



# eLITERATURE REVIEW

## eDiabetes Review Podcast Issue

Jointly presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing

Supported by educational grants from Eli Lilly and Company, Bristol-Myers Squibb, and Novo Nordisk, Inc.



HOME CME INFORMATION PROGRAM DIRECTORS NEWSLETTER ARCHIVE EDIT PROFILE RECOMMEND TO A COLLEAGUE

### VOLUME 1 – ISSUE 4: TRANSCRIPT

## Featured Cases: CVD Risk Factors in Patients with T2D

Our guest author is Om Ganda, MD, Associate Professor of Medicine at Harvard Medical School, and Senior Physician and Director, Lipid Clinic, and Chair, Clinical Oversight Committee at the Joslin Diabetes Center in Boston, Massachusetts.

After participating in this activity, the participant will demonstrate the ability to:

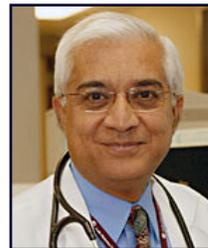
- Discuss managing cholesterol to reduce CVD risk in patients with type 2 diabetes.
- Describe the current evidence for managing dyslipidemia beyond LDL-cholesterol in patients with type 2 diabetes.
- Explain the new recommendations in the management of hypertension in patients with type 2 diabetes.

This discussion, offered as a downloadable audio file and companion transcript, covers the important topic of CVD risk factors in patients with T2D in the format of case-study scenarios for the clinical practice. This program is a follow up to the Volume 1, Issue 3 *eDiabetes Review* newsletter—[CVD Risk Factors in Patients with T2D](#).

### Unlabeled/Unapproved Uses

Dr. Ganda has indicated that his discussion will reference the unlabeled and unapproved use of experimental PCSK-9 inhibitor agents..

### MEET THE AUTHOR



#### Om Ganda, MD

Associate Professor of Medicine  
Harvard Medical School  
Senior Physician and Director, Lipid Clinic  
Chair, Clinical Oversight Committee  
Joslin Diabetes Center  
Boston, Massachusetts

### Faculty Disclosure

Dr. Ganda has indicated that he has received grants and or research funding from Amarin Pharma, Inc., and has served on advisory boards for Amgen and Sanofi.

#### Release Date

July 8, 2014

#### Expiration Date

July 7, 2016

### PROGRAM DIRECTORS

#### Nestoras Mathioudakis, MD

Assistant Professor of Medicine  
Division of Endocrinology,  
Diabetes, & Metabolism  
Associate Director, Inpatient  
Diabetes Management  
The Johns Hopkins University School of  
Medicine  
Baltimore, Maryland

#### Om P. Ganda, MD

Associate Clinical Professor of Medicine  
Harvard Medical School  
Senior Physician and Director,  
Lipid Clinic  
Chair, Clinical Oversight Committee  
Joslin Diabetes Center  
Boston, Massachusetts

#### Susan Porter, MSN, CRNP, CDE

Clinical Nurse Practitioner and Certified  
Diabetes Educator  
The Johns Hopkins University School of  
Medicine  
Baltimore, Maryland

**ACCREDITATION STATEMENTS****Physicians**

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

**Nurses**

The Institute for Johns Hopkins Nursing and the American Nursing Credentialing Center do not endorse the use of any commercial products discussed or displayed in conjunction with this educational activity.

**CREDIT DESIGNATIONS****Physicians**

*eNewsletter:* The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 1.0 *AMA PRA Category 1 Credit(s)*<sup>™</sup>. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

*Podcast:* The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credit(s)*<sup>™</sup>. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

**Nurses**

*eNewsletter:* This 1 contact hour educational activity is provided by the Institute for Johns Hopkins Nursing. Each newsletter carries a maximum of 1 contact hour or a total of 6 contact hours for the six newsletters in this program.

*Podcast:* This 0.5 contact hour educational activity is provided by The Institute for Johns Hopkins Nursing. Each podcast carries a maximum of 0.5 contact hours or a total of 3 contact hours for the six podcasts in this program.

**SUCCESSFUL COMPLETION**

To take the post-test for eDiabetesReview you will need to visit the [Johns Hopkins University School of Medicine's CME website](#) and the [Institute for Johns Hopkins Nursing's website](#). If you have already registered for other Hopkins CE programs at these sites, simply enter the requested information when prompted. Otherwise, complete the registration form to begin the testing process. A passing grade of 70% or higher on the post-test/evaluation is required to receive CE credit.

There are no fees or prerequisites for this activity.

**LAUNCH DATE**

July 8, 2014; activities expire 2 years from the date of publication.

**ESTIMATED COMPLETION**

This activity is estimated to take approximately 30 minutes to complete.

**INTENDED AUDIENCE**

The target audience for this initiative includes: endocrinologists, primary care clinicians, nurse practitioners, physician assistants, Certified Diabetes Educators, and other health care practitioners whose work/practice includes treating patients with T2D.

**INTERNET CME POLICY**

The Office of Continuing Medical Education (CME) at the Johns Hopkins University School of Medicine is committed to protecting the privacy of its members and customers. The Johns Hopkins University SOM CME maintains its Internet site as an information resource and service for physicians, other health professionals, and the public.

Continuing Medical Education at the Johns Hopkins University School of Medicine will keep your personal and credit information confidential when you participate in an Internet-based CME program. Your information will never be given to anyone outside of the Johns Hopkins University School of Medicine's CME program. CME collects only the information necessary to provide you with the services you request.

**STATEMENT OF RESPONSIBILITY**

The Johns Hopkins University School of Medicine takes responsibility for the content, quality, and scientific integrity of this CME activity.

**STATEMENT OF NEED**

- Clinicians do not appropriately intensify therapy as necessary to maintain glycemic control.
- Conflicting data about the safety of incretin agents may unduly deprive patients of treatment benefits.
- Clinicians are not aware of and/or are not implementing strategies to maximize the value of SMBG readings to improve patient outcomes.
- Clinicians do not adequately understand or treat to control CVD risk factors in their patients with T2D.
- Clinicians do not have a sufficiently current knowledge base to effectively consult patients about potential T2D therapeutic advances.
- Clinicians do not adequately counsel and treat their overweight/obese patients with T2D.

**PLANNER DISCLOSURES**

As a provider approved by the Accreditation Council for Continuing Medical Education (ACCME), it is the policy of the Johns Hopkins University School of Medicine Office of Continuing Medical Education (OCME) to require signed disclosure of the existence of financial relationships with industry from any individual in a position to control the content of a CME activity sponsored by OCME. Members of the Planning Committee are required to disclose all relationships regardless of their relevance to the content of the activity. Faculty are required to disclose only those relationships that are relevant to their specific presentation. The following relationship has been reported for this activity:

- **Om P. Ganda, MD**, discloses that he has received grant/research funding from Amarin Pharma.

No other planners have indicated that they have any financial interest or relationships with a commercial entity.

**POLICY ON FACULTY AND PROVIDER DISCLOSURE**

It is the policy of the Johns Hopkins University School of Medicine that the faculty and provider disclose real or apparent conflicts of interest relating to the topics of this educational activity, and also disclose discussions of unlabeled/unapproved uses of drugs or devices during their presentation(s). Johns Hopkins University School of Medicine OCME has established policies in place that will identify and resolve all conflicts of interest prior to this educational activity. Detailed disclosure will be made in the newsletters/podcasts.

**Guest Author Disclosures****CONFIDENTIALITY DISCLAIMER FOR CME CONFERENCE ATTENDEES**

I certify that I am attending a Johns Hopkins University School of Medicine CME activity for accredited training and/or educational purposes.

I understand that while I am attending in this capacity, I may be exposed to "protected health information," as that term is defined and used in Hopkins policies and in the federal HIPAA privacy regulations (the Privacy Regulations). Protected health information is information about a person's health or treatment that identifies the person.

I pledge and agree to use and disclose any of this protected health information only for the training and/or educational purposes of my visit and to keep the information confidential.

I understand that I may direct to the Johns Hopkins Privacy Officer any questions I have about my obligations under this Confidentiality Pledge or under any of the Hopkins policies and procedures and applicable laws and regulations related to confidentiality. The contact information is Johns Hopkins Privacy Officer, telephone: 410-735-6509, e-mail: [HIPAA@jhmi.edu](mailto:HIPAA@jhmi.edu).

"The Office of Continuing Medical Education at The Johns Hopkins University School of Medicine, as provider of this activity, has relayed information with the CME attendees/participants and certifies that the visitor is attending for training, education and/or observation purposes only."

For CME Questions, please contact the CME Office at (410) 955-2959 or e-mail [cmenet@jhmi.edu](mailto:cmenet@jhmi.edu).

For CME Certificates, please call (410) 502-9634.

Johns Hopkins University School of Medicine  
Office of Continuing Medical Education  
Turner 20/720 Rutland Avenue  
Baltimore, Maryland 21205-2195

Reviewed and Approved by  
General Counsel, Johns Hopkins Medicine (4/1/03)  
Updated 4/09

**DISCLAIMER STATEMENT**

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only. Use of The Johns Hopkins University School of Medicine name implies review of educational format design and approach. Please review the complete prescribing information of specific drugs or combination of drugs, including indications, contraindications, warnings, and adverse effects before administering pharmacologic therapy to patients.

**HARDWARE & SOFTWARE REQUIREMENTS**

Pentium 800 processor or greater, Windows 98/NT/2000/XP/7 or Mac OS 9/X, Microsoft Internet Explorer 5.5 or later, 56K or better modem, Windows Media Player 9.0 or later, 128 MB of RAM, sound card and speakers, Adobe Acrobat Reader, storage, Internet connectivity, and minimum connection speed. Monitor settings: High color at 800 x 600 pixels.

**MR. BOB BUSKER:** Welcome to this *eDiabetes Review* Podcast.

Today's program is a follow-up to our newsletter on CVD Risk Factors in Patients with type 2 diabetes. With us today is that issue's author, Dr. Om Ganda, Associate Professor of Medicine at Harvard Medical School, Senior Physician and Director of the Lipid Clinic, and Chair of the Clinical Oversight Committee at the Joslin Diabetes Center in Boston, Massachusetts.

eDiabetes Review is jointly presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. This program is supported by educational grants from Eli Lilly and Company, Bristol-Myers Squibb, and Novo Nordisk, Inc.

Learning objectives for this audio program include:

- Discuss managing cholesterol to reduce CVD risk in patients with type 2 diabetes.
- Describe the current evidence for managing dyslipidemia beyond LDL-cholesterol in patients with type 2 diabetes.
- Explain the new recommendations in the management of hypertension in patients with type 2 diabetes.

Dr. Ganda has indicated that he has received grants and or research funding from Amarin Pharma, Inc., and has served on advisory boards for Amgen and Sanofi. He has advised that his discussion today will reference the unlabeled and unapproved use of experimental PCSK-9 inhibitor agents.

I'm Bob Busker, managing editor of *eDiabetes Review*. Dr. Ganda, thank you for joining us today.

**DR. GANDA:** I'm delighted to be here and to participate in this podcast.

**MR. BUSKER:** In your newsletter issue, doctor, you reviewed newly released guidelines for cholesterol and blood pressure management. What I'd like to do today is look at how that information can inform treatment. So if you would, Doctor Ganda, start us out with a patient description.

**DR. GANDA:** Sure, let me present a patient who is a 48 year old Caucasian male who presents with a

history of type 2 diabetes for 11 years and hypertension for 6 to 8 years. He had a coronary stent placed about 3 years ago after he was found to have an abnormal stress test. His father had a history of stroke at the age of 62 years and his brother had coronary stent placement at the age of 53 years. He works as an accountant, he's a nonsmoker, he has an occasional two or three beers on weekends, his exercise schedule is variable but suboptimal.

On physical exam his BMI was 28.5, his blood pressure was 150/84. He had a mild nonproliferative retinopathy and no other significant findings on physical exam. His medications include metformin, 1,000 mg twice a day, glargine insulin 24 units at bedtime, lisinopril 10 mg daily, hydrochlorothiazide 12.5 mg daily, and simvastatin 40 mg daily, also aspirin, 81 mg.

The pertinent findings on lab results were hemoglobin-A1c of 7.2%, creatinine 1.1, mildly elevated liver enzymes, ALT 44 and AST 60. He had a urine albumin/creatinine ratio of 45, and his lipid levels reveal cholesterol of 170, HDL 48, triglycerides 160, and the calculated LDL cholesterol of 90 mg%.

**MR. BUSKER:** So focusing on this patient's cholesterol — talk to us about the new cholesterol management guidelines from the ACC/AHA. What are the important differences between what just came out and the previous ATP guidelines that most clinicians are familiar with?

**DR. GANDA:** There are several differences which are noteworthy. One of them is that these new guidelines really put more emphasis on preventing cardiovascular disease rather than waiting until the heart attack or stroke has already occurred; in other words, primary prevention, especially in older adults. Because even the so-called normal older adults who don't have diabetes have increased risk of heart disease, and once you have diabetes it becomes even more of a problem. So there is greater emphasis on primary prevention in older adults.

Second, there is a greater emphasis in these new guidelines on the value of statins, because they are the most important evidence based-drug in preventing cardiovascular disease, and compared to other drugs there is much more evidence for them.

Third, the old guidelines gave specific numbers for LDL cholesterol or non-HDL cholesterol. In other words there were specific goals, but in these new guidelines there are no specific goals, but we emphasize the need for a percent reduction in cholesterol based on the intensity of treatment. To decide how intensive the treatment should be, we need to be aware whether the patient has previous cardiovascular disease, and if not, then they should have a risk calculator which should tell us what is the percent risk in 10 years of developing a cardiovascular disease. This is based on a brand new risk calculator that can be easily downloaded online and can even be on your smartphone.<sup>1</sup> Using that number that we'll discuss later, we have to decide how much LDL reduction you need and depending on that, the intensity of the treatment changes.

Finally, the other cholesterol lowering drugs we've used in the past – bile acid sequestrants, ezetimibe, et cetera – are not recommended unless the statin therapy cannot be intensified to a point where it is needed. There is not enough trial evidence for other nonstatin drugs; only the statin drugs have level of that evidence thus far.

**MR. BUSKER:** First, let me point out to our listeners that a link to that risk calculator website Dr. Ganda referred to can be found in the transcript version of this podcast. So Dr. Ganda, the patient you presented has an LDL-C of 90. What should the approach be to lowering his lipids? What do the guidelines say about patients like this?

**DR. GANDA:** Right. So in this particular patient, we know that he already has cardiovascular disease, he had a stent placed, and according to these new guidelines, patients like him should have a greater than 50% reduction in their LDL cholesterol compared to baseline. Unfortunately we don't know the baseline in this patient because this patient already came in taking simvastatin 40 mg daily. But we do know, based on the new guidelines, that in order to get greater than 50 percent reduction in LDL cholesterol, the two recommended drugs are either atorvastatin 40 mg to 80 mg, or rosuvastatin 20 mg to 40 mg. Now not every patient may need that dose, but that is what is recommended for patients like this in general. So because of that, this patient is not on optimal statin therapy at the moment because he is on simvastatin 40 mg daily.

**MR. BUSKER:** His liver enzymes – as you mentioned, they're slightly elevated. What's your interpretation of that?

**DR. GANDA:** One thing we must keep in mind is that patients with diabetes, particularly if they are obese, often have fatty liver. In other words, there is greater accumulation of fat in their liver that can cause mild elevation in liver enzymes, but that is not a contraindication to using lipid lowering drugs such as statins.

However, as physicians, we have to rule out other causes of liver enzyme abnormality, so we should make sure that we rule out causes such as history of hepatitis, a history of alcohol abuse, and so forth. But once again, it's important to recognize that in patients with diabetes, mild liver enzyme problems are very common, and they can easily be reversed by better glycemic control and better attention to diet, and often after statin therapy the liver enzymes may get better rather than stay elevated.

**MR. BUSKER:** These new ACC/AHA cholesterol guidelines – what will they mean for the overall US population?

**DR. GANDA:** I think the most important thing is that many patients who deserve statin therapy have not been treated in the past, particularly older people. So people 60 to 75 in the past have been undertreated with statins, and these new guidelines remind us that these patients are at an increased risk of cardiovascular disease and should be given the benefit of statins to prevent cardiovascular outcomes.

We should also recognize that some people may be overtreated compared to the older guidelines. This is particularly for people over age 60 who may otherwise be quite healthy and may not necessarily be candidates for statin therapy. One has to use clinical judgment, and that's clearly stated in the guidelines.

And finally, the new risk calculator that allows us to calculate the 10 year risk of cardiovascular disease still does not include important things like family history or CRP that can be determinants for cardiovascular outcomes. So far, only white and African American populations have been included in calculating that risk calculator, and we need more data on other ethnic populations such as Asian Americans or even Hispanic Americans.

**MR. BUSKER:** Thank you for that case and that discussion, doctor. And we'll return with Dr. Om Ganda in just a moment.

**SUSAN PORTER:** Hello. I'm Susan Porter, Clinical Nurse Practitioner and Certified Diabetes Educator at the Johns Hopkins University School of Medicine. I'm one of the program directors of *eDiabetes Review*.

If you found us on iTunes or on the web, please be sure to subscribe. This podcast is part of Johns Hopkins *eDiabetes Review*, a new educational program providing monthly activities certified for CME credit and nursing contact hours, with expert commentary and useful practice information for clinicians treating patients with type 2 diabetes.

For more information or to subscribe to receive our newsletters and podcasts without charge, please visit [www.ediabetesreview.org](http://www.ediabetesreview.org). Thank you.

**MR. BUSKER:** Welcome back to this *eDiabetes Review* podcast. I'm Bob Busker, managing editor of the program. Our guest is Dr. Om Ganda from Harvard Medical School and the Joslin Diabetes Center. Our topic is CVD Risk Factors in Patients with type 2 diabetes.

We've been looking at how some of the new information Dr. Ganda discussed in his newsletter issue can be applied in the exam room. So to continue, if you would, doctor, please bring us another patient.

**DR. GANDA:** Let's consider this patient, a 52 year old Hispanic woman who has had type 2 diabetes and hypertension for a number of years. She returns to the office a long time after her last visit. She had missed a couple of appointments and has no specific symptoms at this time, but she has been struggling to lose weight.

Of note, her family history includes a number of people with type 2 diabetes. Two of her four siblings had type 2 diabetes. She doesn't know the details of their health, but her father died at the age of 66 after a heart attack.

On physical exam her BMI is 32, so she is clearly obese; blood pressure is 142/86. The rest of her physical examination is quite normal except for weak pulses on her feet and some varicose veins. Her medications include metformin 1000 mg twice

a day and glimepiride 4 mg daily. The important lab results include an A1c level of 8.2%, her fasting lipids show a cholesterol of 190, triglycerides 240, HDL low at 36, LDL cholesterol 106, and she has moderate elevations in AST and ALT.

**MR. BUSKER:** Using those numbers, how would you interpret her metabolic status?

**DR. GANDA:** I think it's clear that she has type 2 diabetes that is not well controlled. Her A1C is 8.2% on two medications, she has been trying to lose some weight but she has not succeeded yet; in fact, she has multiple risk factors which includes her obesity, her hypertension, and her elevated lipids. Her blood pressure right now is 142/86, and by definition she has 5 out of 5 features of metabolic syndrome. So she has a number of risk factors which can lead to cardiovascular disease.

**MR. BUSKER:** Based on the current recommendations, how would you assess her cardiovascular risk?

**DR. GANDA:** So I think this is a very important question, because according to the new guidelines, in a patient like her who does not have cardiovascular disease, we are talking about primary prevention. We have to calculate her 10 year risk because based on that, we will decide how intensive her treatment should be. Using the calculator that has been introduced by the new guidelines, we calculate the 10 year risk, which includes all of her factors including her age, gender, ethnic background, cholesterol and HDL cholesterol, and her blood pressure.<sup>1</sup>

So based on that, we need to decide if her risk is less than 7.5%, in which case she should receive moderately intensive therapy meaning that her LDL should be reduced by 30% to 50%. But if her 10 year risk is greater than 7.5%, then she needs an LDL reduction greater than 50%. This is a very important consideration and the 10 year risk calculator is very helpful in this regard.

**MR. BUSKER:** So then what would your recommendations be to lower her CVD risk?

**DR. GANDA:** So I think we see that all the time in a patient with type 2 diabetes who are obese and out of control, a lot of times their glycemic control can be improved by diet and exercise and moderate weight

loss and whatever they do to improve their glycemic control indirectly actually has much better impact on lowering triglycerides and even raising HDL, whereas LDL reduction often requires drug therapy.

I should also point out that a patient like her whose cholesterol cannot be controlled with two or three different oral agents often can be helped a lot by even using a simple insulin regimen such as basal insulin. This patient may eventually need that. But by improving glycemic control, all of these measures will help lower her triglyceride and raise her HDL. Those are all important considerations.

I should just mention one other thing: some patients have very high triglycerides, above 500, so we also have to consider the risk of pancreatitis. In such cases, drug such as fibrates or omega-3 fatty acids, the fish oils, can help improve triglycerides from that very high level to a moderate level.

Finally, some new drugs are still being developed in the field of raising HDL cholesterol — one such drug is still in clinical trials — but obviously those drugs are not yet available. The point is, the drugs we have had at our disposal such as niacin, or fibrates to lower triglycerides, have not been shown to be very helpful in evidence-based clinical trials.

**MR. BUSKER:** Talk to us a bit more about what could be done to lower her A1c.

**DR. GANDA:** I can again emphasize the fact that this patient's A1c is 8.2%, she's on maximum dose of metformin, and near maximal dose of glimepiride. At this point we have several options to improve her glycemic control. Number one, she should meet with a nutritionist, she should try to lose some weight, and if those measures are not enough, she will be a candidate either for a GLP-1 analog or a third oral agent or basal insulin. We have a lot of choices, and I think this requires a discussion with the patient and she has to understand that glycemic control cannot always be achieved with an oral agent and these days we have very easy ways to administer an injectable such as a GLP-1 analog or basal insulin.

**MR. BUSKER:** Again, doctor, thank you for bringing us that patient and for that discussion. I'd like to look at one more patient now, if we could please.

**DR. GANDA:** All right, so this next patient is a 56 year old African American patient who has type 2 diabetes for a number of years and high blood pressure for about 10 to 12 years. He has a family history of hypertension and diabetes as well. On physical exam he has some evidence of retinopathy and neuropathy. His BMI is 29, his blood pressure is 148/86, his current medications include metformin, sitagliptin, atorvastatin 20 mg daily, lisinopril, and hydrochlorothiazide. His lab results include an A1c of 7.4%, creatinine of 1.4, and calculated EGFR of 55, meaning that he has stage 3 kidney disease. His urine albumin excretion is 160 µg/mg CRT. His cholesterol is 160, triglycerides also 160, HDL cholesterol 42, and LDL cholesterol 86.

**MR. BUSKER:** How would you assess this patient's cardiovascular risk?

**DR. GANDA:** So this patient has type 2 diabetes for many years in the setting of longstanding hypertension, and he also has early CKD. It's important to recognize kidney disease, because kidney disease is becoming increasingly prevalent with the increasing number of cases of diabetes.

We also know that kidney disease itself is a risk factor for cardiovascular disease, and the combination of diabetes and kidney disease puts an extra burden on the body, so cardiovascular disease becomes even much more common. This has been shown in many studies. These days it's imperative that we assess everybody's kidney function, especially when they have diabetes and hypertension, by GFR, which can be calculated using a calculator that's available online, because creatinine alone is not a good indicator of kidney function, especially in younger people.

This patient's GFR is below 60 which puts him at stage 3 CKD, and given that, we have to make great effort to reduce the progression of kidney disease and prevent development of cardiovascular disease.

**MR. BUSKER:** So this is a patient with very strong CVD risk factors. Let me ask you about the recently released JNC-8 guidelines — how do those differ from previous guidelines and also from the guidance that's been put out by other organizations?

**DR. GANDA:** This is an important question. In the past and even now there have been a lot of controversies about what the blood pressure goal

should be in people at high risk for CVD, such as those with diabetes and those with kidney disease. In the past, the American Diabetes Association said everyone with diabetes should have a blood pressure goal of less than 130/80, but there was not enough evidence behind that. Some of the newer studies, such as the ACCORD blood pressure study, have shown that there is not much advantage in lowering systolic blood pressure below 140, and sometimes there can be adverse consequences of lowering the blood pressure too much.

JNC-8, after a long deliberation over the past several years, recently suggested and introduced a new guideline recommending that all patients with diabetes, with or without kidney disease, should have a blood pressure goal of less than 140 systolic and 90 diastolic. This is based on the best evidence we can gather from all the clinical trials.

They also said that in people above age 60, the systolic blood pressure goal for people without diabetes or kidney disease can be less than 150 rather than 140. This has caused some controversy, because according to some experts there is some data that systolic blood pressure of 150 is too liberal for even people above age 60. Some organizations are saying we should loosen that cutoff of 150 only for people who are above age 80. But again, when it comes to people with diabetes or kidney disease, there seems to be a consensus that the blood pressure goal should be less than 140/90.

**MR. BUSKER:** Now this 56 year old patient you described — you noted that he's African American. Are there ethnic- or racial-based considerations that should affect the choice of an antihypertensive agent?

**DR. GANDA:** A number of studies over the past several years suggest that African American patients respond differently to different therapies. Based on all those considerations, the general recommendation is that African patients should not be given ACE inhibitors or ARBs initially unless they have kidney disease. This is also included now in the JNC-8 guidelines. If they have just diabetes but no kidney disease — no proteinuria in other words — the initial choice should be the thiazide diuretic or calcium channel blockers. The reason for that is that in African American people, ACE inhibitors and ARBs are associated with less protection against stroke and less protection against some of the other cardiovascular outcomes.

Now having said that I should also mention that some of the other guidelines do not necessarily follow that, but I think JNC-8 has really deliberated considerably on this issue and based on some large intervention trials they have chosen to have a different initial drug therapy for patients who are African Americans even in the presence of diabetes.

The other controversy is about the choice of beta blockers as initial antihypertensive drugs. Over the past many years, a number of studies have suggested that now we have so many choices for blood pressure treatment that beta blockers should not be used as the initial therapy. Of course, many patients with diabetes or with kidney disease require multiple drugs to improve blood pressure control and down the line at the second or third line agent, blood pressure agents, beta blockers could be used, especially according to some of the experts in the European Society of Hypertension and Canadian Society of Hypertension. However, according to JNC-8, beta blockers should not be used while we use the other three classes of drugs first. That includes thiazide type diuretics, ACE and ARBs, and calcium channel blockers.

**MR. BUSKER:** For the US population in general, what are the overall implications of these new JNC-8 guidelines?

**DR. GANDA:** I think the overall implication has to be that by relaxing the blood pressure goal to less than 140/90 rather than the old 130/80 or 140/80, we now have many patients, particularly those above age 60, where if we choose the cutoff of 150 in the people without diabetes or kidney disease, we'll end up with many people who were previously not on goal but now would be considered in goal. In fact, it's been calculated that in the United States about 30 million people would not require antihypertensive therapy since they are age 60 and above and their blood pressure is between 140 or 150.

Let me add that there are still a lot of people in the US and the rest of the world where the blood pressure is not being recognized, people have hypertension that is not diagnosed in time, and even if it is diagnosed they are not controlled to a point where they can be considered in goal, even with the looser criteria of the JNC-8. We still have a fair amount of burden of both hypertension and chronic kidney disease that follows the uncontrolled hypertension.

**MR. BUSKER:** Thank you, Dr. Ganda, for today's patients and discussions. I'd like to switch gears and take a moment now to ask you to look to the future for us. Reducing cardiovascular risk by achieving better control of dyslipidemia in patients with type 2 diabetes. What do you see happening in the future?

**DR. GANDA:** In spite of the great value of statins, we made a lot of progress in preventing cardiovascular disease and reducing the second episode of cardiovascular outcome, but many patients still cannot take statin therapy in the dose that they need to take it. In other words, they are not able to get to the goal of 50% reduction in their LDL or less than 50% in the moderate dose category.

I would say about 15% of the patients overall in general practice cannot tolerate statins in the right dose, and a small number are totally statin-intolerant. A lot of work has been going on to try to come up with new drugs that reduce LDL cholesterol but do not have the same side effects as statins.

Once such class of drugs that is currently in clinical trials that looks very exciting is called PCSK-9 inhibitor. PCSK-9 is an enzyme that normally degrades the LDL receptor, so that people with enzyme PCSK-9 cannot achieve an adequate effect of statin or do not have an adequate effect on lowering cholesterol because the LDL receptor is constantly being broken down as a natural mechanism.

It has now been found that certain drugs, several of them in clinical trials, prevent the breakdown of the LDL receptor. These drugs are called PCSK9 inhibitors. These drugs are very effective even in the absence of statin therapy, so that in monotherapy, by preventing the LDL receptor breakdown, they can lower LDL cholesterol almost as much as statins in high doses do, about 50%. In combination with low dose statin for people who can't take the high dose statin, they can lower LDL cholesterol up to 70% or more.

One thing to keep in mind is, these drugs are like proteins. They are injectable, but the good news is that they can be injected once every two weeks or once every four weeks. When they become available, I think they'll provide a very good option for our patients who either cannot take a statin at all or cannot take statins in the right dosage. We're waiting the outcome of these long-term clinical trials in phase III that are currently in progress. Some of them have been

completed up to one year but we need longer term data before they can be subjected to further scrutiny and the FDA approval.

**MR. BUSKER:** Thank you for sharing your thoughts, Dr. Ganda. To wrap things up, I'd like to review today's discussion in light of our learning objectives. So to begin: managing cholesterol to reduce CVD risk in patients with type 2 diabetes.

**DR. GANDA:** The first case we discussed clearly demonstrated the salient differences between the new AHA/ACC cholesterol guidelines and the ATP-3 recommendations we have used in the past. It is clear that in patients with cardiovascular disease we must achieve more intensive statin therapy, which is the best proven therapy thus far for cardiovascular event reduction.

Finally, it's clear from the new guidelines, based on all the evidence, that statins are the most important agent for primary prevention of cardiovascular disease and that for many patients who have high risk of cardiovascular events based on the ten year risk calculator that we use now, we can make better use of statins in primary prevention of cardiovascular disease.<sup>1</sup>

**MR. BUSKER:** And our second objective: managing dyslipidemia beyond LDL cholesterol in patients with type 2 diabetes.

**DR. GANDA:** Our second case was a patient with dyslipidemia who has high triglycerides and low HDL cholesterol, a typical dyslipidemia seen in patients with type 2 diabetes. In the past for patients like this we have drugs like fibrates and niacin, but recently completed trials have shown that if you use intensive statin therapy and reduce the LDL to the optimal goal, the addition of fibrate or niacin beyond the LDL reduction does not provide further protection. This has been quite revealing because we've been using a drug like niacin for the past 50 years. Now we are revisiting this issue because in the past these drugs were used in the absence of statin therapy, but now on top of statin therapy these drugs don't seem to be very effective.

It came down to the fact that in patients with high risk, statins are the best drugs, and until we have better agents to improve HDL cholesterol, we must continue to put much more emphasis on the use of statins and improve other lipid abnormalities such

as triglycerides and low HDL by weight loss, by dietary changes, exercise, and glycemic control.

**MR. BUSKER:** And finally: the new recommendations for managing hypertension in patients with type 2 diabetes.

**DR. GANDA:** Keep in mind that the new recommendation for blood pressure targets are based on a number of evidence-based trials, and it appears that a blood pressure goal of 140/90 as we discussed in case three is a good new guideline from the JNC-8. It is approved and endorsed by a number of other organizations as well. There is still controversy about treating people over age 60: where JNC-8 recommends a systolic blood pressure of less than 150, but other organizations are still insisting on less than 140. However, keep in mind that for patients with diabetes and for patients with chronic kidney disease the blood pressure goal remains less than 140 systolic and less than 90 diastolic.

And finally, for African Americans it is recommended that ACE inhibitors and ARBs may not be the first line of drugs because there is better efficacy and evidence of CVD reduction with thiazide-type diuretics and calcium channel blockers in African Americans, unless kidney disease is present, in which case there is consensus that ACE and ARB inhibitors should be used and can be used as initial therapy.

**MR. BUSKER:** Dr. Om Ganda from the Harvard Medical School, thank you for participating in this eDiabetes Review Podcast.

**DR. GANDA:** Thank you very much, it was a pleasure to participate with you in this very important podcast.

**MR. BUSKER:** To receive CME credit for this activity, please take the post-test at [www.ediabetesreview.org/test](http://www.ediabetesreview.org/test).

This podcast is presented in conjunction with the eDiabetes Review Newsletter, a peer-reviewed literature review certified for CME/CE credit, emailed monthly to clinicians treating patients with type 2 diabetes.

This activity has been developed for endocrinologists, primary care clinicians, nurse practitioners, physician assistants, Certified Diabetes Educators, and other health care practitioners whose work or practice includes treating patients with type 2 diabetes.

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education, through the joint sponsorship of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The Johns Hopkins University School of Medicine designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credits*<sup>™</sup>. Physicians should claim only the credit commensurate with the extent of their participation in this activity.

The Institute for Johns Hopkins Nursing is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

For nurses, this 0.5 contact hour Educational Activity is provided by the Institute for Johns Hopkins Nursing. Each podcast carries a maximum of 0.5 contact hour.

This educational resource is provided without charge, but registration is required. To register to receive eDiabetes Review via email, please go to our website: [www.ediabetesreview.org](http://www.ediabetesreview.org).

The opinions and recommendations expressed by faculty and other experts whose input is included in this program are their own. This enduring material is produced for educational purposes only.

Use of the names of the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing implies review of educational format, design, and approach. Please review the complete prescribing information for specific drugs, combinations of drugs, or use of medical equipment, including indication, contraindications, warnings, and adverse effects, before administering therapy to patients.

eDiabetes Review is supported by educational grants from Eli Lilly and Company, Bristol-Myers Squibb, and Novo Nordisk, Inc.

This program is copyright with all rights reserved, by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing.

## REFERENCE

1. [2013 Prevention Guidelines Tools, CV Risk Calculator](#)