Macleod Diabetes & Endocrine Centre
Royal Devon & Exeter Hospital

"Treatment failure" with diabetes drugs
Continue, Switch, or Add?

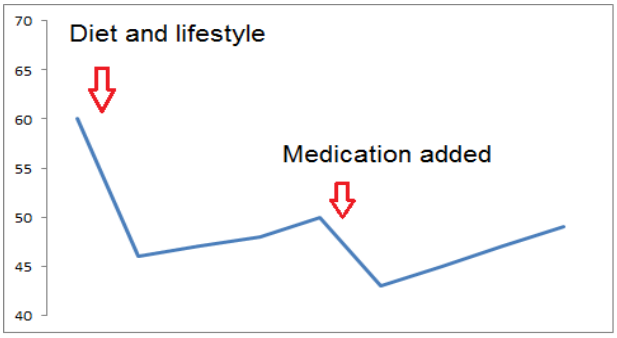
If you start a drug for type 2 diabetes and HbA1c doesn't improve, does this mean the drug isn't working for your patient? And should you just Continue the drug with no change, stop it and Switch to another, or continue it but Add another drug as well?

The short answer is that usually you should Continue if HbA1c is only a little above target, or Add if HbA1c is well above target (by more than 10 mmol/mol). The drug you started is probably working fine, but HbA1c failed to improve for other reasons.

The problem

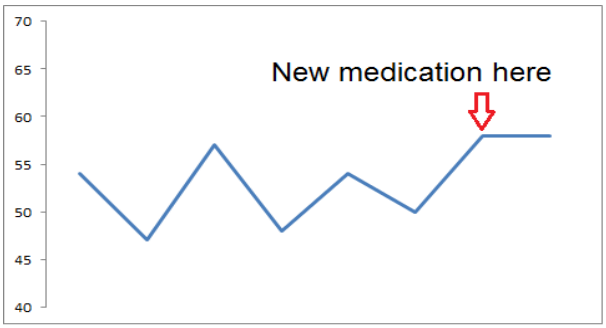
It is natural to assume that if HbA1c doesn't improve, the drug isn't working. This approach is used to assess efficacy in some NICE guidance, particularly for GLP-1 agonists.

In an ideal world, HbA1c would track along like this, with clear response to each treatment.

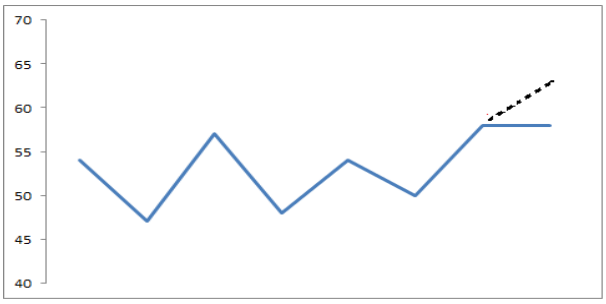


But this isn't a perfect world. HbA1c fluctuates. This might relate to changes in mood, social situation, lifestyle, medication adherence… but in effect the variation is random.

So in the graph to the right, has the new medication helped? It seems not…



…but maybe, without the new medication, HbA1c would have risen, as per the dotted line? Unfortunately, we just can't tell.



So what's new?

The Exeter diabetes research team (**link**) recently published research on this. The team used the CPRD database of primary care patients. They identified several thousand patients

in whom HbA1c failed to improve after a second non-insulin diabetes drug was started (most were already on metformin first-line). They looked at what happened to HbA1c next, according to whether a Continue, Switch or Add decision was made.

With both Continue and Switch, HbA1c fell by about 5-7 mmol/mol. The Switch strategy was only very marginally more effective (an additional ~1 mmol/mol). Firstly, this tells us that in most cases HbA1c will fall if you give it a little longer. Secondly, it doesn't support the notion that if HbA1c doesn't fall then the drug isn't working – if this were true, then Switch should have been clearly more effective.

Following an Add decision, HbA1c fell much more – by 10-15 mmol/mol. So if your patient is a way off target, this is the logical decision.

Does this affect drug choices?

Not much. There wasn't strong evidence for different results with different drugs.

There was a hint that pioglitazone is better at controlling HbA1c, and Continue or Add are particularly appropriate after pioglitazone.

There was a hint that DPP4 inhibitors (gliptins) are less good for HbA1c and Switch might be a little more logical.

Sulphonylureas were in the middle, so this research doesn't support the notion that treatment failure is common with SUs.

There weren't enough patients on GLP1 agonists to give useful results.