## Effect of Nutrition and Exercise Incentive on Weekly Weight Loss Samantha Bothwell | December 11th, 2020

### **Introduction**

Individuals who classified as overweight or obese were enrolled into the study to understand factors that contribute to weight loss. Participants were separated into two groups. One group had a nutritionist, and the other group did not. Both groups received free access to the Wellness center at the University of Colorado Anschutz Medical Campus. Participants were asked to step on a Bluetooth scale once a day over the course of the study. Within the study, there are 3 cohorts. These cohorts indicate participants who started the study around the same time. This study is ongoing, so we do not have access to intervention groupings. Additionally, complete data has not been collected for all participants.

The research questions of interest are :

* What is the trajectory of weight over the duration of time in the study?
* Is there a significant decrease in weight over the course of the study, regardless of intervention group?

### **Methods**

#### **Data Cleaning**

The data received were fairly cleaned for prior analysis. One subject in Cohort 2 was missing Age, Sex, Race and Ethnicity information and was removed. Some participants measured weight once a week, rather than daily. We summarized weight as the average weight each week in the study to account for some of the missing data. One participant had > 80% missing data, after computing weekly averages, and was removed. To analyze trajectories over a year, we truncated the data to 365 days. This allows for some consistency as cohorts had different lengths of measurement time. The outcome measure for analysis was defined as weekly weight difference from baseline. The original data contained baseline ages. To separate out the effects of aging, we added 1/365 to each participant’s weight, for each day in the study. This allows us to use real age for every day, rather than simply baseline age.

#### **Data Analysis**

Data cleaning and visualization was performed in R, version 4.0.2 (The R Foundation, Vienna University). Longitudinal modeling was performed in SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

To understand the trajectory of weight over the duration of time in the study we used the fpca.sc method for regular data in the R refund package, version 0.1-21 (Jeff Goldsmith, et al, 2019). We summarized the results of the mean trajectory for each cohort.

To assess if there is a significant decrease in weight over the course of the study, we fit a change-score linear mixed model in SAS with PROC MIXED. Since time points are equally spaced, we used an AR(1) covariance structure. The model includes a random intercept for participant and

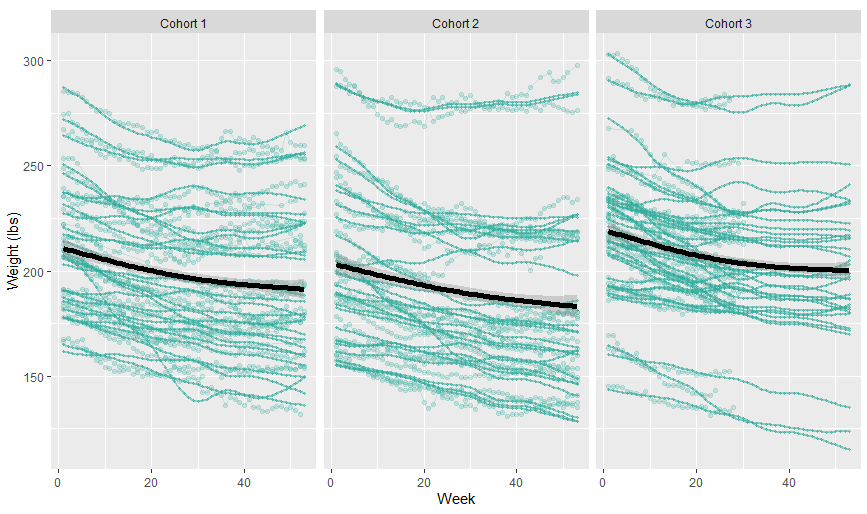
|  | **Cohort 1 (N=29)** | **Cohort 2 (N=25)** | **Cohort 3 (N=36)** | **P-Value** |
| --- | --- | --- | --- | --- |
| **Age** |  |  |  |  |
| Mean (SD) | 41.8 (9.36) | 41.5 (10.5) | 43.6 (8.30) | 0.881 |
| Median  [Min, Max] | 43.2  [26.1, 55.8] | 43.1  [21.9, 55.2] | 42.7  [21.8, 54.9] |  |
| **Sex** |  |  |  |  |
| Female | 21 (72.4%) | 19 (76.0%) | 29 (80.6%) | 0.739 |
| Male | 8 (27.6%) | 6 (24.0%) | 7 (19.4%) |  |
| **Race** |  |  |  |  |
| Asian | 0 (0%) | 1 (4.0%) | 4 (11.1%) | **0.034** |
| Black | 0 (0%) | 3 (12.0%) | 4 (11.1%) |  |
| White | 26 (89.7%) | 21 (84.0%) | 28 (77.8%) |  |
| Other | 3 (10.3%) | 0 (0%) | 0 (0%) |  |
| **Ethnicity** |  |  |  |  |
| Hispanic  or Latino | 4 (13.8%) | 3 (12.0%) | 10 (27.8%) | 0.210 |
| Non Hispanic  or Latino | 25 (86.2%) | 22 (88.0%) | 26 (72.2%) |  |
| **Baseline Weight** |  |  |  |  |
| Mean (SD) | 214 (32.5) | 210 (40.2) | 220 (31.7) | 0.281 |
| Median  [Min, Max] | 210  [166, 285] | 200  [158, 297] | 219  [147, 304] |  |
| **Time Span** |  |  |  |  |
| Mean (SD) | 547 (92.8) | 412 (71.7) | 181 (27.7) | **<0.001** |
| Median  [Min, Max] | 593  [210, 600] | 431  [84.0, 433] | 186  [41.0, 202] |  |

random effects for the linear and quadratic effect of Week. By including random effects for the linear and quadratic terms, we allow predictions for subjects with just a linear trend to not be influenced by the quadratic term.

***Table 1. Cohort Characteristics***

Summaries for categorical variables are represented as N(%) and continuous variables are represented as Median [Range] and Mean (95% CI). P-values were computed using a Kruskal Wallis test for continuous variables and a Chi-Square test for categorical variables.

### **Results**

Table 1 displays the cohort characteristics at baseline stratified by enrollment cohort. Of the 90 participants in the study, 69 are female and 21 are male. The average age for Cohort 3 is slightly higher than cohorts 1 and 2, mean 43.6 years compared to 41.8 and 41.5 years for Cohorts 1 and 2 respectively. In effect, the average baseline weight is highest for Cohort 3. For analysis, we are truncating data to 1 year, or 365 days. However, Cohort 3 is still collecting data, so this cohort has less than a year of data, 181 days on average.

***Figure 1. Weight Trajectories over time***

Figure 1 shows the actual weights vs the smoothed FPCA line for all individuals in their respective cohort. From the curves, there is a general decline in weights over time. The mean trajectories for Cohorts 1 and 2 are fairly comparable. The mean trajectory is higher for Cohort 3 than the other two cohorts, indicating that this group had higher weights on average. A reason for this could be that Cohort 3 was sampled during the Covid-19 pandemic, while Cohorts 1 and 2 were sampled prior to the pandemic. All three mean trajectory lines follow a similar pattern. As time increases, the slope of the line tends to flatten. The FPCA method fills in missing data from full data trends. For Cohort 3, the subjects do not have data after day 200, but FPCA fills in data for the rest of the year to show what they expect the trajectory to be for these subjects. The longitudinal model only uses the data provided and will not incorporate these predicted values given by the FPCA trajectories.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Effect** | **Estimate** | **Standard Error** | **DF** | **T Value** | **Pr > |t|** |
| **Intercept** | -3.6197 | 1.6552 | 81 | -2.19 | **0.0316** |
| **Cohort** |  |  |  |  |  |
| Cohort 1 | -0.6333 | 0.7813 | 3105 | -0.81 | 0.4177 |
| Cohort 2 | -2.7467 | 0.7637 | 3105 | -3.60 | **0.0003** |
| **Sex = Female** | 1.6087 | 0.7175 | 3105 | 2.24 | **0.0250** |
| **Age** | 0.0612 | 0.0333 | 3105 | 1.84 | 0.0659 |
| **Race** |  |  |  |  |  |
| Asian | -0.2756 | 1.3865 | 3105 | -0.20 | 0.8424 |
| Black/African American | 1.1706 | 1.2908 | 3105 | 0.91 | 0.3646 |
| Other | -2.5192 | 1.7693 | 3105 | -1.42 | 0.1546 |
| **Week** | -1.0147 | 0.1015 | 86 | -10.00 | **<.0001** |
| **Week\*Week** | 0.0151 | 0.0011 | 88 | 13.55 | **<.0001** |
| **Week\*Cohort 1** | -0.1239 | 0.1442 | 3105 | -0.86 | 0.3904 |
| **Week\*Cohort 2** | -0.0841 | 0.1497 | 3105 | -0.56 | 0.5745 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **Cohort** | 2 | 3105 | 6.95 | **0.0010** |
| **Sex** | 1 | 3105 | 5.03 | **0.0250** |
| **Age** | 1 | 3105 | 3.39 | 0.0659 |
| **Race** | 3 | 3105 | 0.99 | 0.3985 |
| **Week** | 1 | 86 | 305.49 | **<.0001** |
| **Week \* Week** | 1 | 88 | 183.53 | **<.0001** |
| **Week \* Cohort** | 2 | 3105 | 0.39 | 0.6798 |

Tables 2 and 3 represent the summary output from the linear mixed model. The outcome of interest in this model is the weekly change in weight from baseline. The model incorporates a random intercept, a random effect for the linear and quadratic effects of week and repeated measures across subjects with an AR(1) covariance structure. After adjusting for cohort, sex, age and race, there is a significant relationship between week in study and change in weight (p < 0.0001, NDF = 1, DDF = 86, F = 305.49). On average, a participant will lose 1.1047 lbs for each week in the study, holding all other model covariates constant. There is also a significant effect for the quadratic Week term (p < 0.0001, NDF = 1, DDF = 88, F = 183.53). The quadratic week effect indicates that for each additional week in the study, the slope of Week increases by 0.0151, on average. This agrees with the results of Figure 1, where the trajectory curve starts to flatten over time rather than maintaining a constant decline. An overall test for fixed effects indicated that, in addition to the effects of Week, Cohort and Sex were significantly associated with weight change. From Table 2, Cohort 2 lost 2.75 more pounds, on average, compared to Cohort 3 (p = 0.001, NDF = 2, DDF = 3105, F = 6.95). This agrees with the effect we saw in Figure 1. Additionally, males lost 1.61 more pounds, on average, compared to females (p = 0.025, NDF = 1, DDF = 3105, F = 5.03). Based on the overall test for fixed effects, Age, Race and the Week by Cohort interaction, we all non-significant in relation to weight change.

***Table 2. Linear Mixed Model Effect Estimates (AIC = 13130.5)***

***Table 3. Type 3 Tests for Fixed Effects***

**Note:** Reference levels - Cohort = 3, Sex = Male, Race = White

Figure 2 depicts the actual vs predicted weight change over the course of the study. The predicted weight change lines follow a similar pattern to the actual weight change lines, indicating a good prediction from our model. For a better understanding of how well our model predicts the data, we could perform cross-validation.

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***Figure 2. Actual vs Predicted Weight Change over Study Weeks***

### **Discussion**

The study depended on participants frequently measuring their weights, which is anticipated to result in sufficient missing data. The average proportion of missing data was 10.7% (SD 16.9%), after computing week averages. We assumed that data is missing at random (see Appendix Table 1), which allowed us to proceed with obtaining model estimates under the standard linear mixed model.

The outcome for the final model used weekly weights. This causes some discrepancies as a participant may have 4 measurements on week and all 7 the next. To account for different numbers of measurements each week, we incorporated a weighting factor for every week. Each weighting factor took on a value from 0 – 7, indicating how many measurements were included in the week. When not adjusting for this weighting, our model AIC was 13101.4 which was lower than the model presented, which had an AIC of 13130.5. While the weight factor increased the AIC, it is a more reliable estimate.

As this is an ongoing study, we are unable to evaluate the differences in treatment groups. It may be that the found weight loss over time can be significantly attributed to treatment group, as Cohort 3 overlaps with COVID-19. However, we do not have complete data on Cohort 3 as the study is still collecting data from this cohort. Based on the data we have from Cohort 3, measurements are taken from October of 2019 to April of 2020. When we have a complete year of data from Cohort 3, nearly 60% of the data will be overlapped with COVID-19. We do not know how the treatments were adjusted for this study based on the restrictions of COVID-19. As an extension, it may be of benefit to find data of weight trajectories over the course of COVID-19 for a healthy normal population for comparison. We expect that, on average, people gained weight during COVID due to the inability to access fitness centers, lack of walking to or around school/work and a general inability to travel due to stay-at-home orders. Our results showed that participants lost weight over time, but this trend flattened out near the end of the year. A further analysis can use a similar LMM strategy to effectively evaluate if the change in weight over time is different between Cohort 3 compared to Cohorts 1 and 2, utilizing a full year of Cohort 3 data.

# **References**

Ewen Harrison, Tom Drake and Riinu Ots (2020). finalfit: Quickly Create Elegant Regression Results Tables and Plots when Modelling. R package version 1.0.2. <https://CRAN.R-project.org/package=finalfit>

Jeff Goldsmith, et al (2019). refund: Regression with Functional Data. R package version 0.1-21. <https://CRAN.R-project.org/package=refund>

Jeff Goldsmith, et al. “Corrected Confidence Bands for Functional Data Using Principal Components.” Biometrics, vol. 69, no. 1, 2013, pp. 41–51. Wiley Online Library, doi:https://doi.org/10.1111/j.1541-0420.2012.01808.x.

Matthew Strand and Gary Grunwald (2020). BIOS6643 Analysis of Longitudinal Data Course Notes.

# **Table Appendix**

***Appendix Table 1. Tests for Patterns of Missing Data***

| **Weekly Weight** | **Not missing** | **Missing** | **p** |
| --- | --- | --- | --- |
| **Cohort**  1 | 1311 (86.5) | 204 (13.5) | <0.001 |
| 2 | 1197 (93.6) | 82 (6.4) |  |
| 3 | 869 (90.1) | 96 (9.9) |  |
| **Sex**  Female | 2540 (89.1) | 310 (10.9) | 0.012 |
| Male | 837 (92.1) | 72 (7.9) |  |
| **Race**  Asian | 135 (96.4) | 5 (3.6) | 0.004 |
| Black/African American | 233 (87.9) | 32 (12.1) |  |
| White | 2878 (89.5) | 339 (10.5) |  |
| Other | 131 (95.6) | 6 (4.4) |  |
| **Age**  Mean (SD) | 41.9 (9.3) | 44.6 (9.8) | <0.001 |

**Note**: P-values were computed with Kruskal-Wallis test for continuous variables and Chi-Square Test for categorical variables

***Appendix Table 2. Covariance Parameter Estimates***

|  |  |  |
| --- | --- | --- |
| **Cov Parameter** | **Subject** | **Estimate** |
| Intercept | Participant | 4.2251 |
| Week | Participant | 0.2840 |
| Week\*Week | Participant | 0.000067 |
| AR(1) | Participant | 0.8023 |
| Residual |  | 25.1626 |

# **Code Appendix**

All code can be found on my GitHub: <https://github.com/sjbothwell/BIOS6643_FinalProject>

All data cleaning was performed in R. Data analysis was performed in SAS. Here is some relevant code:

/\* Final Models \*/

/\* 13130.5 \*/

**PROC** **MIXED** DATA = wt\_week ;

CLASS participant\_id cohort sex race(ref = "5");

MODEL weight\_change = cohort sex age race Week Week\*Week cohort\*Week / solution outp = pred1;

RANDOM intercept Week Week\*Week / subject = participant\_id;

REPEATED / SUBJECT = participant\_id type=ar(**1**);

WEIGHT num\_days;

**RUN**;

/\* 13101.4 \*/

/\* Lower AIC but does not account for week weight \*/

**PROC** **MIXED** DATA = wt\_week ;

CLASS participant\_id cohort sex race(ref = "5");

MODEL weight\_change = cohort sex age race Week Week\*Week cohort\*Week / solution outp = pred2;

RANDOM intercept Week Week\*Week / subject = participant\_id;

REPEATED / SUBJECT = participant\_id type=ar(**1**);

**RUN**;

**PROC** **SGPLOT** DATA = pred1;

title 'Predicted Weight Change over Study Weeks';

series x=Week y=pred / group=participant\_id;

**run**;

**PROC** **SGPLOT** DATA = pred1;

title 'Actual Weight Change over Study Weeks';

series x=Week y=weight\_change / group=participant\_id;

**run**;

# Missing Data summary (in R)

explanatory = c("cohort", "sex", "race", "age")

dependent = "mean.wt"

wt.week %>% missing\_compare(dependent, explanatory)

# FPCA Plots (in R)

wt\_fpca = fpca.sc(wt.lb)

# Add yhat varaibles to dataframe

yhat <- as.data.frame(wt\_fpca$Yhat)

wt$wt\_lb\_hat <- c(t(yhat))

colnames(wt.lb) = paste0("time\_", 1:53)

# Actual vs predicted

wt.act <- as\_tibble(wt.lb) %>%

mutate(id = row\_number(), cohort = cohort.list$cohort) %>%

gather(time, value.act, contains("time\_")) %>%

mutate(time = str\_remove(time, "time\_"),

time = as.numeric(time)) # %>%

# filter(id %in% (1:10))

wt.pred <- as\_tibble(wt\_fpca$Yhat) %>%

mutate(id = row\_number(), cohort = cohort.list$cohort) %>%

gather(time, value.pred, contains("V")) %>%

mutate(time = str\_remove(time, "V"),

time = as.numeric(time)) # %>%

# filter(id %in% (1:10))

wt.compare <- cbind(wt.act, wt.pred$value.pred)

colnames(wt.compare)[5] <- "value.pred"

wt.compare$cohort <- ifelse(wt.compare$cohort == 1, "Cohort 1",

ifelse(wt.compare$cohort == 2, "Cohort 2", "Cohort 3"))

ggplot(data = wt.compare[!is.na(wt.compare$value.act),], aes(time, value.act, group = id)) +

geom\_point(alpha = 0.2, color = "#32ad9d") +

geom\_path(alpha = 0.2, color = "#32ad9d") +

geom\_point(data = wt.compare[!is.na(wt.compare$value.pred),], aes(time, value.pred, group = id), alpha = 0.5, color = "#32ad9d", size = 0.75) +

geom\_path(data = wt.compare[!is.na(wt.compare$value.pred),], aes(time, value.pred, group = id), alpha = 0.5, color = "#32ad9d", size = 1) +

facet\_grid(. ~ cohort) +

geom\_smooth(data = wt.compare[!is.na(wt.compare$value.pred),], aes(time, value.pred, group = cohort), lwd = 2, color = 'black') +

xlab("Week") + ylab("Weight (lbs)")