Statistics 571 Midterm 1

Hanlon/Larget, Fall 2010

Name: _____

Instructions:

1. You may use a calculator, but you may not use a laptop computer or phone.
2. The examination is open book, open notes, but not open neighbor. You may use any course handouts including lecture notes and homework solutions.
3. Do all of your work in the space provided. Use the backs of pages if necessary, indicating clearly that you have done so (so the grader can easily find your complete answer).

For Graders' Use:

Question	Possible Score	Score
1	20	
2	20	
3	15	
4	25	
5	20	
Total	100	

1. **(20 points)** Consider a discrete random variable X with $\mathsf{E}(X) = 1.9$. The partial probability distribution of X is given by the following table.

k	-5	-1	?	4	7
$\mathsf{P}(X = k)$	0.15	0.25	0.2	?	0.3

   (a) Fill in the missing values.
   (b) Compute $\mathsf{E}(3X + 7)$.
   (c) Compute $\mathsf{Var}(X)$.
   (d) Compute $\mathsf{Var}(3X + 7)$.

2. **(20 points)** In a certain population of fish, the lengths of the individual fish follow a normal distribution with mean 54.0 mm and standard deviation 4.5 mm. Let $\bar{X}$ represent the mean length of $n = 4$ fish randomly chosen from the population.

   (a) What proportion of individual fish in the population are longer than 60 mm?

   (b) What is the sampling distribution of $\bar{X}$?

   (c) Compute $\mathsf{P}(51 < \bar{X} < 60)$.

   (d) Find the 0.90 quantile of the sampling distribution of $\bar{X}$.

   (e) Find the cutoff values for the middle 80% of the sampling distribution of $\bar{X}$.

   (f) If the underlying population is not normal, but instead is bimodal with a larger peak of lengths centered near 50 mm and a smaller peak of lengths centered near 70 mm, are the above calculations in parts (a), (c), (d), and (e) still justified? Briefly explain. *(One sentence with the key idea is sufficient.)*

3. **(15 points)** The prevalence of color blindness in men is 2 in 100; for woman it is 1 out of 1000. The population consists of 53% men. A person is chosen at random from the population.

   (a) What is the probability that the selected person is color blind?

   (b) What is the probability that the selected person is a color blind woman?

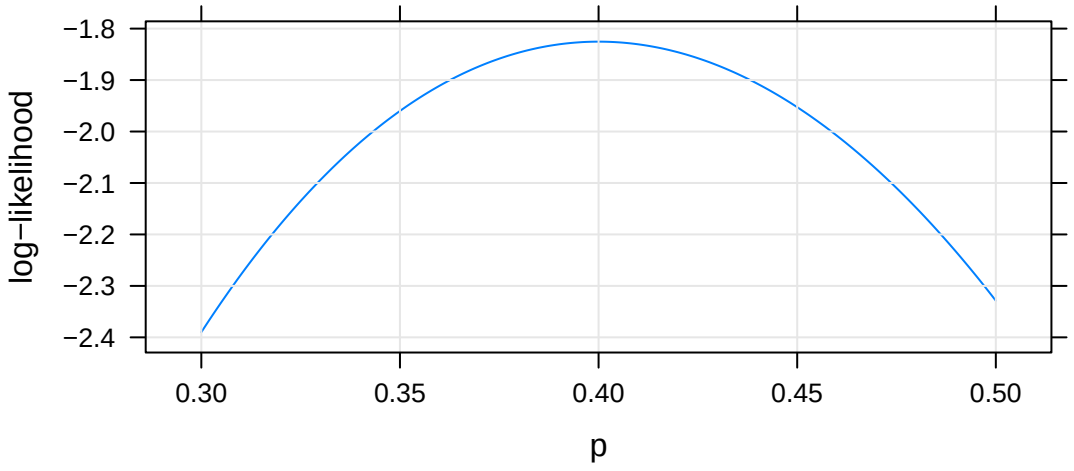
   (c) Given that the selected person is color blind, what is the probability that he is a man?

4. **(25 points)** A plant pathologist hypothesized that if a cotton plant were infested by spider mites, this would spur a number of protective responses that could provide protection against subsequent pathogens, and in particular, a fungus that causes wilt disease. The experiment included 50 individually potted cotton plants. In the first stage of the experiment, 25 of the cotton plants were given an infestation of spider mites and the other 25 plants were infestation-free controls. After two weeks, all spider mites were removed from the treatment group plants. In the second stage of the experiment, all 50 plants were inoculated with the fungus, and after some time, were observed to see if they showed symptoms of wilt disease. The following table summarizes the results.

	Mites	No mites	Total
Wilt disease	10	20	30
No wilt disease	15	5	20
Total	25	25	50

(a) Consider only the 25 plants in the spider mite treatment group. Find a 95% confidence interval for the probability that such a plant in this experimental situation would develop wilt disease. Interpret the interval in the context of the problem.

(b) The following graph displays the log-likelihood of p for a binomial sample where $n = 25$. Use information from the graph to approximate (to two decimal places): (1) the maximum likelihood estimate $\hat{p}$; and (2) the log-likelihood when p is evaluated at its maximum likelihood estimate.



(c) Conduct a G-test to test for independence between treatment (mites or no mites) and the development of wilt disease. State the value of the test statistic and indicate its approximate sampling distribution including degrees of freedom. You need not calculate a p-value, but indicate it size relative to the benchmarks in the following table of quantiles from the χ^2 distribution or from Table A in the textbook. (Quantiles refer to areas to the left, Table A reports areas to the right.) *(For example, say $p < 0.001$ or $0.05 < p < 0.1$.)* Interpret the results in the context of the problem.

	Quantiles of χ^2 Distributions					
df	0.9	0.95	0.975	0.99	0.995	0.999
1	2.71	3.84	5.02	6.63	7.88	10.83
2	4.61	5.99	7.38	9.21	10.60	13.82
3	6.25	7.81	9.35	11.34	12.84	16.27
4	7.78	9.49	11.14	13.28	14.86	18.47

The first number in the table can be found in R by calculating `qchisq(0.9,1)`, for example.

5. **(20 points)** The October 14, 2010 issue of *The New England Journal of Medicine* includes an article titled "Tanezumab for the Treatment of Pain from Osteoarthritis of the Knee". Text and tables from the articles follow the questions. Note that counts of subjects in each treatment group are different in the two tables due to drop out from the study. You are asked to respond to questions about the sampling of individuals for the study and to categorize some of the variables measured. You do not need to read the excerpt for more detail.

   (a) Write one sentence to describe the population about whom the authors are making inferences. *(Use space on the back of this page.)*

   (b) Are the subjects in the study a random sample from the population of interest? Briefly explain. *(One sentence with the key idea suffices. Use space on the back of this page.)*

   (c) Classify each variable in the table below by circling the appropriate values.

Variable	**Explanatory** or **Response**	**Categorical** or **Quantitative**	**Experimental** or **Observational**
Treatment Group	Explan. or Resp.	Cat. or Quant.	Exper. or Obs.
Age	Explan. or Resp.	Cat. or Quant.	Exper. or Obs.
Dose of Tanezumab	Explan. or Resp.	Cat. or Quant.	Exper. or Obs.
Change in WOMAC pain subscore	Explan. or Resp.	Cat. or Quant.	Exper. or Obs.
Response to therapy	Explan. or Resp.	Cat. or Quant.	Exper. or Obs.

Background Increased expression of nerve growth factor in injured or inflamed tissue is associated with increased pain. This proof-of-concept study was designed to investigate the safety and analgesic efficacy of tanezumab, a humanized monoclonal antibody that binds and inhibits nerve growth factor.

Methods We randomly assigned 450 patients with osteoarthritis of the knee to receive tanezumab (administered at a dose of 10, 25, 50, 100, or 200 μg per kilogram of body weight) or placebo on days 1 and 56. The primary efficacy measures were knee pain while walking and the patient's global assessment of response to therapy. We also assessed pain, stiffness, and physical function using the Western Ontario and Mc- Master Universities Osteoarthritis Index (WOMAC); ....

Conclusions In this proof-of-concept study, treatment with tanezumab was associated with a reduction in joint pain and improvement in function, with mild and moderate adverse events, among patients with moderate-to-severe osteoarthritis of the knee.

Study Population We enrolled patients, 40 to 75 years of age, who had osteoarthritis of the knee ... (Kellgren Lawrence grade 2 or higher, on a scale of 0 to 4, with higher numbers indicating more severe signs of osteoarthritis). [There were eligibility conditions including willingness to take certain medications, responses to other medications, and the severity of the pain.] ... At the time of randomization, patients had to have pain while walking on a flat surface (the walking-pain measure of the Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC]) that they rated between 50 and 90 on a visual-analogue scale that ranged from 0 to 100, with 100 indicating maximal pain. [There were other various exclusion criteria including pregnancy.] All participants provided written informed consent.

Study Design and Oversight Patients were recruited between March 30, 2006, and May 3, 2007, at 46 study centers in the United States and were screened within 30 days before randomization. [Treatment was delayed until other medications were out of the system.] Patients rated their knee pain and recorded the score in an electronic diary every day for 3 days before randomization to establish their baseline pain score. Eligible patients were randomly assigned on day 1 . . . to placebo or to tanezumab at a dose of 10, 25, 50, 100, or 200 μg per kilogram of body weight, such that there were equal numbers in each study group.

Table 1. Baseline Characteristics of the Study Patients.*

Characteristic	Placebo (N=74)	Tanezumab, 10 μg/kg (N=74)	Tanezumab, 25 μg/kg (N=74)	Tanezumab, 50 μg/kg (N=74)	Tanezumab, 100 μg/kg (N=74)	Tanezumab, 200 μg/kg (N=74)
Age — yr	58.1±7.7	58.3±8.3	59.9±8.1	60.4±7.7	57.1±8.2	58.4±7.6
Female sex — no. (%)	42 (57)	49 (66)	50 (68)	37 (50)	44 (59)	40 (54)
White race — no. (%)†	66 (89)	62 (84)	67 (91)	66 (89)	67 (91)	64 (86)
Kellgren–Lawrence grade — no./total no. (%)‡						
2	18/73 (25)	21/73 (29)	23/74 (31)	29/74 (39)	22/74 (30)	19/73 (26)
3 or 4	55/73 (75)	52/73 (71)	51/74 (69)	45/74 (61)	52/74 (70)	54/73 (74)
Knee pain while walking§	71.6±10.0	70.6±10.9	71.7±10.5	68.1±10.2	71.1±11.0	72.4±11.5
Patient's global assessment of response¶	48.8±20.8	55.7±20.3	51.0±20.6	51.6±16.9	49.9±19.9	54.4±22.4
WOMAC score‖						
Pain	69.0±11.9	65.8±13.9	69.2±12.5	62.1±12.3	68.3±13.2	68.4±12.0
Stiffness	74.4±13.5	69.7±13.1	75.0±12.4	66.7±17.5	71.2±17.9	73.3±13.1
Physical function	69.0±12.5	63.8±13.6	69.2±14.6	62.6±12.3	67.4±14.8	67.8±14.0

* Plus–minus values are means ±SD.
† Race was self-reported.
‡ A Kellgren–Lawrence score of 2 (minimal signs of osteoarthritis) indicates definite osteophytes without reduction of the joint space; a score of 3 (moderate signs of osteoarthritis) indicates diminished joint space; and a score of 4 (severe signs of osteoarthritis) indicates greatly reduced joint space. Data are from the intention-to-treat population, and missing data are excluded.
§ Knee pain while walking was assessed with the use of a visual-analogue scale that ranged from 0 to 100, with higher scores indicating more pain. Data are from the modified intention-to-treat population.
¶ Patients' global assessment of response to therapy was assessed with the use of a visual-analogue scale that ranged from 0 to 100, with higher scores indicating a better response to therapy. Data are from the modified intention-to-treat population.
‖ Scores on the pain, stiffness, and physical-function subscales of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were assessed with the use of a visual-analogue scale that ranged from 0 to 100, with higher scores indicating more pain, more stiffness, and more limitation of physical function, respectively. Data are from the modified intention-to-treat population.

Table 2. Secondary Efficacy Outcomes.*

Outcome	Placebo (N=73)	Tanezumab, 10 μg/kg (N=74)	Tanezumab, 25 μg/kg (N=75)†	Tanezumab, 50 μg/kg (N=72)	Tanezumab, 100 μg/kg (N=74)	Tanezumab, 200 μg/kg (N=72)
Change in WOMAC score from baseline through week 16						
Pain subscale	–16.2±2.4	–30.1±2.3	–36.0±2.2	–29.0±2.4	–39.6±2.2	–43.5±2.3
Stiffness subscale	–16.3±2.4	–33.5±2.3	–37.7±2.2	–34.5±2.4	–42.7±2.2	–47.8±2.4
Physical-function subscale	–15.2±2.3	–30.1±2.3	–34.9±2.2	–30.8±2.4	–40.5±2.2	–43.8±2.3
Response to therapy according to OMERACT–OARSI criteria by week 16 (% of patients)‡	43.8	74.3	84.0	75.0	93.2	93.1

* Plus–minus values are means ±SE. P<0.001 for all comparisons of the five doses of tanezumab with placebo. These analyses were performed on data from the modified intention-to-treat population.
† One patient who was randomly assigned to receive 25 μg of tanezumab per kilogram of body weight instead received 50 μg per kilogram.
‡ According to the criteria of the Outcome Measures for Rheumatology Committee and Osteoarthritis Research Society International Standing Committee for Clinical Trials Response Criteria Initiative (OMERACT–OARSI), patients were classified as having had a response if the WOMAC pain or physical-function score decreased by 50% or more and by 20 or more points on the visual-analogue scale or if two of the following three findings were observed: a decrease in the WOMAC pain score by 20% or more and by 10 or more points on the scale, a decrease in the WOMAC physical-function score by 20% or more and by 10 or more points on the scale, or an increase in the score on the patient's global assessment by 20% or more and by 10 or more points on the scale.