Critical Review Form
Therapy

B-Type Natriuretic Peptide Testing, Clinical Outcomes, and Health Services Use in Emergency Department Patients with Dyspnea, *Annals of Internal Medicine* 2009; 150:365-371

Objective: **To assess "whether patients who presented with shortness of breath would be managed differently and hospitalization rates would be altered if BNP was measured". (p. 366)**

Methods: **Randomized, controlled single-blind trial at two Australian ED's (Prahan and Epping, Victoria) for all patients presenting with severe dyspnea (triage category 1 to 3) from August 2005 to March 2007. Exclusion criteria included age < 40, trauma or cardiogenic shock related dyspnea, or creatinine > 2.8 mg/dL.**

Physicians received four CHF educational sessions during the enrollment periods, including advice that BNP < 100 ng/L excludes CHF and < 500 ng/L makes AHF likely. With each patient recruited (to either arm), treating physicians received written guidelines on COPD and CHF management. A registrar or consultant assessed all patients in the ED. In the BNP group physicians received the BNP-level within 60-minutes.

The 1-day outcome was hospital admission rates and length of stay for which the study had 80% power with two-sided *P* values to detect absolute admission rate reduction of 10% (80% to 70%) and relative reduction of 20% (8.0 to 6.4 days) in hospital length of stay if sample size 300 patients. Investigators also assessed medical management 30-day mortality, and re-admission rates as secondary outcomes.

Two physicians (one a Cardiologist) made the diagnosis of heart failure blinded to the BNP result but with access to all other clinical data. These physicians used the European Society of Cardiology guidelines to establish the diagnosis of AHF. If they disagreed, a third physician made the diagnosis.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	Yes. "Allocation to the BNP and control group was by random numbers (from computer-generated, random-number tables) in a sealed envelope. The randomization was stratified by site". (p. 366)

2.	Was randomization concealed (blinded)?	Yes. "We blinded patients to the intervention". (p. 366)
3.	Were patients analyzed in the groups to which they were randomized?	Yes. "Statistical analysis was done by intention to treat". (p. 367)
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	"The 2 groups were similar in age, sex, smoking history, frequency of ischemic heart disease, and history of chronic obstructive pulmonary disease. (**Table 1**). About 20% in both groups were diabetic, and 10% had a history of renal impairment. Hypertension and a history of heart failure were more frequent in the BNP group. Patients in the BNP group reported orthopnea more frequently, whereas about 50% of patients had cough, and 25% in both groups had sputum production. Both groups had similar dyspnea grades, heart rates, blood pressure, and oxygenation status (**Table 1**). The initial respiratory rate was increased to a similar extent in both groups". (p. 368)
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	No – see above.
2.	Were clinicians aware of group allocation?	Yes. "We did not blind physicians to the group assignment, but we did blind them to the BNP results". (p. 367)
3.	Were outcome assessors aware of group allocation?	No, " Trained research assistants, who were not blinded to the group assignment, collected baseline demographic characteristics, admission rates, length of hospital stay, and clinical information from hospital records", but adjudicating physicians were not aware of BNP result. (p. 367)
4.	Was follow-up complete?	Yes. "We achieved complete follow-up on all study participants". (p. 367)

II.	What are the results (answer the questions posed below)?	

1.	How large was the treatment effect?	• 612 patients were randomly assigned, but 10 patients in BNP group had no BNP due to lab error. As per intention-to-treat protocol they were nonetheless analyzed in the BNP group.
		• AHF was the diagnosis in 44.8% (48.4% BNP vs. 41.2% controls) with good agreement among adjudicating physicians ($\kappa = 0.79$ for the BNP group and $\kappa = 0.82$ for controls).
		• There were <u>no differences or trends between BNP and controls for any of the outcomes</u>:
		  ○ admission rates (85% vs. 86.6%)
		  ○ ICU admissions (1% vs. 3%)
		  ○ length of stay (median 4.4 vs. 5.0 days)
		  ○ 30-day mortality (6.5% vs. 6.9%)
		  ○ re-admission rates (15% vs. 18%)
		• These <u>results were not changed when analyzed by hospital site and were unchanged after logistic regression analysis to adjust for differences in HTN history, CHF history or hospital site.</u>
		• Knowledge of BNP did not impact clinicians' use of bronchodilators, diuretics, vasodilators, steroids, ACE-inhibitors, or NIPPV.
		• Median BNP for no CHF 99 ng/L vs. CHF 830 ng/L.

2.	How precise was the estimate of the treatment effect?	No significant differences were noted between the two arms of the study, so the CI's widely overlap.

III.	How can I apply the results to patient care (answer the questions posed below)?	
1.	Were the study patients similar to my patient?	Probably -- ED patients with *severe* dyspnea of unclear etiology.
2.	Were all clinically important outcomes considered?	Yes.
3.	Are the likely treatment benefits worth the potential harm and costs?	No, not based upon their study.

Limitations

1) **Limited external validity to severe dyspnea patients.**

2) **No clear description of how researchers distinguish "severe dyspnea" from "non-severe dyspnea".**

3) **No assessment of clinician pre-test probability (but that was the point-to emphasize that this test should not be ordered indiscriminately).**

4) **Inadequate cut-points recommended, failing to use BNP as a continuous variable .**

Bottom Line

BNP should not be ordered indiscriminately on ED dyspnea patients since it does not alter length of stay, admission rates, or mortality in these populations. A more reasoned (and evidence-based) approach entails incorporation of BNP into those patients with indeterminate pre-test probability.