Investigation of a Pregnancy Lifestyle Intervention Using Mediation Analysis and a Power Analysis Simulation

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by

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Abstract

In this report, we attempt to assess how a behavioral intervention on pregnant women achieved its success with regard to specific weight gain and weight loss outcomes. The study established the significance of the intervention in limiting gestational weight gain and promoting the return to pre-pregnancy weight, but the way in which the intervention was successful has yet to be explored. We explain how mediation analysis can be used to investigate certain variables, and introduce the methods necessary for conducting such analysis. We proceed to apply these techniques to various behavior variables as well as perform a power analysis simulation to better understand the relationship between true mediated effect size, sample size, and power to detect the mediated effect.

1 Introduction

We will begin by giving some background on the study and its main results. We will then explain how we arrived at mediation analysis and what we hope to answer with this type of analysis.

1.1 The Study

The *Fit for Delivery* study was a randomized trial on pregnant women with around 400 initial participants (Phelan et al., 2011). Its aims were to assess the effectiveness of a lifestyle intervention on pregnancy weight gain and postpartum weight loss of the participants. Participants in the study were classified into one of two weight groups: Normal Weight, or Overweight/Obese, according to their pre-pregnancy Body Mass Index (BMI) which was calculated from their height and self-reported pre-pregnancy weight. The women were randomly assigned to a lifestyle intervention or standard pregnancy care within weight group and clinic site. This lifestyle intervention was administered during pregnancy and included extra nutrition information, phone calls from a nutritionist, and personalized weight graphs.

Specifically, the study investigated whether the treatment group was more successful at staying within their weight gain guidelines, and whether those women who received the treatment during pregnancy were more successful at returning to their pre-pregnancy weights by six months postpartum. Several covariates were included in all models: age, race, log of weeks gestation at delivery, multiparity, weight group, and clinic site.

Multiple logistic regression models were run to evaluate the treatment effect on each outcome of interest. Those receiving the lifestyle intervention were significantly more likely to stay within weight gain guidelines for the Normal Weight group, but not for women in the Overweight group. Those having received the lifestyle intervention during pregnancy were significantly more likely to return to their pre-pregnancy weight by six months postpartum than those having received standard pregnancy care, for both the Normal Weight and Overweight groups.

1.2 Arriving at a Method of Analysis

Initially, multivariate analysis was conducted on the data. Since the original study focused solely on the women's weights at delivery and at 6 months postpartum, we decided to conduct analysis on the full weight profiles. This also included weight measurements at study entry, at 30 weeks gestation, at 6 weeks postpartum, and at 12 months postpartum. We then conducted profile analysis to compare the weight trajectories between treatment and control groups, accounting for the same covariates as in the original study. We had insufficient evidence to conclude that the weight profiles are not parallel between treatment and control groups for either the Normal Weight group or the Overweight/Obese group (See Appendix Section 2 for more details).

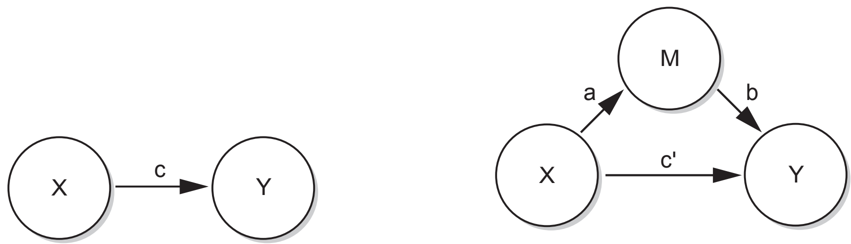
After investigating the data with multivariate analysis, we began reconsidering the original study. While the study yielded some information on the success of the treatment, we still did not know how the treatment achieved its success. Given that the treatment was a lifestyle intervention, in which change can only take place through behavior changes in the women, it seems reasonable to ask whether any of the measured behavior changes played a role in their success. Specifically, we ask whether the women receiving the treatment changed certain behaviors. And furthermore, do we have evidence to suggest that these behaviors were associated with their success?

We found mediation analysis to be a useful method in this investigation of the behavior variables. Mediation analysis allows us to investigate intermediate variables through which some of the effect from an independent variable to a dependent variable may be taking place. Regarding the study, our independent variable is the lifestyle intervention. For the weight gain outcome of the study, we have exceeding weight gain guidelines, and for the weight loss outcome, we have returning to pre-pregnancy weight by six months postpartum as our dependent variable.

2 Mediation Analysis

Mediation analysis allows us to better explain the causal process from an independent variable to a dependent variable by investigating intermediate variables through which some of the effect may be taking place. We will refer to the independent variable as X and the dependent variable as Y. It may be the case that part of the effect from X to Y is transmitted through an intermediate variable, call it M. If a significant part of the relationship between X and Y happens through M, we say that M *mediates* the relationship between X and Y, and so we call M a *mediator*. Mediation analysis involves breaking down the total effect of X on Y into an indirect effect, the effect of X on Y through M, and a direct effect, the remaining effect of X on Y uninfluenced by M.

We can also think about these effects as paths, in which we start out with a significant relationship between X and Y, but with further investigation, find that we can better explain the relationship in terms of two paths, one via the mediator, and one from X directly to Y.



(a) Significant relationship between X and Y

(b) Two paths from X to Y: One via the mediator (indirect effect) and the remaining effect of X on Y (direct effect)

Figure 1: Path diagrams for mediation analysis

Figure 1 provides a visual representation of the relationships between variables. We now introduce the three models which contain the information on these relationships:

$$
\begin{aligned}
Y &= i_1 + cX + \epsilon_1 \\
Y &= i_2 + c'X + bM + \epsilon_2 \\
M &= i_3 + aX + \epsilon_3
\end{aligned}
$$

Naturally, we need a way to quantify the impact of a mediator, or *mediated effect*.

Many methods have been suggested to gauge the mediated effect, though some are more suitable than others, depending on the complexity of the models.

2.1 Estimators of the Mediated Effect

In the simple case where the dependent variable is continuous, there are two equivalent estimates of the mediated effect.

In Figure 1(a) we have the direct effect of X on Y, where the magnitude of this relationship is captured in the coefficient $\hat{c}$. Once we introduce the mediatior, M, into the model, the magnitude of the remaining direct effect of X on Y after accounting for M is given by the coefficient $\hat{c}'$. So, one way to quantify the significance of the mediator is to gauge the change in the direct effect of X on Y. An estimate of the mediated effect is then given by: $\hat{c} - \hat{c}'$. Another estimate of the mediated effect uses information contained in the indirect path from X to Y through M. It is the product of $\hat{a}$, the magnitude of the effect of X on M, and $\hat{b}$, the magnitude of the effect of M on Y. So our other mediated effect estimate is given by: $\hat{a}\hat{b}$.

In the case of linear regression models, these two estimators are equivalent. We have that the total effect of X on Y in Figure 1(a) equals the sum of the indirect effect and the direct effects in Figure 1(b), i.e. $\hat{c} = \hat{c}' + \hat{a}\hat{b}$, which yields $\hat{c} - \hat{c}' = \hat{a}\hat{b}$.

Once one of these estimates has been obtained and its standard error computed, we can then form a confidence interval for the mediated effect. We can then test its significance by looking to see if zero is contained in the confidence interval.

2.2 Mediation Analysis with a Categorical Dependent Variable

Mediation analysis with a categorical dependent variable is not as straightforward as the case of a continuous outcome variable. We will focus on one particular method to assess the mediated effect which involves standardization of coefficients.

MacKinnon and Dwyer conducted a simulation of point estimates and showed that the difference in coefficients and the product of coefficients methods are not equivalent for a categorical dependent variable (1993). The reason for this has to do with the scales across equations in logistic regression. Recall that the first two models in our analysis are logistic regression models, with the same binary dependent variable, Y.

For the pregnancy weight gain outcome, $Y = 1$ if the woman exceeds her weight gain guidelines and $Y = 0$ if the woman remains within her weight gain guidelines. For the postpartum weight loss outcome, $Y = 1$ if the woman is at or below her pre-pregnancy weight by six months postpartum, and $Y = 0$ if her weight at six months postpartum is greater than her pre-pregnancy weight.

As we are dealing with logisitic regression models, Y is treated as a latent continuous variable, representing the log odds of the event of interest occurring, which we will denote $Y^\star$. That is, $Y^\star = ln[P(Y=1)/(1-P(Y=1))]$. Since the variance of the residuals in a logistic model is fixed at $\frac{\pi^2}{3}$, the variance of $Y^\star$ varies depending on the other variables in the model (D. P. MacKinnon & Dwyer, 1993).

The models to be used in mediation analysis with a categorical dependent variable are then:

$$Y^\star = i_1 + cX + \epsilon_1 \tag{1}$$

$$Y^\star = i_2 + c'X + bM + \epsilon_2 \tag{2}$$

$$M = i_3 + aX + \epsilon_3 \tag{3}$$

where $Y^\star$ is the latent continuous variable and $\sigma^2_{\epsilon_1} = \sigma^2_{\epsilon_2} = \frac{\pi^2}{3}$.

In order to make the scales equivalent across equations, D. P. MacKinnon and Dwyer suggest standardizing the regression coefficients in these logistic models (see Appedix Section 3 for standardization procedure). The difference of coefficients method would then involve the difference of standardized $\hat{c}$ and $\hat{c}'$. The product of coefficients estimator is then the product of the unstandardized $\hat{a}$ and standardized $\hat{b}$ coefficients. After standardization, these estimators are more similar than they were prior to standardization. We will focus our attention on the product of coefficients method.

To test the significance of the mediated effect, MacKinnon and Dwyer suggest dividing the $\hat{a}\hat{b}$ estimate by its standard error and comparing to a normal distribution. They also put forth an alternative method of computing confidence limits in order to gauge the statistical significance of the true mediated effect using critical values from a normal distribution.

However, use of a confidence interval based on the normal distribution can be especially inaccurate for small sample sizes, as shown in a simulation gauging the proportion of times a confidence interval lay to the left or right of the true mediated effect (D. P. MacKinnon, Warsi, & Dwyer, 1995). It was later suggested to make use of an asymmetric confidence interval based on the distribution of the product, to account for the fact that the product of two normally-distributed random variables is not necessarily normally distributed (D. MacKinnon, 2008, chap. 4). The R package *RMediation* gives the option of using several different methods to construct confidence intervals for the mediated effect, including Distribution of the Product (DOP) (Tofighi & D. MacKinnon, 2011). Along with the documentation for the *RMediation* package, Tofighi and MacKinnon give a comparison of confidence interval types based on proportion coverage which suggests the superiority of the distribution of the product method.

3 Mediation Analysis on Behavior Variables

We return to our application of mediation analysis on the behavior variables.

We apply our mediation analysis techniques to the dataset from the previously described study on a lifestyle intervention for pregnant women. Here we conduct mediation analysis with a categorical dependent variable, and we use the method of standardization of coefficients for assessing the mediated effect.

In order for an intermediate variable to be considered for mediation analysis, we must have a signficant relationship between the independent variable and the intermediate variable (Baron & Kenny, 1986). We accordingly restrict our analysis to those behavior variables for which women in the intervention group behaved significantly differently to those women who received standard care.

In keeping with the analysis from the original study, the following covariates were included in each model: clinic site, log of weeks gestation at delivery, race, age, and multiparity. Since the covariates are not individually pertinent to mediation analysis, we will simply acknowledge their existence in each model with: *covariates*.

The following are the models we will use for this application of mediation analysis:

$$Y^\star = i_1 + cX + covariates + \epsilon_1 \tag{4}$$
$$Y^\star = i_2 + c'X + bM + covariates + \epsilon_2 \tag{5}$$
$$M = i_3 + aX + covariates + \epsilon_3 \tag{6}$$

3.1 Pregnancy Weight Gain

Here we will focus on the pregnancy weight gain outcome of exceeding weight gain guidelines. We have evidence to conclude that the intervention decreased the proportion of normal weight women who exceeded their weight gain guidelines (OR : 0.51; 95% CI : 0.28, 0.96; P = 0.036). For women in the Overweight group, we have insufficient evidence to conclude that the intervention decreased the proportion of women who exceeded their weight gain guidelines (OR : 1.35; 95% CI : 0.67, 2.74; P = 0.40). Since a treatment effect was significant in the Normal Weight group but not the Overweight group, we will analyze behavior variables for the Normal Weight subgroup only.

To obtain our list of mediator candidates, we run Equation 6 for various behavior variables, M. If we have evidence to conclude that women in the intervention group behaved significantly differently to women receiving standard care, then we will consider each of these behavior variables for further analysis. We obtain the following list of behavior variables:

Mediator candidates:
Changes in Restraint with Food, Percentage of Calories From Carbohydrates, Amount of Time Spent Sitting/Watching TV*, Number of Times Consuming Fast Food Per Week*, Percentage of Calories From Fat, Percentage of Calories From Protein.
* Normality condition seems questionable.

Note that each of these behavior variables is not just a measurement at one time point, but rather a *change* in value from study entry to 30 weeks gestation. In this way, we can better reflect the adjustment of behavior over the course of the pregnancy.

We present the results from our mediation analyses below. We list the mediator candidate, the $\hat{a}$ and standardized $\hat{b}$ coefficients and standard errors underneath, and the 95% confidence interval for the true mediated effect.

Mediator Candidate	$\hat{a}$ coefficient	$\hat{b}_{standard.}$ coefficient	95% CI
Restraint with Food	1.46 (0.431)	0.044 (0.029)	(-0.018, 0.170)
Percentage of Calories from Carbs	2.88 (0.993)	0.0054 (0.012)	(-0.057, 0.097)
Time Spent Sitting/Watching TV	-6.94 (3.30)	-0.0062 (0.0038)	(-0.010, 0.127)
Fast Food Consumption Per Week	-1.19 (0.522)	-0.0044 (0.023)	(-0.057, 0.071)
Percentage of Calories from Fat	-1.67 (0.745)	-0.019 (0.017)	(-0.022, 0.110)
Percentage of Calories from Protein	-0.908 (0.398)	0.0070 (0.0304)	(-0.072, 0.054)

Table 1: Mediation analysis results on behavior variables for pregnancy weight gain outcome, Normal Weight group

For a detailed account of the mediation analysis procedure, see Appendix Section 6: Mediation Analysis on Restraint with Food.

Observe that zero lies within each of the above confidence intervals, so we have insufficient evidence to conclude that any of these behavior variables significantly mediates the relationship between the intervention and the pregnancy weight gain outcome for Normal Weight women.

3.2 Postpartum Weight Loss

We now address the postpartum weight loss outcome of returning to pre-pregnancy weight by six months postpartum. Since the intervention was found to be significant for the Normal Weight group and the Overweight group, we will analyze the behavior variables within each group separately.

Since the outcome is recorded at the six months postpartum timepoint, we examine behavior changes from study entry to six months postpartum. Each variable is then the change in the particular behavior across this time period.

3.2.1 Normal Weight Group

Before looking into the behavior variables, we first verify that women in the Normal Weight group receiving the intervention performed significantly better with regard to the postpartum weight loss outcome. We have strong evidence to conclude that the intervention increased the proportion of normal weight women who returned to their pre-pregnancy weight by six months postpartum (OR : 2.60; 95% CI : 1.27, 5.31; P = 0.009). Now we may consider the behavior variables as a way to better understand how the intervention brought about its changes.

Recall that we arrive at our list of mediator candidates by identifying behavior variables for which women receiving the intervention behaved significantly differently to those women receiving standard care. None of the behavior variables satisfied this criterion for the postpartum outcome. Since the women receiving the intervention did not significantly alter these behaviors compared to the women receiving standard care, we are unable to draw any conclusions about how the intervention achieved its effects.

3.2.2 Overweight Group

While the original study cited a significant treatment effect for the Normal Weight and Overweight groups, it seems that this analysis was conducted with both groups in the same model. However, in conducting subgroups analysis, we cannot draw the same conclusion about the Overweight group. We have insufficient evidence to conclude that the intervention increased the proportion of overweight women who returned to their pre-pregnancy weight by six months postpartum (OR : 1.85; 95% CI : 0.80, 4.30; P = 0.151).

As a result, we will not continue with our investigation of the behavior variables, as we are specifically interested in discovering how the intervention achieved its success.

3.3 Considerations

In our application of mediation analysis to the behavior variables, we were unable to conclude that any of the mediator candidates significantly mediated the relationship between the lifestyle intervention and the weight gain/loss outcomes.

Specifically, the investigation into the restraint with food variable as a potential mediator yielded some interesting, albeit statistically insignificant, findings. A positive coefficient for the restraint variable in the full model suggests that if it had been significant, an increase in restraint score over the course of the pregnancy was associated with exceeding weight gain guidelines. This is peculiar, since we would have thought that exercising more restraint with food would help to keep the participant's weight under control and make it more likely for them to stay within their healthy weight gain range.

There are a few potential explanations for why we observed this relationship between the restraint variable and the dependent variable. Considering that the restraint scores were self-reported, it is possible that women in the treatment group reported showing higher restraint with food when they perhaps did not practice as much restraint. Participants in the lifestyle intervention group received more education on nutrition than those in the standard care group. This would likely have motivated those in the treatment group to claim higher restraint, since this was a more pressing expectation on them. Alternatively, it is possible that the restraint variable was not an accurate measure of the actual restraint shown by the participants. The measurements were a sum of ranked responses to various questions regarding restraint with food. Perhaps the questions were not worded clearly or focused more heavily on certain aspects of restraint that were not as closely tied to weight gain.

More generally, there could be a number of reasons why we did not identify any of the behavior variables as significant mediators. The majority of these variables were self-reported and measured by means of questionnaires. As such, there are likely to be inconsistencies in a participant's responses as well as large variation across participants so that relationships between variables are less clear. It is also possible that there were some omitted behavior variables that accounted for a large part of the success of the intervention program.

We might have also been limited in our ability to detect a mediated effect by our sample sizes. While we initially had information on 363 participants, subgroup analysis of the Normal and Overweight groups separately reduced the sample sizes to 186 and 177, respectively. There were additionally some missing values across the covariates and behavior variables that further reduced these sample sizes somewhat. It is probable that the low sample sizes contributed to our inability to detect a mediated effect, if a true mediated effect existed. We chose to do further investigation by conducting simulations to obtain the power to detect the mediated effect for varying effect sizes and sample sizes.

4 Power Analysis Simulation

Here we investigate the relationship between true mediated effect size, sample size, and power to detect the mediated effect. We explain the procedure used to set up our simulations, provide the simulation results, and comment on our findings.

4.1 Procedure

We are interested in assessing the power to detect the mediated effect for various sample sizes as well as various effect sizes. For the sample sizes, we will use 50, 100, 200 and 500. Regarding the mediated effect sizes, we wish to analyze a few different combinations of a and b coefficients so that their products will yield a few different mediated effect sizes (see Appendix Section 4 for determination of parameter levels). For each combination of a and b parameter values and each sample size, we generate data for X, M, and Y and run the three models given by Equations 1, 2 and 3. We then standardize the coefficients from the logistic regression models according to the standardization procedure for these models (see Appendix Section 3). We then estimate the mediated effect, compute an asymmetric confidence interval for the true mediated effect, and record whether the confidence interval excludes zero or not. This equates to whether or not we would have concluded a significant mediated effect from our sample. We run 1,000 simulations and determine the fraction of those simulations that yield a conclusion of a significant mediated effect. This is taken to be the power to detect the mediated effect.

The following table gives the results from these simulations:

4.2 Results

		b path		
a path	Sample size	$Small(.14)$	$Medium(.36)$	$Large(.51)$
$Small(.283)$	50	.02	.06	.10
	100	.04	.16	.27
	200	.10	.42	.61
	500	.28	.92	.94
$Medium(.721)$	50	.07	.22	.38
	100	.13	.43	.69
	200	.21	.69	.93
	500	.32	.97	.99
$Large(1.02)$	50	.11	.26	.43
	100	.13	.42	.64
	200	.18	.65	.88
	500	.28	.93	.99

Table 2: Power to detect mediated effect $\hat{a}\hat{b}$ for various effect sizes and sample sizes

4.3 Discussion

We can see from the simulation results that we have especially low power to detect the mediated effect for sample sizes around 50 and 100. Also, for a small $\hat{b}$ path, the power appears to be consistently low, even for larger sample sizes.

In most of our analyses on the behavior variables, we observed a large $\hat{a}$ coefficient but a very small $\hat{b}$ coefficient. If the population coefficients were similar in magnitude to the estimated coefficients, then it seems that we would likely have very low power to detect the mediated effect, even for larger sample sizes.

5 Further Use of Mediation Analysis

Mediation analysis can be very useful in better understanding the mechanisms through which a treatment achieved its effects. In our case, had the intent to conduct mediation analysis on behavior variables been present from the study design stage, we might have had a more thoughtful selection of behavior variables to investigate. MacKinnon (2008) outlines the steps a researcher should take to develop a study from a mediation analysis perspective. He states that an important component for future mediation analysis is to "identify the conceptual theory of how the outcome occurs" so as to construct a list of mediator candidates (42).

If mediation analysis successfully identifies some candidates as being significant mediators, then knowledge of these variables can be used for treatment improvement. MacKinnon and Dwyer (1993) suggest that by understanding more about how a program works through mediation analysis, we can potentially reduce the cost of prevention programs (155). This would be especially true if the program involves a number of distinct components, where some can be eliminated and others enhanced based on knowledge obtained from mediation analysis. Ideally, to validate that the identified mediators play a significant role in the treatment's success, we would want to conduct another randomized trial using the enhanced treatment and show that it was more effective than the original treatment (Kraemer, Wilson, Fairburn, & Agras, 2002).

6 Conclusion

We set out to conduct further exploration of a dataset from a study on pregnant women. Its primary objectives were to test the effectiveness of a lifestyle intervention on limiting excessive weight gain during pregnancy and promoting the return to pre-pregnancy weight by six months postpartum. Significant treatment effects were found for Normal Weight women regarding the pregnancy weight gain outcome, as well as for Normal Weight and Overweight/Obese women regarding the postpartum weight loss outcome. While the lifestyle intervention appeared to be somewhat effective, an important question that remained unanswered was: Through what mechanisms was the intervention successful? Considering that the intervention involved extra nutrition information and weight monitoring, participants would have achieved success from the intervention through behavior changes. The dataset contained several behavior variables, recorded at the different time points. We came upon mediation analysis to assess the significance of the behavior variables as intermediate variables in the relationship between the intervention and weight gain/loss outcomes.

While assessing a mediation effect is fairly simple in the case of a continuous dependent variable, each of our dependent variables was binary. Applying the method originally proposed by MacKinnon and Dwyer, we standardized the coefficients in our logistic regression models prior to estimating the mediated effect of each behavior variable (1993). We focused on the product of coefficients method as our estimate of the mediated effect. We analyzed several behavior variables for which women in the intervention group behaved significantly differently to those receiving standard care. We were unable to conclude that any of these behavior variables significantly mediated the relationship between the lifestyle intervention and the weight gain/loss outcomes.

To investigate how sample size might have affected our ability to detect the mediated effect, we conducted a power analysis simulation. This involved generating data with specific magnitudes of association between variables to yield various mediated effect sizes. We also specified different sample sizes, and for each combination of sample size and mediated effect size, computed the power to detect the mediated effect. The power differed greatly across sample size levels, though power remained low across all sample sizes when the magnitude of the path from the mediator to the dependent variable was small.

7 Appendix

7.1 Data Management

Some changes were made to the original JMP data file to allow for more clarity and consistency. A few blank observations were removed, as were some weight change variables which were recomputed as new variables for the purposes of validation. Some variables were renamed and/or recoded to complete the partial value labels which would make future interpretation easier. Due to the partial value labels in the original file, data types were misjudged when brought into *R*, so many variables required the appropriate data type to be specified. These data modifications were performed in *R* and documented in an *R* script entitled "Data Transform.R".

7.2 Multivariate Analysis on Weight Profiles

We are trying to answer the question of whether the nature of the weight changes significantly differs between those women receiving the intervention and those receiving standard care.

We conduct a test of parallel for the weight profiles of treatment and control groups to assess the treatment effect. The weight profiles include weights at study entry, 30 weeks gestation, delivery, 6 weeks postpartum, 6 months postpartum, and 12 months postpartum. We retain the same covariates as the original study, which include clinic site, log of weeks gestation at delivery, race, age, and multiparity. We also analyze the Normal Weight and Overweight/Obese groups separately in order to adhere to the study. This test of parallel collectively compares the changes in average weight between successive time points of the treatment and control groups, accounting for the covariates.

We have insufficient evidence to conclude that, after accounting for the covariates, the weight profiles of the treatment and control groups are not parallel for the Normal Weight group ($F_{5,114} = 0.576$, P = 0.719) or the Overweight/Obese group ($F_{5,94} = 1.097$, P = 0.368).

7.3 Standardizing Coefficients in Logistic Regression Models

We must first compute the variance of $Y^\star$ for each logistic regression equation:

$$\hat{\sigma}^2_{Y^\star} = \hat{c}^2\hat{\sigma}^2_X + \frac{\pi^2}{3} \tag{7}$$

$$\hat{\sigma}^2_{Y^\star} = \hat{c}'^2\hat{\sigma}^2_X + \hat{b}^2\hat{\sigma}^2_M + 2\hat{c}'\hat{b}\hat{\sigma}^2_{XM} + \frac{\pi^2}{3} \tag{8}$$

We then divide each regression coefficient in the logistic equation and the standard error of each coefficient by the standard deviation of $Y^\star$. This yields standardized coefficients and standard errors, which we then use to estimate the mediated effect.

Note that if we have other covariates in the model, we must incorporate their variances and covariances with the other variables and with each other into the calculation of the variance of $Y^\star$. Letting k_i = the coefficient of X_i, the i^{th} independent variable in the model with $1 \leq i \leq n$, the computation is then given by:

$$\hat{\sigma}^2_{Y^\star} = \sum_{i=1}^{n} \hat{k_i}\hat{\sigma}^2_{X_i} + \sum_{i=1}^{n-1}\sum_{j=i+1}^{n} 2\hat{k_i}\hat{k_j}\hat{\sigma}^2_{X_iX_j} + \frac{\pi^2}{3}.$$

We coded this in R as part of a function that standardized a given set of coefficients.

7.4 Determination of Parameters for Simulation

The following procedure is based on the method used by Thoemmes, MacKinnon, and Reiser (2010).

From Equation 3 we obtain the following equation for the variance of M:

$$\sigma^2_M = a^2\sigma^2_X + \sigma^2_{\epsilon_M} \tag{9}$$

Note that X is a binary independent variable with values of 0 for the control and 1 for the treatment. Since the treatment was randomized to the participants, each outcome has a probability of 0.5 of occurring. Therefore, for our simulations we set:

$$\sigma_X^2 = (0.5)(0.5) = 0.25$$

In our simulations, we construct the X variable first, and use this variable to help construct the M variable, as we intentionally set up relationships of varying strengths between these variables for the purpose of imposing varying mediated effect sizes. Since X and M are not independent in our simulations, their covariance is not necessarily zero, and we address this in Section 5: True Standardized Mediated Effect. If we included covariates in the model for simulation, then all the covariances with X would be zero since they would be indepedent with X.

We wish to determine the necessary values of the parameters so as to set up various mediated effect sizes in our population. We use the effect sizes of 0.02, 0.13, and 0.26 proposed by Cohen as our small, medium and large effects, respectively (1988). These were based on the R^2 metric and were developed to apply to studies in the social sciences. In order to obtain all possible combinations of the parameter values, we set effect sizes for the a and b paths and proceed to solve for a and b.

Here we will find the necessary values of our parameters a and b that will establish a medium-large mediated effect size in our population. Let's say we want the explained variance of the a path to be 0.13 and the explained variance of the b path to be 0.26. We will set the explained variance of the c' path at 0.02.

To set up the relationship between X and M, first recall that $M = aX + \epsilon_M$. We will work backwards to find the value of a for which a particular amount of the variance of M is explained by X. We can set up this relationship by defining a proportion of the variance of M that is explained by X and the remaining proportion that is unexplained by X. Since we want the explained variance of the relationship between X and M to be 0.13, for simplicity we can set the variance of M to be 1 and set the variance of the residuals of M to be $(1 - 0.13)$, the proportion of the variance that is unexplained by X. Note that this requires $a^2\sigma_X^2$ in the equation below to be equal to 0.13, as desired. This will allow us to solve for the parameter a in Equation 9:

$$\begin{aligned}
\sigma_M^2 &= a^2\sigma_X^2 + \sigma_{\epsilon_M}^2 \\
1 &= a^2 * 0.25 + (1 - 0.13) \\
1 &= a^2 * 0.25 + 0.87 \\
\frac{1 - 0.87}{0.25} &= a^2 = 0.52 \\
a &= 0.721
\end{aligned}$$

Since the explained variance of the c' path is 0.02, we have:

$$\begin{aligned}
c'^2 * \sigma_X^2 &= 0.02 \\
c'^2 * (0.25) &= 0.02 \\
c' &= 0.283
\end{aligned}$$

We will keep c' fixed at 0.28 for all simulations since we are specifically interested in the power of the ab estimator of the mediated effect.

Since the explained variance of the b path is 0.26, we have:

$$\begin{aligned} b^2 * \sigma_M^2 &= 0.26 \\ b^2 &= 0.26 \\ b &= 0.51 \end{aligned}$$

Continuing in this manner for various effect sizes, we obtain the following parameter values to use in our simulations:

$$\begin{aligned} a &= 0.283, 0.721, 1.02 \\ (\sigma_{\epsilon_M}^2 &= 0.98, 0.87, 0.74) \\ b &= 0.14, 0.36, 0.51 \end{aligned}$$

7.5 True Standardized Mediated Effect

Continuing with the situation in the previous section, we find the true variance of $Y^\star$, and use it to standardize the b parameter:

We use Equation 8 for the variance of $Y^\star$:

$$\sigma_{Y^\star}^2 = c'^2 \sigma_X^2 + b^2 \sigma_M^2 + 2c' b \sigma_{XM}^2 + \pi^2/3$$

We must first find the covariance between X and M. Note that since we construct the M variable using our X variable, then X and M are not independent, and so their covariance is not necessarily zero. We derive an alternate equation for the covariance between X and M that uses our values of a and σ_X^2:

$$\begin{aligned} \sigma_{XM}^2 &= E(XM) - E(X)E(M) \\ &= E\{X(aX + \epsilon_M)\} - E(X)E(aX + \epsilon_M) \\ &= aE(X^2) + E(X\epsilon_M) - E(X)\{aE(X) + E(\epsilon_M)\} \\ &\quad \text{(Since } X \text{ and } \epsilon_M \text{ are independent and } E(\epsilon_M) \text{ is assumed to be zero,} \\ &\quad \text{then } E(X\epsilon_M) = E(X)E(\epsilon_M) = 0) \\ &= a\{E(X^2) - E(X)^2\} \\ &= a * \sigma_X^2 \end{aligned}$$

We then compute the covariance:

$$\begin{aligned} \sigma_{XM}^2 &= a * \sigma_X^2 \\ &= 0.721 * 0.25 = 0.18 \end{aligned}$$

We can now solve for the true variance of $Y^\star$:

$$
\begin{aligned}
\sigma^2_{Y^\star} &= c'^2\sigma^2_X + b^2\sigma^2_M + 2c'b\sigma^2_{XM} + \pi^2/3 \\
&= (0.283)^2 * 0.25 + (0.51)^2 * 1 + 2 * (0.283) * (0.51) * (0.18) + \pi^2/3 \\
&= 3.621 \\
\sigma_{Y^\star} &= 1.903
\end{aligned}
$$

We can find $b_{standardized}$ by dividing b by $\sigma_{Y^\star}$:

$$
\begin{aligned}
b_{standardized} &= b/\sigma_{Y^\star} \\
&= 0.51/1.903 = 0.268
\end{aligned}
$$

Then the true standardized mediated effect is:

$$a * b_{standardized} = (0.721) * (0.268) = 0.193$$

7.6 Mediation Analysis on Restraint with Food

The mediator candidate is the change in reported restraint with food scores from study entry to 30 weeks gestation.

Since the covariates are not individually pertinent to mediation analysis, we will simply acknowledge their existence in each model with: *covariates*.

After running the three models necessary for mediation analysis, we obtain the following results:

$$
\begin{aligned}
\text{Model 1} : Y^\star &= i_1 + cX + covariates + \epsilon_1 \\
\hat{Y}^\star &= -21.84 - 0.681X + covariates
\end{aligned}
$$

$$
\begin{aligned}
\text{Model 2} : Y^\star &= i_2 + c'X + bM + covariates + \epsilon_2 \\
\hat{Y}^\star &= -22.96 - 0.824X + 0.089M + covariates
\end{aligned}
$$

$$
\begin{aligned}
\text{Model 3} : M &= i_3 + aX + covariates + \epsilon_3 \\
\hat{M} &= 3.806 + 1.461X + covariates
\end{aligned}
$$

The key coefficients and their standard errors are: $\hat{c} = -0.681, s_{\hat{c}} = 0.325; \hat{c}' = -0.824, s_{\hat{c}'} = 0.342; \hat{b} = 0.089, s_{\hat{b}} = 0.058; \hat{a} = 1.461, s_{\hat{a}} = 0.431$.

From Model 3 we conclude that those in the intervention group had a significantly higher change in reported restraint with food than those women who received standard care, after accounting for age, race, multiparity, clinic, and weeks gestation at delivery ($\hat{a} = 1.461$, SE $= 0.431$, P $= 0.00086$).

From Model 1 we conclude that women in the intervention group were significantly less likely to exceed their weight gain guidelines than women receiving standard care, after accounting for the covariates (OR: 0.51; 95% CI: 0.27, 0.96; P = 0.036).

From Model 2 we conclude that women in the intervention group were significantly less likely than women receiving standard care to exceed their weight gain guidelines, after accounting for change in restraint with food and the covariates (OR: 0.44; 95% CI: 0.22, 0.86; P = 0.016). However, restraint with food is not significantly associated with exceeding weight gain guidelines, after accounting for the treatment and covariates (OR: 1.09; 95% CI: 0.97, 1.23; P = 0.128).

Notice that the unstandardized coefficient of the intervention variable actually increases in magnitude once we introduce the restraint variable into the first model. Since we are dealing with a binary dependent variable, we must equate the scales across the logistic models in order to accurately gauge the change in coefficients. We will standardize the coefficients according to the previously described method (see Appendix Section 3 for the details).

For the standard deviation of the dependent variable in the first two models, we obtain 2.006 and 2.026, respectively. This yields the following standardized coefficients and their associated standard errors: $\hat{c} = -0.339, s_{\hat{c}} = 0.162; \hat{c}' = -0.407, s_{\hat{c}'} = 0.169; \hat{b} = 0.044, s_{\hat{b}} = 0.029$.

We obtain an estimated mediated effect size of $\hat{a} * \hat{b}_{standardized} = 0.064$. Using the *medci()* function in the *RMediation* package, we arrive at a 95% CI of (-0.0176, 0.1705). Since zero is contained in the confidence interval for the true mediated effect, we have insufficient evidence to conclude that the change in reported restraint with food significantly mediates the relationship between the intervention and the weight gain outcome.

References

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: conceptual strategic and statistical considerations. *Journal of Personality and Social Psychology*, *51*(6), 1173–1182.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates.

Kraemer, H., Wilson, G., Fairburn, C. G., & Agras, W. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry*, *59*(10), 877–883.

MacKinnon, D. P., & Dwyer, J. H. (1993). Estimating mediated effects in prevention studies. *Evaluation Review*, *17*(2), 144–158.

MacKinnon, D. P., Warsi, G., & Dwyer, J. H. (1995). A simulation study of mediated effect measures. *Multivariate Behavioral Research*, *30*(1), 41–62.

MacKinnon, D. (2008). *Introduction to statistical mediation analysis*. Mahwah, NJ: Lawrence Erlbaum Associates.

Phelan, S., Phipps, M. G., Abrams, B., Darroch, F., Schaffner, A., & Wing, R. R. (2011). Randomized trial of a behavioral intervention to prevent excessive gestational weight gain: the fit for delivery study. *The American Journal of Clinical Nutrition*, *93*(4), 772–779.

Thoemmes, F., MacKinnon, D. P., & Reiser, M. R. (2010). Power analysis for complex mediational designs using monte carlo methods. *Structural Equation Modeling: A Multidisciplinary Journal*, *17*(3), 510–534.

Tofighi, D., & MacKinnon, D. (2011). Rmediation: an R package for mediation analysis confidence intervals. *Behavior Research Methods*, *43*(3), 692–700.