of salt restriction for stable heart failure, some studies suggest that low-sodium diets may increase activation of the renin-angiotensin-aldosterone system potentially translating into worse clinical outcomes. The PROHIBIT (Prevent Adverse Outcomes in Heart Failure by Limiting Sodium) study will evaluate adherence to different levels of sodium restriction and provide pilot data on the feasibility and design of a pivotal trial of dietary sodium intake (4).

In addition, although cardiac rehabilitation has been shown to be safe and have a modest effect on quality of life in patients with chronic heart failure, data for cardiac rehabilitation is limited to stable outpatients (5). Patients hospitalized for acute heart failure are phenotypically different than those with ambulatory heart failure and may lack the ability to participate in and/or derive a robust benefit from a structured aerobic exercise program. Thus, the role of cardiac rehabilitation after hospitalization for acute heart failure remains uncertain and is the focus of the ongoing REHAB-HF (A Trial of Rehabilitation Therapy in Older Acute Heart Failure Patients; NCT02196038) trial.

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Amiodarone and Beta-Blockers in Patients With Heart Failure and Atrial Fibrillation

We appreciate the editorial by Piccini and Allen (1), which critically appraises the evidence for and against a survival benefit associated with β-blockers in patients with heart failure with reduced ejection fraction and concomitant atrial fibrillation. The balanced analysis highlights the divergent results obtained in the patient-level meta-analysis by Kotecha et al. (2) and the recently published β-blocker substudy from the AF-CHF (Atrial Fibrillation and Congestive Heart Failure) trial (3). Methodological challenges confronted by these 2 observational studies were discussed. It was insightfully contended that limitations largely stem from the fact that the studies included in the meta-analysis were not designed to assess the population with atrial fibrillation, and that β-blockers were not randomized in the AF-CHF trial.

We deemed it necessary, however, to clarify an important inaccuracy. Piccini and Allen (1) state that the authors of the AF-CHF β-blocker substudy “did not account for the potential impact of β-antagonism from amiodarone.” Accounting for amiodarone is, indeed, a critical issue considering that it was the drug of choice for patients randomized to rhythm control therapy and that it has β-antagonism properties. Moreover, prescription bias resulting from withholding β-blockers in patients on amiodarone following myocardial infarction has previously been proposed to explain the absence of all-cause mortality reduction despite fewer arrhythmic deaths (4,5). For these reasons, it was regarded as essential to adjust for amiodarone. As such, amiodarone was a key variable included in generating the propensity score to match patients with and without β-blockers to control for potential selection bias and confounding by indication. Balance in pseudorandomized treated and untreated groups was empirically verified across observable patient characteristics. More specifically, after propensity matching, 42% of patients with and 42% of those without β-blockers received amiodarone (3). The absolute standardized difference of 1.6% was far lower than the 10% cutoff value indicative of residual bias.

Considering the totality of evidence and the lack of a clear biologically plausible mechanism to explain how atrial fibrillation nullifies salutary effects of β-blockers
in the setting of heart failure, we fully support the conclusion by Piccini and Allen (1) that it is premature to dismiss the potential impact of β-blockers in improving survival in patients with atrial fibrillation and heart failure with reduced ejection fraction.

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