Philippine Practice Guidelines on the Diagnosis and Management of Diabetes Mellitus

A Project of

UNITE FOR Diabetes Philippines:
A Coalition of Organizations Caring for Individuals with Diabetes Mellitus

Diabetes Philippines (Formerly Philippine Diabetes Association)
Institute for Studies on Diabetes Foundation, Inc (ISDF)
Philippine Society for Endocrinology and Metabolism (PSEM)
Philippine Center for Diabetes Education Foundation (PCDEF)

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(Consensus) Panel of Experts:

<table>
<thead>
<tr>
<th>Associations/Agencies</th>
<th>Representative</th>
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<tr>
<td>Diabetes Philippines</td>
<td>1. Dr. Susan Yu-Gan</td>
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<td>2. Sanirose S. Orbeta, MSRD, FADA</td>
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<td>5. Dr. Jimmy Aragon</td>
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<td>6. Dr. Augusto D. Litonjua</td>
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<td>Dr. Carolyn Narvacan-Montano</td>
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<td>8. Dr. Rima Tan</td>
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<td>9. Dr. Ernesto Ang</td>
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<td>11. Dr. Laura Trajano-Acampado</td>
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<td>12. Dr. Bien J. Matawaran</td>
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<td>Philippine Association of Diabetes Educators (PADE)</td>
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<td>14. Dr. Ronaldo Toledo</td>
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<td>Philippine Society for Pediatric Metabolism &amp; Endocrinology (PSPME)</td>
<td>15. Dr. Susana Padilla-Campos</td>
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<td>American Association for Clinical Endocrinology (AACE), Phil Chapter</td>
<td>17. Dr. Jose Carlos Miranda</td>
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<td>18. Dr. Yvette Amante</td>
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<td>Association of Diabetes Nurse Educators Philippines (ADNEP)</td>
<td>19. Leyden F. Florido, RN, MAN</td>
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<td>Association of Municipal Health Officers of the Philippines (AMHOP)</td>
<td>20. Dr. Leonardo Afable Jr.</td>
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<td>Department of Education (DepEd)</td>
<td>21. Dr. Minda U. Meimban</td>
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<td>Representatives of Diabetic Persons (Lay or non-medical representatives)</td>
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<td>Nutritionists and Dietitians Association of the Philippines (NDAP)</td>
<td>25. Nieves Serra, RND</td>
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<td>Philippine Academy of Family Physicians (PAFP)</td>
<td>26. Dr. Alex J.B. Alip Jr.</td>
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<td>Philippine Association of Medical technologists (PAMET)</td>
<td>27. Leila M. Florento, RMT, PhD</td>
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<td>Philippine College of Occupational Medicine (PCOM)</td>
<td>28. Dr. Rustico Jimenez</td>
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<td>Philippine College of Physicians</td>
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<td>Philippine Heart Association (PHA)</td>
<td>29. Dr. Jose Antonio Bautista</td>
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<td>PhilHealth (NON-VOTING)</td>
<td>30. Dr. Shirley Domingo</td>
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<td>Philippine Lipid and Atherosclerosis Society (PLAS)</td>
<td>31. Dr. Abdias V. Aquino</td>
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<td>Philippine Medical Association (PMA)</td>
<td>32. Dr. Arthur Catli</td>
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<tr>
<td>Philippine Obstetrics and Gynecology Society (POGS)</td>
<td>Representative Unable to Attend</td>
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<tr>
<td>Philippine Pediatric Society (PPS)</td>
<td>33. Dr. Susana Padilla-Campos</td>
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<td>34. Dr. Abdias V. Aquino/</td>
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<td>Dr. Norbert Lingling Uy</td>
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<tr>
<td>Philippine Society of Nephrology (PSN)</td>
<td>35. Dr. Benjamin Balmores Jr.</td>
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Objectives of the CPG on DM Development Initiative:

To develop clinical practice guidelines on the screening, diagnosis and management of diabetes which reflect the current best evidence and which incorporate local data into the recommendations, in view of aiding clinical decision making for the benefit of the Filipino patient.

Epidemiology of Diabetes in the Philippines:

The prevalence of diabetes mellitus in the Philippines for the last 10 years according to the National Nutrition and Health Survey is as follows:

<table>
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<tr>
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<tbody>
<tr>
<td>FBS &gt; 125</td>
<td>3.9</td>
<td>3.4</td>
<td>4.8</td>
</tr>
<tr>
<td>DM based on history</td>
<td>---</td>
<td>2.6</td>
<td>4.0</td>
</tr>
<tr>
<td>FBS or OGTT or History</td>
<td>---</td>
<td>4.6</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

Adding on those who have pre-diabetes (impaired fasting glucose or impaired glucose tolerance or both) which has a prevalence of 10.6%, this figure balloons to 17.8% or nearly 20%. In simple terms, 1 out of every 5 Filipino could potentially have diabetes mellitus or pre-diabetes.

Scope of the Guidelines:

The main focus of this set of guidelines is the outpatient management of adult patients with Type 2 diabetes mellitus. Type 1 diabetes will also be briefly mentioned in relation to screening and diagnosis, but management will not be tackled as this group of patients are typically under the care of physicians with specialized training such as endocrinologists or diabetologists. Likewise, the management of diabetes in children will not be tackled. Finally, guidelines on the inpatient management of diabetes mellitus will not be discussed in this document but will be developed in future clinical practice guidelines.

The guideline statements will cover 4 general areas:
1. Screening and Diagnosis of Diabetes
2. Screening for and Prevention of Complications
3. Treatment (Pharmacologic and Non-pharmacologic) of Diabetes
4. Special Populations: Gestational diabetes, diabetes in the elderly

Intended users:

These guidelines are intended for all physicians who are caring for patients with diabetes including diabetologists, endocrinologists, general practitioners, family physicians and general internists, as well as for medical students, resident trainees of internal medicine or family medicine, and endocrine or diabetology fellows-in-training.
**Anatomy of guidelines**

Each of the guideline statements will follow this structure
- Question or Issue
- Statement of the Guideline Recommendation
- Summary of Evidence
- Evidence Grade
- Strength of Recommendation
- Comparison with other guidelines

**Keywords:** Clinical practice guidelines, diabetes mellitus, Philippines

**Executive Summary**

Clinical practice guidelines are user-friendly statements that bring together the best external evidence (research) and clinical experience for rational decision making about a specific health problems. These evidence based guidelines should ideally be cost-effective, adapted to the local setting, incorporates patient’s values in decision making and in a developing country like the Philippines, considers issues of equity. In drafting the guidelines, there was a conscious effort to write it not only for those who could afford the tests and treatments, but also for those who may not have access nor financial means.

This CPG used two main methods for guideline development: (1) Guideline adaptation using the ADAPTE process ([www.adapte.org](http://www.adapte.org)) and (2) de novo development of guideline statements whenever there are no guidelines on certain issues. The latter is the strategy used for developing statements regarding the use of alternative methods for diagnosis of diabetes and herbal medications or alternative medicines for the treatment of diabetes mellitus.

The rationale for the ADAPTE process is to take advantage of existing guidelines and reduce duplication of effort, thereby shortening the amount of time needed for guideline generation.

“The **ADAPTE process** provides a systematic approach to adapting guidelines produced in one setting for use in a different cultural and organizational context. The process has been designed to ensure that the adapted guideline not only addresses specific health questions relevant to the context of use but also is suited to the needs, priorities, legislation, policies, and resources in the targeted setting. The ADAPTE process has been developed to meet the needs of different user groups, including guideline developers, health care providers, and policy makers at the local, national, and international level, as well as groups with lesser or greater resources interested in developing or implementing guidelines. The process is designed to be flexible, depending on the application. The transparent and explicit reporting of the adaptation process if followed will enhance the quality and validity of the adapted guideline.” (from [http://www.adapte.org](http://www.adapte.org)) (Appendix A)
Local researches on epidemiology, prognosis, and clinical trials (for drugs and interventions) on diabetes mellitus will be included in the review of evidence whenever available. Sources for local literature are the research database of the Philippines Society of Endocrinology and Metabolism; the list of abstracts of researches of the Institute for Studies on Diabetes Foundation, Inc (ISDFI); the Philippine Council for Health Research and Development (PCHRDP) HERDIN database; and the local journal of the Philippine College of Physicians, the Philippine Journal of Internal Medicine.

At the end of this CPG development process, gaps in research and opportunities for improvement in the way we care for diabetic patients will be identified.

The following are the steps in the development of clinical practice guidelines:

**Step 1: Research Question Generation**

The technical and administrative groups, and other members of the 4 organizations in UNITE for DM held a meeting to define the scope of the CPG. Questions were developed covering 4 general areas:

1. screening and diagnosis of diabetes;
2. follow-up care and screening for complications;
3. prevention and treatment diabetes and
4. gestational diabetes.

This volume will only cover the first section of the practice guideline, which has already been presented and approved by stakeholders.

Research questions will also tackle issues for special populations like pregnant women (gestational diabetes), children (diagnosis and screening of diabetes in children, and prevention of Type 2 DM) and the elderly (targets for control, precautions in the use of anti-diabetic agents).

**Step 2: Search and Retrieval of Guidelines**

We began the guideline development by searching the National Guideline Clearing House ([www.guideline.org](http://www.guideline.org)), MEDLINE in PUBMED ([www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)) in September 2008. From the National Guideline clearing house using the key term "diabetes"; a total of 515 guidelines were listed. From MEDLINE using the key terms “diabetes”, “diabetes mellitus” and “practice guidelines” 129 guidelines on diabetes were identified. These 2 lists were merged and unified to eliminate duplicate publications, and eliminated references that were not guidelines. Subsequently, only 152 guidelines were left.

These guidelines were then assessed using predetermined criteria as follows:

**Inclusion Criteria:**

a. Guideline must be about diabetes in the outpatient setting
b. General guidelines (entire scope of diabetes) as well as specific types and questions will also be retrieved: pre-conception care, GDM, prevention of DM, foot care, prevention of complications
   c. Published (in text or on-line) since the details of the review must be available
d. Written in English or with English translation,
e. Published in the last five years (2003 onwards) to ensure that evidence base is current. In case that the guideline has an update, then both the original guideline and the update will be retrieved and reviewed.
f. Only evidence-based guidelines will be included (guideline must include a report on systematic literature searches and explicit links between individual recommendations and their supporting evidence)
g. Only national and/or international guidelines will be included (see exclusion b)

Exclusion

a. For duplicate guidelines (e.g. update or revision of previous guidelines) reviewers will only consider the most current
b. Guidelines commissioned by or published by HMO's will not be included since the intent and the use of these guidelines is different from the intended users of this guideline
c. Guidelines for special situations which may be unique to the western population will not be included e.g. care of institutionalized patients, homeless, nursing homes, etc.
d. Guidelines written by a single author not on behalf of an organization, in order to be valid and comprehensive, a guideline ideally requires multidisciplinary input
e. Guidelines published without references – as the panel needs to know whether a thorough literature review was conducted and whether current evidence was used in the preparation of the recommendations

The inclusion and exclusion criteria were used to assess each of the guidelines. After applying these criteria only 41 guidelines were left. The 41 guidelines were again reviewed and another 5 were removed from the list because they did not fulfill the inclusion criteria (post-transplant DM guidelines; use of antipsychotics; diabetes in the long-term care setting; DKA guidelines in children; pre-gestational DM –consensus statement only) leaving 36 guidelines.

The breakdown of the 36 guidelines are as follows:

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>10</td>
</tr>
<tr>
<td>DM Foot</td>
<td>4</td>
</tr>
<tr>
<td>PRE-GDM</td>
<td>6</td>
</tr>
<tr>
<td>HPN in DM</td>
<td>4</td>
</tr>
<tr>
<td>LIPIDS IN DM</td>
<td>4</td>
</tr>
<tr>
<td>DIET</td>
<td>4</td>
</tr>
<tr>
<td>DM PREVENTATION</td>
<td>4</td>
</tr>
</tbody>
</table>

The 10 clinical practice guidelines which dealt with comprehensive aspects of diabetes management (labeled as “general” guidelines) included:

2. American Diabetes Association Standards of Medical Care 2008 (update 2009, 2010) [ADA]
3. ADA-EASD Consensus Algorithm for the Initiation and Adjustment of Therapy (eventually removed because it was not a practice guideline)
5. Canadian Diabetes Association 2008 [Canadian]
6. ESC-EASD consensus statement (eventually removed from the list because it is not a guideline)
7. International Diabetes Federation (General Guidelines) [IDF]
8. IDF Western Pacific Guidelines [IDF West Pac]
9. New Zealand Diabetes Guidelines [NZ]
10. Singapore Clinical Practice Guidelines [Sing]

Aside from these guidelines, we included another guideline that was missed when the systematic literature search was done. This is the National Institute for Health and Clinical Excellence (NICE) clinical guidelines on Type 2 diabetes which were published in 2002, and updated 2008 and 2009.

Although many of the general guidelines already include statements on diabetes in children, additional references were retrieved using the key terms, “diabetes mellitus” and “children OR child OR pediatric OR less than 18 years”. An additional 17 guidelines were retrieved; however, only 3 of them fulfill the inclusion and exclusion criteria.

Again, for gestational DM, many of the general guidelines already include recommendations regarding this problem. We were able to identify an additional 7 guidelines on gestational diabetes mellitus.

As the guideline development process progressed, updates of some of the international guidelines were completed and published. These updates were retrieved and are incorporated into the local CPG whenever applicable.

Step 3: Assess Guidelines Using the AGREE tool for critical appraisal (focusing on Rigour of Methodologic development)

The Appraisal of Guidelines Research & Evaluation (AGREE) Instrument provides a framework for assessing the quality of clinical practice guidelines. The AGREE tool is the method that is recommended by the ADAPTE for assessing the quality of the clinical practice guidelines that were retrieved. This checklist consists of 23 items that are used to assess the methods used for developing the guideline and the quality of the reporting. (Appendix C)

Each guideline was assessed by at least 2 members of the TRC using the AGREE tool. Each of the 23 items were evaluated and then an overall assessment was made. The following aspects of the guidelines were assessed using the AGREE tool:

1. Scope and Purpose – 3 items
2. Stakeholder involvement- 4 items
3. Methodology (Rigour of guideline development) - 7 items
4. Clarity and Presentation – 4 items
5. Applicability – 3 items
6. Methodology (Funding and conflicts of interest) - 2 items

After appraising the 23 items, an overall recommendation is made. This overall assessment item allows appraisers to make a judgment on the quality of the guideline as a whole, as to whether they would ‘strongly recommend,’ ‘recommend with alterations,’ ‘would not recommend,’ or are ‘unsure’ about recommending the guideline. A training resource toolkit is available on the AGREE Web site (www.agreetrust.org).

Step 4: Decide and Select Guidelines for Inclusion

At the onset of the project, the TRC members decided on the following criteria for inclusion of studies based on the outcome of the appraisal process using AGREE:

   a. Should obtain a grade of 3 in at least 4 of the 7 categories of rigour
   b. Should also obtain an overall rating of at least 60%
   c. Obtain an overall assessment of strongly recommend or recommend with alterations.

A guideline will be included if all 3 criteria are fulfilled. Two out of the 11 clinical practice guidelines were excluded:

1. The IDF-Western Pacific guideline which obtained a score of 34.52% for methodologic rigour and had a consistent overall recommendation of "would not recommend" for the 4 reviewers
2. The Singapore clinical practice guideline which obtained a score of 52.38% for rigour of methodology and with 4 categories having a score average of 2.
   Regarding the overall assessment, 2 out of 4 reviewers gave a “recommend with alterations” rating while 2/4 gave a rating of “unsure”.

The final list of guidelines that were included are the following:

2. American Diabetes Association Standards of Medical Care 2008 (update 2009, 2010) [ADA]
3. ADA-EASD Consensus Algorithm for the Initiation and Adjustment of Therapy (eventually removed because it was not a practice guideline)
5. Canadian Diabetes Association 2008 [Canadian]
Step 5: Draft Guideline Report

The research questions were then answered by obtaining the guideline statements from the 8 CPG’s which were tabulated and summarized, noting both the actual content (the statement giving the recommendation), and the levels of evidence and strengths of the recommendation. Subsequently, a draft statement for each question was made with a corresponding strength of recommendation based on the levels of evidence. The original evidence or references used as the basis for the statements were also retrieved by the TRC to ensure that the grade of the evidence given in the original guidelines were correct.

The UNITE for DM CPG used the Oxford Centre for Evidence-based Medicine Levels of Evidence (March 2009 version) for grading the levels of the evidence and the strength of recommendations (Appendix D: CEBM Levels of Evidence and Strength of Recommendation). Briefly, the levels of the evidence are graded according to Arabic numerals 1-5, considering the hierarchy of literature (e.g., for questions of therapeutic efficacy, randomized controlled trials are ranked higher than non-blinded or non-randomized trials or observational studies).

The strength of the guideline recommendation is indicated by the letters A to D as follows:

- Grade A is the strongest recommendation based on consistent level 1 studies (strong recommendation to use or not to use an intervention or test);
- Grade B strength is derived from consistent level 2 or 3 studies or extrapolations from level 1 studies (Moderately strong recommendation);
- Grade C strength is from level 4 studies or extrapolations from level 2 or 3 studies (intermediate strength of recommendation); and
- Grade D is based on level 5 evidence or troublingly inconsistent or inconclusive studies of any level (Weak recommendation).
Issue 1. Classification of Diabetes: How is diabetes classified?

Diabetes mellitus is classified into four clinical types according to etiology:

- Type 1 diabetes mellitus (formerly insulin dependent diabetes mellitus or Juvenile diabetes mellitus): results from auto-immune beta-cell destruction, leading to absolute insulin deficiency
- Type 2 diabetes mellitus (formerly non-insulin dependent diabetes mellitus or adult-onset DM): results from a progressive insulin secretory defect on the background of insulin resistance
- Gestational diabetes mellitus (GDM): diabetes first diagnosed during pregnancy
- Secondary diabetes e.g. genetic defects in beta cell function or insulin action, diabetes of the exocrine pancreas (pancreatitis, cystic fibrosis), drug- or chemical-induced diabetes (such as from the treatment of AIDS, after organ transplantation, glucocorticoids), other endocrine diseases (Cushing’s syndrome, hyperthyroidism)

References:
Standards of Medical Care in Diabetes- 2010. Diabetes Care, Volume 33, Supplement 1, January 2010

Screening and Testing for Diabetes In Asymptomatic Individuals

2. Screening

**Issue 2:** Should universal screening be done and how should screening be done?

Statement 2.1 All individuals being seen at any physician’s clinic or by any health care provider should be evaluated annually for risk factors for type 2 diabetes and prediabetes. (Table 1) (Grade D, Level 5]

Statement 2.2 Universal screening using laboratory tests is not recommended as it would identify very few individuals who are at risk. [Grade D, Consensus)

3. Testing for Diabetes in Asymptomatic Individuals

**Issue 3.1:** Who should undergo laboratory testing for diabetes/prediabetes?

Laboratory testing for diabetes and pre-diabetes is recommended for individuals with any of the risk factors for Type 2 diabetes mellitus. (Table 1) [Level 3-4, Grade B]
• Testing should be considered in all adults ≥ 40yo

• Consider earlier testing if with at least one other risk factor as follows:
  • History of IGT or IFG
  • History of GDM or delivery of a baby weighing 8 lbs or above
  • Polycystic ovary syndrome (PCOS)
  • Overweight: Body Mass Index (BMI)² of ≥ 23 kg/m² or
    Obese: BMI of ≥ 25 kg/m², or
  • Waist circumference ≥ 80 cm (females) and ≥ 90 cm (males), or
    Waist-hip ratio (WHR) of ≥ 1 for males and ≥ 0.85 for females
  • First degree relative with Type 2 diabetes
  • Sedentary lifestyle
  • Hypertension (BP ≥ 140/90 mm Hg)
  • Diagnosis or history of any vascular diseases including stroke, peripheral arterial
    occlusive disease, coronary artery disease
  • Acanthosis nigricans
  • Schizophrenia
  • Serum HDL < 35 mg/dL (0.9 mmol/L) and/or
  • Serum Triglycerides > 250 mg/dL (2.82 mmol/L)

Summary of the evidence:

All CPG’s reviewed recommend laboratory testing for confirmation in individuals at risk
for diabetes mellitus. ADA, CDA and AACE specifically enumerated the risk factors for
diabetes, with concordance among the three CPG’s with regards majority of the risk
factors. IDF did not particularly mention any risk factors.

According to the Canadian Diabetes Association 2008 recommendation, although the
relatively low prevalence of diabetes in the general population makes it unlikely that
mass screening will be cost-effective, testing for diabetes in people with risk factors for
type 2 diabetes or with diabetes-associated conditions is likely to result in more benefit
than harm and will lead to overall cost savings (1,2). Routine testing for type 2 diabetes is,
therefore, justifiable in some but not all settings (3).

The ADA 2010 recommends routine testing for all individuals age 45 years old and above.
CDA 20088 recommends routine laboratory testing for all adults age 40 and above, as
screening individuals as early as age 40 in family physicians’ offices has proved to be
useful in detecting unrecognized diabetes (4). In the Philippines, the 7th National
Nutrition and Health Survey of 2008 showed that the significant burden of diabetes
begins at age 40 years, approximating the national prevalence (5). In a 2002 study by
Baltazar et al among Luzon residents, the over-all prevalence of diabetes was 5.1% with a
sharp rise in trend noted at 40 years and above (6).

Among the risk factors enumerated, presence of IGT, IFG, PCOS and history of GDM are
correlated strongly with DM occurrence (see Table 2).
### Table 2. Risk factors for diabetes mellitus and their corresponding strengths of association.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Strength of Association</th>
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<tbody>
<tr>
<td>Previously identified IGT or IFG</td>
<td>both IGT and IGT RR 12.13 (4.27-20.00) $^7$</td>
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<tr>
<td></td>
<td>isolated IGT RR 5.52 (3.13-7.91) $^7$</td>
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<td></td>
<td>isolated IFG RR 7.54 (4.63-10.45) $^7$</td>
</tr>
<tr>
<td>GDM</td>
<td>RR 7.43 (4.79-11.51) $^8$</td>
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<td></td>
<td>OR for IGT (BMI-matched) 2.54 (1.44, 1.47) $^9$</td>
</tr>
<tr>
<td></td>
<td>OR for DM2 (BMI-matched) 4.00 (1.97, 8.10) $^9$</td>
</tr>
<tr>
<td>PCOS</td>
<td>OR for IGT (BMI-matched) 2.54 (1.44, 1.47) $^9$</td>
</tr>
<tr>
<td></td>
<td>OR for DM2 (BMI-matched) 4.00 (1.97, 8.10) $^9$</td>
</tr>
<tr>
<td>Overweight or obesity</td>
<td>OR 2.13 (1.22-3.71) $^{13}$</td>
</tr>
<tr>
<td>WC $^{10}$</td>
<td>BMI $^{10}$ $\geq$ 25 kg/m$^2$ (OR men 1.52 women 1.59) $^{11}$</td>
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<tr>
<td></td>
<td>WC $^{10}$ $\geq$ 90 cm for males and $\geq$ 80 cm for females (OR men 1.54 women 1.70) $^{11}$</td>
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<td></td>
<td>Waist-hip ratio $^{12}$ $\geq$ 1 for males and $\geq$ 1.05 for females (OR men 1.53 women 1.50) $^{11}$</td>
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<tr>
<td>First-degree relative with DM (parents or siblings)</td>
<td>OR 1.97 (1.48-3.32) $^{13}$</td>
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<tr>
<td>Sedentary lifestyle</td>
<td>RR for DM based on average hours spent watching TV per week (0-1, 2-10, 11-20, 21-40, $&gt;40$): RR 1.00, 1.66, 1.64, 2.16, and 2.87 $^{14}$</td>
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<tr>
<td>Conditions assoc with insulin resistance (acanthosis nigricans)</td>
<td>Increased blood pressure, per 1 SD:</td>
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<tr>
<td>HPN</td>
<td>Systolic: RR 1.56 (1.31-1.85) $^{13}$</td>
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<tr>
<td></td>
<td>Diastolic: RR 1.52 (1.27-1.83) $^{13}$</td>
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<tr>
<td>CVD</td>
<td>DM as a CVD risk factor (age- and sex-adjusted): HR 2.5 (1.9 to 3.2) $^{16}$</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>OR 2.07 (1.03 to 4.15) $^{17}$</td>
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<tr>
<td></td>
<td>Increased triglycerides, per 1 SD: OR 1.70 (1.62-1.78) $^{13}$</td>
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<td></td>
<td>Increased apolipoprotein A-I, per 1 SD: OR 0.76 (0.62–0.92) $^{13}$</td>
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</tbody>
</table>

### Issue 3.2 In what setting/s should testing for diabetes be done?

- Testing should ideally be carried out within the health care setting (clinics, hospitals, local health centers) because of the need for follow-up and discussion of abnormal results by qualified health care professionals (nurse, diabetes educator, physician). [Level 3, Grade B]
• Testing at any setting should be supervised by a qualified health care professional. [Level 5, Grade D]

Summary of evidence

ADA 2010 states that “… community screening outside a health care setting is not recommended because of 3 reasons: People with positive tests may not seek, or have access to, appropriate follow-up testing and care; there may be failure to ensure appropriate repeat testing for individuals who test negative; and community screening may also be poorly targeted, i.e., it may fail to reach the groups most at risk and inappropriately test those at low risk (the worried well) or even those already diagnosed”. The CDA and AACE did not specifically mention as to what setting it should be done. IDF stated that “Each health service should decide whether to have a programme to detect people with undiagnosed diabetes … based on prevalence of undiagnosed diabetes and on resources available to conduct the detection programme and treat those who are detected.”

No randomized controlled trials (RCT’s) regarding screening have been conducted. Population-based and selective screening programs in community settings (outreach programs, health fairs, or shopping malls) have uniformly demonstrated low yield of <1% and poor follow-up (18).

Issue 3.3 If initial test/s are negative for diabetes, when should repeat testing be done?

• Repeat testing should ideally be done annually. (Level 5, Grade D)

Summary of evidence

The ADA 2010, CDA 2008 and IDF 2005 are of the opinion to do repeat testing at least at 3-year intervals since there is little likelihood that an individual will develop significant complications of diabetes within 3 years of a negative result. The ADA 2010 recommends repeat testing annually for those with IFG and/or IGT. The CDA 2008 recommends more frequent testing in those with multiple risk factors. AACE 2007 recommends annual testing for all those with risk factors.

We recommend repeat testing annually for Filipinos with risk factors owing to the significant prevalence and burden of diabetes in our country. In a local study among newly-diagnosed diabetics in Manila, about 20% already had peripheral neuropathy, 42% had proteinuria, and 2% had diabetic retinopathy (19).
4. Screening and Diagnosis of Diabetes in Children

Issue 4.1 Should screening be done for Type 1 diabetes mellitus?

Screening for Type 1 DM is not recommended at the moment for the following reasons:

a. The disease is of low prevalence although an increasing trend is observed. Exact prevalence/incidence has yet to be established. Screening using serologic markers are not available readily and expensive making screening not cost-effective.

b. Since clinical trials for interventions to prevent or delay Type 1 diabetes have not been proven effective, screening for T1 diabetes is NOT recommended.

Summary of the Evidence:

In the Philippines there are no nationwide prevalence or incidence studies on Type 1 diabetes mellitus. A survey done in a municipality in Bulacan showed only 7 cases of Type 1 DM among children aged 0-14 year old during a 10 year period from 1989 to 1998. (1) In the U.S., the rate of new cases among youth was 19 per 100,000 each year for type 1 diabetes and 5.3 per 100,000 for type 2 diabetes. (US 2002-2003).


Issue 4.2 Should screening for Type 2 DM be done in children?

Recommendation: Screening for pre-diabetes and Type 2 DM is recommended among asymptomatic children commencing at age 10 years or at onset of puberty, if puberty occurs at a younger age (ADA) with the following risk factors: (Grade C, Level 4)

- Overweight (BMI > 85\textsuperscript{th} percentile for age and sex, weight –for-height > 85\textsuperscript{th} percentile, or weight > 120\% of ideal for height) OR

- Obese: BMI >95\textsuperscript{th} centile or \geq +2SD (WHO)

- Plus any (two) of the following risk factors
  - Family history (especially parents and grandparents) of Type 2 DM
  - Signs of insulin resistance (Acanthosis nigricans, hypertension, dyslipidemia, PCOS, or small for gestational age birth weight)
  - Maternal history of diabetes or GDM during the child’s gestation
5. Diagnosis of Diabetes.

ISSUE: Diagnosis of Diabetes. What tests and criteria should be used to diagnose diabetes?

Statement 5.1 The diagnosis of Diabetes Mellitus can be made based on the following criteria*:  [Level 2, Grade B]

1. Plasma glucose $\geq$ 126 mg/dL (7.0 mmol/L) after an overnight fast. Fasting is defined as no caloric intake for at least 8 hours up to a maximum of 14 hours.

   OR

2. Two-hour plasma glucose $\geq$ 200 mg/dl (11.1 mmol/l) during an Oral Glucose Tolerance Test.
   The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water after an overnight fast of between 8 and 14 hours.

   OR

3. A random plasma glucose $\geq$ 200 mg/dl (11.1 mmol/l) in a patient with classic symptoms of hyperglycemia (weight loss, polyuria, polyphagia, polydipsia) or with signs and symptoms of hyperglycaemic crisis.

*Among ASYMPTOMATIC individuals with positive results, any of the three tests should be REPEATED within two weeks for confirmation.  (Level 4, Grade C)

Issue 5.2 Who should undergo the OGTT as the preferred initial test for screening for diabetes?

Statement 5.2 A 75-gram OGTT is preferred as the first test in the following individuals who have: (Level 3, Grade B)

1. A previous FBS showing Impaired Fasting Glucose  (100 to 125 mg/dL or 5.6 to 6.9 mmol/L)
2. Previous diagnosis of Cardiovascular Disease (Coronary Artery Disease, Stroke, Peripheral Arteriovascular Disease) or who are at high risk for cardiovascular disease.
3. A diagnosis of Metabolic Syndrome

Issue 5.3 Can other laboratory Tests be Used for the Diagnosis of Diabetes?

Recommendation 5.3: At the present time, we cannot recommend the routine use of the following tests for the diagnosis of diabetes: (Level 3, Grade C)

- HBA1c
- Capillary Blood Glucose
• Fructosamine

However, if a result is available upon consultation due to prior testing, it should be interpreted with caution and should be confirmed by any of the three tests that are considered standard: Fasting Plasma Glucose, Oral Glucose Tolerance Test or Random Plasma Glucose. (Level 2, Grade B)

Recommendation 5.2.2: We do not recommend the following tests for the diagnosis of diabetes: (Level 3, Grade B)

• Urine glucose
• Plasma Insulin

ISSUE 5.4: Diagnosis of Pre-Diabetes. What criteria can be used to diagnose Pre-diabetes?

Statement 5.4 The criteria for Pre-Diabetes is:

1. Impaired Fasting Glucose defined as FBS of 5.6 mmol/L (100 mg/dL) upto 125 mg/dL or 6.9 mmol/L [Level 2, Grade B]

2. Impaired Glucose Tolerance defined as Random/casual blood glucose ≥ 7.7 to 11.0 mmol/L (140-199 mg/dL) OR 2-hr blood sugar in the 75-gm OGTT ≥ 7.7 (140 mg/dL) upto 11.0 mmol/L (199 mg/dL). [Level 2, Grade B]

ISSUE 5.5 What is the criteria for normal blood sugar?

Statement 5.5> Normal blood is sugar is defined as:

1) An FBS < 5.6 mmol/L (100 mg/dL), or
2) Random/casual blood glucose < 7.7 (140 mg/dL), or
3) 2-hr blood sugar in the 75- gm OGTT < 7.7 (140 mg/dL) [Level 2, Grade B]

Summary of the evidence:
The ADA developed the diagnostic criteria for diabetes based on the occurrence of retinopathy as a microvascular event among subjects not previously diagnosed with diabetes. All the other guidelines are similar to the ADA recommendation. Several Asian studies have also tested these criteria using venous blood samples among their population but using the 2nd-hour OGTT level as standard instead of microvascular outcomes. The ADA lowered the threshold for diagnosis of impaired fasting plasma glucose in 2003 in order to approximate the prevalence of IFG similar to IGT. Other groups such as the World Health Organization and the International Diabetes Federation have not adapted this because their reviews of evidence using cardiovascular outcomes mainly among American Caucasian and Europeans showed significant correlation only with IFG level above 6.1 mmol/L or 110 mg/dL. The New Zealand CPG resolved this in their setting by saying that the cut-off for IFG that will indicate the need for an OGTT should be based on ethnicity and race- using the higher cut-off 6.1 mmol/L (110 mg/dL) for European descendants, and 5.6 mmol/L (100 mg/dL) for others. If the endpoint is earlier detection and intervention of pre-diabetes before it
progresses to DM, several studies among the Japanese and Thai population noted lower threshold with better ROC at the 5.6 to 6.9 mmol/L (100-125 mg/dL). 47, 54, 55 If the endpoint is the detection of IGT for earlier cardiovascular risk assessment, then we rely on the review of the DECODA group in 12 Asian countries including the Philippines as previously discussed. 20, 25

Statement 5.6: If initial test/s are negative for diabetes, repeat testing should ideally be done annually. (Level 5, Grade D)

In some countries, 20% to 50% of cases already have complications at the time of diagnosis. 10, 20 The international guidelines recommend repeat testing from one to three years depending on co-existence of other risk factors. In the Philippines, one study cohort showed that 42% of newly diagnosed DM type 2 patients already have proteinuria, 20% already have peripheral neuropathy, and 12% already have clinically significant retinopathy. 53 We recommend that patients at risk should therefore be tested more frequently, at least annually if initial tests are negative.

6. Screening and Diagnosis of Diabetes in Pregnant Women

6.1 Should universal screening for diabetes be done among pregnant women?

Recommendation: All pregnant women should be screened for gestational diabetes (Level 2, Grade B).

The American Diabetes Association (ADA) recommends screening for all except very low risk women, i.e. those belonging to an ethnic group with a low prevalence of diabetes. Filipino women will not fall under the low risk category as data from the ASGODIP (AFES Study Group on Diabetes in Pregnancy) has shown a prevalence of 14% in 1203 pregnancies. 2 Furthermore in a UK cohort, relative risk was increased sevenfold for women of South East Asian descent 3 (RR 7.6 [95%CI 4.1,14.1]). Hence, universal screening should apply in our population. The DIPSi 4 guideline also recommends universal screening for Indian women, because of the high prevalence of gestational diabetes in their population.

The National GDM Technical Working Party of New Zealand recommends that all pregnant women be offered screening for GDM. 5 The NICE guideline 6 recommendation is similar to that of the ADA where testing is offered to women with any risk factor for gestational diabetes.

2 Litonjua AD et al. AFES Study Group on Diabetes in Pregnancy: Preliminary Data on Prevalence. PJIM 1996; 34:67-68
Screening is undertaken to detect disease and to provide early care that morbidity and mortality may be avoided. Gestational diabetes has been associated with increased risk of perinatal morbidity: macrosomia, shoulder dystocia, birth injuries and hypoglycemia. Subsequently these infants have a higher risk of abnormal glucose tolerance and obesity.

Screening for gestational diabetes and treatment to reduce maternal glucose levels has been shown to be beneficial in the Australasian Carbohydrate Intolerance Study (ACHOIS)\(^7\). In the intervention group, the rate of serious perinatal complications was significantly decreased as compared to routine care (RR 0.33 [95%CI 0.14-0.75], \(p=0.01\)). Treatment of even mild gestational diabetes\(^8\) (defined as fasting glucose below 95 mg/dL on screening OGTT) has also been shown to reduce the risks of fetal overgrowth (RR 0.41 [97%CI 0.26,0.66], \(p<0.001\)) and shoulder dystocia (RR 0.37 [97%CI 0.14-0.97], \(p=0.02\)).

Gestational diabetes has also been associated with preeclampsia/gestational hypertension and an increased rate of cesarean sections. Women with a history of gestational diabetes are also at an increased risk to develop type 2 diabetes. The trial on mild gestational diabetes\(^8\) also showed decreased risk for cesarean delivery (RR 0.79 [97%CI 0.64, 0.99], \(p=0.02\)) and hypertensive disorders (RR 0.63 [97%CI 0.42,0.96], \(p=0.01\)) for the women in the intervention group.

Screening for GDM identifies a group of young women at risk of developing type 2 diabetes allowing early and targeted intervention. A study looking at risk factors for development of type 2 diabetes in a Filipino-American population found gestational diabetes to be an independent risk factor (OR 21.65 [95% CI 6.73,69.67]). In a cohort of Filipino women\(^9\) followed up 2 years after a GDM pregnancy, nearly half had abnormal glucose tolerance (16.9%with type 2 diabetes and 32% with impaired glucose tolerance). A meta-analysis\(^11\) involving 675,455 women and 10,559 type 2 diabetic events showed that women with gestational diabetes had an increased risk of developing type 2 diabetes (RR 7.43, 95% CI 4.79-11.51). Once identified, women with GDM benefit from intensive lifestyle and metformin therapy which reduce the incidence of diabetes by approximately 50%.\(^12\)

6.2 For pregnant women, when should screening be done?

**Recommendations:**

a. All pregnant women should be evaluated at the first prenatal visit for risk factors for diabetes (Level 4, Grade C).

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\(^10\) Isip Tan IT & Solimen D. Abnormal glucose tolerance and metabolic syndrome in Filipino women with previous gestational diabetes. Unpublished.


The ADA\textsuperscript{1} recommends that a woman’s risk for gestational diabetes be assessed at the first prenatal visit, as those at high risk are offered testing at this visit. The New Zealand guideline also recommends risk stratification where “women at high risk of undiagnosed type 2 diabetes should be screened at booking.”\textsuperscript{5} The NICE guideline\textsuperscript{6} recommends that “women who have had gestational diabetes in a previous pregnancy should be offered early self-monitoring of blood glucose or an OGTT at 16-18 weeks.”

Table 2 shows risk factors for diabetes among pregnant women. The odds ratios and positive predictive values from the literature are provided. Note that the ADA\textsuperscript{1} defines macrosomia as birth weight more than 4000 grams while the ASGODIP\textsuperscript{18} sets the cutoff at 8 pounds.

### Table 2. Risk Factors for Diabetes Among Pregnant Women

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior history of GDM\textsuperscript{1}</td>
<td>23.6 (95%CI 11.6, 48.0)\textsuperscript{13}</td>
</tr>
<tr>
<td>Glucosuria\textsuperscript{1}</td>
<td>9.04 (95%CI 2.6, 63.7)\textsuperscript{14}</td>
</tr>
<tr>
<td></td>
<td>PPV 50%\textsuperscript{15}</td>
</tr>
<tr>
<td>Family history of diabetes\textsuperscript{1,6}</td>
<td>7.1 (95%CI 5.6, 8.9)\textsuperscript{16}</td>
</tr>
<tr>
<td>First-degree relative with type 2 diabetes</td>
<td>PPV 6.7%\textsuperscript{14}</td>
</tr>
<tr>
<td>First-degree relative with type 1 diabetes</td>
<td>PPV 15%\textsuperscript{14}</td>
</tr>
<tr>
<td>Prior macrosomic baby\textsuperscript{6}</td>
<td>5.59 (95%CI 2.58, 11.7)\textsuperscript{13}</td>
</tr>
<tr>
<td>Age (\geq 25) years old\textsuperscript{1}</td>
<td>1.9 (95%CI 1.3, 2.7)\textsuperscript{16}</td>
</tr>
<tr>
<td></td>
<td>3.37 (95%CI 1.45, 7.85)\textsuperscript{13}</td>
</tr>
<tr>
<td>Diagnosis of polycystic ovary syndrome\textsuperscript{1}</td>
<td>2.89 (95%CI 1.68, 4.98)\textsuperscript{17}</td>
</tr>
<tr>
<td>Overweight or obese before pregnancy</td>
<td></td>
</tr>
<tr>
<td>(\text{BMI} \geq 27) kg/m\textsuperscript{2}</td>
<td>2.3 (95%CI 1.6, 3.3)\textsuperscript{16}</td>
</tr>
<tr>
<td>(\text{BMI} \geq 30) kg/m\textsuperscript{2}</td>
<td>2.65 (95%CI 1.36, 5.14)\textsuperscript{13}</td>
</tr>
<tr>
<td>Macrosomia in current pregnancy\textsuperscript{18}</td>
<td>PPV 40%\textsuperscript{15}</td>
</tr>
</tbody>
</table>

\textsuperscript{13} Ostlund I, Hanson U. Occurrence of gestational diabetes mellitus and the value of different screening indicators for the oral glucose tolerance test. Acta Obstetricia et Gynecologica Scandinavica 2003;82(2):105-8.
\textsuperscript{18} Litonjua AD et al. ASEAN Federation of Endocrine Societies (AFES) Study Group on Diabetes in Pregnancy. PJIM 1996;34:37-42.
Polyhydramnios in current pregnancy\textsuperscript{18} PPV 40\%\textsuperscript{15}

Intake of drugs affecting carbohydrate metabolism\textsuperscript{18}

b. High-risk women should be screened at the soonest possible time (Level 3, Grade B).

A woman with any of the above risk factors is considered high risk. The ADA\textsuperscript{1} defined the criteria for very high risk as follows: severe obesity, prior history of GDM or delivery of LGA infant, presence of glucosuria, diagnosis of PCOS and strong family history of type 2 diabetes. The NICE\textsuperscript{6} guideline considers women with previous history of GDM as high risk.

Early screening is feasible as according to the DIPSI\textsuperscript{4} guideline as “the fetal beta cell recognizes and responds to maternal glycemic level as early as 16th week of gestation.” However, the US Preventive Services Task Force (USPSTF)\textsuperscript{19} identified no randomized controlled trials on screening and treatment of gestational diabetes before 24 weeks of gestation. Nonetheless, one prospective cohort study showed that women with early-onset GDM were likely to be hypertensive (18.6\% vs 5.9\%, \textit{p}=0.006) and to have need of insulin therapy (33.8\% vs 7.1\%, \textit{p}=0.0000) as compared to women who developed GDM later.\textsuperscript{20}

c. Routine testing for gestational diabetes is recommended at 24 to 28 weeks age of gestation for women with no risk factors (Level 3, Grade B).

Women without risk factors should still be screened. In an observational study\textsuperscript{21}, more than one-third of women with gestational diabetes who had no historical risk factors would have been missed if only those with risk factors were tested.

The US Preventive Services Task Force (USPSTF)\textsuperscript{19} found no evidence that screening after the 24th week leads to reduction in morbidity and mortality. However, the ACHOIS\textsuperscript{2} provides evidence that treatment of GDM after the 24th week of gestation does reduce complications. The ADA\textsuperscript{1} recommends screening “greater than low-risk women” for gestational diabetes at 24 to 28 weeks gestation. The NICE\textsuperscript{6} guideline states that women with any risk factor other than previous gestational diabetes, should be offered an OGTT at 24-28 weeks.

Testing for gestational diabetes should still be carried out in women at risk, even beyond 24 to 28 weeks age of gestation (Level 3, Grade C).

ASGODIP data\(^2\) has shown that as much as 3.6% of low-risk and 40.4% of high-risk women are diagnosed to have gestational diabetes when testing is done beyond the 26th week. In the ASGODIP cohort from the Cardinal Santos Medical Center\(^{22}\), more than 75% of their GDM cases were diagnosed from the 26th to 38th weeks of gestation, with more of these women delivering macrosomic infants. In the ASGODIP cohort from Veterans Memorial Medical Center\(^{23}\), half of the GDM cases were diagnosed between the 31st to 40th weeks of gestation.

6.3 Which tests should be used to screen pregnant women for gestational diabetes?

Recommendation: An oral glucose tolerance test (OGTT), preferably the 75-g OGTT, should be used to screen for gestational diabetes (Level 3, Grade B).

Both the NICE\(^6\) and DIPSI\(^4\) recommend the use of the 75-g OGTT. The ADA\(^1\) recommends either a one-step procedure with the OGTT (75-g or 100-g) or a two-step procedure using a 50-g glucose challenge test (GCT) followed by an OGTT. The ASGODIP recommends a GCT for low-risk women at the first prenatal visit and a 75-g OGTT for high-risk women. The International Association of Diabetes and Pregnancy Study Groups (IADPSG)\(^24\) consensus panel recommends either a fasting plasma glucose, HbA1c or random plasma glucose at the initial visit. If test results are not diagnostic, the panel recommends doing a 75-g OGTT at 24 to 28 weeks of gestation.

The NICE\(^6\) no longer recommends using the GCT. It reviewed the use of the 50-g GCT in 4 studies involving 2437 women. The qualitative strength of the GCT as a screening tool is only fair with a calculated positive likelihood ratio of 4.34 (95%CI 1.53-12.26) and a negative likelihood ratio of 0.42 (95% CI 0.33-0.55). A local study\(^25\) showed that the 50-g GCT had a positive predictive value of 44.6%. The 50-g GCT is also only moderately reproducible,\(^26\) more likely to be positive if conducted in the afternoon,\(^27\) and the results are significantly affected by the time since the last meal.\(^28\)

\(^{22}\) Sy RAG et al. Viewpoints on Gestational Diabetes: Report from ASGODIP Participating Hospital: Cardinal Santos Medical Center. PJIM 1996;34:45-48
\(^{25}\) Carlos-Raboca J et al. Maternal fetal outcome among Asians diagnosed by 2-h 75-g oral glucose tolerance test. JAFES 2002;20:19-24
\(^{27}\) McElduff A & Hitchman R. Screening for gestational diabetes: the time of day is important. MJA 2002; 176(3):136
A one-step approach using the OGTT is recommended as 10%\textsuperscript{15} to 23%\textsuperscript{29} of women fail to return for an OGTT after an initial GCT. Locally, in a study\textsuperscript{30} which used a two-step approach to screen for GDM, 36% of the women failed to return for the diagnostic OGTT after a positive GCT result. In the ASGODIP data, two hospitals reported that 17.8%\textsuperscript{31} and 48%\textsuperscript{32} of women with positive GCT results failed to return for OGTT.

The 75-g OGTT appears to have a slight advantage in two small trials that directly compared outcomes of women diagnosed with gestational diabetes using the 75-g vs the 100-g OGTT. Pettitt\textsuperscript{33} et al compared the utility of the 75-g vs the 100-g OGTT in predicting macrosomia and cesarean section in Pima Indians. There were 5 discrepant results and in each case, the 75-g OGTT result was abnormal while the 100-g was not. In a study conducted in Thailand\textsuperscript{34}, it was demonstrated that of 14 women who delivered macrosomic infants, 6 women had abnormal 75-g OGTT test results while only 3 had abnormal 100-g OGTT results.

The 100-g OGTT is more cumbersome, with blood samples taken at 4 time points, a duration of 3 hours and with a high glucose load that is often unpalatable to pregnant women. Furthermore, the 75-g OGTT has been the international standard for the diagnosis of diabetes in non-pregnant adults and it use in pregnancy would allow direct comparison with the postpartum OGTT.

### 6.4 What criteria will be used to interpret the 75-g OGTT?

**Recommendation:** The criteria put forth by the International Association of Diabetes & Pregnancy Study Groups (IADPSG) will be used to interpret the 75-g OGTT(Level 3, Grade B).

There are several ways by which the 75-g OGTT has been used to diagnose gestational diabetes (Table 3). The IADPSG\textsuperscript{24} recommendations have the advantage of having been based on an analysis of the HAPO study\textsuperscript{35} results which enrolled an “ethnically diverse cohort of ~25,000 women in the third trimester of gestation.” Blood glucose levels at which odds ratios for specific outcomes reached predefined values were used to determine the recommended thresholds.


\textsuperscript{30} Isip-Tan IT; Celzo F. & Abrahah MA. Comparison of the 75-g vs 100-g OGTT in diagnosing gestational diabetes in Filipino women. Unpublished.

\textsuperscript{31} De Asis TP et al. Incidence of gestational diabetes mellitus at Veterans Memorial Medical Center PJIM 1996; 34:63-66

\textsuperscript{32} Chua-Ho C et al. Screening for gestational diabetes mellitus: Report from ASGODIP Participating Hospital FEU-NRMFH  PJIM 1996; 34:43-44


Table 3. Interpreting the 75-g OGTT results

<table>
<thead>
<tr>
<th>75-g OGTT</th>
<th>Threshold(s) for diagnosing gestational diabetes (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IADPSG*</td>
</tr>
<tr>
<td>FBS</td>
<td>92</td>
</tr>
<tr>
<td>1-hour</td>
<td>180</td>
</tr>
<tr>
<td>2-hour</td>
<td>153</td>
</tr>
<tr>
<td>3-hour</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Any one value meeting threshold is considered gestational diabetes.

** Two values must meet thresholds to be considered gestational diabetes.

6.5 Can we use other tests to screen pregnant women for diabetes?

Statement 6.7 The following tests should not be used for the diagnosis of diabetes in pregnancy: Capillary Blood Glucose, FBS, RBS, HbA1c, Fructosamine, Urine Glucose. However, if patients already have FBS or RBS at the time of consultation, thresholds for DM will be the same as non-pregnant individuals. Those with glucosuria, elevated CBG or HbA1c should undergo OGTT.

6.6 How should we follow up women who develop diabetes during pregnancy?

Statement 6.6.1 Postpartum recommendation. A 75-gram oral glucose tolerance test should be done 6–12 weeks after delivery in the GDM women who do not have diabetes immediately postpartum. (Grade D, Level 4-5)

Statement 6.6.2 An FBS or RBS is not recommended for the long term follow-up and reclassification of women with previous GDM. (Grade , Level ). However, if patients already have FBS or RBS at the time of consultation, thresholds for DM will be the same as non-pregnant individuals. (Grade D, Level 4-5)
Summary of the Evidence:

It is very important to do laboratory testing or retesting after delivery to identify glucose intolerance among women with GDM. After GDM, 35–60% of women develop type 2 diabetes within 10 years. Identification of abnormalities in glucose metabolism allows the initiation of strategies for primary prevention of diabetes.

The guidelines reviewed all recommend that retesting after GDM should be done within 6-12 weeks after delivery. The 5th International GDM workshop, the ADA 2009 and the Diabetes in Pregnancy study group of India all recommend that retesting be done using the 75-gm OGTT. The NICE however, recommends that an FBS should be done within 6 weeks after delivery.

Several studies have shown that measuring only the fasting plasma glucose level postpartum is not sufficiently sensitive to identify all women who have IGT or type 2 diabetes. Post partum data indicates that only 34% of the women with IGT or type 2 diabetes had impaired fasting glucose and that 44% of those with type 2 diabetes had fasting levels <100 mg/day (<5.5 mmol/l).

Status of glucose metabolism should be assessed periodically with an 75-gram oral glucose tolerance test. Fasting plasma glucose alone has low sensitivity of to detect IGT and diabetes. Large population studies have not established an optimum testing frequency or evaluated modified testing strategies based on risk factors. Without such data, it is recommended that after initial postpartum testing, an oral glucose tolerance test should be repeated in 1 year and, at a minimum, every 3 years thereafter.

GDM identifies women at high risk for diabetes representing a unique opportunity and a responsibility to educate the patient and health care system for primary diabetes prevention. Lifestyle change and use of metformin or thiazolidinediones (rosiglitazone and pioglitazone) can prevent or delay the progression of IGT to type 2 diabetes after GDM.

Recommendation 6.6.3

Women with previous GDM should also undergo screening for other cardiovascular risk factors and components of metabolic syndrome. [Grade D, Level 4-5]

Summary of the Evidence:

Many women with prior GDM exhibit characteristics of the metabolic syndrome (e.g., glucose intolerance, insulin resistance, central obesity, elevated triglycerides, and low HDL cholesterol) and inflammatory markers (e.g., high-sensitivity C-reactive protein
and interleukin-6). They may manifest short-term endothelial dysfunction during late pregnancy that is manifested as transient hypertension. Long-term endothelial dysfunction may be associated later in life with increased risk of chronic hypertension and CVD.

Insulin resistance may be implicated in transient hypertension and has been associated with inflammatory responses. Chronic insulin resistance may produce chronic inflammation, adversely affecting vascular reactivity and atherogenesis, and set up future hypertension and ischemic vascular disease in these women. Standard screening guidelines for CVD risk factor assessment should be followed at the times that glucose metabolism is evaluated.

Reference:
REFERENCES

Clinical Practice Guidelines that were Included in the UNITE for DM CPG: (General Guidelines)

1. American Association for Clinical Endocrinology (AACE)


2. American Diabetes Association Guidelines


   Standards of Medical Care in Diabetes- 2010. Diabetes Care, Volume 33, Supplement 1, January 2010


   Amir Qaseem, MD, PhD, MHA; Sandeep Vijan, MD, MS; Vincenza Snow, MD; J. Thomas Cross, MD, MPH; Kevin B. Weiss, MD, MPH; and Douglas K. Owens, MD, MS, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Glycemic Control and Type 2 Diabetes Mellitus: The Optimal Hemoglobin A1c Targets. A Guidance Statement from the American College of Physicians. Ann Intern Med. 2007;147:417-422.

4. Canadian Diabetes Association 2008 [Canadian]


5. International Diabetes Federation (General Guidelines) [IDF]


6. New Zealand Diabetes Guidelines [NZ]

   Management of Type 2 Diabetes, published December 2003 by the New Zealand Ministry of Health.


**Excluded were the following:**

1. ADA-EASD Consensus Algorithm for the Initiation and Adjustment of Therapy – excluded because it was not a practice guideline
2. IDF Western Pacific Guidelines [IDF West Pac]

**Guidelines Included for Gestational DM:**

1. American Diabetes Association Guideline
   Gestational Diabetes Mellitus. Diabetes Care, Volume 27, Supplement 1, January 2004


Preconception Care of Women With Diabetes. Diabetes Care, Volume 27, Supplement 1, January 2004

2. Australasian Guideline

3. 5th International Workshop Conference

4. New Zealand Guidelines on gestational Diabetes Mellitus
5. NICE Antenatal and NICE GDM Guidelines


6. ACOG Guideline


7. US preventive Services Task Force Recommendation Statement


8. IDC


Not Included:

1. Indian Clinical Practice Guideline on GDM

APPENDIX A. The ADAPTE PROCESS

- Set Up Phase
  - PREPARE FOR ADAPTE PROCESS
  - DEFINE HEALTH QUESTIONS
  - SEARCH AND SCREEN GUIDELINES
  - ASSESS GUIDELINES
  - DECIDE AND SELECT
  - DRAFT GUIDELINE REPORT

- Finalization Phase
  - EXTERNAL REVIEW
  - PLAN FOR FUTURE REVIEW AND UPDATE
  - PRODUCE FINAL GUIDELINE

- Associated Modules
  - Preparation
  - Scope and Purpose
  - Search and Screen
  - Assessment
  - Decision and Selection
  - Customization
  - External Review
  - Aftercare planning
  - Final Production
### Appendix B. ADAPTE TOOL 8

#### Tool 8: Table for Summarizing Guideline Content

<table>
<thead>
<tr>
<th>Health question #1</th>
<th>Health question #2</th>
<th>Health question #3</th>
<th>Health question #4</th>
<th>Health question #5</th>
<th>Health question #6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Insert definition here</td>
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<tr>
<td>Intervention(s)</td>
<td>Insert definition here</td>
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<td>Professionals/patients</td>
<td>Insert definition here</td>
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<tr>
<td>Outcome</td>
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<tr>
<td>Healthcare setting</td>
<td>Insert definition here</td>
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</tbody>
</table>

**Actual content of guidelines (CPG)**
(indicate with ☐ if included in guideline)

<table>
<thead>
<tr>
<th>CPG #1</th>
<th>CPG #2</th>
<th>CPG #3</th>
<th>CPG #4</th>
</tr>
</thead>
<tbody>
<tr>
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*Draft. Do not photocopy.*
Appendix C: The AGREE instrument

Appendix D. CEBM Levels of Evidence and Strength of Recommendation

Table: Steps in finding evidence (“Levels”) for different types of question

<table>
<thead>
<tr>
<th>Question</th>
<th>Step 1 (Level 1)</th>
<th>Step 2 (Level 2)</th>
<th>Step 3 (Level 3)</th>
<th>Step 4 (Level 4)</th>
<th>Step 5 (Level 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How common is it? (E.g., Pre-test probabilities)</td>
<td>Most relevant local and current random sample survey (or censuses)</td>
<td>Systematic review of current surveys</td>
<td>Systematic review of local non-random sample</td>
<td>Systematic review of case-series</td>
<td>Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms</td>
</tr>
<tr>
<td>Is this test accurate? (Diagnostic accuracy)</td>
<td>Systematic review of cross-sectional studies</td>
<td>Systematic review of cross-sectional studies With consistently applied reference standard and blinding</td>
<td>Systematic review of non-consecutive studies, or studies without consistently applied reference standards.</td>
<td>Systematic review of case-control study, or cross-sectional study with non-independent reference standard</td>
<td>Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms</td>
</tr>
<tr>
<td>What will happen if we do nothing? (Prognosis)</td>
<td>Systematic review of inception cohort studies</td>
<td>Inception cohort studies</td>
<td>Cohort or control arm of randomized trial</td>
<td>Systematic review of case-series</td>
<td>Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms</td>
</tr>
<tr>
<td>Does this treatment help? (Treatment Benefits)</td>
<td>Systematic review of randomized trials or n=1 trial</td>
<td>Randomized trial or (exceptionally) observational studies with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up study</td>
<td>Systematic review of case-control studies, historically controlled studies</td>
<td>Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms</td>
</tr>
<tr>
<td>What are the COMMON harms? (Treatment Harms)</td>
<td>Systematic review of randomized trials or n=1 trial</td>
<td>Systematic review of nested case-control or dramatic effects</td>
<td>Non-randomized controlled cohort/follow-up study</td>
<td>Case-control studies, historically controlled studies</td>
<td>Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms</td>
</tr>
<tr>
<td>What are the RARE harms? (Treatment Harms)</td>
<td>Systematic review of case-control studies, or studies revealing dramatic effects</td>
<td>Randomized trial or (exceptionally) observational study with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up study</td>
<td>Case-control studies, historically controlled studies</td>
<td>Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms</td>
</tr>
<tr>
<td>Is early detection worthwhile? (Screening)</td>
<td>Systematic review of randomized trials</td>
<td>Randomized trial</td>
<td>Non-randomized controlled cohort/follow-up study</td>
<td>Case-control studies, historically controlled studies</td>
<td>Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms</td>
</tr>
</tbody>
</table>

* Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of Inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.

NOTE: Please take note of the asterisk below the table. Following the spirit of the GRADE System, we can downgrade or upgrade the level of evidence given the considerations stated:

Grades of Recommendation
A consistent level 1 studies
B consistent level 2 or 3 studies or extrapolations from level 1 studies
C level 4 studies or extrapolations from level 2 or 3 studies
D level 5 evidence or troublingly inconsistent or inconclusive studies of any level

Oxford Centre for Evidence-based Medicine Levels of Evidence (March 2009)
(For definitions of terms used see glossary at http://www.cebm.net/?o=1116)
*Extrapolations* are where data is used in a situation that has potentially clinically important differences than the original study situation.
Appendix E

APPENDIX: Procedure for 75-gram Oral Glucose Tolerance Test:

Guidelines
The oral glucose tolerance test (OGTT) is recommended by the WHO for diagnosis of T2DM.

Preparation and cautions
The OGTT should be performed in the morning, after at least three days of unrestricted carbohydrate intake (more than 150 g of carbohydrate daily). The test should not be done during an acute illness, as the results may not reflect the patient’s glucose metabolism when healthy. A full test dose of glucose for adults should not be given to a person weighing less than 43 kg, due to the fact excessive amount of glucose may produce a false positive result.

The OGTT procedure
The test should be implemented after an overnight fast of 10 to 16 hours (water is allowed). [The American Diabetes Association states 8 to 14 hours as used for criteria in the United States NHANES protocol] Smoking or physical activity is not permitted during the test. Usually the OGTT is scheduled to begin the morning (7–9 am) as glucose tolerance exhibits a diurnal rhythm with a significant decrease in the afternoon. At baseline, the blood sample for glucose determination is taken. The patient is then given a glucose solution to drink. The standard dose is 75 g of glucose in 250–300 ml of water. It should be ingested within 5 minutes. For children, the test load should be 1.75 g per kg of body weight, up to a maximum of 75 g of glucose. The next blood sample is collected at 120 min after the glucose load.

Plasma glucose measurement in blood samples
The processing of the samples after collection is important to ensure accurate measurement of plasma glucose. This requires rapid separation of the plasma after collection. Laboratory measurements rely upon the use of separated plasma and only immediate separation can prevent the lowering of the glucose in the sample. Only if the plasma separation is completely impossible to be done immediately upon collection, glycolysis inhibitors, e.g. sodium fluoride (6mg per ml of the whole blood) can be used. Rapid cooling of the sample may also be helpful in reducing the loss of glucose if the plasma cannot be immediately separated. In this case, the sample should be placed immediately after collection into ice water but the plasma separation should occur within 30 minutes. The plasma should be frozen until the glucose concentration can be measured.

International Federation of Clinical Chemistry (IFCC) recommended that all glucose measuring devices report the results in plasma values. The reason for this recommendation is the fact that plasma glucose values are approximately 11% higher than the values of whole blood glucose measured in the same sample. Moreover, WHO recommendations is that venous plasma glucose should be the standard method for measuring and reporting. However, it should be noted if one converts from venous to capillary plasma glucose the conversion is different in the case of fasting or post-load glucose values. Fasting values for venous and capillary plasma glucose are identical, while the conversion is necessary only for post-load glucose.

Reference: Paulweber B et al. IMAGE-Guideline for Diabetes Prevention Horm Metab Res 2010; 42 (Suppl. 1): S3–S36