# Diabetes monitoring

## Frequently asked questions

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### Which blood glucose values are important – before or after meals?

All blood glucose values over 24 hours contribute to overall glycaemic control and to the potential risk of microvascular complications. However, if the blood glucose before a meal is high, the blood glucose afterward will invariably be higher.

Unless preprandial blood glucose values are within the target range agreed by both the patient and the diabetes professional team, there is little value in testing postprandially.

Postprandial blood glucose testing has another limitation – the high intra-individual variability associated with food intake. The 'glycaemic index' (GI) concept is simple – the differing carbohydrate composition of foods will produce diverse glycaemic responses because of the rate of their digestion and absorption. The GI is calculated by comparing the food in question with a standard food (usually white bread or glucose) and gives a specific value between 0 and 100.[1] Unfortunately this implies a degree of scientific precision that doesn't occur in the 'real world'.

Therefore a GI of 80 could range between 47–113 (90% confidence interval).[2] This may seem surprising at first, but think about the varied contributors to postprandial glycaemia in diabetes (especially type 1 diabetes):

- preprandial glycaemia
- direction and rate of movement of preprandial blood glucose
- prevailing insulinaemia and insulin response (either from intrinsic or injected insulin or from an insulin secretagogue)
- insulin sensitivity (changeable by activity, medication or food type)
- rate of gastric emptying (affected by food type and autonomic nerve function)
- amount of carbohydrate in the food (total glycaemic load)
- foods in the meal, their preparation, temperature (eg. cold cooked potatoes have a lower GI than hot cooked potatoes), additives (acids such as lemon juice lower GI).

The most obvious is the glycaemic load (GL), which is calculated as [GI x carbohydrate (g)]/100. Therefore while a food may have a high GI, if one only eats a very small amount, the GL will be low.[3] One suggested sequence for blood glucose control is:

- get the fasting blood glucose on target
- get the blood glucose before the evening meal on target
- check the A1C. If on target, keep checking the two basal blood glucose levels. If A1C is off target, look for hidden hyperglycaemia in the middle of the day or postprandially, or less usually, in the middle of the night.

The short answer is that the top three blood glucose measurements are fasting, before the evening meal and before lunch.

### All the blood glucose levels are okay, but the A1C is high. How does this happen?

This story is not unusual. Beverley's diary says: 4–8 mmol/L, which implies an average around 6 mmol/L. The A1C says 8.6%, which seems a bit high. From previous studies we know that the mean blood glucose value and A1C are approximately related by the following equation[4]: mean BG = (2 A1C–6) which indicates that Beverley's A1C should only be 6% when her daily mean blood glucose is 6.0 mmol/L. Which glycaemic measure would we consider to be more reliable?

Usually the A1C, as blood glucose monitoring can mislead in many ways. In Beverley's case she was only testing and recording the fasting blood glucose values. She did not measure during the rest of the day when blood glucose values are much higher. Hence this type of testing protocol would result in a falsely low estimate of the actual mean daily blood glucose level.

The recommended full blood glucose profile is at least eight tests per day. Even if Beverley was doing some or all of these tests, she might still be getting unreliable results. After all, blood glucose monitoring requires an accurate meter, strip, finger prick technique and recording of results – and you won't know what the blood glucose value was unless it's recorded in her diary. Sometimes people don't record values because they 'know' the value is unusual or the particular

circumstances that caused it. Sometimes they may be tempted to give you the values you want to see. That way, both of you are happy! Scrolling through the meter's memory may be useful in checking for values that may have not been recorded, incorrectly transcribed, or simply not done. There must be a strong motivation for 'good' results, as a hidden memory in the meter showed that pregnant women misreported values despite their obvious interest in a good outcome for the pregnancy, their babies and themselves.[5]

Sometimes the meter or strip is at fault and a quality control check (fluid date) will identify the problem. Another useful check is to get the blood glucose monitoring values immediately before and after blood is taken for a fasting value (eg. when cholesterol is checked). That way the patient (and you) can check both precision (the difference between the two blood glucose monitoring values) and accuracy (closeness to the laboratory value).

Occasionally the A1C result may be erroneous.[6] Falsely high A1C values are typically related to interference in certain laboratory methods due to the presence of uraemia or hemoglobinopathies. There is also evidence that some nonhaemolytic anaemias may be a primary cause of elevated A1C levels. As A1C reflects a weighted average of blood glucose levels over the preceding 6–8 weeks, any sudden loss of old cells (eg. bleeding), blood transfusion or presence of haemolytic anaemia, will dramatically lower the A1C value, ie. falsely low because of a primary cause. Again hemoglobinopathies can also lead to falsely low A1C values, but this relates directly to the laboratory method used. For patients with nonhemolytic anaemias starting treatment, or renal patients having erythropoietin injections, a rapid decrease of A1C levels will result due to increased reticulocyte formation.

If in any doubt, contact the laboratory and discuss whether their method is susceptible to the problems mentioned above. HPLC methods based on boronate affinity columns or the Bayer DCA 2000 procedure are acknowledged as the most reliable with respect to known causes of interference.

It is also important to restate that measured blood glucose values must be reliable (in both accuracy and precision), particularly if the patient is unaware of hypoglycaemia and/or striving for ideal glycaemic control. An inaccuracy of 1–2 mmol/L doesn't matter at a blood glucose value of 10 mmol/L, but means the difference between consciousness and loss of consciousness if the blood glucose level is 3–4 mmol/L.

## Six months ago the A1C was 6.6% and now it's 7.4%. Is that a significant change?

This actually represents two different questions about the change.

- Is the change in statistically significant, ie. is it a 'true' change or just apparent because of the variability of the laboratory method in this patient over time?
- Is the change clinically significant, ie. how is the change likely to affect patient outcomes and does the change 'cross' any clinically defined target thresholds?

The order of answering these questions is important. If the change is attributed to background 'noise' there is no point in asking the questions about clinical significance.

To answer the first question one needs to know the overall variability of the A1C method associated with longitudinal measurements for an individual. This includes both method and biological variability. For A1C determinations the total coefficient of variation ($CV_T$) is about 6%.[7] The formula to estimate the least significant change (LSC) at a particular statistical significance (z) is: $LSC = z \sqrt{2} \times CV_T$.

It follows therefore, that one needs to decide how confident you are that it is a real change and not just 'noise'. For greater statistical confidence (increased z) a larger change is required, but the 'trade-off' is that you may ignore a lesser but clinically significant change. For example, to be 80% confident that a true change has occurred between the 6 month serial A1C estimations: $LSC = 10.9\% [1.28 \times 1.414 \times 6]$

The actual change is 12.1% $([(7.4/6.6) - 1] \times 100$ which is greater than the LSC calculated above. Thus the change between the initial and final A1C measurements can be classified as statistically significant, at a 20% false alarm probability.

The second question relates to potential outcomes associated with the change and requires clinical information about outcomes associated with changes in the biological measure. For A1C in type 1 and type 2 diabetes, we have data from the Diabetes Control and Complications Trial[4] and United Kingdom Prospective Diabetes Study.[8] As the change in A1C has been determined as significant, we can infer the likely associated clinical consequences. Assuming the patient has type 2 diabetes, adverse microvascular outcomes increase by approximately 30% for each 1% change in A1C. Therefore an absolute increase of 0.8% would be associated with a clinically significant increase in risk of microvascular outcomes (eg. progression of retinopathy) of about 24%. The increase in A1C has also elevated the patient's A1C above a decision A1C threshold (>6.9%), but not above the 8% level, where immediate action is generally advocated.[6] Accordingly a focus for the patient and diabetes team will be to once again achieve an A1C level less than 7.0%, to minimise long term complications.

In the above example, if the final A1C was 7.1% instead of 7.4%, the increase would have been only 7.6%, which is less than the calculated LSC. Therefore, the change between A1C measurements would be attributed to method variability rather than true change. Accordingly we would conclude that the patient's A1C status was essentially unchanged.

Conflict of interest: none declared.

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