STAT3004: Basic Methods in Biomedical Statistics
Assignment 4
Due date: 2 December 2020, 5pm

The following problems are based on questions that can be found in *Fundamentals of Biostatistics, 8th Ed.* by Bernard Rosner, unless stated otherwise.

1. **Problems 13.19-13.20 in Rosner**
   A study was performed assessing the association between lifetime analgesic intake and change in estimated glomerular filtration rate (GFR) as measured from two blood samples obtained in 1989 and 2000 among 1645 participants in the Nurses' Health Study. GFR is a commonly used index of kidney function with lower levels indicating worse kidney function. The data were presented in Table 1 relating lifetime intake of acetaminophen (the active ingredient in Tylenol) in grams and a decline of more than 30% in estimated GFR, which is considered a clinically meaningful decline in kidney function (denoted as a case).

Group	Acetaminophen (g) (lifetime intake)	Median Intake (unit = 100g)	# of Subjects	# of Cases
A	< 100	0.5	819	66
B	$100 - 499$	3.0	186	19
C	$500 - 2999$	17.5	288	34
D	≥ 3000	40.0	352	52
	Total		1645	171

Table 1: Relationship between change in GFR vs. lifetime acetaminophen intake

   (a) What is the estimated odds ratio for being a case comparing Group D to Group A?

   (b) Provide a 95% CI for the OR computed in (a).

2. **Problems 13.80-13.84 in Rosner**
   A study of raloxifene and incidence of fractures was conducted among women with evidence of osteoporosis. The women were initially divided into two groups: those with and those without pre-existing fractures. The women were then randomized to raloxifene or placebo and followed for 3 years to determine the incidence of new vertebral fractures, with the results shown in Table 2.

   (a) Among those with no pre-existing fractures, test whether raloxifene affects the incidence of new fractures.

   (b) Among those with no pre-existing fractures, compute the relative risk of new fractures among those randomized to raloxifene vs. placebo, along with its associated 95% CI..

No pre-existing fractures			
	New fractures	No new fractures	Total
Raloxifene	34	1466	1500
Placebo	68	1432	1500
Total	102	2898	3000

Pre-existing fractures			
	New fractures	No new fractures	Total
Raloxifene	103	597	700
Placebo	170	630	800
Total	273	1227	1500

Table 2: Comparison of fracture incidence between raloxifene- and placebo-treated women

(c) Test the association of study agent with new fractures combining both groups of those with and without preexisting fractures.

(d) Combining both groups, compute the standardized RR for raloxifene vs. placebo and new fractures.
Hint: Use the total population as the standard.

(e) Is pre-existing fracture a confounder in these data?

3. **Problems 14.53-14.56 in Rosner** A study was performed to compare breast cancer incidence between postmenopausal women who used PMH vs. women who did not. A group of 200 women who were current PMH users and 1000 women who were never PMH users in 1990 in the NHS were identified. All women were postmenopausal and free of cancer as of 1990. The 1200 women were ascertained for incident breast cancer by mail questionnaire every 2 years up to the year 2000. However, not all women had complete follow-up. For simplicity, we will assume that women can only fail every 2 years, i.e., in 1992, 1994,..., 2000. The results are given in Table 3. Failed means developed breast cancer

(a) What does a censored observation in 1992 mean in the context of these data?

(b) Estimate the 10-year incidence of breast cancer in each group.

(c) What test can be used to compare the incidence of breast cancer between the 2 groups, taking into account the time when breast cancer develops and the length of follow-up of each subject?

(d) Implement the test in (c), and report a p-value (two-tailed).

Current PMH users			
	Number of women		
Year	In risk set	Failed	Censored
1990	200	0	1
1992	199	3	2
1994	194	2	2
1996	190	4	1
1998	185	2	50
2000	133	2	131

Never PMH users			
	Number of women		
Year	In risk set	Failed	Censored
1990	1000	0	12
1992	988	3	10
1994	975	9	22
1996	944	7	23
1998	914	5	193
2000	716	9	107

Table 3: Relationship between PMH use and breast cancer incidence