TYPE 2 DIABETES AND CARDIOVASCULAR RISK TOOLKIT

There are many missed opportunities to intensify cardiovascular (CV) risk reduction strategies among cardiovascular disease (CVD) patients with Type 2 diabetes. Cardiology clinicians will need to play a more active role in both educating patients and helping to shift the focus from predominantly glucose-lowering to broad-scale CV risk assessment and reduction to optimally manage CV risk in patients with diabetes.
OVERVIEW

The American College of Cardiology (ACC) and its collaborating partners are teaming up to help educate clinicians and patients alike about the link between type 2 diabetes and CVD, both of which carry heavy costs and burdens. There is also quickly emerging research and new treatment options, including two novel classes of antiglycemic medications, that should ideally be integrated into disease management plans to more optimally manage CV risk in some patients, thereby reducing morbidity and mortality.

This toolkit, *Getting to the Heart of the Matter: What You and Your Patients Need to Know About Managing Diabetes and CV Risk*, offers tips for talking with patients about diabetes and cardiovascular risk, as well as the heart-related benefits of two classes of antiglycemic medications. It provides a roadmap for what’s needed to more optimally manage CV risk in people with diabetes, as well as tools to help facilitate conversations with patients at the point of care that can empower them to take action. Also included is a quick snapshot on when to consider using Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors or Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RAs).

These resources are part of the ACC's *Succeed in Managing Cardiovascular Risk in Diabetes (SIM – CVRiD)*. SIM-CVRiD is an initiative aimed at building awareness around approaches to comprehensive CVD risk reduction management in patients with type 2 diabetes.

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GETTING TO THE HEART OF THE MATTER:
What You and Your Patients Need to Know
About Managing Diabetes and CV Risk

Despite advances in medical care, CVD remains the leading cause of morbidity and mortality in people with
type 2 diabetes. Yet many patients remain unaware of the clear-cut connection between these two conditions
and, in turn, may not be taking appropriate steps to reduce their CV risk. Additionally, both conditions intersect
in terms of shared risk factors, as well as targeted treatment approaches, which make efforts to facilitate
quality coordination of care even more essential.

A GROWING ISSUE
Globally, diabetes continues to rise at alarming rates. The prevalence of diabetes (type 2 diabetes and type
1 diabetes) is expected to jump by 54 percent to more than 54.9 million Americans between 2015 and 2030.

Today, more than 100 million U.S. adults are living with diabetes or prediabetes, a precursor to full-blown type
2 diabetes, which typically manifests within 5 years without efforts to prevent it.

SOBERING STATISTICS

- **2-4x** – how much greater the risk of coronary artery disease (CAD) and stroke is in someone with diabetes
  compared to those without it

- **2 out of 3** – the number of deaths in people with diabetes attributed to CVD

- **Nearly two-thirds** – people with diabetes who also develop some form of heart failure

- **54 percent** – the expected jump in the prevalence of diabetes between 2015 and 2030

- **Half of women** who have gestational diabetes, which affects 1 out of 10 pregnancies, will go on to develop
type 2 diabetes, and possibly heart disease as a result, but most don’t follow up on this risk factor
AT A CROSSROADS: A CALL-TO-ACTION TO IMPROVE CV RISK MANAGEMENT

Diabetes is among the strongest risk factors for heart disease. Because the macrovascular and microvascular changes associated with elevated blood sugar levels start early, the heightened risk for heart disease begins years, possibly decades, before diabetes is diagnosed.

People with type 2 diabetes are at increased risk for developing atherosclerotic cardiovascular disease (ASCVD) and microvascular complications. These can include:

- Myocardial infarction
- Stroke
- Coronary artery disease (CAD)
- Peripheral artery disease (PAD)
- Heart failure
- Declines in renal function
- Eye problems, including blindness
- Neuropathies

In addition, many people with established CVD could also have type 2 diabetes or be at risk for developing it, but not know it due to a lack of routine blood glucose testing. As such, there are many missed opportunities to intensify CV risk reduction strategies and an urgent need to step up efforts to clinically manage CV risk in patients with diabetes or prediabetes.

It’s important to keep the following in mind:

- **Many people aren’t aware that they have diabetes or prediabetes.** Even when they have been diagnosed with diabetes, the may not be fully educated about the related CV risk.

- **CV insults from elevated glucose levels often start well before someone is diagnosed with glycemic abnormalities.** Some patients will present with chest pain or a myocardial infarction prior to receiving a diabetes diagnosis.

- **Based on what we know, there is an urgent need to shift the predominant focus on glucose control to one that incorporates a comprehensive and ongoing assessment of patients’ CV risk and recommendations for aggressive risk reduction.** Cardiology clinicians will need to play a more active role in educating patients and managing this risk.

- **A firm understanding of the net clinical benefit of the novel anti-diabetic, cardioprotective agents is crucial.** Patients with diabetes and CVD frequently follow-up with a cardiology specialist. Such encounters are an ideal time to review each patient’s overall management and consider whether these agents should be recommended to favorably impact patient care and outcomes.
TALKING ABOUT DIABETES AND CV RISK: IT’S NOT JUST ABOUT GLUCOSE

It’s important to talk to patients with diabetes – as well as those with both diabetes and heart disease – about their risk of heart disease, including heart attacks, stroke and heart failure. We know from surveying patients that simply saying, “you’re at higher risk for heart issues” isn’t enough.

Try to set aside sufficient time to explain the connection between these conditions and help empower your patients to lower their CV risk.

Below are some general discussion points that might help. We have also developed At-a-Glance: Talking Points About Diabetes and CV Risk and the Role of Novel Diabetes Medications that provide suggested language for answering and addressing common questions about diabetes and CV risk.

THE ESSENTIAL BASICS – HOW TO TALK ABOUT DIABETES AND CV RISK IN 5 MINUTES

The old adage, “Knowledge is power” is particularly salient when it comes to discussions about diabetes and CV risk. Patients need to be informed enough about how diabetes affects the heart and blood vessels to be able to take action and help optimize their CV health and prevent further complications.

✓ The risk for heart disease or stroke is real.

- Almost 7 in 10 people with type 2 diabetes over age 65 will die of some type of heart disease. About 1 in 6 will die of stroke.
- Most people with diabetes – 9 out of 10 – also have one or more additional risk factors for heart disease (for example, smoking, high cholesterol, high blood pressure). These also need to be discussed and managed.
- Sadly, many people with diabetes don’t know they have heart disease until they have a heart attack or notice chest pain and shortness of breath with simple exercise or when walking.
- Some studies suggest that compared to men, women with diabetes are at greater risk of having a heart attack or developing heart failure.
Diabetes can change or injure the inside lining of blood vessels often long before someone knows that they have prediabetes or diabetes. These changes make someone more likely to develop various forms of heart or vascular problems.

These may include:

- blockages in the arteries of the heart or related chest pain or tightness, as well as in the extremities (called PAD)
- heart attacks
- stroke
- heart failure – this is when the heart becomes weakened or stiff so it may not pump well enough to meet the body’s needs

In addition, plaque in the heart’s arteries appears to be less stable and more likely to rupture in people with diabetes. This can lead to heart attack or stroke.

The good news is that patients can take steps to help optimize their heart health and lower the risk of CVD.

Bottom line: managing diabetes doesn’t and can’t stop with monitoring blood glucose levels.

- In addition to yearly eye exams and daily foot care, routine blood sugar testing, patients also need to be mindful of their heart health and risk of heart attack or stroke.
- Even when glucose levels are reasonably controlled, there can still be ongoing CV and inflammation (swelling) in the blood vessels that must be monitored.
- Reinforce the need to work together to carefully assess and track individual patient’s heart and vascular health over time.

Having diabetes and CVD without one or both being well managed can also result in poorer outcomes, or may make another heart attack, stroke or related complications more likely.

There are steps patients can take to lower the risk of developing heart disease or stroke, having repeat heart attacks or stroke or dying.

For example, making a commitment to:

- Heart healthy eating
- Regular exercise
- Achieving and maintaining a healthy weight
- Avoiding tobacco, including exposure to other peoples’ smoke
- Monitoring key health risk factors, including blood pressure, cholesterol, A1c levels
- Reducing stress and feeling more in control
- Taking medications as prescribed
- Committing to regular follow up visits to check blood sugar levels and other CV risk factors

KEY QUESTIONS PATIENTS SHOULD BE ASKING AND HAVE THE ANSWERS TO

Again, it’s important to encourage open and ongoing dialogue about the interplay between type 2 diabetes and CVD. If your conversation about diabetes and CVD and risk factors are effective, your patient should ideally have the answers to the following questions:

- What exactly does having type 2 diabetes mean for my heart health?
- What can I reasonably do to lower this risk (taking into account individual preferences and risk tolerance)?
- How can we best keep tabs on my heart health while also managing my blood sugar level?
- When and how often should I have exams or tests to check my heart and vessels?
- I heard there are diabetes drugs that can also cut the chance of heart attack, stroke or related death or hospitalizations. What are these therapies and how do they work?
- What signs suggest developing or worsening CVD?
- If my blood sugars are well controlled, does that mean I can breathe easy about my heart health?

Answers to some of these and other questions are provided below. Many also help to address some common misconceptions about diabetes and CV risk reduction.
Patients consistently share that they want accurate and hopeful messages about their health and health risks. Below are some questions your patients may ask—or should be asking—about diabetes and CV risks, along with suggested answers. As always, your advice should be tailored to each individual patient and be based on your professional clinical assessment and judgment.

### QUESTIONS PATIENTS MAY ASK RELATED TO DIABETES AND HEART DISEASE

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<thead>
<tr>
<th>Question</th>
<th>Suggested Language</th>
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<td>I’ve heard diabetes and heart disease are related. But how?</td>
<td>It’s true. People with diabetes are much more prone to developing heart issues.</td>
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<td>I was told that having diabetes means heart issues are more likely. How does diabetes hurt the heart?</td>
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<td>• <strong>Diabetes is one of the strongest risk factors for heart and vascular disease</strong> – it’s right up there with smoking and high cholesterol or blood pressure.</td>
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<td>• <strong>Heart disease is also by far the most common cause of death in people with diabetes.</strong></td>
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<td>What’s the connection?</td>
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<td>• First, diabetes and CVD share important risk factors – things that make a disease more likely. These include:</td>
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<td>- High cholesterol</td>
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<td>- High blood pressure</td>
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<td>- Being overweight</td>
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<td>- Not exercising regularly or sitting for long periods of time</td>
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<td>- Tobacco use/avoiding second hand smoke</td>
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<td>• Second, over time, high levels of sugar (or glucose) in the blood can:</td>
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<td>- Change the way your heart works, and</td>
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<td>- Damage the inside of your blood vessels, acting like shards of glass.</td>
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<td>This can result in swelling (inflammation) and also create an environment that makes it easier for plaque and other fatty substances to stick, accumulate and harden in the blood vessels.</td>
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<td>When this happens, the blood vessels supplying the heart can become narrowed or blocked. This can disrupt or stop the normal flow of blood.</td>
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<td>SUGGESTED LANGUAGE TO CONSIDER WHEN TALKING WITH AND ENGAGING PATIENTS</td>
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<td>But, diabetes is also linked to:</td>
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<td>• Stroke</td>
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<td>• Heart failure – (nearly 2 out of 3 people with diabetes will develop some type of heart failure)</td>
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<td>• PAD (blockages in the arteries of the legs and arms)</td>
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<td><strong>The good news is that knowing the heightened risks, we can map out a plan that works for you to help protect your heart health.</strong></td>
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<td><strong>How does diabetes worsen existing heart or vascular disease?</strong></td>
<td>It does so in several ways. For example, it can:</td>
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<td>• Damage the inside lining of the blood vessels</td>
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<td>• Affect how well your body circulates blood to vital organs</td>
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<td>• Place added stress on the heart</td>
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<td><strong>That's why it is so important that we encourage collaboration among all of your providers, your endocrinologist, primary care provider and cardiology specialists to be able to optimally manage both diseases.</strong></td>
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<td><strong>How high is my risk of heart disease?</strong></td>
<td>Even by itself, diabetes puts you at greater risk for heart disease. Damage to the blood vessels often occurs well before someone finds out they have diabetes, and those changes help set the stage for heart disease.</td>
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<td>But just how likely you are to develop heart disease will depend on other factors too. We use risk estimators to help us gauge how likely someone is to have a heart attack or stroke in the next 10 years. This includes things like:</td>
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<td>• Blood pressure</td>
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<td>• Cholesterol levels</td>
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<td>• Body weight</td>
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<td>• How often you exercise</td>
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<td>• Tobacco use</td>
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<td>• Family history</td>
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<td><strong>Your risk can be managed through both lifestyle habits and other treatments, if needed.</strong></td>
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<td>Besides keeping my blood sugar numbers down, what other things can I do to curb my risk of a heart attack or stroke?</td>
<td>You can take steps to boost your heart health, and lower your chance of having a heart attack or stroke or developing heart failure.</td>
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<td>1. An important step—for preventing new or worsening heart disease—is to <strong>focus on lifestyle changes</strong>. Making healthy choices everyday is at the heart of preventing CVD.</td>
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<td>For example:</td>
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<td>- Getting regular exercise</td>
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<td>- Eating heart healthy foods</td>
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<td>- Losing weight, if needed, or staying at your current weight</td>
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<td></td>
<td>- Avoiding tobacco</td>
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<td>- Coping with stress</td>
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<td>It may seem overwhelming, but there are resources and people available to help. You don't need to tackle all of these changes at the same time; every little bit helps.</td>
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<td>It’s also essential to tell us about any <strong>barriers that might make it difficult for you to adopt or keep up with healthy behaviors</strong>.</td>
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<td>For example:</td>
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<td>- Lack of time</td>
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<td>- Feeling overwhelmed (not knowing where or how to start, setting realistic goals, enlisting support from others)</td>
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<td>- Cost</td>
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<td>- Factoring in other health issues you are managing</td>
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<td>- Not fully understanding the link between diabetes and heart disease</td>
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<td>2. <strong>When you think about diabetes, think about your heart too.</strong> That means, in addition to yearly eye exams and daily foot care and routine blood sugar testing, you must also be mindful of your heart health.</td>
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<td>3. <strong>Take your diabetes medications as directed.</strong> Well controlled diabetes is better for your heart.</td>
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<td>4. If you already have heart disease in addition to diabetes, there are <strong>certain diabetes medications</strong> that are traditionally used to lower blood sugar, that can also <strong>cut the likelihood of having another heart attack or stroke or dying as a result</strong>. We can discuss this option, if appropriate.</td>
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| If my blood sugar level is well controlled, I don’t have to worry about developing (or worsening) heart problems. | • Diabetes can change or “scuff up” the lining of the blood vessels often well before you know you have it. Unfortunately, this promotes heart and vascular problems.  
• Even when your blood sugar is reasonably controlled, the risk of CV problems can still persist. But good control of diabetes can lower the likelihood of problems.  
• It’s important to:  
  – Monitor your blood sugar  
  – Aggressively manage your:  
    ○ blood pressure  
    ○ cholesterol  
  – Take your medications as directed  
  – Ask for help if you need assistance with:  
    ○ meal planning  
    ○ weight loss  
    ○ learning what exercise you should engage in and how often  
    ○ avoiding tobacco  
    ○ coping and stress management |
| What heart and vascular disease warning signs should I look out for? | • Signs of a heart attack may include:  
  – Pressure, squeezing, fullness, and pain in the chest or upper body  
  – Shortness of breath.  
Women may feel a heart attack differently, and sometimes have:  
  – Nausea and vomiting  
  – Fatigue perhaps for days  
  – Pain in the back, shoulders and/or jaw  
Call 9-1-1 immediately if you suspect you are having a heart attack or stroke. It can save your life. |
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<td><em>(continued)</em></td>
<td>• <strong>Signs of heart failure may include:</strong></td>
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<td>- Shortness of breath (even when doing simple tasks like dressing or walking a flight of stairs)</td>
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<td>- Swelling in the ankles, feet, legs, abdomen, or veins in the neck (edema)</td>
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<td>- Extreme tiredness (fatigue)</td>
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<td>- Feelings of weakness</td>
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<td>- Rapid or irregular heartbeat</td>
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<td>- Fast weight gain (usually 3 lbs in on day or 5 lbs in one week), or rapid fluctuations in weight</td>
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<td>- Pressure or heaviness in the chest when lying flat</td>
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<td>If you experience any of these symptoms, let us know right away.</td>
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<td>• <strong>Signs of blockages in your extremities (called peripheral artery disease or PAD) may include:</strong></td>
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<td>- Pain, tiredness or numbness in the legs with or without exercise</td>
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<td>- Issues with circulation in your legs or arms</td>
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<td>It’s important to know if you have these symptoms because you can’t take an SGLT2 inhibitor if you have PAD.</td>
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<td>QUESTIONS PATIENTS MAY ASK ABOUT MEDICATIONS</td>
<td>SUGGESTED LANGUAGE TO CONSIDER WHEN TALKING WITH AND ENGAGING PATIENTS</td>
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| **Am I taking the right medications to manage my CV risk?** | There are a number of medications that can be used to lower your likelihood of having a heart attack or stroke if you already have blockages in your arteries and diabetes. These may include:  
  - **Statins** are advised for most people with diabetes  
  - **Low-dose aspirin therapy** may be used to thin the blood so it is less likely to clot and clog blood vessels, but whether this is recommended depends on your age and risk of bleeding problems  
  - **Metformin**, which is first line treatment for diabetes and also seems to help lower the risk of heart disease  
  - **Two classes of diabetes drugs** that have recently been shown to help lower the risk of heart attack or stroke in people who also have heart disease and also lower blood sugar  
  - **ACE-inhibitors or ARBs** to help lower blood pressure and/or kidney complications |
| **I'm already on three diabetes medications. Why do we need to add another?** | • Having diabetes makes you very likely to develop heart disease or vascular problems, and many patients with diabetes also have heart disease.  
  • Certain medications that were originally developed to help control glucose have also been shown in clinician trials to help patients with both diabetes and heart disease reduce their risk for heart attack, stroke or dying as a result.  
  • So if you have heart disease – and even if you’ve already had a heart attack or stroke – these medications can help you maintain glucose control while also lowering your CV risk to prevent future events.  
  • Based on studies, these therapies can also lower blood pressure and help with weight loss, which also benefits the heart. |
| **How do these novel medications work to lower heart disease and stroke?** | We’re not entirely sure, but they’ve been shown to have secondary effects that benefit how the heart functions.  
With SGLT2 inhibitors, we know there are secondary benefits of weight loss, lowering blood pressure and circulating fluid levels. This also means less stress on the heart and kidneys.  
GLP-1RAs also have been linked to weight loss and lowering blood pressure, which can be heart protective. These may also have direct action within the lining of the blood vessels themselves. |
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<tbody>
<tr>
<td>Do I need to adjust my other diabetes medications if I start on an SGLT2 inhibitor or GLP-1RA?</td>
<td>If we decide to start you on one of these medications, we will review your other diabetes medications and decide whether you should stop taking any and/or if we need to adjust the amount (dose) you take.</td>
</tr>
<tr>
<td>Are there any special considerations I should be aware of in taking an SGLT2 inhibitor or GLP-1RAs?</td>
<td>Always report any concerns that you have related to taking these and other medications. GLP-1RAs can slow how quickly food leaves your gut and is processed into glucose in your bloodstream. If you eat too much or too quickly when taking this medicine, you may feel overly full or nauseous. Make sure to report any vomiting. You will be started on a lower dose or amount of the medication. As the amount is increased, you may want to eat smaller meals to see how it affects you. Typically, these symptoms get better once you’ve been on the medications for a period of time. With SGLT2 inhibitors, it’s important to: • Stay hydrated • Report any dizziness or faint feelings or foot ulcers that don’t seem to be healing • Watch for signs of yeast or urinary tract infections – burning or traces of blood with urinating – and practice good hygiene to prevent problems</td>
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IMPROVING OUTCOMES, MANAGING CV RISK IN THE CONTEXT OF DIABETES: WHAT’S NEEDED

In order to improve outcomes related to diabetes and concomitant CV risk and meaningfully enhance patients’ quality of life, there’s an urgent need to:

✓ **Shift and expand the predominant focus on glucose control** to include a comprehensive and ongoing assessment of patients’ CV risk and recommendations for aggressive risk reduction. ACC has developed tips and suggested talking points about diabetes and CV risk.

✓ **Encourage a collaborative, multidisciplinary approach** that can help bridge the gap between diabetes care and cardiology. Clinicians involved in CV care will need to play a larger, more active role in helping to risk stratify patients and optimally manage their CV health.

This can help guard against missed opportunities to better manage CV risk in patients with type 2 diabetes. A significant proportion of patients seen for CV disease management also have type 2 diabetes, undiagnosed diabetes or prediabetes. One study revealed only 13 percent of people with CAD who are cared for by cardiologists are screened for diabetes.

✓ **Step up efforts to screen for diabetes or heart problems** among people living with or at high risk of either disease and with the assistance of guidelines and expert consensus pathways.

✓ **Talk with patients about their personal CV risk.** Simply telling patients with diabetes that they may also be at risk for heart issues isn’t enough to encourage them to take action.

It’s also important to build in opportunities during appointments and follow up visits to revisit their CV risk and make risk reduction an ongoing conversation. CV risk and treatments frequently change over time. See the *Essential Basics – How to Talk About Diabetes and CV Risk in 5 Minutes* section above for conversation starters and answers to commonly asked questions on pages 6.

✓ **When appropriate consider adding an SGLT2 inhibitor or GLP-1RA** to lifestyle changes and other antidiabetes treatments. In clinical outcomes trials, these classes of glucose-lowering medications have been shown to significantly reduce the risk of major atherosclerotic CVD events and related deaths in patients with type 2 diabetes and who are at high risk for heart disease or stroke.

See the *Quick Snapshot: When and What to Consider in Using/Prescribing SGLT2s of GLP-1RAs for Risk Reduction* section below.

“It’s important to convey to patients that cardiovascular disease can and often does happen. I didn’t understand just how likely it was or what it really meant. Patients need information to help them take the elevated risk seriously – for example, what does it look like to live with heart failure? – and also know there are things they can do to manage their health. But they need to be compliant to do so.”

Robin Driscoll, diagnosed with diabetes in 2014, a heart attack in on New Year’s Day 2017 and heart failure later that same year.
SIX HIGH-LEVEL STEPS FOR OPTIMIZING CARDIOVASCULAR RISK REDUCTION AMONG PATIENTS WITH DIABETES

CV risk reduction must be a priority in order to optimally manage diabetes in patients and improve outcomes. This is even more critical among people with diabetes and established CVD.

Note the following steps aren’t intended to be all-inclusive. Read more about this topic in the 2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease at ACC.org/CVDinDMDecisionPathway.

1. **Educate people who have diabetes about other factors – in addition to poorly controlled blood sugars – that might hasten declines in CV health.**
   For example:
   - Smoking
   - Being overweight
   - Being inactive/lack of routine exercise or sitting for long periods
   - High blood pressure
   - Unhealthy cholesterol levels
   - Family history of heart disease, especially at younger ages

2. **Put patients’ CV risk into perspective, and in a way that helps individual patients understand the threat and feel empowered to take action.**
   - Explain that heart check ups are as important as controlling blood sugar and doing routine eye, skin and foot care, and that there are lifestyle changes and medications that can help.
   - Review each individual’s CV risk with available tools and share the potential benefits and options for lowering CV risk.
   - Ask patients about their personal preferences and goals for lowering CV risk.
3. **Develop an individualized plan to assess and manage CV risk on an ongoing basis to optimize heart and vascular health.** Revisit this plan over time.

4. **Make sure diabetes is optimally controlled.** About half of patients with type 2 diabetes fail to achieve adequate glycemic control.

   In accordance with the clinician’s and patient’s goals, work to collaboratively devise a realistic plan for adopting lifestyle changes and adhering to other guideline-directed therapy, including glucose-lowering therapy (e.g., metformin).

   Lifestyle changes are the foundation for controlling diabetes and have important CV health benefits too. Take an inventory of patients’ health habits and work with them to set realistic and measurable goals.

   For example:
   - Most adults with diabetes should try to engage in 150 minutes or more of moderate-to-vigorous intensity aerobic activity each week (e.g., brisk walking/running, swimming, tennis, fitness classes, cycling).
   - If a patient is overweight/obese, losing 5 percent of their body weight (7 percent is even better) can benefit glycemic control, lipids and blood pressure.
   - Cut out sugary drinks.

5. **Consider prescribing novel antihyperglycemic therapies, when appropriate.** Several SGLT2 inhibitors and GLP-1RAs have been shown, in both completed and ongoing outcomes trials, to carry the dual benefit of controlling diabetes and lowering CV risk and death in some patients, thereby improving survival and quality of life.

   These therapies, which are used for blood glucose lowering, have also been shown in clinical trials to cut the risk of CV events or death from a heart attack or stroke in adults with type 2 diabetes and established heart disease.

   As one example, data from the completed EMPA-REG OUTCOME trial showed that, compared to placebo, empaglifozin led to a significant reduction in:
   - Total CV events (heart attacks, heart-related deaths)
   - Overall heart-related deaths
   - Overall death
   - Hospitalizations from heart failure
In trials, these medications also appear to have:

- A low risk of hypoglycemia when used on their own or when used in combination with metformin, which continues to be recommended as the first line medication for type 2 diabetes.*
- Secondary benefits of weight loss and blood pressure lowering.
- Efficacy in patients with type 2 diabetes who were on a wide range of therapies, most frequently metformin.

*Other oral glucose lowering medications may potentially increase the risk of hypoglycemia

For more information about integrating these medications, please refer to *When and What to Consider in Using SGLT2 inhibitorss of GLP-1RAs for Risk Reduction.*

6. **Assess adherence and identify hurdles.**

There are a host of reasons patients may not adhere to their treatment plans. Chief among those reported are:

- Perceived treatment efficacy – why is this medication needed and how will it help improve outcomes and quality of life?
- Costs of treatment
- Side effects
- Treatment complexity and convenience
- Incongruence with their preferences or priorities

Patients may not always want to share these concerns, but it’s essential to ask and help find solutions.
QUICK SNAPSHOT: WHEN AND WHAT TO CONSIDER IN PRESCRIBING SGLT2 INHIBITORS OR GLP-IRAs FOR RISK REDUCTION

WHEN THESE MEDICATIONS MIGHT BE CONSIDERED FOR CV RISK LOWERING

These medications should be used:

1. In concert with guideline-directed medical therapy including lifestyle changes, anti-platelet, blood pressure, lipids and
2. In the context of guideline-directed diabetes care.

Many people with type 2 diabetes and existing heart or blood vessel disease benefit from adding a novel diabetes medicine to help manage blood sugar and heart risks.

Opportunities to initiate these therapies within this context include:

- At the time of type 2 diabetes diagnosis in patients with clinical ASCVD
- At the time of diagnosis with ASCVD in a patient with type 2 diabetes
- In a patient with type 2 diabetes who is not meeting glycemic targets and has clinical ASCVD
- At hospital discharge after admission for an ASCVD- or diabetes-related clinical event

In patients with type 2 diabetes and additional risk factors for CVD, it may be reasonable to initiate these two classes of medications for primary prevention of CVD. Factors to consider include:

- Age > 65 years
- Poorly controlled hypertension (BP > 140/90 mm Hg)
- Hyperlipidemia (LDL-C >100mg/dl or non-HDL >130mg/dl)
- Ongoing tobacco use
- Presence of significant subclinical atherosclerosis (coronary artery calcium score >100)
- Chronic kidney disease stage III or higher
While current evidence for these medications is relevant to people with type 2 diabetes and heart disease, there are data to suggest these medications may have an added benefit, even among those people living with diabetes without currently diagnosed or known heart disease.

**HOW TO CHOOSE BETWEEN A SGLT2 INHIBITOR OR GLP-1RA**

- **Factor in patient and clinician preferences and priorities**
  
  For appropriate patients, engage in an informed discussion to determine if one of these medications could be a suitable option within the context of patient and clinician preferences and priorities.

- **What to think about when initiating and monitoring each**
  
  In addition to factoring in patient preference and medical history to guide decisions about these medications, the tables below from the *2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways* provide some additional things to consider:

> “Given the emerging data, it’s quite possible that we may prescribe these medications for CV risk lowering much the same way we put patients on an ACE or ARB to protect their kidneys.”

*Melissa L. Magwire RN, MSN, CDE, Haverty Cardio Metabolic Center of Excellence*
### TABLE 11
Patient and Clinician Preferences and Priorities for Considering SGLT2 Inhibitors with Demonstrated CV Benefit Versus GLP-1RAs With Demonstrated CV Benefit

<table>
<thead>
<tr>
<th>Consider Using an SGLT2 Inhibitor First When Patient and Clinician Priorities Include:</th>
<th>Consider Using a GLP-1RA First When Patient and Clinician Priorities Include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reducing MACE and CV death</td>
<td>Reducing MACE and CV death</td>
</tr>
<tr>
<td>Preventing heart failure hospitalization</td>
<td>Substantial weight loss</td>
</tr>
<tr>
<td>Reducing blood pressure</td>
<td>Once weekly (subcutaneous) dosing</td>
</tr>
<tr>
<td>Orally administered therapies</td>
<td>Therapy when eGFR consistently &lt;45 ml/min/1.73 m²*</td>
</tr>
</tbody>
</table>

Consider alternative agents if:
- Significant CKD*
- History of prior amputation, severe peripheral arterial disease, neuropathy, or diabetic foot ulcers (avoid canagliflozin)
- History of recurrent genital candidiasis
- History of diabetic ketoacidosis
- History of osteoporosis (avoid canagliflozin)

Consider alternative agents if:
- Persistent nausea, even at low doses
- History of pancreatitis
- History of gastroparesis
- History of MEN2 or medullary thyroid cancer
- History of proliferative retinopathy (consider alternative to semaglutide)

* eGFR <45 ml/min/1.73 m² is currently a caution due to a decrease in glycemic efficacy (not due to safety), but SGLT2 inhibitors are currently being investigated for nephroprotection in these patients.

CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; GLP-1RA = glucagon-like peptide-1 receptor agonist; MACE = major adverse cardiovascular event; MEN2 = multiple endocrine neoplasia type 2; SGLT2 = sodium-glucose cotransporter-2.

### TABLE 13
Considerations for Drug Initiation and Monitoring in Patients Starting a GLP-1RA With Demonstrated CV Benefit

- If A1C well-controlled at baseline, or known history of frequent hypoglycemic events, reduce dose of sulfonylurea by 50% or basal insulin dose by 20% when starting therapy.
- Discontinue DPP-4 inhibitor before starting (if applicable)
- Start at lowest dose and up-titrate slowly to mitigate nausea to the doses used in CV outcome trials*
- Instruct patients to more closely monitor glucose at home for the first 4 weeks of therapy
- Advise patients to undergo appropriate, guideline-recommended eye examinations before starting therapy if not done within the last 12 months
- Increase in diabetic retinopathy complications (for semaglutide)

*Higher doses of GLP-1 RA can sometimes be used for weight loss, but have not been shown to offer additional CV risk reduction.

A1C = hemoglobin A1C; CV = cardiovascular; DPP4 = dipeptidyl peptidase-4; GLP-1RA = glucagon-like peptide-1 receptor agonist.
HELPFUL RESOURCES FOR CLINICIANS AND PATIENTS

<table>
<thead>
<tr>
<th>Institution</th>
<th>Description</th>
</tr>
</thead>
</table>
| **American College of Cardiology** | 2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease: A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways. [ACC.org/CVDinDMDecisionPathway](http://ACC.org/CVDinDMDecisionPathway)  
Clinician Tool: Key Considerations in use of GLP-1RAs and SGLT2is for CV Risk Reduction in Patients with ASCVD and T2D. [ACC.org/CVDinDMClinicianTool](http://ACC.org/CVDinDMClinicianTool)  
ASCVD Risk Estimator Plus App. [ACC.org/Apps](http://ACC.org/Apps) |
| **ACC's CardioSmart.org** | For more about Diabetes and Heart Disease, including patient infographics, go to [CardioSmart.org/DiabetesandHeartDisease](http://CardioSmart.org/DiabetesandHeartDisease). |
| **Centers for Disease Prevention and Control** | Diabetes, Heart Disease, and You. [https://www.cdc.gov/features/diabetes-heart-disease/index.html](https://www.cdc.gov/features/diabetes-heart-disease/index.html) |

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