STAT 592 SAMPLE FIRST MIDTERM EXAM

Problem 1. (50pts) In this problem you are asked to read carefully the passage given below and to answer the questions that follow.

****

"Radiotherapy Can Prevent Spread of Small-Cell Lung Cancer to the Brain"

Source
American Society of Clinical Oncology (ASCO) annual meeting, Chicago, June 2, 2007.

Summary
Radiation therapy to the head, given to patients who had responded to chemotherapy for advanced small-cell lung cancer, reduced by about two-thirds the risk that patients' tumors would spread to the brain, thus extending patients' lives. These findings are likely to change the standard of care for this group of patients.

Background
Lung cancer is the leading cause of cancer death among both men and women. Small-cell lung cancer (SCLC) accounts for about 15 percent of lung cancer cases in the United States. It tends to grow quickly and to spread widely through the body. At diagnosis, about two-thirds of patients with SCLC have disease that has spread beyond the chest cavity.

It is common for SCLC to spread, or metastasize, to the brain. In about 20 percent of patients, the disease has already spread to the brain at diagnosis; after two years, more than 50 percent of patients have brain metastases. With currently available treatments, patients with brain metastases of SCLC survive for a median of six months to a year.

In studies published in the early 1990s, radiation therapy to the head (known as prophylactic cranial irradiation, or PCI) reduced the risk of tumors spreading to the brain and improved survival among patients with early-stage SCLC whose tumors had disappeared after chemotherapy. PCI had not been tested, however, in patients with advanced SCLC.

The Study
A total of 286 patients with SCLC took part in the study, which began in May 2001. All of them had already been treated with chemotherapy. Although their tumors had shrunk in response to the chemotherapy, 75 percent still had tumors in their lungs and in 70 percent the disease had spread to other organs, although not yet to the brain.

The patients were assigned at random to receive either PCI or no additional treatment (the control group). The two groups (each with 143 patients) were well balanced regarding baseline characteristics. Those assigned to PCI were treated with doses of radiation comparable to those used to treat brain metastases after they develop.

The study's principal investigator was Ben Slotman, M.D., Ph.D., of VU University Medical Center in Amsterdam, the Netherlands.

Results
After one year, 14.6 percent of the patients treated with PCI had developed symptomatic brain metastases compared with 40.4 percent of the patients in the control group. Moreover, 27.1 percent of patients in the PCI group were alive after one year, compared with 13.3 percent of those in the control group.

PCI caused some side effects, including headache, nausea, vomiting, and fatigue, but for the most part these adverse effects were mild.

****

Answer the following questions:

(a)(5pts) Is the described clinical trial a phase III trial? Why?

(b) (5pts) How many groups were tested in the trial? Describe them.

(c) (5pts) Were the data monitored sequentially? Why or why not?

(d) (5pts) What group sample size was used in the trial?

(e) (5pts) What were the endpoints of the trial? List them.

(f) (5pts) Describe the innovative treatment under investigation.

(g) (5pts) Was the PI of the trial a medical doctor, as it is supposed to be?

(h)(5pts) Even though it is not stated explicitly in the text, but what do you think, the trial was held in the United States or Europe? Give your argument.

(i) (5pts) Write down the conclusion regarding the efficacy of the new treatment.

(j) (5pts) Could it be a double-blinded trial? Explain.

Problem 2. (25pts) Psoriasis is a common skin condition that causes skin redness and irritation. Most persons with psoriasis have thick, red skin with flaky, silver-white patches called scales. Persons with psoriasis may receive medicines to suppress the body's immune response. The best drug known on the market so far is Methotrexate. Dermatologists are interested in testing a new drug Etanercept. They suspect that patients with mild psoriasis would respond to the new drug differently than subjects with severe psoriasis.

(a)(10pts) Suggest a prognostic factor that could be used in the proposed trial. How many strata will there be in the randomization procedure?

(b)(5pts) How many groups should be in this trial?

(c) (10pts) Carry out an actual randomization procedure based on your results for parts (a) and (b). Use blocks on size four. As your answer, give first three blocks in each strata. The table of random digits is here to assist you:

19223 95034 05756 28713 96409 12531 42544 82853
73676 47150 99400 01927 27754 42648 82425 36290
45467 71709 77558 00095 32863 29485 82226 90056
52711 38889 93074 60227 40011 85848 48767 52573
95592 94007 69971 91481 60779 53791 17297 59335
68417 35013 15529 72765 85089 57067 50211 47487
82739 57890 20807 47511 81676 55300 94383 14893
60940 72024 17868 24943 61790 90656 87964 18883

Problem 3. (25pts) Researchers propose a clinical trial to investigate the metabolic changes that occur after state-of-the-art, less invasive metabolic surgery called sleeve gastrectomy. The primary endpoint will be the rate of developing gastric ulcers, which is considered a very adverse event. It is calculated that 360 patient-years would be required to complete the trial. Researchers would like to use the Bayesian approach, hoping to minimize the resources for the trial. However, they are unsure that the surgery will actually reduce the rate of the complication.

(a)(5pts) What kind of prior density of the rate is appropriate in this case? Enthusiastic or skeptical? Explain.

(b)(10pts) Which distribution should be used to model the number of occurrences? Which conjugate family of distributions should be used as the prior?

(c)(10pts) The table below summarizes the results of the Bayesian interim analysis. Explain in simple words what this table says.

Number of patient-years, t	Number of occurrences, n	$P(H_1)$	Number of patient-years, t	Number of occurrences, n	$P(H_1)$
120	1	0.9789	120	7	0.0681
	2	0.9499		8	0.0492
240	4	0.9533	240	11	0.0551
	5	0.9307		12	0.0377