PubH 7420 Homework 1 Answer Key
Due: Thursday, February 1
50 points

1) The Center for the Evaluation of Nicotine in Cigarettes (CENIC) project 1, study 2 ,was a randomized trial to understand the impact of cigarette nicotine content on tobacco use behavior with and without nicotine replacement therapy (NRT). Subjects were randomized in a 2x2 factorial design to receive one of normal nicotine content (NNC) or very low nicotine content (VLNC) cigarettes and either nicotine patch or no patch. The four treatment groups would then be: NNC + patch, NNC + no patch, VLNC + patch, and VLNC + no patch. This problem will ask you to develop randomization schedules using the following sequence of random numbers:

   5, 3, 7, 2, 3, 2, 2, 3, 4, 6, 3, 2, 8, 7, 5, 1, 4, 2, 4, 4

   a) Assume that participants will be randomized to the four groups in a 1:1:1:1 ratio. Briefly describe how you would use the sequence of random numbers provided above to develop a randomization schedule assuming simple randomization and provide the randomization schedule for the first 10 subjects. (5 points)

   b) Instead, assume that the trial was not designed as a factorial design, but as a three group design with the groups being NNC + no patch (control), VLNC + no patch, and VLNC + patch in a 1:1.5:1.5 ratio, which will randomize more participants to the two VLNC groups. Briefly describe how you would use the sequence of random numbers provided above to develop a randomization schedule assuming simple randomization and provide the randomization schedule for the first 10 subjects. (5 points)

   c) Finally, consider the three-group design described in part c, but instead randomize participants to NNC + no patch (control), VLNC + no patch, and VLNC + patch in 1:1:1 ratio with ***permuted block*** randomization. Provide two possible block sizes. In addition, briefly describe how you would use the sequence of random numbers provided above to develop a randomization schedule assuming permuted block randomization and provide the randomization schedule for at least the first 10 subjects assuming the smallest possible block size. (10 points)

   d) Briefly describe an algorithm for completing permuted block randomization with random block sizes. (5 points)

2) In cluster randomized trials, groups or clusters of individuals (e.g., schools, medical practices, communities), rather than the individuals themselves are randomized. A cluster randomized trial was conducted to evaluate treatments for back pain in primary care, and 26 practices were randomized to use one of two different back pain interventions. The allocation of practices to the interventions was 1:1; 13 practices were assigned to use a novel back pain intervention for patients with low back pain and 13 were assigned to use what was considered a standard intervention. In the methods section of the report describing their trial, the investigators state "Following practice randomization,…, practice nurses prospectively identified patients consulting with their general practitioner with low back pain and invited them to take part in the trial." Even though the practices were similar in size, the number of patients treated in each cluster differed substantially (165 vs 66 patients). Considering how randomization of the 26 practices was implemented and when eligible patients were identified, cite a potential bias. (5 points)

3) CENIC, project 2 was a randomized trial to evaluate the impact of immediate vs. gradual reduction in the nicotine content of cigarettes. Subjects will be randomized to one of three groups: immediate reduction (IR), gradual reduction (GR) and a normal nicotine control group (NNC).

   a) Assume that 750 participants were randomized to IR:GR:NNC in a 2:2:1 ratio. How many patients do the investigators plan to randomize in each of the three treatment groups – IR, GR, and NNC? (Give the planned sample size for each group.) (5 points)

   b) Now, assume that the investigators plan to use a stratified design with strata corresponding to the following three factors: age (< 30 vs. 30+), menthol status (menthol vs. non-menthol), and site (8 sites). If a separate randomization schedule is prepared for each stratum, how many schedules will have to be prepared for this study? (5 points)

   c) If a single block size is to be used for each schedule, what is the smallest block size that can be used? (5 points)

   d) What is the primary disadvantage to implementing stratified randomization? How might the investigators achieve the same benefits without stratified randomization? (5 points)