CHARLES BRUCE: Greetings. My name is Charles Bruce. I'm from the Mayo Clinic in Rochester. And it gives me great pleasure to be able to discuss remote monitoring and how this can potentially impact the science of health care delivery. This has been a group effort. Kevin Bennet, Paul Friedman, Lyle Olson, and Virend Somers have been working together on developing a remote monitoring solution that we will discuss briefly today.

This talk will initially outline our vision for remote monitoring and how this could potentially impact health care delivery. We'll then describe what we consider to be a great opportunity, looking specifically at heart failure. And Lyle will address this and the vexing problem of hospital readmissions for this condition.

Paul Friedman will then briefly discuss noninvasive determination of electrolytes and the tantalizing opportunity of doing this using an adhesive patch. And Virend Somers will then look at the opportunity of screening for obstructive sleep apnea using a remote monitoring solution. Finally, we'll sum up, basically addressing how potentially remote monitoring can allow us to impact the lives of patients not only within Olmsted County, Minnesota, nationally, but even globally.

Our vision dates back to the late 1990s, when we wanted to develop an integrated adaptable system. You could think of it much like a dashboard that you'd have in your motor vehicle. But rather than a dashboard with sensors looking at tire pressure, for example, this would be a dashboard looking at overall health and well-being, principally aimed at screening, but more importantly prevention of disease, and then if you happened to have to have the disease, perhaps help with management, principally with the aim of lengthening independence.

When you think about our practice here at Mayo Clinic or an institution like ours, we're very busy. Last year we saw over a million unique patients, 123,000 hospital admissions, over half a million hospital days of patient care, and certainly requiring a large personnel to accomplish this, 56,000 of us.

If you think about that in the context of patients and health overall, this really represents the very tippy top of the pyramid. Patients who already have identified active disease, they rest on the shoulders of patients who have disease but don't have symptoms. They don't have their symptoms yet, but the disease is still lingering. They rest on an even broader shoulder of the population, those patients who don't have disease yet but have overt risk factors for that problem. And, of course, they rest on an even broader base of the pyramid, people who have genetic and dietary predispositions to these conditions.

So what our hope is is that we are able to move down this pyramid, not just impacting patients who already have active disease, but hopefully having an impact earlier on in trying to prevent the disease from even starting in the first place. Our principle has been to focus on a person, not a patient, because hopefully they'll never become a patient, and doing this by an ecosystem of sensors that communicates via a hub to an infrastructure.

And that this infrastructure is not simply a repository for information, but rather takes knowledge from information that then can be utilized by numerous members in the health care environment, the health care provider, the person's relatives, even device companies, or even the pharmacy. And although this is a cardiovascular application that we're describing now, the opportunity for this platform is far-reaching, extending across the spectrum of medical conditions.

Sensors in the infrastructure, particularly smart algorithms, looking at, for example, at how we take that knowledge, at least that data, and turn it into actionable knowledge. And then what's exciting is that you can imagine something inanimate, like an intelligent medical cabinet, interacting with this ecosystem in a smart way, delivering just the right amount of treatment for that particular individual based on the parameters that are being monitored.

And we feel that Mayo can bring to bear expertise at multiple levels. So our approach has been principally to develop a long-term unobtrusive monitoring system to promote the mobility and independence of patients, focusing on the emerging epidemics of atrial fibrillation, congestive heart failure, and obstructive sleep apnea, but importantly, taking data and signals and integrating these, ensuring that the system is nonproprietary, adaptable, and integrated.

Our proof of concept has been a heart failure monitor. We have an adhesive-style bandage that has a rechargeable unit that is capable of acquiring an electrocardiogram, determining activity level based on a three-way accelerometer by impedance measurements, leading us to respiratory rate estimation and a wireless transmitter that's capable of communicating with off-body sensors, like a scale and blood pressure cuff, and importantly, having diagnostic and treatment algorithms embedded in the solution.

Here you see the current embodiment of this platform. You see here in the right-hand corner the rechargeable unit affixed to the adhesive bandage applied to the chest, that then communicates with a smartphone, that then communicates with the internet and the cloud, that then can present the data on a user interface like an iPad or a user workstation. This particular device right now is capable of measuring an electrocardiogram, respiration rate, the body position, as well as physical activity.

It's with a platform like this that allows us to address something that was featured in our local newspaper just a few weeks ago, the vexing problem of rehospitalization for patients with heart failure and understanding that there's a pressing need to address this because of the financial burden that this has been placed on our health care system. And with that introduction, I'll introduce Lyle Olson, who will address this opportunity.

LYLE OLSON: The scope of the problem of heart failure in the United States is huge. It's estimated at present that there are 6.6 million individuals over age 18, affecting 2.8% of the population. And it's estimated that by the year 2030, that this frequency will increase to 3.5% for a total of 9.5 million individuals with heart failure. The Incidence has been stable for the past several years at approximately 680,000 new cases per year.

It accounts for 57,000 deaths per year, as of 2008, which is more than all cancer combined. It's been estimated that heart failure contributes to mortality in another 250,000 cases per year. Morbidity is also extremely high. It is now the most common discharge diagnosis in patients over the age of 65 years and accounts for 12 million annual office visits. It's estimated that the lifetime risk for the development of heart failure in patients over age 40 is now one in five.

There are tremendous costs associated with this diagnosis in the US. More than 80% of hospitalized heart failure patients are over age 65. It is now the most common DRG diagnosis. More Medicare dollars are spent for heart failure than any other single diagnosis. The estimated total cost by the year 2015 will be $46 billion per year. Hospital costs account for approximately 60% of direct costs, and a substantial Medicare cost is related to heart failure rehospitalization, which will be the focus of subsequent comments.

These graphs came from a recent publication in circulation, an American Heart Association policy statement that projected the prevalence and direct costs of heart failure going forward. At the present time, direct costs are approximately $25 billion per year. And this is projected to increase to $75 billion per year as the prevalence of heart failure increases from 2.5% to 3.5% of the population by the year 2030.

Hospital discharges have increased markedly in the past 30 years. In 1979, there were approximately 377,000 hospital discharges. And in 2009, that figure is 1.1 million. Now, there are less than 1.1 million individuals that were discharged from hospital, as the significant proportion of these discharges or individuals have been hospitalized more than one time.

Medicare has looked at this issue, and it's summarized in this demographic slide from data obtained in 2004, which shows the rate of hospitalization at 30 days for all diagnoses for Medicare patients. And it's approximately 18% to 22% across the United States. The leading reason for rehospitalization is heart failure, compared to all other causes. And in fact, if we look at heart failure patients alone, the readmission rate is approximately 25% at 30 days.

The US government has responded to this issue by legislating heart failure outcome quality measures, such that at the present time, heart failure mortality and readmission rates at 30 days are publicly reported. And in the future, beginning this next coming month, heart failure readmission rates will be linked to Medicare reimbursement.

With this kind of background in mind, it's obvious that new models of care have become necessary. It's been proposed that home monitoring systems may have a favorable effect on heart failure outcomes. This table is from a publication in circulation in 2012 by Dr. Marvin Konstam from Boston, which summarizes outcomes for telephone or telemonitoring of patients with heart failure compared to usual care. And it shows significant reductions in the risk for all-cause mortality, heart failure hospitalization, and all-cause hospitalization.

There are also implantable technologies that have become available on an investigational basis. This slide summarizes two recent studies, the CHAMPION study and the COMPASS Heart Failure study, which tested devices which are implanted into the right heart. These studies were had a study design that was randomized and controlled and demonstrated reduction of hospitalization of 30%, in the case of the CHAMPION study, at six months, which was highly statistically significant.

This figure is from a recent editorial published the *New England Journal of Medicine* by Dr. Desai and Doctor Stevenson, which summarized five steps necessary for a successful home heart failure management using remote monitoring, including accurate assessment of physiologic indicators of decompensation, successful data transmission by the patient, the receipt and processing of data, the interpretation of the data by care providers, subsequent contact with the patient, and therapeutic implementation.

Opportunities going forward include creation of frameworks for delivering appropriate and timely care. We have proposed a model of a dedicated telemedical center that operates 24/7, which we hope will promote practice integration, improve outcomes, and lead to cost savings. Thank you very much.

PAUL FRIEDMAN: When you think about it, when a patient is dismissed from a hospital service with congestive heart failure, that patient has a gradient improvement in his or her health care, but a step function drop-off in the extent of monitoring. Instead of daily blood tests, they may be done in a week or two. Instead of continuous ECG monitoring, it's discontinued.

And if you look at this study done in a province of Canada with a population of approximately 12 million people, note that in 1999, following the publication of the RALES study that demonstrated a benefit of spironolactone in patients with heart failure, there was a significant increase in the number of hospitalizations and the number of deaths for hyperkalemia, showing both what happens when we translate clinical trials to clinical practice and showing the fragile state of patients with congestive heart failure.

If there were some way to continue outpatient monitoring, these kinds of changes perhaps could be mitigated. Now, any medical student can look at an ECG and diagnose marked hyperkalemia or hypokalemia. We know that potassium-- and there are a number of analytes that we'd be interested in monitoring, but I'll focus initially just on potassium-- values when they're markedly abnormal, lead to marked changes in the surface ECG.

The question is, would there be a way that we could continuously record clinically significant but much smaller changes that perhaps lead to changes that are almost invisible on the surface ECG? We've dubbed this concept bloodless blood test. Instead of extracting blood-- which is painful, unpleasant, inconvenient, difficult to deal with-- from a patient and running it through chemical analysis, the idea is to look at the physiologic effects of the content in the blood we want to measure, and then determine the value of that analyte in blood that gave rise to that change.

And the reason small changes are important is shown in this study, published in 2012 in the *Journal of the American Medical Association.* In this study, post-admission serum potassium levels are shown, and mortality in-hospital, as demonstrated on the y-axis. Note a couple of things. First, for relatively small changes in potassium, there's a significant increase in the mortality rate.

The other striking finding is that this orange line shows the ventricular fibrillation rate. The majority of these deaths are actually not related to arrhythmias caused by the potassium abnormalities, but more likely the potassium changes reflect a lack of cardiorenal reserve, so that these patients are sicker and less well able to maintain homeostasis, and thus more prone to getting into trouble.

So the question is, are we able to measure these relatively small changes within the normal range in patients with surface ECG? Well, imagine if you had a Band-Aid that continuously recorded the surface ECG, and that it also has an accelerometer so it can determine whether the patient is moving or not so you can get a clean signal, determine body position.

You could then perform signal averaging. And if we amplify, for example, the T wave on this tracing, you'll see that in the green line is shown a single tracing, which has noise. So it's not a very clean tracing. But noise is a random variable centered typically around 0, so that if you take hundreds or even thousands of complexes, line them up, and average them, the noise averages to 0, leaving you with what is shown here, the red line or the signal average line, which significantly boosts the signal to noise ratio, giving you microvolt level changes. And by processing these, we hypothesized we would be able to determine potassium levels.

So here's our approach. First, this is a very individualized form of medicine. We record a template so that we know the individual's baseline ECG. It would be impossible to look at an unknown ECG and determine a potassium 4.5 or 4.9. But if we know what the template is, then we can detect minute changes from that baseline.

We make physiologic correlations for body position ectopy and other factors that may perturb repolarization or other components of the T wave. We signal average to the microvolt level. And then we apply intelligence, a number of different mathematical models-- much of this has been done working collaboratively with colleagues at Ben-Gurion University-- to then determine what the analyte levels are.

For our first approach, we studied patients undergoing dialysis. They're an excellent model, because potassium levels may change relatively dramatically within the clinical range over a fairly short time period. And look at these T waves that have been processed from one of our early patients. And note that as the potassium level drops from 5.4 to 3.6, there are easily discernible changes in the processed signal. And there are a number of parameters that are being analyzed.

On the basis of this, we've had a very high predictability of potassium levels. And there are a number of parameters which can be studied using this noninvasively. In addition to analytes, there are drug effects as well as sudden death risk factors.

VIREND SOMERS: The classic symptoms of heart failure-- orthopnea, paroxysmal nocturnal dyspnea, fatigue-- are intimately linked to sleep. Orthopnea, shortness of breath when you lie flat, paroxysmal nocturnal dyspnea, shortness of breath occurring intermittently during sleep, and fatigue may occur because of inadequate or poor quality sleep.

Now, one of the reasons for the link between sleep and heart failure is the hemodynamic effect of lying flat. When you lie flat, the hydrostatic consequences result in increase in cardiac filling pressure, with consequent increases in pulmonary and vascular congestion. Now, patients know this, and this is why they sleep with three or four pillows in a semi-upright position.

There are other mechanisms linking sleep to heart failure, and these include sleep apnea, of which there are two kinds. The first is obstructive sleep apnea, which is the disruptive snoring kind of apnea where you have strenuous breathing efforts. And apnea occurs because of upper airway collapse during inspiration. Central sleep apnea is the more quiet kind of apnea, also known as Cheyne-Stokes breathing, where the apnea occurs because of an intermittent loss of central respiratory drive.

Now, in order to establish the prevalence of sleep apnea and heart failure, let's look at this pie chart, which shows severe obstructive apnea, mild obstructive apnea, severe central sleep apnea, and mild central sleep apnea. And the message from this slide is that about 20% of heart failure patients are free from sleep disorder breathing, which means that 8 out of 10 heart failure patients are likely to have some kind of sleep apnea.

Now, the problem with investigating sleep apnea and heart failure is a very high prevalence of heart failure and the considerable expense of in-hospital polysomnography. And here you see that sleep studies, a overnight polysomnogram requires a hospital admission with extensive and complex instrumentation, and is also an operator-intensive exercise and can cost between $2,000 to $3,000. And remember, this is a measure of sleep apnea at a single night in time. So it doesn't follow the trend in sleep apnea severity from one week to the next, from one year to the next, and as heart failure severity changes.

Now, you saw the slide earlier from Charles's presentation. And what you saw was that the remote patient monitor that we are working on provides measurements of EKG, respiration, body position, and physical activity. Now, what we are working on is adding oximetry, EEG, electroencephalogram, and EOG, electrooculogram, to the options for sensor acquisition. And that will allow us in a patient at home on multiple occasions to obtain assessments of sleep apnea presence and severity, and very importantly, change in the sleep apnea profile from one year to the next.

Now, we're working on another aspect of sleep apnea monitoring, and that is recording the sounds of sleep, specifically looking at people's snoring. And here we see a schematic of an iPhone application that we are developing for analyzing sleep sounds, particularly looking at the differences between apneic and simple snoring. And essentially, what we do is analyze a sound for apnea patterns and use sophisticated signal processing algorithms to differentiate between simple and apneic snores. And those of you who have spouses with sleep apnea will find resonance in the fact that we actually use an earthquake detection algorithm to differentiate between the simple and the apneic snoring.

Now, the sleep analyzer is being validated against a comprehensive overnight polysomnography in a sleep lab. And the target that we are going for is an accuracy of more than 80% in a snoring population, namely an accuracy of predicting the AHI to within 80% of the polysomnographic measurement of sleep apnea severity. We're using a very conservative approach and analysis to minimize false negatives. And it's important to know that this application is supported for both an iPhone and an iPod, and uses both built in and external microphones to provide increased quality of sound acquisition.

A third component of the service that we're hoping to provide with this app is a sleep educational resource. So essentially, what we're hoping to do is provide a gateway to the diagnostics--