# Combining fasting plasma glucose and glycosylated hemoglobin improved the accuracy for detecting patients with diabetes

Anand SS, Razak F, Vuksan V, et al. **Diagnostic strategies to detect glucose intolerance in a multiethnic population.** Diabetes Care. 2003;26:290-6.

## QUESTION

In a multiethnic cohort randomly assembled in Canada, is a combination of fasting plasma glucose (FPG) and glycosylated hemoglobin ($HbA_{1c}$) more accurate than FPG alone for diagnosing impaired glucose tolerance (IGT) and diabetes?

## DESIGN

Optimal diagnostic criteria using FPG, 2-hour postglucose–load plasma glucose, and $HbA_{1c}$ to identify patients with IGT and diabetes were determined (using the 1998 WHO diagnostic criteria as the "gold standard") and compared. Cut points were determined from receiver-operating characteristic curves.

## SETTING

3 cities in Canada.

## PARTICIPANTS

936 Canadians of South Asian, Chinese, and European descent.

## DESCRIPTION OF TESTS AND DIAGNOSTIC STANDARD

FPG and 2-hour post–glucose-load (i.e., after ingestion of 75 g of oral glucose) plasma glucose were measured using enzymatic methods with a hexokinase reference. $HbA_{1c}$ was analyzed using high-performance liquid chromatography. The 1998 WHO diagnostic criteria were used as the "gold standard" to classify the participants into 3 categories: normal (FPG < 7.0 mmol/L and a 2-h glucose < 7.8 mmol/L), IGT (FPG < 7.0 mmol/L and a 2-h glucose 7.8 to 11.0 mmol/L), or diabetic (FPG ≥ 7.0 mmol/L or a 2-hour glucose ≥ 11.1 mmol/L). The American Diabetes Association criteria were also applied, and participants were classified into the 3 categories: normal (FPG < 6.1 mmol/L), impaired fasting glucose (FPG 6.1 to 6.9 mmol/L), or diabetic (FPG ≥ 7.0 mmol/L).

## MAIN OUTCOME MEASURES

Sensitivity and specificity, and positive and negative likelihood ratios.

## MAIN RESULTS

According to WHO criteria, 6.4% and 15.2% of participants had diabetes and IGT, respectively. FPG and $HbA_{1c}$ optimal cut points, with the corresponding sensitivity and specificity and positive and negative likelihood ratios for diagnosing diabetes, are in the Table; combining FPG and $HbA_{1c}$ improved the specificity and positive likelihood ratio (Table). The American Diabetes Association criteria had a sensitivity of 48% (95% CI 36 to 61) for diagnosing diabetes. FPG or $HbA_{1c}$ alone or in combination did not yield satisfactory diagnostic properties for diagnosing IGT.

## CONCLUSION

In a multiethnic cohort randomly assembled in Canada, a combination of fasting plasma glucose and glycosylated hemoglobin had greater specificity and positive likelihood ratio than fasting plasma glucose alone for diagnosing diabetes.

*Sources of funding: Not stated.*

*For correspondence: Dr. S. S. Anand, McMaster University, Hamilton, Ontario, Canada. E-mail anands@mcmaster.ca.*

**Diagnostic properties of fasting plasma glucose (FPG) and glycosylated hemoglobin ($HbA_{1c}$) for detecting patients with diabetes**

| Test (cut point) | Sensitivity (95% CI) | Specificity (CI) | +LR (CI) | -LR (CI) |
|---|---|---|---|---|
| FPG (≥ 5.7 mmol/L) | 83% (74 to 93) | 88% (86 to 90) | 7 (6 to 8) | 0.2 (0.1 to 0.3) |
| $HbA_{1c}$ (≥ 5.9%) | 75% (64 to 86) | 79% (76 to 82) | 4 (3 to 4) | 0.3 (0.2 to 0.5) |
| FPG (≥ 5.7 mmol/L) and $HbA_{1c}$ (≥ 5.9%) | 72% (60 to 83) | 95% (94 to 96) | 14 (10 to 19) | 0.3 (0.2 to 0.4) |

*Diagnostic terms defined in Glossary; LRs and CI calculated from data in article.

## COMMENTARY

In the study by Anand and colleagues, the overall sensitivity of fasting glucose (American Diabetes Association recommendations) for diagnosing diabetes was low (48%). A dual cut point of FPG > 5.7 mmol/L and $HbA_{1c}$ > 5.9% had a sensitivity of 72% and a specificity of 95%, and in South Asian people 85% and 91%, respectively.

In clinical practice, we prefer to know which patients with normal or impaired FPG have diabetes according to the oral glucose tolerance test (OGTT). Patients with cardiovascular risk factors and increased risk for mortality cluster in this group (1, 2). If they have abnormal glucose metabolism, different follow-up and management may be required. In patients with FPG < 7.0 mmol/L, can we limit further work-up for diabetes to those at high risk for diabetes, or with cardiovascular risk factors or impaired FPG? Because of the burden of screening a large population we have no other choice, although in certain populations the FPG levels might miss a small percentage of patients with diabetes. If we decide to continue beyond determination of FPG levels, do we offer an OGTT, determination of $HbA_{1c}$, or close follow-up with repeated determinations of FPG? OGTT may offer better sensitivity and specificity for development of macrovascular and microvascular complications of diabetes. Besides of the high cost, $HbA_{1c}$ measurement requires additional testing to evaluate its performance.

Although the question about screening does not have clear-cut answers, some conclusions may be drawn: First, persons with normal or impaired FPG should be stratified according to their risk for diabetes. Factors to consider include ethnic origin, obesity, and family history. A formal index should be developed and validated for that purpose. Second, persons at high risk for diabetes and cardiovascular morbidity should be closely followed even if FPG is normal. Third, the decision to use OGTT, a combination of FPG values and $HbA_{1c}$, or close follow-up depends on the local population, as well as the cost of the tests. Fourth, serious and continuous effort should be made in these patients to modify risk factors and maintain healthy lifestyles.

*Leonard Leibovici, MD*
*Rabin Medical Center*
*Petah Tiqva, Israel*

***References***

1. Consequences of the new diagnostic criteria for diabetes in older men and women. DECODE Study (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe). Diabetes Care. 1999;22:1667-71.
2. **Harris TJ, Cook DG, Wicks PD, Cappuccio FP.** Impact of the new American Diabetes Association and World Health Organisation diagnostic criteria for diabetes on subjects from three ethnic groups living in the UK. Nutr Metab Cardiovasc Dis. 2000;10:305-9.