

## KDBH Podcast #5: ASCVD Risk Calculator

- Salim Virani: 00:04 Welcome and thank you for joining this podcast on cardiovascular disease and diabetes for healthcare professionals. The goal of this ongoing series is to reduce cardiovascular death and incidents of heart attacks and strokes in people with diabetes and is based on the new collaborative initiative between the American Heart Association and the American Diabetes Association, Know Diabetes by Heart™.
- Salim Virani: 00:28 This series is brought to you by founding sponsors, Boehringer Ingelheim and Eli Lilly and Company Diabetes Alliance, and Novo Nordisk, and national sponsors, Sanofi and AstraZeneca.
- Salim Virani: 00:41 I am Salim Virani from Baylor College of Medicine and the Michael E. DeBakey Medical Center and I will be discussing the ASCVD, or the Atherosclerotic Cardiovascular Disease risk calculator, which is a tool, as you may know, that enables healthcare providers and patients to estimate ten-year risk of Atherosclerotic Cardiovascular Disease or ASCVD.
- Salim Virani: 01:09 The first thing that clinicians may ask is, 'Why should we perform ASCVD or Atherosclerotic Cardiovascular Disease risk assessment?' Throughout this podcast, I will talk about ASCVD risk assessment in general, as well as why do we need to do it in patients who have diabetes. The first question, as I said, was that anybody who would ask, 'Why should we perform ASCVD risk assessment?' And the reasons are many.
- Salim Virani: 01:36 The first is, we know that any therapy we use for ASCVD risk reduction ... the benefit of that therapy ... is dependent on the absolute risk reduction that we get from that therapy. What do I mean by that? Let's say we talk about statin therapy. We know that statin therapy lowers risk of Atherosclerotic Cardiovascular Disease in any patient that we use it in. But for the same amount of LDL cholesterol lowering associated with statin therapy, the absolute risk reduction and the benefit is more for a patient who has higher baseline risk.
- Salim Virani: 02:10 For example, if we lower LDL cholesterol by one millimole, or forty milligrams per deciliter, for a patient whose ten-year risk is less than five percent, we reduce major vascular events in six patients out of a thousand who are treated. But if we do the same LDL cholesterol lowering in a patient whose ten-year risk is more than 30%, then we prevent sixty major vascular events for every thousand patients that we treat. We would not know how many events we are preventing if we do not do a ten-year risk calculation. The same holds true for reduction in systolic blood pressure or diastolic blood pressure as well. So, any preventive therapy we undertake in our patients ... the

magnitude of benefit that our patients derive is dependent on the ten-year, or global cardiovascular disease risk. So, it's extremely important for us to perform that.

- Salim Virani: 03:06 The second is, multiple studies have shown that when we perform that ten-year risk calculation, it actually is associated with a reduction in ten-year risk down the line as well as better control of risk factors. Importantly, this is free, and it is not associated with any harm.
- Salim Virani: 03:27 And last but not the least, when a patient is provided with numbers in terms of what their ten-year risk of having a heart attack or stroke or dying from one is, they are more likely to adhere to the therapies that we prescribe. Both in terms of lifestyle modification as well as, possibly, the use of medications to reduce that risk.
- Salim Virani: 03:49 This next question that the clinicians may ask is, 'What are some tools available to calculate a ten-year risk or estimate a ten-year risk of ASCVD events in our patients?' And then, 'Who should we do it in and how often should we do it?'
- Salim Virani: 04:05 The first question is, 'What are some commonly available tools that we have?' If we look at some of the major tools that are available in the U.S., those include the Framingham General Cardiovascular Disease or CVD Risk Calculator, the Pooled Cohort Risk Equations, which is available by the American College of Cardiology/American Heart Association, and we have the Reynolds Risk Score. In the Europeans, we also have SCORE Risk Calculation, which was mostly derived in the European population, so I'm not going to talk about that any further. But of the three that we have available here, which is the Framingham CVD Risk Calculator, as we know, this was derived in mostly a very specific white population and, therefore, the results may not be generalizable to the entire U.S. population.
- Salim Virani: 04:53 After the Framingham Risk Score, we have the Reynolds Risk Score, in which, apart from other risk factors, one also uses HSCRP or High Sensitivity C-Reactive Protein, and family history of cardiovascular diseases as to other input variables and calculates a ten-year risk. But, this, obviously, requires the use of a test, which adds another extra layer of complexity when calculating ten-year risk on a patient.
- Salim Virani: 05:20 So, the one that is recommended by the major American College of Cardiology/American Heart Association guidelines, is the use of Pooled Cohort Risk Equations, which was derived from five major epidemiologic cohorts in the U.S. and these are

sex and race specific equations. The other important aspect of Pooled Cohort Risk Equations is that it gives us the ten-year risk of having hard ASCVD events. So what it includes is: risk of coronary heart disease related death, non-fatal myocardial infarction, fatal or nonfatal stroke. It is extremely important for the clinicians to know that when we are calculating a ten-year risk, it actually includes those four outcomes. And all those are hard outcomes. For example, coronary heart disease associated death, nonfatal MI, fatal or nonfatal stroke.

Salim Virani: 06:12 The other thing that the clinicians may ask is, 'What are the variables that we have to put in to get the ten-year risk?' And those include age, sex, race of the patient, total cholesterol level, HDL cholesterol levels, systolic blood pressure, use of antihypertensive therapy, history of diabetes, or current smoking. Once those variables are inserted, one gets a ten-year risk of heart ASCVD events in their patients and, as I said earlier, this is sex and race specific. We know that in our African-American patients, as well as in women, stroke related outcomes may be more important at times than actually coronary heart disease associated outcomes. And they may be more prevalent in some of the subgroups that might be important when we are treating those patients.

Salim Virani: 07:01 The other question is, 'How often and when should the use of ten-year risk calculations start?' Since most of the patients who were included in these cohorts from which the Pooled Cohort Risk Equations was derived were between the ages of 40 to 79, the guidelines mostly recommend that the ten-year risk calculation be performed in patients between the ages of 40 to 75. Obviously, between 75 to 79 one can perform a ten-year risk calculation, but the risk is always going to be high because age gives the most points when you're calculating a ten-year risk. To summarize, risk assessment should be performed in patients who are between the ages of 40 to 75.

Salim Virani: 07:42 The equations are mostly derived for patients who are white or African-American. If there is a patient who belongs to other ethnic or racial group, in those cases, generally, one would mark as other category when you're doing it online but the estimates you get are generally derived using the white population. These are readily available online, on the website for American Heart Association as well as American College of Cardiology.

Salim Virani: 08:08 The other important thing for Pooled Cohort Risk Equations, which is what is recommended by the guidelines is, that this equation has been validated in multiple U.S. cohorts and this is the equation that has been used for reclassification using other

biomarkers as well as the imaging test. For example, Coronary Artery Calcium Score, which is now recommended by the guidelines to be used for further risk reclassification.

- Salim Virani: 08:37 Important aspect when we talk about our patients with diabetes is, did we all know that patients with diabetes are at a higher risk of ASCVD events. So, in those patients, for example, patients with diabetes between the ages of 40 to 75, the guidelines recommend that we do not need to perform a ten-year risk assessment to identify which patients should be on statin therapy. But, ten-year risk actually helps us to identify what should be the intensity of statin therapy. So, all patients with diabetes should be on statin therapy, because we know that statins work in patients with diabetes. But, ten-year risk is performed rather to identify whether it should be moderate or high intensity statin therapy. For patients who may have a ten-year risk that's above 7.5 percent, clinicians may want to use a high intensity statin therapy to further reduce the risk of ASCVD.
- Salim Virani: 09:33 The other aspect of using Pooled Cohort Risk Equations, which is important for clinicians to understand is that now even the hypertension guidelines recommend the use of ten-year ASCVD risk, because we know that even the efficacy of antihypertensive therapies depends on the patient's ten-year risk. As I said, the magnitude of risk reduction we get from both systolic and diastolic blood pressure lowering is actually dependent on the patient's absolute ten-year risk of ASCVD events. For example, the guidelines tell us that in patients who have systolic blood pressure between 130 to 139 or diastolic blood pressure between 80 to 89, if the ten-year ASCVD risk is above 10%, in those patients, apart from lifestyle therapy, medication should be used to lower systolic blood pressure to below 130, whereas, if the ten-year risk is less than 10%, then clinicians can continue with lifestyle therapies.
- Salim Virani: 10:35 So the next question we have is, 'What are the limitations of any risk assessment tool?' We know that risk assessment tools work the best in the populations that they're derived in. But when we try to generalize those than they may not be totally generalizable. When we talk about the Pooled Cohort Risk Equations, in general, it works very well around the decision thresholds for statin therapy which is usually about 7.5%.
- Salim Virani: 11:02 And for blood pressure lowering, which is about 10%. So, in that 7.5 to 10%, in most of the studies, it is usually well calibrated, but as one would expect, when we try to use Pooled Cohort Risk Equations in a population where most of the sample is derived from more affluent population or population that is more likely

to receive preventive therapies, for example: statins, aspirin or antihypertensive therapy, it may overestimate risk.

- Salim Virani: 11:31 On the other hand, if we use this in populations that are of low-socio-economic status or in patients who have inflammatory disorders, for example: HIV, lupus, psoriasis or other ethnic groups, for example, South Asians. In those cases, the risk may be underestimated and, therefore, it is extremely important to use this ten-year risk ASCVD risk assessment as a guidepost. But, around that, one needs to look at the patient in front of them and then use other, what we call, risk specific enhancers to further estimate this risk in a more precise manner and make the risk more personal to the patient that's in front of us.
- Salim Virani: 12:17 We will talk about that as to what those risk enhancers are in our next segment.
- Salim Virani: 12:22 So the next question we have is, 'Once a ten-year risk is estimated, how can clinicians use this ten-year risk and decide on what are the therapies that they should use? We know as far as the cholesterol guidelines are concerned, once a ten-year risk is estimated, patients can be divided up into four major categories. One is patients who are low risk. Those with ten-year ASCVD risk less than 5%. In these patients, lifestyle therapies, for example, a heart healthy diet as well as physical activity ... Those recommendations are the only recommendations that we need to follow.
- Salim Virani: 13:01 On the other hand, patients who are very high risk, for example: those who have a ten-year risk of greater than or equal to 20%. In those patients, lifestyle plus statin therapy is recommended. In patients who fall between the five to 7.5% which is what we call borderline risk. 7.5 to 20% risk, which is called the intermediate risk category, in these patients if the clinician and patient are comfortable starting therapy, for example, statin therapy, to reduce their future risk of ASCVD events, it's a Class One recommendation to go ahead and do that. But if there is any concern that the risk may be overestimated, then in those cases, clinicians could use risk enhancing factors to further personalize the risk.
- Salim Virani: 13:51 That's when we're talking about a general patient who comes to our clinic to talk about their ASCVD risk. What about a patient with diabetes? For a patient with diabetes, the guidelines recommend that we do not do ten-year risk assessment to identify who's going to derive benefit from statin therapy, because we know that patients with diabetes have a high ASCVD risk. Every patient who is between the ages of 40 to 75

years should be on statin therapy. The reason we would do the ten-year risk assessment in those patients is to identify the intensity of statin therapy. So, if there is a patient with diabetes and their ten-year risk is above 7.5%, then in those patients clinicians should try to use high intensity statin therapy, because they will derive the most absolute risk reduction from the use of statin therapy.

Salim Virani: 14:45

And as we discussed earlier, the same holds true when we are talking about blood pressure management. And there the threshold that's used is 10% if a patient's ten-year risk is above 10% and their systolic blood pressure is between 130 to 139. In those patients, clinicians should use both lifestyle modification as well as medications with the target goal of blood pressure less than 130 millimeters of mercury.

Salim Virani: 15:12

So let's talk about once we have done a ten-year risk calculation, how can we further personalize this risk for a patient who's in front of us. Because as we discussed, that risk can be underestimated or overestimated in a particular patient. These equations work very well at the population level, but at the individual patient level, we have to personalize this risk for the patient who's in front of us.

Salim Virani: 15:37

And that's why the guidelines have introduced the concept of risk enhancers. What are these risk enhancers? These are variables that may or may not independently provide prognostic information on top of the ten-year risk assessment using Pooled Cohort Risk Equations. But at an individual patient level, they may be associated with a higher ASCVD event rate and, therefore, these variables may push the clinician and the patient towards earlier initiation of risk reduction therapies.

Salim Virani: 16:08

All of these variables make intuitive sense. For example, family history of premature ASCVD. We know that patients who have family history of premature ASCVD are at a higher risk of having a premature event themselves. So, if the ten-year risk is, let's say 8%, but the patient has premature family history of cardiovascular disease, but the patient and the clinician may decide that they want to be treated early or with a higher intensity of statin therapy.

Salim Virani: 16:35

The same holds true for family hypercholesterolemia of 160 to 190 milligrams per deciliter. Now we know that in patients whose LDL cholesterol level is above 190, we do not do a risk assessment. We just treat them because they have very high lifetime risk of ASCVD events. But when LDL cholesterol is between 160 to 189, that may serve as a risk enhancer and push

the clinician and patient to consider a therapy early on. Presence of metabolic syndrome, presence of chronic kidney disease, South Asian ancestry, having chronic inflammatory disorders like psoriasis, rheumatoid arthritis, HIV, or AIDS. None of those are captured by Pooled Cohort Risk Equations or other risk equations. So even if the risk is borderline or intermediate, clinicians may want to start risk reduction therapies early on in those patients.

Salim Virani: 17:27 For the first time in guidelines, we're talking about risk that are specific to women. For example: history of premature menopause, or history of pregnancy associated conditions like preeclampsia, or hypertension during pregnancy, diabetes during pregnancy. We know that women who have these conditions have a higher lifetime risk of having cardiovascular disease events. So, if they are in the borderline to intermediate risk categories, by risk assessment, these patients may derive from earlier initiation or increasing the intensity of their statin therapy.

Salim Virani: 18:01 And then there are some lipid or biomarkers. If they are measured, then those could be used to further personalize this. Those include elevated levels of high sensitivity CRP, elevated Lp(a) levels, elevated apoB levels, or having an ankle-brachial index less than .9.

Salim Virani: 18:19 So those were for the general population. The guidelines also talk about risk enhancers in patients with diabetes. For example, the duration of diabetes. If a Type 1 diabetic patient has had diabetes for more than 20 years, or a Type 2 diabetic had diabetes for more than 10 years, that's a risk enhancer. If a diabetic patient has end organ damage, for example: nephropathy, neuropathy, retinopathy, then those are risk enhancers for patients with diabetes. A patient with diabetes who also has subclinical peripheral arterial disease by having ABI less than .9, that is a diabetes specific risk enhancers. In patients with diabetes, if they have these diabetes specific risk enhancers, then the guidelines would tell us that in those patients we should increase the intensity of statin therapy from moderate to high. Because these patients have a higher risk of having cardiovascular events.

Salim Virani: 19:19 So to summarize for patients with diabetes, the ten-year risk calculation is not done to identify who should be on statin therapy. Ten-year risk is done to identify what should be the intensity of statin therapy. If the ten-year risk is high, those patients should likely be treated with high intensity statin therapy. Similarly, for a patient with diabetes who has diabetes

specific risk enhancers, a long duration of diabetes and organ damage with diabetes, presence of subclinical peripheral arterial disease as evident by a low ABI, in these patients high intensity statin therapy should be used.

Salim Virani: 19:58 Up until now, we have discussed why we should perform risk assessment. We've talked about what are the available tools. We've talked about how a clinician should use those tools to calculate a ten-year risk. We've talked about the concept of risk enhancers. And we've talked about the concept of how ten-year risk, as well as risk enhancers should be used for a patient with diabetes. We've talked about risk assessment and we've talked about the risk enhancers.

Salim Virani: 20:28 The third concept in risk assessment is the concept of risk reclassification. So, when one performs a ten-year risk, calculation looks into risk enhancers, whether it's for an average patient or a patient with diabetes, there could still be times when there is uncertainty on the part of the clinician or the patient whether they should be taking preventive therapies. For example, statin therapy. In those cases, the guidelines would tell us that a Coronary Artery Calcium Score, or what is also known as CAC, can be performed to further risk stratify those patients. If the Coronary Artery Calcium Score is zero, in those patients, one could defer therapy for four to five years and then perform risk assessment, possibly a calcium scanning again.

Salim Virani: 21:17 In patients whose Coronary Artery Calcium Score is greater than or equal to 100, those patients, in general, are at very high risk of ASCVD events and those patients should be treated. When it's between one to 99, the guidelines would tell us that these patients do have subclinical atherosclerosis and these patients should be treated ... most of them, at least should be treated, but clinical judgment is required when we look at scores between one and 99. Similarly, if the score is greater or equal to 75th percentile for a patient's age as well as their sex, then those patients are high risk and should be treated.

Salim Virani: 21:58 Now the guidelines tell us that in patients who are diabetic patients, patients who are currently smoking, patients who have family history of Atherosclerotic Cardiovascular Disease events, or those who may have chronic inflammatory disorders, for example: psoriasis, or have HIV, in these patients, the utility of CAC may be limited. So, for most of our patients with diabetes, in general, they should be treated taking into account risk enhancers and the use of Coronary Artery Calcium scoring should be very, very limited in those patients.



- Salim Virani: 22:33 So the clinicians sometimes would ask, 'How do we assess risk in young individuals?' For example, patients who are between the ages of 20 to 39. As we said, the Pooled Cohort Risk Equations is not validated for younger adults. So how do we perform risk assessment in those individuals? The guidelines would tell us that in those patients, one could use what we call a 'lifetime risk of ASCVD.' And that is based on the notion that even one uncontrolled risk factor in young adulthood could be associated with a higher risk of ASCVD events over the patient's lifetime. So in patients between the ages of 20 to 39, clinicians should perform individual risk factor assessment every four to six years as well as if they want to use a communication tool, they could use a lifetime risk. And that lifetime risk is not used to determine the therapy or intensity of therapy in terms of medications, but yet, could be a very powerful tool in terms of communicating risk with the patients to move them towards a healthier lifestyle.
- Salim Virani: 23:38 So I would urge all our listeners to also look at those younger adults so we can start those therapies. For example, lifestyle related therapies, diet and physical activity in our younger adults so they don't develop Atherosclerosis in the first place.
- Salim Virani: 23:55 Let's say that we have done a ten-year risk calculation, we have used our risk enhancers, whether we have a patient with diabetes or without diabetes, and now we want to talk about that risk with our patient. So, we'll want to perform a risk discussion. What are some of the important things that we need to keep in mind? What are some of the principles that we want to keep in mind when we're communicating that risk with our patient?
- Salim Virani: 24:21 The few things that ... I usually put it as a model called Five P Model. The first thing is preference. What does the patient prefer in terms of which risk factors they would like to work on? What are their values? What is their priority?
- Salim Virani: 24:35 The second P is for precision. How confident are we that the risk we have assessed is the actual risk of that patient? And, again, this is to remind us that we need to take patient specific risk enhancers into account.
- Salim Virani: 24:49 The third P is participation. How motivated is the patient to participate in the ongoing care?
- Salim Virani: 24:56 Fourth is potency. What is the treatment dose that we're going to use? Are we going to use low intensity statin therapy, moderate intensity statin therapy, or high intensity statin

therapy? And we discussed a little bit as to what are some of the things that could help us in determining the dose of therapy.

Salim Virani: 25:13

And the last P is for price. It is extremely important to understand what is going to be the cost to the patient?

Salim Virani: 25:21

And that is why it is extremely important to keep all those five P's as part of discussion. So those five P's again include: patient preference, precision, participation, potency, and price.

Salim Virani: 25:34

Once we keep those five P's into consideration, we can discuss those with the patient and come up with a plan that is acceptable to the patient. Because by keeping all these things as part of our discussion with the patient, our patients are more likely to adhere to lifestyle recommendations that we provide to them as well as any use of medications that we prescribe to our patients.

Salim Virani: 26:00

So in the last part of this segment, I would like to summarize what we have discussed thus far for our clinicians.

Salim Virani: 26:07

The most important thing is, first, to assess risk or calculate ten-year risk on a patient between the ages of 40 to 75. The first thing we do is we calculate risk using Pooled Cohort Risk Equations. Remember, in patients with diabetes, we calculate risk not to assess whether they should be on statin therapy, but we calculate risk to identify what intensity of statin therapy they should be on.

Salim Virani: 26:33

The second part of this is to use risk enhancers. We talked about risk enhancers in the general population and we talked about diabetes specific risk enhancers. That's the second step.

Salim Virani: 26:45

The third step is risk reclassification. And that's done in very limited number of patients if there is uncertainty after doing the first two steps. That is the step of risk assessment and further personalizing that risk based on risk enhancers.

Salim Virani: 27:01

And the term that I would put out there for clinicians to remember is CPR. So, again, this is CPR in primary prevention. To prevent the patient from needing real CPR. This was a term that was coined by Don Lloyd-Jones and it is easy to remember when you use this. C is for calculate ASCVD risk. P is to personalize that risk using risk enhancers. R is to reclassify risk in select individuals using Coronary Artery Calcium.

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Salim Virani:	27:33	And, as we discussed, that for patients with diabetes, there are specific risk enhancers that we need to keep in mind.
Salim Virani:	27:41	So I hope that from this discussion, our clinicians would start doing more and more risk assessment for their everyday patients that they see in their clinics, as well as patients with diabetes, who we know are very high risk in terms of future risk of ASCVD events.
Salim Virani:	28:01	With this, I would thank you very much for listening and stay tuned for the upcoming podcasts.
Salim Virani:	28:07	Thank you.