Homework 4 (due Mon, Feb 3):

Read the following article:

> Anderson GL, et al. Monitoring and reporting of the Women's Health Initiative randomized hormone therapy trials. Clinical Trials 2007; 4: 207–217.

Answer these questions with regard to the "E+P Trial."

1. Who provided input into the monitoring plan? What process was used to achieve consensus?

2. A substantial difference in lag-time to full effect of the hormones between the primary outcome of CHD (three years) and the primary safety outcome of breast cancer (10 years) was anticipated.

   2.1 How was the test statistic modified to achieve comparability in the face of different anticipated follow-up times?
   2.2 How frequently were these two outcomes monitored and how many analyses were planned if the trial did not stop early?
   2.3 After how many interim analyses was the trial stopped?
   2.4 Were the intervention effects summarized using relative statistics or absolute statistics or both? What was the rationale behind this choice?
   2.5 For these outcomes, were boundaries defined to evaluate both benefit and harm? If so, were they symmetric or asymmetric? How was this represented in the 95% CIs for CHD at the end of the trial?
   2.6 If the boundary for CHD benefit was crossed early but the breast cancer comparison strongly suggested harm, what action did the monitoring plan advise?
   2.7 What was the estimated treatment effect for the CHD outcome? How was the 95% CI interpreted?
   2.8 What were the clinical and statistical bases for stopping the trial? Why was the decision so controversial?

3. Comment on the role of the Global index.

Required Reading:

> Home PD, Pocock SJ, et al. RECORD Study Group. Rosiglitazone evaluated for cardiovascular outcomes--an interim analysis. N Engl J Med. 2007; 357:28-38.