Critical Review Form
Therapy

Randomized trial of computerized quantitative pretest probability in low-risk chest pain patients: effect on safety and resource use. Ann Emerg Med. 2009 Jun;53(6):727-35.

Objectives: **To test the hypothesis "that the written output of this previously validated, computerized, Web-based, quantitative, pretest probability device would safely reduce resource use in very-low- risk ED patients with chest pain." (p. 728)**

Methods: **This was a prospective, randomized trial including patients enrolled between October 17, 2005 and September 18, 2007 at Carolina's Medical Center in Charlotte, NC. Patients were screened for enrollment by one of 3 trained research coordinators from 7 AM to 11 PM, 6-7 days a week; eligibility requirements included adults with a chief complaint of chest pain who had an ECG performed. Screening occurred immediately following performance of the ECG. Inclusion criteria included ordering of a troponin test, printed computer interpretation of the ECG devoid of the words "ischemia" or "infarction," and a clinician response of "no" to the question: "Do you have a definite plan to admit this patient?" Exclusion criteria included recent (<72 hours) cocaine use, coronary revascularization in the prior 30 days, pregnancy, reasonable suspicion of inability to contact the patient for follow-up, or referral to the ED by a physician or physician's representative.**

After inclusion and consent, the research coordinator compiled data needed to populate a computerized, pretest probability device. This pre-test probability was calculated by first obtaining 8 predictor variables:

1) **Age (divided into 4 subcategories)**
2) **Sex (dichotomous)**
3) **Race (dichotomized as black or other race)**
4) **History of coronary artery disease (dichotomous)**
5) **Chest wall tenderness that reproduces chest pain (dichotomous)**
6) **Diaphoresis (dichotomous)**
7) **ST depression > 0.5 mm in at least 2 leads (dichotomous)**
8) **T-wave inversion > 0.5 mm in at least 2 leads (dichotomous)**

A computer program would then extract from a large database of previously evaluated patients only those with the exact same profile of predictor variables. The percentage of these extracted patients who had acute coronary syndrome is then used as the pre-test probability.

The clinicians were asked, immediately after performing a history and physical exam, to estimate the percent probability that the patient would have an acute

coronary syndrome-defining event in the next 45 days, using implicit judgment alone. Every effort was made to obtain this probability estimate before knowledge of lab results.

The research coordinator then retrieved a sealed, opaque sequentially numbered envelope containing a computer-generated random assignment to the intervention or control group. In the intervention group, both clinicians and patients received a printout of the attribute-matching pre-test probability, displayed as both a numeric percentage and graphically using an icon plot. Those in the control group did not receive a printout, and the pre-test probability was not determined by attribute-matching until more than 45 days later. The decision to admit the patient and perform further testing was at the discretion of the patient and clinician, with no input from the research staff.

Disposition (hospital admission, initial admission to an ED-based chest pain evaluation unit, or discharge home) was then physically observed by the research coordinator. Follow-up occurred by telephone interview at 7 and 45 days by a researcher blinded to group assignment, using a standardized script. The 7-day phone interview included inquiring about return ED visits, subsequent hospital readmission, and satisfaction (using a 5-question satisfaction survey). The 45-day phone interview utilized a structures method to record results of all cardiac-related laboratory tests, imagining procedures, treatments or interventions, and all diagnoses.

The primary safety endpoint was the rate of delayed or missed acute coronary syndrome. There were 5 resource-oriented efficacy endpoints. One of these was the rate of hospital admission in patients with no significant cardiovascular diagnosis within 45 days, determined by two independent emergency physicians, blinded to group allocation. The second efficacy endpoint was the performance of imaging tests that imparted > 5 mSv of radiation (nuclear imaging, CT angiography, or conventional angiography). The final 3 efficacy endpoints were length of stay, patient satisfaction, and rate of readmission.

A total of 400 patients were enrolled, of whom 31 were excluded due to either cocaine use or elopement from medical care; 184 were randomized to the control group and 185 to the intervention group. Patients were similar with respect to age, sex, race, vital signs, BMI, symptoms, past medical history, and ECG findings. All patients had an initial troponin sent, which was normal (<0.05 ng/mL) in 368 and borderline (>0.04-<1.01 ng/mL) in 11 patients (4 in the control group, 7 in the intervention group). The mean (SD) pretest probability estimate from clinicians was 4% (5%), while the mean computerized estimate was 4 (6%).

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. Permuted block randomization was used with a sequence generated by a non-study associated researcher.
2.	Was randomization concealed (blinded)?	Yes. Opaque sequentially numbered envelopes containing the random group assignment were retrieved by a study coordinator following enrollment.
3.	Were patients analyzed in the groups to which they were randomized?	No. Following randomization, 31 patients were excluded. Of these, 18 (9 in each group) were excluded because of cocaine metabolites found in the urine or patient disclosure of recent cocaine use, and 13 (7 in the control group and 6 in the intervention group) eloped from medical care. The remainder of patients enrolled were analyzed by intention to treat analysis.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to age, sex, race, vital signs, BMI, symptoms, past medical history, and ECG findings (Table 1 in the article).
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?	Yes. Patients in the intervention group were made aware of the computer-derived pre-test probability, while those in the control group were not. Given the nature of the intervention, it would not have been possible to blind participants.
2.	Were clinicians aware of group allocation?	Yes. Clinicians in the intervention group were made aware of the computer-derived pre-test probability, while those in the control group were not. Given the nature of the intervention, it would not have been possible to blind the clinicians.
3.	Were outcome assessors aware of group allocation?	No. Follow-up occurred by telephone interview at 7 and 45 days by a researcher blinded to group assignment, using a standardized script. Two independent emergency physicians, blinded to group allocation, used the medical record to determine whether or not patients had a significant cardiovascular diagnosis within 45 days of the index visit.

4.	Was follow-up complete?	Likely yes. The authors do not specifically mention any patients being lost to follow-up, and it seems likely that all patients were contacted at 7 and 45 days for telephone interview, partly as one of the exclusion criteria was suspicion of inability to contact the patient on follow-up. Outside of phone interview and review of medical records from Carolina's Medical Center, no other form of follow-up was utilized. It is possible that patients presented to other hospitals where additional testing or interventions were performed, and that patients may have been unable to accurately report this information.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	There were 8 (2.1%) total patients with acute coronary syndrome diagnosed within 45 days, 3 (1.6%) in the control group and 5 (2.7%) in the intervention group. There was one missed/delayed diagnosis of acute coronary syndrome in the control group, and none in the intervention group. Hospital admission in patients with no significant cardiovascular diagnosis within 45 days was similar between the groups: 20 (11%) in the control group vs. 10 (5%) in the intervention group, for a difference of 6% (95% CI -0.2% to 11.0%; p = 0.059). The rate of thoracic imaging that imparted > 5 mSv and was negative was higher in the control group (n = 36, 19.5%) vs. the intervention group (n = 16, 8.7%), with a difference of 10.8% (95% CI 3.8% to 18%, p = 0.004). The rate of positive imaging was similar between the groups: 11 (6%) in the control group vs. 15 (8%) in the intervention group. Median length of stay was similar between the control and intervention groups: 11.4 hours vs. 9.2 hours (p = 0.36). Significantly more patients in the intervention group reported being "very satisfied" (n = 90, 49%) compared to the control group (n = 79, 38%) with a difference of 11% (95% CI 0.9% to 21%, p = 0.01). Patients in the intervention group were less likely than

		controls to be readmitted to the hospital within 7 days: 11% vs. 4%, for a difference of 7% (95% CI 2.5% to 13.2%, p = 0.001).
2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	Yes. These were patients presenting to a large, urban ED with the chief complaint of chest pain who had essentially normal or nondiagnostic ECGs. This was a typical urban US population with a significant proportion of African American patients, high mean BMI (30 in the control group and 31 in the intervention group), and a similar mix of cardiovascular risk factors.
2.	Were all clinically important outcomes considered?	Yes. The investigators assessed the tool's impact on hospital admission, length of stay, rates of negative imaging, rates of imaging associated with significant radiation exposure, and hospital readmission. While the study did not assess rates of invasive angiography, such rates would be expected to correlate with the rates of positive imaging, which were similar between the groups. The study also did not look at cost, but again this would be expected to correlate well with admission/readmission rates and length of stay.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. Attribute matching did not reduce the risk of the primary safety endpoint (missed acute coronary syndrome) and did not affect hospital admission rates or length of stay. While there was a reduction in thoracic imaging that imparted > 5 mSv of radiation and was negative, this reduction was NOT the result of reduced provocative testing in the intervention group. There were 129 total provocative tests ordered in the intervention group vs. 124 in the control group. While there was reduced ordering of tests that imparted radiation in the intervention group (31 vs. 47) it is unclear why the intervention would affect the ordering of these tests without impacting overall provocative test ordering.

Limitations:

1. **Exclusion of patients the investigators felt they could not obtain follow-up from limits external validity in a population of lower socioeconomic status.**

2. **Follow-up was limited to chart review of the Carolinas Medical Center record and telephone follow-up. It is possible that acute coronary events occurred at outside institutions that were not accurately reported.**

3. **Multiple efficacy endpoints were employed, increasing the risk of a Type I error.**

4. **The attribute matching method used in this study is a proprietary entity and is not free to use.**

Bottom Line:

The use of attribute matching did not affect the rate of missed acute coronary syndrome, but also did not reduce the overall rates of provocative test ordering. While the tool did reduce the rate of negative testing associated with significant radiation exposure, this effect was the result of reduced radiologic testing and increased non-radiologic testing in the intervention group; it is unclear why attribute matching would cause such a shift in the type of tests ordered by the clinician. Further benefit should be shown prior to widespread implementation of the tool in clinical practice, especially given its proprietary nature.