# The Role of In-Hospital Initiation of Cardioprotective Therapies to Improve Treatment Rates and Clinical Outcomes

Gregg C. Fonarow, MD

Division of Cardiology, UCLA School of Medicine, Los Angeles, CA

*Patients with heart failure face a very high risk of hospitalizations and mortality. Despite the compelling scientific evidence that ß-blockers reduce hospitalizations and mortality in patients with heart failure, this lifesaving therapy continues to be underutilized. A number of studies in a variety of clinical settings have documented that a significant proportion of patients with heart failure are not receiving treatment with this guideline-recommended, evidence-based therapy when guided by conventional care. A similar treatment gap has been documented for lipid-lowering therapy in patients with coronary heart disease. The demonstration that initiation of lipid-lowering and other cardioprotective medications prior to hospital discharge for atherosclerotic cardiovascular events results in a marked increase in treatment rates, improved long-term patient compliance, and better clinical outcomes has led to national guidelines being revised to endorse this approach as the standard of care. In-hospital initiation of ß-blocker therapy for heart failure could be reasonably expected to result in similar improvements in treatment rates and clinical outcomes. Recent data suggest that ß-blockers can be safely and effectively initiated in heart failure patients prior to hospital discharge, and that clinical outcomes are improved. Adopting in-hospital initiation of ß-blocker therapy as the standard of care for patients hospitalized with heart failure could dramatically improve treatment rates and thus substantially reduce the risk of future hospitalizations and prolong life in the large number of patients hospitalized each year.* [Rev Cardiovasc Med. *2002;3(suppl 3):S2–S10*]



**Key words:** Heart failure • β-blockers • Coronary heart disease • Lipid-lowering therapy • Myocardial infarction

There is compelling clinical trial evidence that β-blocker therapy reduces the risk of hospitalization and substantially improves survival in patients with heart failure.[1-4] Despite this evidence, as well as national and international clinical guidelines recommending β-blocker treatment in patients with heart failure due to systolic dysfunction, a number of studies have documented low

treatment rates in this patient population.[5-7] The conventional approach to starting β-blocker therapy in patients with heart failure was to delay initiation of therapy until a period of outpatient clinical stability.[8] In general, β-blockers have not been started in heart failure patients during hospitalization. Unfortunately, in the majority of heart failure patients, β-blocker therapy is not initiated during outpatient follow-up.

This "treatment gap" in heart failure is parallel to the treatment gap that has existed with the use of lipid-lowering therapy in patients with coronary heart disease (CHD).[9] The conventional approach to the initiation of lipid-lowering therapy was not to start therapy in-hospital for patients with CHD; instead the national guidelines recommended waiting until the patient was metabolically stable as an outpatient.[10] Based on scientific evidence demonstrating that the in-hospital initiation of lipid-lowering medications resulted in a marked increase in treatment rates, improved long-term patient compliance, and improved clinical outcomes, this approach has been integrated into the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) and American Heart Association/American College of Cardiology (AHA/ACC) Secondary Prevention Guidelines and is now considered the standard of care.[11-13]

The underuse of β-blocker therapy in patients with heart failure represents a major clinical practice and public health issue, just as the underuse of lipid-lowering therapy in patients with CHD does. As such, a similar approach may be required to bridge the β-blocker treatment gap in heart failure. This article reviews the rationale for in-hospital initiation of β-blockers in heart failure, reviews successful programs that have been demonstrated to improve treatment rates, and presents the evidence supporting this becoming the standard of care in patients hospitalized with heart failure.

**Table 1**
**Barriers to Implementing Cardioprotective Therapies in Patients with Cardiovascular Disease**

- Physicians focused on acute problems
- Time constraints and lack of incentives, including lack of reimbursement
- Lack of physician training including inadequate knowledge of benefits and lack of prescription experience
- Lack of resources and facilities
- Lack of specialist-generalist communication, passing on responsibility
- Costs of therapy, inadequate prescription medication benefits, restrictive formularies
- Guidelines that call for delaying initiation of therapy and call for multiple steps, time points, and treatment options

*In the majority of heart failure patients, ß-blocker therapy is not initiated during outpatient follow-up.*

## The Gap in Applying Guideline-Recommended Therapy in Coronary Heart Disease

Patients with CHD remain at high risk for recurrent cardiovascular events and mortality. Despite the wealth of scientific evidence and guideline recommendations regarding risk reduction, there has been an extensive body of evidence documenting that CHD patients have been receiving inadequate treatment to reduce their risk of cardiovascular events and that guidelines have been failing to fulfill their purpose.[9,14–16] A study of over 138,000 patients enrolled in the National Registry of Myocardial Infarction found that only 31.7% of patients hospitalized with an acute myocardial infarction (MI) received lipid-lowering therapy upon discharge.[14] Underuse was seen in both men and women and across all age groups.

The treatment gap that begins in the hospital under conventional management continues on an outpatient basis. The Quality Assurance Project (QAP) analyzed treatment rates in 48,586 outpatients with documented CHD from 140 medical practices (80% cardiology) and found that only 39% of these patients were treated with lipid-lowering medications, and only 11% were documented to have low-density lipoprotein (LDL) cholesterol of 100 mg/dL or less.[15] In the Lipid Treatment Assessment in Practice (L-TAP) study, only 18% of outpatients with CHD treated for hyperlipidemia had LDL cholesterol below 100 mg/dL.[16] Together, these studies demonstrate that under conventionally guided management, regardless of the health

care delivery system, an unacceptably large number of CHD patients were left untreated and undertreated with lipid-lowering therapy. Barriers to implementing lipid-lowering therapy in patients with CHD were highlighted at the 27th Bethesda Conference of the American College of Cardiology.[17] The barriers included physicians being focused on acute problems, time constraints and lack of incentives, lack of training, and poor communication between specialists and primary care physicians (Table 1).

Provider awareness of the NCEP guidelines has been shown not to be sufficient to ensure effective implementation of lipid-lowering treatment. In the L-TAP study, 95% of the surveyed physicians reported that they were knowledgeable about the NCEP guidelines, and 65% reported that they follow the guidelines with most patients, yet only 18% of outpatients with CHD being treated for hyperlipidemia by these physicians had LDL cholesterol below 100 mg/dL.[16]

It has more recently been recognized that the setting in which treatment is initiated may be a very important factor influencing treatment rates.[11] Past treatment guidelines and algorithms such as NCEP ATP-I and ATP-II recommended delaying baseline lipid assessment and treatment until 6 weeks after acute presentation, recognizing that the acute phase response triggered by acute myocardial infarction and coronary artery bypass grafting can substantially lower total and LDL cholesterol.[10] There was also concern that these patients were not metabolically stable and that the early use of lipid-lowering therapy might be harmful.[10] As a result, the first opportunity for beginning treatment was delayed to a time when the patient might have felt that he or she was no longer at risk for recurrent events. The failure of cardiologists and other in-patient physicians to initiate therapy during a period of hospitalization may have lead to long-term management problems in the outpatient setting. Indeed, patients, their family members, and primary care physicians likely perceive inadequate treatment received in the hospital as a lack of endorsement for the cardioprotective medications.[9]

## Does In-Hospital Initiation of Lipid-Lowering and Other Cardioprotective Therapy Improve Treatment Use and Clinical Outcomes?

Although overwhelming clinical trial evidence demonstrated that lipid-lowering drug therapy was associated with a significant reduction in clinical events, recommendations for when to initiate drug therapy were controversial.[18] A lack of data concerning therapeutic benefits, associated risks, and the costs involved in early versus delayed drug treatment added to this controversy.[10,18] Indeed, the majority of clinical trials of statins in patients with CHD, for example the Scandinavian Simvastatin Survival Study (4S), initiated therapy not less than 3 months after an acute event.[19] Studies had shown that lipid levels are lowered following a cardiovascular event, leading to the recommendations in NCEP ATP-I and II that lipid levels should not be assessed until 6 weeks after an event.[10] In addition, conventional wisdom was that patients hospitalized for a cardiovascular event or procedure are too distracted and overwhelmed for secondary prevention measures to be initiated.[10] Whereas it was standard practice to delay the use of lipid-modifying medications in patients with atherosclerotic vascular disease, recent evidence has demonstrated that in-hospital initiation provides substantial benefits with respect to patients' long-term compliance with their treatment and the likelihood of their achieving lipid treatment targets.[11,18]

Proof of concept that in-hospital initiation of lipid-lowering and other cardioprotective medications improves treatment rates and long-term patient compliance was provided by the University of California, Los Angeles, Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP).[11] This program, initiated in a university hospital setting in 1994, focused on initiation of aspirin, statin (titrated to achieve LDL cholesterol below 100 mg/dL), β-blocker, and angiotensin-converting enzyme (ACE) inhibitor therapy in conjunction with dietary and exercise counseling in patients with established CHD prior to hospital discharge. Preprinted orders, care maps, discharge forms, physician/nursing education, and treatment utilization reports were employed to facilitate program implementation.

*The setting in which treatment is initiated may be a very import factor influencing treatment rates.*

Lipid-lowering medication use at the time of discharge increased from 6% before initiation of the program to 86% after CHAMP was implemented ($P < .001$).[11] Improved utilization of aspirin, β-blockers, and ACE inhibitors was also observed (Table 2). Significantly, the in-hospital initiation of lipid-lowering medications

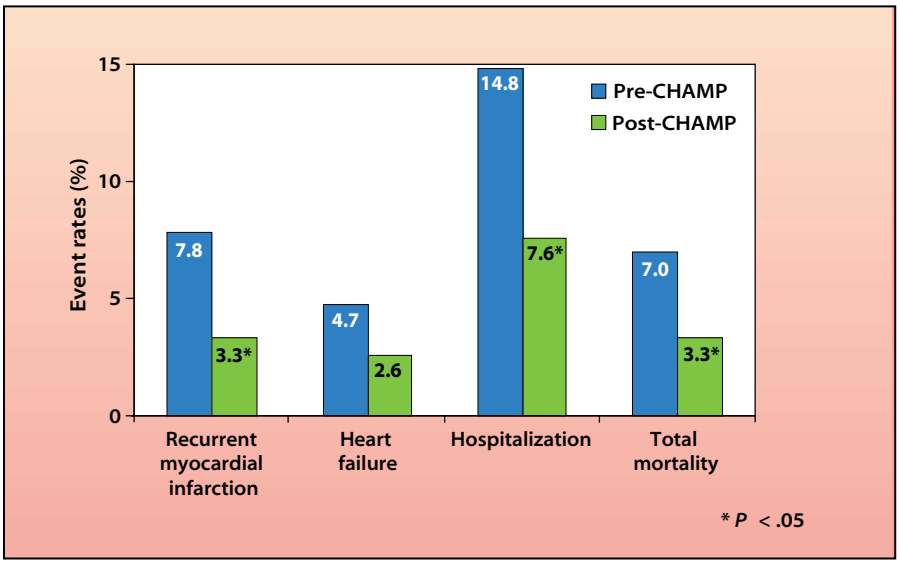


**Figure 1.** *Clinical event rates during the first year after discharge in patients before and after the Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP) study intervention. * P < .05 vs pre-CHAMP.*

had a dramatic effect on long-term treatment rates and patient compliance. With CHAMP, 1 year after hospital discharge 91% of CHD patients were treated with statins and 58% were documented to have LDL cholesterol under 100 mg/dL, compared with 10% and 6%, respectively, with conventional management before CHAMP was implemented ($P < .01$). This improved use of lipid-lowering medications, along with other cardioprotective therapies, was associated with a significant reduction in clinical events in the first year after discharge: the death and nonfatal myocardial infarction rate decreased from 14.8% to 7.3% (odds ratio 0.43; $P < .01$) (Figure 1).[11] These improved treatment rates have been sustained over an 8-year period.[20]

The data generated by CHAMP suggest that postponing the initiation of lipid-lowering therapy by several weeks or months following a cardiovascular event may reduce drug compliance and could contribute to the mismanagement of cardiovascular event risk reduction. Hospitalization can thus serve as a teaching moment for patients and their physicians regarding the importance of cardioprotective therapy to their long-term cardiovascular health.[18]

The CHAMP results have now been replicated in other hospital settings. In an integrated health system of 10 hospitals, this model of care increased the statin treatment rate at discharge after CHD-related hospitalization from 18% at baseline (1994–1997) to 88% postintervention (1999–2000).[21] One-year readmission rates and 1-year mortality rates were also significantly reduced. The American Heart Association has recently launched a national program called Get With the Guidelines based on CHAMP. In a pilot phase conducted in 24 New England hospitals in the year 2000, the use of lipid-lowering therapy increased from 54% pre-intervention to 78% post-intervention ($P < .01$).[22] Hospital-based systems for implementing cardioprotective therapy have been demonstrated to be equally successful in the university and community, teaching and nonteaching, and urban and rural settings. The NCEP-ATP III, AHA/ACC Secondary Prevention 2001, and ACC/AHA Acute Coronary Syndromes 2002 guidelines recommend in-hospital initiation of lipid-lowering medications

*The American Heart Association has recently launched a national program called Get With the Guidelines.*

**Table 2**
**Treatment Rates at Hospital Discharge and at 1-Year Follow-Up with the Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP)**

| | Pre-CHAMP (n = 256) | | Post-CHAMP (n = 302) | |
|---|---|---|---|---|
| Therapy | Discharge | 1 Year | Discharge | 1 Year |
| Aspirin | 78% | 68% | 92% | 94% |
| Beta-Blocker | 12% | 18% | 61% | 57% |
| ACE Inhibitor | 4% | 16% | 56% | 48% |
| Statin | 6% | 10% | 86% | 91% |
| LDL < 100 | – | 6% | – | 58% |

in appropriately selected patients hospitalized with cardiovascular disease.[12,13] Thus in-hospital initiation of lipid-lowering therapy is now recommended as the standard of care in patients with CHD.

## Beta-Blocker Therapy for Heart Failure

There is compelling clinical trial evidence that all patients with heart failure due to left ventricular systolic dysfunction, from asymptomatic left ventricular dysfunction to class IV symptoms, of any etiology should be treated with β-blocker therapy in addition to ACE inhibitors, in the absence of contraindications.[23] Beta-blocker therapy in heart failure reduces mortality by 34%–35%, with additional benefits including reductions in hospitalizations, sudden death, and myocardial infarction.[2-4] National and international guidelines recommend β-blocker therapy as the standard of care in patients with heart failure.[23,24]

Whereas the clinical outcome trials of ACE inhibitors in heart failure studied outpatient initiation of therapy, it has become standard practice to initiate and dose-adjust ACE inhibitor therapy during hospitalization for decompensated heart failure.[23] In contrast, initiation of β-blocker therapy has conventionally been delayed until the heart failure patient was discharged and demonstrated to be stable as an outpatient for 2–4 weeks.[8] Concern existed that early initiation of even low-dose β-blocker therapy in patients during hospitalization could destabilize the patient.[25] It was also felt that it took a few months before the benefits of β-blocker therapy were realized.

## The Gap in Applying Guideline-Recommended Therapy in Heart Failure

Despite the wealth of scientific evidence and guideline recommendations regarding the benefits of β-blockers in patients with heart failure, there is an extensive body of evidence documenting that the conventional approach to initiating β-blockers has left the majority of heart failure patients untreated with this lifesaving treatment.[5-7] In a registry study of patients with left ventricular ejection fraction of 0.35 or below from 105 study centers in eight countries in North America and Europe, only 26% of patients were being treated with β-blockers.[5] Of the 5010 patients with NYHA Class II-IV heart failure due to systolic dysfunction enrolled in the Valsartan Heart Failure Trial (Val-HeFT), only 35% were being treated with β-blockers.[6] In a study of patients with heart failure referred to a university hospital heart failure disease management program, 52% of patients were taking β-blocker therapy.[7] In a registry study conducted in 33 university hospitals in 2000, only 28% of patient hospitalized with decompensated heart failure who had a prior history of heart failure were receiving β-blocker therapy as part of their heart failure regimen prior to hospitalization.[26]

Together, these studies demonstrate that under conventionally guided management regardless of the health care delivery system, an unacceptably large number of heart failure patients are left untreated with β-blocker therapy. Given the substantial number of patients at risk and the benefits of therapy, there is an urgent need to adopt effective strategies that will improve the number of heart failure patients who are being effectively treated with β-blocker therapy. Treatment rates in patients participating in heart failure disease management programs have been higher than rates seen with conventional outpatient management.[5,7,26] This would seem to indicate that β-blocker medication use is impacted by physician education and the process of care in place within the health care delivery system and thus could be favorably impacted by educational initiatives, quality improvement programs, and treatment systems.

## Safety and Efficacy of Beta-Blockers in Heart Failure Patients with Recent Decompensation

Although there had been concern among many physicians that patients with recent decompensation and/or severely symptomatic heart failure would not tolerate the initiation of β-blocker therapy, recent clinical trial evidence demonstrates that treatment of these patients is both safe and effective. The Carvedilol Prospective Randomized Cumulative Survival Study (COPERNICUS) studied the impact of β-blockade in patients with severe heart failure symptoms. This trial enrolled 2289 patients with heart failure symptoms at rest or on minimal exertion and an ejection fraction of under 25%.[4] The study drug could be started while the patient was still hospitalized, but the patients could not be in a CCU/ICU or have been on intravenous inotropic agents in the previous 4 days.

Treatment with carvedilol resulted in a significant 35% reduction in all-cause mortality rates and a significant reduction in the combined risk of death or hospitalization in this severely symptomatic heart failure population. Benefits were seen across all subgroups of patients examined, including patients with recent and/or recurrent decompensation and those with left ventricular ejection fraction below 0.20.[4] Carvedilol was very well tolerated in this severe heart failure patient

population, with more patients withdrawn from the placebo group due to adverse events than from the carvedilol group.[4]

The COPERNICUS trial thus demonstrated that therapy could be safely and effectively initiated, including in hospitalized patients, after initial stabilization. Although patients with acutely decompensated heart failure and those dependent on intravenous inotropic medications should not have β-blockers initiated until they are in a compensated state on oral agents, this frequently occurs within a few days of hospitalization.[4] Thus in-hospital initiation of β-blocker therapy can be considered in the vast majority of patients hospitalized with heart failure but who have achieved clinical stability. Current guidelines also recommend that for patients admitted to the hospital with acutely decompensated heart failure who were previously receiving β-blockers, therapy may be continued during the hospitalization as long as the patient is not in cardiogenic shock or showing signs of systemic hypoperfusion.[23] Thus in-hospital continuation of β-blockers in patients hospitalized with heart failure is already a recommended clinical practice standard.

## In-Hospital Initiation of Beta-Blocker Therapy for Heart Failure

Just as it has proved an effective approach for improving the use of lipid-lowering therapy in CHF, in-hospital initiation of β-blockers would be expected to be effective for heart failure patients (Table 3). Institution of β-blocker therapy in the inpatient setting for patients hospitalized with decompensated heart failure has a number of potential advantages over outpatient initiation. Measurement of ventricular function, if not previously performed, can be systematically integrated into the diagnostic testing performed during cardiac hospitalization through the use of preprinted orders and care maps. The fact that in the COPERNICUS trial patients with severe, chronic heart failure (including in-hospital stabilized patients) tolerated initiation of carvedilol, without an early hazard and with evidence of a reduction in death and hospitalization in the first 8 weeks, removes a perceived barrier to initiating β-blocker therapy in the hospital setting.[4] The structured setting within the hospital can facilitate the initiation of β-blocker treatment through the use of physician prompts and reminders such as care maps, preprinted order sets, discharge forms, and involvement of other health care professionals. Hospital-based initiation of therapy may help to alleviate patient concerns regarding initial β-blocker tolerability and side effects. Linking the initiation of β-blocker and other heart failure medications to the patient's hospitalization conveys the message that this therapy is essential for the prevention of recurrent hospitalizations and is an essential part of the patient's long-term treatment.

Other evidence provides support to the concept that in-hospital of initiation of β-blocker medications could be a more effective way to ensure that treatment is started and continued. It has been demonstrated that ACE inhibitors initiated at the time of hospitalization as part of a disease management program resulted in higher utilization rates at 6 months as compared to treatment utilization rates in conventionally managed outpatients.[27] The use of an institutional heart failure discharge medication program in 10 hospitals and 19,083 patients within an integrated health care system has been shown to increase ACE inhibitor use at time of discharge from 65%–95%.[28] Rates of readmission were reduced from 46.5% to 38.4% and mortality from 22.7% to 17.8% at 1-year follow-up.[28] Although the randomized trials of ACE inhibitors in heart failure involved only outpatients with heart failure, recognition of the safety and improved treatment rates with in-hospital initiation of ACE inhibitors

**Table 3**
**Parallels Between In-Hospital Initiation of Lipid-Lowering Medications for Atherosclerotic and Beta-Blockers for Heart Failure**

| Lipid Lowering for Cardiovascular Disease | Beta-Blockers for Heart Failure |
|---|---|
| Overwhelming clinical trial evidence | Overwhelming clinical trial evidence |
| Large treatment gap | Large treatment gap |
| Concerns about metabolic stability (therapy well tolerated) | Concerns about physiologic stability (therapy well tolerated, with appropriate dosing) |
| Concerns about safety of in-hospital use (safety demonstrated) | Concerns about safety of in-hospital use (safety demonstrated) |
| Concerns about inappropriate patient Rx (effective treatment systems) | Concerns about inappropriate patient Rx (effective treatment systems) |
| Question of benefits in-hospital vs delay (early benefit suggested) | Question of benefits in-hospital vs delay (early benefit suggested) |

has led to treatment rates at the time of hospital discharge to be deemed a performance indicator for heart failure care in the Accessing the Care of Vulnerable Elders project and by the Joint Commission of Accreditation for Hospital Organizations.[29,30]

In-hospital initiation of therapy can also work in a complementary fashion with outpatient heart failure disease management programs.[27,31] With the initiation of therapy beginning in the hospital, fewer titration steps are necessary to achieve target doses. Although studies have demonstrated that patients managed in heart failure disease management programs have improved treatment rates with ACE inhibitors and β-blockers, these systems are often applied to a selected patient population representing only a small proportion of the patients with heart failure being cared for in the health care delivery system from which the patients were drawn.[7,31] In-hospital initiation of therapy can help to ensure that β-blocker therapy is started in patients who will not have access to specialized outpatient heart failure disease management programs. Outpatient systems to ensure appropriate monitoring of patients and uptitration of medical therapy to target doses remain essential for these patients who will not be followed in a heart failure management program, but they would still be expected to be better off on low doses of β-blockers than never having this therapy initiated.[32]

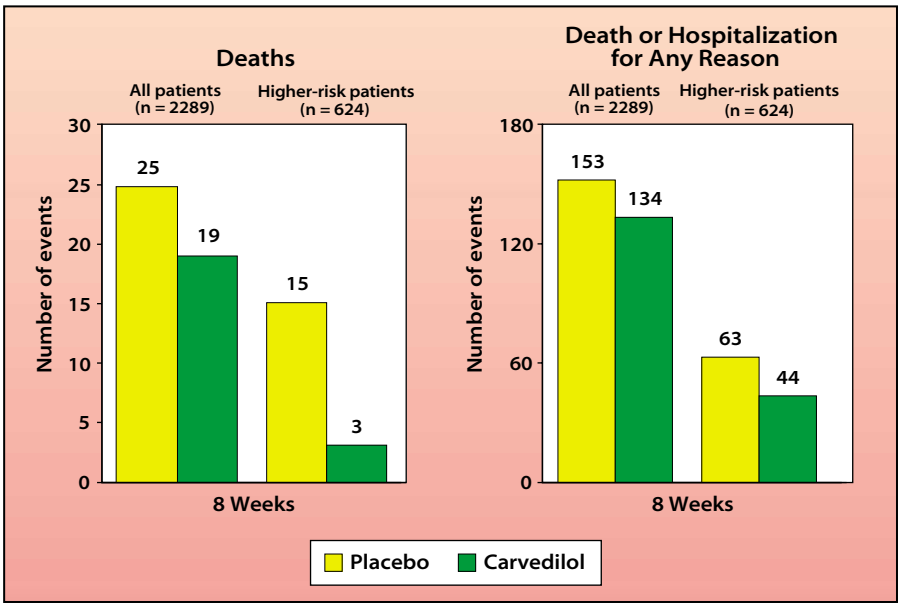


**Figure 2.** *Early clinical event rates in the COPERNICUS trial for the overall study patient population and for higher-risk patients with recent or recurrent decompensation.*

## Early Benefits of Beta-Blocker Treatment

Beyond the long-term benefits of improved treatment use, in-hospital initiation of β-blocker therapy may also be associated with an early ben-

## Main Points

- Evidence shows that heart failure patients and coronary heart disease patients have been receiving inadequate treatment to reduce their risk of cardiovascular events and that guidelines have been failing to fulfill their purpose.
- Past treatment guidelines recommended delaying coronary heart disease treatment with lipid-lowering medications and heart failure treatment with β-blockers until many weeks after hospital discharge.
- The failure of cardiologists and other in-patient physicians to initiate therapy during a period of hospitalization may have lead to long-term management problems in the outpatient setting.
- In-hospital initiation of lipid-lowering and other cardioprotective medications result in a marked increase in treatment rates, improved long-term patient compliance, and improved clinical outcomes.
- The death and nonfatal myocardial infarction rate in the CHAMP program decreased from 14.8% to 7.3%, and these improved rates have been sustained over an 8-year period.
- Rates of treatment with β-blockers have been higher in patients participating in heart failure disease management programs than with conventional outpatient management.
- As β-blocker therapy has now been shown to be safely initiated in-hospital for patients with heart failure and benefits can be seen within in the first 8 weeks of treatment, hospital-based systems for in-hospital initiation of β-blockers can be utilized to bridge the heart failure treatment gap.

efit in reducing heart failure hospitalizations and mortality, one that could be missed if therapy is delayed. In COPERNICUS, there was a reduction in death and hospitalizations seen in the first 8 weeks in the overall patient cohort and in patients with recent and/or recurrent decompensation (Figure 2).[4] Early initiation of carvedilol therapy was safe and well tolerated, with no difference in the withdrawal rate between carvedilol and placebo treatment.[4] As patients discharged after decompensated heart failure are at high risk for recurrent hospitalization and fatal events,[33,34] early initiation of β-blocker therapy can ensure that the patient will not miss out on the risk reduction provided by β-blocker therapy.

As reviewed in this article, it has been clearly documented that not enough has been done to ensure the use of β-blockers in patients with heart failure. Projecting available data nationwide, in the year 2001 there were over 400,000 potentially eligible patients discharged home without β-blocker therapy after being hospitalized with heart failure due to systolic dysfunction. Under conventional management, fewer than 25%–50% of these patients will be started on β-blocker therapy on an outpatient basis. A review of the evidence from recent trials and clinical studies provides a compelling argument for implementing β-blocker therapy in-hospital as part of a systematic approach to addressing the underlying pathophysiology of heart failure. With optimal use of β-blocker therapy in heart failure patients, as many as 21,000 additional lives could be saved each year.

## Conclusions

Despite compelling scientific evidence of the benefits of β-blocker therapy, a substantial proportion of heart failure patients are not on this treatment. Applying hospital-based systems to ensure the initiation of lipid-lowering medications and other cardioprotective therapies has been demonstrated to improve treatment rates, long-term patient compliance, and clinical outcomes in patients with CHD. As β-blocker therapy has now been shown to be safely initiated in-hospital for patients with heart failure and benefits can be seen within in the first 8 weeks of treatment, a similar approach can be utilized to bridge the heart failure treatment gap. Widespread application of hospital-based β-blocker treatment initiation programs for heart failure could dramatically increase rates with this proven, cost-effective therapy and thus substantially reduce the risk of recurrent hospitalizations and death in the large number of patients hospitalized with heart failure every year. ■

## References


1. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group. *N Engl J Med*. 1996;334:1349–1355.
2. MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF). *Lancet*. 1999;353:2001–2007.
3. CIBIS-II investigators and committee. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomized trial. *Lancet*. 1999;353:9–13.
4. Packer M, Coats AJS, Fowler MB, et al. Effect of carvedilol on survival in severe chronic heart failure. *N Engl J Med*. 2001;344:1651–1658.
5. Bart BA, Ertl G, Held P, et al. Contemporary management of patients with left ventricular systolic dysfunction. Results from the Study of Patients Intolerant of Converting Enzyme Inhibitors (SPICE) Registry. *Eur Heart J*. 1999;20:1182–1190.
6. Cohn JN, Tognoni G, Valsartan Heart Failure Trial Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. *N Engl J Med*. 2001;345:1667–1675.
7. Whellan DJ, Gaulden L, Gattis WA, et al. The benefit of implementing a heart failure disease management program. *Arch Intern Med*. 2001;161:2223–2228.
8. Heart Failure Society of America (HFSA) practice guidelines. HFSA guidelines for management of patients with heart failure caused by left ventricular systolic dysfunction—pharmacological approaches. *J Card Fail*. 1999;5:357–382.
9. Fonarow GC. Statin therapy after acute myocardial infarction: are we adequately treating high risk patients? *Curr Atheroscler Rep*. 2002;4: 99–106.
10. Adult Treatment Panel II: Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 1993;269:3015–3023.
11. Fonarow GC, Gawlinski A, Moughrabi S, et al. Improved treatment of cardiovascular disease by implementation of a cardiac hospitalization atherosclerosis management program: CHAMP. *Am J Cardiol*. 2001;87:819–822.
12. Smith SCJ, Blair SN, Bono RO, et al. AHA/ACC Guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update. *Circulation*. 2001;104:1577–1579.
13. Adult Treatment Panel III. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486–2497.
14. Fonarow GC, French WJ, Parsons LS, et al, for the National Registry of Myocardial Infarction 3 Participants. Use of lipid-lowering medications at discharge in patients with acute myocardial infarction: data from the National Registry of Myocardial Infarction 3. *Circulation*. 2001;103:38–44.
15. Sueta CA, Chowdhury M, Boccuzzi SJ, et al. Analysis of the degree of undertreatment of hyperlipidemia and congestive heart failure secondary to coronary artery disease. A*m J Cardiol*. 1999;83:1303–1307.
16. Pearson TA, Laurora I, Chu H, et al. The lipid treatment assessment project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. *Arch Intern Med*. 2000;160:459–467.
17. Twenty-Seventh Bethesda Conference. Matching the intensity of risk factor management with the hazard for coronary disease events. *J Am Coll Cardiol*. 1996;27:957–1047.
18. Fonarow GC, Ballantyne CM. In-hospital initiation of lipid lowering therapy for patients with coronary heart disease: the time is now. *Circulation*. 2001;103:2768–2770.
19. The 4S Investigators. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet*. 1994;344:1383–1389.
20. Fonarow GC, Gawlinski A, Watson KA, Moughrabi S. Sustained improvement in the treatment of cardiovascular hospitalization atherosclerosis management program: CHAMP. *Circulation*. 2001;104:II–711.
21. Pearson RR, Horne BD, Maycock CA, et al. An institutional discharge medication program

reduces future cardiovascular readmissions and mortality: an analysis of 43,841 patients with coronary artery disease. *J Am Coll Cardiol*. 2002;39:452A.
22. McCarthy M. US heart-guidelines program makes a promising start. *Lancet*. 2001;358:1618.
23. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2001;38:2101–2113.
24. Remme WJ, Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J*. 2001;22:1527–1560.
25. Pfeffer MA, Stevenson LW. β-adrenergic blockers and survival in heart failure. *N Engl J Med*. 1996;334:1396–1397.
26. New cardiac project is first to tackle clinical and operational issues. *Health Benchmarks*. 2001;8:1–12.
27. Fonarow GC, Stevenson LW, Walden JA, et al. Impact of a comprehensive heart failure management program on hospital readmission and functional status of patients with advanced heart failure. *J Am Coll Cardiol*. 1997;30:725–732.
28. Pearson RR, Horne BD, Maycock CA, et al. An institutional heart failure discharge medication program reduces heart failure readmissions and mortality: an analysis of 19,083 heart failure patients. *Circulation*. 2001;104:II838.
29. Fonarow GC. Quality indicators for the management of heart failure in vulnerable elders. *Ann Intern Med*. 2001;135:694–702.
30. Landis NT. JCAHO selects core performance measures. Joint Commission on Accreditation of Healthcare Organizations. *Am J Health Syst Pharm*. 2000;57:632–635.
31. Rich MW. Heart failure disease management: a critical review. *J Card Fail*. 1999;5:64–75.
32. Bristow MR, Gilbert EM, Abraham WT, et al. Carvedilol produces dose-related improvements in left ventricular function and survival in subjects with chronic heart failure. MOCHA Investigators. *Circulation*. 1996;94:2807–2816.
33. Cuffe MS, Califf RM, Adams KF Jr, et al. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. *JAMA*. 2002;287:1541–1547.
34. Clinical Quality Improvement Network Investigators. Mortality risk and patterns of practice in 4606 acute care patients with congestive heart failure. The relative importance of age, sex, and medical therapy. *Arch Intern Med*. 1996;156:1669–1673.