Webinar Transcript:
**Therapeutic Considerations for Hypertension**

**Crystal Welch:** Welcome to HHQI's Therapeutic Considerations for Hypertension clinicians’ webinar. The purpose of this webinar is to assist clinicians with improving their knowledge of blood pressure medication classifications and the therapeutic considerations. We will review actions, possible side effects, contraindications, and clinical considerations. There is a clinical resource, Antihypertensive Medication Reference, that may be helpful with this webinar if you have not already downloaded the document.

We are pleased to have Jerad Bailey with HHQI to present today on blood pressure medication classifications. Jerad graduated magna cum laude from Marshall University, with a bachelor of Arts degree and cum laude from West Virginia University with a doctorate of Pharmacy. He's currently the lead pharmacist at Cabin Creek Health Systems in West Virginia and serves as a pharmacy consultant for several organizations. There's a lot of content he will be covering in this session, so let's begin. Jerad, I'll turn it over to you.

**Jerad Bailey:** Thanks, Crystal. Again, my name is Jerad Bailey. I'll be presenting today, and I apologize, I was the one manning the slides here, but I do want to reference this clinicians’ resource here that will be available for download. Some of the content that I'm talking about today will come from this resource. I am using a lot of other pharmacy resources as well, but this could be a very good resource for you to use, to go along with this presentation, along with the slides which should be made available for you to also take a look at.

Today I will be talking about the Therapeutic Considerations for Hypertension. My goals today are to review blood pressure and the condition "hypertension," current treatment protocols, the therapeutic classes used for the treatment of hypertension, and the effects, side effects, and considerations to be made in the outpatient setting with these medications.

Blood pressure is defined as the force of blood against arterial walls as it circulates through the body. When we typically get a blood pressure for a patient, we get the two numbers, the 120 over 80. Those numbers represent the systolic blood pressure and the diastolic blood pressure. Systolic blood pressure is when the left ventricle is most contracted, so a high pressure state, hence the higher number, and the diastolic blood pressure, in which the left ventricle is most relaxed, so we have low pressure. A quick review of our cardiac cycle. We know that the atriums and the ventricles of the heart alternate between being contracted and relaxed.
When these chambers are relaxed, the heart is filling with blood, and they contract in a kind of a 1, 2 motion, so the atrium will contract and the ventricle will contract. During this contraction, we have a high pressure state in which blood is being ejected from the heart throughout the circulatory system feeding the entire body with oxygenated blood. There's several things that factor in the blood pressure, such as our cardiac output, the viscosity of our blood, and something called total peripheral resistance, which I'll call TPR because I'm going to reference it so many times throughout this presentation.

Cardiac output consists of 2 different things. First of which is heart rate. The faster your heart is beating, the more blood that's going to flow into your circulatory system. Our sympathetic nervous system, which mainly controls our fight or flight response ... Say, for example, a grizzly bear just comes through the door. Our heart's going to start racing because our body is prepared to either run away from this threat or to fight it off. It's kind of the main function of our sympathetic nervous system to get us prepared for this. The faster our heart beats, the more blood we can get, we're more prepared for this. Faster pumping means greater fluid movement.

Also, for cardiac output, we have to think about stroke volume. I put a picture of a bucket brigade here which is the old-timey way of putting out fire. A full bucket is more effective than a half-empty bucket, when we have our bucket brigade going here. A larger stroke volume will traditionally allow some more blood to circulate with each heartbeat. It is the efficiency of the heartbeat. A stroke volume is not really targeted with many of these therapies regardless of whether we're in a fight or flight response or relaxed. Stroke volume shouldn't vary on much throughout the day or throughout activities during the day.

Next is blood viscosity. Naturally, the thicker somebody's blood is or the thicker fluid is, the more difficult it is to flow through. I've got a picture of honey and a honeycomb here. Honey does not flow as quickly as, say, regular water. A thinner fluid requires less effort to move and flows more freely. A lot of these medications will actually decrease blood viscosity by removing the water from the blood.

Last is total peripheral resistance. An amount of fluid following through a smaller area is under more pressure than flowing through a larger area. If anybody has ever played with a water hose without the faucet on it in, you may have placed your thumb over the ends to squirt somebody really good from a very far distance. When you put your thumb over the opening, you're reducing the area for which the water is able to flow through. You create pressure. The water is actually actively pushing against your thumb, so you can feel that pressure as you're doing it, and that's the amount of pressure there's also being pushed against all surfaces of this hose. A lot of these drugs will reduce this resistance.
They'll open up these circulatory flows, so that there's less resistance and less work every time your heart beats.

What is normal blood pressure? Well, the American Heart Association has defined some thresholds. 120 over 80 is generally the accepted number almost across the board. As we increase, we start getting the prehypertension, at the beginning of high blood pressure all the way up to hypertension crisis, which we're not going to speak much about today. Generally, 120 over 80, we normally don't freak out too much about. Once we start getting at the prehypertension stage, we start counseling our patients on lifestyle modification to be able to drop those numbers down a bit.

Hypertension is a very insidious disease. It's very difficult to explain to a patient why we might need to treat them for something that doesn't really have any immediate ill effect on them. The issue with hypertension is that it makes the heart and blood vessels have to work harder to overcome this increased pressure. Because of the increased pressure, we can decrease blood perfusion to the heart, we can dislodge blockages or burst arteries leading to the brain, or we can call something called renal artery stenosis, which eventually will lead to kidney failure. We kind of have to scare patients into thinking, "Okay, this is what could happen if you don't take this medications or you don't get your blood pressure under control."

Hypertension has been a very hot topic for a long period of time. The Joint National Committee, which has been responsible for creating a list of best practices for treatment of hypertension, most recently revised their best practices in 2014. What we commonly refer to JNC 8. JNC 8 is a combination of lifestyle modifications and pharmacotherapeutic interventions to use with patients with hypertension. The lifestyle modifications, I won't get into these very much. They include what we normally tell our patients: watch your diet, decrease the amount of salt you eat, exercise a bit more, lose a little weight, stop smoking, limit alcohol, manage stress. That stuff. Good luck with that one, I'm sure. These are some of the things that have proven to reduce blood pressure and in some cases when a patient is prehypertensive, this might be enough to prevent them from having to use any blood pressure medications at all. We generally want to start with lifestyle modifications because just about every single drug that we're going to talk about today may have some type of side effect.

As far as starting pharmacologic therapy, JNC 8 guidelines suggest these particular criteria. Now, for patients over the age of 60, they don't recommend starting treatment until 150 over 90. For just about every other population, it's 140 over 90. In my experience, just about every clinician I've worked with has stuck with the 140 over 90 as their target, so that's probably the important one to remember for
general purposes. Also, in the state of West Virginia, where diabetes is so prevalent, very frequently you also have comorbidity on board, so 140 over 90 is generally our target.

There are a lot of therapeutic options. There are over a dozen medication classes with indications to treat hypertension. Some of them have anywhere between one and 10 medications in the particular class, so what do we choose? Which ones are better? It's often a question I get from doctors. Where should I start with this particular patient? Thankfully, JNC 8 has come up with a starting lineup of medications that we can use as frontline therapies for these patients. The four classes we're going to talk about first are Thiazide Diuretics, Calcium Channel Blockers, Angiotensin-Converting Enzyme Inhibitors, you've probably heard of ACE inhibitors, or angiotensin receptor blockers, which are ARBs.

Now thiazide diuretics, the big one we always talk about is hydrochlorothiazide. It is certainly the most prevalent of all of the thiazide diuretics available. You'll notice that throughout this presentation I have bolded some of these medications. Medications that are in bold are actually one of the top 200 dispensed drugs in year 2013, which was the most recent data I was able to find. It's from Pharmacy Times magazine. If you're going to remember one of each class, I would recommend that'd be the bolded one because these are the most likely ones that you're going to be seeing in practice.

Hydrochlorothiazide, we commonly refer to as HCTZ, because hydrochlorothiazide is an absolute mouthful. It's the most common of the thiazide diuretics. Thiazide diuretics inhibit sodium and chloride re-absorption in the kidney. The kidney is constantly trying to recycle sodium, chloride, potassium, many of the other electrolytes from being excreted into the urine. The thiazide diuretics prevent this from happening, so because sodium and chloride are osmotically active, since they're not being reabsorbed by the kidney, they're going to pull water along with them, so we create the diuretic effect. Since we now have less water in the body, which means there's less water in the blood, there's less work for the heart to be able ... It makes it easier for the heart to pump the blood across the circulatory system.

Now because this is a diuretic, one of the major side effects is frequent urination. Also, since we're dealing with dieresis, these can cause electrolyte imbalance. Low potassium, low magnesium, because we're getting rid of a lot of the as well, we actually called them an increase in calcium within the blood. These agents should also be avoided in patients who are prone to gout and renal failure, due to you're increasing the amount of work that the kidney is having to do. Also, the potential for rash and photosensitivity with thiazide diuretics. You're
essentially dehydrating an individual, there's less water in the skin, so therefore they're more prone to burning as well.

Important considerations for thiazide diuretics, the first and foremost is rehydrate. These medications are actively getting water or removing water from the body and this does need to be replaced quite frequently. Also, increased sun sensitivity. We're in the summer months right now, and we're trying to encourage patients to be more active, get outside and lose weight, and now we're planning on giving them a medication that's going to cause them to get a sunburn more easily, so we need to counsel these patients to make sure that they're using adequate sunscreen while they're getting out, doing work in the yard, whatever they plan on doing. Last, since these medications can cause some electrolyte imbalance, you want to try to get some baseline and periodic labs to make sure that we aren't causing any major issues with their electrolytes.

Next class I'd like to talk about is calcium channel blockers. Calcium channel blockers can be divided into two different classes. On the left, you'll see the dihydropyridines and on the right the nondihydropyridines. The dihydropyridines all end in "pin" or "pine" so Amlodipine, Felodipine, Isradipine, etc. The nondihydropyridines don't really have a naming convention, regretfully. Diltiazem and Verapamil. Even though they aren't in bold, I do see these quite frequently. They are very common drugs. These aren't rarities unlike the ones on the left, where Amlodipine was the main star of the dihydropyridines.

The muscles in your body, and your cardiac muscle especially, require an influx of calcium ions in order to contract, and calcium channel blockers prevent this from happening. Calcium ions aren't getting in the muscle tissue, which means your heart is not beating as frequently, and the muscles, the small muscles inside of the arteries are not contracting, which means you have a more relaxed artery. Dihydropyridine, like Amlodipine, mainly target the muscles and the arteries. So you have a relaxed blood vessel, which means total peripheral resistance is decreased.

Nondihydropyridines mainly target the cardiac muscle. This reduces the patient's heart rate and the contractility of the heart. Now, because we are dealing with ... We're changing the rhythm of the heart, we run the risk of AV block in some of these patients, and also since we are essentially making the heart less efficient, the heart is not really able to pump all the blood it needs to during every beat, so we can pooled in the veins, or edema, and also fatigue and dizziness, because we aren't getting as much circulation to the brain as we're normally used to.

Again, a common trend with these blood pressure medications is going to be skin conditions, in this case rash, can occur. Major considerations for calcium channel
blockers, we talk about conductivity changes, so electrocardiograms periodically, make sure we don't have AV blockers, QT prolongation, or anything else that might be a major issue with these patients. Calcium channel blockers are subject to a lot of drug-drug interactions. Calcium channel blockers are CYP 3A4 substrates, which you might have to go back to pharmacotherapy and kinetics, but Cytochrome P450 is an enzyme that metabolizes many of these drugs, and calcium channel blockers are substrates, which means there're some drugs that can increase their concentration. There're some drugs that could decrease their concentration. They can bit a bit complex to manage in patients that have a lot of drugs on their medication profile. Someone who has a lot of comorbidities, calcium channel blockers might not be the right first-line choice.

Next, I'm going to speak about ACE inhibitors. ACE inhibitors all end in "pril" so Benazepril, Lisinopril, Captopril. Lisinopril is definitely a major one of this particular group. ACE inhibitors work by ... They inhibit ACE, which is an abbreviation for angiotensin converting enzyme. There is an enzyme in the body called angiotensin I, that angiotensin converting enzyme converts to angiotensin II. Angiotensin II is an extremely potent vasodilator which will increase our blood pressure. ACE inhibitors prevent I from becoming II, which means that there's less II floating around in our body, we're going to have less of this vasodilation, which means that we are going to have a reduced TPR.

The major side effects for ACE inhibitors, these can cause electrolyte imbalance. The main thing is hyperkalemia. We will going to return to this later because there are a lot of medications here that can affect our potassium. Skin conditions are fairly rare, but it's something we actually can visualize and see on these patients. The most common one is actually this dry cough. This is a cough that really has no really good etiology. There's no allergies or anything precipitating. It's just a dry nagging cough. For some patients, they can take several years on ACE inhibitors before it actually precipitates, so it's something we always need to remain cognizant of. Renal artery stenosis is a potential issue because this can affect the blood flow to the kidneys. Last is angioedema, which is actually more common in African-Americans. This consideration we'll talk about a little bit later.

As far as considerations for ACE inhibitors, the renal artery stenosis ... ACE inhibitors and ARBs are usually selected for patients because they have some renal protective properties at low doses. They can protect the kidney. However, one of the major side effects is that they can damage the kidney too, so you have to remain cautious about using these medications because it's a double-edged sword with these. We're giving someone a medication that could protect their kidneys, but may also damage them as well.
ACE inhibitors tend to have a pretty pitiful pregnancy category as well. Most of them are pregnancy category D if not C, so if we have a female patient who is considering becoming pregnant or is pregnant or is of child bearing age, we might not want to make an ACE inhibitor our frontline therapy.

Last, ACE inhibitors and ARBs work very similarly. There's actually therapeutic duplication and really no reason that both of these agents should be used simultaneously in a patient. Angiotensin receptor blockers, or ARBs, are kind of a close cousin of ACE inhibitors. You'll notice that there are quite a few medications that are in our top 200, including two brand name medications. Diovan and Benicar, in 2013, were top sellers. Now, Diovan just recently was made available as a generic in January 2015 is now starting to be listed and our pharmacies are dispensing it. However, Benicar does not have a generic available yet. We're still waiting on that one, but Lozartan is actually still pretty popular and a lot of doctors have transitioned to that just because it is a generic alternative or generic option available in the ARB group.

Again, with the ACE inhibitors, we were preventing angiotensin I from converting into angiotensin II. ARBs will essentially just block the action of angiotensin II. We are not reducing the amount of angiotensin II in the body, we're just preventing it from doing its job essentially. We get the same end result as taking an ACE inhibitor, but we get a reduced instance of the coughing that is one of the major reasons people want to discontinue ACE inhibitors, which are a pretty good drug with the exception of the prevalence of that one side effect.

Dry cough is still reported when they were doing their research on this drug, but it's certainly less prevalent than in ACE inhibitors. They essentially have the same side effect profile, with the exception of the addition of upper respiratory infections that they found during their research. This could have something to do with patients not coughing as frequently and therefore they're not clearing bacteria that could be harbored in the chest. There's not really a lot of conjecture as to why this could be the case. All they know is that the research does show that this does exist more so than when they tested it with placebo or with other ACE inhibitors.

The same considerations need to be made as with ACE inhibitors. Pregnancy categories are still not very great, and there is the therapeutic duplication with ACE inhibitors, but also of the four classes we've talked about so far, ARBs are the newest. Like I said, two of those were brand name medications. Those are not cheap. These are the most expensive of our four frontline therapies and therefore patients ... The populations I work with are typically low income, which means I try not to go to these agents very quickly because they tend to be the most
expensive, when we have other options that have been around for years and years and years, that are generic and very cheap for these patients to get first.

As to selecting first-line therapy, many clinicians are more comfortable with some drugs than others. I do have some doctors who prefer to start with an ACE inhibitor regardless of any type of compelling indications to start with something else or some might like hydrochlorothiazides first. Honestly, for the general population, any of these agents are very viable. If we’re dealing with a patient that has severe hypertension, we can start with two therapies simultaneously. A lot of these medications are available as combination products and typically they’re combined with hydrochlorothiazides for the most part.

There are a couple of considerations. The major ones that JNC 8 suggests are African-American, there's a preference for calcium channel blockers, thiazide diuretics because, like I said earlier, ACE inhibitors and ARBs have that increased risk of angioedema, which they're a pretty serious side effect for African-Americans. On the flip side of that, there's a preference for ACE inhibitors and ARBs in patients with chronic kidney disease because of the renal protective properties. Additional ones that don't appear on this slide, we talked about pregnancy categories. If you have a female of child bearing age, you might not want to pick an ACE or an ARB.

If you have a patient that has financial constraints, you might not want to pick an ARB. Some of these medications, actually, are not great to pair up with diabetes medication. Again, we have a large number of patients who are diabetic in our state. Hydrochlorothiazide tends to complicate control of blood sugar, so that might not be a great first-line option for us to pick. There're a lot of things to consider before we select one of these medications. The goal is that, hopefully, with the use of one medication, we can get a patient into a therapeutic range on their blood pressure but sometimes that's not the case.

When we need to escalate therapy, the first thing we could do is max-out the current therapy before adding additional agents. The issue with this is that when we increase the dose of a medication, let's say we have someone on Lisinopril 10 and we decide to 20 or even 40 for this patient, there is marginal benefit for increasing the dose, but we do have a substantial increase and risk of getting one of those side effects like the renal artery stenosis or the dry cough. It's not always the case, but we do increase the risk every single time we increase the dose.

Our second option is to add an additional agent before we do max-out our current therapy. In the case of a patient that might be on Lisinopril 10, we might want to add a hydrochlorothiazide at 12.5 or 25 milligrams, which the concerns there are that a patient is now taking two medications instead of one, so there is the
potential for adherence issues or there is the potential for drug-drug interactions now that we have introduced a second agent into the mix, especially if they have other comorbidities we're concerned about.

Now, in the event that we require a third therapy, we generally want to use the remaining frontline option unless there's compelling contraindication. Like we said before, if we're concerned about the angioedema in an African-American patient or if we have a lady who is considering becoming pregnant, for example. Those might be sufficient reasons to rule out one of these frontline therapies in favor of something else. I did talk before about there being a considerable number of therapeutic classes to choose from. I got the seven here listed that I'm going to talk about. The remainder are not available in the States or no longer available here. These are the major ones that we're going to talk about that we actually see in practice.

The first one we'll speak about is beta-blockers. You've probably heard a lot about these. The examples I listed is not an exhausted list. There're a considerable number of these available commercially. You'll see Atenolol, carvedilol and metropolol – which is actually available in both a short-acting and long-acting version – appear on our top 200. Beta-blockers work centrally and also peripherally. They ultimately cause a decreased heart rate and total peripheral resistance. Any time we start working on the heart, we have to start worrying about fatigue and also decreased exercise tolerance in these patients. The first couple of weeks a patient starts on a beta-blocker, it can cause some GI upset and it can also mask hypoglycemia because some of the effects of beta-blockers actually look a lot like hypoglycemia. Sometimes a patient can just disregard it like, "Oh, this is just this medication," when in fact they might actually be hypoglycemic at the time.

A patient we put on a beta-blocker, exercise intolerance is a major issue initially, because again, we're telling these patients they need to get outside and exercise. Beta-blockers act like [inaudible 00:29:08] on the heart. If we go back to the example of the grizzly bear barreling into the room, beta-blockers prevent the heart from actually doing its job, so a patient will get very tired very quickly. Eventually the heart will overcome this by becoming more efficient and get a bit stronger, even though it can't beat as frequently, it can beat stronger and kind of overcome this. Initially exercise intolerance is a major issue.

Beta-blockers are also pharmacotherapeutically antagonized by asthma medications like albuterol which is a beta agonist. These medications can interact with one another. Lastly, the pregnancy category of beta-blockers is typically D if not C in the first trimester of pregnancy. The problem with this is that many females will not discover they're pregnant or have confirmed pregnancy until they're very late
into the first trimester. Again, these agents might not necessarily be safe in an individual who is thinking about becoming pregnant. However, they do become viable once we start getting into the second and third trimesters. Still a category C in most cases, when they’re in the third trimester, but they become an option in a patient that we absolutely need to get their blood pressure under control if the benefit out-weighs the risk to the fetus.

The next class is loop diuretics. The major one here is furosemide. Loop diuretics work very similarly to the thiazide diuretics. They're inhibiting the reabsorption of sodium and chloride; this creates the diuretic effect. Less water in the blood, less work for the heart. Again, diuretics are going to cause dehydration, going to cause electrolyte imbalance, and it can also cause hyperglycemia because you’re getting rid of water but you’re not getting rid of glucose in the blood. The concentration actually does rise.

However, loop diuretics are very good for patients with fluid overload or renal failure. They're very good at eliminating a lot of this excess water that the patient may have accumulated due to different comorbidities or some of the medications that we’re going to be talking about later. Loop diuretics are also notorious for interacting with just about every diabetes medication. Regardless if it's an oral agent or insulin, loop diuretics will typically decrease the efficacy of all of these drugs across the board. If you have a patient with diabetes, you may have to escalate some of their other medications to compensate for the fact that they’re on a loop diuretic.

In the same vein is potassium sparing diuretics. Triamterene is the most major of the class. Honestly, triamterene, you're going to see most likely paired with hydrochlorothiazide in a combination product. I don't believe I have ever seen it used as a singular agent. Typically they always pair it with hydrochlorothiazide. Again, similar effects to the loop and thiazide diuretic, except it only works on a certain part of the kidney, and by doing so, we actually spare potassium from being excreted into the urine. Because of this, hyperkalemia becomes an issue. Again, we talked about agents such as ACEs and ARBs which also cause hyperkalemia, so we wouldn’t necessarily want to combine these agents with each other.

Also, agents that you might want to avoid in male patients, mainly because of the risk of gynecomastia, which is the increase or growth of breast tissue and sexual dysfunction, which tends to manifest a bit more frequently in the male population. Also these agents, because we are again messing with water levels and electrolytes, we should avoid in patients with diabetes, cholesterol and gout because it can complicate our control of these. Essentially across the board
diuretics, we want to keep an eye on our diabetic patients, patients with high cholesterol, and patients with gout. It can make all those potentially worse.

Next we're going to get into a series of drugs that pretty much just work on total peripheral resistance in various ways. Alpha-adrenergic blockers prevent vasoconstriction in the arterioles and veins. Because they act centrally, they do tend to work a bit more aggressively. The heart will try to compensate for this, but we do get some edema and palpitations in patients that are taking these, as well as postural or orthostatic hypertension. Because of the edema, we will typically try to pair these medications up with some type of diuretic to help remove that excess fluid. Some of these agents are actually beneficial to give to the men because research has shown that these alpha-adrenergic blockers will actually target the arteries in the prostate. So these agents can be beneficial for men with BPH. The flip side of this coin is that there are drug-drug interactions with phosphodiesterase inhibitors which are our erectile dysfunction drugs, such as Viagra, Cialis, Levitra. The comorbidities usually go hand-in-hand in some patients. Even though it's great for BPH, we still have to be careful because they do kind of act like nitrates in that line.

Speaking of nitrates ... vasodilators and nitrates, there's really only two in this particular class, hydralazine and minoxidil, which we don't really see in oral form that frequently. These cause a relaxation in the smooth muscle and arterioles, decreasing TPR. Again, we're going to get fluid retention. Since we're not having an effect on the heart, if we have fluid retention, the heart is actually going to attempt to beat faster to be able to move this fluid, which case we do get tachycardia. An interesting side effect of minoxidil is hirsutism, which is hair growth in places that you may or may not want hair growth. There're actually shampoos that use minoxidil as an active ingredient to help stimulate hair growth. It's one of those cases where a side effect actually had a benefit when applied in a different manner.

Again, since these agents will cause tachycardia and fluid retention, you want to pair them up with stuff that will help slow the heart down like a beta-blocker or a calcium channel blocker and an agent that will help offset the fluid retention such as one of our diuretics. These agents are reserved for treatment-resistant patients. We're scraping the bottom of the barrel here. We're getting into our last line of therapies as we progress through this list.

Next are our alpha agonists. These literally are last-line therapy. These include clonidine which actually I see quite frequently in spite of the fact that they're considered last-line therapy.
Now, alpha agonists reduce nerve activity in the sympathetic nervous system. This decreases heart rate and total peripheral resistance. Decreased heart rate, we have to worry about bradycardia. With the lower heart rate, we're also going to get some sedation and even potentially heart block. Also, since it's acting centrally, we can get some dry mouth. Agents like clonidine and the alpha agonists have an atrocious side effect profile. They do tend to have a drug-drug interactions with a considerable number of medications and also the longer list of side effects.

Adherence is also a problem because coming off of these medications can cause something called “rebound hypertension” where the blood pressure will actually go significantly higher than where we were pre-treatment. We have to make sure these patients are taking their medication, are being completely adherent with their medication, because they can create a problem that was much bigger than what we started with. Clonidine regimens can be as frequent as three times a day, so being adherent to a medication three times a day can be rather difficult.

The last agent that I'd like to talk about today are renin inhibitors or actually renin inhibitor, because there's only one drug in the class right now, Tekturna. Tekturna decreases renin activity, which – we go back to our ACEs and ARBs – interferes with conversion of angiotensinogen to angiotensin I. Less angiotensin I, less angiotensin II, reduced TPR. Again, we're back to ACEs and ARBs. A very similar side effect profile. We don't see the cough as much, but we do see increased frequency of diarrhea. So pick your poison; I know which one I would pick.

Also, the considerations are going to be almost exactly the same as our ACEs and ARBs, with the exception that they found that you need to avoid these drugs in diabetes, which is quite the opposite of what we do with ACEs and ARBs, because we typically will throw an ACE or an ARB onto a patient with diabetes just because of the renal protective properties. In this particular case, we do not get that, so another drug that kind of acts like ACEs and ARBs.

Here’s my list of references. The Joint National Committee 8 or JNC 8, there's quite a few protocols available online to take a look at. I would highly encourage the use of Epocrates. It's a very handy and free tool that can help with brand generic names or figuring out what class a medication is or pulling up side effects. It's pretty handy regardless of whether you're on-the-go or in the office or anything like that. I thank you very much for your time. I know this was a very dense presentation, but I appreciate your patience, and I hope you best wishes in your practice and hope that you can use this information to help your patients out wherever you might be. Thank you.
Crystal Welch: Thank you, Jared. I just wanted to wrap-up and mention that on this slide, we have some HHQI Blood Pressure Resources. There’re additional resources provided in the Master the Maze of Blood Pressure Medications course on HHQI University, which many of you may be in the middle of taking right now. Just a reminder that all these resources are free and they can be shared as well.

We would just really like to thank Jared Bailey very much for the great information in this presentation. We would also like to thank each of you for attending the session and hope that you can apply information to your daily practices as nurses, therapists, to assist patients to better manage their high blood pressure and reduce their risk for heart attack and stroke. With that, I thank you for attending. Thank you very much.