Predicting Quality of Life Improvement During Rural Obesity Trial

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Introduction

Lack of access to medical facilities is one of many of the issues faced by rural populations in healthcare. Doctors' offices are often too far from rural patients' residences to maintain regular visits for effective treatment. As a consequence of this barrier, obesity has been shown to have higher prevalence in rural areas than urban areas. To address this issue in rural Kansas, The University of Kansas Medical Center conducted a cluster randomized clinical trial for rural obesity treatment, called the RE-POWER study [1, 2].

There were three treatments in this study. The Fee-for-Service (FFS) model, characterized by in-clinic individual treatment, is the current standard of care and was considered as the control for this study [3, 4]. The two treatments of interest, Patient Centered Medical Home (PCMH) and Disease Management (DM), are two strategies that were predicted to improve weight loss for rural patients [4, 5, 6]. PCMH is an in-clinic group treatment, while DM utilizes group therapy over the phone with a licensed professional.

To simplify the logistics of administering treatment, randomization occurred at the clinic level rather than the patient level. Randomization was stratified based on clinic size across treatment arms to remove any potential confounding.

The study consisted of two major phases. The initial 0-6 months focused on weight loss treatment, with regular meetings and intervention. This was followed by months 7-24 consisting of maintenance meetings to assess whether weight loss and quality of life were maintained post-intensive treatment.

The goal of the primary analysis for the RE-POWER study was to determine what factors, including treatment, were most effective for weight loss [1, 2]. Building from this, the research aim for our analysis was to determine which factors predict baseline quality of life and change in quality of life during weight loss treatment, as we know this is a factor in weight loss.

Methods

Variables

The original dataset contains over 100 variables. For the purposes of this study, we utilized or created the following variables of interest.

Study Design Variables

Site is the clinic at which patient care was housed, which was stratified across treatment arms by size. Sites were assigned a number from 1 to 80.

Affiliation, the stratification variable, refers to the medical center overseeing the site. The three oversight locations were KUMC, UNMC, and Marshfield Clinic. The majority of sites (58.4%) were overseen by KUMC, 28.3% by Marshfield Clinic, and 13.4% by UNMC.

Treatment arm indicates which of the three treatments (FFS, PCMH, and DM) a patient was assigned to. The values of this variable were in-person individual, in-person group, and phone group.

Demographic Predictors

Age refers to the age (in years) of the patient at the beginning of the study. The minimum age of the cohort was 21 and the maximum age was 75.

Sex was recorded for each patient. These data only contain patients of male or female sex. There were 1081 females (76.8%) and 326 males (23.2%) in the study.

Rurality was categorized into three levels: large rural, small rural, and isolated rural. 659 (46.8%) of the enrolled patients were classified as Isolated Rural, 250 (17.8%) as Small Rural, and 498 (35.4%) as Large Rural.

Health Predictors

BMI (body mass index) was calculated for each patient at the beginning of the study according to the following formula: $(weight(kg)_0 * 2.20462/height^2) * 703$.

Percent weight change was calculated for each patient at each follow-up time point as follows: $100 * ((weight_t - weight_0)/weight_0)$.

Mental Health Disorder(s) was a variable we defined as the presence (1) or absence (0) of one or more recorded mental health disorders. The three variables from the dataset we used to create this proxy variable were depression, anxiety, and other mental health disorder.

Comorbidities (2+) was another proxy variable defined by our group. Any patient with a history of 2 or comorbidities was designated as a 1, otherwise they were designated as a 0. The comorbidities considered were: high cholesterol, asthma, respiratory condition(s), ulcerative colitis or Crohn's, hip and/or knee replacement, gallbladder disease or gallstone, heart failure, angina, stroke, cludication or peripheral arterial disease, arthritis, hyperthyroidism, hypothyroidism, hypertension, diabetes, cancer, and problems with muscles, bones, or joints that cause pain preventing walking for at least 20 minutes.

Outcomes

Our outcome of interest for this study was the Impact of Weight on Quality of Life-Lite (IWQOL-L) survey score. The survey consisted of 31 questions on scale of 1-5 (1=Always, 2=Usually, 3=Sometimes, 4=Rarely, 5=Never). There were 5 subcategories of the IWQOL survey: physical function, self-esteem, sexual life, public distress, and work. Raw scores for each category were summed and scaled by the number of questions for the given category. The total IWQOL score was then computed by summing the scores for each category, and had range from 0-100 in order of increasing quality of life. The IWQOL survey was given to patients at 0 months, 6 months, and 24 months.

We also created the variables iwqol_delta_0to6 and iwqol_delta_0to24, representing the change in IWQOL total score from 0 to 6 months and 0 to 24 months respectively. Each variable was calculated by taking the difference of IWQOL total score at the final timepoint and the IWQOL total score at 0 months.

The three outcomes that we considered were 1) IWQOL at baseline (0 months), 2) change in IWQOL after the intensive treatment period (6 months), and 3) change in IWQOL at the end of the study (24 months).

We aimed to determine whether baseline demographic factors (gender, age, rurality category) and health factors (percent weight loss, BMI, depression/mental health disorders, and having 2 or more comorbidities) differentially impacted the change in quality of life during this weight loss study.

Modeling

To account for correlations between patients at the same site and clinic stratification across treatment arms, we used mixed modeling. Affiliation was treated as a fixed effect, while site was designated at a random effect.

We first fit univariate linear regression models for IWQOL using the demographic and health predictors of interest. All variables with univariate p-value < 0.1 were considered for the multiple linear models. From the full models, we then utilized a manual backwards selection strategy, removing variables with least significance one-at-a-time until all variables remaining in the models had p-value < 0.05. Based on the final reduced models, variance inflation factors were assessed to ensure the absence of multicollinearity (VIF < 5), and then estimates for the beta coefficients and 95% confidence intervals were calculated.

Results

0 Months

We first fit the univariate linear models for IWQOL total score at baseline with each of the predictors, treating affiliation as a fixed effect and site as a random effect.

Table 1: Univariate Table - 0 Months

Variable	p-value
Affliation	0.048
Treatment Arm	0.064
Age	0.003
Sex	0.000
Rurality	0.068
BMI	0.000
Mental Health Disorder(s)	0.000
Comorbidities (2+)	0.005

All variables were found to be significantly associated with IWQOL total ($p < 0.1$), so all were considered for the full multiple linear model.

Table 2: Full Model - 0 Months

Variable	Sum Sq	Mean Sq	Num DF	Den DF	F value	Pr(>F)
Affliation	1208	604	2	30.8	2.44	0.104
Treatment Arm	1503	751	2	28.2	3.03	0.064
Age	261	261	1	1388.4	1.05	0.305
Sex	10670	10670	1	1105.6	43.04	0.000
Rurality	1904	952	2	151.2	3.84	0.024
BMI	43058	43058	1	1388.7	173.70	0.000
Mental Health Disorder(s)	25583	25583	1	1393.5	103.20	0.000
Comorbidities (2+)	972	972	1	1394.7	3.92	0.048

The full model was then trimmed down by removing the variable with largest p-value (if $p > 0.05$) and fitting a new model to the remaining variables. This process was repeated until all variables remaining had $p < 0.05$. The intermediate models are omitted for brevity. To summarize, the variables removed were age ($p = 0.305$), comorbidities ($p = 0.090$), affiliation ($p = 0.118$), and treatment arm ($p = 0.105$).

The final model is given below.

Table 3: Final Model - 0 Months

Variable	Sum Sq	Mean Sq	Num DF	Den DF	F value	Pr(>F)
Sex	10750	10750	1	1136	43.33	0.000
Rurality	2141	1071	2	182	4.32	0.015
BMI	46874	46874	1	1393	188.93	0.000
Mental Health Disorder(s)	27954	27954	1	1401	112.67	0.000

To ensure the absence of multicollinearity, we assessed the variance inflation factors for each of the variables. Rurality is a categorical variable with 3 levels, so generalized variance inflation factor (GVIF) was needed.

Table 4: Variance Inflation Factors for the Final Model - 0 Months

Variable	GVIF	DF	GVIF^(1/(2*DF))
Sex	1.04	1	1.02
Rurality	1.00	2	1.00
BMI	1.00	1	1.00
Mental Health Disorder(s)	1.03	1	1.02

No variance inflation factors were greater than 5, so we concluded that multicollinearity is not present in our model.

We then calculated estimates and 95% confidence intervals for the final model.

Table 5: Estimates and 95% Confidence Intervals - 0 Months

Variable	Estimate	95 Percent Confidence Interval
Intercept	122.119	[114.32, 130.07]
Male	6.934	[4.88, 9]
Large Rural	3.040	[0.88, 5.19]
Small Rural	-0.052	[-2.64, 2.53]
BMI	-1.473	[-1.68, -1.26]
Mental Health Disorder(s)	-9.199	[-10.92, -7.51]

The average baseline IWQOL total score for males was about 7 points higher than for females. Similarly, the average IWQOL total score for patients with at least one mental health disorder was about 9 points lower than for patients without a mental health disorder. For a one-unit increase in BMI, baseline IWQOL score decreased by about 1.5 points. Finally, relative to patients living in areas classified as isolated rural, those in large rural areas had baseline IWQOL score about 3 points higher. There was no difference in IWQOL score between isolated rural areas and small rural areas.

6 Months

For the 6 month timepoint, we shifted to assessing change in IWQOL total score from baseline. We again fit univariate linear models, now including percent weight change as a predictor. As before, we treated affiliation as a fixed effect and site as a random effect.

Table 6: Univariate Table - 6 Months

Variable	p-value
Affliation	0.124
Treatment Arm	0.769
Age	0.006
Sex	0.008
Rurality	0.372
BMI	0.130
Mental Health Disorder(s)	0.084
Comorbidities (2+)	0.137
Percent Weight Change	0.000

In this case, only age, sex, mental health disorder(s), and percent weight change were significantly associated with change in IWQOL total ($p < 0.1$). Only these four variables were considered for the full model.

Table 7: Full Model - 6 Months

Variable	Sum Sq	Mean Sq	Num DF	Den DF	F value	Pr(>F)
Age	297	297	1	1249	1.85	0.174
Sex	1980	1980	1	1249	12.35	0.000
Mental Health Disorder(s)	1832	1832	1	1249	11.43	0.001
Percent Weight Change	30227	30227	1	1249	188.62	0.000

Age was removed from the model ($p = 0.174$), resulting in the reduced model below.

Table 8: Final Model - 6 Months

Variable	Sum Sq	Mean Sq	Num DF	Den DF	F value	Pr(>F)
Sex	1819	1819	1	1250	11.3	0.001
Mental Health Disorder(s)	1723	1723	1	1250	10.7	0.001
Percent Weight Change	31523	31523	1	1250	196.6	0.000

Variance inflation factors were calculated for these three variables. None of the variables were categorical with 3 or more levels, so GVIF was not necessary.

Table 9: Variance Inflation Factors for the Final Model - 6 Months

Variable	VIF
Sex	1.03
Mental Health Disorder(s)	1.04
Percent Weight Change	1.01

None of the variance inflation factors were concerning ($VIF < 5$), so we concluded that our model was free of multicollinearity. We then generated estimates based on this model.

Table 10: Estimates and 95% Confidence Intervals - 6 Months

Variable	Estimate	95 Percent Confidence Interval
Intercept	5.459	[4.06, 6.86]
Male	-2.922	[-4.62, -1.22]
Mental Health Disorder(s)	2.403	[0.97, 3.84]
Percent Weight Change	-0.765	[-0.87, -0.66]

The average change in IWQOL total score for males was ~2.9 points lower than for females. Meaning, the change in IWQOL for females was ~2.9 points higher than for males. Since the females had a lower initial IWQOL, we believe this makes sense, as females had more room to improve.

Similarly, the average change in IWQOL total score for patients with at least one mental health disorder was ~2.4 points higher than for patients without a mental health disorder. We make a similar observation relative to the baseline: patients with mental health disorders had a lower baseline IWQOL, and thus more room to improve.

For a one-unit decrease in percent weight change (indicating weight loss), change in IWQOL score increased by ~0.8 points. This indicates that weight loss improves quality of life, as expected.

24 Months

We again assessed the change in IWQOL total score from baseline, this time at 24 months. We fit univariate linear models with the same predictors as before. We again treated affiliation as a fixed effect and site as a random effect.

Table 11: Univariate Table - 24 Months

Variable	p-value
Affliation	0.502
Treatment Arm	0.965
Age	0.041
Sex	0.032
Rurality	0.488
BMI	0.220
Mental Health Disorder(s)	0.091
Comorbidities (2+)	0.336
Percent Weight Change	0.000

Similar to the 6 month timepoint, age, sex, mental health disorder(s), and percent weight change were significantly associated with change in IWQOL total ($p < 0.1$). These four variables were considered for the full model, given below.

Table 12: Full Model - 24 Months

Variable	Sum Sq	Mean Sq	Num DF	Den DF	F value	Pr(>F)
Age	22.2	22.2	1	1032	0.115	0.734
Sex	1595.9	1595.9	1	907	8.260	0.004
Mental Health Disorder(s)	1284.9	1284.9	1	1160	6.650	0.010
Percent Weight Change	38649.1	38649.1	1	1162	200.035	0.000

Again, age was removed from the model ($p = 0.734$), leaving sex, mental health disorder(s), and percent weight change in the final model.

Table 13: Final Model - 24 Months

Variable	Sum Sq	Mean Sq	Num DF	Den DF	F value	Pr(>F)
Sex	1576	1576	1	829	8.16	0.004
Mental Health Disorder(s)	1266	1266	1	1161	6.56	0.011
Percent Weight Change	40008	40008	1	1165	207.18	0.000

Variance inflation factors were assessed for these three variables in the 24 month final model.

Table 14: Variance Inflation Factors for the Final Model - 24 Months

Variable	VIF
Sex	1.04
Mental Health Disorder(s)	1.04
Percent Weight Change	1.01

No concerning variance inflation was present, so we proceeded to generate estimates for the model.

Table 15: Estimates and 95% Confidence Intervals - 24 Months

Variable	Estimate	95 Percent Confidence Interval
Intercept	8.274	[6.97, 9.58]
Male	-2.826	[-4.76, -0.89]
Mental Health Disorder(s)	2.130	[0.5, 3.76]
Percent Weight Change	-0.684	[-0.78, -0.59]

Resembling to our results at 6 months, the average change in IWQOL total score for males was ~2.8 points lower than for females. Meaning, the change in IWQOL for females was ~2.8 points higher than for males. The average change in IWQOL total score for patients with at least one mental health disorder was ~2.1 points higher than for patients without a mental health disorder. For a one-unit decrease in percent weight change, change in IWQOL score increased by ~0.7 points. As with the 6 month results, weight loss improved quality of life. Women and patients with mental health disorders had more room for improvement in quality of life and did in fact have a larger change over the course of the study.

Discussion and Conclusion

Many social determinants of health and medical conditions were found to be associated with quality of life at the beginning of the study. Whenever considered together, however, a few key predictors emerge. Sex, rurality category, BMI, and mental health disorder status have differential impacts on initial quality of life.

When considering how quality of life improves over the course of the weight loss study, fewer conditions and demographic variables have significant associations. For both the 6 month and 24 month timepoints, we again see sex, mental health disorder status, and the relevant weight-related variable (percent weight change) as key predictors for quality of life improvement.

Utilizing these results, we are able to better understand and predict how effective weight loss clinical trials will be for obesity patients in rural Kansas. Women and patients with mental health disorders have more quality of life to gain from participating in these weight loss clinical trials.

In future work, we plan to conduct analyses using the five IWQOL subcategories as outcomes to determine which areas improved the most during the course of the study. We also want to determine whether baseline quality of life affects percent weight change. To do this, we will fit logistic regression models to the clinically significant thresholds of 5% and 10% weight loss.

Reflection

While working on this project, I experienced handling longitudinal data and mixed modeling for the first time. Dr Brown's experience with coding and mixed modeling is in SAS, but my expertise is in R. Through this experience, we got the chance to work together to understand and apply the lmer package to conduct mixed modeling in R.

I also learned about different strategies for model selection. In this study we chose to employ a manual backward selection strategy, since automated stepwise selection methods have not worked very well in Dr. Brown's experience with mixed modeling. Best subsets could have been a good method to use, but neither Dr. Brown nor I were aware of a package in R that could perform best subsets analysis on mixed models. We plan to conduct a confirmatory best subsets analysis in SAS.

Finally (and arguably most importantly), this semester I learned that the term "multivariate" does not mean multiple predictors, but multiple outcomes. I had no idea that multivariate regression had a separate meaning from multiple regression, and since learning this have caught several mistaken uses of the terms. Although we did have the option to conduct multivariate analysis due to the longitudinal nature of the study, we chose to analyze the timepoints separately to get more specific information about the progression of quality of life.

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