Barriers to weight loss and the effect of intermittent energy restriction on weight loss and diabetes risk in women who have had gestational diabetes.

By

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Glossary and Abbreviations

AAS	Active Australia Survey
ADIPS	Australian Diabetes in Pregnancy Society
ADF	Alternate Day Fasting
AusDiab	Australian Diabetes, Obesity and Lifestyle Study
BMI	Body Mass Index
CDC	Center for Disease Control
CER	Continuous Energy Restriction
COM-B	Capability, Opportunity, Motivation-Behaviour
CVD	Cardiovascular Disease
CSIRO	Commonwealth Scientific and Industrial Research Organisation
CVI	Content Validation Index
DEXA	Dual Energy X-ray Absorptiometry
DHQIII	Diet History Questionnaire III
DPP	Diabetes Prevention Program
GDM	Gestational Diabetes Mellitus
HAPO	Hyperglycemia and Adverse Pregnancy Outcome Study
HbA1c	Glycated Haemoglobin A1c
HDS	Healthy Diet Score
HOMA-IR	Homeostatic Model of Insulin Resistance
I-CVI	Item-Content Validation Index
IER	Intermittent Energy Restriction
LDL-C	Low Density Lipoprotein Cholesterol
NDSS	National Diabetes Services Scheme
NHMRC	National Health and Medical Research Council
OGTT	Oral Glucose Tolerance Test
PARF	Population Attributable Risk Fraction
PCOS	Polycystic Ovary Syndrome
PPWR	Post-Partum Weight Retention
PSQI	Pittsburgh Sleep Quality Index
RCT	Randomised Control Trial
T2DM	Type 2 Diabetes Mellitus
TDF	Theoretical Domains Framework
TRF	Time Restricted Feeding
WOWO	Week-on-Week-off

Executive Summary

The incidence of gestational diabetes is on a sharp rise in Australia and around the world, and is associated with a high risk of developing type 2 diabetes in the years following birth. Obesity is also strongly associated with type 2 diabetes. Therefore, women who have had both a diagnosis of gestational diabetes and are also above a healthy weight range are at an even greater risk of developing type 2 diabetes. Modest weight loss of five to seven percent can reduce this risk by more than half. The primary approach to achieve weight loss is by restricting energy intake by 25 to 30% every day. However, becoming a mother is a profoundly life-changing experience, and the ability for women in this population to adhere to daily energy restriction presents a major hurdle. Alternative evidence-based diet strategies which may improve compliance are therefore of interest. Intermittent energy restriction involves periods of severely restricting energy intake interspersed with periods of habitual food intake. Studies in adult populations with or without disease show that intermittent energy restriction can result in weight loss and improvements in disease risk markers that are comparable to continuous energy restriction. However, prior to this thesis, the effectiveness of this diet approach in women with previous gestational diabetes was unknown. There were also few large Australian studies investigating barriers to weight loss in this population. The aims of the research presented in this thesis were therefore to explore barriers to weight loss after gestational diabetes, to gather opinions regarding intermittent dieting, and to compare the effects of an intermittent two day a week very low energy diet (‘the 5:2 diet”) to continuous energy restriction in women with overweight or obesity who have had gestational diabetes.

The work in this thesis involved four studies from two overarching projects. Firstly, an online survey of women with previous gestational diabetes in Australia was developed. The survey was reviewed by a panel of experts for content validation and pilot tested before being run. These results are presented in chapter 3. The final survey was administered online to 429 women with previous gestational diabetes in Australia and these results are presented in chapter 4. Our findings indicated that the majority of women who have had gestational diabetes in Australia do not perceive themselves to

be at a high risk for developing type 2 diabetes, and experience barriers to weight loss that are overwhelmingly intertwined with their family environment and responsibilities. Women also cited poor behavioural regulation with their eating habits. Opinions of intermittent energy restriction were varied. A 12 month randomised control trial was then undertaken to compare the effects of intermittent energy restriction and continuous energy restriction on weight loss and diabetes risk markers in women with overweight or obesity and previous gestational diabetes. Chapter 5 presents this study. Weight loss and improvements in diabetes risk markers were similar when following both an intermittent or a continuous energy restriction regime. However, the trial experienced high attrition in both diet strategies, indicating that although effective, barriers remain that impact adherence to both intermittent and continuous energy restriction. Finally, we conducted an exploratory secondary analysis of our clinical trial using survey and dietary quality data. This study is presented in chapter 6. An interesting finding in this study was that the continuous energy restriction group showed superior improvement in dietary quality compared to the intermittent energy restriction group between 0 and 12 months ($p=0.05$).

In summary, the main findings from this thesis are that women with overweight or obesity who have previously had gestational diabetes experience significant barriers to weight loss and the home environment is at the forefront of this. Difficulties with behavioural regulation are also common. Intermittent energy restriction was found to achieve comparable weight loss to continuous energy restriction over 12 months and may be an alternative for women with previous gestational diabetes who have not had success with continuous energy restriction. However, long term adherence to both intermittent and continuous energy restriction remains challenging. The results from this thesis will provide a valuable contribution to the field and will be useful for researchers to consider in the future design and implementation of diabetes prevention interventions, as well as for clinicians who are prescribing diabetes prevention and weight loss advice to women with overweight or obesity and prior gestational diabetes.

Signed Declaration

I declare that:

This thesis presents work carried out by myself and does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; to the best of my knowledge, it does not contain any materials previously published or written by another person except where due reference is made in the text; and all substantive contributions by others to the work presented, including jointly authored publications, is clearly acknowledged.

Kristy Gray

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Publications Arising from this Thesis

1. **Gray KL,** Grebenshchikova M, O'Reilly SL, McKellar L, Clifton PM & Keogh JB 2021, 'Development and validation of an online survey to assess perception of diabetes risk and barriers and facilitators to weight loss following gestational diabetes', *International Journal of Environmental Research and Public Health*, vol. 18, no. 480 https://doi.org/10.3390/ijerph18020480

   (Chapter 3)

2. **Gray KL,** McKellar L, O'Reilly SL, Clifton PM & Keogh JB 2020, 'Women's barriers to weight loss, perception of future diabetes risk and opinions of diet strategies following gestational diabetes: an online survey, *International Journal of Environmental Research and Public Health*, vol. 17, no. 9180 https://doi.org/10.3390/ijerph17249180

   (Chapter 4)

3. **Gray KL,** Clifton PM & Keogh JB 2021, 'The effect of intermittent energy restriction on weight loss and diabetes risk markers in women with a history of gestational diabetes: a 12-month randomized control trial', *American Journal of Clinical Nutrition*, vol. 114, issue. 2 :794-803 https://doi.org/10.1093/ajcn/nqab058

   (Chapter 5)

4. **Gray KL,** Clifton PM & Keogh JB, 2021, 'Barriers to weight loss and dietary quality of intermittent and continuous dieters in women with a history of gestational diabetes', *International Journal of Environmental Research and Public Health,* vol. 18, no. 10243 https://doi.org/10.3390/ijerph181910243

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Conference Presentations

International

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- Oral presentation at the American Society for Nutrition Annual Conference, Baltimore, USA, June 2019

National

Gray KL, Clifton PM & Keogh JB 2020, 'The effect of intermittent energy restriction on weight loss and diabetes risk markers in women with a history of gestational diabetes: a 12-month randomized control trial'.

- Oral presentation at Nutrition Society of Australia's Annual Conference. Virtual Conference, December 2020
- Oral presentation at The University of South Australia School of Pharmacy Higher Degree Research Symposium, September 2019 *

**Best presentation awarded*

Format of Thesis

This thesis is submitted as a Thesis Containing Published Research in accordance with the University of South Australia Academic Regulations for Higher Degrees by Research Clause 16.1.1.b.

The thesis is presented in seven chapters. Chapters 1 and 2 provide background and literature reviews as an introduction to the thesis. Chapters 3 through to 6 are presented as published journal articles which have been published in international peer-reviewed journals. A brief preface is included to each chapter presented as a publication. Chapter 3 presents the development and validation process of the online survey and chapter 4 presents the results of the final online survey. Chapter 5 presents the main results from the 12 month clinical trial and chapter 6 presents results from a secondary analysis of the clinical trial. Chapter 7 provides a discussion of the main findings in this thesis and outlines future directions. Chapter 8 lists the references in the unpublished chapters. The contributions of each author to the published articles are stated in the authorship statements, which are included as appendices in chapter 9. A copy of the online survey is also included as an appendix.

1. Literature Review 1: Gestational Diabetes and Type 2 Diabetes

1.1. Gestational Diabetes

Gestational diabetes (GDM) is defined as hyperglycemia that first occurs during pregnancy [1, 2]. During a normal pregnancy, placental hormones cause a physiological shift in metabolism which reduces maternal glucose utilization by 50% to ensure the fetus receives an adequate supply of glucose for proper growth and development [3, 4]. There is a 60% decrease in insulin sensitivity during pregnancy and subsequently insulin secretion is increased to maintain euglycemia [3, 5]. GDM typically occurs when there is a failure to generate the increased insulin required, and carries a risk of complications to both mother and baby throughout pregnancy and birth including maternal pre-eclampsia, and neonatal macrosomia, respiratory distress, and shoulder dystocia [6-8]. Numerous factors contribute to the development of GDM including placental hormones, obesity and excess weight gain during pregnancy, physical inactivity, older age at conception, ethnic background, having a genetic predisposition to insulin resistance, and changes to the gut microbiota [3]. Although GDM is a transient disease which typically resolves shortly after birth, long term maternal health risks remain including an increased risk of developing type 2 diabetes (T2DM), cardiovascular disease (CVD), metabolic syndrome, kidney disease and cancer [8-11]. Maternal hyperglycemia also increases the risk of health consequences in offspring, including obesity and abnormal glucose metabolism from childhood, and adverse effects to neurocognitive development [12]. The risk of T2DM is highest in the first three to six years following GDM however remains markedly raised after this time frame [13]. Factors including high body mass index (BMI), family history of T2DM, non-white ethnicity and advanced maternal age are associated with a higher risk of developing T2DM [14].

The prevalence of GDM has been on a steep rise over the last decade, with 13% of pregnancies in Australia resulting in a live birth in 2019 being complicated by the disease, totalling 40,848 cases [15, 16]. The global prevalence is now one in five pregnancies, with an estimated 20.4 million births from GDM pregnancies [1]. The rise

in GDM is largely due to the change in maternal demographics including pregnancy occurring at an older age, an increase in BMI, and inadequate physical activity levels [17-20]. In 2017-2018, 60% of women aged 18 and older in Australia were classified with overweight (BMI ≥25 - 29.9 kg/m^2) or obesity (BMI ≥ 30 kg/m^2) [19]. A meta-analysis by Chu et al. (2007) of 20 studies including over 500,000 women reported the risk of developing GDM was two, four and eight times higher among women who were overweight, obese or severely obese compared to women with a BMI in a healthy range (unadjusted odds ratio (OR) overweight: 2.14 [95% CI 1.82 to 2.53]; obese: 3.56 [95% CI 3.05 to 4.21]; severely obese 8.56 [95% CI 5.07 to 16.04] [18]. A systematic review and meta-analysis of 70 studies and 671,945 women similarly reported a risk of GDM that increases as BMI increases (overweight: relative risk (RR) 1.97 [95% CI 1.77 to 2.19]; moderately obese: RR 3.01 [95% CI 2.34 to 3.87]; and morbidly obese: RR 5.55 [95% CI 4.27 to 7.21]) [21]. A recent prospective cohort study published in 2020 (n=912) examined the associations of BMI to both diet-controlled GDM and insulin-dependent GDM while correcting for age, parity, previous hypertension in pregnancy, gestational weight gain, smoking and fertility treatments. This study reported women with obesity to be three times more likely to develop diet-controlled GDM compared to women with a BMI <25 kg/m^2; (adjusted OR: 2.99 [95% CI 1.71 to 5.25]), and 12 times more likely to develop insulin-dependent GDM (adjusted OR: 11.88 [95% CI 3.67 to 38.48]) [22]. One large study of 66,689 women with a singleton birth reported that over half of GDM could potentially be prevented if all women who had overweight or obesity became a healthy weight (population attributable risk fraction (PARF) 57% [95% CI 54.2 to 59.9%]) [23], and an earlier study reported the prevalence of GDM in women in a healthy weight range to be 2.3% [24].

A recent change in diagnostic criteria has also contributed to the rising prevalence of GDM [25]. In the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, hyperglycemia in pregnancy was found to be an independent risk factor for adverse outcomes, with strong correlations between maternal glucose levels at 24 to 32 weeks and adverse maternal and neonatal outcomes [26]. In 2014, the Australian Diabetes in Pregnancy Society (ADIPS) recommended a change in GDM diagnostic criteria, lowering the acceptable fasting and 2-hr glucose tolerance levels in pregnancy [27]. A

2-hr 75 g oral glucose tolerance test (OGTT) is routinely performed on all pregnant women in Australia between 24 to 28 weeks of pregnancy, and GDM is now diagnosed with either a fasting plasma glucose of 5.1 to 6.9 mmol/L; 1-hr post OGTT of ≥10 mmol/L; or 2-hr post OGTT of 8.5 – 11 mmol/L [27]. A fasting plasma glucose > 6.9 mmol/L or a 2-hr OGTT >11 mmol/L indicates the individual has T2DM previously undiagnosed rather than GDM [27].

1.2. Type 2 Diabetes

T2DM continues to present a major global public health challenge. There were an estimated 417 million people living with the disease worldwide in 2019 [1]. T2DM is a metabolic disorder characterized by hyperglycemia resulting from insulin resistance and subsequent pancreatic beta cell dysfunction [1]. It is a serious disease that massively contributes to the burden of mortality worldwide, with an estimated 4.2 million deaths resulting from diabetes complications in 2019 [1]. The Australian Diabetes, Obesity and Lifestyle Study (AusDiab 2012) reported that women with diabetes have a mortality rate 5.5 times higher than women without diabetes (27.7 deaths compared to five deaths per 1,000 person-years) [28]. T2DM also leads to the development of other chronic diseases including CVD, kidney disease, diabetic retinopathy, stroke, risk of amputations, some types of cancer and dementia [29-31]. Excess body fat is the greatest modifiable risk factor for the development of T2DM [32]. The United States Center for Disease Control (CDC) reported that 89% [95% CI 86.6 to 91.1%) of adults with diagnosed T2DM have a BMI above 25 kg/m^2 [33], and a meta-analysis of nine prospective cohort studies in 2009 showed that women with obesity are 12 times more likely to develop T2DM compared to women in a healthy weight range (RR 12.41 [95% CI 9.03 to 17.06]) [34].

1.3. Gestational Diabetes and Risk of Type 2 Diabetes

Following birth, women who have had GDM retain a risk of developing T2DM that is significantly higher than that of women who do not develop GDM, with up to half of the women who had GDM developing T2DM later in life [9, 11, 35, 36]. In the last 12 years, four large-scale meta-analyses have attempted to quantify the risk of T2DM after GDM

and have reported the risk to be between seven and 10 times higher than women who do not develop GDM [9, 11, 13, 35].

Being in an overweight or obese weight range increases the risk of both the development of GDM and the progression to T2DM [1, 14, 37]. A cohort study of over 8,000 women in the National Health and Nutrition Examination Survey (NHANES) reported that the absolute risk of T2DM after GDM was much higher in women with obesity (BMI ≥30 kg/m^2) compared to women who were not overweight (BMI <25 kg/m^2) (26.1% vs. 9.7%, p < 0.001) [38]. The relative risk of T2DM after GDM was reported in a meta-analysis of 95,750 women by Rayanagoudar et al. in 2016, who showed that women with previous GDM who have a BMI above a healthy weight range are twice as likely to develop T2DM compared to women who have had GDM and are within a healthy weight range (RR 1.95 [95% CI 1.60 to 2.31], p<0.001), and the risk increased with BMI categories (BMI ≥30 kg/m^2 RR 2.85 [95% CI 2.21 to 3.69], p<0.001) [14].

Weight gain after a GDM pregnancy increases the risk of diabetes further still [39]. A cohort study by Peters et al. (1996) demonstrated that for every 4.5 kg weight gained after delivery there was a doubling in risk for T2DM development after adjustments for confounding variables (RR 1.95 [95%CI 1.63 to 2.33] [40], while Bao et al. (2015) reported a 27% higher risk of developing T2DM for each 5 kg of weight gained following GDM (adjusted hazard ratio (HR) 1.27 [95% CI 1.04 to 1.54]) [37]. Bao et al. (2015) also found that women who had both a BMI ≥30.0 kg/m^2 at baseline (time when GDM was first reported) and who gained ≥5 kg after GDM were 43 times more likely to develop T2DM compared with women who had a BMI <25.0 kg/m^2 at baseline and gained <5 kg after GDM (adjusted HR 43.19 [95% CI 13.60 to 137.11]) [37]. Of the 717 women in the study with a baseline BMI of <25 kg/m^2, only 31 developed T2DM (4.3%), compared to 228 of the 971 women who had a baseline BMI ≥25 kg/m^2 (23.4%) [37].

1.4. Prevention of Type 2 Diabetes after Gestational Diabetes

GDM identifies a high-risk population early, offering an opportunity for lifestyle intervention to prevent T2DM in younger adults [41]. Earlier onset of T2DM is linked to a higher risk of cardiovascular disease complications [42], therefore preventing or

delaying T2DM in this population is of paramount importance. In 2001 and 2002, two ground-breaking diabetes prevention clinical trials were published, which established the importance of weight loss in the prevention of T2DM; the Finnish Diabetes Prevention study [43] and the Diabetes Prevention Program (DPP) [44]. Both studies demonstrated a reduction of T2DM incidence of up to 58% through lifestyle modification resulting in weight loss of five to seven percent of total body weight [43, 44]. This was found to be more effective than treatment with metformin alone (31% reduction) [44]. While these studies were not specific to women with previous GDM, they did prompt further investigation in this population. A 2008 study using a subset of women from the DPP with prior GDM (n=350) provided evidence that weight loss from diet and lifestyle modification can significantly reduce the risk for developing T2DM after GDM, with a 53% reduction in T2DM incidence compared to women with prior GDM who had no weight loss intervention [45]. Furthermore, a 10 year follow up from the DPP study showed that the effect of lifestyle modification on diabetes prevention is maintained in the long term with a 34% risk reduction at 10 years [46]. Similarly, a ten year follow up study of the DPP that studied a subgroup of women with previous GDM reported a 35% reduction in progression to T2DM following lifestyle intervention, compared to women without a history a GDM [47]. These results were solidified in a meta-analysis of 10 randomised control trials (RCTs) (n=1733) investigating the effect of postpartum lifestyle intervention on long term risk of T2DM after GDM, showing that lifestyle intervention which commenced within three years of birth reduced the risk of T2DM after GDM by close to half (pooled RR 0.57 [95% CI 0.42 to 0.78], p = 0.32) [48].

Despite strong evidence that weight loss interventions can significantly reduce the risk of developing T2DM after GDM, long term weight loss and subsequent weight maintenance is difficult in this population [49]. Many women do not lose weight after pregnancy and retain on average 0.5 to 4.0 kg 12 months after birth [50]. In-fact, women of child-bearing age (18 - 35 years) have the highest risk of weight gain compared to women in other age groups [51-54]. A prospective cohort study of women with GDM reported that at one year post-partum, two-thirds of women (66.4%, n=259) had post-partum weight retention (PPWR). Mean PPWR was 4.0 ± 7.4 kg. Women with PPWR at

one year also had adverse metabolic consequences including higher increase in fasting glucose and hemoglobin A1c (HbA1c) levels [55].

A review of 30 studies which examined interventions to prevent T2DM after GDM identified that while lifestyle interventions are effective, participation in programs can be low [56]. The Mothers After Gestational Diabetes Australia Diabetes Prevention Program (MAGDA-DPP) provides a good example of this. MAGDA-DPP was a lifestyle intervention trial for women with recent GDM, consisting of one individual session, five group sessions and two telephone sessions over 12 months (n=573). At 12 months, the intervention group had a mean weight reduction of -0.23 kg [95%CI -0.89 to 0.43 kg] while the usual care group gained 0.72 kg [95% CI 0.09 to 1.35 kg). Only 10% of women attended all sessions [57]. Review articles have had similar findings. A review of 18 articles of lifestyle behaviours after GDM found that women with previous GDM rarely met dietary and physical activity recommendations [58], and two meta-analyses of lifestyle interventions for diabetes prevention after GDM support these findings, reporting that lifestyle interventions resulted in a mean difference (MD) of around one kilogram of weight loss compared to no intervention [49, 59].

Similar difficulties encompassing lifestyle changes and achieving weight loss have also been reported in postpartum women without previous GDM. A recent meta-analysis published in 2020 showed that while lifestyle interventions effectively reduce body weight in a general population of post-partum women, to date many interventions have failed to translate this into successful weight loss outcomes in the real world [60]. Further implementation based research is needed to help this high risk population engage in behavioural lifestyle changes for weight loss and diabetes prevention [60].

1.5. Summary

In summary, the evidence presented clearly shows that a history of GDM is one of the most predictive risk factors for developing T2DM, that pre-pregnancy BMI and weight gain are influential factors in the progression to T2DM after GDM, and that weight loss can delay or prevent the onset of T2DM in many cases. However, weight loss is challenging in this population.

2. Literature Review 2: Intermittent Energy Restriction

2.1. Background, History and Mechanism of Intermittent Energy Restriction

Weight loss through dietary restriction has been shown to effectively prevent or delay the onset of T2DM in a general population of people with overweight or obesity as well as women with previous GDM [43, 44, 47, 48, 61], and given the high risk of developing T2DM, the time following a GDM pregnancy presents a crucial window to intervene. However, as discussed in chapter 1, long-term adherence to dietary restrictions and lifestyle programs proves to be difficult, particularly in a population of women who have recently had a baby or have a young family at home [62, 63]. Adherence to daily energy restriction typically declines after several months, and as dietary adherence is directly associated with amount of weight lost, finding ways to improve adherence is imperative to weight loss success [63-67]. In recent years, alternative weight loss strategies such as intermittent energy restriction (IER) has been of interest to researchers. As opposed to continuous energy restriction (CER), which requires moderate energy restriction of around 25-30% of energy requirements every day [63], IER offers a more flexible model of dieting, allowing periods of unrestricted eating interspersed with periods of little or no energy intake each week [68]. There are numerous types of IER with varying periods of energy restriction or fasting. For example; alternate-day-fasting (ADF) alternates a day of ad-libitum eating with a day of fasting, and the twice-a week method, commonly referred to as 'the 5:2 diet', requires two days of severe energy restriction each week and five days of ad-libitum eating [67, 68]. The severity of a fast also varies between regimes, with some diets requiring a full abstinence from any caloric intake during the fasting period, and other regimes allowing up to 25% of caloric requirements on fasting days [68]. Time-restricted feeding (TRF) is a sub-class of IER in which food intake is restricted to a number of hours each day, typically eight hours or less [63].

The concept of fasting is not novel. Researchers have studied the physiological effects of partial and complete fasting in humans and animals dating back to the 1800s [69]. Historically, variations of intermittent fasting were used to promote spiritual and physical health in ancient civilizations around the world [70, 71], and these practices still continue in some religions today, such as Ramadan, which is observed by Muslims and involves

a month of fasting every day from dawn until dusk [72]. Prolonged fasting as a treatment for obesity and diabetes gained attention in the 1950s to 1960s but resulted in severe side effects including cardiac arrhythmias, anemia, breakdown in electrolyte homeostasis, and death in some cases [67]. Over the last 20 years, research focus has turned to intermittent fasting for weight loss and disease prevention and treatment, and the term 'intermittent fasting' has now become well known in the dieting community [67]. Animal studies have shown profound beneficial effects from intermittent fasting with benefits exceeding that which is seen from daily caloric restriction, including reduced body weight, increased life span, improved glucose regulation and lipid metabolism, lower inflammatory markers and reduced incidence of cardiovascular diseases, diabetes, cancer and neurological disorders [73-78]. However, these benefits have not yet been proven in humans.

Along with the increased flexibility around food intake that an intermittent diet offers, researchers have speculated several mechanisms that may elucidate beneficial metabolic effects of IER. Firstly, CER induces adaptive thermogenesis, that slows or halters weight loss, and IER may attenuate these adaptions by allowing periods of unrestricted eating [79]. Moreover, as hepatic glycogen stores are depleted between 12 to 36 hours after cessation of energy intake, IER may induce ketosis, which mobilizes fatty acids, activating ketogenic pathways in the liver which can in turn reduce hunger and aid with dietary adherence [67, 80]. IER is also thought to induce periodic mild metabolic stress which induces adaptive changes by activating antioxidant mechanisms, resulting in an increase in stress resistance [77, 81]. Resistance to oxidative stress may have beneficial effects in disorders involving inflammation and therefore increase resistance to disease [77, 81]. Johnson et al. (2007) showed that markers of inflammation and oxidative stress were decreased following eight weeks of IER in adults with obesity [81]. IER may also affect the gut microbiome favorably [82-84]. Recent research found that 30 days of ADF induced the formation of beige adipose tissue and improved metabolic homeostasis in mice [84], while a longer term study by Beli et al. (2018) found that IER in the form of ADF created beneficial changes in the gut microbiota of mice after seven months [83]. Furthermore, daily fasting regimes that restrict caloric intake to daytime hours and extend the nighttime fast influence circadian

biology and may improve metabolic regulation [70]. However, these beneficial mechanisms have not been proven in human studies and ongoing research is required [63].

The following review will focus on the effects of intermittent energy restriction for weight loss and diabetes prevention in adults and discuss the evidence available on the effects of IER specifically in women.

2.2. Intermittent Energy Restriction and Weight Loss

As discussed in chapter 1, weight loss of five to seven percent of body weight can reduce the incidence of T2DM in people with overweight or obesity by 58%, and women with overweight or obesity and a history of GDM by 53% [43, 61]. Weight loss from IER has shown to range from -4.6% to -13% after eight weeks to one year with no significant differences between IER and CER, suggesting IER produces clinically meaningful weight loss and thus is a suitable alternative to CER [63, 68]. One review of adults with overweight or obesity and without diabetes reported slightly superior weight loss in CER compared to IER in studies lasting from three to 24 weeks (CER -4% to –14% after six to 24 weeks of treatment; IER -3% to -8% after three to 24 weeks of treatment), but concluded that both strategies are comparable and effective [85]. A recent meta-analysis compared IER to CER in 17 RCTs lasting a minimum of 12 weeks in adults with overweight and obesity, and reported IER resulted in clinically meaningful weight loss (mean -5.8 kg; range −2.3 to −11.9 kg), with no meaningful between group differences observed for weight loss (mean difference (MD) −0.55 kg [95% CI: −1.01 to −0.09 kg], n = 13 studies) or fat mass loss (MD −0.66 kg, [95% CI: −1.14 to −0.19 kg] n = 10 studies) [86]. This study also included subgroup analyses for the IER regime, sex, study length, and disease status with no significant differences observed [86]. Their findings consolidate results from Harris et al. (2018) where weight loss was found to be slightly better although not statistically significant following IER compared to CER (-1.03 kg [95% CI -2.46 to 0.40 kg], p = 0.156) [87], and Enríquez Guerrero et al. (2021) where 13 out of the 17 articles reviewed showed no significant difference in body weight following IER or CER [88]. One meta-analysis has shown IER results in statistically significant reduction in BMI compared to CER (MD -0.75 kg/m^2 [95% CI -1.44 to -0.06

kg/m^2], p = 0.033). However total body weight was not different between IER and CER either before or after intervention (weight loss for IER compared to CER after intervention: MD -1.94 kg [95% CI -5.20 to 1.31 kg], p = 0.241), and the greater reduction in BMI seen in IER was attributed to one study in the meta-analysis whose IER protocol of alternate day zero calorie fasting was a greater energy deficit than the CER protocol of -1670 kJ (-400 kCals) per day [89, 90]. The meta-analysis was also limited by the short length of the trials included, lasting between four and 12 weeks, and small numbers in the trials, ranging from 20 to 56 participants. Additionally, several of the clinical trials comprised of adults in a healthy weight range undertaking a resistance training or exercise program, limiting the generalization of the results to a general population. Weight loss typically plateaus after six months as adherence to diet drops and weight gain can reoccur [91], therefore studies lasting six months or longer are needed to evaluate the effectiveness of a diet in the longer term [91, 92]. Only one meta-analysis has investigated weight loss outcomes in IER trials lasting a minimum of six months [91]. Weight loss from IER was found to be no different to CER (MD 0.08 ± 0.11 kg, p=0.458) [91]. The authors also noted that the length of interventions was not associated with more weight loss, reinforcing the challenges of long-term weight loss for both IER and CER [91].

2.3. Intermittent Energy Restriction and Metabolic Markers

Although animal studies have shown IER produces superior improvements to CER in metabolic markers independent of weight loss, this has not been proven in human studies [63, 67]. Considerable heterogeneity exists between IER studies, including differences in IER and CER protocols, whether meals are provided to participants or not; the use of liquid meal replacements; exercise requirements; timing of blood sample collection; and length of intervention, making direct comparisons and generalization of findings difficult [68].

A recent 12 month study by Gabel et al. (2019) comparing ADF to CER and control (usual diet) in adults with insulin resistance reported minor improvements in fasting glucose levels that were not significantly different between the three groups by six or 12 months (12 months: ADF −3 ± 3 mg/dL; CER −4 ± 2 mg/dL; control +4 ± 4 mg/dL,

p>0.05, n=43) [93]. Similar findings were also shown in a review article of IER for weight loss and diabetes prevention by Barnosky et al. (2014). Minor decreases in fasting glucose levels of 3% to 6% were seen following eight to 12 weeks of IER in individuals with prediabetes (treatment by time p<0.05), while CER studies showed no effect on fasting glucose concentration after six to 12 weeks [85]. Fasting insulin appears to be more responsive to dietary treatment. Barnosky et al. (2014) reported improvements in fasting insulin levels ranging from 20% to 31% following eight to 12 weeks of IER (treatment by time p<0.05) and 11% to 41% following six to 12 weeks of CER (treatment by time p<0.05), while Gabel et al. (2019) found that ADF results in a significantly greater decrease in fasting insulin when compared to CER and control after six (−44 ± 6%) and 12 months (−52 ± 9%) (p<0.05, n=43) [85, 93]. Homeostatic model of insulin resistance (HOMA-IR) also decreases following both IER and CER. Gabel et al. (2019) reported that reductions in HOMA-IR were significantly greater for ADF after six (−48 ± 6%) and 12 months (−53 ± 9%) of dietary intervention when compared to CER and control (p<0.05, n=43) [93]. However, the review paper by Barnosky et al. (2014) suggests that the level of energy restriction is the determining factor for the amount of improvement in insulin and HOMA-IR regardless of the diet strategy [85]. Several meta-analyses have suggested that greater improvements in glycemic markers are seen following IER compared to CER [89, 94]. One meta-analysis reported superior improvements in fasting glucose (WMD -4.16 mg/dL [95% CI, -6.92 to -1.40 mg/dL], p = 0.003) and HOMA-IR (-0.54 [95% CI, -1.05 to -0.03]; p = 0.038) in IER [89]. However, these findings can be explained by the greater reduction in BMI found in IER and was limited by the small clinical trials included with short intervention lengths, as well as the population, which included adults who were metabolically healthy and not overweight [89]. Furthermore, one of the trials included in the analysis did not match the level of energy restriction between IER and CER. Another meta-analysis of the effect of IER for the treatment of overweight and obesity in six RCTs reported superior reduction in fasting insulin concentration from IER in comparison to CER (WMD: -4.66 pmol/L [95% CI -9.12 to -0.19 pmol/L], p = 0.041) [95], and one other meta-analysis also reported slight improvements in fasting insulin resulting from IER compared to CER (MD − 0.89 μU/mL [95% CI − 1.56 to − 0.22 μU/mL], p = 0.009), although concluded this is unlikely

to be a clinically meaningful difference [94]. They reported no group differences in HOMA-IR, fasting glucose, HbA1c, lipids or blood pressure, although this meta-analysis included clinical trials of overweight adults both with and without diabetes [94]. However, other systematic reviews and meta-analyses have shown no difference between changes in intermediate disease markers in IER and CER, including fasting glucose and insulin, HOMA-IR, HbA1c, LDL cholesterol, triglycerides, and blood pressure [68, 86, 91, 94]. The heterogeneity of studies limits the ability to make direct comparison of the effect of IER compared to CER on biomarkers such as fasting glucose and insulin [68]. Reduced fasting glucose and insulin levels are more pronounced following a day of fasting, which reflects lower circulating glucose and insulin levels due to the absence of food intake and therefore lack of glucose available for absorption rather than improved pancreatic function [96]. Therefore, results from fasting blood samples taken during IER studies will vary depending on whether the sample was collected following a fasting day or fed day. For example, a study by Harvie et al. (2011) investigating the effects of IER and CER looked at serum markers over one week in subset of participants (n=30). The IER group experienced brief reductions in fasting insulin (-23%) and HOMA-IR (-29%) following two days of severe energy restriction, which returned to normal levels within two days of resuming usual diet. There were no significant changes in the CER group [97].

Collectively, the majority of evidence regarding IER for diabetes prevention in humans suggests that improvements in diabetes risk markers resulting from IER are related to the degree of energy restriction and subsequently weight loss. IER does not appear to confer metabolic benefit over CER however does appear to be a suitable alternative to CER for diabetes prevention.

2.4. Intermittent Energy Restriction in Women

Systematic reviews and meta-analyses of IER in humans have been in adult populations with or without disease but to date they have not been specific to females. One study of 75 men and women with obesity who participated in a 12 week ADF study found no differences in percentage of weight loss or metabolic markers based on sex or menopausal status (weight loss: premenopausal women −4.6 ± 3.2%; postmenopausal

women; −6.5 ± 3.2%; and men −6.2 ± 4.4%, p>0.05) [98]; and a meta-analysis of the effects of IER and CER in adults showed no sex related differences in a subgroup analysis [86]. Nevertheless, men and women may respond differently to treatment for obesity, with aspects to consider including sex-related factors which are related to genetic and metabolic pathways, and gender related factors which are influenced by social and cultural factors [99]. Therefore, research investigating the effectiveness of an IER style of diet on weight, glycemic markers and adherence in women who with overweight or obesity is beneficial.

Several clinical trials investigating the effects of IER for weight loss and metabolic improvements in women without diabetes have been conducted with varying results [97, 100, 101]. Harvie and colleagues ran two clinical trials investigating IER in women who were overweight without diabetes [97, 100]. The first was a six month RCT published in 2011, of 107 premenopausal women. IER and CER at 75% of energy requirements were found to be equally effective for weight loss (IER -6.4kg [95% CI -7.9 to -4.8kg], CER -5.6kg [95% CI -6.9 to -4.4kg], p=0.4) as well as fat mass and other anthropometric measures. No significant changes in fasting glucose were seen in either group, however IER saw greater improvements in fasting insulin (-1.2 μU ml^{-1} [95% CI -1.4 to -1.0 μU ml^{-1}], p=0.04) and HOMA-IR (-1.2 μU ml^{-1} [95% CI -1.5 to -1.0 μU ml^{-1}], p=0.04) at six months compared to CER [97]. The same authors also reported superior improvements in serum insulin and HOMA-IR in IER in a three-armed clinical trial of women who were overweight with a family history of breast cancer (n=115) [100]. This RCT included two different intermittent diets with carbohydrates restricted to <40g/day on fasting days. One of the IER regimes was less restrictive, allowing unlimited lean protein and mono- and poly-unsaturated fat on fasting days (IECR+PF), and the other did not (IECR). At three months, serum insulin and HOMA-IR showed significantly superior reductions following IECR compared to CER, but not IECR+-PF compared to CER. There were no changes in fasting glucose. Mean fat loss was also greater for both IECR and IECR+PF compared to CER at three months (IECR: -3·7 kg [95% -2·5 to -4·9 kg], p=0.007; IECR+PF: -3·7 kg [95% CI -2·8 to -4·7 kg], CER: -2·0 kg [95% CI -1·0 to 3·0 kg], p=0·019), despite no differences in total weight loss between diet groups [100]. However, there were no differences between groups in reductions in insulin, HOMA-IR,

weight and fat loss following a one month weight-maintenance phase in which the two IER groups restricted their intake for one day a week and the CER group consumed estimated energy requirements daily [100]. Hutchison et al. (2019) also reported greater reductions in fat mass and total body weight in an eight week study investigating IER as three non-consecutive days of fasting each week at 70% and 100% of energy requirements (IER70 and IER100) compared to CER (CER70) and control in women who were overweight (weight loss: IF100 -2.7 ± 0.5 kg, IER70 -5.4 ± 0.5 kg, CER70 -3.9 ± 0.4 kg; fat loss: IF100 -2.3 ± 0.4 kg, IER70 -3.9 ± 0.4 kg, CER70 -2.8 ± 0.4 kg, n=88). Changes in fasting glucose were minor and between group differences were seen following a fast day only in IER70 compared with CER70 and after a fed day only in IER70 compared with IER100. Fasting insulin also improved for both IER and CER at 70% of energy requirements (IER70 -3.6 ± 1.0 mU/L, CER70 -1.2 ± 1.1 mU/L, p=0.70). However, IER at 100% of energy requirements resulted in a transient increase in fasting insulin after fed day (IER100 2.9 ± 1.4 mU/L) despite modest weight loss, suggesting that IER should be prescribed with overall energy deficit [101]. Harvie et. al. (2013) and Hutchison et al. (2019) both used IER protocols which restricted carbohydrates on fasting days. Restriction of carbohydrates can induce ketosis which may result in higher rates of fat oxidation and therefore greater loss of fat mass [102, 103], however the sustainability of this type of IER in the long term remains unknown. The improvements in fasting insulin concentrations and HOMA-IR seen in Harvie et. al. (2011), Harvie et. al. (2013) and Hutchison et. al. (2019) suggests that IER at 70% to 75% of estimated energy requirements could create superior metabolic benefits in the short term in women without diabetes, however this has not been proven in larger studies of adults, and there are limited IER studies specifically in women. Changes in fasting glucose levels appear to be minor following IER in a non-diabetic population, which is expected when glucose levels are within a normal range at baseline. Larger scale and longer-term studies of IER in women with overweight or obesity are needed to investigate the effects of IER on weight and diabetes risk markers further.

The largest clinical trial to date comparing IER to CER was by Headland et al. (2018) who ran a 12-month RCT comparing a 5:2 diet to week-on-week off (WOWO) energy restriction and CER in adults who were overweight. Although this study did not

specifically recruit women, the majority of completers were female (female; n=124, male; n=22). At 12 months weight loss was significant over time but not by diet groups (CER -6.6 ± 6.1kg, WOWO -5.1kg ± 4.9kg, 5:2 diet -5.0 ±4.9kg, p=0.2) [104]. There were no differences in fat mass and lean mass changes, assessed by dual energy X-ray absorptiometry (DEXA) amongst the three diet groups, and no significant changes were seen in fasting glucose levels for either diet group at 12 months. The authors also conducted a follow up 12 months after the intervention completed (24 months from baseline), and reported that IER prescribed as WOWO or 5:2 was equally effective compared to CER with no differences between 5:2 and CER or WOWO and CER after two years (CER -4.5 ± 4.9 kg; WOWO -2.8 ± 6.5 kg; 5:2 diet -3.5 ± 5.1 kg, p value between WOWO and CER p=0.84, p value between 5:2 and CER p= 0.41, n=109). Weight gain occurred in all groups between the intervention finishing at 12 months and follow up at 24 months (CER 2.7 ± 3.4 kg, WOWO 2.5 ± 4.4 kg WOWO, 5:2 diet 1.6 ± 5.9 kg), although fasting glucose, total cholesterol and LDL cholesterol remained unchanged, suggesting that despite some weight regain, benefits from weight loss remained. No dietary intake data was collected at the 24 month visit, however as improvements in dietary quality can benefit cardiometabolic health independent of weight loss, it is possible that some of the dietary changes made during the 12 month intervention were continued through to the 24 month follow up despite overall energy consumption being above requirements.

2.5. Adherence to Intermittent Energy Restriction

It is well known that adherence to CER declines over time and can result in weight regain [64, 92]. One of the main reasons that intermittent dieting has gained public attention in recent years is because of the increased flexibility this style of dieting can offer compared to daily calorie restriction [105]. Furthermore, IER prescribed at less than 3,400 kJ per fasting day, or prescribed with carbohydrate restriction of 40 g to 60 g per fasting day has the possibility of inducing ketosis which can reduce hunger and could improve adherence [67, 80]. One study comparing the effects of IER to CER in overweight women reported better adherence to IER than CER, with 70% adherence to IER and 39% adherence to CER after three months [100]. A recent meta-analysis also found adherence to IER to be slightly better than CER in adults with a BMI above 25

kg/m^2 (IER 76% [range 44% to 98%], CER 62% [range 32% to 78%]) [86]. However, adherence to an IER diet regime has not consistently shown to be greater than CER [79]. Welton et. al. (2020) reported similar adherence to both styles of energy restriction [68], and other systematic reviews have shown attrition, which is an indicator of adherence, to be similar between IER and CER in clinical trials [79, 91, 106].

2.6. Summary

The evidence to date indicates that IER is a safe and suitable alternative to CER for diabetes prevention in individuals with overweight or obesity, producing weight loss that is equivalent to CER when matched for energy restriction. Improvements in glycemic and metabolic markers appear to be at least comparable to CER in adults without diabetes. However, substantial heterogeneity exists amongst IER interventions, and there is a paucity of long-term studies investigating the effects of IER for weight loss and disease prevention, especially in women. Intermittent dieting has not yet been investigated in women who have a BMI above a healthy weight range and a history of GDM. Given their high risk of T2DM, together with the challenges these women can experience adhering to CER, further research investigating the effectiveness of an intermittent style of dieting in this specific population is warranted and has the potential to reduce the burden of T2DM in women with previous GDM.

2.7. Theoretical Domains Framework

Implementing sustainable behaviour change is a complex process. Theory-based health research allows scientists to identify which influences on behavior are most relevant in the target population and design appropriate interventions to increase the possibility of successful behavior change [107, 108]. The Theoretical Domains Framework (TDF) is a validated theoretical framework consisting of 14 domains and 84 constructs to classify attitudes and behaviors, barriers, and facilitators to behaviour change [109]. The framework was developed by behavioural scientists and implementation researchers in 2005, and later updated in 2012 [109]. The TDF can be used in conjunction with the COM-B model (Capability, Opportunity, Motivation – Behaviour model) which states that one's capability, opportunity and motivation interact to produce behaviour [110]. Together, the TDF and COM-B model can be used to map attitudes and behaviours,

barriers and facilitators to behaviour change, which can be used to pinpoint areas of focus when designing implementation interventions. The survey questions in chapters 3, 4 and 6 of this thesis utilize the TDF linked to the COM-B model to classify sources of behaviour deductively which will assist with the future development of targeted strategies for weight loss and diabetes prevention in women with previous GDM. Table 2.1 shows the domains and constructs within the TDF, and Table 2.2 shows how the TDF is integrated into the COM-B model.

Table 2.1: The Theoretical Domains Framework (adapted from Atkins et al. 2017, pg. 3-5) [109].

Domain	Constructs
1. Knowledge	Knowledge, Procedural knowledge, Knowledge of task environment
2. Skills	Skills, Skills Development, Competence, Ability, Interpersonal skills, Practice, Skills assessment
3. Social / Professional role and identity	Professional identity, Professional role, Social identity, Identity, Professional boundaries, Professional confidence, Group identity, Leadership, Organisational commitment
4. Beliefs about capabilities	Self-confidence, Perceived competence, Self-efficacy, Perceived behavioural control, Beliefs, Self-esteem, Empowerment, Professional confidence
5. Optimism	Optimism, Pessimism, Unrealistic optimism, Identity
6. Beliefs about consequences	Beliefs, Outcome expectancies, Characteristics of outcome expectancies, Anticipated regret, Consequents
7. Reinforcement	Rewards, Incentives, Punishment, Consequents, Reinforcement, Contingencies, Sanctions
8. Intentions	Stability of intentions, Stages of change model, Trans theoretical model and stages of change
9. Goals	Goals (distal/proximal), Goal priority, Goal/target setting, Goals (autonomous/controlled), Action planning, Implementation intention
10. Memory, attention, and decision processes	Memory, Attention, Attention control, Decision making, Cognitive overload/tiredness
11. Environmental context and resources	Environmental stressors, Resources/material resources, Organisational culture/climate, Salient events/critical incidents, Person × environment interaction, Barriers and facilitators
12. Social influences	Social pressure, Social norms, Group conformity, Social comparisons, Group norms, Social support, Power, Intergroup conflict, Alienation, Group identity, Modelling
13. Emotion	Fear, Anxiety, Affect, Stress, Depression, Positive/negative affect, Burn-out
14. Behavioural regulation	Self-monitoring, Breaking habit, Action planning

Table 2.2: The Theoretical Domains Framework integrated into the COM-B model (Capability, Opportunity, Motivation – Behaviour) (adapted from Cane et al. 2012, pg. 15) [110] .

COM-B component		TDF domain
Capability	Psychological	Knowledge
		Cognitive and interpersonal skills
		Memory, attention, and decision processes
		Behavioural regulation
	Physical	Physical skills
Opportunity	Social	Social influences
	Physical	Environmental context and resources
Motivation	Reflective	Social/professional role and identity
		Beliefs about capabilities
		Optimism
		Intentions
		Goals
		Beliefs about consequences
		Reinforcement
	Automatic	Emotion

2.8. Scope of Thesis

Women with overweight or obesity who have a history GDM have a high risk of developing T2DM, and although weight loss can substantially lower their risk, this population typically has low success with weight loss programs in the long term. Hence, there is a need to explore alternative weight loss methods which may improve adherence and subsequently increase weight loss. IER is a promising comparable alternative to CER for weight loss and diabetes prevention in adults, however the effectiveness of this style of dieting specifically in women who have previous GDM is not known. Additionally, there is a need

to gain a better understanding of the barriers to weight loss these women face for healthcare providers and researchers to be able to incorporate appropriate strategies into future weight loss programs. Therefore, the aims of this PhD are:

- To identify barriers to weight loss and investigate women's perception of their risk of T2DM after GDM, and;
- To determine the effects of two day a week IER over 12 months on weight loss and diabetes risk in women who have had GDM and are also overweight.

The first study in this PhD includes two publications from our cross-sectional online survey which explored barriers and enablers to weight loss, perception of diabetes risk and opinions of various diet strategies including IER after GDM. The first publication (chapter 3) relates to the development, content validation and pilot testing of the survey and the second publication (chapter 4) outlines the results from the final survey. The survey was undertaken as there were limited large Australian studies gathering women's views and opinions of their disease risk, barriers to weight loss and preferences for weight loss program delivery and content.

The second study in this thesis also includes two publications and adds to the limited number of studies investigating the effect of IER on weight loss and diabetes risk over a period of 12 months. Most IER studies in humans to date last six months or less. This is also the first study investigating IER in a population of women with previous GDM. The evidence from the literature review in chapter 1 highlighted that women with previous GDM have poor adherence and subsequently low success achieving and maintaining weight loss. Given the increased flexibility an intermittent diet offers, an intermittent diet was worthwhile investigating in this population. The first publication for this study (chapter 5) presents the main results from our 12 month clinical trial. The second publication (chapter 6) is a secondary analysis from the clinical trial and provides greater insight into how barriers to weight loss may affect weight loss success in intermittent and continuous dieters and investigates differences in dietary quality between intermittent and continuous dieters over time. The evidence presented in the literature reviews highlights a profound need for alternative weight loss strategies for women with prior GDM. The work in this thesis addresses a gap in the literature by

gathering specific information on weight loss barriers, views and opinions of future disease, and bringing it together with research from a promising alternative method of restricting energy intake.

2.8.1. Hypothesis

Two non-consecutive days of very low energy intake a week (2100 kJ twice a week with ad-libitum intake for five days a week) can produce weight loss and reduction in diabetes risk that is not inferior to CER (prescribed at 6000 kJ daily) in women with prior GDM who have a BMI above 25 kg/m^2.

3. Development and Validation of an Online Survey to Assess Perception of Diabetes Risk and Barriers and Facilitators to Weight Loss Following Gestational Diabetes

3.1. Preface

It was recognized that much of the research on barriers to weight loss and perception of T2DM risk after GDM came from semi-structed interviews and focus groups, with limited large studies published. Additionally, most of this research targeted women in the first one to two years following birth, and although this is the optimal time to lose weight, it may also be the hardest time for women who are recovering from childbirth or are otherwise busy with the demands that come with raising a new baby. As such, we identified a need to develop a new survey tool to explore barriers to weight loss and perception of diabetes risk on a larger scale as well as understand women's views on IER as a diet strategy.

Content validation and pilot testing are important steps in developing a new survey instrument. The process of content validity draws on expertise from a panel of specialists in the field and ensures that each question or item in a new survey appropriately measures the construct it was designed to measure. Pilot testing is also an important step which helps to identify potential problems prior to implementation of the full survey. Using both a panel of experts and a sample of participants from the target population in the survey development ensured that the final survey appropriately addressed our research aims and would be interpreted correctly and accepted in the target population.

This aim of this chapter was therefore to present the survey development and review process used to achieve content validation prior to the final survey administration. The results for the final survey are presented in chapter 4.

3.2. Published Article

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Development and Validation of an Online Survey to Assess Perception of Diabetes Risk and Barriers and Facilitators to Weight Loss Following Gestational Diabetes

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Abstract: Our objective was to describe the development and validation of a survey investigating barriers to weight loss, perception of diabetes risk, and views of diet strategies following gestational diabetes (GDM). The survey underwent three stages of development: generation of items, expert evaluation, and pilot testing. A content validation index (CVI) was calculated from expert responses regarding item relevance, coherence, clarity, and response options. Experts also responded to the domain fit of questions linked to the Theoretical Domains Framework (TDF). Pilot responders answered the survey and responded to review questions. Six experts in the field of nutrition, midwifery, psychology, or other health or medical research completed the expert review stage of the survey. In the pilot test, there were 20 responders who were women with previous GDM and who were living in Australia. The overall CVI from the expert review was 0.91. All questions except one received an I-CVI of >0.78 for relevance (n = 35). Fourteen of the 27 items linked to the TDF received an agreement ratio of <1.0. Twenty-seven of the 31 pilot questions were completed by ≥90% of responders. Pilot review questions revealed an agreement percentage of ≥86% (n = 12) regarding the survey's ease to complete, understand, importance, length, and interest level. The final survey tool consists of 30 items and achieved content validation through expert evaluation and pilot testing.

Keywords: survey development; gestational diabetes; diabetes prevention; content validation; Theoretical Domains Framework

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1. Introduction

Diabetes mellitus poses a major public health problem around the world, affecting approximately 463 million people and accounting for 4.2 million deaths in 2019 [1]. Type 2 diabetes (T2DM) accounts for around 90% of all diabetes cases [1]. Gestational diabetes (GDM) affected 16% of pregnancies resulting in live births in the world in 2019 [1] and is associated with a risk of developing T2DM in the years following pregnancy, which is 10 times higher than women who do not develop GDM in pregnancy [2]. Women who have GDM and are in an overweight or obese category are twice as likely to develop T2DM than women with previous GDM who are in a healthy weight range [3,4]; therefore, weight loss after GDM is a vital part of diabetes prevention. Women who develop GDM that are in a healthy BMI range should aim to return to their pre-pregnancy weight following pregnancy and maintain a healthy lifestyle to minimize risk of T2DM development [5]. Previous research has investigated barriers to weight loss and the perception of T2DM risk following GDM; however, these studies typically target women in the first one to two years following birth [6–8]. Much of the research around lifestyle behaviors and barriers to weight loss after GDM has come from semi-structured interviews and focus groups [8].

There are limited large studies that investigate the risk perception of T2DM and barriers to weight loss beyond this immediate postpartum period. There is also limited research investigating the weight loss strategies that women with previous GDM have tried and where they source information on weight loss following a GDM pregnancy. Theory-based health investigations allow researchers to identify which determinants of behavior are most relevant in the target population and design interventions that will appropriately address barriers and increase the likelihood of successful behavior change [9]. The Theoretical Domains Framework (TDF) is a theoretical framework consisting of 14 domains to classify attitudes and behaviors, barriers, and facilitators to behavior change [10]. This survey sought to explore women's perception of their T2DM risk after GDM and use the TDF to identify barriers to weight loss and identify diet strategies, programs, or services that these women feel would be suitable at any time after GDM. Opinions of an intermittent '5:2' diet were of interest. This paper presents the survey development and review process used to achieve content validation prior to the final survey administration. The final survey was designed to be an exploratory, cross-sectional online survey of women living in Australia with previous GDM.

2. Materials and Methods

There were three stages to the development and content validation of the survey: initial survey development, expert evaluation, and pilot study testing.

Stage 1: Survey Development

The survey was developed by an accredited dietitian in October 2017 following a review of literature on diabetes prevention after GDM, which revealed limited large studies past 12 months post-pregnancy that investigated barriers to weight loss, diet strategies or services, or perception of diabetes risk following GDM. The TDF was used to guide the development of the survey and categorize beliefs, barriers to weight loss, and perception of diabetes risk as well as structure for the data analysis plan. Table A1 (Appendix A) shows the TDF domains. The survey was developed using the LimeSurvey software package (LimeSurvey, Hamburg, Germany) and contained 36 questions including yes/no multiple-choice and Likert-scale rankings with optional open text comments for several questions. There were five parts to the survey: (1) demographic information and personal characteristics, (2) perception of diabetes risk and views on weight loss after pregnancy; (3) barriers to weight loss; (4) opinions of diet strategies and services; and (5) opinions and use of an intermittent two-day diet (the '5:2' diet). Opinions of an intermittent diet were of interest, as this study was part of a larger research project investigating intermittent energy restriction for weight loss in overweight women with previous gestational diabetes. A plain-language approach was used for questions, and the level of readability was assessed using the Gobbledygook formula, determined to be at a Grade 10 reading level (15–16 years old) [11]. Six questions were linked to the TDF. Questions regarding barriers to weight loss, perception of diabetes risk, and opinions of diet strategies were more heavily informed by the TDF. Question 29 asked participants to respond with their level of agreement to a list of 22 barriers, facilitators, and opinions regarding weight loss. The statements were mapped to a specific TDF domain by the primary researcher.

Stage 2: Expert Review

Invitations to participate in the survey expert review stage were sent via email to 50 recognized experts in the fields of nutrition, midwifery, psychology, or other health or medical research, with six experts completing the expert review (12% response rate). A sample of 3–10 expert reviewers is deemed adequate for content validation of a new survey [12]. Experts were identified from the author lists of journal articles in relevant areas and searches on various university departmental staff pages. Of the six reviewers, four were Accredited Practicing Dietitians, one had a background in midwifery and nursing, and one a background in health and exercise psychology and behavior. All six reviewers worked in research and academia settings. Recruitment occurred between November and

December 2017. An email invitation outlining the study with a link to the online survey, instructions for rating each item, and an information sheet outlining the TDF domains was sent to each potential reviewer. Reviewers were asked to respond to the relevance, clarity, coherence, and answer options for each question on a four-point Likert scale [13]. The definition of each item and scoring was provided to reviewers as follows: relevance (Is the question going to help achieve an answer to the research objectives?), clarity (Is the question clear and specific? Does it make sense to the reader?), coherence (Is this question logical, consistent, and reasonable in the context of the research problem being addressed?), and answer options (Are the answers appropriate for the question being asked?). The answer options for the four-point Likert scale were 1 = not acceptable, 2 = below expectations, 3 = meets expectations, and 4 = exceeds expectations. Reviewers were also asked "Is there anything else you would like to say about the question (e.g., item rewording, answer order/options, or anything else)." For the TDF-linked questions, reviewers were also asked to rate the fit of the identified TDF domain on a four-point Likert scale (1 = absolutely does not fit, 2 = doubtful fit, 3 = fair fit, 4 = exact fit). At the end of the survey, reviewers were asked for any other overall comments or feedback about the survey.

Stage 3: Pilot Test

Following changes made to the survey from the expert review, a pilot test was undertaken to evaluate the usability of the survey, identify any procedural problems, and receive overall survey feedback from participants. The inclusion criteria for the pilot and final study were the same: women with previous GDM, living in Australia, aged 18 years or older, and no diagnosis of diabetes prior to GDM. Recruitment occurred between December 2017 and January 2018 and was achieved through a social media advertisement. A convenience sample of 21 women participated in the pilot survey, but $n = 1$ was ineligible. Recruitment was through social media advertisement until the required number of responses were received ($n = 20$), and as such, a response rate could not be determined. A sample size of $n = 20$ was deemed adequate based on recommendations by Julius (2005), who specified a minimum of 12 participants per group needed to pilot a study [14]. Comparable numbers have been used to pilot cross-sectional surveys in similar populations [15–17]. Participants responded to the survey questions and an additional question covering how easy the survey was to understand and complete as well as the survey's length, importance, and if it was interesting using a 5-point agreement Likert scale. Participants were also asked to provide any extra comments or feedback as free text.

2.1. Statistical Analysis

2.1.1. Expert Review

Results from the expert review stage were used to determine the initial retention, deletion, and modification of survey items. The content validation index (CVI) is an inter-rater agreement calculated based on expert reviewers' ratings [12]. It is a widely used tool for quantifying the relevance of a multi-item tool to the construct of interest and commonly used in the development of questionnaires and surveys in health and nursing research [12]. The content validation of each item was performed by a panel of experts ($n = 6$) and was achieved through calculating the content validation index (I-CVI) (number of expert answers with a score of 3 or 4 divided by the total number of expert answers) in the dimensions of relevance, clarity, coherence, and answer options [12]. An overall CVI of the survey was also determined by calculating the mean index from the I-CVI relevance index. A CVI of at least 0.83 is commonly considered acceptable when six expert reviewers rate the items, reflecting one expert who disagreed and five who agreed the question was appropriate in the dimension being measured. A CVI of $\leq$0.78 reflects two experts disagreeing and four agreeing, is considered unacceptable when there are six reviewers, and requires modification [12].

Data were analyzed using Microsoft Excel (Office 2016 for Microsoft, Redmond, WA, USA). Questions that received an I-CVI of $\leq$0.78 were modified or removed [12]. The TDF domain fit responses were analyzed by calculating the number of experts who scored the

chosen domain fit at 3 (fair fit) or 4 (exact fit) divided by the number of expert reviewers. All open text comments for each question and the overall survey from the reviewers were read and changes were made based on the suggestions. Analysis of the expert review stage was performed using Microsoft Excel (Office 2016 for Microsoft, Redmond, WA, USA).

2.1.2. Pilot Test

The pilot test determined the final retention, deletion, and modification of survey items. Data analysis was undertaken using IBM SPSS Statistical software v25 for Windows (IBM, Chicago, IL, USA) and Microsoft Excel (Office 2016 for Microsoft, Redmond, WA, USA). A descriptive analysis of the demographic information for the pilot test was also performed. Data were tested for normality using Q–Q plots, histograms, and Shapiro–Wilk tests. As most data were skewed data, they are presented as the median and IQR, unless otherwise stated. An answer percentage was calculated for each question (number of the responders who answered each question divided by the number of responders who were presented with the question, multiplied by 100). The percentage of participants who responded with a score of $\geq$4 (agree or strongly agree) for the positively phrased review questions or $\leq$2 (disagree or strongly disagree) for the negatively phrased review question was also calculated for each of the pilot test review questions.

2.1.3. Ethics

The research was conducted according to the NHMRC National Statement on Ethical Conduct in Human Research. Ethics approval was granted by The University of South Australia's Human Research Ethics Committee prior to the project commencing (Protocol No. 200231). Reviewers and pilot responders provided informed consent electronically prior to commencing the survey.

3. Results

3.1. Expert Review

The overall CVI was 0.91. For relevance, clarity, coherence, and response options, there were 1, 10, 3, and 12 items, respectively, that received an I-CVI score of $\leq$0.78. Table 1 shows the index scores for each survey item and the changes made. The one question that received an I-CVI score of $\leq$0.78 for relevance was a screening question needed to determine eligibility for the survey. The four eligibility screening questions were regrouped into one question at the start of the survey, which asked participants if they met all the eligibility requirements or not.

All 36 items received expert comments. As a result, 32 items were modified, and 10 items were merged into 4 items. The answer mode or question wording of four items that received acceptable I-CVIs across all measures were minimally modified based on expert-panel-written suggestions. Question order was also modified to improve survey flow, and the online platform was changed to Survey Monkey (SurveyMonkey Inc., San Mateo, CA, USA) to improve the user interface and allow for more specialized functions such as skip logic.

Fourteen of the 27 TDF items had an agreement ratio of <1.0 for the TDF framework fit review. The question that listed barriers to weight loss and asked responders to rate their agreement or disagreement with the statements was found to be too lengthy by reviewers, and some statements were repetitive; therefore, the question was reduced from 22 to 15 statements. Four items that were originally linked to the TDF domain 'Environmental Context and Resources' were changed to the domain 'Beliefs about Capabilities', one item that was linked to the 'Behavioral Regulation' domain was also changed to 'Beliefs about Capabilities', and two items that were linked to the domain 'Knowledge', were changed to the domains 'Beliefs about Consequences' and 'Social/Professional Role and Identity'. Four of the barriers to weight loss statements that were negatively phrased were changed to be positively phrased based on reviewer suggestions that responders whose first language is not English may find these statements difficult to understand.

Table 1. Content validation index (I-CVI) scores from expert evaluation for each item and changes made *.

Version 1 of Survey: Items Constructed by the Research Team						Version 2 of Survey: Items MODIFIED Following Expert Review (Administered to Pilot Test)	
Question No.	**Question**	**Relevance**	**Clarity**	**Coherence**	**Response Options**	**New Question No.**	**Changes Made Following Expert Review**
1	Informed consent	N/A	N/A	N/A	N/A	1	
2	Have you ever been diagnosed with gestational diabetes during a pregnancy?	1.00	1.00	1.00	1.00	2	Definition of gestational diabetes added. Responses changed to agree to all inclusion criteria.
3	Did you have either type 1 or type 2 diabetes before your gestational diabetes pregnancy?	**0.67**	0.83	**0.67**	**0.67**	2	Question wording changed and merged into the eligibility question (Question 2)
4	Are you aged 18 years or older?	1.00	1.00	1.00	1.00	2	merged into one eligibility question (Question 2)
5	Do you live in Australia?	1.00	1.00	1.00	1.00	2	merged into one eligibility question (Question 2)
6	What is your postcode?	1.00	1.00	1.00	1.00	3	Wording of why postcode data are collected slightly modified
7	Are you currently pregnant?	1.00	1.00	1.00	1.00	6	
8	In what year were you diagnosed with gestational diabetes? (If you have had gestational diabetes more than once, enter your most recent diagnosis)	0.83	1.00	1.00	1.00	15	
9	Did you require insulin injections during your gestational diabetes pregnancy to manage the diabetes?	1.00	**0.67**	1.00	**0.67**	16	Wording and responses changed
10	Since your gestational diabetes pregnancy, have you been diagnosed or told by a doctor or other healthcare professional that you have type1 diabetes, type 2 diabetes, prediabetes, or impaired glucose tolerance?	0.83	1.00	1.00	1.00	17	Wording modified slightly

Table 1. *Cont.*

Version 1 of Survey: Items Constructed by the Research Team						Version 2 of Survey: Items MODIFIED Following Expert Review (Administered to Pilot Test)	
Question No.	**Question**	**Relevance**	**Clarity**	**Coherence**	**Response Options**	**New Question No.**	**Changes Made Following Expert Review**
11	Do you have a family history of diabetes?	0.83	1.00	1.00	1.00	14	Dropdown answer changed to radio buttons
12	When was your youngest child born? (in what month and year did your most recent pregnancy end)	0.83	**0.50**	0.83	**0.67**	8	Wording modified
13	How many children do you have living at home with you?	1.00	**0.67**	1.00	0.83	7	Wording modified
14	What is your age in years?	1.00	1.00	1.00	1.00	5	
15	What is your height in cm without shoes on? (If you do not know your height in centimeters (cm), you can use the following link to convert your height from feet and inches into cm)	1.00	1.00	1.00	**0.67**	9	Included hyperlink to convert height from imperial to metric units
16	What is your current weight in kilograms (kg) without shoes and in light or no clothing? (If you have a set of bathroom scales, please weigh yourself and enter your weight in here. If you are unable to weight yourself but you know how much you weigh, please use that weight)	1.00	0.83	1.00	1.00	10	Wording modified and hyperlink added
17	For the last question about your weight, did you weigh yourself or estimate your weight?	1.00	1.00	1.00	1.00	11	
18	What is your employment status?	1.00	1.00	1.00	0.83	4	Added ‘other’ option
19	Do you think you are at risk of developing type 2 diabetes?	1.00	**0.67**	0.83	**0.67**	13	Answer mode and options changed

Table 1. *Cont.*

Version 1 of Survey: Items Constructed by the Research Team						Version 2 of Survey: Items MODIFIED Following Expert Review (Administered to Pilot Test)	
Question No.	**Question**	**Relevance**	**Clarity**	**Coherence**	**Response Options**	**New Question No.**	**Changes Made Following Expert Review**
20	Do you consider yourself to be under, within, or over a healthy weight?	0.83	0.83	1.00	**0.67**	12	Answer options changed
21	Since you have had gestational diabetes, have you been told by a doctor or other healthcare professional (e.g., a dietitian, midwife, diabetes nurse, etc.) that you need to lose weight?	0.83	**0.67**	1.00	**0.67**	18	Wording modified
22	Have you lost, gained, or maintained your weight since your last baby was born?	0.83	**0.50**	1.00	0.83	22	Wording modified
23	Since your gestational diabetes pregnancy, have you gone on any diets or tried to lose weight?	1.00	1.00	1.00	1.00	23	Wording slightly modified based on TDF fit
24	Have you tried any of the following diets, programs, or procedures since having gestational diabetes?	1.00	**0.50**	**0.67**	0.83	24	Merged Q24 and Q25 and wording changed
25	Are there any other types of diets or weight loss programs or services you have tried for weight loss? (please specify what you have tried and if it worked for you or not)	1.00	1.00	1.00	0.83	24	Merged Q24 and Q25 and wording changed
26	How long after having a baby do you think it is safe to start to try and lose weight?	1.00	0.83	1.00	**0.60**	20	Answer mode and responses changed

Table 1. *Cont.*

Version 1 of Survey: Items Constructed by the Research Team						Version 2 of Survey: Items MODIFIED Following Expert Review (Administered to Pilot Test)	
Question No.	**Question**	**Relevance**	**Clarity**	**Coherence**	**Response Options**	**New Question No.**	**Changes Made Following Expert Review**
27	Do you think it is safe to lose weight while you are breastfeeding?	1.00	1.00	1.00	0.83	19	Added 'I don't know' option
28	Did you breastfeed your baby after your gestational diabetes pregnancy?	1.00	0.83	1.00	**0.67**	21	Answer options changed
29	Please read the following statements about weight loss and answer each question how much you agree or disagree with the statement	1.00	**0.67**	1.00	**0.5**	25	Merged Q29 and 30. Answer wording 'neither agree or disagree' changed to 'not sure' for simplicity
30	Are there any other things not listed above that might make weight loss hard for you right now?	1.00	1.00	1.00	1.00	25	Merged Q29 and 30.
31	The following statements will ask you what kind of weight loss program or service you think might work for you at the moment. Please read each statement and answer according to how much you agree or disagree that each one could work for you.	1.00	0.83	1.00	0.83	26	Wording slightly changed and question merged with Q32
32	Are there any other things you think could help you to lose weight right now?	1.00	0.83	0.83	1.00	26	Merged with Q31
33	Where would you go for information on how to lose weight?	1.00	1.00	1.00	0.83	27	Wording changed "Where have you or would you go to look for information on how to lose weight?"

Table 1. *Cont.*

Version 1 of Survey: Items Constructed by the Research Team						Version 2 of Survey: Items MODIFIED Following Expert Review (Administered to Pilot Test)	
Question No.	**Question**	**Relevance**	**Clarity**	**Coherence**	**Response Options**	**New Question No.**	**Changes Made Following Expert Review**
34	Have you heard of the 5:2 diet?	1.00	**0.67**	1.00	0.83	28	wording changed (This is also known as an intermittent or fasting diet)
35	If you answered 'yes' to the last question, have you ever tried the 5:2 diet?	1.00	0.83	1.00	**0.67**	29	typographical error corrected. Skip logic added to the previous question
36	Do you think the 5:2 diet could be a good option for you right now? Please feel free to comment if you would like to add any further thoughts.	0.83	**0.67**	**0.50**	**0.67**	30	Wording changed

* Items that received a score of $\leq$0.78 are shown in boldface.

3.2. Pilot Test

Participants had a median (IQR) age of 36 (5) years (n = 20) and were 2 (4) years post-GDM (n = 19), with a BMI of 27.3 kg/m^2 (11.7 kg/m^2) (n = 18). Eleven and six women, respectively, were in the overweight or obese (61%) and healthy weight range (28%), and one woman was underweight (9%). Two participants did not provide their weight; therefore, their BMI could not be established.

Twenty-seven questions were answered by ≥ 90% of responders. Skip logic was used for questions on diet types and intermittent dieting (Questions 23 and 28), and as a result, only 13 participants were shown the more detailed questions on diet types (Question 24), 15 on intermittent dieting (Question 29a), and five on the suitability of intermittent dieting (Question 29b). The final four survey questions had response rates of 60–73%. Table 2 shows the percentage of participants who answered each question. All review questions received an agreement percentage of ≥86% (n = 12) for the positively phrased statements, and 14% (n = 2) agreed with the statement "The survey took too long" (Figure 1). All participants agreed that the survey was easy to understand and that the survey was important. One participant answered the survey as not easy to complete, and one found the survey not interesting. Of the twelve participant free text comments, eight were positive and four commented that they disliked the question on diets tried and how well they worked because it contained a forced choice where they had to select answers, even if a particular type of diet was not applicable to them. Subsequently, the answer mode for this question was changed. No other changes were made following the pilot survey test.

Table 2. Number and percentage of questions answered for each item in the pilot test.

Question No.	Question	No. Presented with Question	No. Who Answered Question	% Answered
1	Consent	21	21	100%
2	Eligibility	21	21	100%
3	Postcode	20	18	90%
4	Employment status	20	20	100%
5	Age	20	20	100%
6	Pregnant	20	20	100%
7	Number of children at home	20	20	100%
8	Year youngest child born	20	20	100%
9	Height	20	20	100%
10	Weight	20	18	90%
11	Weight measured or estimated	20	20	100%
12	Perception of weight status	20	20	100%
13	Perception of diabetes risk	20	19	95%
14	Family history of diabetes	20	19	95%
15	Year diagnosed with GDM	20	19	95%
16	Medication during GDM pregnancy	20	19	95%
17	Diagnosis of diabetes since GDM	20	19	95%
18	Has a healthcare professional told you to lose weight?	20	19	95%
19	Do you think it is safe to lose weight while breastfeeding?	20	19	95%
20	How long after having a baby do you think it is safe to start trying to lose weight (breastfeeding and not breastfeeding)?	20	19	95%
21	Did you breastfeed your baby after your GDM pregnancy?	20	19	95%
22	Has your weight changed since your last baby was born?	20	19	95%
23 *	Since having GDM, have you thought about or tried losing weight?	20	19	95%
24	Diets tried and how well they worked?	13	13	100%
25	Barriers to weight loss (Likert scale)	20	18	90%
26	Weight loss programs or services tried	20	18	90%

Table 2. *Cont.*

Question No.	Question	No. Presented with Question	No. Who Answered Question	% Answered
27	Where would you go for information on how to lose weight?	20	18	90%
28 *	Have you heard of the 5:2 diet?	20	18	90%
29a	Have you tried the 5:2 diet?	15	11	73%
29b	Do you think the 5:2 diet could be a good option for you?	5	3	60%
30	Pilot review question (ease to complete, understand, length and importance) (Likert scale)	20	14	70%
31	Pilot review question—We would like to hear your thoughts about the survey	20	12	60%

* Skip logic used at this question. GDM: gestational diabetes.

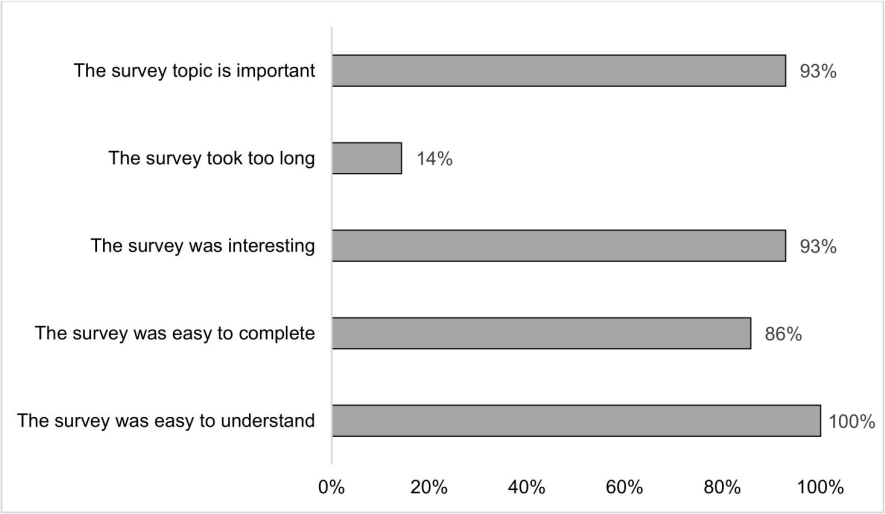


Figure 1. Pilot test review. Percentage of responders who agreed or strongly agreed on the Likert-scale survey review questions (n = 14); responses were received on a five-point Likert-scale (1 = strongly disagree, 2 = disagree, 3 = not sure, 4 = agree, 5 = strongly agree).

4. Discussion

This study developed and tested the content validity of a questionnaire. Content validity assesses whether the content of a test or instrument is measuring the constructs of interest (barriers to weight loss, perception of diabetes risk, and views of diet strategies following GDM) [18]. Content validity was achieved in this study through acceptable levels of expert agreement in the areas of relevance, clarity, coherence and item response options, and a good response rate with positive feedback from the pilot test stage. The overall CVI value from the expert review also shows good relevance to the constructs being measured. Together, results from the expert review suggest that the elements in the survey are appropriate to assess the constructs of interest.

Items' clarity and response options received the greatest number of I-CVI scores of $\leq$0.78 (10 and 12, respectively), while items' relevance and coherence only received an I-CVI score of $\leq$0.78 for one and three items, respectively. This suggests that initial issues with the survey at the expert review stage were not related to the question itself but more how the question and response options were worded. The pilot test showed promising results, with a high response rate for most of the questions and high agreement ratios to the survey review questions, including the survey being easy to understand and easy to complete.

Results from the pilot test suggest that the final survey questions were appropriate for the target population.

The final survey tool consists of 30 questions, including 6 questions linked to the TDF, with the purpose to assess women's barriers to weight loss, perception of diabetes risk and views of diet strategies, and services following gestational diabetes in a cross-sectional study. The consequences of T2DM are substantial and include a risk of developing chronic complications including cardiovascular disease, kidney disease, cancer, and early death [1,19]. With the growing percentage of women being diagnosed with GDM [20] and a nearly ten-fold increased risk of these women developing T2DM [2], understanding the barriers to weight loss, perception of disease risk, and views on different diet strategies is a critical step needed to design appropriate diabetes prevention interventions. The TDF provides a validated way to categorize constructs of behavior change and pinpoint areas to focus intervention on such as providing education to increase knowledge or teaching the target population self-monitoring techniques to improve behavioral regulation [9].

Daily energy restriction, although an effective strategy for weight loss, is difficult to adhere to in the long term [21]. Alternative weight loss strategies such as intermittent fasting have become popular in recent years, appealing to many people due to the increased flexibility for eating on non-fasting days [22]. Research to date suggests that an intermittent diet is a suitable alternative to continuous energy restriction for overweight adults, producing comparable weight loss and metabolic improvements to a conventional daily diet [23–25]; however, more research in the area is needed, particularly focusing on longer-term outcomes. This survey adds to the body of research on intermittent fasting by investigating the popularity and opinions of this diet strategy in a population of women who are at high risk for developing T2DM.

The main limitation in the development of this survey was that no second round of expert evaluation was undertaken; therefore, experts did not have the opportunity to respond to the changes made following their initial review. However, results from this stage showed acceptable I-CVI scores for the survey items as well as a good overall CVI. Most of the changes made to the survey following the expert review were minor, involving modification of question wording for clarity and coherence as well as changing the response options or mode and changing the survey platform to a more user-friendly interface and allowing the skip logic function. The survey assessed socioeconomic diversity by gathering postcode data; however, questions regarding ethnicity were not included in the survey. This would be worthwhile data to collect in future studies given the large Asian population in Australia, the increased risk of GDM in these women, and a lower BMI threshold where the risk of comorbidities is increased [26]. One of the main goals for GDM management is to control weight gain during pregnancy. The focus of this survey is on weight loss following a GDM pregnancy rather than GDM management; therefore, we did not include questions regarding weight gain in pregnancy or pre-pregnancy weight status. We did assess current BMI and asked whether participants had lost the weight they gained in pregnancy. However, pre-pregnancy weight and weight gain in pregnancy could influence the perception of diabetes risk and would be worth including these questions in future studies.

The final survey will be administered as an online cross-sectional survey to women with previous GDM. The TDF will help to identify barriers to weight loss, perception of diabetes risk and diet strategies that are found to be achievable based on different family circumstances and years past GDM.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by University of South Australia's Human Research Ethics Committee (Protocol No. 200231 29 October 2017).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Table A1. The Theoretical Domains Framework domains and constructs *.

Domain		Constructs
1.	Knowledge	Knowledge, Procedural knowledge, Knowledge of task environment
2.	Skills	Skills, Skills Development, Competence, Ability, Interpersonal skills, Practice, Skills assessment
3.	Social/Professional Role and identity	Professional identity, Professional role, Social identity, Identity, Professional boundaries, Professional confidence, Group identity, Leadership, Organizational commitment
4.	Beliefs about Capabilities	Self-confidence, Perceived competence, Self-efficacy, Perceived behavioral control, Beliefs, Self-esteem, Empowerment, Professional confidence
5.	Optimism	Optimism, Pessimism, Unrealistic optimism, Identity
6.	Beliefs about Consequences	Beliefs, Outcome expectancies, Characteristics of outcome expectancies, Anticipated regret, Consequents
7.	Reinforcement	Rewards, Incentives, Punishment, Consequents, Reinforcement, Contingencies, Sanctions
8.	Intentions	Stability of intentions, Stages of change model, Transtheoretical model and stages of change
9.	Goals	Goals (distal/proximal), Goal priority, Goal/target setting, Goals (autonomous/controlled), Action planning, Implementation intention
10.	Memory, attention, and decision processes	Memory, Attention, Attention control, Decision making, Cognitive overload/tiredness
11.	Environmental context and resources	Environmental stressors, Resources/material resources, Organizational culture/climate, Salient events/critical, incidents, Person × environment interaction, Barriers and facilitators
12.	Social Influences	Social pressure, Social norms, Group conformity, Social comparisons, Group norms, Social support, Power, Intergroup conflict, Alienation, Group identity, Modeling
13.	Emotion	Fear, Anxiety, Affect, Stress, Depression, Positive/negative affect, Burn-out
14.	Behavioral Regulation	Self-monitoring, Breaking habit, Action planning

* Adapted from Cane J, O'Connor D and Michie S, 2012 (1).

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4. Women's Barriers to Weight Loss, Perception of Future Diabetes Risk and Opinions of Diet Strategies Following Gestational Diabetes

4.1. Preface

The literature review in chapter 1 highlighted that women of childbearing age are a high-risk group for weight gain. Furthermore, women in this age bracket who are already overweight and have a history of GDM have an exceptionally high risk for developing T2DM. There is no question that weight loss can dramatically lower the likelihood of developing T2DM after GDM. However, low levels of engagement and high attrition in this population are extremely common, and the incidence of T2DM continues to rise. Much of the available research on barriers to weight loss in this population arose from qualitative studies with a small sample size, therefore we identified a need to develop a new large-scale online survey. The aim of this survey was to investigate barriers to weight loss, perception of future diabetes risk, opinions of IER following GDM, and preferences for delivery of weight loss programs or services. The Theoretical Domains Framework was used to deductively categorize questions and free text comments into clear sources of behaviour. The results of the survey presented in this chapter provide a broader picture than was previously available regarding barriers to weight loss experienced by women with a history of GDM in Australia, as well as opinions of IER and program delivery preferences. The findings are a valuable addition to the field, providing usable information for consideration in both the development of future diabetes prevention programs as well as in clinical settings.

4.2. Published Article

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Women's Barriers to Weight Loss, Perception of Future Diabetes Risk and Opinions of Diet Strategies Following Gestational Diabetes: An Online Survey

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Abstract: Weight loss after gestational diabetes (GDM) reduces the risk of type 2 diabetes (T2DM); however, weight loss remains challenging in this population. In order to explore perceptions of T2DM risk, barriers to weight loss, and views of diet strategies in women with previous GDM, a cross-sectional online survey of n = 429 women in Australia aged ≥18 years with previous GDM was conducted. Opinions of intermittent energy restriction (IER) were of interest. Seventy-five percent of responders (n = 322) had overweight or obesity, and 34% (n = 144) believed they had a high risk of developing T2DM. Within the Theoretical Domains Framework, barriers to weight loss were prominently related to Environmental Context and Resources, Beliefs about Capabilities, and Behavioural Regulation. Exercising was the most tried method of weight loss over other diet strategies (71%, n = 234) and weight loss support by a dietician was appealing as individual appointments (65%, n = 242) or an online program (54%, n = 200). Most women (73%, n = 284) had heard of IER (the "5:2 diet"), but only 12% (n = 34) had tried it. Open comments (n = 100) revealed mixed views of IER. Women in Australia with previous GDM were found to lack a self-perceived high risk of developing T2DM and expressed barriers to weight loss related to their family environment, beliefs about their capabilities and behavioural regulation. IER is appealing for some women with previous GDM; however, views vary.

Keywords: diabetes risk; gestational diabetes; weight loss barriers; diet strategies; intermittent energy restriction; theoretical domains framework

1. Introduction

Gestational diabetes (GDM), defined as glucose intolerance that begins or is first recognized during pregnancy [1], is a growing health issue around the world. In 2016–2017, 40,000 (15%) pregnancies in Australia were affected by GDM [2]. Globally, GDM affected 16% of live births in 2019, with 20.4 million babies being born from a GDM pregnancy [3]. Although GDM typically resolves shortly after birth, the risk of developing type 2 diabetes (T2DM) is nearly 10 times higher for women with a history of GDM compared to women who did not have GDM in pregnancy [4]. Being in an overweight or obese weight category further increases the risk of developing T2DM after GDM [5,6]. A 2010 study

found the overall adjusted population-attributable fraction of GDM due to overweight and obesity to be 46.2% (95% CI = 36.1, 56.3) [6].

Globally, T2DM is a major health problem, with an estimated 463 million adults in the world currently living with the disease [7]. Lifestyle modification resulting in weight loss can significantly reduce the risk of T2DM after GDM [8]; however, weight loss is not easily achieved or maintained in this population [9]. Understanding the high risk of developing T2DM associated with GDM is important for women to improve motivation to overcome barriers and make behavioural changes to prevent T2DM [10]. Exploring barriers to weight loss after GDM is also necessary to be able to implement appropriate and effective interventions [11]. Previous research investigating factors that influence lifestyle behaviour modification for diabetes prevention in women who previously had GDM identified such factors as tiredness, lack of time, lack of family support, diet not fitting into family meals, lack of affordable weight loss programs, access to child-minding services, and further pregnancies as barriers to weight loss [12–14]. These studies tend to target women who have given birth within the last 12 months. Although this may be the optimal time to lose weight [15], women with a history of GDM who are greater than one year postpartum may respond better to a weight loss program once a more stable lifestyle has resumed [10].

There are few large studies investigating risk perception of T2DM, barriers to weight loss, or diet strategies for women with previous GDM beyond the 12-month postpartum period. The purpose of this survey was to explore women's perception of their risk of T2DM after GDM, to use the Theoretical Domains Framework (TDF) to identify barriers to weight loss, and to identify diet strategies, programs, or services that these women feel would be suitable to them at any time after GDM. Views and opinions of IER were of particular interest.

2. Materials and Methods

2.1. Participants and Recruitment

This study was an exploratory, cross-sectional online survey. Recruitment occurred between March and September 2018 and was done online through advertising on Facebook and Australian online parenting websites and forums, as well as a mailout (n = 1600) and email (n = 2560) by the Australian National Diabetes Services Scheme (NDSS). Facebook advertisements appeared on the newsfeed webpage of potential participants who met a predefined criterion (women, aged ≥18 years, located in Australia). The mail and email were sent by the NDSS to women on the National Gestational Diabetes Register, and included information about the survey, as well as the URL and links to access the survey and consent form. The research team did not receive the names, contact information, or any other information about anyone who clicked on the survey link from the advertisements. Since 2011, all women in Australia who are diagnosed with GDM are automatically added to the National Gestational Diabetes Register unless they opt out, and therefore, the survey advertisements reached potential participants with a diverse background. Responders were women aged ≥18 years living or residing in Australia who had been diagnosed with GDM during a pregnancy any length of time ago. Women were excluded if they had a diagnosis of type 1 diabetes (T1DM) or T2DM prior to a GDM pregnancy, or if they were pregnant with their first child (n = 3). Women who were currently pregnant with GDM were included if they also had GDM in a previous pregnancy. Diagnoses of GDM, T1DM, T2DM, and impaired glucose tolerance or prediabetes were self-reported. As recruitment was achieved through potential participants following a link to the survey, the research team did not have access to any medical records.

2.2. Survey Development

The initial survey was developed online using Survey Monkey by a dietician at the University of South Australia. The survey underwent content validation by a panel of experts in the fields of nutrition, midwifery, psychology, and health/medical research (n = 6). Experts responded to the clarity,

coherence, relevance, and response options for each question, as well as the fit of the chosen domain within the TDF. The TDF is a theoretically-based approach to classifying attitudes and behaviours, barriers, and facilitators to behaviour change [16]. The 14 domains of the TDF can be integrated into the COM-B model (Capability, Opportunity, Motivation—Behaviour) allowing for further identification of the determinants of a behaviour [17]. The survey achieved content validation with an overall content validity index (overall CVI) of 0.91, and all questions except one received an individual CVI (I-CVI) of >0.78 for relevance (n = 35). Following the expert evaluation, the adapted survey was piloted in women with a history of GDM (n = 20) who responded to questions on the length, importance, interest, and ease to complete and understand the survey, and provided further comments. The pilot test review questions revealed an agreement percentage of ≥86% (n = 12) regarding the survey's ease to complete, understand, importance, length, and interest level, and 87% of the survey questions (n = 27) were answered by >90% of the pilot responders. Minor changes were made based on the pilot feedback prior to the final survey being run.

2.3. Survey Questions

The final survey consisted of five sections: demographic information; perception of diabetes risk and views on weight loss after pregnancy; barriers to weight loss; diet strategies and services; and opinions and use of an intermittent two-day diet (the "5:2" diet). The 5:2 diet was of particular interest as this survey formed part of a larger project investigating whether an intermittent diet would be a suitable alternative to continuous energy restriction in women with previous GDM. The survey comprised of 28 questions and included single- and multiple-choice questions and Likert scales. Several questions allowed space for optional open-text comments. The level of readability was determined to be at Grade 10 reading level (15 to 16 years old) using the Gobbledygook formula [18]. Skip logic was used at several points throughout the survey so that women were not burdened with questions that were not relevant to them. The question regarding diet strategies asked responders which (if any) diet strategies they had tried from a provided list of 12 weight loss methods, and if they had tried an approach, how well that approach worked for them. No explanation for the individual diet strategies was provided based on their wide use within this population. The question assessed how many people had tried the different diet strategies listed, and did not ask participants to rate or provide views of the different strategies. The questions regarding the 5:2 diet at the end of the survey did include information about what the 5:2 diet is and what it involves, as this was assessing participants' views and opinions of the diet.

2.4. Statistics

A sample size of n = 384 was required to provide results that are indicative of the population of women in Australia who have had GDM with 95% confidence level and a 5% margin of error [19]. The number of 384 was based on the Australian Bureau of Statistics (ABS) calculator using a population size of 40,000. The default response rate of 50% was used.

Data were analyzed using IBM SPSS Statistical Software version 26 for Windows (IBM, Chicago, IL, USA). Data were tested for normality using Q-Q plots, histograms, and Kolmogorov–Smirnov tests. Variables were not normally distributed and remained skewed after log transformation, and therefore were analyzed using Kruskal–Wallis non-parametric tests. Pearson's chi squared test was used for categorical variables. A binomial logistic regression was run to ascertain if there were any effects of age, family history of diabetes, and body mass index (BMI) on self-reported diagnoses of T2DM or prediabetes following GDM. Significance was set at $p < 0.05$. Descriptive data are presented as the % of respondents (total number of respondents) for categorical variables and the median, and IQR for continuous variables. Results from 5-point Likert scales were collated to a three-point scale by grouping "Agree" and "Strongly Agree" responses and "Disagree and Strongly Disagree" responses together. Questions and comments from the "barriers to weight loss" section were categorized into domains of the TDF within the COM-B model using a double-coding method by two of the authors (KG and SOR). Supplementary Table S1 shows the TDF domains integrated into the COM-B

model. Comments received regarding the diet strategies attempted and thoughts on the 5:2 diet were categorized into common themes arising from the comments. Body mass index (BMI) was calculated from self-reported height and weight. Responders' answers were included in the analysis for as many questions as they had valid answers for. Women who were pregnant (n = 20) were excluded from the weight question and BMI calculation, as well as the question, "Do you consider yourself to be in a healthy weight range?". Australian postcode data were used to determine Socio-Economic Indexes for Areas (SEIFA).

2.5. Ethics

The research was conducted according to the National Health and Medical Research Council's (NHMRC) National Statement on Ethical Conduct in Human Research. Ethics approval was granted by The University of South Australia's Human Research Ethics Committee prior to the project commencing (protocol #200231). Responders provided informed consent electronically before commencing the survey.

3. Results

Four hundred and thirty-two women began the survey. Three women were excluded as they were pregnant with their first child. There were 429 valid responses, with 77% (n = 329) completing the entire survey. The overall response rate could not be calculated as there were no data available on how many people saw the online advertisements; however, n = 4160 invitations were sent through mail and email. The median, IQR age was 36.0, 8.0 years, respectively, and BMI was 30.0, 9.8 kg/m^2. Seventy-five percent of women (n = 322) were above the healthy BMI range of 18.5–24.9 kg/m^2, and five women were underweight (1%). Women were 3.0, 5.0 years post-GDM (2.4, 3.6 years postpartum). Table 1 shows the personal and demographic characteristics of the responders.

Table 1. Characteristics of survey responders.

Characteristic	All Responders
Age, y	36.0, 8.0
Weight, kg	82, 27
BMI, kg/m^2	30.1, 9.7
SEIFA *, index	6.0, 5.0
- Decile 1, *n* (%)	43 (10)
- Decile 2, *n* (%)	27 (6)
- Decile 3, *n* (%)	53 (13)
- Decile 4, *n* (%)	40 (10)
- Decile 5, *n* (%)	38 (9)
- Decile 6, *n* (%)	54 (13)
- Decile 7, *n* (%)	41 (10)
- Decile 8, *n* (%)	63 (15)
- Decile 9, *n* (%)	34 (8)
- Decile 10, *n* (%)	29 (7)
Years postpartum ** y	2.5, 3.5
Years since GDM, y	3.0, 5.0
GDM managed, *n* (%)	
- Diet/Exercise	248 (7)
- Metformin	46 (11)
- Insulin	135 (31)
Children living at home, n	2, 1
Employment, *n* (%)	
- Full-time work/study	99 (23)
- Part-time work/study	180 (42)
- Stay-at-home /maternity leave	126 (29)
- Retired/unemployed/other	24 (5)
Family history of diabetes, *n* (%)	268 (62)
Lost weight gained in pregnancy, *n* (%)	
- Yes	218 (62)
- No	177 (42)
- "I don't know"	30 (7)
Breastfeeding time, *n* (%)	
- Did not breastfeed	40 (9)
- Breastfed up to 3 months	99 (24)
- Breastfed 4–6 months	46 (11)
- Breastfed 1 year or longer	147 (35)

Data is median, IQR. * Socio-Economic Indexes for Areas (decile 1 = most disadvantaged, decile 10 = least disadvantaged), ** from most recent pregnancy.

Just over 50% of women had lost the weight they gained during pregnancy (n = 217). Of the women who were at least 12 months postpartum (n = 330), 53% (n = 175) had lost all the weight they gained during pregnancy. Two-thirds of respondents breastfed their baby after GDM for more than three months (67%, n = 285) and one-third (34%, n = 147) breastfed for more than 12 months. Length of time breastfeeding was not associated with losing pregnancy weight (p = 0.14, n = 423).

Six women were diagnosed with T2DM since having GDM, and 10% (n = 43) were told they had pre-diabetes or impaired glucose tolerance (IGT). Ninety-five responders (22%) answered that they had not been tested for diabetes since having GDM. Of the responders who had not been tested for T2DM, 19% (n = 18) were either in an underweight or healthy weight range. Eleven women had not seen a healthcare professional since having GDM, and 38% (n = 164) had been told by a healthcare professional that they needed to lose weight. In a binomial logistic regression, family history of diabetes and age were significantly related to a self-reported diagnosis of prediabetes or T2DM after GDM; however, BMI was not ($p \leq 0.001$, $r^2 = 0.167$ for the model).

3.1. Knowledge of Weight, Weight Loss, and Perception of Risk of T2DM

Women who were in an overweight (n = 115) or obese (n = 207) weight category mostly knew that they were overweight. Only eight women who had overweight or obesity answered that they thought they were a healthy weight, and one responder with an overweight BMI identified as underweight. Women with a higher BMI were more likely to respond that they thought they were very overweight ($p < 0.001$, n = 413).

One-third of women (34%, n = 144) thought they were at high risk of developing T2DM, 41%(n = 176) answered moderate risk, 20% (n = 86) answered low risk, and 5% (n = 22) answered that they did not think they were at risk for developing T2DM. Higher BMI was associated with a higher perceived risk of developing T2DM ($p < 0.001$, n = 412). There was a statistically significant association between family history of GDM and higher perceived risk of developing T2DM ($p < 0.001$). GDM management method was also significantly associated with perceived risk of T2DM with 44% (n = 60) of responders who took insulin during a GDM pregnancy responding they thought they had a high risk of developing T2DM, compared to 36% (n = 16) of responders who took metformin and 27% (n = 67) who were diet-controlled (p = 0.008).

Eighty-three percent (n = 358) reported that they had thought about or tried losing weight since having GDM. Of the 65 women who had not thought about or tried losing weight since having GDM, 62% (n = 40) were in an underweight or healthy weight range.

Around three-quarters of responders (74%, n = 318) believed that gradual weight loss while breastfeeding was safe, 4% (n = 19) answered that you should not lose weight while breastfeeding, and 12% (n = 50) answered they did not know if it was safe to lose weight while breastfeeding.

3.2. Barriers and Enablers to Weight Loss after GDM

The most common barriers to weight loss were family responsibilities taking priority (63%, n = 240) (TDF domain: Environmental Context and Resources) and finding it hard to deal with hunger (56%, n = 206) (TDF domain: Behavioural Regulation). Most women agreed or strongly agreed that they knew what sorts of foods they should eat to lose weight (86%, n = 335) (TDF domain: Knowledge) and that their family would support them to lose weight (82%, n = 321) (TDF domain: Social Influences). Figure 1 shows the levels of agreement to each statement regarding barriers to weight loss. Responders who were postpartum longer were more likely to strongly disagree with the statement, "It is hard to deal with hunger while losing weight" (p = 0.03, n = 389) (TDF domain: Emotion) and "I don't need to lose weight" (p = 0.02, n = 389). There were no other significant associations with barriers to weight loss and years postpartum.

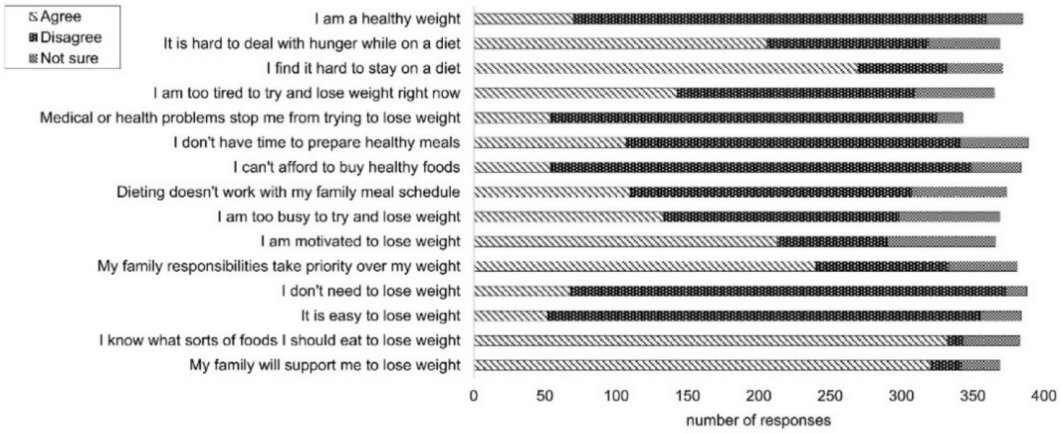


Figure 1. Barriers and enablers to weight loss. Data n = 389 responses for each statement listed. Responses were received as a 5-point Likert scale (strongly agree, agree, not sure, disagree and strongly disagree). Responses for "strongly agree" and "agree" have been grouped together as "agree", and responses for "strongly disagree" and "disagree" have been grouped together as "disagree". Responses for "not applicable" are not shown.

There were 114 comments received in the open-text comment box regarding barriers to weight loss, which resulted in 172 phrases being categorized within the TDF. Environmental Context and Resources, and Beliefs about Capabilities were the most prominent domains within the TDF, with n = 48 and n = 27 comments sitting in the respective domains. Figure 2 shows the frequencies of each domain within the TDF categorized for this question. Supplementary Table S2 highlights some of these comments and the domain they were categorized into.

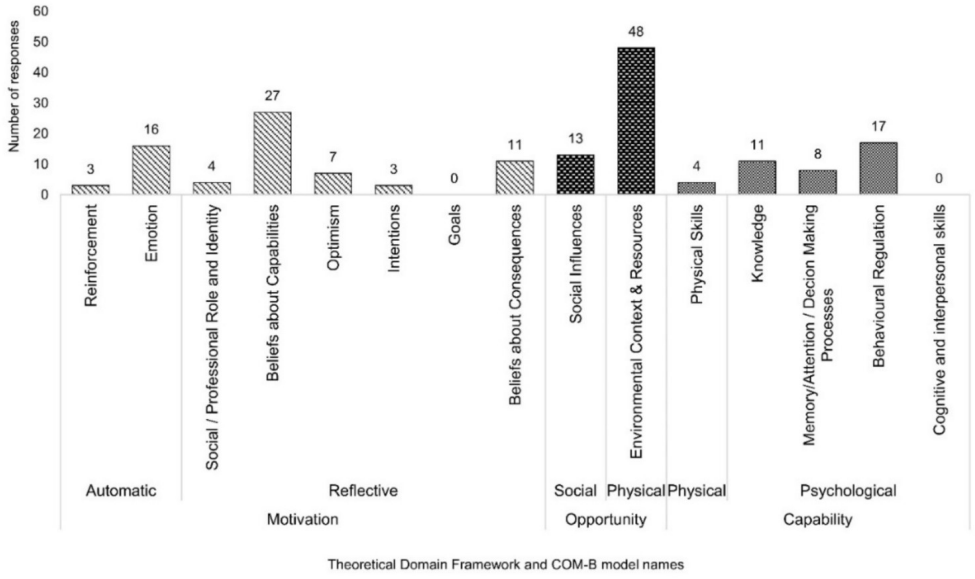


Figure 2. Barriers to weight loss categorized into the Theoretical Domains Framework and the COM-B (Capability, Opportunity, Motivation- Behaviour) model from responders' comments.

3.3. Diet Strategies

Exercising to lose weight was the most tried method of dieting with 71% (n = 234) of women reporting they had tried this method, and only 14% (n = 45) responded that exercising did not work for them. A nonspecific diet (eating less food overall) was the second most tried method of dieting,

with 61% (n = 201) of women reporting they had tried this, and only 20% (n = 67) reporting that this did not work for them. Eighteen percent (n = 60) had used an online program to lose weight and 33% (n = 109) had used a mobile application. Figure 3 shows results for the types of diets and weight loss strategies tried and how well they worked for the responders.

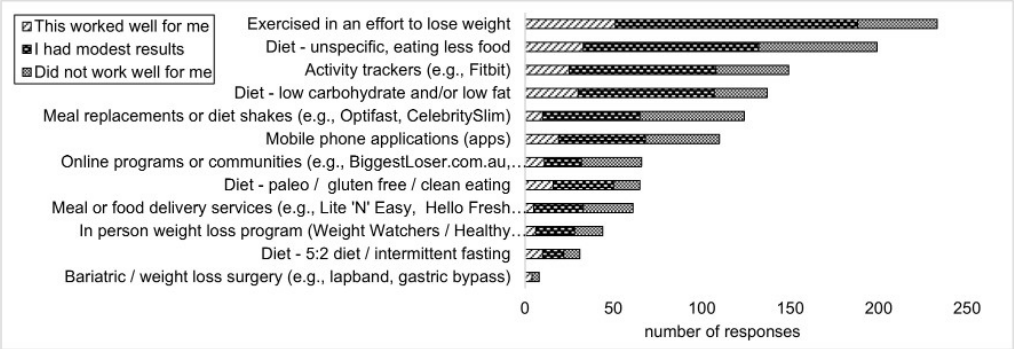


Figure 3. Diet strategies tried and how well they worked.

Age was positively associated with the use of weight loss center programs. There was no significant difference in the age for responders who had or had not tried meal replacements, meal delivery services, online programs, mobile applications, bariatric surgery, low-carbohydrate or low-fat diets, intermittent fasting, paleo or gluten-free diets, eating less food, exercising, or using an activity tracker.

Other approaches that women added in the open-text comments (n = 64) included: the Mediterranean diet, vegan diet, avoiding processed foods, prescription weight-loss medication, "quitting sugar", limiting sweetened beverages such as soda, self-hypnosis, psychological support, listening to podcasts, maintaining dietary changes made in GDM pregnancy, breastfeeding, keeping a food diary, and paid diet programs.

3.4. Weight Loss Services, Programs, and Information

Responders were asked what kind of weight loss program or service they thought would work for them. Services delivered by a nutritionist or dietician were the most popular choices, either as individual appointments (62% (n = 242) agreed or strongly agreed) or within an online program (51%, n = 200 agreed or strongly agreed). Group sessions run by a dietician or nutritionist were less popular (38%, n = 146 agreed or strongly agreed). Mobile applications were also a popular choice, with 50% (n = 194) agreeing this would be a good option for them. There was a statistically significant difference in years postpartum across the levels of agreement for group sessions with a dietician, with responders who were further post-pregnancy more likely to disagree that group sessions would work for them (p = 0.002, n = 389). These responders were also less likely to agree that an online community with other mothers (p = 0.03, n = 389) or using a mobile application (p = 0.001, n = 389) for weight loss would be helpful.

Responders were asked where they have or would go to look for information on how to lose weight. Internet searches were the most popular choice for seeking information to lose weight (n = 308) followed by a doctor, dietician, or nutritionist (n = 234), online forums or online communities (n = 167), family or friends (n = 163), diet books (n = 137), gym instructor/lifestyle coach (n = 129), television shows (n = 45), midwife or nurse (n = 41), and a psychologist or counsellor (n = 24).

3.5. Intermittent Fasting (the 5:2 Diet)

Seventy-three percent of responders (n = 284) had heard of the 5:2 diet, but only n = 34 had tried the diet (n = 27 tried it and lost weight, n = 7 answered that they tried it and it was not right for them) and 26% (n = 73) had thought about the diet but had not yet tried it. Responders who had not heard

of the 5:2 diet were given information explaining the diet. Of the responders who had not heard of the 5:2 diet and thought they needed to lose weight (n = 87), 60% (n = 52) answered that it sounded like it could be a good option for them, 18% (n = 16) answered that the diet would not suit them, and 22% (n = 19) were unsure. Common themes that emerged from comments regarding the 5:2 diet (n = 100) included concerns around how the fasting days would fit in with family routines and the influence or messages this may portray to their children, as well as concerns about feeling too hungry and overeating on non-fasting days. Several women commented that they thought the diet sounded interesting or appealing but would need support and advice on how to do it, as well as meal ideas. Other women commented that they have found the diet easy and/or achievable or have heard positive stories from family and friends about the diet (Supplementary Table S3).

4. Discussion

Enabling lifestyle behaviour changes is a complex process [20]. One of the main findings in this survey was that although responders had good knowledge of their weight status, this did not translate to a high level of perceived T2DM risk. These findings add to the body of evidence that most women with previous GDM lack an understanding of the high risk of T2DM development [21]. Understanding the high risk of T2DM after GDM, particularly for women with overweight or obesity, is important as it offers motivation to lose weight and implement changes in behaviour to reduce the risk of diabetes [22,23]. Under the TDF and COM-B model, the question regarding perception of T2DM risk in this survey is related to an individual's belief or acceptance of the significance of developing T2DM. Motivation to change behaviour depends on the value attached to the consequences of one's behaviour [24], suggesting that responders may not believe that the consequence of developing T2DM is important enough to motivate the individual to change their behaviour. Other studies have also shown that women with previous GDM who held a higher perceived risk of developing T2DM were more likely to change their behaviors [22]. The cumulative incidence of T2DM after GDM is 9% within five years [4], which may not be perceived as very high by the responders. Only six responders in our study reported to have developed T2DM since GDM, and 10% (n = 43) had been diagnosed with prediabetes. Most responders had their GDM managed through lifestyle modification rather than medication, and this was associated with a lower perceived risk of T2DM. The lack of a high perceived risk of developing T2DM could also be in part due to most responders reporting to have received normal results from their most recent diabetes screening test, which could lessen their notion of risk. However, close to one quarter of the responders in this survey had not been tested for diabetes following their GDM pregnancy. Low levels of diabetes screening in this population are well-recognized [25], highlighting a missed opportunity for diagnosis and early intervention.

Understanding the barriers to weight loss that women with previous GDM may experience can help to guide the development of appropriate and effective interventions. Results from this survey suggest that the Environmental Context and Resources, Behavioural Regulation, and Beliefs about Capabilities are key domains of the TDF regarding weight loss barriers that women with previous GDM may experience. Using the COM-B model, this highlights a perceived lack of opportunities and a lack of motivation to make lifestyle changes. Many of the comments categorized to the Environmental Context and Resources domain relate to family responsibilities, with factors such as needing to cook separate meals for children and/or partners, not having time to exercise, and breastfeeding frequently being cited in this domain. Medical issues were also commonly mentioned. The barriers to weight loss identified in this study are not unique to women with previous GDM. Family responsibilities, tiredness, and self-regulation issues are also commonly cited as barriers to weight loss in a general population of postpartum women with overweight or obesity [26]. Responders in this survey who were further postpartum showed better self-regulation in dealing with hunger than responders who had recently had a baby. These findings are consistent with recent evidence which shows that women who are less than two years postpartum benefit from lifestyle modification that includes strategies

such as self-monitoring to improve behavioural regulation, setting and reviewing goals, and problem solving, rather than information provision to increase knowledge [27].

Exercising for weight loss was the most tried approach to lose weight by the responders in this survey. Exercising alone for weight loss requires no change in dietary behaviors. Given the difficulties women mentioned around changing dietary behaviors with a young family at home, this could be one reason why women are choosing exercise for weight loss. While exercise improves body composition and holds an important role in the prevention of T2DM, weight loss from exercise alone is typically small, and energy restriction through dietary changes is also required to achieve clinically significant weight loss [15,28].

In recent years, alternative weight loss strategies, such as intermittent energy restriction (IER) have become popular in general populations. There are many forms of IER, with one of the most common being the "5:2 diet", requiring severe energy restriction for two days per week and habitual eating for five days per week [29]. This is appealing to some, given it only requires a behavioural change for two days each week, therefore creating less disruption to daily life [30]. Given the barriers to weight loss that women in this study have identified, specifically factors relating to lack of time and family responsibilities, as well as a lack of motivation to change, a two-day-a-week diet may be an achievable weight loss strategy for some women with previous GDM. The results from this survey presented equivocal views and opinions of the 5:2 diet, including some women who thought the diet was an excellent approach, and others who strongly felt this would not be a good diet for them, reinforcing that there is no single approach that will work for everyone. A qualitative study of women's experiences following the 5:2 diet for reduced risk of breast cancer reported positive psychological results, with many participants finding the 5:2 diet easier to adhere to and less demanding than a continuous diet, and that it increased their motivation and self-efficacy [31]. However, the women in this study were in a different life stage to the responders in the current study and may not experience the same barriers to weight loss related to caring for a young family. Further research investigating the qualitative aspects of this diet approach in women with previous GDM or postpartum women would be beneficial. Additionally, over 200 participants in the survey reported dealing with hunger as a barrier to weight loss, which needs to be considered for people commencing a 5:2 diet, given the severe energy restriction on fasting days. However, other research has found that hunger is not increased on an intermittent diet, can produce weight loss and metabolic benefits comparable to a continuous diet, and is a suitable alternative weight loss strategy to a continuous diet [32,33].

5. Limitations

There were several limitations in this study. One of the aims of this study was to explore women's perceptions of their risk of developing T2DM after GDM. Participants were offered four levels of risk to choose from (high, moderate, low risk, or not at risk). However, the perception of level of risk is somewhat subjective, and we did not provide an explanation of what high-, medium-, or low-risk meant. However, our results were consistent with other research in the area showing that women with previous GDM do not perceive themselves to be at high risk for developing T2DM. Future research could use focus groups to gather a deeper understanding of perceived level of risk; however, this is a trade-off for achieving the large sample size that we did. The second aim of our survey was to use the TDF to identify barriers to weight loss at any time after GDM. The limitation of this aim was that the TDF question items were not equally spread in number for each TDF domain, and therefore domain ranking could not be performed. However, the barriers to weight loss responses showed Environmental Context and Resources, Beliefs about Capabilities, and Behavioural Regulation as key domains. We did encourage free text comments in this question and linked these to the TDF, which allowed us to see which domains in the TDF participants expressed barriers to weight loss in addition to the provided list. Further research investigating barriers to weight loss after GDM should include an equal number of barriers assigned to each domain to allow for domain ranking. Our sample corresponds to approximately 1% of the 40,000 women who gave birth in Australia in

2016–2017 diagnosed with GDM. We recognize this was a small sample size and may not represent the views of the overall population with GDM in Australia. However, we believe it provides insight into the perception of future diabetes risk in this group of women, and a larger survey would help clarify this. This survey aimed to reach a diverse population of women with previous gestational diabetes by including a letter and email sent out for recruitment by the NDSS to women on the Gestational Diabetes Register. Although we cannot be sure how many participants participated in the survey after receiving the letter or email and how many participated after seeing an advertisement on Facebook or an online parenting website, the SEIFA index, which ranks the level of disadvantage based on postcode data in deciles, showed participants were predominantly living in a middle-of-the-range socio-economic area, with a large IQR and with a good spread of diversity across the SEIFA deciles. Another consideration was the lack of eligibility criteria set for weight or BMI in this study. As weight was self-reported in this study and women who are overweight commonly underestimate their weight [34], it was useful to include women who may not know that they are overweight. Further to this, as this survey investigated opinions of the effectiveness of different diet strategies, it was valuable to include the experiences from women who may have previously been overweight and were now classified into a healthy weight range.

6. Conclusions

This large Australian survey found that, overall, women with previous GDM do not perceive themselves to have a high level of risk for developing T2DM. Diabetes prevention interventions need to consider the restrictions to lifestyle changes imposed on women with a young family and facilitate improving self-regulation and motivation. The 5:2 diet may be an achievable option for some women with previous GDM who are above a healthy weight range; however, further research in this area is needed.

Supplementary Materials: The following are available online at http://www.mdpi.com/1660-4601/17/24/9180/s1, Table S1: The Theoretical Domains Framework integrated into the COM-B model (adapted from Cane et al 2012, pg. 15), Table S2: Responder comments on barriers to weight loss mapped to the Theoretical Domains Framework, Table S3: Responder comments regarding opinions of the '5:2 diet'.

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Conflicts of Interest: The authors declare no conflict of interest.

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5. The Effect of Intermittent Energy Restriction on Weight Loss and Diabetes Risk Markers in Women who have had Gestational Diabetes: A 12 month Randomised Control Trial

5.1. Preface

The literature review in chapter 2 showed that IER is an effective alternative strategy to CER, resulting in comparable weight loss and improvements in disease risk markers. However, evidence regarding the long-term effectiveness of intermittent dieting in women was scarce, and there were no studies investigating IER in a population of women with prior GDM. Chapter 4 demonstrated that although weight loss is an effective treatment to lower the risk of T2DM after GDM, significant barriers adhering to lifestyle programs are present during this life stage, much of which is centered around the family environment and poor behavioural regulation. As IER minimizes disruption to eating patterns over the week as a whole, we were interested in whether an intermittent two-day-a-week diet might address some of the barriers to weight loss expressed by many of the responders in the survey, and thus be a strategy that women with prior GDM are able to integrate into their lives. We therefore conducted a 12 month RCT to study the effects of two day a week IER compared to CER on weight loss and diabetes risk markers in women with previous GDM. We hypothesized that weight loss following a two day a week intermittent diet would not be inferior to an energy matched continuous diet over 12 months in women with overweight or obesity and previous GDM.

5.2. Published Article

Gray KL, Clifton PM & Keogh JB 2021, 'The effect of intermittent energy restriction on weight loss and diabetes risk markers in women with a history of gestational diabetes: a 12-month randomized control trial', *American Journal of Clinical Nutrition*, vol. 114, issue. 2 :794-803 https://doi.org/10.1093/ajcn/nqab058

The effect of intermittent energy restriction on weight loss and diabetes risk markers in women with a history of gestational diabetes: a 12-month randomized control trial

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ABSTRACT

Background: Weight loss after gestational diabetes (GDM) can prevent or delay the onset of type 2 diabetes. Intermittent energy restriction (IER) may offer an alternative to continuous energy restriction (CER) for weight loss.

Objectives: We compared the effects of IER (2 days per week) to daily CER over 12 mo on weight loss and diabetes risk markers in overweight women with previous GDM.

Methods: Overweight females ($n = 121$) ≥18 y were randomized 1:1 to either IER [2-d 500 kcal (2100 kJ); $n = 61$] or CER [1500 kcal (6000 kJ); $n = 60$] in this 12-mo noninferiority trial.

Results: The trial was completed by 62 participants with a median age of 39.6 y [Quartile (Q) 1 to Quartile 3, 34.9 to 43.9 y] with a median BMI of 32.6 kg/m^2 (Q1 to Q3, 28.5 to 37.9 kg/m^2) at a median of 2.9 y after GDM (Q1 to Q3, 2.1 to 6.4 y; 49% attrition; IER $n = 29$; CER $n = 30$; $P = 0.8$). The mean ± SD weight loss was significant over time ($P < 0.001$) but not by diet group (IER −4.8 ± 5.0 kg; CER −3.2 ± 5.0; $P = 0.2$). The mean between-group difference was −1.6 kg (95% CI: −4.2 to 1.0 kg; $P = 0.2$). There were no significant between-group differences in change in HbA1c, fasting plasma glucose, fasting serum insulin, HOMA-IR or 2-h oral glucose tolerance at 12 mo ($p>0.05$). The trial was registered at https://www.anzctr.org.au/ (ACTRN12617001476325).

Conclusions: IER produces comparable weight loss to CER over 12 mo in overweight women with previous GDM. The high dropout rate in this study is a limitation in the interpretation of these results. Larger studies are needed to confirm noninferiority of IER compared to CER. *Am J Clin Nutr* 2021;114:794–803.

Keywords: intermittent energy restriction, intermittent fasting, diabetes prevention, gestational diabetes, weight loss, women, overweight

Introduction

In 2016–17, 15% of pregnancies resulting in a live birth in Australia were affected by gestational diabetes (GDM) (1). A diagnosis of GDM in Australia is based on the Australian Diabetes in Pregnancy Society's criteria of a fasting plasma glucose level 5.1–6.9 mmol/L or a 2-h 75 g oral glucose tolerance of 8.5–11.0 mmol/L during pregnancy (2). Globally, around 1 in 5 pregnancies are affected by GDM (3), with 18.4 million births from GDM pregnancies in 2017 (4). Women with GDM have a nearly 10-fold risk of developing type 2 diabetes mellitus (T2DM) compared to women who do not develop GDM (5), and up to half of these women develop T2DM later in life (6). T2DM has lifelong consequences that can lead to the development of other chronic diseases, including heart disease and cancer early in life (7, 8), making diabetes a major health concern in Australia and globally (4) and raising the importance of diabetes prevention.

GDM is more prominent in women who are overweight or obese, who have double the risk of T2DM compared to those in a healthy weight range (6). Weight loss interventions are effective in reducing the risk of T2DM (9); however, engagement is low in this population (10). Weight loss of 5 kg reduces the risk of developing T2DM by half in women with impaired glucose tolerance and prior GDM (11); however, factors such as fatigue, a lack of family support, diet not fitting into family meals, family responsibilities, and further pregnancies make weight loss difficult for women with children (12–14).

Continuous energy restriction (CER) remains the most common strategy for weight loss and diabetes prevention (15), and requires individuals to restrict their energy intake by 25–30%,

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Abbreviations used: AAS, Active Australia Survey; CER, continuous energy restriction; GDM, gestational diabetes mellitus; HbA1c, glycated hemoglobin; IER, intermittent energy restriction; OGTT, oral-glucose-tolerance test; PSQI, Pittsburgh sleep quality index; Q, quartile; T2DM, type 2 diabetes mellitus.

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or 500–600 kcal (2100–2500 kJ), daily (16, 17). This diet is difficult to adhere to in the long term (18). Alternative weight loss regimes, such as intermittent energy restriction (IER), have gained attention recently. IER involves periods of severe energy restriction followed by periods of habitual eating, and may provide more flexibility with less disruption to daily life than CER. IER has been found to produce weight loss and metabolic benefits comparable to those of CER (15, 19–21); however, to our knowledge an IER diet has not been tested in overweight women with a history of GDM. The purpose of this study was to investigate the effects of a 2-d 500 kcal (2100 kJ) IER regime to CER over 12 mo on weight loss and diabetes risk markers in overweight women with previous GDM. The hypothesis was that weight loss resulting from an IER diet would not be inferior to that from a CER diet at 12 mo.

Methods

Participants

Recruitment occurred between March 2018 and March 2019. Recruitment was achieved through a mail-out by the National Diabetes Services Scheme to women registered on the Australian Gestational Diabetes Register, interviews on television and local radio, advertisements on social media, posts on online parenting websites, and flyers displayed on community and university notice boards. Participants were females aged ≥18 y with a previous diagnosis of GDM during pregnancy and a current BMI ≥ 25 kg/m^2. The following exclusion criteria applied: diagnosis of type 1 or type 2 diabetes; taking any diabetes or other medications that could affect glucose levels; pregnant or less than 12 wk postpartum; previous bariatric surgery; participating in any other clinical study involving medical or lifestyle interventions; had been following an intermittent diet in the last 3 mo; non-English speaking; or diagnosis of an eating disorder or any significant illness or disease. Due to low levels of recruitment, the eligibility criteria were changed from a diagnosis of GDM in the previous 5 y to include women with a diagnosis of GDM at any time. This change occurred after the recruitment of 19 participants. The eligibility criteria were also modified to allow women who reported having a history of an eating disorder to be considered if it was completely treated and a letter was sent to their medical practitioner (n = 1). Participants were randomized 1:1 at their baseline visit to either an intermittent or continuous diet. Randomization was undertaken using an online random number generator (www.randomization.com) and was stratified by the number of years since GDM (≤5 y and >5 y) and BMI (<30 kg/m^2 and ≥30 kg/m^2). Participants received $50 upon completion of the 12-mo trial.

Dietary intervention

Participants in the IER diet were advised to follow a very low–energy diet of 500 kcal (2100 kJ) per day (40% protein, 35% carbohydrates, and 25% fat with 7.5% saturated fat) for 2 nonconsecutive days each week. They were encouraged to follow their habitual eating pattern for the remainder of the week, but no specific guidance on energy restrictions was given. Participants in the CER group were advised to follow a diet of 1500 kcal (6000 kJ) per day (30% protein, 45% carbohydrates, and 25% fat with 7.5% saturated fat) for 7 days a week. Both diets provided approximately 25% energy restriction per week. Participants were seen by a qualified dietitian at each visit (0, 1, 2, 3, 6, 9, and 12 mo). All participants received a detailed diet plan, education on how to adhere to their diet, information on the energy content of foods, and sample meal plans. No food was provided. Participants were encouraged to engage in at least 30 min of physical activity on most days of the week. They were asked to keep diet records for 2 days each week to help with compliance and were asked to return the completed records at each subsequent visit. Diet records for 1 wk prior to visits at 3 and 12 mo were analyzed (IER n = 23; CER n = 20) using an Australian dietary analysis program (FoodWorks Version: 10.0.4266 Xyris Software Brisbane Australia Pty Ltd). Women who were breastfeeding (n = 12) were advised on a modified diet that provided up to an extra 500 kcal (2100 kJ) per day, depending on the age of the infant and whether supplemental formula or solids had been introduced. Breastfeeding mothers were provided with a set of bathroom scales and were required to weigh themselves weekly at home to ensure weight loss did not exceed 0.5 kg per week. These women received fortnightly contact with the study dietitian for the first 3 mo and a minimum of monthly follow-ups after.

Clinical measurements

Participants attended the University of South Australia's Health Research Clinical Trials Facility 7 times over 12 mo; they visited monthly for the first 3 mo and then every 3 mo to the 12-month time point (**Figure 1**). Participants were also offered a noncompulsory visit with the dietitian between the 3 monthly visits. The primary outcome was weight loss and secondary outcomes were BMI, glycated hemoglobin (HbA1c) level, fasting glucose and insulin levels, HOMA-IR score, and 2-h oral-glucose-tolerance test (OGTT) results. Height was measured at the baseline visit without shoes using a wall-mounted stadiometer (SECA) and was recorded to the nearest 0.1 cm. Body weight was measured at each visit in light clothing without shoes using calibrated electronic digital scales (SECA) and was recorded to the nearest 0.1 kg. BMI was calculated as weight(kg)/height(m^2). Participants fasted overnight for their weight measurements at baseline, 3 mo, and 12 mo. HbA1c was measured by finger-prick analysis using disposable lancets and a Diabetes Care Analyzer Vantage Analyser (Siemens Healthcare Diagnostics) at baseline, 3 mo, and 12 mo. The machine was calibrated monthly. A 2-h 300-ml 75-g OGTT (Carbotest, ThermoFisher Scientific Australia) was administered at baseline and 12 mo following an overnight fast. Blood was taken by finger-prick at 0, 60, and 120 min using disposable lancets and a glucometer (Freestyle Optium H, Abbott Australia). The 2-h OGTT was changed from a venous blood draw to the finger-prick method after 8 participants had been recruited to allow volunteers to receive their results immediately (n = 2 of these participants declined the 2-h OGTT). None of the participants who had their 2-h OGTT taken via a venous blood draw completed the study. A venous blood sample to measure fasting glucose and fasting insulin and to calculate HOMA-IR was also taken at 0, 3, and 12 mo. Participants in the IER group were told to consume their usual diet and not to fast on the day before an appointment, to avoid potential acute effects on glucose and insulin levels

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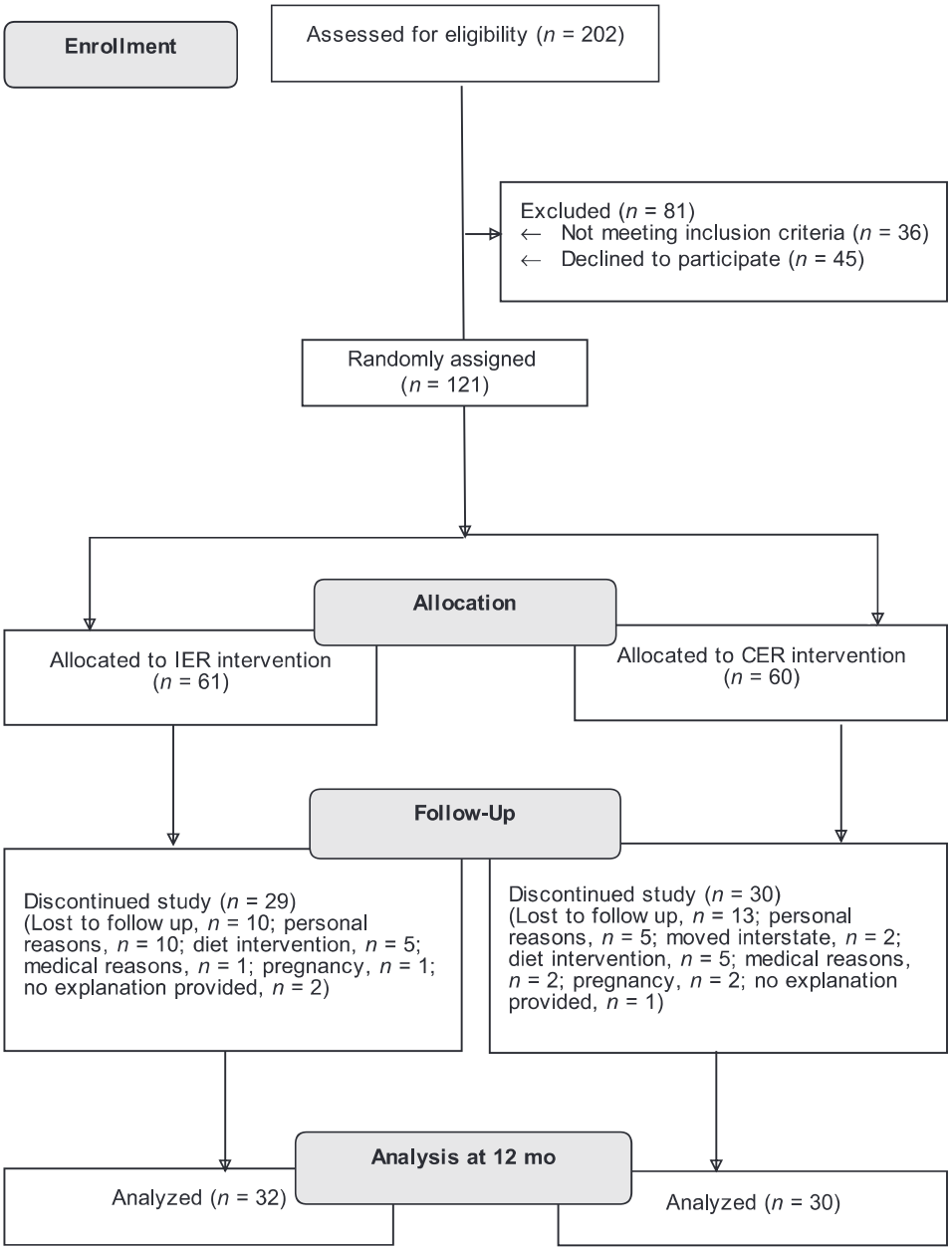


FIGURE 1 Experimental design and measurements at each visit. Abbreviations: CER, continuous energy restriction; IER, intermittent energy restriction.

from fasting. They were also asked to attend the clinic for blood samples in the same condition at each visit, so that individuals had the same number of days after a fasting day for each blood sample. Blood samples for plasma glucose were collected into a tube with sodium fluoride EDTA and were placed on ice immediately until processing. Blood samples for serum insulin were collected into a tube with no additives and remained upright at room temperature for 30 min to clot before being placed on ice until processing. Blood samples were separated via centrifuge (Universal 32R; Hettich Zentrifugen) at 4000 × *g* at 4°C for 10 min and were stored at −80°C until study completion. Plasma glucose was measured using an automated spectrophotometric analyzer (KoneLab 20XTi, ThermoFisher Scientific). Serum insulin was measured using commercial ELISA kits (Mercodia Insulin ELISA, lot# 29,991, Mercodia AB). HOMA-IR was calculated from the plasma glucose and serum insulin analysis using the equation (fasting insulin mU/L × fasting glucose mmol/L)/22.5. Physical activity and sleep quality were assessed at each visit using the Active Australia Survey (AAS) and Pittsburgh Sleep Quality Index (PSQI).

Statistics

This was a randomized noninferiority trial. A completion sample size of 70 participants ($n = 35$ each for IER and CER) was needed to demonstrate noninferiority of IER using 80% power, a P value < 0.05, and a 95% CI noninferiority limit of +3.3 kg with an SD of 6.0 kg, which was based

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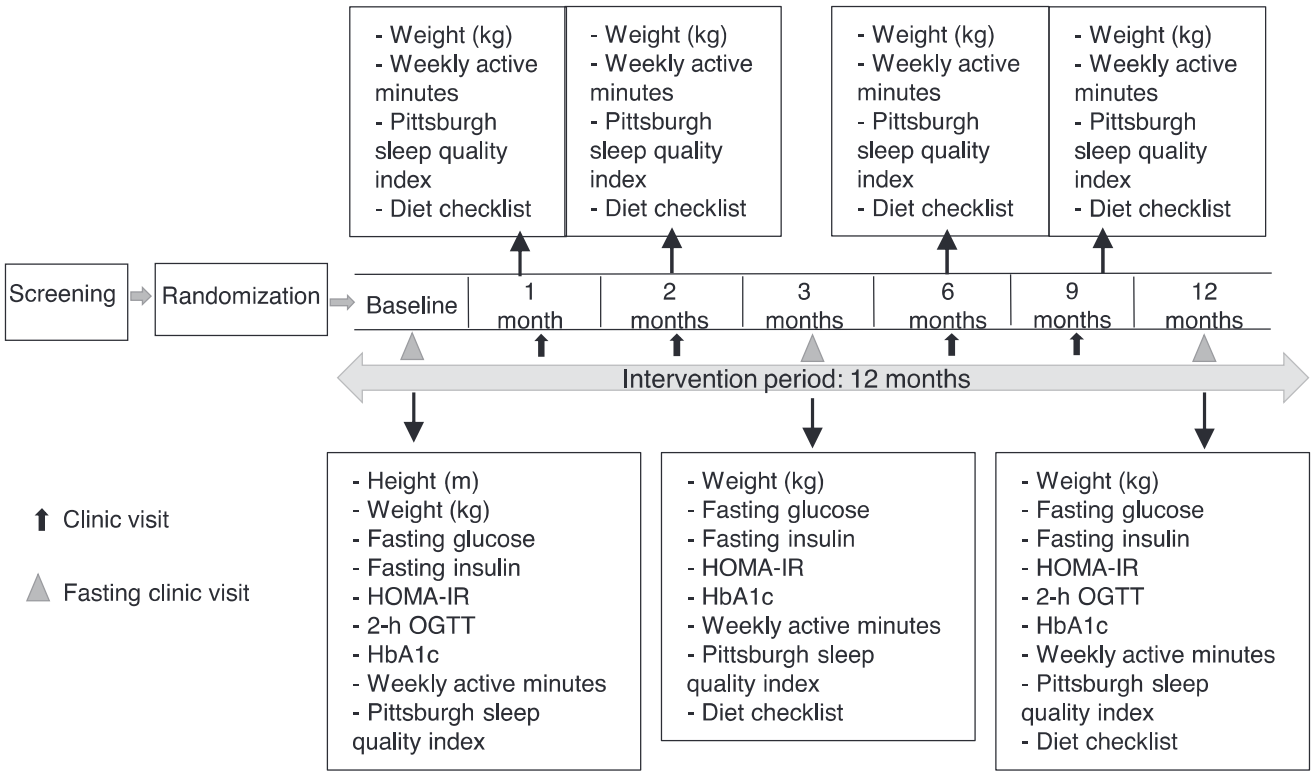


FIGURE 2 Participant flow diagram. Abbreviations: HbA1c, glycated hemoglobin; OGTT, oral-glucose-tolerance test.

on results from a 12-month controlled weight loss study in a comparable population (22). We hypothesized that a 3.3-kg weight difference between diets (66% of a desirable 5-kg weight loss) would be clinically meaningful and have an impact on the future diabetes risk. A noninferiority limit was set for the primary outcome only; superiority tests were performed for all other outcome measures. Data were analyzed using IBM SPSS Statistical Software version 26 for Windows. Significance was set at a P value < 0.05. Data were tested for normality using Q-Q plots, histograms, and Shapiro-Wilk tests. Variables that were not normally distributed were log transformed. Variables that remained skewed after log transformation were analyzed using nonparametric tests. Independent-sample t-tests and Pearson χ^2 tests were used to compare differences at baseline between diet groups and between completers and noncompleters. A general linear model of repeated measures was used to assess change over time and time × treatment interactions. Both completer and intention-to-treat analyses were performed. The intention-to-treat analysis was performed using the last measure carried forward on the primary outcome only. A descriptive analysis of dietary intake, physical activity, and sleep quality was performed, and within-group differences were assessed with a paired-sample t-test for normally distributed variables and a Wilcoxon signed rank test for nonnormally distributed variables. Data for normally distributed variables are presented as means ± SDs and data for nonnormally distributed data are presented as medians (IQRs).

Ethics

The research study was approved by The University of South Australia's Human Research Ethics Committee (protocol number 200,165) and was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12617001476325). All participants gave written informed consent.

Results

Of the 202 women assessed for eligibility, 166 satisfied the inclusion criteria and 121 women were randomly assigned. There were 61 participants randomly assigned to the IER group and 60 participants randomly assigned to the CER group. In total, 62 participants completed the trial to 12 mo (49% attrition). The withdrawal rates were similar between diet groups [IER, 48% (n = 29); CER, 50% (n = 30); P = 0.8]. **Figure 2** shows the recruitment and withdrawal of participants. Baseline characteristics were similar between the IER and CER group and between completers and noncompleters (**Table 1**). There were 6 volunteers whose baseline 2-h OGTT measurements were taken by plasma glucose, and there was no significant difference in glucose levels at fasting (n = 105; P = 1.0) or after 1 h (n = 105; P = 1.0) or 2 h (n = 105; P = 0.7) when these participants were excluded from the analysis. Participants were predominately in the obese weight category, with a median BMI of 32.6 kg/m^2 (IQR, 9.4 kg/m^2), had a median age of 40 y (IQR, 9 y) and were 3 y (IQR, 4 y) postpartum (IQR = Quartile 3 − Quartile 1) at baseline. There were 26 participants (22%) with a baseline HbA1c level of ≥5.7% (IER n = 17; CER n = 9), and 43 (36%) with a fasting plasma glucose level >5.5 mmol/L (IER n = 22; CER n = 21). At commencement of the trial, 12 mothers were breastfeeding (IER n = 8; CER n = 4), and 9 of these participants completed the trial to 12 mo (IER n = 6; CER n = 3).

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TABLE 1 Baseline characteristics of participants

Characteristic	All Participants $n = 121$	IER $n = 61$	CER $n = 60$	P value	Completers $n = 62$	Noncompleters $n = 59$	P value
Age, y	39.6 (9.0)	39.3 (8.9)	40.2 (9.2)	0.75	41.2 (11.2)	38.3 (7.7)	0.21
Years postpartum, y	2.9 (4.2)	2.4 (5.4)	3.1 (4.0)	0.81	3.2 (5.2)	2.3 (3.0)	
Times had GDM, n	1.0 (1)	1.0 (1)	1.0 (0)	0.77	1.0 (1)	1.0 (0)	0.27
GDM managed, *n* (%)				0.96			0.06
Diet	65 (54.2)	33 (53.2)	32 (55.2)		40 (64.5)	25 (43.1)	
Metformin	12 (10)	6 (9.7)	6 (10.3)		4 (6.5)	8 (13.8)	
Insulin	43 (35.8)	23 (37.1)	20 (34.5)		18 (29)	25 (43.1)	
Children, *n*	2.0 (0)	2 (0)	2.0 (1.0)	0.43	2.0 (0)	2.0 (0)	0.98
Weight, kg	89.9 (27.1)	90.3 (26.7)	87.0 (21.9)	0.12	89.3 (20.6)	90.4 (28.8)	0.65
BMI, kg/m^2	32.6 (9.4)	34.8 (9.6)	32.6 (8.4)	0.19	32.4 (9.6)	34.3 (9.5)	0.47
HbA1c, %	5.4 ± 0.6	5.4 ± 0.4	5.3 ± 0.4	0.24	5.3 ± 0.4	5.4 ± 0.4	0.73
Fasting glucose, plasma, mmol/L	5.5 ± 0.5	5.5 ± 0.6	5.5 ± 0.5	0.74	5.4 (0.7)	5.5 (0.8)	0.99
Fasting insulin, mU/L	10.0 (8.1)	10.0 (5.9)	10.2 (9.6)	0.24	9.1 (4.8)	10.3 (10.2)	0.08
HOMA-IR	2.3 (2.2)	2.3 (1.3)	2.4 (2.8)	0.25	2.2 (1.5)	2.5 (2.5)	0.08
Fasting glucose, finger-prick, mmol/L	5.4 ± 0.5	5.4 ± 0.6	5.3 ± 0.5	0.29	5.4 ± 0.7	5.4 ± 0.8	0.48
1-h OGTT, finger-prick, mmol/L	10.4 ± 2.3	10.4 ± 2.5	10.4 ± 2.1	0.98	10.5 ± 2.3	10.4 ± 2.3	0.73
2-h OGTT, finger-prick, mmol/L	8.2 (2.4)	7.9 (2.2)	8.3 (2.0)	0.99	7.9 (2.8)	8.3 (2.2)	0.64
Weekly physical activity, min	180 (315)	240 (430)	170 (290)	0.11	203 (337)	170 (313)	0.21
PSQI	7 (6)	7 (5)	7 (6)	0.42	7 (6)	6.5 (4)	0.42

Data are available for IER ($n = 61$), CER ($n = 60$), completers ($n = 62$), and noncompleters ($n = 59$) for all variables except HbA1c and fasting finger-prick glucose (IER, $n = 61$; CER, $n = 59$; completers, $n = 62$; noncompleters, $n = 58$); 1-h glucose and 2-h glucose (IER, $n = 57$; CER, $n = 53$; completers, $n = 58$; noncompleters, $n = 52$); and fasting plasma glucose, fasting insulin, and fasting HOMA-IR (IER, $n = 51$; CER, $n = 54$; completers, $n = 54$; noncompleters, $n = 50$). Results are displayed as medians [IQRs (IQR = Quartile 3 − Quartile 1)] for variables that were not normally distributed: age, years postpartum, number of times had GDM, number of children, weight, BMI, 2-h glucose, fasting insulin, fasting plasma glucose (completers and noncompleters only), HOMA-IR, weekly physical activity minutes, and PSQI. HbA1c, fasting finger-prick glucose, 1-h finger-prick glucose, and fasting plasma glucose (all participants and IER and CER) were normally distributed and are displayed as means ± SDs. The categorical variable "GDM managed" is displayed as a count (percentage). *P* values were obtained from independent-sample t-tests. Variables that were not normally distributed were log transformed. A Mann-Whitney U test was used for variables that remained skewed after log transformation [number of times had GDM, number of children, BMI, fasting glucose finger-prick (completers and noncompleters only), and PSQI]. The *P* value for "GDM managed" was obtained from Pearson's chi-square test.

Abbreviations: CER, continuous energy restriction; GDM, gestational diabetes; HbA1c, glycated hemoglobin; IER, intermittent energy restriction; OGTT, oral-glucose-tolerance test; PSQI, Pittsburgh sleep quality index.

Weight loss

Weight and BMI data were not normally distributed. Results were obtained from a repeated-measures ANOVA using log transformation for weight. The *P* values for weight loss were obtained from the Kruskal-Wallis test for the between-group delta (diet × time) and the Friedman's test for the change over time, as these variables remained skewed after log transformation. Weight loss between baseline and 3 mo was not normally distributed; however, weight loss between baseline and 12 mo was normally distributed.

Weight loss was statistically significant over time ($P < 0.001$) but not time by diet group at 12 mo (IER, −4.8 ± 5.0 kg; CER, −3.2 ± 5.0 kg; $P = 0.2$; $n = 62$; **Table 2**). Results from an intention-to-treat model did not differ [IER median, −4.2 kg (IQR, 7.4 kg); CER median, −2.9 kg (IQR, 7.6 kg); $P = 0.06$; $n = 121$]. The mean between-group difference for weight loss for the IER compared to CER group at 12 mo was −1.6 kg (95% CI: −4.2 to 1.0 kg; $P = 0.2$; $n = 62$), which fell within the noninferiority margin of +3.3 kg.

At 12 mo, participants had lost an average (mean ± SD) of 4.3 ± 5.5% of their starting weight (IER, 5.0 ± 5.4%; CER, 3.5 ± 5.6%; $P = 0.3$) and 37% ($n = 23$) of participants had lost ≥5 kg (IER $n = 13$; CER $n = 10$; $P = 0.6$). At 3 mo, 29% (IER $n = 7$; CER $n = 11$; $P = 0.3$) had lost ≥5 kg of their starting weight. At 12 mo, 21% (IER $n = 5$; CER $n = 8$; $P = 0.6$) of participants had no overall weight loss and 14.5% (IER $n = 5$; CER $n = 4$; $P = 1.0$) lost >10% of their starting body weight.

In a stepwise linear regression, there were no significant associations between weight loss and age, years postpartum, years past GDM, months breastfeeding, change in sleep quality, or change in the weekly number of active minutes. Results did not differ in an intention-to-treat model.

Dietary compliance

Completion of the food records was variable; 35 participants provided records at 3, 6, and 12 mo and 43 provided records at 3 and 12 mo (IER $n = 23$; CER $n = 20$). Diet recalls were taken when participants failed to return their records ($n = 17$). An analysis of the records at 3 and 12 mo showed no changes in energy intake in the IER group [59 ± 787 kJ (95% CI: −281 to 399; $P = 0.7$) and 14 ± 188 kcal (95% CI: −67 to 95; $P = 0.7$), respectively] on fasting days or in the CER group [−86 ± 1021 kJ (95% CI: −564 to 392; $P = 0.7$) and −21 ± 244 kcal (95% CI: −135 to 94; $P = 0.7$), respectively]. There were no statistically significant between-group differences from 3 to 12 mo between the IER and CER groups in either the changes in energy intakes [145 ± 276 kJ (95% CI: −413 to 702; $P = 0.60$) and 35 ± 66 kcal

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TABLE 2 Changes in primary and secondary outcomes for individuals who completed the study

		Baseline	3 mo	12 mo	*P* value, time	*P* value, diet × time
Primary outcome						
Weight, kg	IER	90.0 (20.5)	85.8 (20.0)	85.3 (17.8)	<0.001	0.22
	CER	87.6 (20.9)	83.8 (22.9)	81.3 (22.7)		
Weight loss, kg	IER	—	−3.5 (2.0)	−4.8 ± 5.0		0.17
	CER	—	−4.3 (4.5)	−3.2 ± 5.0		
Secondary outcomes						
BMI, kg/m^2	IER	32.4 (10.3)	31.6 (9.3)	32.2 (7.6)	<0.001	0.17
	CER	32.4 (8.8)	31.0 (9.1)	31.0 (7.6)		
HbA1c, %	IER	5.3 ± 0.4, [5.2–5.4]	5.2 ± 0.3, [5.1–5.3]	5.2 ± 0.3, [5.1–5.3]	<0.001	0.34
	CER	5.4 ± 0.4, [5.2–5.5]	5.1 ± 0.2, [5.0–5.2]	5.2 ± 0.3, [5.1–5.3]		
Fasting plasma glucose, mmol/L	IER	5.5 ± 0.5, [5.3–5.7]	5.4 ± 0.6, [5.2–5.6]	5.8 ± 0.5, [5.6–6.0]	<0.001	0.17
	CER	5.5 ± 0.4, [5.3–5.6]	5.2 ± 0.5, [5.0–5.4]	5.5 ± 0.5, [5.3–5.7]		
Fasting serum insulin, mU/L	IER	8.8 (4.5)	6.1 (4.9)	6.7 (4.2)	<0.001	0.25
	CER	9.1 (8.7)	7.5 (5.0)	9.3 (6.9)		
Fasting HOMA-IR, index	IER	2.2 (1.2)	1.5 (1.4)	1.7 (1.2)	<0.001	0.68
	CER	2.2 (2.4)	1.8 (1.0)	2.3 (1.9)		
Fasting finger-prick glucose, mmol/L	IER	5.4 (0.7)	5.4 (1.0)	5.7 (1.3)	0.65	0.29
	CER	5.3 (0.7)	5.2 (0.3)	5.3 (0.6)		
1-h OGTT finger-prick, mmol/L	IER	10.0 ± 2.4, [9.2–10.8]	—	10.4 ± 3.1, [9.4–11.3]	0.72	0.29
	CER	11.1 ± 2.0, [10.2–11.9]	—	10.9 ± 1.9, [9.9–11.9]		
2-h OGTT finger-prick, mmol/L	IER	7.5 (2.6)	—	7.8 (1.6)	0.87	0.59
	CER	8.4 (2.8)	—	8.3 (3.8)		

Data are available for IER ($n = 32$) and CER ($n = 30$) for weight, BMI, and HbA1c; fasting finger-prick glucose IER ($n = 31$) and CER ($n = 30$); 1-h and 2-h OGTT finger-prick IER ($n = 31$) and CER ($n = 27$); fasting plasma glucose, fasting serum insulin, and fasting HOMA-IR IER ($n = 24$) and CER ($n = 27$). Results are displayed as medians (IQRs) (IQR = Quartile 3 − Quartile 1) for variables that were not normally distributed (weight, weight loss at 3 mo, BMI, fasting serum insulin, fasting HOMA-IR, fasting finger-prick glucose, and 2-h finger-prick glucose). Weight loss at 12 mo, HbA1c, fasting plasma glucose, and 1-h OGTT finger-prick data were normally distributed and are displayed as means ± SDs [95% CIs]. Results were obtained from a repeated-measures ANOVA using log transformation for weight, fasting finger-prick glucose, fasting serum insulin, fasting HOMA-IR, and 2-h OGTT finger-prick. *P* values for weight loss and BMI were obtained from the Kruskal-Wallis test for the between-group delta (diet × time) and from Friedman's test for the change over time, as these variables remained skewed after log transformation. *P* values for HbA1c, fasting plasma glucose, and 1-h OGTT finger-prick were obtained from a repeated-measures ANOVA using the raw data, as these variables were normally distributed. Abbreviations: CER, continuous energy restriction; HbA1c, glycated hemoglobin; IER, intermittent energy restriction; OGTT, oral glucose tolerance test.

(95% CI: −99 to 168; $P = 0.60$), respectively] or the changes in intakes of fat, saturated fat, mono- or poly-unsaturated fat, cholesterol, carbohydrate, fiber, total sugar, protein, caffeine, or alcohol ($P > 0.05$; **Table 3**). There were no statistically significant within-group differences in the changes in total energy intake or in fat, saturated fat, mono- or poly-unsaturated fat, cholesterol, carbohydrate, fiber, total sugar, protein, caffeine, or alcohol intakes between 3 and 12 mo (Table 3).

Secondary outcomes

Results were obtained from a repeated-measures ANOVA using log transformation for fasting finger-prick glucose, fasting serum insulin, fasting HOMA-IR, and 2-h OGTT finger-prick data, as these variables were not normally distributed. The *P* values for HbA1c, fasting plasma glucose, and 1-h OGTT finger-prick data were obtained from a repeated-measures ANOVA using the raw data, as these variables were normally distributed.

At 12 mo, HbA1c levels ($n = 62$), fasting plasma glucose levels ($n = 51$), fasting serum insulin levels ($n = 51$), and HOMA-IR scores ($n = 51$) showed significant changes over time ($P < 0.001$), with no significant between-group differences (Table 2). There were no significant changes in finger-prick fasting glucose levels ($n = 61$), 1-h OGTT results ($n = 58$), or 2-h OGTT results ($n = 58$) over time, with no time × diet interactions at 12 mo. Changes in fasting plasma glucose levels, serum insulin levels, and HOMA-IR scores followed a similar pattern over time, with reductions seen in the first 3 mo and levels increasing between 3 and 12 mo (Table 2).

In stepwise linear regression, baseline weight was positively correlated with a reduction in HbA1c (adjusted $r^2 = 0.06$; $P = 0.03$). A change in HbA1c levels was correlated with weight loss ($P = 0.03$). Weight loss was positively correlated with a reduction in fasting insulin levels, accounting for 9% of the variance in the change of fasting insulin levels (adjusted $r^2 = 0.07$; $P = 0.03$). Weight loss also accounted for 9% of the variance in the change in HOMA-IR scores (adjusted $r^2 = 0.08$; $P = 0.03$).

Physical activity and sleep quality

Between baseline and 12 mo, the weekly number of active minutes (AAS) decreased by a mean of −11 ± 191 min for the IER group ($n = 31$) and −2 ± 269 min for the CER group ($n = 27$; $P = 0.9$). The weekly number of active minutes

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TABLE 3 Dietary intake and physical activity for IER and CER groups at 3 and 12 mo, assessed by 2-d/wk diet checklists

	IER				CER				
	3 mo $n = 23$	12 mo $n = 23$	Difference $n = 23$	P value	3 mo $n = 20$	12 mo $n = 20$	Difference $n = 20$	P value	Between-group difference P value
Energy, kJ	2594 ± 770	2653 ± 652	59 ± 787 [−281 to 399]	0.72	6407 ± 1152	6321 ± 1454	−86 ± 1021 [−564 to 392]	0.71	0.60
Energy, kcal	620 ± 184	634 ± 156	14 ± 188 [−67 to 95]	0.72	1531 ± 275	1511 ± 348	−21 ± 244 [−135 to 94]	0.71	0.60
Protein, g	50 ± 15	55 ± 13	6 ± 18 [−2 to 13]	0.16	91 ± 19	89 ± 19	−2 ± 22 [−12 to 9]	0.74	0.25
Protein, % of energy	33 ± 4	36 ± 8	3 ± 10 [−2 to 7]	0.21	25 ± 6	25 ± 7	0 ± 6 [−2 to 3]	0.76	0.39
Total fat, g	23 ± 12	19 ± 7	−4 ± 111 [−9 to 1]	0.14	57 ± 18	50 ± 18	−7 ± 20 [−17 to 3]	0.14	0.49
Total fat, % of energy	31 ± 8	26 ± 8	−5 ± 12 [−10 to 1]	0.08	33 ± 6	29 ± 6	−3 ± 8 [−7 to 1]	0.83	0.71
Saturated fat, g	7 ± 4	6 ± 3	−1 ± 4 [−3 to 1]	0.19	21 ± 6	19 ± 8	−3 ± 8 [−7 to 1]	0.18	0.46
Saturated fat, % of energy	10 ± 3	8 ± 4	−2 ± 4 [−4 to 0]	0.11	12 ± 3	11 ± 3	−1 ± 4 [−3 to 1]	0.16	0.92
Cholesterol, mg	260 ± 161	242 ± 161	−18 ± 162 [−88 to 52]	0.61	336 ± 172	296 ± 108	−39 ± 187 [−127 to 48]	0.36	0.69
Polyunsaturated fat, g	3 ± 2	3 ± 2	0 ± 2 [−1 to 1]	0.60	9 ± 5	7 ± 3	−2 ± 4 [1 to −4]	0.05	0.11
Monounsaturated fat, g	10 ± 5	8 ± 3	−2 ± 5 [−4 to 0]	0.09	22 ± 7	20 ± 8	−2 ± 10 [−7 to 3]	0.38	0.99
Carbohydrate, g	47 ± 15	52 ± 25	5 ± 24 [−5 to 15]	0.32	145 ± 32	152 ± 49	6 ± 36 [−10 to 23]	0.43	0.88
Carbohydrate, % of energy	30 ± 7	31 ± 8	2 ± 9 [−2 to 5]	0.36	37 ± 5	39 ± 8	2 ± 10 [−3 to 6]	0.46	0.99
Total sugar, g	37 ± 10	37 ± 9	0 ± 12 [−4 to 6]	0.76	73 ± 17	69 ± 25	−3 ± 21 [−13 to 6]	0.49	0.43
Fiber, g	14 ± 4	15 ± 5	1 ± 5 [−2 to 3]	0.52	23 ± 8	24 ± 6	2 ± 8 [−3 to 6]	0.38	0.69
Fiber, % of energy	5 ± 1	5 ± 2	0 ± 1 [−1 to 1]	0.84	3 ± 1	3 ± 1	0 ± 1 [0–1]	0.15	0.54
Caffeine, mg	0 (112)	4 (71)		0.95	60 (184)	126 (309)		0.06	0.13
Alcohol, g	1 ± 2	0 ± 2	0 ± 2 [−1 to 0]	0.33	4 ± 7	6 ± 11	−2 ± 12 [−8 to 3]	0.39	0.15
Physical activity, mins	337 ± 259	292 ± 228	−46 ± 254 [−139 to 47]	0.32	324 ± 298	264 ± 240	−60 ± 239 [−153 to 33]	0.19	0.79

Data are available for IER ($n = 31$) and CER ($n = 28$) participants for minutes of physical activity. All other variables have data available for IER ($n = 23$) and CER ($n = 20$) participants. Data are presented as means ± SDs [95% CIs] with P values obtained from paired-sample t-tests for the within-group time trend for all variables except caffeine. Caffeine was not normally distributed and data are displayed as medians (IQRs), (IQR = Quartile 3 − Quartile 1) with a P value obtained from a Wilcoxon signed-rank test. P values for differences between groups from the within-group changes in dietary intake between 3 and 12 mo were calculated using independent-sample t-tests for all variables except caffeine, which was obtained from a Mann-Whitney U test. Abbreviations: CER; continuous energy restriction; IER; intermittent energy restriction.

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increased between baseline and 3 mo by a median of 20 min (IQR 275 min) for the IER group ($n = 46$) and 20 min (IQR 158 min) for the CER group ($n = 38$; $P = 0.7$). Between 3 and 12 mo, the weekly number of active minutes decreased by a mean of -46 ± 254 min (95% CI: -139 to 47; $P = 0.3$) in the IER group ($n = 31$) and by -60 ± 239 min (95% CI: -153 to 33; $P = 0.2$) in the CER group ($n = 28$; Table 3).

There was an overall improvement in the sleep quality score (PSQI) in both the IER and CER groups, with a mean difference from baseline to 12 mo of -2 ± 3 index points for the IER group ($n = 31$) and -2 ± 3 index points ($n = 27$) for the CER group ($P = 0.96$). The sleep quality scores improved by medians of -1 index point (IQR, 4 index points) for the IER group and -1 index point (IQR, 4 index points) for the CER group between 0 and 3 mo ($P = 0.2$). Between 3 and 12 mo, sleep quality showed a median change of 0 index points (IQR, 3 index points) in the IER group and an improvement of 0.5 index points (IQR, 4 index points) in the CER group ($P = 0.4$).

Discussion

This randomized controlled trial was designed to determine whether an intermittent 2-d very low–calorie diet was noninferior to moderate daily caloric restriction over 12 mo in overweight women with previous GDM. IER has previously been investigated in overweight women; however, to our best knowledge, this is the first study that investigated the effects of IER compared to CER in women with previous GDM. The results demonstrated that a 2-d 500 kcal (2100 kJ) IER diet can result in comparable weight loss to a daily 1500 kcal (6000 kJ) CER diet in this population. This outcome may be confounded by the high attrition rate, which resulted in fewer completers than planned in the study. Although the analysis indicated that the difference between the groups remained within the predetermined noninferiority margin, we cannot confirm noninferiority with any degree of confidence due to the high number of dropouts.

The present study adds to the growing body of research showing that IER can produce comparable weight loss to CER in overweight or obese men and women. A recent systematic review comparing IER to CER in overweight and obese adults included 12 studies ranging from 8 wk to 1 y in duration, and found that weight loss ranged from 4.6% to 13% of the starting body weight, with no significant between-group differences (19). Weight loss in the present study was slightly lower at 12 mo (4.3 ± 5.5%); however, only 2 studies in the review lasted for 12 mo or longer, and these studies reported weight loss of 5.6% and 6.8% (23, 24). Our study focused on a population of women with previous gestational diabetes, who often achieve lower levels of weight loss (25), which may explain why weight loss was slightly less in our study than in other 12-mo IER studies. In the present study, most of the weight loss was seen in the first 3 mo of the trial, with some weight gain seen in the CER group from 3 to 12 mo and a small amount of weight loss seen from 3 to 12 mo in the IER group; however, there was no significant between-group effect. Other IER studies lasting 12 mo or longer have shown similar weight loss patterns, with weight decreasing for 3 to 6 mo and plateauing or rising thereafter (21, 23), reinforcing the complexities around long-term lifestyle changes and weight management with both IER and CER.

Weight loss of 5 kg resulting from lifestyle changes has been shown to reduce the risk of diabetes by 53% in women with previous GDM (11). In the present study, mean weight loss was less than this at 3 mo (IER -3.5 ± 2.0 kg; CER -4.3 ± 4.5 kg) and 12 mo (IER -4.8 ± 5.0 kg; CER -3.2 ± 5.0 kg); however, improvements in HbA1c levels, fasting plasma glucose levels, fasting serum insulin levels, and fasting HOMA-IR scores were still seen at 3 mo. There were no significant between-group differences in diabetes risk factors at 3 or 12 mo, which is consistent with other recent research comparing IER to CER (26). The improvements in fasting glucose levels, insulin levels, HOMA-IR scores, and glucose tolerance observed at 3 mo were attenuated at 12 mo, suggesting participants were in a hypercaloric state for the final blood draw. An analysis of the dietary checklists suggests that both IER and CER participants were consuming close to their allocated energy allowance; however, to minimize the participant burden, these checklists were only completed for 2 days a week (fasting days for IER and any "usual day" for CER). It is likely that some participants were either overeating on their nonrecording days or underreporting their food intake, which is a common problem in dietary interventions (27). Many participants lost weight throughout the 12 mo, which suggests they were complying with the diet. Despite weight loss maintenance, the 2-h glucose values from the OGTT remained just above the desirable levels at 12 mo, suggesting the group had continuing glucose intolerance. Overall, the participants remained in the obese category. HbA1c levels, which are a measure of longer-term average plasma glucose levels, are less sensitive to sudden dietary changes and remained slightly improved at 12 mo in both the IER and CER groups. The higher weight loss for the IER group, although not statistically superior to that of the CER group, might explain the improvements in insulin levels and HOMA-IR scores observed at 12 mo in the IER group but not in the CER group. It is also possible these results are confounded by the high attrition rate, by wide variation in the ages of the participants, or by starting weights.

There were some limitations to our study. The high withdrawal rate, which resulted in a smaller completion sample than required, is a serious limitation. Low levels of engagement in long-term weight loss interventions in this population are well documented (10), and our study showed that adherence to either an IER or CER regime is challenging for women with previous GDM. In order to minimize the participant burden, we did not measure body composition or satiety, which is another limitation to the study. Furthermore, as we only assessed dietary compliance for 2 days a week, we are unable to compare total weekly energy intakes between the 2 groups. We also altered our method to test 2-h glucose tolerance using a finger-prick test with capillary whole blood instead of venous plasma, to reduce the participant burden. The finger-prick method allowed participants to receive their results immediately. Women who have had GDM are recommended to have a 2-h glucose tolerance test every 1–2 y in Australia; by withholding results until study completion, the women would have been required to have another test with their physician. Capillary blood glucose has previously been shown to be suitable for use in health-care settings for a GDM diagnosis where a laboratory analysis is

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not available (28), and is accepted as a screening tool in large epidemiological studies in developing countries (29). In addition to the smaller-than-planned sample size at the end of the study, other confounders may include previous episodes of weight gain or the number of attempts to lose weight since a diagnosis of GDM.

Our study shows that IER produces comparable weight loss to CER, with similar improvements in diabetes risk markers, suggesting that IER is as effective as CER for weight loss in overweight women with previous GDM. However, the high dropout rate is a limitation in our interpretation of the results, as well as a potential limitation in the sustainability/implementation of both interventions. Larger long-term studies with better adherence investigating the effects of IER on weight loss and diabetes risk markers in women with previous GDM would be beneficial.

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The authors' responsibilities were as follows—JBK: designed the research (project conception, development of overall research plan and study oversight); KLG: contributed to the study design and conducted the research (submitted the ethics application, hands-on conduct of the experiments and data collection), performed the laboratory analysis and initial statistical analysis, and drafted the manuscript; PMC: contributed to the study design, provided medical oversight for the project, and supervised the statistical analyses. JBK, PMC: contributed to the interpretation of the data and critically reviewed the manuscript; and all authors: read and approved the manuscript.

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Data Availability

Deidentified data will be made available upon request pending approval from the University of South Australia's Human Research Ethics Committee.

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6. Weight Loss Barriers and Dietary Quality of Intermittent and Continuous Dieters in Women with a History of Gestational Diabetes

6.1. Preface

Our 12 month clinical trial found that while IER does appear to result in comparable weight loss to CER, attrition was not improved in the IER group, with both diet groups experiencing close to 50% withdrawal. This suggests that while an IER diet can work for some women with prior GDM, barriers to weight loss remain that may not be addressed by a change in diet protocol alone. The aim of this chapter was therefore to gain a better understanding of how barriers to weight loss identified at baseline may have affected actual weight loss of IER and CER participants during the intervention. This chapter presents results from a retrospective investigation using a questionnaire which consisted of several of the items used in the survey in chapter 4. The other aim of this chapter was to investigate how overall dietary quality changed during the intervention for both intermittent and continuous dieters. Dietary quality was assessed at baseline and 12 months using the Commonwealth Scientific and Industrial Research Organisation's (CSIRO's) Healthy Diet Score (HDS). The results from this chapter are a valuable addition for consideration in the development of future IER interventions in this population.

6.2. Published Article

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Weight Loss Barriers and Dietary Quality of Intermittent and Continuous Dieters in Women with a History of Gestational Diabetes

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Abstract: Weight-loss after gestational diabetes (GDM) lowers the risk of type-2 diabetes (T2DM). Intermittent energy restriction (IER) produces comparable weight-loss to continuous energy restriction (CER), but long-term adherence remains difficult in this population. This exploratory secondary analysis of a 12-month trial comparing IER to CER following GDM examined weight-loss and dietary quality associated with barriers to weight-loss or T2DM risk perception as assessed in a Likert scale questionnaire at baseline. The participants had a median (IQR) BMI of 32.6 (9.4) kg/m^2 and 3 (4) years postpartum (n = 121). Forty-five percent (n = 54) of the participants thought they were at a high risk of developing T2DM. Greater affordability of healthy food was related with greater weight-loss at 3 months (p = 0.044, n = 85). At 12 months, there was no significant relationship between weight-loss and the barriers to weight-loss ($p > 0.05$). CER had superior improvement in dietary quality at 12 months (CER 11 ± 10, IER 6 ± 5.6, n = 42, p = 0.05). Under the Theoretical Domains Framework, the barriers were predominantly related to behavioral regulation (n = 83, 69%; n = 76, 63%) and environmental context and resources (n = 67, 56%). Interventions for diabetes prevention in this population should include behavioral regulation strategies, consider the family home environment, and ensure that the risk of T2DM is conveyed. Women choosing IER may benefit from education to improve their dietary quality.

Keywords: diabetes prevention; gestational diabetes; weight loss; women; intermittent energy restriction; intermittent fasting; theoretical domains framework; weight-loss barriers

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1. Introduction

Women with a history of gestational diabetes (GDM) have a nearly 10-fold risk of developing type-2 diabetes (T2DM) compared with women with no GDM in pregnancy, making GDM one of the highest single risk factors for T2DM development [1]. Despite this, research shows that women with previous GDM typically do not perceive themselves to be at a high risk for T2DM development [2–5]. Women with a history of GDM who are overweight can significantly reduce their risk of developing T2DM through lifestyle changes resulting in weight-loss [6,7]. However, they face multifaceted barriers to achieving weight-loss, and family responsibilities interfering with weight-loss attempts and motivation are often at the forefront of this [2,8,9].

Intermittent energy restriction (IER) has become a popular weight-loss strategy in recent years and may offer more flexibility in eating over the week compared with a continuous diet [10,11]. Research to date suggests that IER can achieve comparable but not superior weight loss and metabolic improvements to continuous energy restriction (CER), but long-term adherence does not appear to be improved in intermittent dieters compared with continuous dieters [10,12,13]. The results from our 12-month randomized

control trial (RCT) investigating the effect of IER on weight-loss and diabetes risk markers in women with previous GDM showed that IER can produce comparable weight-loss and metabolic improvements. However, there was close to 50% attrition, which limited the conclusions that could be drawn from the study [14]. Low participation and high dropout in this population have been previously reported, highlighting poor long-term adherence to lifestyle changes in women with previous GDM [15–18].

Understanding the barriers to weight-loss assists with successful intervention development by identifying individual characteristics that may help or hinder weight-loss efforts and adherence to a diabetes prevention program [19]. Interventions aiming to improve health outcomes in women with a history of GDM need to consider these individual characteristics that may predict health-related behaviors and encompass individual needs into such interventions [17,20]. Additionally, the development of interventions that require behavior changes should be underpinned by an appropriate behavior change theory or framework [21]. The Theoretical Domains Framework (TDF) incorporates theories of behavior change into one integrative framework and allows researchers to classify the determinants of a behavior to inform implementation [22,23]. This paper reports the results from an exploratory secondary analysis of our 12-month clinical trial. The results from the primary outcomes of the clinical trial have been published elsewhere [14]. Here, we use the TDF integrated into the Capability, Opportunity, Motivation-Behavior model (COM-B model) [23] to examine whether the weight-loss of the participants in a 12-month clinical trial investigating IER compared to CER in women with previous GDM was associated with barriers to weight-loss and perception of the risk of T2DM at baseline. Furthermore, we present dietary quality data from the clinical trial and investigate how barriers to weight-loss and the perception of diet risk may have influenced the overall diet quality in 12-month IER and CER weight-loss intervention in women with a history of GDM.

2. Materials and Methods

2.1. Participants and Study Design

The participants were enrolled in a 12-month RCT between March 2018 and March 2019 which investigated IER as an alternative diet strategy to CER. The study design and recruitment processes have been previously reported [14]. Briefly, the participants were females aged ≥18 years with previous GDM, no diagnosis of any other type of diabetes and a BMI ≥25 kg/m^2. The participants were randomized 1:1 to either an IER (500 kcal (2092 kJ) per day; 40% protein, 35% carbohydrate and 25% fat with 7.5% saturated fat for 2 non-consecutive days each week) or CER diet (1500 kcal (6276 kJ) per day; 30% protein, 45% carbohydrate and 25% fat with 7.5% saturated fat for 7 days a week). Both diets provided approximately 25% energy restriction per week. The participants were asked to complete diet checklists for 2 days a week in the month leading up to their clinic appointments, and the results of their dietary intake were published [14]. Randomization was achieved using an online random number generator (www.randomization.com, accessed on 1 August 2021) and was stratified by the number of years since GDM (≤5 years and >5 years) and BMI (<30 kg/m^2 and ≥30 kg/m^2).

2.2. Measurements

Height was measured at the baseline visit without shoes on using a wall-mounted stadiometer (SECA, Hamburg, Germany) and recorded to the nearest 0.1 cm. Weight was measured at baseline, 3 and 12 months after an overnight fast and in light clothing without shoes using calibrated electronic digital scales (SECA, Hamburg, Germany) to the nearest 0.1 kg. The BMI was calculated from the height and weight using the equation BMI = [weight(kg)/height(m)^2].

Participants were asked to complete a questionnaire at their baseline visit which included questions about barriers to weight-loss and the perception of risk of developing T2DM. The barriers to weight-loss questionnaire listed 10 items and asked participants to respond on a 5-point Likert scale (“Strongly agree”, “Agree”, “Not sure”, “Disagree”

or "Strongly disagree"). Space for open text comments was provided for participants to list any other barriers to weight-loss. The participants were also asked if they thought they were at risk of developing T2DM and responded on a 4-point scale ("Yes, high risk", "Yes, moderate risk", "Yes, low risk" or "No, I am not at risk"). The questions were linked to the Theoretical Domains Framework (TDF). All the items in the questionnaire underwent expert review for content validation and were used in our previous survey of women in Australia with a history of gestational diabetes [2,24]. The questionnaire items are listed in Table 1. Dietary quality was assessed at baseline and after 12 months using the Commonwealth Scientific and Industrial Research Organisation (CSIRO) Healthy Diet Score (HDS). This is a validated online dietary quality assessment tool that includes questions regarding the quantity, quality and variety of an individual's diet. The scoring algorithm compares the intake across the different food groups as well as discretionary intake against the Australian Dietary Guidelines (ADGs), with each food group being assigned a maximum of 10 points and discretionary intake being assigned a maximum of 20 points [25]. Upon completion, the results are immediately displayed as a score, with a maximum score of 100. A higher score represents greater compliance with the ADGs, and a lower score indicates a lower quality diet. The users do not receive information regarding their score from each of the food groups or discretionary categories, but three personalized suggestions on how they could improve their diet, such as lowering discretionary intake, including more wholegrains or consuming more vegetables, are provided with the score.

Table 1. Barriers to weight-loss and the perception of future diabetes risk at baseline in a randomized control trial investigating IER in women with previous GDM [1].

	All (*n* = 120)	**IER (*n* = 61)**	**CER (*n* = 59)**	***p* Value**
My family will support me to lose weight (*n*) (%)				0.89
- Agree or strongly agree	112 (93)	58 (95)	54 (92)	
- Not sure	7 (6)	3 (5)	4 (7)	
- Disagree or strongly disagree	1 (0)	0 (0)	1 (2)	
It is easy to lose weight * (*n*) (%)				0.81
- Agree or strongly agree	9 (8)	6 (10)	3 (5)	
- Not sure	11 (9)	4 (7)	7 (12)	
- Disagree or strongly disagree	97 (83)	48 (83)	49 (83)	
My family responsibilities take priority over my weight (*n*) (%)				0.84
- Agree or strongly agree	67 (56)	34 (56)	33 (56)	
- Not sure	24 (20)	13 (21)	11 (19)	
- Disagree or strongly disagree	29 (24)	14 (23)	15 (25)	
I am motivated to lose weight (*n*) (%)				0.67
- Agree or strongly agree	112 (93)	58 (95)	54 (92)	
- Not sure	4 (3)	1 (2)	3 (5)	
- Disagree or strongly disagree	4 (3)	2 (3)	2 (3)	

Table 1. *Cont.*

	All (n = 120)	IER (n = 61)	CER (n = 59)	p Value
Dieting doesn't work with my family meal schedule (n) (%)				0.93
- Agree or strongly agree	16 (13)	8 (13)	8 (14)	
- Not sure	29 (24)	15 (25)	14 (24)	
- Disagree or strongly disagree	75 (63)	38 (63)	37 (63)	
I can't afford to buy healthy foods (n) (%)				0.16
- Agree or strongly agree	6 (5)	2 (3)	4 (7)	
- Not sure	9 (8)	3 (5)	6 (10)	
- Disagree or strongly disagree	105 (88)	56 (92)	49 (83)	
I don't have time to prepare healthy meals (n) (%)				0.10
- Agree or strongly agree	18 (15)	8 (13)	10 (17)	
- Not sure	17 (14)	7 (11)	10 (17)	
- Disagree or strongly disagree	85 (71)	46 (75)	39 (66)	
I am too tired to try and lose weight right now (n) (%)				0.17
- Agree or strongly agree	14 (12)	4 (66)	10 (17)	
- Not sure	12 (10)	9 (15)	3 (5)	
- Disagree or strongly disagree	94 (78)	48 (79)	46 (78)	
I find it hard to stay on a diet (n) (%)				0.44
- Agree or strongly agree	83 (69)	43 (70)	40 (68)	
- Not sure	19 (16)	10 (16)	9 (15)	
- Disagree or strongly disagree	18 (15)	8 (13)	10 (17)	
It is hard to deal with hunger while on a diet (n) (%)				0.73
- Agree or strongly agree	76 (63)	41 (67)	35 (59)	
- Not sure	14 (12)	6 (10)	8 (14)	
- Disagree or strongly disagree	30 (25)	14 (23)	16 (27)	
Do you think you are at risk of developing T2DM? (n) (%)				0.96
- Yes, high risk	54 (45)	29 (48)	25 (42)	
- Yes, moderate risk	47 (39)	21 (34)	26 (44)	
- Yes, low risk	17 (14)	10 (16)	7 (12)	
- No, I am not at risk	2 (2)	1 (2)	1 (2)	

* n = 117 for all responders, n = 58 for IER responders (n = 3 did not complete this question). CER: continuous energy restriction; [1] GDM: gestational diabetes; IER: intermittent energy restriction; T2DM: type-2 diabetes mellitus.

2.3. Statistical Analysis

The data were analyzed using IBM SPSS Statistical Software version 26 for Windows (IBM, Chicago IL, USA). Significance was set at $p < 0.05$. The data were tested for normality using Q-Q plots, histograms and Shapiro–Wilk tests. The results for categorical variables were presented as numbers (%). Results for the continuous variables were presented as

the mean ± SD for normally distributed data and the median (IQR) for non-normal data. The results from the 5-point Likert scales were collated to a 3-point scale by grouping "Agree" and "Strongly agree" responses and "Disagree" and "Strongly disagree" responses together for the descriptive analysis. Independent t-tests were used to determine the differences between the groups. For the association analysis, the results from the barriers to weight-loss were collated to a 2-point scale ("Agree" and "Disagree"), omitting the "Not sure" responses. Spearman's correlation was used to determine the associations with the ordinal variables and the dependent variables. Variables found to be correlated to the dependent variable were entered into Kruskal–Wallis non-parametric tests as the data were not normally distributed. Intention-to-treat analyses were run for the weight loss associations that were significant in the completers' analysis using the last weight carried forward.

Each barrier was linked to a previously determined TDF domain. Open text comments (n = 32) for the barriers to weight-loss were categorized into the domains of the TDF (n = 37) by the primary researcher (K.L.G.). Supplement S1 shows the TDF and COM-B model.

This was an exploratory secondary analysis of a 12-month clinical trial; therefore, no power calculation was undertaken to determine a required sample size for the variables reported here, and no correction for multiple testing was performed.

3. Results

One hundred twenty-one participants were randomized to the clinical trial, and 62 participants completed the trial to 12 months (49% attrition). Withdrawal was similar between both diet groups (IER 48% (n = 29), CER 50% (n = 30), p = 0.8). One participant withdrew at the baseline appointment after randomization and did not complete the questionnaire. There were 120 responses for the perception of diabetes risk question and 9 of the 10 barriers to weight-loss items measured at baseline. Three participants did not provide an answer to the barrier "It is easy to lose weight" (n = 117). The demographics, weight loss and diabetes marker outcome results were previously reported [14]. Briefly, the participants were predominantly in the obese weight category with a median (IQR) BMI of 32.6 (9.4) kg/m^2, had a median (IQR) age of 40 (9) years and were 3 (4) years postpartum at baseline (Table 2). Weight-loss was statistically significant over time ($p < 0.001$) but not over time by diet group at 12 months (IER −4.8 ± 5.0 kg, CER −3.2 ± 5.0 kg, p = 0.17, n = 62).

Table 2. Baseline characteristics of participants [1].

Characteristic	All Participants (n = 121)	IER (n = 61)	CER (n = 60)	p Value
Age (y)	39.6 (9.0)	39.3 (8.9)	40.2 (9.2)	0.75
Years postpartum (y)	2.9 (4.2)	2.4 (5.4)	3.1 (4.0)	0.81
Times had GDM (n)	1.0 (1)	1.0 (1)	1.0 (0)	0.77
GDM managed (n) (%)				0.96
- Diet	65 (54.2)	33 (53.2)	32 (55.2)	
- Metformin	12 (10)	6 (9.7)	6 (10.3)	
- Insulin	43 (35.8)	23 (37.1)	20 (34.5)	
Children (n)	2.0 (0)	2 (0)	2.0 (1.0)	0.43
Weight (kg)	89.9 (27.1)	90.3 (26.7)	87.0 (21.9)	0.12
BMI (kg/m^2)	32.6 (9.4)	34.8 (9.6)	32.6 (8.4)	0.19
HbA1c (%)	5.4 (0.6)	5.4 (0.4)	5.3 (0.4)	0.24
Fasting glucose, plasma (mmol/L)	5.5 (0.5)	5.5 (0.6)	5.5 (0.5)	0.74

[1] Data are available for IER n = 61, CER = 60 for all variables except HbA1c (IER n = 61, CER n = 59) and fasting plasma glucose (IER n = 51, CER n = 54). HbA1c and fasting finger-prick glucose were normally distributed and are displayed as means (SD). All other variables were not normally distributed and are shown as medians (IQR). CER: continuous energy restriction; GDM: gestational diabetes; IER: intermittent energy restriction.

3.1. Barriers to Weight-Loss and the Perception of Diabetes Risk

The most common barriers to weight-loss from the list in the questionnaire were "finding it hard to stay on a diet" (n = 83, 69%) (TDF domain: behavioral regulation), "finding it hard to deal with hunger while on a diet" (n = 76, 63%) (TDF domain: behavioral regulation) and "family responsibilities taking priority over weight-loss" (n = 67, 56%) (TDF domain: environmental context and resources). Ninety-three percent (n = 112) of participants agreed that their family would support them to lose weight (TDF domain: social influences) and that they were motivated to lose weight (TDF domain: beliefs about capabilities). There were no significant differences between the diet groups and barriers to weight loss ($p > 0.05$). Table 1 shows the number and percentage of participants who responded with "Agree", "Not sure" or "Disagree" to each item. Close to half of the participants reported that they thought they were at high risk for developing T2DM (TDF domain: beliefs about consequences) (n = 54, 45%), 39% (n = 47) answered moderate risk, 14% (n = 17) answered low risk, and 2% (n = 2) answered that they did not think they were at risk for developing T2DM (Table 1). There were no significant differences between IER and CER and the perceived risk of developing diabetes (p = 0.96). There were no significant correlations with the perception of diabetes risk or barriers to weight-loss between completers and non-completers ($p > 0.05$, n = 120).

Thirty-two comments were received regarding other barriers to weight loss in the baseline questionnaire, which were coded into 37 domains within the TDF. "Environmental context and resources" (n = 11), "beliefs about capabilities" (n = 8) and "social influences" (n = 8) were the most commonly allocated domains. Four comments were allocated into the domain "emotion", while "memory, attention and decision processes" received three comments, "skills" received two comments, and "reinforcement" received one comment. Supplement S2 shows the comments received regarding barriers to weight-loss.

3.2. Barriers to Weight-Loss: Perception of Diabetes Risk and Weight-Loss

In a Spearman's correlation matrix, only 1 of the 10 barriers was correlated with weight loss at 3 months (n = 85) ("I can't afford to buy healthy foods", p = 0.043, TDF domain: environmental context and resources). When entered into a Kruskal–Wallis test, being able to afford to buy healthy foods was related to more weight loss at 3 months in the completers' analysis (p = 0.044, n = 85), and this remained significant in an intention-to-treat model (p = 0.009, n = 111). There were no significant correlations to weight-loss at 12 months with barriers to weight-loss ($p > 0.05$). The perception of diabetes risk was not correlated with weight loss at 3 months (p = 0.835, n = 89) or 12 months (p = 0.369, n = 62).

3.3. CSIRO Healthy Diet Score and Weight-Loss Outcomes

Ninety-eight CSIRO Healthy Diet Scores (HDS) were completed at baseline. The results were missing from n = 23 participants due to difficulties using the website, forgetting to complete it or withdrawing from the study after the first visit and not returning a completed CSIRO HDS. The mean CSIRO HDS at baseline was 56 $\pm$ 10. There was no significant difference in the CSIRO HDS between IER (mean 56 $\pm$ 9, n = 50) and CER (55 $\pm$ 11, n = 48) at baseline (p = 0.47). The baseline CSIRO score was not correlated with weight loss at three (p = 0.18, n = 89) or 12 months (p = 0.24, n = 62).

Forty-four of the 62 completers returned the CSIRO HDS at 12 months. The results were missing from n = 18 participants due to difficulties using the tool, not being able to complete the tool at baseline or forgetting to complete it. The mean CSIRO HDS at 12 months was 64 $\pm$ 10 (IER 62 $\pm$ 9, n = 25; CER 65 $\pm$ 12, n = 19, p = 0.34). The CSIRO scores improved between 0 and 12 months by 8 $\pm$ 6 points. The CER group showed a weak statistically significant improvement compared with the IER group in the CSIRO HDS between 0 and 12 months (CER 11 $\pm$ 10, IER 6 $\pm$ 5.6, n = 42, p = 0.05).

3.4. Barriers to Weight-Loss: Perception of Diabetes Risk and CSIRO Healthy Diet Score

There were no significant correlations between the baseline HDS and barriers to weight-loss ($p > 0.05$). There were no responders who completed the HDS at 12 months who disagreed to the statement "I am motivated to lose weight" ($n = 41$ agreed). The statement "Dieting doesn't work with my family meal schedule" was correlated with change in the HDS between the baseline and 12 months ($p = 0.035$, $n = 31$). When entered into a Kruskal–Wallis test, agreement to this statement was associated with a larger improvement in HDS scores between 0 and 12 months ($p = 0.038$, $n = 31$). No other barriers to weight-loss, perception of T2DM risk or diet group were significantly correlated with the HDS at baseline or at 12 months. There were no correlations between the barriers to weight-loss, perception of diabetes risk, diet group or change in the HDS over 12 months.

4. Discussion

This exploratory secondary analysis of a 12-month RCT investigating IER compared to CER in women with previous GDM found several relationships between the barriers to weight-loss at baseline, weight-loss and changes in dietary quality. We found no differences in the barriers to weight-loss and weight-loss success between the intermittent and continuous dieters. However, we did find that the CER group had better improvement in their dietary quality between the baseline and 12 months than the IER group. The barriers to weight-loss were centered around behavioral regulation and environmental context and resources, which was apparent despite high levels of self-reported motivation and family support.

Not being able to afford to buy healthy foods was associated with weight-loss at 3 months in this study. However, this association was lost at 12 months. Due to the small sample size, we were unable to draw any firm conclusions from this finding. Furthermore, only six completers in the study agreed they could not afford to buy healthy foods. The affordability of food varies greatly in different areas [26], and the population in the current study was largely living in a metropolitan location in Adelaide, South Australia, where food is accessible and more affordable than in rural locations. Other studies have shown that women with previous GDM report affordability of healthy foods as a barrier to weight loss [27]. In our study there were no correlations with the IER and CER diet groups in any of the models with barriers to weight-loss. However, the high attrition rate in our study is a limitation in our results, and given that affordability of healthy food is a well-known social determinant of health [28], further research investigating the affordability of an intermittent diet compared with a continuous diet would be valuable. Our analysis also showed that the participants who reported that dieting did not work with their family mealtimes at baseline had greater improvement in their diet quality scores at 12 months. This question only related to mealtimes and did not assess how participants felt about limiting discretionary snacks or changing meals they ate outside of the family environment. The HDS scoring algorithm has higher weighting for discretionary intake; each food group is assigned a maximum of 10 points, and discretionary intake is assigned a maximum of 20 points, with better adherence to the Australian Dietary Guidelines receiving a higher score in each group [25]. Therefore, removing indulgent foods independent of family meals will result in HDS improvement.

From the participants' comments, the most common barriers to weight-loss at baseline in this cohort were related to behavioral regulation within the TDF. Environmental context and resources were also evident as a weight-loss barrier, with over half of the participants agreeing that their family responsibilities took priority over their weight-loss. Together, these findings outline a perceived lack of opportunity and capability to make the behavioral changes required for weight-loss. These findings are similar to our large observational survey of barriers to weight-loss in women with previous GDM, which found that almost two-thirds of the participants gave priority to their family responsibilities over weight-loss and over half reporting behavioral regulation as a key barrier [2].

The high withdrawal rate in this clinical trial limits the conclusions that can be drawn from our results. However, low levels of engagement and high attrition rates are common in this population [18], and we believe our study provides valuable results in the field which would benefit from further investigation with larger numbers. Additionally, our study design utilized a validated framework (TDF and COM-B model) to classify the barriers to weight-loss into determinants of behavior, which will help to inform the implementation of future interventions.

Another limitation to consider is that the questionnaire only listed 10 statements regarding barriers to weight-loss, and of the 120 women who completed the questionnaire, only 32 added comments regarding their own barriers to weight-loss. There may be other barriers to weight-loss that were not presented in the questionnaire list or comments. A more extensive questionnaire or focus groups could help to identify other weight-loss barriers in future studies. However, our findings suggest that behavioral regulation strategies and working around the limitations of the family environment setting are key to weight-loss success in this population. These findings are consistent with our previous research, which surveyed 429 women with previous GDM using the same questions [2], as well as a recent meta-analysis of strategies to improve healthy eating behaviors after pregnancy, which showed that interventions encompassing strategies to improve behavioral regulation and goal setting are more effective in this population than information provision aimed at increasing nutritional knowledge [17]. Together, these results reinforce evidence highlighting the need for interventions to be structured around the family when implementing health-related behavior change strategies in a family home setting with children [29].

The CER group in this study had a significantly improved CSIRO HDS score at 12 months compared with the IER group. This is consistent with the findings from an earlier study in which the Healthy Eating Index improved in the CER group compared with the IER group [30]. Weight-loss for IER in the primary results of this clinical trial was comparable to CER at 12 months (IER -4.8 ± 5.0 kg, CER -3.2 ± 5.0 kg, $p = 0.2$, $n = 62$) [14]. However, the CSIRO HDS scores suggest that despite comparable weight-loss, CER may result in better dietary improvements in the long term. This may be because dietary changes are required 7 days a week in a CER diet compared with only 2 days in an IER diet and help healthy eating habits to be developed. Our results suggest that for women with previous GDM choosing an IER diet for weight-loss and diabetes prevention in the long term, it may be beneficial to include education on healthy, unrestricted eating for non-fasting days to improve diet quality once a stable IER diet has been established. However, given the high attrition and small numbers in the study, our results do need to be interpreted with caution, and larger long-term studies which include a more comprehensive dietary quality assessment would be beneficial. The CSIRO HDS was chosen as it is a relatively quick and easy form of assessment, creating less burden on the participant than a food frequency questionnaire. However, it does not provide specific information on the intake of food groups or nutrients [25].

5. Conclusions

The findings from this study add insight to the results of our clinical trial, suggesting that despite self-reported high motivation, long-term weight-loss is difficult, and women with previous GDM face multiple barriers to weight-loss which are centered around the family environment and behavioral regulation. Furthermore, in the long term, women choosing an intermittent diet for weight-loss may benefit from an intervention that has a focus on improving dietary quality on non-fasting days. The high dropout rate in this study presents a serious limitation for interpreting the results, and larger studies are needed to confirm our findings. However, our findings are consistent with other research and suggest that interventions for diabetes prevention in women with previous GDM need to ensure that the risk of future T2DM is conveyed, that strategies to improve behavioral regulation are included and that the difficulties encompassing dietary change in the family home

setting are considered. Qualitative research investigating the barriers and motivators for weight-loss in women with previous GDM following an IER or CER diet would provide further insight to assist with behavior change interventions.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/ijerph181910243/s1. Supplement S1: The Theoretical Domains Framework integrated into the COM-B model (adapted from Cane et al. 2012, pg. 15 [22]); Supplement S2: Participant comments on barriers to weight loss at baseline visit commencing 12-month RCT, linked to the TDF and COM-B model.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author, subject to approval from the University of South Australia's Human Research Ethics Committee.

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7. Discussion, Future Directions and Conclusion

7.1. Discussion

Weight loss through diet and lifestyle modification is the primary approach for diabetes prevention in women who have a BMI above a healthy weight classification and have also had GDM. The literature review presented in chapter 1 showed that weight loss of five to seven percent can reduce the risk of T2DM by over half [43, 44]. However, obesity and diabetes levels are continuing to rise in this population in Australia and worldwide [19]. This presents a major public health problem. Daily caloric restriction amounting to a 25 to 30% energy deficit is the most common diet strategy for weight loss, and although effective, adherence typically declines after three to six months [62, 63]. Alternative methods of energy restriction which may improve adherence are therefore of interest to researchers as well as women who are trying to lose weight. The literature review presented in chapter 2 showed that IER produces comparable weight loss and improvements in diabetes risk markers to CER in adults with overweight or obesity, however the majority of published interventions lasted six months or less, therefore the long-term efficacy of intermittent dieting remained unknown. Furthermore, there were limited studies investigating intermittent energy restriction specifically in women. Importantly, prior to this thesis intermittent dieting had not been studied in a population of women with overweight or obesity and have a history of gestational diabetes. Given the low adherence to CER, investigation of IER as an alternative strategy for weight loss and diabetes prevention was warranted. Additionally, diabetes prevention research in this cohort typically includes women in the first year after GDM, and although this is the optimal time to lose weight, women may find a lifestyle program more achievable once they are past this post-partum period. However, research past one year post-partum was scarce. There were also limited large studies investigating barriers to weight loss in this cohort, with much of the work arising from semi-structured interviews, focus groups or other smaller studies.

Therefore, the primary aims of this research were:

1) To investigate women's perception of their risk of T2DM after GDM; to identify barriers to weight loss; and to explore women's opinions of intermittent energy restriction after GDM.

2) To compare the effects of two day a week IER compared to CER on weight loss and diabetes risk markers over 12 months in women with overweight or obesity who have also had GDM.

The work in this thesis involved two overarching projects involving women with a previous diagnosis of GDM:

- An online survey (chapters 3 and 4: aim 1).
- A 12 month randomised clinical trial (chapter 5: aim 2, chapter 6: aims 1 and 2).

The key findings from the survey were:

- Responders did not perceive themselves to be at a high risk for developing T2DM.
- The most common barriers to weight loss were family responsibilities taking priority and finding it hard to deal with hunger, particularly for women who were more recently post-partum.
- Responders expressed mixed opinions of IER.

The key findings from the 12 month clinical trial were:

- A two-day a week IER diet is a suitable alternative to CER for weight loss and improvements in diabetes risk markers in women with overweight or obesity who have had GDM. However, the high withdrawal rate in the study reinforces the difficulties with long term adherence to both diet strategies in this population.
- Despite comparable weight loss between intermittent and continuous dieters, the continuous diet group had a superior improvement in dietary quality at 12 months.

Together, within the Theoretical Domains Framework and COM-B model, the findings from this thesis showed that women in Australia with overweight or obesity who have

also had GDM lack an understanding of the high risk of developing diabetes, and experience barriers adhering to diet programs which often stems from a perceived lack of opportunities centered around their familial responsibilities; a lack of belief about their physical capabilities, and a lack of motivation to make lifestyle changes. IER may provide part of the solution for some women, by presenting less disruption to daily life throughout the week and appears to result in similar levels of weight loss to CER over 12 months. An interesting finding from the secondary analysis of the clinical trial was that despite comparable weight loss between diet groups, the continuous group showed superior improvements in their dietary quality at 12 months as assessed by the CSIRO Healthy Diet Score. Although this finding was not powered to confirm that CER results in superior diet quality improvements, it warrants further investigation as improvements in dietary quality can have beneficial effects on health independent of weight loss [111]. Part of the appeal of intermittent dieting is that there are no restrictions to the diet on non-fasting days, however our finding suggests that it may be beneficial to emphasise the importance of healthy choices despite unrestricted consumption on non-fasting days once stable adherence to an intermittent diet has been established.

7.2. Strengths

The year-long design of our clinical trial is a key strength of this thesis. Our findings added to the currently small body of research about the efficacy of intermittent dieting for weight loss and diabetes prevention over a minimum of 12 months. It was also the first trial to investigate an intermittent style of dieting in women with previous GDM. Furthermore, the trial was designed to be as close to a real-world setting as possible by providing support from a dietitian and not providing food to participants. The only monetary incentive given was a $50 gift card if they attended their final 12 month clinic visit. The inclusion of the secondary analysis from the clinical trial provided greater depth and insight into how barriers to weight loss may affect weight loss success in intermittent and continuous dieters as well as see differences in how dietary quality changed over time. Our Australia-wide online survey underwent thorough review by a panel of experts as well as pilot testing prior to implementation. The advertising methods used for the survey which included social media and a large-scale mail-out and subsequent email-out by Diabetes Australia to participants registered on the

National Gestational Diabetes Register ensured we achieved a high reach to women with diverse backgrounds.

7.3. Limitations

The high withdrawal rate in our clinical trial was the most significant limitation in this thesis as we did not have sufficient statistical power to confirm non-inferiority of intermittent compared to continuous energy restriction. High withdrawal and low success rates in weight loss programs are well documented in women with previous GDM [59, 112, 113], which is the reason this thesis sought to investigate IER as an alternative approach to CER. Other groups of women in their reproductive years such as women who have recently had a baby [62], and women with polycystic ovary syndrome (PCOS) [114, 115] also have low levels of success with weight loss. An intention-to-treat analysis was undertaken in our clinical trial, and weight loss remained comparable between groups when non-completers were included using the last weight carried forward method. Another consideration is that although the study was designed to be similar to a real-world clinical setting, the high level of support from an Accredited Practicing Dietitian at no cost to participants over 12 months is not typical in a community setting. Furthermore, the inclusion requirements for participants limits the cohort recruited and therefore generalizability of our findings for women who did not enrol in the trial due to being unable to commute to appointments, work or family responsibilities, or being unable or unwilling to provide blood samples or complete diet checklists.

7.4. Future Directions

The research presented in this thesis highlights areas for further research. Future research of IER in both a general population of adults with a body weight above a healthy weight classification, as well as women with previous GDM should focus on the long-term effectiveness of this diet approach. The majority of IER research conducted to date has intervention periods of six months or less, particularly in studies using the 5:2 diet approach. However, several 12 month RCTs which used similar IER diet protocols to our clinical trial are worth noting. Carter et al. (2018) speculated that weight loss may be superior in IER compared to CER after 12 months in adults with pre-existing T2DM

(CER – 5.0 [0.8] kg; IER –6.8 [0.8] kg; p = 0.25) although the between group difference was not significant and the study was not powered to detect superiority of the diet. They calculated a sample size of more than 300 participants would be needed to confirm superiority of IER over CER for weight loss after 12 months with 80% power [116]. Headland et al. (2018) reported no between group differences in weight loss after 12 months of intervention in a population of adults with a BMI ≥ 25 kg/m^2 without diabetes (CER -6.6 kg; WOWO – 5.1 kg; 5:2 -5.0 kg, p=0.2 time by diet), or at a 24-month follow up appointment (CER -4.5 ± 4.9 kg; WOWO -2.8 ± 6.5 kg; 5:2 -3.5 ± 5.1 kg (p>0.5 time by diet) [117, 118]. Although Headland et al. (2018) did not specifically recruit women, the majority of participants were female (male n= 22, female n=124), therefore the results are of particular interest to the population studied in this thesis. However, the participants in both studies were older than the participants in our clinical trial (Headland et al. (2018) mean age 49 ± 14 years; Carter et al. (2018) mean age 61.0 ± 9.1 years) and likely did not experience the same set of barriers to weight loss that is connected to younger women who have recently been pregnant and are raising infants or young children. Further 12 month intervention studies of women with previous GDM will require a larger sample size to confirm non-inferiority of IER to CER in this population.

In particular, adherence and dietary quality should be measured in future IER interventions. Although food checklists and diet histories can increase participant burden, increasing the checklist requirements from two to three days to include one non-fasting day a week for the intermittent group would provide greater insight into energy consumption and dietary quality over each week. A more comprehensive validated dietary quality assessment tool at baseline and 12 months such as the National Cancer Institute's Diet History Questionnaire III (DHQIII) would also give a more thorough picture of changes in dietary quality over a year. This is worth investigating as our clinical trial suggested that CER could result in greater improvements in dietary quality than IER. Additionally, asking participants to complete exit surveys would allow us to better understand factors that cause an individual to withdraw from the study which may be useful when designing future interventions.

With regard to the high withdrawal observed in our 12 month clinical trial as well as many other weight loss interventions in women of childbearing age [62, 112, 114], future interventions should consider strategies known to improve retention rates, including providing monetary incentives or gift cards at each visit attended; providing food; and offering free child-minding services during appointments. Offering virtual appointments when blood work is not required, as well as extended hours may also make appointments more accessible to women with young children at home. Furthermore, it is important that future weight loss interventions in this population address the myriad of barriers to weight loss discussed in this thesis, regardless of whether an IER or CER diet is prescribed. Weight loss and diabetes prevention interventions in this population need to incorporate diabetes risk education and provide structured behavioural support which includes strategies to improve behavioural regulation that can be integrated within the family. Our findings regarding barriers to weight loss are supported by more recent work undertaken by Lim et al. (2020a) and Lim et al. (2020b) [119, 120]. Lim et al. (2020a) identified effects of various behavioural strategies on energy intake in a general population of post partum women [119], while Lim et al. (2020b) reviewed implementation challenges of DPPs after GDM and provided direction for future implementation of such programs in context of the COM-B model [120]. Their findings follow on from the work undertaken in this thesis, and future weight loss programs in a population of women with prior GDM should consider the recommendations in these papers; specifically, that future DPPs need to address the unique challenges to weight loss experienced by women with prior GDM to optimize penetration, implementation, and participation in programs. Long term evaluation is also recommended so that incidence of T2DM after GDM following participation in a DPP can be measured directly [121].

Time restricted feeding (TRF) is a form of IER that involves restricting energy intake to a number of hours each day rather than several days per week. Protocols vary, however a typical feeding pattern limits consumption of energy intake to an eight hour window each day followed by 16 hours of fasting. The TRF cycle is designed to optimize alignment with the body's daily circadian rhythm and has been shown to promote weight loss in the short term compared to control (WMD: −1.07 kg [95%CI −1.74 to −0.40];

$p = 0.002$; $I^2 = 56.2\%$) [122]. Weight loss is likely due to an overall energy deficit which occurs as a natural result of limiting the number of hours that food can be consumed [122]. Improvements in diabetes risk markers including insulin sensitivity and glucose have been observed in both animal and human TRF studies independent of weight loss, although the evidence from human studies generally comes from small studies with short intervention lengths [70, 122]. Clinical trials investigating TRF suggest high adherence and retention in adults with overweight or obesity in the short term [123, 124], however to date there have not been any trials investigating this form of dieting specifically in mothers. While the simplicity of TRF may appeal to some women with young children at home, timing of the allowed eating window would likely affect adherence. Regularly skipping the evening meal may not be practical for women with children at home, and the importance of family mealtime needs to be considered before recommending such a regime to mothers. From a practical standpoint, extending the morning fast and having an early dinner with no further consumption in the evening may be an achievable strategy for women who have had GDM to adopt, and has the potential to improve glucoregulatory levels and promote behavioural regulation by limiting snacking to only a number of hours each day. Further research of TRF in a population of women with previous GDM is needed.

More thorough studies investigating the effects of IER in breastfeeding women and their infants would also be valuable. Observational studies of Muslim women fasting during Ramadan demonstrate that thousands of lactating Muslim women fast during Ramadan with no reported adverse effects on themselves or their infants [125], and RCTs suggest that short term fasting (<24 hours) does not affect milk supply [126, 127]. Weight loss of 0.5 kg per week while breastfeeding is safe and recommended in well-nourished women with overweight or obesity, and the macronutrient composition and concentrations of major minerals in human milk are not affected under these conditions [128, 129]. However, most clinical trials investigating intermittent energy restriction for weight loss exclude breastfeeding mothers. In our clinical trial, breastfeeding women were included (n=12) and were provided with a modified diet plan which allowed up to an extra 2100 kJ per day depending on the age of the infant, how often the infant was breastfed and whether supplemental formula or solids had been introduced [130].

Adequate protein intake of 1.1 g/kg per day was also ensured and participants were advised to take a pre-natal vitamin daily [131]. Nevertheless, it is possible that women who were eligible did not enrol in the clinical trial as they did not want to undertake either intermittent or continuous energy restriction while breastfeeding. In our survey, breastfeeding was commonly cited as a barrier to weight loss, with women commenting that it was either not safe to restrict energy intake while breastfeeding; that it would affect their milk supply; or that breastfeeding made them too hungry to attempt energy restriction. These barriers have the potential to result in women either ceasing breastfeeding to attempt weight loss or delaying weight loss attempts until the infant has been weaned. Breastfeeding is associated with improved postpartum glucose tolerance and reduced risk of developing T2DM [132]. In a population of women with previous GDM, breastfeeding for six to 12 months was shown to reduce the incidence of T2DM by 61% compared to not breastfeeding at all; and breastfeeding for up to six months reduced the incidence by 47% over 30 years [133]. However, women who have had GDM are less likely to initiate breastfeeding than women who do not have GDM [120]. Gradual weight loss while breastfeeding should be encouraged in these high-risk women, and such support needs to address the barriers and beliefs about the safety of energy restriction in nursing mothers. Furthermore, the effectiveness of different forms of IER in breastfeeding mothers has not been studied. While a 5:2 style of dieting may appeal to some breastfeeding mothers who do not want to focus on daily energy restriction, others may have safety concerns about the impact that severe energy restriction several days of the week could have on milk supply or find themselves too hungry to adhere to fasting days. A daily TRF regime may be an appealing option for some women as it does not require formal energy restriction during the allowed eating window, however consideration needs to be taken as to how such a regime would fit into family meal routines. Therefore, it would be beneficial to conduct an intervention which investigates the effects of and adherence to both a 5:2 and a TRF regime in breastfeeding mothers and their infants. Future diabetes prevention interventions should also include strategies aimed at improving breastfeeding rates.

Finally, further qualitative research investigating the experiences and opinions of intermittent and continuous dieting in women with previous GDM will provide greater

insight and inform future program development. Semi-structured interviews were conducted in a sub-sample of completers in our clinical trial during their final 12 month visit (n=12) for thematic analysis. However, as recruitment for the clinical trial took longer than projected, the interviews were conducted at a later time frame that did not allow for the analysis to be included within this thesis. Analysis and publication of this data is expected in 2022.

7.5. Conclusion

The findings from this thesis show that women with overweight or obesity who have previously had GDM experience significant barriers to weight loss that are frequently centered around the family environment. Behavioural regulation is often difficult, particularly for women who are more recently post-partum, and there is a low level of understanding of the high risk associated with the progression to T2DM following GDM. IER was shown to achieve similar levels of weight loss and similar improvements in diabetes risk markers to CER in this population, and therefore offers an alternative for women who have not had success with daily energy restriction. However, the need for these women to have access to professional dietetic support that offers an individualized plan, considers the whole family, assists with goal setting and improving self regulation, and includes diabetes risk education is emphasized.

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Appendices

Appendix 1: Copy of Online Survey

University of South Australia Health Research: Life After Gestational Diabetes







Researchers at The University of South Australia are looking for women who have had diabetes during pregnancy (gestational diabetes) and would like to take part in research that will help women lose weight and may reduce their risk of Type 2 Diabetes (the most common type of diabetes).

Gestational Diabetes is a type of diabetes that first develops during pregnancy and usually goes away once the baby is born. This is different to having pre-existing diabetes – (either type 1 or type 2) which are lifelong conditions and don't go away after you have your baby.

We are currently running two research projects you may be eligible to participate in:

- a 12 month weight loss study

and

- an online survey

Participation is voluntary. If you would like more information please contact Ph: 8302 1365 or Email: sansom.researchvolunteers@unisa.edu.au. The projects have been approved by The University's Human Research Ethics Committee.

Before you decide whether to take part in this research it is important that you understand what the research is for and what you will be asked to do. Please take time to read the following information and discuss it with your family, friends and health professional if you wish.

* 1. **Are you interested in participating in a 12 month weight loss study with a qualified Dietitian at The University of South**

Australia in Adelaide?

The weight loss study will investigate a diet method called intermittent energy restriction, commonly known as the "5:2 diet" on weight loss and blood sugar levels over 12 months.
Volunteers will be asked to follow a set diet plan (either the 5:2 diet or a conventional daily diet) and will have regular contact with a qualified dietitian throughout the 12 month study who will provide you with information and support. Participants who complete the 12 month trial will receive a $50 honorarium.

To be eligible to participate you need to meet the following criteria:

- Have been diagnosed with Gestational Diabetes (pregnancy-induced diabetes) in a pregnancy at any time.
- Do not have Type 1 or Type 2 Diabetes.
- Overweight or obese with a Body Mass Index (BMI) of 25kg/m2 or higher (we can help you work this out if you're not sure).
- Able to come in to the University of South Australia Sansom Institute Clinical Trials Facility on Frome Road in Adelaide for seven appointments with the Dietitian over the 12 month study.
- Aged 18 years or older.

You will not be eligible to participate in this weight loss study if you:

- Have had surgery for weight loss in the past (e.g. lap-band or gastric bypass).
- Have ever been diagnosed with an eating disorder or if you think you might have an eating disorder
- Have a serious illness e.g. cancer being actively treated, liver or kidney disease.
- Have been following the 5:2 diet in the last 3 months.
- Are pregnant or less than 12 weeks post-partum.
- Are currently involved in any other ongoing dietary study.

Breastfeeding Mothers

If you are breastfeeding you may still be able to participate in the trial. You will be given a modified version of the diet , requiring extra calories to cover the energy and

nutrition your baby takes from your breastmilk. The study Dietitian will contact you to discuss this and work out your individual nutritional requirements.

Participation is voluntary. If you would like more information please contact Ph: 8302 1365 or Email: sansom.researchvolunteers@unisa.edu.au. The projects have been approved by The University's Human Research Ethics Committee.

- ◯ Yes
- ◯ No



2. Please provide your contact details so we can get in touch with you about the weight loss study.

Your details will be stored securely and will not be used for any other reason than to contact you about the study. We will contact you with more information shortly and to check if you are eligible to participate.

Note*

If you would prefer not to provide your contact details here but are interested in participating in the study, please contact The University of South Australia's Sansom Institute for Health Research directly for more information.

phone:08 8302 1365

email: sansom.researchvolunteers@unisa.edu.au

Name	
Email Address	
Phone Number	

* 3. **Would you like to complete the short online survey about lifestyle and weight after having gestational diabetes?**

The survey is a one-off online questionnaire you can complete now. It will take approximately 15 minutes. The responses we get will help us to find out what sorts of things can make losing weight difficult after having a baby and what type of program or service could help, plus you can go into a draw to win $50!

If you select Yes here you will be taken to the survey now. The next page will give you more information about the survey before you start. You can exit the survey at any time if you change your mind by closing your web browser.

If you have any questions please read through the information on the next page or contact The University of South Australia's Sansom Institute for Health Research.
phone: 08 8302 1365
email: sansom.researchvolunteers@unisa.edu.au

- ◯ Yes
- ◯ No



INFORMATION SHEET

PLEASE TAKE THE TIME TO READ THROUGH THE FOLLOWING INFORMATION BEFORE YOU START THE SURVEY.

Project Description

The purpose of the survey is to gather information from women who have had gestational diabetes (pregnancy-induced diabetes) about their knowledge, awareness and attitudes about maintaining a healthy weight and to find out what things what sorts of things might influence a woman's ability or decision to lose weight after having their child. We want to gather information to find out what might make weight loss hard for women who have had gestational diabetes and what sorts of diet or programs could help. The results from this survey will help us to design and develop programs for these women that are accessible and can fit into their lives.

What does this survey involve?

This is an online survey that will take approximately 15 minutes to complete. There is no further participation or follow up required. You can participate now once you have read all the information. There are no right or wrong answers, we are asking about your experiences and situations. Most of the questions are multiple choice. There are a few questions where we will ask you to tell us how much you agree or disagree with some particular statements, and a few places where you will be able to type some more information if you would like to. We would also like to know your height and your current weight. If you have a set of scales at home, we would appreciate if you could weigh yourself for this question (take your shoes and any other heavy clothing off). If you aren't able to weigh yourself now but have had your weight taken recently or know how much you weigh you can use that. If you don't know how much you weigh you can leave the question blank.

What are the benefits of participating in the study?

This is an observational survey - this means that you will not receive any dietary advice or assessments from us. While you will not benefit directly from this study, you will be providing a valuable contribution to the knowledge in this field of study and helping the researchers to design and develop suitable programs and diets for women like yourself. As a thank you for participating in our study you can also go into a draw to win a $50 voucher (you will need to provide your name and phone number for this so we can contact you if you win). If you would like to receive a summary of the research findings please enter your contact details at the end of this survey or contact the research team at sansom.researchvolunteers@unisa.edu.au or ph 8302 1365.

Are there any risks involved?

We foresee no risks involved in this survey, however some questions may be of a personal nature, such as questions about your weight, pregnancies and family history of diabetes. All of your answers are confidential and de-identified. This means that we do not store your contact details (if you provide them) with your survey answers. All of the survey answers will be analysed together will all the other responders' answers, your answers will not be singled out. Participation is voluntary; you are free to withdraw from the survey at any time by closing your web browser. However once you submit your survey, if you have not included your name or contact details we would be unable to remove your response as it would be impossible to identify your individual data.

Eligibility

To be eligible to participate in the study you need to meet the following criteria:

- Aged 18 years or older
- Have been diagnosed with gestational diabetes during a pregnancy
- Living or residing in Australia
- Have access to a computer with the internet

You will not be eligible to participate in this study if:

- You were diagnosed with type 1 or type 2 diabetes before your gestational diabetes pregnancy

Is my privacy protected?

All information collected as part of the study will be retained for a period of five years in electronic copy at the University of South Australia, City East Campus, in the School of Pharmacy and Medical Sciences. Data is stored in on password protected files on a computer on the university's server in a locked office. Only the researchers listed below will have access to these files. Your responses will be de-identified by the researcher and stored anonymously. You will not be identified in the reporting of the research. All records containing personal information will remain confidential and no information which could lead to identification of any individual will be released unless required by law. Our results will show summary data only. We will not collect or store your IP address. However the researcher cannot guarantee the confidentiality or anonymity of material transferred by email or the internet.

Questions?

Please feel free to email or call us if you have any questions about the information in this document or the survey. Please contacthe Sansom Institute for Health Research **ph: 8302 1365**, **email: sansom.researchvolunteers@unisa.edu.au**.

Contact details for the research team are listed below.

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This research will be conducted according to the NHMRC National Statement on Ethical Conduct in Human Research. This project has been approved by the University of South Australia's Human Research Ethics Committee. If you have any ethical concerns about the study please feel free to contact the Ethics Officer: P:8302 3118; E: vicki.allen@unisa.edu.au. Participants or third parties who wish to lodge a complaint about either the study or the way it is being conducted should contact the Executive Officer of UniSA HREC in the first instance, email: humanethics@unisa.edu.au or Ph: 8302 3118.

* 4. **CONSENT FORM**

Please read the information below. If you agree to take part in the survey please provide your consent by clicking the 'I agree' button below. You will then be taken to the first survey question. If you do not wish to take part in the survey you may close your web browser or click on the 'I do not agree' option.

STUDY NAME: Why Weight? Life after Gestational Diabetes

INVESTIGATORS:

Mrs Kristy Gray, BND, APD E: kristy.gray@mymail.unisa.edu.au

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Dr. Peter Clifton, FRACP, PhD, MRCP, MBBS E: peter.clifton@unisa.edu.au

- I have read the Participant Information above. I understand and agree to take part in this survey.
- I understand that I may not benefit from taking part in this survey.
- I understand that, while information gained during the study may be published, I will not be identified and my personal results will remain confidential subject to The Privacy Act.
- All information collected as part of the study will be retained for a period of five years in both hard copy and electronic at the researcher's office at the University of South Australia, City East Campus, in the School of Pharmacy and Medical Sciences. Information is stored in a locked office and on password protected files. Only the researchers listed above will have access to these files. Personal Identification will be removed at the end of data collection, so no information will be individually identifiable.
- I understand that my participation is voluntary and I can withdraw from the study at any stage by closing my web browser.

◯ I agree

◯ I do not agree



* 5. **To be eligible to participate in the study you need to meet the following criteria:**

- Aged 18 years or older

- Have been diagnosed with gestational diabetes during a pregnancy*

- Living or residing in Australia

*Gestational Diabetes is a type of diabetes that develops during pregnancy and usually goes away once the baby is born. This is different to having pre-existing diabetes – (either type 1 or type 2) which are lifelong conditions and occur independently of pregnancy status.

Please only chose "Yes" option if you satisfy **all** of the following:

- I have been **diagnosed with gestational diabetes** in one or more of my pregnancies
- **Before** my diabetic pregnancy I had **not** been diagnosed with type 1 or type 2 diabetes
- I am aged **18 years or older**
- **I live** or reside **in Australia**

◯ Yes

◯ No

* 6. What is your postcode?

This information will not be used to identify you in any way. Postcode data helps us to gather anonymous statistical information.

* 7. What is your employment status?

- [ ] Full time employment
- [ ] Part time employment
- [ ] Full time study
- [ ] Part time study
- [ ] Other (please specify)
- [ ] Stay at home mum
- [ ] Maternity leave
- [ ] Retired
- [ ] Unemployed

* 8. What is your age in years?

* 9. Are you currently pregnant?

- ◯ Yes
- ◯ No

* 10. How many children do you have living at home with you?

Please include your own children as well as any other children living with you that you are responsible for.

* 11. When was your youngest child born? (month and year e.g. 10/2010 or October 2010)

This question will help us with some of your responses about losing weight after a pregnancy.

12. What is your height in centimetres (cm) without shoes on?

If you do not know your height in centimetres (cm) you can use the following link to convert your height from feet and inches into cm.

http://www.height-converter.com/

13. What is your current weight in kilograms (kg) without shoes and in light or no clothing?

If you have a set of bathroom scales please weigh yourself and enter your weight in here. If you are unable to weigh yourself but you know how much you weigh at the moment please use that weight.

If you don't know what your weight is approximately, you can leave this answer blank.

If you do not know your weight in kg you can use the following link to convert your weight from pounds (lb)to kilograms (kg).

http://www.metric-conversions.org

* 14. For the previous question about your weight, did you weigh yourself or estimate your weight?

- ◯ This is my actual weight - I weighed myself today
- ◯ This was my actual weight taken recently (not today)
- ◯ This is my approximate / estimated weight
- ◯ I did not enter my weight into the last question
- ◯ Other (please specify)

* 15. Do you consider yourself to be under, within or over a healthy weight?

- ◯ Very underweight
- ◯ Moderately underweight
- ◯ A little underweight
- ◯ I think I am a healthy weight
- ◯ A little overweight
- ◯ Moderately overweight
- ◯ Very overweight

* 16. Do you think you are at risk of developing Type 2 Diabetes?

Type 2 Diabetes is the most common type of diabetes. It can occur when your body doesn't make enough insulin or doesn't use the insulin in your body properly. This leads to high levels of glucose (sugar) in your blood.

Yes, high risk	Yes, moderate risk	Yes, low risk	No, I am not at risk
○	○	○	○

* 17. Do you have a family history of diabetes?

Answer yes if you have a parent, grandparent, sibling, son/daughter, aunt or uncle with diabetes.

- ○ Yes
- ○ No
- ○ I don't know

* 18. In what year were you diagnosed with gestational diabetes?

If you have had gestational diabetes more than once, enter your most recent diagnosis.

* 19. Did you require any of the following medications to manage your gestational diabetes?

- ☐ Insulin
- ☐ Diabetes tablets (eg. Metformin)
- ☐ No, my diabetes was controlled by diet alone
- ☐ Other (please enter a comment)

* 20. Since you had your baby following gestational diabetes, has a doctor or healthcare professional said that you have any of the following?

- [ ] Type 2 Diabetes
- [ ] Type 1 Diabetes
- [ ] Pre-diabetes or Impaired Glucose Tolerance
- [ ] I have not had a glucose/sugar test for diabetes since my gestational diabetes
- [ ] My doctor or healthcare professional has told me my blood glucose/sugar levels are normal



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* 21. Since you had your baby following gestational diabetes, has a doctor or other healthcare professional (e.g. a dietitian, midwife, diabetes nurse etc.) told you that you need to lose weight?

- ◯ Yes
- ◯ No
- ◯ I haven't seen a healthcare professional since my gestational diabetes pregnancy
- ◯ I don't remember

* 22. Do you think it is safe to lose weight while you are breastfeeding?

- ◯ Yes, unrestricted weight loss is fine while breastfeeding
- ◯ Yes, gradual weight loss only while breastfeeding
- ◯ No, you should not lose weight while breastfeeding
- ◯ I don't know

* 23. How long after having a baby do you think it is safe to start trying to lose weight?

	< 1 month	1-2 months	3-4 months	5-6 months	7-9 months	10-12 months	Longer than 12 months
Breastfeeding	○	○	○	○	○	○	○
Not breastfeeding	○	○	○	○	○	○	○

Other (please tell us what you think)

* 24. Did you breastfeed your baby after your pregnancy when you had diabetes?

- ○ No, I did not breastfeed
- ○ Yes, for less than 1 month
- ○ Yes for between 1 - 3 months
- ○ Yes for between 4 - 6 months
- ○ Yes for between 7 - 12 months
- ○ Yes for 1 year or longer

* 25. Have you lost the weight you gained during your last pregnancy?

If you are currently pregnant, had you lost your pregnancy weight from your previous pregnancy before becoming pregnant again?

- ○ Yes
- ○ No
- ○ I don't know

* 26. Since your gestational diabetes, have you thought about or tried losing weight?

- ○ Yes
- ○ No

* 27. Have you tried any of the following things to lose weight since you have had children? Please select all that you have tried and how well they worked for you.

If you are doing this survey on your ***mobile device****, you may need to rotate your device (change the view to the landscape mode) to be able to see the full question.*

	Have you tried this?	How well did this work for you?
Meal replacements or diet shakes (e.g. Optifast, CelebritySlim etc)		
Lite 'N' Easy, Hello Fresh or other meal or food delivery services		
Weight Watchers / Healthy Inspirations or other similar program		
Online programs or communities (e.g. BiggestLoser.com.au, SparkPeople.com etc)		
Mobile phone applications (apps)		
Bariatric / weight loss surgery (e.g. lapband, gastric bypass)		
Diet - low carbohydrate and/or low fat		
Diet - 5:2 diet / intermittent fasting		
Diet - paleo / gluten free / clean eating		
Diet - unspecific, eating less food		
Exercised in an effort to lose weight		
Activity trackers (e.g. Fitbit)		

Other (please tell us what they are and how well it worked for you)

* 28. Please read the following statements about healthy diet and weight loss and select how much you agree or disagree to each one.

	Strongly agree	Agree	Not sure	Disagree	Strongly disagree	N/A
My family will support me to lose weight	○	○	○	○	○	○
I know what sorts of foods I should eat to lose weight	○	○	○	○	○	○
It is easy to lose weight	○	○	○	○	○	○
I don't need to lose weight	○	○	○	○	○	○
My family responsibilities take priority over my weight	○	○	○	○	○	○
I am motivated to lose weight	○	○	○	○	○	○
I am too busy to try and lose weight	○	○	○	○	○	○
Dieting doesn't work with my family meal schedule	○	○	○	○	○	○
I can't afford to buy healthy foods	○	○	○	○	○	○
I don't have time to prepare healthy meals	○	○	○	○	○	○
Medical or health problems stop me from trying to lose weight	○	○	○	○	○	○

	Strongly agree	Agree	Not sure	Disagree	Strongly disagree	N/A
I am too tired to try and lose weight right now	○	○	○	○	○	○
I find it hard to stay on a diet	○	○	○	○	○	○
It is hard to deal with hunger while on a diet	○	○	○	○	○	○
I am a healthy weight	○	○	○	○	○	○

Are there any other things not listed above that might affect your decision to lose weight or make weight loss hard for you right now?

* 29. The following statements ask you what kind of weight loss program or service you think might work for you. Please read each statement and select how much you agree or disagree.

If you are currently pregnant please respond to this question based on what you think might work for you after this pregnancy.

	Strongly agree	Agree	Not sure	Disagree	Strongly disagree	N/A
Individual appointments with a dietitian or nutritionist	○	○	○	○	○	○
Group sessions with other mothers and a dietitian or nutritionist	○	○	○	○	○	○
Online program run by a dietitian or nutritionist	○	○	○	○	○	○
Online education program with a community of other mothers	○	○	○	○	○	○

	Strongly agree	Agree	Not sure	Disagree	Strongly disagree	N/A
Smartphone applications	○	○	○	○	○	○
Sessions with a dietitian or lifestyle coach over the phone	○	○	○	○	○	○
Information and resources given to me by a doctor, dietitian, midwife etc.	○	○	○	○	○	○
I like to do my own research and try to lose weight my own way	○	○	○	○	○	○
I am not trying to lose weight right now	○	○	○	○	○	○
I don't need to lose weight	○	○	○	○	○	○

* 30. Where have you or would you look for information on how to lose weight?

- ☐ Internet searches
- ☐ Diet books
- ☐ Online forums or communities
- ☐ Doctor or dietitian / nutritionist
- ☐ Midwife or Child and Family Health nurse
- ☐ Friends or family
- ☐ TV shows
- ☐ Psychologist or counsellor
- ☐ Gym instructor / lifestyle coach
- ☐ I don't need to find information on how to lose weight
- ☐ Other (please specify)

* 31. Have you heard of the 5:2 diet? (This is also known as Intermittent or Fasting diet)

- ○ Yes
- ○ No

***This is the last page ! Don't forget to click NEXT* at the bottom of the page to submit your answers!**

* 32. Have you ever tried the 5:2 diet?

! Breastfeeding mothers should talk to their healthcare professional (e.g. a doctor, dietitian or nutritionist) before starting any type of diet.

- ◯ Yes, I tried the diet and lost weight
- ◯ Yes, I tried the diet and it wasn't for me
- ◯ I have thought about trying the 5:2 diet but haven't yet
- ◯ No, I haven't tried the 5:2 diet

We would appreciate your comments about 5:2 diet

33. **If you would like to receive a summary report from this survey or if you are interested in participating in a weight loss study (clinical trial) for women who have had gestational diabetes in the last 5 years at The University of South Australia please select the options below and enter your contact details.**

This is optional. We will not store your contact details with your survey responses. Your survey responses will remain anonymous.

If you choose to be contacted about the weight loss study we will store the contact details you provide in a secure and confidential database until we have contacted you, for a period of up to one year. We will not contact you about other studies or give your contact details to anybody. The weight loss study is only available to women living in South Australia. If you would like us to remove your details from the contact list at any time or if you have any queries about this you can email kristy.gray@mymail.unisa.edu.au.

- [ ] **I would like to receive a copy of the report from this survey.**
- [ ] **I would like to be contacted about participating in a weight loss study (South Australian residents only).**

Name and email address (or postal address) or phone number if you would prefer a call.

34. **If you would like to go in to the draw to win a $50 voucher please enter your name and phone number.**

Going in to the draw is optional. If you do we will not store your contact details with your survey responses. Your survey responses will remain anonymous.

Name	
Phone number	

Please make sure you click the **NEXT** *button to save your responses.*

We would appreciate if you could spread the word and share this survey and LIKE the Facebook page.

Thank you very much for your participation!

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This is the last page ! Don't forget to click DONE at the bottom of the page to submit your answers!

* 35. **The 5:2 diet, also known sometimes as Intermittent Energy Restriction or Intermittent Fasting, involves following a very low calorie diet (500 calories) for 2 days of the week and eating normally, but sensibly, for the other 5 days, compared to a more traditional diet where you reduce your energy (or calories) by a smaller amount but stay on the diet every day.**

! Breastfeeding mothers should talk to their healthcare professional (e.g. a doctor, dietitian or nutritionist) before starting any type of diet.

Do you think the 5:2 diet could be a good option for you right now?

- [ ] Yes, the 5:2 diet sounds like it could be a good option for me
- [ ] No, the 5:2 diet doesn't sound like it would suit me
- [ ] I don't know
- [ ] I don't need to lose weight
- [ ] Please feel free to comment if you would like to add any further thoughts.

36. If you would like to receive a summary report from this survey or if you are interested in participating in a weight loss study (clinical trial) for women who have had gestational diabetes in the last 5 years at The University of South Australia please select the options below and enter your contact details.

This is optional. We will not store your contact details with your survey responses. Your survey responses will remain anonymous. If you choose to be contacted about the weight loss study we will store the contact details you provide in a secure and confidential database until we have contacted you, for a period of up to one year. We will not contact you about other studies or give your contact details to anybody. The weight loss study is only available to women living in South Australia. If you would like us to remove your details from the contact list at any time or if you have any queries about this you can email kristy.gray@mymail.unisa.edu.au.

- [ ] I would like to receive a copy of the report from this survey.
- [ ] I would like to be contacted about participating in the weight loss study (**South Australian residents** only).

Name and email address (or postal address) or phone number if you would prefer a call.

37. If you would like to go in to the draw to **win a $50 voucher** please enter your name and phone number.

Going in to the draw is optional. If you do we will not store your contact details with your survey responses. Your survey responses will remain anonymous.

Name	
Phone number	

Please make sure you click the DONE button to save your responses.

We would appreciate if you could spread the word and share this survey and LIKE the Facebook page.

Thank you very much for your participation!

Appendix 2: Statement of Authorship: Development and Validation of an Online Survey to Assess Perception of Diabetes Risk and Barriers and Facilitators to Weight Loss Following Gestational Diabetes

STATEMENT OF AUTHORSHIP

Chapter 3

Development and Validation of an Online Survey to Assess Perception of Diabetes Risk and Barriers and Facilitators to Weight Loss Following Gestational Diabetes

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Contributed to the conceptualization and study design, conducted the study, performed data collection and formal analysis, interpreted data and prepared the manuscript.

I hereby certify that this statement of contribution to the above-named paper is correct, and I give permission for the inclusion of the paper in the thesis.

Signed:  Date: 25/01/2022

Author 2: Maya Grebenshchikova

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Appendix 3: Statement of Authorship: Women's Barriers to Weight Loss, Perception of Future Diabetes Risk and Opinions of Diet Strategies Following Gestational Diabetes

STATEMENT OF AUTHORSHIP

Chapter 4

Women's Barriers to Weight Loss, Perception of Future Diabetes Risk and Opinions of Diet Strategies Following Gestational Diabetes

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Appendix 4: Statement of Authorship: The Effect of Intermittent Energy Restriction on Weight Loss and Diabetes Risk Markers in Women who have had Gestational Diabetes: A 12 month Randomised Control Trial

STATEMENT OF AUTHORSHIP

Chapter 5

The Effect of Intermittent Energy Restriction on Weight Loss and Diabetes Risk Markers in Women who have had Gestational Diabetes: A 12 month Randomised Control Trial

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Appendix 5: Statement of Authorship: Weight Loss Barriers and Dietary Quality of Intermittent and Continuous Dieters in Women with a History of Gestational Diabetes

STATEMENT OF AUTHORSHIP

Chapter 6

Weight Loss Barriers and Dietary Quality of Intermittent and Continuous Dieters in Women with a History of Gestational Diabetes

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