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## Refining Strategies for Enhancing Cardiorenal Outcomes With SGLT2 Inhibitors: Optimizing the Cardiometabolic Care Model

### Announcer:

Welcome to CME on ReachMD. This replay of a live broadcast, titled "Refining Strategies for Enhancing Cardiorenal Outcomes with SGLT2 Inhibitors: Optimizing the Cardiometabolic Care Model", is provided by Medtelligence and supported by independent educational grants from Boehringer Ingelheim Pharmaceuticals, Inc. and Eli Lilly and Company.

### Ms. Magwire:

Good afternoon. I'm Melissa Magwire, a practicing nurse clinician and certified diabetes care and education specialist and the program director for the Cardiometabolic Center Alliance. It's my privilege this afternoon to be joined with this panel. I'm going to have you introduce yourselves.

### Dr. Miller:

I'm Keith Miller. I'm a cardiologist with Bryan Heart in Lincoln, Nebraska.

### Ms. Denicola:

I'm Dawn Denicola, a nurse practitioner at Our Lady of the Lake in Louisiana Cardiology in Baton Rouge, Louisiana.

### Dr. Bullington:

I'm Matthew Bullington, an ambulatory care pharmacist with Major Health Partners Primary and Specialty Care in Shelbyville, Indiana.

### Ms. Magwire:

Thanks so much for joining me. I know this is going to be a phenomenal conversation today. We'll be talking about refining strategies for enhancing cardiorenal outcomes with SGLT2 inhibitors, optimizing the cardiometabolic care model. These are, again, our faculty. And again, thanks for joining us.

I'm going to start with you, Dr. Keith, and I want you to kind of outline the role of what you are doing in the setting of being a practicing clinician in a cardiovascular center.

### Dr. Miller:

Great. Thanks again for the introduction, Melissa.

### Ms. Magwire:

And I'm going to get your slides up here in just a second. There you go. These are our learning objectives today. And again, we're going to talk about the cardiologist best practices in the management of cardiometabolic renal outcomes in your setting.

### Dr. Miller:

So when I see a patient with cardiometabolic and renal disease, there's certain things that I think about and go through, and I want to try and capture some of that in our discussion today. I think kind of doing a comprehensive cardiac assessment really encapsulates it well, because we're not just thinking about their cardiac problems anymore, because we really have to incorporate an understanding of the other comorbidities that come into play and that affect the management of our patients, especially when it comes to heart failure with

reduced ejection fraction, and how that interplays with our patients' chronic renal disease and our patients' type 2 diabetes.

The guideline-directed medical therapy for patients with heart failure with reduced ejection fraction have been completely rewritten in just the last 2 years. And the biggest rewrite really comes in the use of SGLT2 inhibitors for patients with heart failure with any ejection fraction, but especially with reduced ejection fraction. So I want to talk about that a little bit, and how the management of those heart failure patients, irrespective of their ejection fraction, but especially the low EF group, interplays with their type 2 diabetes since now one of the 4 pillars of treatment for those patients with HFrEF is a diabetes drug that's used and does affect glycemic control. So we have to consider things like chronic kidney disease and diabetes when we're thinking about their heart failure treatment.

Along with that, it's really important in our clinics that we focus on patient education and counseling, because they're not used to having their cardiologist talk to them about medications that are used typically to treat diabetes. So it's really been a game changer for us.

Let me start with a case study. A 68-year-old man, and this is very typical for someone that we might see in our cardiometabolic clinic or our general cardiology clinic, for that matter. A 68-year-old man with a history of type 2 diabetes, hypertension, chronic kidney disease stage 3b, and heart failure with reduced ejection fraction. And he happens to have an EF of 38%. And on this particular clinic day, he reports with complaints of worsening heart failure symptoms, an elevated hemoglobin A1c, and a serum of 1.8 mg/dL.

So when I walk into a room with a patient like this and with that particular complaint of worsening heart failure, I'm thinking about their heart failure first and foremost, but also how it relates to their other conditions. If they're talking about some decompensation or something has changed in their heart failure experience, I'm thinking about what might have been the thing that tipped them into a decompensation. Could there be some progression of valvular heart disease? Might they, for example, have developed atrial fibrillation, a common comorbidity that can tip people into congestive heart failure, or potentially coronary artery disease progression or incidents, depending on whether they've had that history in the past? And then I always ask people about compliance with other medications. Maybe they've been on a loop diuretic in the past that they haven't been compliant with for one reason or another. Or the use of nonsteroidal anti-inflammatory drugs or steroids for some other medical problem that might have tipped them into congestive heart failure.

So I consider all those things and think about is there anything else that we might do to further evaluate why they're decompensating and address those problems, manage the rhythm, the valve disease or the coronary disease if appropriate. But then really redirect the focus to guideline-directed medical therapy for their reduced ejection fraction heart failure with a focus on the 4 pillars of therapy for these HFrEF patients, which are all now Class IA indicated.

And it's important because one of those therapies is a diabetes medication, SGLT2 inhibitors, that we consider their other comorbidities in that regard. This patient, for example, we don't know for sure if he has atherosclerotic cardiovascular disease, but we do know he's at high risk. And we know that because he's over the age of 55 and he has multiple additional cardiovascular risk factors. So according to the American Diabetes Association Guidelines, that puts him in a high-risk category. So he is a candidate already and Class I indicated for medications like GLP-1 RAs, SGLT2 inhibitors, in addition to RAS inhibitors and statins. And that's codified into multiple different clinical guidelines – endocrinology guidelines, cardiology guidelines, in addition to the diabetes guidelines. Of course we're going to be thinking about hypertension; we always do. And we want to treat to an aggressive goal, generally, including a RAS inhibitor.

We want to think about the chronic kidney disease, and that's something we haven't always been great about thinking about in cardiology clinic. This patient almost certainly has an indication to be on a RAS inhibitor and an SGLT2 inhibitor, based on the current KDIGO guidelines, as well as the American Diabetes Association. And really best practice would be, in this patient, in addition to knowing what his GFR is, we really should be measuring his urine albumin-to-creatinine ratio to get a further idea of what his risk of progression of chronic renal disease is, according to the KDIGO heat maps.

So we want to think about all those things and incorporate those considerations and how we're crafting his therapy. And if you look at this gentleman's history, he has Class IA indications, all 4 of the Class IA indications to be on an SGLT2 inhibitor. He has type 2 diabetes, so he has the indication for glycemic control. He has high risk for ASCVD events, so he has the indication to reduce major adverse cardiac events as a type 2 diabetic with high risk. And he's got chronic kidney disease, and he has congestive heart failure. Multiple reasons to be on this drug class, which really is not just glycemic-lowering therapy anymore.

Aside from the diabetes indication, this drug class is indicated, as I've said, for cardiovascular risk reduction, for treatment of congestive heart failure, now regardless of the ejection fraction, and also to reduce the progression of chronic kidney disease. These patients are in our clinics every day, so patients with these comorbidities are ones that we need to be thinking about carefully and optimizing their therapy.

Some of the compelling data for use of SGLT2 inhibitors in heart failure with reduced ejection fraction come from the EMPEROR-

Reduced clinical trial. This trial enrolled people with ejection fractions of 40% or less, almost 4,000 patients randomized 1:1 to empagliflozin 10 mg or placebo, with the primary outcome of either cardiovascular mortality or hospitalization for heart failure. And in a remarkably short follow-up interval of just 16 months, they were able to demonstrate a 25% relative risk reduction in that primary outcome measure, which equates to a 5.3% absolute risk reduction, or a number needed to treat of just 19 patients to prevent 1 primary cardiac death or hospitalization for heart failure in 16 months of follow-up. And at least as remarkable as that is how quickly the advantages seemed to accrue. If you look at all heart failure worsening episodes, not just first hospitalizations or deaths, they were able to demonstrate a statistically significant benefit within 12 days of initiation of empagliflozin.

And for that reason, and really the body of evidence behind this drug class, it's not just one trial, there's very strong evidence from the dapagliflozin group of clinical trials as well, and also from the cardiovascular outcome trials with this class that were done and started to be published in 2015. These drugs consistently have shown advantages for congestive heart failure.

And the heart failure with reduced ejection fraction guidelines were updated in 2022, as shown on this slide, to codify the benefits of this drug class, SGLT2 inhibitors, as now a Class I-indicated therapy, along with the renin-angiotensin system inhibitors, beta-blockers, and the mineralocorticoid receptor antagonist drug classes. So they are part of the standard of care. There is no question about that at this point.

In this patient, then, I would be really thinking about trying to individualize his heart failure treatment. Of course, he should be on a beta-blocker for his HFrEF. We should be having him on a RAS inhibitor, and consider whether that best would be served with Entresto [sacubitril/valsartan]. And I would say at this moment in time, with a decompensation, early initiation of an SGLT2 inhibitor has a really powerful role for him, because he needs better A1c control; we know that. And also there are rapid benefits in reducing heart failure risk, really just within a few weeks of initiating the drug class. He also has the indications of chronic kidney disease and ASCVD risk reduction. So for all those reasons, he's a great candidate for this drug class. I would follow him up closely after that with close blood glucose monitoring, checking his kidney function, and over the next 2 or 3 months, trying to optimize his guideline-directed medical therapy to include those 4 pillars at optimal doses.

So that's a classic example of how our practice has changed in the last 10 years. It's not enough to look at coronary disease, heart failure, lipid management, and hypertension anymore. We need to be thinking about comorbidities much more carefully in our cardiology practice, including type 2 diabetes and chronic kidney disease, and making that really a cornerstone of our therapy for these patients with multiple chronic disease states.

**Ms. Magwire:**

Thank you, Keith. That was an excellent outline of what it takes to be that really comprehensive approach in a really complex patient. If you had to give me maybe one more pearl of what you think it takes to kind of coordinate that care and get that patient off from the right standpoint, what would you say?

**Dr. Miller:**

Yeah, it's a great question. I think if you're getting into this area as a cardiologist, coordination of care is so important because we are starting to dabble into the management of a diabetic patient's glycemic-lowering therapies. And if they're already on treatment for their type 2 diabetes, there needs to be close coordination and communication with primary care doctors. And I think we also have to get used to the idea of asking what is their hemoglobin A1c and are they checking their blood sugars at home so we can make appropriate adjustments to other medications.

**Ms. Magwire:**

Perfect. That kind of tees me up for the nursing best practices in the management of cardiometabolic renal outcomes.

So to your point, there are a lot of comorbid conditions for this patient that really require that coordinated approach. So kind of think back, level-set the stage with this patient who's living with type 2 diabetes, also heart failure and chronic kidney disease. So this patient may be seeing a nephrologist who may have a nurse practitioner on board as well, probably a general cardiologist, probably somebody in the heart failure clinic, then their primary care practitioner, who hopefully has a nurse practitioner and a PharmD as well, and then maybe even being seen in the endocrinology clinic with a nurse practitioner, a CDCES, a dietitian. And then, because they're living with diabetes, they may also have to see an ophthalmologist. They need to see a podiatrist, their dentist, maybe someone in sports medicine for an exercise program. These patients are living with a lot of different care plans coming at them, and they really need a coach or someone to coordinate that approach. And so that coordination is really kind of a key aspect to their education and really establishes kind of that needed successful plan for these patients. So keeping that in mind, that not only are they dealing with all of these care plans, they're balancing their life, their family, their friends as well. So really, education, I think, is going to be key.

And so one of the things that I spend a lot of time doing with folks living with CKM disease is making that connection for them. What is

the connection between the cardiovascular, the kidney, and the metabolic system? And really kind of letting them know that it's estimated that about 1 in 3 folks living in the United States has at least 3 risk factors that can contribute to cardiometabolic kidney disease; be that extra body fat, especially around the waist, prediabetes or diabetes, high triglycerides, high blood pressure. And that having one or more CKM condition really puts them at risk for developing others. So really laying that groundwork for them to understand that they really kind of need to look at this as a cardio-kidney-metabolic constellation of disease states that they need to address.

One of the other things that we touch on a lot in our clinic is that so goes the heart, goes the kidney. And really ensuring that these patients understand the link between heart disease and diabetes, but kidney disease and diabetes, but also the heart and the kidney. And some of the heart failure education points that I cover with patients is that heart failure is a term used to describe the heart that can't keep up with the body's needs for oxygen and blood. And while that sounds simplistic, we often really scare patients by saying heart failure, and patients tend to sort of tune out sometimes. So really challenging practitioners to use verbiage or explain the verbiage they're using so that the patient understands and realizes there are steps they can take.

Then the other key term when we talk about heart failure is their ejection fraction, and giving that to them in patient-friendly terms, saying that the injection fraction really compares the amount of blood in the heart to the amount of blood that's pumped out with each heartbeat so that they understand, when we're tossing around these terms, what they mean.

Then when we look at their kidney, DKD and CKD education points, explaining the necessity for a urine albumin-creatinine ratio and an eGFR and giving it to them in terms they understand. Again, a uACR that measures kidney damage and an eGFR that measures kidney function. One of the key terms or goals that I give patients is to let them know that reducing their albuminuria levels can slow progression of kidney disease. And so in patients living with chronic kidney disease or diabetic kidney disease who have a uACR that's greater than 30%, a reduction of 30% or greater can actually slow down CKD progression. So giving them a target. We often give them A1c levels to live by if they're living with diabetes, but giving them this actual endpoint or reduction point actually helps as well. And it's estimated that about 60% of patients with heart failure have some form of kidney disease as well. So again, so goes the heart, goes the kidneys. And really helping patients make that connection.

Empowering patients to take an active role in their health, I think, is one of the keys to actually having an engagement that leads to a successful care plan. So using this from the American Heart Association, this is the Life's Essential 8 that came out from the AHA just recently. And I think it really sets the stage for patients to take an active role in their healthcare. So we're going to go through these fairly quickly, but know that there's a lot online that you can work with with your patients.

So getting healthy sleep. I think sleep is actually a cardiovascular risk factor in itself that we don't often address. And really talking to patients, advising them that they should have at least 7 to 9 hours of sleep per night, and that sleep health, talking to them about sleep apnea, those types of things, how lack of sleep in itself can be a risk factor. Obviously, one of the biggest ones on here is to quit smoking. We are doing tobacco cessation counseling or questioning with every patient that walks across our door and understanding that that's still something that we need to be taking an active role in with these patients. Managing blood pressure. Keeping blood pressure in the range of 120/80 is optimal. You'd be surprised how many patients that we talk to on a daily basis who don't understand that a blood pressure of 130/80 is actually considered high blood pressure. Controlling cholesterol. Non-HDL and LDL levels and their targets, and what those targets should be for our folks who are living with CKD disease. Also eating healthier, whole foods, fruits and vegetables, lean proteins, nuts and seeds. Being more active. It's all well and good to tell someone, "Hey, you need to exercise more," but we really need to set up tangible targets for our patients, aiming for that 150 minutes a week of moderate or 75 minutes of intense physical activity. I often tell patients, I don't care what they do, they can stand in the middle of the room and flap their arms. That works if they can move, but really giving them some goals that they can work towards. Managing blood sugar. Dr. Miller actually talked about the link between diabetes and folks and risk of disease. So monitoring A1c levels, monitoring glucose levels, and taking an active role in that. And then finally managing the weight and achieving it and maintaining a healthy weight. Optimal BMI is between 18.5 and less than 25. And we know that in the US, average BMI is much larger than that. So really working with these patients to maintain their weight and understand that that is a risk factor in itself.

And then finally, explaining guideline-directed medical therapy to patients in a manner that resonates with them. So really understanding that you need to explain the who, the why, the where, and the when of medications to ensure successful adherence. So who would benefit from an SGLT2 inhibitor? Anyone living with type 2 diabetes, anyone with heart failure, anyone with kidney disease, anyone at high risk or already has ASCVD. So often, patients would come into the clinic, have diabetes, they're living with diabetes, and their glucose is under good control, and we go to add an agent like an SGLT2 inhibitor, and the patient thinks, "Well, my diabetes is already under control." Explaining to the patient that you are adding this agent for other issues like heart failure or chronic kidney disease or ASCVD will help ensure that patient understands why you're adding to their medication regimen.

So why should they take that? Well, the why of that we've sort of already explained. It helps deal with that heart failure, with chronic

kidney disease, decreasing the ASCVD risk as well as that glycemic control. The when. When to take it is usually first thing in the morning, because we do know that it can cause glucosuria and increased urination, so we have folks take it first thing in the morning. And we talked about the why and the where. Where it works. It works within the kidneys. I know Matthew is going to do a really good analogy of how that works, the mechanism of action. But where it works within the kidneys and to excrete excess glucose off.

And then finally, we want to talk to patients about potential mitigation of any side effects. We want to talk to patients about staying hydrated, watching their glucose levels to avoid hypoglycemia, as well as avoiding mitigating potential risk for genital mycotic infections, and looking at any of the other benefits they may have, such as a slight lowering of blood pressure and even a few pounds of weight loss. So again, really explaining the who, the why, the where, and the when really helps ensure success adherence.

So on that, Matt, I'm going to throw it over to you and have you kind of talk to the pharmacy best practices in the management of cardiometabolic renal outcomes.

**Dr. Bullington:**

Thank you very much. And today we're going to look at, we've heard about all of the ways that SGLT2 inhibitors work in a cardiometabolic patient, and now we'll look at how they do that.

So we've got the drug class listed there, all the different medications available. What you want to remember here is that there are some slight differences in the effects of the medications. So if you find a patient doesn't respond as well to one of the members of the class, that doesn't necessarily mean that you have to scrap the whole class. It may be worth a shot to try a different medication still in the same class because of all the different benefits that these medications provide.

So as far as the diabetic patient, we see a lower A1c by 0.4% to 1.16%. And those numbers are from the clinical trial data. So anecdotally, we can see better A1c reduction even than that. So we can also see a reduce in systolic and diastolic blood pressure by 4 to 6 mmHg and 1 to 2 mmHg, respectively.

One concern in using it in a patient living with diabetes would be the concern of hypoglycemia. Fortunately, when an SGLT2 inhibitor is used with, say, metformin or a GLP-1, that risk is almost nonexistent. However, when you use an SGLT2 inhibitor with a sulfonylurea like glimepiride or insulin, that is something that you do have to take into account and do have to monitor. And there really is a pretty clean drug-to-drug interaction profile for this class of medications. You do see the potent UGT enzyme inducers such as rifampin, phenytoin, phenobarbital, and ritonavir can decrease area under the curve with canagliflozin, which that does not seem to occur with other medications in the class. But it is something to keep in mind. So if you have a patient that is on rifampin, phenytoin, phenobarbital, or ritonavir, another member might be the best option.

And you can have polypharmacy concerns as we're treating cardiometabolic patients. We all know that these patients typically have quite a few medications in their medication profile. So with the SGLT2 inhibitors, what we see more often than not is the concern is that the other medications are going to accentuate the effect of the SGLT2 inhibitor. So if you're using an SGLT2 inhibitor with a diuretic, you're going to want to make sure that you talk to the patient about getting plenty of hydration, drinking plenty of water, so that they can be aware that that might be something they want to monitor.

So where do the sodium glucose transporters work? They work in the proximal tubule in the kidney. And what they do is they cause natriuresis and glycosuria, ketogenesis, altered sodium-hydrogen exchanger activity, and reduced plasma uric acid levels. So these are their main effects. This leads to decreased intrarenal RAS activation, decreased cardiac pre and afterload, increased vascular function, and decreased arterial stiffness. And in these effects are how the SGLT2 inhibitors not only reduce blood sugar by blocking 90% of the reabsorption of glucose in the kidney, but they also can exert their renal and cardiovascular effects.

So here we've got the guideline-directed medical therapy optimization for the particular patient that we are talking about today. Now, as a pharmacist, I tend to think of this as guideline-directed medication therapy. What can I say? I mean, I'm a pharmacist; I deal in drugs. So you've got the type 2 diabetes with chronic kidney disease, you see an SGLT2 inhibitor, RAS blockade, a nonsteroidal MRA like finerenone, and a high-intensity statin. And for your heart failure patient with reduced ejection fraction, you've got the SGLT2 inhibitor with an ARNI and a steroidal MRA and a beta-blocker and a diuretic. So as you can see, the SGLT2 inhibitors are in both classes of medications. So that is why we want to be able to utilize these medications in as many of these patients as we can. It's very beneficial for the patient, and it can treat more than one medical issue at a time.

And we also have seen in multiple trials the clinical benefits of GDMT and the SGLT2 inhibitors when used in conjunction with other medications required for guideline-directed medication therapy.

So we must try to keep the patients on these medications if we can, by letting them know what types of side effects they can expect, how to treat those side effects. So the side effects that you could expect would be dehydration or urinary tract infection or a yeast



infection. And really, when we approach those types of infections, the treatment is fairly straightforward. So if we can get the patient to understand that so that they might not just have one and say, "Well, I'm done taking an SGLT2 inhibitor," if we can help them get through that, then maybe they can stay on it, and maybe they won't have a return of the UTI or the yeast infection. Because we also want to give them different avenues of prevention for those infections, so stay adequately hydrated and good genital hygiene can help patients stay on the SGLT2 inhibitors and realize their full benefit.

**Ms. Magwire:**

Great. Thanks, Matt. That was a great overview of the polypharmacy. And before we go to Dawn, I just wanted to ask you, I think your role is pivotal in this care coordination, because you've outlined how many different medications a lot of these folks are living with. So a little bit about your role and the importance of that within your care team.

**Dr. Bullington:**

Sure. What we like to do is we like to present the best and clearest picture to the practitioner of exactly the whole patient, their whole medication list. And we want to make sure that the patient also realizes, hey, we're just not throwing another medication on because, again, if we can decrease the number of medications that this patient might be on, which the SGLT2 inhibitors do give us the option of doing that, then that's a real benefit to the patient and can really increase their buy-in.

**Ms. Magwire:**

Great. Thank you.

Well, Dawn, we're going to have you talk today about best practices in your role as you see it.

**Ms. Denicola:**

Perfect. Thanks. Yeah, I'm going to talk about the advanced practice provider and the best practices in the management of cardiometabolic renal outcomes.

Some of the things we'd like to discuss today is really how my assessment is going to complement that of the primary cardiac provider, even the primary care provider. When I first see a patient, I find it's really important to discuss their medical history, of course, but kind of dive deeper into that too, when they were diagnosed with diabetes, what treatments they were started with, how their heart failure progressed, whether it was because of the diabetes or ischemia from cardiovascular disease, and then when their chronic kidney disease came into play.

Targeting any of their worsening heart failure, if they've just been in the hospital for an admission for heart failure or a readmission, this is really going to affect which medications we think about starting and also our plan of care for them.

Evaluating and initiating guideline-directed medical therapy, dose adjustments based on that renal function and their eGFR. For this, I find that making sure they have all of the most up-to-date lab work, looking at not only hemoglobin A1c but also the eGFR and the microalbumin creatinine urine, to see which medications are going to be best for them and explaining to them those functions.

Providing education for these patients is incredibly important. Understanding why they're on a medicine, not just that they need to take it because it's a guideline, becomes very important in their everyday life. I think that we have to talk about social determinants of health and really the environmental factors that are coming into play. If we sit in the clinic and we have all of the best medications and the best diagnoses, but we don't think about if they can get these from the pharmacy or if they have support at home, we're really missing a big piece that can have an effect on their health.

Lifestyle promotion. We've talked a little bit about that today. If you have a patient that currently is not active, American Heart suggests 150 minutes a week, but it's taking a stepwise process with these patients, saying, "Okay, let's go for 15 minutes in one day," and really get them used to moving their bodies more so there's not frustration and feelings of failure, and they can progress to those goals that are really going to benefit them the most.

Ongoing dose adjustments and making a plan for how often we'll see them, bringing them into the clinic, as well as telephone follow-ups and video visits are going to be some of the best ways that we are able to meet them where they are geographically and in their diagnoses.

So talk a little bit about review of ongoing assessment. Again, where they started with these, how they understand their diagnoses. So when they were first diagnosed, is this something that they've taken an active role in? Have they been given treatments and not really understood what they're for? And really finding out, for them, what the barriers have been. When I see them in my clinic it's because typically some aspect of their cardiometabolic disease has been difficult to treat or difficult to get to goal. So what have those barriers been? Is it socioeconomic? Is it they don't understand the need for the daily blood sugar checks or the daily blood pressure checks? And meeting them where they are in that education.

As I discussed, their most recent lab work and testing. And I think this is important. A lot of times, we'll tell patients your lipids look good, or your A1c is better, but giving them on that first visit, the goal, where we want them to be for each of those numbers and sharing with them their progression or regression with each visit to let them know, okay, the plan that we have is actually working, or we need to double down and make adjustments.

Again, review of social determinants of health and referring to social workers when needed to help them, whether it be food, utilities, all of this plays a really big part in their medical care.

Heart failure status. Evaluating the stage and class, it makes a big difference in understanding where the patient is. It's not just a matter of what their ejection fraction is and what their numbers are, but being able to stage this in stage A, B, C, or D can help us with the guidelines, but also their class of symptoms. And for me, we use the KCCQ, so I'm able to show the patient we're better, we're not better. Because a lot of times they'll come and tell me, "Oh, my breathing is good." "My breathing is not good." I don't know what that means, so actually being able to give it a number on their symptom management helps them to see, okay, this is actually quantified and getting a little bit better.

Whether or not they've had recent hospital stays. We talked a little bit about the SGLT2 inhibitors and how they work so quickly, within 12 days, really, to help improve patients. And this includes 30-day readmissions. So getting these patients on the SGLT2 inhibitor as soon as possible, before they leave the hospital if they've had a hospitalization, is very important in helping them to understand why we're adding another medication to their regimen.

Advanced therapies come into play with these assessments. When we talk about, do they need to go to an advanced therapy center? Is it time for us to talk about palliative cardiology and goals of care and symptom management or hospice as well?

Education and lifestyle. In Baton Rouge, where I live, a lot of this is education with these patients, and I know it is nationwide too, but I find for me, the benefit of my cardiometabolic clinic has been time to spend with patients and really seeing where they are in their health continuum. They may be very well versed in their disease process, or they may be at the very beginning. We may have just diagnosed them with diabetes because they came to us with a triglyceride level that was out of control, and now we're dealing with something new. And it's really scary. So helping them understand how these dots can be connected between kidney disease, heart disease, as well as living with diabetes, and how slowing the progression of any of these is going to benefit the whole.

Again, the SGLT2 education such as what to expect. We're going to have them monitor their blood pressure, because you can get a little bit of a dip with blood pressure with this medication, as well as looking for any genital mycotic infections. So staying well hydrated, good personal hygiene, and letting them know if this happens, please keep us posted. Don't just stop your medicine, because we can help treat you with these symptoms, is really important so they know that we could potentially expect some of these things and help them when they start getting symptoms.

Lifestyle modification. These are tools. These medications, all of the guideline-directed medications are great to help with progression of disease and help patients live better lives. But they're tools, so we need that change underlying lifestyle and really help them find out what their goal is. I can't set their goals for them. So where would they like to see themselves? And so what stepwise process do we need to see to get there. And setting them and with each visit saying, "Have we met these goals?" If not, all right, what do we need to do to get back there? Planning for follow-up can include, "I'm going to call you in 2 weeks and see how you're doing on this medication, if you've had any issues." Depending on medical records, they can message us back through the system and see how they're doing. We have a life coach, if you will, that can also call patients and check in on them with their activity to see if they're meeting their goals. Set these 1-month follow-ups if we're making transitions to higher doses of medications or new medications, and also following remote blood pressure monitoring, remote heart rate and rhythm monitoring, if that's necessary for our AFib patients, as well as continuous glucose monitoring, which has been a huge change in teaching lifestyle for these patients. They may not want to be on a continuous glucose monitor forever. I have a lot of patients that seem to be a little resistant, but putting them on one for 2 to 4 weeks so they can continuously see the foods that are elevating blood sugars has been a big eye-opener for most of our patients.

**Ms. Magwire:**

Great. Well, that was phenomenal on how you see your role and in the work that you do within your center.

But I kind of want to pull this all together and talk a little bit on this panel. And one of the things that I want to go to is you kind of talked about how cardiologists didn't typically step into this space, and they were really kind of singly focused. We were all practicing in our silos. And what do you think has really been the driving force between that type of approach and now? And I think one of the things we see the most hesitance is our cardiology peers not wanting to kind of dip their toe into the pool of glycemic-lowering agents. So maybe we could start with that.

**Dr. Miller:**

Yeah, it's a great question. I finished internal medicine training quite a long time ago, and then went off to cardiology training, and I was more than happy to say I probably will never have to manage diabetes again. And then here I am managing diabetes way more than I ever expected.

In the last 8 years, it's become 100% clear that it's untenable for a cardiologist not to have a working knowledge of diabetes medications, at least to the point where we can identify a need, just like the patient we talked about, this 68-year-old diabetic patient with heart failure, and say, well, here's a patient that has a very compelling indication to be on an SGLT2 inhibitor. If they're not diabetic or they're not on any diabetes medications, it's pretty straightforward. There's really no difficulty there. But what if they are?

And I think every practitioner has to wrestle with this in their own practice to some extent. And to the listeners that are in a cardiology practice, or cardiologists themselves, I think they need to work through this. At a minimum, I think if you're seeing a patient like this, you need to be able to recognize, oh, they're on other diabetes medications, but the need for this SGLT2 inhibitor is so compelling, I need to find room in their regimen for this.

So what is at least the minimum that I need to do to make sure that I can safely start that medication on this patient? You need to know what is their hemoglobin A1c and are they on other medications that, when combined with an SGLT2 inhibitor, could cause hypoglycemia, and take measures to try and adjust the other medications appropriately. And then communicate, communicate, communicate with the patient's primary care provider or whatever other providers might be involved. Maybe a nephrologist is involved in their care. Communication becomes very important.

And I'm sure these guys have other thoughts about how to coordinate the other diabetes management.

**Ms. Magwire:**

Yeah. Dawn, I know you're in a cardiology practice as well. So how do you kind of navigate that, sort of steering out of your lane which is no longer your lane, but how do you kind of navigate that?

**Ms. Denicola:**

Carefully. Continuous glucose monitoring, to that point, I find is very helpful at this stage because it can really tell us very closely if they're having lows. If a patient is having lows, even if they're not feeling them but we're kind of getting to that level, I'm going to be really careful about their insulin and sulfonylureas. Very close communication with primary care or endocrinology. If a patient comes in and they are experiencing lows and they're symptomatic, I will have them dose back on their insulin. A lot of these patients, they manage this insulin based on their blood sugars anyway, so they're very familiar with how many units at a time. Maybe sometimes more than me, because cardiology is kind of where I hang my hat, not endocrinology. But if it takes picking up the phone, if I'm really concerned, or sending a message through the electronic record. You know, "I saw this patient today. This is where we are. For this reason, they need to be on SGLT2 inhibitor, but these are my concerns. Please advise. How would you best take care of this?" And I think that's going to help gain mutual respect as we start or continue to cross these lines and break down our silos. We may need to make changes, but you're still the expert, you know, teach me what I need to know.

**Ms. Magwire:**

Yeah, great. And then, Matt, I know you come from a primary care perspective and are doing a lot of the titrating and all. And how do you manage that when they have multiple care providers within your care team?

**Dr. Bullington:**

Yeah, I think it's really important that we communicate not just with the other providers, but also with the patient so that we're not communicating around the patient; we're communicating through the patient so that the patient can understand why we feel that this is the best course. So it's very important that we make sure that the patient has buy-in. And we also aren't afraid to utilize diabetic educators and dietitians. We have so many tools at our disposal, so all of the different disciplines in the medical field, if we work together and keep the patient at the center, we can accomplish so much.

**Ms. Magwire:**

As we're looking at guidelines, and we'll talk about those again in a minute, but multi-pharmacy or polypharmacy, and you hit on the pillars of care within heart failure, now we're looking at pillars of care for CKD and DKD. Do you start all the guideline-directed medical therapy meds at the same time? One at a time? And how do you titrate?

**Dr. Miller:**

Yeah, it's a great, important question. And I think there's no question, I think, in the guidelines and the expert communities on managing heart failure. There's been sort of a growing recognition that we take too long getting people onto and titrated up to good target doses of



guideline-directed medical therapy drugs. And a push. And this is, if you read the newer heart failure guidelines that have come out in the last 2 years, they've made an emphasis of trying to get people on, really, all of the 4 pillars of therapy quite quickly. And I've also gotten burned on that a couple of times when I was probably a little bit too aggressive and somebody, their blood pressure really couldn't tolerate it or their kidneys rebelled a little bit. So I think you have to use clinical judgment.

I think the more you can get initiated early, I think I'd rather see them on a lower dose of a beta-blocker, RAS inhibitor, and an SGLT2 inhibitor right out of the gates and then titrate incrementally as you go, rather than starting one, waiting a month, starting a second one and starting a third. I think it's better for compliance for the patients. I think it helps them psychologically recognize the importance of the therapy.

Dawn mentioned, I think, a really important point, which is the value of starting patients on drug in the hospital if they've been hospitalized with an acute heart failure decompensation, because if you discharge a heart failure patient from the hospital not having initiated an SGLT2 inhibitor, the likelihood they'll be on that drug a year down the road is very small. So they're much more likely to stay on the drug. So as much as you think they can tolerate multiple drugs right out of the gate and then titrating over to – I really have a goal to get them on their optimal regimen within 3 months, is kind of my rule of thumb.

**Ms. Magwire:**

Yeah, because you really don't lose them to follow-up.

Matthew, on that standpoint, we know that we've talked a lot about education, and we probably will a couple more times before we're done here. But do you feel like educating the patient when you approach them to say, "Okay, you're going to be on 4 different classifications for medication, just for this one episode that you may have had," in the case of our patient that had a heart failure, new diagnosis, or exacerbation?

**Dr. Bullington:**

Yeah. I think it's critical to help the patient understand what each medication is doing, how they interact with each other, what other types of effects that they might see. In doing so, you just increase your chances of them staying with the whole GDMT therapy. Patients that don't know and have surprises will tend to associate those surprises with any number of medications that get started.

And I think you also have to explain to them the necessity in starting multiple medications. Because in some cases, we've got time on our side, and we don't need to start multiple medications at the same time. And if we can do that, then that makes it easier for the patient to get used to one medication at a time. But in some of these more critical cases, they do need that medication therapy, and they need multiple drug classes all at the same time, so we need to make sure that they're educated on what they're looking for, for each drug class. If they say, "I'm having this problem," they need to have one to go to maybe to where we can talk with them about that and see if there's a different alternative medication.

**Ms. Magwire:**

Yeah. And then, Dawn, did you find if they understand the heart and metabolism and the kidney connection, that they're a little bit more apt to take an active role in the multi-therapy that we're looking at in this case?

**Ms. Denicola:**

Yeah, absolutely. I think understanding that these don't happen in silos, that they are affected, and how living with diabetes increases your risk for heart disease, the vascular as a whole as well, including the kidneys.

Also with these patients, helping them to understand that if you're hospitalized for a heart failure exacerbation, your risk of coming back in the hospital within the first 30 days is really high. That's why we do 7- to 14-day follow-ups, and getting them on these medications as soon as possible really can help keep them out of the hospital and kind of prevent chipping away, as you will, of the strength of the heart.

**Ms. Magwire:**

Great.

I'm going to pick on you again, Dawn, because I know we do a lot of counseling for female patients who have, maybe in the past, had a history of genital mycotic infections. One of the things we at least do in our clinic, we do ask about that, but we also look at glycemic control. And we explain to the patients, the higher the glucose, the more likelihood that you may experience, even off that medication, a urinary tract infection and/or a genital mycotic infection. Anything else in the male or female population when you're talking to them about mitigating those potential for side effects?

**Ms. Denicola:**

No. We've talked about hydration, which you have to balance if you have heart failure patients versus kidney patients, and you have to

kind of find the sweet spot for each patient, what that increased fluid level may look like without causing a problem. Personal hygiene is really important. Making sure that patients are paying very close attention to that and helping them understand that, kind of what we always talk about, is the closer you are to goal, the better you're going to feel. So with this, we get your blood sugar down closer to where it needs to be, we really have less of a chance of having these infections that can cause so much discomfort.

**Ms. Magwire:**

One of the other things that we deal with, at least in our clinic, on a daily basis, and I'm hoping you're not seeing this, but you probably are, are folks that we're seeing for the first time who are living with some stage of chronic kidney disease and aren't aware of that. And I think we talked offline the other day about how cardiologists didn't used to see the uACR as a test that they needed to do, but maybe you could talk about the importance of anyone who's seeing that patient living with CKM disease, really ensuring that these patients are getting tested.

**Dr. Miller:**

Yeah, 100%. I can't tell you how many patients that I was the first one to break to them that they had chronic kidney disease, and I mentioned it because that's part of my thought process when I'm seeing a patient now. So, yeah, they are surprised about that.

But I think if you haven't spent any time with the KDIGO guidelines, one of the most important graphics in that guideline is the heat map, where they correlate GFR and urine albumin with risk of progression of chronic kidney disease. And it's a potent multiplier. So if there's protein in the urine, the risk of progression is significantly higher than if there's not for any given GFR. So it's really ideally not enough to know just the GFR. And uACR is inexpensive. It's very easy to do. And any cardiology clinic can get it.

If you find somebody that has a very high albumin in the urine, you may want to be referring them to a nephrologist, and many of them will have nephrologists involved in their care. But in our market, and I think a lot of markets, it does take time to get in to see a nephrologist. So we don't shy away from those people. We actually feel a greater sense of urgency, if anything, to the people with microalbuminuria.

So certainly, we try to incorporate it into our day-to-day workflow. It's just now part of the discussion. It's like GFR or ejection fraction is to heart failure as uACR is to chronic kidney disease.

**Ms. Magwire:**

Dawn, do you feel like the cardiologists within your sphere, those that you work with, your peers, are kind of making that connection now between the uACR and their overall heart failure?

**Ms. Denicola:**

Yeah, I really think they're starting to. And we've talked about education a lot, of our peers as well. So as we learn things, helping cardiologists who may not work in the cardiometabolic space understand that this is something that we need to start looking at. And so yeah, starting to understand that a little bit better, and also staying in conversation with our nephrology partners and saying, "Hey, we've got this patient, we went ahead and started them on SGLT2." And they're appreciative and agree.

**Ms. Magwire:**

Well, I know I don't want to speak for you, but I know your primary care peers that you work with probably wouldn't care if somebody from a cardiovascular clinic did a uACR. But I know you guys have done a really strong campaign on ensuring that patients know. So some of the education you're doing with patients?

**Dr. Bullington:**

Yeah, we actually have talked with patients about the uACR and the importance. And a lot of it's just using that KDIGO heat map. If you can show a patient the KDIGO heat map and show them how if your GFR can be in the green zone, be just fine, but if your uACR is elevated or extremely elevated, you're still in danger of quickly dropping down to the next level. And so I think our practitioners, our nurses, everyone's done a great job at really prioritizing patients, knowing where they're at with that. I think it's very beneficial. Because and then that way, instead of maybe catching something on the back end where we're trying desperately to save a patient, we can get out ahead of it and maybe just make it to where the patient really doesn't know that there was ever a problem.

**Ms. Magwire:**

Yeah, great.

**Dr. Miller:**

Yeah, I would strongly recommend collaborating with your nephrology groups in your area, if you're a cardiology group, or even primary care. Invite them over for lunch, sit down with them, and just talk about who are the appropriate patients to refer, and what data would you like to see before we send them over? Should we just go ahead and order a renal ultrasound and GFR, uACR, whatever? And our

groups have been very receptive to that.

**Ms. Magwire:**

Great. We've had a couple questions about the ACC and AHA guidelines, Dr. Miller, and the level of recommendation for SGLT2s versus GLP-1s, or in combination with GLP-1s.

**Dr. Miller:**

Yeah. We talked about the heart failure guidelines that have been updated in 2022 and 2023, and the SGLT2 inhibitors have really become, as I said before, Class IA indicated for heart failure. And for preserved EF heart failure or mildly reduced EF heart failure, they are really the strongest recommended drug class now, over and above all the other ones that we've thought about in the past, RAS inhibitors, etc. So they're critical, pivotal drugs, standard of care for heart failure.

The ACC and AHA did come out with an updated guideline on chronic, stable coronary disease in the last year. And for the type 2 diabetic patients in that guideline, they recommend both those drug classes as Class IA recommended, that's GLP-1s and SGLT2 inhibitors. And they actually gave strong economic value to both of those interventions. We think of these, these are brand-name drugs, they come with a cost, but the pharmacoeconomic data is very favorable for these medication classes. So I think we should be thinking of them in our chronic coronary disease patients as just as strongly indicated as statins, anti-platelet drugs, and good blood pressure control.

**Ms. Magwire:**

Great. Thank you.

Well, one last quick question, very quickly, is what about SGLT2s in hospitalized patients with heart failure? Should you wait until they're more stable or not? And, Dawn, I'll throw this one to you.

**Ms. Denicola:**

No. What we found, and what we've seen in the research, is that adding this on, it's not like a beta-blocker. With those, I'm going to wait until my patient is a little more stable. Go ahead and add the SGLT2. It's likely not going to have a lot of effect on their blood pressure. So you can continue diuresing them, and then when they kind of more stabilize, we can start adding the ARNI as well as the MRA, and then the beta-blocker back, of course checking chemistries. But to answer the question, no, start them as soon as you can.

**Ms. Magwire:**

Thanks. So, Matt, I'm going to toss it to you, and then we'll hit each one of you, but really quick, one or two words you think that are the key to coordinated care and putting this all together for our patients.

**Dr. Bullington:**

Multidisciplinary team.

**Ms. Magwire:**

Great. Thank you.

**Ms. Denicola:**

Absolutely patient education. What the goals are, where they are, and how we can not get them to where we want them to be, but really meet them where they are and move them closer to those goals and communication with the team.

**Ms. Magwire:**

Keith?

**Dr. Miller:**

Yeah, in our practice, this has been a great utilization of APPs and clinical pharmacists. They've really helped our practice grow. It's a great use of a multidisciplinary team.

**Ms. Magwire:**

Well, thank you. And thank you to our audience for joining us today, and thank you to the spectacular panel. Really appreciate your time. That's all we have for today. Thank you.

**Announcer:**

You've been listening to a replay of a live broadcast titled "Refining Strategies for Enhancing Cardiorenal Outcomes with SGLT2 Inhibitors: Optimizing the Cardiometabolic Care Model". This activity was provided by Medtelligence and is supported by Boehringer Ingelheim Pharmaceuticals, Inc. and Eli Lilly and Company.

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