A Summary of the Philippines UNITE for Diabetes Clinical Practice Guidelines for the Diagnosis and Management of Diabetes (Part I: Screening and Diagnosis of DM)

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Introduction

Clinical practice guidelines are systematically developed statements intended to assist practitioners and patients in making decisions about appropriate health care.[1] They are user-friendly statements that bring together the best external evidence (research) and clinical experience for rational decision-making about specific health problems. These recommendations are intended to improve the quality of medical care delivered by doctors or groups of doctors, leading to better outcomes such as disease prevention, prevention of complications, and an overall improvement in the quality and quantity of life of patients. For guidelines to be able to achieve these objectives they must ideally be evidence-based; adapted to the local setting; incorporate patients' values in decision-making; and in a developing country like the Philippines, consider issues of equity.

The Philippine Practice Guidelines on the Diagnosis and Management of Diabetes Mellitus is a pilot project of the UNITE FOR DM organization, a coalition of organizations caring for individuals with diabetes mellitus. This coalition is made up of the following organizations: The Diabetes Philippines (formerly The Philippine Diabetes Association); the Institute for Studies on Diabetes Foundation, Inc (ISDFI); the Philippine Society for Endocrinology and Metabolism (PSEM); and the Philippine Center for Diabetes Education Foundation (PCDEF). The objective of this project is 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.

This guideline is a response to the call of the International Diabetes Federation (IDF) for concerted efforts worldwide to develop systematic initiatives to halt the progression of diabetes and its complications. The global projection for diabetes is an increase in total number from 246 million diabetics in 2007 to 380 million or 55 percent increase in prevalence by the year 2025.[2] In the Philippines, the national prevalence was predicted to be 7.9% 08.

For the last 10 years, the prevalence of diabetes mellitus in the Philippines according to the National Nutrition and Health Survey is as follows:[3]

	1998	2003	2008
FBS > 125	3.9	3.4	4.8
DM based on history	---	2.6	4.0
FBS or OGTT or History	---	4.6	7.1

Adding on those who have pre-diabetes (impaired fasting glucose or impaired glucose tolerance), this figure is likely to exceed 10percent. In simple terms, one out of every 10 Filipinos could potentially have diabetes mellitus or prediabetes.

Summary of the Methodology for Guideline Development

The main focus of the Philippine guidelines is the outpatient management of adult patients with Type 2 diabetes mellitus. Type 1 diabetes was also briefly discussed in relation to screening and diagnosis, but management will not be addressed as this group of patients are typically under subspecialty care. The management of diabetes in children will also not be included. 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) follow-up care and screening for complications; (3) prevention and treatment of diabetes and (4) gestational diabetes. This synopsis will only cover the first section of the practice guideline, which has already been presented and approved by stakeholders.

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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.

This CPG used two main methods for guideline development: (1) guideline adaptation using the ADAPTE process, 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 the use of herbal medications or nutraceuticals for the treatment of diabetes mellitus.

The rationale for using 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.[4] The full methodology of the ADAPTE process is available at the website www.adapte.org.

The UNITE for DM CPG used the Oxford Centre for Evidence-based Medicine Levels of Evidence (March 2009 version) for grading the levels of evidence and strength of recommendations.[5] Briefly, the levels of 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 recommendation is indicated by the letters A to D, with A being the strongest recommendation based on consistent level 1 studies; Grade B strength is derived from consistent level 2 or 3 studies or extrapolations from level 1 studies; Grade C strength is from level 4 studies or extrapolations from level 2 or 3 studies; and Grade D is based on level 5 evidence or troublingly inconsistent or inconclusive studies of any level.

Summary of the Recommendations

The following are the clinical practice guideline recommendations for the screening and diagnosis of diabetes in the Philippines:

Issue 1. Classification of Diabetes: How is diabetes classified?

Diabetes mellitus is classified into 4 clinical types according to etiology:

- Type 1 diabetes mellitus (formerly insulin dependent diabetes mellitus or juvenile diabetes mellitus): results from autoimmune 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 in 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)

Screening and Testing for Diabetes in Asymptomatic Individuals

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 pre-diabetes. (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]

Issue 3.1: Who should undergo laboratory testing for diabetes/pre-diabetes?

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]

Table 1. Demographic and Clinical Risk Factors for Type 2 DM

- Testing should be considered in all adults $\geq$ 40 years old
- 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 $\geq$ 23 kg/m^2 or Obese: BMI of $\geq$ 25 kg/m^2, or
  - Waist circumference $\geq$ 80 cm (females) and $\geq$ 90 cm (males), or Waist-hip ratio (WHR) of $\geq$ 1 for males and $\geq$ 0.85 for females
  - First degree relative with Type 2 diabetes
  - Sedentary lifestyle
  - Hypertension (BP $\geq$ 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)

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

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

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]*

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. The exact prevalence/incidence has yet to be established. Screening using serologic markers is not readily available and expensive, so that screening is not cost-effective.

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

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

Screening for prediabetes 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 > 85th percentile for age and sex, weight –for-height > 85th percentile, or weight > 120percent of ideal for height) OR
- Obese: BMI >95th centile or $\geq$ +2SD (WHO criteria)
- Plus any (two) of the following risk factors
  - o Family history (especially parents and grandparents) of Type 2 DM
  - o Signs of insulin resistance (Acanthosis nigricans, hypertension, dyslipidemia, PCOS, or small for gestational age birth weight)
  - o Maternal history of diabetes or GDM during the child's gestation

Diagnosis of Diabetes

Issue 5.1 What tests and criteria should be used to diagnose diabetes?

The diagnosis of diabetes mellitus can be made based on any of 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.
2. Two-hour plasma glucose $\geq$ 200 mg/dl (11.1 mmol/L) during an Oral Glucose Tolerance Test (OGTT). 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.
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 hyperglycemic 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 OGTT as the preferred initial test for screening for diabetes?

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?

Issue 5.3.1. At present, we cannot recommend the routine use of the following tests for the diagnosis of diabetes: HBA1c, capillary blood glucose and fructosamine. [Level 3, Grade C] 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].

The HbA1c is currently not yet recommended as a diagnostic test for diabetes mellitus in the Philippines due to unavailability in many areas of the country and the lack of standardization of the test in our setting.

Recommendation 5.3.2: The use of routine urinalysis (for urine glucose) and plasma insulin are NOT recommended for the diagnosis of diabetes. [Level 3, Grade B]

Issue 5.4: What criteria can be used to diagnose prediabetes?

The criteria for prediabetes are:

1. *Impaired Fasting Glucose defined as FBS of 100 mg/dl (5.6 mmol/L) up to 125 mg/dl (6.9 mmol/L) [Level 2, Grade B]*
2. *Impaired Glucose Tolerance defined as a 2-hr blood sugar in the 75-gm OGTT $\geq$ 140 mg/dl (7.7mmol/L) up to 199 mg/dl (11.0 mmol/L) [Level 2, Grade B]*

Issue 5.5 What are the criteria for normal blood sugar?

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

Issue 5.6: If initial test(s) are negative for diabetes, when should the tests be repeated?

Repeat testing should ideally be done annually. [Level 5, Grade D]

Gestational Diabetes: Screening and Diagnosis of Diabetes in Pregnant Women

Issue 6.1 For pregnant women, HOW should screening be done?

*All pregnant women should be evaluated at the **first prenatal visit** for risk factors for diabetes [Level 5, Grade E]. These risk factors include: age ≥ 25 years old; overweight or obese before pregnancy; history of abnormal glucose metabolism; history of poor obstetric outcome (abnormal glucose tolerance, macrosomia [>8 lbs], congenital malformations, recurrent abortions, unexplained intrauterine death); family history of diabetes (first-degree relative); intake of drugs affecting carbohydrate metabolism, i.e. steroids; and glucosuria.*

Risk evaluation is done to determine the urgency for doing screening laboratory tests; those with any of the risk factors are considered to be high risk and must undergo laboratory testing as soon as possible.

Issue 6.2 Timing of Laboratory Testing

Routine testing for gestational diabetes mellitus (GDM) is recommended at 24-28 weeks age of gestation [Grade A]. High-risk women should be screened at the soonest possible time [Grade B].

Issue 6.3 Which tests should be used to screen pregnant women for GDM?

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

Issue 6.4 What criteria should be used to interpret the 75-g OGTT?

The criteria put forth by the International Association of Diabetes & Pregnancy Study Group (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 recommendations have the advantage of having been based on an analysis of the HAPO study[6] 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.

Table 2. Interpreting the 75-g OGTT results

75-g OGTT	Threshold(s) for diagnosing gestational diabetes (mg/dl)		
	IADPSG*	ADA**	ASGODIP & DIPSI
FBS	92	95	NA
1-hour	180	180	NA
2-hour	153	155	140
3-hour	NA	140	NA

* *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?

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. [Grade D, Level 4-5]

Issue 6.6 FOLLOW-UP. How should we follow up women who develop diabetes during pregnancy?

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

6.6.2 An FBS or RBS is not recommended for the long term follow-up and reclassification of women with previous GDM. 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]

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

Recommendations

Clinical practice guidelines are tools to improve the quality of patient care. In order for clinical practice guidelines to achieve its objectives, it must be well disseminated to the end-users. Its acceptability, compliance and eventual impact on health outcomes must be assessed. It must also reflect current best evidence. Hence, a system for updating practice guidelines to incorporate new findings from researches must be developed and incorporated into the methodology of the guideline.

Finally, physicians must realize that guidelines are meant to enlighten the way they practice and are not intended to replace sound clinical judgment. Decisions about the care of patients must be individualized in the context of unique or specific clinical circumstances that may be encountered in daily practice.

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The full document is available at the PSEM website http://www.endo-society.org.ph and the Philippine Diabetes Association website http://www.diabetesphil.org.

References
1. Field MJ, Lohr KN (editors). Guidelines for clinical practice: from development to use (publication of the Committee on Clinical Practice Guidelines, Institute of Medicine). Washington (DC): National Academy Press, 1992.
2. Diabetes Atlas 3rd Edition. http://www.eatlas.idf.org. Accessed 25 January 2007.
3. The 7th National Nutritional and Health Survey 2008 (preliminary data). [unpublished]
4. The ADAPTE Resource Toolkit for Guideline Adaptation (Version 1.0). http://www.adapte.org. Accessed October 21, 2008.
5. The Oxford Centre for Evidence-based Medicine Levels of Evidence (March 2009). http://www.cebm.net. Accessed July 09, 2010.
6. Bellamy L. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009; 373(9677):1773-9.