

## PREFERRED TREATMENT METHODS FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE

THESIS

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### THESIS

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# PREFERRED TREATMENT METHODS FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE

## THESIS

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### Abstract

Shared decision making is the concept of physicians involving patients in the planning process in terms of their treatment methods. The University of Maryland Medical Center is interested in applying shared decision making to the treatment of patients with Inflammatory Bowel Disease (IBD), which has three types: Crohn's disease, ulcerative colitis, and indeterminate-type. There are several treatment methods for IBD, but the two of focus in this study were medical management and ileal pouchanal anastomosis (IPAA) surgery. To explore patient preferences between these two alternative treatment methods, a discrete choice experiment (DCE) was employed in which respondents were asked to answer 14 choice sets. The responses for the DCE were binary, and therefore logistic regression models were explored. The conditional logistic regression model was determined to be the most appropriate for this analysis. After step-wise regression was performed, a final conditional logistic regression model was analyzed. The results suggested that IPAA was the preferred method of treatment amongst all patient profiles. The 30-year risk of being diagnosed with colorectal cancer and the risk of needing emergent surgery were the two factors that were the most influential to patient preferences. Both of these attributes had favorable levels for the IPAA alternative, which was further support for IPAA being the most preferred alternative among patients. Furthermore, education of alternatives is a driving factor in patient preferences.

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# Table of Contents

|   | Page   |
|---|--|
| Abstract  | iv   |
| Acknowledg  | gementsv   |
| List of Figu  | ıres   |
| List of Tabl  | les  |
| I. Introd   | luction  |
| 1.2 P   | Background1Problem Statement2Research Objectives2  |
| II. Literat   | ture Review  |
| 2.2 In<br>2.3 D<br>2.4 A  | Overview    4      Inflammatory Bowel Disease & Patient Preferences    4      Discrete Choice Experiments    5      Inalysis of Discrete Choice Experiments    6      Comparing Models    11   |
| 2.6 C<br>2.7 M<br>2.8 In<br>2.9 B   | Coefficients of Logistic Regression Models12Induitible Factor Analysis12Inputation14Bootstrapping15Itility Modeling15  |
| III. Metho  | odology  |
| 3.2 In<br>3.3 R<br>3.4 M<br>3.5 B<br>3.6 M<br>3.<br>3.6 M<br>3.<br>3.7 M<br>3.8 Id<br>3.9 A | Dverview17nitial Survey Data17ceduction of Columns and Imputation20fultiple Factor Analysis21Bootstrapping21fodeling22.6.1 Modeling in JMP22.6.2 Modeling in R23fodeling Comparisons24lentification of Significant Factors24opplication of Models25Tinal Comparisons26 |

## Page

| IV.   | Analy   | vsis and Results  |
|-------|---|---|
|       | 4.2 F<br>4.3 S<br>4.4 In<br>4.5 M<br>4.6 S<br>4.7 A<br>4<br>4<br>4<br>4<br>4<br>4.8 C | Dverview27Results of Multiple Factor Analysis27Significance of Missing Values29nitial Regression Models30Modeling with Interaction Terms32Step-Wise Regression34Application of Models36.7.1 Effect Marginals36.7.2 Utility Profiler37.7.3 Probability Profiler39Comparison to Initial Patient Preferences40 |
| V.    |   | Chapter Summary 42   usions and Recommendations 43  |
|       | 5.1 C<br>5.2 F  | Conclusion43Recommendations45Future Work46  |
| Appe  | endix A   | A. Survey   |
|       | 1.2 S<br>1.3 C  | Attribute Levels47Survey Construct48Original Data56Clean Data57   |
| Appe  | endix I   | B. R Code   |
| Bibli | 2.2 N<br>2.3 C<br>2.4 S   | Data Cleaning and Imputation59Multiple Factor Analysis60Conditional Logistic Regression61Step-Wise Regression62N63  |

# List of Figures

| Figure | Page  |
|--------|---|
| 1      | Frequency of Responses for Each Attribute                 |
| 2      | Percentage of Variability Explained by Factors            |
| 3      | Individual Factor Map                                     |
| 4      | Marginal Effects of Main Attributes                       |
| 5      | Utility Profiler Example (Medical Management alternative) |
| 6      | Probability Profiler Example                              |

# List of Tables

| Table | Page   |
|-------|--|
| 1     | Breakdown of Demographics, Current Meds, Past Meds, & Symptoms         |
| 2     | Initial Regression Model Results                                       |
| 3     | Model Comparison: AIC, BIC, & -2*LogLikelihood31                       |
| 4     | Variables with Odds Ratios $> 2$                                       |
| 5     | Breakdown of Most Influential Attributes by Percentage<br>of Responses |

# PREFERRED TREATMENT METHODS FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE

### I. Introduction

#### 1.1 Background

There has been a movement in recent years to focus more on patient involvement in treatment decisions. Previously, there were mixed thoughts on how involved patients should be in their treatment decisions. Studies conducted by Stewart *et al* [1] and Guadagnoli [2] provided evidence for these claims. However, newer evidence supports that patients are more comfortable in treatment decisions when they are involved in the process. Shared decision making is the concept of allowing patients to be more involved in determining which treatment methods their doctors recommend. For shared decision making to be successful, communication and education between the physicians and the patients is paramount. In fact, Longo *et al* [3] concluded that patients are continually more likely to appreciate shared decision making the more they experience it. Efforts to introduce shared decision making into the doctor and patient relationships are important to a flourishing medical environment.

One of the diseases of interest for incorporating shared decision making is Inflammatory Bowel Disease (IBD), which effects approximately 1.3% of adults in the United States [4]. IBD can be split into three different types: ulcerative colitis, Crohn's disease, and indeterminate-type. Generally, the type of IBD a patient has will influence the treatment approach since each type comes with its own implications including courses of action for treatment planning. Furthermore, the type of disease can indicate complications from IPAA surgery or pouch failure. In some cases, it is difficult to diagnose the disease as ulcerative colitis or Crohn's disease, which will therefore result in the diagnosis of indeterminate-type. Patients with indeterminate-type IBD tend to have an even higher rate of pouch issues [5].

#### 1.2 Problem Statement

In order to improve patient care, data must be collected and analyzed. In the medical field, this generally comes in the form of observational data on patients instead of a deliberate designed experiment. Because of this, it can be difficult to accurately draw conclusions through the use of standard statistics methods. Therefore, more advanced operations research techniques can be employed.

The University of Maryland Medical Center in Baltimore is interested in catering to the preferred treatment methods of patients with IBD. The subject matter expert for this research was Dr. Bryce E. Haac, MD, who is a surgical resident and researcher at the University of Maryland Medical Center. She and her associates desire to be better equipped to offer treatment options to patients battling IBD. For this effort, a discrete choice experiment was used. The survey was developed using D-optimal, two-factor factorial design with 14 choice sets designed for this study. Demographics data was also collected in the survey process to determine which, if any, of these factors contribute to patient preferences. Dr. Haac and her team determined the 12 attributes under consideration in this study. Furthermore, the two levels for each attribute were established and not altered.

#### **1.3 Research Objectives**

In this research, regression techniques, factor analysis, and decision analysis techniques are used to determine the preferences of individual patients for treatment methods for IBD. Medical management and IPAA surgery were the two treatment methods of focus for this study. Both of these options are viable for patients with all types of IBD. The objective of the study is to highlight any attributes or patient characteristics that influence a patient's preference of medical management or IPAA. In doing so, the physicians at University of Maryland Medical Center will have a better understanding of which types of treatment methods should be offered to which types of patients, as well as inferring the shortcomings of the current methods. This information will allow Dr. Haac and her team to successfully employ shared decision making for patients with IBD.

## II. Literature Review

#### 2.1 Overview

This chapter provides relevant background of studies performed that offer insight into the techniques used for this study. It includes statistical techniques and medical studies that inspired the methodology and analysis of the research.

#### 2.2 Inflammatory Bowel Disease & Patient Preferences

Since there is a wide variety of approaches to treating IBD, physicians have become more interested in the preferences of the individual patient. In 2009, Siegel [6] suggested that previously in IBD, the methods of treatment were "step-up" in nature. That is, they tended to start at the least potent type of treatment available and alter treatment approaches when necessary, leaving surgery as the last resort. He concluded that communication between physicians and patients should focus on risk and benefits of all types of treatment methods from the start.

A study conducted by Gregor *et al.* [7] in 2015 used a discrete choice experiment (DCE) to understand patient preferences concerning IBD treatment options. This Willingness-To-Pay (WTP) designed study surveyed 586 IBD patients with Crohn's disease (68.9%) or ulcerative colitis (31.1%). The study consisted of 12 attributes with anywhere from 2 to 5 levels of each attribute. The conclusion of the study was that IBD patients were more willing to prioritize short-term outcomes, such as reduction in pain of treatment, over long-term outcomes, such as symptom relief. These results were surprising and important since physicians typically suggested treatment options based on their long-term effects with less concern for the short-term benefits.

While there has been an increase in accounting for patient preferences, O'Connor et al. [8] caution against relying on patients' judgements of the benefits and risks of treatments. The use of patient decision aids are critical since "patients have unrealistic expectations of treatment benefits and harms, clinicians are poor judges of patients' values, and, as a consequence, there is over-use of treatment options that informed patients do not value".

#### 2.3 Discrete Choice Experiments

This research takes advantage of a DCE, which is a practice widely used in medical research. In this case, DCE was used to draw insights about patient preferences between two IBD treatment options. There were 12 attributes with a different level for each treatment option. Because of this, a two-level fractional factorial design was used to build the survey. It was deemed that high-order interactions were negligible, and this technique was validated through concepts from Montgomery [9]. DCE allows the respondent to choose between two options in a series of choice sets. The choice sets are devised through combinations of the levels of each of the attributes. They are then compared against one another to drive the analysis of what the preferences are among the respondents [10].

In 2017, Haac *et al.* [11] conducted a DCE for patients with venous thromboembolism prophylaxis to determine benefit-risk trade-off estimations. The study used a Bayesian D-optimal design to develop the 40 choice sets administered in the survey. The DCE was split into four independent surveys, and required over 200 respondents to accomplish the desired power of the study and assess the associated demographics appropriately. Since Haac had successfully implemented a D-optimal design in a previous study, this was the approach used in this survey as well.

#### 2.4 Analysis of Discrete Choice Experiments

The objective of conducting a DCE is to estimate the treatment options a physician should offer to a specific patient provided his/her demographics, background, medical history, lifestyle, and preferences. Some of the methods for analyzing large data sets of medical information and demographics include propensity score matching and regression modeling [12], as well as linear discriminant analysis [13].

Haac *et al.* [11] took advantage of multinomial logistic regression in their study of venous thromboembolism prophylaxis. Logistic regression is a technique in which the dependent variable is comprised of two distinct outcomes [14]. Since, in this research, like in that of Haac *et al.*'s [11] previous work, the focus is to determine between two alternative treatment methods, logistic regression is a reasonable method of analysis for the DCE results.

There are two main logistic regression models of interest in this study: multinomial logistic regression and conditional logistic regression. Hoffman and Duncan [15] go into detail comparing the two methods. The main takeaway from their research is that it is most appropriate to employ conditional logit when the dependent variable is modeled as a function of the alternative characteristics, instead of the characteristics of the respondents. The multinomial logit model uses the choice probabilities from Equation (1), while the conditional logit model uses the probabilities from Equation (2), where *i* represents the individual respondents, *j* represents an alternative choice among the total alternatives J,  $Z_{ij}$  represents the characteristics of the  $j^{th}$  alternative for each individual with  $\beta$  and  $\alpha$  representing parameter vectors,  $X_i$  represents the characteristics of the individual, and  $P_{ij}$  represents the probability of the individual choosing alternative *j*.

$$P_{ij} = \frac{\exp\left(X_i\beta_j\right)}{\sum_{k=1}^{J}\exp\left(X_i\beta_k\right)} \tag{1}$$

$$P_{ij} = \frac{\exp\left(Z_{ij}\alpha\right)}{\sum_{k=1}^{J}\exp\left(Z_{ik}\alpha\right)} \tag{2}$$

When there is an interest in both of these techniques, a mixed logistic regression model may be appropriate. The mixed logistic regression model uses Equation (3).

$$P_{ij} = \sum_{k=1}^{J} \frac{\exp\left(X_i\beta_j + Z_{ij}\beta\right)}{\exp\left(X_i\beta_k + Z_{ik}\alpha\right)} \tag{3}$$

In research conducted by Bridges *et al.* [16] in 2011, a 10-step approach was developed concerning the use of conjoint analysis to include DCE. The steps are: 1) research question, 2) attributes and levels, 3) construction of tasks, 4) experimental design, 5) preference elicitation, 6) instrument design, 7) data collection, 8) statistical analyses, 9) results and conclusions, and 10) study presentation. The focus of this paper includes steps 8 and 9. There are many approaches to statistical analysis of the data of DCE. Many of the approaches are discussed by Hauber *et al.* [17], including the use of a linear probability models, linear regression using ordinary least squares (OLS), conditional logit with preference weights, conditional logit with a continuous variable, random-parameters logit, hierarchical Bayes, and the latent-class finite-mixture model.

The linear regression technique of OLS is a common method that produces estimates of the coefficients for the slope and parameters. The benefit of OLS is that it is easy to interpret, but there are limitations. Since OLS relies on a linear function, alternative methods are more appropriate in the case of a binary response. For this reasons, OLS is not the best approach for this study [17].

Logistic regression, or logit regression, is a common method for analyzing binary data. In this study, choice sets have two options producing binary results. Therefore, logit regression is a method worthy of exploring. Conditional logit analysis is a method coined by McFadden [18] in 1974 through his research in qualitative choice behavior. He discusses the difficulty of "understanding human choice behavior", which he defines as the choice sets and their alternatives, the characteristics of the decision-maker, and the ability to model behavior pertaining to choices in general.

One of the benefits of conditional logit is that it coincides with random utility theory [18]. Utility theory is used to identify which choice preferences drive the respondents' decisions the most. Conditional logit uses the log-likelihood values to determine the goodness of fit for the model since an R-squared calculation is not possible like in standard linear regression models. Log-likelihood (LL) values are independently determined from sample size of the test. So, they must be manipulated to determine useful information similar to that of an R-squared value. Hauber *et al.* [17] identifies three formulas for determining likelihood ratios:

likelihood ratio 
$$\chi^2 = -2 * (LL \text{ models without predictors} - LL \text{ of model})$$
 (4)

likelihood ratio  $\chi^2 = -2 * (LL \text{ of restricted model} - LL \text{ of unrestricted model})$  (5)

McFadden's pseudo 
$$R^2 = 1 - \frac{\text{LL of model}}{\text{LL model without predictors}}$$
 (6)

Conditional logit analysis is valuable in that it takes into account the preference weights of the respondents which influence the results of the survey. Hauber *et al.* [17] discusses effects-coding and dummy-variable coding, as well as coding the efficacy attribute as a linear continuous variable. While conditional logit analysis is a better candidate for analysis than OLS linear regression, it still has its limitations. The key limitation to conditional logit is the assumption that each choice set captures the respondents' utility equally.

Random parameters logit is similar to conditional logit, but it provides a mean

and a standard deviation of effects across the sample, whereas conditional logit only provides a mean. Random parameters logit assumes a distribution among preferences for individuals, and has an associated choice-probability model, shown here.

$$Pr(\text{choice}_n = i) = \frac{\exp\left(V(\beta_n, x_i)\right)}{\sum_j \exp\left(V(\tilde{\beta_n}, x_j)\right)}$$
(7)

The function  $\tilde{\beta}_n = f(\beta, \sigma | v_n)$  is typically assumed to be normally distributed where the parameters for the mean,  $\beta$ , and the standard deviation,  $\sigma$ , must be estimated based on individual preferences and their variation represented by the variable  $v_n$ , where *n* indexes respondents. However, it is difficult to ascertain the true distribution of personal preferences prior to sampling since their weights are not directly interpretable. Furthermore, fitting a random parameters logit model can be taxing to the researcher since the maximum likelihood estimation is simulated in a manner that could result in differing answers. Yielding a stable solution for the estimator is not always guaranteed [17].

Similar to random parameters logit, hierarchical Bayes requires an assumption of the distribution of preference weights and uses a choice-probability model to represent the responses for each individual. In this method, Equation (7) is used to establish the lower level of a two-level evaluation. The upper level, which is typically assumed to be normal for each preference weight, describes the fluctuation of preferences among respondents and is represented by the relation  $\beta_n \sim N(b, W)$ , where  $\beta_n$  is the individual-specific preference weight parameters, b is the overall preference mean, and W is the variance-covariance matrix of preferences across respondents. In most practical applications, hierarchical Bayes and random parameters logit will generate similar results. In cases in which it is not desirable to assume a common scale across respondents, hierarchical Bayes has the upper hand over random parameters logit, which requires such an assumption [17]. Latent-class finite-mixture model is a method that combats heterogeneity of preferences among respondents. The model produces classes in which the respondents in a given class are homogeneous, but the classes themselves contain heterogeneity among them. Like the aforementioned methods, latent-class finite-mixture models also use choice-probability equations (conditional logit) to determine preference weights. The number of classes is decided by the researcher, and each class will have an associated choice-probability equation to determine preference weights. Once the number of classes is established, the latent-class finite-mixture model applies a special case of a multinomial logit function,  $\pi_q$ , which expresses the probability of the respondent being in each class. The choice probability then becomes:

$$Pr(\text{choice} = 1) = \sum_{q} Pr(\text{choice} = i|\beta_q)\pi_q$$
 (8)

It can be difficult for the researcher to determine the appropriate number of classes, and as with random parameters logit, multiple starting points should be considered to ensure that the model converges to a stable solution. In latent-class fixed-mixture models, the observations from one respondent are independent of one another, but they are assumed to be in the same class. Furthermore, in analyzing results from this method, ratios should be used instead of direct qualitative evaluations for comparisons across classes [17].

Hanson and Jack [19] used utility functions in a multi-dimensional space to assess a DCE which was used to predict whether or not doctors and nurses would accept assignments to rural areas of Africa. They informed the utility function through regression techniques and probability functions based on the responses and demographics of the participants.

#### 2.5 Comparing Models

There are three main values to inspect when analyzing a choice model: Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and negative loglikelihood (the negative of the natural logarithm of the likelihood function). Most software programs will report at least one, and usually all three, of these values. They are a way of comparing models to one another.

AIC is calculated using Equation (9), where k is the number of estimated parameters and  $\hat{L}$  is the maximum value of the likelihood function.

$$AIC = 2k - 2ln(\hat{L}) \tag{9}$$

BIC is calculated using Equation (10), where n is the sample size, k is again the numer of estimated parameters, and  $\hat{L}$  is the maximum value of the likelihood function.

$$BIC = ln(n)k - 2ln(\hat{L}) \tag{10}$$

The negative log-likelihood is a function of the maximum likelihood that is used by the regression models. Since this is a maximization equation, it is advantageous to work with the negative of the log-likelihood. Furthermore, to more accurately approximate large samples, this value is multiplied by two [20]. The second part of Equations (9) and (10) are 2 times the negative log-likelihood. The objective of AIC and BIC is to penalize increasing the complexity of the regression model. BIC places a heavier penalty on more complex models. In practice, Kuha [21] suggests finding models in which both AIC and BIC are favored.

#### 2.6 Coefficients of Logistic Regression Models

When using logistic regression models, it is imperative to understand the output. Unlike linear regression models, the coefficients of logit models are not easily interpretable. The coefficients initially are probabilities, and must therefore be manipulated into odds, and then odds ratios. These odds ratios can be interpreted as the amount of influence a variable has on the outcome. A simple equation from Gould [22] demonstrates the odds ratio in words.

$$\frac{odds(\text{if the corresponding variable is incremented by 1})}{odds(\text{if variable not incremented})}$$
(11)

For the conditional logit model, the exponentiated coefficients are used and are interpreted in the same manner as the ordinary logit model estimates. As the name suggests, conditional logit produces probabilities conditioned on groups that the analyst defines. Therefore, the unconditional probabilities must be determined in order to evaluate odds ratios.

In a multinomial logit model with only two outcomes, the results are considered the same as the ordinary logit models. One of the two outcomes is considered the base outcome, and the exponentiated coefficients are the behavior of the variables in comparison to the base outcome [22].

### 2.7 Multiple Factor Analysis

When a dataset has many variables, sometimes it is advantageous to determine if the number of variables can be reduced. There are several methods for this based on the type of variables under consideration; namely, Principal Component Analysis, Multiple Correspondence Analysis, and Factor Analysis. Each of these techniques are meant to discover underlying relationships in order to reduce the number of dimensions in the dataset.

Principal Component Analysis (PCA) is a technique used for reducing the dimensions of the dataset when the variables are continuous. PCA builds principal components based on linear combinations of existing variables. Since this dataset is mostly categorical in nature, it was deemed that PCA alone was not the most appropriate method. Multiple Correspondence Analysis (MCA) is used for nominal categorical variables. It is used to identify any underlying relationships between variables that can be exploited for dimension reduction. Since the variables in this dataset are of varying types, it was deemed that a special case of Factor Analysis would be most appropriate. Multiple Factor Analysis (MFA) is a Factor Analysis method that combines techniques from both PCA and MCA. The continuous variables are treated similarly to PCA, while the categorical variables are treated similarly to MCA. The result of MFA is identification of which factors account for the highest percentage of the variance in the data [23].

The results of MFA can be viewed in a scree plot. This plot shows the percentage of the variance accounted for by some number of factors. An indication of a useful factor analysis is an "elbow" in the plot; that is, a clear indication in the dropoff of variance explained between two dimensions. For example, consider the third dimension explained 20% of the data and the fourth only explained 5%, then the analyst would consider keeping the first three dimensions.

In determining how many factors to keep, there are generally two guidelines to follow. The first is to choose the number of factors that cumulatively explain 70% or more of the variance, though this is oftentimes difficult with social science data [24]. The second is to include the dimensions that have eigenvalues  $\geq 1$ , which means that these factors explain at least as much variance as a single variable. Rahn [25] claims it would not be advantageous to keep factors that explain less variance than a single variable. She also cautions using this technique because it could cause unwanted exclusions of factors with eigenvalues just below 1.

#### 2.8 Imputation

With any survey data, there is a chance of missing data. Filling in the blanks in a dataset is referred to as imputation. There are many techniques to imputing a dataset, including but not limited to: listwise deletion, single imputation, and multiple imputation. Listwise deletion is a method in which any sample with a single missing value is deleted all together. Single imputation is a term referring to multiple techniques in which the blanks are filled in creating the new dataset. Multiple imputation refers to iteratively imputing the dataset and keeping an average of all of the iterations. Like single imputation, there are also multiple techniques for executing multiple imputation.

For each of these imputation techniques, the analyst should consider the underlying reason for the missing values in the dataset. The data could be missing at random, missing not at random, or missing completely at random. In these cases, the probability of obtaining a missing value is related to observed variables, unobserved variables, or neither, respectively [26]. The determination of the type of missing values in the dataset is important to executing appropriate imputation techniques.

Single imputation techniques considered include mean, mode, hot-deck, cold-deck, and regression. Mean and mode imputation take the mean or mode of the variable and uses it to fill in the blanks of that column. Hot-deck and cold-deck imputation rely on the responses of other individuals to fill in the missing values. A respondent with similar answers otherwise is chosen at random and the appropriate value is used to fill in the missing variable. In general, hot-deck uses a respondent in the dataset being analyzed, whereas cold-deck takes a response from an individual not included in the analysis otherwise. Regression imputation predicts the value of the missing variable based on a regression model of the other respondents. The main technique for multiple imputation considered was multivariate imputation by chained equations. While this method is useful in reducing the bias and accounting for uncertainty in the missing values, it can be difficult to implement when considering variables of differing types [27].

### 2.9 Bootstrapping

In a case where there are more samples needed to ensure the robustness of the modeling techniques used, bootstrapping can be a beneficial method. Bootstrapping is a resampling technique that takes the current samples and generates additional data from them. Like imputation, there are many bootstrapping techniques. Bootstrapping is typically performed on a statistic or metric of a dataset. In the case of a dataset that is mostly categorical variables, the empirical distribution of the columns can be used for bootstrapping [28].

#### 2.10 Utility Modeling

The main objective in a DCE is to identify the utility of alternatives for individual patients. The utility is the sum of observable and unobservable components, shown in Equation (12), where j is an alternative.

$$U_j = V_j + \epsilon_j \tag{12}$$

The observable component,  $V_j$  can be defined as  $V_j = \beta'_j x_j$ , where  $\beta_j$  are the coefficients of the independent variables  $x_j$  in the regression model. The unobservable component is an error term injected into the model by the nature of the respondents

in the discrete choice experiment. It is assumed that the patients select the alternative with the highest utility to them. That is, alternative k is chosen when  $U_k > U_j$  for all cases when  $k \neq j$ . In this case, there are only two alternatives. As a result, the following conditions can be applied resulting in alternative 1 or alternative 2 being chosen, respectively.

$$(U_1 - U_2) = (V_1 - V_2) + (\epsilon_1 - \epsilon_2) > 0$$
$$(U_2 - U_1) = (V_2 - V_1) + (\epsilon_2 - \epsilon_1) > 0$$

Each of these conditions can be simplified to be in terms of the error.

$$\epsilon_2 < (V_1 - V_2) + \epsilon_1$$
  
$$\epsilon_1 < (V_2 - V_1) + \epsilon_2$$

This leads to a probability of selecting alternative 1 or 2, respectively.

$$(P_1|\epsilon_1) = P(U_1 > U_2)$$
  
 $(P_2|\epsilon_2) = P(U_2 > U_1)$ 

To find the unconditional probability, the integral must be taken.

$$P_1 = \int (P_1|\epsilon_1) f_1(\epsilon_1) \ d\epsilon_1$$
$$P_2 = \int (P_2|\epsilon_2) f_2(\epsilon_2) \ d\epsilon_2$$

While the probabilities and utilities can be calculated in this manner, every individual will have a utility function associated with each possible alternative. Therefore, through the use of discrete choice experiments and the analyses associated, results can be produced that offer information regarding which factors drove the decisions for respondents in the surveys overall [29].

## III. Methodology

#### 3.1 Overview

This chapter expands on the material discussed in Chapter II by discussing the applications of the methods used for analysis of the data. The first step upon receiving the data from Dr. Haac and her team was to clean the data. Once the data was cleaned, several methods were explored to analyze the data. Multiple software packages were used, namely R and JMP. The survey, original data set, and cleaned data set can be found in Appendix A.

#### 3.2 Initial Survey Data

The initial survey data consisted of responses from 45 individuals. Each respondent was asked to provide demographics information, as well as current IBD medications, past IBD medications, and current IBD symptoms. The breakdown of how the respondents answered are found in Table 1.

| Demographics           |              |    |   | Current Medications |             |    |   | Symptoms                      |             |    |
|------------------------|--------------|----|---|---------------------|-------------|----|---|-------------------------------|-------------|----|
|                        | Minimum      | 24 |   |                     | Yes         | 37 |   |                               | Yes         | 7  |
| Age                    | Maximum      | 71 |   | Biologic Therapy    | No          | 8  |   | Bleeding                      | No          | 38 |
|                        | Median       | 40 |   |                     | No Response | 0  |   |                               | No Response | 0  |
| _                      | Black        | 6  | 1 |                     | Yes         | 13 |   |                               | Yes         | 17 |
|                        | White        | 37 |   | Immunomodulator     | No          | 32 |   | Frequent<br>Bowel Movements   | No          | 28 |
| Race                   | Asian        | 1  |   |                     | No Response | 0  |   |                               | No Response | 0  |
|                        | No Response  | 1  |   |                     | Yes         | 7  |   |                               | Yes         | 10 |
|                        | High School  | 4  | 1 | Steroid             | No          | 38 |   | Pain                          | No          | 34 |
| Education              | Some College | 15 |   |                     | No Response | 0  |   |                               | No Response | 1  |
|                        | Bachelor's   | 12 |   | Aminosalicylate     | Yes         | 8  |   | Unintentional                 | Yes         | 10 |
|                        | Master's     | 10 |   |                     | No          | 37 |   | Unintentional<br>Weight Loss  | No          | 35 |
|                        | Doctoral     | 4  |   |                     | No Response | 0  |   |                               | No Response | 0  |
|                        | < \$20k      | 2  | 1 |                     |             |    |   |                               | Yes         | 16 |
|                        | \$20 - 40k   | 3  |   |                     |             |    |   | Bloating                      | No          | 28 |
|                        | \$40 - 60k   | 3  |   | Past Me             | edications  |    |   |                               | No Response | 1  |
|                        | \$60 - 80k   | 6  |   |                     | Yes         | 32 | 1 |                               | Every Day   | 4  |
|                        | \$80 - 100k  | 8  |   | Biologic Therapy    | No          | 13 |   | Interference in<br>Daily Life | Most Days   | 3  |
| Household              | \$100 - 120k | 2  |   |                     | No Response | 0  |   |                               | Some Days   | 9  |
| Income                 | \$120 - 140k | 4  |   |                     | Yes         | 20 |   |                               | Rarely      | 22 |
|                        | \$140 - 160k | 3  |   | Immunomodulator     | No          | 25 |   |                               | Never       | 6  |
|                        | \$160 - 180k | 2  |   |                     | No Response | 0  |   |                               | No Response | 1  |
|                        | \$180 - 200k | 0  |   |                     | Yes         | 35 | 1 |                               |             |    |
|                        | > \$200k     | 10 |   | Steroid             | No          | 10 |   |                               |             |    |
|                        | No Response  | 2  |   |                     | No Response | 0  |   |                               |             |    |
| Relationship<br>Status | Married      | 30 |   |                     | Yes         | 19 | 1 |                               |             |    |
|                        | Single       | 11 |   | Aminosalicylate     | No          | 26 |   |                               |             |    |
|                        | Divorced     | 4  |   |                     | No Response | 0  |   |                               |             |    |

Table 1. Breakdown of Demographics, Current Meds, Past Meds, & Symptoms

In addition to these responses, participants were asked to answer the 14 choice sets. Each question consisted of 12 attributes consisting of different outcomes for Treatment A and Treatment B. The respondents chose either Treatment A or B based on the levels of the attributes for each choice set. The frequency of responses for each of the 12 attributes are shown in Figure 1.



Figure 1. Frequency of Responses for Each Attribute

To finish out the survey, the respondents were asked if their physician had discussed treatment via IPAA surgery, medication management, both, or neither. They were also asked which treatment method they would prefer based on their current knowledge. Lastly, they were asked to identify their top three of the 12 attributes that most heavily influenced their choice set responses.

#### 3.3 Reduction of Columns and Imputation

Out of the 45 responses initially received from the survey, eight of the respondents had at least one choice set that they did not respond to. Of these eight, four individuals had three or fewer missing responses. The other four had 6, 10, 12, and 13 missing responses. Before excluding these samples, they were analyzed to determine if the fact that these responses were blank was significant in the models. Once this was determined, further exploration of the missing values determined whether or not it was necessary to keep the blanks in the dataset for model building.

The remaining missing responses were then filled in using imputation. Imputation was done using the R package "imputeMissings" [30]. Since the data were simple binary responses and the missing values were missing completely at random, the imputation method chosen was to use the mode of the variables. Some of the respondents also left missing answers for some of the demographics and medical history information. These missing values were also imputed using the mode technique. Furthermore, several of the variables were considered additional information since they were dependent upon a previous response, and not necessary for modeling of the data. These columns included average number of bowel movements, number of abdominal surgeries, whether or not pain medication was required, the amount of weight lost and in how many months, whether or not a patient had needed blood transfusion(s), and if the respondent answered "Yes" to being Hispanic (only one of the original respondents). After elimination and imputation, the final raw dataset consisted of 42 rows (41 respondents) and 53 columns.

The section of the survey in which respondents were asked to identify their most influential factors made up 12 of the columns in the dataset. This section of the survey was considered additional information and was removed for the majority of the analysis. The final dataset then consisted of 42 rows and 41 columns. The final edit made to the dataset was the levels for the income of the respondents. They were originally put into 10 levels of household income. But to reduce the dimensions in the models, the median was taken and the responses were separated into two levels.

#### 3.4 Multiple Factor Analysis

Often, when there are so many variables in the dataset, one can explore if the number of variables can be reduced somehow. There are several methods of doing this including Principal Component Analysis and Factor Analysis. Generally, these methods require all of the variables to be continuous. Since most of the variables in this dataset were categorical, another method was needed. Multiple Factor Analysis is a variation of Factor Analysis that allows the analyst to identify the types of variables in the dataset. It uses Principal Component Analysis on the continuous variables in conjunction with Multiple Correspondence Analysis for the categorical variables. The R packages "FactoMineR" [31] and "factoextra" [32] are designed for executing Multiple Factor Analysis (MFA). The data under consideration were those associated with each respondent. These data consisted of 26 variables divided into six categories: age (since it is continuous, it remained in its own group), demographics, current IBD medications, past IBD medications, current IBD symptoms, and responses to the two questions concerning physician education and preferred treatment. Through MFA, a scree plot was produced identifying how much of the variability was explained by each of the factors. In general, the desired outcome of a scree plot is for a large proportion of the variance to be explained by as few factors as possible.

#### 3.5 Bootstrapping

With so few respondents in the original dataset, one method to increase the robustness of the models was to perform bootstrapping. In this case, bootstrapping was conducted in Excel. The distribution of each of the columns was identified and an additional 955 respondents were generated for a total of 1000 respondents. Having this many rows of data eliminated any issues with overfitting the model due to a lack of responses for the vast number of variables included. It was assumed that the initial respondents were representative of the entire population, and the analyses were conducted using the bootstrapped dataset.

#### 3.6 Modeling

This section describes the methods used to model the data. Modeling was conducted in both R Version 3.6.1 [33] and JMP Pro 13 [34].

#### 3.6.1 Modeling in JMP

As with any software tool, there are some nuances to JMP in terms of the data and its format. Formatting was performed in Excel prior to importing. When using the Choice Model tool, there are two options: one table format and multiple table format. In the multiple table format, the data is divided into three tables which identify response data, profile data, and subject data. The response data is pulled from a table containing the actual responses to the choice sets. The profile data is pulled from a table containing the attributes of each of the choice sets. The subject data is a table containing the demographics and medical history of the respondents. The one table format pulls all of the same information but from a single table. For this analysis, the one table format was used. To be sure that the data was in the appropriate format before importing, Excel Visual Basic for Applications was used to alter the data from its original format. The resulting dataset contained 28 rows for each respondents, for a total of 28,000 rows. Each respondent had two rows for each of the 14 choice sets, with one of those two rows indicating which of the options they chose. The columns included the alternative level (0 for non-preferred alternative, 1 for preferred alternative). These alternatives in conjunction with the indication of the choices made are the drivers of the Choice Model tool.

The inputs for the Choice Model from one table included the indication of the choice, the subject ID number, and the choice set ID for the response section. The construct effects were the twelve attributes for each of the choice sets. The profile effects were the remaining columns consisting of demographics and medical information of each of the respondents.

This tool allows for the user to select a few options in reference to the execution of the model, namely inclusion of firth-bias adjusted estimation and hierarchical Bayes. For the purpose of this analysis, firth-bias adjusted estimation was used, but hierarchical Bayes was not since there were so many variables in the model. Regardless of the options chosen here, JMP Choice Model builds a conditional logistic regression model.

#### 3.6.2 Modeling in R

There are many statistical packages built for execution in R. The packages used specifically for model-building in this case were "mlogit" [35], "clogitL1" [36], and "survival" [37]. Each of these packages include functions which build regression models. The "mlogit" [35] package is designed for the execution of multinomial logistic regression models. The "clogitL1" [36] package was designed for the execution of conditional logistic regression models. The "survival" [37] package has a broad scope of functions to execute for various problems, but the main execution used here was a function to build conditional logistic regression models.

Similar to JMP, there are nuances to formatting the data appropriately to import into R for analysis. Again, this formatting was conducted in Excel using Visual Basic for Applications. The format of the data was nearly identical to that of the JMP dataset, with the exception of a logical column for the selection of a specific choice instead of a binary 0/1. The data for R also included a column called "strata" which was a code that included the respondent number and the question. For example, the code for the fifth question that the third respondent answered would be 305. This column was called in the conditional logistic regression models as a way to group the respondents and their answers.

#### 3.7 Modeling Comparisons

Before any additional exploration of modeling was conducted, the models in JMP and R were compared with one another. The comparisons were based on three measurements: AIC, BIC, and log-likelihood. Each of these three measurements rely on the maximum likelihood in calculating their values. The values themselves don't inherently have any meaning, but instead they are used to compare models to one another. In general, the lower the value for each of these, the better. In some cases, the AIC and BIC will have conflicting results due to the level of penalty each applies given the number of variables in the model.

#### 3.8 Identification of Significant Factors

In any regression model, the desired outcome is identification of significant factors that explain the dependent variable(s), which in this case was the choice in each choice set. Since there were so many factors considered in these models, there were variables that were deemed insignificant in each of the models. Therefore, to produce the most efficient and significant model possible, the insignificant variables were methodically removed. There are several subset selection approaches to determining the most appropriate model including forward step-wise regression, backward step-wise regression, and exhaustive search. These processes take into consideration factor interactions that may or may not be significant in the models. While exhaustive search is generally the most thorough of these subset selection techniques, forward and backward step-wise regression are much quicker. Furthermore, the backward step-wise technique is typically preferred to ensure that all interaction terms are considered [14].

In logistic regression models, the odds ratios are reported as the exponentiated coefficients. The odds ratios are important for determining the value of terms in the model for consumers and were therefore used to draw inferences about the data. Furthermore, McFadden's pseudo  $R^2$  was calculated using Equation (6) as a measure to determine the quality of the model.

#### 3.9 Application of Models

The logistic regression models identified factors that are relevant to patients. Taking this and applying it in the field required the development of utility models that the physicians can use to guide which treatment methods to consider when dealing with each of their patients. For the majority of this analysis, JMP was used. In the Choice Model of JMP, there are multiple built-in tools for applying models to determine patient preferences. One such tool is the Probability Profiler. This tool allows for the analyst to quickly determine which of the attributes contribute the most to the likelihood of a patient preferring one alternative over another. Another useful tool is the Effect Marginals. This tool allows the analyst to inspect the marginal probability and marginal utility for each main attribute in the model; that is, the analyst can determine what the value of each of the attributes are to the patients given all other attributes do not change. Another tool in JMP is the Utility Profiler, which is similar to the Probability Profiler. With this tool, the analyst is able to infer relationships between the attributes of an alternative and the characteristics of the individuals.

### 3.10 Final Comparisons

The last step in the analysis was to compare the responses from the initial 41 respondents to the questions concerning their treatment preference based on their current knowledge and the questions concerning the most influential attributes to their decision making in the 14 choice sets. These results were compared to those produced by the modeling techniques, and in doing so, validated the models.
## IV. Analysis and Results

### 4.1 Overview

This chapter presents the results and analysis of the methods discussed in Chapter III using both R and JMP. The techniques applied in each of these software programs yielded similar results.

## 4.2 Results of Multiple Factor Analysis

The first results from the methodology were from the MFA conducted. The scree plot in Figure 2 shows the result from the MFA conducted in R.



Figure 2. Percentage of Variability Explained by Factors

In this case, the most influential factor explained 10% of the variance. Further-

more, the scree plot has no such indication of a drop-off in explained variance since the line is fairly smooth from top left to bottom right. In order to achieve 70% explanation of variance in the dataset, 12 factors are needed. While this reduces the number of variables from 26, it is not all that useful. To enhance the reduction, eigenvalues were analyzed for the variables. The first six factors had eigenvalues > 1, but only explained 48% of the variability.

The individual factor map was another R tool that was implemented in analyzing the results of the MFA.



Figure 3. Individual Factor Map

Figure 3 shows the individual factor map with the five factors used for the multiple factor analysis. This map suggests that current symptoms contribute most to the variability explained by the first dimension (Dim 1), and that current medications play a large part in determining the variability explained by the second dimension (Dim 2). However, as seen here and in the scree plot, the total variability explained by the first two dimensions was only 20%, which leaves a lot to be desired from this MFA.

Multiple Correspondence Analysis in JMP was also conducted to compare the results with those produced through the methods in R. These results were similar, and it was concluded that it would be best to conduct the analysis with all of the original factors in the model.

#### 4.3 Significance of Missing Values

Prior to removal of the blanks, a model was built to see if they were significant. The model was built in JMP using the Choice Model. The check box for "No Choice" was selected for this analysis. In this case, the respondents were essentially allowed to not select either option in choice sets. The Choice Model reported the results of the conditional logistic regression model, and significance of terms was determined through likelihood-ratio tests and p-values. The results of the model showed that the missing values were significant. One interpretation of this result is that for those individuals, it was difficult for them to determine the difference between alternatives. To further determine how to interpret motivation for individuals not responding to questions, these specific samples were explored further. There was no clear indication of similarities or patterns in the missing data that would suggest these missing values were not random. That is, there was no additional insight that could be gained from exploring the blanks in the dataset. Therefore, these missing values were excluded for the individuals that did not respond to six or more choice sets, and were imputed for individuals that did not answer three or fewer choice sets.

### 4.4 Initial Regression Models

The initial regression models were built in both JMP and R using the bootstrapped dataset. It was advantageous to compare the results of each of these software platforms. For model comparisons, the Choice Model in JMP was used which builds a conditional logistic regression model, the "clogit" function in R's "survival" [37] package was used which also builds a conditional logistic regression model, and the "mlogit" function in R's "mlogit" package [35] was used which builds a multinomial logistic regression model. The results yielded coefficients and p-values at a 95% confidence level. These results were used in comparison of models and significant terms throughout the iterations.

In this iteration of modeling, the intention was to determine which of the 12 attributes were significant. That is, which of the 12 attributes did respondents consider the most important. The models from JMP and R using the training dataset resulted in 10 out of 12 attributes being significant. The two that were not significant were risk of side effects and stool frequency. The results from both R and JMP can be seen in Table 2. Both the conditional logit model and the multinomial logit models yielded the same results.

| Attribute                            | Estimate (JMP) | P-Value <mark>(</mark> JMP) | Estimate (R) | P-Value (R) | Significant |
|--------------------------------------|----------------|-----------------------------|--------------|-------------|-------------|
| 30-yr risk of colorectal cancer      | -0.88          | < 0.0001                    | 1.76         | < 0.0001    | Yes         |
| Need for prolonged meds              | -0.41          | < 0.0001                    | 0.81         | < 0.0001    | Yes         |
| 2-yr health care costs               | 0.17           | < 0.0001                    | -0.34        | < 0.0001    | Yes         |
| Need for ostomy                      | -0.78          | < 0.0001                    | 1.57         | < 0.0001    | Yes         |
| Risk of bowel obstruction            | -0.54          | < 0.0001                    | 1.08         | < 0.0001    | Yes         |
| Risk of leak                         | -0.28          | < 0.0001                    | 0.55         | < 0.0001    | Yes         |
| Risk of sexual dysfunction           | -0.06          | 0.004                       | 0.13         | 0.004       | Yes         |
| Risk of difficulty becoming pregnant | 0.13           | < 0.0001                    | -0.25        | < 0.0001    | Yes         |
| Need for emergent surgery            | -0.93          | < 0.0001                    | 1.86         | < 0.0001    | Yes         |
| Avg hospitalizations in 2 yrs        | -0.15          | < 0.0001                    | 0.29         | < 0.0001    | Yes         |
| Risk of side effects                 | 0.03           | 0.210                       | -0.06        | 0.211       | No          |
| Avg stool frequency                  | -0.04          | 0.090                       | 0.08         | 0.088       | No          |

 Table 2. Initial Regression Model Results

Notice the estimates between the models are different. The results of the Choice Model in JMP reports the estimates as part-worths; whereas, the logit models from R report estimates that coincide with probabilities. In either case, the estimates are not directly interpretable for the purposes of this study. However, the key takeaway was that the same 10 attributes were significant in all of the models.

Before continuing with the analysis, the three models were compared using AIC, BIC, and log-likelihood. The AIC, BIC, and log-likelihood for each are reported in Table 3.

Table 3. Model Comparison: AIC, BIC, & -2\*LogLikelihood

| Model Type               | AIC       | BIC       | -2*LogLikelihood |
|--------------------------|-----------|-----------|------------------|
| Multinomial Logit in R   | 10,380.04 | 10,648.23 | 10,372.12        |
| Conditional Logit in R   | 10,374.41 | 10,460.76 | 10,350.41        |
| Conditional Logit in JMP | 10,374.45 | 10,460.77 | 10,350.42        |

The conditional logit models from both platforms produced nearly identical AIC, BIC, and log-likelihood values. This could be considered validation for the use of each of the platforms moving forward. Each of the values for the multinomial logit model were just slightly higher than those for the conditional logit models. Furthermore, it is important to recall that BIC has a heavier penalty for increased complexity of a model. Therefore, for the sake of comparison, BIC was the criteria of focus for this model comparison. The conditional logit models in both R and JMP outperformed the multinomial logit model. Therefore, the conditional logit models were used moving forward.

Before considering interaction terms in the model, the two insignificant terms were removed and the models were run again. While the estimates changed slightly, the results were essentially the same. Therefore, without considering interactions from patient characteristics, all attributes except risk of side effects and average stool frequency could be valuable to the patient.

## 4.5 Modeling with Interaction Terms

After exploring models with the main attributes, the patient characteristics were introduced as interaction terms. The odds ratios of the conditional logit model in R were analyzed with all of the terms included. The odds ratios are reported as the exponentiated coefficients in R. Out of all of the odds ratios reported in the model, there were only four which had odds ratios greater than 10. These terms were risk of cancer, need for ostomy, risk of obstruction, and risk of emergent surgery. The odds ratio for risk of emergent surgery was the greatest at 48.89. This means that for every unit decrease of risk of emergent surgery, the odds of the respondent choosing that alternative were increased by a factor of 48.89. Ultimately, there were only six variables that had odds ratios over 2, which can be seen in Table 4. The four that were previously mentioned, as well as need for prolonged medications and risk of leak. These results suggested that those were the most influential factors to the respondents.

| Attribute                 | Odds Ratio |
|---------------------------|------------|
| Need for Emergent Surgery | 48.89      |
| Risk of Cancer            | 33.59      |
| Need for Ostomy           | 18.11      |
| Risk of Obstruction       | 11.12      |
| Prolonged Meds            | 7.62       |
| Risk of Leak              | 2.90       |

Table 4. Variables with Odds Ratios > 2

To gain additional insight to the value of the variables being added to the model, each of the 24 variables that described the individuals were introduced to the original 12 attributes one at a time. The results were compared to each other to draw inferences about how each of the covariates behaved in relation to the other terms in the model. For this, the conditional logit in R was used. The p-values were assessed at an alpha level of 0.05. Sex, history of ostomy, current steroid, current aminosalicylate, history of an immunomodulator, history of an aminosalicylate, bleeding as a current symptom, and pain as a current symptom had no effect on the model. Education, relationship, history of abdominal surgery, current biologic therapy, current immunomodulator, and frequent bowel movements as a current symptom were terms that were not significant as interactions. But, they did alter which of the original 12 attributes were significant. The terms that did produce significant interactions were age, race, income, IBD type, years diagnosed, history of biologic therapy, history of a steroid, unintentional weight loss, bloating as a current symptom, and frequency of symptoms interfering with daily life. The results of these independent interactions being introduced to the model were compared to the model with all two-term interactions included. The risk of difficulty becoming pregnant and stool frequency were terms that were not significant in any interactions. While risk of difficulty becoming pregnant was significant in many of the models without an interaction, it was not significant in the full model. Stool frequency was not significant in the full model, nor the original model. Stool frequency only became significant when race, frequent bowel movements, and frequency of symptoms interfering with daily life were independently introduced into the model, but none of the interaction terms were significant. The behavior of the characteristic terms in the model were similar to the models in which they were individually introduced. There were 14 of these terms that had no significance in the model: sex, education, relationship, history of abdominal surgery, history of ostomy, current biologic therapy, current immunomodulator, current steroid, current aminosalicylate, history of immunomodulator, history of aminosalicylate, and current symptoms of bleeding, frequent bowel movements, and pain.

## 4.6 Step-Wise Regression

In order to rid the model of insignificant terms, backward step-wise regression was conducted. This technique was selected because it performs better than forward step-wise regression when large subsets are being analyzed [14]. In backward stepwise regression, F-statistics are used to determine which variables enter and exit the model. While any subset selection technique has its limitations, backward step-wise regression is quicker than alternative methods and considers all possible interaction terms. Therefore, it was used as the model selection method for this analysis.

The step-wise regression started with all two-factor interactions in the model and removed variables until only significant terms remained in the final model. These processes were hierarchical models meaning main effects would remain in the model if significant interaction terms depended on them, even if the main effects themselves were not significant.

The next phase of modeling was to include all of the attributes and their interactions. Although the risk of side effects and stool frequency were considered insignificant in the original models, they were kept in the first models including interaction terms. If they were involved in interactions that were significant, then they would be kept in further iterations of modeling.

The model with two-factor interactions resulted in a total of 420 terms in the model. There were seven out of 12 of the attributes that were significant on their own: 30-yr risk of colorectal cancer, need for prolonged medication, 2-yr health care costs, need for ostomy, risk of obstruction, risk of leak, and need for emergent surgery. With that being said, there were interaction terms that included insignificant attributes, which included: risk of side effects\*race, stool frequency\*education, stool frequency\*relationship, stool frequency\*bleeding as a current symptom, risk of side effects\*frequency of symptoms interfering with everyday life.

The only attribute that was not significant independently or with an interaction term was the average hospitalizations over a two-year period. Since this was a significant term in the initial model, it could not be removed after this iteration. However, many interaction terms were insignificant.

The model produced through backward step-wise regression in JMP had 24 terms. Stool frequency was the only attribute that was not significant on its own or in interaction terms. Each of the other covariates were significant to an alpha level of 0.05 with the exception of risk of sexual dysfunction and risk of side effects. These terms remained in the model because they were significant in interaction terms. The model produced through backward step-wise regression using the "stepAIC" function from the "MASS" package [38] in R also resulted in 24 terms. Of these covariates, all were significant to an alpha level of 0.05 with the exception of risk of sexual dysfunction. This term remained in the model because its interaction with frequency of symptoms interfering with everyday life was significant.

The McFadden's pseudo  $R^2$  was calculated in R using the "support.CEs" package [39]. The "gofm" command reports goodness-of-fit measures for a model, including the McFadden's pseudo  $R^2$  for a conditional logistic regression model. The McFadden's pseudo  $R^2$  for this model was 0.24. This result indicated a well-fit model since McFadden [18] claims that a model with a McFadden's pseudo  $R^2$  between 0.2 and 0.4 is considered a very good fit. Therefore, analysis using this model could be confidently conducted.

## 4.7 Application of Models

Since both R and JMP produced similar useful models, further analysis was conducted using the tools in the JMP Choice Model platform: Effect Marginals, Utility Profiler, and Probability Profiler.

#### 4.7.1 Effect Marginals

The first tool used was the Effect Marginals. The marginal probability and marginal utility were displayed for each of the main attributes in the model, and are shown in Figure 4. For each of these attributes, the 0 represents the less desirable option and 1 represents the more desirable option. For example, the 0 for cancer represents an 18% chance of the patient being diagnosed with colorectal cancer in the next 30 years, whereas the 1 represents a 0.06% chance of being diagnosed with colorectal cancer in the next 30 years (see Appendix A for details on the levels for each

attribute). The marginal probability is interpreted as how likely the patient would be to choose 0 or 1 based on all other attributes remaining at their same level. The marginal utility offers similar information, but the utilities for each level are reciprocals instead of probabilities on a [0,1] scale. The more drastic the difference between each level of an attribute, the more valuable that attribute is to the respondents.



Figure 4. Marginal Effects of Main Attributes

In the results of the Effect Marginals, there were clearly dominating attributes in the model. The risk of cancer, need for ostomy, and risk of emergent surgery were the three main attributes that most heavily influenced which alternative the patients preferred.

#### 4.7.2 Utility Profiler

The next tool utilized was the Utility Profiler. This tool allows the analyst to view the impact that each attribute and characteristic term have on the overall utility. The utility is calculated with a 95% confidence interval. For example, a patient whose characteristics are all at the default levels and viewing the medical management alternative has a utility of -1.01 with a confidence interval of [-1, 23, -0.80], as shown in Figure 5. The more drastic the slope between the levels of an attribute, the greater influence that attribute had on the utility of a choice.



Figure 5. Utility Profiler Example (Medical Management alternative)

The utility function is such that the utility for the IPAA alternative is the reciprocal of the medical management alternative. In the example above, this patient would have a utility for IPAA of 1.01. Whichever alternative has a positive utility is the preference for the patient, so in this example the IPAA alternative was preferred. By adjusting the characteristic terms, the utility for any type of patient could be determined. The main objective was to identify whether or not there was any point in which one alternative would be preferred for one patient, but the other alternative would be preferred for another patient. With the given construct, there were over 16.7 million combinations of patient characteristics. Therefore, only the effects that were significant in the model were inspected. These characteristic terms included age, sex, IBD type, history of steroid, unexpected weight loss as a current symptom, and frequency of symptoms interfering in daily life. Age was the only continuous variable, so minimum age and maximum age were considered. Furthermore, each of the characteristics were examined at their highest and lowest levels. This resulted in a much more manageable 64 combinations. In every patient profile explored, the IPAA alternative had the higher utility. This was due to the major impact that the risk of cancer and the risk of emergent surgery had on the model. Both of these attributes were at the low levels for the IPAA alternative. Since there were no patient profiles that displayed a preference for medical management, other combinations making up patient profiles were explored. None of these additional profiles had a utility in favor of medical management, but one result had a confidence interval that contained 0. This patient profile was for a female patient, any age, with a history of steroid, weight loss as a current symptom, and symptoms interfering with daily life some days or most days. The confidence interval containing 0 illustrates that given this patient profile, there is a chance that this patient would prefer IPAA over medical management.

#### 4.7.3 Probability Profiler

The last tool used in the JMP platform was the Probability Profiler. Similar to the Utility Profiler, this tool allows the analyst to compare preferences given patient profiles. This tool asks for the user to define what the levels of each attribute are for the "baseline". In this case, the baseline levels were those for the medical management alternative. Once the baseline was established, the analyst can then set the levels of the attributes to compare other alternatives to medical management. Since the only other alternative was IPAA, the attribute levels were set accordingly in the Probability Profiler. Based on the default levels for the characteristics of the patient, the result was that the probability this patient would choose IPAA over medical management was 88%, as seen in Figure 6. The greater the slope between the levels of an attribute, the more influence that attribute had on the probability of an individual preferring one alternative over the other.



Figure 6. Probability Profiler Example

Beyond the attribute levels, the user can also design patient profiles. The results mirrored those of the Utility Profiler. For any patient profile, the probability of him/her preferring the IPAA alternative was greater than medical management. The patient profile that yielded the confidence interval containing 0 in the Utility Profiler was analyzed here as well. In this case, the patient would elect IPAA over medical management 62% of the time. The other patient profiles that were tested were around 80% probability of preferring IPAA over medical management.

## 4.8 Comparison to Initial Patient Preferences

In the survey, the patients were asked to identify which treatment they would prefer with their current knowledge, as well as ranking the most influential attributes to their decisions in the choice sets. It was valuable to compare the results of these responses to those yielded through the modeling techniques. The responses from the original 41 responses were analyzed for this comparison. Again, it was assumed that these respondents are representative of the entire population.

Out of the 41 respondents, only three claimed to prefer the IPAA alternative over medical management based on their current knowledge. The distribution of the responses for education patients have received from their medical staff was aligned with the preferences: over 63% responded that their medical staff had not spoken to them about either alternative, 20% had received education on both, 0% were taught exclusively about IPAA, and 17% were taught exclusively about medical management. Out of all the respondents that had received some sort of education on treatment alternatives, nearly half of them were only taught about medical management. Therefore, it is logical for patients to prefer the medical management alternative, which was not the result of the model. This provides evidence for a need of an increase in education, especially for IPAA.

The respondents were asked to identify their top three most influential attributes in rank order. The results of the top four overall attributes are displayed in Table 5.

Table 5. Breakdown of Most Influential Attributes by Percentage of Responses

| Attribute                |     |     |     |       |
|--------------------------|-----|-----|-----|-------|
| Attribute                | 1   | 2   | 3   | Total |
| Risk of Cancer           | 46% | 5%  | 10% | 61%   |
| Need for Ostomy          | 34% | 12% | 15% | 61%   |
| Risk of Emergent Surgery | 10% | 15% | 9%  | 34%   |
| Risk of Obstruction      | 7%  | 7%  | 20% | 34%   |

Nearly half of the respondents considered the risk of cancer to be their most influential attribute throughout the choice sets. The next top choices for the most influential were need for ostomy, risk of emergent surgery, and risk of obstruction, respectively. These four attributes contributed to 25% of the overall responses for this question. For the top four, at least one-third of the respondents agreed that these were the most influential attributes. These results can be considered a validation of the results from the models. When cross referenced with the Effect Marginals output, it is obvious that these two results align with one another. The four attributes that offer the highest utility for the patients in both cases were the same. Therefore, the model used for this analysis can be utilized for future patients in determining treatment plans.

Comparing the driving factors was important, but the least important factors

were also compared. The three attributes that were consistently the least significant across all the models were risk of sexual dysfunction, risk of side effects, and stool frequency. Therefore, these three attributes were compared to the results of the original 41 respondents. There were three individuals that considered risk of sexual dysfunction as one of their driving factors, whereas only two respondents claimed risk of difficulty becoming pregnant to be a driving factor. While this is interesting, it is important to note that the risk of difficulty becoming pregnant was only a factor for females, which made up 23 out of 41 of the original respondents. There were five respondents who considered stool frequency and seven who considered risk of side effects to be in their top three most important factors. There were two other factors that were considered less influential with only four respondents selecting each: two-year health care costs and risk of leak.

## 4.9 Chapter Summary

In this chapter, methods and techniques used to analyze the data were discussed. This included MFA, exploration of logit models, subset selection, and interpretation of the results. In particular, the final model had 24 variables and the results generally coincided with the responses from the initial respondents. The utility for the IPAA and medical management alternatives were analyzed. For all patient profiles, the utility of IPAA was greater. These results were driven by the probability of patients selecting an alternative with the more desirable levels for the risk of cancer and risk of emergent surgery attributes.

## V. Conclusions and Recommendations

This chapter provides an overview of the analytics conducted in this study. The conclusions are discussed and recommendations for future work are offered.

#### 5.1 Conclusion

With analytic approaches complete, conclusions could be drawn regarding the preferred method of treatment for patients with inflammatory bowel disease. These conclusions were made from the use of logistic regression models and the responses from the original 41 surveys. Based on the given models, a physician is able to determine which treatment type is likely preferred by a patient with any profile of characteristics.

The first discovery from all of the modeling techniques was that 10 out of the 12 main attributes were considered significant when patient profiles were not considered. The two that were not significant were stool frequency and risk of side effects. When incorporating the patient characteristics as interaction terms, the risk of sexual dysfunction, the risk of difficulty becoming pregnant, and the average hospitalizations in a two-year period also become insignificant. Although there were five insignificant attributes with a full logit model, there was also a lot of noise. Because of this, all attributes remained in the model until noise-inducing covariates were removed.

After completing step-wise regression, a final model was used to draw conclusions concerning probabilities and utilities for patients. The final model consisted of 24 variables, in which all main attributes except stool frequency were included. The remaining terms were interactions of the main attributes with age, sex, IBD type, history of steroid, weight loss as a current symptom, and frequency of symptoms interfering with daily life. From this model, marginal effects were determined, which included the marginal probability and marginal utility for each of the main attributes in the model. The results of these marginal effects clearly indicated that three attributes were the most influential for patients. Risk of cancer, need for ostomy, and risk of emergent surgery all had marginal probabilities over 75%. That is, the preferential level of these attributes were chosen over 75% of the time. In addition, these three attributes also carried the highest utility for the patients, as well as the highest odds ratios.

The results from modeling indicated that the utility of IPAA is greater than medical management for every patient profile. The only instance in which this may not be the case is for female patients with a history of steroid, weight loss as a current symptom, and symptoms interfering with daily life some days or most days. For this patient profile, the utility is estimated to be greater for IPAA, but there is a slight chance that she would prefer medical management. Overall, for any given patient profile, the probability of that patient preferring IPAA to medical management was around 80%, with the aforementioned patient profile preferring IPAA to medical management with a probability of 62%.

The patients were initially asked to identify their three most influential attributes in the survey. A comparison was made between these results and the results of the model. The three most influential attributes according to the model were risk of cancer, risk of emergent surgery, and need for ostomy. The responses the patients gave in the survey mirrored these results. In the cases of risk of cancer and need for ostomy, 61% of respondents claimed that these attributes were one of their three most important factors, with 46% saying that risk of cancer was their number one most influential. 34% of individuals considered risk of emergent surgery to be one of their three most influential attributes. The same number of individuals also considered risk of obstruction to be in their top three. This also mirrors the results of the model in that risk of obstruction had the fourth highest marginal effect.

The patients were also asked if their physicians had discussed either of the methods with them, and which of the two methods they preferred based on their current knowledge. The question concerning patient education showed that 63% of respondents had not received any education from their physicians, 17% had received education on medical management only, and 20% had received education on both medical management and IPAA. There were only 7% of the individuals that would prefer IPAA to medical management, all of which had received education on both treatment methods. These respondents makes up 38% of the respondents that had received education on both methods. The results from these questions suggest that patient preferences are driven by the education they receive.

#### 5.2 Recommendations

Based on the conclusions, recommendations can be made to Dr. Haac and her associates at University of Maryland Medical Center. The main takeaway is to focus on educating patients on the attributes and their levels, specifically risk of cancer, need for ostomy, risk of obstruction, and risk of emergent surgery. The initial survey results suggested that without education, patients prefer medical management. Properly educating the patients on the attributes and their levels results in the patients preferring IPAA. Furthermore, the patient characteristics that were most important in determining preferences were weight loss as a current symptom and frequency of symptoms interfering with daily life.

The original number of survey respondents was 45, with 41 usable samples. Techniques were employed to overcome the minimal number of samples. However, these techniques come with assumptions. To ensure more concrete results, more samples are needed.

## 5.3 Future Work

The model approaches used for this research included conditional logistic regression and multinomial logistic regression. In the literature review, several other approaches were discussed. With an extended period of time, the mixed logistic regression model should be considered. Furthermore, there are many types of model selection techniques. Methods beyond backward step-wise regression could be considered.

In the modeling, the levels were simplified to high and low, but the respondents still saw the actual attribute levels in each of the choice sets. The levels were determined by Dr. Haac and her team of experts, but if the levels were to ever change, the responses of the individuals might change accordingly. Therefore, sensitivity analysis on the attribute levels could be conducted to see what the impact of this would be. Since the attribute levels were reduced to high and low levels, an entirely new round of surveys would need to be conducted to determine the impact that changing attribute levels would have on patient responses.

In addition to the design of this survey, a continuous column of prices would be beneficial to add to the study. In doing so, a willingness-to-pay model could be created. This would afford the physicians the opportunity to see how much patients are "willing to pay" for a change in one of the attribute levels. This is an additional feature of the JMP Choice Model that could be employed with the appropriate data, and is generally easy to interpret in comparison to the output of the logit models used here.

# Appendix A. Survey

## 1.1 Attribute Levels

| Attribute                            | Medical Management | IPAA Surgery                                   |
|--------------------------------------|--------------------|--|
| 30-yr risk of colorectal cancer      | 18%                | 0.06%  |
| Need for prolonged meds              | 90%                | 50%  |
| 2-yr health care costs               | \$15,700           | \$6,400  |
| Need for ostomy                      | No                 | Temporary                                      |
| Risk of bowel obstruction            | 0%                 | 20% (8% requiring operative intervention)      |
| Risk of leak                         | 0%                 | 10%  |
| Risk of sexual dysfunction           | 0%                 | 3% impotence in men<br>8% dyspareunia in women |
| Risk of difficulty becoming pregnant | 25%                | 40%  |
| Need for emergent surgery            | 1%                 | 0.05%  |
| Avg hospitalizations in 2 yrs        | 4.8                | 1.4  |
| Risk of side effects                 | Yes                | No   |
| Avg stool frequency                  | 10                 | 6  |

# 1.2 Survey Construct

## PART I: Baseline Characteristics

| 1)       | Age in years:              |              |           |            |                |                  |                                 |
|----------|----------------------------|--------------|-----------|------------|----------------|------------------|---------------------------------|
| 2)       | Sex (circle one):          | Male         |           | Female     | 9              | Prefer not to re | spond                           |
| 3)       | Race (circle one):         |              | Black     |            | White          | Asian            | other:                          |
|          | a. Hispanic (circle        | e one):      | yes       | no         |                |                  |                                 |
| 4)       | Education (circle one):    |              |           |            |                |                  |                                 |
|          | less than High School      |              | High S    | chool/GE   | D              |                  | Some College/Associate's Degree |
|          | Bachelor's Degree          |              | Gradu     | ate Degr   | ee             |                  | Doctoral Degree                 |
| 5)       | Gross annual househol      | d income     | e (circle | one):      |                |                  |                                 |
| less tha | an \$20,000                | \$20,00      | 0-\$40,0  | 00         |                | \$40,000-\$60,00 | \$60,000-\$80,000               |
| \$80,00  | 0-\$100,000                | \$100,0      | 00-\$120  | ),000      |                | \$120,000-\$140, | 000 \$140,000-\$160,000         |
| \$160,0  | 00-\$180,000               | \$180,00     | 00-\$200  | ),000      |                | more than \$200  | ),000                           |
| 6)       | Relationship status (cir   | cle one):    |           | Marrie     | d              | Single           | Divorced                        |
| 7)       | Type of IBD (circle one    | ):           | Crohn     | 's         | Ulcerat        | ive Colitis      | Indeterminate-type              |
| 8)       | History of abdominal s     | urgery fo    | r IBD (c  | ircle one  | ):             | yes no           |                                 |
|          | a. If yes, number          | of previo    | ous surg  | eries:     |                |                  |                                 |
|          | b. History of osto         | my:          | yes       | no         |                |                  |                                 |
| 9)       | Current IBD medication     | ns (circle   | all that  | apply)     |                |                  |                                 |
|          | Biologic therapy           | An Imn       | nunomo    | odulator   |                | Steroids         | An Aminosalicylate              |
| 10)      | Past IBD medications (     | circle all t | that app  | oly)       |                |                  |                                 |
|          | Biologic therapy           | An Imn       | nunomo    | odulator   |                | Steroids         | An Aminosalicylate              |
| 11)      | Current IBD-related sy     | mptoms       | (circle a | ll that ap | ply)           |                  |                                 |
|          | Bleeding (if yes, is ther  | e a need     | for bloo  | od transf  | usion? )       | (es or No)       |                                 |
|          | Frequent bowel mover       | nents (if    | yes, ave  | erage nur  | nber of        | daily bowel mov  | ements:)                        |
|          | Pain (if yes, is chronic p | oain med     | ication   | required   | ? <u>Yes o</u> | r No)            |                                 |
|          | Unintentional weight l     | oss (if yes  | s, specif | ý:         | number         | of pounds in     | months)                         |
|          | Bloating                   |              |           |            |                |                  |                                 |
| 12)      | How often do the abov      |              |           | erfere wi  |                |                  |                                 |
|          | Every day                  | Most d       | ays       |            | Some o         | lays             | Rarely Never                    |

## PART II: Choice Sets (for each of the following scenarios, check which treatment you would prefer)

#### Choice Set 1

| Attribute   | Treatment A  | Treatment B |
|---|--|-------------|
| 30-year risk of colorectal cancer   | 18%  | 0.06%       |
| Need for long term medications to control disease   | 90%  | 50%         |
| 2-year health care costs  | \$15,700   | \$6,400     |
| Need for ostomy   | Temporary  | No          |
| Risk of obstruction   | 20% (8% requiring operative intervention)                        | 0%          |
| Risk of leak  | 0%   | 10%         |
| Risk of sexual dysfunction  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women | 0%          |
| Risk of difficulty becoming<br>pregnant   | 40%  | 25%         |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | Yes  | No          |
| Stool frequency (BM/day)  | 6  | 10          |
| Average number of hospitalizations over 2-year period   | 4.8  | 1.4         |
| Need for emergent surgery   | 0.05%  | 1%          |
| Check which treatment you prefer  |  |             |

| Attribute   | Treatment A | Treatment B |
|---|-------------|-------------|
| 30-year risk of colorectal cancer   | 0.06%       | 18%         |
| Need for long term medications to control disease   | 90%         | 90%         |
| 2-year health care costs  | \$15,700    | \$15,700    |
| Need for ostomy   | No          | No          |
| Risk of obstruction   | 0%          | 0%          |
| Risk of leak  | 10%         | 10%         |
| Risk of sexual dysfunction  | 0%          | 0%          |
| Risk of difficulty becoming pregnant  | 40%         | 40%         |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | Yes         | No          |
| Stool frequency (BM/day)  | 10          | 10          |
| Average number of hospitalizations over 2-year period   | 1.4         | 1.4         |
| Need for emergent surgery   | 1%          | 0.05%       |
| Check which treatment you prefer  |             |             |

| Attribute   | Treatment A  | Treatment B |
|---|--|-------------|
| 30-year risk of colorectal cancer   | 0.06%  | 18%         |
| Need for long term medications to<br>control disease  | 90%  | 50%         |
| 2-year health care costs  | \$15,700   | \$6,400     |
| Need for ostomy   | No   | Temporary   |
| Risk of obstruction   | 20% (8% requiring operative intervention)                        | 0%          |
| Risk of leak  | 10%  | 0%          |
| Risk of sexual dysfunction  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women | 0%          |
| Risk of difficulty becoming<br>pregnant   | 25%  | 40%         |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No   | Yes         |
| Stool frequency (BM/day)  | 6  | 10          |
| Average number of hospitalizations over 2-year period   | 1.4  | 4.8         |
| Need for emergent surgery   | 0.05%  | 0.05%       |
| Check which treatment you prefer  |  |             |

| Attribute   | Treatment A | Treatment B                               |
|---|-------------|---|
| 30-year risk of colorectal cancer   | 18%         | 18%                                       |
| Need for long term medications to control disease   | 50%         | 90%                                       |
| 2-year health care costs  | \$15,700    | \$6,400                                   |
| Need for ostomy   | No          | No  |
| Risk of obstruction   | 0%          | 20% (8% requiring operative intervention) |
| Risk of leak  | 10%         | 10%                                       |
| Risk of sexual dysfunction  | 0%          | 0%  |
| Risk of difficulty becoming<br>pregnant   | 25%         | 25%                                       |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | Yes         | Yes                                       |
| Stool frequency (BM/day)  | 10          | 10  |
| Average number of hospitalizations over 2-year period   | 4.8         | 4.8                                       |
| Need for emergent surgery   | 0.05%       | 0.05%                                     |
| Check which treatment you prefer  |             |   |

| Attribute   | Treatment A  | Treatment B |
|---|--|-------------|
| 30-year risk of colorectal cancer   | 18%  | 18%         |
| Need for long term medications to<br>control disease  | 90%  | 90%         |
| 2-year health care costs  | \$6,400  | \$6,400     |
| Need for ostomy   | Temporary  | No          |
| Risk of obstruction   | 0%   | 0%          |
| Risk of leak  | 0%   | 0%          |
| Risk of sexual dysfunction  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women | 0%          |
| Risk of difficulty becoming<br>pregnant   | 25%  | 40%         |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | Yes  | Yes         |
| Stool frequency (BM/day)  | 6  | б           |
| Average number of hospitalizations over 2-year period   | 4.8  | 4.8         |
| Need for emergent surgery   | 0.05%  | 0.05%       |
| Check which treatment you prefer  |  |             |

| Attribute   | Treatment A                               | Treatment B  |
|---|---|--|
| 30-year risk of colorectal cancer   | 18%                                       | 18%  |
| Need for long term medications to control disease   | 50%                                       | 50%  |
| 2-year health care costs  | \$6,400                                   | \$6,400  |
| Need for ostomy   | No  | No   |
| Risk of obstruction   | 20% (8% requiring operative intervention) | 20% (8% requiring operative intervention)                        |
| Risk of leak  | 0%  | 10%  |
| Risk of sexual dysfunction  | 0%  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women |
| Risk of difficulty becoming<br>pregnant   | 25%                                       | 40%  |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | Yes                                       | Yes  |
| Stool frequency (BM/day)  | 10  | 10   |
| Average number of hospitalizations over 2-year period   | 4.8                                       | 1.4  |
| Need for emergent surgery   | 0.05%                                     | 0.05%  |
| Check which treatment you prefer  |   |  |

| Attribute   | Treatment A                                  | Treatment B                                  |  |  |  |  |  |  |
|---|--|--|--|--|--|--|--|--|
| 30-year risk of colorectal cancer   | 0.06%  | 0.06%  |  |  |  |  |  |  |
| Need for long term medications to control disease   | 50%  | 50%  |  |  |  |  |  |  |
| 2-year health care costs  | \$6,400                                      | \$6,400                                      |  |  |  |  |  |  |
| Need for ostomy   | Temporary                                    | Temporary                                    |  |  |  |  |  |  |
| Risk of obstruction   | 20% (8% requiring operative<br>intervention) | 20% (8% requiring operative<br>intervention) |  |  |  |  |  |  |
| Risk of leak  | 10%  | 0%   |  |  |  |  |  |  |
| Risk of sexual dysfunction  | 0%   | 0%   |  |  |  |  |  |  |
| Risk of difficulty becoming<br>pregnant   | 40%  | 40%  |  |  |  |  |  |  |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No   | No   |  |  |  |  |  |  |
| Stool frequency (BM/day)  | 6  | 10   |  |  |  |  |  |  |
| Average number of hospitalizations over 2-year period   | 4.8  | 1.4  |  |  |  |  |  |  |
| Need for emergent surgery   | 1%   | 1%   |  |  |  |  |  |  |
| Check which treatment you prefer  |  |  |  |  |  |  |  |  |

| Attribute   | Treatment A                                  | Treatment B |
|---|--|-------------|
| 30-year risk of colorectal cancer   | 18%  | 18%         |
| Need for long term medications to<br>control disease  | 90%  | 90%         |
| 2-year health care costs  | \$15,700                                     | \$6,400     |
| Need for ostomy   | No   | No          |
| Risk of obstruction   | 20% (8% requiring operative<br>intervention) | 0%          |
| Risk of leak  | 0%   | 0%          |
| Risk of sexual dysfunction  | 0%   | 0%          |
| Risk of difficulty becoming<br>pregnant   | 25%  | 25%         |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No   | Yes         |
| Stool frequency (BM/day)  | 10   | 6           |
| Average number of hospitalizations over 2-year period   | 4.8  | 4.8         |
| Need for emergent surgery   | 0.05%  | 0.05%       |
| Check which treatment you prefer  |  |             |

| Attribute   | Treatment A  | Treatment B  |  |  |  |  |  |  |
|---|--|--|--|--|--|--|--|--|
| 30-year risk of colorectal cancer   | 18%  | 0.06%  |  |  |  |  |  |  |
| Need for long term medications to<br>control disease  | 90%  | 90%  |  |  |  |  |  |  |
| 2-year health care costs  | \$6,400  | \$6,400  |  |  |  |  |  |  |
| Need for ostomy   | No   | No   |  |  |  |  |  |  |
| Risk of obstruction   | 0%   | 0%   |  |  |  |  |  |  |
| Risk of leak  | 0%   | 0%   |  |  |  |  |  |  |
| Risk of sexual dysfunction  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women |  |  |  |  |  |  |
| Risk of difficulty becoming pregnant  | 25%  | 25%  |  |  |  |  |  |  |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No   | No   |  |  |  |  |  |  |
| Stool frequency (BM/day)  | 10   | 10   |  |  |  |  |  |  |
| Average number of hospitalizations over 2-year period   | 4.8  | 4.8  |  |  |  |  |  |  |
| Need for emergent surgery   | 1%   | 0.05%  |  |  |  |  |  |  |
| Check which treatment you prefer  |  |  |  |  |  |  |  |  |

| Attribute   | Treatment A | Treatment B                                  |
|---|-------------|--|
| 30-year risk of colorectal cancer   | 18%         | 18%  |
| Need for long term medications to control disease   | 90%         | 50%  |
| 2-year health care costs  | \$15,700    | \$15,700                                     |
| Need for ostomy   | Temporary   | Temporary                                    |
| Risk of obstruction   | 0%          | 20% (8% requiring operative<br>intervention) |
| Risk of leak  | 10%         | 0%   |
| Risk of sexual dysfunction  | 0%          | 0%   |
| Risk of difficulty becoming pregnant  | 25%         | 25%  |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No          | No   |
| Stool frequency (BM/day)  | 10          | 6  |
| Average number of hospitalizations over 2-year period   | 4.8         | 4.8  |
| Need for emergent surgery   | 1%          | 1%   |
| Check which treatment you prefer  |             |  |

| Attribute   | Treatment A  | Treatment B                                  |
|---|--|--|
| 30-year risk of colorectal cancer   | 0.06%  | 18%  |
| Need for long term medications to<br>control disease  | 90%  | 50%  |
| 2-year health care costs  | \$15,700   | \$6,400                                      |
| Need for ostomy   | Temporary  | No   |
| Risk of obstruction   | 0%   | 20% (8% requiring operative<br>intervention) |
| Risk of leak  | 0%   | 10%  |
| Risk of sexual dysfunction  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women | 0%   |
| Risk of difficulty becoming<br>pregnant   | 40%  | 25%  |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No   | Yes  |
| Stool frequency (BM/day)  | 10   | 6  |
| Average number of hospitalizations over 2-year period   | 4.8  | 1.4  |
| Need for emergent surgery   | 1%   | 0.05%  |
| Check which treatment you prefer  |  |  |

| Attribute   | Treatment A  | Treatment B |
|---|--|-------------|
| 30-year risk of colorectal cancer   | 0.06%  | 0.06%       |
| Need for long term medications to control disease   | 90%  | 90%         |
| 2-year health care costs  | \$6,400  | \$15,700    |
| Need for ostomy   | No   | Temporary   |
| Risk of obstruction   | 0%   | 0%          |
| Risk of leak  | 10%  | 10%         |
| Risk of sexual dysfunction  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women | 0%          |
| Risk of difficulty becoming<br>pregnant   | 25%  | 25%         |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No   | No          |
| Stool frequency (BM/day)  | 6  | 6           |
| Average number of hospitalizations over 2-year period   | 4.8  | 1.4         |
| Need for emergent surgery   | 1%   | 1%          |
| Check which treatment you prefer  |  |             |

| Attribute   | Treatment A  | Treatment B  |
|---|--|--|
| 30-year risk of colorectal cancer   | 0.06%  | 18%  |
| Need for long term medications to<br>control disease  | 50%  | 90%  |
| 2-year health care costs  | \$6,400  | \$15,700   |
| Need for ostomy   | Temporary  | No   |
| Risk of obstruction   | 20% (8% requiring operative intervention)                        | 20% (8% requiring operative<br>intervention)                     |
| Risk of leak  | 10%  | 0%   |
| Risk of sexual dysfunction  | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women |
| Risk of difficulty becoming<br>pregnant   | 40%  | 25%  |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No   | Yes  |
| Stool frequency (BM/day)  | 6  | 6  |
| Average number of hospitalizations over 2-year period   | 4.8  | 4.8  |
| Need for emergent surgery   | 0.05%  | 0.05%  |
| Check which treatment you prefer  |  |  |

| Attribute   | Treatment A | Treatment B  |
|---|-------------|--|
| 30-year risk of colorectal cancer   | 0.06%       | 18%  |
| Need for long term medications to<br>control disease  | 90%         | 50%  |
| 2-year health care costs  | \$6,400     | \$15,700   |
| Need for ostomy   | Temporary   | No   |
| Risk of obstruction   | 0%          | 20% (8% requiring operative intervention)                        |
| Risk of leak  | 0%          | 10%  |
| Risk of sexual dysfunction  | 0%          | 3% impotence in men;<br>8% dyspareunia (painful sex)<br>in women |
| Risk of difficulty becoming<br>pregnant   | 40%         | 25%  |
| Risk of side effects<br>(bone fracture, severe infection<br>requiring hospitalization, abnormal<br>liver function, hair loss) | No          | Yes  |
| Stool frequency (BM/day)  | 6           | 10   |
| Average number of hospitalizations over 2-year period   | 1.4         | 4.8  |
| Need for emergent surgery   | 1%          | 1%   |
| Check which treatment you prefer  |             |  |

#### PART III: Treatment Preference

| Has your physician discussed the benefits a (IPAA) surgery with you? (circle one) | nd risks of Medical Manag | ement and Ileal Pouc  | ch-Anal Anastomosis |
|---|---------------------------|-----------------------|---------------------|
| Medical Management Only   | IPAA Only                 | Both                  | Neither             |
|   |                           |                       |                     |
| Based on your current knowledge, which tr   | eatment method would yo   | u prefer? (circle one | )                   |
| Medical Management  | IPAA surgery              |                       |                     |
|   |                           |                       |                     |

#### PART IV: Most Important Attributes

Identify the three most driving attributes to you from 1 to 3.

# 1.3 Original Data

| - 44 | 6 3 | 1   | 0 | 3 | 2  | 2 | 2 | 3 | 0 | 0  | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 6   | 1 |   | 1 | 15 | 9 | 1 | 2 |
|------|-----|-----|---|---|----|---|---|---|---|----|---|---|---|---|---|---|---|---|---|---|---|---|-----|---|---|---|----|---|---|---|
| 5    | 1 : | 2   | 0 | 4 | 7  | 1 | 2 | 4 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 | 4 |
| - 40 | 0 0 | ) 2 | 0 | 5 | 5  | 3 | 2 | 2 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 | 4 |
| 3    | 1 : | 2   | 0 | 6 | 11 | 1 | 1 | 4 | 1 | 1  | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 0 |   | 0 |     | 1 | 0 | 0 |    |   | 1 | 3 |
| 51   | 8 ( | 2   | 0 | 3 | 5  | 1 | 3 | 4 | 0 | 0  | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 35   | 9 ( | 2   | 0 | 5 | 7  | 1 | 1 | 3 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |   | 1 | 4   | 0 |   | 1 |    |   | 1 |   |
| 55   | 5 : | 2   | 0 | 6 | 11 | 1 | 2 | 4 | 0 | 0  | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 31   | 6 : | 2   | 0 | 2 | 2  | 1 | 1 | 2 | 0 | 0  | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 |   | 1 | 4.5 | 1 | 0 | 0 |    |   | 1 |   |
| 31   | 8 : | 2   | 0 | 6 | 11 | 1 | 1 | 2 | 1 | 1  | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 |   | 1 |     | 1 |   | 1 |    |   | 0 |   |
| 35   | 9 : | 2   | 0 | 4 | 11 | 1 | 1 | 4 | 1 | 2  | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 4    | 5 : |     | 0 | 3 | 4  | 2 | 1 | 4 | 1 | 1  | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 0 |   | 1 |     | 1 |   | 0 |    |   | 1 |   |
| 3    | 0 : | 2   | 0 | 4 | 9  | 2 | 1 | 3 | 1 | 2  | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |   | 1 |     | 0 |   | 0 |    |   | 1 |   |
| 24   | 4 ( | 2   | 0 | 3 | 2  | 2 | 1 | 4 | 1 | 1  | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 1 |   | 0 |     | 1 |   | 0 |    |   | 0 |   |
| 4    |     |     | 0 | 5 | 11 | 1 | 1 | 4 | 1 | 12 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 1 |   |
| 43   | 3 : | 2   | 0 | 3 | 4  | 1 | 1 | 4 | 1 | 1  | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 21   |     |     | 0 | 3 | 4  | 1 | 1 | 2 | 1 | 1  | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |   | 1 | 4   | 1 | 0 | 0 |    |   | 1 |   |
| 31   | 8 : | 2   | 0 | 5 | 5  | 2 | 1 | 4 | 1 | 2  | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 3    | 3 : | 2   | 0 | 4 | 5  | 2 | 2 | 4 | 0 | 0  | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 1 |   |
| 35   | 9 ( | 2   | 0 | 5 | 9  | 1 | 1 | 4 | 1 | 2  | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 4    | 7 : | 2   | 0 | 3 | 1  | 3 | 1 | 4 | 1 | 3  | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 8   | 1 | 1 | 1 |    |   | 1 |   |
| 6    | 2 0 | 1   | 0 | 4 |    | 3 | 2 | 4 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 40   | 0 0 | ) 1 | 0 | 2 | 5  | 2 | 1 | 3 | 1 | 1  |   | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |   | 0 |     |   |   | 1 |    |   |   |   |
| 4    |     | 2   | 0 | 3 | 8  | 1 | 2 | 2 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 1 |   |
| 7:   | 1 0 | 2   | 0 | 3 | 5  | 1 | 2 | 3 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |   | 1 | 2   | 0 |   | 0 |    |   | 0 |   |
| 40   | 0 : | 2   | 0 | 5 |    | 1 | 1 | 4 | 0 | 0  | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 4    |     | 2   | 0 | 3 | 7  | 1 | 2 | 2 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 4   | 1 | 0 | 1 |    |   | 0 |   |
| 2    |     | 2   | 0 | 2 | 3  | 1 | 1 |   | 1 | 2  | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 4    |     |     |   | 4 | 11 | 1 |   | 4 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 3    | 5 ( | 2   | 0 | 3 | 5  | 1 | 2 | 3 | 0 | 0  | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 3    |     |     | 0 | 4 | 6  | 1 | 1 | 2 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 34   |     | 2   | 0 | 6 | 8  | 1 | 2 | 4 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 4    |     | 1   | 0 | 3 | 3  | 2 | 1 | 4 | 1 | 2  | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 0 |   |
| 31   | 8   | 2   | 0 | 4 | 6  | 1 | 1 | 4 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |   | 1 | 4   | 0 |   | 0 |    |   | 1 |   |
| 51   |     |     | 0 | 4 | 11 | 1 | 1 |   | 1 | 3  | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 |    |   | 1 |   |
| 4    |     | 2   | 0 | 4 | 7  | 2 | 3 | 4 | 0 | 0  | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |   | 1 | 3   | 0 |   | 1 | 10 | 4 | 0 |   |
| 3    |     |     | 0 | 5 | 11 | 1 | 1 | 3 | 1 | 1  | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 | -  |   | 1 |   |
| 3    |     |     | ő | 3 | 3  | 1 | 1 | 4 | 1 | 2  | 0 | 1 | 1 | 0 | 0 | 0 | ô | 1 | 0 | 0 |   | 1 |     | 0 |   | ő |    |   | 0 |   |
| 4    |     |     | 0 | 2 | 4  | 3 | 1 | 2 | 1 | 2  | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 |     | 0 |   | 0 |    |   | 1 |   |
| 2    |     | 3   | 0 | 5 | 11 | 1 | 1 | 2 | 0 | 0  | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | - | 0 |     | 0 |   | 0 |    |   | 1 |   |
| 6    |     |     | ő | 3 | 4  | 1 | 2 | 4 | 0 | ő  | 0 | 1 | 1 | 0 | 1 | 0 | ő | 0 | Ô | 0 |   | 1 | 3   | 0 |   | ő |    |   | ō |   |
| 4    |     | 1   | 0 | 5 | 4  | 2 | 1 | 4 | 1 | 2  | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 |   | 0 |     | 0 |   | 1 | 20 | 4 | 0 |   |
| 5    |     |     | 0 | 4 | 5  | 1 | 1 | 4 | 1 | 4  | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8   | 1 | 0 | 1 | 20 |   | 0 |   |
| 3    |     |     | ő | 4 | 8  | 1 | 2 | 2 | - |    |   | 1 | ō | 0 | 0 | 1 | ô | 1 | ô | ō |   | 1 |     | ō |   | ô |    |   | 0 |   |
| 4    |     |     | 1 | 5 | 11 | 1 | 2 | 3 | 1 | 3  | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |   | 1 |     | 0 |   | 1 | 10 | 3 | 0 |   |
|      |     | 2   | 0 |   | 1  | 2 | 1 | 2 | 0 | 0  | 0 | 1 | 0 | 0 | 0 | 1 |   | 1 | 0 | 0 |   | 0 |     | 0 |   | 0 | 10 | ~ | 0 |   |

| study_id |   |   |   |   |   | CS_6 |   |   |   |   | CS_11 | CS_12 |   | CS_14 |   | med.v.ipaa |   | prolonged_med |   |   | obstruction |   |   |   |   |   |   | emergent_surg |
|----------|---|---|---|---|---|------|---|---|---|---|-------|-------|---|-------|---|------------|---|---------------|---|---|-------------|---|---|---|---|---|---|---------------|
| 1        | 0 | 0 | 1 | 0 | 1 | 1    | 0 | 1 | 0 | 0 |       |       | 0 |       | 3 | 1          | 1 | 0             | 0 | 0 | 1           | 1 | 0 | 0 | 0 | 0 | 0 | 0             |
| 2        | 1 | 0 | 1 | 0 | 1 | 1    | 1 | 1 | 1 | 0 | 1     | 1     | 0 | 0     | 3 | 0          | 1 | 0             | 0 | 0 | 0           | 0 | 0 | 0 | 0 | 0 | 1 | 1             |
| 3        | 1 | 0 | 1 | 0 | 1 | 1    | 1 | 1 | 1 | 0 | 1     | 0     | 1 | 1     | 4 | 0          | 0 | 1             | 1 |   | 0           | 0 | 0 | 0 | 0 | 0 | 1 | 1             |
| 4        | 1 | 0 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 0     | 0     | 0 | 0     | 1 | 0          | 1 | 0             | 0 | 3 | 0           | 0 | 0 | 2 | 0 | 0 | 0 | 0             |
| 5        | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 0     | 0     | 0 | 0     |   |            | 1 | 0             | 0 | 2 | 0           | 0 | 0 | 0 | 3 | 0 | 0 | 0             |
| 6        | 1 | 1 | 0 | 0 | 1 | 1    | 0 | 1 | 1 | 1 | 0     | 1     | 0 | 0     | 4 |            | 0 | 0             | 0 | 0 | 3           | 0 | 0 | 0 | 0 | 1 | 0 | 2             |
| 7        | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 1     | 0     | 1 | 0     | 4 | 0          | 0 | 0             | 0 | 1 | 1           | 1 | 0 | 0 | 0 | 0 | 0 | 0             |
| 8        | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 0 | 1     | 1     | 0 | 0     |   |            | 0 | 0             | 0 | 0 | 0           | 0 | 0 | 0 | 1 | 0 | 3 | 2             |
| 9        | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 0 | 0     | 0     | 0 | 1     | 4 | 0          | 1 | 0             | 0 | 2 | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 3             |
| 10       | 1 | 0 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 0 | 1     | 0     | 1 | 1     | 1 | 0          | 0 | 0             | 0 | 1 | 2           | 0 | 3 | 0 | 0 | 0 | 0 | 0             |
| 11       | 1 | 1 | 0 | 0 | 1 | 1    | 1 | 1 | 1 | 1 | 1     | 0     | 0 | 1     | 4 | 0          | 0 | 1             | 0 | 2 | 0           | 0 | 0 | 0 | 0 | 0 | 3 | 0             |
| 12       | 1 | 1 | 0 | 0 | 0 | 0    | 0 | 1 | 1 | 1 | 0     | 1     | 0 | 1     | 3 | 1          | 0 | 3             | 0 | 0 | 0           | 0 | 0 | 1 | 0 | 2 | 0 | 0             |
| 13       | 1 | 0 | 0 | 0 | 1 | 0    | 0 | 1 | 1 | 1 | 1     | 1     | 0 | 0     | 3 | 0          | 2 | 0             | 0 | 1 | 3           | 0 | 0 | 0 | 0 | 0 | 0 | 0             |
| 14       | 1 | 0 | 0 | 0 | 1 | 0    | 0 | 1 | 1 | 1 | 1     | 1     | 0 | 0     | 3 | 0          | 0 | 0             | 0 | 1 | 0           | 0 | 0 | 0 | 0 | 2 | 3 | 0             |
| 15       | 1 | 1 | 1 | 0 | 1 | 1    | 1 | 1 | 1 | 1 | 1     | 0     | 1 | 1     | 1 | 0          | 1 | 0             | 0 | 1 | 0           | 1 | 0 | 0 | 0 | 0 | 0 | 0             |
| 16       | 1 | 1 | 1 | 0 | 1 | 0    | 1 | 1 | 1 | 0 | 0     | 1     | 0 | 0     |   |            | 0 | 0             | 0 | 2 | 3           | 0 | 1 | 0 | 0 | 0 | 0 | 0             |
| 17       | 1 | 0 | 0 | 0 | 1 | 1    | 1 | 1 | 1 | 0 | 1     | 1     | 0 | 0     |   |            | 3 | 0             | 0 | 0 | 0           | 0 | 0 | 0 | 0 | 0 | 1 | 2             |
| 18       |   | 1 |   | 0 |   |      |   |   |   |   |       |       | 0 | 0     | 4 |            | 0 | 0             | 2 | 0 | 0           | 0 | 0 | 0 | 0 | 1 | 0 | 3             |
| 19       | 1 | 1 | 0 | 1 | 1 | 1    | 1 | 1 | 1 | 1 | 1     | 0     | 1 | 0     | 4 | 0          | 1 | 0             | 0 | 1 | 0           | 0 | 0 | 0 | 0 | 0 | 1 | 0             |
| 20       |   |   | 0 |   |   |      |   |   |   |   |       |       |   |       | 4 | 0          | 0 | 0             | 0 | 0 | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0             |
| 21       | 1 | 0 | 0 | 0 | 0 | 0    | 0 | 0 | 0 | 0 | 1     | 0     | 0 | 0     | 4 | 0          | 1 | 0             | 3 | 0 | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 2             |
| 22       | 1 | 0 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 0 | 1     | 0     | 1 | 1     |   | 0          | 3 | 0             | 0 | 1 | 2           | 0 | 0 | 0 | 0 | 0 | 0 | 0             |
| 23       | 1 | 0 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 1     | 1     | 0 | 0     | 4 | 0          | 1 | 0             | 2 | 0 | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 3             |
| 24       | 0 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 1     | 0     | 0 | 0     | 4 | 0          | 0 | 1             | 0 |   | 0           | 0 | 0 | 0 | 2 | 3 | 0 | 0             |
| 25       | 1 | 1 |   | 0 | 1 |      | 1 | 0 | 1 | 0 |       |       |   |       |   |            |   |               |   |   |             |   |   |   |   |   |   |               |
| 26       | 1 | 1 | 0 |   | 1 | 0    |   | 1 | 0 | 1 | 0     | 0     | 1 | 1     | 4 |            | 0 | 0             | 0 | 1 | 3           | 0 | 0 | 0 | 2 | 0 | 0 | 0             |
| 27       | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 0     | 1     | 0 | 0     | 3 | 1          | 1 | 0             | 0 | 0 | 3           | 0 | 0 | 0 | 0 | 0 | 2 | 0             |
| 28       | 1 | 0 | 0 | 0 | 1 | 1    | 0 | 1 | 1 | 1 | 1     | 0     | 1 | 1     | 3 | 0          | 3 | 0             | 0 | 1 | 0           | 0 | 0 | 0 | 0 | 0 | 2 | 0             |
| 29       | 0 | 1 | 0 | 0 | 1 | 1    | 1 | 1 | 1 | 1 | 1     | 1     | 1 | 0     | 4 | 0          | 1 | 0             | 0 | 3 | 0           | 0 | 0 | 0 | 0 | 2 | 0 | 0             |
| 30       | 1 | 0 | 0 | 0 | 1 | 1    | 1 | 1 | 1 | 0 | 0     | 0     | 0 | 0     | 4 |            | 1 | 0             | 0 | 3 | 2           | 0 | 0 | 0 | 0 | 0 | 0 | 0             |
| 31       | 1 | 0 | 0 | 0 | 1 | 0    | 1 | 0 | 1 | 1 | 0     | 0     | 0 | 0     | 4 | 0          | 1 | 0             | 0 | 3 | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 2             |
| 32       | 1 | 0 |   |   |   |      |   |   |   |   |       |       |   |       |   |            |   |               |   |   |             |   |   |   |   |   |   |               |
| 33       | 1 | 0 | 0 | 0 | 1 | 0    | 1 | 0 | 1 | 0 | 1     | 0     | 1 | 0     | 1 | 0          | 1 | 0             | 0 | 3 | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 2             |
| 34       | 1 | 0 | 0 | 0 | 1 | 1    | 1 | 1 | 1 | 0 | 1     | 1     | 0 | 0     | 1 | 0          | 1 | 0             | 0 | 2 | 3           | 0 | 0 | 0 | 0 | 0 | 0 | 0             |
| 35       | 0 | 1 | 0 | 1 | 1 | 1    | 1 | 0 | 1 | 0 | 0     | 1     | 0 | 0     | 4 | 0          | 0 | 0             | 0 | 0 | 1           | 0 | 0 | 0 | 0 | 0 | 1 | 1             |
| 36       | 1 | 1 | 0 | 0 | 1 | ō    | 1 | 1 | 1 | 1 | 0     | 1     | 0 | 0     | 4 | 0          | 1 | 2             | 0 | 0 | 0           | 0 | 0 | 0 | 3 | 0 | 0 | 0             |
| 37       | 1 | 0 | 0 | 1 | 1 | 0    | 1 | 1 | 1 | 0 | 1     | 0     | 0 | 0     | 1 | 0          | 3 | 0             | 0 | 1 | 0           | 0 | 0 | 0 | 2 | 0 | 0 | 0             |
| 38       | 1 | 0 | - | 1 | 1 | 0    | 1 | 1 | 1 | 1 | 1     | 0     | 0 | 0     |   |            | 1 | 0             | 0 | 0 | 3           | 2 | 0 | 0 | 0 | 0 | 0 | 0             |
| 39       | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 1     | 1     | 0 | 0     | 4 | 0          | 1 | 0             | 0 | 3 | 0           | 0 | 0 | 0 | 0 | 0 | 2 | 0             |
| 40       | 1 | 1 | 0 | 0 | 1 | 1    | - | 1 | 1 | 1 | 1     | 0     | 0 | 0     | 4 | 0          | 2 | 3             | 0 | 1 | 0           | 0 | 0 | 0 | 0 | 0 | 0 | 0             |
| 41       | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 0 | 1     | ō     | 1 | 1     | 4 | -          | 0 | 0             | 0 | 1 | 3           | 0 | 0 | 0 | 0 | 0 | 0 | 1             |
| 42       | 1 | 1 | 1 | 1 | 1 | 0    | 1 | 1 | 1 | 1 | 1     | ō     | ō | 1     | 4 | 0          | 0 | 3             | ō | 0 | 0           | 0 | ő | 0 | 1 | 0 | 2 | 0             |
| 43       | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 1 | 1 | 1 | 1     | ŏ     | 0 | Ô     | 4 | ő          | 1 | 2             | 3 | 0 | 0           | 0 | ő | 0 | 0 | 0 | 0 | 0             |
| 44       | 1 | 1 | 0 | 0 | 1 | 0    | 1 | 0 | 1 | 1 | 1     | 0     | 1 | 1     | 3 | 0          | 0 | 0             | 0 | 1 | 0           | 0 | 2 | 0 | 0 | 0 | 0 | 3             |
| 45       | 1 | 1 | 0 | 1 | 1 | 1    | 1 | 1 | 1 | 0 | 0     | 0     | 0 | 1     | 1 | 0          | 0 | 0             | 0 | 1 | 0           | 0 | 0 | 0 | 0 | 0 | 2 | 3             |
|          |   |   |   |   |   |      |   |   |   | ~ | 2     | 9     |   | *     |   | ~          |   | 2             |   |   | ~           | ~ |   |   |   | v |   | 3             |

## 1.4 Clean Data

|    |    |   |   |   |   |   |   |   |   |   |   |   |   |   |   | hx_immunomod |   |   |   |   |   |   |   |   |
|----|----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|--------------|---|---|---|---|---|---|---|---|
| 1  |    |   |   | 3 | 0 | 2 | 2 | 3 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 0            | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 2 |
| 2  |    | 1 | 2 | 4 | 1 | 1 | 2 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0            | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| 3  | 40 | 0 | 2 | 5 | 0 | 3 | 2 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0            | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| 4  |    |   | 2 | 6 | 1 | 1 | 1 | 4 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1            | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 3 |
| 5  |    |   |   | 3 | 0 | 1 | 3 | 4 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1            | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| 6  | 39 | 0 | 2 | 5 | 1 | 1 | 1 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1            | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 4 |
| 7  | 55 | 1 | 2 | 6 | 1 | 1 | 2 | 4 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 1            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 4 |
| 8  | 36 | 1 | 2 | 2 | 0 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0            | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 3 |
| 9  | 38 | 1 | 2 | 6 | 1 | 1 | 1 | 2 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 0            | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 2 |
| 10 | 39 | 1 | 2 | 4 | 1 | 1 | 1 | 4 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 5 |
| 11 | 45 | 1 | 2 | 3 | 0 | 2 | 1 | 4 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0            | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 |
| 12 | 30 | 1 | 2 | 4 | 1 | 2 | 1 | 3 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1            | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 3 |
| 13 | 24 | 0 | 2 | 3 | 0 | 2 | 1 | 4 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1            | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 4 |
| 14 | 44 | 0 | 2 | 5 | 1 | 1 | 1 | 4 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 0            | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 4 |
| 15 | 43 | 1 | 2 | 3 | 0 | 1 | 1 | 4 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 4 |
| 16 |    | 1 | 2 | 3 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 0            | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 1 |
| 17 | 38 | 1 | 2 | 5 | 0 | 2 | 1 | 4 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 0            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 4 |
| 18 |    | 0 | 2 | 5 | 1 | 1 | 1 | 4 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0            | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| 19 | 62 | 0 | 1 | 4 | 1 | 3 | 2 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 4 |
| 20 | 40 | 0 | 1 | 2 | 0 | 2 | 1 | 3 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0            | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 3 |
| 21 | 40 | 1 | 2 | 3 | 1 | 1 | 2 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1            | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 3 |
| 22 | 71 | 0 | 2 | 3 | 0 | 1 | 2 | 3 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0            | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 5 |
| 23 | 45 | 0 | 2 | 3 | 1 | 1 | 2 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0            | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 2 |
| 24 | 25 | 0 | 2 | 2 | 0 | 1 | 1 | 4 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 5 |
| 25 | 48 | 1 | 2 | 4 | 1 | 1 | 1 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 5 |
| 26 | 35 | 0 | 2 | 3 | 0 | 1 | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0            | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| 27 | 35 | 0 | 2 | 4 | 1 | 1 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0            | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| 28 | 34 | 1 | 2 | 6 | 1 | 1 | 2 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1            | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 5 |
| 29 | 38 | 1 | 2 | 4 | 1 | 1 | 1 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0            | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 4 |
| 30 | 56 | 1 | 2 | 4 | 1 | 1 | 1 | 4 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 0            | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 4 |
| 31 | 40 | 1 | 2 | 4 | 1 | 2 | 3 | 4 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1            | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 4 |
| 32 | 36 | 1 | 2 | 5 | 1 | 1 | 1 | 3 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1            | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 4 |
| 33 | 39 | 0 | 2 | 3 | 0 | 1 | 1 | 4 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0            | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 4 |
| 34 | 42 | 1 | 1 | 2 | 0 | 3 | 1 | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0            | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 3 |
| 35 | 29 | 1 | 3 | 5 | 1 | 1 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0            | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 4 |
| 36 | 64 | 0 | 2 | 3 | 0 | 1 | 2 | 4 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 0            | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 |
| 37 |    |   | 1 | 5 | 0 | 2 | 1 | 4 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1            | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 3 |
| 38 | 55 |   | 2 | 4 | 0 | 1 | 1 | 4 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1            | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 3 |
| 39 | 30 | 0 | 2 | 4 | 1 | 1 | 2 | 2 | 0 | 0 | 1 | 0 | ō | 0 | 1 | 0            | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 3 |
| 40 | 41 | 0 | 2 | 5 | 1 | 1 | 2 | 3 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 0            | 1 | 0 | 0 | 1 | 0 | 1 | 0 | 4 |
| 41 |    | 1 |   | 3 | 0 | 2 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1            | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |

|          |   |   |   |   |   |   |   |   |   |   |   |   |       |   |   | med.v.ipaa | cancer | prolonged_med |   | ostomy | obstruction |   | sexual_dysfn |   | side_effects |   | hospitalization |   |
|----------|---|---|---|---|---|---|---|---|---|---|---|---|-------|---|---|------------|--------|---------------|---|--------|-------------|---|--------------|---|--------------|---|-----------------|---|
| 1        | 0 | 0 | 1 | 0 |   | 1 |   | 1 |   | 0 |   | 0 |       | 0 | 3 | 1          | 1      | 0             | 0 | 0      | 1           | 1 | 0            | 0 | 0            | 0 | 0               | 0 |
| 2        | 1 |   | 1 | 0 |   |   | 1 |   |   | 0 | 1 | 1 |       | 0 | 3 | 0          | 1      | 0             | 0 | 0      | 0           | 0 | 0            | 0 | 0            | 0 | 1               | 1 |
| 3        | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 |       | 1 | 4 | 0          | 0      | 1             | 1 | 0      | 0           | 0 | 0            | 0 | 0            | 0 | 1               | 1 |
| 4        | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 0 |       | 0 | 1 | 0          | 1      | 0             | 0 | 3      | 0           | 0 | 0            | 2 | 0            | 0 | 0               | 0 |
| 5        | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 0 |       | 0 | 4 | 0          | 1      | 0             | 0 | 2      | 0           | 0 | 0            | 0 | 3            | 0 | 0               | 0 |
| 6        | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | <br>) | 0 | 4 | 0          | 0      | 0             | 0 | 0      | 3           | 0 | 0            | 0 | 0            | 1 | 0               | 2 |
| 7        | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 |       | 0 | 4 | 0          | 0      | 0             | 0 | 1      | 1           | 1 | 0            | 0 | 0            | 0 | 0               | 0 |
| 8        | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | <br>) | 0 | 4 | 0          | 0      | 0             | 0 | 0      | 0           | 0 | 0            | 0 | 1            | 0 | 3               | 2 |
| 9        | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | <br>) | 1 | 4 | 0          | 1      | 0             | 0 | 2      | 0           | 0 | 0            | 0 | 0            | 0 | 0               | 3 |
| 10       | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 1     | 1 | 1 | 0          | 0      | 0             | 0 | 1      | 2           | 0 | 3            | 0 | 0            | 0 | 0               | 0 |
| 11       | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | <br>) | 1 | 4 | 0          | 0      | 1             | 0 | 2      | 0           | 0 | 0            | 0 | 0            | 0 | 3               | 0 |
| 12       | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 1 | <br>) | 1 | 3 | 1          | 0      | 3             | 0 | 0      | 0           | 0 | 0            | 1 | 0            | 2 | 0               | 0 |
| 13       | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | <br>) | 0 | 3 | 0          | 2      | 0             | 0 | 1      | 3           | 0 | 0            | 0 | 0            | 0 | 0               | 0 |
| 14       | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | <br>) | 0 | 3 | 0          | 0      | 0             | 0 | 1      | 0           | 0 | 0            | 0 | 0            | 2 | 3               | 0 |
| 15       | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1     | 1 | 1 | 0          | 1      | 0             | 0 | 1      | 0           | 1 | 0            | 0 | 0            | 0 | 0               | 0 |
| 16       | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 1 | )     | 0 | 4 | 0          | 0      | 0             | 0 | 2      | 3           | 0 | 1            | 0 | 0            | 0 | 0               | 0 |
| 17       | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | )     | 0 | 4 | 0          | 3      | 0             | 0 | 0      | 0           | 0 | 0            | 0 | 0            | 0 | 1               | 2 |
| 18       | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |       | 0 | 4 | 0          | 1      | 0             | 0 | 1      | 0           | 0 | 0            | 0 | 0            | 0 | 1               | 0 |
| 19       | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2     | 0 | 4 | 0          | 1      | 0             | 3 | 0      | 0           | 0 | 0            | 0 | 0            | 0 | 0               | 2 |
| 20       | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 |       | 1 | 4 | 0          | 3      | 0             | 0 | 1      | 2           | 0 | 0            | 0 | 0            | 0 | 0               | 0 |
| 21       | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 2     | 0 | 4 | 0          | 1      | 0             | 2 | 0      | 0           | 0 | 0            | 0 | 0            | 0 | 0               | 3 |
| 22       | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 |       | 0 | 4 | 0          | 0      | 1             | 0 | 0      | 0           | 0 | 0            | 0 | 2            | 3 | 0               | 0 |
| 23       | 1 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 0 |       | 1 | 4 | 0          | 0      | 0             | 0 | 1      | 3           | 0 | 0            | 0 | 2            | 0 | 0               | 0 |
| 24       |   | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 |       | 0 | 3 | 1          | 1      | 0             | 0 | 0      | 3           | 0 | 0            | 0 | 0            | 0 | 2               | 0 |
| 25       | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |       | 1 | 3 | 0          | 3      | 0             | 0 | 1      | 0           | 0 | 0            | 0 | 0            | 0 | 2               | 0 |
| 26       | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |       | 0 | 4 | 0          | 1      | 0             | 0 | 3      | 0           | 0 | 0            | 0 | 0            | 2 | 0               | 0 |
| 27       | 1 |   | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |       | 0 | 4 | 0          | 1      | 0             | 0 | 3      | 2           | 0 | 0            | 0 | 0            | 0 | 0               | 0 |
| 28       | 1 |   | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 0 |       | 0 | 4 | 0          | 1      | 0             | 0 | 3      | 0           | 0 | 0            | 0 | 0            | 0 | 0               | 2 |
| 29       | 1 |   | 0 | 0 | 1 | 0 | 1 | 0 | 1 | Ô | 1 | ő |       | 0 | 1 | 0          | 1      | ő             | 0 | 3      | 0           | 0 | 0            | 0 | 0            | 0 | 0               | 2 |
| 30       | 1 |   | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 |       | 0 | 1 | 0          | 1      | 0             | 0 | 2      | 3           | 0 | 0            | 0 | 0            | 0 | 0               | 0 |
| 31       |   | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 1 |       | 0 | 4 | 0          | 0      | 0             | 0 | 0      | 1           | 0 | 0            | 0 | 0            | 0 | 1               | 1 |
| 32       |   | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 |       | 0 | 4 | 0          | 1      | 2             | 0 | 0      | 0           | 0 | 0            | 0 | 3            | 0 | 0               | 0 |
| 33       | 1 |   | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 |       | 0 | 1 | 0          | 3      | 0             | 0 | 1      | 0           | 0 | 0            | 0 | 2            | 0 | 0               | 0 |
| 34       | 1 |   | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 |       | 0 | 4 | 0          | 1      | 0             | 0 | 0      | 3           | 2 | 0            | 0 | 0            | 0 | 0               | 0 |
| 35       |   | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |       | 0 | 4 | ő          | 1      | 0             | 0 | 3      | 0           | 0 | 0            | 0 | 0            | 0 | 2               | 0 |
| 35<br>36 | 1 |   | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |       | 0 | 4 | 0          | 2      | 3             | 0 | 1      | 0           | 0 | 0            | 0 | 0            | 0 | 0               | 0 |
| 37       |   | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 |       | 1 | 4 | 0          | 0      | 0             | 0 | 1      | 3           | 0 | 0            | 0 | 0            | 0 | 0               | 1 |
| 38       | 1 |   | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 |       | 1 | 4 | 0          | 0      | 3             | 0 | 0      | 0           | 0 | 0            | 0 | 1            | 0 | 2               | 0 |
| 39<br>39 |   | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 0 |       | 0 | 4 | 0          | 1      | 2             | 3 | 0      | 0           | 0 | 0            | 0 | 0            | 0 | 0               | 0 |
|          |   |   | ~ | 0 |   | 0 |   | 1 | 1 | 1 |   | 0 |       | 1 | 3 | 0          | 0      | 0             | 0 |        | 0           | 0 | 2            | 0 | 0            | 0 | 0               | 3 |
| 10       | 1 |   | 0 |   | 1 |   | 1 | 0 | 1 | 1 | 1 |   |       |   |   |            |        |               |   | 1      |             |   |              |   |              |   |                 |   |
| \$1      | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | <br>) | 1 | 1 | 0          | 0      | 0             | 0 | 1      | 0           | 0 | 0            | 0 | 0            | 0 | 2               | 3 |

## Appendix B. R Code

## 2.1 Data Cleaning and Imputation

```
#import raw dataset
library(readxl)
rawDataTotal <- read excel("C:/Users/james/OneDrive/Documents/Thesis/Data/original.xlsx")
rawData <- rawDataTotal #make a copy of the raw data
#delete unwanted columns
rawData$hispanic <- rawData$num_abd_surg <- rawData$transfusion <- rawData$avg_bm <- rawData$painmed <- rawData$pound
s <- rawData$months <- rawData$cancer <- rawData$prolonged med <- rawData$cost <- rawData$ostomy <- rawData$bstructi
on <- rawData$leak <- rawData$sexual_dysfnc <- rawData$pregnancy <- rawData$side_effects <- rawData$stool_freq <- raw
Data$hospitalization <- rawData$emergent_surg <- NULL
#rename columns to not have numbers in the names
names(rawData)[names(rawData) == "5asa"] <- "asa"</pre>
names(rawData) [names(rawData) == "hx_5asa"] <- "hx_asa"</pre>
#eliminate samples that have 6 or more missing answers from choice sets
for (i in 1:length(rawData$ID)) { c <- 0</pre>
 if (is.na(rawDataCS_1[i])) {c = c + 1}
 if (is.na(rawData$CS 2[i])) {c = c + 1}
 if (is.na(rawData$CS 3[i])) {c = c + 1}
 if (is.na(rawData$CS_4[i])) {c = c + 1}
 if (is.na(rawData$CS_5[i])) {c = c + 1}
 if (is.na(rawData$CS 6[i])) {c = c + 1}
 if (is.na(rawData$CS_7[i])) {c = c + 1}
 if (is.na(rawData$CS 8[i])) {c = c + 1}
  if (is.na(rawData$CS_9[i])) {c = c + 1}
  if (is.na(rawData$CS 10[i])) {c = c + 1}
 if (is.na(rawData$CS 11[i])) {c = c + 1}
  if (is.na(rawDataCS_{12[i]}) {c = c + 1}
  if (is.na(rawData$CS_13[i])) {c = c + 1}
 if (is.na(rawData$CS 14[i])) {c = c + 1}
 else \{c = c\}
  if (c > 5) {rawData <- rawData[-i,]}</pre>
  }
#impute the remaining missing cells
#set the columns to appropriate type
library(dplyr)
```

library(magrittr)
rawData[,-2] %<>% mutate\_if(is.numeric,as.factor)

#impute using mode
library(imputeMissings)



rd.long <- reshape(rd, varying = c(26:39), direction = "long", idvar = "ID", sep = "\_", timevar = "choice\_set")

## 2.2 Multiple Factor Analysis

```
#Multiple Factor Analysis
#load data
library (FactoMineR)
library(readxl)
RD <- read_excel("C:/Users/james/OneDrive/Documents/Thesis/Data/Raw Data.xlsx", sheet="rawDataReduced")
RD MFA <- RD
#get only necessary columns
RD MFA$CS 1<-RD MFA$CS 2<-RD MFA$CS 3<-RD MFA$CS 4<-RD MFA$CS 5<-RD MFA$CS 6<-RD MFA$CS 7<-RD MFA$CS 8<-RD MFA$CS 9<-
RD_MFA$CS_10<-RD_MFA$CS_11<-RD_MFA$CS_12<-RD_MFA$CS_13<-RD_MFA$CS_14<-NULL
#convert the columns (except age) to factors instead of numeric
library(dplyr)
library(magrittr)
RD MFA %<>% mutate if(is.numeric,as.factor)
RD_MFA$age <- as.numeric(RD_MFA$age)
RD_MFA$study_id <- NULL
RD MFA$physician <- NULL
RD_MFA$med.v.ipaa <- NULL
#run multiple factor analysis
res <- MFA(RD_MFA, group = c(1,9,4,4,6), type = c("c","n","n","n","n"), ncp = 3,
          name.group = c("age", "demographics", "current.meds", "past.meds", "symptoms"))
```

plot(res,choix="ind",partial="all")

#factoextra scree plot
library(factoextra)

reseig <- get\_eigenvalue(res)
summary(reseig)</pre>

## 2.3 Conditional Logistic Regression

## #build full conditional logit model including all interaction terms library(survival)

clogit.model <- clogit(choice ~ cancer+prolonged\_med+cost+ostomy+obstruction+leak+sexual\_dysfnc+pregnancy+side\_effect</pre> s+stool freg+hospitalization+emergent surg+cancer:age+prolonged med:age+cost:age+ostomv:age+obstruction:age+leak:age+ sexual\_dysfnc:age+pregnancy:age+side\_effects:age+stool\_freq:age+hospitalization:age+emergent\_surg:age+cancer:sex+prol onged\_med:sex+cost:sex+ostomy:sex+obstruction:sex+leak:sex+sexual\_dysfnc:sex+pregnancy:sex+side\_effects:sex+stool\_fre q:sex+hospitalization:sex+emergent surg:sex+cancer:race+prolonged med:race+cost:race+ostomy:race+obstruction:race+lea k:race+sexual dvsfnc:race+pregnancy:race+side effects:race+stool freg:race+hospitalization:race+emergent surg:race+ca nccr:edu+prolonged\_med:edu+cost:edu+ostomy:edu+obstruction:edu+leak:edu+sexual\_dysfnc:edu+pregnancy:edu+side\_effects: edu+stool\_freq:edu+hospitalization:edu+emergent\_surg:edu+cancer:income+prolonged\_med:income+cost:income+ostomy:income +obstruction:income+leak:income+sexual dysfnc:income+pregnancy:income+side effects:income+stool freq:income+hospitali zation:income+emergent surg:income+cancer:relationship+prolonged med:relationship+cost:relationship+ostomy:relationsh ip+obstruction:relationship+leak:relationship+sexual\_dysfnc:relationship+pregnancy:relationship+side\_effects:relation  $ship+stool\_freq:relationship+hospitalization:relationship+emergent\_surg:relationship+cancer:IBD\_type+prolonged\_med:IB$ D\_type+cost:IBD\_type+ostomy:IBD\_type+obstruction:IBD\_type+leak:IBD\_type+sexual\_dysfnc:IBD\_type+pregnancy:IBD\_type+sid e effects:IBD type+stool freq:IBD type+hospitalization:IBD type+emergent surg:IBD type+cancer:years dx+prolonged med: years\_dx+cost:years\_dx+ostomy:years\_dx+obstruction:years\_dx+leak:years\_dx+sexual\_dysfnc:years\_dx+pregnancy:years\_dx+s ide\_effects:years\_dx+stool\_freq:years\_dx+hospitalization:years\_dx+emergent\_surg:years\_dx+cancer:abd\_surg+prolonged\_me d:abd surg+cost:abd surg+ostomy:abd surg+obstruction:abd surg+leak:abd surg+sexual dysfnc:abd surg+pregnancy:abd surg +side effects:abd surg+stool freq:abd surg+hospitalization:abd surg+emergent surg:abd surg+cancer:hx ostomy+prolonged med:hx\_ostomy+cost:hx\_ostomy+ostomy:hx\_ostomy+obstruction:hx\_ostomy+leak:hx\_ostomy+sexual\_dysfnc:hx\_ostomy+pregnancy :hx\_ostomy+side\_effects:hx\_ostomy+stool\_freq:hx\_ostomy+hospitalization:hx\_ostomy+emergent\_surg:hx\_ostomy+cancer:biolo gic+prolonged\_med:biologic+cost:biologic+ostomy:biologic+obstruction:biologic+leak:biologic+sexual dysfnc:biologic+pr egnancy:biologic+side\_effects:biologic+stool\_freq:biologic+hospitalization:biologic+emergent\_surg:biologic+cancer:imm unomod+prolonged\_med:immunomod+cost:immunomod+ostomy:immunomod+obstruction:immunomod+leak:immunomod+sexual\_dysfnc:imm unomod+pregnancy:immunomod+side effects:immunomod+stool\_freq:immunomod+hospitalization:immunomod+emergent surg:immuno mod+cancer:steroid+prolonged med:steroid+cost:steroid+ostomy:steroid+obstruction:steroid+leak:steroid+sexual dysfnc:s teroid+pregnancy:steroid+side\_effects:steroid+stool\_freq:steroid+hospitalization:steroid+emergent\_surg:steroid+cancer :asa+prolonged med:asa+cost:asa+ostomy:asa+obstruction:asa+leak:asa+sexual dysfnc:asa+pregnancy:asa+side effects:asa+ stool freq:asa+hospitalization:asa+emergent surg:asa+cancer:hx biologic+prolonged med:hx biologic+cost:hx biologic+os tomy:hx\_biologic+obstruction:hx\_biologic+leak:hx\_biologic+sexual\_dysfnc:hx\_biologic+pregnancy:hx\_biologic+side\_effect s:hx\_biologic+stool\_freq:hx\_biologic+hospitalization:hx\_biologic+emergent\_surg:hx\_biologic+cancer:hx\_immunomod+prolon ged\_med:hx\_immunomod+cost:hx\_immunomod+ostomy:hx\_immunomod+obstruction:hx\_immunomod+leak:hx\_immunomod+sexual\_dysfnc:h x immunomod+pregnancv:hx immunomod+side effects:hx immunomod+stool freg:hx immunomod+hospitalization:hx immunomod+eme rgent\_surg:hx\_immunomod+cancer:hx\_steroid+prolonged\_med:hx\_steroid+cost:hx\_steroid+ostomy:hx\_steroid+obstruction:hx\_s teroid+leak:hx\_steroid+sexual\_dysfnc:hx\_steroid+pregnancy:hx\_steroid+side\_effects:hx\_steroid+stool\_freq:hx\_steroid+ho spitalization:hx steroid+emergent surg:hx steroid+cancer:hx asa+prolonged med:hx asa+cost:hx asa+ostomy:hx asa+obstru ction:hx\_asa+leak:hx\_asa+sexual\_dysfnc:hx\_asa+pregnancy:hx\_asa+side\_effects:hx\_asa+stool\_freq:hx\_asa+hospitalization: hx\_asa+emergent\_surg:hx\_asa+cancer:sx\_bleed+prolonged\_med:sx\_bleed+cost:sx\_bleed+ostomy:sx\_bleed+obstruction:sx\_bleed +leak:sx\_bleed+sexual\_dysfnc:sx\_bleed+pregnancy:sx\_bleed+side\_effects:sx\_bleed+stool\_freq:sx\_bleed+hospitalization:sx bleed+emergent surg:sx bleed+cancer:sx BM+prolonged med:sx BM+cost:sx BM+ostomy:sx BM+obstruction:sx BM+leak:sx BM+s exual\_dysfnc:sx\_BM+pregnancy:sx\_BM+side\_effects:sx\_BM+stool\_freq:sx\_BM+hospitalization:sx\_BM+emergent\_surg:sx\_BM+canc er:sx\_pain+prolonged\_med:sx\_pain+cost:sx\_pain+ostomy:sx\_pain+obstruction:sx\_pain+leak:sx\_pain+sexual\_dysfnc:sx\_pain+p regnancy:sx\_pain+side\_effects:sx\_pain+stool\_freq:sx\_pain+hospitalization:sx\_pain+emergent\_surg:sx\_pain+cancer:sx\_weig ht+prolonged med:sx weight+cost:sx weight+ostomy:sx weight+obstruction:sx weight+leak:sx weight+sexual dysfnc:sx weig  $\label{eq:htpregnancy:sx_weight+side_effects:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_weight+hospitalization:sx_weight+emergent_surg:sx_weight+stool_freq:sx_wweight+stool_freq:sx_wweight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:sx_weight+stool_freq:stool_freq:sx_weight+stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_freq:stool_$ cancer:sx\_bloating+prolonged\_med:sx\_bloating+cost:sx\_bloating+ostomy:sx\_bloating+obstruction:sx\_bloating+leak:sx\_bloating+lea ting+sexual\_dysfnc:sx\_bloating+pregnancy:sx\_bloating+side\_effects:sx\_bloating+stool\_freq:sx\_bloating+hospitalization: sx bloating+emergent surg:sx bloating+cancer:sx frequency+prolonged med:sx frequency+cost:sx frequency+ostomy:sx freq  $uency+obstruction: sx\_frequency+leak: sx\_frequency+sexual\_dysfnc: sx\_frequency+pregnancy: sx\_frequency+side\_effects: sx\_frequency+sexual\_dysfnc: sx\_frequency+pregnancy: sx\_frequency+sexual\_dysfnc: sx\_freq$ equency+stool freq:sx frequency+hospitalization:sx frequency+emergent surg:sx frequency+strata(STR), originalData

summary(clogit.model)

# 2.4 Step-Wise Regression

#backward step-wise regression based on AIC of models
step.clogit <- stepAIC(clogit.model, direction = "backward", trace = F, k = 3.8415)</pre>

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# **REPORT DOCUMENTATION PAGE**

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| a. REPORT    | b. ABSTRACT   | c. THIS PAGE | ABSTRACT | OF<br>PAGES | Lt Col Andrew J. Geyer, Ph.D., AFIT/ENC  |  |  |  |  |
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