Background: The use of plasma levels of B-type natriuretic peptides (BNPs) to guide treatment of patients with chronic heart failure (HF) has been investigated in a number of randomized controlled trials (RCTs). However, the benefits of this treatment approach have been uncertain. We therefore performed a meta-analysis to examine the overall effect of BNP-guided drug therapy on cardiovascular outcomes in patients with chronic HF.

Methods: We identified RCTs by systematic search of manuscripts, abstracts, and databases. Eligible RCTs were those that enrolled more than 20 patients and involved comparison of BNP-guided drug therapy vs usual clinical care of the patient with chronic HF in an outpatient setting.

Results: Eight RCTs with a total of 1726 patients and with a mean duration of 16 months (range, 3-24 months) were included in the meta-analysis. Overall, there was a significantly lower risk of all-cause mortality (relative risk [RR], 0.76; 95% confidence interval [CI], 0.63-0.91; \( P = .003 \)) in the BNP-guided therapy group compared with the control group. In the subgroup of patients younger than 75 years, all-cause mortality was also significantly lower in the BNP-guided group (RR, 0.52; 95% CI, 0.33-0.82; \( P = .005 \)). However, there was no reduction in mortality with BNP-guided therapy in patients 75 years or older (RR, 0.94; 95% CI, 0.71-1.25; \( P = .70 \)). The risk of all-cause hospitalization and survival free of any hospitalization was not significantly different between groups (RR, 0.82; 95% CI, 0.64-1.05; \( P = .12 \) and RR, 1.07; 95% CI, 0.85-1.34; \( P = .58 \), respectively). The additional percentage of patients achieving target doses of angiotensin-converting enzyme inhibitors and β-blockers during the course of these trials averaged 21% and 22% in the BNP group and 11.7% and 12.5% in the control group, respectively.

Conclusions: B-type natriuretic peptide–guided therapy reduces all-cause mortality in patients with chronic HF compared with usual clinical care, especially in patients younger than 75 years. A component of this survival benefit may be due to increased use of agents proven to decrease mortality in chronic HF. However, there does not seem to be a reduction in all-cause hospitalization or an increase in survival free of hospitalization using this approach.

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B-type natriuretic peptide (BNP) is a neurohormone secreted predominantly from the ventricle of the heart in response to intracardiac volume loading. B-type natriuretic peptide functions as a counter-regulatory hormone to angiotensin II, nor-epinephrine, and endothelin, having vasodilatory and diuretic effects. The precursor of BNP is pro-BNP, stored in secretory granules in myocytes. Pro-BNP is split by a protease enzyme into BNP and N-terminal pro-BNP (NT-pro-BNP). Compared with BNP, NT-pro-BNP is a longer peptide sequence than BNP (76 vs 32 amino acids) and has a longer half-life (60-120 minutes vs 15-20 minutes). Both BNP and NT-pro-BNP plasma concentration have been shown to be useful in the diagnosis of acute decompensated HF. In addition, these peptides can be used as prognostic indicators in prediction of mortality and clinical outcome in patients with chronic HF.
els may increase temporarily in the following long-term treatment with natriuretic peptide plasma levels also fall.

To determine whether the therapeutic benefit of BNP-guided treatment in chronic HF, by performing a meta-analysis of RCTs comparing BNP-guided treatment and usual clinical care.

**DATA SOURCES AND SEARCHES**

Clinical RCTs were identified via MEDLINE (source, PubMed, 1966 to December 2008), EMBASE (1974 to December 2008), the Cochrane Controlled Clinical Trials Register Database (through December 2008), and the ClinicalTrials.gov Web site (through December 2008). Each search query included the keywords and corresponding MeSH terms for brain natriuretic peptide, pro-brain natriuretic peptide, heart failure, and therapy. Manual reference checking of the bibliographies of all retrieved articles was also performed. To identify studies reported only at scientific meetings, searches were undertaken both manually and electronically of the abstracts of annual scientific sessions of the American Heart Association (2005-2008), the European Society of Cardiology (2005-2009), the American College of Cardiology (2005-2009), the European Heart Failure Society, and the Heart Failure Society of America (through 2009). Eligibility assessment and data abstraction were both performed independently in an unblinded standardized manner by 2 reviewers (P.P. and P.P.).

**METHODS**

**DATA SYNTHESIS AND ANALYSIS**

Results were pooled with Stata statistical software (version 10; StataCorp, Cary, North Carolina) using the Mantel-Haenszel model for a meta-analysis. Trials included were those by Troughton et al, Beck-da-

**QUALITATIVE FINDINGS**

Eight trials, with a total of 1726 patients, met the specified criteria for meta-analysis. Trials included were those by Troughton et al, Beck-da-

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Table 1. Patient Characteristics in Included Trials

<table>
<thead>
<tr>
<th>Source</th>
<th>Patients, No.</th>
<th>Duration of Follow-up, Mo.</th>
<th>Age, y</th>
<th>Male, %</th>
<th>NYHA FC, Mean</th>
<th>NYHA FC Class II, %</th>
<th>NYHA FC Class III, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NH</td>
<td>C</td>
<td>NH</td>
<td>C</td>
<td>NH</td>
<td>C</td>
<td>NH</td>
</tr>
<tr>
<td>Troughton et al</td>
<td>33</td>
<td>36</td>
<td>9.5</td>
<td>68</td>
<td>72</td>
<td>78</td>
<td>75</td>
</tr>
<tr>
<td>Beck-da-Silva et al</td>
<td>21</td>
<td>20</td>
<td>3</td>
<td>64.5 (15.2)</td>
<td>65.6 (13.5)</td>
<td>33.33</td>
<td>35</td>
</tr>
<tr>
<td>Esteban et al</td>
<td>30</td>
<td>30</td>
<td>18</td>
<td>Similar in both groups</td>
<td>Similar in both groups</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>STARS-BNP</td>
<td>30</td>
<td>30</td>
<td>18</td>
<td>Similar in both groups</td>
<td>Similar in both groups</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>TIME-CHF</td>
<td>251</td>
<td>248</td>
<td>18</td>
<td>76</td>
<td>77</td>
<td>80</td>
<td>82</td>
</tr>
<tr>
<td>BATTLESCARRED</td>
<td>121</td>
<td>121</td>
<td>24</td>
<td>76</td>
<td>76</td>
<td>83</td>
<td>67</td>
</tr>
<tr>
<td>PRIMA</td>
<td>174</td>
<td>171</td>
<td>24</td>
<td>71</td>
<td>72</td>
<td>83</td>
<td>67</td>
</tr>
<tr>
<td>SIGNAL-HF</td>
<td>126</td>
<td>124</td>
<td>9</td>
<td>&gt;18</td>
<td>&gt;18</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: BATTLESCARRED, NT-pro-BNP-AsisiTed Treatment to LEssen Serial CARdiac REadmissions and Death; BNP, B-type natriuretic peptide; C, control group; Cr, creatinine; Imm, Immunofluorometric; NA, not available; NH, neurohormonal group; NT-pro-BNP, pro-BNP split by a protease enzyme into BNP and NT-terminal pro-BNP; PRIMA, Pro-brain-natriuretic peptide-guided therapy of chronic heart failure IMProve heart failure morbidity And mortality; STARS-BNP, Systolic Heart Failure Treatment Supported by BNP; TIME-CHF, Trial of Intensified vs standard Medical therapy in Elderly Patients with Congestive Heart Failure.

a Values are expressed as mean (SD).

b Inclusion criteria, patients older than 18 years.

c Data are given in picograms per milliliter.

d Data are given in milligrams per deciliter per meter.

e Data are given in millimeters per liter.

f San Diego, California.

g Data are given as micromoles per liter.

Patient characteristics in these trials are summarized in Table 1. The studies varied in terms of the number of patients, duration of the intervention, and primary end points. In studies where all-cause mortality or all-cause hospitalization was not the primary end point, they were included as secondary end points. The total number of patients in each study ranged from 41 to 499, and the duration of follow-up time varied from 3 to 24 months (mean duration, 17 months). All studies were performed in patients with New York Heart Association (NYHA) class II or greater and left ventricular ejection fraction less than 50%. The participants’ ages ranged from 18 to 85 years. Most were men, with the exception of the study by Beck-da-Silva et al, in which the percentage of males was around 35% in each group. Three studies, including those by Beck-da-Silva et al and Esteban et al and the STARS-BNP study, used the BNP level as a monitor to guide medication doses in the intervention group, whereas the other 4 studies (Troughton et al, BATTLESCARRED study, the TIME-CHF study, PRIMA study, and the SIGNAL-HF study) used NT-pro-BNP levels.

Target plasma BNP or NT-pro-BNP level in the intervention group and clinical aims in the control group of each trial are summarized in Table 2. In the BATTLESCARRED study, there were 3 study arms: hormone-guided care, intensive clinical care, and usual care. “Usual care” in this trial involved no adjustment of medication or further contact with the research team other than an enquiry after 3 months to document medications, adverse events, readmissions to hospital, and death. Consequently, this...
CI indicates confidence interval. PRIMA27 Individual NT-pro-BNP target (lowest level during the first 2 wk after treatment of HF) together with clinical assessment

Table 2. Treatment Group Targets in Included Trials

<table>
<thead>
<tr>
<th>Source</th>
<th>Target BNP/NT-Pro-BNP–Guided Therapy</th>
<th>Target Control Group</th>
<th>Medical Adjustment Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troughton et al25</td>
<td>NT-pro-BNP &lt;1700 pg/mL</td>
<td>HF score &lt;2 (based on Framingham criteria)</td>
<td>ACEI, diuretic, digoxin, aldactone, metolazone then additional vasodilator (isosorbide dinitrate and felodipine)</td>
</tr>
<tr>
<td>Beck-da-Silva et al22</td>
<td>Based first on BNP level and then clinical status evaluation; BB up-titrated when: 1. BNP level is lower + unchanged or better clinical status 2. There are mild signs of congestion but BNP level &gt;10% lower than previous value 3. BNP is within ±10% previous level, clinical signs were primarily considered</td>
<td>Up-titrated medication when no sign of deterioration (worsening FC, HR &lt;55, BP &lt;80, increase congestion)</td>
<td>Only BB (ACEI or ARB and digoxin were unchanged)</td>
</tr>
<tr>
<td>Esteban et al23</td>
<td>NA</td>
<td>Framingham score Based on PE + usual paraclinical + biological parameter</td>
<td>NA</td>
</tr>
<tr>
<td>STARS-BNP24</td>
<td>BNP &lt;100 pg/mL</td>
<td></td>
<td>BB, ACEI, aldactone, diuretic</td>
</tr>
<tr>
<td>TIME-CHF25</td>
<td>NT-pro-BNP + FC $\leq$ II &lt;400 pg/mL ($\leq$75 y), &lt;800 pg/mL ($&gt;75$ y)</td>
<td>FC $\leq$ II</td>
<td>BB, ACEI, or ARB, aldactone, diuretic, nitrate</td>
</tr>
<tr>
<td>BATTLESCARRED26</td>
<td>NT-pro-BNP &lt;1300 pg/mL</td>
<td>HF score $&lt;2$</td>
<td>BB, ACEI, aldactone, diuretic, metolazone, digoxin</td>
</tr>
<tr>
<td>PRIMA27</td>
<td>Individual NT-pro-BNP target (lowest level during the first 2 wk after treatment of HF) together with clinical assessment</td>
<td>Clinical assessment</td>
<td>BB, ACEI, or ARB, aldactone, diuretic, digoxin</td>
</tr>
<tr>
<td>SIGNAL-HF28</td>
<td>NT-pro-BNP plus clinical symptoms and signs</td>
<td>Clinical symptoms and signs</td>
<td>BB, ACEI, or ARB, aldactone</td>
</tr>
</tbody>
</table>

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, β-blocker; BNP, B-type natriuretic peptide; BP, blood pressure; FC, functional class; HF, heart failure; HR, heart rate; NA, not available; NT-pro-BNP, pro-BNP split by a protease enzyme into BNP and N-terminal pro-BNP; PE, physical examination. See Table 1 footnote for study name abbreviations.

4Heart failure score based on Framingham data for a diagnosis of HF with major criteria each scoring 1 point and minor criteria each scoring 0.5 point.

Figure 2. All-cause mortality meta-analysis of individual trials. Fixed-effects model ($\chi^2$=3.75; $P=.59$). CI indicates confidence interval.

GROUP ANA

The risk of all-cause mortality was significantly lower in the neurohormonal (BNP)-guided treatment group (RR, 0.76; 95% CI, 0.63-0.91; $P=.003$ (Figure 2) compared with the clinical-guided treatment group. This effect was dominated by the TIME-CHF study,25 which contributed 49.6% of the weight. There was no significant heterogeneity between the trials (heterogeneity $\chi^2$ of 3.81; $P=.80$). Funnel plot analysis suggested that there was little in the way of publication bias in this result (Figure 3).

A subgroup analysis was performed in the TIME-CHF25 and BATTLESCARRED26 studies, which provided data on patients younger than 75 years or 75 years or older. All-cause mortality was significantly lower in younger patients treated with BNP-guided therapy (RR, 0.52; 95% CI, 0.33-0.82; $P=.005$) than in those in the clinical guided group with a heterogeneity $\chi^2$ of 0.57 ($P=.45$). In contrast, all-cause mortality of those 75 years or older was not significantly different between groups (RR, 0.94; 95% CI, 0.71-1.25; $P=.70$ [heterogeneity $\chi^2$ of 1.14; $P=.29$]).

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HOSPITALIZATION

Three studies\textsuperscript{21,22,24} provided data on all-cause hospitalization. There was no significant difference seen in the BNP-guided therapy group on all-cause hospitalization vs clinical guidance (RR, 0.82; 95% CI, 0.64-1.05; \(P= .12\)) (\textbf{Figure 4A}), with a heterogeneity \(\chi^2 \) of 0.78 (\(P= .68\)). For this end point, the effect was dominated by the STARS-BNP study\textsuperscript{24} with around 80.4% of the weight.

Survival free of any hospitalization was reported in 2 trials. There was a nonsignificant difference in survival free of any hospitalization between the 2 groups (RR, 1.07; 95% CI, 0.85-1.34; \(P=.58\)) (\textbf{Figure 4B}), with a heterogeneity of \(\chi^2 \) 0.00 (\(P=.98\)). This was predominated by the TIME-CHF study,\textsuperscript{25} with approximately 81.6% of the weight.

NUMBER OF DAYS ALIVE AND NOT HOSPITALIZED

The STARBRITE\textsuperscript{18} and PRIMA\textsuperscript{27} studies provided data on the number of days that patients were alive and not hospitalized. The number of days they were alive and not hospitalized was higher in the BNP-guided group than in the clinical control group, but the difference was not significant in both studies (mean [SD], 85 [12.1] days vs 80.4 [20.6] days in the STARBRITE study\textsuperscript{18} and 685 days vs 664 days in the PRIMA study\textsuperscript{27}). Unfortunately, we are unable to perform a formal meta-analysis of this outcome because of differences in the presentation of data.

DRUG THERAPY

The STARS-BNP\textsuperscript{24} and PRIMA\textsuperscript{27} studies presented the percentages of patients having medical treatment adjustment during the study period. Patients in the BNP-guided group had doses of their HF medication adjusted more than those in the clinical care group (\textbf{Figure 5A}; 75% vs 58% in diuretics, 13.4% vs 8.2% in aldactone, 49.6% vs 30.9% in ACE inhibitors or ARBs, and 51.1% vs 41.6% in \(\beta\)-blockers).

The mean percentage of patients reaching their target dose of ACE inhibitors and \(\beta\)-blockers during the study were calculated from the STARS-BNP\textsuperscript{23} and TIME-CHF studies.\textsuperscript{25} Approximately double the number of patients in the BNP-guided therapy group had their doses up-titrated and reached their target level of ACE inhibitors and \(\beta\)-blockers compared with the clinical usual care group (\textbf{Figure 5B} (21.2% and 22.0% in the BNP group vs 11.7% and 12.5% in the usual care group, respectively).}

OTHER PARAMETERS

Change of functional class, quality-of-life (QOL), and left ventricular (LV) ejection fraction (LVEF) could not be meta-analyzed. In terms of functional class, the TIME-CHF\textsuperscript{23} and STARS-BNP\textsuperscript{24} studies showed improvement in both groups; however, Beck-da-Silva et al\textsuperscript{22} and Esteban et al\textsuperscript{23} found no change. The TIME-CHF\textsuperscript{23} study reported a significant improvement in both the BNP and control groups on QOL, particularly during the first 12 months, but the difference between the 2 groups was not significant. However, statistical improvement in QOL in the BNP-guided therapy group (\(P=.03\)) was observed in the study by Beck-da-Silva et al\textsuperscript{22} (\(P=.03\)). Troughton et
Spironolactone, ACE inhibitors, and BNP-guided therapy have been shown to improve clinical outcomes in patients with chronic heart failure (HF). We performed a meta-analysis of clinical RCTs of this therapy, including those used in the present meta-analysis showed promising results regarding the potential clinical benefits of measuring the plasma BNP level to guide the treatment.

Sensitivity analysis was also performed for the end point of all-cause hospitalization (Table 3). The point estimates for all-cause hospitalization were stable under a range of assumptions, and although studies favored BNP-guided therapy, significance was not achieved under any scenario.

Figure 5. Patients having medical treatment adjustment. A, Percentage of patients having doses of medication increased; B, percentage change of patients reaching target dose. ACE indicates angiotensin-converting enzyme; BNP, B-type natriuretic peptide.

We found that using this approach can decrease all-cause mortality of these patients significantly compared with usual clinical care, particularly in patients younger than 75 years. The number of days that patients were alive and not hospitalized was also significantly higher in the BNP-guided group; nevertheless, all-cause hospitalization and survival free of hospitalization between the 2 groups were not significantly different.

One case report and 1 case series of 76 patients with LV dysfunction showed promising results regarding the potential clinical benefits of measuring the plasma BNP level to guide the treatment. Larger studies using BNP monitoring in the treatment of patients with chronic HF suggested the effectiveness of this approach, with demonstrable improvements in clinical outcomes, including rates of death and rehospitalization. However, subsequent RCTs of this therapy, including those used in this meta-analysis, have found variable results. The overall findings of our study suggest that BNP-guided treatment reduces all-cause mortality in patients with chronic HF. This observation is supported by a recently published evaluation that included some (but not all) of the studies used in the present meta-analysis.

We found that the mortality benefit observed with BNP-guided therapy was restricted primarily to those patients in a younger age group (<75 years). In general, these patients have high mortality rates despite use of proven medications and/or devices. Use of ACE inhibitors, β-blockers, and spironolactone reduce morbidity and mortality in patients with chronic HF. As a result of treatment using BNP-guided modification, it was shown that there is an increase in prescribing of these HF medications (spironolactone, ACE inhibitors, and β-blockers) compared with clinically guided treatment. Specifically, the percentage of patients achieving their target dose of ACE inhibitors and β-blockers in the BNP-guided group were increased to approximately 2-fold higher than those in the control group. Therefore, mechanisms underlying decreased mortality in the BNP-guided therapy group could relate to the higher percentage of patients achieving the target dose of drugs with proven prognostic efficacy. Alternatively, there may be other, as-yet unidentified factors contributing to the mortality benefit.

The BATTLESCARRED and TIME-CHF studies showed that the group of patients younger than 75 years derived considerable clinical benefit from BNP-guided therapy, including decreased all-cause mortality. In contrast, in the older age group (≥75 years), the mortality benefit was not substantive. The reason for this is uncertain. Older patients may have more comorbid diseases, including hypertension, chronic kidney disease, diabetes mellitus, and dysrhythmia, that make them less able to tolerate target doses of medication than those in younger age group. They may also be less responsive to these therapies. In the TIME-CHF study, patients in the older age group had a mean age of 82 years (compared with 69 years in the younger group) and had more prevalent comorbidities (eg, hypertension [77% vs 61%], atrial fibrillation [36% vs 26.7%], and kidney disease [62% vs 44%], and more were classified as having NYHA functional class III disease (80% vs 65%). The TIME-CHF study also suggested that the less severe the comorbidities, the more favorable the effects of NT-pro-BNP-guided therapy. Older patients are also more likely to have noncardio-
vascular diseases such as cancers and chronic lung and liver diseases. Thus, these may contribute to mortality in patients of advanced age, and BNP-guided therapy would not alter these outcomes.

The optimal target level of BNP to which therapy should be guided is difficult to decide on. Confounding effects include age, sex, and weight; BNP levels are higher in females and those of advanced age. Furthermore, too aggressive a reduction in BNP levels by up-titration of diuretics, ACE inhibitors, and β-blockers may potentially result in worsening rather than improvement in clinical outcomes, especially in elderly individuals, by causing hypotension and worsening renal failure.

Rates of all-cause hospitalization and survival free of hospitalization were not significantly different between the 2 study groups (Figure 4). However, there was a trend toward lower risk of all-cause hospitalization and more survival free of any hospitalization in this group. This may be explained in part by the contribution of non–HF events on which BNP-guided therapy would not have an impact. Unfortunately, we could not calculate the impact on HF hospitalization owing to a lack of data.

A major limitation of this evaluation of BNP-guided therapy is that we were not able to meta-analyze some key clinical end points on which this approach may have a beneficial impact. In particular, hospitalization for HF is one such end point, where BNP-guided therapy and accompanying intensification of use of standard HF pharmacological therapies should theoretically have a favorable impact on this outcome.

We identified 3 ongoing trials of BNP-guided therapy: the NorthStar study,1 the PROTECT trial,42 and the EXIMPROVE CHF trial.43 The NorthStar study41 is a clinical RCT conducted in Denmark and involving 720 patients with follow-up for 30 months, in which there were 3 arms: treatment in general practice, a standard follow-up program in an HF clinic, and follow-up with plasma NT-pro-BNP levels monitored in an HF clinic. The PROTECT trial42 is an RCT in Massachusetts General Hospital, Boston, that includes 300 patients with follow-up for 1 year. There are 2 arms: standard of care and NT-pro-BNP–guided groups. The EXIMPROVE CHF (Improvement of patients with Chronic Heart Failure Using NT-pro-BNP) study43 is an RCT in St Michael’s Hospital, Toronto, Ontario, Canada, using NT-pro-BNP–guided care, with follow-up for 2 years.

Based on the findings of the present meta-analysis, future studies will require a larger number of patients and careful matching of age, sex, and other key clinical variables to definitively address the true effectiveness of BNP-guided treatment in the treatment of chronic HF. Prospective evaluation of relevant study end points for which BNP-guided therapy may be expected to have a beneficial impact on outcomes (eg, hospitalization for HF) would also be of great importance.

In summary, the present study demonstrates that BNP-guided therapy can significantly lower all-cause mortality rate in patients with chronic HF compared with those receiving usual clinical care, particularly in patients younger than 75 years but not in those of advanced age. However, this approach does not seem to either reduce all-cause hospitalization or increase survival free of hospitalization.

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Financial Disclosure: None reported.

Table 3. Sensitivity Analysis of the Effect of BNP-Guided Medical Therapy on All-Cause Mortality and All-Cause Hospitalization

<table>
<thead>
<tr>
<th>Source</th>
<th>Trials, No.</th>
<th>Patients Evaluated, No.</th>
<th>All-Cause Mortality, RR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality; analysis with all studies except</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troughton et al21</td>
<td>7</td>
<td>1657</td>
<td>0.78 (0.65-0.94)</td>
<td>.008</td>
</tr>
<tr>
<td>Beck-da-Silva et al22</td>
<td>7</td>
<td>1685</td>
<td>0.76 (0.63-0.92)</td>
<td>.004</td>
</tr>
<tr>
<td>STARS-BNP24</td>
<td>7</td>
<td>1666</td>
<td>0.75 (0.62-0.90)</td>
<td>.002</td>
</tr>
<tr>
<td>TIME-CHF23</td>
<td>7</td>
<td>1506</td>
<td>0.76 (0.63-0.92)</td>
<td>.005</td>
</tr>
<tr>
<td>BATTLESCARRED26</td>
<td>7</td>
<td>1227</td>
<td>0.76 (0.58-1.00)</td>
<td>.052</td>
</tr>
<tr>
<td>PRIMA27</td>
<td>7</td>
<td>1484</td>
<td>0.74 (0.61-0.89)</td>
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</tr>
<tr>
<td>SIGNAL-HF28</td>
<td>7</td>
<td>1381</td>
<td>0.74 (0.59-0.93)</td>
<td>.009</td>
</tr>
<tr>
<td>All-cause hospitalization; analysis with all studies except</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troughton et al21</td>
<td>2</td>
<td>261</td>
<td>0.84 (0.65-1.09)</td>
<td>.19</td>
</tr>
<tr>
<td>Beck-da-Silva et al22</td>
<td>2</td>
<td>289</td>
<td>0.84 (0.65-1.08)</td>
<td>.18</td>
</tr>
<tr>
<td>STARS-BNP24</td>
<td>2</td>
<td>110</td>
<td>0.63 (0.31-1.31)</td>
<td>.22</td>
</tr>
</tbody>
</table>

Abbreviations: BNP, B-type natriuretic peptides; CI, confidence interval; RR, relative risk. See Table 1 footnote for study name abbreviations.
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3. Dickstein K, Cohen-Solal A, Filippatos G, et al; Task Force for Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of European Society of Cardiology; ESC Committee for Practice Guidelines; Document Reviewers. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology: developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). Eur J Heart Fail. 2008;29(19):2388-2442.


