

THERAPY UNIT

Objectives:

The objective of this unit is to determine the validity (risk of bias) of a randomized trial and determine what were the results and how they might apply to a clinical scenario.

Assignment:

Review the clinical scenario, read the attached articles, critically appraise the trial using the attached worksheet, and come prepared to discuss in the context of the scenario.

Clinical Scenario:

You are an attending physician on a general medicine teaching ward. A 65-year-old diabetic male with previously stable coronary artery disease is on your ward team with a presentation of exertional chest tightness and dyspnea and has ruled out for acute myocardial infarction. Given his known coronary disease and change in symptom pattern, he underwent a coronary angiography to assess for progression of his coronary disease. It is the intern's first day on the team and she is getting familiar with her new patients. She suggests that this diabetic patient is at increased risk of contrast-induced nephropathy and asks why the patient did not receive Acetylcysteine to prevent kidney injury. She recalls reviewing an RCT when she was a medical student that suggested benefit. The resident states that a newer RCT did not show benefit, thus the patient did not receive acetylcysteine. The intern asks, how do you decide what to do if there is conflicting evidence? You suggest it would be a useful exercise to look at these competing articles and discuss. And, being familiar with this paper and the evidence, you advise that the quickest way to begin this search is via ACP Journal Club (ACP-JC).

Sitting at the computer in the team room, with your help the medical student identifies 2 ACP-JC summaries that have different conclusions. The team agrees that this will be tonight's reading for discussion tomorrow on rounds.

Enclosed Materials:

1. ACT Investigators. Acetylcysteine for prevention of renal outcomes in patients undergoing coronary and peripheral vascular angiography: main results from the randomized Acetylcysteine for Contrast-induced nephropathy Trial (ACT). *Circulation*. 2011;124:1250-9.
2. James M, Manns B. N-acetylcysteine prevented contrast-medium-induced nephropathy in primary angioplasty. *ACP J Club*. 2006 Nov-Dec;145(3):63.
3. Saklayen MG. Acetylcysteine did not reduce kidney injury in at-risk patients having vascular angiography. *Ann Intern Med* 2012 Jan 17;156(2):JC1-8.
4. Walsh M, Perkovic V, Manns B, Srinathan S, Meade M, Devereaux PJ, and Guyatt G. Therapy (Randomized trials). In Guyatt G, Meade MO, Cook DJ, Rennie D. *Users' Guides to the Medical Literature: A Manual for Evidence-based Clinical Practice*. 3rd ed. New York, NY: McGraw-Hill; 2014.

5. Worksheet for the evaluation of an article on Therapy.

Activities:

- Read the ACT trial (ref #1) and the relevant chapter of the Users' guide.
 - Complete the worksheet for the ACT trial and discuss the issues that threaten the validity of the results. What were the results?
 - How might these results apply to in the clinical scenario provided?
- ACP–JC comparison: review the ACP-JC summary by James (ref #2).
 - Calculate Number Needed to Treat for the outcomes listed in the ACP-JC table
 - Compare the trial described and its results to the ACT trial and identify reasons for the conflicting findings. Note that there is also an ACP JC for the ACT trial (ref #3) which can be used to facilitate discussion.

Notes: Whether you are using this package to teach or to learn how to practice EBM yourself, there are multiple take home lessons in this package.

- This scenario comes from a real life example in which learners on a ward team identified different practices standards (using Acetylcysteine prior to catheterization versus not) and each identified RCT evidence to support their view. The presence of an ACP-JC summary for each of the papers (references #1 and #3) allowed very rapid access to evidence to discuss this comparison. At the same time, the ACT trial is a well done trial that is clearly reported. Reading the whole article allows more in depth appraisal.
- Both for learners and teachers, the materials in this package can be used flexibly to focus on a number of curricular goals, including:
 - ACP Journal club: how to search ACP-JC and its strengths and weaknesses.
 - Therapy Math: you can only teach Number Needed to Treat in an article which shows a difference in treatment arms (the ACT trial does not), thus you can use the ACP Journal Club table to discuss risk ratios, risk differences, and NNT.
 - Evolution of evidence on a particular question: this scenario allows discussion of how we need to remain cautious about positive results from initial small trials on a topic, and how a well done large RCT can change the practice paradigm.
 - The relationship between individual trials (both large and small) and Systematic Review / Meta-analysis: The ACT authors perform and report a systematic review in the paper that allows you to put the ACT trial into context.