**Type 2 Diabetes NICE Guidelines Update Transcript**

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0:01 **Chair:** Good evening, everyone. My name is Dr Nimish Shah I'm the GP Lead for South Wales. I'm really pleased to introduce Sarah Davis. She's a UK diabetes clinical champion and knows so much about diabetes and is also such a passionate speaker and always gets her point across very, very clearly. There's been new NICE guidelines on Type 2 diabetes. Really we're going to be focussing on those and the changes from the previous guidelines and how we can implement them in general practise. So over to you Sarah thank you.

0:40 **Speaker:** Thanks Nimish and thank you indeed to everybody for joining us. Yes, one of those days where it looks beautiful outside but is absolutely freezing, isn't it? I've got an 11 year old in Storey Arms at the moment, up in Brecon, and they've had snow there, so that's rather magical for them. I think.

0:58 **Speaker:** Right let’s get my screens organised and we will kick off, right? Good evening, everyone. Brilliant to be joining you and plenty of people logging on this evening, which is fantastic. Thank you for spending an hour of your precious evening with us this evening. Yes, this evening is going to be all about updates in prescribing for Type 2 diabetes in primary care, with very much a focus on that brand new update to the NICE Type 2 diabetes guideline which hit the press gosh it must be about six weeks ago now on the 15th of February of this year.

1:35 **Speaker:** So this evening's learning objectives are indeed going to be focussed around those NICE guidance. I want to look at what is new, what do we need to know that is new in those guidelines? What do I feel is good? And maybe what do we all feel is not so good? They wouldn't be NICE guidelines unless there was some controversy now would they. I want to illustrate the changes to the guidelines, with a few case studies very much trying to bring them to life, thinking about actually how will this affect what we do in everyday clinical practise and then how on earth in this day and age when we're under so much pressure and time and lack of resources, are we going to put guidelines such as this into practise and indeed we’ll look at some resources to support us to do just that.

2:27 **Speaker:** OK, what we certainly know is that over the last few years, there's been a real flurry of national and international guidelines for the management of Type 2 diabetes. And of course, that's because there's been major changes in the evidence base around prescribing in Type 2 diabetes, particularly for those new agents. I don’t think you can go to a talk can you without hearing about SGLT2 inhibitors at the moment. You know they really have hit the headlines, particularly in the Type 2 diabetes world, but of course now also beyond Type 2 diabetes as well. The previous NICE guideline around prescribing came out in 2015. So actually before any of those cardiovascular outcome trials and beyond for the SGLT2 inhibitors and indeed the GLP1 receptor agonists really came out. So it was well overdue an update, you can see on the slide there that over the last four years there has been a flurry of other guidelines that have been updated. We have the SIGN guidance from Scotland at the end of 2017, which started to move in the direction of taking into account the cardiovascular outcome trial evidence for the newer agents. And really what I've been using over the last few years while we waited for the NICE update was the ADA/EASD consensus report. And if you've seen me talk over the last couple of years, you would have seen me allude to that and I will just mention it during this evening as well. That's one of those really up to date living, working, breathing documents. We even had a guideline for managing diabetes from the European Society of Cardiology in the middle of 2019 because of this increasing evidence around looking at cardiovascular morbidity and mortality in people living with diabetes and altering our thoughts around prescribing because of that. So NICE NG28 update was much waited for and it came out as I said on the 15th of February. So just about six weeks ago.

4:33 **Speaker:** So what is new? What is not so new? Well, even back in 2015, NICE, very much promoted individualised care, particularly around setting individualised HBA1c targets, depending on the person sat in front of us. I think this was really helpful and something we have indeed I think moved towards QOF in the past is very much driven us towards one size fits all for an HBA1c target. And of course, we've got HBA1c targets back in QOF for this year in Wales. What NICE have come up with is this quite useful visual patient decision aid around setting a target HBA1c so we can give this document to our patients living with Type 2 diabetes. They can read it through, the advantages and disadvantages of a tight versus more relaxed HBA1c target and NICE mentioned a number of things you want to take into account when we're setting up individualised HBA1c targets, so personal preference of the patient. Most importantly, their co-morbidities and potential risks from polypharmacy. Many of our patients living with Type 2 diabetes now particularly, are frailer older patients. Of course, we're looking at multiple morbidity, aren't we? Complex management and definitely polypharmacy. We also want to think about the likelihood of benefiting from long term intervention. We know that as people get frailer and older and have had Type 2 diabetes for a longer period of time, actually the benefits of tight glycaemic control in terms of reducing long term complications and indeed the potential benefits in terms of cardiovascular risk reduction from our newer agents will diminish. And this, of course, is really important, particularly in multimorbidity and frailty that we relax HBA1c targets, and NICE in their updated guidance very much promoting this. However, despite the mention of individualised targets, they do still have the same general principles of HBA1c targets for the majority of our patients with Type 2 diabetes. So this hasn't changed from the 2015 iteration. So when someone's on monotherapy i.e. Metformin, we'd be aiming for an HBA1c of less than 48, slightly more relaxed if they were on a Sulfonylurea and then adding therapy once their HBA1c is above 58 mmol/mol generally aiming for that target of around 53 mmol/mol or less once a patient is on multiple therapies. What NICE haven't reviewed in this guidance is anything around education, around diet and lifestyle support, around management of complications. The real focus of this NICE update has been on the prescribing. So of course, structured education still vitally important. Individualised diet and lifestyle support remains crucial, but the majority of today's presentation will focus on the prescribing because that's where the big changes have come in this new NICE guideline. So what NICE have come up with is two new algorithms. If you remember in the 2015 guidance, we have sort of a single page algorithm that was incredibly complicated to follow. So this time they've come up with two separate algorithms.

07:54 **Speaker:** This is the first one. So this is for choosing first line medication. So once a person has been diagnosed with Type 2 diabetes, what should we prescribe? The second one, as you might imagine, is for additional medications further down the line. It's actually quite simple to follow. It looks a little complicated. It's perhaps a little busier with text than I might have hoped for. But actually, once you get your head around it, it's quite simple to follow. And what I've done is I've adapted it a little bit on our next slide to really walk us through what it actually says.

08:28 **Speaker:** So this is first line treatment, patients have been diagnosed with Type 2 diabetes with further structured education. We've given diet and lifestyle advice. What NICE want us to do then is assess HBA1c set an individualised target, but also at this early stage, take into account cardiovascular risk and kidney function. In patients who already have established heart failure or established atherosclerotic cardiovascular disease, that’s ASCVD and you can see in the green box in the top right there that can include atherosclerosis at any vascular site. So they might have had an MI in the past or they might have had a TIA. They may have peripheral arterial disease. So in those patients newly diagnosed with Type 2 diabetes who already have heart failure or atherosclerotic cardiovascular disease, NICE say we should go for Metformin and offer an SGLT2 inhibitor from the start as dual therapy. Interesting. Not something we're used to doing is it, dual therapy from the outset. And I’ll go into a bit more detail in the next slide in terms of whether we're starting those together or one after the other. We also are going to assess in patients who do not have established cardiovascular disease their cardiovascular risk status and NICE want us to do that using something we're really familiar with that is integrated into our computer systems, which is QRISK2. So in all, patients newly diagnosed with Type 2 diabetes who have a QRISK2 score above 10 percent. So exactly the same cut-off as what we might be thinking about, talking about lipid lowering therapies. NICE say we should give Metformin and consider an SGLT2 inhibitor as dual therapy from the outset. Now that is the majority of our patients living with Type 2 diabetes isn't it, that’s the first thing I thought when I saw this. Because, of course, by the nature of the disease itself, the majority of people from the beginning will have a QRISK of greater than 10 percent. We do have another flow on the left here for our patients who are not in either of those groups. So do not have heart failure or cardiovascular disease and have a QRISK of less than 10 percent. So perhaps our younger patients may fall into this group. For those patients, we're still going to give Metformin monotherapy. So important to always notice the language that NICE use. So when something's got really strong evidence, they say offer. When the evidence is there but slightly less strong, they say consider. So for that group in the middle with heart failure or established cardiovascular disease, they say, offer the dual therapy from the beginning. For the group on the right, QRISK above 10 percent they say consider the dual therapy from the beginning. A few other bits and pieces to remind ourselves of, again I’m trying to make it a bit simpler than the actual algorithm from NICE. They mention reminders and sometimes this can be useful but if someone has got symptomatic hypoglycaemia at the time of diagnosis of their Type 2 diabetes, so perhaps they present not feeling great, they're got an HBA1c above 100. They've got osmotic symptoms that they’re weeing all the time, they're desperately thirsty. In that situation, we might want to consider a Sulfonylurea such as Glipizide or Insulin initially as rescue therapy, perhaps for the first six or eight weeks, and then transfer onto Metformin with or without the SGLT2 inhibitor. In terms of whether we start them together or one then the next, what they say is actually we should start the Metformin first and then add the SGLT2 inhibitor once Metformin tolerability is confirmed and on the next slide I'm going to go into a bit more detail about what I think that means. What about patients who can't tolerate Metformin? It happens doesn’t it, those horrible GI side effects. Sometimes people cannot tolerate Metformin. In that middle group who've got cardiovascular disease already they say we should use an SGLT2 inhibitor on its own. The right-hand group QRISK above 10 percent consider an SGLT2 inhibitor as monotherapy from the beginning and on the left, those at lower cardiovascular risk if they can't tolerate Metformin. Ideally, they suggest Sulfonylurea or Pioglitazone from the beginning or an SGLT2 inhibitor,and they would prefer us to choose an SGLT2 inhibitor over a DPP4 inhibitor in terms of cost effectiveness.

13:13 **Speaker:** Okay, let's break it down for a bit more detail then shall we? Well I think the first thing that certainly strikes me, is this means we're going to be using SGLT2 inhibitors a lot more alongside Metformin from the very outset of treatment. I like it, you know I think the evidence around this group of agents is very strong, but I think this is a big change for us. NICE look very clearly at both clinical effectiveness and cost effectiveness, and they feel that the cost effectiveness of that combination, particularly in our highest risk groups, is very clear. And of course, what we're doing here is we're using an SGLT2 inhibitor beyond glycaemic control. So say you've got a patient HBA1c is I don't know, 58 or 53 at diagnosis. We're going to start Metformin, we've decided to do so. But actually, even though they're HBA1c will probably come down to where we want it to be, we should still think about adding the SGLT2 inhibitor if they're high risk, for those additional benefits of the cardiovascular and renal protection, rather than really anything to do with glycaemic control. That's a big change in the way we think about this group of agents and almost I think, we feel now perhaps more like a statin. So QRISK above 10 percent. Let's think about getting the SGLT2 inhibitor there almost as a preventor drug, just like statin therapy for primary prevention of cardiovascular disease. So how quickly should we add the SGLT2 inhibitor to the Metformin? So what NICE say in their small print, is we should add the SGLT2 inhibitor without delay to ensure that people do not remain on Metformin monotherapy for prolonged periods of time. They do not specify how long. So what I think is in those very high risk groups so the person whose got heart failure or established cardiovascular disease. We're going to start the patients on Metformin and then if they tolerate that Metformin titration quite well, think about adding that SGLT2 inhibitor after about four weeks, once they've established onto the Metformin. In the lower risk group, those with a QRISK above 10 percent I actually think it's reasonable to think about adding the SGLT2 inhibitor around that 10 to 12 week mark when you're probably getting the patient back in for an HBA1c and a review of how things are going anyway. That's my suggestion, it doesn't specify in NICE just that we should get them onto the SGLT2 alongside the Metformin in that high risk group as soon as possible. Which SGLT2 inhibitor? Well interesting so what NICE say is we should use an SGLT2 inhibitor with proven cardiovascular benefits. Now, of course, all of the cardiovascular outcome trials have been slightly different. The evidence base for the SGLT2 is all a little bit different. It's probably very much a class effect, but we have most certain data for cardiovascular and renal benefits that Dapagliflozin Empagliflozin and Canagliflozin. When NICE looked at cost effectiveness, they thought that Dapagliflozin had the most consistent evidence for cost effectiveness for that outset combination therapy. But actually all of them met that clinical and cost effectiveness criteria. When you look at the data, well, so Dapa had good evidence in primary prevention. It's got good evidence in heart failure. Empagliflozin was the only one that showed cardiovascular benefit in terms of reducing cardiovascular mortality. So the others showed benefits but Empagliflozin was the only one in established cardiovascular disease that reduced cardiovascular mortality. Canagliflozin good evidence in diabetic kidney disease. So all slightly different in terms of their evidence base. Actually I think the important thing is probably to choose one and to learn the dose and the licences and stick with it.

17:05 **Speaker:** The second algorithm is this, as you might imagine, its treatment escalation. So we've got one for how to choose your first line medications and then one for how to choose further medications as the Type 2 diabetes progresses. Again I’ve broken it down a little bit. It's fairly simple, actually. So if someone's cardiovascular risk or their status changes we should review things. So say somebody does not have heart failure or cardiovascular disease, but develops it, something of course we often see in Type 2 diabetes. If they're not already on an SGLT2 inhibitor, they should be put onto one, whether that's in addition to their other therapies or as a switch. If someone was previously low cardiovascular risk, less than 10 percent, you see where this is going. If they become more than 10 percent, then we should again think about adding or switching to an SGLT2, if they're not already on one. What about in patients where the HBA1c is above an individual target? They're either already on an SGLT2 inhibitor or they're low risk, and so they're not on one. Well here we can of course use combination therapy, we mustn’t forget about glycaemic control. I suppose the interest from this NICE update is around the cardiovascular protective effects of the SGLT2s. But actually, of course, we still need to think about glycaemic control and we will of course need to use additional agents as Type 2 diabetes progresses in order to try and reach those individualised HBA1C targets. And we can use really any combination of therapies, according to this NICE update, which is great. So we've got glyptins, DPP4 inhibitors, Pioglitazone, Sulfonylureas, SGLT2 inhibitors and of course insulin as well. What about GLP1s I hear you cry. I'm sure there's a big hoo ha about those as well. Well, this perhaps is the most controversial part of the NICE guideline update, because GLP1 receptor agonists are still right at the bottom of the treatment pathway. So once a person is on triple oral therapy and they require increased glycaemic control, that's when we can consider switching one of those oral agents to a GLP1. But they still have that criteria for BMI and indeed stop criteria as well. I'm going to go into that and perhaps the reasons why in a little bit more detail in just a moment or two.

19:29 **Speaker:** NICE have also come up with a really useful guide in terms of when we are adding additional medication, should we switch or should we add and they sort of go through some points that we need to think about in terms of which one we're going to do? So obviously, if someone's not tolerating a medication then we just think about switching and we need to think about how effective something was when it was first started, and I think this part that I put in red here is really interesting. So we should stop medications that have had no impact on glycaemic control or weight. Unless there is an additional clinical benefit, such as cardiovascular or renal protection. So particularly now thinking about the SGLT2s, if someone's on the SGLT2 and that was started for that cardiovascular and renal protection, even if it didn't do a lot for glycaemic control, which particularly we’ll see that at lower EGFRs and I’ll mentioned that a little bit later on. We should still carry on prescribing it because it's still giving the cardiovascular and renal protection and then use additional medications for glycaemic control. So that's a situation where we're probably going to be adding rather than switching. So we're unlikely to stop the SGLT2 once we've started it, it's more likely we’ll add additional agents when we need that additional glycaemic control.

20:54 **Speaker:** So what about the GLP1s? Why are they still right there down at the bottom? And you know, there's been a big outcry from large national groups, including a few that I sit on, the Primary Care Diabetes society and the Cardiorenal Metabolic Group about this really. And I think it was probably hoped that the GLP1s would be higher up the treatment pathway because also they have shown cardiovascular benefits, particularly in terms of stroke and atherosclerotic disease. But they are still very much down the pathway. So when someone, as I said, is on triple oral therapy, then we can consider it. But NICE state in the study to have a BMI of greater than 35 adjusted according to ethnic group or potentially a lower BMI if insulin would be particularly problematic or if weight is a big problem and we've still got the stop criteria, so you still need to have a reduction in HBA1c and weight in order to continue using them. What’s slightly better and has improved, is that they can now use GLP1s in any combination of treatment. So the previous iteration of the guidance, it was really only advised to use a GLP1 alongside Metformin and a Sulfonylurea. But now we can use them alongside anything in a wider range of combinations, including alongside the SGLT2 inhibitors. And I think that's a really interesting combination of treatments something I've used quite a lot over the last couple of years and was starting to get a bit of data now from the research about that combination and the potential benefits that it brings. As I said that stop criteria remains so a reduction of HBA1c of 11 mmol/mol and weight of three percent after six months of a GLP1. So this is definitely the controversial bit. Why have NICE done this, so NICE have been very clear in their descriptions as to why they've done this, because they, I think, knew this was going to be a more controversial part of this guideline. Well, firstly, they consider GLP1s and the SGLT2s as a group and within the GLP1s is a lot more of a mixture in terms of their efficacy and cardiovascular benefit. So only Dulaglutide Liraglutide and injectable Semaglutide have shown these cardiovascular benefits. The others have not, but they only considered as a whole group. They also looked at the cost effectiveness, but only consider the cost effectiveness in terms of the cardiovascular outcome trials. They didn't incorporate the really quite marked glycaemic lowering and weight lowering, that of course we see with the GLP1s as well. So a little controversial. Am I disappointed? Yes, a bit. Will I still use the GLP1s a little earlier on in the right patients? Probably. You know these are guidelines they’re not tramlines but certainly been really interesting to see.

23:50 **Speaker:** And this as I mentioned earlier, is the guidance that perhaps I'd be following over the last few years the ADA/EASD consensus statement. And you can see it's not come out brilliantly, but we could see that the GLP1s figure much highly in this treatment pathway. Second line to Metformin in patients with atherosclerotic cardiovascular disease in patients where hypoglycaemia is a concern and in patients where weight is a concern, so certainly not following that lead. But I totally understand that NICE need to think about cost effectiveness within the NHS.

24:25 **Speaker:** Anything else we need to know that I haven't told you already. Well, I think just a quick mention and a nod to kidney disease. So back at the end of 2021, I think it was probably October. There was also an update to the NICE chronic kidney disease guideline, and I think it probably went under the radar a little bit. I can’t imagine why I don’t know why everyone is not out there reading the chronic kidney disease guidelines hmm or not, probably better things to do, but indeed they incorporated it into this NICE Type 2 diabetes guideline update as well, because it's this. We're all aware that in our patients with Type 2 diabetes who have a raised albumin creatinine ratio above 3, we should have those patients on an ace inhibitor or an ARB, which is titrated to maximum tolerated dose. However the SGLT2 inhibitors come in here again. So because of the evidence of slowing kidney disease, particularly albuminuria kidney disease that we often see in Type 2 diabetes and also reducing cardiovascular events and mortality in the renal outcome trials, in patients with an ACR greater than 30, NICE say we should offer an SGLT2 inhibitor in addition to that ACE inhibitor or ARB. So look at the language again so offer is strongly worded in patients with an ACR between 3 and 30. We should consider an SGLT2 in addition to that ACE inhibitor or ARB, that's not on the algorithm it is in the small print. And as I said, it was in the NICE CKD guidance there was updated in 2021 and then that ACR of 3 to 30 considering an SGLT2 inhibitor was then added a little bit later on. And certainly I think there is a lovely quality improvement activity to be done here, particularly in your patients with the high ACRs because there won't actually be that many with an ACR above 30, plenty between 3 and 30, but not that many people with Type 2 diabetes and an ACR greater than 30, and those patients now should be offered an SGLT2 inhibitor to slow their kidney disease and protect their heart as well. And I'll show you a really easy way to find and identify those patients without having to write a tricky search particularly if you are on vision in just a moment or two. However, I hear you cry, but don’t we need an EGFR of 60 in order to start an SGLT2 inhibitor. Some of these patients are inevitably going to have lower EGFRs. Well over the last few years in light of all the evidence for this class of agents, the licences and the indications have changed rapidly.

27:14 **Speaker:** And frankly, it's been hard for me to keep abreast of what's been going on. And if you've not got a particular interest in diabetes. I think it would have been completely impossible. So on this slide I have summarised the current situation for the four SGLT2 inhibitors their licence indications and their EGFR requirements. So very briefly, Dapagliflozin is now indicated for three things, for Type 2 diabetes, for chronic kidney disease and for heart failure with reduced ejection fraction and those second two indications are for people with and without Type 2 diabetes. And we can start it for all of those indications down to an EGFR of 15. Canagliflozin licenced for Type 2 diabetes and when we say Type 2 diabetes here we don't just mean for glycaemic control also for the reduction of cardiovascular morbidity and mortality. Cana for Type 2 diabetes then and diabetic kidney disease. So Canagliflozin we can now start it down to an EGFR of 30 and actually carry on prescribing down to end stage renal disease in patients with an ACR of greater than 30 that is for the 100 mg dose. You need to have an EGFR of more than 60 to use the 300 dose. Empagliflozin licence for Type 2 diabetes and heart failure with reduced ejection fraction for patients with and without Type 2 diabetes. For Type 2 diabetes you need an EGFR of at least 60 to start unless they've got established cardiovascular disease so if they're high risk with established cardiovascular disease, we can now start Empagliflozin 10 mg down to an EGFR of 30. If you're using it because someone's got heart failure with reduced ejection fraction, we can start it down to an EGFR of 20. In order to use the 25 mg dose, though, we do have an EGFR of greater than 60. Ertugliflozin is the more limited one at the moment. Only licenced for Type 2 diabetes need an EGFR of more than 60 to start it. It is confusing, isn't it? As I said I it's probably a good idea to try and remember one and pretty much stick with it.

Or sometimes I'll change which one I'm using, depending on the person, because of the evidence base for that particular agent. But certainly keeping abreast of these changes is challenging. So I hope that that is helpful.

29:31 **Speaker:** And for this, renal licences have changed. What does this mean? Is it safe to use these SGLT2s at these lower licences? Well, absolutely. When we start a SGLT2 inhibitor, you do get an initial little drop in EGFR about three to five mils in the first week or so, which then recovers. That is actually a correction of the hyper filtration that we see in diabetic kidney disease and it then recovers. So no need to check EGFR using these at two weeks like perhaps with an ACE inhibitor. I didn't do anything beyond normal monitoring. So it's important to remember that the evidence is very strong and indeed NICE now supports that in their guidance that SGLT2s are nephroprotective not nephrotoxic. What is however vital to realise, is that at a lower EGFR, you will not get much in the way of glycaemic load. So below an EGFR of about 45, you really won't get much in the way of glycaemic lowering at all. You will still get the cardiovascular and renal protection. So it's still going to start it for that, for that guardianship drug. But if you need further glycaemic control, we're going to need to use additional agents. For that reason, I think it's quite useful to recall the indication for starting the SGLT2 from the beginning. So have you started it because that patients got kidney disease? Have you started it because they’ve got heart failure? Have you started it for that glycaemic lowering? I think that's useful because obviously we know another member of the multidisciplinary team might be seeing that patient further down the line and making that decision about whether to continue the therapy or to switch. I think it could be useful to recall the reason that we started it. I hope your’e getting the flavour. There is definitely a big shift towards this CRM, this cardio renal metabolic approach to Type 2 diabetes management very much using these agents beyond glycaemic control, just more like a statin for that cardiovascular and also renal protection. Of course, if we're going to be using SGLT2 inhibitors for almost everybody with Type 2 diabetes from the outset, we better be able to use them safely, haven't we?

31:42 **Speaker:** And I know some of you will have some concerns around the safety of this group of drugs. So let's just whiz through where we're at before we look at some case studies. Commonest side effects, definitely mycotic genital infections. So thrush is something we often see, don't we? And some patients won't be able to continue treatment because of recurrent thrush. Often it will settle in my experience, but not for everyone. Fournier's gangrene that necrotising fasciitis of the perineal region, we did have some warnings about that. I mean there's no definite association. There haven't been cases shown in the big trials. But of course, we're going to give good hygiene advice and if someone presents with some severe pain, perineal tenderness etc.. of the perineal region, we're going to get them seen straight away. UTIs is an interesting one. So there was definitely a concern early on with these agents that there were going to be more UTIs, and would therefore avoid them in people with recurrent UTIs. Actually the trials have not shown that, all these massive trials and they've been huge these trials haven’t they and they have not shown an increase in UTIs so we're moving away from that being a concern. What about lower limb amputations? What about people with diabetic foot disease? So remember, there was a signal wasn't there an increase in toe amputations from CANVAS, which was the cardiovascular outcome trials for Canagliflozin. Again the evidence base now is moving away from concern, so it hasn't been shown in any of the other trials. And now we're getting some really big real world data as well. So we had a big retrospective study published in the European Heart Journal last May. This looked at millions of patients who have been treated with different agents and the SGLT2 didn't seem to be associated with any increase in amputations. And in fact both the SGLT2s and the GLP1s seem to be associated with a lower risk of amputations than gliptins or other agents. Which should kind of make sense because we know that people who are at risk of amputations are likely to have peripheral arterial disease, and they probably improve outcomes in that group of patients. So what am I doing now? Well, of course I'm still ensuring that good foot care advice is in place, but I'm no longer as concerned that this is an issue with this group.

33:55 **Speaker:** This one however we do need to be aware of don’t we DKA. So it is a rare side effect across the class, previously quoted at about one in a thousand. But actually some recent observational studies have suggested it’s a bit more common. More like one in five hundred or so. If it's going to happen, it’s most likely to happen in the first six months of treatment. But a really useful bit of guidance from Association of British Clinical Diabetologist ABCD and Diabetes UK that was published about a year ago, which I will recommend having a look at, I’ve popped the link there on the slide for you. And essentially, they give us some ideas in terms of which patients we should avoid using an SGLT2 in because their DKA risk will be increased and which groups you want to use with caution. So in somebody that has not got Type 2 diabetes, say they got Type one diabetes, if you think they might have LADA so latent autoimmune diabetes of adult onset, if they've got Type 3C or pancreatic diabetes because of a history of chronic pancreatitis perhaps, we should not be using SGLT2 inhibitors. That's because the risk of DKA is greater when someone is insulinopenic. So if somebody is going to be insulinopenic because they've got Type one diabetes or because they become acutely unwell, then we should be avoiding SGLT2 inhibitors. Anyone with a history of DKA, I wouldn't use them. And also this actually comes up in the NICE guidance. Anyone that's undertaking a ketogenic diet is not advised to use an SGLT2 because of the theoretical risk of DKA. And what about groups to use with caution? So people who have got a lower BMI or people who are losing weight would be cautious. That's because they might not have Type 2 diabetes or they might just be insulinopenic, so I'm much more cautious in that kind of lean person with a probable diagnosis of Type two diabetes when I'm using an SGLT2. Also someone with a very high starting A1c so if someone's got an A1c above eighty six, I will use an SGLT2 inhibitor but because the theoretical risk of DKA is higher with high high blood glucose levels, I will again just be more cautious. Make sure they've got really good sick day advice. If we see someone on SGLT2 who is unwell vomiting, abdominal pain, drowsiness, we've definitely got to rule out a DKA, so we should check for ketones. Remember, it can be euglycaemic, so the blood glucose might be relatively normal. We still want to check for ketones. Ideally capillary rather than urine dipstick.

36:33 **Speaker:** I'm going to skip through sick day guidance because I'm sure you know it already. I want to get some case studies and time as always is racing on, there’s some really good resources out there to help us give good sick day guidance and there’s a reminder on the slide there of the medications that we should temporarily pause when somebody becomes unwell. The primary care diabetes society has got great guidance you can see on the right there, how to give sick day advice. And trenddiabetes as always, an excellent resource and patient information leaflets. This is so useful, Type 2 diabetes What to do when you are ill. A really good one to use.

37:11 **Speaker:** There's lots of other guidance out there as well, in fact this one was published just a little bit too late for me to properly incorporate into my slides. It was just published last week in Diabetes Therapy by some colleagues of mine. This is again a traffic light guidance in terms of safety for prescribing SGLT2 inhibitors. We’ve got the red group, people with Type one diabetes, ketogenic diet and so on. Amber and green. And again I’ve put the citation there on the slide, but I'm more than happy for you to drop me an email if you'd like me to send you a PDF copy of that very recently published traffic light guidance.

37:54 **Speaker:** Lots of other resources out there as well. One of my colleagues Claire Davis is a clinical pharmacist in North of England, and she's come up with some really nice advice for primary care around the safe use of SGLT2 inhibitors. She keeps up to date in a Google Drive folder, actually. And again, I put the link there for you on the slide. If you drop me an email, though, I'll just send you those links right back. Very helpful.

38:07 **Speaker:** And this is interesting, if you want a different way to access the NICE guidance and you like sort of interactive clicky type approach. A colleague Amjid Rehman in England is a GP with special interest in diabetes produces these that are called clinicalpathways.io. If you just search for SGLT2 inhibitors or the ng28 guidance, it comes up with this really interactive, very clever way of showing you and talking you through the guidance. So if that's your sort of approach, do have a look at those that are completely free to access and he’s more than happy to receive feedback. And he was more than happy for me to promote them to everyone today.

38:48 **Speaker:** Ok let's just spend the last ten minutes on a couple of case studies to bring this all to life a little bit shall we? So this is Samantha. So Samantha is a 53 year old lady past medical history of hypertension. She's on Ramipril 5, and she has just been diagnosed with Type 2 diabetes. HBA1c is 59 We've repeated that, it's confirmed. We've got her LDL it’s 3.2. Renal functions ok, urinary ACR is alright her BMI is 32 so it's raised and her blood pressure is 150 over 80. She works in an office or from home over the last couple of years, she's got a couple of children at university. She struggled to do any regular exercise, and she has struggled with her weight for a long time. Her mum died of a stroke when she was 73, so she's absolutely desperate to avoid any risk of stroke. So as part of our assessment, be it for lipid lowering therapy or now indeed to decide what to do with her medication for her Type 2 diabetes. We're going to assess her cardiovascular risk status.

39:51 **Speaker:** QRISK2, her 10 year cardiovascular risk score is 13 percent. OK, so of course, I know I haven’t focussed much on this today. The first thing we’re going to do with Samantha is discuss ways to talk about her diet and lifestyle. Just a quick signpost to this, you may already be aware, which is brilliant, that everybody in Wales has got free access to mydesmond. This is online digital education for Type 2 diabetes. They just go to mydesmond.wales and they'll be able to just register for free when they go on to that. So really, really good I do recommend having a look at mydesmond and of course, we're going to refer to our local dietetic services, depending what's available by your local dietician team and indeed local projects, whatever might be helpful for her. We're going to address her cardiovascular risk factors, so we definitely want to work on a blood pressure. I'm going to talk about potentially statin therapy as well, because her QRISK is above 10 percent.

40:54 **Speaker:** So what about her Type 2 diabetes, now previously would you have given a three month trial of diet and exercise? Yeah, maybe, absolutely. And certainly I might have done, and I still might. It'll depend on the patient. We know, don't we, that lifestyle change is pivotal to the management of Type 2 diabetes. We also know from the direct study that if she can lose enough weight in this next year or so she's got a good chance of putting Type 2 diabetes into remission. However, we also know that tight early glycaemic control helps to reduce long term complications and using an SGLT2 inhibitor early in Type 2 diabetes will help to protect her heart and her kidneys. So we definitely need to make an individualised decision I think now with our patients, you know, I think if you talk to Samantha and she says, I can't stand having this diagnosis, I can't have Type 2 diabetes. I know what I need to do. I'm going to get rid of this. I'm going to lose this weight. And of course, I think that there is definitely an argument for giving her that chance and supporting her with that. However, we also know that early pharmacological intervention might well be helpful as well and I think we need to have honest conversations with our patients about the benefits of each approach.

42:13 **Speaker:** We talked to her about it, we talk to her about Metformin. She's happy to start Metformin and then we talk about adding an SGLT2 inhibitor. And now this conversation I'm having and my practise nurses are having with all patients is different. So we're now saying, let's put you on Metformin that's going to bring your HBA1c down, help with you Type 2 diabetes. And then we need to think about discussing adding another agent and this tablet is going to help to protect your heart and to protect your kidneys, which can be affected by Type 2 diabetes in the longer term. So we start Metformin, we titrate it because she’s in that QRISK more than 10 percent group I'm going to review her at 12 weeks, and we do an HBA1c again. Her HBA1c has come down to 50 mmol/mol. Now previously, I might have left things alone there but because of the NICE guidance, we do discuss adding an SGLT2 inhibitor for reasons beyond glycaemic control to protect Samantha's heart and kidneys. And we add Dapagliflozin 10 mg with that sick day guidance.

43:13 **Speaker:** Let’s look at one more case. David is 68. He's had Type 2 diabetes for eight years, so he's a bit more into his Type 2 diabetes journey. He's on Metformin, Sitagliptin, Ramipril and Atorvastatin. His HBA1c is 50, and he's come for his review 50 mmol/mol. We’ve got his renal function so his EGFR is 50, so a bit reduced and his urinary ACR is 25 so quite raised, it’s been raised for a couple of years. So we look at his chronic kidney disease stage. He's Stage G3a because of his EGFR, A2 because of his raised urinary ACR so quite high risk. His BMI is 28 with a blood pressure of 140 over 76. So we're seeing him at review and actually at first glance, I might think, well OK we'll think about what we can do let’s have a look at blood pressure. Perhaps we can be a bit tighter there with our blood pressure control to protect his kidneys. HBA1c probably quite happy with that, but actually, now we know we can probably upgrade his treatment. What do you think that gliptin is doing for David. And I think I've got quite a lot of patients who probably are on gliptins, you know, rightly so perhaps because they need the benefit of glycaemic control. They're well tolerated, but it's not giving any additional benefits.

44:31 **Speaker:** He’ll definitely benefit from SGLT2 inhibitor. He’s high cardiovascular risk, we didn't do his QRISK but we know it will be high and he's got a raised ACR with a slightly reduced EGFR. Are we going to add the SGLT2 inhibitor to his Metformin and gliptin. Or are we going to switch? Well, we have a look back, when he started on his gliptin it did improve the HBA1c by about 4 to 6 mmol/mol. So not a great deal. We don't see a great deal of lowering with a gliptin. But it hasn’t helped his weight, as you wouldn’t expect it to, and isn't giving any additional benefits. He's getting on okay with everything, though. So I think in this situation I would switch, so I'd stop his DPP4 inhibitor and start him on the SGLT2 inhibitor. I am aware his EGFR is a little bit low, so I might not get the amount of glycaemic control from the SGLT2 inhibitor, that I would always expect from the group of agents, so I may need to monitor that and use something else further down the line. But he's definitely a patient where at the review, I'm going to be looking at cardiovascular risk status at renal status and thinking now, is he one that should be on an SGLT2?

45:45 **Speaker:** Sounds like hard work folks doesn't it? How on earth are we went to implement these guidelines now when we're under such pressure in primary care? Well, this is my idea, my thoughts around this. So I think our highest risk group, we probably could identify those lists, do a virtual review, perhaps in line with our clinical pharmacist colleagues, a sort of quality improvement type project. So identifying the patients who have got Type 2 diabetes with heart failure or established atherosclerotic cardiovascular disease, potentially a fairly big group and definitely those who've got Type 2 diabetes with a urinary ACR above 30. So those groups, I forget those lists, and I'm going to show you how to get them really easily after easter and review them virtually, are they on a SGLT2 if they're not, perhaps it is worth having a look at actively adding them in. But everybody else, those with a QRISK above 10 percent. Of course, it's not realistic for us to call all of those patients in and whack them on to SGLT2 inhibitors, if appropriate. I think that's perfectly all right to be doing throughout the year when we're seeing patients for their annual diabetes review. A quick word then to the to the data before we go to some questions, I'm more than happy to take questions before we finish by eight o'clock this evening. Now many of you may be using the Audit+ national diabetes audit support module for diabetes, and is really helpful for looking at how we're doing on national diabetes audit in terms of completing the essential care processes and reaching our treatment targets. But what I have done is I have massively extended the module and it's going to launch the week after Easter, so it's going to be called the All Wales diabetes module on Audit+ it's going to have its own little emblem and I've put loads and loads of data for you to access on there, including easily identifying your patients with Type 2 diabetes who have cardiovascular disease and your patients with Type 2 diabetes who have chronic kidney disease, specifically those with raised ACRs. I've also put some searches in there around frailty and diabetes, so identifying our older frailer patients who might be overtreated and suitable for de prescribing, you're going to be easily able to access your prescribing data so you can see your patients on insulin for example who’ve got Type 2 diabetes. How many have you got on an SGLT2 inhibitor, how many on Glipizide and so on and also those with the highest HBA1c those with the highest BMI, and perhaps we can think about targeting our highest risk patients.

48:20 **Speaker:** I've got a couple of screenshots. This is from the Woodlands data, which is my surgery in Cardiff, so it's a bit small on your slide, but there's just some examples. So at the top there, we've got HBA1c ranges. So on the left there the smallest bar is those with an HBA1c of greater than 100. So our very high HBA1cs coming all the way down to those with HBA1cs less than 58, less than 53. And you can just click through on these bars to bring up your list of patients. The bottom right there is the frailty one, so here we can see patients with frailty and we use the Electronic Frailty Index score for this one. But also there’s another one that's typically based on age. I can see there actually in Woodlands, we've got over 30 patients with a high frailty score with an HBA1c of less than 48, so they potentially are over treated and we know that's quite common as frailty ensues. So there's definitely a NICE quality improvement project for me to crack on with there. These are the ones for identify co-morbidities. So the top one there is people with Type 2 diabetes in your practise who have chronic kidney disease. So you can see this is again as my Woodlands data, we've got about 500 patients with diabetes, about 420 with Type 2 diabetes, quadrant fifty I think Type 2 diabetes. I can see there actually on the right hand side of the blue bars only about seven of those have got an ACR of greater than 30. So as I said, not a huge group to review and to see if they're on an SGLT2 inhibitor, slightly larger group with that ACR over 3, but hopefully really easy to identify your patients. And then bottom right there is your patients with cardiovascular disease, definitely a bigger group. You can break it down into those with angina, those who’ve had a stroke, those with heart failure, and so on and so forth. So this will launch the week after Easter it's going to come with a how to guide you’ll be delighted to hear. I'm going to attach lots of ideas I've got in terms of the way you might want to use this data to improve your diabetes outcomes.

50:15 **Speaker:** Finally before I stop talking a quick plug if I may, for a save the date. So I sit on the Primary Care Diabetes Society committee and we are doing a face to face Welsh PCDS conference this year. Hooray! Brilliant be so nice to do a face to face conference. It is in Cardiff completely free to attend of course, it’s on the 12th of May in the Jury's Inn. So if you fancy coming along to the Welsh PCDS Conference, do go to the website diabetesonthenet and register and it’ll be fantastic to catch up with some of you there.

50:51 **Speaker:** I'm definitely going to stop talking. I've talked for long enough. I'm more than happy to take any of your questions this evening or if you think of something afterwards or you'd like me to send you some of those PDFs of the safe prescribing in SGLT2s for example, do drop me an email. I'm Sarah.davies78 on the global email. Thank you very much.

51:13 **Chair:** Thank you very much, Sarah. That was really interesting. There aren't any questions in the chat bar, which is surprising, but I think it's obviously the GLP1s the most controversial part of it, and these guidelines aren't reviewed that frequently on there I think they missed a bit of a boat there really. Patients are going to be asking for theirs, difficult. There's one thing, it was talking about if the medication isn't effective you should stop and move on to another one. And yet then some of the guidelines says that you can only go on GLP1 if they are on three medications, not considered, not tried three medications. So actually, if you’re stopping some of these medications you’ll never get according to the guidelines in a position where you could start it.

51:58 **Speaker:** I think there's a little bit of wiggle room there, I call it in Nimesh a bit of wiggle room. So, you know, I think you could say if a patient has tried a triple oral therapy and it hasn't been successful, then a GLP1 is an option. And you know, it'll be interesting to see what local guidance does, whether it's sort of very much sticks with NICE or is a little bit more relaxed in the approach the GLP1s. And you're right, patients want them. We know that some of them now are being licenced for weight loss, specifically at higher doses. I'm sure many of us will have had those conversations with our patients asking if we are able to prescribe in that scenario, which we're not in primary care at the moment, sadly.

52:38 **Chair:** Thank you. And there aren't any other questions, I'm glad that we approved that audit+ module. When I saw your documentation originally, it didn't quite make as much sense as those two slides did, so that was pretty good.

52:53 **Speaker:** Yeah, I think it'll be really helpful Nimesh. I'm hoping we might get a nice kind of national quality improvement project out of it, perhaps. I think it's got great potential and it's just an easy way to be able to do these searches, especially if you haven't got someone tech savvy in the practice, that’s able to write them and come up with them. So I'm hoping that’ll be really good for people.

53:15 **Chair:** And so I think there are no further questions. Obviously, there's quite a lot to take in and I think the more you use it will make that a little bit more easier and some really good little tips there and some sort of pointers as to where we can get further information. So that's really really good. Have a pleasant evening. Thank you very much, Sarah.

53:54 **Speaker:** Thanks, everyone. See you soon.