WILL YOU USE HBA1C TO SCREEN & MONITOR DIABETES?

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Diabetes is clinically well defined by glycation of proteins

1. True
2. false

So far, diabetes has been defined as “a clinical condition of elevated glucose concentration in blood”

High A1C represents high glycation of proteins in the body, which is a substantially different biochemical abnormality, although it is certainly secondary to high blood glucose

Moreover, high A1C is only observed subsequently to an increase in blood glucose, but there are few data on how long the delay is.

Regardless of the length of this delay (weeks, months), diagnosis of diabetes using A1C would occur later than with blood glucose assessment.

In many cases, such a delay might have negative clinical consequences.

Diabetes is clinically defined by high blood glucose and not by glycation of proteins

On screening for newly diagnosed diabetics by HbA1c and traditional fasting &PPG:

1. HbA1c will detect more cases
2. HbA1c will detect less cases
3. No great difference between them

?

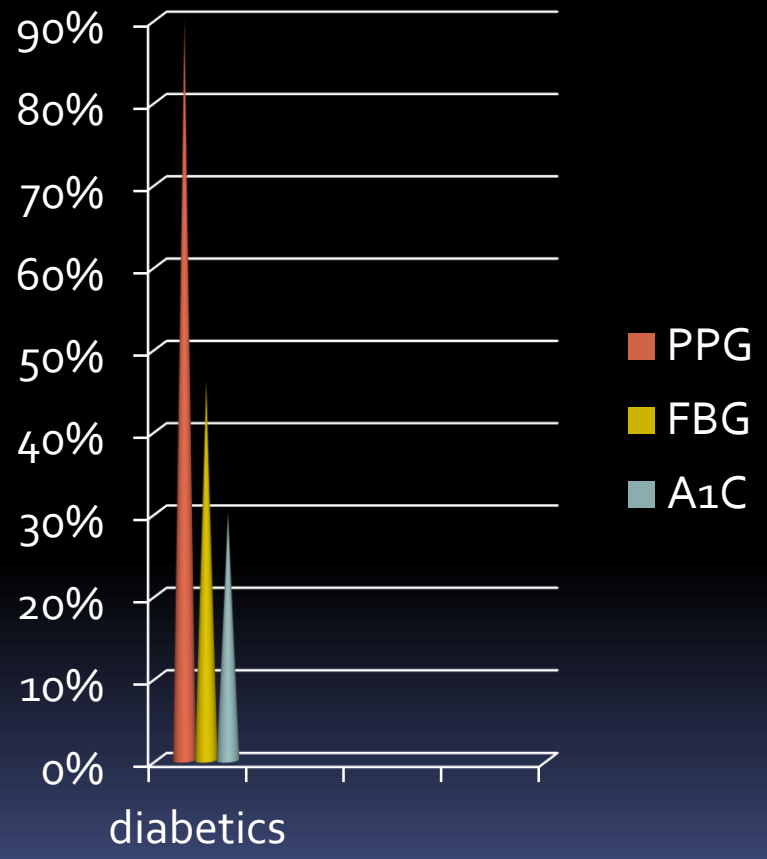
Epidemiological studies carried out in the general population showed that:

A1C and plasma glucose (FPG and/or 2-h OGTT) identify partially different groups of diabetic subjects!!!

Prevalence of diabetes and high risk for diabetes using A1C criteria in the U.S population in 1988–2006. Diabetes Care 2010

These findings are based on several studies, including

the 2003–2006 U.S. National Health and Nutrition Examination Survey (NHANES)



Analysis of U.S. NHANES data revealed that:

Overall, only 25% of individuals with a 'positive' OGTT had an HbA1c >6.5%

45% of individuals who exceeded both the fasting and 2hr glucose criteria were not diagnosed with diabetes using HbA1c.

suggesting that A1C might reduce the number of people diagnosed as having diabetes from that using current glycemic criteria

Prevalence of diabetes and high risk for diabetes using hemoglobin A1c criteria in the U.S. population in 1988–2006. *Diabete Care 2010; **33: 562–568.***

A1C has poor sensitivity in diabetes diagnosis and would change the epidemiology of diabetes

A1C is a marker of all pathophysiological abnormalities in diabetes

1. True
2. False

The exposure to elevated blood glucose levels in people with diabetes involves two components:

- chronically sustained hyperglycemia → reflected in HbA1c
- the acute daily fluctuations of glucose from peaks to nadirs reflecting intermittent acute glucose toxicity → HbA1c reveals little about individual daily glucose fluctuations.

OGTT and 2-h pp levels reflect the pathophysiology behind diabetes better than other glycemic parameter.

They provide information on what occurs in the postprandial state, when glucose levels are at the highest levels during the day and when the health of the pancreatic b-cell is essential.

Diabetes Metab Res Rev 2010;26:280-286

A1C is a poor indicator of what occurs in the postprandial state. A1C captures only chronic hyperglycemia, but it will miss acute hyperglycemia which reflects an impaired b-cell function .

Diabetes Metab Res Rev 2010;26:280-286

A growing body of evidence indicates that recurrent and/or periodic blood glucose fluctuations with large amplitude levels beyond near-normoglycemic limits play a much more serious role in diabetic vascular damage than chronically sustained hyperglycemia.

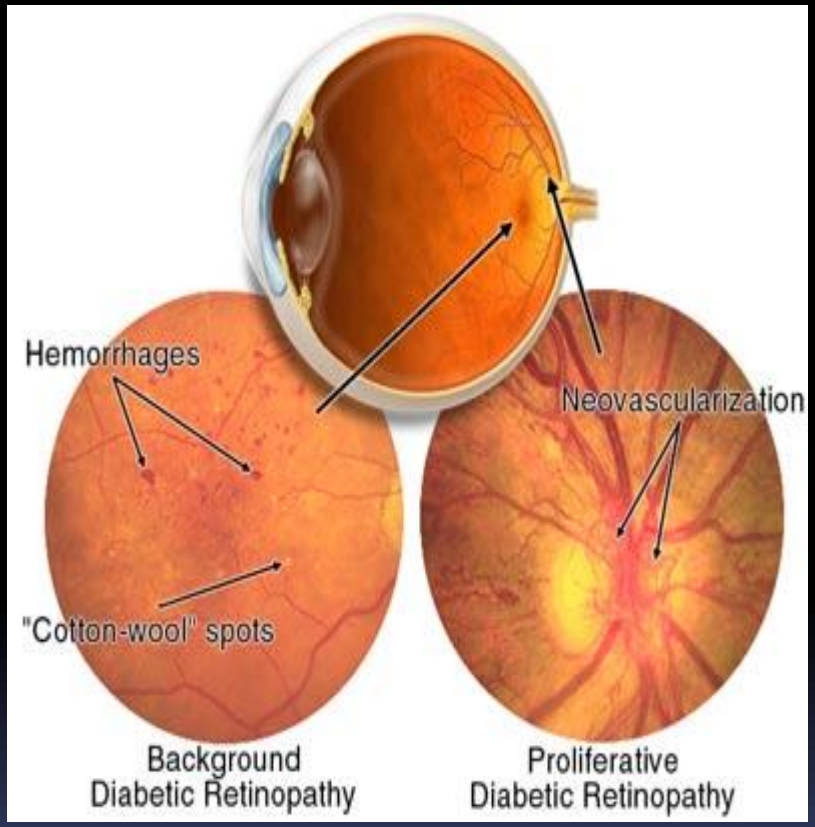
Diabetes. 2008;57(5):1349-54.

A1C is a poor marker of important pathophysiological abnormalities featuring diabetes

HbA 1c and prediction of diabetic complications:

1. More sensitive in prediction of microvascular complications
2. More sensitive in prediction of macrovascular complications
3. Poor predictor of all complications
4. Sensitive predictor of all complications

≥6.5%


Hemorrhages
"Cotton-wool" spots
Neovascularization
Background
Diabetic Retinopathy
Proliferative
Diabetic Retinopathy

Because high glucose is toxic and causes many types of tissue damage, any indicator of hyperglycemia is predictive of diabetes complications

FPG → poor marker of mortality and future CVD events

2-h PG and A1C → better predictors when analyzed jointly

only 2-h PG remains a statistically significant predictor of mortality and CVD

Two prospective studies found that elevated 2-hr glucose predicted mortality independent of fasting glucose and HbA1c. J Clin Epidemiol 2004;57:590–596

One of the main issues is that people with IGT have ~40% increased mortality compared with normoglycemic people.

HbA1c is acknowledged to be poor at identifying patients with impaired fasting glucose (IFG) or IGT

the ADA raised the prospect of making HbA1c between 5.7% and 6.4% identifying patients at high risk of developing diabetes and its complications.

↑HB A1c towards the diabetic cutoff will→

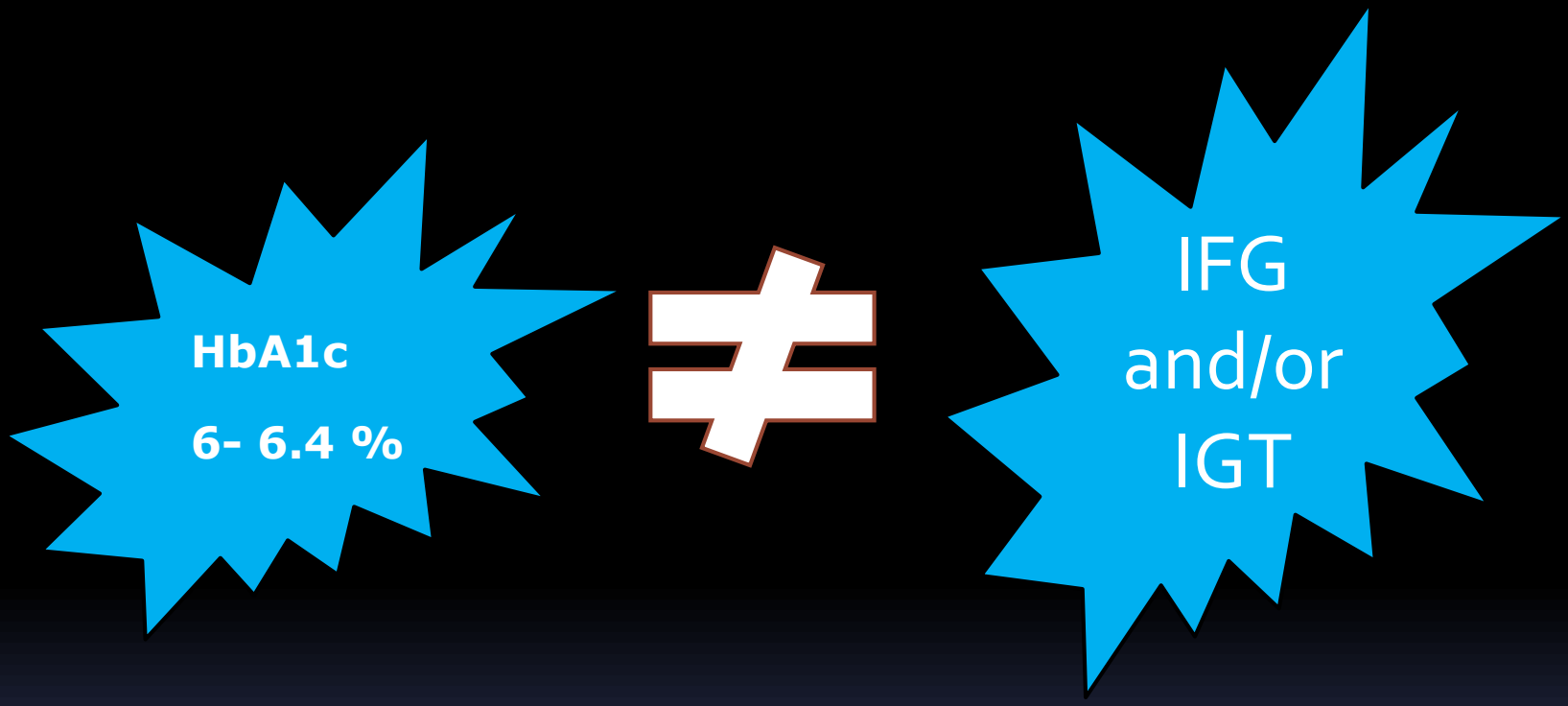
↑The risk of diabetes

(i.e 6-6.4% have higher risk than 5.7-6%)

1. True
2. False

Individuals found to be in the Expert Committee 'high risk' state (HbA1c of 6.0–6.4%) belong to a group which is about 10 times smaller in size than identified as having either IFG or IGT

International expert committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care. 2009;32:1327-1334.*


HbA1c
6- 6.4 %
≠
IFG
and/or
IGT

In addition, lifestyle intervention has been shown to prevent the progression from IGT to diabetes and also reduce their mortality risk to the level observed among normoglycemic people.

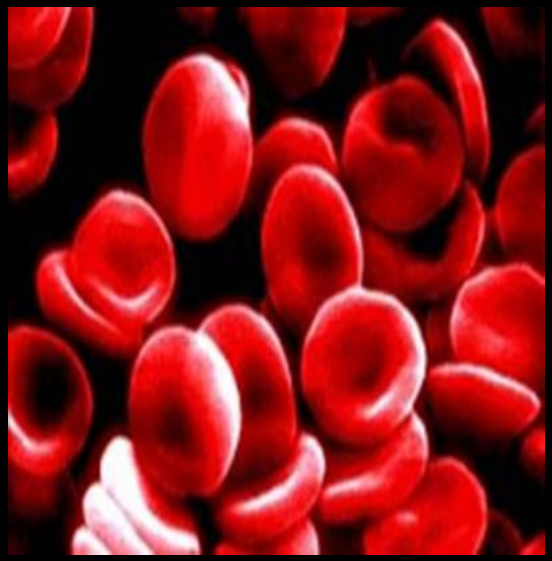
Such prevention trial evidence does not exist for A1C.

2-h Glucose level and IGT are stronger predictors of CVD than A1C

From the factors unlikely to cause misleading A1C results:

1. S. TG
2. S. Bilirubin
3. S. Iron
4. All of the above
5. Non of the above

Abnormal hemoglobin traits are not uncommon in many regions of the world, and they significantly interfere with A1C assay even without any indication that a problem might exist



ABCD position statement on haemoglobin A1c for the diagnosis of diabetes *Pract Diab Int 2010*

- Around 1/3 of HbA1c instruments in routine use there will give a clinically significant error in the presence of these haemoglobins

- Guidance already exists on alerting clinicians to diabetes patients of African, Mediterranean or South-east Asian heritage who may have problems when using HbA1c for monitoring.

Also, there are several clinical conditions that influence erythrocyte turnover e.g.

malaria, iron difficiency anemia, uremia, pregnancy, smoking, hypertriglyceridemia, hyperbilirubinemia, chronic use of salicylates and/or vitamin C

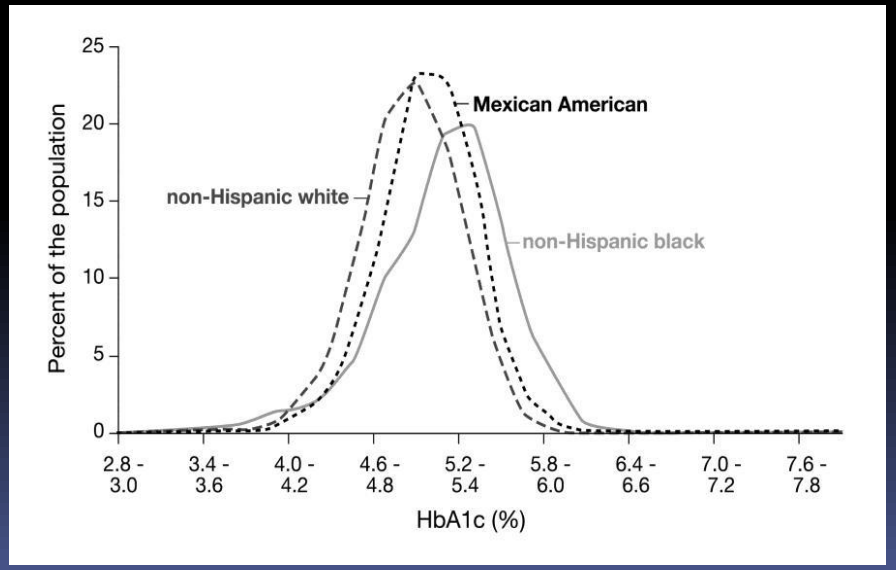
misleading A1C results

Hemoglobin A1c for the diagnosis of diabetes. Practical considerations. *Pol Arch Med Wewn. 2010;120:37-41.*

Ageing and ethnicity:

It has been identified that older non-diabetic subjects appear to have higher HbA1c values than younger individuals,

Differences in the HbA1c have also been consistently found between individuals from different races



Diagnostic strategies to detect glucose intolerance in a multiethnic population. Diabetes Care 2003;26:290–296

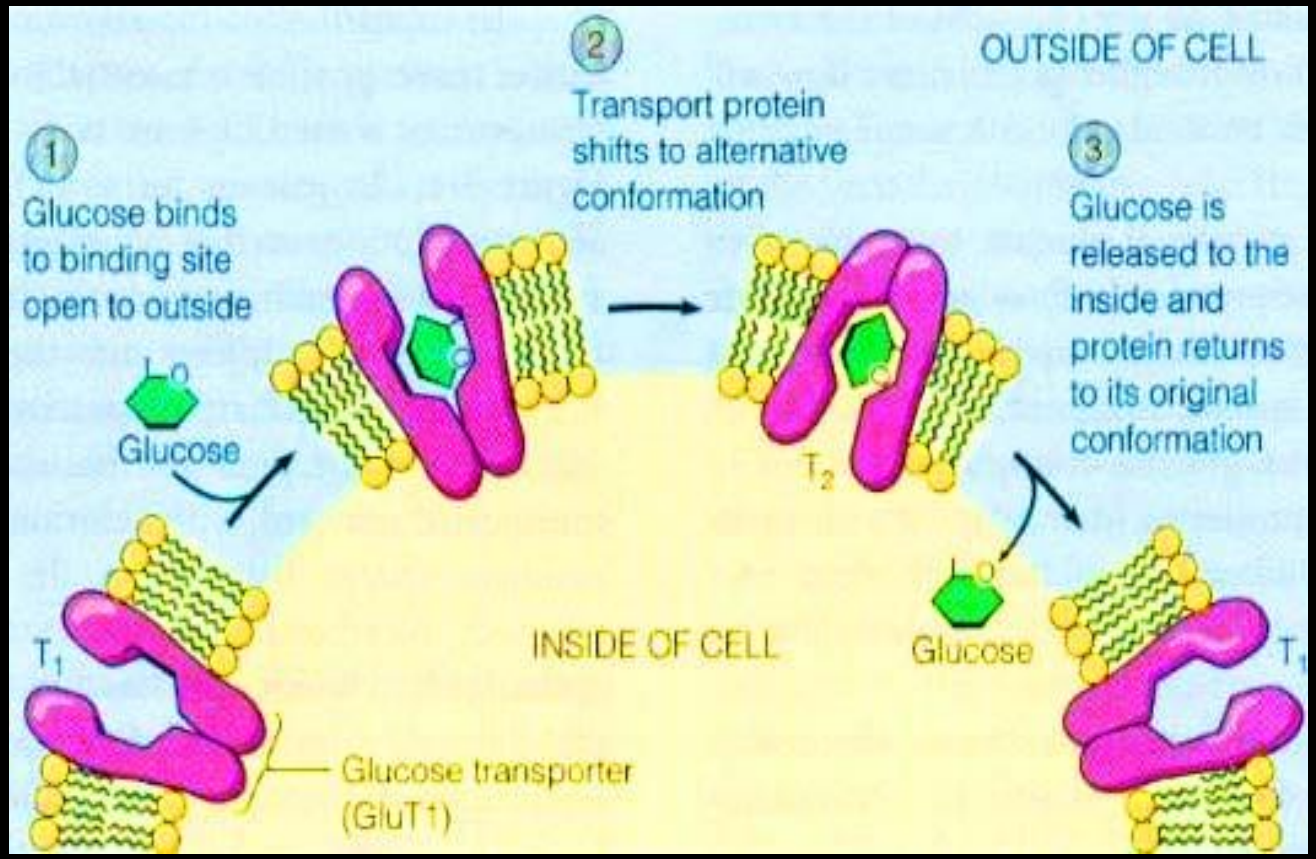
- it is possible that some patient would be misdiagnosed by a single HbA1c cutoff.
- In turn, this could necessitate the use of age-related and race-related diagnostic thresholds for HbA1c.

Glycaemia-independent ethnic differences in HbA1c in subjects with impaired glucose tolerance. *Diabet Med 2009;* ***26: 1068–1069.***

A1C assay is unreliable and can be misleading in many subjects

Diabetics with identical average plasma glucose will sure have nearly the same HbA1c levels:

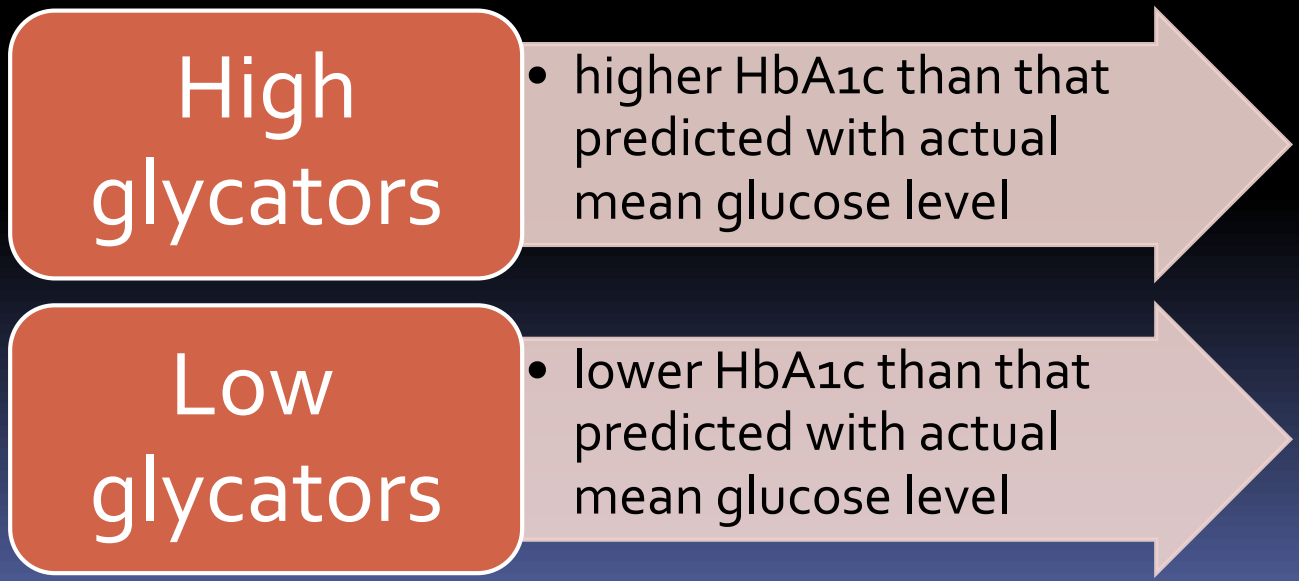
1. True
2. False



However, people with identical blood glucose concentrations may have different glucose concentrations in their red blood cells

Evidence for interindividual heterogeneity in the glucose gradient across the human red blood cell membrane and its relationship to hemoglobin glycation. Diabetes. 2008;57(9):2445-52.

A disadvantage of the measurement of HbA1c for screening and diagnosis of diabetes is an incomplete correlation between HbA1c and average plasma glucose



Hemoglobin A1c in diabetes diagnosis: Time for caution. *Endocr Pract. 2010;16:5-6*

The use of HbA1c levels as absolute "goals" for diagnosis and treatment is "inappropriate if not coupled with glucose measurements."

Hemoglobin A1c in diabetes diagnosis: Time for caution. *Endocr Pract. 2010;16:5-6.*

- Although IFCC standardisation of HbA1c measurement is a step forward in improving comparability between laboratories, but there is still a long way to a global standardization of the A1Cassays  there are still clinically significant differences between laboratories using different instruments different manufacturers

A1C assay is more expensive than glucose assay, and it will thus remain so despite the speculative claim that the cost of A1C assay will become less expensive when used more extensively

In addition, many individuals at high risk of diabetes would need other laboratory tests that require fasting (e.g., lipid profile, hepatic profile, etc.), and therefore adding a glucose determination to the panel is not really a major issue.

less developed societies in which diabetes diagnosis is made with plasma glucose:

developed societies in which diabetes diagnosis is made with A1C

such a division should be avoided. It would add to the inequities in health and health care.

Change
Def of DM

Pathophysiol. abnormalities
featuring diabetes

Low sensitivity in diabetes diagnosis

Not ideal to identify risk
of macrovascular complications

Not reliable to use in any subject

Hyperglycemia is not the only contributing factor

more expensive
Lake of standardization

- **Will you use HbA1c**

  to screen & monitor diabetes?

1.Yes **2.No**

Thank you for your Attention