

Nathan Wong: 00:03

Welcome, everyone. And thank you for joining this podcast. The major objective of this podcast is to help your patients with type 2 diabetes understand their risk for cardiovascular disease and the importance of blood pressure, lipid and glucose control in particular in managing risk. With the central theme, really being that diabetes is more than a blood sugar problem, it is a cardiovascular problem that warrants addressing its associated cardiovascular risk. The purpose of this podcast series is to reduce cardiovascular deaths, heart attacks, strokes, and heart failure in people living with type 2 diabetes.

Nathan Wong: 00:47

And it's based on the collaborative initiative between the American Heart Association and the American Diabetes Association, called Know Diabetes by Heart™. This series is brought to you by founding sponsor Novo Nordisk and national sponsor Bayer. My name is Nathan Wong and I'm a cardiovascular epidemiologist and professor and director of the Heart Disease Prevention Program at the University of California, Irvine. And I'm also a past president of The American Society for Preventive Cardiology.

Nathan Wong: 01:23

And joining me is Dr. Colette Knight, an endocrinologist and diabetes and metabolism specialist. She is also chair of the Inserra Family Diabetes Institute and division director of endocrinology at Hackensack University Medical Center. Let's begin just by making a few points about the epidemiology and background of this issue. As we discussed, diabetes is more than a blood sugar problem, it really must be viewed as a cardiovascular condition, since heart diseases, particularly coronary heart disease and heart failure, as well as cerebral vascular diseases, such as strokes are principle causes of death in persons with diabetes.

Nathan Wong: 02:14

We really need to get our patients to know their numbers. In particular, their lipid levels, such as LDL cholesterol, but also triglycerides, blood pressure, A1C in particular, these should be all checked on a regular basis. But we also need to make sure patients understand their numbers and targets, such as for BMI and waist circumference, smoking status, dietary, and physical activity habits as well. Also since chronic kidney disease is a major complication of diabetes, knowing an eGFR or an albumin-creatinine ratio is also very important.

Nathan Wong: 03:01

Why is blood pressure control, lipid management and glucose so important? Well, these are really the key metrics that your patients need to understand to be well controlled. And this can really make the difference between whether or not they're going to suffer a heart attack, stroke or heart failure event. We have known for a long time from numerous clinical trials that tight blood pressure control can reduce not only microvascular, but also macrovascular

complications, such as a 44% reduction in stroke or 56% reduction in heart failure as seen in UKPDS.

Nathan Wong: 03:43

Also, as we know, there's a large evidence base of statin trials that show that statins are just as effective in preventing cardiovascular complications in people with versus without diabetes. About a 20 to 25% reduction in risk for every 40 milligram per deciliter reduction in LDL cholesterol. And finally, our newer anti-diabetes medications, namely the SGLT-2 inhibitors and GLP-1 receptor agonists have revolutionized diabetes treatment, because of their impact on cardiovascular outcomes. And Dr. Knight might like to add a few points to this.

Colette Knight : 04:32

In my own practice, I find that it's the most difficult concept for patients to understand until they begin to actually have symptoms of chest pain, shortness of breath or things like that, and then they're able to understand their association. In terms of managing patients with diabetes, the treatment plan has to be personalized and there are a number of factors that we have to take into consideration. The type of diabetes, how long that patient has had diabetes, because that might actually affect the severity of hyperglycemia. We also have to look at what other medical issues do they have in addition to diabetes? So, do they have high blood pressure, high cholesterol? Is there an issue of weight that we also need to address?

Colette Knight: 05:36

And one key thing is to really think about the patient's preference in terms of management. Many might be surprised to realize that patients actually come into the office already having some sense of what treatment they want to use. I certainly agree that the use of SGLT-2 inhibitors and GLP receptor agonists have absolutely changed and in some ways revolutionized the treatment that we are able to pursue for diabetes. And with that, we have seen significant improvements with weight loss and glucose control. But it's really important to be able to say to the patient that we now have medications that can lower glucose, improve A1C, but also improve heart health.

Nathan Wong: 06:25

Yes, those are very important points, Dr. Knight, and really the whole shared decision-making concept about deciding together with the patients what are the most appropriate therapies for them is really, really important in really making them understand that the therapies that reduce cardiovascular risk really need to be prioritized, because it's cardiovascular disease that is more likely to kill them rather than, for example, amputation or retinopathy. These are very important points.

Nathan Wong: 07:15

One very important theme of this podcast is the importance of composite risk factor management. And so, this is, in particular, managing together not only to blood sugar, but also blood pressure and LDL cholesterol. And we have data, for example, that we have published from pulling three major U.S. prospective studies in cardiovascular disease that was published in Diabetes Care in 2016, showing that achieve and control of A1C, blood pressure and LDL together was associated with approximately 60% lower risk of cardiovascular outcomes compared to having none of these under control. And, in fact, the results, I might mention, were especially striking for the African American populations that were included in those studies.

Nathan Wong: 08:29

We also know that other studies such as the Steno-2 clinical trial done in Europe shows more than 50% lower risk when in people receiving multifactorial risk factor control. But the sad state of affairs in America and throughout much of the world is that despite our advanced healthcare here in the U.S. and generic therapies that are available for addressing all these factors, we have 25% or fewer adults with diabetes at target for all three of those factors.

Nathan Wong: 09:12

And this is from data we published in the U.S. Diabetes Collaborative Registry, as well as the National Health and Nutrition Examination Survey. There is really a huge gap in achieving these guideline recommended targets together. And I'm curious with you being an important clinician in this field, how do you feel we can best improve this clinically inertia problem?

Colette Knight: 09:52

Well, I certainly agree that inertia is an issue and it's an issue certainly among providers, but also among patients. So, I think with the patient, we need to be very clear in our communication and emphasize that, yes, we want to manage glucose, but that treating cholesterol and also blood pressure are important parts of this management. We need to explain to the patients the therapies that we are using, why they're important and how we expect those treatments might help them. For example, if someone is using an ACE inhibitor or an ARB for blood pressure, we should also emphasize that these have kidney protective effects. I think if we allow patients to see that a single drug can have multiple purposes, they're more likely to follow through. Patients need to have a team that works with them. That includes the educator, the endocrinologist, or diabetologist, and the primary care doctor and other specialists who might be involved.

Colette Knight: 10:57

But those providers should also be communicating, so that when the patient sees them, we continue the same message of adherence to treatment and

looking at targets. It's important for patients, after they've done their blood test, to show them the trends, but also to remind them what the target is. And when they improve, we really need to emphasize that they have done a good job. I think sometimes patients simply don't know how they're doing. And if they don't get any feedback, they don't really know if they should continue. A lot of the times when patients come to us in the practice, they are often very confused about why they should continue a statin therapy if their total cholesterol is less than 200 or if the LDL is at goal. But we always have to emphasize to them that at least from the studies that we've seen published several years ago now, that at any LDL, a statin drug is important for cardiovascular health.

Colette Knight: 11:59

In terms of inertia among physicians, a lot of that sometimes comes from their experience. A lot of physicians have significant challenges in terms of accelerating the treatment to injectable therapies, use of insulin, for example. And there are many times when they are also not as familiar with the newer drugs. As you know, we've had many new medications recently, and these medications were developed after many of us left a more formal training setting.

Colette Knight: 12:34

And so, one has to invest a lot of time to really learn about these new medications and how to use them. As an endocrinologist, I'm invested in this, but you can imagine a primary care doctor, who is overwhelmed with so many other medical conditions they have to manage. And so, we have to think about how we can disseminate the education to these providers so that they can learn about these medications, learn how to use them fairly quickly, and so that they can implement them in their own practice.

Colette Knight: 13:05

Cost is also an issue why sometimes we are stuck using some medications that may not be optimal, because the newer medications, though they have great efficacy, they are out of reach for so many of our patients.

Nathan Wong: 13:20

Well, thank you for those comments. I think you really hit the nail on the head. We really need to have this multidisciplinary, what we call a cardio diabetes care team really instituted at every hospital to really address the spectrum of risk in our patients with diabetes. I might also point out that I think we really, now that many of our institutions have very sophisticated, electronic medical record systems, there's really a significant potential to leverage these to improve quality of care, really by, for example, identifying and sending messaging out to physicians whose patients say have not had a recent lipid profile or A1C or blood pressure check in a reasonable amount of time, or who are not at target, or who are not at recommended therapy, such as statin

therapy. And so, there's a lot we can do to utilize the EMR also to educate physicians and through use of the patient portal mechanisms to even educate patients. This is really going to be a dramatic area, I think, in the future.

Nathan Wong: 15:05

Now, one of the things is we should talk a little bit about what targets would be appropriate. And as we know, there have been recommendations to get the A1C below 7%, maybe even lower in our healthier diabetes patients. But perhaps we can be more lenient in the more complicated patients with diabetes, such as those with extensive microvascular disease or macrovascular complications, or longstanding diabetes, or labile glucose control has been pointed out by Silvio Inzucchias well as others and the ADA guidelines.

Nathan Wong: 15:58

Also remember that while we don't have specific LDL cholesterol targets, since our guidelines are really based on prescription of different statin intensities with a high-intensity statin recommended for those at highest risk, most clinicians really like to see the LDL below 100 or ideally below 70, and those at highest risk, particularly if macrovascular disease is present. Then finally the blood pressure target, as we know, has been specified to be less than 130 over 80, since the 2017 guidelines. And perhaps there are some other targets, Dr. Knight, that you would like to see patients achieve?

Colette Knight: 16:47

Absolutely. I think the A1C is one to address because I think it's still for most of us to measure that we use to assess glucose control. And for any patient, the provider should be very clear about what that patient's A1C should be. And I agree that for the young, healthy, usually less than 7% is fine. For my older patients with significant underlying illnesses, 8% could be appropriate for that group. But certainly, over the last few years, as we've been using continuous glucose monitors that have really allowed patients to track glucose in real time, to provide that data to their physicians, to assess and evaluate, time in target has now become another metric that sometimes we have found to be just as important and maybe even more important than A1C, because it really allows you to know if the patient is at goal. And for many of us that time in target is a glucose level of 70 to 180.

Colette Knight: 18:00

And if the patient is achieving that 70% of the time, then they are actually in target. And I think why that is helpful is because the patient can see those numbers in real time. And being able to look at glucose excursions on a daily basis, they can actually act on that. They may change the way they eat. They may adjust certain behaviors because they now understand that they can actually be proactive about assessing their glucose control. I think looking at weight, weight loss improvements in that is also another metric because weight is such an important issue in terms of how patients respond to treatment.

Colette Knight: 18:46

If they gain weight, they become resistant to insulin. They need maybe more treatment. If they lose weight, they become more sensitive, but they also sometimes become more motivated, but it also improves the risk for other illnesses. And so, I think that we have the standard metrics that we assess, and I think that those are a good baseline, but we certainly need to look at other metrics that the patients can actually be engaged in measuring. And I think that that is really how we can get them more engaged in their management.

Nathan Wong: 19:22

Yeah. And I'm happy that you mentioned a point about weight loss because as we know, from the recent American Diabetes Association, there was a debate. And whether perhaps weight loss should be the new A1C, right? Whether a 15% weight loss should be the new diabetes target. Perhaps it's too premature to say that should replace A1C, but I think we can probably all agree that it is reasonable to make that one of the key targets. And we of course now have newer therapy such as semaglutide as shown in the step one trial, as well as tirzepatide shown in a Surmount trial that really give the patient more tools to reduce their weight and potentially also dramatically reduce their cardiovascular risk. So really a lot of interest in data on that.

Colette Knight: 20:42

I agree. And I think the shift that we are seeing now is that patients want to use medical management for weight loss. They're active, they're calling, they're requesting these new therapies. And the advantage is that you can use these new GLP agonists, whether or not you have a history of diabetes. And so, it really opens up to a much larger group. And I have found that one because they're given once a week, the burden of taking a medication is significantly reduced. So many patients find them relatively easy to use, even those who might be adverse to using an injectable therapy, many of them have certainly come around to using these treatments.

Colette Knight: 21:32

I think that the next few weeks and months are going to be quite an eye-opening and even an exciting time to see how some of these newer therapies impact our patients. We've had a several years now of use with semaglutide. And we've certainly seen in the benefits in terms of glucose lowering, weight loss, and certainly the cardiovascular benefits have been published in the sustained trial. And now we have tirzepatide and that certainly from the most research Surmount trial, the weight loss potential of at least 20% is quite significant. And I think that these medications will certainly improve the life and certainly the outcomes of a lot of our patients.

Nathan Wong: 22:22

Wonderful. Yeah, no, I think there's incredible potential in some of these newer therapies, towards improving not only diabetes control, but the cardiovascular

risk associated with diabetes. I think it's very important that we make a few points about how can we address different patient barriers to achieve an optimal care? We certainly know that for example, with there's a lot of fear around statin use and it's very, very important that we educate our patients that yes, while statins may slightly worsen the glucose levels and some were able to treat that, but you can actually prevent five or more heart attacks and strokes for every situation where the glucose could increase.

Nathan Wong:

23:32

And they really do need to understand this whole risk benefit ratio, social determinants of health are also extremely important. There's all sorts of issues regarding healthcare access, the neighborhood built environment, and such as those with lack of access to healthcare or living in food deserts or without safe places to exercise really have greater risk. And I'm curious, Dr. Knight, your thoughts on what are the best ways that we can address some of these patient barriers.

Colette Knight:

24:20

Yes, certainly, it's really important to think about social determinants of health whenever you're thinking about diabetes and heart disease, because in many ways these are social illnesses. There are many ways that an institution or a physician can begin to address that. First of all, we need to understand which determinants are actually affecting our patients? Several months ago, really because of the COVID pandemic and some of the issues that we're seeing, we did a small little pilot study. We have the SDOH questions, the social determinants of health questions already in our EMR. And so, they are available for any provider to ask the patients.

Colette Knight:

25:04

And so, we basically decided to have every patient with diabetes, answer those questionnaires over three to four months. And we were certainly surprised that the patients who had issues with housing insecurity, that we did not know about or food insecurity that wasn't known to us, or some who had significant issues with depression and so on that would not have come out if we were just doing a standard medical visit. When we think about diabetes management, yes, we have the medical aspect with the treatment, but we have to think about the social aspects as well.

Colette Knight:

25:45

We also have to think about how do we reach those communities that may not necessarily come into our academic centers? So, we have to go into those communities. We have to go to the community centers, faith based centers. We have to meet with their local leaders so that they can begin to have some rapport with the medical institutions and centers that are in their community so that they can certainly come in to have the treatment that they need, so I think that... But it won't necessarily be a single institution or provider in order to

really change the barriers that affect social determinants of health, these will require significant policy changes both at the local level, regional level, even the national level.

Colette Knight: 26:38

But I think as we begin to engage in these discussions and as more and more providers begin to see the importance of understanding them and thinking about how to address them, I mean, something as simple as having access to a behavioral health specialist in a diabetes program is incredibly helpful. They can help patients navigate issues around insurance, issues around mental health, even housing applications. Something as simple as that is important. If a hospital provides medications for patients who are being discharged, you might be able to prevent a readmission for someone who may not be able to afford insulin because you provided the medication.

Colette Knight: 27:21

They may only need it for a short time, and then they can actually get better and take a medication that they can actually use. Now is the time I would say for every provider to really take ownership in terms of what they can do to help patients address those issues, but also the institution as well, to think about how they can have broader programs for identification, for assessment, and if possible, to address how they can mitigate these factors that for so many people are actually preventing them from getting the care that they need.

Nathan Wong: 27:58

Thank you so much. I think that was really a beautiful overview about all the different ways that we can try to address these patient barriers. And I completely agree with you that this really requires change at the society level, and we have to get the governments involved, both local, state and of course, the national level to address these problems in our underserved communities in particular. Let me switch gears and go back to cardiovascular risk and remember that in order to decide how intensively and what the best therapies that should be used in a particular patient are, we really need to start with understanding our patient's risk. And we can, for example, as recommended in our ACCAHA, multi society guidelines to use the pulled cohort risk score to initially estimate someone's tenure risk of a cardiovascular event.

Nathan Wong: 29:31

And this is recommended also in people with diabetes, because there's a wide spectrum of risk seen in those with diabetes, not everyone is necessarily a coronary heart disease risk equivalent, which really was an older concept that came out about 20 years ago. But there are of course majors, not in the risk score, such as A1C and duration of diabetes and newer risk scores under development may help address some of these. I should also mention there are also important diabetes, specific risk enhancement factors. Those I just mentioned, but also presence of microalbuminuria, chronic kidney disease, even

subclinical atherosclerosis, we've done some work with coronary calcium that was published from the Multi-Ethnic Study of Atherosclerosis for example, showing that there's a tenfold variation in future cardiovascular event risk. And those with diabetes dependent under level of coronary calcium. Event rates range from 0.4% per year in those with a zero calcium score to tenfold greater, 4% per year, higher than even many people with preexisting cardiovascular disease if the score was 400 or higher.

Nathan Wong:

31:14

This really speaks to the point that diabetes is not necessarily risk equivalent and we need to do proper risk assessment. Also, the guidelines pointed out certain female specific risk enhancement factors, such as we know that someone with a history of gestational diabetes or preeclampsia, this can further add to their risk and thus can help the physician decide to treat this patient more aggressively. I think these are very important points to consider doing a comprehensive cardiovascular risk assessment. And I'm curious maybe if there are other further tools that Dr. Colette Knight might recommend to further assess how aggressively someone should be treated based on their cardiovascular as well as other diabetes risk.

Colette Knight:

32:36

I absolutely agree that actually this coronary calcium score has actually become quite important in our management. And I find that it's been helpful to have that information as I am working with the patient to understand the best treatment, or maybe why we should be using a statin, because that is certainly something that you can use as evidence. I certainly, usually for each patient, I would calculate the cardiovascular risk scores because the patient needs to understand that and learn how to use that information. You mentioned two groups that I think are quite high risk, those with gestational diabetes and those with preeclampsia. And those are two groups that remain at risk because for the patient with gestational diabetes, they have this notion that once the pregnancy has ended, then the risk of developing diabetes has ended. And that is clearly not the case.

Colette Knight:

33:46

So, for those patients, it's important to continue to assess them, maybe during a glucose tolerance test, several weeks after continuing with education, they should have A1C checked at least once a year, so that they understand that having had gestational diabetes, the risk of long term diabetes is still present. Preeclampsia as you know is a mixed disease that we know a lot about. And yet we are still learning, but also very concerning. And it's not unusual to have a patient who have both of these conditions at the same time. And so there certainly is a lot more.

Colette Knight:

34:29

For my patients, I usually want to have a very clear understanding of what the cardiovascular disease is because now we have targeted therapies that can be used to actually act on heart disease. If someone has heart failure, that's been clearly defined, then I might consider using an SGLT-2 inhibitor in that patient because we have studies showing that they do improve heart function. If someone has atherosclerotic cardiovascular disease, I might be more inclined to use a GLP receptor agonist. And so, I think the better that we can understand and define the other cardiac related conditions, the better we will be able to determine risks, but also to treat these patients.

Nathan Wong: 35:23

Yeah, there's no question about it that we do need to know what... Have a complete cardiovascular history. And whether or not the patient has a history of heart failure, that's going to help you in deciding whether some of these newer therapies like SGLT-2s may be most appropriate. I think that's a critical point. We have covered an awful lot of really interesting points in this podcast. And I really want to, again, thank the American Heart Association, the American Diabetes Association, and the Know Diabetes by Heart initiative for the opportunity. And also, especially Dr. Colette Knight, who has really shared a lot of her valuable, clinical experience in terms of what she feels are really important priorities. I think we can all agree on what our important cause to action regarding this program.

Nathan Wong: 36:48

Really, we have focused on the importance that we get our patients to know their numbers, not just A1C, but also blood pressure and lipids. We talked about the importance of weight control, perhaps as a very important primary target that we need to focus on. And really the whole concept of making sure that these risk factors are managed together. Too often, either the patient or the clinician or both, their focus might be on one of these, like A1C. And we don't pay enough attention to the other risk factors. And clearly there is evidence that if we control these risk factors together, that we can dramatically lower future cardiovascular risk by 50 or 60% or more. This message really is extremely important. We recommend that you download resources such as a new pocket guide and a shared decision making guide that are available at <https://www.knowdiabetesbyheart.org/> all one word.

Nathan Wong: 38:13

Also, we encourage you to look for further information about this initiative that is constantly being released by going to that website, [knowdiabetesbyheart.org](https://www.knowdiabetesbyheart.org). And we want to hear from you as our audience, if you have suggestions for future content, by emailing Know Diabetes by Heart at knowdiabetesbyheart@diabetes.org. It's our very important mission to reach as many listeners as possible with this lifesaving information. And if you enjoy this podcast and are listening on iTunes or Google Play, don't forget to leave us a rating and subscribe. Again, I want to thank Dr. Knight as well as our staff at the

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