Part 1, Question 1: Continuous Outcomes

In this series of questions, we examine data from a study of 158 infants who visited Northbay Healthcare in Solano County, California for a Vitamin K shot. Assume that the infants in the study are a representative sample from all infants in Northbay Healthcare.
Nurses administered a Vitamin K shot to each infant. Infants were randomized to two different protocols to study how to reduce pain experienced by the infants due to the shot. The infants were divided into two groups – the control group, where standard protocol for handling the infants was used; and an intervention group, where mothers held their infants prior to, during, and after administration of the shot. Pain was measured using the Neonatal Infant Pain Score (NIPS) (Lawrence et. al 1993). The variables in the dataset are described below:

- id – unique identifier for each infant
- group – 1 if intervention group, 0 if control
- pain0 – NIPS score 0 seconds after shot
- pain30 – NIPS score 30 seconds after shot
- pain60 – NIPS score 60 seconds after shot
- pain120 – NIPS score 120 seconds after shot
- crytime – total time that the infant cried in seconds

Use the babies.dta dataset to answer the questions below.
These data were made available through SOCR (http://www.socr.ucla.edu/).
Source: Lawrence J, Alcock D, McGrath P, Kay J, MacMurray SB, Dulberg C. (1993) The development of a tool to assess neonatal pain, Neonatal Network, 12:59-66.

Exploratory analysis. Before jumping into analyzing the babies.dta dataset, first explore the dataset using summary statistics and graphical analyses.

1. Calculate the average cry time in each group. Calculate the median cry time in each group.

```
mean crytime, over(group)

Mean estimation                     Number of obs    =     158

      control: group = control
 intervention: group = intervention

--------------------------------------------------------------
        Over |       Mean   Std. Err.     [95% Conf. Interval]
-------------+------------------------------------------------
crytime      |
     control |   39.20253   2.624219       34.0192    44.38586
intervention |   29.60759   2.430496      24.80691    34.40828
--------------------------------------------------------------
```

```
bysort group: sum crytime, detail
-------------------------------------------------------------------------------
-> group = control

            Total time infant cried, in seconds
-------------------------------------------------------------
      Percentiles      Smallest
 1%             0              0
 5%             2              0
10%            11              0       Obs                  79
25%            20              2       Sum of Wgt.          79

50%            37                      Mean           39.20253
                       Largest       Std. Dev.      23.32457
75%            56             81
90%            73             84       Variance       544.0354
95%            81             86       Skewness       .3022815
99%           100            100       Kurtosis       2.394307

-------------------------------------------------------------------------------
-> group = intervention

            Total time infant cried, in seconds
-------------------------------------------------------------
      Percentiles      Smallest
 1%             0              0
 5%             0              0
10%             5              0       Obs                  79
25%            11              0       Sum of Wgt.          79

50%            27                      Mean           29.60759
                       Largest       Std. Dev.      21.60272
75%            43             72
90%            64             73       Variance       466.6774
95%            72             73       Skewness         .53556
99%            78             78       Kurtosis       2.238552
```

Group	Mean	Median
Control	39.20253	37
Intervention	29.60759	27

Part 1, Question 2: Paired Data

To help measure standard infant reactions to the shot without the intervention, we first restrict our analysis to the control group. Among the controls, we examine whether NIPS scores decreased within 30 seconds of receiving the shot. Restrict your analysis in the following questions to the control group. In Stata, you can use the command "drop if group == 1".

Generate a new covariate reflecting change in NIPS score over the 30 second interval (NIPS score at 30 seconds minus NIPS score at time of shot).

1. What is the mean change in cry time over the 30 second interval? The median? Is the distribution symmetric?

First, examine some descriptive statistics.

What is the mean change in NIPS score over the 30 second interval? -2.177215

```
mean paindiff

Mean estimation                     Number of obs    =      79
------------------------------------------------------------------
             |       Mean   Std. Err.     [95% Conf. Interval]
-------------+----------------------------------------------------
    paindiff |  -2.177215   .3226591      -2.81958    -1.53485
------------------------------------------------------------------
```

What is the median change in NIPS score over the 30 second interval? -1

```
sum paindiff, detail
                          paindiff
-------------------------------------------------------------
      Percentiles      Smallest
 1%           -7             -7
 5%           -7             -7
10%           -7             -7       Obs                  79
25%           -4             -7       Sum of Wgt.          79

50%           -1                      Mean           -2.177215
                      Largest         Std. Dev.       2.867857
75%            0              1
90%            0              2       Variance        8.224602
95%            1              4       Skewness        .0347357
99%            7              7       Kurtosis        3.05753
```

Is the distribution of change in NIPS score over the 30 second interval symmetric?
No

2. Test the null hypothesis that the average change in NIPS score over the 30 seconds is equal to 0, versus the alternative that the average change in NIPS score is different from 0. Conduct the test at the 0.05 level of significance. Assume that the change in NIPS score is normally distributed.

```
. ttest paindiff == 0

One-sample t test
------------------------------------------------------------------------------
Variable |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
paindiff |      79   -2.177215    .3226591    2.867857    -2.81958    -1.53485
------------------------------------------------------------------------------
    mean = mean(paindiff)                                         t =  -6.7477
Ho: mean = 0                                     degrees of freedom =       78

    Ha: mean < 0                 Ha: mean != 0                 Ha: mean > 0
 Pr(T < t) = 0.0000         Pr(|T| > |t|) = 0.0000          Pr(T > t) = 1.0000
```

What is the absolute value of the test statistic? 6.7477

What is the distribution of the test statistic under the null?

a)Standard normal
b) t-distribution with 78 df
c) t-distribution with 156 df

What is your p-value? < 0.001

What is your conclusion?

a) there is evidence that NIPS score decreases on average over the 30 seconds
b) there is not evidence that NIPS score changes on average over the 30 seconds
c) none of the above

2. Now, conduct an analogous non-parametric test, testing the null hypothesis that the median change in NIPS score is equal to 0, versus the alternative that the median change in NIPS score is different from 0. Conduct the test at the 0.05 level of significance. Use the most powerful non-parametric test that you have available.

```
signrank pain30 = pain0

Wilcoxon signed-rank test

        sign |      obs   sum ranks    expected
-------------+--------------------------------
    positive |        7         292      1453.5
    negative |       50        2615      1453.5
        zero |       22         253         253
-------------+--------------------------------
         all |       79        3160        3160

unadjusted variance    41870.00
adjustment for ties     -178.63
adjustment for zeros    -948.75
                     ----------
adjusted variance      40742.63

Ho: pain30 = pain0
            z =  -5.754
    Prob > |z| =   0.0000
```

What is the p-value? < 0.001

What is your conclusion?

a) there is evidence that median NIPS score decreases over the 30 seconds
b) there is not evidence that median NIPS score changes over the 30 seconds
c) none of the above

3. Examine the distribution of change in NIPS score. Compare the results of the parametric test that assumes normality versus the non-parametric test. Are you surprised that these two tests above gave somewhat similar conclusions? Why?

a) Yes, the t-test is always more powerful than the non-parametric test
b) No, there are no severe outliers or extreme skewness in the distribution and the sample size is sufficiently large
c) No, the results of non-parametric tests usually match up with the results of parametric tests

Tests for a change in mean and a change in median will behave similarly (i.e. both reject or both fail to reject) when the distribution of the outcome is not severely skewed and there are not extreme outliers.

Part 1, Question 3: Parametric Test For Infants Experiencing Severe Pain

In this question, we examine average cry time by group among infants who initially experienced severe pain. *Restrict your analysis to infants with a NIPS score of 7 immediately after receiving the shot.*

Make sure that you start this question with the full babies.dta dataset at the top of this webpage. Then, use the covariate pain0 to construct the relevant subset. In Stata, you can use the command "drop if pain0 < 7" to restrict to the appropriate subset.

Assume that, within group, cry time among infants who initially experienced severe pain follows a normal distribution

1. Among infants with initial severe pain, estimate the average cry time in each group, with a corresponding 95% confidence interval.

Now, we base our inferences off of the t-distribution. The easiest ways to construct a confidence interval using the t-distribution are using the ci command or ttest command in Stata

```
bysort group: ci crytime

-------------------------------------------------------------------------------
-> group = control

    Variable |        Obs        Mean    Std. Err.       [95% Conf. Interval]
-------------+---------------------------------------------------------------
     crytime |         59    40.64407    2.896597         34.8459    46.44224

-------------------------------------------------------------------------------
-> group = intervention

    Variable |        Obs        Mean    Std. Err.       [95% Conf. Interval]
-------------+---------------------------------------------------------------
     crytime |         47    36.91489    3.006442        30.86324    42.96655
```

Control: (34.8459, 46.44224)
Intervention: (30.86324, 42.96655)

2. Among infants with initial severe pain, conduct a test of the null hypothesis that the two groups have equal means versus the alternative hypothesis that the means are not equal at the 0.05 level of significance. Assume that the variances within each group are equal.

```
ttest crytime, by(group)

Two-sample t test with equal variances
------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
 control |      59    40.64407    2.896597    22.24919     34.8459    46.44224
interven |      47    36.91489    3.006442    20.61113    30.86324    42.96655
---------+--------------------------------------------------------------------
combined |     106    38.99057    2.090001    21.51788    34.84648    43.13465
---------+--------------------------------------------------------------------
    diff |            3.729174    4.211379               -4.622148     12.0805
------------------------------------------------------------------------------
    diff = mean(control) - mean(interven)                         t =   0.8855
Ho: diff = 0                                     degrees of freedom =      104
    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.8110         Pr(|T| > |t|) = 0.3779          Pr(T > t) = 0.1890
```

What is the absolute value of your test statistic? 0.8855
How many degrees of freedom does the test statistic have under the null? 104
What is the p-value? 0.3779

What do you conclude from this test?

a) the means in the two groups are different
b) the means in the two groups are not different
c) none of the above

We conclude that there is not evidence in the data that the means are different, which is absolutely not the same as concluding that the means in the two groups are not different.

3. When presenting these results, should this analysis be described as:

a) An intent-to-treat analysis
b) An "as-treated" analysis
c) A subgroup analysis
d) a and b
e) a and c

4. Suppose instead we wanted to examine the change in NIPS score from time 0 to time 120. Construct a new covariate that represents this change in NIPS score. Use graphical summaries to examine the distribution of this covariate. Which of the following tests would be appropriate to analyze the data:

a) Paired t-test
b) signed-rank test
c) wilcoxon rank sum test

The data is highly skewed but is not paired, so a Wilcoxon rank sum test is most appropriate.

```
gen paindiff = pain120 - pain0
histogram paindiff, by(group)
```

Part 2, Question 3: Case Control Study

The following tables show the crude and sex-specific results from a Density-Type Case Control Study that examines the association between a binary exposure (E) and a disease.

Full Data

	Cases	Control	Total
E+	740	350	1090
E-	260	650	910
Total	1000	1000	2000

Sex-Specific Data

Males

	Cases	Controls	Total
E+	640	250	890
E-	160	250	410
Total	800	500	1300

Females

	Cases	Controls	Total
E+	100	100	200
E-	100	400	500
Total	200	500	700

1. What is the value for the Crude Odds Ratio in this study?
OR = (740/260) / (350/650) = 5.2857

2. Calculate a 95% confidence interval for the crude odds ratio.
(4.36, 6.40)

3. Test the null hypothesis that there is no marginal association (ignoring sex) between disease and exposure using a Pearson Chi-square test at the 0.05 level of significance.

True or false: equivalently, the null hypothesis for this test is that the risk difference is equal to zero. False

What is the value of the test statistic? 306.68

What is the sampling distribution of the test statistic under the null hypothesis?

a) Standard Normal
b) Binomial
c) Chi-squared with 1 df

What is your p-value? 0.0000

What is the conclusion?

a) Reject the null hypothesis
b) Fail to reject the null hypothesis
c) Inconclusive

4. Suppose that you decide to estimate a conditional odds ratio for the effect of exposure on disease, holding sex constant, using logistic regression modeling. Using the tables above, consider whether sex is a confounder and/or an effect modifier. Using this information, which of the following logistic regression models is most appropriate for modeling the conditional odds ratio?

a) Include sex and exposure in the model for the log-odds
b) Include only exposure in the model for the log-odds
c) Include sex, exposure, and an interaction between sex and exposure in the model for the log-odds

Suppose a colleague performs a Case Control Study using the same cases as in the previous study but selecting a different Control group by selecting one control for each case, matching by sex. Complete the following tables with the expect values for B, D, B_1, D_1, B_0 and D_0.

Full Data

	Cases	Control	Total
E+	740	B=440	1180
E-	260	D=560	820
Total	1000	1000	2000

Sex-Specific Data

Males

	Cases	Controls	Total
E+	640	B_1=400	1040
E-	160	D_1=400	560
Total	800	800	1600

Females

	Cases	Controls	Total
E+	100	B_0=40	140
E-	100	D_0=160	260
Total	200	200	400

5. Using your values for B and D, what is the value for the Crude Odds Ratio in this study?

OR = 3.6224

6. Which value for the Odds Ratio best reflects the unconfounded effect of exposure (enter the letter of your best answer from the options listed below)?

a) The crude Odds Ratio from the first study since sex is not a confounder in that study
b) The crude Odds Ratio from the first study since sex is a confounder in that study
c) The sex-adjusted Odds Ratio in the first study since sex is a confounder in that study
d) The sex-adjusted Odds Ratio in the first study since sex is not a confounder in that study
e) The crude Odds Ratio in the second study since matching eliminates confounding in a case control study

7. Suppose we used the matching procedure described above and came up with the following output:

		Cases		
		E+	E-	Total
Controls	E+	340	100	440
	E-	400	160	560
	Total	740	260	1000

Test the hypothesis that there is no marginal association between disease and exposure at the 0.05 level of significance.

```
mcci 340 400 100 160

                 | Controls               |
Cases            |   Exposed   Unexposed  |      Total
-----------------+------------------------+------------
         Exposed |       340         400  |        740
       Unexposed |       100         160  |        260
-----------------+------------------------+------------
           Total |       440         560  |       1000

McNemar's chi2(1) =    180.00    Prob > chi2 = 0.0000
Exact McNemar significance probability       = 0.0000

Proportion with factor
        Cases             .74
        Controls          .44     [95% Conf. Interval]
                       ---------  --------------------
        difference          .3      .2593138   .3406862
        ratio         1.681818      1.557482   1.816081
        rel. diff.    .5357143      .4823884   .5890401

        odds ratio           4      3.205359   5.031359   (exact)
```

What is the value of your test statistic? 180.00

What is the null distribution of the test statistic?

a) Standard Normal
b) Binomial
c) Chi-squared with 1 df

What is the p-value? 0.0000

What is your conclusion?

a) Reject null hypothesis
b) Fail to reject null hypothesis