Part I: Hemodynamic Monitoring for Heart Failure: Background and Rationale
Akshay S. Desai MD, MPH

Desai/Fig.1: **Presentation Title**

Desai/Fig.2: **Growing Burden of HF**
It is now well established that heart failure (HF) is a growing problem for the American healthcare system and even worldwide. The American Heart Association projects that the total number of prevalent cases of patients with HF will increase from roughly 5 million in the current era to nearly 8 million by 2030 – an increase of about 46%.[1] That means that in 2030 nearly 1 in every 33 people will have HF, a staggering burden of morbidity for the current healthcare system to manage.

Desai/Fig.3: **Increasing Costs of Care**
The growth of HF in the population is associated with an increasing burden of cost to the American healthcare system. The current cost of HF is estimated to be around $30 billion annually, and this is projected to double, to $60 billion annually, by 2030.[1] Nearly 80% of the direct cost associated with HF care is associated with hospitalization. Hospitalization for HF is the leading cause of hospitalization in the Medicare-age population in the United States, and readmissions for HF are increasingly a target of both payers and patients for improving the quality of care in the US system.

Desai/Fig.4: **Imperative - Reduce Readmissions**
Marked variation between hospitals in the rates readmission early after HF hospitalization and the belief that early readmissions after HF hospitalization may signal inadequate inpatient or transitional care has led many payers to target readmission rates (particularly those at 30-days) as a hospital performance metric.. It is envisaged that strategies targeted at readmission reduction might simultaneously improve both the quality and cost of care.

In 2009 the Centers for Medicare and Medicaid Services (CMS) began public reporting of all-cause readmission rates for a number of conditions, including HF, and in 2010 with the passage of the Patient Protection and Affordable Care Act, CMS were instituted financial penalties for hospitals with worse-than-expected 30-day readmission rates for HF, myocardial infarction, and pneumonia. Since penalties are applied against total hospital reimbursement, the financial consequences for excessive rates of 30-day readmission are substantial. At our hospital, for example, nearly $15–20 million of Medicare dollars were at risk between the years 2012 and 2015. These data, coupled with the negative prognostic implications of recurrent hospitalization for HF patients, underscore the financial and clinical imperative for physicians to focus attention on prevention of heart failure readmissions.

Desai/Fig.5: **Risk for Readmission**
While the 30-day metric for HF readmissions is the focus of CMS financial penalties, all physicians who care for HF patients understand that these patients are at risk for readmission well beyond the first 30 days after they leave the hospital. Most studies of the lifetime risk of admission for HF patients highlight at least two distinct peaks in readmission rates.[2] The first happens early (up to 60 or 90 days) after hospitalization, as patients transition to care in the ambulatory setting; There is a plateau in the rates of readmission as the disease is stabilized and patients are engaged with longitudinal HF management, and then as the disease advances toward the end-stage and patients approach the end of life, there is a spike again in the rates of hospitalization.

Desai/Fig.6: **Cycle of Congestion**
Most cardiovascular hospitalizations in patients with HF are related to worsening congestion and volume overload. It is well established that congestion drives most of the typical symptoms of effort limitation, orthopnea, paroxysmal nocturnal dyspnea, and peripheral edema in HF patients.

Beyond simply making patients feel poorly, however, congestion may actually perpetuate or enhance the progression of the HF syndrome; patients with worsening filling pressures have worsening ventricular wall stress, more mitral regurgitation, secondary rises in pulmonary pressures, increased myocardial oxygen demand, and increasing load on the right ventricle – and this syndrome of progressive myocardial ischemia, worsening wall stress, and worsening pulmonary hypertension may result in progression of the biventricular dysfunction and perpetuation of a downward spiral of hemodynamic deterioration in HF.

Desai/Fig.7: **Efficacy of Decongestion**
For hospitalized HF patients, the extent of residual congestion at the time of discharge is one of the most potent predictors of their risk for readmission and death. **Figure 7** illustrates one measure of this association, using pre-discharge levels of B-type natriuretic peptide (BNP) as a surrogate for the efficacy of decongestion at the time of discharge. As shown, patients with the lowest tertile of BNP (eg, <350 ng/L shown in the Figure) at hospital discharge had nearly 15-fold lower rates of hospitalization and death at 180 days than patients with the highest tertile of BNP (here > 700 ng/L).[3] Accordingly, effective management of congestion prior to discharge is a key goal for hospitalized patients, even if it comes at the expense of prolonging the length of stay.

Desai/Fig.8: **Congestion State Post Discharge**
Data from two key randomized trials of patients hospitalized with HF, the DOSE-HF (Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure) trial and the CARRESS-HF (Cardiorenal Rescue Study in Acute Decompensated Heart Failure) trial conducted within the NHLBI HF network, have clarified the relationship between decongestion and the risk of HF readmissions. In these trials, 48% of the patients remained congested at the time of discharge, and predictably those patients had higher rates of readmission.[4] But even among the 52% of patients who left the hospital in a clinically decongested state, about two-thirds of those patients developed recurrent congestion by 60 days of follow-up.

These data highlight that not only is congestion an important target within the hospital for optimal management of patients, but that longitudinal monitoring of patients for recurrence of congestion in early post-discharge interval may be a critical target for improving clinical outcomes.

Desai/Fig.9: **Smoothing the Transition**
In aggregate, the various strategies deployed by clinicians to keep HF patients well and out of the hospital are classified under the rubric of multidisciplinary HF disease management. Operationally, HF disease management differs in its specifics from institution to institution, but typically includes a few core components.

The first is often nurse or pharmacist-led predischarge education, in order to educate and provide patients with the substrate and tools to self-manage their disease.

The second is nurse-directed coordination of care at the time of discharge, to facilitate continuity of care and a warm handoff from inpatient to outpatient providers.

Finally, there is some component of postdischarge surveillance. In many hospitals this includes both periodic trans-telephonic surveillance of weight and vital signs (telemonitoring) and access for patients who are developing worsening symptoms to providers with specialty expertise in HF.

When applied effectively, HF disease management is extremely effective in improving HF outcomes. In meta-analyses these interventions are associated with a 25% reduction in overall mortality, a 26% reduction in HF readmissions, and about a 19% reduction in hospitalization for any cause over time.[5]

The advantage to HF disease management is that because of the savings from prevention of readmissions, which is such an important cost driver, these programs are often cost-saving or cost-neutral. In the end, although it is difficult to say specifically which components are the most relevant, a central focus on early identification and treatment of worsening congestion is common to all.

Desai/Fig.10: **Rise in Filling Pressures**
Data from trials of implantable hemodynamic monitors for HF have revealed a lot about the evolution of HF decompensation. **Figure 10**, drawn from data from the COMPASS-HF (Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure Study) trial,[6] underscores that whether patients had a low ejection fraction (in blue) or a preserved ejection fraction (in red), filling pressures rose very gradually, often over 2–3 weeks in anticipation of the HF event.

So while to many patients and clinicians HF decompensation sometimes appears to be an abrupt phenomenon, these data suggest that it develops gradually over the course of time, independent of ejection fraction. This window of gradual rise in filling pressures (shown in blue in the Figure), which often precedes the development of typical symptoms of HF, represents a key opportunity to intervene to prevent HF decompensation well before it happens.

Desai/Fig.11: **Blind Management**
The challenge, of course, is that most patients with HF spend a small fraction of their lives in the clinic, in front of either HF practitioners or electrophysiology (EP) specialists. Patients spend the vast majority of the time living their lives at home, well outside the vision and reach of providers, making most days of HF management largely blind, with heavy reliance on patients to self-report symptoms of clinical deterioration.

Unfortunately, patients frequently underreport symptoms because they make unconscious adjustments to their day-to-day life to accommodate subtle changes in effort tolerance or they fail to report changes with sufficient lead time to implement changes in therapy to prevent hosptialization.

Desai/Fig.12: **Assessment of Congestion**
In the clinic physicians have a number of ways to assess when congestion is developing in patients. Most of these are physical exam-based, some require laboratory testing, and some exploit available in-dwelling technology such as defibrillators and pacemakers. Of the parameters shown in Figure 12, physical exam parameters and biomarkers such as jugular venous pressure, hepatojugular reflux, an S3 gallop, pulmonary rales, or measurement of brain (B-type) natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (NT-pro-BNP) are challenging to use outside of the clinic setting because they really require a face-to-face encounter with the patient. Accordingly, they are not of much help in managing patients remotely or in triaging patients who call with worsening symptoms.

Key to abbreviations in Figure:
BNP – brain natriuretic peptide
JVP – jugular venous pressure
LVEDP – left ventricular end-diastolic pressure
PCWP – pulmonary capillary wedge pressure
RAP – right atrial pressure
S3 – third heart sound

Desai/Fig.13: Daily Weight Measurements

Beyond physical exam and laboratory parameters, serial monitoring of weight or data from implantable devices has been used to facilitate remote HF management. The most common physiologic parameter that we use to monitor HF patients is daily measurements of weight, and most HF longitudinal management programs instruct patients to monitor their weights on a daily basis to track potential changes in fluid status. (I often give my patients guidance about contacting the HF clinic if their weight exceeds a gain of 2 lb in 2 days or 5 lb in a week.) The challenge is that the sensitivity of that kind of weight change for anticipating a HF hospitalization, and the specificity of weight change for predicting HF events, is much lower than we would like.

In general, if we look at changes in body weight in anticipation of a HF hospitalization, many patients are admitted to hospital with little or no change in weight, and when there is a change in weight it is often minute, maybe 2–3 lb, not as dramatic as one might expect. If we correlate changes in body weight with changes in filling pressure, using data from implantable hemodynamic monitors, we see that often there are dramatic swings in pressure that anticipate HF events but are not reflected in day-to-day changes in body weight. So, while weight measurements are not irrelevant to HF management, they are often not a terribly sensitive sign of HF decompensation.[6-8] When weight changes do happen, they often happen so proximate to HF events that intervening to prevent a hospitalization is not possible.

Desai/Fig.14: TIM-HF

Data suggesting that weight and vital sign monitoring is ineffective as a stand-alone HF management strategy are supported by several large randomized clinical trials. **Figure 14** shows the results of one, the TIM-HF (Telemedical Interventional Monitoring in Heart Failure) trial, published in 2011, which used a particularly elaborate automated telemonitoring system for HF that tracked daily weights and vital signs on a routine basis from a centralized telemonitoring center.[9]

In this trial, use of telemonitoring to assist treatment of HF resulted in no significant impact over usual care on the rates of HF hospitalization or, indeed, the rates of mortality in this trial. These data add to a growing body of literature suggesting that there does not appear to be an incremental benefit of longitudinal monitoring of weights and vital signs over standard HF management for improving HF outcomes.

So while it seems intuitively clear that patients should do better with daily weight monitoring, it is not clear that this is an adequate form of longitudinal surveillance for HF patients.

Desai/Fig.15: Remote Monitoring

In general the optimal signal for managing HF patients would be one that tracks closely with filling pressure, is easily discernible and accurately measurable, is rapidly transmitted from the patient to the provider, is actionable/interpretable by a variety of clinicians, and is responsive, in that the intervention that is directed by the change of pressure produces a measurable change in the parameter so that the information–intervention feedback loop can then repeat.

Figure 15 displays the concept of a loop of remote monitoring where some data are transmitted upon action by the patient, the data are received and processed by a central provider, the patient is then contacted and implements an intervention, and then the response to that patient-initiated intervention can be detected so that further intervention can be implemented if needed.[10]

Even with an effective signal of decompensation, it may not be possible to keep patients well and out of the hospital unless all elements of this information–intervention loop can be completed in an efficient fashion.

Desai/Fig.16: Acute Decompensation

So the challenge of HF management remains the question that if daily weight measurements are not useful, what other strategies are available for monitoring HF patients? **Figure 16** illustrates how weights are a late marker and often, if present at all, do not help prevent decompensation in HF patients.[11] There are other parameters that can be assessed, such as intrathoracic impedance or heart rate variability, that due track much better with rises in filling pressures and that do predict risk for impending decompensation with greater efficiency.

The challenge with those measures is that they are not often as actionable as we might like. It is difficult for clinicians to interpret a change in impedance or heart rate variability in a way that translates into effective medical therapy to prevent decompensation, and often therefore these data, when systemically studied in randomized trials, have not yielded the hoped-for incremental benefit with regard to outcomes.

What are we really trying to estimate with weights, changes in impedance, or heart rate variability changes? The answer is changes in filling pressure, which until recently we have not had the ability to measure directly.

Desai/Fig.17: Other Approaches

Some trials have suggested that periodic BNP monitoring might enhance the efficacy of guideline-directed medical therapy, but it is not yet clear how serial BNP levels should be optimally leveraged to facilitate HF management. As well, variability in BNP levels is confounded by a number of factors that make them only a loose surrogate for the degree of volume overload/congestion.

Desai/Fig.18: DOT-HF

In general, data from randomized trials suggest that there is really no benefit for longitudinal monitoring of device-based parameters for enhancing HF management, and this provides an important cautionary note that more data do not always equate to more information.

Looking for example at the results from DOT-HF (Diagnostic Outcome Trial in Heart Failure),[12] which randomized HF patients to management with or without guidance from impedance data, the clinicians who had access to the impedance data were no better at keeping their patients alive, and actually were worse at keeping their patients out of the hospital, than the physicians who relied on traditional information. This may have been because the impedance signal was overly sensitive, or perhaps because when impedance dropped in these HF patients, clinicians felt compelled to refer patients to the emergency department for evaluation, where they were frequently admitted.

The paradoxical increase in the rates of hospitalization in impedance-guided strategies suggests that perhaps this is not the signal that we need for monitoring HF patients.

Desai/Fig.19: Higher PAP = Hospitalizations

What we do know from the results from hemodynamic monitoring trials is that direct measurement of filling pressures correlates strongly with risk of HF events, and that in patients in whom we are able to effectively reduce filling pressures, we are often able to prevent hospitalization. Data from the COMPASS-HF (Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure Study) trial of an implantable pulmonary artery diastolic pressure monitoring device suggested that the risk of the HF hospitalization correlates very closely with measured pulmonary artery diastolic pressure. In that study patients had a linear increase for the risk for HF hospitalization once the pulmonary artery diastolic pressure exceeded 18 mmHg.[13]

In other words, overall the data from COMPASS-HF suggest very strongly that perhaps the signal that we have been missing in longitudinal HF management is the ability to directly monitor filling pressures, and pulmonary artery diastolic pressure in particular.

Desai - References

[1] Heidenreich PA, Albert NM, Allen LA, et al; American Heart Association Advocacy Coordinating Committee; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Stroke Council. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. *Circ Heart Fail*. 2013;6:606-619.

[2] Desai AS, Stevenson LW. Rehospitalization for heart failure: predict or prevent? *Circulation*. 2012;126:501-506.

[3] Logeart D, Thabut G, Jourdain P, et al. Predischarge B-type natriuretic peptide assay for identifying patients at high risk of re-admission after decompensated heart failure. *J Am Coll Cardiol*. 2004;43:635-641.

[4] Lala A, McNulty SE, Mentz RJ, et al. Relief and recurrence of congestion during and after hospitalization for acute heart failure: insights from Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure (DOSE-AHF) and Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARESS-HF). *Circ Heart Fail*. 2015;8:741-748.

[5] McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. *J Am Coll Cardiol*. 2004;44:810-819.

[6] Zile MR, Bennett TD, St John Sutton M, et al. Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. *Circulation*. 2008;118:1433-1441.

[7] Lewin J, Ledwidge M, O'Loughlin C, et al. Clinical deterioration in established heart failure: What is the value of BNP and weight gain in aiding diagnosis? *Eur J Heart Fail*. 2005;7:953-957.

[8] Abraham WT, Compton S, Haas G, et al; FAST Study Investigators. Intrathoracic impedance vs daily weight monitoring for predicting worsening heart failure events: results of the Fluid Accumulation Status Trial (FAST). *Congest Heart Fail*. 2011;17:51-55.

[9] Koehler F, Winkler S, Schieber M, et al. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: the telemedical interventional monitoring in heart failure study. *Circulation*, 2011;123:1873-1880.

[10] Desai AS, Stevenson LW. Connecting the circle from home to heart-failure disease management. *N Engl J Med* 2010;363:2364-2367.

[11] Adamson PB. Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: new insights from continuous monitoring devices. *Curr Heart Fail Rep*. 2009;6:287-292.

[12] van Veldhuisen DJ, Braunschweig F, Conraads V, et al; DOT-HF Investigators. Intrathoracic impedance monitoring, audible patient alerts, and outcome in patients with heart failure. *Circulation*. 2011;124:1719-1726.

[13] Stevenson LW, Zile M, Bennett TD, et al. Chronic ambulatory intracardiac pressures and future heart failure events. *Circ Heart Fail*. 2010;3:580-587.

Part II: Background and Rationale for Implantable Hemodynamic Monitoring
William T. Abraham, MD

Abraham/Fig.1: Presentation Title

Abraham/Fig.2: CHAMPION Trial Design
Dr. Desai has nicely described the rational for considering pulmonary artery pressure (PAP) as a target for heart failure (HF) therapy. To test the hypothesis that lowering PAP can reduce the risk of HF hospitalization for decompensation episodes, 550 patients were randomized into the prospective, multicenter, controlled, single-blind CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients) trial,[1] with all of the subjects followed until the last patient had reached 6 months of follow-up. The primary efficacy endpoint was the rate of HF-related hospitalizations at 6 months, to test the hypothesis that PAP-guided HF management could lower the rate of HF hospitalization.

As shown in **Figure 2**, all 550 patients were implanted with the CardioMEMS PAP sensor system (see next Figure); 270 were randomized to a treatment arm and 280 to a control arm; the two arms differed in that those randomized to the treatment arm were managed according to the PAP levels recorded by their implanted PAP monitoring device, whereas the physicians were blinded to PAP levels for the subjects in the control arm and the patients were managed strictly on the basis of standard of care. The primary endpoint was HF hospitalization at 6 months, but patients were followed for an average follow-up exceeding 15 months in order to evaluate the durability of effect.

Abraham/Fig.3: PAP Measurement System
The PAP measurement system evaluated in the CHAMPION Trial[1] is illustrated in **Figure 3**. The implantable sensor is shown in the upper right-hand corner of the Figure. It is a small MEMS-based pressure sensor about the size of a small paperclip. There is no battery. There are virtually no moving parts. There is nothing to wear out, or to run out, or to be replaced, and now with 10 years' experience with using this sensor, there have been no sensor failures. The sensor is implanted using a simple right-heart catheter-based delivery system, and it can be implanted by virtually any type of cardiologist, from invasive or interventional cardiologists, electrophysiologists, HF specialists, or general cardiologists.

The home electronic system makes it easy for the patient to use. The patient simply lies back on the specialized pillow, shown on the lower left-hand corner of the Figure, and pushes one button. When the patient pushes that button, the device is simultaneously powered via radio frequency, the pressure waveform information is extracted from the sensor, and then the information is sent from the cellular base station to a secure web site via a cellular link for clinician inspection.

And at the lower right-hand corner of the Figure is a typical trend plot for PAPs derived from this PAP measurement system, where systolic, diastolic, and mean PAPs are shown in red, green, and blue, respectively. This also illustrates the paradigm that was tested in the CHAMPION Trial where, as seen in this example, the patient started with high PAP; medications were then adjusted to lower the pressures into the target range depicted by the blue shading, and kept there, allowing the patient in this particular example to remain well and out of the hospital without further HF hospitalizations.

Abraham/Fig.4: CHAMPION PA Target Pressures
The CHAMPION trial assessed managing PAP levels to target values so that regardless of patient signs or symptoms, regardless of whether or not the patient felt well, and regardless of whether the clinician thought that the patient looked well, the trial protocol encouraged the treating physicians to lower patient PAP levels into the target ranges shown in **Figure 4**.[1,2] For example, the target range for pulmonary artery diastolic pressure was 8–20 mmHg [systolic 15–35 mmHg, mean 10–25 mmHg].

This was accomplished with very simple protocol-driven treatment algorithms, such as the one shown in **Figure 4**. If the PAP values were elevated, implying that the patient was wet, the investigator was encouraged to add or increase the dose of a diuretic. If that medication adjustment alone did not result in a reduction in the PAP, then the investigator was encouraged to add or to increase the dose of a vasodilator.

Abraham/Fig.5: Clinical outcomes
The result of application of the simple CHAMPION trial protocol illustrated in **Figure 5** was a significant reduction in HF hospitalizations.[3] Over the entire period of the randomized, single-blind, controlled follow-up, there was a 33% reduction in the risk of HF hospitalizations. But importantly, beyond that there was also a significant reduction in the combined endpoint of death from any cause or HF hospitalizations, and [indicated by the red outline] there were also significant reductions in all-cause hospitalizations and in the composite of all-cause death or all-cause hospitalizations. This latter observation is important because it shows that there is no trade-off with PAP-guided HF therapy; ie, there is no increase in other types of hospitalizations associated with the reduction in HF hospitalizations. In other words, use of PAP-guided HF therapy results in a win in terms of the effects on both HF morbidity and mortality.

Abraham/Fig.6: PAP-M: Reduces hospitalizations
Further analysis of the CHAMPION trial results explored the effects of PAP-guided HF management in certain important patient subpopulations. The trial enrolled patients regardless of their left ventricular (LV) ejection fraction (EF), so that patients with either reduced EF (HFrEF) or preserved EF (HFpEF) were included in the trial.

Randomization was stratified on the basis of LVEF and there was a prespecified analysis based on EF (data published in Circulation HF in 2014[4]). **Figure 6** reproduces a table from that publication, showing that both patients with preserved EF (EF ≥40%), as well as those patients with normal EF (EF ≥50%) demonstrated highly statistically significant and clinically meaningful reductions in the risk of HF hospitalization. Specifically, for patients with EF ≥40% (ie, preserved EF), the relative risk reduction for HF hospitalization was 50%.

Abraham/Fig.7: PAP-M: Benefits and comorbidities
Other important subgroups in the CHAMPION Trial were investigated, particularly those HF patients with common comorbidities – such as history of myocardial infarction,[5] chronic obstructive pulmonary disease (COPD),[6] pulmonary hypertension,[7] atrial fibrillation,[8] or chronic kidney disease (CKD).[9] As depicted in **Figure 7** reporting data from several sources of information, there were consistent reductions in HF hospitalizations across all of these CHAMPION patient subpopulations with common HF comorbidities.

For example, the COPD population represents a particularly challenging group of HF patients (because it is often difficult to know if their worsening shortness of breath is related to worsening HF or to worsening or exacerbation of their COPD), and yet in these challenging patients PAP-guided HF therapy produced a 41% reduction in the risk of HF hospitalization.[6] Similarly, in another high-risk population, HF patients with CKD, PAP-guided HF management was both safe and effective, and moreover was not associated with any worsening of renal function.[9]

Abraham/Fig.8: PAP-M: Better than GDMT
Another population subset explored in the CHAMPION Trial was the cohort of HF with reduced EF (HFrEF) patients on optimal guideline-directed medical therapy (GDMT). This was important because after the CHAMPION results were shown to be successful, one of the questions was whether PAP-guided HF management primarily helps patients who aren't already managed very well, or is this approach valuable even in patients who are successfully managed with GDMT?

In the CHAMPION Trial about half of the enrolled patients were on GDMT, meaning that these HFrEF patients were on good doses on beta blockers and ACE inhibitors or ARBs, at a minimum. If indicated, these patients had received CRT and ICD devices, and many were also on aldosterone antagonists. Yet as shown in **Figure 8**, analysis of the CHAMPION GDMT patient subset demonstrated a further 43% reduction in the risk of HF hospitalization on top of GDMT.[10]

In other words, use of PAP-guided HF management reduces hospitalizations and adds value on top of well-managed GDMT alone.

Abraham/Fig.9: **PAP-M: Lowers mortality**
In addition to the further reduction in hospitalizations discussed in Figure 8, this analysis also suggested that PAP-guided management could produce a reduction in the risk of mortality. As shown in **Figure 9**,[10] a 43% relative risk reduction (57% hazard ratio) for patients treated with PAP-guided HF management in addition to GDMT provides a strong suggestion that a reduction in HF hospitalizations with PAP-guided HF management may also result in a reduction in mortality. However because this was a retrospective analysis of a subgroup of the CHAMPION population, this information cannot be taken as definitive.

Abraham/Fig.10: **CHAMPION lowers 30-day readmissions**
Another frequent question that has arisen from the CHAMPION Trial data concerns whether there was an effect on 30-day hospital readmissions? There is evidence that PAP-management reduces HF readmissions at 6 months and over longer follow-up, but there is now a strong focus on 30-day readmission rates. To perform this further retrospective analysis we looked at Medicare-eligible CHAMPION patients who were admitted to hospital during the follow-up of the study – ie, those ≥65 years – and compared them to the Medicare database for 30-day readmissions and HF hospitalizations, looking at patients with PAP-managed care versus standard of care. Looking at 30-day outcomes following these hospitalizations, the results showed statistically significant and clinically meaningful reductions in all-cause readmissions and HF hospitalizations in the PAP-guided treatment group compared with control patients. For example, as seen in **Figure 10** the reduction in 30-day all-cause readmissions was 58%, and in HF 30-day readmissions was 78%, for PAP-guided management vs standard care.[11]

Abraham/Fig.11: **CHAMPION: Effect on CMS HRRP**
To look at the hospitalization data in a different way, we compared the CHAMPION results to the CMS hospital readmission reduction program (HRRP) index. This is the index that CMS uses to penalize hospitals for excess 30-day readmissions: an index >1 results in a penalty, whereas an index <1 results in no penalty.

Figure 11 shows hospital readmission data from all of the hospitals in the United States, shown by grey dots, with the same data from the CHAMPION study sites highlighted in green.[11] It can be seen that in general about half of the gray dots fall above the index line for 1.00 and half fall below the line. But when the same 30-day readmission index for the PAP-treatment patients in the CHAMPION sites is calculated, the index was 0.74 – ie, lower than what has been produced by any hospital in the United States. Again, these are preliminary data and they do not tell the complete story, but these data suggest quite strongly that the use of PAP-guided management will also lower 30-day hospitalization readmission rates.

Abraham/Fig.12: **CHAMPION: Longitudinal analysis(1)**
Some additional supportive data from a longitudinal analysis of the CHAMPION Trial is shown in **Figure 12**, showing what happened after the many months of experience with PAP-guided therapy in the randomized single-blind phase of the study.[12] At that point the clinicians who had been managing their patients with PAP-guided therapy were allowed to continue; however for the first time in a real world setting the clinicians who had been managing the control patients with standard care alone were allowed to begin managing them using the information from their PAP monitoring devices. The prediction would be that if this works, one would expect the rate of HF hospitalizations in the control patients to fall significantly as they were crossed over from control to active management using PAP guidance, as seen in the next Figure.

Abraham/Fig.13: CHAMPION: Longitudinal analysis(2)
As described in **Figure 13**, the control patients in CHAMPION were followed for an average of 17.5 months in the randomized portion of the trial, and then for an additional open-access follow-up averaging 13 months, during which the control patients transitioned to providing information from the hemodynamic monitoring device.[12] As shown in Figure 13, during this follow-up with active PAP monitoring these former control patients demonstrated a 48% reduction in HF hospitalizations.

So, in summary, the CHAMPION Trial results have demonstrated that PAP-guided HF management can have a very significant effect on reducing the risk of HF hospitalizations, and that this occurs regardless of the patient's LVEF. It occurs in important subpopulations of HF patients, such as those with common HF comorbidities, and it also occurs in those patients who are well treated with guideline directed medical therapy (GDMT).

Abraham - References

[1] Abraham WT, Adamson PB, Bourge RC, et al; CHAMPION Trial Study Group. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. *Lancet*. 2011;377:658-666.

[2] Adamson PB, Abraham WT, Aaron M, et al. CHAMPION trial rationale and design: The long-term safety and clinical efficacy of a wireless pulmonary artery pressure monitoring system. *J Cardiac Fail*. 2011;17:3-10.

[3] Adamson PB, Abraham W, Stevenson L, et al. Benefits of pulmonary artery pressure monitoring extend to reduction of all-cause rehospitalization. *J Am Coll Cardiol.* 2014;63I(12): A746.

[4] Adamson PB, Abraham WT, Bourge RC, et al. Wireless pulmonary artery pressure monitoring guides management to reduce decompensation in heart failure with preserved ejection fraction. *Circ Heart Fail.* 2014;7:935-944.

[5] Strickland WL, Parrott CW, Abraham WT, et al. The utility of remote wireless pulmonary artery pressure monitoring in patients with or without a history of myocardial infarction: Experience from the CHAMPION Trial. *J Am Coll Cardiol.* 2011;58(20 Suppl B):B130. Abstract TCT-479.

[6] Krahnke JS, Abraham WT, Adamson PB, et al; Champion Trial Study Group. Heart failure and respiratory hospitalizations are reduced in patients with heart failure and chronic obstructive pulmonary disease with the use of an implantable pulmonary artery pressure monitoring device. *J Card Fail*. 2015;21:240-249.

[7] Benza RL, Raina A, Abraham WT, et al. Pulmonary hypertension related to left heart disease: Insight from a wireless implantable hemodynamic monitor. *J Heart Lung Transplant.* 2015;34:329-337.

[8] Miller AB, Teerlink J, Carson P, et al. Impact of remote, wireless pulmonary artery hemodynamic monitoring in patients with atrial fibrillation and chronic heart failure: insights from the CHAMPION trial. *J Am Coll Cardiol.* 2012;59(13 suppl):E868.

[9] Abraham WT, Adamson PB, Stevenson LW, et al. Benefits of pulmonary artery pressure monitoring in patients with NYHA Class III heart failure and chronic kidney disease: Results from the CHAMPION trial. *J Cardiac Fail.* 2014;20(8 suppl):S93. Abstract 233.

[10] Abraham WT, Adamson P, Stevenson L, et al. Pulmonary artery pressure management in heart failure patients with reduced ejection fraction significantly reduces heart failure hospitalizations and mortality above and beyond background guideline-directed medical therapy. *J Am Coll Cardiol.* 2015;65(10S):A790.

[11] Adamson PB, Abraham WT, Bauman J, Yadav J. Impact of wireless pulmonary artery pressure monitoring on heart failure hospitalizations and all-cause 30-day readmissions in Medicare-eligible patients with NYHA Class III heart failure: Results from the CHAMPION trial. *Circulation*. 2014;130:A16744.

[12] Abraham WT, Stevenson LW, Bourge RC, et al. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. Lancet, published online November 8, 2015.