

**Dietary and Lifestyle Advice for Women to Prevent and  
Treat Pregnancy Hyperglycaemia: Identifying and Closing  
Research Gaps**

Shanshan Han

Discipline of Obstetrics and Gynaecology

School of Paediatrics and Reproductive Health

Faculty of Health Sciences

March 2014

# INDEX

Pages

<b>Table of contents .....</b>	<b>ii</b>
<b>List of tables and figures .....</b>	<b>viii</b>
<b>List of abbreviations.....</b>	<b>xi</b>
<b>Abstract .....</b>	<b>xiv</b>
<b>Declaration .....</b>	<b>xvii</b>
<b>Acknowledgements .....</b>	<b>xviii</b>

# Table of contents

Pages

<b>1</b>	<b>Literature review on prevention and management of hyperglycaemia in pregnant women.....</b>	<b>1</b>
<b>1.1</b>	<b>Introduction.....</b>	<b>1</b>
<b>1.2</b>	<b>Hyperglycaemia and gestational diabetes mellitus .....</b>	<b>2</b>
<b>1.3</b>	<b>Aetiology and pathogenesis of hyperglycaemia in pregnancy .....</b>	<b>3</b>
1.3.1	Higher insulin resistance when compared with a normal glucose tolerance in pregnancy.....	4
1.3.2	Pancreatic $\beta$ -cell dysfunction.....	4
1.3.3	Genetic predisposition .....	4
<b>1.4</b>	<b>Risk factors for Gestational Diabetes Mellitus.....</b>	<b>5</b>
1.4.1	Advanced age at conception .....	5
1.4.2	Pre-pregnancy overweight or obesity .....	6
1.4.3	Excessive weight gain since age of 18 years .....	6
1.4.4	Excessive gestational weight gain during pregnancy .....	7
1.4.5	History of having a macrosomic infant.....	7
1.4.6	Previous history of GDM.....	7
1.4.7	Family history of Diabetes Mellitus .....	8
1.4.8	High or low maternal birthweight.....	8
1.4.9	Ethnicity.....	8
1.4.10	Parity.....	9
1.4.11	Polycystic ovarian syndrome .....	9
1.4.12	Diet with low fibre and high glycemic load .....	9

1.4.13	Physical inactivity.....	10
<b>1.5</b>	<b>Identifying strategies that can prevent pregnancy hyperglycaemia .....</b>	<b>10</b>
<b>1.6</b>	<b>Screening for Gestational Diabetes Mellitus .....</b>	<b>11</b>
1.6.1	Australian recommendations on screening for GDM.....	15
<b>1.7</b>	<b>Diagnosis of Gestational Diabetes Mellitus.....</b>	<b>16</b>
1.7.1	Recommendations in Australia and New Zealand for the diagnosis of GDM	19
<b>1.8</b>	<b>Adopting the new IADPSG criteria and prevalence of hyperglycaemic disorders during pregnancy and GDM.....</b>	<b>20</b>
<b>1.9</b>	<b>Health outcomes for gestational diabetes mellitus.....</b>	<b>22</b>
1.9.1	Fetal outcomes for GDM when untreated.....	22
1.9.2	Maternal outcomes for GDM when untreated .....	23
<b>1.10</b>	<b>A review of the evidence base for treatment of women with GDM: specific treatment compared with standard antenatal care .....</b>	<b>25</b>
1.10.1	Current recommendations on treatment and management for GDM .....	26
1.10.2	Management and treatment recommendations in Australia for GDM .....	27
<b>1.11</b>	<b>Evidence for management and treatment of Borderline Gestational Diabetes Mellitus.....</b>	<b>28</b>
1.11.1	Introduction.....	28
1.11.2	Perinatal health outcomes of untreated pregnant women with intermediate glucose intolerance without meeting current diagnostic criteria for GDM – evidence from observational studies.....	28
1.11.3	A review of the evidence base for treatment of women with glucose intolerance not meeting current diagnostic criteria for GDM.....	32

1.11.4	Diagnosis of glucose intolerance not meeting current diagnostic criteria for GDM - impact on the women of diagnosis - evidence from qualitative studies .....	32
1.11.5	Longer health outcomes of pregnant women with glucose intolerance not meeting current diagnostic criteria for GDM – evidence from observational studies .....	34
<b>1.12</b>	<b>Summary of research gaps identified.....</b>	<b>36</b>
<b>2</b>	<b>Cochrane systematic review: Exercise for pregnant women for preventing gestational diabetes mellitus.....</b>	<b>38</b>
<b>2.1</b>	<b>Statement of Authorship .....</b>	<b>39</b>
<b>3</b>	<b>Cochrane systematic review: Different types of dietary advice for women with gestational diabetes mellitus .....</b>	<b>90</b>
<b>3.1</b>	<b>Statement of Authorship .....</b>	<b>91</b>
<b>4</b>	<b>Cochrane systematic review: interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria.....</b>	<b>172</b>
<b>4.1</b>	<b>Statement of authorship .....</b>	<b>173</b>
<b>5</b>	<b>A qualitative study of women’s views on their diagnosis and management for borderline gestational diabetes mellitus.....</b>	<b>219</b>
<b>5.1</b>	<b>Background .....</b>	<b>219</b>
<b>5.2</b>	<b>Methods.....</b>	<b>220</b>

5.2.1	Participants and procedure.....	220
5.2.2	The interview .....	221
5.2.3	Ethics .....	222
<b>5.3</b>	<b>Results .....</b>	<b>223</b>
5.3.1	Participants.....	223
5.3.2	Women’s reactions to being diagnosed with borderline GDM .....	224
5.3.3	Women’s attitudes towards managing their borderline GDM.....	226
5.3.4	Information seeking and plans for diet and exercise .....	226
5.3.5	The influence of family history of diabetes mellitus on women’s feelings and experiences.....	227
5.3.6	Enablers and barriers for women to achieve intended diet and exercise changes.....	227
5.3.6.1	<b>Enablers.....</b>	<b>229</b>
5.3.6.2	<b>Barriers.....</b>	<b>231</b>
5.3.7	Women’s needs to overcome barriers.....	233
<b>5.4</b>	<b>Discussion.....</b>	<b>233</b>
<b>5.5</b>	<b>Conclusion .....</b>	<b>236</b>
<b>6</b>	<b>The In-depth IDEAL 4 to 12 month Follow-Up Study - maternal and infant health outcomes after receiving diet and exercise advise during pregnancy or routine care for managing borderline gestational diabetes mellitus.....</b>	<b>237</b>
<b>6.1</b>	<b>Introduction.....</b>	<b>237</b>
<b>6.2</b>	<b>Study aims and hypotheses for the In-depth IDEAL 4 to 12 month Follow-Up Study.....</b>	<b>238</b>

<b>6.3</b>	<b>Methods.....</b>	<b>239</b>
6.3.1	Participants eligible for the In-depth IDEAL 4 to 12 month Follow-Up Study .....	239
6.3.2	The IDEAL Trial: summary of research methods .....	239
6.3.2.1	Eligibility criteria for the IDEAL Trial .....	239
6.3.2.2	Exclusion criteria for the IDEAL Trial .....	239
6.3.2.3	Trial entry and randomisation .....	240
6.3.2.4	The IDEAL Trial study groups and interventions.....	240
6.3.3	Contact with the families and recruitment procedures for the In-depth IDEAL 4 to 12 month Follow-Up Study .....	241
6.3.4	Data collection and assessments made at the In-depth IDEAL 4 to 12 month Follow-Up Study.....	242
6.3.4.1	Maternal assessment.....	242
6.3.4.2	Infant assessment.....	243
6.3.5	Study outcomes for the In-depth IDEAL 4 to 12 month Follow-Up Study .	243
6.3.6	Sample size for the In-depth IDEAL 4 to 12 month Follow-Up Study.....	246
6.3.7	Statistical analyses .....	247
<b>6.4</b>	<b>Results .....</b>	<b>249</b>
6.4.1	Recruitment and flow of participants.....	249
6.4.2	Maternal baseline characteristics .....	251
6.4.3	Primary outcomes .....	253
6.4.3.1	Infant outcomes .....	253
6.4.3.2	Maternal outcomes .....	255
6.4.4	Secondary outcomes .....	255
6.4.4.1	Infant outcomes .....	255

6.4.4.2	Maternal outcomes .....	261
<b>6.5</b>	<b>Discussion.....</b>	<b>264</b>
6.5.1	Strengths and limitations of this study.....	269
<b>6.6</b>	<b>Conclusions.....</b>	<b>270</b>
6.6.1	Implications for clinical practice .....	270
6.6.2	Implications for research .....	270
<b>7</b>	<b>Summary conclusions .....</b>	<b>272</b>
<b>7.1</b>	<b>Conclusions from the three Cochrane systematic reviews on pregnancy hyperglycaemia .....</b>	<b>272</b>
<b>7.2</b>	<b>Conclusions from the qualitative semi-structured interview study .....</b>	<b>277</b>
<b>7.3</b>	<b>Conclusion for the In-depth IDEAL 4 to 12 month Follow-Up Study.....</b>	<b>278</b>
<b>7.4</b>	<b>Overall conclusions .....</b>	<b>280</b>
<b>8</b>	<b>References .....</b>	<b>281</b>
<b>9</b>	<b>Appendix.....</b>	<b>320</b>
<b>9.1</b>	<b>Semi-structured question list used in interviews.....</b>	<b>320</b>



## List of tables and figures

pages

Table 1.1 Modifiable and not modifiable risk factors for gestational diabetes .....	11
Table 1.2 Selected international recommendations on screening for GDM .....	14
Table 1.3 Selected international recommendations on diagnosis of GDM.....	17
Table 1.4 Clinical outcomes among women with borderline GDM (140 women) compared with women with a normal OGCT (1596 women) .....	30
Table 1.5 Clinical outcomes among babies born to women with borderline GDM (139 babies) compared with women with a normal OGCT (1583 babies) .....	31
Table 1.6 Adjusted odds ratios for associations between maternal glycaemia as a continuous variable and primary and secondary perinatal outcomes in the HAPO Study .....	31
Table 1.7 Research questions addressed in the thesis of “Dietary and lifestyle advice for women to prevent and treat pregnancy hyperglycaemia: identifying and closing research gaps” .....	37
Figure 5.1 Flowchart of recruitment.....	223
Table 5.1 Characteristics of women approached for the study .....	224
Table 5.2 Women’s experience after being told they had borderline GDM .....	225
Table 5.3 Enablers and barriers for women to achieve their lifestyle goals .....	228
Table 5.4 Summary of needs raised by women to help with overcoming barriers .....	234
Figure 6.1 Study flowchart for the In-depth IDEAL 4 to 12 month Follow-Up Study.	248

Table 6.1 Maternal baseline characteristics for the Follow-Up Study cohort and the IDEAL Trial cohort .....	250
Table 6.2 Baseline characteristics of women enrolled in the Follow-Up Study by treatment group .....	252
Table 6.3 Infant anthropometric outcomes based on WHO 2006 growth standards at follow-up by treatment group .....	254
Table 6.4 Maternal anthropometric outcomes at four months postpartum by treatment group .....	256
Table 6.5 Infant anthropometric outcomes at four months of age by treatment group .....	259
Table 6.6 Maternal BMI category change between IDEAL Trial entry and 4 months postpartum .....	263
Table 7.1 Summary of ‘ <i>Exercise for pregnant women for preventing gestational diabetes mellitus</i> ’ Cochrane systematic review .....	273
Table 7.2 Summary of ‘ <i>Different types of dietary advice for women with gestational diabetes mellitus</i> ’ Cochrane systematic review .....	274
Table 7.3 Summary of ‘ <i>Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria</i> ’ Cochrane systematic review .....	276
Table 7.4 Summary of the research findings for the qualitative semi-structured interview study.....	277

Table 7.5 Summary of the research findings for the In-depth IDEAL 4 to 12 month

Follow-Up Study.....279

## List of abbreviations

ABS	Australian Bureau of Statistics
ACHOIS Trial	Australian carbohydrate intolerance study in pregnant women trial
ADA	America Diabetes Association
ADIPS	Australasian Diabetes in Pregnancy Society
ACOG	American College of Obstetricians and Gynaecologists
AIHW	Australian Institute of Health and Welfare
BGL	blood glucose level
bGDM	borderline gestational diabetes mellitus
BMI	body mass index
BP	blood pressure
CDA	Canadian Diabetes Association
CI	confidence intervals
COREQ	consolidated criteria for reporting qualitative research
cyclic GMP	cyclic guanosine monophosphate
CYWHS	the Children, Youth and Women's Health Service
dl	decilitres
DM	diabetes mellitus
EASD	European Association for the Study of Diabetes
g	grams
GDM	gestational diabetes mellitus
GI	glycaemic index
h	hour
HAPO Study	hyperglycaemia and adverse pregnancy outcome study

HBGM	home blood glucose monitoring
HDL	high-density lipoprotein
HR	heart rate
HRmax	max heart rate
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IDEAL Study	investigation of dietary advice and lifestyle for women with borderline gestational diabetes
IDF	international diabetes federation
IGTP	impaired glucose tolerance of pregnancy
IOM	Institute of Medicine
IUGR	intrauterine growth restriction
kg	kilos
L	litres
LGA	large-for-gestational age
m	meters
mg	milligrams
MiG Trial	metformin in gestational diabetes trial
mm Hg	millimetres of mercury
mmol	millimoles
MODY	maturity-onset diabetes of the young
MOH	Ministry of Health
NA	not applicable
NDDG	National Diabetes Data Group
NICE	National Institute for Health and Clinical Excellence

NIH	National Institutes of Health
NIPerIER	National Institute of Perinatology Isidro Espinosa de los Reyes
NZ	New Zealand
OGCT	oral glucose challenge test
OGTT	oral glucose tolerance test
RANZCOG	Royal Australian and New Zealand College of Obstetrics and Gynaecology
RR	relative risk
RCT	randomised controlled trial
SD	standard deviation
SEIFA	socio-economic indexes for areas
SGA	small-for-gestational age
SMBG	self-monitored blood glucose
T1DM	type1 diabetes mellitus
T2DM	type 2 diabetes mellitus
WCH	Women's and Children's Hospital
WHO	World Health Organization
WOMBAT	Women and babies health and wellbeing: action through trials
wk	weeks
yr	years

# **Abstract**

## **Background**

Increased glycaemia during pregnancy is associated with adverse health outcomes for women and their babies. This thesis aimed to investigate and evaluate the strategies used for preventing, diagnosing and managing pregnancy hyperglycaemia.

## **Methods**

Research methodologies used included Cochrane systematic review, qualitative semi-structured interview and a follow-up cohort study of women and babies within a randomised trial.

## **Results**

Three Cochrane systematic reviews were conducted in identified research gaps. The first review assessed the effects of physical exercise for preventing gestational diabetes mellitus (GDM). Evidence from five randomised controlled trials involving 922 women and their babies suggested no differences in the incidence of GDM, caesarean section or operative vaginal birth between women who received additional exercise interventions and those having routine antenatal care.

The second review assessed nine randomised trials involving 429 women and 436 babies investigated eleven different types of dietary advice within six different comparisons. No one type of dietary advice was more effective than others in reducing the risk of caesarean section, operative vaginal birth, large-for-gestational age or macrosomic infants.

The third review assessed the effects of different types of management strategies for pregnant women with borderline GDM. Evidence from four randomised controlled trials involving 521 women and their babies suggested additional interventions, including dietary counselling and metabolic monitoring, helped reduce the number of macrosomic and large-for-gestational-age babies without increasing the risks of caesarean section or operative vaginal birth. All three systematic reviews highlighted the need for further, larger, well-designed trials.

The qualitative semi-structured interview study explored women's views on their diagnosis and management for borderline GDM. Twenty-two women attended the interviews. The diagnosis of borderline GDM caused concern for one third of women. The majority of women believed managing their borderline GDM was important and they planned to improve their lifestyle. Factors affecting women's ability to achieve intended lifestyle changes varied greatly. The most important enabler was thinking about baby's health. The most significant barrier was a lack of family support.

The follow-up cohort study within a randomised trial followed 245 mother-baby pairs at four to 12 months after birth to assess their health. Additional lifestyle interventions during pregnancy for women with borderline GDM had no impact on primary outcomes of maternal weight retention at four months postpartum or their babies' weight at four to 12 months of age, or any secondary outcomes, except infant subcutaneous adiposity at four months of age.

## **Conclusion**

Synthesis of available evidence on different strategies for preventing and managing pregnancy hyperglycaemia does not yet permit clear guidance for clinical practice but indicates the need for further trials with long-term follow up to assess impact on



mothers and their children. A diagnosis of borderline GDM appears to be a powerful motivator for women to change diet and exercise patterns. As new health knowledge becomes available from further completed trials, a timely update of the relevant Cochrane reviews to include these trials is warranted.

## **Declaration**

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future be used in a submission for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

The author acknowledges that copyright of published works contained within this thesis resides with the copyright holder(s) of those works.

I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library catalogue and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

Shanshan Han

March 2014

## Acknowledgements

I feel extremely grateful to my supervisors Professor Caroline Crowther and Philippa Middleton for their continuing guidance, encouragement, support and constructive comments. I would also like to thank the Discipline of Obstetrics and Gynaecology at the University of Adelaide for providing the opportunity to undertake my PhD study.

During my candidature, I have received great help and support from many people. I would like to thank the following people in no particular order:

Research staff from the Royal Women's Hospital (Melbourne) for their support and help in recruitment, assessment and data collection for the In-depth IDEAL 4 to 12 month Follow-Up Study.

Pat Ashwood and Daniela Gagliardi for their assistance in trial coordinating for the In-depth IDEAL 4 to 12 month Follow-Up Study.

Dr Thach Tran for his help in providing invaluable advice in statistical analyses and performing the analyses for the In-depth IDEAL 4 to 12 month Follow-Up Study.

Yu Zhang and Vincent Ball for their great support in database and data management for the In-depth IDEAL 4 to 12 month Follow-Up Study.

Kaye Robinson and Caroline Holst for their assistance in data entry for the In-depth IDEAL 4 to 12 month Follow-Up Study.

Tanya Bubner for her involvement in the qualitative data analysis for the semi-structured qualitative interview study.

Elen Shute and Claire Binnion for their assistance in transcribing interviews for the semi-structured qualitative interview study.

All of the staff at the Clinical Trials Unit within ARCH (Australian Research Centre for Health of Women and Babies) for their friendship and PhD support.

My family, particularly my husband Yu and my daughter Angelina, my Mum and Dad, parents-in-law for being supportive and accommodating my thesis into our lives.

I am also so grateful for the financial support I received from the Australian Postgraduate Awards provided by the Australian Federal Government, as well as the PhD Top-up Scholarship from the Robinson Institute, University of Adelaide.

Finally I would like to thank all of the women and their babies who volunteered to take part in my PhD project.