Chapter 4
The Risk of Comparative Effectiveness Analysis for Decision Making Purposes

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Abstract. The purpose of comparative effectiveness analysis is ordinarily defined as a means to compare the benefits of drug A versus drug B. However, particularly in relation to cancer drugs, there is only drug A, and comparative effectiveness analysis tends to compare drug A to a quality adjusted threshold value, with a frequent conclusion that the cost of the drug is not worth the additional life given to the patient. Ordinarily, a societal perspective is used to deny the drugs, since the additional life may be worth the drug cost for the patient, although not to the payer. The British organization, the National Institute for Clinical Excellence (NICE) has denied many cancer drugs to their patients because the cost exceeds a threshold value. The Centers for Medicaid and Medicare are examining a similar process to deny treatments that exceed a quality adjusted price of $50,000. There are similar provisions in the Healthcare Reform Act. With the emphasis upon medications, medical procedures are not as subject to this comparative effectiveness scrutiny; procedures can frequently exceed the cost of medication treatments. However, each medication is considered separately; no analysis examines the total contribution of the treatment to the overall cost of healthcare. We examine different aspects of comparative analysis using techniques of data mining.

1 Introduction

In many ways, comparative effectiveness analysis is used to inflate the actual cost of treatment based upon the perceived quality of life of patients generally. Quality of life is defined lower for patients who are older or disabled, or both compared to younger, healthier patients. The adjusted cost, then, does not necessarily reflect the actual required reimbursement for treatment. In addition, the payer does not pay the adjusted cost, only the actual cost. However, if the adjusted cost is above a threshold value, that threshold is justified by the payer as a reason to deny the treatment rather than to use the actual cost that would actually be paid.

We will examine different aspects of comparative effective analysis and some of the problems that are not considered generally when defining the models but where data mining techniques can greatly enhance the process. Otherwise, there are some missing pieces that result in a risk that inferior drugs are deemed as the most cost effective, or that medications are denied because of a poor understanding of quality of life.

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Currently, the focus on the definition of quality of life is on functioning; relationships are ignored. That there are differing perspectives in terms of quality of life is clear because most patients opt for treatment once presented with options such as chemotherapy or heart surgery. While do not resuscitate orders are common, these are generally signed when they are hypothetical rather than real. Group identity is used to define quality of life rather than individual identity; levels of productivity and quality of life are considered equal across the patient base. We will demonstrate how text analysis can improve upon the concept currently in use for quality of life.

2 Preprocessing Data

In claims data, prescriptions are separated from inpatient and outpatient treatments as well as office visits and home health care. Because all of this information is stored in different files in a one-to-many relationship with a patient's identification number, the most important aspect of using these databases is to convert them to a one-to-one relationship after filtering down to the condition under study. We take advantage of the data step and the use of summary statistics to do both. Each patient claim is identified by an ICD-9 code as to the primary reason for the medication or treatment. Osteoporosis, for example, is identified by the codes, 733.0x where x can vary from 0 to 9 (http://icd9cm.chrisendres.com/). Each of the datasets has a column for the primary code. We can use an if...then statement in a data step to isolate patients with a specific condition.

Once the different data sets have been filtered down to a specific condition, we need to convert them to a one-to-one relationship. We then choose one of the datasets to serve as the primary set and merge the datasets using a left or a right join, depending upon the order of the data sets. In addition, we have to be concerned about whether medication is discontinued, or if the patient switched to a different treatment medication.

Because the database has accurate dates for prescriptions, we can investigate in more detail the occurrence of medication switching using survival data mining. In order to do this, we need to transpose both date and medication. Doing a similar code to transpose the medication date, we then merge the two transposed datasets together so that both medication and date are in the same dataset.

We then need to search for the first prescription that involves switching, and the date when the switching occurs. If no switching occurs, we define the final date as a censoring value. The censoring variable can be modified to search for specific endpoint medications. For example, if we want to know whether the change is equal to the drug, Boniva, then we define Boniva=0 if medchange='Boniva' and =1 otherwise. Then we apply survival analysis, stratifying by the initial medication using the start of the year, 2006, as time=0. In doing this, we make the assumption that future medication choice depends on the present medication and not on the past medications.

Because SAS software (SAS Institute, Inc.; Cary, NC) is used so commonly in medical research and drug development, we provide the SAS code for the preprocessing in the appendix, using SAS version 9.2.

3 Comparison of Multiple Drugs for Best Value

We provide an example of a comparison of multiple medications for the treatment of osteoporosis. We want to see if there is a difference in the medical tests performed given the different medications to include this information in a comparison between drugs. In this example, we combine different datasets taken from the Medical Expenditure Panel Survey (http://www.meps.ahrq.gov/mepsweb/).

We want to see if patients taking different medications have different types of other treatments that can increase costs. We first looked at the costs for each type of care: medications, inpatient, outpatient, office visits, and home health care. We also looked at the issue of patient compliance in relation to the medications. It is possible that patients are more likely to comply with one medication over another, and compliance might reduce the overall costs in terms of treatment. Table 1 gives the costs of the medications used to treat osteoporosis along with the different payers.

Table 1. Total Cost for Osteoporosis Medications

Year	N Obs	Variable	Mean	Sum	N
2005	3733	selfpay	50.1955746	187380.08	3733
		medicare	2.9947924	11179.56	3733
		medicaid	10.4126493	38870.42	3733
		private	27.2414894	101692.48	3733
		va	0	0	3733
		total	94.2722127	351918.17	3733
2006	4179	selfpay	36.7708279	153665.29	4179
		medicare	27.6511079	115553.98	4179
		medicaid	2.7505288	11494.46	4179
		private	17.6373654	73706.55	4179
		va	0	0	4179
		total	88.2418689	368762.77	4179

Table 1 indicates that the average prescription went from $50 self-pay to $36 while Medicare again increased 10-fold and Medicaid paid 1/3 of the amount in 2006 that it paid in 2005 for these medications. Private insurance declined considerably from $101,692 in 2005 to $73,707 in 2006 for this cohort of patients. The results suggest that most of the patients prescribed these medications are in the Medicare eligible population. The patients were just shifted in terms of payment and payer for their continuing medication.

Table 2 gives the frequency count for the medication, Actonel, which is a once-a-week prescription. In a year's time, there should be 12 prescriptions, with each prescription equal to 4 doses. Possibly, there are 90-day prescriptions of 12 tablets, so we need to take this into consideration as well. We do this by computing the product of the frequency of the prescription by the average quantity per prescription by patient. Note that the most frequent number of prescriptions per patient is for just one. The patients who get just one prescription most probably had difficulty with the medication and discontinued its use.

Table 2. Frequency Count for Number of Actonel Prescriptions

FREQ	Frequency	Percent	Cumulative Frequency	Cumulative Percent
1	23	20.91	23	20.91
2	13	11.82	36	32.73
3	10	9.09	46	41.82
4	13	11.82	59	53.64
5	9	8.18	68	61.82
6	8	7.27	76	69.09
7	7	6.36	83	75.45
8	6	5.45	89	80.91
9	6	5.45	95	86.36
10	1	0.91	96	87.27
11	5	4.55	101	91.82
12	3	2.73	104	94.55
13	3	2.73	107	97.27
15	1	0.91	108	98.18
16	2	1.82	110	100.00

Figure 1 gives the spread of the number of doses for Boniva. Boniva is taken once per month. In a year's time, there should be 52/4, or 13 prescriptions per patient; however, only 6 patients have achieved that number.

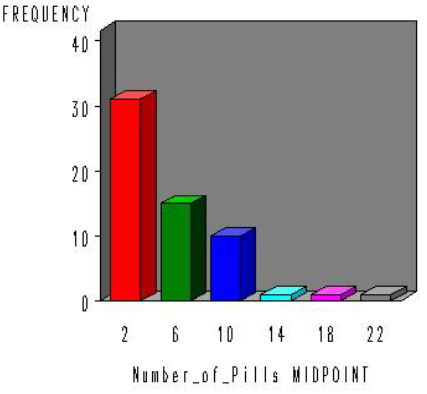

Fig. 1. Number of Doses for Boniva

The mode in Figure 1 is for 4 doses or fewer when it should be for 12 or 13. Again, it does not appear that patients are taking the full medication. It is possible that the patients are switching medications because of adverse effects, so we need to take switching into consideration as we define compliance.

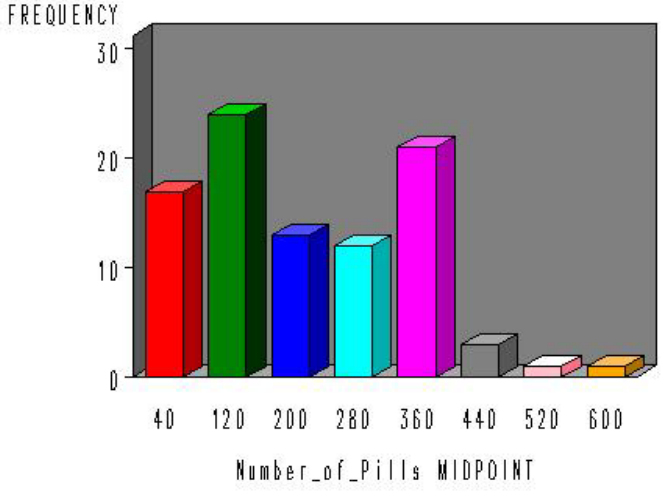

Fig. 2. Number of Doses for Evista

Evista is used daily, which suggests that a patient should have approximately 365 doses in a year's time. While there are many who have that number of doses, there are many more who do not, which suggests a lack of compliance with the medication requirements.

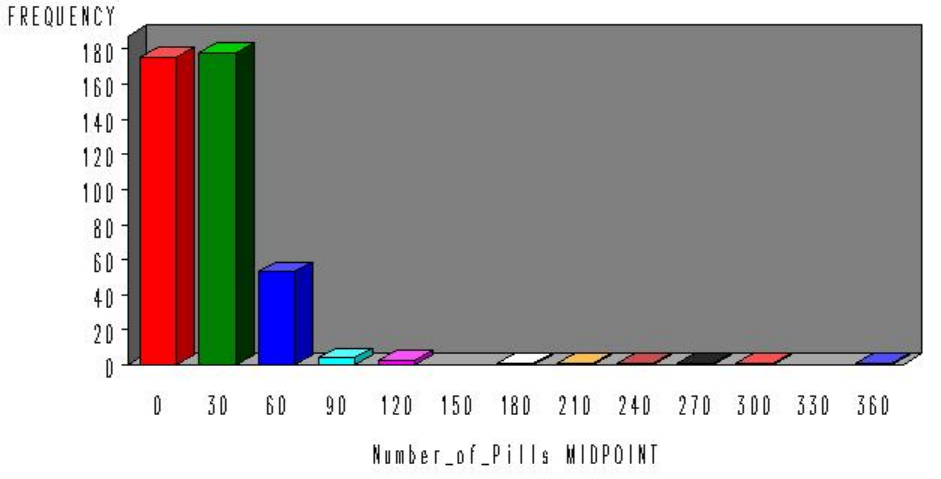

Fig. 3. Number of Doses for Fosamax

This medication (Fosamax), too, should have 52 doses in a year, although there is a daily dose (which appears to be taken by very few patients). There are some extreme outliers, but most patients are getting fewer than the 52 doses.

While this preliminary investigation indicates that most of the patients are not in compliance, concluding this result can be misleading. If a patient switches from Actonel to Fosamax during the middle of the year, that patient will appear to be out of compliance for both medications. Therefore, we must change the observational unit to reflect the total doses for each drug. First, we separate the patients with more than one medication from those with exactly one medication.

Table 3 shows the number of patients who switched medications. The number is fairly small. It is sufficiently large so that patients who switch need to be taken into consideration when defining compliance. Note that most of the switching is to Fosamax.

Table 3. Second Medication and Number Who Switched

RXNAME	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Boniva	5	15.15	5	15.15
Evista	1	3.03	6	18.18
Fosamax	27	81.82	33	100.00

In order to work with medication combinations, we first need to standardize the value. Therefore, we compute a simple ratio for each medication taken, $c(med_i)$=number of doses prescribed/number of doses needed for full compliance. Then we add the sum of $c(med_i)$ for each medication. For example, suppose a patient takes Fosamax for 2/3 of a year and Boniva for the remaining 1/3 of a year. Then, compliance for Fosamax=36/52 and compliance for Boniva=3/12 for that patient. The sum of these values is equal to 36/52+3/12=0.69+0.25=0.94, or very close to one, the ideal identified as full compliance. Finally, we have to make certain that we distinguish between a once-a-day dose and a once-a-week dose. A patient who has 240 doses is on a once-a-day prescription.

We also want to look in the patient conditions listed with the prescriptions for these patients with medications for osteoporosis to ensure that they have been properly diagnosed. Therefore, we consider the ICD9 codes that are associated with each of the medications. For Actonel, there are 646 (out of a total of 996) primary codes given as 733, or Other disorders of bone and cartilage. The specific codes for osteoporosis are 733.01 (Senile osteoporosis or postmenopausal osteoporosis), V17.81 (Osteoporosis), 733.02 (Idiopathic osteoporosis), 733.03 (Disuse osteoporosis), 733.0 (Osteoporosis), and 733.00 (Osteoporosis, unspecified). However, there are other primary patient conditions listed for Actonel that include 714 (Rheumatoid arthritis and other inflammatory polyarthropathies), 715 (Osteoarthrosis and allied disorders), 716 (Other and unspecified arthropathies), 718 (Other derangement of joint), and 719 (Other and unspecified disorders of joint). Actonel is not approved for arthritis and is not considered effective for its treatment. It is possible that arthritis is primary and osteoporosis is secondary as a patient condition. It is also possible that Actonel is used off-label to treat arthritis. However, 733 is not listed as a secondary ICD9 code for Actonel. Either the Actonel is prescribed improperly, or the ICD9 code is inappropriately listed, or the use is off-label.

Evista similarly has 296 out of 690 primary ICD9 codes listed as 733, but unlike Actonel, it has 5 secondary codes also listed as 733. While there are also diagnoses listed for arthritis (715-716), there are 88 primary codes for V68 (Encounters for administrative purposes). This code suggests that the purpose of the encounter was to write a new prescription for a recurring medication.

For Fosamax, there are 1531 primary codes out of 2009 for osteoporosis. There are an additional 88 primary codes for arthritis, 46 primary codes for V68, and 61 for V82 (Special screening for other conditions). In contrast, none of the primary codes for estrogen are for osteoporosis or arthritis. The primary code listed is for 627 (Menopausal and postmenopausal disorders). It suggests that the estrogen prescriptions are not for osteoporosis.

We want to look at the relationship between the level of compliance to the need for treatment for bone fractures that result from the condition of osteoporosis. The number of such patients is quite small; 12 inpatients and 19 outpatients are identified as having treatment for bone breaks, while also having the condition of osteoporosis.

Note that for patient #8, the primary code is for infection; it is the secondary code that reveals the bone fracture related to the infection. This problem of infection is frequently related to orthopedic treatments.

Table 4. Osteoporosis Medications by Inpatient Fractures

Row number	RXName	Dose Strength	Quantity of Prescription	ICD9 Code	ICD9 Code	ICD9 Code
1	Actonel	35	12	821, Fracture of other and unspecified parts of femur	-1	-1
2	Actonel	35	12	821, Fracture of other and unspecified parts of femur	-1	-1
3	Fosamax	70	90	822, Fracture of patella	-1	-1
4	Evista	60	150	724, Other and unspecified disorders of back	733, Other disorders of bone and cartilage	807, Fracture of rib(s), sternum, larynx, and trachea
5	Actonel	35	24	827, Other, multiple, and ill-defined fractures of lower limb	-1	-1
6	Fosamax	70	4	808, Fracture of pelvis	922, Contusion of trunk	-1
7	Fosamax	70	28	820, Fracture of neck of femur	707, Chronic ulcer of skin	-1
8	Fosamax	70	12	041, Bacterial infection in conditions classified elsewhere and of unspecified site	805, Fracture of vertebral column without mention of spinal cord injury	787, Symptoms involving digestive system
9	Fosamax	70	8	824, Fracture of ankle	-1	-1
10	Fosamax	35	24	824, Fracture of ankle	-1	-1
11	Actonel	35	12	812, Fracture of humerus	-1	-1
12	Fosamax	70	4	820, Fracture of neck of femur	812, Fracture of humerus	814, Fracture of carpal bone(s)

The patients taking Actonel in this group appear to be complying with the number of doses for a once a month treatment. The patients treated with Fosamax do not seem to be complying with the medication. If this is the case (and as shown previously, it is also true for patients generally prescribed the medication), it would be worthwhile to determine just why patients are not complying with the medication and how compliance can be improved.

This table does suggest that there are patients at high risk for fractures who are not complying with their medications. We can see if this remains the case for outpatient visits for fractures (Table5).

Table 5. Osteoporosis Medications by Outpatient Fractures

Row number	RXName	Dose Strength	Quantity of Prescription	ICD9 Code	ICD9 Code	ICD9 Code
1	Fosamax	35	4	805, Fracture of vertebral column without mention of spinal cord injury	-1	-1
2	Fosamax	70	12	825, Fracture of one or more tarsal and metatarsal bones	-1	-1
3	Fosamax	70	156	824, Fracture of ankle	-1	-1
4	Fosamax	70	156	824, Fracture of ankle	-1	-1
5	Fosamax	70	156	824, Fracture of ankle	-1	-1
6	Fosamax	70	156	824, Fracture of ankle	-1	-1
7	Fosamax	70	156	824, Fracture of ankle	-1	-1
8	Fosamax	70	156	824, Fracture of ankle	-1	-1
9	Fosamax	70	156	824, Fracture of ankle	-1	-1
10	Fosamax	70	156	824, Fracture of ankle	-1	-1
11	Fosamax	70	156	824, Fracture of ankle	-1	-1
12	Fosamax	70	156	824, Fracture of ankle	-1	-1
13	Fosamax	70	156	824, Fracture of ankle	-1	-1
14	Fosamax	70	156	824, Fracture of ankle	-1	-1

Row number	RXName	Dose Strength	Quantity of Prescription	ICD9 Code	ICD9 Code	ICD9 Code
15	Actonel	30	32	823, Fracture of tibia and fibula	-1	-1
16	Actonel	30	32	823, Fracture of tibia and fibula	-1	-1
17	Actonel	30	32	823, Fracture of tibia and fibula	-1	-1
18	Fosamax	70	4	820, Fracture of neck of femur	812, Fracture of humerus	814, Fracture of carpal bone(s)
19	Fosamax	70	4	820, Fracture of neck of femur	812, Fracture of humerus	814, Fracture of carpal bone(s)

There is a red flag on the 156 doses of Fosamax to consider; this patient is taking the daily treatment. This list also suggests that patients receive multiple follow up visits for treatment and there are actually just 5 patients in the sample receiving outpatient treatment for fractures. Preprocessing needs to isolate episodes of treatment rather than just a list of treatments.

It would be of interest to determine whether patients who are taking the medications just as a preventative measure to avoid osteoporosis are the ones with limited compliance compared to patients who already have the disease, and who have complications related to the disease. It is said that "an ounce of prevention is worth a pound of cure". However, if the patients do not accept the prevention, it will do little good.

To examine some of these potential problems, we look to the physician visits and laboratory tests datasets restricted to the patients prescribed osteoporosis medications.

Table 6. Treatment Performed in Physician Visit by Medication (Percent of Patients)

Treatment Performed	*IV Therapy*	*Lab Tests*	*X-Rays*	*MRI/CATSCAN*	*Medication Prescribed*
Actonel	1.20	13.08	10.94	15.97	3.38
Boniva	0	13.54	3.09	3.09	4.64
Evista	0	22.49	4.54	13.84	6.51
Fosamax	0.22	18.88	6.72	11.58	4.22
	EKG	**EEG**	**Other Test**	**Surgical Procedure**	
Actonel	3.45	0.26	16.34	7.45	
Boniva	2.04	0	4.51	6.80	
Evista	3.30	0	24.21	21.51	
Fosamax	2.24	0.50	20.72	11.84	

There are differences in the percentage of patients with the type of treatment given the different medications. Patients taking Actonel are much more likely to have an X-Ray or an MRI; those taking Boniva are much less likely. It could be that patients with more serious conditions are given Actonel while Boniva is used more for prevention; or it could be that physicians prescribing Actonel are more knowledgeable about needed follow up to guard against side effects. It could also mean that patients taking Actonel are more likely to be tested for fractures. The EKG and EEG are heart-related, and are more likely with Actonel and Evista compared to Boniva and Fosamax. Surgical procedures, too, are more likely with Evista. Therefore, there are additional consequences that are related to the medication choice.

Of course, this is a non-terminal, treatable disease. Terminal illnesses will always be cheaper not to treat. If not treated, the patient dies and is removed from the healthcare system. It is this reason for a threshold value when performing comparative effectiveness analysis; the healthcare system will pay so much and no more. That is why cancer patients are problematic. They are terminal if not treated and it will cost less not to treat and reduce the time of survival. Therefore, these patients are at the mercy of the threshold value.

4 Effectiveness Analysis Using a Threshold Value

In this section, we investigate the problem of defining a patient's quality of life in relationship to treatments when the choice is not between drug A and drug B, but the effectiveness is measured against a financial threshold value, as has become common in cancer treatments as well as other chronic diseases for which few options are available for patients.

4.1 NICE

The National Health Service in Britain has been using comparative effectiveness analysis for quite some time. NICE stands for the National Institute for Health and Clinical Excellence. This organization has defined an upper limit on treatment costs, and if the cost exceeds this pre-set limit, then the treatment is denied. It does not matter if the drug is effective or not. That means that there are many beneficial drugs that are simply not available to patients in Britain where fully 25% of cancer patients are denied effective chemotherapy medications. (Devlin 2008; Mason and Drummond 2009) The number of chemotherapy drugs denied is increasing regardless of their effectiveness.

NICE is not comparing drug A to drug B for chemotherapy. Instead, the organization compares the cost of a drug to the value the organization places on your life. If it costs too much to keep you alive given your defined value, or to improve your life, then you are denied treatment. Similar types of rationing have also come to the United States. Oregon has become notorious in its Medicaid benefit, denying cancer drugs to patients, but making the same patients aware that assisted suicide is available. Oregon will not make available drugs that can prolong a patient's life; it will make available a drug to end it (which will then save additional medical costs). Currently, pharmaceutical companies have been subsidizing Oregon's Medicaid by providing these drugs to patients who have been denied by Medicaid. (Smith 2009) It has been

suggested that euthanasia is cheaper than end of life care, and more cost-effective than treating many patients with terminal illnesses. (Sprague 2009)

Just recently, the Food and Drug Administration has considered retracting approval of a chemotherapy drug for breast cancer on the basis of cost effectiveness rather than effectiveness. In this case, the definition of effectiveness has changed. The drug was approved based upon an improvement in disease-free survival. The intent is to withdraw approval because effectiveness is now defined as overall survival. The public outcry resulted in a postponement of a decision to remove approval at least for 4 months. (Anonymous-WSJ 2010; Perrone 2010) However, as of December, 2010, the FDA has voted to disapprove the drug for breast cancer.

4.2 QALY

A comparative effective analysis starts with the perceived patient's utility given the disease burden. The QALY, or quality of life-adjusted years, is an estimate of the number of years of life gained given the proposed intervention. Each year of perfect health is assigned a value of 1.0. A patient in a wheelchair is given a correspondingly lower value as is a patient who is elderly; this value is not clearly defined and is rarely based upon patient input. (Prieto and Sacristan 2003)

Consider an example. Suppose a cancer drug for patients with liver cancer allows a patient to live an average of 18 months compared to not using the drug. However, as with most cancer drugs, there are potent side effects. Suppose that the analyst decides that the quality of life is only 40% of perfect health (giving a weight of 0.4). Then the drug gives 1.5*0.4=0.6 QALYs to the patient. Suppose that at the initial introduction of this drug, it costs $1000 per month, or about $18,000 for the anticipated additional life of the patient. Then the cost per QALY is equal to 18,000/0.6=$30,000 per year of life saved. According to the NICE organization, this drug then would be too costly regardless of the fact that there is no comparable drug that is effective in prolonging the patient's life. However, suppose the analyst uses a measure of 60% of perfect health. Then the drug gives 1.5*0.6=0.9 QALYs to the patient at a cost of $20,000, which brings the amount closer to the pre-set value defined by NICE. Therefore, this definition of a scale of perfect health is of enormous importance. In fact, NICE has often denied such a cancer drug because of its cost. (Anonymous-NICE 2004; anonymous-NICE 2008; Anonymous-bevacizumab 2009; Anonymous-MedicalNews 2009; Anonymous-NICEreview 2009; Anonymous-NICEreview 2009)

If a person is otherwise young and healthy and a drug costs $10,000 per year, then the QALY is $10,000. However, if a patient is older and has a chronic condition, then that patient's utility may be defined as exactly half that of a young and otherwise healthy person. In that case, the QALY is $20,000 for the same drug. If the patient is old and has two or more chronic conditions, then the patient's utility could be defined as 25% that of a young and healthy person. In that case, the QALY IS $40,000 per year of life saved. By defining $15,000 as the upper limit for treatment, it is easy to see how the definition of a person's utility can be used to deny care to the elderly.

However, the cost of treating the disease is not restricted to the cost of medications. Therefore, we must look at all aspects of treatment, including physician visits, hospital care, and home health care. We must also look at the impact of patient compliance on the overall cost of healthcare. If patients have specific diseases that can be treated,

but who do not use the treatment, then outcomes will not be the same compared to patients who do comply. Also, patients who switch treatments may suffer from adverse events of the first treatment that are not present in the second treatment. Therefore, we must examine the totality of patient care.

4.3 Definition of Concepts

There are a number of concepts used in developing comparative effectiveness models. These concepts are particularly important when only one drug is compared to a threshold value. There are several ways that are currently in use to define a patient's quality of life. However, each method deals with a hypothetical situation rather than one that is real, bringing into question the validity of the entire process. The methods are listed below (McNamee, Glendinning et al. 2004; Puhan, Schunemann et al. 2007):

- Time Trade Off (TTO): Respondents are asked to choose between remaining in a state of ill health for a period of time, or being restored to perfect health but having a shorter life expectancy.

In other words, individuals are given the choice between taking a "happy pill" that will guarantee them perfect health for a period a time, after which they will drop dead versus spending a longer period of time in imperfect health. Would you be willing to take this happy pill if you had ten years of perfect health followed by death? Suppose you had 20 years? 30 years? At what point will you take this happy pill? If you refuse to take this pill, then you will have imperfect health of some type, say arthritis, diabetes, or asthma for, say 30 years. Is ten years of perfect health better than 30 years of imperfect health? It is not a real choice since such a "happy pill" does not exist, and probably never will.

- Standard gamble (SG): Respondents are asked to choose between remaining in a state of ill health for a period of time, or choosing a medical intervention, which has a chance of either restoring them to perfect health, or killing them.

This, too, is a hypothetical situation. A medical intervention is offered to a patient if the benefit outweighs the risk for a patient in ill health. There is no current intervention where the choice is perfect health or death. There is also no indication of the actual risk involved. Suppose there is a 1% chance of death versus a 25% chance of death. The patient decision, even as a hypothetical, may be different.

- Visual Analogue Scale (VAS): Respondents are asked to rate a state of ill health on a scale from 0 to 100, with 0 representing death and 100 representing perfect health.

This scale assumes that individual patients have a reasonable concept of perfect health. Since the term is very vague, it is not certain how patients are reflecting upon the terminology in order to make a reasonable assessment. Moreover, this scale does not allow patients to indicate their quality of life, which also should be taken into consideration.

4.4 Use of Text Analysis

Because the concepts of perfect health and quality of life are important to the definition of comparative effectiveness models, we also need to know how the concepts are interpreted by patients as they complete the basic surveys used to define quality of life. We used text analysis and open ended surveys to see how individuals view these basic concepts. Text analysis goes beyond simple frequency counts of words. It examines how words and concepts are linked within sentences.

Generally, a document is converted into a row in a matrix. This row has a column for any word contained within the dataset of documents. The matrix value is equal to the number of times that word occurs in the document. The matrix will consist mostly of zeros since the list of words is much longer than the list of documents. Therefore, the next step is to reduce the dimension of the matrix. This is done through the process of singular value decomposition. This feature is extremely valuable for calls into customer service, for example, for chart notes, and to examine advertisements from the competition.

There are variations to this general methodology depending upon what you want to discover. For example, if you want to determine what documents contain a specific word for flagging purposes, this can be done through filtering. However, if you want to look at connections within the text structure itself, you can find much greater meaning using the word structure itself. The basics of text analysis are as follows:

1. Transpose the data so that the observational unit is the identifier and all nominal values are defined in the observational unit.
2. Tokenize the nominal data so that each nominal value is defined as one token.
3. Concatenate the nominal tokens into a text string such that there is one text string per identifier. Each text string is a collection of tokens.
4. Use text mining to cluster the text strings so that each identifier belongs to one cluster.
5. Use the clusters defined by text mining in other statistical analyses.

The general process of text analysis is outlined below:

The SVD of an N x p matrix A having N documents and p terms is equal to $A=U\Sigma V$ where U and V are N x p and p x p orthogonal matrices respectively. U is the matrix of term vectors and V is the matrix of document vectors; Σ is a p x p diagonal matrix with diagonal entries $d_1 \geq d_2 \geq \ldots \geq d_p \geq 0$, called the singular values of Σ. The truncated decomposition of A is when SVD calculates only the first K columns of U, Σ and V. SVD is the best least squares fit to A. Each column (or document) in A can be projected onto

the first K columns of U. Similarly, each row (or term) in A can be projected onto the first K columns of V. The columns projection (document projection) of A is a method to represent each document by K distinct concepts. So, for any collection of documents, SVD forms a K dimensional subspace that is a best fit to describe data.

Cluster analysis, also called data segmentation, has a variety of goals. All goals relate to grouping or segmenting a collection of objects into subsets or "clusters" such that those elements within each cluster are more closely related to one another than the objects assigned to different clusters. An object can be described by a set of measurements or by its relation to other objects.

In addition, another goal is to arrange the clusters into a natural hierarchy. The arranging involves successively grouping the clusters themselves so that at each level of the hierarchy, clusters within the same group are more similar to each other than those in different groups. Cluster analysis is used to form descriptive statistics to assess whether or not the data consist of a set of distinct subgroups; each subgroup representing objects with substantially different properties.

Central to all of the goals of cluster analysis is the notion of the degree of similarity or dissimilarity between the individual objects being clustered. A clustering method attempts to group the objects based on the definition of similarity supplied to it. Clustering algorithms fall into three distinct types: combinatorial algorithms, mixture modeling and mode seeking.

Text analysis has as its basis the Expectation Maximization Algorithm. The expectation maximization (*EM*) algorithm uses a different approach to clustering in two important ways:

1. Instead of assigning cases or observations to clusters to maximize the differences in means for continuous variables, the *EM* clustering algorithm computes probabilities of cluster memberships based on one or more probability distributions. The goal of the clustering algorithm is to maximize the overall probability or likelihood of the data, given the final clusters.

2. Unlike the classic implementation of k-means clustering, the general *EM* algorithm can be applied to both continuous and categorical variables.

The expectation-maximization algorithm is used to estimate the probability density of a given set of data. EM is a statistical model that makes use of the finite Gaussian mixtures model and is a popular tool for simplifying difficult maximum likelihood problems. The algorithm is similar to the K-means procedure in that a set of parameters is re-computed until a desired convergence value is achieved. The finite mixture model assumes all attributes to be independent random variables.

4.5 Text Analysis of Open Ended Questions

Approximately 100 pre-nursing students were surveyed and asked to define "health", "perfect health", and "quality of life". The results show that there is some ambiguity amongst the students, but the general consensus appears to be focused on physical functioning or lifestyle habits rather than social functioning and social networks. We first look at the definition of "health" using text analysis. Table 7 shows the terms that were used in text analysis to define the different clusters.

Table 7. Text Clusters Representing the Term, "Health"

Cluster Number	*Description*	*Percentage*
1	Physically, health, emotionally	0.08
2	Happy, ability, own, one life	0.28
3	Bad, good, +will, life	0.08
4	+enjoy, in alive, +thing, +not	0.164
5	Need, +do, +can, on, patient	0.2
6	+disease, independent, healthy, life	0.08
7	Physical, with, well, emotional, able	0.08

The concept that exists in clusters 1,2,5,6, and 7 primarily focus on physical functioning while clusters 3 and 4 focus on the ability to enjoy life. These clusters indicate that there are two prime considerations held by different groups of people when attempting to define "health". Moreover, these two groups would tend to approach surveys on quality of life in completely different ways. Similarly, Table 8 shows the text clusters defined for "quality of life".

Table 8. Text Clusters for "Quality of Life"

Cluster Number	*Description*	*Percentage*
1	+ condition, mental, medical, +problem, + illness	0.26
2	+absence, human body, human, within, +ability	0.14
3	Perfect health, perfect, +do, +not, health	0.24
4	When, diet, with, without, in	0.2
5	Stable, mentally, well, state, free	0.16

There is one group that defines "quality of life" by "perfect health" while a second cluster indicates that it is equivalent to the absence of illness. This cluster shows the ambiguity in the terms as the definition is circular. Two groups focus on a person's mental condition to define "quality of life". The final cluster defines quality as a lifestyle habit, primarily related to diet. Table 9 shows the clusters for the concept of "perfect health".

Table 9. Text Clusters for "Perfect Health"

Cluster Number	*Description*	*Percentage*
1	Disease, free, exercise, medical, eat	0.15
2	State, overall, individual, physical, well	0.30
3	Problem, health, not, living, health	0.1
4	Feeling, good diet, have, diet, lifestyle	0.04
5	Life, mentally, physically, do, basis	0.41

Three groups focus on the lack of disease and physical well being. Cluster number 5 includes mental well being while cluster number 4 looks at feeling good and lifestyle, including diet.

Another feature of text analysis is that links between terms can be visualized. Figure 4 examines the links to the term, health.

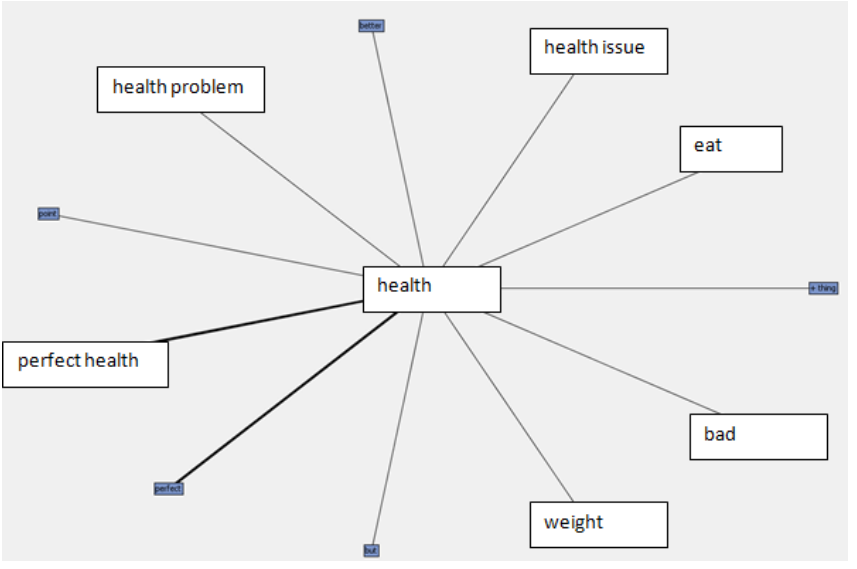

Fig. 4. Links to the Term, Health

Other than having some type of health problem, the links are to lifestyle concepts, eating and weight. There are no links to mental or social functioning. Similarly, Figure 5 examines the concept of life. Again, the emphasis appears to be upon physical functioning and the ability to do what one wants to do.

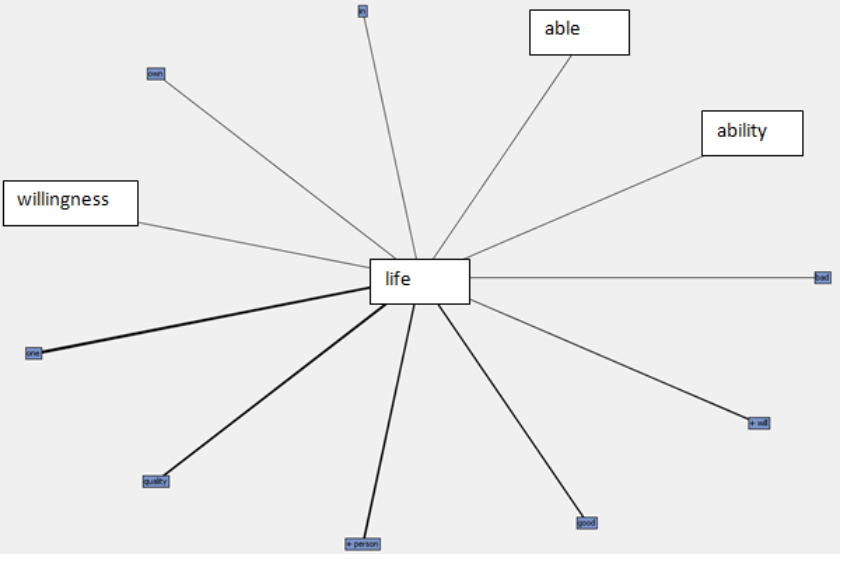

Fig. 5. Links to the Term, Life

Because of the critical nature of these concepts in the comparative effectiveness models, it is absolutely essential to discover how patients put meaning to the terms and to compare their understanding of the concepts to the understanding held by those who develop the models; if there are considerable differences in understanding, difficulties will arise when and if rationing occurs.

5 Discussion

The concepts used in comparative effectiveness analysis, such as quality of life and time trade off need to be examined closely; otherwise, the validity of the results are in doubt. Patient input should be as comprehensive as possible, and text analysis allows for them to demonstrate their different viewpoints with regard to the concepts. Patient understanding should also be compared to the understanding of those who perform comparative effectiveness analysis.

In addition, there is a considerable difference in using comparative models when comparing drug A to drug B to determine which drug provides both better cost and more benefit as opposed to comparing drug A to a threshold value. There should be some meaningful justification for the threshold. In addition, the full cost of treatment, including inpatient and outpatient treatments as well as physician visits and laboratory tests should be considered as the complete cost of treatment as opposed to just the cost of medication. The overall impact on the future development of medications and treatments should also be assessed.

If the quality of life is sufficiently lowered, it is almost always possible to exceed any fixed threshold value. The consequences of miscalculations can result in patient deaths because they are deprived of medications that are medically effective but not defined as cost effective. In other words, the perspective of the individual patient should be considered along with the perspective of society in terms of dollars spent upon healthcare.

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Appendix: SAS Code for Preprocessing

Many-to-One

```
  TITLE;
  TITLE1 "Summary Statistics";
  TITLE2 "Results";
  FOOTNOTE;
  FOOTNOTE1    "Generated    by    the    SAS    System
(&_SASSERVERNAME,              &SYSSCPL)             on
%TRIM(%QSYSFUNC(DATE(),          NLDATE20.))          at
%TRIM(%SYSFUNC(TIME(), NLTIMAP20.))";
  PROC MEANS DATA=WORK.SORTbyID
       FW=12
       PRINTALLTYPES
       CHARTYPE
       NWAY
       VARDEF=DF
             MEAN
             STD
             MIN
             MAX
             N      ;
       VAR  TOTTCH06  OBTTCH06  OPVTCH06  OPOTCH06  AMETCH06
AMATCH06  AMTTCH06  AMTOTC06  ERDTCH06  ZIFTCH06  IPFTCH06
DVTOT06    DVOTCH06    HHNTCH06    VISTCH06    OTHTCH06
RXTOT06;
       CLASS cost_Sum /    ORDER=UNFORMATTED ASCENDING;

  RUN;
```

Merge Datasets

```
  PROC SQL;
     CREATE                                                TABLE
SASUSER.QUERY_FOR_SUMMARYOFCONDITIONS_SA AS
           SELECT t1.patientID,
            t1.remaining variables from dataset,
            t2.variables from second dataset
  FROM  claims.summaryofconditions  AS  t1  RIGHT  JOIN
claims.h105 AS t2 ON (t1.patientID = t2.patientID);
  QUIT;
```

Transpose Data

```
proc transpose data=medications out=medicationbyid
     prefix=med_;
    id patientid;
run;
```

Defining Number of Prescriptions

```
  data sasuser.survivaldata;
    set medicationbytranspose;
    array meds(379) med_1 - med_379;
    array dates(379) date_1 - date_379;
  do j=1 to 379;
     if dates(j)=. then dates(j)='31dec2004'd;
     censor=1;
    end;
    do i=1 to 379;
      if i=1 then temp=meds(i);
      if meds(i) ne temp then do;
        med_num=i;
        date_num=dates(i);
       medchange=meds(i);
       censor=0;
        i=379;
       end;
    end;
  run;
```

Create Censoring Variable

```
if date_num = . then date_num='12dec2006'd;
if (medchange eq ' ') then censor=1;
if (medchange eq 'Drug_1') then drug_1=0;
else drug_1=1;
if (medchange eq 'Drug_2') then Drug_2=0;
else drug_2=1;
finaldate=input(newlastdate,anydtdtm17.);
format finaldate datetime17.;
final=datepart(finaldate);
       format final date9.;
```

Survival Analysis

```
PROC LIFETEST DATA=sasuser.survival data ALPHA=0.05
;
      BY medchange;
      STRATA med_1;
      TIME Days * censor (1);

RUN;
```