[MUSIC PLAYING]

ESRA KARSLIOGLU FRENCH: I am Esra Karslioglu French. I'm a clinical associate professor of medicine here at UPMC AT department of medicine, in division of endocrinology. Welcome to the lecture, Diabetes Mellitus, Who Needs to See an Endocrinologist and How? The goal of this lecture is to give you the updates from diabetes world. I also want to make you aware of new care pathways we created in division of endocrinology, so you can reach out to endocrinologists in an efficient way when you need to.

Here is the lecture road map. We are first going to look at the numbers, the prevalence, the cost, and the complications of diabetes. How does the next 20 years look for our diabetes population? We are going to discuss about diabetes technology, sensors, closed loop systems. We are going to discuss two medication groups, SGLT2 inhibitors and GLP-1 agonists.

I'll try to give you tips how you can incorporate these medications to your workflows. We are going to discuss everything new. And I would like to point you to resources while navigating all these new medications and technology. In the background, we are going to discuss 2020 ADA guidelines. At the very end, we are going to talk about innovative models of care, eConsults, and RAVE clinic.

34 million Americans, or 10% of the population, have diabetes. Most of these patients have Type 2 diabetes. 1.6 million have Type 1 diabetes. Seven million people are undiagnosed. 26% of all seniors have diabetes. 1.5 million Americans are diagnosed with diabetes every year. Most of the diabetics who are younger than 20 years old are Type 1 diabetics.

Diabetes is a growing global problem. This is not a North America problem anymore. If you look at the next 20 years, by 2045, western Pacific countries, including China, will have 183 million diabetes patients, followed by southeast Asia, 151 million people with diabetes. Middle East and North African countries is following this by 82 million.

Diabetes is an expensive disease. One of every five health care dollars is spent caring for people with diabetes. One in three Medicare dollars is spent caring for people with diabetes. The largest components of medical expenditures are hospital inpatient care, which is 30% of total medical cost, followed by prescription medications to treat complications of diabetes. Anti-diabetes agents and diabetes supplies also account for 15% of this cost, followed by physician office visits by 13%.

In addition to being costly and common, diabetes affects survival and decreased life expectancy. A patient who is in their 60s, if they have diabetes, their life expectancy is six years less compared to another patient without diabetes. A patient who is 60 years old who has diabetes and had an MI has a life expectancy of 12 years less. Compared to a patient without diabetes.

Diabetes is the leading cause of cardiovascular disease, kidney failure, blindness, and lower limb amputation. 50% to 80% of people with diabetes die of cardiovascular disease. 44% of new kidney failure cases are observed in patients with diabetes. 30% of people with diabetes age older than 40 have diabetic retinopathy.

Heart failure is under-recognized diabetes complication. Here is the risk of complications in patients with diabetes relative to patients without diabetes. CHF is very on the top. In patients with type 2 diabetes, heart failure represents the complication with the largest excess risk as compared to non-diabetic peers.

Over the last five years, the way we approach diabetes changed, as we had more data about the different diabetes agents. Five years ago, this is how our guidelines looked like. We started with lifestyle changes, healthy eating, weight control, increased physical activity, diabetes education, followed with metformin. Then we had this menu of medications, and it was A1C which drove the decision which medication to add or take away.

Whereas in 2020, the guidelines look very different. A1C is not the major driver to choose the agent, but the risk factors are. As you can see, if patients have indicators of high risk or established cardiovascular disease, chronic disease, chronic kidney disease, or heart failure, we consider SGLT2 inhibitors and GLP-1 agonists independent of A1C target.

And for patients who we care about minimizing hypoglycemia, we choose a certain type of agent. And most of the time, these are DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors. And TZDs. If cost is a major issue, which usually is a major issue, sulfonylureas TZDs and sometimes insulin might be the way to go. If weight loss is the goal, again, GLP-1 agonists and SGLT2 inhibitors are our choice.

So we discuss about the prevalence, complications, and achieving a hemoglobin A1C goal will decrease, especially microvascular complications. Hypoglycemia is the biggest barrier to optimal glucose control. The good news is we have a solution, and it is diabetes technology.

I'd like to share with you a letter I received from my patient's parents. My patient is in his 40s now. He was diagnosed with Type 1 diabetes at age 16. I never met his parents, but they sent me this thank you note after I placed him on a CGM, continuous glucose monitor.

His parents said, "our son has type 1 diabetes since age 16. During the last three decades, we have experienced highs and lows of this dreadful disease. Since he has a CGM, he has a new twinkle in his eyes. This technology changed his life."

I think we all try to do our best to change our patients' lives in the best way we can. And diabetes technologies are here now to help us do that. Hypoglycemia is the biggest barrier to reach our optimal A1C goal. Patients with severe hypoglycemia are more likely to have major macrovascular events, microvascular events, to die from any cause, and have cardiovascular disease. So eliminating hypoglycemia is essential.

Hypoglycemia causes disruption, fear. Patients lose their driver's licenses due to hypoglycemia. They develop complications. It is associated with high medical costs, and there's a ripple effect. As hypoglycemia is the biggest barrier to optimal glucose control, patients, clinicians, and medical societies relax their push for an A1C less than 7%. This is unfortunate. After two decades of gradual improvement in national levels of glucose control, average A1C levels increase.

This paper was published in *Jama* in 2019. It shows trends in diabetes management among US adults between 1999 to 2016. Blood pressure control is getting better. LDL levels are getting lower, whereas A1C has been trending up in the last 10 years. In 2020 and beyond, we must figure out how to achieve both optimal glycemic control and minimal hypoglycemia, and it starts with technology to minimize the ripple effect of hypoglycemia.

This is how my desktop looks at work. I have shortcuts to three different softwares, Tidepool, LibreView, Dexcom Clarity. That's where patients share with me their sensor data through cloud technology. If you have diabetes educators in your practices, ask them to help you to set up these workflows. If you don't have diabetes educators, feel free to chat to me outside of this lecture, and I'll be happy to set up the workflow, or give you ideas how to incorporate these life-changing technologies, so we can all care for our patients in a better way.

Continuous glucose monitors decrease hypoglycemia by 40%. This trial was in type 1 diabetic patients who were in intensive insulin therapy. Patients who use sensors compared to patients who were using finger sticks had 40% less hypoglycemia. We talked about prevalence of the disease, complications, the barriers, which is hypoglycemia, and how technology can help us to overcome these barriers.

Another piece of technology is a closed loop system. It is also known as artificial pancreas. I found that terminology is a little bit misleading, because we are still far from pancreas, but we are in the right path.

So here you see a download of a closed loop pump. On the top part, you're going to see patient's sensor. This is the glucose data. Then in the middle row, when patient eats, they put in the carbohydrate data. They ate 20 grams of carbs et cetera.

And when they put the carbohydrate information into the pump, the pump gives them a bolus formula. In the background, this is the basal rate. In our traditional pumps, these basal rates kind of stayed the same, according to whatever rate we put in. But with the closed loop systems, now the pumps are able to micro-bolus if the blood sugars are high between meal boluses, according to the algorithms that are built in.

This closed loop has been a long journey for diabetics. It is a six-step plan, and we're currently in number four. Step one was for pump to shut off when user not responding to low glucose alarm, and this is achieved. Step two was predictive hypoglycemia causes alarms, followed by reduction or cessation of insulin, kind of preventing hypoglycemia before it happens. Currently, this piece of technology has been also achieved.

The third step was to create the pump that turns off when there's hypoglycemia, but also gives more insulin if there's hyperglycemia. And current technology also is able to do that. And the fifth step is automated basal hybrid closed loop. It's a closed loop system at all times. The only thing patient is doing at this time is meal time manual bolusing. So here we are in 2020, and step four, five, and six are the future goals.

Step five is full automated insulin closed loop, meaning patient puts the pump and sensor on, and they forget they have diabetes. And the last one is currently in the closed loop we only have insulin, whereas a multi-hormone closed loop, where glucagon in addition to insulin is available also is another goal. It's likely to be achieved pretty soon. So better outcomes are achievable with closed loop systems, less hypoglycemia, less hyperglycemia, and quality of life is better, and our patients are much happier.

So I'll give you a quick update about diabetes technology, and how it can help your patients' barriers to achieve better A1C and overall better quality of life. Now I'd like to switch gears to complications again, and I'd like to talk about heart failure. Actually, I'm going to talk about heart failure quite a bit during this lecture that you might think this is a cardiology lecture. But no, you're in the right place, this is endocrinology.

All right, so heart failure represents a substantial global burden, with significant morbidity and mortality. Heart failure is as malignant as some of the common cancers in both men and women. Five year survival rate for heart failure is 50%. The one month mortality rate following a first hospitalization for heart failure is 11%.

Type 2 diabetes is a major risk factor for development of heart failure, which occurs as early, is often undetected in patients with type 2. It is frequent, forgotten, and often fatal in patients with type 2 diabetes. Early identification and diagnosis is important to modify the adverse outcomes. Multiple guideline directed evidence-based therapies exist for HFrEF, with studies underway for HFpEF patients.

In 2015, the first EMPA trial was published in the*New England Journal,* followed by CANVAS trial in 2017, and later again followed by DAPA in 2019. EMPA-REG, CANVAS and DECLARE all showed positive outcomes, major mortality and morbidity risk reduction cardiovascular disease in patients with type 2 diabetes. The fourth trial, VERTIS-CV, probably will be published by the time we have this conference. While this lecture is prerecorded, I don't have the outcomes yet.

DAPA-HF is unique, because not only it looked at diabetes patients with heart failure, and the effect on the cardiovascular death, heart failure hospitalization, and urgent heart failure visits, it also looked at the patients who didn't have diabetes. And they also had better outcomes. Again, ADA updated its approach. And as we discussed, in the beginning of the disease, independent of individualized A1C targets, we now take into account the risk factors or established history of cardiovascular disease, chronic kidney disease, or heart failure while choosing therapy.

Especially patients who are high risk, age older than 55, they have LVH, coronary, carotid, or lower extremity artery stenosis is more than 50%, considered as agents. Patients with heart failure, a chronic kidney disease, especially HFrEF patients with a low ejection fraction, and chronic kidney disease, specifically with eGFR of less than 60, and macroalbuminuria considered again, these agents. And we have ample evidence that they control these risk factors.

Now we have multiple recommendations to support use of SGLT2 inhibitors to manage heart failure risk in patients with type 2 diabetes. And after the DAPA heart failure trial, FDA approved dapaglifozin as a new treatment for heart failure. Patients do not have to have diabetes anymore. So here's a summary of SGLT2 inhibitors in heart failure. This is exciting times with new glucose-lowering therapies.

There is overwhelming evidence that SGLT2 inhibitors reduce the risk of heart failure hospitalization in patients with type 2 diabetes. We are using this in patients with HFrEF even without diabetes now. And they are shown to reduce death, as well as hospitalizations. And we are waiting on the results of trials with HFpEF.

EMPA-REG and CANVAS declare the primary outcome was cardiovascular disease. And they do decrease heart failure hospitalizations, cardiovascular death. CREDENCE primary outcome was the kidney disease. And in addition to all other trials, all these four trials basically showed the same thing, basically, SGLT2 inhibitors are cardio risk reducing drugs, with glucose lowering as a beneficial side effect. What does that mean? That means that SGLT2 inhibitors are not only endocrinologist medications more.

I'd like to share with you some tips about SGLT2 inhibitors. Because as endocrinologists, we've been using these medications for a longer period of time, and now we're all going to use this for diabetes control to decrease cardiorenal risk factors, even patients who don't have diabetes. And we learned some lessons during this time. One, lower doses appear as effective as higher doses. So if your goal is to reduce risk, you can stay in the low dose. You only need to advance the dose if additional glucose lowering is needed.

Patients should be cautioned about the likelihood of increased urinary output and frequency, and the need to maintain adequate hydration at all times. Avoid dehydration while on these medications. If you are starting this medication on a patient with controlled diabetes-- let's say their A1C is less than 7, and they're already on insulin or sulfonylurea you should consider decreasing the insulin and sulfonylurea dose to prevent hypoglycemia. Whereas if you're using this in a non-diabetic patient diabetic patient not using sulfonylurea or insulin, there's essentially no risk of hypoglycemia.

Consider dose reductions of other diuretics in any signs of volume contraction. But you don't need to change doses of other hypertension medications. Consider other agents and patients with urinary incontinence, or men with advanced prostatic disease and obstructive voiding symptoms.

Genital mycotic infections are the most common side effect, but they're easily treated. If recurrent, may need to discontinue this therapy. UTI may occur. It is rare. But do not use with history of severe UTIs, like pyelonephritis, urosepsis, or those at increased risk, like patients with indwelling urinary catheters, stents, or significant stone burden.

One SGLT2 inhibitor, canagliflozin, doubled the risk of lower extremity amputation in one study. We need more information. Although not reported with other members of this class, consider other therapies if a patient has severe peripheral artery disease, active foot ulcers, and/or prior amputations. Do not use in advanced kidney disease.

GFR limit depends on specific agents. Most can be used safely down to an estimated GFR of 30, and even some studies suggest 25. But glucose lowering usually diminishes after 45, while other benefits appear to be maintained. Avoid these medications in patients with hypotension, orthostasis, unexplained syncope or dizziness. These medications are not approved for patients with type 1 diabetes, or other patients who may be ketosis prone.

So I saved the best till the last. This is very important. We need to halt SGLT2 inhibitors three days prior to major surgical procedures when patients will be NPO to avoid ketosis. We don't understand very well, but we know that when patients are NPO, the risk of euglycemic DKA is higher, and euglycemic DKA means patient is in diabetic ketosis. But since they urinate glucose through the SGLT2 inhibitor effect, their blood sugar is not that high, so this can be missed, and it can be fatal.

So when our patients call our office saying, I'll be NPO for a surgery, how do I adjust my insulin, this or that medication, we usually decrease basal insulin by 30% the night before the surgery. And we halt the SGLT2 inhibitors for three days. Also, we recommend halting these medications temporarily when patients are ill or hospitalized, again, to avoid ketosis.

The second class of medications I'd like to discuss, which is the GLP-1 receptor agonist. We've been all using this class of agents for a while now. I think most of us are very comfortable with using them. Especially, the weight loss side effect has been very welcome.

I'd like to point you to this meta-analysis that was published in *The Lancet* in 2019, which looks at seven trials, with a combined total of 56,000 participants. GLP receptor agonist treatments reduce MACE by 12%. It reduced all-cause mortality by 12%. Broad composite kidney outcome, which was development of new-onset macroalbuminuria, declined in GFR, progression to end stage kidney disease were all decreased by 17%.

As you know, GLP-1 receptors come in different flavors, daily use, weekly use. Some weekly agents come with needles on them, some of them you need to order needles, et cetera, so it can be a little bit confusing. And I'll show you some resources to help you. Again, some tips for success with GLP receptor agonists.

Start low dose, titrate slowly. Nausea, vomiting, diarrhea are the most common side effects. Caution patients to eat smaller meals, and to eat slowly. If starting medication in a patient who is already on insulin or sulfonylurea, again decrease insulin or sulfonylurea around 20% to avoid hypoglycemia. Otherwise, if the patient is not on sulfonylurea or insulin, you don't need to worry about hypoglycemia.

Do not use in patients with gastroparesis. Do not use in patients with a history of medullar or thyroid cancer, or MEN2, which are both very rare disorders, but you will need to ask the family history. Most importantly, do not use in patients with a history of pancreatitis.

Consider other therapies if weight loss is not desirable. Most of the time, our patients with type 2 diabetes mellitus are obese, and GLP-1 agonists help with weight loss. But if you have a patient with a normal BMI, or low normal BMI, you might prefer to avoid these medications, as weight loss might not be the goal.

I'd like to show you the timeline of important discoveries in the history of diabetes. So 1922, the first exogenous insulin administered to human. Until now, almost in the last 100 years, there was a quiet time from 1922 to 2000, where in the last 20 years, multiple new agents were discovered, which is great. Now we have multiple options.

But this can also be a problem. Do we have multiple options? Do we have too many options? This is like going to a grocery store to buy pasta sauce, and you look at the shelves, you have too many options, you don't know which one to choose.

Here are a couple of options. We have Humulin 70/30. This is a mixed insulin. We have U-500. This is a regular insulin concentrated five times. Pharmacokinetics are really different. It acts like a long-acting insulin. We prefer this in patients who require more than 200 units of insulin a day.

Now we have NPH. It has been around for a long time. Patients know it as cloudy insulin. Apidra is a short-acting insulin.

Tresiba is degludec. This is one of the new long-acting insulins. The half-life is 24 hours. And in our patients who can't administer their Lantus exactly the same time every day, like our shift workers, Tresiba works great, due to the long half-life.

Novolog mix comes as 70/30. There is Fiasp, very rapid short acting insulin. You know Lantus, and it's now went off patent, so you can see it as Basaglar a glargine U-100. Humalog comes as mixed 50/50 as well as mixed 75/25.

Don't forget about Levemir, which is detemir. Humalin-R is short-acting insulin. Humalog is analog short-acting insulin. And we have inhaled insulin. And don't forget these mixed paths basically. Xultophy is a combination of degludec and GLP-1 agonist. So do you see the problem here?

So here's a question for you. You have a 56 six-year-old female with type 2 diabetes admitted to hospital for lower extremity cellulitis treatment. At home, she's on Toujeo, which is U-300 glargine, and she takes 50 units once a day. Her diabetes is under good control. Her A1C is 6.8.

Now when she's admitted, Toujeo is not formulary in your hospital. Now you need to switch to glargine U-100, which is the preferred medication. So how would you convert to Toujeo 50 units to Lantus 50? Would you simply give Lantus 50 units? The answer is actually you need to decrease Toujeo to Lantus by 20%, because Lantus is more potent. And if it's a patient with tight blood sugar control, if you give the same dose, 1:1 conversion-- you can cause hypoglycemia.

Too many options. This can be really confusing. So as a division of endocrinology, we are creating these resources for all our trainees. One is in Infonet. So if you go to Infonet, and if you type diabetes resources, you will see all these inpatient hyperglycemia reference cards, different insulin formulations, as well as GLP-1 agonist treatments, which needs PAM, which doesn't, et cetera. These were all created by Amy Donihi, PharmD. And it is in your fingertips to, again, give better patient care in this confusing world with many options.

We also created an app. This is under Comp Portal, MyGuide app. You can download it to your iOS device or Android device. And you will see our impatient hyperglycemia management protocol, which can be handy while caring for patients in the hospital.

The last thing I'd like to show you-- Rapid Access Clinic via telemedicine. Like many clinics, in endocrine, we created different care pathways with telemedicine just to give efficient and rapid access to endocrinologists. Traditionally, when primary care physicians assigned a patient to endocrinology, patients had to wait a month to three months, according to where the location of the practice was. So this was really not optimal.

Now we have eConsults, where primary care physicians can put an eConsult in Epic, and an endocrinologist will be consulted. At the end of this consult, we either give some treatment recommendations, and we never meet the patient, or we triage the patient face to face or video visit in endocrine clinic. We also offer same-day 30-minute video visits when patients call central scheduling.

High risk patients can be converted to face to face after a first video visit. But we do, again, in an efficient way, triage patients. Patients with hypoglycemic crisis, we help engage diabetes educators, social workers, and avoid admissions or ED visits.

How about patients who present at emergency room with pure hyperglycemia, no electrolyte abnormalities? Sometimes, these patients are admitted because the primary care physician and the emergency room doctor are worried that the patient will not get timely endocrine care, and they want to avoid a crisis. Now, instead of admitting these patients, some patients might be just triaged in video visit with one of our experienced APPs, who have been trained for hyperglycemia crisis, within 24 hours.

All new patients are offered video visits. That helps us pool our resources together, and decrease patient waiting times. We're a team of physicians, APPs, diabetes educators. Post-hospital discharges with type 2 diabetes patients or patients with diabetes are at very high risk for readmission. And we are offering video visits one week after discharge, again, with our experienced APP clinic. Our APPs and best practice providers are trained through our fellowship program, where we immerse them into a very dense packed inpatient/outpatient diabetes training program.

A little bit about endocrine eConsults before we end. So you can put an eConsult in Epic order. You can place it during the office visit or phone encounter. You can indicate the reason for the consult in comments. Here's a snapshot of our eConsult volume so far.

30% of our eConsults are diabetes. The other 30% is thyroid. And others are osteoporosis calcium disorders, as well as neuroendocrine. 33 of the 50 patients with diabetes had an A1C of more than 8. And 43% of the patients of all 50 diabetes eConsults were managed by eConsult only.

So we just give some recommendations to a primary care physician. seven of these visits were triaged to face to face, or video visit, or CDE visit. So I have follow-up A1C on only nine patients. And 7 out of 9 patients after an eConsult had a reduction in their A1C. So I'm really excited about this.

Here's an eConsult example, where a primary care physician was worried about their patient. They wanted fast, efficient care. New diagnosis of diabetes, thin patient 29 years old. So we really escalated this pathway and so this patient with a video visit the next day. And turns out, she had new onset type 1 diabetes. So PCP orders the eConsult, we review it, and we either give you instructions, or we say we will need to see this patient by video visit, either endocrinologists, APP, or CDE.

So here we are, and 2021 will be 100th anniversary of the discovery of insulin. This is Banting and Best in a picture with the first dog they treated by injecting insulin back after he developed diabetes. So we have multiple options to care for our patients. I hope you found some useful tips. I'll be happy to answer any questions you have. Thank you.