

CLINICAL PRACTICE GUIDELINES

2017 MOH/P/PAK/353.17(GU)

MANAGEMENT OF *DIABETES IN PREGNANCY*



Ministry of Health
Malaysia



Malaysian Endocrine
& Metabolic Society



Perinatal Society of
Malaysia



Family Medicine
Specialists
Association of
Malaysia



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Available on the following websites:

<http://www.moh.gov.my>

<http://www.acadmed.org.my>

<http://www.mems.my>

<http://www.perinatal-malaysia.org>

<http://www.fms-malaysia.org>

Also available as an app for Android and IOS platform: MyMaHTAS

STATEMENT OF INTENT

These clinical practice guidelines (CPG) are meant to be guides for clinical practice based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions, corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on the websites mentioned above.

UPDATING THE CPG

These guidelines were issued in 2017 and will be reviewed in a minimum period of four years (2021) or sooner if new evidence becomes available. When it is due for updating, the Chairman of the CPG or National Advisor of the related specialty will be informed about it. A discussion will be done on the need for a revision including the scope of the revised CPG. A multidisciplinary team will be formed and the latest systematic review methodology used by MaHTAS will be employed.

TABLE OF CONTENTS

No.	Title	Page
	Levels of Evidence and Formulation of Recommendation	i
	Key Recommendations	ii
	Guidelines Development and Objectives	v
	Development Group	viii
	Review Committee	ix
	External Reviewers	x
	Algorithm A: Screening and Diagnosis of Diabetes in Pregnancy	xi
	Algorithm B: Intrapartum Glucose Monitoring for Diabetes in Pregnancy in Active Labour	xii
	Algorithm C: Insulin Infusion and Titration in Active Labour	xiii
1.	INTRODUCTION	1
2.	SCREENING AND DIAGNOSIS	1
	2.1 Overt Diabetes in Pregnancy	2
3.	MANAGEMENT OF PREGNANT WOMEN AT RISK OF DEVELOPING GESTATIONAL DIABETES MELLITUS	4
	3.1 Medical Nutrition Therapy	4
	3.2 Exercise	6
4.	MANAGEMENT OF WOMEN WITH PRE-EXISTING DIABETES	7
	4.1 Preconception Care and Counselling	7
	4.2 Contraception	8
	4.3 Glycaemic Control	8
	4.4 Folic Acid Supplementation	8
5.	ANTENATAL MANAGEMENT OF DIABETES IN PREGNANCY	10
	5.1 Glycaemic Control	10
	5.2 Medical Nutrition Therapy	12
	5.3 Oral Antidiabetic Agents	13
	5.4 Insulin	14
	5.5 Pre-eclampsia Prophylaxis	17
	5.6 Assessment of Complications of Diabetes	18
	5.7 Fetal Surveillance	19
	5.8 Timing and Mode of Delivery	20

TABLE OF CONTENTS

No.	Title	Page
6.	INTRAPARTUM GLYCAEMIC CONTROL FOR DIABETES IN PREGNANCY	22
7.	POSTPARTUM MANAGEMENT OF DIABETES IN PREGNANCY	23
	7.1 Postpartum Glucose Monitoring	23
	7.2 Postpartum Use of Metformin	23
	7.3 Breastfeeding	24
	7.4 Postpartum Contraception	24
	7.5 Postpartum Lifestyle Intervention	24
8.	MANAGEMENT OF NEONATES OF MOTHERS WITH DIABETES	26
9.	MANAGEMENT OF SPECIAL CONDITIONS IN DIABETES IN PREGNANCY	27
	9.1 Continuous Subcutaneous Insulin Infusion	27
	9.2 Corticosteroids	27
	9.3 Fasting	27
10.	REFERRAL TO SECONDARY/TERTIARY CARE	28
11.	IMPLEMENTING THE GUIDELINES	29
	REFERENCES	31
	Appendix 1: Examples of Search Strategy	37
	Appendix 2: Clinical Questions	38
	Appendix 3: Carbohydrate Content of Common Malaysian Foods	39
	Food Groups and Exchange Lists	40
	Glycaemic Index List	44
	Sample Menu	45
	Appendix 4: Medication Table	46
	Appendix 5: Preparation of Insulin Infusion	48
	List of Abbreviations	49
	Acknowledgement	50
	Disclosure Statement	50
	Source of Funding	50

LEVELS OF EVIDENCE

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II-1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

SOURCE: US / CANADIAN PREVENTIVE SERVICES TASK FORCE 2001

FORMULATION OF RECOMMENDATION

In line with new development in CPG methodology, the CPG Unit of MaHTAS is in the process of adapting **Grading Recommendations, Assessment, Development and Evaluation (GRADE)** in its work process. The quality of each retrieved evidence and its effect size are carefully assessed/reviewed by the CPG Development Group. In formulating the recommendations, overall balances of the following aspects are considered in determining the strength of the recommendations:-

- overall quality of evidence
- balance of benefits versus harms
- values and preferences
- resource implications
- equity, feasibility and acceptability

KEY RECOMMENDATIONS

The following recommendations were highlighted by the guidelines Development Group as the key clinical recommendations that should be prioritised for implementation.

Screening

- Screening for gestational diabetes mellitus based on risk factors using 75 gram oral glucose tolerance test (OGTT) should be done at booking.
 - If the test is negative, it should be repeated at 24-28 weeks of gestation.
- For women at the age of 25 or more with no other risk factors, OGTT should be done at 24-28 weeks of gestation.
- Overt diabetes in pregnancy should be managed as pre-existing diabetes.

Preconception Care

- Preconception care of women with pre-existing diabetes which involve a multidisciplinary team should be fully implemented in all healthcare facilities.

Antenatal Management of Diabetes in Pregnancy

- Self-monitoring of blood glucose (SMBG) should be done in diabetes in pregnancy. The blood glucose targets should be as the following:
 - fasting or preprandial: ≤ 5.3 mmol/L
 - 1-hour postprandial: ≤ 7.8 mmol/L
 - 2-hour postprandial: ≤ 6.7 mmol/L
- The frequency of SMBG in diabetes in pregnancy should be individualised based on mode of treatment and glycaemic control.
- Pregnant women with pre-existing diabetes on multiple daily insulin (MDI) injection regimen should perform SMBG at least three times daily. It can be done at fasting, preprandial, postprandial or bedtime.
- Women with gestational diabetes mellitus (GDM) on MDI injection regimen should perform SMBG two to three times daily, for two to three days a week.
- Pregnant women with type 2 diabetes mellitus or GDM on diet and exercise therapy, oral antidiabetic agents (OAD), single-dose intermediate-acting or long-acting insulin should perform fasting and postprandial SMBG at least once daily until blood glucose targets are reached.
- Pregnant women who are on insulin or OAD should maintain their capillary blood glucose level >4.0 mmol/L.

- Pregnant women with diabetes should be given individualised medical nutrition therapy which includes carbohydrate-controlled meal plan and monitoring of gestational weight gain.

- In gestational diabetes mellitus, metformin should be offered when blood glucose targets are not met using changes in diet and exercise within 1-2 weeks.
 - It should be prescribed after consultation with specialists.
- Metformin should be continued in women who are already on the treatment before pregnancy.

- Insulin therapy can be initiated at outpatient setting in pregnant women with diabetes.
- The preferred choice of insulin regime in diabetes in pregnancy is multiple daily injections.
- Insulin analogues should be continued during pregnancy in women with pre-existing diabetes who are already on the treatment and have established good blood glucose control before pregnancy.
- Rapid-acting insulin analogue may be considered as an option, particularly in patients with frequent hypoglycaemia or postprandial hyperglycaemia using human insulin during pregnancy.

- Pregnant women with pre-existing diabetes should be offered ultrasound scan at:
 - 11-14 weeks of gestation for dating and major structural malformation
 - 18-20 weeks of gestation for detailed structural anatomy scan (by a trained specialist or ultrasonographer)
- In women with pre-existing diabetes and gestational diabetes mellitus, serial growth scan should be performed every four weeks from 28 to 36 weeks of gestation.

- In women with pre-existing diabetes or gestational diabetes mellitus who develop maternal or fetal complications, elective delivery before 37+0 weeks should be considered.

Intrapartum Management of Diabetes in Pregnancy

- In women with diabetes, capillary blood glucose should be maintained between 4.0-7.0 mmol/L during labour and delivery.

Postpartum Management of Diabetes in Pregnancy

- In women with history of gestational diabetes mellitus, oral glucose tolerance test should be performed at six weeks after delivery to detect diabetes and prediabetes. If negative, annual screening should be performed.

GUIDELINES DEVELOPMENT AND OBJECTIVES

GUIDELINES DEVELOPMENT

The members of the Development Group (DG) for these CPG were from the Ministry of Health (MoH) and Ministry of Higher Education (MoHE). There was active involvement of a multidisciplinary Review Committee (RC) during the process of the CPG development.

A systematic literature search was carried out using the following electronic databases/platform: Guidelines International Network (G-I-N), Medline via Ovid, Cochrane Database of Systemic Reviews (CDSR) and Pubmed. Refer to **Appendix 1** for **Example of Search Strategy**. The inclusion criteria were all diabetes in pregnancy regardless of study design. The search was limited to literature published in the last 10 years, on humans and in English. In addition, the reference lists of all retrieved literature and guidelines were searched and experts in the field contacted to identify relevant studies. All searches were conducted from 3 October 2015 to 21 March 2016. Literature search was repeated for all clinical questions at the end of the CPG development process allowing any relevant papers published before 30 June 2017 to be included. Future CPG updates will consider evidence published after this cut-off date. The details of the search strategy can be obtained upon request from the CPG Secretariat.

Reference was also made to other guidelines as listed below:

- Ministry of Health Malaysia - CPG on Management of Type 2 Diabetes Mellitus (5th Edition) (December 2015)
- National Institute for Clinical Excellence (NICE) - Diabetes in Pregnancy: Management of Diabetes and its Complications from Preconception to the Postnatal Period (February 2015)
- New Zealand Guideline Group (NZGG) - Screening, Diagnosis and Management of Gestational Diabetes in New Zealand (December 2014)

These CPGs were evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II prior to it being used as reference.

A total of 13 clinical questions were developed under different sections. Members of the DG were assigned individual questions within these sections. Refer to **Appendix 2** for **Clinical Questions**. The DG members met 22 times throughout the development of these guidelines. All literatures retrieved were appraised by at least two DG members using Critical Appraisal Skill Programme checklist, presented in evidence tables and further discussed in each DG meetings. All statements and recommendations formulated after that were agreed upon by both the DG and RC. Where evidence was insufficient, the recommendations were made by consensus of the DG and RC. Any

differences in opinion were resolved consensually. The CPG was based largely on the findings of systematic reviews, meta-analyses and clinical trials, with local practices taken into consideration.

The literatures used in these guidelines were graded using the US/ Canadian Preventive Services Task Force Level of Evidence (2001) while the grading of recommendation was done using the principles of GRADE (refer to the preceding page). The writing of the CPG follows strictly the requirement of AGREE II.

On completion, the draft CPG was reviewed by external reviewers. It was also posted on the MoH Malaysia official website for feedback from any interested parties. The draft was finally presented to the Technical Advisory Committee for CPG, and the HTA and CPG Council MoH Malaysia for review and approval. Details on the CPG development by MaHTAS can be obtained from Manual on Development and Implementation of Evidence-based Clinical Practice Guidelines published in 2015 (available at http://www.moh.gov.my/penerbitan/mymahtas/CPG_MANUAL_MAHTAS.pdf)

OBJECTIVES

The objectives of the CPG are to provide evidence-based recommendations on diabetes in pregnancy on these aspects:

- i. Screening and diagnosis
- ii. Management (pre-pregnancy, antenatal, intrapartum and postpartum period)

CLINICAL QUESTIONS

Refer to **Appendix 2**

TARGET POPULATION

Inclusion Criteria

- i. Women with diabetes planning for pregnancy
- ii. Pregnant women at risk of diabetes
- iii. Pregnant women with pre-existing diabetes and gestational diabetes mellitus

Exclusion Criteria

Pregnant women with secondary causes of diabetes

TARGET GROUP/USER

This CPG intends to guide those involved in the management of diabetes in pregnancy either in primary or secondary/tertiary care in public and private practice namely:

- i. Medical officers and specialists
- ii. Allied health professionals
- iii. Trainees and medical students
- iv. Patients and their advocates
- v. Professional societies

HEALTHCARE SETTINGS

Outpatient, inpatient and community settings

DEVELOPMENT GROUP

Chairperson

Dr. Nurain Mohd. Noor
Consultant Endocrinologist
Hospital Putrajaya, Putrajaya

Members (alphabetical order)

Assoc. Prof. Dr. Barakatun Nisak
Mohd Yusof
Lecturer & Dietician
Faculty of Medicine and Health
Sciences
Universiti Putra Malaysia, Selangor

Ms. Nazatul Syima Idrus
Pharmacist & Principal Assistant
Director
Pharmaceutical Services Division
Ministry of Health Malaysia, Selangor

Dr. Hanin Farhana Kamaruzaman
Senior Principal Assistant Director
Health Technology Assessment Section
Ministry of Health Malaysia, Putrajaya

Dr. Noor Lita Adam
Consultant Endocrinologist
Hospital Tuanku Ja'afar, Negeri Sembilan

Dr. Hoong Farn Weng Michael
Consultant Obstetrician & Gynaecologist
Hospital Wanita & Kanak-kanak Sabah
Sabah

Assoc. Prof. Dr. Norasyikin Abdul Wahab
Lecturer & Consultant Endocrinologist
Faculty of Medicine
Universiti Kebangsaan Malaysia
Kuala Lumpur

Professor Dr. Imelda Balchin
Consultant Maternal Fetal Medicine
Faculty of Medicine
Universiti Malaya, Kuala Lumpur

Assoc. Prof. Dr. Norlaila Mustafa
Lecturer & Consultant Endocrinologist
Faculty of Medicine
Universiti Kebangsaan Malaysia
Kuala Lumpur

Dr. Lili Zuryani Marmuji
Family Medicine Specialist
Klinik Kesihatan Gunung Rapat, Perak

Dr. Ranjit Singh Dhaliwal
Obstetrician & Gynaecologist
Hospital Ampang, Selangor

Dr. Mastura Ismail
Consultant Family Medicine Specialist
Klinik Kesihatan Seremban 2
Negeri Sembilan

Assoc. Prof. Dr. Rohana Abdul Ghani
Lecturer & Consultant Endocrinologist
Faculty of Medicine
Universiti Teknologi MARA, Selangor

Dr. Mohd. Aminuddin Mohd. Yusof
Head of CPG Unit & Public Health
Physician
Health Technology Assessment Section
Ministry of Health Malaysia, Putrajaya

REVIEW COMMITTEE

The draft CPG was reviewed by a panel of experts from both public and public sectors. They were asked to comment primarily on the comprehensiveness and accuracy of the interpretation of evidence supporting the recommendations in the CPG.

Chairperson

Dr. Zanariah Hussein
Senior Consultant Endocrinologist &
National Advisor of Endocrinology Services
Hospital Putrajaya, Putrajaya

Members (alphabetical order)

Dr. Carol Lim Kar Koong
Consultant Obstetrician & Gynaecologist
(Maternal Fetal Medicine)
Hospital Sultan Haji Ahmad Shah
Pahang

Ms. Noraini Mohamad
Deputy Director
Pharmacy Practice & Development
Division
Pharmaceutical Services Programme
Ministry of Health Malaysia, Selangor

Dato' Dr. Ghazali Ismail
Senior Consultant Obstetrician &
Gynaecologist
Hospital Sultan Ismail, Johor

Dr. Norraliza Md. Zain
Consultant Family Medicine Specialist
Klinik Kesihatan Lanang, Sarawak

Dr. J. Ravichandran Jeganathan
Senior Consultant Obstetrician &
Gynaecologist & National Advisor of
O&G Services
Hospital Sultanah Aminah, Johor

Dr. Norzaihan Hassan
Consultant Family Medicine Specialist
Klinik Kesihatan Bandar Kota Bharu
Kelantan

Dr. Junainah Sabirin
Deputy Director & Public Health
Physician
Health Technology Assessment Section
Ministry of Health Malaysia, Putrajaya

Professor Dato' Dr. Sivalingam Nalliah
Lecturer & Senior
Consultant Obstetrician & Gynaecologist
Faculty of Medicine
International Medical University
Negeri Sembilan

Dr. Noor Aziah Zainal Abidin
Senior Principal Assistant Director
Medical Development Services Section
Ministry of Health Malaysia, Putrajaya

EXTERNAL REVIEWERS (in alphabetical order)

The following external reviewers provided feedback on the draft:

Dr. Ernieda Md Hatah
Senior Lecturer, Clinical Pharmacy Discipline
Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Kuala Lumpur

Assoc. Prof. Dato' Dr. Hamizah Ismail
Head of Department & Consultant Obstetrician & Gynaecologist
Kulliyyah of Medicine, International Islamic University Malaysia, Pahang

Dr. Iskandar Firzada Osman
Consultant Family Medicine Specialist
Klinik Kesihatan Jaya Gading, Kuantan, Pahang

Professor Dato' Dr. Mafauzy Mohammed
Professor of Medicine & Senior Consultant Endocrinologist
School of Health Sciences, Universiti Sains Malaysia, Kelantan

Dr. Navin Kumar a/l Loganadan
Clinical Pharmacist
Hospital Putrajaya, Putrajaya

Mdm. Nurul Huda Ibrahim
Senior Principle Assistant Director (Dietetic)
Primary Care Sector
Family Health Development Division, Ministry of Health, Putrajaya

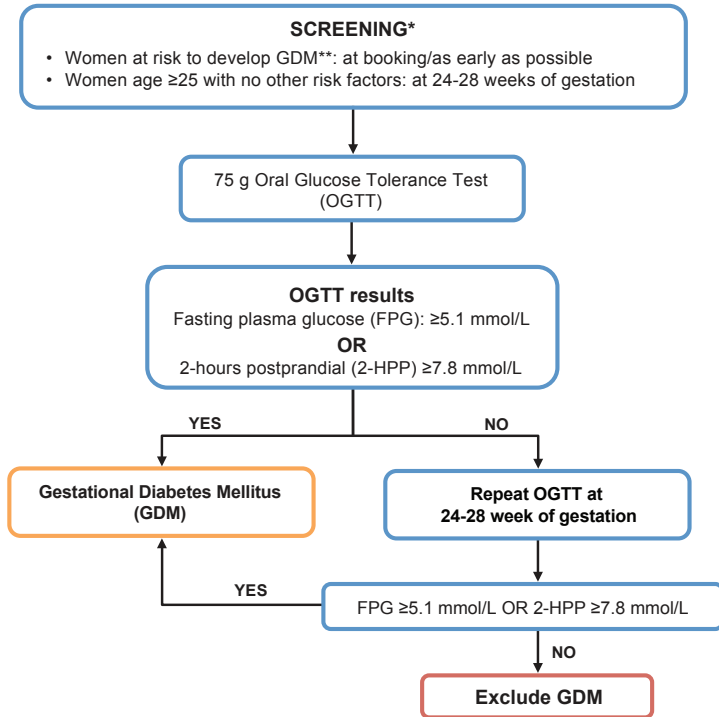
Dr. Shari Nor
Maternal Fetal Medicine Specialist & Consultant Obstetrician & Gynaecologist
Hospital Wanita & Kanak-kanak Sabah, Sabah

Professor Dr. Siti Zawiah Omar
Head of Department & Professor of Obstetrics & Gynaecology
Faculty of Medicine
Universiti Malaya, Kuala Lumpur

Professor Dr. Winnie Chee Siew Swee
Professor of Food Science & Nutrition
Dean of School of Health Sciences
International Medical University, Kuala Lumpur

Professor Dr. Zalilah Mohd Shariff
Professor of Community Nutrition
Department of Nutrition and Dietetics
Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Selangor

ALGORITHM A: SCREENING AND DIAGNOSIS OF DIABETES IN PREGNANCY



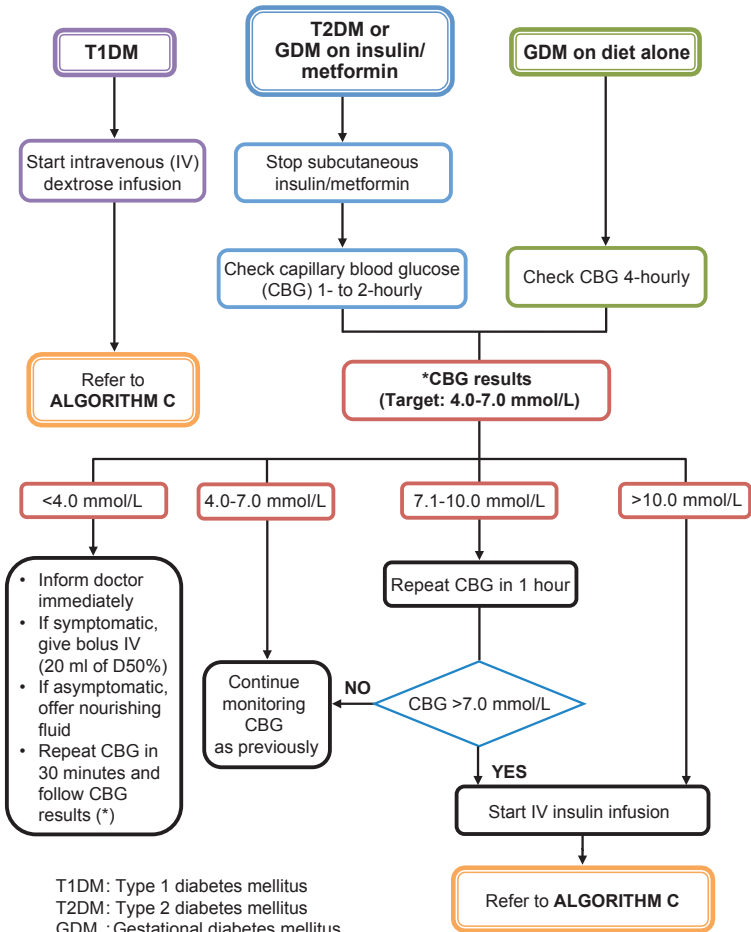
***Overt DM is suspected in the presence of at least one of the following:**

- FPG ≥ 7.0 mmol/L
- Random plasma glucose (RPG) ≥ 11.1 mmol/L
- However, the diagnosis of overt DM should be confirmed with a second test (FPG/RPG/OGTT).

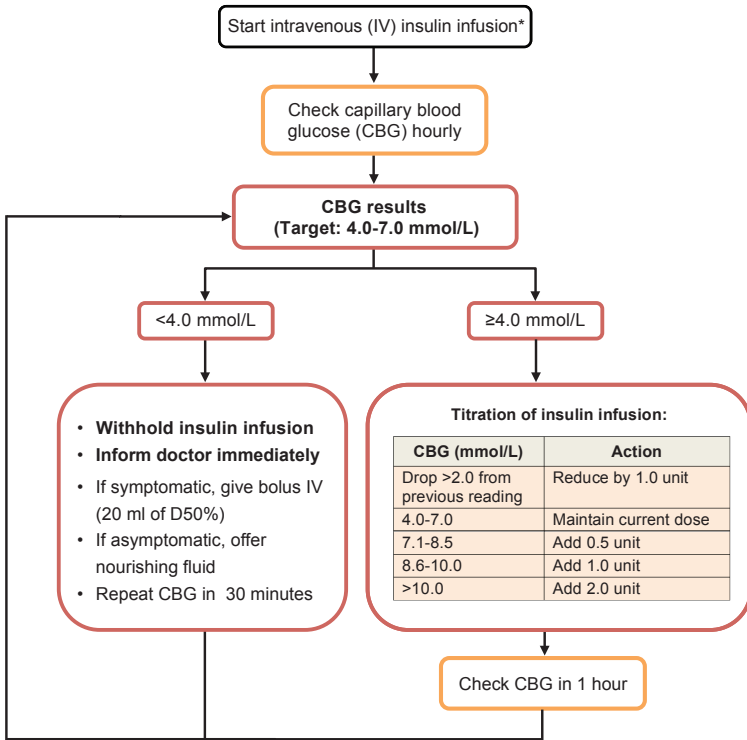
**** Presence of any risk factors:**

- Body mass index > 27 kg/m²
- Previous history of GDM
- First degree relative with diabetes mellitus
- History of macrosomia (birth weight > 4 kg)
- Bad obstetric history
- Glycosuria $\geq 2+$ on two occasions
- Current obstetric problems (essential hypertension, pregnancy-induced hypertension, polyhydramnios and current use of corticosteroids)

ALGORITHM B: INTRAPARTUM GLUCOSE MONITORING FOR DIABETES IN PREGNANCY IN ACTIVE LABOUR



ALGORITHM C: INSULIN INFUSION AND TITRATION IN ACTIVE LABOUR



* IV insulin infusion initiation rate

- Type 1 diabetes mellitus: 0.01-0.02 unit/kg/hour
- Type 2 diabetes mellitus/gestational diabetes mellitus: 0.05-0.07 unit/kg/hour
- If requirement exceed 0.1 unit/kg/hour, refer the endocrinologist/physician

Refer to **Appendix 5** for preparation of insulin infusion.

1. INTRODUCTION

The National Health Morbidity Survey 2015 showed that the prevalence of diabetes was 17.5%. Generally, the prevalence of diabetes increases with age.^{1, level III} This is a concern especially in the reproductive age group as this will adversely affect their fertility and pregnancy.

Diabetes in pregnancy is associated with risks to the woman and her developing fetus. National Obstetric Report involving 14 tertiary hospitals showed the incidence of diabetes in pregnancy was 8.66% in 2011 and 8.83% in 2012. The caesarean section rates in this group of patients were around 13% in 2011 and 2012. In both years approximately 16% babies born to diabetic mothers weighed 4 kg and more. There was a 2-fold increase in macrosomia in diabetes patients in both years as compared to nondiabetes and this could have contributed to the increased caesarean section rates. These figures were obtained from only a few tertiary hospitals and the actual prevalence was expected to be higher.^{2, level III}

There are variations in local clinical practice management of diabetes in pregnancy at different levels of care. To date, there is no specific local CPG addressing this issue. This CPG, therefore, provides a comprehensive evidence-based guideline in screening and management of diabetes and its complications in pregnancy. This CPG would assist healthcare providers in delivering high quality care.

2. SCREENING AND DIAGNOSIS

Screening for diabetes in pregnant women is important to identify asymptomatic patients who may have overt diabetes before they manifest symptoms such as excessive thirst and urination, or fatigue. Two main screening strategies are 'universal' where all women undergo a screening test for gestational diabetes mellitus (GDM) and 'selective' where only those women at high risk are screened.

In a Cochrane systematic review, there was insufficient evidence to determine if screening for GDM and types of screening can improve maternal and fetal health outcome in view of small studies and poor quality evidences. However, one of the included study showed that universal screening was better than selective screening at detecting GDM (RR=0.44, 95% CI 0.26 to 0.75).^{3, level I}

Ideally, universal screening should be adhered to. However, if resources are limited, selective screening is acceptable focusing on individuals at risk of developing GDM.⁴

- **Women at risk to develop GDM include:**⁴
 - a. Body mass index (BMI) >27 kg/m²
 - b. Previous history of GDM
 - c. First-degree relative with diabetes mellitus (DM)
 - d. History of macrosomia (birth weight >4 kg)
 - e. Bad obstetric history [unexplained intrauterine death, congenital anomalies (i.e. neural tube defects, cardiac defects), shoulder dystocia]
 - f. Glycosuria ≥2+ on two occasions
 - g. Current obstetric problems (essential hypertension, pregnancy-induced hypertension, polyhydramnios and current use of corticosteroids)

Increasing age has been associated with an increased risk of developing GDM. Based on consensus between RC and DG CPG, pregnant women ≥25 years old without other risk factors should have screening for GDM at 24-28 weeks.

Another Cochrane systematic review found that the evidence was insufficient to conclude the best strategy to diagnose GDM.^{5, level I} However, oral glucose tolerance test (OGTT) has been recommended by international guidelines on the issue.^{6, 7-8, level III} It should be done at booking for high risk women, and repeated at 24-28 weeks of gestation if the initial result was negative^{4, 6}

There is insufficient evidence to suggest HbA1c alone as a useful diagnostic test for GDM and thus, it is not a useful alternative to OGTT.^{9, level III}

In a meta-analysis on screening for GDM, random blood sugar measurement was found to be an inadequate test to screen for GDM.^{10, level II-2}

2.1 OVERT DIABETES IN PREGNANCY

There is no universally accepted definition of overt diabetes in pregnancy. However, the diagnosis is made when blood glucose level is high (refer to yellow box in page 3) during the first trimester. In the case of overt diabetes, a second test either using fasting plasma glucose (FPG), untimed random plasma glucose (RPG), HbA1C, or OGTT, must be performed on another day to confirm the diagnosis.^{11, level III} If results indicate overt diabetes, treatment and follow-up should be carried out as for pre-existing diabetes.^{8, level III; 12}

- GDM is diagnosed in the presence of any one of these results:⁴
 - FPG ≥ 5.1 mmol/L
 - 2-hour postprandial (2-HPP) ≥ 7.8 mmol/L
- Overt DM is suspected in the presence of at least one of the following:¹³
 - FPG ≥ 7.0 mmol/L
 - RPG ≥ 11.1 mmol/L with symptoms
- However, the diagnosis of overt DM is confirmed with a second test (FPG/RPG/OGTT).¹³

Recommendation 1

- Screening for gestational diabetes mellitus based on risk factors* using 75 gram oral glucose tolerance test (OGTT) should be done at booking.
 - If the test is negative, it should be repeated at 24-28 weeks of gestation.
- For women at the age of 25 or more with no other risk factors, OGTT should be done at 24-28 weeks of gestation.
- Overt diabetes in pregnancy should be managed as pre-existing diabetes.

*Refer to the above yellow box on women at risk to develop GDM above.

3. MANAGEMENT OF PREGNANT WOMEN AT RISK OF DEVELOPING GESTATIONAL DIABETES MELLITUS

There are many adverse effects of obesity on maternal and perinatal outcomes. Obesity in pregnancy is associated with a significant risk of GDM and hypertensive disorders of pregnancy including pre-eclampsia. Caesarean section rates are high and infants of obese mothers are at greater risk of large for gestational age (LGA), macrosomia, shoulder dystocia, congenital malformation and stillbirth. Thus, lifestyle modification strategies such as exercise, diet and weight management are important to prevent GDM.

3.1 MEDICAL NUTRITION THERAPY

Medical nutrition therapy (MNT) consists of nutritional diagnosis and therapy that include dietary intervention and counselling. It is crucial at any stage of pregnancy in women who are at risk of GDM. This can be achieved by choosing healthy food with appropriate gestational weight gain (GWG).^{14, level III}

Women at risks of GDM should receive individualised MNT as needed, preferably by a dietitian. A small group counselling (2-4 women) may also be provided. A nonrandomised trial has shown that small group counselling produced similar improvement in nutrition knowledge compared to individual counselling.^{15, level II-2}

In a meta-analysis of RCTs among pregnant women (mostly with BMI >25 kg/m²), combined dietary intervention and physical activity reduced the risk of GDM by 18% (p=0.0091) compared with standard care. The benefits were particularly prominent when the intervention was started before 15 weeks of gestation.^{16, level I}

A Cochrane systematic review suggested a possible reduction in GDM risk in women receiving dietary intervention compared with standard care. However, no significant difference was observed between different types of dietary intervention to prevent GDM. There were no adverse events reported in all of the included studies.^{17, level I}

GWG rate which is higher than the recommended range especially in early pregnancy may increase the risk of GDM. Excessive GWG increases the risk of postpartum weight retention and maternal obesity later in life. The recommended weight gain is determined based on each woman's pre-pregnancy BMI (refer to **Table 1**).^{18, level III}

Table 1: Total and rate of weight gain recommendations during pregnancy

Pre-pregnancy body weight status (BMI in kg/m ²)	Total weight gain (ranges in kg)	Rates of weight gain in second and third trimester [mean (range) in kg/wk]
Underweight (<18.5 kg/m ²)	12.5-18.0	0.51 (0.44-0.58)
Normal weight (18.5-24.9 kg/m ²)	11.5-16.0	0.42 (0.35-0.50)
Overweight (25.0-29.9 kg/m ²)	7.0-11.5	0.28 (0.23-0.33)
Obese (≥30 kg/m ²)	5.0-9.0	0.22 (0.17-0.27)

- In the local setting, the BMI criteria for overweight is 23.0-27.4 kg/m² and obesity is ≥27.5 kg/m².¹⁹ There is no recommendations on total and rates of weight gain for local population. However, targeting GWG to the lower range in **Table 1** may be recommended to improve pregnancy outcomes.

GWG is the major determinant of incremental energy needs during pregnancy. Energy prescription should be individualised based on pre-pregnancy BMI, weight gain, fetal growth pattern, physical activity, food and blood glucose records.

- For women with normal pre-pregnancy BMI, energy prescriptions (approximately ranges from 30-35 kcal/kg body weight depending on activity level) should be given as per normal pregnancy based on the Recommended Nutrient Intakes for Malaysia.⁴
- For obese women, a 30-33% of calorie restriction of their estimated energy needs (approximately 25 kcal/kg body weight) can be prescribed to reduce the rate of GWG without inducing maternal ketosis and compromising fetal growth or birth weight. The GWG must be closely monitored, and the additional energy needs during pregnancy should be modified accordingly.^{20, level III}

- General recommendations on MNT:
 - MNT should be given to pregnant women with these conditions:
 - at risk of GDM
 - pre-existing diabetes
 - at diagnosis of GDM
 - at initiation of insulin therapy
 - postpartum care
 - MNT should be individualised according to nutritional needs and cultural preference to ensure positive maternal and fetal outcomes.

Recommendation 2

- Pregnant women at risk of gestational diabetes mellitus should be offered medical nutrition therapy which includes monitoring of gestational weight gain.

3.2 EXERCISE

Structured moderate physical exercise programmes during pregnancy significantly decrease the risk of Gestational Diabetes Mellitus.

^{21-22, level I} They also reduce maternal weight gain with no adverse events to the mother and neonate.^{22, level I}

Examples of safe physical activities during pregnancy are:^{23, level III}

- Brisk walking
- Swimming
- Stationary cycling
- Low impact aerobics
- Modified yoga or pilates
- Strength training
- Racquet sport

These exercise and physical activities can be performed for at least 20 to 30 minutes per day on most or all days of the week and adjusted accordingly as indicated.^{23, level III}

Absolute contraindications to aerobic exercise in pregnancy are:^{23, level III}

- Haemodynamically significant heart disease
- Restrictive lung disease
- Cervical incompetence with or without cerclage
- Multiple gestation at risk for premature labour
- Persistent second or third trimester bleeding
- Placenta praevia after 26 weeks gestation
- Threatened preterm labour
- Ruptured membranes
- Pregnancy induced hypertension

Recommendation 3

- All pregnant women with uncomplicated pregnancies should be encouraged to exercise especially those at risk of developing gestational diabetes mellitus.

4. MANAGEMENT OF WOMEN WITH PRE-EXISTING DIABETES

4.1 PRECONCEPTION CARE AND COUNSELLING

Women with pre-existing Type 1 DM (T1DM) and Type 2 DM (T2DM) will benefit from preconception care because it reduces the incidence of congenital malformation, preterm delivery and perinatal mortality. Preconception care also lowers the HbA1c level of these women in the first trimester.^{24, level II-2} However, the role of preconception care in women with history of GDM remains unclear due to lack of evidence.^{25, level I}

Before conceiving, women with pre-existing diabetes are advised to reduce their weight if they are overweight or obese. The recommended exercise schedule is 150 minutes per week.⁴ Blood pressure (<130/80 mmHg) and HbA1c should be kept to the optimal (<6.5% or 48 mmol/mol). Screening for diabetic retinopathy and nephropathy should be organised prior to conception. Women with multiple cardiovascular risk factors on contraception should undergo cardiovascular risk assessment before withdrawal of the contraception. Additionally, folic acid supplementation should be given three months before withdrawal of contraception.⁴

Preconception care, including counselling on the risk and expected management during pregnancy for women with pre-existing diabetes, should be provided by a multidisciplinary team.^{26, level III}

- Preconception care, provided by a multidisciplinary team, consists of:⁶
 - discussion on timeline for pregnancy planning
 - lifestyle advice (diet, physical activities, smoking cessation and optimal body weight)
 - folic acid supplementation
 - appropriate contraception
 - full medication review (discontinue potentially teratogenic medications)
 - retinal and renal screening
 - relevant blood investigations
- Women with pre-existing diabetes should be informed of the glycaemic control targets and empowered to achieve control before conception. They should also be counselled on the risks and expected management strategies during pregnancy.

- Medication review
 - Women with T2DM who are planning a pregnancy should switch from oral antidiabetic agent (OAD) to insulin for glycaemic control. Patients who are already on metformin may continue treatment.⁶
 - Women with pre-existing diabetes who also have polycystic ovarian syndrome may continue metformin for ovulation induction.
 - Prior to conception or upon detection of pregnancy, the following medications should be discontinued: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers and statins.⁶

4.2 CONTRACEPTION

Women with pre-existing diabetes are encouraged to have a planned pregnancy. Their choice of contraception is based on their own preferences and any risk factors according to the Medical Eligibility Criteria.⁶ The use of oral contraceptive pills are allowed. However, intrauterine contraceptive device is the preferred method. Caution should be exercised when using Depo-Provera since it may worsen glycaemic control.^{27, level III}

4.3 GLYCAEMIC CONTROL

NICE guidelines recommend that women with pre-existing diabetes who plan for pregnancy to aim for HbA1c <6.5% (48 mmol/mol) if this is achievable without causing hypoglycaemia. Any reduction in HbA1c level towards the target is likely to reduce the risk of congenital malformations in the baby. Those with HbA1c level >10% (86 mmol/mol) are advised not to get pregnant because of the associated risks.⁶

For each 1% decrement in HbA1c, the risk of pre-eclampsia reduces by 12% in pre-pregnancy period to 53% at 34 weeks of gestation in T1DM.^{28, level I}

Women with pre-existing diabetes who plan to become pregnant need to increase the frequency of self-monitoring of blood glucose (SMBG) by including fasting, pre- and postprandial levels.⁶

4.4 FOLIC ACID SUPPLEMENTATION

The synthetic form of folate is folic acid (FA) which is often used in supplements and fortified foods. The main function of folate is to act as the co-enzyme in one-carbon transfer during the methylation cycle, an essential process for the syntheses of nucleic acids, which form part of deoxyribonucleic acid and neurotransmitters. Folate also plays an

essential function in protein synthesis, metabolism and other processes associated to cell multiplication and tissue growth.²⁹

Daily FA supplementation (alone or in combination with other vitamins and minerals) in women who become pregnant or are ≤ 12 weeks pregnant is effective in preventing neural tube defects (NTDs) compared with no intervention/placebo or vitamins and minerals without FA (RR=0.31, 95% CI 0.17 to 0.58). It also has protective effect for recurrence of NTDs (RR=0.34, 95% CI 0.18 to 0.64). However, there is no significant evidence of preventive effect on cleft palate, cleft lip, congenital cardiovascular defects and miscarriages.^{30, level I}

Lack of periconceptional (during a month before conception or first three months of pregnancy) use of vitamins or supplements that contain FA is associated with an excess risk of NTDs in diabetes.^{31, level II-2}

All women with diabetes should be counselled regarding intake of foods high in FA, folate-fortified foods and appropriate FA supplementation of 4 to 5 mg per day during the preconception period and in the first 12 weeks of gestation.^{32, level III} This is supported by NICE and Canadian guidelines.^{6; 33, level III} Local guidelines and Canadian guidelines recommend that FA supplementation should be taken at least three months prior to conception.^{4; 33, level III}

Recommendation 4

- Preconception care of women with pre-existing diabetes which involve a multidisciplinary team should be fully implemented in all healthcare facilities.
- Supplement of 5 mg folic acid per day should be given to women with diabetes who plan to become pregnant at least three months prior to conception and continue until 12 weeks of gestation.

5. ANTENATAL MANAGEMENT OF DIABETES IN PREGNANCY

5.1 GLYCAEMIC CONTROL

Self-monitoring of blood glucose (SMBG) in all pregnant women with pre-existing diabetes or GDM is recommended to achieve glycaemic control and improve pregnancy outcomes.^{6; 11} It serves to assist patients in adjustments of their medications particularly multiple daily insulin (MDI) therapy to achieve the desired glycaemic targets. Furthermore, it helps to prevent hypoglycaemia or hyperglycaemia episodes.

Monitoring of blood glucose is preferably done at home. The traditional blood sugar profile (BSP) performed in the hospital may not reflect the actual day-to-day blood sugar levels.⁴ In local setting when SMBG is not feasible, clinic-based BSP may be done to assess the glycaemic control. The frequency of BSP is once in two weeks until delivery or more frequent.

In a Cochrane systematic review on pregnant women with pre-existing diabetes, there was no significant advantage of any monitoring technique on maternal and fetal outcomes.^{34, level I}

In a meta-analysis on GDM, treatment consisting of diet modification, insulin and glucose monitoring was effective in reducing the incidence of:

- pre-eclampsia (RR=0.62, 95% CI 0.43 to 0.89)
- shoulder dystocia (RR=0.42, 95% CI 0.22 to 0.77)
- macrosomia (RR=0.50, 95% CI 0.35 to 0.71)

However, these interventions did not significantly change the rates of caesarean section, induction of labour (IOL), small for gestational age (SGA) and admission to neonatal intensive care unit (NICU).^{35, level I}

There is no benefit for glycaemic targets of FPG between 3.33-5.00 mmol/L and 4.45-6.38 mmol/L in T1DM. Very tight blood sugar control increases the risk of maternal hypoglycaemia (RR=22.0, 95% CI 11.07 to 32.93). There is evidence of harm (increased risk of pre-eclampsia, caesarean section and LGA) for FPG >7 mmol/L.^{36, level I}

Glycaemic targets that have been recommended by guidelines are:^{6; 11; 33}

- fasting: ≤ 5.3 mmol/L
- 1-HPP: ≤ 7.8 mmol/L
- 2-HPP: ≤ 6.4 - 6.7 mmol/L

SMBG should be done at the following times (performed over a few days):⁴

- fasting (following an 8-hour overnight fast) and preprandial
- 1 or 2 hours after the start of each meal (postprandial)
- bedtime and during the night when indicated

In poorly controlled diabetes, more frequent monitoring is essential. Monitoring should be done at home to reflect the actual day-to-day blood glucose levels. Refer to **Table 2** on self-monitoring blood glucose.

There is no evidence on the effectiveness of HbA1c monitoring in predicting adverse outcomes in pregnancy.

Table 2: Timing for Self-monitoring Blood Glucose⁴

Timing of SMBG & mode of treatment	Breakfast		Lunch		Dinner	
	Pre	Post	Pre	Post	Pre	Post/Prebed
Diet only	✓	✓		✓		✓
OAD or single dose insulin	✓	✓		✓		✓
Multiple dose insulin	✓	✓	✓	✓	✓	

Recommendation 5

- Self-monitoring of blood glucose (SMBG) should be done in diabetes in pregnancy. The blood glucose targets should be as the following:
 - fasting or preprandial: ≤ 5.3 mmol/L
 - 1-hour postprandial: ≤ 7.8 mmol/L
 - 2-hour postprandial: ≤ 6.7 mmol/L
- The frequency of SMBG in diabetes in pregnancy should be individualised based on mode of treatment and glycaemic control.
- Pregnant women with pre-existing diabetes on multiple daily insulin (MDI) injection regimen should perform SMBG at least three times daily. It can be done at fasting, preprandial, postprandial or bedtime.
- Women with gestational diabetes mellitus (GDM) on MDI injection regimen should perform SMBG two to three times daily, for two to three days a week.
- Pregnant women with type 2 diabetes mellitus or GDM on diet and exercise therapy, oral antidiabetic agents (OAD), single-dose intermediate-acting or long-acting insulin should perform fasting and postprandial SMBG at least once daily until blood glucose targets are reached.
- Pregnant women who are on insulin or OAD should maintain their capillary blood glucose level >4.0 mmol/L.

5.2 MEDICAL NUTRITION THERAPY

MNT for pregnant women with diabetes focuses on carbohydrate (CHO)-controlled meal plan. The aim is to achieve and maintain optimum glycaemic levels and appropriate GWG, while meeting essential nutrients to promote positive maternal and fetal outcomes.⁴

Evidence on the ideal amount of CHO for pregnant women with diabetes to achieve good glycaemic control is limited, but a minimum of 175 g CHO daily has been recommended.^{37, level III} In a meta-analysis of RCTs on GDM, lower CHO diets [40-45% of total energy intake (TEI)] showed no significant difference in maternal and neonatal outcomes compared with CHO intake of 55-60% TEI. This could be due to the small number of studies included.^{38, level I}

The ideal macronutrients distribution for pregnant women with diabetes is not known. Macronutrient distribution should be individualised. A general recommendation to promote a balance diet would be 45-60% CHO, 15-20% protein and 25-35% fat of total energy requirement.⁴

Both the amount and type of CHO influence glycaemic control. The type of CHO is best described using glycaemic index (GI) concept. In a meta-analysis on GDM, a low GI diet was more effective in reducing insulin requirement (RR=0.767, 95% CI 0.597 to 0.986) compared with high GI diet.^{38, level I} In a recent Cochrane systematic review on GDM, low-to-moderate GI showed no significant benefits in maternal outcomes (severe hypertension or pre-eclampsia, eclampsia and rate of caesarean section) and LGA compared with moderate-high GI diet. However, the primary papers used in the review were of low quality.^{39, level I}

The components of CHO-meal plan include the following:⁴

- monitoring of total CHO intake using grams, exchange list, household or hand measures as long as it is practical for women to comprehend and follow
- distributing total CHO exchanges according to SMBG, lifestyle and medications
- choosing appropriate type of CHO which is lower in GI
- sucrose (e.g. sugars) intake must be counted as part of the total CHO intake; excess sucrose intake contributes to calories and may cause excessive GWG
- non-nutritive sweeteners do not impact glycaemic level. However, it should not exceed the acceptable recommended daily intake.^{40, level III}

Refer to **Appendix 3** on CHO food, exchange list and GI diet.

- MNT provided by a dietitian, SMBG and insulin therapy are effective in reducing the rate of serious perinatal complications and tend to improve maternal quality of life.^{41, level I}
- Early nutritional intervention should be initiated at the time of diagnosis. Refer to **Appendix 3** for suggested menu plan.

Recommendation 6

- Pregnant women with diabetes should be given individualised medical nutrition therapy which includes carbohydrate-controlled meal plan and monitoring of gestational weight gain.

5.3 ORAL ANTIDIABETIC AGENTS

Metformin and glibenclamide are OAD that have been used in GDM. Glibenclamide has limited human data and should only be used if potential benefit outweighs the potential risk. Metformin is labelled as FDA pregnancy category B while glibenclamide is in category C.

A meta-analysis showed that compared with glibenclamide, metformin had significantly lower maternal weight gain, neonatal birth weight, macrosomia and LGA. However, there was no significant difference in glycaemic control (FPG and postprandial plasma glucose), caesarean section, preterm birth, stillbirth and neonatal hypoglycaemia.^{42, level I}

In four meta-analyses on GDM, there was no significant difference in glycaemic control between OAD and insulin. Compared with insulin, metformin was associated with less maternal weight gain^{43-46, level I} but higher incidence of premature birth (<37 weeks gestation).^{44-46, level I}

Two of the above meta-analyses compared glibenclamide and insulin. Glibenclamide was associated with less maternal hypoglycaemia but higher maternal weight gain.^{44, level I} For neonatal outcomes, it was associated with higher incidence of macrosomia, neonatal birth weight and neonatal hypoglycaemia.^{42, level I; 44, level I}

Category B: Animal studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Category C: Animal studies have shown an adverse effect on the fetus and adequate and well-controlled studies in humans were not available.

NICE guidelines state that metformin should be offered to women with GDM if diet and exercise do not control the blood glucose adequately within 1-2 weeks.⁶

Refer to the medication table in **Appendix 4**.

Recommendation 7

- In gestational diabetes mellitus, metformin should be offered when blood glucose targets are not met by modification in diet and exercise within 1-2 weeks.
 - It should be prescribed after consultation with specialists.
- Metformin should be continued in women who are already on the treatment before pregnancy.

5.4 INSULIN

5.4.1 Initiating Insulin Therapy

Common current practice involves hospital admissions for initiation of insulin therapy in insulin-naïve pregnant women and GDM. There is no evidence to support inpatient or outpatient settings for more effective treatment. However, local expert opinion recommends that insulin therapy could be initiated in the outpatient setting if the patient is agreeable, able to equip herself with adequate SMBG and able to titrate the required insulin doses to achieve glycaemic targets without hypoglycaemia. This may provide a more practical real-life experience in the comfort of her home as she attempts to make the necessary diet and lifestyle changes.

However, specialists may opt for hospital admission if deemed necessary due to logistic reasons, the need for referral to other multidisciplinary teams, closer monitoring for hyperglycaemia or hypoglycaemia and other factors.

Insulin should be initiated when MNT and/or metformin therapy failed to achieve optimum glycaemic control. There are multiple insulin regimes available in managing diabetes in pregnancy. However, the preferred choice of insulin regime is MDI.⁴ Initiation and optimisation of insulin therapy is illustrated in **Appendix 4**.

Insulin should be initiated when:⁶

- blood glucose targets are not met after MNT and metformin therapy
- metformin is contraindicated or unacceptable
- FPG ≥ 7.0 mmol/L at diagnosis (with or without metformin)
- FPG of 6.0-6.9 mmol/L with complications such as macrosomia or polyhydramnios (start insulin immediately, with or without metformin).

5.4.2 Human Insulin

The use of human insulin, both short acting (regular) and intermediate or long acting [Neutral Protamine Hagedorn (NPH)] have been established in pregnancy. They are generally considered safe and effective and labelled as FDA pregnancy category B. In the local setting, human insulin is the preferred choice of insulin in view of its cost and availability.

5.4.3 Insulin Analogues

Insulin analogues mimic natural insulin physiology. There are rapid and long acting (basal) insulin analogues which are currently used in pre-existing diabetes during pregnancy and GDM. Insulin lispro and aspart are labelled as FDA pregnancy category B. On the other hand, insulin glulisine and glargine are labelled as FDA pregnancy category C (refer footnote in page 13).

A. Rapid-acting Insulin Analogues

i. Insulin lispro

Insulin lispro significantly improves HbA1c and reduces total insulin requirement in pre-existing diabetes in pregnancy compared with regular insulin. Apart from that, it is associated with greater mean birth weight and lower hyperbilirubinaemia. There is no significant difference in other maternal and fetal outcomes.^{47, level II-2}

ii. Insulin aspart

Insulin aspart (IAsp) is as effective and safe as regular insulin when used in basal-bolus therapy with NPH in pregnant women with T1DM. It also offers some benefits in terms of postprandial glucose control and preventing severe hypoglycaemia.^{48, level I} Fetal outcomes using IAsp is comparable with regular insulin with a tendency towards fewer fetal losses, preterm deliveries, congenital malformations and neonatal hypoglycaemia.^{49, level I}

B. Long-acting (Basal) Insulin Analogues

i. Insulin detemir

There is no difference in HbA1c when comparing insulin detemir with NPH in pregnant T1DM women although insulin detemir group has significantly lower FPG at 24 and 36 weeks. Insulin requirement and rate of hypoglycaemia are similar in both groups.^{48, level I} There is no significant difference in the incidence of composite pregnancy outcomes which include fetal and perinatal mortality, and major malformations.^{49, level I}

ii. Insulin glargine

In pre-existing diabetes, there is no difference in the glycaemic control between insulin glargine and NPH. However, there is significantly lower insulin requirement in patients treated with insulin glargine. Maternal complications i.e. worsening pre-existing retinopathy and nephropathy, pre-eclampsia, and all types of hypoglycaemia are significantly higher in NPH-treated patients. Meanwhile in GDM, there is significantly higher FPG and insulin dose requirement in NPH-treated patients.^{50, level II-2}

In a systematic review on diabetes in pregnancy, there were no significant differences in main neonatal outcomes between insulin glargine and NPH.^{51, level II-2}

C. Premixed Insulin Analogues

i. Premixed insulin aspart 30

The use of premixed insulin aspart 30 in T2DM during pregnancy shows no significant difference in glycaemic control, maternal weight gain and neonatal outcomes compared with premixed human insulin 30. However, there is lower mean total insulin dose requirement with premixed insulin aspart 30.^{52, level I}

- Human insulins are the preferred choice in pregnant women who need insulin therapy.
- Both rapid- and long-acting (basal) insulin analogues are as efficacious as human insulin in pregnant women with pre-existing diabetes and GDM.
- Insulin analogues are associated with fewer incidences of hypoglycaemia.
- Long-acting analogues have benefit in diabetic pregnant women with repeated nocturnal hypoglycaemia.
- Insulin glulisine and glargine can be given only when potential benefit outweigh the potential risk.
- There is no evidence to support the use of glulisine in pregnancy.

Recommendation 8

- Insulin therapy can be initiated at outpatient setting in pregnant women with diabetes.
- The preferred choice of insulin regime in diabetes in pregnancy is multiple daily injections.
- Insulin analogues should be continued during pregnancy in women with pre-existing diabetes who are already on the treatment and have established good blood glucose control before pregnancy.
- Rapid-acting insulin analogue may be considered as an option, particularly in patients with frequent hypoglycaemia or postprandial hyperglycaemia using human insulin during pregnancy.

5.5 PRE-ECLAMPSIA PROPHYLAXIS

Pregnant women with pre-existing diabetes have a five-fold increased risk of pre-eclampsia (OR=5.74, CI 95% 5.31 to 6.20) compared to women without diabetes.^{53, level II-2}

In a large RCT on women with pre-existing diabetes, low dose aspirin supplementation (60 mg) did not reduce the risk of pre-eclampsia. There was also no evidence of harm to mothers or neonates.^{54, level I} However, existing guidelines recommend 75 mg aspirin daily from 12 weeks of gestation until delivery in patients with high risk of developing pre-eclampsia, which includes diabetes.^{55; 56, level III}

In three multicentre RCTs on women with pre-existing diabetes, supplementation of vitamin C and E did not reduce the risk of pre-eclampsia.^{57-59, level I} In fact, it was significantly associated with the following complications:

- fetal growth restriction^{59, level I}
- low birth weight^{59, level I}
- fetal loss or perinatal death (RR=2.20, 95% CI 1.02 to 4.73)^{57, level I}
- preterm prelabour rupture of membrane (RR=1.97, 95% CI 1.31 to 2.98)^{57, level I}

A Cochrane systematic review reported that high dose calcium supplementation (>1g/day) reduces the risk of pre-eclampsia (RR=0.45, 95% CI 0.31 to 0.65), especially for women with low calcium diets and those at high risk of pre-eclampsia.^{60, level I} Lower dose calcium may be effective, but needs to be confirmed by larger, high quality trials.^{61, level I}

The World Health Organisation (WHO) recommends calcium supplementation with 1.5-2.0 gram elemental calcium daily from 20 weeks of gestation in populations with low dietary calcium intake, to reduce the risk of pre-eclampsia.^{62-63, level III}

Recommendation 9

- Low dose aspirin (75-150 mg daily) should be given to prevent pre-eclampsia in women with pre-existing diabetes from 12 weeks of gestation until term.
- Vitamin C and E supplementation should not be given to prevent pre-eclampsia in women with diabetes.

5.6 ASSESSMENT OF COMPLICATIONS OF DIABETES**5.6.1 Retinal Assessment during Pregnancy**

Pregnant women with pre-existing diabetes should receive retinal assessment at booking, and again at 28 weeks, if initial findings were normal.⁶ If diabetic retinopathy is detected, referral to an ophthalmologist is required.

In a population-based study on pre-existing diabetes during pregnancy, 25.9% of patients who received two or more retinal assessment had progression of retinopathy. Significant factors associated with progression of retinopathy were higher systolic blood pressure during booking, higher HbA1c at first trimester and greater drop of HbA1c between first and third trimester.^{64, level III}

In women who present with high HbA1c and diabetic retinopathy in early pregnancy, rapid optimisation of blood glucose control should still be considered.⁶

5.6.2 Renal Assessment during Pregnancy

If renal assessment has not been done in the preceding three months in women with pre-existing diabetes, arrange it during the first antenatal visit. Referral to a nephrologist should be considered when:⁶

- serum creatinine is abnormal (120 $\mu\text{mol/L}$ or more); estimated glomerular filtration rate should not be used during pregnancy
- the urinary albumin: creatinine ratio (ACR) >30 mg/mmol
- total protein excretion exceeds 0.5 g/day

Thromboprophylaxis should be considered for women with nephrotic range proteinuria above 5 g/day (ACR >220 mg/mmol).⁶

Pregnant women with pre-existing renal disease should be managed in a combined clinic by multidisciplinary specialists.

Recommendation 10

- In women with pre-existing diabetes,
 - retinal assessment should be performed at booking and repeated at least once throughout the pregnancy
 - renal assessment should be performed at booking; those with pre-existing renal disease should be managed in a combined clinic

5.7 FETAL SURVEILLANCE

A meta-analysis of observational studies showed a higher risk of major congenital malformations in babies of women with GDM compared with reference group (RR=1.16, 95% CI 1.07 to 1.25). The risk was higher in women with pre-existing diabetes compared with reference group (RR=2.66, 95% CI 2.04 to 3.47).^{65, level II-2}

In women with GDM, ultrasound-guided management reduces the risk of LGA/SGA (RR=0.64, 95% CI 0.45 to 0.93) and macrosomia (RR=0.32, 95% CI 0.11 to 0.95), but increases the need for insulin treatment (RR=1.58, 95% CI 1.14 to 2.20) compared with conventional management.^{66, level I}

Fetal surveillance using ultrasound scan in women with pre-existing diabetes is as follows:⁶

Timing	Parameters
11-14 weeks of gestation	<ul style="list-style-type: none"> • Early scan is performed to: <ul style="list-style-type: none"> ○ confirm gestational age using crown-rump length measurement ○ assess for major structural malformation including acrania and anencephaly
18-20 weeks of gestation	<ul style="list-style-type: none"> • Detailed structural anatomy scan which includes the spine and heart (four-chamber, outflow tract and three-vessel views)
28-36 weeks of gestation	<ul style="list-style-type: none"> • Serial growth scan is performed every four weeks to assess fetal growth and amniotic fluid volume • The rate of fetal growth should be used to facilitate decisions with treatment, and timing and mode of delivery

Recommendation 11

- Pregnant women with pre-existing diabetes should be offered ultrasound scan at:
 - 11-14 weeks of gestation for dating and assessment of major structural malformation
 - 18-20 weeks of gestation for detailed structural anatomy scan (by a trained specialist or sonographer)
- In pregnant women with pre-existing diabetes and gestational diabetes mellitus, serial growth scan should be performed every four weeks from 28 to 36 weeks of gestation.

5.8 TIMING AND MODE OF DELIVERY

In two systematic reviews on pregnant women with GDM and pre-existing T2DM requiring insulin, active IOL at 38 weeks gestation reduced the risk of macrosomia compared with expectant management until 42 weeks (RR=0.56, 95% CI 0.32 to 0.98). There was no significant increase in rates of caesarean section, shoulder dystocia, neonatal hypoglycaemia or perinatal deaths. However, the RCT included had small sample size and did not permit firm conclusion to be drawn.^{67-68, level I}

In a systematic review on GDM, observational studies suggested a potential reduction in macrosomia and shoulder dystocia rates with elective IOL and caesarean section for estimated fetal weight indications. However, the quality of evidence was low.^{67, level I}

Management of delivery recommended by NICE guidelines in pregnant women with:⁶

- pre-existing diabetes with no maternal or fetal complications, deliver* between 37+0 and 38+6 weeks
 - pre-existing diabetes with maternal and/or fetal complications, deliver* before 37+0 weeks
 - GDM with no maternal or fetal complications, deliver* no later than 40+6 weeks
 - GDM with maternal and/or fetal complications, deliver* before 40+6 weeks
- **elective delivery by IOL or caesarean section*

Diabetes itself should not be considered a contraindication to attempting vaginal delivery after a previous caesarean section. Pregnant women with diabetes who have an ultrasound-diagnosed macrosomic fetus should be counselled about the risks and benefits of vaginal delivery, IOL and caesarean section.⁶

Recommendations from other guidelines are:

- pregnant women with GDM or pre-gestational diabetes should be offered IOL between 38-40 weeks depending on their glycaemic control and other comorbidities.^{33, level III}
- for women with GDM,¹²
 - if ultrasound at 36-37 weeks reports normal fetal growth (<90th percentile) and there are no maternal or fetal comorbidities, plan delivery at 40 weeks
 - If growth is >90th percentile or there are maternal and/or fetal comorbidities, plan delivery for 38 to 39 weeks

Antenatal corticosteroids is administered to women who have spontaneous or planned preterm delivery to accelerate fetal lung development. This will prevent respiratory distress syndrome. However, the use of corticosteroids is associated with a significant worsening of glycaemic control requiring adjustment in insulin dose.⁶

Recommendation 12

- The following should be planned for pregnant women with pre-existing diabetes:
 - without complications, delivery between 37+0 and 38+6 weeks
 - with maternal or fetal complications, delivery before 37+0 weeks
- The following should be planned for women with gestational diabetes:
 - on diet alone with no complications, delivery before 40+0 weeks
 - on oral antidiabetic agents or insulin, delivery between 37+0 and 38+6 weeks
 - with maternal or fetal complications, deliver before 37+0 weeks
- Mode of delivery should be individualised, taking into consideration the estimated fetal weight and obstetric factors.
- Women with diabetes who receive antenatal corticosteroids for fetal lung maturation should have close monitoring of blood glucose levels and insulin dose adjusted accordingly.

6. INTRAPARTUM GLYCAEMIC CONTROL FOR DIABETES IN PREGNANCY

Maternal hyperglycaemia during labour increases the risks of neonatal hypoglycaemia and fetal distress.^{6; 33, level III}

Insulin requirements decrease during delivery due to less calories intake and increased metabolic demand during the period. Adequate glucose must be provided during labour to meet its high requirement.^{33, level III}

A small RCT among pregnant women with diabetes requiring insulin, titrated insulin infusion versus alternating intravenous fluid regime with insulin as needed showed no difference in intrapartum maternal glycaemic control and neonatal hypoglycaemia.^{69, level I} There is no other evidence on the optimal method of maintaining glycaemic control during delivery.

Current recommendations for intrapartum glycaemic control are:^{6; 33, level III}

- monitor CBG every hour during labour and delivery, and ensure that it is maintained at 4.0-7.0 mmol/L
- use IV dextrose and insulin for women with
 - T1DM from the onset of established labour
 - CBG >7.0 mmol/L

For intrapartum glycaemic management in women with pre-existing diabetes and GDM, refer to **Algorithm B** and **C**.

Recommendation 13

- In women with diabetes, capillary blood glucose should be maintained at 4.0-7.0 mmol/L during labour and delivery.
- Monitoring of capillary blood glucose during labour and delivery in women with diabetes should be done:
 - 1- to 2-hourly in women on insulin treatment
 - 4-hourly in women not on insulin treatment

7. POSTPARTUM MANAGEMENT OF DIABETES IN PREGNANCY

Postpartum management is important in both GDM and pre-existing diabetes. This section covers aspects in glucose monitoring, diabetes prevention, pharmacotherapy, contraception, breastfeeding and lifestyle modification in the postnatal period.

7.1 POSTPARTUM GLUCOSE MONITORING

- Women with insulin-treated pre-existing diabetes should reduce their insulin immediately after birth and monitor their blood glucose levels carefully to establish the appropriate dose.⁶
- Most women diagnosed with GDM should be able to discontinue their insulin immediately after delivery.⁴
- Explain to women with insulin-treated pre-existing diabetes that they are at increased risk of hypoglycaemia in the postnatal period, especially when breastfeeding, and advise them to have a meal or snack available before or during feeds.⁶

In women with history of GDM,

- postpartum 75 g OGTT within one year of delivery yields higher detection rate of diabetes and pre-diabetes compared with FPG alone.^{70, level III}
- FPG (≥ 6.1 mmol/L) has a sensitivity of 90% and specificity of 91% for detection of diabetes. However, it will miss those with abnormally high 2-hour glucose levels post glucose challenge [diabetes >11.1 mmol/L and impaired glucose tolerance (IGT) >7.8 mmol/L] with sensitivity of 61% and specificity of 93%.^{71, level II-3}
- postpartum HbA1c is inferior to OGTT in the detection of diabetes and pre-diabetes.^{72-73, level III} However, the use of HbA1c ($>5.7\%$) in addition to OGTT provides an additional detection of 10.6% of patients with pre-diabetes.^{74, level III}
- FPG test is offered at 6-13 weeks after delivery to exclude diabetes, preferably during the 6-week postnatal follow-up.⁶
- annual screening for diabetes should be performed.⁴
- OGTT should be performed six weeks postnatally.⁴

7.2 POSTPARTUM USE OF METFORMIN

Postpartum metformin therapy significantly prevents newly-diagnosed diabetes in women with history of GDM compared with placebo (risk reduction=50.4%).^{75, level I} However, there is no significant benefit on weight loss or achievement of pre-pregnancy weight.^{76, level I}

7.3 BREASTFEEDING

Breastfeeding of more than three months in women with history of GDM is associated with lower risk of diabetes (HR=0.55, 95% CI 0.35 to 0.85).^{77, level II-2} Breastfeeding of more than nine months is associated with lower incidence of metabolic syndrome ($p=0.03$) compared with shorter duration.^{78, level II-2} Breastfeeding reduces the odds of abnormal OGTT at 12 weeks compared with bottle-feeding (OR=0.418, 95% CI 0.199 to 0.888).^{79, level II-2}

The optimum duration for breastfeeding is unknown. Breastfeeding for at least three months is recommended and longer duration is encouraged to reduce the risk of diabetes.

7.4 POSTPARTUM CONTRACEPTION

In pre-existing diabetes, there is insufficient evidence to demonstrate any significant difference in contraceptive efficacy and diabetes control between hormonal and non-hormonal contraceptions.^{80, level I}

There is limited data to demonstrate that Levonorgestrel-intrauterine system does not negatively affect glucose tolerance, i.e. IFG and IGT, compared with copper intrauterine device or tubal sterilisation in women with history of GDM.^{81, level III}

7.5 POSTPARTUM LIFESTYLE INTERVENTION

Postpartum lifestyle intervention includes MNT, physical activity and behavioural modification. It has been shown to be effective in reducing weight and insulin resistance, and development of T2DM among women with history of GDM.^{82, level I}

Intensive lifestyle intervention (addition of moderate physical activity, 50-60 minutes, four days per week) is effective in reducing cumulative incidence of diabetes during a 3-year study compared with conventional care ($p=0.003$).^{83, level I} It is also effective in reducing postpartum weight retention, waist circumference, insulin resistance, LDL-cholesterol and triglycerides, and increase intensity of vigorous physical activity level.^{83-84, level I}

Postpartum weight loss of more than 2 kg is significantly associated with smaller increase in FPG and reduction in 2-hour glucose levels post glucose challenge.^{85, level I}

In an RCT, intensive lifestyle intervention delivered via educational programme showed no significant differences in waist circumference, fasting blood glucose and lipids. This may be due to low subjects participation to the scheduled visits.^{86, level I}

Recommendation 14

- In women with history of gestational diabetes mellitus,
 - oral glucose tolerance test should be performed at six weeks after delivery to detect diabetes and pre-diabetes; If the result is negative, annual screening should be performed
 - metformin and intensive lifestyle intervention during postpartum period should be considered to prevent diabetes
 - breastfeeding of at least three months or longer should be encouraged to reduce the risk of diabetes

8. MANAGEMENT OF NEONATES OF MOTHERS WITH DIABETES

Optimal glycaemic control during pregnancy reduces the incidence of perinatal morbidity and mortality. Recognised neonatal complications of mothers with diabetes include macrosomia, traumatic birth injuries, neonatal hypoglycaemia and hyperbilirubinemia. Women with diabetes should deliver in hospitals where neonatal resuscitation services are available.

Management of neonates of mothers with diabetes are listed below:⁶

- The neonates should stay with their mothers unless there are clinical complications or signs that warrant admission for special or intensive care.
- Perform blood glucose testing routinely in neonates at 2-4 hours after birth to detect hypoglycaemia. Perform blood tests for polycythaemia, hyperbilirubinaemia, hypocalcaemia and hypomagnesaemia if clinical signs present.
- Only discharge neonates after 24 hours of delivery, provided that they are maintaining satisfactory CBG levels and feeding well.

9. MANAGEMENT OF SPECIAL CONDITIONS IN DIABETES IN PREGNANCY

9.1 CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

Insulin pump or continuous subcutaneous insulin infusion (CSII) is a small device that is used to administer subcutaneous insulin continuously. It has been used in non-pregnant diabetes patients especially in T1DM.

In a Cochrane systematic review, there is no evidence to support the use of CSII over multiple doses insulin for pregnant women with pre-existing diabetes and GDM. The RCTs used in the review were small and of low quality.^{87, level I}

- CSII does not confer additional maternal or fetal benefits compared with MDI. However, those who are already using the device can continue it throughout pregnancy.

9.2 CORTICOSTEROIDS

Corticosteroids are administered during pregnancy to accelerate fetal lung maturation. It is known to elevate plasma glucose levels and worsen glycaemic control of diabetes in pregnancy.

In two observational studies, both fasting and postprandial plasma glucose were elevated after corticosteroids administration in pregnant women with diabetes.^{88-89, level III} Most of them had to increase the insulin doses to less than double of their regular doses.^{88, level III}

There is no evidence on the use of oral or inhaled corticosteroids for other indications in diabetes with pregnancy.

- Women with diabetes who are given corticosteroids during pregnancy need regular plasma glucose monitoring (at least four times a day, for 48 hours from the first dose) and adjustment of their insulin dose accordingly.

9.3 FASTING

Pregnant women with diabetes should be strongly advised against fasting during Ramadhan. However, some of them might wish to observe the religious obligation.⁹⁰

In a local study on pregnant women with diabetes who fasted during Ramadhan, most of them who were on NPH insulin (79.2%) were able to fast for more than 15 days without any hypoglycaemia or

fetal complications. Thus, once or twice daily NPH insulin is safe and tolerable for this group of pregnant women.^{91, level III}

Women with pre-existing diabetes and GDM with good glycaemic control prior to Ramadan continue to have good control throughout and after Ramadan.^{92, level II-2}

Recommendation 15

- Pregnant diabetes women should consult their healthcare providers if they wish to observe fasting.

10. REFERRAL TO SECONDARY/TERTIARY CARE

All women with pre-existing diabetes should receive continuous specialist care to detect complications, review medications and optimise glycaemic control.^{33, level III} Similarly, women with GDM who have poor glycaemic control and fetal complications should receive specialist care.

Referral to a dietitian is necessary to ensure balanced diet and achievement of good glycaemic control. Assessment for retinopathy and nephropathy should be performed regularly during pregnancy.⁶

At postpartum, these women should be referred back to their health facilities to continue with their diabetes care. Ophthalmology review should be performed at least six months after delivery.⁶

Recommendation 16

- Pregnant women with pre-existing diabetes and women with GDM who have poor glycaemic control or fetal complications should be referred to secondary or tertiary care.

11. IMPLEMENTING THE GUIDELINES

Implementation of CPG is important as it helps in providing quality healthcare services based on best available evidence applied to local scenario and expertise. Various factors and resource implications should be considered for the success of the uptake in the CPG recommendations.

11.1 Facilitating and Limiting Factors

The existing facilitating factors in implementing the recommendations in the CPG are:

- availability of CPG to healthcare providers (hardcopies and softcopies)
- regular conferences and updates on management of diabetes in pregnancy involving professional societies or bodies (Malaysian Endocrine and Metabolic Society, Obstetrics and Gynaecology Society of Malaysia, Family Medicine Specialist Association, Academy of Family Physician Malaysia, National Diabetes Institute, etc.)
- public awareness campaigns on diabetes in pregnancy during World Diabetes Day, etc.

The existing limiting factors in implementing the recommendations in the CPG are:

- different levels of care and wide variation in practice due to expertise, facilities and financial constraints
- lack of awareness among high risk women on the risk of developing diabetes in pregnancy

11.2 Potential Resource Implications

To implement the CPG, there must be dedicated efforts to:

- ensure widespread distribution of CPG to healthcare providers
- provide regular training to healthcare providers via effective seminars and workshops
- involve multidisciplinary team at all levels of health care
- strengthen the National Obstetric Registry

To assist in the implementation of the CPG, the following are proposed as clinical audit indicators for quality management:

1. Screening at booking in women at risk of GDM

$$\text{Percentage of women at risk of GDM screened with 75-g OGTT at booking (target >85\%)} = \frac{\text{Number of women at risk of GDM screened with 75-g OGTT at booking in a period}}{\text{Total number of women at risk of GDM at booking in the same period}} \times 100\%$$

2. Postpartum OGTT in women with GDM

$$\text{Percentage of women with GDM who had OGTT at six weeks postpartum (target >70\%)} = \frac{\text{Number of women with GDM who had OGTT at six weeks postpartum}}{\text{Total number of women with GDM}} \times 100\%$$

Implementation strategies will be developed following the approval of the CPG by MoH which include Quick Reference and Training Module.

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Appendix 1

EXAMPLE OF SEARCH STRATEGY

Clinical Question: What are the effective and safe screening strategies for diabetes in pregnancy?

1. DIABETES, GESTATIONAL/
2. (gestational adj1 diabetes mellitus).tw.
3. (diabetes adj1 (pregnancy-induced or pregnancy induced or gestational)).tw.
4. PREGNANCY IN DIABETICS/
5. pregnancy in diabet*.tw.
6. DIABETES MELLITUS/
7. diabetes mellitus.tw.
8. DM.tw.
9. DIABETES MELLITUS, TYPE 1/
10. iddm.tw.
11. (diabetes mellitus adj1 (insulin-dependent or insulin dependent or insulin-dependent 1 or insulin dependent 1 or type 1)).tw.
12. DIABETES MELLITUS, TYPE 2/
13. niddm.tw.
14. (diabetes mellitus adj1 (non-insulin-dependent or noninsulin-dependent or noninsulin dependent or non insulin dependent or type 2)).tw.
15. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. PREGNANCY/
17. pregnanc*.tw.
18. 16 or 17
19. 15 and 18
20. 1 or 2 or 3 or 4 or 5 or 19
21. MASS SCREENING/
22. screen*.tw.
23. (mass adj1 screen*).tw.
24. 21 or 22 or 23
25. 20 and 24
26. limit 25 to (english language and humans and yr="2006 -Current")

Appendix 2**CLINICAL QUESTIONS**

1. What are the effective and safe screening strategies for diabetes in pregnancy?
2. What are the methods to diagnose GDM?
3. Are the following interventions effective and safe in pre-existing diabetes? (preconception care and counselling, exercise, contraception, glycaemic/metabolic control, supplementations)
4. Are the following antenatal management effective and safe in non-diabetes pregnant women at risk of gestational diabetes? (lifestyle modification, exercise, medical nutrition therapy [MNT])
5. Are the following antenatal management effective and safe in pre-existing diabetes and gestational diabetes? (glycaemic/metabolic control, timing and mode of delivery, pre-eclampsia prophylaxis, MNT, fetal surveillance, screening for congenital malformation)
6. Are oral antidiabetic agents effective and safe in pre-existing diabetes and gestational diabetes?
7. Is insulin analogue effective and safe in pre-existing diabetes and gestational diabetes?
8. Are the following intrapartum management (spontaneous vaginal delivery/caesarean section) effective and safe in pre-existing diabetes and gestational diabetes? (blood glucose target, insulin regime)
9. Are the following postpartum management effective and safe in pre-existing diabetes and gestational diabetes? (postpartum glucose monitoring, modification of the treatment, breastfeeding, contraception counselling)
10. What are the effective and safe management of specific conditions in pregnancy? (use of corticosteroids, use of insulin pumps, fasting)
11. What are the effective and safe management for infants of diabetic mothers?
12. What are the indications for referral to secondary/tertiary care?

Appendix 3

CARBOHYDRATE CONTENT OF COMMON MALAYSIAN FOODS

Foods	Serving	Calories (kcal)	CHO content (g)	Approx. CHO exchanges*
Cooked rice	1 bowl (159 g)	207	48	3
Roti canai	1 piece (95 g)	301	46	3
Chappati	1 piece (100 g)	300	47	3
Curry mee	1 bowl (450 g)	549	55	4
Fried noodles (mee/mee hoon)	1 plate (30 g)	281	41	3
Bread (white/ wholemeal)	1 slice (30 g)	70	15	1
Biscuits, unsweetened	2 pieces (18 g)	80	14	1
Curry puff	1 piece (40 g)	128	17	>1
Potato	1 medium (90 g)	90	16	1
Dhal (raw)	½ cup (98 g)	98	64	4
Full cream milk	1 cup (250 ml)	187	18	1
Low fat milk	1 cup (250 ml)	131	12	1
Skim milk powder	4 tbsp (28 g)	100	16	1
Condensed milk, sweetened	2 tbsp (40 g)	126	21	1.5
Apple/orange	1 medium (114 g)	40	9	<1
Banana (pisang mas)	1 small (50 g)	40	9	<1
Star fruit	1 medium (260 g)	56	11	1
Durian local	5 small seeds (189 g)	64	12	1
Langsat/grapes/ longan	8 small (233 g)	52	12	1
Guava	½ fruit (100 g)	50	11	1
Watermelon/papaya/ pineapple	1 slice (160 g)	56	11	1
Mango	1 small (100 g)	50	11	1

*1 CHO food exchange = 15 g

tbsp = tablespoon

- Sources: 1. Tee ES, Mohd Ismail N, Mohd Nasir A, et al. Nutrient Composition of Malaysian Foods. Kuala Lumpur: Institute for Medical Research (IMR);1997.
2. Shahr S, Yusoff NM, Safii NS, et al. Atlas of food exchanges & portion sizes (3rd edition). Kuala Lumpur: MDC Publishers; 2015.

Appendix 3

FOOD GROUPS AND EXCHANGE LISTS

Cereals, Grain Products and Starchy Vegetables (Each item contains 15 g carbohydrate, 2 g protein, 0.5 g fat and 75 calories)	
Cereals, Grain and Bread	
Rice, white unpolished (cooked)	½ cup or ⅓ Chinese rice bowl
Can be exchanged for	
Rice porridge	1 cup
Kuey teow	½ cup or ⅓ Chinese rice bowl
Meehoon	
Tang hoon	
Spaghetti	
Macaroni	
Mee, wet	
Idli	1 piece (60 g)
Putu mayam	1 piece (40 g)
Thosai, diameter 20 cm	½ piece
Chappati, diameter 20 cm	⅓ piece
Bread (wholemeal, high fibre, white/brown)	1 slice (30 g)
Plain roll	1 small (30 g)
Burger bun	½ piece
Pita bread, diameter 6"	½ piece
Oatmeal, cooked	¼ cup
Oats, uncooked	3 rounded tbsp
Muesli	¼ cup
Flour (wheat, rice, atta)	3 rounded tbsp
Biscuits (plain, unsweetened) e.g. cream crackers, Ryvita	3 pieces
Small thin, salted biscuits (4.5 x 4.5 cm)	6 pieces
Starchy Vegetables	
*Baked beans, canned	1/3 cup
*Lentils	1/3 cup
(*Contains more protein than other foods in the list i.e. 5 g/serve)	
Corn kernel (fresh/canned)	½ cup
Peas (fresh/canned)	½ cup
Sweet potato	½ cup (45 g)
Tapioca	
Yam	
Breadfruit (sukun)	1 slice (75 g)
Pumpkin	1 cup (100 g)
Corn on the cob, 6 cm length	1 small
Potato	1 small (75 g)
Potato, mashed	½ cup
Waterchestnut	4 pieces
<ul style="list-style-type: none"> • 1 cup = 200 mL in volume = ¾ Chinese rice bowl (11.2 cm in diameter x 3.7 cm deep) • Tablespoon (tbsp) refers to dessert spoon level (equivalent to 2 teaspoons) 	

Adapted: Malaysian Dietitians' Association. Medical Nutrition Therapy Guidelines for Type 2 Diabetes Mellitus. 2013.

Appendix 3

FOOD GROUPS AND EXCHANGE LISTS (continue)

Fruits (Each item contains 15 g carbohydrate and 60 calories)	
Orange	1 medium
Can be exchanged for	
Banana	1 small (60 g)
Apple	1 medium
Custard apple (buah nona)	
Star fruit	
Pear	
Peach	
Persimmon	
Sapodilla (ciku)	
Kiwi	
Hog plum (kedondong)	6 whole
Mangosteen	2 small
Plum	2 small
Duku langsung	8 pieces
Grapes	
Langsat	
Longan	
Water apple (jambu air), small	
Lychee	5 whole
Rambutan	5 whole
Pomelo	5 slices
Papaya	1 slice
Pineapple	
Watermelon	
Soursop (durian belanda)	
Guava	½ fruit
Cempedak	4 pieces
Jack fruit (nangka)	4 pieces
Prunes	3 pieces
Dates (kurma), dries	2 pieces
Raisin	20 g
Durian	2 medium seeds
Mango	½ small

Adapted: Malaysian Dietitians' Association. Medical Nutrition Therapy Guidelines for Type 2 Diabetes Mellitus. 2013.

Appendix 3

FOOD GROUPS AND EXCHANGE LISTS (continue)

Lean Meat, Fish and Meat Substitutes (Each serving of meat and substitutes contain 7 g of protein. These foods contain varying amounts of fat and energy, but negligible carbohydrate)				
	CHO (g)	Protein (g)	Fat (g)	Energy (kcal)
Lean meat / meat substitutes	0	7	4	65
Fish / shellfish	0	7	1	35
Lean Meat				
Chicken (raw, without skin)	½ drumstick			
<i>Can be exchanged for</i>				
Lean meat (all varieties)	1 small serve (40 g)			
Poultry (young)	40 g raw/30g cooked			
Egg (hen)	1 medium			
Soya bean curd (taukua)	½ piece (60 g)			
Soya bean curd (soft, tauhoo)	¾ piece (90 g)			
Soya bean curd, sheet (fucok)	1½ sheets (30 g)			
Tempeh	1 piece (45 g)			
Cheese, cheddar	2 thin slices (30 g)			
Cottage cheese	¼ small cup			
Fish/Shellfish				
Fish (e.g. kembong, selar)	½ piece (40 g)			
Fish cutlet	¼ piece (40 g)			
Squid	1 medium (40 g)			
Crab meat	¼ cup			
Lobster meat				
Prawn meat				
Cockles	20 small			
Prawn	6 medium			
*Beans and lentils are good sources of protein but they also contain carbohydrate				

Milk (Milk contains varying amount of carbohydrate, fat and protein depending on the types)				
	CHO (g)	Protein (g)	Fat (g)	Energy (kcal)
Skimmed (1% fat)	15	8	Trace	90
Low fat (2% fat)	12	8	5	125
Full cream	10	8	9	150
Fresh cow's milk	1 cup (240 ml)			
UHT fresh milk				
Powdered milk (skimmed, full cream)	4 rounded			
Yogurt (plain/low fat)	¾ cup			
Evaporated (unsweetened)	½ cup			

Adapted: Malaysian Dietitians' Association. Medical Nutrition Therapy Guidelines for Type 2 Diabetes Mellitus. 2013.

Appendix 3

FOOD GROUPS AND EXCHANGE LISTS (continue)

Fat (Each item contains 5 g of fat and 45 calories. Some of the foods in the list, e.g. nuts and seeds also contain small amounts of carbohydrate and protein)	
Oil (all types)	1 level teaspoon (5 g)
Can be exchanged for	
Butter, margarine	1 level teaspoon
Mayonnaise	
Shortening, lard	
Peanut butter (smooth or crunchy)	2 level teaspoons
Cream, unwhipped (heavy)	1 level tbsp
Cream cheese	
Salad dressing	
Cream, unwhipped (light)	2 level tbsp
Coconut, shredded	
Coconut milk (santan)	
Non dairy creamer, powder	
Almond	6 whole
Cashew nut	6 whole
Walnut	1 whole
Peanut	20 small
Sesame seed	1 level tbsp
Watermelon seed (kuachi) with shell	¼ whole

Adapted: Malaysian Dietitians' Association. Medical Nutrition Therapy Guidelines for Type 2 Diabetes Mellitus. 2013.

Appendix 3

GLYCAEMIC INDEX LIST

Food Category	Low GI (< 55)	Intermediate GI (56-70)	High GI (>70)
Rice	Barley	Basmati Rice Brown rice Parboiled rice Red rice	Glutinous rice Jasmine rice Instant porridge White rice Sago
Bread and cereals products	All brand breakfast cereals Muesli Wholegrain bread varieties	Capati Idli Oatmeal Pita bread, wholemeal Wholemeal barley flour bread	Cornflakes Rice crackers Roti canai White flour bread Wholemeal (whole wheat) Wheat flour bread
Noodle and Pasta	Lasagne pasta sheets, Spaghetti, white, boiled Spaghetti, wholemeal, boiled	Spaghetti, white, durum Wheat semolina Udon noodles, plain Wheat noodles	Fried macaroni Fried meehoon Fried rice noodles Rice noodle (kuey teow)
Milk	Full fat milk Low fat milk Skimmed milk Soy milk (without added sugar) Yogurt	Ice cream Sweetened condensed milk	Teh tarik
Fruits	Apple Mango Oranges Plum	Banana Dates Papaya Pineapples Raisin	Lychee Watermelon
Legumes	Baked beans Chickpeas Lentils Mung bean		
Tubers	Cassava, boiled	Pumpkins, boiled Sweet corn, boiled	Potato, boiled Sweet potato, boiled

- Sources:**
- Atkinson FS, Foster-Powell K, Brand-Miller JC. International tables of glycemic index and glycemic load values: 2008. *Diabetes Care*. 2008;31(12):2281-2283.
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Appendix 3

**SAMPLE MENU
(FOR 2000 KCAL/DAY*)**

(This sample menu provides ~ 48% carbohydrate, 18% protein and 34% fat from energy)

Suggested meal time	Suggestion for serving size and foods
Breakfast (8-9 am)	<ul style="list-style-type: none"> • 1 cup wheat noodles or spaghetti, preferably soups than fried, or • 1 piece chapatti/2 pieces idli with dhal curry, or • 5 tbsp oats with 1 tbsp powder milk and 1 tbsp fruits cutlets <p style="text-align: center;">AND</p> <ul style="list-style-type: none"> • 1 glass (250ml) milk
Morning Tea (10-11am)	<ul style="list-style-type: none"> • 1 piece curry puff, or • Egg sandwich (2 pieces of whole grain bread, 1 boiled egg, salads), or • 1 container plain yogurt, or • 1 glass milk
Lunch (12-2 pm)	<ul style="list-style-type: none"> • 2 ladles of rice (preferably low-to-medium glycaemic index) • ½ ekor fish/1 piece (asam rebus, soup) • ½ cup tempeh/tauhu (preferable baked) • 1 ladle of vegetables • ½ piece guava, 1 slice papaya, 1 apple/orange/pear/lai • Plain water
Afternoon Tea (4-5 pm)	<ul style="list-style-type: none"> • ½ cup barley water and 1 chickpea, or • 1 tab plain yogurt, or • 4-5 piece cream cracker with low fat cheese, or • 1 glass milk
Dinner (6-8 pm)	<ul style="list-style-type: none"> • Same as lunch, or • 1 cup spaghetti (bolognaise or soup), salads and with 1 exchange fruit (apple/orange/pear), or • Noodles soup with slices of chicken, salads and with 1 exchange of fruit (apple/orange/pear), or • Chicken sandwich (2-3 pieces of whole grain bread, 1 slices baked chicken, salads) with 1 (apple/orange/pear)
Supper (9-10 pm)	<ul style="list-style-type: none"> • 1 glass milk

*This is a menu planned for women with a normal pre-pregnancy BMI. Patients who are underweight, overweight or obese should be referred to a dietitian/nutritionist. The same applies to those with excessive gestational weight gain.

Appendix 4

MEDICATION TABLE

Oral Antidiabetic Agents

Drugs	Formulations	Minimum Dose	Maximum dose
Metformin	Metformin 500 mg tablet	Initial dose 500 mg OD Usual dose 1500 mg OD	1000 mg TDS
	Metformin SR 850 mg	Usual dose 850 mg BD	850 mg TDS
	Metformin XR 500 mg/750 mg	Initial dose 500 mg OD Usual dose 1500 mg OD	2000 mg OD

Insulin

Types of Insulin preparation	Onset of Action	Peak Action (hours)	Duration of Action	Timing of Administration of Insulin
PRANDIAL				
Short-acting, Regular Actrapid Humulin R Insugen R Insuman R	30-60 min	2-4	6-10	30 min before meal
Rapid-acting, Analogues Aspart Lispro	0-20 min	1-3	3-5	5-15 min immediately before/after meals
BASAL				
Intermediate-acting, NPH Insulatard Humulin N Insugen N Insuman N	1-2 hour	4-8	8-12	Pre-breakfast /pre-bed
Long-acting Analogues Glargine Determir	30-60 min	Less peak	16-24	Same time everyday (flexible once daily injection)
PREMIXED INSULIN				
Mixtard 30	30 min	Dual	18-23	30-60 min before meals
Humulin 30/70	30 min	Dual	16-18	30-60 min before meals
Novomix 30	10-20 min	1-4	16-20	5-15 min before meals
Humalog mix 25/75	15 min	0.25-2.5	16-18	5-15 min before meals
Humalog mix 50/50	15 min	0.25-2.5	16-18	5-15 min before meals

Initiating Insulin Therapy in Pregnancy

Glycaemic abnormality	Suggested Insulin Type and Dose
FPG >5.3 mmol/L	Start 0.2 units/kg of intermediate-acting insulin at bedtime, increase by 2 units every 3 days until targets are reached.
1-hour postprandial >7.8 mmol/L 2-hours postprandial >6.7 mmol/L	Start 6 units of short-acting insulin, increase by 2 units every 3 days until targets are reached. If preprandial short-acting insulin dose exceeds 16 units TDS, consider adding 6-10 units intermediate-acting insulin in the morning and titrate accordingly until targets are achieved.

Estimation of total daily insulin requirement by gestation/trimester

Pregnancy gestation	Total daily insulin requirement
1 st trimester	0.7 units/kg/day
2 nd trimester	0.8 units/kg/day
3 rd trimester	0.9 units/kg/day

Blood Glucose Targets in Pregnancy

Timing of Blood Glucose	Target Value (mmol/L)
Fasting or preprandial	5.3
1-hour after the start of a meal	7.8
2-hours after the start of a meal	6.7

- Sources:**
1. Malaysian Endocrine & Metabolic Society and Ministry of Health Malaysia. Management of Type 2 Diabetes Mellitus (5th Edition). Kuala Lumpur: MEMS & MOH; 2015.
 2. Malaysian Endocrine & Metabolic Society and Ministry of Health Malaysia. Practical Guide to Insulin Therapy. Kuala Lumpur: MEMS & MOH; 2011. (Available at: http://www.mems.my/file_dir/3308086634dc0e0f9e1c72.pdf)

Appendix 5

PREPARATION OF INSULIN INFUSION

Principles of infusion:

Glucose is infused intravenously at a fixed rate. Insulin is administered intravenously at a variable rate. CBG is checked hourly and insulin infusion rate adjusted accordingly to maintain target CBG range.

Women with T1DM need to have some insulin in their system at all times to avoid diabetic ketoacidosis. Those with T2DM or GDM may or may not require insulin infusion. Insulin requirements decrease after delivery of the placenta.

Intravenous insulin infusion protocol

Dilute insulin to a concentration of 1 unit/mL. Use either 20 units short-acting human insulin (actrapid) made up to 20 mL with 0.9% saline solution in a 20 mL syringe or 50 units short-acting human insulin made up to 50 mL with 0.9% saline solution in a 50 mL syringe. Administer insulin infusion via a syringe pump.

Based on serum potassium (K⁺) result, prepare a separate dextrose-potassium chloride (KCl) mixture as below:

K ⁺ result	Amount of KCl to add to 500 mL of 5% dextrose solution
<3.5 mmol/L	3 g (39 mmol)
3.5-4.5 mmol/L	2 g (26 mmol)
>4.5 mmol/L	1 g (13 mmol)

Note: One ampoule of 10 mL KCl 10% contains 13.4 mmol of K⁺.

- Initiate IV insulin infusion as detailed in Algorithm C.
- Maintain a constant infusion of dextrose-KCl over six hours, at a rate of 83 mL/hour.
- The patient would require one dedicated IV cannula with both infusions administered concurrently through infusion pumps, connected via a 3-way stopcock to the IV cannula.

LIST OF ABBREVIATIONS

ACR	albumin:creatinine ratio
BD	twice daily
BMI	body mass index
CBG	capillary blood glucose
CI	confidence interval
CPG	Clinical Practice Guidelines
CSII	continuous subcutaneous insulin infusion
DG	Development Group
FA	folic acid
FPG	fasting plasma glucose
GDM	gestational diabetes mellitus
HbA1c	glycosylated haemoglobin
HPP	hours postprandial
HPT	hypertension
HR	hazard ratio
IAsp	insulin aspart
IOL	induction of labour
IV	intravenous
LGA	large for gestational age
MaHTAS	Malaysian Health Technology Assessment Section
MDI	multiple dose injections
NICE	National Institute for Health and Care Excellence
NICU	neonatal intensive care unit
NPH	Neutral Protamine Hagedorn
OAD	oral antidiabetic agents
OGTT	oral glucose tolerance test
OD	once daily
PG	plasma glucose
PIH	pregnancy-induced hypertension
RC	Review Committee
RCT	randomised controlled trial
RPG	random plasma glucose
RR	relative risk / risk ratio
SC	subcutaneous
SGA	small for gestational age
SMBG	self-monitoring blood glucose
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
tbsp	tablespoon
TDS	thrice daily

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**MALAYSIAN HEALTH TECHNOLOGY
ASSESSMENT SECTION**

Medical Development Division
Ministry Of Health Malaysia
Level 4, Block E1, Precinct 1
62590 Putrajaya,
Malaysia

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