Assessing Impact of an Oral Nutritional Supplement Program for Patients with COPD

by
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A master's paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Science in Public Health in the Department of Health Policy and Management, Gillings School of Global Public Health

Chapel Hill
May 3, 2016

Approved by:

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Abstract

**Objective:** The purpose of this study was to assess the cost-effectiveness of an oral nutritional supplement program for patients with Chronic Obstructive Pulmonary Disorder (COPD) versus standard of care, which is no intervention in patient nutrition, from the perspective of a private payer in the United States.

**Methods:** A probabilistic Markov Model was used to calculate total costs, quality adjusted life years, and number of exacerbations for a population of 500,000 COPD patients. The two alternatives were standard of care and the use of an oral nutritional supplement twice a day for a year. Cost estimates came from the literature and data from the Medical Expenditure Panel Survey, which was based on average reimbursement rates across the United States. Quality of life scores and transition probabilities were based on data from the literature.

**Results:** On average, the total cost of care for patients with oral nutritional supplements is lower than the standard of care. The oral nutritional supplement program also resulted in fewer exacerbations and more QALYs. The results estimate that the program can save $12,290/QALY gained for COPD patients.

**Conclusion:** Results suggest that the oral nutritional supplement program is cost-saving for the COPD population and should be a serious consideration for insurance companies and health systems.
I. Research Objective

COPD is an enormous and growing problem for the American healthcare system. It is an expensive chronic condition and one that leaves patients unable to fully take care of themselves and perform regular daily tasks. For COPD patients, an important part of how well they are able to live with the disease is what medications and services are covered by their health insurance. Using data from the literature and a Markov model, I assessed the balance of costs and benefits of providing COPD patients with oral nutritional supplements, specifically two nutritional supplements each day for a year. The key outputs that I examined for this modeling approach were total exacerbations, Quality Adjusted Life Years (QALYS), total cost, and incremental cost effectiveness ratio (ICER). The goal of this research is to look at the cost effectiveness and possible quality of life and health impacts to determine if the coverage of non-traditional items such as nutritional supplements could make sense for insurance companies to cover as part of care plans. This is particularly important as more and more people, especially seniors on Medicare Advantage plans and people on Medicaid managed care plans, are insured in capitated systems. If these low cost solutions can make a difference it can mean better health for patients and more revenue for insurance companies, which could encourage insurance companies to pilot and offer more preventative and non-traditional programs for patients.

II. Background

COPD is a preventable, chronic progressive lung disease that is becoming increasingly important in healthcare because of the cost of treatment and the number of deaths resulting from the disease. COPD is a rising cause of death in the United States and a disease that affects 6.3% of adults in the US -- about 24 million patients. This rate may be an underestimate because many people do not know they have COPD and the disease often goes undiagnosed for a long
Patients with COPD are classified into different stages of the disease based on the COPD Global Initiative for Chronic Obstructive Lung Disease (COPD GOLD). The stages, mild, moderate, severe, and very severe, are based on a patient’s ability to blow air out, which gives a good indication of air flow limitations. More information on the staging can be seen in appendix item A. There are well established risk factors for COPD; according to the Mayo Clinic the most significant risk factors are "smoking, having asthma and smoking, occupational exposure to dust and chemicals, age, and genetics." The rate of COPD varies significantly across the United States, with many states in the Southeast having the highest prevalence. This map shows COPD prevalence by congressional district and highlights the large discrepancies in COPD prevalence even within states.

**Image 1. COPD Prevalence by Congressional District**

![COPD Prevalence by Congressional District](image1)

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1. (Centers for Disease Control.)
2. (WebMD)
3. (Mayo Clinic Staff, 2015)
4. (Centers for Disease Control, 2014)
In addition to a high prevalence in the US, COPD is a growing problem globally. With an aging global population, chronic diseases are becoming more common -- especially COPD. Around the world, smoking tobacco is a significant cause of COPD. The World Health Organization estimates that "73% of COPD mortality is related to smoking, with 40% related to smoking in nations of low and middle income."\(^5\) The rates of COPD also vary by gender, which can be attributed to differences in smoking rates and the different types of jobs held by men and women. The following chart shows the differences in COPD rates by gender for different countries.

**Image 2. Graph of COPD prevalence by gender globally\(^6\)**

![Graph of COPD prevalence by gender globally](image)

The cost of caring for patients with COPD from an insurance perspective is substantial; researchers found that the cost of the average patient with COPD is about $6000 more in medical costs than patients who were not diagnosed with COPD.\(^7\) The costs associated with COPD are mostly paid by government programs: in 2010 51% of the cost associated with COPD were paid

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\(^5\) Mannino & Buist, 2007
\(^6\) Mannino & Buist, 2007
\(^7\) Centers for Disease Control
by Medicare and 25% of the costs associated with COPD were paid by Medicaid.\(^8\) In addition to the direct healthcare costs paid for COPD related care, there are significant absenteeism costs from COPD, which greatly increase the disease’s burden on society; absenteeism costs in 2010 were estimated to be about $3.9 billion.\(^9\)

One often overlooked side-effect that is highly correlated with COPD is malnutrition. The prevalence of malnutrition among patients with COPD ranges from 20% to 70% depending on patient demographics and comorbidities. Malnutrition is an independent predictor of mortality for COPD patients and patients with lower weights have lower five-year survival rates.\(^10\) Patient with COPD lack energy to exercise and perform daily activities and begin to lose muscle and experience wasting especially in their extremities. This can lead to reductions in body cell mass, the diaphragm, and respiratory muscles. This further compounds the problem because the muscle loses result in even greater reduction in endurance and the ability to perform daily activities.\(^11\) A review of studies that examined Protein Energy Malnutrition (PEM) and chronic nonmalignant disorders found that in studies that focus on patients with COPD “nutritional treatment of PEM in connection with COPD may positively affect body composition as well as muscular strength and respiratory function.”\(^12\)

Insurance companies and other types of payers that take on risk based contracts feel the impact of the increasing COPD population and the high costs of their care. COPD patients can be a very costly population for ACOs and managed care organizations. Currently, few insurance companies or managed care organizations cover nutritional supplements for patients. Some

\(^8\) (Centers for Disease Control)  
\(^9\) (iv Ford, Murphy, Khavjou, Giles, & Holt, 2015)  
\(^10\) (Aknar, 2001)  
\(^11\) (Ezzell, 2000)  
\(^12\) (Aknar, 2001)
ACOs and managed care organizations are considering offering nutritional supplements to patients with COPD and protein energy malnutrition as a way of bringing down costs and helping to improve the lives and health of their patients.

The concept of insurance companies covering non-traditional health related items is increasing in the United States. In New York, the New York State commissioner of Health and the New York State Medicaid Director have both publicly argued for housing to count as healthcare for chronically homeless populations. The argument they made was that the system would significantly save money in the long run by helping to pay for housing for these people. This type of thinking is different from how healthcare and health insurance have traditionally operated where the providers would prescribe things but did not really think about what was happening outside of the walls of the doctor’s office or hospital. Using modeling techniques to show the potential cost savings and impact of an oral nutritional supplement program could make a serious contribution to this current and relevant debate.

III. Research Overview

The connection between nutritional status and COPD outcomes is very apparent, but data about potential interventions that can benefit the patient and the payer is lacking. In order to evaluate the possibility of using oral nutritional supplements to bring a patient back up to an energy level where they are able to better care for themselves and perform everyday activities, a Markov model, data from the literature, and probabilistic sensitivity analysis can be used to estimate important end points and outcomes. Data was collected from various meta-analyses and research done in the COPD and nutrition fields. The perspective of an payer was chosen as

13 (Aronczyk, 2014)
opposed to a global perspective because the implication of the research is to see if it could make sense for insurance companies both traditional, fee for service, healthcare insurers and managed care organizations, which have more of a population health approach already, to cover oral nutritional supplements for some of their COPD patients. These results could have an impact on how insurance companies think about what they cover for patient care especially as the US healthcare system transitions over to more of a pay for performance model.

IV. Specific Aims

The first aim of the study is to determine if an oral outpatient nutritional supplement intervention reduces the cost of caring for COPD patients from the perspective of a payer. My hypothesis is that the use of oral nutritional supplements will reduce the total cost of care at the one year end point. This end point was chosen because it is enough time to show substantial health changes. In addition, insurance companies and managed care organization often consider yearly costs and benefits.

Using a Markov model and data from the literature, my second aim is to determine if a nutritional supplement improves quality of life of COPD patients. Quality of life measures are closely connected to functional status of patients, so this measure can show an impact both in a patient’s ability to do daily activities and their overall health status. In this study quality of life is measured in QALYS, with the QALY data coming from the literature. My hypothesis is that the oral nutritional supplement intervention will, on average improve COPD patients’ QALYs.

Using a Markov model and data from the literature, my third aim is to determine if a nutritional supplement intervention improves the number of total exacerbations for patients with COPD. Exacerbations, both severe and non-severe, are closely tied with inpatient hospital stays
and sharp spikes in the cost of caring for a patient with COPD. My hypothesis is that an oral nutritional supplement intervention reduces the number of exacerbations that a COPD patient experiences in a one-year time frame.

V. Literature Review

COPD Care Information

The standard of care for COPD patients is put forward by the American Thoracic Society and the European Respiratory Society. They recommend a step-wise treatment called the Global Initiative for Chronic Obstructive Lung Disease more commonly referred to as the GOLD treatment algorithm. This treatment involves variations on a management program with the goal of slowing disease progression, addressing symptoms, improving health status and ability to exercise, and avoiding complications and exacerbations.14

Nutritional Supplements and Chronic Disease

Protein-energy malnutrition (PEM) is something that often occurs in connection with chronic diseases, including COPD. One reason for this is that many chronic diseases impact the body’s metabolic functions and can cause decreased nutrient intake. There is lots of research that established the relationship between patients with PEM and chronic disease and an increase in “morbidity, mortality, and extended hospital stays.”15 The causality between the treatment of PEM and improved symptoms for the chronic disease vary with both the chronic disease and the severity of the patient. There has been a lot of research that looks into this connection especially among elderly populations. One study published in the American Journal for Clinical Nutrition looked at the connection between PEM and COPD, chronic heart failure (CHF), stroke,

14 (Minkoff, 2005)
15 (Aknar, 2001)
dementia, rehab following a hip fracture, chronic renal failure, rheumatoid arthritis, and other diseases that commonly impact the elderly. A meta-analysis published in Clinical Nutrition Supplements in 2007 specifically looked at the use of oral nutritional supplements. Disease-related malnutrition increases mortality particularly for elderly patients in the hospital or those recently discharged from the hospital.16

COPD and PEM

A review of studies involving PEM and chronic diseases in the American Journal for Clinical Nutrition found 14 nutrition intervention trials specifically focused on COPD patients. Most of these were randomized control trials, but a few were observational trials.17 There is a large number of patients with PEM and COPD, but the estimates vary widely, from 20% to 70% of COPD patients. The group that is most likely to have PEM among COPD patients is those that have COPD and emphysema.18 It takes a lot of effort for COPD patients to perform basic functions, so people with COPD frequently have an “imbalance between energy expenditure and dietary intake”. This impact is further increased when patients experience exacerbations of their COPD.19 The problem compounds itself because as a patient losses lean body mass they often have reduced diaphragm mass, making it even harder for a patient with breathing issues to breathe. Weight loss has been recognized as a problem for COPD patients for a long time. Even in the 1970s it was seen that patients with COPD and weight loss had a significantly lower five year survival rate than patients with COPD alone.20 An examination of the observational and randomized control trials involving COPD and nutritional supplements in the review found the

16 (Stratton & Elias, 2007)
17 (Stratton & Elias, 2007)
18 (Aknar, 2001)
19 (Aknar, 2001)
20 (Vandenbergh, van de Woestijine, & Gyelesen, 1967)
following: 9 of the 14 studies showed positive effects on body weight, 8 studies saw functional improvements, and 5 found both positive impacts on body weight and functional status. Overall the review found that “nutritional treatment of PEM in connection with COPD may positively affect body composition as well as muscular strength and respiratory function.”

A meta-analysis specifically focused on oral nutritional supplements examined the efficacy in many different health conditions including COPD. For the COPD trials the meta-analysis method found a significant weight change when patients used oral nutritional supplements as opposed to routine care. The study also found that a weight gain of more than 2kg was correlated with improved functioning for the patient.

Modeling the issue

Lots of research has been done on the clinical side using trials to identify the impact of nutritional supplements on patients with chronic diseases, especially COPD. There have been fewer models to examine the impact of nutritional supplements on this population as a whole. One article published in Value in Health by Oosterbrink et al. used a probabilistic Markov model to look at COPD patients and what a change in their use and type of bronchodilators could do to change the number of exacerbations, QALYS, and total cost. This study was done looking at patients in both the Netherlands and Canada, but the information can be applied to patients in the United States. This probabilistic Markov model was created using data from clinical trials. It had a one year end point and moved the populations through both baseline COPD health states and COPD exacerbations, which very accurately reflects how a COPD patient’s health status can change quickly.

Another important COPD model that informed this research was also a

21 (Aknar, 2001)
22 (Stratton & Elias, 2007)
23 (Oosterbrink, Rutten-van Molken, Monz, & Fitzgerald, 2005)
Markov model, but modeled the impact of home-based COPD management programs on patients from an economic perspective. This study moved patients through health states in two different buckets: stable and unstable. However the health states in this study did not correspond to the COPD GOLD stages that are commonly accepted in the treatment of COPD. This study examined the possible impact of using a telehealth program to reduce the clinical and economic burden of patients with COPD.24

Implementation

There has been significant research done to look at the impact of nutritional supplements in improving the care of chronic disease patients. Some of this research has caused action to be taken to implement policies to support the use of nutritional supplements. Many of the studies in the meta-analysis by Stratton and Elia were used to help set and influence policies created by NICE and other European health organizations.25 For example, NICE now covers nutritional supplements for patients with malnutrition or who are at risk of becoming malnourished. However in the US, one of the major insurance companies, Aetna, only covers nutritional supplements provided by feeding tube or intravenously unless mandated by state law. Other insurance companies do cover oral nutritional supplements, but adoption is not consistent or wide-spread.

VI. Conceptual Model

The overall idea is that patients with COPD lack the energy and nutrition necessary to perform daily activities and take care of themselves. By adding an oral nutritional supplement, they are better able perform the activities to keep themselves healthy and out of the hospital. Therefore

24 (Xin Liu, Lee, Atakkhorymi, & al., 2013)
25 (Stratton & Elias, 2007)
the implementation of a regular use of oral nutritional supplements will reduce the probability of transitioning to a worse COPD GOLD stage from one month to the next. See the image below for a diagram of the conceptual model for this research.

**Image 3. Conceptual Mod**

VII. Research Methods

*Creation of Model*

A probabilistic Markov model was used to assess the impact of oral nutritional supplements in COPD patients. This type of model was chosen because COPD patients do not pass from one health state to the next linearly, they can cycle back through different states. For this reason a Markov model would more accurately match what happens to these patients than a decision tree or other types of models. The model used was based off of the research done by
Oosterbrink et al. and published in Value in Health. This model was chosen because of how it combined patients moving between health states and having exacerbations in those states. The study also used published data and had good information about transition probabilities for the patients in the standard of care arm of the model. This model served as a good base for creating a model to examine the impact of oral nutritional supplements on patients with COPD.

Collecting Inputs

The inputs in the model came from the literature and large public databases. The transition probabilities for the current state model come from the standard of care portion of the Oosterbrink study. The modifications to the transition probabilities in the intervention model came from a meta-analysis of the effectiveness of nutritional supplements in patients with chronic diseases. This meta-analysis found a 1.53% increase in the probability of a patient improving, so for example in the intervention the probability of moving from the severe state to the moderate state was increased by that factor while the probability of moving from the severe state to the very severe state was decreased by that factor. The transition probabilities for both the standard of care and intervention arm are shown in Table 1. The population size for the model was based off of CDC estimates of the prevalence of COPD in North Carolina. The cost estimates used information about inputs and health services usage from the Oosterbrink study and data from the Medical Expenditure Panel Survey (MEPS) database about the mean expenses per person for different services related to specific health states. The cost of the supplement was from online information about the cost of buying the supplement Ensure in bulk. Using the base Markov model and the MEPS data together it was possible to come up with estimates for the cost

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26 (Oosterbrink, Rutten-van Molken, Monz, & Fitzgerald, 2005)
27 (Stratton & Elias, 2007)
of caring for COPD in the United States.\textsuperscript{28} These annual costs were divided into monthly costs to fit with the models time increments. The QALY scores associated with the different health states and whether or not an exacerbation occurred were taken from the Oosterbrink study as well. These QALY estimates were based on an observational study about the quality of life associated with the various COPD GOLD stages that was published in Value in Health.\textsuperscript{29}

\textit{Evaluating Outcomes}

The model and inputs resulted in point estimates of the impact of the outcomes of interest: exacerbations, QALYS, total cost, and Incremental Cost Effectiveness Ratio (ICER). Using Crystal Ball and either reported standard errors or a 20\% range around an input, which was used for inputs that did not have reported variability, one thousand runs of the model were used to give a better understanding of the range of possible impact that could be expected if this intervention were to be implemented. A one-way sensitivity analysis of certain key inputs was used to delve deeper into the impact of estimates that were deemed the most important using a tornado chart on select outcomes. The tornado chart is included in the appendix.

\textbf{VIII. Description of Model and Inputs}

\textit{Model Design}

The probabilistic Markov model moves patient through three of the stages of COPD according to the COPD GOLD system: Moderate COPD, Severe COPD, and Severe COPD. The model used as a basis for this research did not include a death state because of the very low number of deaths in the trials upon which they were basing their transition probabilities. Therefore the model for this research also excludes a death state in the model design. In each

\textsuperscript{28} (Agency for Healthcare Research and Quality)
\textsuperscript{29} (Briggs, Ericsson, Wedzicha, & al., 2004)
state, for every month patients have a chance of either having no exacerbation, a nonsevere exacerbation, or a severe exacerbation. A first short stage of 8 days is included in the model, this is because of an initial jump in energy that occurs with the beginning of starting an oral nutritional supplement in COPD patients who are often malnourished or who have protein calorie malnutrition. See below for diagrams of both the model design and the conceptual model.

**Image 4. Model structure for Markov Model evaluating COPD**

![Diagram of the model structure for Markov Model evaluating COPD]

**Model Inputs**

The basis for the model inputs are described above in the research methods section. The model inputs are from a combination of previously published articles and information from national survey data. The inputs and their sources can be seen below in Table 1. The estimate for the model population was based on the population of North Carolinians with COPD. This was chosen so that the number would be useful if this data were to be presented to a large insurance company so they could envision the impact of the program on a large population. The majority of the probabilities in the model are derived from the Oosterbrink study. The transition probabilities indicate the probability of moving from one state to the next in a month. The model
assumes that the individuals are in a given state for the full month. Once the population has been
assigned a given state for that month, then the probability of having an exacerbation is assigned
to that subgroup. The probability of exacerbation increases as the severity of COPD increases.

Table 1. Probabilistic Markov Model Inputs

<table>
<thead>
<tr>
<th>Input</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model Population 500,000 people</td>
<td>(Centers for Disease Control.)</td>
</tr>
<tr>
<td>Starting probability Moderate COPD</td>
<td>(Oosterbrink, Rutten-van Molken, Monz, &amp; Fitzgerald, 2005)</td>
</tr>
<tr>
<td>Starting probability Severe COPD</td>
<td>(Oosterbrink, Rutten-van Molken, Monz, &amp; Fitzgerald, 2005)</td>
</tr>
<tr>
<td>Starting Probability Very Severe COPD</td>
<td>(Oosterbrink, Rutten-van Molken, Monz, &amp; Fitzgerald, 2005)</td>
</tr>
</tbody>
</table>

Transition probabilities, per month (Standard of Care) (Oosterbrink, Rutten-van Molken, Monz, & Fitzgerald, 2005)

<table>
<thead>
<tr>
<th>From:</th>
<th>To: Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>0.957</td>
<td>0.04</td>
<td>0.003</td>
</tr>
<tr>
<td>Severe</td>
<td>0.023</td>
<td>0.954</td>
<td>0.023</td>
</tr>
<tr>
<td>Very Severe</td>
<td>0.001</td>
<td>0.045</td>
<td>0.954</td>
</tr>
</tbody>
</table>

Transition probabilities, per month (Intervention) (Oosterbrink, Rutten-van Molken, Monz, & Fitzgerald, 2005), (Stratton & Elias, 2007)

<table>
<thead>
<tr>
<th>From:</th>
<th>To: Moderate</th>
<th>Severe</th>
<th>Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>0.957</td>
<td>0.04</td>
<td>0.003</td>
</tr>
<tr>
<td>Severe</td>
<td>0.0383</td>
<td>0.954</td>
<td>0.0077</td>
</tr>
<tr>
<td>Very Severe</td>
<td>0.001</td>
<td>0.0603</td>
<td>0.9387</td>
</tr>
</tbody>
</table>

Exacerbation probabilities, per month (Standard of Care and Intervention) (Oosterbrink, Rutten-van Molken, Monz, & Fitzgerald, 2005)

<table>
<thead>
<tr>
<th>From:</th>
<th>Exacerbation</th>
<th>Severe Exacerbation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>0.852</td>
<td>0.097</td>
</tr>
<tr>
<td>Severe</td>
<td>0.789</td>
<td>0.136</td>
</tr>
<tr>
<td>Very Severe</td>
<td>0.712</td>
<td>0.192</td>
</tr>
</tbody>
</table>
The difference between the standard of care transition probabilities and the intervention probabilities are based on the information found in the meta-analysis by Stratton and Elias. The modification from the meta-analysis increases the probability of moving from Severe COPD to Moderate COPD and increases the probability of going from Very Severe to Severe. So that the probabilities for each state still sum to 1, the increase in probability from severe to moderate is matched by a decrease in the probability of going from severe to very severe. For the increased probability of moving from Very Severe to Severe the change is matched by a decrease in the probability of staying in the Very Severe state from one month to the next. For example the probability of transitioning from severe to moderate in the standard of care state is 0.023 and in the intervention state it is increased to 0.0383.

The other key estimates for the model are the cost estimates and QALYs for the various disease states. The information for the cost data comes from the Oosterbrink study, the MEPS survey data, and estimates of the cost of providing nutritional supplements to each patient.

### Table 2. Cost estimates for the different COPD health states

<table>
<thead>
<tr>
<th>Estimated total cost of care per patient, per month (Standard of Care), units 2016 USD</th>
<th>(Oosterbrink, Rutten-van Molken, Monz, &amp; Fitzgerald, 2005), (Agency for Healthcare Research and Quality)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Exacerbation</td>
<td>Exacerbation</td>
</tr>
<tr>
<td>Moderate</td>
<td>$256.02</td>
</tr>
<tr>
<td>Severe</td>
<td>$2,514.49</td>
</tr>
<tr>
<td>Very Severe</td>
<td>$26,326.10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Estimated total cost of care per patient, per month (Intervention), units 2016 USD</th>
<th>(Oosterbrink, Rutten-van Molken, Monz, &amp; Fitzgerald, 2005), (Agency for Healthcare Research and Quality) (Perkins, 2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Exacerbation</td>
<td>Exacerbation</td>
</tr>
<tr>
<td>Moderate</td>
<td>$327.72</td>
</tr>
<tr>
<td>Severe</td>
<td>$2,586.19</td>
</tr>
<tr>
<td>Very Severe</td>
<td>$26,397.80</td>
</tr>
</tbody>
</table>
The moderate state with no exacerbation includes the cost of out-patient physician visits, prescription medications, and any services. These three cost buckets match with the resource use described in the Oosterbrink study. The cost for the Severe and Very Severe states with no exacerbation is scaled from the Moderate state estimate using cost information from the Oosterbrink study from the Netherlands. So for example in the Netherlands the cost of severe COPD is 7.8 times the cost of moderate COPD. This same factor was used to increase the cost of moderate COPD in the US to find an estimate of the cost of severe COPD in the US. The base level costs between the US and the Netherlands were not comparable but the scale-up of services used as the disease state worsens can make for a useful comparable for estimating costs. The same basic idea is used for estimating the cost of an exacerbation on top of the care needed without an exacerbation. The services utilized for an exacerbation are hospital inpatient stay, ER visit, home health, and other services. A Severe Exacerbation is assumed to cause a longer and more complicated hospital stay so the cost of a Severe Exacerbation is scaled up from an Exacerbation using the cost estimates from the Oosterbrink study. The oral nutritional supplement program in this model is very scalable and just involves the cost of the supplement. The idea behind this is that the insurance company would ship a biweekly or monthly supply to patients in the program. This puts the cost of the intervention at just the cost of two Ensure a day for a year per patient. Most insurance companies already have the ability to ship prescriptions to patients so shipping Ensure would not need much increased capability to be shipped.

The quality data comes from the Oosterbrink study as well. This came more directly from the study because the quality adjusted life year scores are much more comparable from one country to another than cost data. The QALY estimates in the Oosterbrink study came from an article published in Value in Health by Briggs et al. In this study they used observation data to
come up with average QALY scores for the different COPD GOLD stages and then modified those scores for exacerbations and severe exacerbations.

Table 3. QALY estimates for the different COPD health states

<table>
<thead>
<tr>
<th>Estimated QALY per patient, per month (Standard of Care and Intervention)</th>
<th>(Oosterbrink, Rutten-van Molken, Monz, &amp; Fitzgerald, 2005), (Briggs, Ericsson, Wedzicha, &amp; al., 2004)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Exacerbation</td>
<td>Exacerbation</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.755</td>
</tr>
<tr>
<td>Severe</td>
<td>0.748</td>
</tr>
<tr>
<td>Very Severe</td>
<td>0.549</td>
</tr>
</tbody>
</table>

The associated quality of life scores indicate a large drop off in quality of life if a patient moves from the Severe stage of COPD to the Very Severe. There is only a 0.007 difference in QALYs if a patient moves from the Moderate COPD health state to the Severe COPD health state. This difference seems very small when using quality adjusted life years as a measure, but comes out to about 2.52 days per patient, which with a large patient population can make a large difference. There is also a sharp decrease in QALYs if a patient has a severe exacerbation versus just a regular exacerbation. Severe exacerbations generally mean more hospital time, a longer recovery, and much higher chance of complications. An ICER for QALYs was measured by determining the differential Total Cost for the model and the incremental total QALY score. The incremental total cost was divided by the incremental QALY score to find the ICER for QALYs.

IX. Results

Base Case

In the base case resulted in relevant and impactful data. The base case results are shown below in Table 4. The outputs of interest for this model were total cost, number of exacerbations in total and for the two subcategories of exacerbations and severe exacerbations, total Quality Adjusted Life Years, and the Incremental Cost Effectiveness Ratio. In the base case of this
model, using the inputs in the previous tables the model found cost savings, reduced exacerbations, and increased quality adjusted life years. This means that the intervention would have a negative ICER indicating that implementing this strategy would both save money for whoever is paying for the healthcare costs and result in a better quality of life and less time in the hospital for the patients.

Table 4. Base Case Results from Probabilistic Markov Model

<table>
<thead>
<tr>
<th>COPD Population at Risk</th>
<th>Exacerbations</th>
<th>Nonsevere Exacerbations</th>
<th>Severe Exacerbations</th>
<th>Total QALYs</th>
<th>Inc. QALYs</th>
<th>ICER (QALYs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternative</td>
<td>Total Costs</td>
<td>Inc. Costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard of Care</td>
<td>$26,170,636,685</td>
<td>445,236</td>
<td>841,531</td>
<td>3,864,151</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nutritional Supplement</td>
<td>$24,337,962,688</td>
<td>- $1,832,673,997</td>
<td>414,079</td>
<td>776,502</td>
<td>4,013,261</td>
<td>149,110 -$12,290</td>
</tr>
</tbody>
</table>

Sensitivity Analysis

While the base case results for the model are very promising, it is important to remember that they are based off of estimates with some uncertainty. For this reason it is important to apply sensitivity analysis to the model. This model contained a lot of different estimates and transition probabilities, so a probabilistic sensitivity analysis allows for changing all of the probabilities at once. This gives a better understanding of the range of possible impacts that a oral nutritional supplement program could have as opposed to just making decisions off of the base case. The Oosterbrink article that the transition probabilities and QALY data came from gave both point estimates and standard errors for these probabilities. Using this information a triangle distribution was applied to all of probabilities. A triangle distribution was chosen because some of the probabilities were either very close to 1 or very close to 0 and this allowed for the range of the probability to be capped at the logical bounds. For the triangle distributions
the most likely value was the point estimate and the minimum and maximum were three standard errors above or below that, unless that would give a number outside of the 0 to 1 range in which case a cap of 0 or 1 was used. The minimum and maximum for the cost estimates were 20% above or below the point estimate.

The probabilistic sensitivity analysis was performed using the Crystal Ball software. This analysis produced similar results to the base case, with the intervention generally resulting in lower costs, higher QALYs, and fewer exacerbations. These results can be seen in the charts included in Appendix B. There is a noticeable difference between the standard of care and intervention for both total cost and QALYs, with lower cost and higher QALYs for the intervention arm. The difference between the total exacerbations for the standard of care and intervention arms of the model are the most distinct with two separate peaks for the two charts. This chart is available in Appendix B.

Image 5. ICER Plane for Total Cost and QALYs from probabilistic Markov Model
Another important output of the probabilistic sensitivity analysis is the Incremental Cost effectiveness ratio. To show the possible ICER’s for the oral nutritional supplement intervention, Crystal Ball was used to create an ICER plane. In the ICER plane, the y-axis is the difference in total cost between the standard of care arm and the intervention arm. A negative cost difference costs were lower for the intervention arm than the standard of care arm. The x-axis is the difference between QALYs for the two arms of the model. An ICER plane is useful for thinking about how to make the decision to implement a new program. If most of the outcomes are in the top left quadrant than the program results in higher cost and lower QALYs and is a dominated strategy that is likely a poor idea to implement. The bottom left and top right quadrants are interventions that would require a tradeoff, so either higher cost but more QALYs or lower cost but few QALYs. The bottom right chart is where most of the runs for the model were located for this Markov Model. This means that in 92% of cases this model predicts that implementing the oral nutritional supplement program would cause lower costs and increased QALYs.

X. Discussion

The outcomes from this model are encouraging because they show the potential for low cost interventions to have a significant impact on patient health. The sensitivity analysis is critical because the estimates of transition probabilities and cost may vary based on location, population, and many other factors. The sensitivity analysis shows that while, for the most part, this program results in better quality of life and cost savings, there is a wide range of possible health outcomes and total costs. According to the sensitivity analysis 92% of runs were cost saving and quality improving and 8% of runs were cost saving but did not improve quality of life. Further
research could be done to modify the transition probabilities and other estimates based on comorbidities. COPD patients often have other chronic diseases so being able to predict the impact of the intervention on a specific subset of the patient population. These modifications could also be key to convincing insurance companies to cover oral nutritional supplements for more groups of COPD patients.

The outputs from the model and sensitivity analysis are very useful for looking at the possible impact of covering supplements for patients. It is important to combine this information with knowledge of the industry and how coverage decisions are made and how similar programs have performed to understand the likelihood of an organization being willing to invest in and implement this type of a program. It is also critical to consider things like the logistics of running this type of program and how likely patients are to stick to a twice a day oral nutritional supplement regimen. This assessment is important for making recommendations and which types of insurance companies or healthcare organizations to push to use this type of intervention. The results from this model show that there is significant potential in the use of low cost nutritional supplement interventions to improve care for patients with COPD, but further research and investigation is likely needed.

XI. Limitations

This model has some important limitations and areas where more information would improve the model and its predictive capabilities. One key limitation is the patient adherence to the program over an entire year is likely to be much lower than 100%, the impact factor used from the meta-analysis did not have information about how adherence would modify the impact. The adherence problem is particularly important because oral nutritional supplements like Ensure are commonly complained about by patients because of the taste. If a patient does not
like the taste they are much less likely to have high adherence to the regimen. Better cost data specific to a certain population or area would be useful in order to create a more robust and meaningful model. The cost information is very high level and more precise micro-costing could give a better estimate. The cost information for the Ensure supplement excludes shipping costs. There is likely a cost to this but it is ultimately much smaller than the cost savings found and so would not be consequential if included in the model. Using insurance claims data, possibly even broken down for distinct areas, could give a more accurate cost estimate. This could be important to include because COPD prevalence in the United States is very high in some rural areas. Another important limitation is that the model does not include possible negative effects of using oral nutritional supplements such as nausea and vomiting. This could be important to know because it may be better to only enroll patients in the oral nutritional supplement program if they are in the worse COPD GOLD stages because of the possibility for side effects and low adherence. Despite some important limitations, this study has some important findings that can inform the discussion about possible ways to care for patients with COPD.

XII. Implications

The findings from this model have interesting implications for both the current state of healthcare in the United States and where the trends in healthcare are going. In its current form, the two best types of organizations for adopting a program like the proposed oral nutritional supplement program are managed care organizations or hospitals/health systems that have taken on risk-based population health contracts. These types of organizations tend to have a better line of communication with the physicians, have an incentive structure that aligns with the ideas of the program, and are often focused on the Medicare population where COPD is very common. An oral nutritional supplement program could also be implemented on a smaller scale by
hospitals. Instead of giving the supplements to a larger group, hospitals could offer the program to COPD patients who are frequent visitors to the Emergency Department as a way to reduce the number of costly ED visits those patients have in a year. As the US healthcare system transitions to more of a fee-for-performance system, this type of program should become more common and embraced by insurance companies and health systems.

XIII. Conclusion

Preliminary results reveal that an oral nutritional supplement program for patients with COPD can result in total cost savings for caring for the population and improved quality of life measures. On a per patient basis, the intervention results in approximately $3,665 in savings per year and 0.298 more QALYs, which is equivalent to 108 days. The goal for this evaluation was to show the potential impact of creating and implementing low cost interventions for patients with chronic diseases like COPD that can keep them feeling healthier and out of the hospital. From a business perspective this is also compelling evidence for an insurance company or managed care organization that an investment in a program like this can result in significant savings. This is particularly important because of the growth of the COPD population in the United States and around the world. Based on the results, we recommend further research into the potential uses of oral nutritional supplements and other ways to improve patient nutrition as well as research to better understand how to create interventions for patients with multiple chronic diseases.
Acknowledgements

Finally, I would like to thank the following people without whom this project would not have been possible: Justin Trogdon, PhD (First Reader); Kristen Hassmiller Lich, PhD (Second Reader); Elvin Perkins (Unofficial Advisor); Morris Weinberger, PhD (Master’s Thesis Seminar Leader); and Bruce Fried, PhD (Master’s Thesis Seminar Leader).
Appendix.
Appendix A. COPD GOLD staging criteria

<table>
<thead>
<tr>
<th>Stage</th>
<th>COPD Type</th>
<th>FEV1/FVC &lt; 0.70</th>
<th>FEV1 ≥</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mild COPD</td>
<td>FEV1/FVC &lt; 0.70</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>II</td>
<td>Moderate COPD</td>
<td>FEV1/FVC &lt; 0.70</td>
<td>50-79%</td>
</tr>
<tr>
<td>III</td>
<td>Severe COPD</td>
<td>FEV1/FVC &lt; 0.70</td>
<td>30-49%</td>
</tr>
<tr>
<td>IV</td>
<td>Very Severe COPD</td>
<td>FEV1/FVC &lt; 0.70</td>
<td>&lt; 30%</td>
</tr>
</tbody>
</table>

- Usually, this means requiring long-term oxygen therapy.

Appendix B. Probabilistic Sensitivity Analysis of Total Cost of Care, QALYs, and Total Exacerbations
**In this chart “Home Health” refers to the cost bucket of home health services for patients recovering from an exacerbation. The “Modification factor” is the amount that the transition probabilities are changed by in the intervention branch of the model.**
Bibliography

Agency for Healthcare Research and Quality. (n.d.). *Table 7a: Mean Expenses per person with Care for Selected Conditions by type of service: United States, Average Annual 2012-2013.*


