Consultant:
David Levy

2.5/3

BIOSTATISTICS CONSULTING WORKSHEET

UCLA FIELDING SCHOOL OF PUBLIC HEALTH, DEPARTMENT OF BIOSTATISTICS

Date: 4/23/18

Client Information:

- **Name(s):**
  H.C. Yoon, A. Emerick, J. Hill and J. Goldin

- **Department:**
  Department of Diagnostic Imaging, Kaiser Moanalua Medical Center
  Department of Radiological Sciences, UCLA.

- **Phone:**
  Contact information unavailable

- **Name of PI:**
  H.C. Yoon

Purpose:

- **Statement of research hypotheses:**
  The rate of CAC progression is gender specific, being greater in men than in women.

- **Statement of statistical hypotheses:**
  H_0: There is no difference in the mean rate of CAC progression (volume change per unit

time) between males and females. ($\mu_m = \mu_w$)
H_1: There is a significant difference in the mean rate of CAC progression (volume change per unit time) between males and females. ($\mu_m \neq \mu_w$)

Background & References:

- Background:

"Recent reports indicate that electron-beam computed tomography (EBCT) can document the presence and monitor the progression of atherosclerotic coronary artery calcification (CAC) in the general adult population as well as in those with increased cardiovascular risk (1-3). In addition, EBCT can measure changes in the extent of CAC in adults treated with lipid-lowering agents. Interpretation of the clinical significance of different coronary artery calcium scores in the same patient is dependent on several factors including measurement variation and expected rate of progression of coronary calcium."

- References:

1. Maher JE; Bielak LF; Raz JA; Sheedy II PF; Schwartz RS; Peyser PA. Progression of Coronary Artery Calcification: A Pilot Study. Mayo Clin Proc 1999; 74:347-355. 1999.

2. Goodman WG, Goldin J, Kuizon BD, Yoon C, Gales B, Sider D, Wang Y, Chung J, Emerick A, Greaser L, Elashoff RM, Salusky IB. Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. N Engl J Med. 2000;342:1478-83.

3. Budoff MJ; Lane KL; Bakhsheshi H; Mao S; Grassmann BO; Friedman BC; Brundage BH. Rates of Progression of Coronary Calcium by Electron Beam Tomography. Am J Cardiol 2000; 86:8-11.

Descriptions:

- **Study design:**

A retrospective study investigated the imaging results from 217 asymptomatic subjects. "For the purpose of this study, asymptomatic was defined as having no history of documented ischemic heart disease including no abnormal electrocardiogram, stress test,

or coronary angiogram, and no prior history of myocardial infarction or coronary bypass surgery. Standard EBCT acquisition protocols were followed and, from 30 to 40 contiguous axial images were obtained in a single breath hold to include the entire heart. Each study was scored for CAC volume using the default values of three or more contiguous pixels with density 130HU or greater in the expected location of an epicardial artery. The volume of each lesion was the product of the pixel area and the slice thickness. The sum of all lesion volumes yields the total calcium volume score (CVS) in units mm^3."

- **Population(s):**

  Asymptomatic patients.

- **Sample(s):**

  Convenience sample of patients who underwent at least two EBCT studies at Imatron Corp, in San Francisco, CA for the detection of CAC as a part of a clinical screening program.

- **Dependent variable(s):**

  Sex

- **Independent variable(s):**

  Rate of CAC progression, defined as the difference in volumes between first and second screenings divided by the number of days elapsed, $\frac{mm^3}{day}$

Analysis:

- Continuous/discrete:

  Continuous

- Descriptive/inference:

  Inference

- Single/multifactor:

  Single factor

- Univariate/multivariate:

  Univariate

Tools for Analysis:

The statistical software R was used to analyze this dataset. Data import and cleaning were achieved using the licensed libraries "tidyverse" and "readstata13". All calculations and inferential procedures were conducted using the R software's base package. Those measures included descriptive statistic calculations, an F-test for equal variance, and a two-sided, two-sample t-test for equal means with unequal variances.

Results:

The data collected for this study did ***not*** provide sufficient evidence to reject the null hypothesis that asymptomatic men and women have equal mean CAC progression. This result holds with the use of both one-sided and two-sided t-tests. More detailed analysis results are attached.

Follow-up:

- Appointment:

  N/A

- Report:

  N/A

- Conclusions:

  N/A

Consulting Assignment 3

David Levy

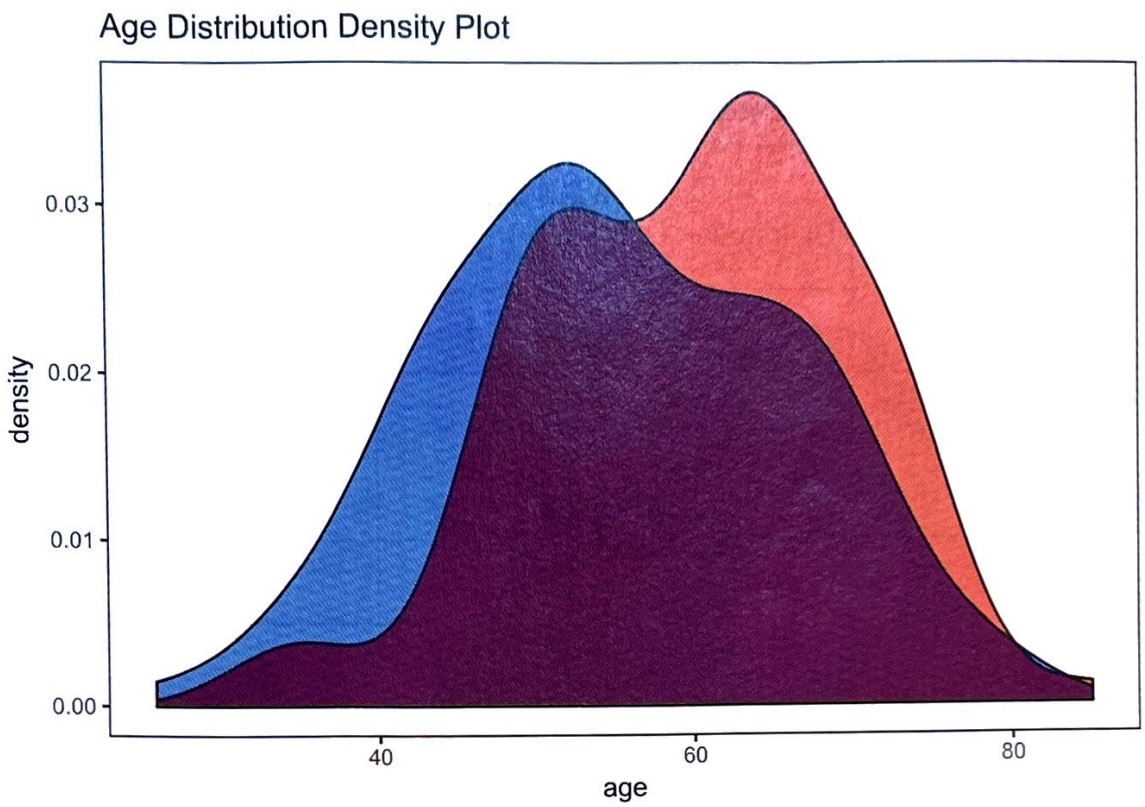
4/22/2018

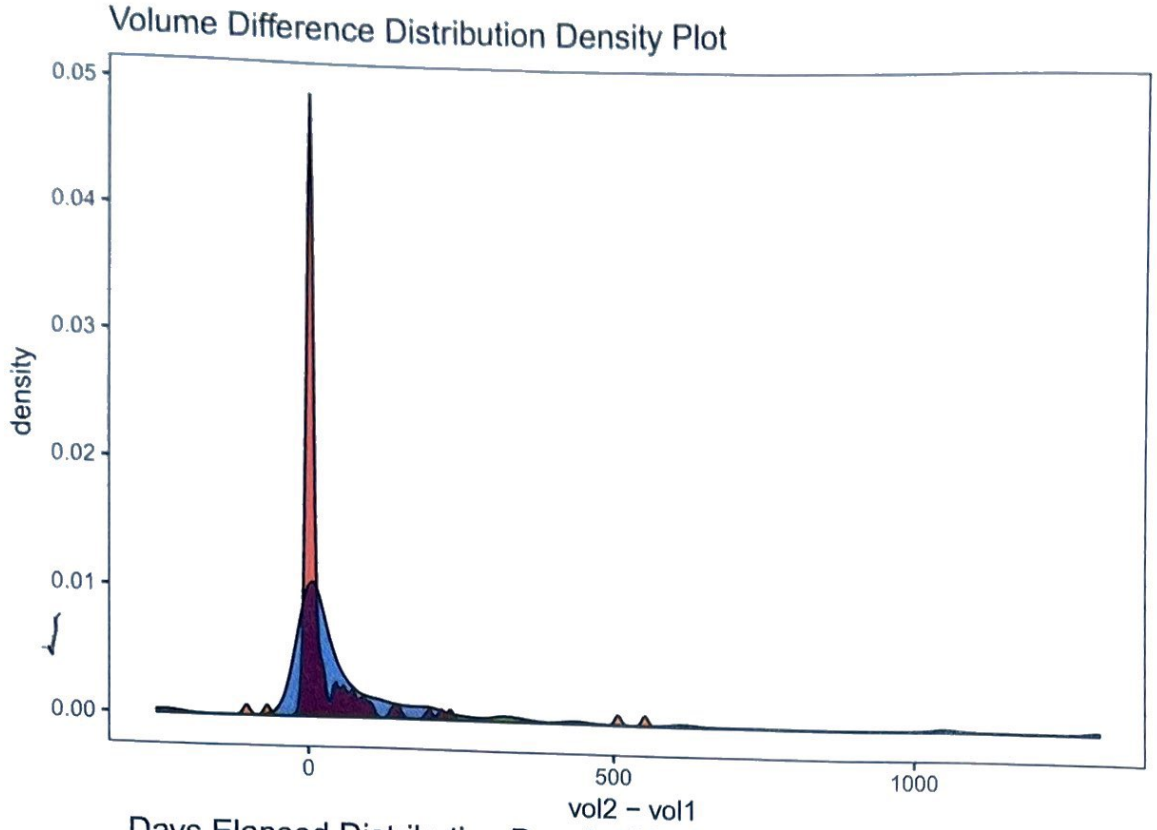
Note that the variable of interest is not included in the dataset. Instead, we'll need to define the "rate of CAC progression" as the differences in the first and second CVS measures divided by the number of days elapsed between visits:

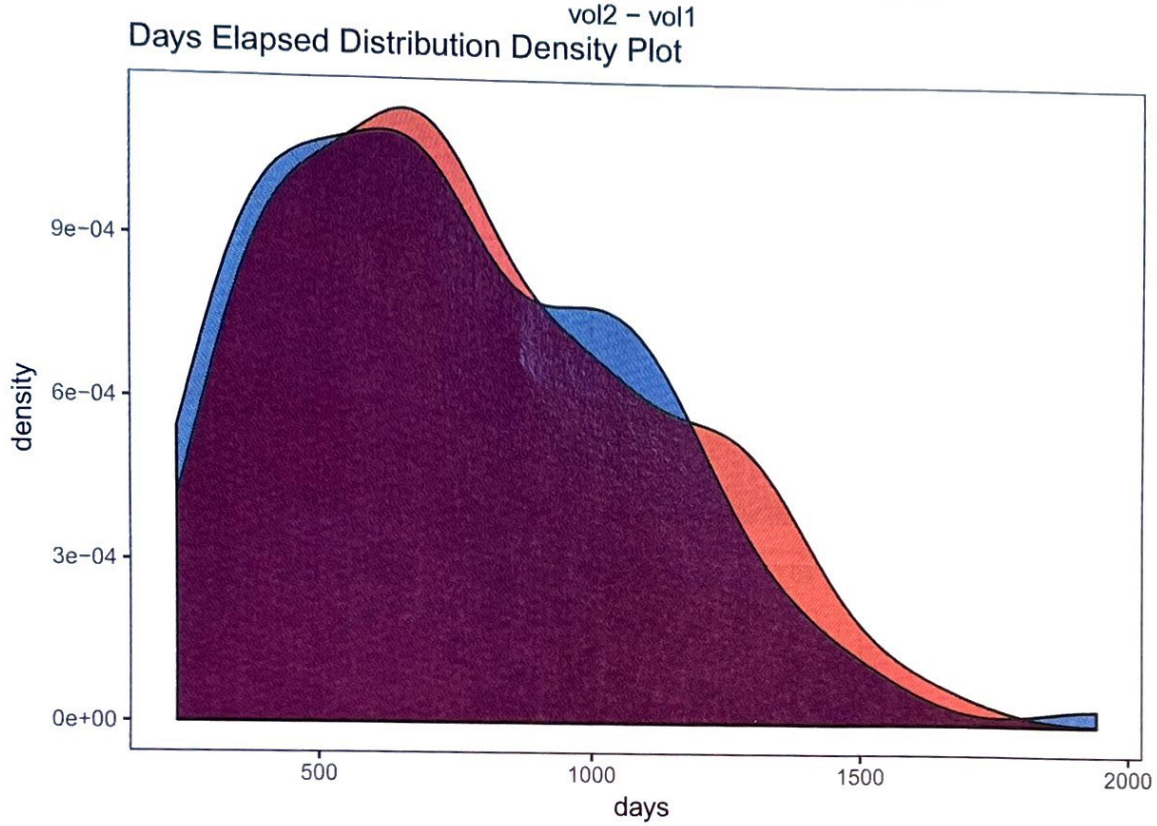
The table below shows the study group split by sex.

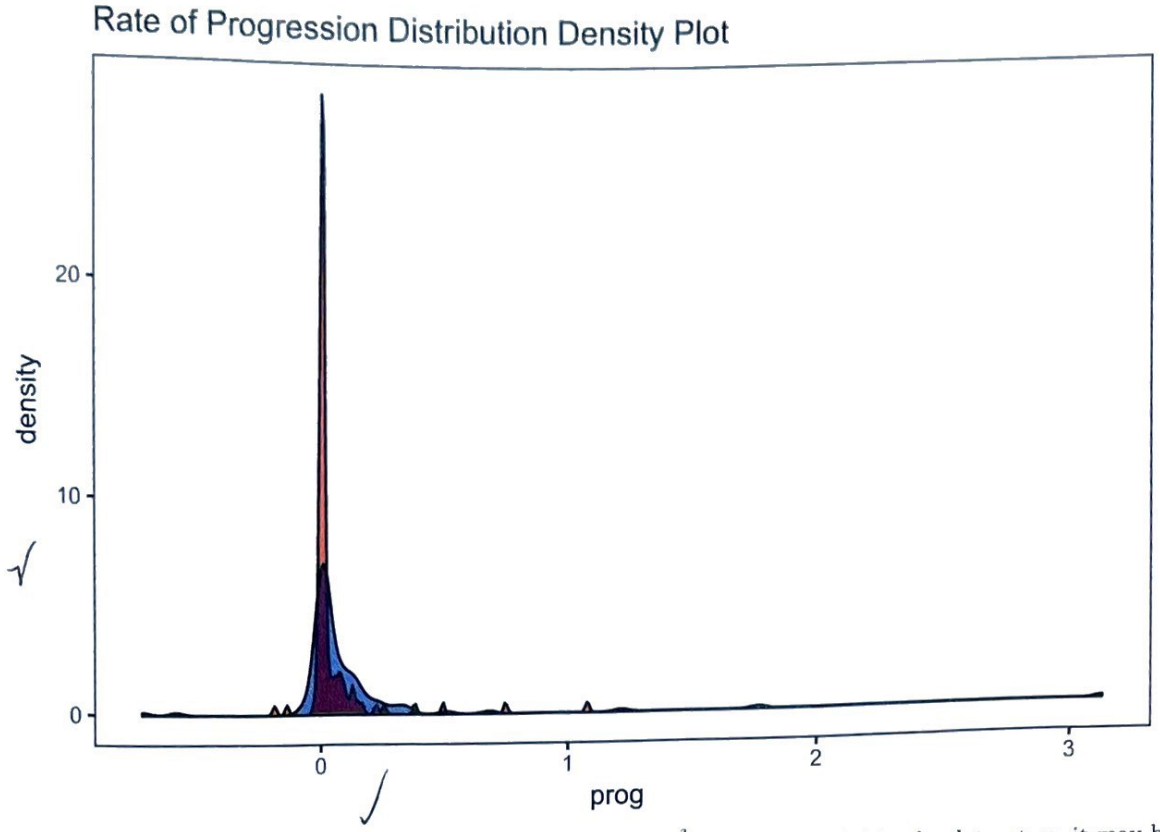
Sex	$n = 217$
Female, count (%)	103 (47.5%)
Male, count (%)	114 (52.5%)

Below, we visualize the distribution of each variable included in the dataset:




Volume Difference Distribution Density Plot
density
0.05
0.04
0.03
0.02
0.01
0.00
0
500
1000
vol2 − vol1


Days Elapsed Distribution Density Plot
density
9e−04
6e−04
3e−04
0e+00
500
1000
1500
2000
days



Interestingly there is a large spike of rate distributions at 0 $\frac{mm^3}{day}$. Age is included in the dataset, so it may be prudent from here to sratify on age in order to determine whether it has any effect on progression rates.

The table below shows descriptive statistics for the full cohort, the female group and the male group respectively.

Characteristic	Full cohort ($n = 217$)	Female ($n = 103$)	Male ($n = 114$)
Age, yrs, mean ± SD	57.2 ± 11.0	59.7 ± 10.1	54.9 ± 11.2
CVS difference, mm^3, mean ± SD	51.6 ± 147.0	28.9 ± 85.2	72.1 ± 184.0
Days elapsed, mean ± SD	761.5 ± 333.8	779.7 ± 332.7	745.0 ± 335.3
CAC progression, $\frac{mm^3}{day}$, mean ± SD	0.078 ± 0.291	0.046 ± 0.148	0.108 ± 0.375

Based on the graphical display of the distribution of the CAC progression measure, we suspect that the male and female groups have unequal variances. We test that suspicion below with an F-test:

```
##
##  F test to compare two variances
##
## data:  cac_male$prog and cac_female$prog
## F = 6.3884, num df = 113, denom df = 102, p-value < 2.2e-16
## alternative hypothesis: true ratio of variances is not equal to 1
## 95 percent confidence interval:
##  4.358023 9.329685
## sample estimates:
## ratio of variances
```

```
##              6.388409
```

Considering the results of the F-test above, we have sufficient evidence to suggest that the variances are indeed unequal, and so we conduct a two-sample t-test with unequal variances in order to test the statistical hypothesis of interest. In this case, the null hypothesis states that the means of the male and female CAC progression measures are equal. The results are shown below:

```
##
##  Welch Two Sample t-test
##
## data:  cac_female$prog and cac_male$prog
## t = -1.6473, df = 150.54, p-value = 0.1016
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -0.13783575  0.01249761
## sample estimates:
##  mean of x  mean of y
## 0.04554485 0.10821393
```

As noted above, we have addressed the client's question, but should pursue additional analysis techniques. First and foremost, age stratification is recommended. The other variables included in the dataset require investigation, but were not explored here because they were not defined.