THERAPY UNIT

Objectives:

The objective of this unit is to determine the risk of bias of the results of a randomized controlled trial, determine what the results were, and how the results 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 in a general medicine outpatient clinic supervising a medical resident. The resident just reviewed a 65 year-old male with type 2 diabetes and a history of stable angina with an angiogram that demonstrated no critical lesions last year. His blood glucose is reasonably well controlled with metformin, and a dipeptidyl peptidase-4 inhibitor with a hemoglobin A1C of 7.0% and his blood pressure is controlled on an angiotensin converting enzyme inhibitor and thiazide diuretic with a reading in the office today of 125/80 mmHg. His kidney function is normal (estimated GFR >60 ml/min). He is receiving cholesterol lowering medication.

The patient is feeling well but the resident notes that his 10-year risk for cardiovascular disease is >30% and wonders if any more can be done to reduce his risk. You suggest that perhaps a quick literature search for treatments to reduce cardiovascular events in patients with type 2 diabetes is in order and that the ACP Journal Club would be a suitable place to start.

Searching ACP Journal Club for “type 2 diabetes cardiovascular” brings up a long list of article but when sorted by date your attention is drawn to a recent review titled, “In patients with type 2 diabetes and CV disease, empagliflozin reduced a composite of CV events at 3.1 years.”

Enclosed Materials:

Zinman et al for the EMPA-REG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes and mortality in type 2 diabetes. New England J Med. 2015: 373 (22): 2117-2128.

Shekelle, P. In patients with type 2 diabetes and CV disease, empagliflozin reduced a composite of CV events at 3.1 years. Ann Int Med. 2016: 164 (2): JC2.

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. 3nd ed. New York, NY: McGraw-Hill; 2014.

Worksheet for the evaluation of an article on Therapy.

Activities:

- Read the EMPA-REG trial (ref #1) and the relevant chapter of the Users' guide.
    - Complete the worksheet for the EMPA-REG trial and discuss the issues that increase the risk of bias. What were the results?
    - How might these results apply to the clinical scenario provided?
- ACP-JC
    - The ACP-JC reviewer cited several reasons that weakened his belief in the results. Are they valid? How would you expect each potential issue to affect the RRR and NNT for the primary outcome and the safety outcome?
    - Does the patient described in this scenario meet the description of patients enrolled in the EMPA-REG trial? How might a deviation from the EMPA-REG eligibility affect the applicability of the results to this patient?

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

- New treatments with both a patient-important and statistically significant benefit are not common. Applying the evidence generated from these trials requires readers and reviewers to assess both the risk of bias of the results as well as the generalizability to patients in their practice.
    - Risk of bias is established by assessing the methods of the trial to ensure they are robust
    - Generalizability / external validity requires the reader to estimate whether the results apply to the patient(s) they are treating and in particular, whether differences between their patients or methods of using the treatment will change the expected benefits and risks of the treatment.
    - New evidence is typically generated quickly for new treatments and the consistency of effects (i.e., the reproducibility of the treatment effect) is powerful evidence. This requires clinicians to update their knowledge regularly.