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EDITORIALS AND VIEWPOINTS

Heart Failure in the Lifetime of *Musca Domestica* (The Common Housefly)

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In patients with heart failure (HF), hospitalization events represent important clinical endpoints for gauging therapeutic efficacy, both in clinical trials and clinical practice. Interest in this endpoint has skyrocketed since the Patient Protection and Affordable Care Act (PPACA) called for institution of hospital payment penalties by the Centers for Medicare and Medicaid Services (CMS) for excessive 30-day all-cause re-admission rates following index hospitalization for HF, acute myocardial infarction, or pneumonia (1). Much effort has gone into developing approaches—mostly system-based strategies—to improve hospital performance on this metric. The 30-day time frame has taken on greater importance in the minds of clinicians and investigators, who have begun to explore drug effects within this narrow time window. One example is the recent presentation from the DIG (Digitalis Investigation Group) trial (2), showing a 34% (95% confidence interval: 14% to 49%) hazard reduction for 30-day all-cause hospitalization within the subpopulation of patients age ≥65 years with chronic HF and reduced left ventricular ejection fraction. These efforts are a cause for reflection on the relevance of the CMS metric (Table 1): its focus on all-cause readmissions, to the exclusion of mortality, and its focus on 30 days—the approximate lifetime of *Musca domestica*, the common housefly, but a fairly arbitrary and irrelevant timeframe in a patient's life.

A focus on hospitalizations is well-justified. Hospitalization directly detracts from the quality of a patient's life, separating him or her from home, loved ones, and sources of productivity and gratification. It is a marker of disease severity. One-year mortality following HF hospitalization has been estimated at between 26% and 33% (3,4). Every drug class known to reduce mortality in chronic HF also reduces HF hospitalization rates (5–8). Hospitalization is expensive, accounting for approximately 80% of the estimated $24.7 billion in direct costs for HF care in the United States (9).

Although there are many reasons to reduce hospitalization rates, it is cost alone that drove construction of the PPACA metric. Annually, approximately $17.5 billion are expended caring for the nearly 2 million Medicare beneficiaries who are re-hospitalized within 30 days following discharge, representing 19.6% of all index hospitalizations for any cause, including 26.9% of index hospitalizations for HF (10,11). Reducing Medicare expenditure is a needed and worthy aspiration. However, all-cause 30-day readmission is a limited and blunt instrument, when it comes to assessing patient benefit (12). If the goal of cost containment were balanced with improvement in patient well-being, the readmission endpoint would be structured differently.

A re-hospitalization metric centered on patient benefit would consider the competing risk of death. Clinicians, statisticians, and regulatory agencies alike would scorn an endpoint that ignores this important confounder. The 30-day mortality rate following HF hospitalization among Medicare fee-for-service beneficiaries has been estimated at 10.7% (13). The construct of the PPACA metric would imply that death is an acceptable outcome, as long as it occurs without re-hospitalization. In fact, out-of-hospital mortality benefits a hospital's performance by eliminating the patient's opportunity to become counted as a re-hospitalization. It creates the perverse disincentive to re-hospitalize a rapidly declining patient, at least until day 31. Although much has been made of regional and hospital-specific variability in readmission rates (10), there is an inverse correlation between a hospital's 30-day readmission rate and mortality rate following an index HF hospitalization (14,15). Between the years 1993 and 2006, among patients admitted for HF under Medicare fee-for-service, both in-hospital and 30-day mortality decreased, whereas 30-day readmission rates increased (13). Beyond the issue of competing risk, it has been speculated that appropriately planned procedural re-hospitalizations, contributing to the readmission endpoint, may decreases mortality risk (14).

The CMS focus on all-cause hospitalization has its appeal: after all, cost is cost, regardless of admitting diagnosis. But we have yet to discover a magic bullet—drug, device, or disease management intervention—that will cure all of man's ills. A reduced rate of readmission for HF likely implies disease improvement, with associated long-term benefit. There is need to perfect systemic strategies that monitor, assess, and intervene early in labile, ambulatory HF patients. The keys to successful HF disease management

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Table 1 Advantages and Disadvantages of Elements of the 30-Day All-Cause Readmission Metric

	Metric Characteristic	Advantages	Disadvantages
Endpoint	Readmission alone	• Hospitalizations are costly. • Hospitalizations are unpleasant for patients. • Hospitalizations are a marker for disease activity.	• It does not account for the competing risk of death. • Out-of hospital death favors the metric. • There is inverse correlation between a hospital's rates of 30-day mortality and 30-day readmission.
Diagnostic type	All-cause	• Hospitalizations are costly, regardless of admitting diagnosis.	• Interventions that improve heart failure exert greatest benefit on cause-specific hospitalizations and translate into long-term patient benefit.
Time frame	30-day	• Short time frame rationalizes assigning accountability to the discharging hospital.	• Short-term effects are less relevant to the patient than longer-term outcomes. • Hospitals and payment models are not constructed to support needed system implementation. • Short-term metrics create perverse incentives, discouraging use of treatments with minor short-term risk and major long-term benefit. • Systems developed with short-term focus ignore longer-term patient needs.

programs are: 1) a system that drives timely therapeutic responses to monitored changes in clinical status (16); and 2) a long-term focus on patient education and treatment adherence (17). Many such strategies drive demonstrable reduction in cause-specific readmission rates (18), but not necessarily non-HF–related events (19). Although the net effect is generally a modest reduction in all-cause hospitalization, ongoing ambulatory monitoring may identify new medical problems, including known adverse effects of HF treatments, which may require early readmission. So if the purpose of a metric is to gauge net benefit to the patient, it should focus on cause-specific, not all-cause, readmission. In the long-term, cost reduction will follow.

And what about the 30-day time point? The federal government appears well-focused on promoting our nation's health over the entire human lifespan (20,21). It seems odd, then, that PPACA would target the lifetime of the common housefly for its readmission metric. For patients, there is nothing special about the 30-day timeframe (12). Within the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan) trial, over a median follow-up of 9.9 months, 77% of readmissions fell beyond the 30-day window (22). It seems highly unlikely that an intervention specifically and exclusively targeting the first 30 days would make a substantial impact overall, particularly if clinicians are incentivized to delay needed admissions until the 31st day. Furthermore, the 30-day window perversely drives treatment goals toward a short-term focus, at the expense of longer-term outcomes. Beta-blockers offer substantial long-term outcome improvement, and there is a strong rationale for initiating them during hospitalization (23). But they require months to exert their benefit (24), and bradycardia, hypotension, or bronchospasm may drive early re-hospitalization, incentivizing a metric-conscious clinician to withhold therapy. Similarly, it may be tempting for a provider to cite mild azotemia or marginal blood pressure as an excuse to withhold a renin-angiotensin-aldosterone system antagonist, thereby depriving the patient of long-term benefit, rather than risking an early readmission.

Presumably, the CMS believes that within our disjointed healthcare environment, hospitals should at least take ownership over the first 30 post-discharge days. The fallacy of this notion is exemplified best among urban academic centers, serving as safety nets for diverse, multicultural, often mobile populations within a fee-for-service payment model, and disproportionately harmed by the CMS penalty. The $280 million in penalties (expected to triple over the next 2 years) exacted across over 2,200 hospitals in October 2012 (11), while challenging the viability of many struggling hospitals, will be insufficient to justify the required magnitude of investment to develop the broad-based disease management enterprises necessary to effect the program's goals (1). It simply will not work. Hospitals will opt to suffer the penalty. A program of misguided penalties is no substitute for restructuring our nation's overall payment model to facilitate long-term longitudinal patient management.

With so much fanfare about "effectiveness" research, the CMS seems to have forgotten the effectiveness side of the cost-effectiveness equation. Cost analyses have shown clear evidence of cost effectiveness for long-term (not 30 days) HF disease management programs (16,18). Depending on program costs, these efforts may also be cost saving (16). But we need to be clear about this distinction. If the primary goal of the CMS is cost control, regardless of net patient benefit, then we should abandon the pretense of striving toward cost effectiveness. We need a payment structure that will incentivize construction of integrated health systems and implementation of disease management programs, not designed to prevent hospitalization for 30 days, but to maintain the long-term health of our patients in a cost-effective manner.

Returning to the question of drug therapy, neurohormonal antagonists are well established to reduce long-term HF hospitalization rates (5–8), in parallel with survival benefits. Few patients were enrolled in these trials during, or immediately following, hospitalization. The recently presented retrospective analysis adds to what we already knew from the original pre-specified DIG analysis (25), namely that digoxin reduced the risk of HF hospitalization by 28% (95%

confidence interval: 21% to 34%) and all-cause hospitalization by 8% (95% confidence interval: 2% to 13%) over a mean follow-up of 37 months, resulting in 6% fewer total hospitalizations. There was no effect on survival. The latest reanalysis, focusing on 30 days in patients age ≥65 years, must be applied cautiously to the goal of improving a hospital's performance on the CMS metric, since: 1) patient care during the conduct of the DIG trial differed substantially from contemporary practice, including dramatically lower beta-blocker use; and 2) the 30-day period in question was from time of randomization in a chronic HF population, not from time of hospital discharge. A study presently under consideration by the National Heart, Lung, and Blood Institute's Heart Failure Network proposes to investigate the clinical impact of nitrates and digoxin (factorial design), initiated during a HF hospitalization, with a 60-day primary composite endpoint including death or hospitalization for HF. Although examining an intervention's impact on all-cause 30-day re-hospitalization is relevant to the CMS metric, it is less relevant to understanding the impact on disease activity and on patients' well-being than is a focus on longer-term, cause-specific re-hospitalization, accounting for the competing risk of death.

Real solutions will only come through major systemic change. We have the tools to improve our patient's health, but our payment and delivery system does not provide for, or incentivize, their deployment. We should move away from the blunt and ineffective approach of penalizing hospitals for performance on misguided, arbitrary metrics. We must think and act holistically over our patients' remaining lifespans, not in units of time more appropriately geared toward *Musca domestica*. We should move toward aligning incentives from patient to provider, through bundled payments, medical homes, and, ultimately, through integrated systems, competing to provide population management, based on the overall quality, outcome, patient experience, and cost of care.

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