Critical Review Form
Diagnostic Test

Reed MJ, Newby DE, Coull AJ, Jacques KG, Prescott RJ, Gray AJ. Role of brain natriuretic peptide (BNP) in risk stratification of adult syncope. Emerg Med J.2007 Nov;24(11):769-73.

Objectives: **"to assess the value of a near-patient BNP test to predict medium term (3 month) serious outcome for syncope patients presenting to a UK ED, and to compare the performance of BMP with our existing departmental syncope guidelines..." (p. 769)**

Methods: **This prospective, observational study was conducted in the ED of the Royal Infirmary of Edinburgh between November 7, 2005 and February 7, 2006. Consecutive patients aged 16 years or older presenting for syncope were eligible for inclusion. Patients who had previously been recruited, who could not given consent, or who had a history of seizure with a prolonged post-ictal phase were excluded. Patients underwent a standardized assessment using multiple predetermined variables on history, physical examination, and electrocardiogram. All patients who were "medium or high risk" according to local guidelines had near-patient BNP testing, the results of which were available to the treating clinician. The investigators decided *a priori* to use cut-offs of 100 pg/ml and 1000 pg/ml as abnormal and "rule in" values for BNP.**

The primary endpoint was "serious outcome" at 3 months, defined as all-cause death, acute myocardial infarction, life-threatening arrhythmia, implantation of a pacemaker or defibrillator, pulmonary embolus, cerebrovascular accident, intracranial or subarachnoid hemorrhage, hemorrhage requiring a blood transfusion of at least 2 units during inpatient stay, or need for acute surgical procedure or endoscopic intervention "secondary to a suspected cause of syncope." Follow-up was performed by review of the hospital's electronic medical records, or by phone call in the case of 2 patients who were from outside the hospital's region.

A total of 99 patients were enrolled during the study period. Of these, 44 patients were admitted and 55 were discharged home from the ED. There were 11 patients (11.1%) with a serious outcome, of whom 5 died. All 11 had been admitted to the hospital. Of the 99 patients enrolled, 82 were "medium to high risk," and only 72 had BNP levels measured. Nine of these patients (12.5%) had a serious outcome.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did clinicians face diagnostic uncertainty?**	Yes. This study enrolled consecutive patients presenting to the ED with undifferentiated syncope whose etiology was not yet clear.

		The fact that near-patient BNP levels were only checked on patients at "medium or high risk" according to hospital guidelines could introduce spectrum bias when trying to generalize the results to all emergency department patients, which would affect the reported measures of diagnostic accuracy.
B.	**Was there a blind comparison with an independent gold standard applied similarly to all patients? (Confirmation Bias)**	No. There is no single gold standard test in the evaluation of syncope and no single test to determine if a patient's syncope was of cardiac etiology. The authors report patient outcomes rather than final diagnoses, and do not report what testing each patient underwent. It is quite likely that testing varied from patient to patient, with not all patients undergoing cardiac monitoring, cardiac ECHO, coronary artery cathterization, etc., which could potentially lead to differential verification bias and partial verification bias. In addition, clinicians were specifically NOT blinded to BNP results, and it is possible that these values affected the decision to perform additional testing (i.e. patients with elevated BNP levels would be more likely to undergo cardiac ECHO).
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard? (Ascertainment Bias)**	Uncertain. Again, there is no true gold standard test. It is unlikely that the results of the BNP influenced the decision to perform additional testing, but the authors do not specifically mention blinding of clinicians to BNP results.
II.	**What are the results?**	
A.	**What likelihood ratios were associated with the range of possible test results?**	Among 72 patients with a BNP level drawn, the test characteristics of BNP > 100 pg/mL are as follows: • Sensitivity 0.67 (95% CI 0.31-0.91) • Specificity 0.70 (95% CI 0.57-0.80) • PPV 0.24 (95% CI 0.10-0.46) • NPV 0.94 (95% CI 0.81-0.98) • LR+ 2.21 (95% CI 1.22-4.01) • LR- 0.48 (95% CI 0.19-1.22) The test characteristics of BNP > 1000 pg/mL are as follows: • Sensitivity 0.33 (95% CI 0.09-0.69) • Specificity 1.00 (95% CI 0.93-1.00) • PPV 1.00 (95% CI 0.31-1.00) • NPV 0.91 (95% CI 0.81-0.96) • LR+ ∞ (95% N/A)

		• LR- 0.51 (95% CI 0.23-1.12)
III.	**How can I apply the results to patient care?**	
A.	**Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?**	Yes. This is a standard blood test offered in most (if not all) hospitals and emergency departments across the United States. While different assays exist and different forms of natriuretic peptide are checked, it would be easy to adjust the cutoff for these various forms of the test.
B.	**Are the results applicable to the patients in my practice?**	Yes. This study enrolled a group of patients presenting to the ED with undifferentiated syncope. While they did use local guidelines to identify patients at "medium to high risk" and only evaluated BNP values in this subgroup, it would be possible to use similar guidelines to risk-stratify patients in our emergency department. Unfortunately, the majority of eligible patients were not recruited (for unclear reasons) which is likely to bias the findings.
C.	**Will the results change my management strategy?**	No. This was a fairly small, pilot study with only 72 patients having BNP levels checked. The resulting diagnostic test characteristics are associated with rather wide 95% confidence intervals. Additionally, the likelihood ratios associated with a BNP < 100 pg/mL are quite poor and would have very little effect on post-test probability.
D.	**Will patients be better off as a result of the test?**	No. This study did not assess the impact of BNP on disposition and testing among patients presenting to the ED with syncope. The test characteristics associated with BNP were rather poor in this study, with the exception of a BNP value > 1000 pg/mL, which demonstrated a high positive likelihood ratio, but would not have likely changed management in the small number of patients (n = 3) with a value this elevated.

Limitations:

1. **Despite this reportedly being a consecutive sample of patients, review of electronic records revealed that only 37.6% of eligible patients were enrolled.**

2. **Ten out of 82 (12.2%) medium to high-risk patients did not have a BNP level measured.**

3. **While the authors do not specify what testing was performed on patients in the study, it is unlikely that all patients underwent the same evaluation in this study, with a variety of tests (ECHOcardiography, telemetry monitoring, stress testing, etc.) performed only certain patients. Given this fact, some patients may have had dysrhythmias or structural lesions that were not identified (due to lack of testing), which would result in inaccurate measures of diagnostic accuracy (differential verification bias and partial verification bias).**

4. **Clinicians were not blinded to BNP results, which may have influenced disposition decisions and further testing, leading to ascertainment bias.**

5. **The resulting diagnostic test characteristics were rather poor; specifically, the likelihood ratios associated with a BNP > 100 pg/mL demonstrate that the test results would have very little impact on post-test probability.**

Bottom Line:

This small study conducted at a single ED in the UK evaluating the diagnostic value of near patient BNP testing in "moderate to high risk" patients presenting with syncope found rather poor diagnostic test characteristics using a cut-off of > 100 pg/mL (LR+ 2.21, LR- 0.48). Using a cutoff of > 1000 pg/mL, the LR- remained poor (0.51) while the LR+ was infinite. Unfortunately, such a result only applied to 3 patients (~4%) and would not likely have affected the management of this small subset of patients. This study was plagued by issues with patient selection (only 37% of eligible patients were enrolled) and is very small in size; in addition, it was not designed to look at the clinical impact of testing.