**Cardiovascular Risk in Diabetes Transcript**

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0:01 **Chair**: Good evening, I'd like to welcome you to today's HEIW webinar. This is part of the continuing diabetes series. So without further ado, I'm going to hand you over to Sarah Davies, who's a UK diabetes champion, and she’s presented before. I'm sure most of you have seen her before. Really knows her stuff about diabetes. Really enthusiastic presenter. I'm sure it'll be a great presentation. Thank you, Sarah.

0:33 **Speaker**: Thank you very much Nimish for that kind introduction. It's going to be lively if we're going to do diabetes on a Tuesday evening, folks hasn’t it. So thank you very much for joining us and thank you very much for inviting me.

0:45 **Speaker**: So good evening everyone. My name is Sarah Davies. I am a GP first and foremost, I work in Woodlands Medical Centre, in Ely in Cardiff, and I'm also the CD for diabetes in Cardiff and Vale for primary care. And as Nimish said, if anyone’s seen me before I’m really passionate about great quality diabetes care in the primary care setting. But today, I suppose, is a little bit of a different focus for me but incredibly important. And hopefully that will really become apparent during today's talk. And I think it can be very indicative of just how complicated it is to look after people living with Type 2 diabetes in primary care. We are talking managing cardiovascular risk in diabetes.

**1:31** **Speaker**: Of course, we're all more than aware that diabetes is associated with multiple complications. That's what we're constantly, of course, trying to reduce or indeed even prevent. And we can divide those broadly into the microvascular complications. So retinopathy for example, diabetic kidney disease, neuropathy. But today's focus is on those macrovascular complications, stroke, heart disease and peripheral vascular disease.

**2:02 Speaker:** So what is the excess risk for someone living with diabetes? Well people living with diabetes have about a 2 to fold increase in both coronary heart disease and stroke, so twice or more likely to suffer from atherosclerotic cardiovascular disease or indeed suffer a stroke, with markedly increased risk of increase in mortality as well compared to someone without a diagnosis of diabetes. They also have a significant increased risk of both heart failure and peripheral arterial disease. I think heart failure is a really interesting one, I'm not talking a great deal about heart failure this evening, but certainly something that's very much come into the forefront, particularly as the SGLT2 inhibitors have emerged as indeed treatments for heart failure in their own right. We've become increasingly aware of the risk of heart failure in people living with Type 2 diabetes and the fact that it’s probably somewhat under diagnosed. I’d certainly say once you start looking for early heart failure in people with Type 2 diabetes, you most definitely start to find it. And indeed, we know that peripheral arterial disease also tends to probably be under diagnosed, again look for it and we probably will find it. And we know, of course, that if someone's got atherosclerotic disease, they will often have atherosclerotic disease in multiple vascular beds. So if someone's got coronary heart disease, it is indeed likely they may also have a degree of peripheral vascular disease or indeed multivessel disease in the brain. It's a fascinating paper that came out in The Lancet just before Christmas that I wanted to share with you. So vascular disease is most definitely the leading cause of death in people with diabetes worldwide. But interestingly, and in the most up to date data is actually looking at data from England from 2018. In the UK actually cancer is now the leading cause of death in people with diabetes. It's very recently overtaken vascular disease as that leading cause of death because outcomes of vascular disease have of course been improving. On the primary prevention side, of course, with us doing a fabulous job and also of course in how secondary prevention takes place in terms of interventions, particularly in the acute setting. However, as we can see from that paper, the excess mortality risk related to vascular disease in people with diabetes is still markedly that than those without diabetes. This is, as I said, is the data from England 2018. And you can see that the more vascular related mortality rate for men 7.5 per 1000 patient years if you've got diabetes, 4.3 if you haven't and similar figures for women, so just less than twice as likely to have vascular related mortality than someone without diabetes.

4:47 **Speaker**: This is a real and eye-opening slide, in my opinion that I just wanted to share with you, really bringing into focus what we're talking about in terms of numbers years of life loss, potentially for somebody with diabetes and coexisting cardiovascular disease. This comes from the Emerging Risk Factors collaboration data. So if you take a 60 year old with Type 2 diabetes, that sixty year old, if you're a man, can expect to die just less than six years earlier than a man without diabetes. A woman just less than seven years earlier than somebody without diabetes. So we see that just the diagnosis of diabetes reduces years of life. But we really see those numbers becoming, I think quite scary is in people with diabetes and established cardiovascular disease. Where actually somebody of the age of 60 with both of those diagnoses can expect to die 11 years prematurely in a man or 14 years prematurely in a woman. I think those are quite shocking and stark figures. And of course, remind us that actually secondary prevention of the highest risk patients once somebody has had a cardiovascular event, they’re then the highest risk for losing years of life. So of course, what do we want to do, put in those interventions earlier on, isn't it, to try and prevent a cardiovascular event ever happening in the first place.

6:11 **Speaker:** So why does Type 2 diabetes carry this increased cardiovascular risk? You'll be extremely relieved to hear I am not going to go through the complex pathophysiological pathways involved in these processes because frankly, I am not that way inclined. I want to get to the practicalities, but essentially hypoglycaemia itself carries links with pathways that are pro atherogenic so their production of advanced glycation end product we see on the left bottom hand side of this slide here.

Activation of protein kinase C associated with hyperglycaemia drives atherogenysis. So does hyper-insulinaemia, which of course, is linked to the underlying insulin resistance that we typically see in Type 2 diabetes. That leads to disturbance of intracellular fatty acid metabolism, activation of protein kinase again and indeed TNF type pathways, which drive atharogenysis. Of course, many people living with Type 2 diabetes will also have hypertension and hyperlipidaemia, which again are pro atherogenic pathway generating mechanisms. So we start to see our targets here to reduce cardiovascular risk. So targeting insulin resistance of hyperinsulinaemia, targeting hyperglycaemia, hypertension and, of course, dyslipidaemia.

7:36 **Speaker:** So what I want to do this evening is very much to hang our learning onto a pretend case study, a sort of think through what could easily be a real life patient that you or I might see in the surgery tomorrow. This is David. Let's meet David, and we going to sort of weave David through the next half an hour, 40 minutes. So David is a 49 year old chap. He's been very recently diagnosed with Type 2 diabetes just in the last six months, past medical history of hypertension. So that's how his Type 2 diabetes was identified. He was having his cardiovascular risk screening bloods. In terms of his lifestyle he's an ex smoker, managed to stop a few years ago, and he works in an office or indeed over the last couple of years has work mainly from home, fairly sedentary in terms of his lifestyle. Current medications, so he's been put on metformin for his Type 2 diabetes he’s on maximum dose 1 gram twice daily, and he's also on an ace inhibitor, ramipril 10 mg. And we've got some data about David when he comes for his review. So his BMI is 30. His blood pressure is 142 over 86. We've got a lipid profile, total cholesterol 5.8 an LDL of 2.3 and an HDL of 1.3. What do you think? His eGFR is greater than 90, but his urinary ACR is slightly raised at 4mg/mmol. And his HBA1c is 54 mmol/mol. A lot of data, often I think that Type 2 diabetes can be quite data heavy, of course you want to think about David as a whole person. But certainly this amount of data is quite hard to process. And where on earth do we start? Where do we prioritise things? Well, let's consider David's HBA1c just to start off with. So his current HBA1c is 54 mmol/mol. Gosh, it's an awful lot lower than a lot of the HBA1c’s I've been seeing recently, certainly as we try and recover from COVID, a lot of people with very very high HBA1c triple figures, I wonder if that's your experience as well. But what about David's target HBA1c status?

9:54 **Speaker:** This is where I get to see if the polls are working folks, I've got a poll question for you, this should just pop up onto your screen and you can just vote for your answer. So what do you think is David's optimal HBA1c target? Do you think you'd like to get it to less than 48 mmol/mol? Less than 53 mmol/mol. Or are you quite happy at 54, you want to keep it less than 58 mmol/mol? So what do you think is your optimal target when you're having a chat to David and you're looking at his glycaemic control? What do you think you would like to get it towards? It's 54 at the moment remember, just give everyone a minute to vote, and hopefully then the answers will just pop up by magic.

Lovely, thanks everyone. So most people want to go for the tightest target less than 48 mmol/mol followed by the 53, and some of you are happier going for less than 58. And we know, of course, glycaemic control is really important in Type 2 diabetes isn’t it and for a long time we have focussed really I think almost solely on glycaemic control. It's been a really important part of management of Type 2 diabetes and of course continues to be and I absolutely agree. David’s young, he’s very early in his Type 2 diabetes journey. We definitely want to get that HBA1c down and keep it there for as long as possible. And I agree. I think going for less than 48 is very appropriate in this gentleman. But what will that do for him?

11:25 **Speaker:** So what do we know about the role of glycaemic control and cardiovascular risk? What difference is it going to make for him? Well of course, can one go to a diabetes talk without hearing about the seminole UKPDS study? Gosh, it's an old study now, but it's still a goodie, and we base quite a lot of what we do upon it. So of course, the UKPDS study compared intensive glycaemic control to a more relaxed approach in people newly diagnosed with Type 2 diabetes. So just like David our patient, and what they showed is that after 10 years of intensive glycaemic control, there was a significant risk in microvascular events, especially retinopathy twenty five percent relative risk reduction, but actually not a statistically significant reduction in cardiovascular events. That did become more significant when they went back 10 years later, 10 years after the study affinity went back again and there was a more significant effect on cardiovascular events at that time. But the reduction microvascular events was definitely the biggest outcome that was seen from the UKPDS study, and indeed you can see this rather complicated forest plot. But the other big studies looking at intensive glycaemic control have showed the very same, that actually the benefit on macrovascular risk is not that great. You can see that all of those little horizontal lines and shapes are just to the left of our vertical line, favouring more intensive control but none of them are particularly significant when you band together all these big studies. So Accord Advance UKPDF and VADT, you get just about a significant reduction in major cardiovascular events of about nine percent relative risk reduction, which is mainly driven by a reduction in myocardial infarction. So what does this tell us? Yes, glycaemic control is important, particularly in reducing microvascular complications, but not so important in reducing cardiovascular risk.

13:25 **Speaker:** And really, this has led to a, I suppose, a change in the way that we think about the overall management of people with Type 2 diabetes, very much driven by the cardiovascular outcome trials for some of our newer agents. And I really like this way of thinking about things. So whereas previously we might have been quite glucocentric, so focussing very much on HBA1c, and that's certainly something that I have done over the years. We're now moving to try and think more about overall cardiovascular risk and indeed reducing mortality for our patients living with Type 2 diabetes when we think about those numbers of years of life lost from that previous slide. Of course, if we can do anything to reduce those and help our patients live longer, this is something that I'd be rather pleased to achieve. So instead of being glucocentric, I like to think about it now as a three way thing. So first of all, yes, I still want to reduce HBA1c, particularly to reduce those microvascular complications. But I also want to tackle multifactorial cardiovascular risk factors. So blood pressure, lipids, weight reduction, smoking cessation and so on. And we want to think about prioritising the medications that reduce cardiovascular events, particularly in patients with established cardiovascular disease or those at particularly high risk. The SGLT2 inhibitors and some of the GLP-1 receptor agonists. So we've talked about glycaemic control. It remains important, of course it does, particularly in microvascular risk. And certainly with David, we want to bring it down less than 48 mmol’s, if at all possible, and keep it there for as long as possible to reduce his exposure to glycaemic load over the next 5, 10, 15, even 20 years of his Type 2 diabetes journey. But what about multifactorial intervention? What about tackling all of those other cardiovascular risk factors?

15:23 **Speaker:** This is one of my favourite studies that really always reminds me of just how important it is to try our best to tackle all of these cardiovascular risk factors. It was called the STENO 2 study. It wasn't a big study it was set in Denmark. It started a long time ago. And it looked at patients with Type 2 diabetes and microalbuminuria. Important to remember, of course, that microalbuminuria is, of course, an early warning sign of diabetic kidney disease, but also an independent cardiovascular risk factor all of its own. And remember David our friend in this case study does indeed have a raised urinary ACR and microalbuminuria. So in this STENO 2 study, not a big study just a hundred and sixty patients they randomised in the intervention group to patients having intensive management of all of these risk factors for eight years. So they had intensive control of their blood pressure, very low lipid targets, help with smoking if it was required and intensive glycaemic control and all of those things were very well addressed for an eight year period. And what they showed was at the end of the eight years, significant reductions in cardiovascular deaths and indeed of death from any cause. You see there an absolute risk reduction of cardiovascular death of 13 percent and an absolute risk reduction of any cause of mortality of 20 percent. Those are massive, absolute risk reductions. And so we know that if we can tackle all of these things, we can make a significant difference. But what I really like about this study is they went back twenty one years later. So after eight years, they left the patients alone and their blood pressures came up a bit. The lipids came up a little bit. Glycaemic control drifted up as well. When they went back twenty one years later and looked again, they found that those patients that had had that multifactorial control for eight years still had significantly less cardiovascular disease than those that did not. So a 15 percent absolute risk reduction in stroke and eight years additional life expectancy compared to the group that didn't get the multifactorial intervention. So again, talking about numbers of years of life that we might be able to add onto patients if we can try and address all of these factors. But it's not easy, is it? You know, we have got limited time. We've got complex patients with multimorbidity and polypharmacy. How can we tackle glycaemic control, blood pressure, lipids, lifestyle weight reduction and so on in one single review? Well, indeed, I think it's really very difficult.

18:02 **Speaker:** So if you have to prioritise, where should it be? Where’s the biggest bang for our buck, if you like in terms of cardiovascular risk reduction? So this is very much epidemiological population level study data, but it gives us a good idea into hierarchy of interventions and reduction of cardiovascular events. Let's just look at the data in that table there, so we're looking here at what happens when you do certain interventions in terms of number of cardiovascular events that you prevent for every 1000 patients over five years. So if you lower HbA1c by 0.9 percent, so that's what 10 mmols mol in new money, you'll prevent eight of those cardiovascular events. If you lower cholesterol, total cholesterol now by 1 mmol per litre. You prevent 23 of the events. And if you lower blood pressure by 10 over 5 mmols of mercury, you prevent 29 of those cardiovascular events. I think it's a really useful reminder, if you know if you're going to prioritise and your main priority is cardiovascular risk reduction. Actually great blood pressure control is the most important factor, followed very closely by very good active lipid management, followed by glycaemic control. A really good reminder, I think, of prioritisation. OK, then what are we going to do for David? Where on earth are we going to start with his cardiovascular risk reduction? We've already worked out his glycaemic control.

19:34 **Speaker:** But what about lifestyle interventions? Of course each and every consultation for Type 2 diabetes will always start with this, a reminder about lifestyle. How can we support David to make those healthy choices to help him with his diet, to help him with exercise? It can be really difficult can’t it. Where are we with the evidence? So alcohol, of course, is always something to talk about with somebody like David. Is he drinking very much? Is that perhaps adding to his cardiovascular risk? And certainly we've got well proven links between high alcohol consumption and increased cardiovascular risk. In fact, generally speaking, there's a linear relationship that’s been demonstrated with most cardiovascular diseases showing the lower the better in terms of alcohol consumption, certainly below 12 units a week. Smoking, of course, a well-established link with cardiovascular risk. I don’t need to show you that, we're going to support David, although it does say he’s an ex smoker. We want to very much keep it that way to reduce his cardiovascular risk. What about diet? Always a controversial one, isn't it? What diet are you going to recommend to David to maximise his cardiovascular risk reduction? So good evidence levels about reduction in caffeine and salt in terms of reducing hypertension of course. What about which diet after that? Well, the problem is there's not brilliant, randomised, controlled trial evidence for one diet over another at the moment. This is one published in the New England Journal of Medicine that was called the PREDIMED study a couple of years ago, which did show that perhaps the Mediterranean diet approach has the biggest impact in reducing cardiovascular events in people with high risk of cardiovascular disease. Do you know what I always say, though, actually is it's the diet that the patient can sustain, stick with and afford. And that has to be it, doesn't it? Individualised dietary advice. Exercise of course, definitely closely linked with reducing cardiovascular risk. This is one of my favourite documents around exercise actually it’s a few years old now. It was a joint Royal Colleges report called ‘Exercise the miracle cure and the role of the doctor in promoting it’ well worth the read it draws together lots of the evidence around multiple different diseases, including cardiovascular disease as well of course, and a good reminder that actually even just getting somebody who's completely sedentary to become moderately active will significantly reduce cardiovascular death. They quote reduction in cardiovascular death, for getting just that person up and moving by about 31 percent. So a real important reminder that we can make a serious difference, even if it doesn't feel like perhaps you are. In terms of aerobic exercise, we know the aerobic exercise has a significant impact on reducing blood pressure. So there was a network Meta-analysis in the British Journal of Sports Medicine back a couple of years ago in 2019, which showed actually that regular aerobic exercise has the same blood pressure lowering ability as starting a common antihypertensive. That's a lovely conversation to have, isn't it? Well, your blood pressure is up a bit, but actually, if you could start doing some regular exercise, it might be that we can avoid adding this extra medication and bring that blood pressure down to where it needs to be. And what about weight management, of course, we want to support Dave to reduce his weight and have a healthy weight. And there's been some really interesting studies around weight and cardiovascular risk, including one called the EPIC study, which actually is looking mainly at cancer risk and overweight and obesity. But they’ve also done a cardiovascular offshoot from this study, which showed that excess weight is associated with increased cardiovascular risk even when everything else is controlled. So when HbA1c is okay when blood pressure is OK. Excess weight will still be associated with an increase in cardiovascular risk. And of course, we know in Type 2 diabetes that weight loss reduces insulin resistance, that core patho physiology at the very basis of Type 2 diabetes.

**23:33** **Speaker:** Sometimes motivating lifestyle change though, can be really difficult. And would you describe as heart sink sometimes, some of the conversations with people living with Type 2 diabetes, but like it or not we do see the patients who have the most to gain from making those changes. So as I said, the small change can still be really significant and don't forget the power of our words, the power of brief intervention and the language that we use can make a huge difference. A couple of great resources to remind you of, motivate to move is a Welsh born and bred CPD for general practise, all about motivational interviewing and getting people exercising. There’s some really nice videos on there and some really good motivational interviewing techniques to use in primary care. So do have to look at motivation to move. Another resource I'd recommend is one called Moving Medicine and this has got some disease specific motivational interviewing ideas for us. Whether you've got one minute or five minutes or a bit longer to have the conversation. There's a couple of really useful resources that we might want to utilise to make our brief intervention when we are motivating lifestyle change even more powerful.

**24:46 Speaker:** But let's get to some of the nitty gritty in terms of prescribing then in cardiovascular risk reduction in diabetes. So do you think - this is your second chance for a poll folks. Do you think that David should be on a statin? So to remind you, he's a 49 year old chap just diagnosed with Type 2 diabetes, his BMI is raised and his LDL was 2.3 with a cholesterol above 5. Do you think you he should automatically be put on a statin? Yes or no? What do you reckon? Are you sticking David on some atorvastatin?

OK, lovely. So most of you say yes, but some of you are holding back and saying, well, no, maybe David might get away without a statin at the moment.

**25:36 Speaker:** So where is the evidence base and what are the guidelines saying just now? So first of all, do we need to do cardiovascular risk scoring in our patients with diabetes? Well, the NICE lipid guidance dates back to 2014, so it's a little bit on the old side and they’re planning to do a big update to it next year, in fact. But actually, even when they did the update in 2014, they did say that we should risk score people with Type 2 diabetes to individualise preventative therapy. So previously there was probably very much sort of fire and forget strategy that as soon as somebody was diagnosed with Type 2 diabetes, certainly once they reach the age of 40, we would automatically give a statin. That's very much because it was believed that having a diagnosis of Type 2 diabetes was equivalent to having had a cardiovascular event and therefore more like a secondary prevention approach. But actually, the evidence has really emerged now, and we know that in fact, that's not the case, and the risk actually comes about the same after about eight to ten years of having Type 2 diabetes or in people that develop chronic kidney disease. So sometimes we can postpone giving a statin in people who have a Qrisk of less than 10 percent. It's not a lot of people, but we are seeing younger people being diagnosed aren’t we with Type 2 diabetes. So certainly there are some situations where that Qrisk will be less than 10 percent. Of course we do have to consider lifetime risk in that and remember that Q Risk only gives us a ten year cardiovascular risk score. So you might want to consider what's this person's lifetime cardiovascular risk from having these conversations? And also increasingly, we have to remember women of childbearing age. A lot of us will be managing people with Type 2 diabetes in their 20s 30s. If you're looking after ladies worth considering, is this lady trying for a baby? Am I wanting really to put her on a statin? Is she using good contraception at the moment? The other reason it's worth mentioning Qrisk I think beyond in fact statin therapy, is that also is going to become important in making other treatment decisions, particularly things like early use of SGLT2 inhibitors. Nimish alluded to it very briefly, but next week there's a big event happening, folks. The first NICE Type 2 diabetes guidelines for seven years is due to come out next week. I've seen the draft. I’ll share the draft very briefly with you in just a moment or two, but certainly they are looking at using Qrisk to decide whether we should use SGLT2 inhibitors, particularly early on in Type 2 diabetes.

28:11 **Speaker:** So if we put David's information into the Qrisk risk calculator, this is QRisk 3, by the way, there was a big update to Qrisk 2 that happened in 2018, but is not part of anyone's primary care systems yet very much still curious to integrate it onto our systems and the same across England as well. It's got a few new important cardiovascular risk factors there such as severe mental illness, rheumatoid arthritis and a few others probably coming to an update near us in the next few years may. But if we put this information into Qrisk, his ten year cardiovascular risk score is over 15 percent. So I think probably we are going to consider offering or maybe encouraging David to have a statin.

28:54 **Speaker:** So let’s remind ourselves what the NICE guidance says. I'm mainly talking about Type 2 diabetes this evening. That's our bread and butter in primary care. Worth just reminding ourselves of the Type one guidance I think because I wonder how much this is adhered to. So this is what NICE says in Type one diabetes, we should consider atorvastatin for all adults over the age of 18 with Type one and offer it to all people with Type one diabetes over the age of 40 or those that have had Type one for ten years or more. Now remember if someone's diagnosed in childhood that ten years comes around very early on or indeed those with other risk factors. It's a quite widespread advised use of statins in Type one diabetes. I suspect that doesn't necessarily happen, very interesting to know about. In Type 2 diabetes you are familiar with this of course, we should offer atorvastatin 20 mg if the ten year cardiovascular risk score is more than 10 percent. So definitely a conversation that we want to be having with David around use of statin therapy now to reduce his cardiovascular risk. And remember, of course, in secondary prevention that whacking 80 mg atorvastatin dose.

**30:06 Speaker:** But what target are you aiming for? Now certainly historically, I've had very much a fire and forget approach to statin therapy, so I've decided that David needs to go on atorvastatin 20 mg, I give it to him, job done. But shouldn't we be going back and reviewing targets and uptitrating? Well, the answer is probably yes. So in NICE guidance, it says we should aim for a 40 percent reduction in non-HDL cholesterol. I never really liked that target, and I think that's one of the reasons I probably haven't really paid very much attention to it. We get hundreds of results to go through. Have we got time to calculate whether that was a 40 percent reduction in their non-HDL cholesterol or not. Pragmatically I’m aiming more for perhaps a 1 mmol decrease from baseline total cholesterol or ideally aiming for at less than 5 at least, if I can get it there and NICE do encourage that we should treat to target. So consider increasing the dose, changing to a more potent statin or adding other therapy such as ezetimibe or referring our very high risk patients for a PCSK9 inhibitor if appropriate. Now, interestingly, if we look at the evidence base over the last five, six years since NICE published their guidance, it's very much been a trend towards looking at LDL targets.

A lot of the evidence is showing that LDL is the most atherogenic lipid and the lower the better. There's no J-shaped curve here with LDL. The lower you get your LDL, the lower your cardiovascular risk. And recent guidance from our European colleagues very much follows this. So for every 1 mmol/mol fall in LDL, we see a 22 percent reduction in cardiovascular morbidity and mortality. So the European lipid guidance came out in 2019 and is very much focussed on active management of lipids and low LDL targets. It's a lovely guidance, and it very much stratifies people into levels of cardiovascular risk, and it gives you an LDL target according to that level of risk. I suspect when NICE update their guidance, they will go in a similar direction.

**32:19 Speaker:** So I'm just going to share with you those groups, those risk groups starting at moderate risk. I'm not showing you the low risk group because everybody with diabetes is at least moderate risk of cardiovascular disease, according to this European guideline. So we can see that, for example, if somebody has had diabetes for ten years or more with no target organ damage and has any other additional risk factors so hypertension for example, they would fall in that Middle High-Risk group and I put at the bottom there the LDL target. So you could see they’re quite low. So in that high risk group, in the middle, we've been aiming for an LDL of less than 1.8. But what if someone's got established cardiovascular disease or any target organ damage, including micro albuminuria because that is kidney organ damage, they go into that right hand very high risk of cardiovascular disease group, according to this European guidance, with an LDL target of less than 1.4. Or if you can't get there, a 50 percent reduction from baseline. So actually, our patient, David, would be in that very high cardiovascular risk group and we should aim for a really low LDL target. So yeah, we're going to talk about starting atorvastatin and we’re going to look what that does to his LDL. Generally speaking, you'd get about a 50 percent reduction in LDL with a potent statin so thinking about probably atorvastatin 40 mg, we see about a 50 percent reduction in his LDL. We might need to then increase the dose if necessary or consider adding ezetimibe and perhaps we can talk more about ezetimibe later on. But I'm certainly using it a little bit more widely now well-tolerated and often can get you about another 20 percent reduction in LDL.

**35:05 Speaker:** Last poll question we've done HbA1c. We've done lifestyle intervention, we've done lipids. What about blood pressure? So David's current blood pressure is 142 over 86. What do you reckon, folks? What is David's optimal blood pressure target? What are you aiming to be? Less than 130 over 80 Less than 140 over 90 or Less than 150 over 90. So what would you like David's blood pressure to be, what number have you got in your head for him? We've seen that hypertension is probably the most important thing that we can control in order to reduce his cardiovascular risk. So what do you want to get it down to? Thanks, everyone. Brilliant. So most people, pretty aggressive, want to get it down to less than 130 over 80. I agree again here the lower the better, really, in terms of the evidence, particularly in someone like David, young, not frail, nothing much in the way of co-morbidities. I quite agree. You want to aim pretty low.

**35:10 Speaker:** So where are we with hypertension? What are we meant to be doing? So in terms of the targets, previously in the previous iteration of the NICE Type 2 diabetes guidance, the target in Type 2 diabetes was less than 140 over 80, or a bit lower particularly if somebody had kidney, eye or cardiovascular disease and of course, our friend David has got micro albuminuria. Now, interestingly, NICE have relaxed that target a little bit. So when they did the NICE hypertension guidance in 2019, they included people with Type 2 diabetes, and they say the target is less than 140 over 90 for everybody with Type 2 diabetes. Now our friends across the sea, both in the US and indeed in Europe, do aim for these lower guidance. Less than 130 over 80, particularly in young people, particularly if there's also evidence of chronic kidney disease. And certainly, of course, we want to individualise targets. So, yes, NICE want everyone to have less than 140 over 90 and absolutely that’s the aim isn’t it to get everybody down to less than 140 over 90. I've got loads of people with Type 2 diabetes in my care that have not got blood pressures lower than that. So I definitely want to get everyone down to there. And I agree with what you said in the polls. Someone like David, young, earlier Type 2 diabetes, high lifetime cardiovascular risk, you'll want to get that blood pressure that bit lower again.

**36:40 Speaker:** How should we do it? So what NICE say in their updated hypertension guidance is we should go for an ACEi inhibitor or an angiotensin receptor blocker, first line for hypertension in everybody with Type 2 diabetes, regardless of age. So even in people over the age of 55, if they've got Type 2 diabetes, it should be an ACEi or ARB first line. They do acknowledge that in people of black African or African Caribbean origin, it should be ARB rather than ACEi inhibitor, but also acknowledge that even the ARB may be less affected in people of these ethnic origins, and they may require additional treatment a little bit sooner. Interestingly, going back to our European friends, they very much advocate dual therapy for hypertension from the outset, which is an interesting idea because as we all know, the majority of patients will end up on at least two antihypertensives won’t they and they’ve very much shown there's good evidence for this. But actually going for two from the beginning and get blood pressure down to where you want it to be more quickly with lower doses of medication and therefore potentially less side effects. Interesting idea. The other point, perhaps to pull out around hypertension before we move on to our final little section is that NICE advise that in people with diabetes, we should check standing and seated blood pressures. This is especially relevant, of course, in older adults, and we know that postural falls and blood pressure are much more common in Type 2 diabetes, particularly after a long duration of Type 2 diabetes when there'll be a degree of autonomic neuropathy going on. So certainly well worth checking, standing and seated. And actually, if we identify a postural drop, particularly in older patients, NICE recommend treating to a standing blood pressure target. I think that's a really useful little tip. I don't think we could finish talking about cardiovascular risk management in diabetes without mentioning the new cardiovascular outcome trial data can we.

**38:40 Speaker:** So I'm just going to touch upon it, don't panic I am not going to go into the intense detail of all of these studies but this just shows us all of the cardiovascular outcome trials for the new agents that have come out for managing Type 2 diabetes since 2013. Of course, some of them have been really exciting because some of these trials have demonstrated cardiovascular risk reduction. So positive benefits in terms of cardiovascular disease in people with Type 2 diabetes. And indeed, these are the ones that are highlighted here on this slide that have shown positive benefits. So the SGLT2 inhibitors and a number of the GLP-1 receptor agonists. And that means now when we're choosing medications for managing Type 2 diabetes, we should also take into account potential positive effects on cardiovascular risk from those choices.

39:34 **Speaker:** So I've drawn you a set of scales here, reminding us of which diabetes medications have got evidence of decreasing cardiovascular risk and which have no effect at all. So DPP-4 inhibitors so that’s glyptins, Sulfonylureas and Insulin have no effect on cardiovascular risk either way, Metformin Pioglitazone do have some soft evidence from years ago, so the UKPDS study did show some positive effects at reducing cardiovascular disease, particularly in years down the line and particularly when Metformin was used, only about 340 patients in that study so the numbers were very small. Pioglitazone has got some again soft evidence around reducing cardiovascular disease, particularly stroke, particularly in people with established cardiovascular disease or in those that had a previous MI. However, the evidence for the newer agents so the SGLT2 inhibitors and the GLP1 receptor agonists is absolutely overwhelming. Big studies, huge trials that, of course, have been the buzz of diabetes management over the last few years. So the SGLT2 inhibitors have been especially beneficial in heart failure, they are now heart failure medications all on their own aren’t they. And the GLP-1 receptor agonists good evidence in reducing atherosclerotic cardiovascular disease. That's ASCVD and stroke.

**41:00 Speaker:** This is the guidance that I've therefore been following when I've been prescribing in Type 2 diabetes over the last few years, while we await the NICE update. I'm not going to go through the detail, but this is the European and the American guidance for Type 2 diabetes at the moment. And the difference about the new guidance and NICE is going to go in this similar direction as well although slightly different, is they ask us after Metformin to make a decision as to whether that person has established cardiovascular disease or heart failure, or whether they're particularly high risk of cardiovascular disease. And if they are, we go down the left hand side of this prescribing algorithm. And what they encourage us to do is to add an SGLT2 inhibitor or a GLP-1 receptor agonist onto Metformin independently of the HbA1C. So even if somebody like David, where their HbA1c is 54. And you might be quite happy with their control. If they’re high risk or have got established cardiovascular disease. The advice is that we should be adding these agents on for their cardiovascular risk reduction, regardless of HbA1c. A total different mindset I think about the way that we actually use diabetes medicines in Type 2 diabetes.

**42:14 Speaker:** What are NICE going to do in their update due next week. Much buzz and excitement around, still in draft form at the moment, although a little birdie tells me that it is not going to change very much when it comes out next week. This is a very tiny little snippet from the proposed guidance and again, quite similar asking us very early on to decide if that person has established cardiovascular disease or is high risk for cardiovascular disease and particularly promoting very early use of SGL2 inhibitors in those groups. Let's wait and see the full guidance when it comes out, and I look forward to joining you in the next month I think it is to do a good update around these.

**42:49 Speaker:** So back to David, what are we going to do for David? Where should we start before we go to some questions this evening? We're, of course, going to talk to David about lifestyle interventions. How can we support him with weight reduction, with exercise to reduce his cardiovascular risk. We're going to talk about lipid management, so we're going to offer him a statin and we're going to titrate it and remember he’s in that very high risk cardiovascular group. So we want to aim for really quite a low LDL target, ideally less than 1.4 for his LDL, according to the European guidance. We definitely want to keep his blood pressure less than 140 over 90 it’s just above that at the moment with a systolic of 142. So let's get him doing some home monitoring let’s see what that mean looks like. And really, exactly, as you said, I want to get that a bit lower. Less than 130 would be great, especially because we know he's got micro albuminuria as well. In terms of glycaemic control, yes, it's still important, particularly for microvascular risk. We want to get it less than 53, maybe even less than 48. And I would think now about adding an SGLT2 inhibitor now. Yes, it will help with his HBA1c, but also it's going to protect his heart and his kidneys. Remember, he's got a raised ACR, and the recent NICE CKD guidance says that anyone with an ACR above 3, we should consider an SGLT2 inhibitor along, of course, with his ace inhibitor that he's already taking.

**44:16 Speaker:** So conclusions, I've got a couple of resources to show you, and then I'll definitely going to come to some questions if anybody anybody's got any for us this evening. People living with diabetes are at significantly higher cardiovascular risk than those without. Multifactorial cardiovascular risk control is associated with the best outcomes. If we can try and tackle all of the cardiovascular risk factors, we're going to be on a winner. In terms of dyslipidemia, yes, we should use Qrisk to score cardiovascular risk and offer atorvastatin in Type 2 diabetes when someone's ten year risk is over 10 percent. But titrate to individualised target. Definitely a move globally to look at LDL with aggressive targets being set. We definitely want to control blood pressure we saw it’s the most important cardiovascular risk factor, aiming for at least 140 over 90 and probably lower in younger patients like David. When we're thinking about prescribing our diabetes medications. We want to think about prioritising those glucose lowering medications that come with cardiovascular protection, particularly in our highest risk patients.

**45:22 Speaker:** Before I go to Nimish for your questions there’s a couple of resources, just two or three slides to remind you of. So if you work in Cardiff and Vale, you'll be familiar I'm sure with Community Health Pathways, all of the diabetes community health pathways are there and updated. So do use those and hopefully they are coming further across Wales very soon as well. This is a save the date for you, a shameless plug. I do sit on the Primary Care Diabetes Society committee, but the PCDS conference is always really good to attend and the Welsh one is going to be face to face day on Thursday the 12th of May at Jury’s Inn in Cardiff. So if you fancy booking a place for that completely free to attend, do go on the primary care diabetes website, [www.diabetesonthenet.com](http://www.diabetesonthenet.com) and reserve yourself a free place. It's going to be a fabulous day.

**46:12 Speaker:** Finally, don't forget that everybody in Wales now with Type 2 diabetes has access to online structured education called MyDesmond so anybody can access this. They just go to MyDesmond.Wales and they can sign up for an account. It's completely free. It's an online support tool, essentially lots of education there and resources available for patients diagnosed with Type 2 diabetes. That's a fabulous resource in Wales, and I always like to mention these again. Born and bred in Wales, brilliant resource to use with patients. These are pocket medic videos, short, patient orientated films for people to watch and learn about Type 2 diabetes. Loads of them out there, including on kidneys and diet interventions, remission, so on and so forth. Available in multiple languages as well, so do go to the pocket medic site, which is there on the slide for you.

**47:05 Speaker:** Right Nimish I think it's time I stopped talking now and we've got a few minutes left for any questions if anyone's got any for me.

**47:13 Chair:** Thank you, Sarah. That was an excellent overview of managing cardiovascular risk in diabetes and lots of really interesting little snippets there. There are no questions, either they're all very hungry and they want to get away or you've stunned them with all your knowledge. Right from the very beginning in the early slides the females did worse with mortality is that the post-menopausal effect.

**47:42 Speaker:** Yes there's definitely some degree of that. There's also some evidence that women with diabetes and cardiovascular disease get identified a bit later as having developed that cardiovascular disease. So that's just always worth bearing in mind I think, remembering that our ladies are probably at slightly increased risk rather than anything and to get them identified early on. But yeh that comes with absolutely perimenopausal increased risk as well.

**48:04 Chair:** No, it was really, really good for me. The LDL targets, the microalbuminuria, the checking the Qrisk which is different to what we've been doing in the past, really, really interesting. And obviously the newer medications are going to be really used a lot more. I'm seeing that already coming out of secondary care and I'm sure that they’re going to be more widely used with better outcomes. What about weight loss and using medication like the injectables for that? Obviously, there's a lot of talk around about that and some of the injectables are going to be coming out as a once weekly injectable, which makes it easier to use and maybe not even for the diabetics or the pre-diabetics or the people on the borderline. And I think there's going to be tablets soon as well so that's even easier.

**48:55 Speaker:** Yeah, it's already out Nimish. Yeah so GLP1’s is quite an exciting field actually. So we know the GLP1’s are really effective at reducing HBA1C, but they are very potent weight-loss drugs as well. And you're absolutely right. So when we use them in Type 2 diabetes, you'll often see quite significant weight loss and people don't mind a once weekly injectable and several of them now are once weekly injectable which is great. But there is an oral tablet already available. So once daily tablets oral Semaglutide and we can use that it's a bit of a faff to take it has to be taken on an empty stomach with just a little sip of water and then nothing else for 30 minutes, so a bit of a faff to take because that increases the availability of it, but certainly another option for GLP1’s. But we are definitely going to see the GLP1’s ones coming in to the weight loss field outside of Type 2 diabetes, as well, so already we've got high dose Liraglutide marketed as Saxenda which has been licenced for weight loss outside of Type 2 diabetes. It's had a NICE technology appraisal, and it's quite specific in terms of the group that is recommended for. So it is people with prediabetes under a Tier three weight management clinic so quite specific where we're going to see our use on the NHS, but you may well have patients that are getting prescribed it privately. I've certainly got a few people who go to a private weight management clinic and are on Saxenda or high dose of Liraglutide. And high dose Semaglutide will be the next one that's coming out. Amazing weight loss data from the step trials, which have been released recently. So it's on its way, definitely. But whether we'll get to use it in primary care for weight loss, I suspect not. They are rather pricey.

50:37 **Chair:** Thank you Sarah. Well, there's no other questions. That's been a fantastic talk thank you very much. Thank you very much, Sarah.

50:46 **Speaker:** Thank you very much Nimish for having me. Thank you. Good night, everybody. Thanks.