Exploring Relationships Between Sleep, Physical Activity, Diet And Glycaemic Control During And After Gestational Diabetes: Studies With Activity Monitors

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Contents

I. Declaration

This is to certify that the content of this thesis is my own work. This thesis has not been submitted for any degree at any University. I certify that the intellectual content of this thesis is my original work except where due acknowledgement has been made. The research described in this thesis was conducted over one year from February 2021 to January 2022.

In addition, in cases where I am not the corresponding author of a published item, permission to include the published material has been granted by the corresponding author.

Cellina Ching

17th July 2022

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct..

N Wah Cheung

17th July 2022

II. Acknowledgements

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III. List of abstracts presented to learned societies

Chapter 3 “The Effect Of Physical Activity On Glycaemic Control In Women With Gestation Diabetes” presented to Australasian Diabetes in Pregnancy and Society of Obstetric Medicine of Australia and New Zealand Joint Annual Scientific Meeting 2021

Chapter 4 “The Effect Of Sleep On Glycaemic Control In Women With Gestation Diabetes” presented to Australian Diabetes Society Australasian Diabetes Congress 2021

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VI. List of Abbreviations

ACHOIS	Australian Carbohydrate Intolerance Study In Pregnant Women
ADIPS	Australasian Diabetes In Pregnancy Society
AHIW	Australian Institute Of Health And Welfare
BG	Blood Glucose
BMI	Body Mass Index
CPAP	Continuous Positive Airway Pressure
CRP	C-Reactive Protein
DALY	Disability-Adjusted Life-Years
DEACC	Diabetes Endocrinology And Ambulatory Care Centre
DILGOM	Dietary Lifestyle And Genetic Determinants Of Obesity And Metabolic Syndrome
DPP	Diabetes Prevention Program
DPS	Diabetes Prevention Study
EEG	Electroencephalogram
FINRISK	National Finland Cardiovascular Risk Study
GDM	Gestational Diabetes Mellitus
GEM	Gestational Diabetes Effect On Moms
GI	Glycaemic Index
HAPO	Hyperglycaemia And Adverse Pregnancy Outcome
Hba1c	Glycated Haemoglobin
IADPSG	International Association Of The Diabetes And Pregnancy Study Groups
IGT	Impaired Glucose Tolerance
IL	Interleukin
IVGTT	Insulin-Modified Intravenous Glucose Tolerance Test
JSON	Javascript Object Notation
MESA	Multi-Ethnic Study Of Atherosclerosis
MVPA	Moderate To Vigorous Physical Activity
OGTT	Oral Glucose Tolerance Test
OSA	Obstructive Sleep Apnoea
PSQI	Pittsburgh Sleep Quality Index
RCT	Randomised Controlled Trial
REM	Rapid Eye Movement
SE	Sleep Efficiency
SMS	Short Message Service
SMs2	Smart Mums With Smart Phones 2
SOL	Sleep Onset Latency
T2DM	Type 2 Diabetes Mellitus
TDD	Total Daily Dose
TNF α	Tumour Necrosis Factor
TST	Total Sleep Time
WASO	Wake After Sleep Onset
WHO	World Health Organisation

VI. Abstract

Gestational diabetes (GDM) is one of the most common complications of pregnancy. The adverse perinatal outcomes and consequent need for treatment is well established. However, the long-term sequelae of GDM includes a six-to-seven-fold increase of type 2 diabetes mellitus (T2DM) which results in a significant burden of disease to the individual and population. The need to address this is further amplified by the rising incidence of GDM and T2DM. Lifestyle interventions aimed at diet and exercise are the current mainstays of treatment of GDM and prevention of progression to T2DM. However, there is emerging evidence supporting sleep as an additional modifiable risk factor contributing to T2DM risk and glycaemic control. It has also been shown to influence the currently target lifestyle factors of exercise and diet. Novel technologies such as commercially available activity monitors that can track physical activity and sleep are of growing interest in their ability to support lifestyle programs through their accessibility and interactivity. They also have potential as a useful research tool to collect data beyond currently validated tools as they are simultaneously objective and convenient.

The aims of this thesis are to explore the effect of sleep and exercise on glycaemic control in women with GDM during pregnancy; understand the relationship of sleep on exercise and weight in postpartum women with GDM and investigate the impact of COVID lockdown on physical activity of postpartum women. This revolved around the application of activity monitors for lifestyle interventions and clinical research.

Smart Mums with Smart Phones 2 (SMs2) is a randomised controlled trial that recruited pregnant women diagnosed with GDM with antenatal care at three teaching hospitals for a postpartum lifestyle intervention delivered via text messages and supported with a wrist worn activity monitor (Garmin Vivofit4®). I was involved in the recruitment of participants for SMs2 and their follow-up. The studies undertaken in this thesis are substudies of SMs2 which examined observational data collected before completion of the trial and therefore without unblinding of trial randomisation, The data collected for this thesis comprised demographic, medical and obstetric information obtained at study baseline, glucose levels performed as part of routine care of GDM, and step and sleep data downloaded from the activity monitors. The relationship between these data were explored.

A key finding of this thesis is a trend towards improved post prandial but not fasting blood glucose levels with increased step count during pregnancy. Achieving healthy sleep targets during pregnancy improved the likelihood of reaching glycaemic targets and increased sleep duration after pregnancy was associated with more steps being taken. There was a positive relationship between sleep and postpartum weight but no relationship between steps and postpartum weight. When postpartum activity was examined in relation to periods of COVID lockdown, a paradoxical increase in step count was observed during these times.

This finding of this thesis adds to the accumulating evidence for a relationship between sleep, glycaemic control and diabetes risk. Sleep is an under-recognised risk factor which should be considered during GDM and post-partum. Integration of sleep modification into lifestyle intervention programs for women with GDM during pregnancy and postpartum may potentially can help achieve glucose management and diabetes risk reduction goals. Evolving technologies such as activity monitors may support the optimisation of physical activity and sleep and are also a useful research tool able to collect granular data over prolonged periods of time.

Chapter 1: Introduction

1.1 Gestational Diabetes

1.1.1 Definition

Gestational diabetes (GDM) is a common complication of pregnancy defined as the first onset of glucose intolerance occurring in pregnancy (1, 2).

1.1.2 Incidence

In Australia, GDM currently affects approximate 14% of pregnancies (3). It is the fasting growing subtype of diabetes in Australia with more than twice the number of women affected in 2019 as compared to 10 years prior. This is compared to prevalence of GDM around the world ranging from 4.5% in Japan to up to 31.5% in Norway(4). However, with variation in screening approaches and diagnostic criteria used, the global prevalence is difficult to estimate. Factors contributing to the increasing incidence of GDM in Australia includes increasing obesity up from 56.3% in 1995 to 67% in 2017–18 (5, 6), mean maternal age increasing from 29.9 years in 2007 to 30.6 years in 2017 and number of women from higher risk ethnic background particularly Asian women (6). As such in Australia, women in older age groups have up to twice the incidence of the general population and women born in central and southern Asian more than twice the incidence, affecting 28% of pregnancies (6, 7)

1.1.3 Diagnostic criteria

Another contributing factor to the incidence of GDM is the changing diagnostic processes and thresholds.

O'Sullivan & Mahan provided the first data regarding screening, diagnosis and treatment of new onset hyperglycaemia in pregnant women based on a 3 hour 100g oral glucose tolerance test (OGTT) and the development of diabetes (8). They also established a reduction in the rate of macrosomia (4.3% compared to 13.1%) and perinatal mortality in treating gestational diabetes with diet and insulin (9, 10). Their threshold for diagnosis however was based on the risk of developing future diabetes rather than pregnancy outcomes. Subsequently the 2-hour 75g OGTT that had been established for the diagnosis of diabetes and glucose intolerance was extended to pregnant women by the World Health Organisation (WHO) (11). As limited investigation into its use in this cohort had been conducted, a variety of procedures and criteria were adopted by different organisations.

Following this, the Australasian Diabetes in Pregnancy Society (ADIPS) adopted the 75g OGTT for the diagnosis of GDM (1, 12). This recommended that all women not previously known to have pre pregnancy diabetes or hyperglycaemia in pregnancy should undergo a 75g OGTT at 24 – 28 weeks gestation. The cut-off for diagnosis was established on a statistical basis with fasting glucose based on the 95th percentile of pregnancy and 2-hour fasting glucose based on that which 4-9% of women had been found to have in a European multicentre study and from 3 clinics in Melbourne.

The Hyperglycaemia and Adverse Pregnancy Outcome study (HAPO) (13) was an observational study conducted in 25,505 women across fifteen centres in nine countries investigating adverse pregnancy outcomes associated with maternal hyperglycaemia. They were unable to establish a definitive threshold but instead found a continuous increased risk. The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) was formed in 1998 to facilitate collaboration between various groups that focus on diabetes and pregnancy (14). They established threshold based on the findings from the HAPO study and are the mean glucose levels where the risk of birthweight >90th percentile, percentage body fat >90th percentile and cord c-peptide >90th percentile is increased 1.5 times. From this a diagnosis of GDM is established if at least one of the following criteria are met; fasting glucose is ≥ 5.1mmol/L, 1-hr glucose ≥ 10.0mmol/L or 2-hr glucose ≥ 8.5mmol/L. Subsequently ADIPS and most Australian Centres have adopted these criteria (15).

Although the evolution of GDM diagnosis has resulted in increasing homogeneity, diagnostic criteria still remains dependent on location of practice (16). The change in diagnostic threshold has contributed to the increasing incidence of GDM (17).

1.1.4 Adverse Outcomes – long and short term

The HAPO study (13) was a landmark trial that demonstrated some of the well recognised short term pregnancy outcomes associated with GDM including increased birthweight, cord c-peptide levels, primary caesarean section and neonatal hypoglycaemia. Other associations included pre-eclampsia, shoulder dystocia and birth injury, premature delivery, intensive neonatal care and hyperbilirubinaemia.

Longer term, offspring of mothers with GDM are at risk of abnormal glucose metabolism and obesity later in life (18, 19). There is also evidence to suggest effects on neurocognitive development with increased risk of attention-deficit/hyperactivity disorder (20) and low cognitive scores in children of women with GDM (21).

Women with a history of GDM also suffer long term consequences with an increased risk of cardiovascular events. These findings have been consistent across multiple population groups around the world. A meta-analysis in 2019 by Caroline et al. pooled nine studies of 5,390,591 women and showed women with a history of GDM had a twofold increased risk of cardiovascular events compared to their peers (22). There is also evidence to suggest that women with GDM have an increased prevalence of microalbuminuria (23) and renal morbidity (24). The increased cardiovascular risk and renal outcomes may be partly mediated by the increase in risk factors such as hypertension, metabolic syndrome and type 2 diabetes mellitus (T2DM) (25, 26).

1.1.5 Treatment and effect on outcomes – short and long term

Typically, women with GDM are managed with non-pharmacological interventions such as diet education, physical activity, and weight control prior to the use of pharmacotherapy such as metformin and insulin. Crowther et al. (27) conducted a randomised controlled trial in 490 women to investigate if

treatment of GDM reduced the risk of perinatal complications. Treatment in the intervention group included dietary advice, blood glucose monitoring and insulin therapy. Compared to the routine care group there was a reduced incidence of serious perinatal outcomes which was defined as death, shoulder dystocia, bone fracture and nerve palsy. However, the intervention group had an increase in induction of labour and admission to neonatal nursery and similar rates of caesarean sections to the usual care group. Landon et al.(28) conducted a study similarly looking at the outcomes of women who received treatment for GDM. The treatment group showed reduced birthweight, neonatal fat mass, frequency of large-for-gestational-age infants, shoulder dystocia, caesarean delivery, pre-eclampsia and gestational hypertension.

Despite the improvement in neonatal outcomes in women treated for GDM, this benefit may not translate to long term outcomes. Landon et al. followed up 500 women who were previously enrolled in a study on the treatment of mild GDM and found that there was no reduction in childhood obesity or metabolic dysfunction (29). This finding was consistent with follow up of women in the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) who had mild GDM where despite improvements in macrosomia at birth, body mass index (BMI) did not change at age 4 to 5 years old (30).

1.2 Type 2 Diabetes Mellitus

1.2.1 Risk of T2DM

Another issue of GDM is the long-term risk of developing T2DM in the mother. Although glucose intolerance resolves following the completion of the pregnancy, approximately half of these women will develop type 2 diabetes mellitus (T2DM). In several meta-analysis, there was a six to seven-fold increased relative risk of T2DM in women with prior GDM compared to those that did not have GDM. This effect had a wide range dependent on duration of follow up and diagnostic criteria used. (31-34). GDM contributes substantially to the growing burden of diabetes. Based on population attributable risk, it has been estimated that 10-31% of parous women with T2DM had a history of GDM (33).

1.2.2 The prevalence and impact of T2DM

Type 2 diabetes is the most common form of diabetes. It is a chronic disease where there is insulin resistance with relative insulin deficiency that results in high blood glucose levels. It requires long-term management with lifestyle, oral medication, non-insulin injection therapy or insulin or a combination of these.

The prevalence of diabetes is rising exponentially on a global scale from 108 million in 1980 to 422 in 2014, the majority of which is from T2DM. The International Diabetes Federation have estimated this to increase to 693 million by 2045 if no effective preventative methods are introduced (35). Diabetes is associated with increased mortality from infection, cardiovascular disease, stroke, chronic kidney

disease, chronic liver disease and cancer. In 2017 the global incidence, prevalence, death, and disability-adjusted life-years (DALYs) associated with diabetes has been calculated at 22.9 million, 476.0 million, 1.37 million, and 67.9 million, with a projection to 26.6 million, 570.9 million, 1.59 million, and 79.3 million in 2025, respectively (36).

In Australia, an estimated 1.2 million (4.9%) people had diabetes in 2017-18 based on self-reported data (37). The increasing rates are likely largely driven by increased obesity, aging population, dietary changes and sedentary lifestyles.

T2DM also confers significant mortality and morbidity to those affected. According to the Australian Institute of Health and Welfare (AIHW) National Mortality Database, diabetes contributes to 10.5% of all deaths in 2018, ranking in the top ten leading causes of death in Australia (37). In 2012, Diabetes Australia reported that in Australians with diabetes, 13% are affected by peripheral neuropathy of the lower limbs and 15% suffer from diabetes retinopathy. Diabetes is the leading cause of end stage-renal failure. Cardiovascular disease is the leading cause of death with 65% of cardiovascular deaths occurring in those with diabetes or pre-diabetes. In addition, 41% of people with diabetes experience poor social wellbeing from stress, anxiety and depression associated with managing their disease (38).

These figures translate into a heavy burden on the economic and health system. In 2017-18, there were 1.2 million hospitalisations associated with diabetes, T2DM accounted for approximately 90% with higher risk in males and increasing age (37). The annual cost of T2DM is $6 billion including the cost of healthcare, carers and government subsidies. The average annual healthcare cost per person in $4,025 if there are no associated complications however this can more than double to $9645 when there are micro- and macrovascular complications. Primary prevention can reduce the risk of diabetes by nearly 60% over a 3 years period which converts to saving a lifetime healthcare cost saving of $1087 per person (38).

1.2.3 Current interventions for GDM to prevent T2DM

The increased prevalence of T2DM and its associated long-term morbidity and health care costs prompts the need for preventative interventions. The Diabetes Prevention Program (DPP) (39) and Finnish Diabetes Prevention study (DPS) (40) are both randomised controlled trials that successfully reduced the incidence of T2DM in individuals who were at risk with impaired glucose tolerance (IGT) through lifestyle modification. Both used resource intensive interventions targeted at diet and physical activity and the DPP resulted in 58% lower incidence of T2DM at 4 years whilst the DPS saw 9% of the intervention group develop diabetes compared to the 20% of the control group at 3 years follow up. Given the high risk of T2DM following GDM, and the success of diabetes prevention through lifestyle intervention, studies have sought the opportunity to explore the effect of lifestyle intervention on at risk women with a history of GDM to prevent the progression T2DM in this inherently young population.

However, outcomes from lifestyle intervention have been variable. In a study of 200 women with previous GDM who were randomised to either intensive or routine dietary advice, there was no difference found in the annual incidence of diabetes after a median of 51 months follow up (41). On the other hand, in another study with 260 women with previous GDM who were randomised to either Mediterranean lifestyle or usual care, there were fewer women with glucose disorders after 3 years (42). The largest of these studies was the Gestational Diabetes Effect on Moms (GEM) study which was a cluster randomised controlled trial including 2280 with GDM. Using lifestyle interventions modelled after DPP they found more women were able to meet weight goals at 6 weeks and 6 months follow up, but this effect was attenuated at 12 month follow up. Vigorous intensity physical activity had also significantly increased however there was no difference in diabetes incidence (43).

In an analysis of the women involved in the DPP study, comparison of women 3 years after randomisation to the placebo group demonstrated an estimated cumulative incidence of diabetes of 38.4% for women with a history of GDM compared with 25.7% of those without GDM (44). Interestingly, women with previous GDM had similar reductions in the incidence of diabetes of approximately 50% with either lifestyle or metformin therapy compared to placebo however in the women without GDM history this reduction was only 49% and 14% respectively. Similar trends were found at 10 years of follow up for DPP (45).

There are also post-partum interventions that have also been shown to reduce risk factors for the development of diabetes including weight reduction, improving eating behaviours and physical activity (46-49). A meta-analysis on 15 randomised control trials investigating lifestyle intervention for women with previous GDM to prevent T2DM showed most interventions were focused on diet and physical activity with only one including incentive to breastfeed with follow up of up to 2 years (50). Of the 8 interventions that reported on diabetes, there was a 25% reduction in incidence of diabetes, with number needed to treat of 25 women, however this was only borderline significant. Furthermore, no benefit was found in measures of glycaemia. Trials where intervention was implemented soon after delivery (within 6 months) were more effective.

1.3 Sleep and diabetes

Modifiable lifestyle factors such as diet and physical activity are the two major risk factors for diabetes and targets of interventions however there is increasing evidence that sleep might also play a critical role.

Total sleep time (TST) / Sleep duration	Time spent sleeping during sleep episode
Sleep fragmentation	Interruption of continuous sleep
Sleep chronotype	Time of day preference for sleep
Sleep regularity	Consistency of sleep habits
Sleep onset latency (SOL)	Time to transition from wakefulness to sleep
Sleep efficiency (SE)	Ratio of TST to time in bed
Wake after sleep onset (WASO)	Duration of wakefulness after sleep established
NREM sleep	Non-Rapid eye movement sleep
REM sleep	Rapid eye movement sleep

Table 1. Sleep Definitions

1.3.1 Normal sleep architecture

Sleep architecture is the structural organisation of sleep. Sleep stages 1, 2 and 3 are categorised into non-Rapid eye movement sleep (NREM) and sleep stage 4 is rapid eye movement sleep (REM) sleep (51). These stages represent a continuum of sleep depth and vary in characteristic brain wave patterns, eye movements and muscle tone. Normal sleep cycles through these sleep stages with NREM sleep representing 75 to 80 percent of sleep and REM sleep account for the remainder 20 to 25 percent. The first cycle is typically 70 to 100 minutes with subsequent cycles becoming longer at approximately 90 to 120 minutes. The duration of REM sleep progressively increases with each sleep cycle (52).

1.3.2 Prevalence of sleep problems

The Sleep Health Foundation of Australia recommends 7-9 hours of sleep for adults (53, 54). A national survey conducted in 2016 on 1011 adults above 18 years of age reported that 30-45% of adults had sleep problems including difficulties sleeping a few times a week or daytime sleep-related symptoms. Symptoms varied with age with older age groups more likely to report adequate and refreshing sleep and snoring and breathing pauses more common in middle age groups. Sleep duration was reported at approximately 7 hours on average with significant variability in younger adults. Overall, it was found 12% sleep less than 5 ½ hours and 8% over 9 hours (53).

1.3.3 Sleep duration

Sleep duration is the most widely studied sleep parameter regarding diabetes risk, glucose intolerance and glycaemic control. In a study where sleep was restricted in 11 men aged 18-27 years to 4 hours per night for 6 nights then followed by 6 nights with 12 hours allowed in bed, glucose tolerance was significantly poorer in the shorter sleep setting. The rate of rate of glucose clearance 40% lower, acute insulin response to glucose was 30% lower and glucose response after breakfast was higher (55). Further studies reproduced the association between short sleep and T2DM (56, 57).

The correlation between sleep duration with T2DM and glucose intolerance was further explored in a cross sectional study of 722 men and 764 women, aged 53 to 93 years. A U-shaped relationship was

demonstrated with increased prevalence of IGT and T2DM sleep duration less than 6 hours or greater than 9 hours (58). A meta-analysis looking into the relationship between sleep duration and risk of diabetes included 10 prospective studies with at least 3 years follow up to produce a total of 107,756 participants demonstrated an increase risk with both short and long sleep durations (59). Short sleep duration had a greater effect in men with a relative risk of 2.2 and in women 1.07. When sleep was greater than 9 hours the relative risk of T2DM was 1.38. Definition of short and long sleep varied between studies complicating interpretation of these results. Similar results were found in another meta-analysis of ten prospective studies with the lowest risk was observed in the 7-8hr duration. For every hour of reduced sleep there was a 1.09 relative risk of T2DM when compared to 7 hours of sleep and a 1.14 risk for every hour increment (60).

An analysis comparing the risk of sleep disturbances to traditional risk factors for T2DM found the pooled relative risk with sleeping ≤5 h, 6 h, and ≥9 h/d was 1.48, 1.18 and 1.36 respectively. This is in comparison to the pooled relative risk of being overweight, having a family history of diabetes, and being physically inactive which were 2.99, 2.33 and 1.20. This demonstrates that sleep has a comparable risk to some of the risk factors typically associated with development of T2DM (61).

Risk factor	Relative Risk
≤5 hrs sleep per day	1.48
6 hrs sleep per day	1.18
≥9 h per day	1.36
Physical inactivity	1.20
Family History	2.33
Overweight	2.99

Table 2. Risk of Sleep Duration and Other Factors on T2DM

1.3.4 Sleep duration and mortality

There not only appears to be an association between the duration of sleep and the risk of developing T2DM but there has been data to suggest that sleep duration is associated with mortality.

A meta-analysis of prospective studies of sleep duration and all-cause mortality included 16 studies correlating sleep duration derived from questionnaires and death. Definitions of sleep duration varied between studies with short sleep at least less than seven hours and long sleep at least more than eight hours across all studies. There was a 1.12 relative risk of death in short sleep and 1.3 relative risk with long sleep. (62)

Furthermore, there was a study that specifically assessed mortality in relation to sleep duration in those with T2DM. It reviewed the self-reported sleep hours obtained from the 273,029 adults included

in National Health Interview study 24,212 of whom had type 2 diabetes. They found that extremes of sleep duration were associated with higher all-cause mortality in non-diabetes and diabetes but to a greater degree in the latter group. For non-diabetics, there was a hazard ratio of 1.74 when sleep was less than five hours and 2.72 with more than 10 hours sleep when compared to 7 hours of sleep whereas for the diabetes this was a hazard ratio of 2.78 and 3.67 respectively. (63)

1.3.5 Sleep chronotype

Circadian rhythms are thought to be generated through expression of designated 'clock genes' and their timing varies amongst individuals (64). Chronotype is the preference for the time of day for sleep and daily activities in relation to the circadian rhythm. An individual's timing of this rhythmicity falls on a continuous spectrum where early chronotypes prefer to wake up and perform activities earlier in the day compared to evening chronotypes who wake and are most active in the evening (65, 66). It is also dependent on age with adolescents tending to have a later chronotype that becomes earlier as they age (65). This genetic predisposition can be impacted by environmental factors including light exposure and the impact of sleep debt from working days on work free days (67). The Dietary Lifestyle and Genetic determinants of Obesity and Metabolic Syndrome (DILGOM) substudy of the 2007 National Finland Cardiovascular Risk Study (FINRISK) was a cross-sectional analysis that found an increased risk of T2DM with evening chronotype when compared to morning chronotype (OR 2.6). This was found to be independent of sleep duration and sleep quality (68). Similarly it was found that patients who had T2DM and were evening chronotypes had poorer glycaemic control however this was partially mediated by a larger caloric intake for dinner (69).

1.3.6 Sleep fragmentation

Sleep fragmentation is the disruption in continuity of sleep that can be seen in depression, sleep-disordered breathing, and from other environmental factors. Observations of the number and duration of nocturnal awakenings in 97 participants with T2DM over 7 days and was correlated with the variation of fasting blood glucose (70).

Sleep has been experimentally fragmented to study the effects on glucose metabolism in 11 healthy volunteers. Subjects underwent one night of uninterrupted and two nights of fragmented sleep. Sleep was monitored with polysomnography and fragmentation was induced with auditory and mechanical stimuli until microarousal was elicited on electroencephalogram (EEG) whilst maintaining sleep duration. Frequently sampled insulin-modified intravenous glucose tolerance test (IVGTT) was obtained at baseline and after 2 nights of fragment sleep which involved glucose administration followed by insulin and multiple measurements of glucose thereafter. Sleep fragmentation was shown to significantly reduce the effect of insulin and glucose on glucose disposal by 25.2% and 20.9% respectively (71). Other studies have been conducted looking at deep sleep suppression with similar levels of reduction in insulin sensitivity (72, 73).

1.3.7 Sleep onset latency

Sleep onset latency (SOL) is the duration of the transition from wakefulness to the first sleep stage. In a case control study of 867 people, sleep characteristics of those with diabetes were compared with age and sex matched controls using a self-administered questionnaire. They found that the number of participants with sleep disorders was higher in diabetics and they also had longer SOL (20.2 +/-0.8 compared to 13.7 +/- 0.5) (74).

The impact of sleep quality including SOL has also been assessed in patients with T2DM. The Pittsburgh Sleep Quality Index (PSQI) is a reliable and validated sleeping tool where the participants rate various features of their sleep. This index was administered to 220 participants and a logistic regression analysis was conducted on their global score against their glycated haemoglobin (Hba1c). SOL, sleep disturbance and daytime dysfunction were significantly associated with poorer glycaemic control with an odds ratio (OR) of 2.14, 5.09 and 3.50 respectively (75).

In a study of 92 subjects, sleeping questionnaires were administered as well as fasting glucose, post glucose challenge plasma glucose and homeostatic model assessment-insulin resistance estimation performed. Sleeping parameters were analysed against presence of diabetes and obesity. Diabetic non obese individuals had increased SOL, earlier wake times, more sleep fragmentation, increased snoring and daytime dysfunction compared to their non-diabetic counterparts. Using the Sleep Heart Health Study Sleep Habits Questionnaire, comparison of sleep duration on weekdays in diabetic obese individuals was shorter than their non-diabetic obese counterparts. This may represent the shorter duration of sleep associated with patients with diabetes who may take longer to sleep and wake up earlier, exacerbated during the workdays where extension of sleep time is limited by conventionally wake times that are dictated by work commitments. Across the entire group, SOL was significantly positively associated with fasting glucose, post glucose challenge plasma glucose and homeostatic model assessment-insulin resistance and waist circumference (76).

1.3.8 Daytime napping

Although napping may occur to compensate for short overnight sleep duration, research shows that this is also implicated in poorer health outcomes. Analysis of data obtained from the prospective Sister Study which had 50, 8884 enrolled women aiming to identify environmental and genetic risk factors for breast cancer sought to determine the risk associated with napping. After excluding women with Type 1 diabetes, implausible sleep data, cancer, stroke, transient ischaemic attack or heart disease, there were 39, 071 women included in the study. Data on self-reported sleep duration, latency, awakenings and naps was correlated against the presence of diabetes. Napping was associated with a significantly increased risk of T2DM. Short sleep (<7hrs), latency >30minutes and frequent night awakenings were also positively associated with T2DM risk but this was not statistically significant (77). This association has been reproduced by multiple studies (78-81). Self-reported napping is also associated with poor glycaemic control as evidenced by worse Hba1c (82). A meta-analysis of observational studies on daytime napping and diabetes risk showed napping less than one

hour did not increase diabetes incidence however napping over 1 hour per day was associated with a 31% increased risk of diabetes (83). A dose response meta-analysis demonstrated a J-curve relationship between nap duration and the risk of diabetes or metabolic syndrome where risk began and sharply increased from 40 minutes onwards (84). Another meta-analysis of prospective studies also reported a dose-response relationship between daytime napping with an 11% increased risk of T2DM for each 30 minute per day increment in napping (85).

1.3.9 Sleep regularity

Sleep consistency is often impacted by various lifestyle factors including shift work, jet lag and social norms. This can result in rapid variation in sleep patterns across consecutive days. Variation in sleep can cause circadian misalignment as the rapid day to day variation in sleep schedules is not met by the slower to accommodate intrinsic circadian rhythm (86). Studies of shift workers have shown increased risk of diabetes, suggesting sleep regularity may be an important component of sleep (87).

Associated with this is the concept of social jetlag which occurs when late sleep onset, whether voluntarily or from endogenous chronotype is combined with early arousal from external influences or social demands. This causes an accumulation of sleep debt over the working week that is compensated for by sleep extension during weekends.(88) It is a sleep habit that is related to chronotype and sleep regularity. Shift work is a common form of this that has been shown to be associated with diabetes and poor glycaemia control. (89, 90)

Phillips et al. (91) developed a sleep regularity index to explore circadian function and effect on academic performance. The index determines the probability of an individual being asleep at the same timepoint across different days. Using the sleep regularity index, relationship between sleep regularity and daytime sleepiness, daytime sleep as well as 10-year projected risk of cardiovascular disease, obesity, hypertension and risk of diabetes was examined. This study was based on the Multi-Ethnic Study of Atherosclerosis (MESA) which was a longitudinal observational study of 6814 45-84 year old patients in the United States. Sleep was measured with actigraphy, sleepiness was assessed with self-reported Epworth Sleepiness scale and cardiovascular risk factors of blood pressure, lipid levels, BMI, Hba1c and fasting glycose assessment. Sleep irregularity was associated with delayed sleep timing and evening chronotype irrespective of sleep duration. There was also an association with reduced physical activity, increase daytime sleep and sleepiness. Sleep irregularity was also significantly associated with increased BMI, fasting blood glucose and Hba1c, the directionality of which was not established (92).

A cross-sectional study with 1986 older adults measured sleep parameters through actigraphy over 8 days and showed that sleep variability was independently associated with prevalence of T2DM irrespective of sleep duration (93).

1.3.10 Sleep treatment

The association between sleep and diabetes has been established with investigation of various sleep parameters. However, there are limited studies into whether treatment with sleep prescriptions would be able to address this. Obstructive sleep apnoea (OSA) which is characterised by sleep disturbance with snoring, apnoeic episodes and subsequent daytime sleepiness is associated with T2DM. In the Wisconsin Sleep cohort, severity of OSA was associated with increase prevalence of T2DM (94) and conversely, those with T2DM frequently suffered from OSA. Habitual snoring itself has also been associated with glucose metabolism in both diabetic and non-diabetic patients (95, 96). Babu et al. (97) studied the effect of treatment of OSA with continuous positive airway pressure on changes in glucose levels and Hba1c. They found that continuous positive airway pressure (CPAP) use was associated with significantly decreased 1-hour post prandial BGs. Those with HbA1c greater than 7% had a significant improvement (9.2% ± 2.0% to 8.6% ± 1.8%), the degree of which was correlated with days of use in participants using CPAP at least four hours per day.

Investigation of improvement in sleep found that it could result in improved insulin sensitivity. Sixteen participants were included who had an average self-reported time in bed during the week of 6.5 hours. These participants were all included as they had increased self-reported time in bed during the weekend suggesting sleep restriction during the week and attempted sleep recovery on weekends. Participants were monitored with actigraphy which showed average sleep time of 6 hours at baseline. After instruction to increase their time in bed, participants increased their sleep time by 54± 33 minutes over the 2 first weeks of the intervention, by 48 ± 31 minutes over the 2 middle weeks of the intervention, and by 44 ± 34 minutes over the 2 last weeks of the intervention. The increased sleep time was associated with improved fasting glucose levels and higher insulin-to-glucose ratio suggesting better insulin sensitivity. (98)

Overall, the evidence for the relationship between sleep and its various parameters are increasing however causality and directionality still requires investigation.

1.4 Potential mechanisms for sleep mediating diabetes risk

1.4.1 Appetite hormones

It is thought that shorter sleep duration may result in increased opportunity to eat as well as increased hedonic perception of highly palatable foods (99). However, appetite hormones may be involved in increasing caloric intake. Two of these hormones include ghrelin which is a potent stimulator of appetite and leptin which suppresses food intake and reduces energy expenditure. Spiegel et al. (100) experimentally manipulated sleep duration in 12 healthy young men with average BMI in the normal range and measured the plasma leptin and ghrelin levels and subjective hunger ratings. Sleep restriction was associated with lower anorexigenic leptin levels, increased orexigenic ghrelin levels, with increased hunger and appetite particularly for calorie dense foods with high carbohydrate

content. In an observational study on participants obtained from the Wisconsin Sleep Cohort, a population based longitudinal study of sleep disorders, nocturnal polysomnography, sleep questionnaire and diaries were compared with serum leptin and ghrelin measured the following morning. Sleep duration had a U-shaped relationship with BMI. Short sleep was associated with low leptin and high ghrelin when comparing 5 hours to 8 hours of sleep, independent of BMI (101). Interestingly obesity is typically associated with low levels of ghrelin and high levels of leptin owing to leptin resistance (102). These studies suggest that the effect of short sleep on appetite hormones may result in an increase intake of foods that may lead to obesity and diabetes.

1.4.2 Hypothalamic-pituitary adrenal axis

The hypothalamic-pituitary-adrenal axis follows a diurnal pattern that is linked to the circadian rhythm through its relationship with the central pacemaker found in the suprachiasmatic nucleus (103). The disturbance to circadian rhythm from sleep deprivation resulting in increased levels of cortisol is thought to be another explanation for the relationships between poor sleep and metabolic outcomes.

A study was conducted to evaluate plasma cortisol profiles in three different sleep conditions; normal sleep schedule, partial and total sleep deprivation. Evening cortisol was raised in the evening following total sleep deprivation only (104). These conditions were expanded in a subsequent study with 6 nights of sleep restriction to 4 hours, followed by sleep recovery with 12 hrs allowed in bed for 6 nights. Glucose tolerance and thyrotropin concentration was lower in sleep debt whilst evening cortisol and activity of sympathetic nervous system was higher (55). This relationship was also found when assessing ACTH and cortisol levels in 14 health male subjects. When comparing the half of the group that slept for a shorter duration (476.9 ± 15 minutes) with the half sleeping for a longer duration (596.9 ± 14.4 minutes), plasma cortisol was significantly higher upon waking (105). Interestingly the “shorter sleep” group’s sleep duration falls within sleep recommendations and would be expected to have a lower risk of diabetes and better control than the “longer sleep” group whose duration is >9hrs according to studies on sleep duration. Therefore, a higher plasma cortisol might be expected in the “longer sleep” group for this pathophysiological mechanism to hold true. Alternatively, this may suggest the association between longer sleep duration and diabetes is through a different mechanism.

The studies have been performed on small healthy male cohorts and therefore this relationship is less established and unable to be generalised to the population. Furthermore, a study in a similar cohort showed lower cortisol levels in sleep deprived conditions (106).

1.4.3 Clues from the studies between OSA and T2DM

The association of OSA with T2DM suggests that potentially the sleep fragmentation and hypoxia that results from successive apnoea-hypopnoea episodes mediates metabolic disturbances including activation of the sympathetic nervous system, oxidative stress, systemic inflammation, in conjunction with previously discussed alterations in appetite-regulating hormones and activation of the

hypothalamic-pituitary-adrenal axis, that in turn, favour the development of insulin resistance, glucose intolerance and ultimately T2DM (107).

1.4.4 Sympathetic nervous system activation

During sleep, the parasympathetic nervous system predominates resulting in slowed heart rate, reduced blood pressure, respiration, body temperature and basal metabolism (108). Conversely the inappropriate activation of the sympathetic nervous system may be a mediator of poor sleep and metabolic health. Studies in animal models have demonstrated that epinephrine inhibits insulin secretion, augments hepatic glucose output by stimulating gluconeogenesis and glycogenolysis, impairs skeletal muscle uptake of glucose and decreases metabolic clearance of glucose (109).

The effects of exogenous epinephrine on glucose tolerance in nine normal weighted subjects has been studied. Using insulin clamp technique, glucose was administered at a variable rate to maintain euglycemia, whilst insulin was infused with and without epinephrine and insulin and propranolol were infused with and without epinephrine. The addition of epinephrine lowered glucose metabolism and delayed the suppression of hepatic glucose production. Propranolol had no effect of insulin mediated metabolism but restored glucose metabolism when administered with epinephrine (109). Similar impairments were seen in glucose metabolism with the administration of epinephrine in another study on six healthy volunteers (110). In assessing measures of sympathetic activity including plasma and urinary norepinephrine against movement and arousal in 67 subjects with hypertension and OSA, cortical arousals did not correlate with any of the measured variables. However movement arousals independently predicted baseline plasma norepinephrine study (111). In a cross-sectional analysis of the Whitehall II study that included 2751 participants, self-reported sleep duration and disturbances were independently associated with higher evening cortisol. (112)

1.4.5 Hypoxia

Hypoxia can occur secondary to sleep apnoea or hypopnoea or from disrupted sleep with frequent arousals. In lean healthy mice, intermittent hypoxia was found to reduce insulin sensitivity compared to exposure to synthetic air due to reduced glucose utilization in oxidative muscle fibres and was not restored by autonomic nervous system blockade (113). When 13 healthy human volunteers were subjected to five hours of intermittent hypoxia or normoxia during wakefulness on two separate days, IVGTT showed worsening insulin sensitivity and decreased glucose effectiveness in the former condition with changes in heart rate variability suggesting increased sympathetic nervous system activity (114).

1.4.6 Oxidative stress

Sleep apnoea is also associated with increased concentrations of reactive oxygen species which can inhibit insulin stimulated substrate uptake in muscle and adipose tissue and may damage pancreatic β-cells due to their relatively low concentration of antioxidant enzymes (115, 116). Reactive oxygen species activate pathways that affect cellular signalling such as down-regulation of the cellular

response to insulin, leading to a reduced ability of insulin to promote glucose uptake, and glycogen and protein synthesis (117).

1.4.7 Underlying inflammation

There have been studies that suggest poor sleep may be related to a pro-inflammatory state. Inflammatory cytokines such as interleukin-6, tumor necrosis factor-alpha (TNF α), C-reactive protein (CRP) and interleukin-18 are associated with insulin resistance and T2DM (118, 119). In a systematic review on 72 studies assessing sleep disturbance, sleep duration and markers of inflammation, sleep disturbance and long sleep duration was associated with higher levels of CRP and IL-6, short sleep but not extremes of short sleep was associated with higher levels of CRP but not IL- 6, TNF α was not associated with either sleep disturbance or duration. Experimental sleep restriction was not associated with any of these markers (120).

1.4.8 Mechanisms of risk of diabetes associated with long sleep

The underlying mechanisms relating long sleep duration and diabetes risk is less well understood. Risk factors including depressive symptoms, low socioeconomic status, unemployment, a low level of physical activity, poor health has all been shown to be associated with long duration of sleep (121).

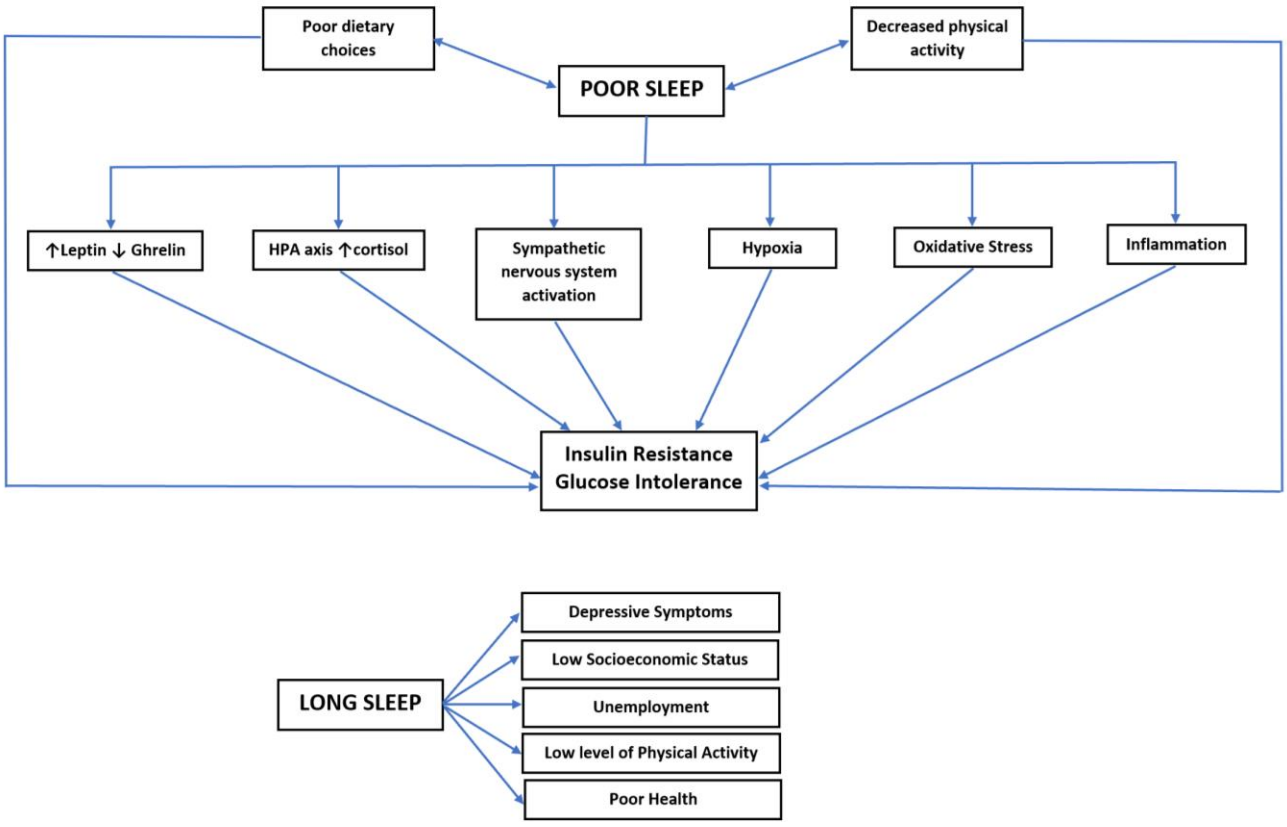

Figure 1. Mechanism of Effect of Sleep Duration on Diabetes Risk

1.5 Sleep, physical activity and diet

Physical activity and diet are well established targets for intervention in prevention and management of T2DM. Given the association established between sleep and diabetes, there are studies exploring how sleep is related to physical activity and diet which adds to our knowledge of the complexity of their associations with diabetes.

1.5.1 Sleep and physical activity

The relationship of exercise and sleep has been explored for at least the last two decades and is thought to be bidirectional (122, 123). In a sample of 827 university students, assessment of sleep quality and physical activity surveyed annually over three years found sleep quality indirectly predicted increased physical activity over time and vice versa (124). Similar bidirectional relationships were found in middle age adults who were periodically surveyed over a 2 year period (125). This bidirectionality was also seen in longitudinal analysis of a mean of 6.9 years on 38601 United Kingdom biobank participants. Those who had poorer sleep patterns at baseline had higher odds (1.24 -1.65 OR) of physical inactivity at follow up. Conversely physical inactivity at baseline and reducing physical inactivity over time resulted in higher odds of poor sleep at follow up (126).

Mechanisms discussed for this bidirectionality suggest that acute or repeated physical activity increases total sleep time by decreasing insulin resistance and the concentration of inflammatory markers, better regulation of circadian rhythm and release of brain derived neurotrophic factors. Sleep deprivation can affect physical activity by increasing cortisol concentration, decreasing growth hormone and prolactin concentration and stimulating inflammatory markers (127).

Experimentally restricted sleep in 18 patients with history of type 2 diabetes was performed in a crossover study between eight and a half hours or five and a half hours of sleep. When time in bed was reduced, total activity reduced by 31%, and reduction in moderate and vigorous physical activity (MVPA) time decreased by 24%. This effects was seen more in regular exercisers (128). Mah et al. investigated the effect of 5-7 weeks of sleep extension on the athletic performance in eleven healthy students in a University basketball team. The mean baseline sleep duration was 470.0 +/- 65.9 minutes and increased to 624.2 +/- 68.4 minutes. Following sleep extension, reaction times improved, fasters sprint times recorded, shooting accuracy improved and daytime sleepiness decreased (129).

Studies on exercise and sleep vary in the time period over which they assessed participants from days to weeks which reflects the acute and chronic effects of exercise on sleep respectively with variable results. Sleep and physical activity were measured over 7 days by accelerometry in 330 young adult women and found that those who woke up later and slept longer had less MVPA throughout the day (130). Wu et al. reviewed sleep quality in 365 primiparous women post-partum with PSQI and triaxial wrist accelerometer for seven days (131). Sleep quality was not found to be associated with 24-hour physical activity. In another study, 112 postmenopausal Iranian women equipped with a pedometer had improved sleep quality, latency, duration, efficiency and daytime dysfunction after increasing their walking distance by 500 steps per week for 12 weeks (132). A meta-

analysis of daily associations between exercise and sleep showed that sleep quality, sleep efficiency and wake after sleep onset was associated with physical activity however the associations were small and varied in direction (133). A meta-analysis was conducted on 41 studies on the effects of acute exercise and 25 studies on regular exercise with the former predominantly within participant designs and the latter randomised controlled trials (RCTs). The effects of acute and regular exercise on sleep were both positive however with they were small effects. Acute exercise improved total sleep time, deep sleep, sleep onset latency and sleep efficiency and wake time after onset. Regular exercise benefited total sleep time, sleep efficiency, sleep onset latency and sleep quality as assessed by PQSI (134). These small effects might be moderated by the variation in exercise protocols, and tendency to study changes in cohorts with good sleepers (135).

Wang et al. explored the effect of physical activity intensity on sleep quality in 14 studies and concluded that moderate physical activity seemed to be more effective than vigorous activity in improving sleep quality. However there were only 2 studies exploring vigorous activity in this review one of which was aimed at assessing how late night vigorous exercise affected sleep quality (136).

Although sleep has been shown to be associated with physical activity in a bidirectional fashion there is evidence that timing of physical activity may be a crucial factor to consider. Exercise in the evening risks negatively impacting sleep by increasing arousal, affecting sleep hygiene and stimulating the autonomic nervous system. Yamanaka et al. (137) experimentally explored the effects of exercise in the morning or evening on circadian rhythm, core body temperature, sleep stages and heart rate variability in 22 healthy young males over 4 consecutive days. Morning exercise enhanced parasympathetic activity whilst night exercise enhanced sympathetic activity as suggested by heart rate in nocturnal sleep. Sleep stages 1 and 2 decreased by 13% without exercise and REM sleep decreased by 10.5% after evening exercise. Alley et al. (138) compared the effects of timing of resistance exercising on sleep found that exercise results in less wake after sleep onset (WASO) time but timing of sleep did not statistically significantly impact sleep stages or nocturnal blood pressure. Stutz et al. (139) conducted a meta-analysis of 23 studies in this area and found that evening exercise did not alter total sleep time but increased REM latency and deep sleep and decreased stage 1 sleep suggesting perhaps more restorative sleep. A higher body temperature at bedtime and higher physical stress was associated with lower sleep efficiency and more wake after sleep onset. Therefore, vigorous evening exercise ending within one hour of bedtime may not be recommended which may be due to insufficient cardiovascular recovery, resulting in increased HR and blunted parasympathetic activity.

Promisingly, as a post primary treatment intervention, inactive breast cancer survivors were enrolled in physical activity intervention that included wearable technology assess sleep over 24 weeks and found that there were improvements in WASO and number of awakenings at 12 weeks. Within groups analysis found this improvement in sleep quality may be sustainable over a longer duration (140).

Overall, it appears that sleep quantity and quality have a reciprocal relationship with physical activity however these effects may only be modest. Other factors such as the type and intensity of exercise may also be important as well as avoiding exercise too close to sleep onset.

1.5.2 Sleep and diet

The importance of diet in diabetes management and the emerging association of the effect of sleep on diabetes raises the question on how sleep may be related to diet.

A study that randomised 27 participants to usual sleep or restricted them to two-thirds of normal found caloric consumption was significantly increased without increase in energy expenditure nor changes in circulating leptin or ghrelin levels (141). In a cross-sectional study of 459 women sleep was measured with actigraphy and sleep diaries and correlated against dietary nutrients derived from food questionnaires. This revealed that napping was significantly correlated with increased fat intake and sleep duration was also negatively associated with fat intake. This may in part account for the increased caloric intake seen in these circumstances (142). Increased snacking is another source of calories that is associated with short sleepers. When sleep was reduced by 122 +/- 25 minutes per night in 11 healthy volunteers, meal intake remained similar between short and longer bedtimes but sleep restriction was accompanied by an increased consumption of snacks with higher carbohydrate content particular in the hours from 7pm to 7am (143). Energy expenditure did not increase significantly. Similar findings were found in a cohort of 240 adolescents when comparing those with less than 8 hours weekday sleep duration to those with at least 8 hours sleep duration. A high proportion of calories was from fats, lower proportion from carbohydrates and 2.1 fold increased odds of consuming at least 475 calories from snacks (144).

The association between macronutrient profile and insomnia was explored in a cross-sectional analysis of 4435 Japanese non-shift workers. Macronutrient intake was assessed using a diet history questionnaire and insomnia symptoms such as difficulty initiating sleep, difficulty maintaining sleep and poor quality sleep were also self-reported. Low protein intake was associated with poor sleep quality and difficulty initiating sleep whereas higher protein intake and lower carbohydrate intake was associated with difficulty maintaining sleep (145). Another study examining sleep quality with dietary habits amongst 3,129 female workers found poor sleep quality was associated with poorer eating habits including lower intake of vegetables and fish, higher intake of carbohydrates, confectionary, noodles, energy drinks and sugar -sweetened beverages. Poor sleep quality was also associated with skipping breakfast and eating irregularly (146). Using similar measures in 495 participants, sleep onset latency >60 minutes has been associated higher intakes of food by weight and energy and lower intakes of wholegrain. Greater insomnia severity was also associated with higher intakes of food by weight and energy but also lower total and unsaturated fats (147).

The Mediterranean diet which is characterised by high consumptions of plant-based foods and whole grains, moderation of fish and increase in olive oil is generally considered to be healthy. To review this, 1596 adults who were at least 60 years of age were assessed on their degree of adherence to a

Mediterranean diet against sleep quality. Those in the highest tertile of adherence to a Mediterranean diet were less likely to have changed their sleep duration after a median follow up of 2.8 years and were at lower risk of poor sleep quality (148). Similar findings were produced when studying 432 women in a prospective cohort study where better compliance with a Mediterranean diet was associated with better sleep quality, higher sleep efficiency and fewer sleep disturbances. Fruit and vegetable consumption were predictive of these same sleep characteristics. Higher legume intake predicted better sleep efficiency (149).

Considering the association between poor sleep and diet, a 4-week randomised feasibility study was performed on 42 participants to assess sleep extension on dietary intake. Sleep extension reduced the intake of free sugar, fat and carbohydrates (150).

Dietary carbohydrates are thought to increase the plasma concentration of tryptophan which is a precursor of serotonin, a sleep inducing hormone (151). Therefore it was investigated how different glycaemic index (GI) carbohydrates affected sleep in twelve healthy volunteers (152). They found a significant reduction in mean sleep onset latency with high GI compared with low GI meals consumed 4 hours before bedtime. A high GI meal 4 hours before bedtime also showed shorter sleep onset latency compared to the same meal one hours before bedtime. A randomised double-blind trial was conducted on 10 young males that explored the effect of a high GI meal against a low GI meal following sprint interval training on the sleep parameters that evening and following day's training. Total sleep time and sleep efficiency were greater with a high GI meal and sleep latency was shortened four-fold with visual reaction time also decreasing by 8.9%. Jumping ability and aerobic endurance performance was not affected (153).

Given the associations established between macronutrient intake and sleep quality, by manipulating the composition of isocaloric diets it was shown that a high carbohydrate low fat diet was associated with decrease slow wave sleep compared to normal diet or low carbohydrate high fat diet. The high carbohydrate low fat diet and low carbohydrate high fat diet were associated with more rapid eye movement sleep compared to normal diet (154). It is thought that cholecystokinin which is released from the duodenum in the presence of lipids and proteins also causes sedation. Following high carbohydrate low fat meals and low carbohydrate high fats meals, it was found that subjects felt sleepier after the latter meal with significantly higher cholecystokinin levels (155). Another study which varied the diets of their 44 participants in a cross over designs found that higher carbohydrate diets were associated with a lower sleep onset latency and high protein diet decreased number of wake episodes (156) .

Alongside these studies that explore how dietary contents may influence the hormones involved in sleep, there is limited evidence that specific food may promote sleep via neurotransmitters and hormone that promote sleep. Subjects who consumed 2 kiwifruits, which naturally contain serotonin, 1 hour before bed for 4 weeks showed improved sleep quality scores, waking time after sleep onset, sleep onset latency, total sleep time and sleep efficiency (157). Tart cherry juice, which reportedly has high levels of melatonin, was administered to 20 volunteers in a randomised, placebo-controlled

crossover study. The cherry juice group showed significant increase in time in bed, total sleep time and sleep efficiency (158).

1.6 Barriers to prevention

Despite evidence to suggest that diabetes can be prevented with lifestyle modifications, successful implementation of these measures can be difficult in practice. Although maternal lifestyle behaviours are more readily modified during pregnancy to benefit the child, following delivery this is often not maintained. Barriers to this include tiredness, childcare demands early in the post- natal period as well as work and family commitment later on (159, 160). In a study performed by Kim et.al examining perception of risk of future diabetes, 90% of women recognised that GDM was a risk for T2DM however only 16% believe they themselves had a high risk of developing T2DM. This increased to 39% when estimating risk if they maintained their current lifestyle (161). In addition social supports, financial constraints and personal preferences influenced postpartum behaviour (162, 163). A study exploring barriers to a healthy lifestyle in women with previous GDM found that timing, reiteration and cultural competence of health information can be a barrier (164, 165). These findings suggest that to increase maintenance of healthy lifestyle behaviours requires increased education with reinforcement and consistency that is affordable, adaptive and accessible.

1.7 Use of health technology

mHealth refers to mobile technologies, including mobile phones, wearing monitoring devices, digital health assistance and other wireless devices to support and enhance public health practice (166). The use of mobile phone devices has increased exponentially over recent years. According to the international telecommunications union, 93% of the world has access to a mobile broadband network with an estimated 105 mobile cellular subscriptions per 100 inhabitants in 2020. 88% of Australian population owns a mobile phone (167). Short message service (SMS) or text messages are frequently used. Their use for interventions come at relatively low cost and can have a wide reach. They allow for effective health communication with the ability to tailor and personalize messages and make them interactive. Because of the low cost, ubiquity and accessibility, frequent reinforcement, mobility, mobile phone based interventions have been trialed to address a variety of health issues including cancer screening, smoking cessation, physical activity, medication adherence and diabetes (168).

There have been studies that explored the efficacy of lifestyle directed text messaging interventions to improve glycemic control in diabetics with modest results. The DTEXT study was a randomized controlled trial using text message intervention over a 6-month period on 395 adults with T2DM and a Hba1c of at least 7.0%. There was no improvement seen in Hba1c at 3 months or 6 months. There was however significant improvement in nutritional aspects with increased self-reported consumption of vegetables and fruit and less discretionary sweets (169). Text to Move (TTM) was a randomized

controlled trial conducted on 126 patients with T2DM to improve their physical activity. It incorporated physical activity monitoring and coaching into text messages to help compared to an active control arm that received only pedometers. They found that step counts were higher in the intervention group at 3 and 4 months but there was no significant difference at 6 months. There was no significant decrease in Hba1c (170). A meta-analysis of 11 RCTs with 1720 participants with interventions using mobile text messaging addressing diet and physical activity in people with T2DM found 5 studies showing significant improvement in Hba1c with remaining studies showing trends to improvement. Overall, there was a significant reduction in Hba1c of 0.38% (171).

There are limited trials that have utilized text messaging to target the at-risk population of women with GDM to prevent progression to T2DM. Cheung et al. therefore investigated the feasibility of using this tool as an alternative to the resource intense lifestyle interventions that have been shown to prevent T2DM. The 6-month pilot study was conducted on 60 women and incorporated customized text messages focusing on lifestyle changes in conjunction with an activity monitor. There was a trend to improvements in diet, increased physical activity and weight loss however significant improvements in dysglycaemia remain to be seen (172).

Text message interventions are also thought to address the economic burden of chronic diseases. The TEXT ME randomized trial used text messages to support and motivate lifestyle changes in adults with coronary heart disease. Low-density lipoprotein cholesterol, systolic blood pressure and BMI were lower at 6 months (173). They estimated the cost effectiveness of such a preventative program of $10.56 million savings from few myocardial infarction, fewer strokes, and improved quality of life (174). Wong et al. investigated the cost -effectiveness of SMS intervention to prevent T2DM in participants with IGT. Using data from previous epidemiological studies and clinical trials, a Markov model was developed found a savings of 118.39 USD per subject over 2 years, increased to 1020.35 USD in the lifetime model (175).

Another benefit of text messages use as a form of mHealth is their accessibility to the general population. Nelson et al. explored engagement in a 12-month text message intervention that supported self- care and medication adherence in 248 patients with diabetes. The median response rate to interactive texts was 91% over 12 months. Nearly half of patient continued text messages for the latter 6 months. Those who discontinued text early reports that text messages and improved their routines sufficiently to not require further texts (176).

1.8 Wearable technologies and monitors

Sleep duration can be measured through a myriad of approaches including self-reported questionnaires, polysomnography and actigraphy. Although they are validated measures, the former tends to be more subjective but able to be conducted amongst larger cohorts for longer time periods that the latter two which are more objective. Technology advances have not only provided an

alternative method of delivering healthcare interventions such as via text messages but the emergence of wearable health technology. Consumer wearable health devices have a variety of features that can include physiological data such as heart rate and sleep patterns as well as physical activity such as steps, distance walked and intensity of physical activity. They are also able to provide feedback, goals and connect to social platforms to improve engagement. The increasing availability and uptake of these technologies by the public allows data collection on these health physiological and activity markers to be obtain on a larger scale in terms of number of people and duration. Areas where wearable technologies are being explored include cardiac monitoring, falls detection and prevention, physical activity, and continuous glucose monitoring in diabetes.

One of the main considerations when employing these novel technologies particularly for research purposes is their validity and accuracy. Factors that influence validity include where sensor is worn, light emitting diode (LED) colour and penetration as well as the algorithm used to process this biodata and output it to the user (177). There are multiple companies producing these devices with data derived from a variety of permutations of sensors and formulas that aren't transparent to the consumer.

Attempting to address the wide variety of devices now available, a systematic review comprising of 169 studies with 5934 participants examined FitBIt, Garmin, Apple, Polar, Misfit, Withings, Samsung, and Zioami. They compared these devices to references standard criterion measures such as accelerometry, electrocardiography and indirect calorimetry. In regard to step count in controlled conditions in particular, the was an overall tendency for underestimation of steps across all devices(mean -9%). This was particularly seen with Withings and Misfit wearables whilst Apple and Samsung devices had less variability although they also had fewer studies. However, in free-living conditions the steps were overestimated (mean 3%). Despite strong interdevice reliability for step count, intradevice comparisons showed significant variability within the same device for steps for Fitbit Charge HR, Fitbit Surge, Fitbit Zip, and Garmin Vivofit. (178).

Consumer sleep tracking devices were compared against the gold standard for research laboratories, polysomnography and the standard for mobile sleep assessment, actigraphy in 34 young healthy adults. They assessed four wearable devices which included Fatigue Science Readiband, Fitbit Alta HR, Garmin Fenix 5S and Garmin Vivosmart 3 and three nonwearable devices. Most of the devices performed as well or better than actigraphy on sleep/wake measures however the Garmin devices were worse. Garmin devices tended to overestimate total sleep time and underestimate wake after sleep onset and the Fitbit Alta HR underestimated sleep onset latency. Detecting sleep stages was inconsistent and performance of the devices was worse on nights with more disrupted sleep(179). A systematic review of the accuracy of Fitbit Models in assessing sleep compared to polysomnography, found that more recent generation models that integrate heart rate variability and body movement to assess sleep stages performed better than earlier generation models that only utilise body movement. Non sleep staging models overestimated total sleep time and sleep efficiency and underestimate

wake after sleep onset with no significant different in sleep onset latency. Sleep staging Fitbit models showed no difference in WASO, TST and SE but underestimated SOL (180).

Aside from using technologies for research purposes and to obtain population level measurement of data, it has been shown that consumer wearable activity trackers invoke behaviour change such as increased physical activity. This can translate into beneficial effects on health outcomes and therefore could be utilised as an adjunct to lifestyle interventions (181, 182).

Comparison of the use of a pedometer that tracks steps against an activity monitor that was able to display steps and exercise intensity for physical activity was performed on subjects with T2DM (183) . In their cohort on 187 subjects, there was a significantly greater reduction in Hba1c in the activity monitor group at 2 months however this effect weakened and was non-significant at 6 months. This suggests that perhaps the ability of the activity monitor to provide feedback resulted in increased motivation to reach target step and activity goal. However despite this, less than 40% of both groups (37.9% activity monitor and 25% pedometer) continued at least 80% of the exercise therapy beyond six months, suggesting that effects were greatest with the novelty of the monitor but ongoing motivators are required (183). This may be an opportunity to integrate other mHealth technologies such as text messaging to increase the durability of the use of activity monitors. Despite these promising findings, this was not supported by the meta-analysis conducted which included twelve trials of 1458 participants. It included both accelerometers and pedometers and showed they increased overall physical activity however there was no significant difference in Hba1c, BMI, blood pressure or lipid profile (184). Consequently, further studies may need to determine in which cohorts and for what purposes these increasingly available technologies should be implemented.

1.9 Aims

Although there is mounting evidence about the influence of sleep on diabetes, less is known regarding this same relationship in GDM. Both during pregnancy and postpartum, physical activity and diet are the focus of lifestyle modification however it is unclear if sleep is another factor that should be targeted. In the following studies, we assess the effect of sleep and physical activity on glycaemic control in GDM and the effect of sleep on physical activity postpartum. Activity monitors are increasing in popularity and uptake and can be used as tool to encourage lifestyle modification whilst simultaneously collecting data. Wrist worn activity monitors are used in these studies to assist in data collection and we indirectly assess their viability as a research tool.

Chapter 2: Methods

Smart Mums with Smart Phones 2 (SMs2) is a randomised controlled trial of postpartum text messaging support for women with GDM. It is a multicentre study that recruited 176 women from 3 Sydney metropolitan hospitals; Westmead, Blacktown and Campbelltown Hospitals. It incorporates the use of a wrist worn activity monitor and integrates the data captured by this device to customize a structured lifestyle modification program delivered via text messages. This study aims to evaluate whether this intervention that has been augmented by modern technologies improves diabetes risk factors, namely weight, physical activity (PA) and diet in postpartum women with GDM.

Recruitment for the study occurred from January to August 2021. Participants underwent randomisation at delivery and were followed up until 12 months postpartum. Therefore, at the time of completion of this thesis, SMs remains ongoing and unblinding of randomisation was not available for analysis. However data captured at baseline, during pregnancy and in the first few months postpartum for women recruited earlier were available and utilised as substudies in the following chapters. These include the relationship between physical activity and sleep and blood glucose levels during pregnancy, the effect of sleep on physical activity postpartum and the effect of a COVID lockdown on physical activity postpartum.

The following methodology describes my involvement in the study design, recruitment, implementation and follow up of SMs2 that allowed for the completion of my substudies.

2.1 Study protocol

SMs2 began recruitment of pregnant with GDM in January 2021. Participants were then randomised at birth to the lifestyle intervention with text message support or usual care and followed up intermittently with self-completed evaluations up until 52 weeks postpartum (Figure 2.)

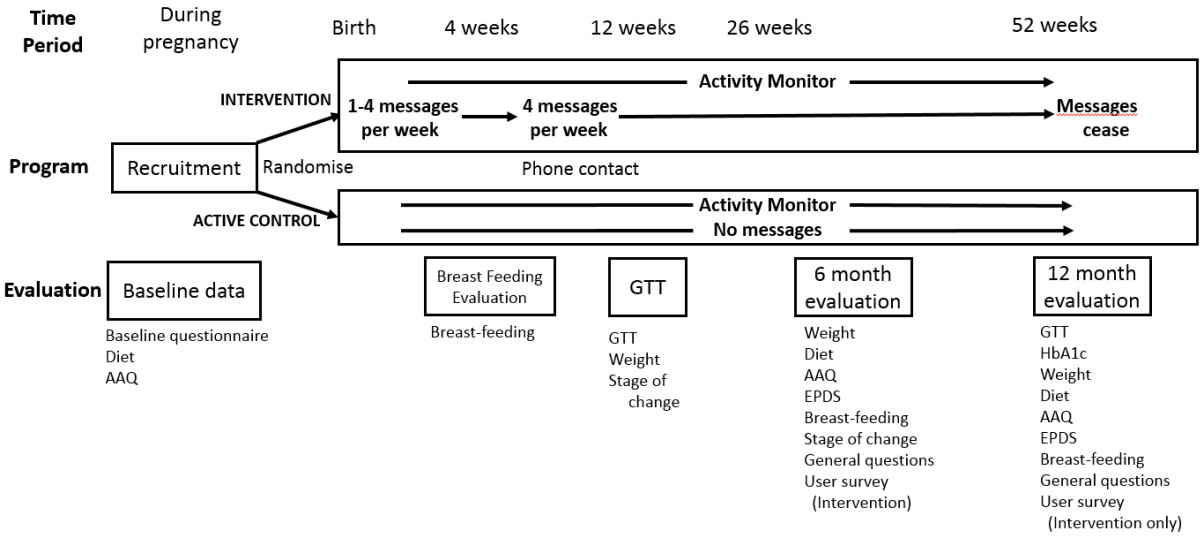

Figure 2. Protocol for Participants in SMs2

2.2 Recruitment

Pregnant women diagnosed with GDM who had a smart phone with internet access were invited to participate. Women were recruited during routine antenatal appointments. We also received referrals from the hospital's Diabetes Education and Ambulatory Care Centre (DEACC). All women who are diagnosed with GDM are referred to DEACC for a group education session and provided with a glucose meter and glucose testing strips. We screened the online antenatal records of these patients to confirm their eligibility by reviewing the women's past medical history, OGTT result and fetal health (Table 3.). The online records of patients attending obstetric and diabetes in pregnancy clinics were reviewed in a similar way. We were able use the online booking system to determine the next appointment for these women and tracked these in a spreadsheet.

These women were then approached by the study coordinator of the respective site at their antenatal clinic or diabetes education visits where the objectives of the study were discussed, and exclusion and inclusion criteria were reviewed prior obtaining informed consent. As these discussions were conducted around existing appointments times, patient files were tagged and monitored on check in systems on appointment days so we could speak to women before, between and after their appointments. Most women were recruited at the initial encounter however some women needed time to consider committing to participation and so were followed up at later appointments for further discussions.

Inclusion criteria

- Diagnosis of GDM on OGTT in accordance with local criteria
  o At Westmead and Blacktown Hospital
  ▪ Fasting glucose ≥5.5mmol/L OR
  ▪ 2-hour glucose level following 75g oral glucose load ≥7.0mmol/L
  o At Campbelltown Hospital
  ▪ Fasting glucose at least ≥5.1 OR
  ▪ 2-hour glucose level following 75g oral glucose load ≥10.0mmol/L
  ▪ 2-hour glucose level following 75g oral glucose load ≥8.5mmol/L
- Owns a smart phone with internet access
- Age > 18 years

Exclusion Criteria
- Already using stand-alone activity monitor (allowing for apply watch and phone activity monitor if agreeable to use study activity monitor) - Has pre-existing diabetes - GTT result in "Diabetes Mellitus in pregnancy" range in first 20 weeks of pregnancy (fasting glucose ≥7.0 mmol/L or 2-hour glucose ≥11.1 mmol/L - On medications which affect glucose metabolism (e.g. metformin, steroids, antipsychotics) - Twin/multiple pregnancy - Significant fetal disorder likely to require increased care in first 6 months post-partum - Planning to spend >1 month overseas within 6 months post-partum - Unable to walk regularly due to physical limitations

Table 3. Inclusion and Exclusion Criteria Smart Mums with Smart Phones 2

2.3 Baseline Data collection

At the initial encounter, contact information was obtained and women completed a baseline questionnaire that included demographics, medical and obstetric history, pre-pregnancy dietary, activity, and sleep habits (Table 4.). The dietary and activity questions were derived from validated questionnaires.

Eligibility checklist was reviewed with the participant before written informed consent was obtained. Data was also collected from medical records regarding the participants' GTT result and booking in information including, height, weight and BMI. All data was collected on paper forms and subsequently transcribed into REDCap, a secure online database management system. Online records were printed and stored with original paper forms and source documents in a secured office. On the next Friday after recruitment, women were sent an automated welcome message with a link to confirm the correct phone number was entered into redcap before further messages are sent postpartum.

Demographics	**Age at expected date of delivery**
	Country of birth and ethnicity
	Marital status
	Education level
	Employment
Obstetric History	Gravidy
	Parity
	Estimated date of delivery
	Booking in date, weight, height
	Previous breastfeeding
Medical History	Previous GDM
	Family history of diabetes
	Polycystic ovarian syndrome, depression, high blood pressure, high cholesterol
Smoking Status	
Alcohol Intake	
Pre-pregnancy Activity	Walking
	Moderate physical activity
	Vigorous gardening
	Vigorous physical activity
Pre-pregnancy Diet	Vegetarian / vegan diet
	Fruit and vegetable intake
	Sugary drinks and fruit juice
	Discretionary foods: takeaway, biscuits, cakes, icecream, chips, chocolates, lollies
Sleep	Normal hours of sleep prior to pregnancy
	Days of perceived sleep insufficiency in last month
OGTT	Date of OGTT
	Fasting
	1-hour glucose
	2-hour glucose

Table 4. Baseline Data Collected

2.4 Garmin Setup

Women were set up with an activity monitor (Garmin Vivofit4®) in the latter half of their pregnancy to allow women to experience the devices and troubleshoot any issues while they were still making regular hospital visits to attend clinic appointments. Study coordinators assisted in the pairing of activity monitors to the smart phone application as well as demonstrating synchronization of these devices. Information on use of the monitor was provided verbally and in a written hand out. Syncing of the activity monitor with the participants phone was also monitored from this early stage to maintain engagement and establish habitual use of the device.

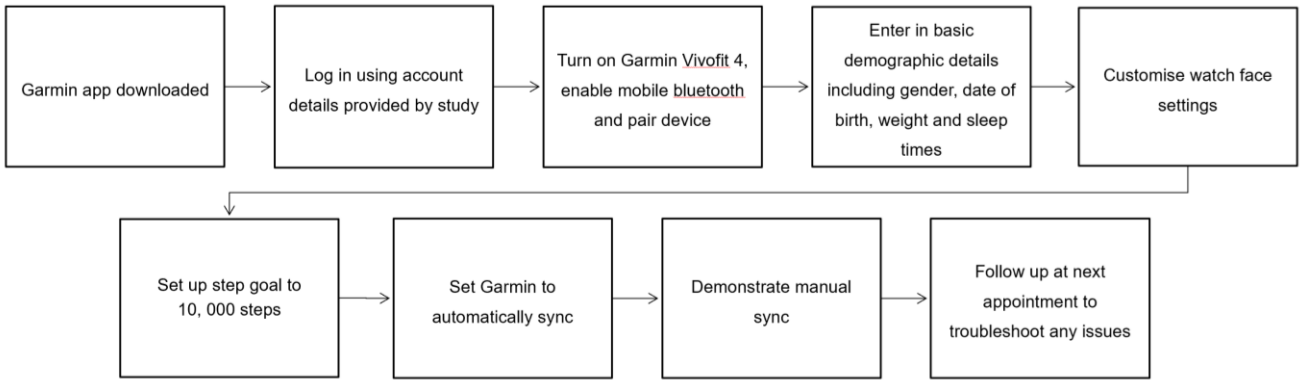

Figure 3. Garmin Set Up Process

2.5 Garmin issues and troubleshooting

During the set-up process we found several issues and solutions were found.

Problem	Solution
Garmin app could not be downloaded on all phone operating systems	Trial an older spare phone OR Trial partner's phone
Garmin app required later versions of the android or iPhone operating systems	Participant to download latest operating system at home then set up Garmin device at next appointment following this
Prolonged time require to download Garmin app	Participant to download Garmin app at home then set up Garmin device at next appointment following this
Complex autogenerated account names and passwords **Password failure when curly bracket included**	Study team contacted to provide new account name OR Trial a difference device with a different account name and password
Difficult pairing Garmin device with phone	Confirm Bluetooth on OR Reinstall Garmin application OR Restart phone OR Trial a difference device with a different account name and password

Table 5. Troubleshooting Problems in Garmin Set Up

Data uploads were reviewed to assess if women were wearing their devices and regularly syncing. At subsequent appointments women were encouraged to continue wearing their devices and any issues were troubleshooted.

Problem	Solution
Rashes from silicone wristband	Recommended wearing the band slightly loose to for breathability Intermittent washing the band to clean off any sweat or debris Keep device in pocket (allows for some tracking but less accurate)
Difficulty wearing device due to pregnancy related weight gain	Larger wristbands provided
Limited data obtained since Garmin set up	Reminded how to manually sync their devices with the mobile application.

Table 6. Troubleshooting Problems Related to Garmin Use

2.6 Postpartum messages and surveys

Lifestyle intervention was delivered via mobile text messages that began postpartum. Some text messages were based on the validated messages used in the TEXT ME trial (173). Additional messages appropriate for use in young mothers according to local and national guidelines were developed, with additional input from experts in the fields of diabetes, nutrition, physical activity, health promotion, and lactation. The themes of the text messages were initially based on newborn health and motherhood before progressing to supporting physical activity, health eating and diabetes prevention. Text messages were also integrated with the activity monitors to further customise text messages with adaptive weekly step goals based on the previous weeks data. Subjects were then followed up via self-reported questionnaires that were completed remotely via a link attached to a text message at 4 weeks, 12 weeks, 26 weeks and 52 weeks postpartum. These surveys were conducted periodically to assess breastfeeding status, weight changes, physical activity, dietary habits and completion of OGTT. Subjects were contacted at 14 weeks postpartum to follow up 3-month survey, OGTT results and weight and then again at 6 months to ensure completion of 6-month survey and weight. Data from these surveys were stored on the online database REDCap.

2.7 Garmin Data

The Garmin Vivofit 4 was used in SMs2 however there were no financial arrangements or conflicts of interest between any of the investigators and the Garmin technology company. It featured a watch face that displayed the time, as well as physical activity targets such as steps taken, distance travelled and intensity minutes. It boasted a 1-year battery life, bypassing the need for regular charging. There were also extended features such as timers and stopwatches. The Garmin Connect mobile phone application displayed number of steps taken, intensity minutes and sleep duration.

Women enrolled in Smart Mums 2 had their Garmin Vivofit set up in their 3rd trimester. Those who wore their device and synced them to their phone had step and sleep data readily available. This data could be accessed by using coding to extract it from the server with the assistance of a data scientist. A log was kept of all accounts and passwords allowing researchers to manually access information stored online on the Garmin Connect application.

2.7.1 Sleep

The Garmin application sleep data shows sleep onset, duration, wake time, and the level of sleep. The user can enter in their normal sleep time into the setup of their Garmin connect app to facilitate the recording of this information. The levels of sleep include deep, light and awake where differentiation is reliant on the degree of movement given the Garmin Vivofit does not have a heart rate monitor to help determine sleep stages. Despite the lack of heart rate monitor, a study exploring the validity of several wearable activity trackers including the Garmin Vivofit compared with self-reported sleep log with a significant correlation with an r value of 0.8 (185). This device is more affordable than one with heart rate monitoring improving its scalability and achieving the primary aims of Smart Mums 2 did not require measurement of sleep.

This information is presented in the application as a user-friendly graph that gives a visual representation of the overall architecture of one night's sleep (Figure 4). Sleep onset and wake time can be manually manipulated retrospectively on the Garmin Connect application. Garmin Vivofit records physical activity in 15 minutely epochs with varying proportion of time classified as sedentary, active or highly active. The physical activity data is presented to the user on the app as a daily step count and weekly intensity minutes. Through trial of these devices several limitations in the algorithms used to determine sleep and physical activities patterns were identified.

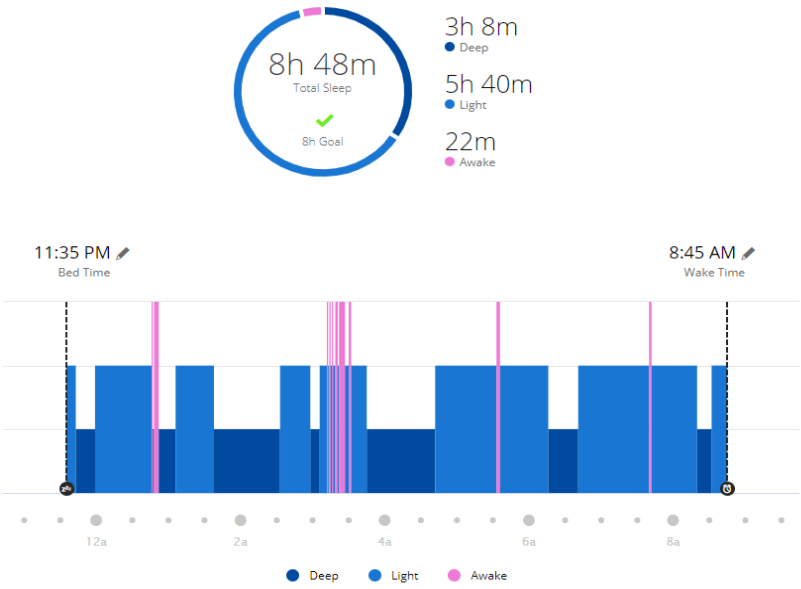

Figure 4. Normal Sleep Pattern as Displayed in Garmin Connect Mobile Application

2.7.1.1 Garmin device removal during sleep

If the Garmin was taken off during normal sleeping hours, the lack of movement is interpreted as deep sleep. This can be easily distinguished as there is deviation from the variations in normal sleep architecture and is homogenously represented as deep sleep >90% of the (Figure 5). When the Garmin is removed during awake hours, this is reported as sedentary activity with no steps recorded.

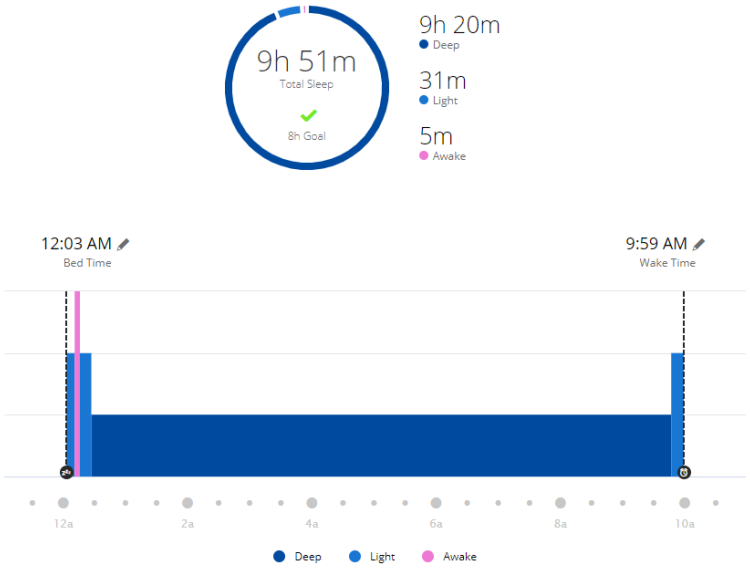

Figure 5. Sleep Pattern Where Garmin Likely Not Worn

2.7.1.2 Missing daytime sleep data

Physical activity epochs and sleep data are recorded with no overlapping times such that physical activity is only recorded when sleep ends. As a result, naps that occur during the day are not registered by the Garmin Vivofit as additional sleep hours. Instead, this is represented as a sedentary period in the physical activity epochs. However, if sleep times are retrospectively manipulated to include the nap period, the nap will be displayed. More than one sleep period cannot be displayed and therefore to have both the night sleep and nap requires a long sleep duration that includes all these times with an awake interval during this sleep.

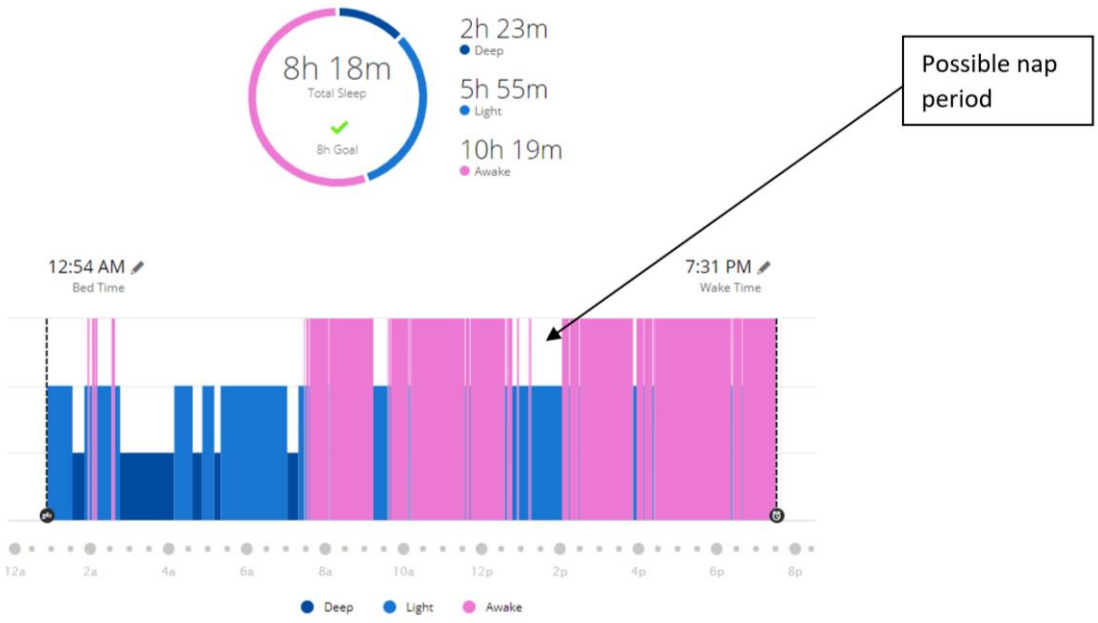

Figure 6. Wake Time Retrospectively Manipulated to Reveal Possible Day Time Nap

Sleep \ Epoch	Sedentary	Active	Very active
Awake	Awake during sleep OR Sedentary during day *	Active	Very active
Light	Nap	Active	Very active
Deep	Garmin removed OR deep sleep **	Active	Very active

*Differentiated by surrounding level of activity

** Differentiated by if associated normal sleep pattern

Figure 7. Interpretation of Garmin Vivofit Activity Epochs

Given this, it is difficult to determine whether prolonged sedentary periods are representative of naps, sedentary physical activity or the user not wearing their device. In order to overcome this, we tried to obtain 24 hours epochs of concurrent sleep and physical activity data which could be cross referenced to obtain more accurate sleep information. However this was unsuccessful as sleep and physical activity data were recorded in exclusion of the other and therefore complete 24 hour data for both could not be obtained

2.7.2 Physical activity

Garmin step data for one day was a cumulative count over a 24-hour period from midnight. Garmin Vivofit does not have a heart rate monitor incorporated into the device, therefore step count relies on arm swing. This could result in overestimation if activities were performed that may mimic an arm swing without walking. Conversely, walking with static arm movement can result in underestimation. This could occur in the scenario of pram pushing or if the device is not being worn on the arm due to an adverse reaction. Furthermore, without heart rate tracking this device is unable to distinguish between sedentary activity or if it is simply not being worn. Consequently, in the following studies we excluded days where less than 1000 steps were taken in a day as this likely represented incomplete data capture.

Garmin determines intensity minutes either through metrics comparing current heart rate to resting heart rate or frequency of steps. The Garmin Vivofit lacks a heart rate sensor therefore only moderate intensity activity is tracked and not vigorous intensity activity. Given that vigorous intensity activity is credited with twice as much intensity minutes as moderate activity, this may underestimate the intensity minutes of users. The intensity minutes were organised in the Garmin files as sedentary, active and highly active minutes. Sedentary minutes corresponded to time spent with no steps and active was time spent with >1 step. No participants had highly active minutes recorded with this device because of the limitations in its tracking ability without a heart monitor. There is research to suggest that minutely step thresholds could be used as a proxy for exercise intensity (186). Theoretically these thresholds could be used to differentiate the physical activity data into moderate and vigorous intensity exercise. However, as the Garmin Vivofit operated on 15-minute physical activity epochs that were subdivided into the previously described activity minutes, we were unable to obtain minutely step data to be able to do this. Therefore, we used Garmin's interpretation of activity minutes to maintain consistency for analysis.

2.7.3 Data organisation

Data recorded by the Garmin Vivofit could be retrieved from the mobile or online application by the user. The data is also uploaded onto a server and stored in JavaScript Object Notation (JSON) format in text files with sleep and physical activity separated. This is a common data representation format that is used to transmit structured data between a server and web application. The data type that is supported includes strings (used to present text data), numbers, Booleans (true or false) and null. Arrays are also supported which are a list of ordered items from any of the previously mentioned data types surrounded by square brackets. Objects is an unordered set of key/value pairs. Keys are string text and values are any JSON supported data. The objects are surrounded by curly brackets, each key is followed by a colon and each pair is separated by a comma.

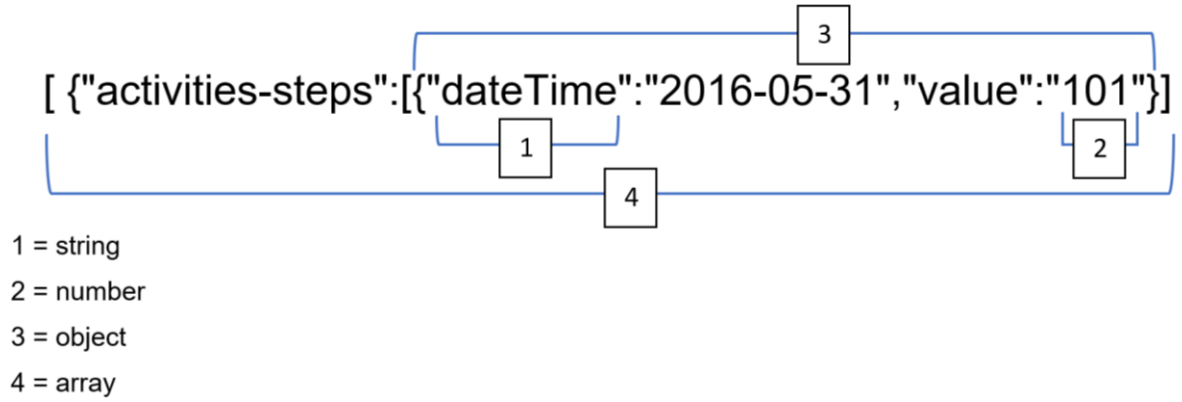

Figure 8. Labelled Example of JSON Activity Data

This JSON data is not presented in an easily accessible format for direct analysis. Given the large volume of data that is obtained in this way for several hundred days across multiple days, it needed to be processed and organised into a format more amenable to analysis. These JSON text files were converted into Microsoft Excel files with the assistance of a data scientist. Following this, data was organised by participant and date with corresponding sleep and physical activity prior to analysis.

Chapter 3: The effect of physical activity on glycaemic control in gestational diabetes

3.1 Introduction

Gestational diabetes has been shown to be associated with adverse perinatal outcomes in the short term and adverse metabolic outcomes in the long term for both mother and child (13, 18). Treatment of GDM through lifestyle modifications has been shown to improve these (27, 28),

Typically, initial management of GDM includes regular blood glucose (BG) monitoring and engaging in lifestyle changes prior to commencement of pharmacotherapy. Exercise is recommended for pregnant women and is also an important component of a non-pharmacological intervention in GDM. It has been shown that the addition of regular exercise to dietary advice can improve glycaemic control (187). These improvement can be seen with both aerobic and resistance exercise performed in supervised programs (188). Some studies have also shown that exercise can improve pregnancy outcomes such as decreased macrosomia and rates of caesarean section (189). Women who have GDM are required to achieve tight BG targets and although exercise has been shown to improve glycaemic control, few studies have explored the effect of physical activity on BG levels during pregnancy on a day-to-day basis.

Mobile health technologies which are being used to support lifestyle interventions include consumer worn devices that can track physiological data including physical activity. Their uptake is relative to their accessibility, convenience, ability to be personalised and relatively low cost but simultaneously they can also provide a larger volume of granular data over longer periods of time than other validated methods such as questionnaires or actigraphy.

In this study we utilized a wrist worn activity monitor to explore the relationship between physical activity and blood glucose levels in women with GDM.

3.2 Method (see Chapter 2)

3.2.1 Study Design and Population

This was a substudy of Smart Mums With Smart Phones 2 (SMs2), a randomised controlled trial of text messaging support for women after GDM at three metropolitan hospitals (190).

As each site had varying methods of reviewing, managing and archiving BG records, we were only able to include women from Westmead Hospital, a tertiary centre, where online records were maintained (Figure 9).

3.2.2 Variables

Baseline data included demographics, medical and family history, physical activity, dietary and sleep habits.

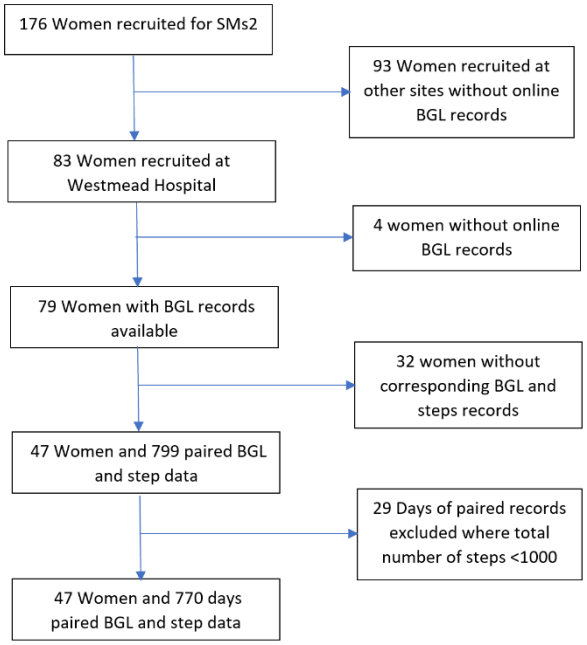

Figure 9. Selection of Study Population

Following diagnosis of GDM women attend a group education session with a diabetes nurse educator and dietitian. As part of routine gestational diabetes care, they are also provided with a glucose meter and women are taught to regularly check and record their fasting and 2-hour post prandial BGs. At Westmead Hospital, women aimed for target fasting BG is between 4.0 – 5.5 mmol/L and post prandial BG between 4.0 – 7.0 mmol/L. These are sent to a hospital email or brought to appointment on usually a 1-2 weekly basis for review by the endocrinology team or diabetes educators. After review, women may have lifestyle measure reinforced or if required clinicians may commence insulin on a individual case by case basis. Data was taken from multiple women across several days with up to four BG readings per day. This data was manually entered into a Microsoft Excel spreadsheet.

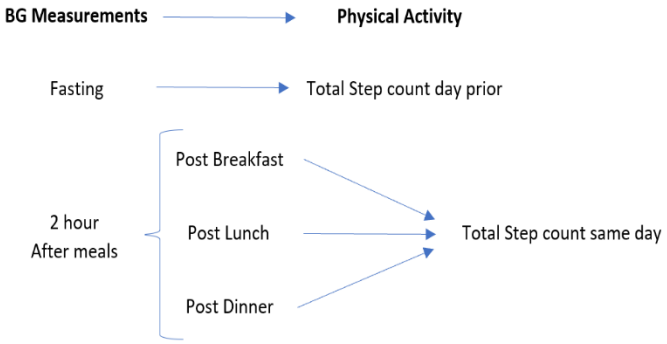

Figure 10. Pairing of Glycaemic Control and Physical Activity Data

Women are provided with a wrist-worn activity monitor (Garmin Vivofit 4®) in their third trimester. This monitor can track and display daily step count.

We collected daily step counts and BG records from days where there was corresponding data. Days where less than one thousand steps were taken were excluded as the device monitor was likely not worn for the entire day. Due to the potential confounding effect of insulin therapy, the data for women on and off insulin were examined separately.

3.2.3 Statistical Analysis

Data were analysed with R Program, version 4.1.0 (*R Core Team, Auckland, New Zealand*). Linear mixed effect models were used to determine the effect of total daily steps on glucose measurements. The effects of steps completed the day prior on the fasting BG the following day was examined, as well as the effect of steps on post prandial BGs on the same day. Step quantity was treated as a fixed effect and the study ID was included as a random effect in the model as multiple readings were obtained from

the same woman. Data are reported as mean ± standard deviation. Statistical significance was taken as a two–sided *p*–value <0.05.

3.3 Results

There were 47 women included in this study with 770 days of paired observations. The mean age at conception was 32.2 ± 4.1, ranging from 25 - 41 years old. Details summarising the demographics of the women included are described in Table 7.

	Group	% (N)	Mean	STD
Age at conception	25-29	31.9 (15)	32.2	4.1
	30-34	35.6 (16)		
	35-40	31.9 (15)		
	>40	2.1 (1)		
Pre pregnancy BMI	Underweight <18.5	0 (0)	27.4	5.3
	Normal 18.5 – 24.9	38.3 (18)		
	Overweight 25-29.9	31.9 (15)		
	Obese >30	29.8 (14)		
Ethnicity	Subcontinental	51.1 (24)		
	South East Asian	2.1 (1)		
	East Asian	4.3 (2)		
	Australian	2.1 (1)		
	European	6.4 (3)		
	Pacific Island	2.1 (1)		
	South American	2.1 (1)		
	Middle Eastern	19.1 (9)		
Education level	Year 10 School Certificate	8.5 (4)		
	Year 12 School Certificate	2.1 (1)		
	Technical and Further Education	17.0 (8)		
	University Undergraduate	38.3 (18)		
	University Postgraduate	35.6 (16)		
Previous GDM	No	68.1 (32)		
	Yes	31.9 (15)		
Family History of Diabetes	No	27.7 (13)		
	Yes	72.3 (34)		
Gravidy	1	36.2 (17)	2.4	1.5
	2-8	63.8 (30)		
Parity	0	42.6 (20)	0.8	0.8
	1-3	57.5 (27)		

Table 7. Demographics and Obstetric History of Women Included

The mean fasting glucose level for all data pairs was 5.0 ± 0.6 mmol/L, post breakfast BG 5.9 ± 1.0 mmol/L, post lunch 6.0 ± 1.0 mmol/L, post dinner BG 6.4 ± 0.9 mmol/L and mean post prandial BG 6.1 ± 0.7 mmol/L. The mean steps taken on the day prior to the measured fasting BG was 4455 ± 251 and mean steps taken on the same day was 4447.0 ± 2481.2. Thirty-five women required insulin

during the period of time where corresponding steps and BG records were available and their mean total daily dose (TDD) of insulin was 35 ± 46 IU.

There were 13 women who did not require insulin during the days where they have paired BG and step data available. The mean BGs and steps for each group are summarised in Table 8.

	All women (n=47)	**Women not on insulin (n=13)**	**Women on Insulin (n=34)**
	Mean BG ± STD (mmol/L)	Mean BG ± STD (mmol/L)	Mean BG ± STD (mmol/L)
Fasting	5.0 ± 0.6	4.8 ± 0.4	5.1 ± 0.6
Post breakfast	5.9 ± 1.0	5.3 ± 0.7	6.1 ± 1.0
Post lunch	6.0 ± 1.0	5.6 ± 0.8	6.2 ± 1.0
Post dinner	6.4 ± 0.9	6.1 ± 0.8	6.5 ± 0.9
Mean post prandial	6.1 ± 0.7	5.6 ± 0.6	6.3 ± 0.6
Steps yesterday	4455 ± 25.18	5032 ± 2493	4250 ± 2498
Steps today	4447 ± 2481	4885 ± 2473	4284 ± 2467
Insulin TDD	35 ± 46		

Table 8. Mean Glucose Readings and Steps Counts for Days Where Paired Data Were Available for all Women Based on Insulin Use

There was no significant relationship between steps taken on the previous day and fasting BG (-0.01mmol/L per 1000 steps, 95% CI -0.03 – 0.01, p=0.36). This was similar for post prandial BGs and steps taken on the same days however we observed a trend towards a reduction in the overall post prandial BG with increased steps (-0.02mmol/L per 1000 steps, 95% CI -0.04 – 0.00, p=0.07).

Legend

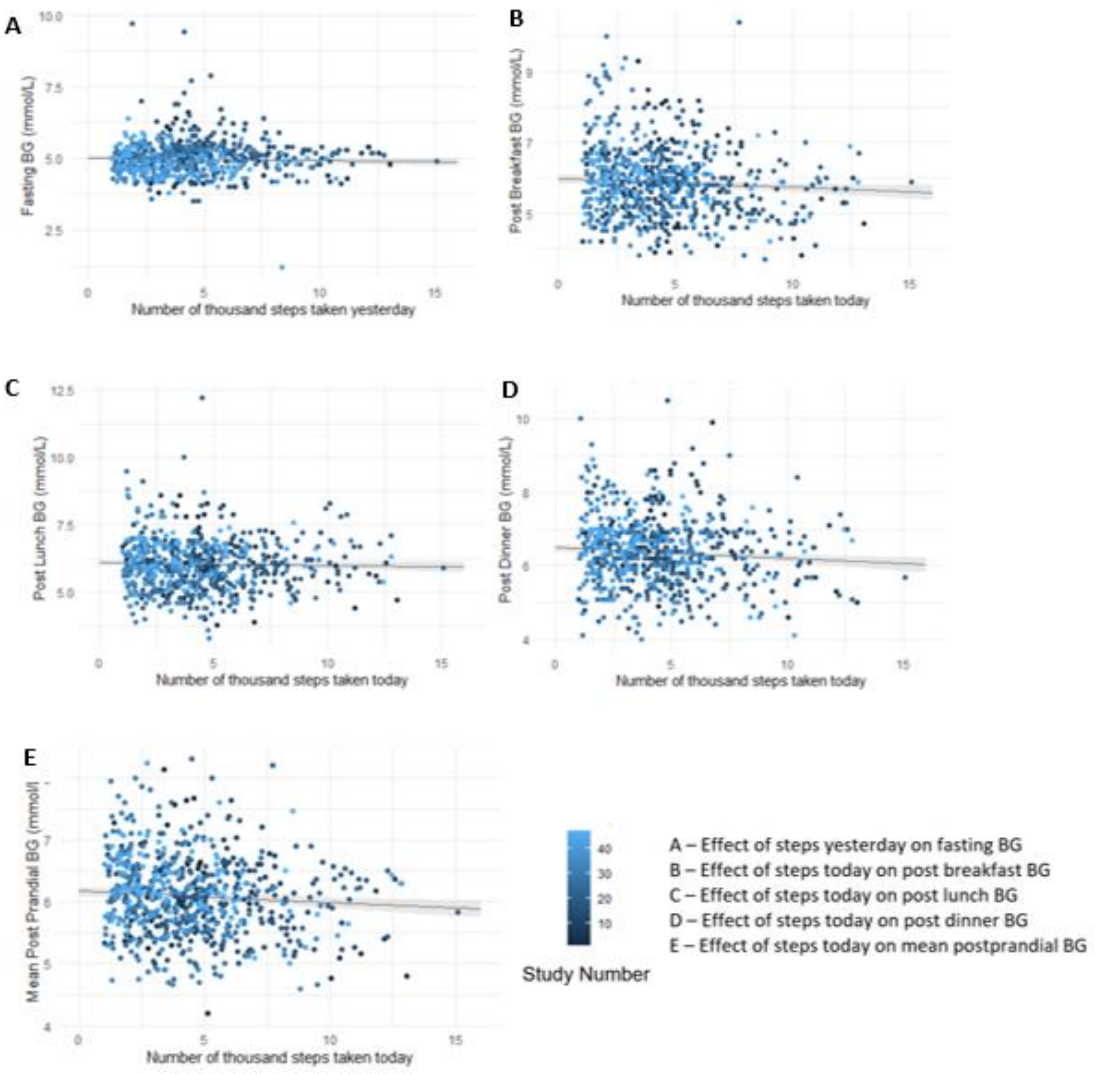

Figure 10. Change in Glucose Per 1000 Steps for all Women

	Women not on insulin (13)			Women on Insulin (34)		
Blood glucose levels (BG)	Estimated change in BG per 1000 steps (mmol/L)	(95% CI)	Linear Trend p-value	Estimated change in BG per 1000 steps (mmol/L)	(95% CI)	Linear Trend p-value
Fasting*	0.00	-0.01, 0.03	0.46	-0.01	-0.04, 0.01	0.33
Post Breakfast	0.02	-0.02, 0.07	0.32	-0.06	-0.10, -0.01	<0.01
Post Lunch	-0.04	-0.09, 0.01	0.15	-0.01	-0.06, 0.03	0.57
Post dinner	-0.07	-0.12, -0.02	<0.01	0.00	-0.05, 0.03	0.73
Mean post prandial	-0.04	-0.08, 0.00	0.07	-0.03	-0.06, 0.00	0.02

** Fasting glucose versus steps recorded on the previous day, all other measurements versus steps on the same day.*

Table 9. Change in Glucose Per 1000 Steps Between Insulin Groups

Women who were not on insulin showed a significant reduction in the BG after dinner of 0.1 mmol/L ($p<0.01$) for every 1000 steps taken on the same day. Women who were on insulin had a BG after breakfast that was significantly reduced by 0.1 mmol/L ($p<0.01$).

As the amount of walking a woman undertakes decreases in late pregnancy, and potentially there is an altered relationship between steps and glucose levels, we divided the data into 2 groups, before and after 36 weeks gestation, for further analysis. The mean daily steps taken prior to 36 weeks were 4427 ± 1998, and after 36 weeks it was 4189 ± 1799. When women were less than 36 weeks gestation, the mean post prandial glucose level improved by 0.1mmol/L for every 1000 steps taken ($p=0.04$). The highest post prandial effect was seen at dinner with 0.1mmol/L reduction in BG per 1000 steps ($p<0.001$). There was no relationship demonstrated between steps and BGs after 36 weeks gestations.

Women who were not on insulin showed a significant reduction in the BG after dinner of 0.07 mmol/L for every 1000 steps taken on the same day (95% CI -0.12 - -0.02, $p<0.01$). Women who were on insulin had a BG after breakfast that was significantly reduced by 0.06 mmol/L (95% CI -0.10 - -0.01, $p<0.01$).

As the amount of walking a woman undertakes decreases in late pregnancy, and potentially there is an altered relationship between steps and glucose levels, we divided the data into 2 groups, before and after 36 weeks gestation, for further analysis. The mean daily steps taken prior to 36 weeks were 4427 ± 1998, and after 36 weeks it was 4189 ± 1799. When women were less than 36 weeks gestation, the mean post prandial glucose level improved by 0.03mmol/L for every 1000 steps taken (95% CI -0.06 – 0.00, $p=0.04$). The highest post prandial effect was seen at dinner with 0.1mmol/L reduction in BG per 1000 steps (95% CI -0.01 – 0.03, $p<0.001$). There was no relationship demonstrated between steps and BGs after 36 weeks gestations.

	Observations <36 weeks gestation (384)			Observations ≥ 36 weeks gestation (386)		
Blood glucose levels (BG)	Estimated change in BG per 1000 steps (mmol/L)	(95% CI)	Linear Trend p-value	Estimated change in BG per 1000 steps (mmol/L)	(95% CI)	Linear Trend p-value
Fasting*	0.00	-0.02, 0.02	0.93	-0.28	-0.63, 0.07	0.12
Post Breakfast	-0.03	-0.08, 0.01	0.17	-0.14	-0.42, 0.12	0.29
Post Lunch	-0.01	-0.06, 0.03	0.6	-0.02	-0.25, 0.22	0.90
Post dinner	-0.07	-0.11, -0.03	<0.01	0.06	-0.19, 0.31	0.64
Mean post prandial	-0.03	-0.06, 0.00	0.04	-0.05	-0.46, 0.35	0.80

** Fasting glucose versus steps recorded on the previous day, all other measurements versus steps on the same day.*

Table 10. Change in Glucose Per 1000 Steps in Women Before and After 36 Weeks Gestation

3.4 Discussion

3.4.1 The relationship between exercise and glycaemic control

Obstetric and diabetes professional organisations recommend that pregnant women should participate in regular aerobic and strength conditioning exercise during pregnancy aiming to be active on most if not all days of week. Goals for duration of exercise is similar to that for non-pregnant women with 150 to 300 minutes of moderate exercise per week, the intensity of which is tailored to each individual (191). Physical activity has been shown to improve glucose control in part by acute effects of contraction-mediated glucose uptake into skeletal muscle (192).

In this study there was a trend towards an inverse relationship between physical activity and glycaemic control in pregnancy. However, the weak effect would not make this clinically significant unless the women were very active. In the subgroup of women who did not require insulin there was a significant effect of a 0.07mmol/L reduction in BG after dinner per 1000 steps. Although a 0.07mmol/L reduction in BG alone is not clinically significant, if the relationship is linear, and the woman is able to achieve the recommended 10, 000 daily steps this would amount to a 0.7 mmol/L drop in BG compared to a woman who was completely sedentary. This could then be clinically significant.

The improvement in blood glucose levels on average post prandially and in particular after dinner is also increased when the women were less than 36 weeks gestation. The effect of exercise at various gestational ages has not been compared to our knowledge. Our finding may just be a reflection of a reduction in the degree of mobility that women have towards the end of their pregnancy. If women walk less late in pregnancy it will be more difficult to discern an effect of activity on BG levels.

In one randomised controlled trial, 19 women were randomised to dietary advice with or without regular exercise for six weeks. There was an improvement in glycaemic parameters in the exercise group as evidenced by lower glycosylated haemoglobin, fasting glucose and 1 hour post prandial glucose (187) The most common type of physical activity that pregnant women engage is in walking as it can be integrated into busy schedules, is cost-free and does not require equipment (193). In a study of 200 women with GDM, those who were instructed to engage in 20 minutes of brisk walking everyday had reductions in post prandial glucose, glycosylated haemoglobin, c-reactive protein, triglycerides and maternal and neonatal complications (194). Although studies have shown that exercise can improve glycaemic control in women with GDM, they are often implemented using supervised physical activity interventions which is not practical for translation to healthcare systems (195). Another study of 24 women with GDM who wore an accelerometer found a negative correlation between random BGs performed at the beginning and end of the study. They also noted a greater effect in participants who walked more than 6000 steps per day (196).

3.4.2 Limitations

With changes in the model of care because of COVID-19, there were fewer face to face appointments, and this may have affected the ability to document glucose levels. Often women did not provide their BGs for review towards the end of their pregnancy if they were not going to have another appointment prior to their delivery. Women were provided with activity monitors at varying times in their pregnancy depending on time of recruitment and antenatal appointments resulting in inconsistent duration of use prior to delivery. These factors limited the number of paired step and BG records that were able to be obtained. Furthermore, it is likely that there were days where the device was not worn for the entire day leading to underestimation of total daily steps.

The daily step count is a cumulative measure of the physical activity performed for the entire day however this is compared to static blood glucose levels measured at different times of the day in relation to food intake. Therefore, although step counts are measured over a set 24hrs period for each participant, there would be variability within and between the time of a participants BGs limiting the validity of direct comparisons between these variables. This may potentially explain why the effect of steps is highest after dinner as this BG would be taken towards the end of the day when more steps had been completed. However, studies on acute effect on BG soon after exercise are inconsistent and this requires further exploration (197, 198).

Consumer wearables devices are not yet validated measurement tools for research purposes particularly with the degree of variability between brands and models and a lack of transparency regarding how output data is derived. There are multiple characteristics that contribute to the accuracy of these devices including where the sensor is worn, the choice of LED emitted from the sensor affecting penetration, motion artefact susceptibility and melanin absorption as well as the algorithm used to process this biodata (177). As the device used in this study was wrist worn and lacked a heart rate monitor, it was dependent on arm swings detected via an accelerometer to count steps. Monitors with a heart rate monitor tend to have higher accuracy. It has also been noted in a

systematic review of validity and accuracies of these devices, the Garmin Vivofit has significant variability within the same device for step count (178). Despite this, the large volumes of data may compensate for the inaccuracies of the devices. The increasing availability and uptake of the devices as well as the finetuning of the technology and algorithms could see their role in research expand as they become more accurate.

3.5 Conclusion

There is a trend to towards an association between overall physical activity and improved glycaemia in GDM, with negative associations between step count and glucose levels at certain times of the day. These results support recommendations for physical activity as part of management of GDM.

Chapter 4: The effect of sleep on glycaemic control in gestational diabetes

4.1 Introduction

Sleep problems are common with many Australians falling short of recommendations for sleep duration (53). This has associated implications on metabolic health including increased cardiovascular risk, poor control of diabetes and higher mortality ((63)). Sleep quality is also an important aspect of sleep health as characteristics such as increased fragmentation (70), later chronotype (68), higher latency (74) and daytime napping (77) can negatively impact diabetes risk and glycaemic control.

Sleep changes during pregnancy are common due to hormonal and physical changes causing increased upper airway resistance that results in snoring, changes in respiratory drive, upward displacement of the diaphragm affecting lung volumes, and nausea, vomiting, urination and back pain decreasing sleep efficiency and increasing fragmentation (199). These issues are particularly reported in the third trimester where mean sleep duration decreases (200), snoring increases, the risk of insomnia is twice as high (201) and more napping occurs (202).

Women with sleep disordered breathing have an increased risk of pregnancy complications such as gestational diabetes, gestational hypertension and preeclampsia, caesarean section and preterm birth. Current models of care in the treatment of GDM through lifestyle modification centre on diet and exercise however few studies have examined other lifestyle factors associated with diabetes such as the effect of sleep on glycaemic control during pregnancy.

The increasing health technologies available consumers such as activity monitors that can obtain physiological data such as heart rate, sleep activity and oxygenation which offers the advantage of detailed objective data for long time periods over conventional methods of polysomnography, actigraphy and questionnaires.

This study examines the relationship between sleep and blood glucose levels in women with GDM with the use of a wrist worn activity monitor.

4.2 Methods

4.2.1 Study Design and Population

We included women who had been recruited for Smart Mums With Smart Phones 2 (SMs2), a randomised controlled trial of text messaging support for women after GDM at three metropolitan hospitals (190) (see Chapter 2 for inclusion and exclusion criteria).

As each site had varying methods of reviewing, managing and archiving BG records, we were only able to include women from Westmead Hospital, a tertiary centre, where online records were maintained (Figure 11.).

4.2.2 Variables

Baseline data included demographics, medical and family history, physical activity, dietary and sleep habits.

Blood glucose levels were routinely monitored by women and records were obtained from diabetes in pregnancy clinic records and correspondence.

Women are provided with a wrist-worn activity monitor (Garmin Vivofit 4®) in their third trimester. This monitor tracks sleep, Sleep data included duration of light sleep, deep sleep and wake after sleep onset (WASO). Total sleep duration was a sum of light sleep and deep sleep and time in bed was a sum of total sleep duration and WASO. Fragmentation was a variable derived of WASO as a proportion of total sleep.

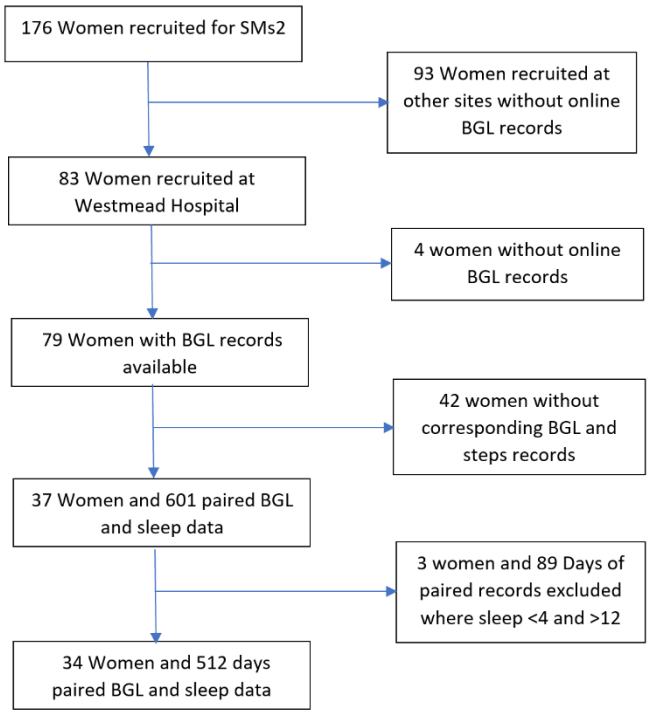

Figure 11. Selection of Study Population

We collected available BG records and obtained sleep data for corresponding dates from data uploads. All BG measurements were correlated with the sleep parameters from the night prior. Days where less than four hours or more than twelve hours of sleep occurred or when more than 90% of sleep was deep sleep were excluded as the device monitor was likely not worn for the entire duration of sleep. Due to the potential confounding effect of insulin therapy, the data for women on and off insulin were examined separately.

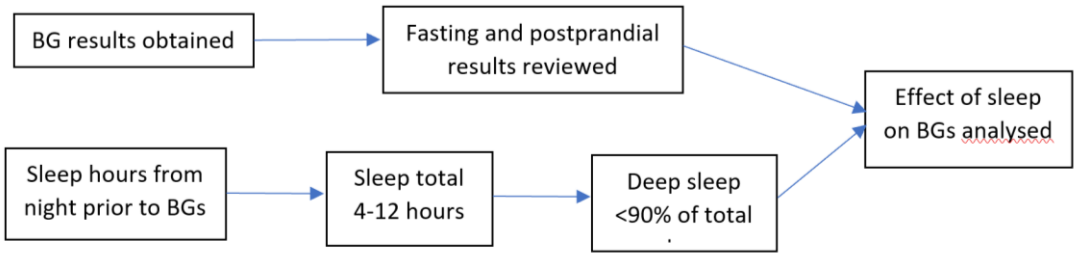

Figure 12. Processing of Sleeping and Blood Glucose Data

4.2.3 Statistical Analysis

Data were analysed with R Program, version 4.1.0 (*R Core Team, Auckland, New Zealand*). Linear mixed effect models were used to determine the effect of sleep duration on glucose measurements. Sleep duration was treated as a fixed effect and the study ID was included as a random effect in the model as multiple readings were obtained from the same woman. Data are reported as mean ± standard deviation. Statistical significance was taken as a two–sided *p*–value <0.05.

4.3 Results

There were 32 women included in this study with 498 days of paired BG and sleep observations. The mean age at conception was 31.9±4.0, ranging from 25 - 39 years old. Details summarising the demographics of the women included are described in Table 11.

	Group	% (N)	Mean
Age at conception	25-29	28.1 (9)	31.9±4.0
	30-34	40.6 (13)	
	35-40	31.2 (10)	
Pre pregnancy BMI	Underweight <18.5	0 (0)	27.4±4.9
	Normal 18.5 – 24.9	37.5 (12)	
	Overweight 25-29.9	31.2 (10)	
	Obese >30	31.2 (10)	
Ethnicity	Subcontinental	59.4 (19)	
	South East Asian	3.1 (1)	
	East Asian	3.1 (1)	
	European	6.3 (2)	
	Pacific Island	3.1 (1)	
	South American	3.1 (1)	
	Middle Eastern	21.9 (7)	
Education level	Year 10 School Certificate	9.3 (3)	
	Year 12 School Certificate	3.1 (1)	
	Technical and Further Education	18.8 (6)	
	University Undergraduate	37.5 (12)	
	University Postgraduate	31.3 (10)	
Previous GDM	No	68.8 (22)	
	Yes	31.2 (10)	
Family History of Diabetes	No	28.1 (9)	
	Yes	71.9 (23)	
Gravidy	1	37.5 (12)	2.3 ±1.3
	2-5	62.5 (20)	
Parity	0	43.8 (14)	0.8±0.8
	1-3	56.3 (18)	

Table 11. Demographics and Obstetric History of Women Included

The mean fasting glucose level for all data pairs was 5.0 ± 0.4 mmol/L, post breakfast BG 5.8 ± 0.6 mmol/L, post lunch 6.0 ± 0.5 mmol/L, post dinner BG 6.6 ± 0.6 mmol/L and mean post prandial BG 6.1 ± 0.5 mmol/L. The mean duration of sleep the night prior to measurement of BGs was 7.8 ± 0.9 hours and time in bed 8.1 ± 0.8 hours. Twenty-seven women required insulin during the time where corresponding sleep and BG data were available with a mean total daily dose (TDD) of insulin of 31 ± 51 IU.

	Mean ± SD
Fasting BG (mmol/L)	5.0 ± 0.4
Post breakfast BG (mmol/L)	5.8 ± 0.6
Post lunch BG (mmol/L)	6.0 ± 0.5
Post dinner BG (mmol/L)	6.6 ± 0.6
Mean post prandial BG (mmol/L)	6.1 ± 0.5
Sleep duration (hours)	7.8 ± 0.9
Time in bed (hours)	8.1 ± 0.8
WASO (hours)	0.3 ± 0.2
Light Sleep (hours)	4.4 ± 0.8
Deep Sleep (hours)	3.4 ± 0.7
Insulin TDD (units)	31 ± 51

Table 12. Mean Glucose Readings and Sleep Data for Days Where Paired Data Were Available

Overall, there was no significant relationship between duration of sleep and fasting BG or mean post prandial BG. However, women who met recommended sleep duration of 7-9 hrs were more likely to have all BGs in target for the following day (OR 1.6,95% CI 1.0 – 2.4, p=0.05). Light sleep duration, proportion of light sleep and proportion of deep sleep were associated with fasting BGs the following day (-0.07 mmol/L per hour of sleep, 95% CI -0.11 – -0.02, p=<0.01; 0.003 mmol/L per hour of sleep, 95% CI -0.01, 0.001 p=0.04, 0.007 mmol/L per hour of sleep, 95% CI 0.001 – 0.01, p=0.02). WASO did not affect fasting or mean post prandial BGs.

Sleep parameter in hours	Fasting BG (mmol/L)	(95% CI)	Linear Trend p-value	Mean Postprandial BG (mmol/L)	(95% CI)	Linear Trend p-value
Sleep duration (hours)	-0.02	-0.06, 0.02	0.25	0.01	-0.2, 0.05	0.46
Time in bed (hours)	-0.02	-0.05, 0.01	0.25	0.02	-0.02, 0.05	0.37
Light sleep (hours)	-0.07	-0.11, -0.02	<0.01	0.03	-0.02, 0.07	0.26
Light sleep (proportion of sleep duration)	0.00	-0.01, 0.00	0.04	0.00	0.00, 0.01	0.54
Deep sleep (hours)	0.04	-0.01, 0.08	0.09	-0.01	-0.05, 0.04	0.81
Deep sleep (proportion of sleep duration	0.00	0.00, 0.01	0.02	0.00	-0.1, 0.0	0.68
WASO (hours)	-0.08	-0.28, 0.13	0.47	0.05	-0.15, 0.25	0.64
Fragmentation	0.24	-1.67, 1.24	0.74	0.43	-1.03, 1.89	0.57

Table 13. Relationship Between Sleep Parameters and BGs the Next Day

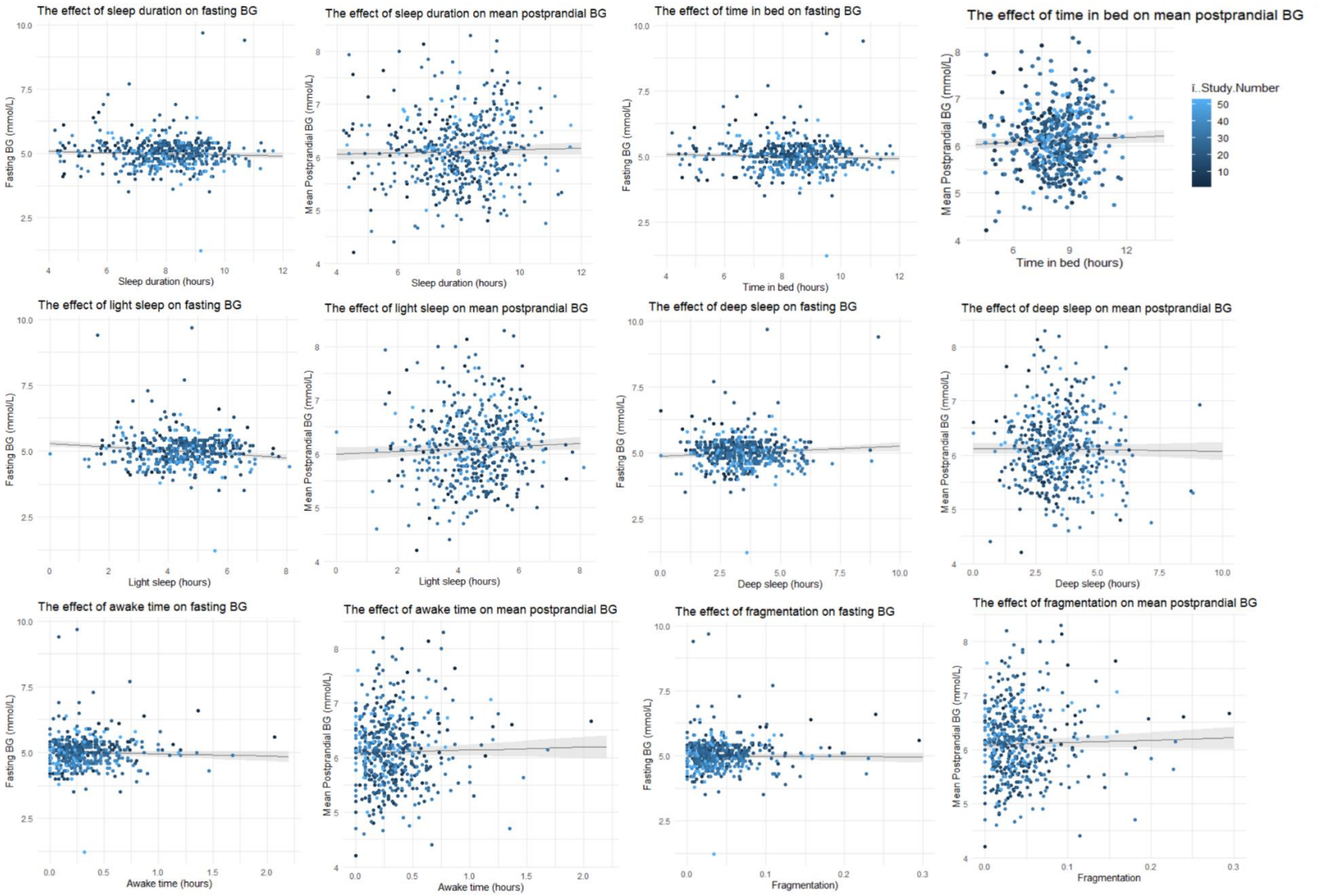

Figure 13. Relationship Between Sleep Parameters and BGs the Next Day

	Odds Ratio	(95% CI)	p-value
All BG in target if sleep duration in target	1.6	1.0, 2.4	0.05
Fasting BG if sleep duration in target	1.4	0.8, 2.4	0.29

Table 14. Odds of Meeting BG Target If Sleep Duration Was In Target

In the insulin group, fasting BG was associated with light sleep and the proportion of sleep duration spent in deep sleep (-0.08 mmol/L per hour of sleep, 95%CI -0.14 – -0.03, p=<0.01; 0.01 mmol/L per hour of sleep, 95%CI 0.00 – 0.01, p=<0.01). There were no other significant differences in the groups.

	Sleep parameter in hours	Fasting BG (mmol/L)	(95% CI)	Linear Trend p-value	Mean Postprandial BG (mmol/L)	(95% CI)	Linear Trend p-value
Insulin Group (N=376)	Sleep duration (hours)	-0.03	-0.08, 0.01	0.20	0.01	-0.03, 0.05	0.63
	Time in bed (hours)	-0.02	-0.07, 0.02	0.24	0.01	-0.03, 0.06	0.55
	Light sleep (hours)	-0.08	-0.14, -0.03	<0.01	0.02	-0.03, 0.07	0.36
	Light sleep (proportion of sleep duration)	0.00	-0.01, 0.00	0.80	0.00	0.00, 0.01	0.54
	Deep sleep (hours)	0.04	-0.01, 0.09	0.10	-0.01	-0.06, 0.04	0.75
	Deep sleep (proportion of sleep duration	0.01	0.00, 0.01	<0.01	0.00	0.00, 0.01	0.49
	WASO (hours)	-0.04	-0.31, 0.23	0.75	0.04	-0.21, 0.29	0.78
	Fragmentation	0.13	-1.76, 2.06	0.89	0.22	-1.57, 2.02	0.81
No Insulin Group (N=122)	Sleep duration (hours)	0.00	-0.05, 0.04	0.83	0.02	-0.05, 0.09	0.53
	Time in bed (hours)	-0.01	-0.06, 0.03	0.55	0.03	-0.03, 0.10	0.37
	Light sleep (hours)	0.00	-0.06, 0.05	0.79	0.06	-0.02, 0.05	0.16
	Light sleep (proportion of sleep duration)	0.00	-0.01, 0.01	0.74	0.00	-0.01, 0.01	0.88
	Deep sleep (hours)	0.00	-0.06, 0.06	0.94	-0.01	-0.10, 0.07	0.71
	Deep sleep (proportion of sleep duration	0.00	-0.02, 0.01	0.57	0.00	-0.01, 0.01	0.46
	WASO (hours)	-0.16	-0.36, 0.05	0.13	0.11	-0.19, 0.41	0.48
	Fragmentation	-1.16	-2.58, 0.31	0.12	0.97	-1.15, 3.04	0.37

Table 15. Relationship Between Sleep Parameters and BGs the Next Day in Insulin and Non-Insulin Group

As sleep becomes more disturbed in later pregnancy, the effect of sleep on BGs may change and so we divided our data into that recorded before and after 36 weeks gestation. Prior to 36 weeks gestation, there was a negative association between sleep and fasting BG (-0.05 mmol/L per hour of sleep, 95%CI -0.09 – -0.01, p=0.03) and time in bed and fasting BG (-0.04 mmol/L per hour of sleep, 95%CI -0.09 – 0.00, p=0.03). There was a positive relationship between mean postprandial BG and WASO hours (0.27 mmol/L per hour of sleep, 95%CI 0.00 – 0.55, p=0.05). When women were greater than 36 weeks gestations, both duration of light sleep and deep sleep were negatively associated with fasting BGs (-0.10 mmol/L per hour of sleep, 95%CI -0.17 – 0.03, p<0.01; 0.08 mmol/L per hour of sleep, 95%CI 0.01 – 0.14, p=0.02). Fasting BGs were also associated with the proportion of sleep duration spent in deep sleep (0.01 mmol/L per hour of sleep, 95%CI 0.00 – 0.02, p=0.03).

	Sleep parameter in hours	**Fasting BG (mmol/L)**	**(95% CI)**	**Linear Trend p-value**	**Mean Postprandial BG (mmol/L)**	**(95% CI)**	**Linear Trend p-value**
Gestation <36 weeks (N=238)	Sleep duration (hours)	-0.05	-0.09, -0.01	0.03	0.03	-0.02, 0.09	0.26
	Time in bed (hours)	-0.04	-0.09, 0.00	0.03	0.04	-0.02, 0.09	0.17
	Light sleep (hours)	-0.03	-0.08 0.02	0.20	0.04	-0.03, 0.10	0.26
	Light sleep (proportion of sleep duration)	0.00	0.00, 0.01	0.12	0.00	-0.01, 0.01	0.82
	Deep sleep (hours)	-0.03	-0.09, 0.02	0.19	0.01	-0.08, 0.05	0.70
	Deep sleep (proportion of sleep duration	0.00	-0.01, 0.01	0.63	0.00	-0.01, 0.01	0.80
	WASO (hours)	0.00	-0.21, 0.21	0.99	0.27	0.00, 0.55	0.05
	Fragmentation	0.21	-1.23, 1.68	0.78	1.82	-0.08, 3.75	0.06
Gestation >36 weeks (N=260)	Sleep duration (hours)	-0.01	-0.07, 0.05	0.76	0.00	-0.05, 0.06	0.86
	Time in bed (hours)	-0.01	-0.06, 0.05	0.81	0.00	-0.04, 0.06	0.75
	Light sleep (hours)	-0.10	-0.17, -0.03	<0.01	0.02	-0.04, 0.08	0.59
	Light sleep (proportion of sleep duration)	0.00	-0.01, 0.0	0.23	0.00	-0.01, 0.01	0.94
	Deep sleep (hours)	0.08	0.01, 0.14	0.02	0.00	-0.06, 0.06	0.94
	Deep sleep (proportion of sleep duration	0.01	0.00, 0.02	0.03	0.00	-0.01, 0.01	0.78
	WASO (hours)	-0.04	-0.38, 0.31	0.83	-0.05	-0.35, 0.25	0.72
	Fragmentation	0.11	-2.33, 2.60	0.93	-0.21	-2.36, 1.96	0.85

Table 16. Relationship Between Sleep Parameters and BGs the Next Day

4.4 Discussion

4.4.1 The relationship between sleep and glycaemic control

There is no recommended sleep duration specific to pregnancy however for the general adult population, it is 7-9 hours. Sleep problems during pregnancy are common with the mean duration of sleep shorter in the third trimester with increased snoring (200) and the risk of insomnia twice as high in the 3rd trimester compared to the first and second (201). Towards the end of pregnancy sleep is more restless and fragmented (203) and women tend to nap more (202). Poor sleep quality has been associated with gestational diabetes and other adverse pregnancy outcomes including increased risk of caesarean delivery and preterm birth throughout pregnancy (204-207) .

We did not find a relationship between duration of sleep and subsequent fasting and post prandial BGs. However, achieving sleep duration targets did improve chances of reaching BG in target for all readings for the next day. This suggests that sleep does affect glycaemic control but perhaps not in a linear fashion. The finding of a relationship between optimal duration of sleep (7=9 hours) and better glucose levels suggests that the relationship may be U-shaped, though this is not obvious from our graphs. There was a small effect of sleep duration and time in bed on fasting BG in women when they were less than 36 weeks gestation however this is unlikely to be clinically significant even if women reach sleep goals for seven to nine hours.

Unlike previous studies, we were also able to examine the effects of other sleep metrics as well as sleep components such as light and deep sleep. Interestingly light and deep sleep had opposite effects on glycaemic control with improvement in fasting BG of 0.10mmol/L for light sleep when gestation was greater than 36 weeks. A similar effect of light sleep on fasting BG was seen in women who were on insulin. This was contrary to what was expected. The Garmin algorithm determines whether a person is in light sleep or deep sleep. Light sleep should represent stage 1 and 2 sleep and deep sleep represents stage 3 and 4 as this would correspond with the level of depth of the sleep stages. Stage 3 and 4 sleep, also know as slow wave sleep is the most restorative sleep stage. Unfortunately, without a heart rate monitor, the Garmin is unable to determine REM sleep. Slow wave sleep suppression but not REM sleep suppression can affect impair glucose metabolism and affect fasting glucose levels (73). This may be because REM sleep causes an increase in sympathetic nervous system activation with elevated blood pressure and heart rate (52). Therefore, to further understand our results, the duration of REM sleep would also need to be determined.

We also found a positive relationship between WASO and mean post prandial BGs which would be consistent with poor quality sleep affecting glucose control. A study of 166 women with GDM who wore actigraphy for up to six nights whilst wearing continuous glucose monitoring found sleep duration was negatively associated with standard deviation glucose. Furthermore, each 10 minute increase in WASO was 16% more likely to be above glycaemic targets which is consistent with our findings (208). Poor quality sleep has been associated with an increased risk of GDM (209) and sleep disturbances are associated with an elevated Hba1c in pregnant women (210). It is thought that

disturbed sleep can increase inflammatory responses that may contribute to adverse pregnancy outcomes such as gestational diabetes, preeclampsia and preterm birth (211, 212)

Although there were some statistically significant associations between proportion of sleep spent in deep sleep and fasting BG in women who were greater than 36 weeks gestation and women on insulin, the effect size was too small to be clinically significant. We were unable to find any other studies that qualitatively assessed the effect of different sleep levels on glycaemic control in GDM.

More than half the women in our study had at least one child prior to the current pregnancy although we do not have details of these children that might suggest the degree to which this might have influenced sleep. It has been shown in a study of 133 women, that compared to nulliparous women, multiparous women reported poorer sleep quality and efficiency with shorter duration in the first trimester, poorer sleep quality and longer SOL in the second trimester, and increased fragmentation in the third trimester (213). This may be related to the impact of greater childcare demands on sleep. As these women may have had poorer quality sleep, increased duration may not have been sufficient to translate into improved glycaemic control.

Although we did not find a relationship between sleep and glucose levels, this has been found in previous studies. A cohort study of 37 women who were recruited in their first week of dietary management of GDM wore an actigraph and completed a sleep diary for 7 days. This was compared against their glucose records and there was a negative association between sleep duration and fasting and one-hour postprandial BG readings (214). Similarly, a study of 65 women in their third trimester had their glucose control assessed using continuous glucose monitoring over 6 days against sleep quality measure by the Pittsburgh Sleep Quality Index. They demonstrated that poorer sleep quality was associated with a lower proportion of time in glucose target, higher glucose variability, higher mean glucose levels and greater number of glucose excursions (215). Despite these studies having a comparable number of participants, the sleep data recorded in our study occurred at various stages of pregnancy which may affect sleep characteristics differently. Therefore, our data perhaps was less consistent than in these studies which were able to find a relationship between sleep and glycaemia.

4.4.2 Limitations

The cohort of the study was limited the number of BG records obtained that had corresponding sleep data. This was impacted by the management of BG records at each site, COVID 19 affecting models of care, and timing of when activity monitors were issues and women reliably providing BG records throughout pregnancy. Consequently, despite the number of women recruited for SMs2, we were only able to include a much smaller number of women impacting the power of this substudy.

Consumer wearables devices are not validated for research particularly considering the numerous and variable devices between and within brands where the mechanism of data collection and processing is not transparent. Factors that influence the accuracy of these devices include location of sensor, sensory LED colour determining penetration, motion artefact susceptibility and melanin

absorption as well as the algorithm used to process this biodata. A study that compared consumer sleep tracking devices to the fold standard for research, polysomnography, found that the Garmin devices included (Fenix 5S and Vivosmart 3) tended to overestimate total sleep time and underestimate wake after sleep onset. Detecting sleep stages was inconsistent and worse on nights of interrupted sleep (179). In a study of Fitbit models, devices that integrated heart rate variability were better than those that relied on body movement alone (180). The device in this study did not have a heart rate monitor. The user can enter their normal sleep times into the settings on the Garmin app which may assist sleep detection. Thus, the sleep data in this study is likely of modest quality compared to other studies on sleep however given the same device was used across the cohort the findings are still valid.

The Garmin Vivofit was only able to determine a few sleep parameters include light sleep, deep sleep and WASO. These categories may correlate to the different sleep stages however there is no information readily available on what is classified as light and deep sleep limiting comparisons with other sleep studies. It also makes interpreting the differing effects of light and deep sleep on glycaemic control difficult. Other sleep characteristics such as REM sleep or sleep latency could not be obtained from this device. Furthermore, Garmin does not detect naps, a sleep habit that increases as pregnancy progress but also results in poorer glycaemic control in the general population of diabetics.

4.5 Conclusion

We found that that there was no relationship between sleep duration and overall glycemic control in women with GDM. However, meeting sleep recommendations improved the likelihood of meeting BG targets. Our data suggests that some measures of sleep quality might influence glucose levels. However in the context of women who are being treated for GDM any effects are small.

Chapter 5: The relationship between sleep and physical activity in postpartum women with gestational diabetes

5.1 Introduction

Gestational diabetes is rising in incidence and its association with not only adverse perinatal outcomes (13) but long term maternal risk of developing T2DM (33, 216) contributes to burden of disease on the individual and population (38). Given the population of women with GDM are inherently young with a high risk of progression to T2DM, this is a cohort who would benefit from preventative intervention. Although trials using lifestyle interventions have reduced the progression from IGT to T2DM (39, 40), the success of similar interventions have varied outcomes in women with GDM (43).

Whilst lifestyle interventions targeting physical activity and diet remain at the forefront of prevention of T2DM, it is important to consider other contributing lifestyle factors. Sleep has been increasingly associated with risk of diabetes. Sleep duration (59) as well as sleep quality including fragmentation (70), latency (74), regularity (92), napping (77) and chronotype (68) can affect glucose tolerance and glycaemic control. There are several mechanisms mediating this relationship that has been proposed such as the effect of sleep on appetite hormones, the hypothalamic pituitary adrenal axis, sympathetic nervous system, inducing oxidative stress and inflammation. The relationship sleep has with diabetes may also be mediated through its effect on physical activity. A bidirectional relationship exists between sleep and physical activity and this effect has been found with both acute and chronic duration however the effect size is modest (126, 134). There are few studies that examine the relationship between sleep and physical activity in the post-partum period which suggest that this relationship may differ in this cohort compared to the general population. Women in this period are more likely to have interrupted and poor-quality sleep as they are affected by newborn sleeping and feeding patterns (217). Poor sleep is associated with negative maternal health outcomes such as increased weight retention (218) and depression (219). Poor sleep may also be associated with less physical activity (126). Therefore, women in the post-partum period may experience a double whammy of poor sleep which exacerbates reduced physical activity that magnifies their long-term risk of diabetes.

Mobile health technologies include mobile phones and wearable devices that can enhance public health services and support healthcare (166). Consumer worn devices are increasingly used and are able to measure physiological parameters such as steps, intensity of physical activity and sleep. Their ability to capture greater volumes of data, over longer time periods for more people allow us to better understand behavior and relationships with health metrics. The demands of new motherhood on women can make study on postpartum sleep habit difficult as polysomnography and actigraphy can be intrusive and sleep diaries and questionnaires may be difficult to complete if suffering from sleep deprivation or depression (217). Consumer worn devices may be a more practical and convenient method to assess sleep and physical activity in a large cohort for a prolonged period of time.

In this study we explore the effect of sleep quantity and quality on physical activity habits in post-partum women who have had GDM. Our hypothesis is that poor sleep is associated with less physical activity the next day. A combination and poor sleep and reduced physical activity may have synergistic effects to increase long-term diabetes and cardiovascular risk.

5.2 Methods (see Chapter 2)

5.2.1 Study Design and Population

We included women who had been recruited for Smart Mums With Smart Phones 2 (SMs2), a randomised controlled trial of text messaging support for women after GDM at three metropolitan hospitals (190). This study is a subanalysis examining the post-partum relationship between physical activity, sleep and weight conducted prior to completion of the trial. Data was collected until the end of October 2021.

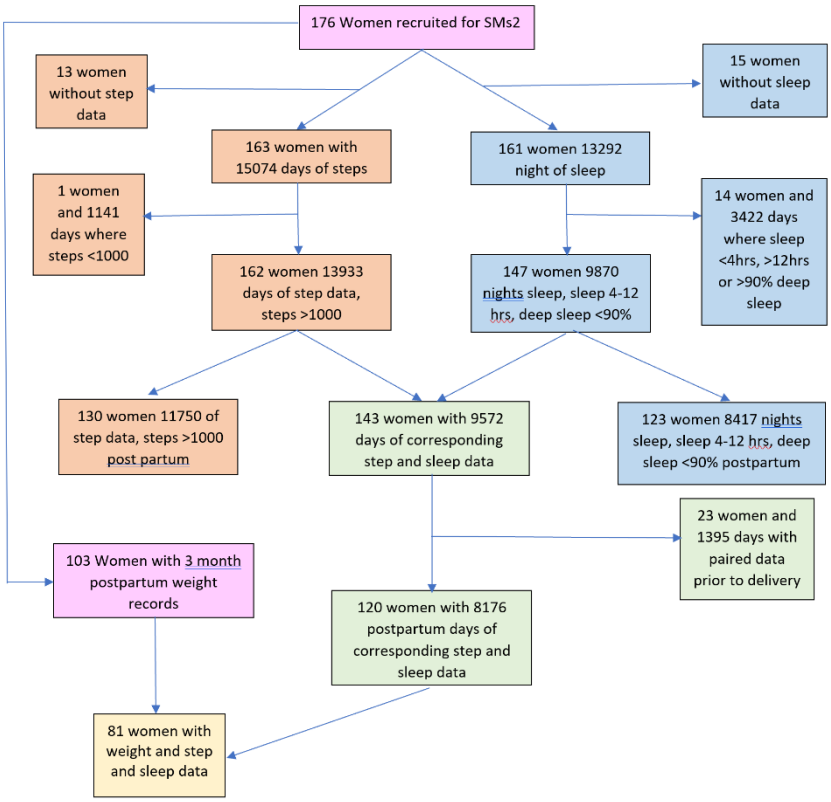

Figure 14. Selection of Study Population

5.2.2 Variables

Baseline data included demographics, medical and family history, physical activity, dietary and sleep habits.

Women are provided with a wrist-worn activity monitor (Garmin Vivofit 4®) in their third trimester. This device tracked sleep data including total sleep duration, light sleep, deep sleep and wake after sleep onset (WASO). Total sleep duration was a sum of light sleep and deep sleep and time in bed was a sum of total sleep duration and time awake. Fragmentation was a variable derived of time awake as a proportion of total sleep. Physical activity data included daily steps, active minutes and sedentary minutes. Sedentariness was calculated as the sedentary time as a proportion of the day not in bed. Days where there was corresponding sleep and step data postpartum were included. We excluded days where data suggested that the device was not worn the entire day including when daily steps were less than one thousand, sleep duration was less than four hours or greater than twelve hours and when deep sleep represented more than ninety percent of total sleep.

At delivery, we obtained the last recorded antenatal weight. Subsequently, at three months and six months postpartum, women were sent a survey link via text message which included a self-reported weight. From this, we were able to determine the change in weight during the postpartum period.

5.2.3 Subanalyses

As we expect physical activity levels to increase as time from delivery increased, we analysed the effect of sleep parameters on physical activity across three two-month time periods postpartum

5.2.4 Statistical analysis

Data were analysed with R Program, version 4.1.0 (*R Core Team, Auckland, New Zealand*). Linear mixed effect models were used to determine the effect of sleep duration on number of steps the following day. Sleep duration was treated as a fixed effect and the study ID was included as a random effect in the model as multiple readings were obtained from the same woman. The mean postpartum steps and sleep for each woman was compared with her three-month and six-month postpartum weight with linear regression. Data are reported as mean ± standard deviation. Statistical significance was taken as a two–sided *p*–value <0.05.

5.3 Results

There were 120 women with 8176 postpartum days of corresponding step and sleep data. The mean age at conception was 32.4 ± 4.4, ranging from 20 - 42 years old.

	Group	% (N)	Mean
Age at conception	<25	4.2 (5)	32.4 ± 4.4
	25-29	20.8 (25)	
	30-34	39.2 (47)	
	35-40	33.3 (40)	
	>40	2.5 (3)	
Pre pregnancy BMI	Underweight <18.5	1.0 (1)	29.3 ± 7.2
	Normal 18.5 – 24.9	33.3 (40)	
	Overweight 25-29.9	25 (30)	
	Obese >30	30.8 (37)	
	>40	10 (12)	
Country of Birth	South Asia	40.8 (49)	
	East Asia	1.7 (2)	
	South East Asia	5.8 (7)	
	Europe	1.7 (2)	
	Pacific Island	4.2 (5)	
	Central America	1.0 (1)	
	South America	1.7 (2)	
	North America	1.0 (1)	
	Middle East	4.2 (5)	
	Australia/New Zealand	35.8 (43)	
	Africa	2.5 (3)	
Education level	No formal education	1.0 (1)	
	Year 10 School Certificate	10.0 (12)	
	Year 12 School Certificate	10.8 (13)	
	Technical and Further Education	22.5 (27)	
	University Undergraduate	25.0 (30)	
	University Postgraduate	30.8 (37)	
Previous GDM	No	64.2 (77)	
	Yes	35.8 (43)	
Family History of Diabetes	No	44.2 (53)	
	Yes	55.8 (67)	
Gravidy	1	25.0 (30)	2.8 ± 2.0
	2-5	75.0 (90)	
Parity	0	32.5 (39)	1.0 ± 1.0
	1-3	67.5 (81)	

Table 17. Demographics and Obstetric History Women Included

The mean steps taken per day was 5241 ± 2497. The mean total sleep for the night prior was 7.3 ± 1.6 hours. (Table 18.)

	Mean
Steps	5241 ± 2497
Sedentariness	14.8 ± 1.7
Active minutes	0.9 ± 0.4
Total Sleep	7.3 ± 1.1
Light Sleep	3.6 ± 1.1
Deep Sleep	3.7 ± 1.3
WASO	0.5 ± 0.3
Time in bed	7.8 ± 1.0
Light Sleep / Total Sleep	49.7 ± 12.4
Light Sleep / Time in bed	46.5 ± 11.9
Deep Sleep / Total Sleep	50.1 ± 12.5
Deep Sleep / Time in bed	47.2 ± 12.5
WASO / Total Sleep	7.1 ± 4.4
WASO / Time in bed	6.3 ± 3.5

Table 18. Mean Steps and Sleep Characteristics of the Night Prior

There was a positive association between duration of total sleep (120.8 steps per hour of sleep, 95% CI 84.1 - 157.5, $p < 0.01$), time in bed (72.1 steps per hour in bed, 95% CI 37.3 - 106.9, $p < 0.01$), light sleep (138.7 steps per hour of light sleep 95% CI 92.8 – 184.8, $p < 0.1$) and deep sleep (51.0 steps per hour of deep sleep, 95% CI 5.9 – 96.0, $p = 0.03$) with steps taken the following day. For the same sleep parameters there was a negative relationship with sedentariness. There was a positive relationship between total sleep (0.8 active minutes per hour of sleep, 95% CI 0.4 1.1, $p < 0.01$), time in bed (0.5 active minutes per hour in bed, 95% CI 0.1 – 0.8, $p < 0.01$) and light sleep (1.0 active minutes per hour of light sleep 95% CI 0.6 – 1.4, $p < 0.1$) and active minutes the following day. There was a negative association between WASO and steps the next day (-606.3 steps per hour of WASO, 95% CI -747.2 - -465.5, $p < 0.01$) and active minutes (-3.9 active minutes per hour of WASO, 95% CI -5.2 - -2.5, $p < 0.0$) (Table 19.).

	Steps			Active Minutes			Sedentariness		
Sleep Parameter	**Effect**	**95%CI**	**P value**	**Effect**	**95%CI**	**P value**	**Effect**	**95%CI**	**P value**
Total sleep	120.8	84.1, 157.5	<0.01	0.8	0.4, 1.1	<0.01	-0.5	-0.5, -0.4	<0.01
Time in bed	72.1	37.3, 106.9	<0.01	0.5	0.1, 0.8	<0.01	-0.4	-0.5, -0.4	<0.01
Light Sleep	138.7	92.8, 184.8	<0.01	1.0	0.6, 1.4	<0.01	-0.5	-0.5, -0.4	<0.01
Light/Total Sleep	3.6	-0.8, 8.0	0.11	0.0	0.0, 0.1	0.15	0.0	0.0, 0.0	0.03
Light Sleep/Time in bed	8.4	3.8, 13.0	<0.01	0.0	0.0, 0.1	<0.01	0.0	0.0, 0.0	<0.01
Deep Sleep	51.0	5.9, 96.0	0.03	0.2	-0.2, 0.7	0.29	-0.3	-0.4, -0.3	<0.01
Deep /Total Sleep	-3.4	-7.7, 1.0	0.13	0.0	-0.1, 0.0	0.19	0.0	0.0, 0.0	0.05
Deep Sleep/Time in bed	0.5	-4.0, 5.0	0.83	0.0	0.0, 0.0	0.83	0.0	0.0, 0.0	0.24
WASO	-606.3	-747.2, -465.5	<0.01	-3.9	-5.2, -2.5	<0.01	0.0	-0.2, 0.1	0.58
WASO/Total Sleep	-45.2	-54.5, -35.9	<0.01	-0.3	-0.4, -0.2	<0.01	0.0	0.0, 0.0	<0.01
WASO /Time in bed	-57.2	-68.7, -45.7	<0.01	-0.4	-0.5 - 0.3	<0.01	0.0	0.0, 0.0	<0.01

Table 19. Effect of Sleep Parameter on Physical Activity the Following Day

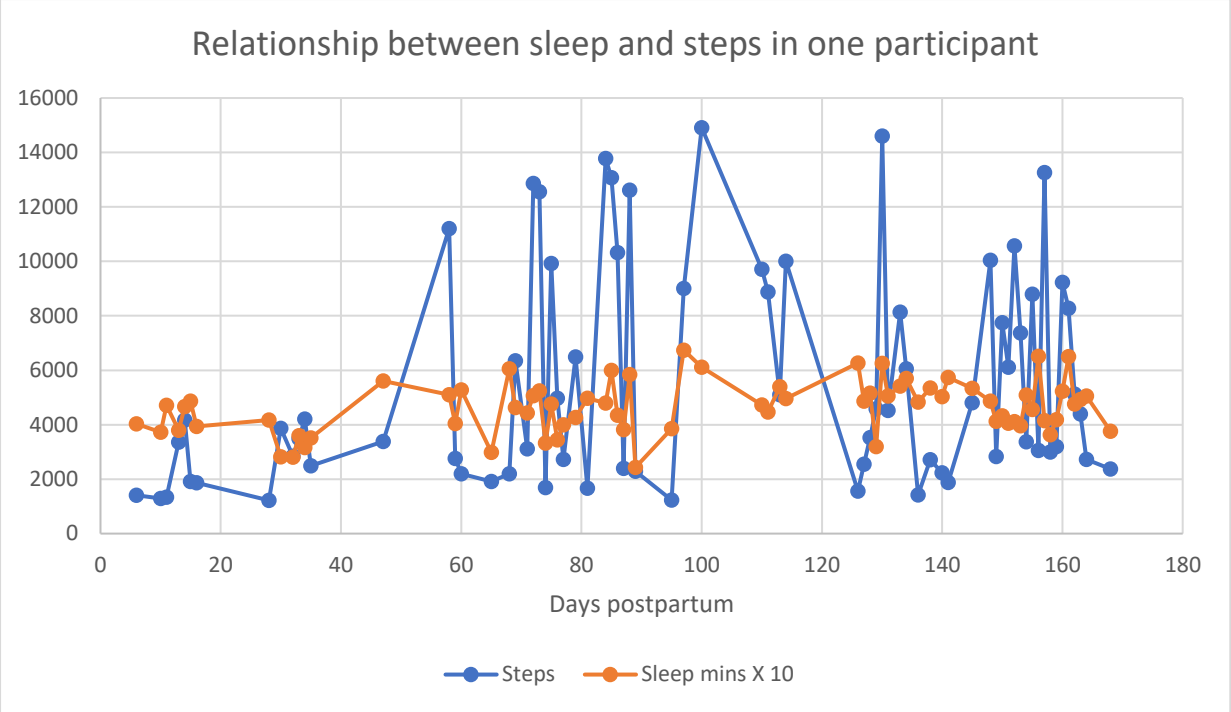

Figure 15. Relationship Between Sleep and Steps in One Participant

There was a mean of 4506 ± 2329 steps, 5802 ± 2655 steps and 5923 ± 2485 in the first 2-month, second 2-month and third 2-month period postpartum respectively. The mean total sleep was 6.8 ± 1.1 hours, 7.5 ± 1.1 hours and 7.7 ± 1.0 for the first 2-month, second 2-month and third 2-month period postpartum respectively.

	First 2 months PP	Second 2 months PP	Third 2 months PP	First vs third 2 months PP P value
Steps	4506 ± 2329	5802 ± 2655	5923 ± 2485	<0.01
Sedentariness	94.1 ± 2.9	92.6 ± 2.9	92.3 ± 3.0	<0.01
Active Minutes	45.3 ± 21.6	54.3 ± 21.2	56.2 ± 21.6	<0.01
Total Sleep	6.8 ± 1.1	7.5 ± 1.1	7.7 ± 1.0	<0.01
Light Sleep	3.4 ± 0.9	3.7 ±1.1	4.0 ± 1.1	<0.01
Deep Sleep	3.5 ± 1.1	3.8 ± 1.4	3.7 ± 1.2	0.25
WASO	0.6 ± 0.3	0.4 ± 0.2	0.4 ± 0.2	<0.01
Time in bed	7.5 ± 1.0	7.9 ± 1.1	8.1 ± 1.0	<0.01
Light Sleep / Total Sleep	49.8 ± 10.9	50.0 ± 13.1	52.7 ± 12.4	0.11
Light Sleep / Time in bed	45.6 ± 10.1	47.7 ± 12.8	50.4 ± 12.0	0.01
Deep Sleep / Total Sleep	50.2 ± 10.9	49.4 ± 13.6	47.2 ± 12.4	0.11
Deep Sleep / Time in bed	46.3 ± 10.9	47.1 ± 13.2	45.2 ± 11.9	0.53
WASO / Total Sleep	9.3 ± 4.8	5.7 ± 3.2	4.7 ± 2.8	<0.01
WASO / Time in bed	8.1 ± 3.8	5.2 ± 2.7	4.4 ± 2.4	<0.01

Table 20. Mean of Physical Activity and Sleep Parameters Over Postpartum Time Periods

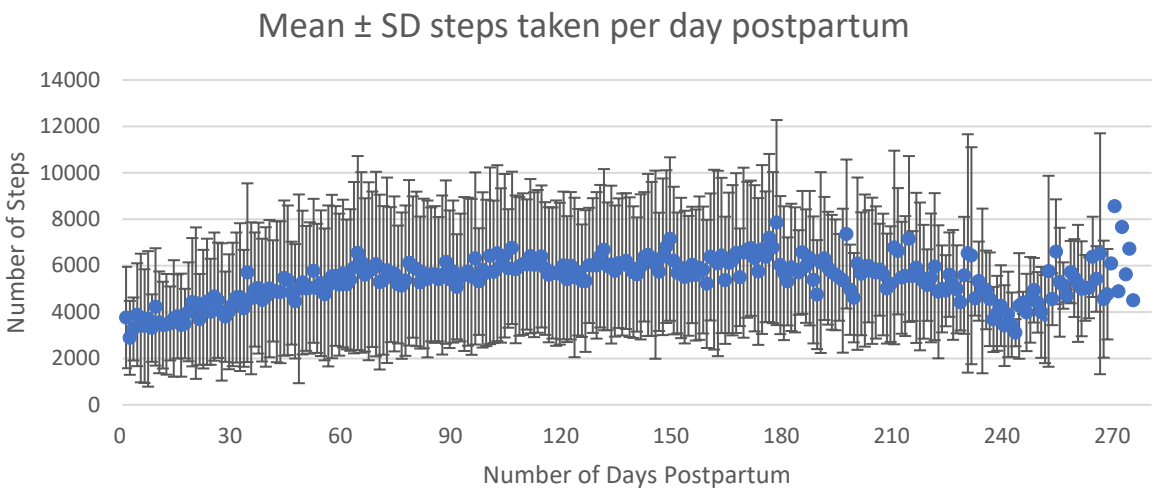

Figure 16. Mean Steps Taken Per Day Postpartum

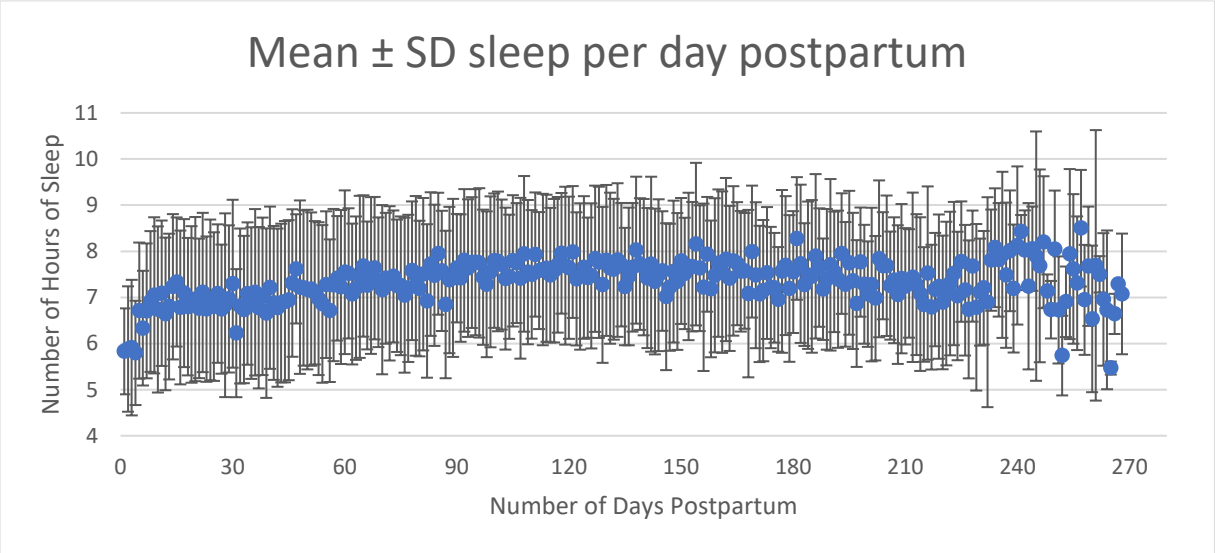

Figure 17. Mean Sleep Duration Per Day Postpartum

Regarding the effects of sleep on physical activity across increasing 2-month time periods from delivery, there remained a positive relationship between total sleep and deep sleep and steps the following day only in the first two-month postpartum period (74.1 steps per hour of total sleep 95% CI 207.2 – 127.8, p=0.01 and 89.1 steps per hour of deep sleep, 95% CI 20.8, 157.5, p = 0.01). The negative association between WASO and steps the following day also persisted in the first two months postpartum (-284.3 steps per hour of WASO, 95% CI -468.7, -100.0, p<0.01). In all postpartum time periods there is a consistent negative association between total sleep and sedentariness (-0.4% for every hour of sleep, 95% CI -0.4 - -0.3, p<0.01 for first 2 month, -0.4% for every hour of sleep, 95% CI -0.5 - -0.4, p<0.01, -0.4% for every hour of sleep for second 2 months, 95% CI -0.5 - -0.3, p<0.01 for third 2 months) and between WASO and sedentariness (-0.4% for every hour of sleep, 95% CI -0.6 - -0.2, p<0.01 for first 2 month, -0.8% for every hour of sleep, 95% CI -1.1 - -0.5, p<0.01, -1.0% for every hour of sleep for second 2 months, 95% CI -1.5 - -0.6, p<0.01 for third 2 months) (Table 21.).

		First 2 months Postpartum n=104 women, 2517 obs			Second 2 months Postpartum n=92 women, 2948 obs			Third 2 months Postpartum n=69 1817 obs		
	Sleep Parameter	**Effect**	**95%CI**	**P value**	**Effect**	**95%CI**	**P value**	**Effect**	**95%CI**	**P value**
Steps	Total sleep	74.1	207.2, 127.8	<0.01	47.1	15.8, 110.1	0.14	-29.3	-110.7, 52.1	0.48
	Time in bed	43.1	-5.9, 92.2	0.09	38.5	-20.1, 97.3	0.20	-19.9	-96.8, 56.9	0.61
	Light Sleep	37.4	-34.7, 109.6	0.31	74.1	-5.0, 153.6	0.07	42.8	-52.7, 138.5	0.38
	Light/Total Sleep	4.8	-11.4, 1.8	0.15	3.5	-4.0, 11.0	0.36	5.6	-3.6, 14.7	0.23
	Light Sleep/Time in bed	-2.2	-9.2, 4.9	0.55	3.5	-4.4, 11.4	0.39	5.5	-4.0, 15.0	0.26
	Deep Sleep	89.1	20.8, 157.5	0.01	6.1	-68.9, 80.9	0.87	-79.4	-174.0, 14.9	0.10
	Deep /Total Sleep	5.0	-1.6, 11.6	0.14	-2.8	-10.4, 4.7	0.46	-5.2	-14.4, 3.9	0.26
	Deep Sleep/Time in bed	7.4	0.7, 14.2	0.03	-2.6	-10.3, 5.1	0.51	-6.1	-15.5, 3.2	0.20
	WASO	-284.3	-468.7, -100.0	<0.01	-47.4	-303.7, 208.9	0.72	173.7	-218.3, 566.9	0.39
	WASO/Total Sleep	-19.8	-31.7, 7.9	<0.01	-4.6	-22.3, 13.1	0.61	12.0	-15.7, 39.8	0.40
	WASO /Time in bed	-28.2	-43.6, -12.9	<0.01	-5.7	-27.2, 15.8	0.60	14.7	-17.7, 47.2	0.38
Active minutes	Total sleep	0.3	-0.1, 0.8	0.15	0.1	-0.6, 0.9	0.72	0.3	-0.1, 0.8	0.15
	Time in bed	0.2	-0.2, 0.6	0.36	0.2	-0.6, 0.9	0.65	0.2	-0.2 , 0.6	0.36
	Light Sleep	0.0	-0.6, 0.7	0.89	1.0	0.0, 2.0	0.05	0.0	-0.6, 0.7	0.89
	Light/Total Sleep	0.0	-0.1, 0.0	0.09	0.1	0.0, 0.2	0.05	0.0	-0.1, 0.0	0.09
	Light Sleep/Time in bed	0.0	-0.1, 0.0	0.26	0.1	0.0, 0.2	0.07	0.0	-0.1, 0.0	0.26
	Deep Sleep	0.5	-0.1, 1.1	0.08	-0.6	-1.5, 0.3	0.19	0.5	-0.1, 1.1	0.08
	Deep /Total Sleep	0.0	0.0, 0.1	0.08	-0.1	-0.2, 0.0	0.07	0.0	0.0, 0.1	0.08
	Deep Sleep/Time in bed	0.1	0.0, 0.1	0.05	-0.1	-0.2, 0.0	0.06	0.1	0.0, 0.1	0.05
	WASO	-1.3	-2.9, 0.2	0.09	0.8	-2.4, 4.0	0.63	-1.3	-2.9 0.2	0.09
	WASO/Total Sleep	-0.1	-0.2, 0.0	0.08	0.1	-0.2, 0.3	0.64	-0.1	-0.2, 0.0	0.08
	WASO /Time in bed	-0.1	-0.2, - 1.1	0.04	0.1	-0.2, 0.3	0.65	-0.1	-0.3, 0.0	0.04
Sedentariness (%)	Total sleep	-0.4	-0.4, -0.3	<0.01	-0.4	-0.5, -0.4	<0.01	-0.4	-0.5, -0.3	<0.01
	Time in bed	-0.4	-0.4, -0.3	<0.01	-0.4	-0.5, -0.4	<0.01	-0.4	-0.5, -0.3	<0.01
	Light Sleep	-0.3	-0.4, -0.3	<0.01	-0.4	0.5, -0.4	<0.01	-0.3	-0.4, -0.2	<0.01
	Light/Total Sleep	0.0	0.0, 0.0	0.50	0.0	0.0, 0.0	0.22	0.0	0.0, 0.0	0.64
	Light Sleep/Time in bed	0.0	0.0, 0.0	0.45	0.0	0.0, 0.0	0.60	0.0	0.0, 0.0	0.95
	Deep Sleep	-0.3	-0.4	<0.01	-0.3	-0.4, -0.2	<0.01	-0.2	-0.3, -0.1	<0.01
	Deep /Total Sleep	0.0	0.0, 0.0	0.49	0.0	0.0, 0.0	0.29	0.0	0.0, 0.0	0.86
	Deep Sleep/Time in bed	0.0	0.0, 0.0	0.63	0.0	0.0, 0.0	0.13	0.0	0.0, 0.0	0.59
	WASO	-0.4	-0.6, -0.2	<0.01	-0.8	-1.1, -0.5	<0.01	-1.0	-1.5, -0.6	<0.01
	WASO/Total Sleep	0.0	0.0, 0.0	0.47	0.0	0.0, 0.0	0.0	0.0	-0.1, 0.0	0.01
	WASO /Time in bed	0.0	0.0, 0.0	0.58	0.0	-0.1, 0.0	0.0	0.0	-0.1 0.0	0.01

Table 21. The Effect of Sleep on Physical Activity Across Postpartum Time Period

There were 81 women with step and sleep data and three-month postpartum weight available. The mean steps was 5397.0 ± 2402.8 and mean total sleep was 7.3 ± 1.1 hours. These women had mean absolute weight change of -5.5 ± 9.8 kilograms postpartum compared to their last recorded weight during pregnancy.

At the time of the current analysis. there were 44 women with step and sleep data and six-month postpartum weight available. The mean steps was 5317.4 ± 2352.4and mean total sleep was 7.3 ± 1.1 hours. These women had mean absolute weight change of -8.3 ± 7.0 kilograms postpartum.

	3 months postpartum mean (N=81)	**6 months postpartum mean (N=44)**
Steps	5397.0 ± 2402.8	5317.4 ± 2352.4
Active Minutes	52.3 ± 21.7	52.1 ± 21.5
Sedentariness	92.9 ± 2.9	93.2 ± 2.8
Total Sleep	7.3 ± 1.1	7.3 ± 1.1
Time in Bed	7.7 ± 1.0	7.8 ± 1.1
Light Sleep	3.7 ± 1.0	3.7 ± 1.2
Deep Sleep	3.6 ± 1.0	3.6 ± 1.0
WASO	0.5 ± 0.2	0.4 ± 0.2
Last antenatal weight (kg)	84.6 ± 20.8	85.5 ± 22.1
3-month postpartum weight (kg)	78.0 ± 20.6	N/A
6-month postpartum weight (kg)	N/A	77.2 ± 21.4
Absolute Postpartum Weight Change (kg)	-5.5 ± 9.8	-8.3 ± 7.0
Weight Change Proportion (%)	-7.5 ± 8.7	-9.8 ± 7.1

Table 22. Mean Steps, Sleep and Weight of Women at Three and Six Months Postpartum

There was no relationship between mean postpartum steps or sleep on the weight change of women at three months or 6 months postpartum. There was a positive relationship between sleep duration and 3-month weight (1.5 kilograms for every hour of sleep, 95% CI 0.2-2.9, p=0.02) and deep sleep and 3-month weight (1.4kilograms for every hour of sleep, 95% CI 0.1-2.6, p=0.03). However, this effect was not seen at 6 months postpartum (Table 23.). We were unable to analyse the effect of insufficient, sufficient and excess sleep on postpartum steps as there were only 3 women with long sleep and a 3-month postpartum weight and 1 woman with long sleep and a 6 month postpartum weight available.

	3-month weight n=81			6-month weight n=44		
Parameter	**Effect**	**95%CI**	**P value**	**Effect**	**95%CI**	**P value**
Steps	-0.4	-1.1, 0.2	0.20	0.5	-0.4, 1.4	0.27
Active Minutes	-0.1	-0.1, 0.0	0.12	0.0	-0.1, 0.1	0.63
Sedentariness	-0.6	-1.4, 0.1	0.11	-0.4	-1.2, 0.4	0.29
Total sleep	1.5	0.2, 2.9	0.02	-0.2	-2.2, 1.8	0.85
Time in bed	1.6	0.2, 3.0	0.03	-0.3	-2.4, 1.7	0.74
Light Sleep	-0.3	-1.9, 1.3	0.74	-1.1	-2.9, 0.7	0.23
Light/Total Sleep	-0.1	-0.2, 0.1	0.29	-0.1	-0.3, 0.1	0.19
Light Sleep/Time in bed	-0.1	-0.2, 0.1	0.40	-0.1	-0.3, 0.1	0.22
Deep Sleep	1.4	0.1, 2.6	0.03	1.3	-0.8, 3.4	0.23
Deep /Total Sleep	0.1	-0.1, 0.2	0.43	0.1	-0.1, 0.3	0.19
Deep Sleep/Time in bed	0.1	-0.1, 0.2	0.29	0.1	-0.1, 0.3	0.17
WASO	-2.9	-9.5, 3.6	0.37	-2.6	-11.4, 6.3	0.56
WASO/Total Sleep	-0.2	-0.6, 0.2	0.31	-0.1	-0.7, 0.4	0.61
WASO /Time in bed	-0.2	-0.7, 0.2	0.35	-0.2	-0.8, 0.5	0.59

Table 23. Effect of Mean of All Postpartum Steps and Sleep on Weight at Three and Six Months Postpartum

Rather than using the mean of all the postpartum step and sleep data available we also examined the effect of mean steps and sleep measured during 0-3 months postpartum on 3 month postpartum weight and mean steps and sleep measure during 3-6 months postpartum on 6 month postpartum weight. The positive relationship between sleep duration and 3-month weight (1.6 kilograms for every hour of sleep, 95% CI 0.2-2.9, p=0.03) and deep sleep and 3-month weight remained (2.2 kilograms for every hour of sleep, 95% CI 0.8-3.6, p<0.01). There was no association between mean physical activity and sleep during 3-6 months postpartum with 6 month weight (Table 24.).

	3 month weight * n = 75			6 month weight ** n = 36		
Parameter	**Effect**	**95%CI**	**P value**	**Effect**	**95%CI**	**P value**
Steps	-0.3	-1.0, 0.4	0.39	0.5	-0.7, 1.7	0.37
Active Minutes	-0.1	-0.1, 0.0	0.14	0.0	-0.1, 0.2	0.72
Sedentariness	-0.9	-1.7, -0.2	0.01	-0.5	-1.5, 0.5	0.33
Total sleep	1.6	0.2, 2.9	0.03	-0.5	-3.3, 2.3	0.72
Time in bed	1.5	0.0, 2.9	0.04	-0.7	-3.7, 2.3	0.63
Light Sleep	-0.7	-2.4, 1.0	0.42	-1.0	-3.4, 1.5	0.43
Light/Total Sleep	-0.1	-0.2, 0.0	0.17	-0.1	-0.3, 0.1	0.44
Light Sleep/Time in bed	-0.1	-0.3, 0.1	0.21	-0.1	-0.3, 0.2	0.48
Deep Sleep	2.2	0.8, 3.6	<0.01	0.6	-1.9, 3.1	0.62
Deep /Total Sleep	0.1	0.0, 0.2	0.17	0.1	-0.1, 0.3	0.43
Deep Sleep/Time in bed	0.1	0.0, 0.3	0.11	0.1	-0.1, 0.3	0.43
WASO	-3.7	-9.7, 2.4	0.23	-3.3	-16.9, 10.3	0.62
WASO/Total Sleep	-0.2	-0.6, 0.2	0.25	-0.2	-1.1, 0.7	0.67
WASO /Time in bed	-0.3	-0.7, 0.2	0.21	-0.2	-1.3, 0.9	0.69

Table 24. Effect of Mean Steps and Sleep between 0-3 Months and 3-6 Month Only on Weight at Three and Six Months Postpartum Respectively

5.4 Discussion

5.4.1 The effect of sleep on steps in postpartum women

There is increasing evidence that disordered sleep is associated with diabetes risk, glucose intolerance and poorer glycaemic control. The duration of sleep has been examined the most and studies demonstrate a U-shaped relationship with increased diabetes risk with both short and long sleep (62). Other features of sleep pertaining to its quality have also been considered. Increased sleep latency, later chronotype, sleep irregularity, more fragmented sleep and daytime napping are adverse sleep qualities when considering diabetes risk. This relationship may be mediated by its effect on physical activity.

Amongst the general population increased sleep duration can influence subsequent exercise performance however in postpartum women this relationship differed. An observational study of 365 women at 6 months postpartum, who wore an accelerometer for 7 days and completed the Pittsburgh Sleep Quality Index (PSQI) found over half the women in this study reported poor sleep quality. They found no significant associations between sleep quality and total activity over 24 hours. They also found that total activity, total minutes of MVPA and total minutes of light activity were all slightly greater in women with poor sleep quality however the difference was only small (131). Similarly,

another study of 530 women found that at 3 months postpartum there was no association between moderate-vigorous physical activities and sleep quality. At 12 months there was a weak association with childcare and recreational moderate-vigorous physical activities at 12 months postpartum (220).

In SMs2 we examined the relationship between sleep and physical activity in the at-risk postpartum women with GDM. In this study there was a significant increase in steps when sleep duration increased the night prior. This is the relationship expected when comparing to broader population studies. Active minutes also increased, and sedentariness decreased with more sleep however the effect may be too small to be clinically significant.

Women report that there is decreased levels of moderate – vigorous physical activity during pregnancy persisting until at least 6 months postpartum (221). Most of the women in this study did not reach high levels of moderate – vigorous physical activity, limiting associations that could be found with sleep. These reduced activity levels during the first 6 months of pregnancy may also explain why we were unable to appreciate increasing effect of sleep on physical activity over time.

Interestingly the negative effect of WASO was five times greater than the positive effect of sleep duration on steps the following day. This suggests that sleep fragmentation and quality of sleep may have a significant influence on physical activity. However, although WASO may exhibit a stronger effect on steps, this may be offset by the lesser duration of WASO compared to total sleep. A meta-analysis on the daily associations between sleep and physical activity found that sleep quality, sleep efficiency and WASO were the only parameters associated with physical activity the next day (133). This metanalysis included studies with objectively and subjectively measured sleep and physical activity. We did not find any other studies that demonstrated this effect in postpartum women.

It was also noted that the relationship between sleep and WASO with steps the following day were present in the first two month postpartum but did not persist through subsequent time periods. Sleep patterns in postpartum women change such that at 1-month postpartum women slept a mean of 7.53 hours per 24-hour period, of which 6.15 were nocturnal compared with the nonpregnant average of 8.43 hours average total (222). In addition to less total sleep time, sleep efficiency is also decreased with increased wake after sleep onset and daytime napping (223, 224). Infant sleep is characterized by multiple sleep and wake periods throughout the 24-hour day. In addition, metabolic demands and stomach volume necessitate frequent feedings. Consequently, nighttime sleep disruption among new mothers is a normative and accepted condition (222). With new motherhood associated with impacts on several domains of sleep quality, improvements in sleep parameters may have a more marked effect.

5.4.2 The effect of physical activity on weight

Excessive gestational weight gain or postpartum weight retention increases the risk of obesity and obesity-related diseases such as diabetes, metabolic syndrome, and cardiovascular disease (225, 226). Diet and exercise are interventions used to assist mothers in losing weight (227). A systematic

review of physical exercise strategies in postpartum women found that exercise improved weight loss with the most effective interventions being programs with objectively defined goals and exercise combined with intensive diet (228). A randomised controlled trial of 66 women who were 6 weeks to 6 months postpartum underwent a 12-week exercise intervention. They were provided with pedometers and encouraged to progressively increase their daily step count to a goal of 10,000 steps per day. They found a significant increase in physical activity over the duration of the intervention and significant weight loss differences between the groups (229). We did not find a relationship between steps, as a measure of physical activity, on postpartum weight change. In the study conducted by Maturi et al., the intervention included an initial counselling session, text messages, phone calls, written information pamphlet which is a more resource intense exercise intervention than was provided in this study. Subsequently the group with the pedometer and exercise program had significant weight loss over those without these interventions. They did not report whether steps alone were an indicator of weight loss. This suggests that steps alone may not be a sufficient intervention. Women were encouraged to reach a 10,000 step goal and the mean steps taken by women in our study was approximately only 5000 which may have been insufficient to cause a significant effect. Furthermore, this study excluded the early postpartum period and so women might have had more opportunity for exercise compared to women in this study

5.4.3 The effect of sleep on weight

Several studies have shown a relationship between sleep duration and postpartum weight. In A study exploring predictors of postpartum weight gain found that self-reported sleep duration less than 5 hours was a predictor of postpartum weight retention at 3 months (230). Similarly another study of postpartum women found that self-reported sleep of less than 5 hours per night was associated with substantial postpartum weight retention at one year (231). In a study where Black and Hispanic women had their sleep objectively measured by actigraphy at 6 weeks and 5 months postpartum and correlated this to their weight change at 6 weeks, 5 months and 12 months postpartum. There was no association between sleep duration at 6 weeks and weight change between 6 weeks and 5 months. However, women who slept less than 7 hours at 5 months had 1.8kg greater weight than women who slept more than 7 hours (232). There were no association between WASO, sleep efficiency or sleep timing with postpartum weight change.

Although there was a mean weight loss in our cohort there was an association between increased sleep duration and a greater weight at 3 months postpartum. In a prospective cohort study of women with GDM, there was a more than double risk of substantial postpartum weight retention in women who slept more than 8 hours at 6-9 weeks postpartum (233). Negative outcomes have been associated with long sleep in the general population such as increased risk of diabetes and glycaemic control. This finding raises the question about whether there is a different relationship between sleep and postpartum weight in women with and without metabolic disturbances such as GDM. Alternatively, there may be a U-shaped relationship that exists between sleep duration and postpartum weight.

However, this relationship did not persist at 6 months in our study which could be related to the fewer 6-month postpartum weights or the impact of new motherhood on healthy weight-related lifestyle habits. Additionally, half of the women recruited for SMs2 were randomised to receive text message support messages encouraging healthy dietary and exercise habits as well as activity monitor use during the time data was collected for this substudy. Therefore, we may have been more likely to obtain sleep and weight data for women who were more engaged because of the text messages. Weight loss that might have been associated with the text message intervention may have obscured the relationship between postpartum sleep and weight change at 6 months.

5.4.4 Strengths and limitations

There are currently no studies examining the relationship between physical activity and exercise in postpartum women who have had GDM. Neither of the studies on physical activity and exercise on post-partum women previously discussed explored the specific features of sleep quality but rather only on overall sleep duration. Furthermore, the use of a commercial device for everyday use enabled us to collect data over a long period of time, longer than any previous study of this nature.

The use of activity monitors allowed for objective measures of multiple sleep and physical activity parameters to be obtained in this young busy cohort that may not otherwise be achieved with conventional measurements such as actigraphy, polysomnography or questionnaires. Although it may be more convenient these devices are limited in the accuracy of the data they obtain as they are not validated measurement methods. A systematic review of these consumer worn devices demonstrated that overall they underestimate steps by of mean of 9% (178). However, as long as the bias is relatively consistent, this would not have affected our findings. When wearing a device for a short period of time, there is a possibility of altered behavior because the subject is conscious that she is in a study. By capturing data over a 6-month period, our data is more likely to reflect true free-living conditions.

The Garmin Vivofit used in this study does not have a heart rate monitor and this deficiency reduces its accuracy in assessing sleep when compared to more recent models that integrate heart rate variability (180). Despite the long battery life, there were several factors that limited the use of the device. These included comfort especially at night, removal for water-based activities, and impact on childcare. Being wrist-worn, it may have impinged on newborn care which may have deterred women from wearing the device. Users who were not engaged with the device may not have monitored their phone app to ensure syncing of the device and data uploads. These aspects may have affected consistent wear of the device impacting on data quality.

Gestational weight gain occurs predominantly from second trimester onwards in a relatively linear fashion varying widely across demographic groups (234). In this study the last recorded weight was used as a comparator to determine postpartum weight change. However, the last recorded weight occurred at their last clinic appointment which may have occurred weeks prior to delivery and

therefore not accurately correspond the participant's peak weight. As a result, weight loss may have been underestimated limiting the effect of physical activity and sleep observed.

As this remains an ongoing study at the time of analysis, fewer women had reached 6 months postpartum reducing the number that could be included at the timepoint for comparison of weight loss with a sleep. This likely also accounts for the increase variability of sleep and reduce steps at 240 days postpartum (Figure 16., Figure 17.)

5.5 Conclusion

Improved sleep may increase physical activity in postpartum women with a history of GDM. Qualitative analysis on other factors that influence sleep and physical activity in this early postpartum may help guide future lifestyle interventions.

Chapter 6: The effect of COVID lockdown on physical activity in postpartum women with gestational diabetes

6.1 Introduction

Smart Mums With Smart Phones 2 (SMs2) is a randomised controlled trial of text messaging support for women with GDM commencing after delivery until 12 months postpartum (190). GDM is a common complication of pregnancy and women with GDM have an up to 50% risk of developing type 2 diabetes mellitus (31). Lifestyle interventions are the preferred initial management strategy for those with pre-diabetes. These interventions have been applied to women with a history of GDM to prevent progression to T2DM with some effect (43). Furthermore improved lifestyle habits can not only improved risk of diabetes but also reduce postpartum weight retention (235) and more broadly reduce cardiovascular risk (236), improve mental health (237), and reduce risk of certain cancers(238). A meta-analysis of postpartum interventions in GDM to prevent T2DM showed most focused on diet and physical activity. In the 8 studies of these studies that commented on diabetes there was a borderline significant 25% reduction in diabetes incidence. Interventions that were implemented within 6 months after delivery were found to be more effective (50).

Women in this trial are encouraged to participate in physical activity, in particular walking. They are provided with an activity monitor which tracks their steps and provides feedback to the women regarding their step targets. Concurrent to this study was the emergence of COVID-19 pandemic which resulted in many countries implementing measures such as social distancing and lockdown to reduce the spread of the disease. Subsequently, studies have shown a reduction in physical activity and associated weight gain associated with COVID 19 (239). During SMs2, Sydney experienced a second wave of COVID-19 prompting a three-and-a-half-month lockdown. We explored how lockdown impacted on the exercise habits of this vulnerable postpartum population.

6.2 Method (see Chapter 2)

6.2.1 Study Design and Population

We included women who had been recruited for Smart Mums With Smart Phones 2 (SMs2), a randomised controlled trial of text messaging support for women after GDM at three metropolitan hospitals (190).

6.2.2 Variables

Baseline data included demographics, medical and family history, physical activity, dietary and sleep habits.

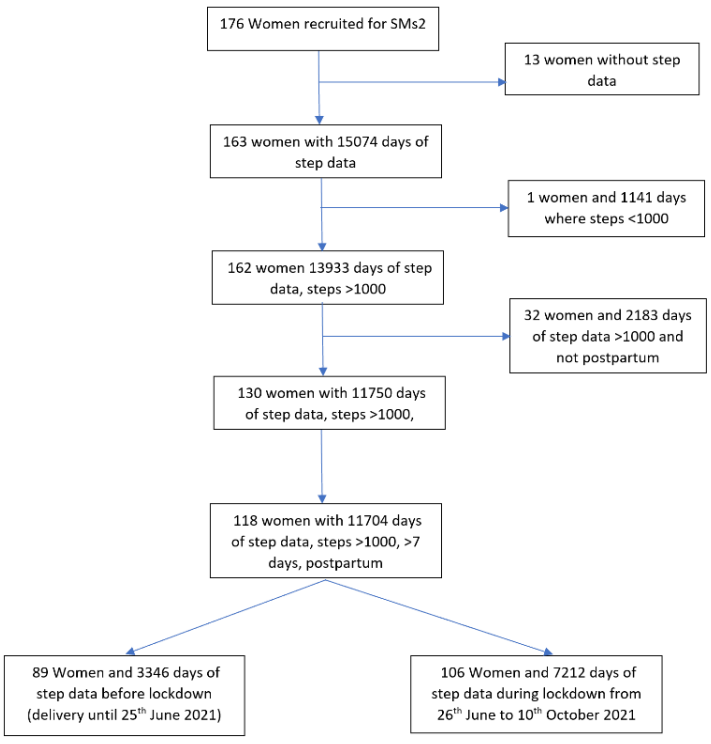

Figure 18. Selection of Study Population

All participants are provided with a wrist-worn activity monitor (Garmin Vivofit 4®) in their third trimester. This monitor tracks steps which is displayed on the device and a mobile phone app that with regular synchronisation to enabled data upload.

Postpartum step data was obtained and days where less than 1000 steps were taken were excluded as it is likely the activity monitor was not worn the entire day. Women who had less than 7 days of postpartum step data were also excluded as it suggested that the device was not being used consistently and may misrepresent their regular activity levels. Data was divided into before and during the implementation of lockdown restrictions in Sydney from 26th June until it began easing on 11th October 2021.

During this time residents of Greater Sydney were subjected to “stay at home orders” that did not allow people to leave their home except for essential reasons such as shopping for food, compassionate needs or medical care, exercise, essential work or education. Non-essential business such as retail stores, gyms, indoor recreational facilities and sporting venues were closed, and restaurants could only provide take away food. Exercise was initially limited to groups of 10 in open spaces such as parks however this was progressively tightened to only 1 person and for up to 1 hour at its peak. Residents could not leave their local government area except for essential reasons.

Mean daily steps taken during 1-3 months postpartum was compared with 3-5 months postpartum before lockdown to determine if there was a change in steps as participants progressed further from delivery. We did this same comparison interrupted by lockdown. This comparison was done only for women who had data for both time points. We included women who had data for at least part of the 1-3 months and 3-5 months postpartum time period. As SMs2 was still ongoing at the time of this sub study, few women were beyond a few months postpartum and these time periods allowed us to capture the most amount of women with a reasonable distribution between the groups to allow for adequate comparison. We also compared different postpartum periods before and during lockdown. We did not compare these steps to the post lockdown period as this analysis was performed only shortly after lockdown restrictions was lifted and there was limited data available at this time.

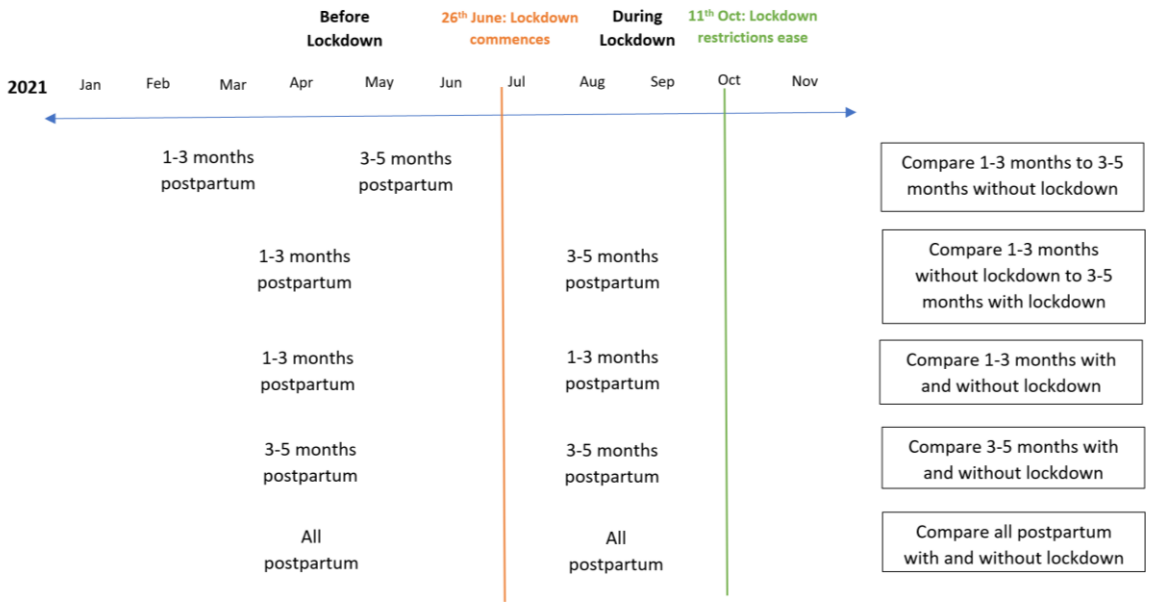

Figure 19. Plan for Analysis of Data

6.2.3 Statistical analysis

Student's t-test was used to compare the data between groups. Data are reported as mean ± standard deviation. Statistical significance was taken as a two–sided *p*–value <0.05.

6.3 Results

Smart Mums 2 recruited 176 women. Of these, there were 118 women with 11704 days of step data during the time period of interest. The mean age at conception was 32.5 ± 4.4, ranging from 20 - 42 years old. The mean daily steps were 4876 ± 2087.

	Group	% (N)	Mean
Age at Delivery			32.5±4.4
Pre pregnancy BMI			29.4±7.2
Country of Birth	Australia/New Zealand	36.4 (43)	
	European	1.7 (2)	
	Pacific Island	4.2 (5)	
	Central America	0.8 (1)	
	South America	1.7 (2)	
	North America	0.8 (1)	
	Middle East	4.2 (5)	
	East Asia	1.7 (2)	
	South East	5.9 (7)	
	South Asia	40.7 (48)	
	Africa	1.7 (2)	
Education level	No formal education	0.8 (1)	
	Year 10 School Certificate	9.3 (11)	
	Year 12 School Certificate	11.0 (13)	
	Technical and Further Education	22.0 (26)	
	University Undergraduate	26.3 (31)	
	University Postgraduate	30.5 (36)	
Previous GDM	No	63.6 (75)	
	Yes	36.4 (43)	
Family History of Diabetes	No	44.9 (53)	
	Yes	55.1 (65)	
Gravidy	1	25.4 (30)	2.8±2.0
	2-15	74.6 (88)	
Parity	0	31.4 (37)	1.0±0.9
	1-4	68.6 (81)	

Table 25. Demographics and Obstetric History of Women Included

There was no difference in daily steps undertaken by women who were 1-3 months postpartum compared to those who were 3-5 months postpartum before lockdown. However, there was a significant difference between these 2 time periods when the 3-5 months postpartum time period was affected by lockdown ($t(48) = 2.67$, $p=0.01$). There was a trend towards increase in steps at 1-3 months and 3-5 months postpartum for women during lockdown compared to before lockdown however these did not reach statistical significance. Overall, there were significantly more steps taken during lockdown (5197 ± 2139) for the same 77 women compared to before lockdown (3972 ± 1742) irrespective of how many months postpartum they were ($t(76) = 6.33$, $p < 0.01$). (Table 26.)

Before lockdown (Delivery until 25/6/21)			During lockdown (26/6/21 – 10/10/21)	P value
Number of months postpartum	**1-3 months**	**3-5 months**		
Mean daily steps N=24	4490 ± 1441	4857 ± 1525		0.16
Number of months postpartum		**1- 3 months**	**3 - 5 months**	
Mean daily steps N=49		4607 ± 1857	5308 ± 2171	0.01
Number of months postpartum		**1-3 months N=58**	**1-3months N=76**	
Mean daily steps		4683 ± 1995	5160 ± 2557	0.15
Number of months postpartum		**3 - 5 months N=25**	**3-5 months N=85**	
Mean daily steps		4875 ± 1496	5531 ± 2343	0.10
		All postpartum	**All postpartum**	
Mean daily steps N=77		3972 ± 1742	5197 ± 2139	<0.01

Table 26. Comparison of Mean Steps Before and After Lockdown

6.4 Discussion

6.4.1 Effect of lockdown on steps during lockdown

In a review of 19 articles on the impact of COVID-19 on weight and weight related behaviours, half of respondents gained weight whilst one-fifth lost weight. Additionally, there was a 36.3% to 59.6% increase in total food consumption and a 67.4% to 61.4% decrease in physical activities (239). These trends raise concerns regarding the impact of COVID-19 on postpartum women with GDM who are at risk for T2DM and ideally should be improving their diet, activity levels and avoiding postpartum weight retention. Across 30 million users, FitBit reported a decrease in steps in many countries including a 4% reduction in Australia (240). Similarly in a study on 455 404 smartphone users across 187 countries there was a 5.5% decrease in mean steps within 10 days of pandemic declaration and a 27.3% decrease in mean steps within 30 days (241). In contrast, we found that physical activity as measured by a daily step count increased during lockdown in postpartum women after a GDM pregnancy.

A study in Belgium found that in adults less than 55 years of age, adults who were not very physically active engaged in more activity during lockdown. Whereas people who were active prior to lockdown but relied on organised sport, exercise classes or other social supports to motivate exercise were more likely to be affected by lockdown (242). Walking is the most common form of exercise undertaken by postpartum women as it is functional, easy and low cost (243). As Australians were still able to exercise outdoors during pandemic lockdowns, unlike those who may rely on gyms or group sport for their physical activity, postpartum women would have still been able to access their main form of exercise during lockdown. The catchment area for SMs2 was largely areas where most people live in stand alone home dwellings and therefore outdoor walking was quite possible, as compared to areas where high rise apartment blocks dominate. As such the impact of lockdown on exercise may have not been so great in these women.

In the UK, pregnant women with gestational diabetes had increased sedentary time and there was a reduction in the number of women meeting physical activity guidelines predominantly accounted for by fear of leaving the house due to COVID 19 (244). Our findings were in contrast to this, possibly because the of the lower infections rates seen in Australia compared to the UK in the earlier waves of COVID 19. Additionally, as outdoor exercise was one of the few reasons to leave the house, and advised by health authorities to be safe given the ability to maintain social distancing, walking may have increased during this time. Therefore, the decrease in physical activity observed in larger population studies may be less applicable to postpartum women in Australia. Furthermore, the external influence of COVID 19 pandemic and subsequent lockdown which brought health and the benefits of exercise to the forefront of people's attention. As a result postpartum women who would ordinarily exercise by walking outdoors may have been more motivated to do this during lockdown.

Interventions for women with GDM have shown that barriers to continuing lifestyle modifications postpartum include tiredness and childcare demands early in the postnatal period (159, 160).

Typically, support from family and friends, or childcare facilities can enable more healthy behaviour by assisting with childcare (159). For example, this can enable the woman to have time to perform purposeful exercise, but it may also allow earlier return to work or pursuit of leisure activities. In our cohort, one may expect that with lockdown, there was reduced access to this support and this would result in less opportunity for exercise. One potential explanation for our unexpected finding is that because of the loss of childcare support women were undertaking more incidental physical activity through their maternal caregiver role, and this was being detected on the activity monitors. Alternatively, although access to support outside of the household may have been reduced, with more people working from home, women may have had substantially more support from their partners or other household family that subsequently allowed women more opportunity to exercise. The reduction in social demands associated with lockdown may have also increased free time that could be reallocated to exercise.

Postpartum women are vulnerable to changes in support networks and accessibility to social care services associated with COVID 19 lockdown. This accounts for the increased prevalence of postnatal depression seen in Australian women during the pandemic (245). Although an increase in mental health issues may have adversely affected exercise, a study of in the United States of pregnant, birthing and postpartum experiences during COVID 19 found that participants reported that self-care included engaging in physical activity suggesting exercise may have been a coping mechanism for the increased stress of lockdown (246).

Our findings may not be generalisable to all post-partum women. The women in our study may have been more motivated as they joined a study of a lifestyle intervention to reduce diabetes risk. However, this would not account for the increase in step count during lockdown. Half of the women were randomised to receive text message support that included physical activity encouragement, links to sources of physical activity support, and progressive step goals. These interventions may have been particularly valuable and effective during lockdown.

A study on activity levels of 181 postpartum women as measured by survey and accelerometer for 1 week at three and twelve months postpartum found there was an increase in step count and less sedentary time at twelve months postpartum. There was no change in moderate and vigorous intensity activity except for an increase in reported indoor household activities (247). We did not find a significant difference in steps as women progressed from 1-3 months postpartum period to 3-5 months postpartum without the interference of lockdown. Given that the women in this study gave birth from January to August 2021, few women had reached beyond a few months postpartum before lockdown restrictions were imposed. We therefore could only assess the changes in physical activity postpartum over a short time that may have been insufficient to detect any change.

6.4.2 Limitations

The Garmin Vivofit used in this study is a wrist worn monitor that does not measure heart rate and therefore is dependent on arm swings detected by an accelerometer to count steps. Monitors that can

measure heart rate have higher accuracy. During trials of the device in SMs2, it was noted that movements associated with settling an infant could overestimate steps and that reduced arm movement with pushing a pram could underestimate steps. In a systematic review examining the validity and accuracy of wearable devices, the Garmin Vivofit has significant variability within the same device for step count (178). However the large volume of step data in this study, with over 11,000 days of step data, minimises the effect of this variability on the outcome.

Other quantitative measurements were not obtained in this study to validate our findings and as there were no qualitative measurements or surveys conducted, we can only speculate on the causes for the increased physical activity during lockdown in these women. The reasons for this will be explored in focus groups following the conclusion of the RCT.

6.5 Conclusion

Our study demonstrates that COVID-19 lockdown does not necessarily reduce physical activity and in post-partum women who have had GDM, there is an increase in activity. The reasons for this are unclear, but this may be due to changes in the home and supportive environment. At least in our context, concerns that lockdown might increase diabetes risk for these women because of reduced physical activity are unfounded.

Chapter 7: Discussion

Gestational diabetes poses a growing problem as a result of its increasing prevalence(4) and significant risk for subsequent T2DM (32, 172) and its associated long-term complications. To address this, lifestyle interventions have been trialled on this cohort with varying degrees of success (41, 42, 44, 45, 47). However, these interventions are largely limited to targeting diet and physical activity and the long-term success that is needed is often hindered by the engagement and competing demands of these women (159, 160, 165). Increasing evidence indicates that sleep influences diet, physical activity and diabetes risk and the current studies explore these effects in women with gestational diabetes and how we can expand lifestyle interventions in attempt to achieve better outcomes. The use of activity monitors in these studies brings into consideration how we can take advantage of developing technologies to provide insights into this relationship and bolster current interventions.

7.1 Measurement of sleep and physical activity

7.1.1 Measurement methods

Polysomnography is the gold standard of sleep measurement however it is expensive, requires laboratory settings, can be intrusive and measurements are limited to a few days which may misrepresent the natural sleep environment. The introduction of actigraphy, a wrist worn device that can tracks activity levels to measure sleep-wake patterns over long time periods, is able to address some of these issues (248). Over several decades, growing research validated their use as an objective sleep measurement tool with a concordance of over 90% with polysomnograhy (249). However as sleep is inferred from lack of movement, they are limited in the their measurement of sleep onset latency and fragmented sleep where the subject may be awake but motionless (250) resulting in an overestimation of sleep and underestimation of wake time (248). Although actigraphy has been accepted as a reliable and validated research tool, procedures for their use are not standardized and variability remains in type of actigraphy use, placement location, sampling and data processing (251). These methodological differences can limit comparisons between studies. Similarly objective measures of physical activity such as direction observation, pedometers and heart rate monitors are limited in their accessibility and expense in the former and accuracy in the latter two (252).

Activity monitors were used in these studies to collect data on sleep and physical activity in favour of these more traditional methods. Mobile health technologies are becoming increasingly accessible and their low cost, mobility, ability to be customised and be interactive has led researchers to include them in various lifestyle interventions(168). Consumer wrist worn devices are one of these technologies that are becoming more available with numerous companies providing a wide variety of devices. These devices have features that capture physiological data beyond actigraphy such as heart rate and sleep patterns as well as physical activity including steps, distance walked, intensity of physical

activity. Their consumer-friendly interface and design make them attractive and practical for use by the general population.

Advancement of data collection methods can result from the convenience of these devices, their availability and population uptake. In these studies, we were able to record a large volume of data over a longer period of time than has been used in most previous studies. This allowed us to demonstrate a relationship between sleep and physical activity in postpartum women with GDM that although had been shown in general population, had not been demonstrated in this cohort in previous studies. These devices are also able to obtain more granular data such as sleep stages and fragmentation than can be achieved by self-reported surveys alone but are not as invasive or time consuming as polysomnography. By providing a greater degree of information, we may be able to better understand the relationship between lifestyle risk factors and create better models of care for patients.

7.1.2 Limitations to consider

An innate problem with using devices developed by private companies is the variability in algorithms and sensors used by these devices are not readily available to scrutinise or validate. Although studies have been performed to compare the accuracy and reliability of these devices compared to standardised measures (178), other implications to consider are how to compare results from studies that use different devices. This issue is compounded by the constant development and production of new devices.

The Garmin Vivofit used in these studies was limited by its lack of heart rate monitor which has been shown to reduce accuracy in sleep tracking and determining sleep stages (179). It also did not detect daytime naps which is an important component of sleep health. This device was also reliant on arm swings to determine steps and therefore exercise without this would be underrecognised whilst sedentary activities with repetitive arm swinging movement would be misconstrued as exercise. Additionally, only moderate intensity exercise was recognised by this device which is important as the duration of vigorous intensity exercise is weighted twice as much as moderate exercise in the assessment of physical activity. Improving the features and data processing of a device to address these issues is inherently coupled with increased cost.

Overall, by using activity monitors we were able to explore relationships and demonstrate associations between sleep, physical activity, weight and glycaemic control in gestational diabetes with greater detail than previous studies. The large volume of data, and extended period of collection may compensate for the inherent inaccuracies of the commercial monitors, and therefore these new technologies have the potential to be an important and useful research tool.

7.2 The impact of lifestyle factors on gestational diabetes

7.2.1 Glycaemic control during pregnancy

Physical activity has an established role in pregnancy. Regular exercise is recommended to all pregnant women and in women with GDM, physical activity is an important part of non-pharmacologic management (191). Several studies have demonstrated the improvement in glycaemic control with exercise in women with GDM (194). More specifically, as pregnant women most commonly engage in walking for exercise, negative correlations between number of steps walking daily and BG have been shown (196). The current study showed trends that echoed these findings and provides support for exercise in GDM management. In this study, there was a trend to increase in daily steps resulting in decreasing postprandial BGs but not fasting. It is possible that a larger sample size, or a program which purposefully aims to increase exercise will show a stronger relationship between physical activity and glycaemic control. It must be kept in mind that in our study, there was no intervention during pregnancy, so we were only observing normal, modest levels of activity in our participants.

More recently, multiple characteristics of sleep have been associated with diabetes risk, glucose tolerance and glycaemic control including duration (59), fragmentation (70), latency (74), regularity (92), napping (77) and chronotype (68). Sleep problems are common in pregnancy particularly in the third trimester where duration is shortened, quality decreased and fragmentation increased (200, 202). Poor sleep quality is associated with the development of gestational diabetes (207). Recently studies have demonstrated a relationship between sleep duration and BG readings as well as sleep quality and glycaemic control (214, 215). In our small cohort of women with GDM at various stages of pregnancy, we could not find a linear relationship between sleep duration and glycaemic control in women with GDM in our small cohort, however there was evidence that achieving sleep duration between seven to nine hours increased likelihood of reaching BG targets for the following day. In the subgroup of women less than 36 weeks gestation, increase sleep duration improved fasting BG the following day. The use of the activity monitor enabled examination of other features of sleep and it was found that WASO which contributes to sleep fragmentation and poor sleep quality negatively affected glycaemic control in GDM which is consistent with previous studies (208). A larger sample size may have been able to demonstrate clearer associations between sleep duration and glycaemic control in GDM as seen in the relationships we found in subgroups; however the magnitude of this effect under normal circumstances may not be clinically significant.

7.2.2 Postpartum weight retention

Excess postpartum weight gain is associated with increased risk of obesity and obesity-related diseases such as diabetes, metabolic syndrome, and cardiovascular disease (225, 226). For women who have had GDM, this is increasingly important as they are already at increased risk of these diseases and weight retention can potentiate these risks (253). In the postpartum period, weight loss in women with GDM is associated with improvement in glucose metabolism (254, 255).

Gestational weight gain is one of the strongest predictors of postpartum weight retention (256, 257). Other factors such as pre-pregnancy BMI (258), breastfeeding duration (259), postpartum exercise and food intake (260), sleep duration, parity(261), depression(262) and vitamin D levels (263) have also been associated with weight retention. Sociodemographic factors such as race, maternal age less than 20 or above 40, unemployment, low education level have also been reported as predictors with varying consistency (230).

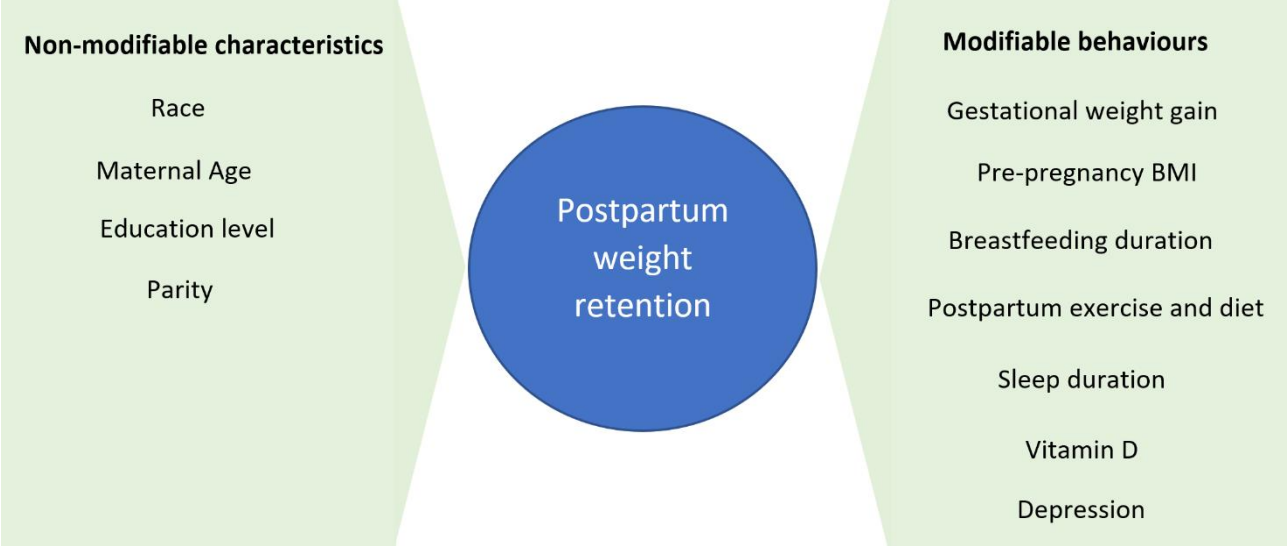

Figure 20. Risk Factors for Postpartum Weight Reduction

In postpartum women, healthy dietary behaviours (264) and physical activity (265) are often suboptimal contributing to weight retention (266). Systematic reviews have shown that interventions targeting diet only can produce weight loss however exercise only programs are not as efficacious (227). Successful lifestyle interventions have intensively targeted both diet and physical activity but are generally of short duration (227, 228, 267, 268). Caloric restriction is primarily responsible for weight loss whereas physical activity has an important role in weight maintenance. Physical activity also has greater reduction in fat mass compared to diet only weight loss and increase muscle mass which can improve insulin resistance and glycaemic control (269). The effectiveness of these interventions can be limited by poor engagement and high attrition rates (48, 270) and their longer term ability to improve weight management are unclear.

There is emerging data that weight is associated with sleep (271). In a cohort of 688 postpartum women, those that reported less than five hours of sleep showed increased weight retention at 3 months postpartum however this was no longer a significant predictor of weight retention at 12 months (230). Another study however did show women who slept less than five hours at 6months had significant postpartum weight retention at 1 year (218). Other studies exploring this relationship have also demonstrated similar findings (272). Obesity is associated with nocturnal sleep disturbance and short sleep duration even in the absence of obstructive sleep apnoea (273, 274). The findings from our study of GDM women instead showed a positive relationship between sleep and weight. This is consistent with another postpartum GDM study where an excess of 8 hours of sleep doubled the risk

of postpartum weight retention. This may represent a U-shaped relationship that has been described between sleep duration and impaired glucose tolerance and T2DM (58, 59) however we were unable to demonstrate this in our postpartum study. Further research could explore the positive relationship that has been demonstrated in postpartum women with GDM.

7.3 The relationship between sleep and currently targeted lifestyle factors

Sleep is associated with the most commonly targeted modifiable lifestyle factors, physical activity and diet. There is thought to be a bidirectional relationship between sleep and physical activity with large population studies showing that poor sleep has higher odds of physical inactivity and vice versa (126). These effects can be seen on both an acute and chronic basis (134). We found that this effect was present in our study of postpartum women with GDM where duration of nocturnal sleep was positively associated with an increase in daily steps the following day.

Sleep restriction is associated with increased caloric consumption, increased intake of fat, carbohydrates, snacks and less vegetables (141-143, 145, 146). Diet considered healthier such as Mediterranean diet are associated with better sleep (147, 148). Furthermore, sleep extension reduced the intake of free sugar, fat and carbohydrates (150).

The relationship between physical activity and diet is less established. Cross sectional studies have shown that increased physical activity was associated with healthier eating habits such as increased intake of fruits and vegetables and lower consumption of saturated fats (275, 276). Furthermore, improvements in fruit and vegetable intake may increase the likelihood of increased physical activity and vice versa (277).

In all likelihood, the modifiable lifestyle factors of physical activity, diet and sleep are all inter-related with bidirectional relationships (Figure 21.).

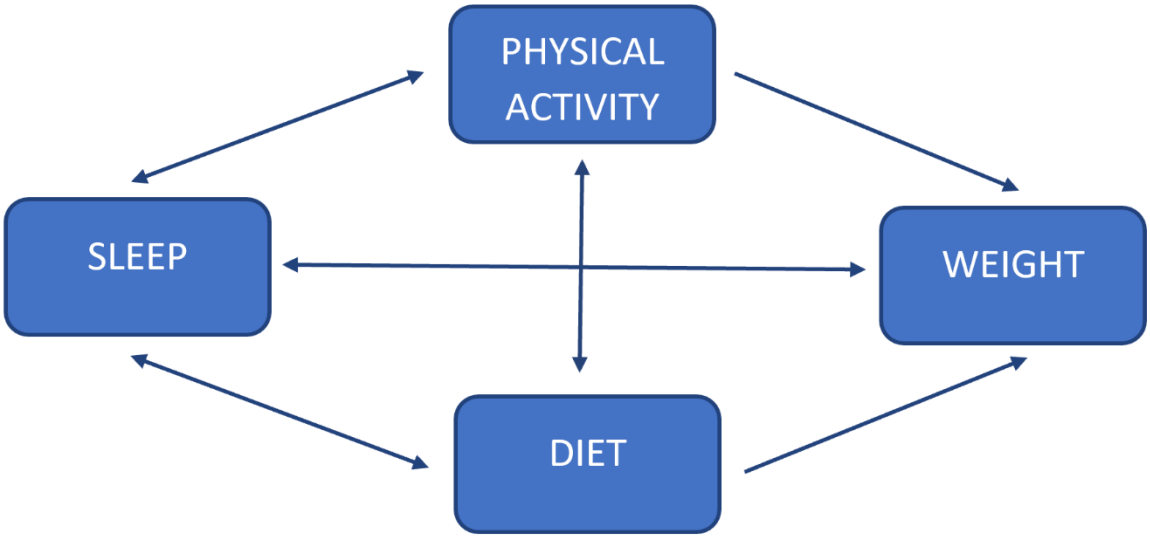

Figure 21. Relationship Between Sleep, Physical Activity, Diet and Weight

7.4 Treating sleep as a modifiable lifestyle risk factor

Sleep has hitherto received very little clinical attention and we suggest that the current scope of lifestyle interventions should be broadened to improve sleep as well, particularly among women with GDM, both during pregnancy and post-partum.

Multiple studies have demonstrated that treating sleep may improve glycaemic control. In a small study of 16 healthy participants who were instructed to increase their sleep time from a baseline mean of 6.5 hours, there was an improvement in fasting glucose levels and higher insulin-to-glucose ratio suggesting better insulin sensitivity (98). A similar study of 21 nondiabetic subjects who reported less than 6 hours of sleep per night found that sleep extension improved glucose metabolism only in individuals who were able to obtain at least 6 hours of sleep per night suggesting a potential threshold effect (278). A study of adolescent patients with type 1 diabetes found that participants randomly assigned to sleep extension for one week had a 7.4% improvement in glucose levels with an increase of 11 hours of glucose time in range (279). In a pilot study of 45 type 2 diabetic patients who slept after midnight, a structured diabetes sleep education program improved sleep quality, reduced HbA1c and fasting glucose at 3 months follow up (280). However a sleep education program applied to 74 women with GDM in a pilot RCT found that there were no differences in the proportion of women achieving glycaemic control during pregnancy or sleep knowledge and quality (281).

The benefits of treating sleep has also been explored in regards to weight management. In a study of 123 overweight and obese women undergoing caloric restriction, sleep duration was positively associated with weight loss and better sleep quality at baseline was associated with greater fat loss (282). Similarly in a study of overweight and obese women who were enrolled in a weight loss program, better subjective sleep quality and sleep duration more than seven hours increased the likelihood of weight loss (283). The preliminary results from a randomised controlled trial of obese short sleepers where nonpharmacologic and behaviour based interventions were used to extend sleep, reported more willingness to exercise and less craving for sweet or salty snacks (284). Furthermore, in a RCT with 80 overweight adults who slept less than 6.5 hours per night, individualized sleep counselling that increased mean sleep duration by 1.2 hours per night was associated with a decrease in energy intake of 270 kilocalories per day after 2 weeks. Theoretically if this reduction were sustained, it could translate into approximately 12 kilogram weight loss over 3 years (285).

Few sleep treatment studies can be seen in postpartum women possibly because of the altered priorities of these women in whom interventions must correspond with the demands of caring for a newborn. A small pilot study that was conducted on twelve women with GDM who were at least 1 year postpartum with less than seven hours of sleep per night found that women randomised to a sleep coaching intervention reported improvement in sleep quality and a trend towards increased physical activity. Follow up OGTT at 6 weeks showed increased fasting and 2 hour glucose levels for both the intervention and control groups but this was worse in the control group (286).

Current research suggests that lifestyle modifications may be augmented by incorporating the potential benefits of sleep. Non-pharmacologic behavioural sleep programs could be adapted from cognitive behavioural therapy for insomnia to pregnant and postpartum women. The general principles of these programs include:

a) Stimulus control therapy to strengthen the relationship between bed and sleep by having consistent sleep and wake times and avoiding non sleep activities in bed
b) Sleep restriction therapy to shorten amount of time in bed not sleeping
c) Sleep hygiene including comfortable and cool environment, avoiding tobacco, alcohol, caffeine and vigorous exercise several hours before bed (287)

The feasibility and benefits of integrating a sleep program with usual lifestyle measures is yet to be studied.

7.5 Utility of commercial wrist worn devices to support lifestyle interventions

Although expanding lifestyle management to be increasingly multimodal by addressing sleep could improve care of gestational diabetes during pregnancy and postpartum, success in their implementation and evaluation would require greater engagement than that seen in the current interventions. The rapid expansion of technology and its ubiquitous use in society has led to the adoption of mHealth which utilizes these mobile technologies to support public health practices (166). The promise of its use if exemplified in a qualitative study that found that women had positive and accepting views of mHealth for lifestyle interventions in antenatal care.

Trials of lifestyle interventions in pregnant women using a smartphone app have been shown to improve dietary behaviours and motivation for exercise but may not improve gestational weight gain (288-291). Another study of 49 women with recent GDM who underwent a 13-week intervention explored the use of a different form of technology with a web-based pedometer programme with individualised and adaptive weekly step goals and education on lifestyle modification. However, there were no significant behavioural changes, or improvements in fasting and 2-hour glucose or weight. There were low enrolment rates in the programme and the investigators suggested that more intensive self-monitoring may be needed to change behaviour (292). This is supported by a meta-analysis of studies promoting healthy dietary and physical activity behaviours which found that interventions with self-monitoring are more effective (293).

Commercially available wrist worn devices are a newer technology that can be used to support lifestyle interventions. In particular they could be advantageous in postpartum women who are managing the childcare demands of new motherhood where engagement and participation might otherwise be limited by traditional data measurement methods such as surveys or polysomnography. It could also be used to address issues with engagement seen in previous lifestyle interventions as it increases self-monitoring, can provide individualised feedback, allows goal setting and can access

social platforms. Furthermore, these devices also tackle the resource and time burden associated with the successful but more intensive lifestyle interventions improving scalability.

A meta-analysis of twelve studies using pedometers and accelerometers in participants with T2DM found an increase in physical activity of one hour per week; however there was no improvement in HbA1c, BMI or blood pressure (184). However a majority of these studies used pedometers and the participants had well controlled baseline HbA1c (294). In a systematic review of 21 studies where activity monitors were used as a feedback tool for physical activity interventions in T2DM patients, there was increase in physical activity and beneficial effect on HbA1c, systolic blood pressure and BMI. Another systematic review demonstrated similar improvements in health outcomes in people with chronic disease (182).

A systematic review exploring interventions using consumer wearable activity monitors on physical activity compared to devices that do not provide feedback found there was a significant increase in daily step count, moderate and vigorous physical activity and energy expenditure (181). In a cohort of people with type 2 diabetes, using an activity monitor that displayed exercise intensity resulted in a greater reduction in Hba1c compared to a pedometer at 2 months. However, at 6 months the effect attenuated and there were significant attrition rates (183). This suggests the feedback provided by these devices may improve engagement in physical activity however these devices may be an insufficient intervention alone in the long term and ongoing motivation and follow up is required.

Supplementing wearable devices with other technologies such as text messaging is an option to address this and has been shown to be beneficial. A study in 27 patients with T2DM who did not regularly engage in physical activity found that the use of a pedometer linked to their smartphone with text messaging feedback and personalised to their compliance increased the amount and pace of physical activity and was associated with a reduction in Hba1c (295). A similar study in T2DM that used individualised text messages with adaptive goals based on daily step counts captured by a pedometer was able to improve step counts and reduce Hba1c (170). In a systematic review of RCTs on improving physical activity in adults with chronic disease found that using mobile apps or activity trackers that allow for self-monitoring and feedback increased daily step count. The effectiveness of these interventions were higher when text messages and personalisation were included (296).

Sustaining the effects of wearable devices is important if an intervention is to translate into better health outcomes however few studies have explored how these complementary technologies fare long-term. Factors that improve maintenance of use include age, internal motivation, social support and recognising long term benefits (297, 298). Text messaging may be able to provide this remote support, motivation and education to assist with the maintenance of lifestyle changes. In a study on improving physical activity in cancer survivors, participants who received an intervention incorporating an activity monitor, follow up calls and tailored text message support were able to maintain recommended levels of moderate to vigorous physicality activity over an 8-week period whereas this declined in the activity monitor only control group. However, the intervention did also include health

coaches which may account for some of the improved outcomes outside of automated mobile health technologies alone (299).

It has been demonstrated that the use of health technologies can be included into multimodal lifestyle interventions. Activity monitors integrated with text messaging feedback can support lifestyle interventions to increase and maintain physical activity and improve health outcomes. Furthermore, adaptive goals and reinforcement has been shown to improve step counts (300) and moderate-to-vigorous activity in adults (301). In the six-month pilot study, Smart Mums 1, customisable text messages linked to an activity monitor utilised goal setting and feedback as part of a lifestyle intervention on postpartum women with GDM and found trends to improved physical activity, diet and weight loss (172). Smart Mums 2 runs on a similar premise but is a larger multicentre study from which we have been able to explore the consequences of lifestyle habits. The study is ongoing and plans to further explore how text messages and activity monitors can increase physical activity and sustain positive behavior change (190).

In regards to wearability of these devices, it was found in Smart Mums 1 that despite most participants providing positive feedback, problems with the device such as minor damaged or technical error cause interruption in their usage limited their participation in and benefits from lifestyle interventions suing activity monitors (172). Similarly in a study of a acceptability and feasibility of using activity monitors to support increased physical activity in an exercise referral scheme for adults found that monitors increased awareness pf physical activity however wearability and malfunctioning were barriers (302). In a physical activity intervention using Fitbit monitor and text messages in cancer survivors with participants had positive attitude toward the intervention an most participants felt that effort required was limited and manageable. However, some felt that the prescribed daily step count took away self-control and interpreted the encouragements as highlighting participants inability to meet goals (303). Wearability could be optimised but having a lead in trial period of these devices so that participants are able to adapt to them and to identify and fix any technical issues prior to the intervention. Further individualisation of messages and increasing interventions adaptability would also improve user satisfaction. At the conclusion of SMs2, focus groups are planned to explore benefits and limitations of the intervention that could be applied to future interventions.

7.8 Conclusion

Sleep and physical activity are important lifestyle factors to consider in management of GDM during and after pregnancy. Health technologies such as wearable devices could be adjunct in lifestyle interventions. Models of care should consider using activity monitors to provide continuous remote support promoting sleep and physical activity.

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