An analysis of the effects of sleep quality and exercise programs on cancer survivors' quality of life

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Abstract

Cancer is a widespread disease that affects millions of people in the United States yearly. It has been found that physical activity improves sleep in healthy populations using objective and subjective methods, and that sleep is impaired in cancer patients and linked to poorer outcomes. It has also been found that increasing physical activity improves quality of life and reduces fatigue in cancer patients and survivors. This paper details an analysis to determine if sleep quality in cancer patients improves following a cancer-patient exercise program, as well as to determine if sleep quality moderates cancer-related fatigue and/or quality of life following a cancer-patient exercise program. The first portion of the analysis was accomplished using the Wilcoxon Signed-Rank test and the results indicated no improvement in sleep quality in cancer patients after a patient exercise program. Linear regression models were used to address the second portion of the analysis question. The response variables tested were change in fatigue and quality of life. The primary predictors were change in strength (walking distance/grip strength) and sleep quality as well as the interaction to test for the moderating effect of sleep quality. All analysis was done using R version 3.5.1 including the dplyr and readxl packages. No interaction was found and there is no evidence of a moderating effect of sleep on the positive impact of exercise on quality of life/fatigue in cancer patients. A significant limiting factor of this analysis is the final sample size and further testing on a larger sample size is a priority for continued research.

Introduction

In 2018 there were an estimated 1.7M (439.2 per 100,000 individuals) new cancer diagnoses made in the United States (National Cancer Institute 2018). The difficulties of coping after a cancer diagnosis are impossible to ignore. The number of cancer survivors has increased in recent years and is expected to continue to rise. Thus it is vital to understand how to adjust to life after diagnosis and treatment of cancer.

The BfitBwell cancer exercise program is designed to assist patients in maintaining a healthy lifestyle during or after cancer treatment with the ultimate goal being to improve their quality of life. In order to qualify, individuals must be a patient of the University of Colorado Cancer Center currently undergoing treatment or must have finished treatment within the last 6 months. Patients participating in the program take a pre-assessment to measure physical fitness, sleep quality, quality of life, and nutrition and diet. The variables used to describe these measures are described in detail in Table 1.They then participate in 3 months of training sessions followed by a post-assessment questionnaire containing the same questions as previously administered.

Table 1: Variable Descriptions

Measure	Description
Physical Fitness: Grip Strength	Grip strength measurement (kg of force)
Physical Fitness: Walking Distance	Continuous feet walked in 6 minutes
Sleep Quality	Patient overall sleep quality rating with 1 being very poor and 5 being very good
Quality of Life	Total score from all survey questions regarding quality of life. Ranges from 0 to 108 where a higher score indicates better quality of life
Fatigue	Combined score from all survey questions related to fatigue. Ranges from 0 to 52 where a higher score indicates less fatigue

The two primary aims of the proposed study were to determine whether sleep quality improved after a physical activity intervention and to determine whether or not sleep quality moderated cancer-related fatigue and/or quality of life in cancer survivors. Two secondary aims of this study were to compare sleep habits and physical fitness before and after the physical activity intervention and to understand changes in quality of life subscales. These subscales were physical status, social interactions, religious/spiritual status, economic status, and physiological status.

Summary Statistics

The initial sample contained observations for 141 participants, though only observations with both pre and post measurements of the main analysis variables are considered, resulting in a final sample size of 37. As seen in Table 2, the majority of participants were female and White/not Hispanic or Latino, with ages ranging from 30-79. Cancer diagnosis was grouped into Breast or Other, with Other being blood/heme, colorectal, other cancer, etc. Most patients were not currently being treated with chemotherapy, radiation therapy, surgery plans, or other treatments (see Table 3).

Table 4 shows pre/post participant counts of sleep quality indicators, and we can see that (i) the same proportion of participants pre and post program awakened feeling rested, (ii) a slightly higher proportion of participants had less frequent awakening during the night (never or 1-3 times a week) post program than pre, and (iii) a slightly higher proportion of participants rated overall sleep quality as good or very good post program compared to pre.

Table 2: Demographics

	N	%
Gender		
Male	10	27%
Female	27	73%
Age		
30-39	6	16%
40-49	11	30%
50-59	5	14%
60-69	12	32%
70-79	3	8%
Race		
Asian	3	8%
Black or African American	1	3%
Mixed Race	3	8%
White	30	81%
Ethnicity		
Hispanic or Latino	3	8%
Not Hispanic or Latino	33	89%
Not Reported	1	3%

Table 3: Cancer diagnosis and treatment

	N	%
Current Cancer Diagnosis		
Breast	14	38%
Other Cancer	23	62%
Blood/Heme	2	5%
Colorectal	4	11%
Esophageal	3	8%
Lung	1	3%
Other	10	27%
Ovarian	1	3%
Pancreatic	1	3%
Prostate	1	3%
Currently on Chemotherapy		
No	21	57%
Yes	16	43%
Currently on Radiation Therapy		
No	25	68%
Yes	12	32%
Have Surgery Planned		
No	29	78%
Yes	8	22%
Currently on Other Treatments		
No	25	68%
Yes	12	32%

Table 4: Quality of sleep evaluation

	Pre	Post
Do you awaken feeling rested?		
1: Yes	18	18
2: No	19	19
How often do you wake up during the night?		
1: Never	1	1
2: 1-3 times a week	10	13
3: 4-6 times a week	8	2
4: Once or twice a night	11	13
5: More than 2 times a night	7	8
During the past 4 weeks, how would you rate your sleep overall?		
1: Very poor	1	1
2: Poor	8	7
3: Fair	15	13
4: Good	9	14
5: Very good	4	2

In order to investigate the relationship between the change in quality of life, change in grip strength/walking distance, and improvement in sleep quality, figures 1 and 2 were inspected.

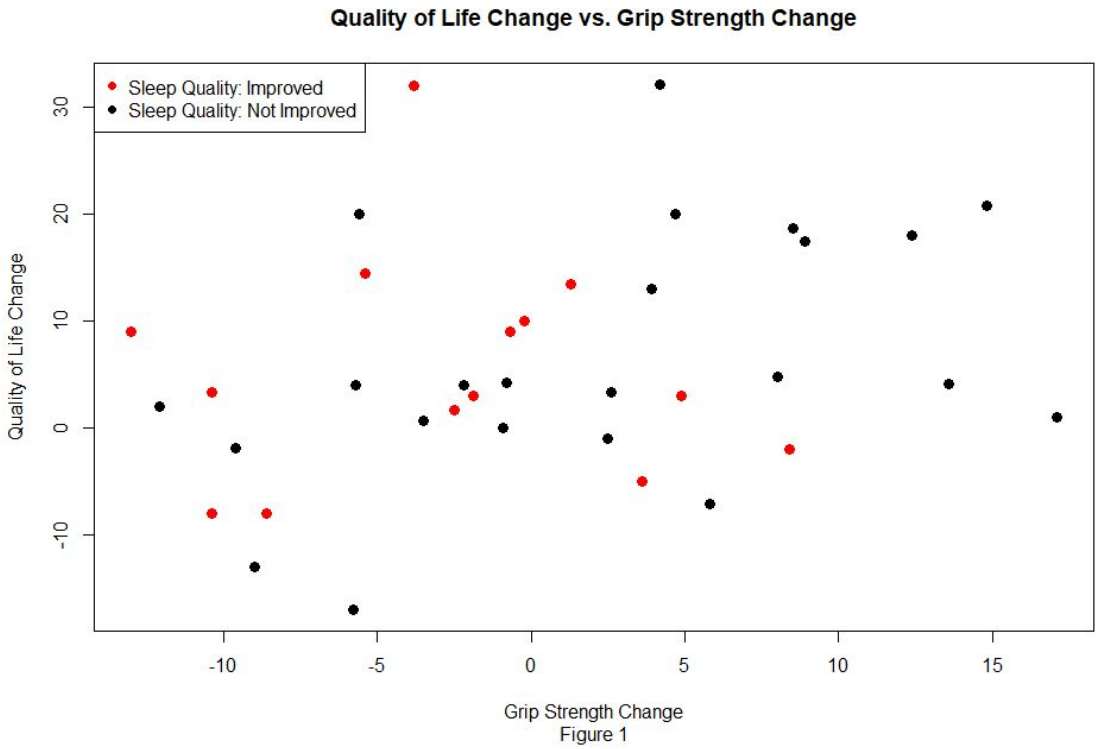

Figure 1

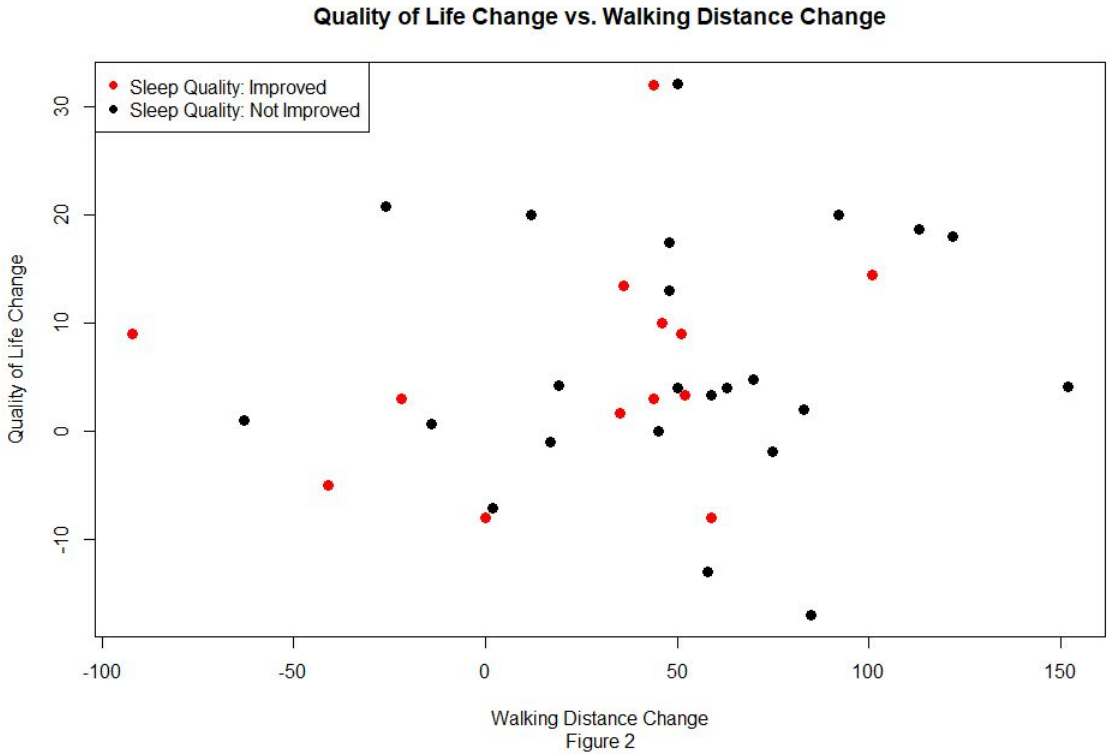

Figure 2

Visual inspection does not indicate a relationship between either predictor and quality of life. It also does not appear that sleep quality improvement moderates the impact of exercise on quality of life. The figures show that quality of life does appear to improve as the majority of individuals change in quality of life is greater than 0. However the primary aim of the study is to investigate the interaction between exercise and sleep quality on quality of life, not the change in quality of life itself.

Methods/Analysis

The first goal of this analysis was to determine whether sleep quality improves following physical activity intervention. The Wilcoxon Signed-Rank test was used on the pre/post responses to the three main survey questions related to sleep quality - (i) Do you awaken feeling rested?, (ii) How often do you wake up during the night?, and (iii) During the past 4 weeks, how would you rate your sleep overall?, which have numerical ratings indicating sleep quality. See Table 4 for the distributions of the levels for these variables. The Wilcoxon Signed-Rank test was used rather than a paired t-test due to non-normality of the response variables, which was verified via the Shapiro-Wilk test. See the Appendix for R output from the Shapiro-Wilk test.

The second goal of this analysis was to determine if the effect of exercise on quality of life and/or fatigue was moderated by sleep quality. The method used to analyze this interaction included fitting four primary linear regression models. In order to fit these models, the change (post - pre) in quality of life, fatigue, grip strength, and feet walked in 6 minutes was calculated. A binary variable for whether or not sleep quality improved was also calculated.

The assumption of the method used was that the data are normally distributed. To check this assumption quantile-quantile (QQ) plots were examined. A QQ plot indicates normality when the points follow a straight line. As can be seen in figures 3 and 4 below the data follows an approximately normal distribution.

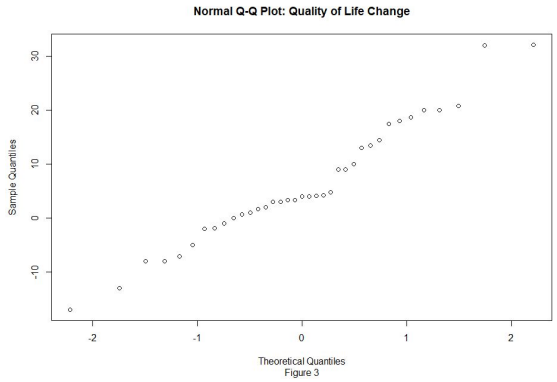

Figure 3

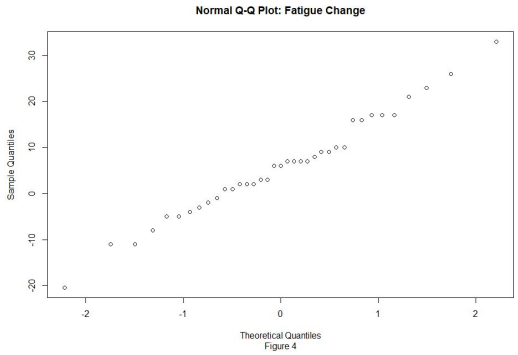

Figure 4

Two models were then fit with the change in quality of life as the response variable. The change in grip strength and binary variable for improved sleep quality as well as the interaction of these two variables were the main predictors. Two additional models were fit with the change in fatigue used as the response variable but the same predictors. The inclusion of additional covariates was tested using stepwise model selection based on AIC. Both forward and backward model selections were tested. The covariates tested were age, gender, race, cancer diagnosis, and the change in sleep habits (post - pre).

Results

The Wilcoxon Signed-Rank test results in a failure to reject the null hypothesis (the median difference (pre-post) = 0) at the α = 0.05 significance level for each of the three sleep quality variables, suggesting no significant sleep improvement in sleep quality following physical activity intervention. R output from the tests is available in the Appendix.

Table 5: Wilcoxon Signed-Rank test for sleep improvement

Variable	$Null\ Hypothesis\ (H_0)$	$Alternative\ Hypothesis\ (H_\alpha)$	Alpha Level	Conclusion
Do you awaken feeling rested?	Median difference (pre-post) = 0	Median difference (pre-post) is > 0	0.05	$Fail\ to\ reject\ H_0$
How often do you wake up during the night?	Median difference (pre-post) = 0	Median difference (pre-post) is > 0	0.05	$Fail\ to\ reject\ H_0$
During the past 4 weeks, how would you rate your sleep overall?	Median difference (pre-post) = 0	Median difference (pre-post) is < 0	0.05	$Fail\ to\ reject\ H_0$

The four primary models discussed previously indicate no interaction between exercise and change in sleep quality. In fact, the only model with results indicating a significant association was the model with grip strength and change in sleep quality as the predictors and quality of life as the response. The significant p-value for grip strength in this model indicates a linear relationship between change in grip strength and change in quality of life. Grip strength returned a coefficient of 0.62 meaning that for every 1 unit increase in grip strength quality of life increased by 0.62 points. However, the variable for sleep quality improvement and the interaction between sleep quality and grip strength did not prove to be significant. The R^2 in this model was 0.13 indicating that only 13% of variation in quality of life can be explained by the predictors. Each of the successive models described in the methods section had a lower R^2 and no indication of linear association.

While no interaction was found between sleep quality and exercise, the small sample size is a limiting factor and indicates a need for further research and analysis. While the number of total participants would normally be sufficient, the lack of pre and post program data for the majority of the participants necessitates a small sample size for the questions of interest. The results of this analysis certainly could and should be either strengthened or changed based on a larger and more inclusive sample.

Author Statement

Both authors contributed to statistical analysis and writing for this report. Both authors read and approved the final report. Taylor Stuart and Kyle Kirkpatrick both performed initial analysis independently and then confirmed results collaboratively. Kyle focused his final analysis and writing on aim 1 while Taylor focused on aim 2. Taylor and Kyle divided up the remaining portions of the paper including the abstract, introduction, and summary statistics.

Appendix A - Data Input

```
library(readxl)
library(dplyr)

# read in data
d <- read_xlsx(file.choose(), na = "NV")
colnames(d) <- tolower(colnames(d))

# subset columns
cols <- c("age","gender","race","raceother","ethnicity","curr_cancer_diag",
          "curr_chemo", "curr_rad","curr_surg", "curr_other",
          "gp7total", "gp7total_2", "gs7total",
          "ge6total", "ge6total_2", "gf7total", "gf7total_2",
          "fact-g total", "fact_g total_2", "gfat_total",
          "gfat_total_2", "gripst_dom", "gripst_dom_2",
          "gripst_ndom", "gripst_ndom_2", "smwt_dist", "smwt_dist_2",
          "wr_sl2", "wr_sl2_2", "wr_sl4", "wr_sl4_2", "wr_sl7",
          "wr_sl7_2", "sleephabits_total", "sleephabits_total_2")

# remove last two rows (they had cell comments)
d <- d[1:(nrow(d)-2),cols]
d <- d[!is.na(d$sleephabits_total) & !is.na(d$sleephabits_total_2),]

# convert to numeric - was cast as string on import
d$gripst_dom <- as.numeric(d$gripst_dom)

# Convert demographic variables to factors
d$race <- factor(d$race, levels = 1:7, labels = c("American Indian/Alaska Native",
"Asian",
                                  "Black or African American",
                                  "Native Hawaiian or Other Pacific Islander",
                                  "White", "Mixed Race", "Other Race"))

d$ethnicity <- factor(d$ethnicity, levels = 1:2, labels = c("Hispanic or Latino",
                                                  "Not Hispanic or Latino"))
```

```
d$curr_cancer_diag <- factor(d$curr_cancer_diag, levels = 1:11,
                             labels = c("Breast", "Prostate", "Colorectal", "Lung",
                                        "Ovarian", "Blood/Heme", "Head and Neck",
                                        "Brain", "Esophageal", "Pancreatic", "Other"))

d$gender <- factor(d$gender, levels = 1:2, labels = c("Female", "Male"))
d$curr_chemo <- factor(d$curr_chemo, levels = 0:1, labels = c("No", "Yes"))
d$curr_rad <- factor(d$curr_rad, levels = 0:1, labels = c("No", "Yes"))
d$curr_surg <- factor(d$curr_surg, levels = 0:1, labels = c("No", "Yes"))
d$curr_other <- factor(d$curr_other, levels = 0:1, labels = c("No", "Yes"))
d$curr_cancer_diag2 <- as.factor(ifelse(d$curr_cancer_diag == "Breast", "Breast",
"Other"))
```

Appendix B - Aim 1

```
# pre/post Shapiro-Wilk test
# "Do you awaken feeling rested?"
shapiro.test(d$wr_sl2)
shapiro.test(d$wr_sl2_2)

# pre/post Shapiro-Wilk test
# "How often do you wake up during the night?"
shapiro.test(d$wr_sl4)
shapiro.test(d$wr_sl4_2)

# pre/post Shapiro-Wilk test
# "During the past 4 weeks, how would you rate your sleep overall?"
shapiro.test(d$wr_sl7)
shapiro.test(d$wr_sl7_2)



# Wilcoxon Signed-Rank Test - Test for improved sleep quality
wilcox.test(d$wr_sl2, d$wr_sl2_2, paired = TRUE, alternative = "greater", exact =
FALSE, correct = TRUE, conf.int = TRUE)
wilcox.test(d$wr_sl4, d$wr_sl4_2, paired = TRUE, alternative = "greater", exact =
FALSE, correct = TRUE, conf.int = TRUE)
```

```
wilcox.test(d$wr_sl7, d$wr_sl7_2, paired = TRUE, alternative = "less", exact = FALSE,
            correct = TRUE, conf.int = TRUE)
```

Appendix C - Aim 2

```
##Calculate Variables
d$qol_change = d$`fact_g total_2` - d$`fact-g total`
d$fatigue_change = d$gfat_total_2 - d$gfat_total
d$gripst_change = d$gripst_dom_2 - d$gripst_dom
d$smwt_change = d$smwt_dist_2 - d$smwt_dist
d$imp_slp_qual = ifelse(d$wr_sl7_2 > d$wr_sl7, "1", "0")
d$imp_slp_qual = as.factor(d$imp_slp_qual)
d$sleephabits_diff = d$sleephabits_total_2 - d$sleephabits_total


##Visualize
plot(d$gripst_change, d$qol_change, col = as.factor(d$imp_slp_qual), pch=19, cex =
1.2, main = "Quality of Life Change vs. Grip Strength Change", xlab="Grip Strength
Change", ylab = "Quality of Life Change", sub = "Figure 1")
legend('topleft', pch = 19, legend = c("Sleep Quality: Improved", "Sleep Quality: Not
Improved"), col = c(2,1))
plot(d$smwt_change, d$qol_change, col = as.factor(d$imp_slp_qual), pch=19, cex =
1.2, main = "Quality of Life Change vs. Walking Distance Change", xlab="Walking
Distance Change", ylab = "Quality of Life Change", sub = "Figure 2")
legend('topleft', pch = 19, legend = c("Sleep Quality: Improved", "Sleep Quality: Not
Improved"), col = c(2,1))
boxplot(d$qol_change ~ d$imp_slp_qual)




## linear Regression
qqnorm(d$qol_change)
qqnorm(d$fatigue_change)

## QOL on Grip and sleep
mod = lm(qol_change ~ gripst_change * imp_slp_qual, data = d, na.action = na.fail)
```

```
summary(mod)

mod2 = lm(qol_change ~ gripst_change * imp_slp_qual
        + age + gender + race + curr_cancer_diag2 + sleephabits_diff, data = d, na.action
= na.fail)

summary(step(mod, mod2, direction = 'forward'))
summary(step(mod, mod2, direction = 'backward'))


## QOL on walking and sleep
mod = lm(qol_change ~ smwt_change * imp_slp_qual, data = d)
summary(mod)

mod2 = lm(qol_change ~ smwt_change * imp_slp_qual
        + age + gender + race + curr_cancer_diag2 + sleephabits_diff, data = d)

step(mod, mod2, direction = 'forward')
step(mod, mod2, direction = 'backward')


## fatigue on Grip and sleep
mod = lm(fatigue_change ~ gripst_change * imp_slp_qual, data = d)
summary(mod)


mod2 = lm(fatigue_change ~ gripst_change * imp_slp_qual
        + age + gender + race + curr_cancer_diag2 + sleephabits_diff, data = d)
summary(mod2)

step(mod, mod2, direction = 'forward')
step(mod2, mod, direction = 'backward')

## fatigue on walking and sleep
mod = lm(fatigue_change ~ smwt_change * imp_slp_qual, data = d)
summary(mod)


mod2 = lm(fatigue_change ~ gripst_change * imp_slp_qual
```

```
        + age + gender + race + curr_cancer_diag2 + sleephabits_diff, data = d)
summary(mod2)

step(mod, mod2, direction = 'forward')
step(mod2, mod, direction = 'backward')
```

Appendix D - Output

Aim 1 Shapiro-Wilk test - All variable tests indicate non-normality

```
> # pre/post Shapiro-Wilk test
> # "Do you awaken feeling rested?"
> shapiro.test(d$wr_sl2)

        Shapiro-Wilk normality test

data:  d$wr_sl2
W = 0.63719, p-value = 2.479e-08

> shapiro.test(d$wr_sl2_2)

        Shapiro-Wilk normality test

data:  d$wr_sl2_2
W = 0.63719, p-value = 2.479e-08

>
> # pre/post Shapiro-Wilk test
> # "How often do you wake up during the night?"
> shapiro.test(d$wr_sl4)

        Shapiro-Wilk normality test

data:  d$wr_sl4
W = 0.89188, p-value = 0.001767

> shapiro.test(d$wr_sl4_2)

        Shapiro-Wilk normality test

data:  d$wr_sl4_2
W = 0.83529, p-value = 7.269e-05

>
> # pre/post Shapiro-Wilk test
> # "During the past 4 weeks, how would you rate your sleep overall?"
> shapiro.test(d$wr_sl7)

        Shapiro-Wilk normality test

data:  d$wr_sl7
W = 0.90666, p-value = 0.004538

> shapiro.test(d$wr_sl7_2)

        Shapiro-Wilk normality test

data:  d$wr_sl7_2
W = 0.8922, p-value = 0.001802
```

Aim 1 Wilcoxon-Signed Rank tests - suggest no improvement pre/post program

```
> # Wilcoxon Signed-Rank Test - Test for improved sleep quality
> wilcox.test(d$wr_sl2, d$wr_sl2_2, paired = TRUE, alternative = "greater", exact = FALSE,
orrect = TRUE, conf.int = TRUE)

        Wilcoxon signed rank test with continuity correction

data:  d$wr_sl2 and d$wr_sl2_2
V = 27.5, p-value = 0.5229
alternative hypothesis: true location shift is greater than 0
95 percent confidence interval:
 -0.9999486        Inf
sample estimates:
(pseudo)median
             0

> wilcox.test(d$wr_sl4, d$wr_sl4_2, paired = TRUE, alternative = "greater", exact = FALSE,
orrect = TRUE, conf.int = TRUE)

        Wilcoxon signed rank test with continuity correction

data:  d$wr_sl4 and d$wr_sl4_2
V = 64.5, p-value = 0.5835
alternative hypothesis: true location shift is greater than 0
95 percent confidence interval:
 -0.9999653        Inf
sample estimates:
(pseudo)median
             0

> wilcox.test(d$wr_sl7, d$wr_sl7_2, paired = TRUE, alternative = "less", exact = FALSE,
+             correct = TRUE, conf.int = TRUE)

        Wilcoxon signed rank test with continuity correction

data:  d$wr_sl7 and d$wr_sl7_2
V = 150, p-value = 0.3584
alternative hypothesis: true location shift is less than 0
95 percent confidence interval:
         -Inf 3.162504e-06
sample estimates:
(pseudo)median
 -2.240679e-05
```

Aim 2

Example output from linear model testing. Only significant variable in this model is grip strength change. All other models had no significant predictors.

```
Call:
lm(formula = qol_change ~ gripst_change * imp_slp_qual, data = d,
    na.action = na.fail)

Residuals:
     Min       1Q   Median       3Q      Max
-18.4248  -7.2083  -0.8927   5.5201  26.5510

Coefficients:
                           Estimate Std. Error t value Pr(>|t|)
(Intercept)                  5.0454     2.3701   2.129   0.0408 *
gripst_change                0.6242     0.2839   2.199   0.0350 *
imp_slp_qual1                0.3286     3.9938   0.082   0.9349
gripst_change:imp_slp_qual1 -0.6440     0.5595  -1.151   0.2580
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 10.95 on 33 degrees of freedom
Multiple R-squared:  0.1296,    Adjusted R-squared:  0.05042
F-statistic: 1.637 on 3 and 33 DF,  p-value: 0.1996
```

References

Agresti, Alan; 2013, Categorical Data Analysis, Third Edition

Herring, Matthew; Monroe, Derek; Kline, Christopher E; O'Connor, Patrick J.; MacDonncha, Ciaran; 2018, Sleep quality moderates the association between physical activity frequency and feelings of energy and fatigue in adolescents, Springer-Verlag GmbH Germany

Higgins, James J; 2004, An Introduction to Modern Nonparametric Statistics

Liu , Wen Liu; Schaffer Lauren; Herrs, Natalie; Chollet, Christine; Taylor, Sarah, 2015, Improved sleep after Qigong exercise in breast cancer survivors: A pilot study, University of Kansas Medical Center

National Cancer Institute, 2018, Cancer Statistics, www.cancer.gov