Example of How to Approach an Article

- Cannon, Christopher P. et. al. "Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes." *The New England Journal of Medicine* 372.25 (2015): 2387-397.

1. What is the study question?

Does further lowering of LDL cholesterol with ezetimibe reduce CDV complications in ACS patients?

2. What study design is used to answer the question?

Randomized, double-blinded , placebo controlled trial

3. What is the exposure/intervention

Addition of ezetimibe to simvastatin in treating ACS.

4. What is the outcome and how is it defined or measured?

Outcome measured by a combined endpoint of CDV death, nonfatal MI, unstable angina, coronary revascularization, or nonfatal stroke.

5. How were the participants selected or recruited for the study?

Multiple centers over several continents. Not volunteers.

6. Who was included in the study?

Age >/= 50. ACS defined as acute MI with or without ST elevation. Also high risk unstable angina. LDL must be 50-125 if statin naive or 50-100 if on statin.

7. Who was excluded from the study?

Planned CABG, creatinine clearance < 30, active liver disease, use of statins stronger than 40 mg simvastatin.

8. If randomization occurred, at what point did it occur?

Within 10 days of the event.

9. What do the authors say about the power/sample size of the study? Is the power adequate to answer the study question?

Needed 5250- events to detect a 9.4% lower relative risk (90% power). Achieved the event numbers at 5314.

10. Are the study groups' characteristics comparable at baseline?

Yes

11. What statistical tests/methods are used in the analysis of the results?

Intention to treat was used. Statistical analysis was chosen appropriately.

12. What are the results of the study?

The primary endpoint was achieved with a 32.7% event rate in the Vytorin group and a 34.7% event rate in the simvastatin group. The absolute risk reduction was 2%. The risk reduction appeared to correlate perfectly with the average drop in LDL from 69.9 to 53.2 at one year.

13. Are the results statistically significant?

Yes P-value was 0.016. 95% confidence interval was 0.89-99 which means you can be 95% sure that the real risk reduction is within this narrow range.

14. Are the results clinically significant?

Yes. A non-statin agent for the first time has improved CDV outcomes. It is highly likely this has occurred because of the LDL lowering.

15. What are the biases/limitations of the study that could cause you to question the author's conclusions?

There was a 42% dropout during the seven years of follow-up, but this is to be expected. There were no cointerventions, early stoppage of the study, differences in the two patient groups, or placebo effects.

16. How does this fit into our current knowledge?

In secondary prevention, the lower the cholesterol the better the outcome.

17. Discuss internal and external validity.

a. Did the authors rule out chance, bias, and confounding factors? Very well.

b. Will these results change your practice? Perhaps not since per guidelines we currently use a high dose "strong" statin in ACS. However, it does raise the question that perhaps measurement of LDL cholesterol may be important in both primary and secondary prevention and that lowering LDL is critical.