**Operator:**
It is now my pleasure to turn today’s program over to Steve Dentel from the American Heart Association. Mr. Dentel, the floor is yours.

**Steve Dentel:**
Thank you so much. And on behalf of the American Heart Association, American Stroke Association, and Get With The Guidelines Heart Failure, I’d like to welcome you all to today's webinar, 2017 update to the guidelines for the management of heart failure. My name is Steve Dentel, and I'm the national director for Field Programs and Integration with the American Heart Association. On today's webinar, we will hear from Dr. Clyde Yancy, who will review the 2017 updates to the Guidelines for the management of heart failure. The focused update represents a second of a two-stage publication along with the 2016 focused update on new pharmacological therapy for heart failure. Our presentation is intended to help you understand recent updates which will help guide providers and their choice of heart failure therapy to produce better outcomes for patients. Today's presentation is designed to offer an opportunity for question and answers with our speaker. We encourage your feedback and participation in this event. As Andrea shared, you can submit questions through the presentation by using the green “Question and Answer” button in the lower corner of your screen. A recording of today’s webinar will be made available on the American Heart Association’s website, heart.org/quality.

It’s my pleasure to introduce our speaker for today. Dr. Clyde Yancy is a chief of cardiology of Northwestern University Feinberg School of Medicine and associate director of the Bluhm Cardiovascular Institute and Northwestern Memorial Hospital. He holds the Magerstadt Endowed Professor of Medicine Chair and holds an appointment as professor of the Medical Social Sciences. He is a Northwestern University Feinberg School of Medicine Vice Dean of Diversity and Inclusion. And his research interests are in heart failure, heart transplantation, quality of care, and healthcare disparities. Dr. Yancy has published over 300 peer reviewed papers, and has an active web-based CME presence. It’s now my pleasure to turn things over to Dr. Yancy. And as you can see on the next slide, if you would want to take a look, here are his disclosures. Take it away, Dr. Yancy.

**Clyde Yancy, MD.:**
Steve, thank you very much. And let me extend a very warm welcome to now nearly 600 of you who have attended today's webinar. This is an exciting opportunity for us to talk about the latest information in heart failure. Several of you were very kind and sent me emails prior to today's webinar looking forward to the information. So I worked very hard not to disappoint. And I'm grateful that you are so committed to really staying current with state-of-the-art information on heart failure. I am deliberately leaving up this slide that reads disclosures, because it should be made clear in a very transparent way, that on the one hand I don't have relationships with industry, I receive no consulting fees, honorary or research support, but on the other hand, my perspective on information on data on evidence is framed by my work as an editor, by my work with guideline writing committees, serving as chair of the Heart Failure Guidelines since 2011, by certain federal appointments I have, and certain volunteer appointments I have. And so that allows you to have the full context of the way in which I develop my thought processes.

Our intent today is to discuss the 2017 American College of Cardiology, American Heart Association, and new for this iteration of the Guidelines, the Heart Failure Society of America as joint organizations on the masthead addressing this focused update of the 2013 Guideline for the Management of Heart Failure. That should be the graphic you see in front of you.

Let's begin. There's several things that I want to be certain we accomplish over the next 30 to 35 minutes, or so. I'd like to give you a brief overview of the newest information we have about heart failure. And then go into exactly what is incorporated in the new clinical practice guidelines, and importantly, let's talk about how practice will be changed by these guidelines. The most important part of today's discussion, I think, will be the mid-portion where we emphasize the newest, latest information we have about the prevention of heart failure. That will be followed by a provocative conversation of an emerging phenotype that we previously described in 2013 but that has taken on more substance since the European guidelines were released in 2016 and with our reassessment of the 2017 update. And then finally, and for the first time, we'll begin to talk about a brand-new set of guidelines statements, the heart failure with preserved ejection fraction, including for the first time a recommendation for a therapeutic option. And we'll close with something that is increasingly important in cardiovascular medicine, but particularly with heart failure, and that is a discussion about the important co-morbidities.

So to get us all on the same page, let's remember that this is a disease, a condition, a circumstance, that is essentially ubiquitous. One in five individuals over the age of 40 will develop heart failure at some time during their existence, equal risk for men and women. So this is no longer a condition about them, it's about us. At present, we have over 600 people that have called in for this webinar. That means 120 of us will experience heart failure during our existence, so this is incredibly important. You may recognize that each January, the American Heart Association releases their Heart and Stroke Facts. For 2017, those facts were chaired by my good friend and colleague, Emelia Benjamin, from Boston University in Boston, Massachusetts, a long-standing expert epidemiologist and long-standing, passionate AHA volunteer. And these facts, Emelia endorsed the notion without any hesitancy that heart failure does have a very high prevalence as we get older. There is some data to suggest, even confirmed, that the incidence is decreasing, but Emelia’s Heart and Stroke Facts make it very clear that as the population ages, more and more people are subject to developing this disease. So, we will have ongoing dialogues about managing the burden of heart failure, less so because the incidents is increasing, and more so because of prevalence will continue to grow.

I'm struck that in the 2017 version of the American Heart Association Heart and Stroke Facts several points are made clear. The first, the prevalence will increase to about 6.5 million and higher as we go forward.

The next, there has been an improvement in the five-year survival. We've always talked about the dismal outcomes in heart failure. We'll need to recalculate the way in which we frame those comments, because these outcome data, albeit data by several years, are demonstrating that we're beginning to see real advances, which I would attribute to better treatments, better use of evidence based care, better prevention and better interruption of some of the circumstances like coronary disease that predispose to heart failure. It’s becoming increasingly evident, and I’ll share this with you later in the presentation, that there is much traction to be had from the American Heart Association’s Life Simple 7 steps towards a healthy existence, because it also appears to lead to a lower lifetime risk of heart failure. I will repeat things of prevention throughout our conversation today because I think it's an important point for you to take away as we go forward with this dialogue.

It's also important to note the following. The numbers are beginning to demonstrate that for those persons that are hospitalized, we really are getting very close to a 50/50 incidence of HFrEF, reduced ejection fraction heart failure, versus are HFpEF. We’re also beginning to recognize some very striking differences in the population. For those persons admitted with reduced ejection fraction heart failure, there is a predominant representation of black men, and for those people admitted to the hospital with symptomatic preserved ejection fraction heart failure, a predominant representation of older white women.

You will see before you, the prototypical graphic that demonstrates the stages of heart failure, the patients on the second tier who are most at risk in each stage, and on the third tier those interventions, those goals of care, those treatments that are most highly regarded. This really is the template, the backbone, for how we think about heart failure. And many of you that have been following the guideline process over the last several years will remember that for 2013 for the first time we brought HFpEF to the front page to make clear that it is of the same level of importance as reduced ejection fraction heart failure, and though we didn't have an evidence-based treatment that we could articulate in 2013, you'll see going forward today that such is no longer the case, and we do have a therapy.

I'll now about to the algorithm that we developed in response from many of you indicating that trying to apply multiple different therapies can become confusing. Can we show a way in which this can follow an algorithmic approach? And indeed, in 2013 we developed this straightforward algorithm for HFrEF, not for HFpEF, indicating the importance of an ACE or ARB, the ACE preferred, and an evidence-based beta blocker and then further suggested that there are three decision trees that have to be followed, neither of which is mutually exclusive. One that deals with indication of diuretics, one that deals with indication prior to LOE C and nitrates, and the persistently symptomatic African-American NHYA class III or IV, and one that deals with the benefit of Aldosterone antagonist when renal function is reasonably intact. Our argument then and now is that in aggregate as you construct the medical regimen with what's indicated, we can see evidence of success.

That success is demonstrated on the next graphic, which reflects a calculus that Dr. Fonarow and I completed with our co-investigators and published now five years ago, demonstrating that for each of the evidence-based therapies as they then existed, there was a significant benefit to be seen in the relative risk reduction and mortality and the relative risk reduction in heart failure hospitalizations. And when we did a thought experiment to standardize the data to similar exposure, in this case 36 months, you can see the numbers needed to treat were surprisingly low.

Here's the first pause moment I want to make clear. Before we get into the newest information, please acknowledge, please remember, heart failure outcomes are getting better. The incidence is lower, prevalence higher, but evidence-based therapy, the legacy therapies, the RAAS inhibition, beta blockers, Aldosterone antagonists, nitrates and hydralazine do work, and work incredibly well, and we should not retreat from those therapies that we know to be good.

So let's begin the first part of our substantive discussion on the 2017 focused update of the new guidelines. What's new, and how will practice change? I was privileged to work with an incredible writing committee, and to have Dr. Mariell Jessup serve as the vice chair. As I’ve already suggested, for the first time the Heart Failure Society of America was officially represented on the committee and shared a masthead with us. We also were benefitted by having European representation from Dr. Gerasimos Filappatos. Additionally, we had primary care physicians, we had pharmacy, we had internal medicine and of course cardiology. So this really represented the full suite of individuals that see patients with heart failure. We were quite pleased. Should you wish to download the citation, there is a link available that is embedded within this slide. And should you have reason to reference this presentation in a publication, please use that same link. Let me offer, then, an extreme amount of gratitude to a group that worked tirelessly to pull this together, and to do so in near record time. The first part of this guideline went from first meeting to publication online in five months, and the second part of this guideline was completed in another seven months to eight months. This is the kind of responsiveness we've been targeting so that our guidelines can stay current with the knowledge base.

So, why did we have to do another set of guidelines? Why not let the 2013 Guidelines stay? This slide, the graphic you see in front of you, which shows the results from paradigm HF was, in fact , game changer. You hear that word all the time. And it has become exhausted. But, in this case, it really was a game changer, because it indicated that we needed to fundamentally revisit how we treat heart failure, and understand how can we incorporate this powerful new tool in the right way for patients with symptomatic heart failure in a manner that avoids harm, allows for us to capture this benefit while still respecting and incorporating everything else we knew. These data were profound. You've seen them before. Number you need to treat is 21, 20% reduction on cardiovascular death of heart failure hospitalization as a primary endpoint study ended early because of the overwhelming evidence benefit. The high degree of certainty portrayed by the P value only adds further impetus to the decision made to revisit our guidelines and understand how we incorporate new therapies. You remember the paradigm HF studied a novel concept, the combination of neprilysin inhibition and RAAS inhibition. The graphic you see before you reminds you that the elaboration of angiotensin-II leads to a cascade of events through hypertrophy, fibrosis, ways of constriction, Aldosterone release, Norepinephrine release that drives progressive and [inaudible] function, while the cascade that elaborates cyclic GMP through the natriuretic peptide receptor and leads to protein kinase G production generates a suite of biological activates that are the antithesis of RAAS activation. That in turn leads us to the newest concepts that involve the alignment of the angiotensin and receptor antagonists and the neprilysin inhibitor in what’s now called the ARNI class, with the intention to inhibit the RAAS system and upregulate the endogenous natriuretic peptide system.

The graphic before you is very important. Please look at the section entitled “B - The Change in NT-proBNP.” There is a different effect of the neprilysin inhibitor Sacubitril/ on NT-proBNP versus BMP, NT-proBNP is not a substrate for Sacubitril. And in panel B, you’ll see the arrow indicating the initiation of the ARNI compound, and the continued fall in NT-proBNP as depicted on this graphic. However, when you look at BNB in panel C, coincident with the introduction of Sacubitril/valsartan, you'll see a continued rise in BNP because it is, in fact, a substrate for the neprilysin inhibitor. So keep this difference in place. And what this means practically is when you’re using the ARNI compound, make certain your laboratory is evaluating NT-proBNP and BNP.

The second reason why we needed to do a new guideline was based on information that emerged for yet another evidence-based therapy that did not previously exist in the armamentarium and this is ivabradine, which is gated towards inhabitation of the hyperpolarization activated cyclic nucleotidegated channels, or the HCN channels . It does only one thing, which is delay diastolic repolarization, effectively leading to a slower heart rate in a patient inside a rhythm already at an increased heart rate, despite being a beta blocker. Evidence has suggested that there's a benefit and a composite endpoint of cardiovascular death or hospital admission for worsening heart failure driven primarily by the hospitalization advantage and less so by the mortality advantage, but nevertheless another important therapy for consideration and treatment of heart failure. So the graphic you see before you is the summary of the first part of the Guidelines published in May of 2016 indicating the novel therapies that were being brought forward that were in addition to what was already existing in the 2016 Guideline. Those therapies have been rearticulated then within the context of stage C, reduced ejection fraction heart failure therapy. The graphic you see before you makes clear as a very first statement that's what's most important is RAAS inhibition which can be accomplished either with an ACE inhibitor or an ARB or the ARNI compound. We don't have the information base to start the ARNI compound in de novo or in the hospital, but as you're treating patients with heart failure, any one of these three qualifies as an inhibition of the RAAS system.

The next Guideline statement restates for a reason the benefit of ACE inhibitors and ARBs. That reason is this: not every patient will tolerate the ARNI compound. That will not subject that patient to inferior care, or inferior outcomes. And ACE inhibitors are appropriate and ARB is appropriate for the caveats noted in this guideline statement and only for the patients that meet.

The next Guideline statement I'll share with you, should we go forward with the ARNI compound. Specifically inpatients with chronic symptomatic reduced injection fraction heart failure, NYHA class II or III, very few patients in class IV, so we left that out of the guideline, even though it’s in the FDA label, who tolerate an ACE inhibitor, or ARB, tolerate is akin to what we saw in the trial and enalapril milligrams twice a day. Replacement by an ARNI is recommended to further reduce morbidity and mortality. This is the second pause moment. It's very important that we emphasize this benefit of this newest therapy as a replacement for certain patients already on an ACE inhibitor, because of the benefit in terms of reduction and morbidity and mortality that can be obtained. It's also important that we are balanced, and we recognize in whom it is we should not use this newer therapy and whom it is we should use this newer therapy. This newest compound should not be given with an ACE inhibitor. We know from past experience from a randomized control trial that the combination of neprilysin inhibition with an ACE inhibitor leads to an unacceptable consequence of angioedema, including fatalities. Moreover, any patient with any history of angioedema should also not be given this compound, less so because we have the randomized trail data, but more so because we believe expert opinion would warrant such a precaution.

What about ivabradine? A little bit less fervor regarding the class recommendation of 2-A. But a high degree of evidence based on randomized trial, demonstrating that for reduced ejection fraction heart failure with a heart rate greater than 70 on beta blockers, then the data would suggest the cut point is closer to greater than 78, the addition of an ivabradine when the patient is in sinus rhythm is associated with a reduction in morbidity and this too should be incorporated into treatment algorithms.

The graphic before you is yet another pause moment. I've used that term several times already, I'll continue to use it as we get something that's important. This is, again, amongst the most important things I can share with you. You will remember the simplicity of the treatment algorithm that I shared with you earlier in the presentation from 2013. For 2017, this is the new treatment algorithm, much more involved necessarily so. Let's be very deliberate here. Step one. Establish the diagnosis of reduced ejection fraction heart failure. That means to assess the volume status, understand the etiologies, that may give you some different directions you can go for therapy, and then initiate guideline and directed medical therapy, or GDNT. Specifically that means ACE or ARB -- you’ve heard me say this before -- the ACE is preferential or an evidence-based beta blocker. Devices as needed, diuretics as needed. This is the class recommendation one. This is step one.

Now, what is step 2? We recognize that we now have six patient scenarios. And each scenario independently prompts yet another intervention. And so the white boxes are the six scenarios, the interconnected arrows make the point that no treatment excludes another treatment, an individual patient may be a candidate for all six, or none of the six. But, depending on your evaluation of the six scenarios, that will prompt the introduction of one of the several therapies that is connected to each scenario, five of which are class recommendation one, one in a different color of ivabradine is a class recommendation 2A.

As you construct the medical regimen on top of what you began with, following all the caveats we've outlined, you get to step 4. And step 4 is a reassessment of symptoms. If the patient’s symptoms have improved, you persist with guideline directed medical therapy with serial reassessment, and optimizing dosing of those meds. And that is the horizontal bar at the bottom of the algorithm. If the symptoms persist, then we are entering stage D, and at that point in time we have four treatment strategies. Class one indicates strategies of palliative care, or hospice, transplantation of ventricular replacement, mechanical circulatory support for a 2A recommendation, or investigational studies.

There are nearly 700 of you online now. Thank you, again, for joining. I'm pausing because I want you to recognize that in my opinion, this is one of the most important things we can share with you. For each of the 700 of you listening, this is your take-away. This is something you should download, put it on a wall, put it in your clinics. I have personally copied this and given it to every advanced practice provider that works with us so we can all be on the exact same page as we’re constructing treatment regimens for patients with reduced injection fraction heart failure.

As a comparator, I’ve included the ESC treatment algorithm, and I want you to recognize the two committees that work over the same time period and released our statements together, can arrive at very different ways in which to treat patients. No approach is right or wrong, but they reflect our different lenses. What is uniquely different here about the European approach is that they would suggest that a mineralocorticoid antagonist be added before any consideration to replace the ACE inhibitor with an ARNI, to add ivabradine, or to consider the need for CRT. And so this is a nuance in the way we approach the treatment of heart failure that reflects different groups of professionals looking at data points and thinking about what's correct.

I told you that the point of emphasis that I most wanted to make, even though we've had several pause moments, is thinking about prevention. And the subtitle here is a new reality in heart failure. I'm going back to the stages, phenotypes, and treatments that we've seen before to remind you that stage A reflects those patients simply at risk without any symptoms. And stage B are those that also without symptoms, but with asymptomatic LV dysfunction. And stage C reflects the onset of symptoms. Why is that important? Because these data are overwhelming. With the development of any, and I emphasize “any” symptoms of heart failure, the outcomes have immediately changed. I recently listened to Marc Pfeffer discuss this, and he made very clear once you are admitted to the heart failure club, your outcomes just can never be as good as they might have been had you never been admitted. It is empiric, intuitive, it is an incredible thrust for all of us to do whatever we can do to prevent patients from progressing from stage A or B to stage C.

How is that possible? Well, let's go back to something straightforward. What identifies the greatest risk for developing heart failure? And that is blood pressure. For individuals with the highest blood pressure, you can see in nearly 30%, not the 20% I told you before, 30% risk for developing heart failure. And these data that should be before you right now, that demonstrate the sub group analysis from the Sprint study. Most important in that landmark study that showed that the treatment of hypertension in at risk individuals to a targeted systolic 120 over 80 was associated with a mortality advantage was this. A 38% relative risk reduction in the onset of symptomatic heart failure. People, that is very important. That is a new dynamic, and it tells us that there is an opportunity to effectively treat heart failure -- to effective prevent heart failure by treating hypertension. This is further endorsed when we aggregate the several hypertension trials for which we have heart failure outcomes and demonstrate across the board between a 30-70% likelihood of the development of heart failure by treating hypertension appropriately. These data cannot be overlooked.

I told you I would get back to the simple seven, and these are data that we’ve developed here at Northwestern demonstrating that for the risk factors of hypertension, diabetes, and obesity, in those individuals with zero risk factors, the red lines, the lifelong risk for heart failure from the age 45 going forward, is less than 10%. For those patients with all three of those risk factors, hypertension, obesity, and diabetes, that lifelong risk goes up to nearly 50%. The message couldn't be more profound. And it's something that reflects an important take home message.

So yet another pause moment. And I appreciate that so many of you remain engaged because this is another statement that is being made for the first time that is different from anything you've ever seen in the heart failure guideline. There’s class recommendation one, level of evidence is BR based on Sprint in patients at increased risk stage A heart failure. The optimal blood pressure in those with hypertension should be less than 130 over 80. If this is your only take away from today, let this be the one that you walk away with incorporating in your practice. The potential of a 40% detriment in the development of heart failure cannot be overlooked and can be achieved by looking at those persons that are at higher risk and are hypertensive and are treating them to a blood pressure in the office less than 130 over 80. Profoundly important information, the potential to fundamentally change the burden of disease, and let's not miss that opportunity.

So, if we think about the new guidelines, and the first set of take away messages, number one, new effective medical therapies like the ARNI compound and ivabradine have now been fully incorporated in evidence-based guideline directed treatment algorithms, and I very deliberately went over this new treatment algorithm. Secondly, there is an increasing complexity in the treatment of HFrEF, and so we need something that allows us to work through these different scenarios. Third, there are powerful new data should drive the PREVENTION-- it's deliberately in all caps -- of heart failure. We should not walk away without thinking about prevention as a new imperative in the management of patients at risk for heart failure. And then fourth, avoid entry into the heart failure club at all costs. Because that is the very best treatment that we have.

So, let's move forward, and talk about this new phenotype. Many of you heard about this notion of heart failure with improved ejection fraction. Are those just errant observations in the echo lab or is this a real phenomenon? Well, the Europeans step forward and in May of 2016 released this new definition of what they call heart failure with mid-range ejection fraction. And really thought that it fit between HFrEF and HFpEF, that’s intuitive, but it also reflected a different construct. Structural heart disease, probably both systolic and diastolic abnormalities, elevated natriuretic peptides, really generating a lot of discussion about what should we do about these patients. Go back to the 2013 Guideline and remember that in 2013 we deconstructed HFpEF and said it is not just patients with an EF greater than 50%, it is those patients with an ejection fraction between 41-49 inclusively, that happen have ventricular functions so measured. But we also identified then that there was a group of patients where the ejection fraction was greater than 40% who previously had HFrEF but had improved, and we indicated that for the research we needed to better categorize these patients and understand who they are and what they represent. A lot of that work is being done now.

I want to share with you just one benefit original research that was recently published that highlights the potential -- this is not proof positive by any circumstance -- but highlights the potential for identifying these patients. In this series of over 2,000 patients followed for over three years at a single large tertiary care referral center, 62% having reduced ejection fraction heart failure and 38% having preserved ejection fraction, there was evidence that of those that had preserved ejection fraction heart failure, 16% previously had reduced EF, EF less than 40%. And this was the stunning part. When you followed those patients over the three years, their mortality was least worrisome, 4.8% versus 16.3 or 13.2%. That's depicted here when you look at the data in aggregate. But to make it more clear, I’ve deconstructed the data for you, looking at cumulative mortality, looking at what I would call the grey line for recovered ejection fraction, 4.8% risk of mortality over 36 months. Looking here at the cumulative event rate, death or heart failure hospitalization, 11.8%. For recovered EF compared to either reduced EF or preserved EF, we're still trying to fully understand what's going on here but it looks like it's a real phenomenon worth pursuing. There was recently a major meeting of the National Heart, Lung and Blood Institute to really think about all the potential mechanisms that might be in play here, abstinence from alcohol, use of beta blockade, critic resymptomization therapy, revascularization valve surgery, RAAS blockage, and really to take advantage of what we do in the transplant space by moving a core of tissue to place an LVAD or doing a transplant and having a necropsy specimen. And looking at these mechanisms very carefully we tried to articulate in 2016 in an editorial in 2016 all the things that may be happening here, spontaneous recovery repair, reverse remodeling, super responders, reversible illnesses, mod cardiac recovery per se, LVAD supported, and indicated that we still have lingering questions about how best to treat this condition. But I think we should all pay attention to the discovery of this group of patients where there's been improvement in the EF. They may represent a very different phenotype.

Let's spend our several minutes that remain together talking about heart failure with preserved ejection fraction and important co-morbidities in heart failure. What about the treatment of HFrEF? You will recognize the graphic before you right now as the data from the TOPCAT study. And these data demonstrating something very striking. If you looked at blood pressure in panel A, serum potassium in panel B, serum creatinine in panel C, and looked at the discrimination of the patient populations according to the Americas versus those in Russia, the former Soviet republic of Georgia. If we just take one thing, and that is looking at blood pressure, you would suggest that if someone took Spironolactone, the blood pressure should fall. And in panel A, the red lines, you see in fact there was a drop in blood pressure, not observed in the purple lines that reflect Russia or the former Soviet republic of Georgia, and those might be blue lines. Potassium is the same thing. You would expect potassium to be increased, Creatinine is the same thing, you’d expect it to be increased. You see that in the Americas population, but you didn't see that in Russia, the Georgian populations. Many of you understand where this is going, but you may not have seen the primary data. So this raised questions that there was some major differences by region.

Then we look at outcomes and look at the primary outcome, then deconstruct the primary outcome to cardiovascular death or heart failure hospitalization. Striking differences between the two regions. And importantly, if one looks at cardiovascular death, you really see an incidence or rate of events in the Russia and Georgia that actually is better than what one would have expected in populations without cardiovascular disease. The most recent contribution to this was published just several weeks ago in the New England Journal of Medicine. And a cohort of patients that remain and whom there were specimens that could be assayed to determine if the active metabolites of spironolactone were present. It was fairly striking. By looking through these data, you can see that for those individuals who reported taking spironolactone and had no detectable quantities in panel B, 3% in the Americas, 30% in Russia. You can then see the same replication of the change in serum potassium level that I shared with you before, making the argument that there were quite a number of patients in TOPCAT who had no physiologic response to the MRAs, no electrolyte response, and had no evidence of having actually taken study drugs. So much so that it puts us in a position where perhaps evaluating the Americas population independently is an appropriate thing.

So let's go through the updated HFpEF Guidelines. First, treat the blood pressure appropriately. That’s the first statement. And use diuretics to relieve volume overload. Next, coronary revascularization is important, very high, can be a common instance of coronary disease in HFpEF, managing atrial fibrillation according to clinical practice guidelines, using beta blockers ACE or ARBs to augment blood pressure control. All of those things are restated from before.

This is the new information, and yet another pause moment. I will read it to you; pay attention to the class recommendation 2B, level of evidence is B-R. So a fairly soft recommendation. In appropriately selected patients with HFpEF, EF greater than 45%, elevated BNP levels or heart failure admission within one year, adequate renal function, aldosterone receptor antagonist might be considered to decrease hospitalizations. This is directly related to our post-oc analysis of TOPCAT suggesting there was a sufficient difference in the patient populations, the Americas versus Russia and the former Soviet republic of Georgia, that we believe there is enough evidence to suggest that you might consider the aldosterone receptor antagonist, provided the caveats are respected as treatments with HFpEF. This is the first appearance of an evidence-based strategy in a clinic practice guideline for heart failure with preserved ejection fraction. You can see there is similarly a lower level of evidence in class recommendation, the use of ARBs might be considered to decrease hospitalizations. Again, it's important for balance to state where the harm equation is. PDE5 inhibitors are nitrates to increase activity and quality of life, not indicted because they’re ineffective. Routine use of nutritional supplements, not recommended because they’re not effective.

Finally, I want to go through the important co-morbidities in heart failure. I want to remind you that anemia is something that we wrestle with over and over again. The available data would say that iron supplementation is something that might be reasonable, class recommendation is 2-B, predominantly is it’s given intravenously, not orally. However, given, erythropoietin-stimulating agents doesn't appear to be of any benefit. We are tentative about iron supplementation because some of the early data are telling us that patients may be at risk for increased hospitalizations. So stay tuned for more data to come from there. But for right now, this is our thought process.

What about hypertension? Well, I've already emphasized the importance of treating those with concomitant risks and hypertension in a manner that will reduce the incidence of heart failure. But what about those that already have symptomatic HFpEF or HFrEF? Well, this restates the first statement of reducing blood pressure as a means to reducing incidence of heart failure. And now for HFrEF, we believe you can extrapolate from the Sprint trial with less conviction that targeting a blood pressure of 130 over 80 or less is the appropriate thing to do. And for HFpEF, again with limited data, and less strong conviction, we believe that the targeted systolic blood pressure in the patient with HFpEF should be less than 130 over 80. You can hear from my words the tentativeness of my language, that that would not be strongly advised.

What about sleep disorders? Well, lots of work has been done thinking about obstructive sleep apnea. In that case, we know that first there should be a formal sleep assessment. The reason for the sleep assessment is because there is a difference in how patients respond with either obstructive sleep apnea or central sleep apnea to available modalities of care. CPAP may be reasonable in those with obstructive sleep apnea because it improves sleep quality and daytime sleepiness, but it does not change cardiovascular outcomes. It does not improve outcomes for heart failure. Using servo- ventilation for central sleep apnea has been associated with harm, and we would not advise that approach for patients with central sleep apnea.

I'm sharing with you a very interesting graphic from the Journal of Cardiac Failure. This is for your edification only. But you can see on the left panel several different important co-morbidities, and on the right panel, seven different specific ways in which heart failure might be impacted. And what I want to point out, which the authors here, Tom Maddox and Bob Mentz, show, which is very striking the bi-directionality of these co-morbidities, that is, heart failure exacerbates some of the co-morbidities but the co-morbidities exacerbate heart failure. This intricacy that is portrayed here really makes the argument quite profound that for obesity with sleep disorder breathing for renal dysfunction, for diabetes, for anemia, for chronic obstructive lung disease, we must acknowledge these co-morbidities, treat them according to guidelines and realize this intersectionality of particularly HFpEF and the co-morbidities. And so be advised of that very intricate relationship.

So as we complete and leave more than sufficient time for questions, let me tell you this next set of takeaways. The first take-away was on medical therapies and prevention, the second take-away was on heart failure with improved ejection fraction. The third set is on these co-morbidities.

Let me start off first by emphasizing yet again that the first evidence-based guideline directed therapy for HFpEF has been endorsed, albeit modestly, by the Guidelines, but more research is needed. That is a major statement all caps, but it is a step forward for the co-morbidities, anemia attributable to iron deficiency, intravenous iron is preferable to oral iron. Sleep apnea, do not use servo control support for central sleep apnea. CPAP only for obstructive sleep apnea. Sleep studies are indicated. No impact on heart failure outcomes but sleep quality is improved. Hypertension, the new target, less than 130 over 80, and heart failure with hypertension systolic or diastolic preserved are reduced. Don't forget the prevention message. Don't overlook the bi-directional effects, the co-morbidities may exaggerate clinic outcomes in heart failure and heart failure may exaggerate the co-morbidities, and it may even be such that the co-morbidities further lead to the development of heart failure with preserved ejection fraction, that's a work in progress.

So here's your final take-away, the treatment of heart failure continues to evolve with new therapies and emerging new devices. New treatment algorithms address increasing complexity of heart failure therapy. A specific intervention is now indicated for HFpEF. Co-morbidities matter; overzealous treatment may lead to harm. And prevention is a new reality. These five points are the key takeaways in our thought process about the treatment of heart failure.

And finally, and to put special emphasis on the messages about prevention is this: There is a Chinese proverb I was given by a nurse, who helped me learn transplant medicine but who is now departed. And I've kept this on my credenza for many, many years, and can bring this back out because of the conversations we’re having about prevention today. “A mediocre physician treats advanced disease… a good physician treats disease… a great physician prevents disease.” We should all aim to be great physicians and great care providers.

Questions. Thank you very much.

**Steve Dentel:**
Thank you so much, Dr. Yancy. And, Andrea, can you remind our participants how to ask a question?

**Operator:**

Absolutely. To ask a question via the web, click the “Q&A” button on the lower left hand corner, type your question in the open area and click “Submit.”

**Steve Dentel:**
So, going into the questions that we have posted so far. Dr. Yancy, one of the questions comes in, it says, “We tend to hold the Aldosterone receptor antagonist until we are sure the patient is going to be compliant with follow-up labs. Do you recommend this also after hearing the new recommendations?”

**Clyde Yancy, MD:**
So I really want to compliment Deanna Jordan for bringing this question forward. Deanna recalls that in the 2005 Guideline, again, the 2013 Guideline, we made special emphasis of the importance of demonstrating that a patient was compliant, had access to laboratory assessments, and we made emphasis that the risk for hyperkalemia was an ever present risk, and so we had to be continually diligent in our surveillance. Deanna, you're correct still, nothing about the new Guidelines changes that. Yes, we have more comfort giving, the Aldosterone receptor antagonist, hyperkalemia has not gone away. You may be aware that there are some newer therapies that will attenuate some of the risk of hyperkalemia but it's not clear whether or not those newer therapies would attenuate the benefit of the Aldosterone receptor antagonist. So yes, everything we've known before we continue to embrace. We should continue to do laboratory assessments; we should be diligent about potassium, we should make certain renal function is intact, make certain that patients don’t begin the process with evidence of hyperkalemia. So thank you for that question.

I can see several other questions. And so if you will, Steve, I'll just work through them so that we can get to as many as possible.

**Steve Dentel:**
Sure.

**Clyde Yancy, MD:**
I'm going back to the beginning, if I can, yeah. So, from Emily Graebel (ph), “Do you have a recommended transition of care team and how it’s instructed?” This is a very important question, Emily, and the answer is involve. But, in essence, heart failure is a team sport. And managing patients with only a physician-only, a physician and nurse is no longer the right thing to do. There should be access to pharmacy, with a pharmaceutical professional, as in a Pharm.D to help construct these complex medical regimens. Nurse and patient education, that is patient education provided by a nurse is incredibly important, probably the most important thing we can share. A mid-level provider, or an advanced practice provider, or a nurse practitioner, physician assistant, incredibly important for the serial follow-up that’s involved. Many, many centers are providing standalone clinics with walk in on demand services to help address the problem of readmission. So there are many iterations of a transition of care team, or a disease management program, many of which have to be tailored to your own environment. But suffice it to say multi-disciplinary is the key consideration, and overrepresentation with education, and nursing care is the right thing to do.

There is a question from David Perez from Tenet, “Can I have a list of the most updated beta blocker, ACE, ARB approved by the AHA?” David, please go to the online representation of the Guidelines. We have a particular table, my memory says it’s Table 2, but it has every drug and dose appropriate for heart failure, and you'll find more than enough information there.

Andrea Paulnitz (ph) from Evansville wants to know if we have recommendations on serum creatinine levels in the discontinuation of ACE/ARB? This is clinically an incredibly important question, because we deal with a lot of tentativeness because of creatinine is elevated. It is a concern. We have to respect that concern. And we don't really have an evidence-based strategy to guide us. We know for the mineral corticoid antagonist, the aldosterone antagonist, we need to respect an estimated GFR of 30CCs per minute. It has to be at least at that threshold or higher to be comfortable giving those compounds if one wanted to be very conservative that would be an appropriate standard to apply to the ACE or ARB, but sometimes when we give the ACE to ARB the renal function might actually get better. It may go up briefly, but then get better. I will tell you my clinical practice, which is not in the Guidelines, but my clinical practice is as long as a creatinine isn't greater than 3, then we try to look at all the different circumstances, and start with a low dose ACE or ARB, hoping that we can have some ACE inhibitor on board, because it changes the natural history.

I’ve got a question from Sheila Gasarey (ph), “If blood pressure is on the low side and reduced ejection fraction heart failure, some patients and some -- for some patients, some providers are hesitant to add additional evidence based therapies, specifically the aldosterone antagonist. We have to remember that blood pressure is oftentimes low in reduced ejection fraction heart failure because we've over diuresed patients, their volume contracted and/or their after load is still increased. So, as we titrate the ACE, as we titrate the beta blocker in particular, something like carvedilol that has some [indiscernible] dilating properties. As we add spironolactone, many times the blood pressure will maintain its adequacy because if cardiac output comes up, even if resistance goes down, blood pressure stays level set. But the real take-home message, Sheila, is to pay attention to your diuretic dose. Invariably when patients have compromised blood pressure and heart failure in evidence based therapies, especially ambulatory outpatients because we’ve over-diuresed them and backing off the diuretics might allow you to let you get more evidence based therapies on board.

Nicole Jones is from close to my home. I grew up in Baton Rouge. She’s at East Jefferson General Hospital. I think that’s on the East bank in New Orleans. I even said New Orleans correctly there, Nicole. Did you recognize that? Nevertheless, “I think I heard you say that there was insufficient evidence to start ARNI in the hospital setting, but is it a quality measure for Get With The Guidelines – Heart Failure?” And I’m so glad you raised this question because that has been a misinterpretation of what’s in our quality of measures. That quality measure is intended to something very important, to give you credit, if in fact the mode of rest and ambition you select is the ARNI compound, but only based on a Guideline-driven, evidence-based approach, not starting the ARNI in the hospital, but having had someone on the ARNI compound who gets admitted, continuing the ARNI in the hospital. This was recently brought to my attention by several senior physicians in the field, we need to modify this quality measure a bit so it shows ACE inhibitor, or ARB, or ARNI to -- for that quality measure. So thank you, thank you very much for bringing this on board.

There is a question from Tammy Horrom from Vista Medical Center East. I'm sorry, Tammy, I don't know where that is. But the question is, “Is anyone working on a slide deck for educational purposes for our physicians, with the 2013, 2016, and 2017?” The 2017 deck is available online, published April 28th. The 2013 may still be available, as well. You can blend the two together and very easily see where the 2017 information supersedes the 2013. It's a little bit of an exercise. We haven't done that for you, but the data all there online.

Maria Peralta from JFK Medical Center wants to know: There was a push at one point where heart failure was a core measure, and now it’s gone on the wayside, what can we do to maintain the focus? Well what's really happened is that we previously really truly emphasized smoking cessation, LVF assessment, ACE inhibitors and discharge orders, and that was the construct for what we put together as core measures for heart failure. Those measures were tried largely because we had feelings where there was global deployment of all those measures, and also because of data that we and others generated to suggest that not all of those measures fundamentally changed outcomes. There should be no sense that there is a de-emphasis on quality measures on heart failure, just that we're looking at very different strategies.

Susan Ward from Mercy Health makes a point that the current Get With The Guidelines database does not really take into account sleep apnea. That is correct, to a certain extent. But, the Guideline information should not be overlooked. The most important message I delivered today was, please do the sleep assessment because you do not want to inappropriately treat central sleep apnea. And you want to find those patients with obstructive sleep apnea and give them the benefit of support for their sleep apnea, because we know that CPAP will in fact improve their sleep quality.

Jan Basil (ph) from Charleston, and I think I know you, Jan, wants to know about CRT use for QRS of greater than or equal 150 milliseconds to the left bundle branch block pattern. Yes, that is different from 130 milliseconds. So the class one recommendation, Jan, is in fact left bundle branch block pattern, QRS greater than 150 milliseconds. We have a recent publication demonstrating how that has changed. The number of patients eligible for CRT, but the number of patients receiving CRT has remained level set, if not gone up because the criteria has been refined. In the European setting, the threshold is at 130 milliseconds. For the U.S. guidelines, 130 is still suitable, no longer a class recommendation one, but especially so when it reflects left bundle branch block pattern. So thank you for that question.

Susan wants to say thank you. So I appreciate that, Susan. Thank you for listening in today.

Are there any other questions? I think I've gone through those that I can access in the queue that we have here. Hearing none, then, or seeing none, I think we have a minute left of our allotted time. So, I really wanted to turn this back over to staff. But in so doing, I would like to thank everyone for listening in. I hope you enjoyed what we discussed today. There's well over 500 of you that have stayed attentive during the process. You can see the graphic on the screen now that gives you a place to visit, it names a contact if you have additional questions. We've got great new information for heart failure. We can change outcomes. And so let's all roll our sleeves up and work together to really get failure out of the notion of heart failure, and start seeing more and more success with this treatment. Liz, Steve, I'll let you close the program today, thank you very much.

**Steve Dentel:**
Thank you so much, Dr. Yancy. And I'd like to thank all of the participants for being on for today's webinar. And in the next week, there will be a recording of today’s webinar, presentation slides will be available on the American Heart Association's website, heart.org/quality. And we also will be emailing you a survey to gather your feedback on today's webinar. Thanks again, and have a great day.

**Operator:**

Thanks to all our participants for joining us today. We hope you found this webcast presentation informative. This concludes our webcast. You may now disconnect. Everyone have a great day.