

A Multiattribute Decision Model for Bipolar Disorder: Identification of Preferred Mood-Stabilizing Medications

Brandon T. Suehs, PharmD; and Tawny L. Bettinger, PharmD, BCPP

Objective: To develop a multiattribute decision model (MADM) to aid in the selection of preferred medications for the treatment of bipolar disorder.

Study Design: Data were obtained via a self-administered online survey among psychiatric pharmacist specialists. These survey data were used to construct a MADM based on multiattribute utility technology.

Methods: Anticonvulsant mood stabilizers, atypical antipsychotics, olanzapine-fluoxetine combination, and lithium carbonate were evaluated using a MADM. Attributes included in the model were effectiveness, safety and tolerability, cost, monitoring burden, and dosing frequency. A survey instrument was developed to score the relative importance of each attribute and the factor scores for each medication. Four iterations of the model were performed to ascertain the medication with the highest total utility score when the effectiveness factors were weighted to consider the following: overall effectiveness, effectiveness in acute mania, effectiveness in acute bipolar depression, and effectiveness in maintenance treatment. Sensitivity analyses were performed to evaluate the stability of the MADM results.

Results: When overall effectiveness, effectiveness in acute mania, or effectiveness in maintenance treatment was considered, lithium carbonate had the highest total utility score. When effectiveness in acute bipolar depression was considered, lamotrigine had the highest total utility score. When considering only atypical antipsychotics, aripiprazole was associated with the highest total utility score for all iterations of the MADM.

Conclusion: The use of a MADM may be a beneficial tool to assist in making formulary or preferred therapeutic agent decisions.

(Am J Manag Care. 2009;15(7):e42-e52)

For author information and disclosures, see end of text.

Bipolar disorder is a cyclical mood disorder characterized by periods of mania or depression punctuated by periods of euthymia. Bipolar disorder affects approximately 2% of Americans.¹ There are various medication treatments aimed at minimizing the duration and severity of symptoms of bipolar disorder. Lithium carbonate, atypical antipsychotics, and mood-stabilizing anticonvulsants have all been shown to be effective in various phases of the disorder and are recommended agents for the treatment of bipolar disorder.^{2,3}

Treatment of bipolar disorder is associated with significant costs, a large portion of which is related to the cost of chronic medication administration.⁴ Medication formularies are increasingly being used to help control the cost of treatment for various medical conditions, as well as for psychiatric disorders such as bipolar disorder. To thoroughly evaluate the utility of a medication, it is important that formulary decisions take into account factors other than just medication cost in the formulary development process. A number of factors such as safety and effectiveness should be considered in addition to acquisition cost. A multiattribute decision model (MADM) attempts to take multiple factors into account when determining what medication alternative has the highest utility.

The MADM presented herein is a form of evaluation using multiattribute utility technology (MAUT). Multiattribute utility technology analysis is a broad technique originally developed to aid in making decisions regarding competing social programs.⁵ The MAUT framework has been extended to a number of other applications such as differentiating among medication interventions for medical conditions, including migraine,⁶ angina,⁷ and schizophrenia.⁸

The objective of this research was to develop a MADM to differentiate mood-stabilizing medications for the treatment of bipolar disorder. We synthesized data from a variety of sources, including focus group discussions, an online survey of psychiatric pharmacist specialists, and relevant clinical information in construction of our MADM.

METHODS

Development of a MADM involves determining the perspective of the model, identifying the treatment alternatives, ascertaining the relevant attributes to be considered, quantifying each attribute for each treatment alternative, and calculating the total utility score for each treatment alternative.⁵ The perspective

In this issue
Take-Away Points / e43
www.ajmc.com
Full text and PDF

Identification of Preferred Mood-Stabilizing Medications

for this MADM was determined to be a hypothetical psychiatric hospital. Lithium, anticonvulsant medications, atypical antipsychotics, and the olanzapine-fluoxetine combination were identified as the possible treatment alternatives. The attributes relevant to a comparison of mood-stabilizing medications were determined by a focus group discussion involving clinical psychiatric pharmacist specialists and academic pharmacy practice researchers. The attributes important to differentiating the various mood-stabilizing medications identified by the focus group were effectiveness, safety and tolerability, cost, monitoring burden, and dosing frequency. The next step in developing our MADM was to determine the relative weight or relative importance of each of these attributes and to assign a score for each medication on each of these attributes. To complete these steps of the analysis, we developed a survey instrument to be administered to a group of psychiatric pharmacist specialists.

Survey

The survey instrument was developed as a self-administered online survey. The target respondent population was psychiatric pharmacist specialists. A psychiatric pharmacist specialist is a pharmacist who has received specialized training or practices in the area of clinical psychopharmacology. Survey respondents were recruited from among the membership of the College of Psychiatric and Neurological Pharmacists, an organization representing more than 700 healthcare professionals in the United States and Canada. Subjects were recruited via the organization's e-mail Listserv. The initial invitation to participate in the survey was followed by a second e-mail invitation 1 week later. Online responses were collected for 14 days. The survey instrument consisted of 3 parts, namely, demographic information, attribute weights, and attribute factor scores. Only completed surveys were included in this analysis.

Demographic Information

Survey questions in this section were designed to obtain demographic information about survey participants. Demographic information collected included the following: sex, number of years in practice, academic degrees obtained, pharmacy residency information, board certifications obtained, and current practice setting.

Attribute Weights

Attribute weights were determined by asking respondents to weight how important each of the attributes (effectiveness,

Take-Away Points

This article describes the process of developing a multiattribute decision model (MADM) to compare mood stabilizers for the treatment of bipolar disorder.

- A MADM takes multiple attributes (eg, effectiveness, safety and tolerability, and cost) into account when determining the most favorable decision alternative.
- According to this model, lithium carbonate and lamotrigine are the mood-stabilizing medications with the highest utility scores.
- Among the atypical antipsychotics, aripiprazole is associated with the highest utility score.
- MADMs based on multiattribute technology are a versatile method that may have applications in the formulary decision-making process.

safety and tolerability, cost, monitoring burden, and dosing frequency) is when considering which medication should be used for a patient with bipolar disorder. Responses were scored on a 10-point scale (10 indicates very important, and 1 indicates not important at all) and were averaged for each attribute. The raw attribute weightings were converted to ratio weights and finally to percentage scores for use in the final model.

Attribute Factor Scores

For each attribute, factors were identified that could be used to quantify the attribute. In light of the differential effectiveness of medications in the different phases of bipolar disorder, we asked respondents to score each medication on the following 3 separate factors related to effectiveness: effectiveness in acute mania, effectiveness in acute bipolar depression, and effectiveness in maintenance treatment. For the safety and tolerability attribute, respondents were asked to score each medication separately on the factors of safety and tolerability. Monitoring burden and costs were each evaluated as a single factor. When rating each of the medications on the cost factor, respondents were asked to rate their "perception of the overall cost" associated with each medication. Dosing frequency was also evaluated as a single factor. Dosing frequency was included in the model to incorporate adherence as a component in the model, as the frequency of medication

■ **Table 1.** Dosing Factor Score Assignment

Daily Dosing Regimen ^a	Raw Dosing Factor Score ^b
3-4	40
3	50
2-3	60
2	70
1-2	80
1	90

^aBased on consensus recommendations and US Food and Drug Administration–approved labeling.

^bRange, 0 to 100.

■ **Equation 1.** Calculation of Factor Utility Score

$$u_f = 100(f - V_{\min}) / (V_{\max} - V_{\min})$$

u_f = factor utility score

f = raw factor score

V_{\max} = maximum plausible factor score

V_{\min} = minimum plausible factor score

administration has been found to be closely related to medication adherence.⁹

Raw factor scores were determined by asking the respondents to score each medication on all of the factors using a 5-point Likert-type scale. The responses were anchored for each factor such that a higher raw factor score indicated a more favorable performance on each attribute. If respondents did not know how to score a particular medication on a given factor, there was a “not sure” response available for them to select. “Not sure” responses were excluded from subsequent calculations on a casewise basis. The mean response scores were then calculated for each of the medications, and this mean response score was used as the raw factor score for each factor. For the dosing attribute, a single factor score based on consensus dosage recommendations and the US Food and Drug Administration–approved dosing frequency was used. The dosing factor score for each medication was assigned a value on a scale from 0 to 100 as given in **Table 1**. This method for attributing dosage factor scores was based on techniques used in a MADM analysis of medication treatments for schizophrenia.⁸

Calculation of Total Utility Score

The final steps of our MAUT analysis involved conversion of the raw factor scores to utility scores, calculation of

the attribute utility scores, and calculation of the total utility score for each medication. The mean raw factor scores were converted to a common utility scale ranging from 0 (the worst plausible value for a factor) to 100 (the best plausible value for a factor) to obtain the factor utility score. **Equation 1** was used to convert the raw factor scores to the factor utility scores. For all of the individual factors, except for the dosing factor, values of $V_{\max} = 5$ and $V_{\min} = 1$ were used. For the dosing factor, values of $V_{\max} = 100$ and $V_{\min} = 30$ were used.

Factor utility scores were weighted and summed, when appropriate, to determine the attribute utility score (see equation 2 herein). For example, because the safety and tolerability attribute score was related to 2 factor scores, the safety and tolerability factor scores (u_{safety} and $u_{\text{tolerability}}$, respectively) were each weighted equally (ie, w_{safety} and $w_{\text{tolerability}}$ were both set to 0.50) to calculate the unified safety and tolerability attribute score (U_{st}). A similar procedure was used to calculate the effectiveness attribute utility score (U_e), as discussed in the following “Model Iterations” subsection. For the monitoring burden, cost, and dosing frequency attributes, the attribute utility score (U_m , U_c , and U_d , respectively) is equivalent to the factor utility score, because only a single factor contributes to the attribute. Finally, attribute utility scores were scaled by their respective attribute weights and were summed to calculate the total utility score. The total utility score is represented in **Equation 2**.

Model Iterations

Four main iterations of the model were performed to compare the total utility scores when effectiveness in acute mania, effectiveness in acute bipolar depression, effectiveness in maintenance treatment, and overall effectiveness were considered. Each of these iterations was performed by adjusting the effectiveness factor weightings (w in equation 2). For example, for the iteration of the model evaluating effectiveness in acute mania, w_{mania} was set to 1, while $w_{\text{depression}}$ and $w_{\text{maintenance}}$

■ **Equation 2.** Calculation of Total Utility Score

$$U_{\text{total}} = (U_e \times W_e) + (U_{\text{st}} \times W_{\text{st}}) + (U_d \times W_d) + (U_m \times W_m) + (U_c \times W_c)$$

$$U_e = (u_{\text{mania}} \times w_{\text{mania}} + u_{\text{depression}} \times w_{\text{depression}} + u_{\text{maintenance}} \times w_{\text{maintenance}})$$

$$U_{\text{st}} = (u_{\text{safety}} \times w_{\text{safety}} + u_{\text{tolerability}} \times w_{\text{tolerability}})$$

U = attribute utility score

W = attribute weight

u = factor utility score

w = factor weight

Identification of Preferred Mood-Stabilizing Medications

were set to 0. For the iteration evaluation of overall effectiveness, each of the effectiveness factors was weighted equally.

Sensitivity Analysis

We also evaluated the stability of our model by varying the methods of calculating the monitoring and cost based on factor scores. Namely, we calculated the monitoring factor score using the number of monitoring interventions recommended instead of the survey response scores. We also calculated the cost factor score by inputting the average wholesale price for a 30-day supply of a typical dosage of each medication instead of using the perception of cost item from the survey. We then compared the results of these models with those of the original model to evaluate the model stability.

To clarify the reporting of results, in cases where a medication is available in both generic and branded forms, we indicate brand in parentheses next to the chemical name for branded versions of the medication. In cases where a medication was only available in a branded formulation at the time of this research, the chemical name is used exclusively. All calculations were performed using SPSS version 14.0 (SPSS Inc, Chicago, IL) and Excel 2007 (Microsoft, Redmond, WA). This research project was ap-

■ **Table 2.** Demographic Characteristics of Survey Respondents and Overall Membership^a

Variable	Survey Respondents	Overall Membership	P ^b
	(n = 116)	(n = 656)	
	No. (%)	No. (%)	
Sex			
Male	34 (29.3)	—	
Female	81 (69.8)	—	
Degree			
BSPHarm	41 (35.3)	134 (20.4)	.05
PharmD	98 (84.5)	535 (81.6)	
MSPHarm	9 (7.8)	34 (5.2)	
PhD	2 (1.7)	21 (3.2)	
Experience, y			
<10	57 (49.1)	—	
10-19	30 (25.9)	—	
≥20	29 (25.0)	—	
Country			
United States	111 (95.7)	625 (95.3)	>.99
Other	5 (4.3)	31 (4.7)	
Geographic region			
Northeast	10 (8.6)	133 (20.3)	.03
South	47 (40.5)	210 (32.0)	
Midwest	27 (23.3)	134 (20.4)	
West	26 (22.4)	141 (21.5)	
Pacific	1 (0.9)	2 (0.3)	
Postgraduate training^c			
Psychiatric pharmacy residency	68 (58.6)	—	
Pharmacy practice residency	24 (20.7)	—	
Pharmacy residency, other	5 (4.3)	—	
Other postgraduate training	5 (4.3)	—	
Board certification			
BCPP	69 (59.5)	313 (47.7)	.23
BCPS	1 (0.9)	21 (3.2)	
BCPS and BCPP	4 (3.4)	14 (2.1)	
Practice in a clinical setting with direct interaction with patients			
Yes	99 (85.3)	—	
No	17 (14.7)	—	
If clinical practice, age of patients seen^c			
Children	34 (29.3)	—	
Adults	94 (81.0)	—	
Geriatric	60 (51.7)	—	
If clinical practice, percentage of patients with a bipolar diagnosis			
<25	36 (31.0)	—	
25-49	53 (45.7)	—	
50-74	10 (8.6)	—	
≥75	0	—	

BCPP indicates Board-Certified Psychiatric Pharmacist; BCPS, Board-Certified Pharmacotherapy Specialist.

^aSome subtotals do not sum to heading totals because of missing responses to questions.

^bFrom χ^2 test comparing frequency distribution of respondents and the College of Psychiatric and Neurological Pharmacists members with available demographic information.

^cCategories are not mutually exclusive.

■ **Table 3.** Raw Attribute Weight, Ratio Weight, and Percentage Weight for Each of the Attributes Among 116 Survey Respondents

Attribute	Weight, Mean (SD) ^a	Ratio Weight ^b	% Weight ^c
Effectiveness	9.83 (0.42)	1.28	23
Safety and tolerability	9.60 (0.68)	1.25	22
Dosing frequency	7.88 (1.58)	1.02	18
Monitoring burden	7.74 (1.57)	1.01	18
Cost	7.70 (1.57)	1.00	18

^aSimple average of the responses (10 indicates very important, and 1 indicates not important).
^bRatio of the mean weight of each attribute to the attribute with the lowest mean weight (ie, cost).
^cPercentage ratio weight for each attribute divided by the sum of the ratio weights of all attributes.

proved by the University of Texas at Austin Institutional Review Board.

RESULTS

The total membership of the College of Psychiatric and Neurological Pharmacists at the time of study recruitment was 735, with 643 individuals subscribed to the organization’s Listserv. The online survey was accessed by 145 individuals, 116 (80%) of whom submitted a completed survey. The overall response rate was 116 of 643 (18%). The demographics of the survey respondents and available overall membership are given in **Table 2**.

The mean raw attribute weights, as well as the corresponding ratio weights and percentage weights, are given in **Table 3**. Effectiveness was identified as the most important attribute to consider during the medication selection process, followed closely by the safety and tolerability attribute. The dosing frequency, monitoring burden, and cost attributes were considered important as well and clustered closely together. The mean raw factor scores and factor utility scores for the effectiveness, safety and tolerability, cost, monitoring burden, and dosing frequency factors are available in **Appendix Tables 1, 2, and 3** to this article.

Total utility scores for each iteration of the model are given in **Table 4**. When only effectiveness in acute mania was considered in the effectiveness attribute score, lithium carbonate was the decision alternative with the highest total score. Among the atypical antipsychotics, aripiprazole was the medication with the highest utility score.

When only effectiveness in acute bipolar depression was considered for the effectiveness attribute score, lamotrigine was the decision alternative with the highest total utility score (**Table 4**). In this iteration, aripiprazole was the atypical antipsychotic with the highest total utility score.

Results for the effectiveness in maintenance treatment iteration of the MADM reveal that lithium carbonate is the

medication with the highest total utility score (**Table 4**). The most highly rated atypical antipsychotic in this iteration of the model was aripiprazole.

The final model constructed was an overall effectiveness model, where each of the 3 effectiveness factors (effectiveness in acute mania, effectiveness in acute bipolar depression, and effectiveness in maintenance treatment) was equally weighted to calculate the attribute utility score (**Table 4**). In this iteration, lithium carbonate was associated with the highest total utility score. As in the other iterations of the model, aripiprazole was associated with the highest score among the atypical antipsychotics.

A sensitivity analysis was also performed. Results showed that the alternate methods of calculating the monitoring and cost factor scores did not affect the overall results of any iteration of the MADM.

DISCUSSION

This article presents an implementation of MAUT analysis in bipolar psychopharmacology. According to the model we developed, lithium carbonate is the medication with the highest total utility score when considering medication treatments for effectiveness in acute mania, effectiveness in maintenance treatment, and overall effectiveness. Lamotrigine is the medication associated with the highest total utility score for bipolar depression.

In light of the high prevalence of atypical antipsychotic use and the high costs associated with the atypical antipsychotics, we also evaluated the results within this class of medications separately. According to our model, aripiprazole is the antipsychotic associated with the highest total utility score for all iterations of this MADM. Evaluations of the individual factor utility scores reveal that aripiprazole scored only moderately well on the effectiveness and cost factors; however, aripiprazole scored highest among all of the antipsychotics on the safety and tolerability and monitor-

Identification of Preferred Mood-Stabilizing Medications

Table 4. Total Utility Scores Associated With Each Medication for the 4 Model Iterations Among 116 Survey Respondents

Medication	Effectiveness in Acute Mania ^a	Effectiveness in Acute Bipolar Depression ^b	Effectiveness in Maintenance Treatment ^c	Overall Effectiveness ^d
Lithium carbonate				
Lithium	64.61	60.69	66.09	63.80
Lithium (brand)	60.53	56.62	62.02	59.72
Antipsychotics				
Aripiprazole	58.95	54.05	59.24	57.41
Olanzapine	51.08	42.89	48.83	47.60
Olanzapine-fluoxetine combination	43.22	49.34	48.41	46.99
Risperidone	55.56	48.70	54.20	52.82
Quetiapine fumarate	54.21	51.41	53.33	52.98
Ziprasidone	50.65	46.73	50.86	49.41
Anticonvulsants				
Carbamazepine IR	54.28	48.88	55.68	52.95
Carbamazepine IR (brand)	48.34	42.94	49.74	47.01
Carbamazepine ER	55.36	49.95	56.76	54.02
Carbamazepine ER (brand)	48.98	43.58	50.38	47.65
Valproic acid/divalproex sodium IR	63.14	54.32	63.49	60.32
Valproic acid/divalproex sodium IR (brand)	59.19	50.37	59.54	56.37
Valproic acid/divalproex sodium MR	59.97	51.14	60.31	57.14
Valproic acid/divalproex sodium ER	62.04	53.22	62.39	59.22
Gabapentin	48.35	48.29	48.55	48.40
Gabapentin (brand)	42.08	42.03	42.29	42.14
Lamotrigine	50.57	60.84	61.47	57.63
Oxcarbazepine	52.24	50.00	53.65	51.96
Topiramate	45.78	45.06	46.70	45.85
ER indicates extended release; IR, immediate release; MR, modified release.				
^a Total utility score when $w_{\text{mania}} = 1.0$, $w_{\text{depression}} = 0.0$, and $w_{\text{maintenance}} = 0.0$ (see equation 2).				
^b Total utility score when $w_{\text{mania}} = 0.0$, $w_{\text{depression}} = 1.0$, and $w_{\text{maintenance}} = 0.0$ (see equation 2).				
^c Total utility score when $w_{\text{mania}} = 0.0$, $w_{\text{depression}} = 0.0$, and $w_{\text{maintenance}} = 1.0$ (see equation 2).				
^d Total utility score when $w_{\text{mania}} = 0.33$, $w_{\text{depression}} = 0.33$, and $w_{\text{maintenance}} = 0.33$ (see equation 2).				

ing burden factors. The contribution of the latter attributes to the overall utility score seems to drive the differences in total utility scores seen between aripiprazole and the other antipsychotics.

It is also notable to highlight the medications with the lowest total utility scores for each of the model iterations. Gabapentin (brand and generic formulations) and topiramate scored poorly on all iterations of the MADM. The low scores for these agents were driven in large part by low effectiveness ratings. These agents are not recommended as mood-stabilizing agents in the Texas Medication Algorithm Project² or American Psychiatric Association³ treatment guidelines. These results suggest that the model is able to discriminate between medications with different levels of con-

sensually recognized utility, even while accounting for factors not explicitly considered in these treatment guidelines (ie, cost, dosing frequency, etc).

The response rate to our online survey using e-mail recruitment was modest (18%). This is a limitation frequently seen with online surveys¹⁰⁻¹² and especially with online surveys of health professionals.¹³ Surveys of health professionals using multiple follow-up recruitment e-mails,¹⁴ postal follow-up,¹⁵ or telephone follow-up¹⁶ have shown higher response rates than studies¹⁷⁻¹⁹ that did not use these recruitment strategies. Our study used only a single follow-up e-mail for study recruitment. A number of other factors, including technical problems accessing the Web-based survey, the timing of the survey, lack of compensation, concerns regarding

confidentiality, length of the survey, and misidentification of the survey recruitment e-mail as spam, may have adversely affected our response rate. We did not account for e-mails that “bounced” or were returned with “out of office” replies in the denominator of the response rate calculation. Despite the modest response rate, our sample was generally representative of the membership of the College of Psychiatric and Neurological Pharmacists with regard to academic degree, board certification, and nationality. Our sample seems to be underrepresentative of members from the northeastern United States and overrepresentative of members from the southern United States. The percentage deviation for the northeastern US region in our sample was -53.9% from the expected value. The percentage deviation for the southern US region was 20.4%. The overrepresentation of membership from the South may be attributable to the authors’ academic affiliations at a southern university.

A limitation of this analysis is that we chose to survey only psychiatric pharmacist specialists. We did not seek to obtain attribute or factor scores from physicians, nurses, psychologists, or other medical professionals. Psychiatric pharmacist specialists were chosen for the sampling frame in this study because of their specialized knowledge in the area of psychopharmacology and their broad knowledge base regarding the attributes included in this MADM. As evidenced by the demographics of our survey respondents, psychiatric pharmacist specialists typically have received advanced postgraduate training in psychopharmacology or pharmacy practice and frequently hold board certification. In addition to a variety of clinical, academic, and industry roles, pharmacists often participate on pharmacy and therapeutics committees in healthcare systems and provide input on medication formulary decisions. Among our survey respondents, 85% (99 respondents) indicate that they practice in a setting with direct patient contact (Table 2). In some states and practice settings, pharmacists may operate under collaborative practice agreements and have prescriptive authority within their defined scope of practice; however, we did not specifically ask our respondents whether they had a collaborative practice agreement in place or had prescriptive authority.

Although it is possible that other healthcare professionals would assign different attribute weights, research has shown that physicians and pharmacists rate the importance of the attributes included in this model similarly with regard to their influence on medication decision making. Schumock et al²⁰ surveyed a group of pharmacists, physicians, and formulary decision makers to determine the influence that a variety of factors have on medication decision making. Among the drug-related attributes assessed, pharmacists and physicians rated the importance of effectiveness, safety, ease of dosing,

monitoring requirements, and cost similarly. The relative importance of each attribute also corresponds to the findings in our survey. Schumock et al found that physicians and pharmacists both rate effectiveness and safety as the most highly influential attributes. Monitoring requirements, ease of dosing, and cost attribute scores clustered closely together, and, as in our study, these attributes were scored lower than the effectiveness and safety attributes. Schumock et al also found that there was a statistically significant difference in the importance that pharmacists and physicians placed on “personal experience” when making medication decisions, with physicians rating personal experience as having a greater influence. Perhaps reflecting these findings, this attribute was not identified for inclusion in our model by our focus group of psychiatric pharmacist specialists.

It is also possible that other healthcare professionals would assign different factor scores to the individual medications included in this study. Research indicates that pharmacists are particularly knowledgeable regarding medication adverse effects. In a study²¹ comparing the knowledge of pharmacists, physicians, and nurses related to medication adverse effects, pharmacists’ and physicians’ scores were similar, and both were higher than nurses’ scores (85.1, 81.3, and 72.3, respectively; $P < .001$, analysis of variance). In addition, studies²²⁻²⁵ have demonstrated that physicians often are unfamiliar with medication costs. In a survey of 203 physicians, 78% of physicians described themselves as “often unaware of actual drug costs.”²² Similarly, in a survey of 189 physicians practicing in 4 academic medical centers, 80% indicated that they “felt unaware of the actual costs of medications.”²³ In our study, only 29% (34 of 116) of pharmacists chose “not sure” or skipped the cost factor scoring for any medication. Seventy-one percent (82 respondents) answered the cost factor item for all of the included medications; however, we made no attempt to determine the accuracy of the respondents’ knowledge of medication-related costs. When a sensitivity analysis using medication average wholesale price in place of the pharmacist-rated overall cost factor scores was conducted, the major findings remained unchanged.

A strength of this method of MAUT analysis is the flexibility and adaptability of the model, as well as its ability to simultaneously incorporate a number of different attributes when comparing treatment alternatives. Using a form of MAUT analysis may be a beneficial tool to aid health systems in making medication formulary decisions. While the attributes that we chose to include in this model were determined via a focus group discussion involving pharmacists with a variety of backgrounds, these attributes may not be all-inclusive. There may exist other attributes important in the decision-making process that were not included. One benefit

Identification of Preferred Mood-Stabilizing Medications

of MAUT analysis is that other attributes can be easily assimilated into the model.

A significant limitation of the MAUT analysis is that it fails to take patient-level data into account. The analysis is performed strictly at the population level and is meant to determine the medication with the highest level of total utility on a population basis. This model cannot and should not be used to determine what medication is most suited to an individual patient. Medication decisions for individual patients should include consideration of a variety of factors that are not included in this MAUT analysis, such as history of response, patient choice, and prescriber preference.

CONCLUSIONS

Multiattribute decision models are a potentially useful tool to assist in formulary decision making. This research demonstrates implementation of a MADM based on the results of a focus group and a survey of psychiatric pharmacist specialists. According to this model, lithium carbonate and lamotrigine are the mood-stabilizing medications with the highest total utility scores. Among the atypical antipsychotics, aripiprazole is associated with the highest total utility scores.

Author Affiliation: College of Pharmacy (BTS, TLB), University of Texas, Austin. Seton Shoal Creek Hospital (TLB), Seton Healthcare Network, Austin, TX.

Author Disclosure: Dr Bettinger reports serving on an advisory board for Eli Lilly. Dr Suehs reports no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Funding Source: None reported.

Authorship Information: Concept and design (BTS, TLB); acquisition of data (BTS, TLB); analysis and interpretation of data (BTS, TLB); drafting of the manuscript (BTS, TLB); critical revision of the manuscript for important intellectual content (TLB); statistical analysis (BTS); and administrative, technical, or logistic support (TLB).

Address correspondence to: Brandon T. Suehs, PharmD, College of Pharmacy, University of Texas, One University Station, Austin, TX 78712. E-mail: bsuehs@mail.utexas.edu.

REFERENCES

1. Merikangas KR, Akiskal HS, Angst J, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey Replication [published correction appears in *Arch Gen Psychiatry*. 2007;64(9):1039]. *Arch Gen Psychiatry*. 2007;64(5):543-552.
2. Suppes T, Dennehy EB, Hirschfeld RM, et al; Texas Consensus Conference Panel on Medication Treatment of Bipolar Disorder. The Texas implementation of medication algorithms: update to the algorithms for treatment of bipolar I disorder. *J Clin Psychiatry*. 2005;66(7):870-886.

3. Hirschfeld RMA, Bowden CL, Gitlin MJ, et al. *Practice Guideline for the Treatment of Patients With Bipolar Disorder*. 2nd ed. Arlington, VA: American Psychiatric Association; 2002.
4. Guo JJ, Keck PE Jr, Li H, Jang R, Kelton CM. Treatment costs and health care utilization for patients with bipolar disorder in a large managed care population. *Value Health*. 2008;11(3):416-423.
5. Edwards W, Newman JR. *Multiattribute Evaluation*. Thousand Oaks, CA: Sage Publications; 1982.
6. Ferrari MD, Goadsby PJ, Lipton RB, et al. The use of multiattribute decision models in evaluating triptan treatment options in migraine. *J Neurol*. 2005;252(9):1026-1032.
7. Schumacher GE. Multiattribute evaluation in formulary decision making as applied to calcium-channel blockers. *Am J Hosp Pharm*. 1991;48(2):301-308.
8. Bettinger TL, Shuler G, Jones DR, Wilson JP. Schizophrenia: multi-attribute utility theory approach to selection of atypical antipsychotics. *Ann Pharmacother*. 2007;41(2):201-207.
9. Jarboe KS. Treatment nonadherence: causes and potential solutions. *J Am Psychiatr Nurses Assoc*. 2002;8(4 suppl):S18-S25.
10. Sheehan KB. E-mail survey response rates: a review. *J Computer-Mediated Communication*. 2001;6(2). <http://www3.interscience.wiley.com/cgi-bin/fulltext/120837811/HTMLSTART>. Accessed August 27, 2008.
11. Kaplowitz MD, Hadlock TD, Ralph L. A comparison of Web and mail survey response rates. *Public Opinion Q*. 2004;68(1):94-101.
12. Sills SJ, Song C. Innovations in survey research: an application of Web-based surveys. *Soc Sci Computer Rev*. 2002;20(1):22-30.
13. Braithwaite D, Emery J, De Lusignan S, Sutton S. Using the Internet to conduct surveys of health professionals: a valid alternative? *Fam Pract*. 2003;20(5):545-551.
14. Gandhi TK, Sittig DF, Franklin M, Sussman AJ, Fairchild DG, Bates DW. Communication breakdown in the outpatient referral process. *J Gen Intern Med*. 2000;15(9):626-631.
15. McLean SA, Feldman JA. The impact of changes in HCFA documentation requirements on academic emergency medicine: results of a physician survey. *Acad Emerg Med*. 2001;8(9):880-885.
16. Fischbacher C, Chappel D, Edwards R, Summerton N. Health surveys via the Internet: quick and dirty or rapid and robust? *J R Soc Med*. 2000;93(7):356-359.
17. Hassenbusch SJ, Portenoy RK. Current practices in intraspinal therapy: a survey of clinical trends and decision making. *J Pain Symptom Manage*. 2000;20(2):S4-S11.
18. Hollowell CM, Patel RV, Bales GT, Gerber GS. Internet and postal survey of endourologic practice patterns among American urologists. *J Urol*. 2000;163(6):1779-1782.
19. Kim HL, Hollowell CM, Patel RV, Bales GT, Clayman RV, Gerber GS. Use of new technology in endourology and laparoscopy by American urologists: Internet and postal survey. *Urology*. 2000;56(5):760-765.
20. Schumock GT, Walton SM, Park HY, et al. Factors that influence prescribing decisions. *Ann Pharmacother*. 2004;38(4):557-562.
21. Markowitz JS, Pearson G, Kay BG, Loewenstein R. Nurses, physicians, and pharmacists: their knowledge of hazards of medications. *Nurs Res*. 1981;30(6):366-370.
22. Kom LM, Reichert S, Simon T, Halm EA. Improving physicians' knowledge of the costs of common medications and willingness to consider costs when prescribing. *J Gen Intern Med*. 2003;18(1):31-37.
23. Reichert S, Simon T, Halm EA. Physicians' attitudes about prescribing and knowledge of the costs of common medications. *Arch Intern Med*. 2000;160(18):2799-2803.
24. Ernst ME, Kelly MW, Hoehns JD, et al. Prescription medication costs: a study of physician familiarity. *Arch Fam Med*. 2000;9(10):1002-1007.
25. Hoffman J, Barefield FA, Ramamurthy S. A survey of physician knowledge of drug costs. *J Pain Symptom Manage*. 1995;10(6):432-435. ■

Appendix Tables follow on next page.

■ **Appendix Table 1.** Raw Factor Scores (*f*) and Utility Factor Scores (*u*) for Effectiveness in Acute Mania, Effectiveness in Acute Bipolar Depression, and Effectiveness in Maintenance Treatment for Each of the Treatment Decision Alternatives Among 116 Survey Respondents^a

Medication	<i>f</i> _{mania}	<i>u</i> _{mania}	<i>f</i> _{depression}	<i>u</i> _{depression}	<i>f</i> _{maintenance}	<i>u</i> _{maintenance}
Lithium carbonate						
Lithium	4.43	85.78	3.75	68.75	4.69	92.24
Lithium (brand)	4.43	85.78	3.75	68.75	4.69	92.24
Antipsychotics						
Aripiprazole	3.33	58.33	2.48	37.01	3.38	59.62
Olanzapine	4.03	75.66	2.60	40.05	3.63	65.87
Olanzapine-fluoxetine combination	2.26	31.55	3.33	58.16	3.16	54.12
Risperidone	3.69	67.32	2.50	37.50	3.46	61.40
Quetiapine fumarate	3.64	66.09	3.16	53.90	3.49	62.28
Ziprasidone	3.18	54.57	2.50	37.50	3.22	55.48
Anticonvulsants						
Carbamazepine IR	3.56	64.04	2.62	40.54	3.81	70.13
Carbamazepine IR (brand)	3.56	64.04	2.62	40.54	3.81	70.13
Carbamazepine ER	3.56	64.04	2.62	40.54	3.81	70.13
Carbamazepine ER (brand)	3.56	64.04	2.62	40.54	3.81	70.13
Valproic acid/divalproex sodium IR	4.43	85.78	2.90	47.41	4.49	87.28
Valproic acid/divalproex sodium IR (brand)	4.43	85.78	2.90	47.41	4.49	87.28
Valproic acid/divalproex sodium MR	4.43	85.78	2.90	47.41	4.49	87.28
Valproic acid/divalproex sodium ER	4.43	85.78	2.90	47.41	4.49	87.28
Gabapentin	1.23	5.80	1.22	5.58	1.27	6.70
Gabapentin (brand)	1.23	5.80	1.22	5.58	1.27	6.70
Lamotrigine	1.90	22.59	3.69	67.24	3.80	70.00
Oxcarbazepine	2.58	39.56	2.19	29.81	2.83	45.67
Topiramate	1.59	14.81	1.47	11.68	1.75	18.81

ER indicates extended release; IR, immediate release; MR, modified release.

^aBased on 5-point Likert-type scale, where 1 indicates not effective and 5 indicates very effective.

Identification of Preferred Mood-Stabilizing Medications

■ Appendix Table 2. Raw Factor Scores (*f*) and Factor Utility Scores (*u*) for Safety and Tolerability for Each of the Treatment Decision Alternatives Among 116 Survey Respondents^a

Medication	<i>f</i> _{safety}	<i>u</i> _{safety}	<i>f</i> _{tolerability}	<i>u</i> _{tolerability}	<i>U</i> _{st}
Lithium carbonate					
Lithium	3.16	54.09	3.10	52.61	53.35
Lithium (brand)	3.16	54.09	3.10	52.61	53.35
Antipsychotics					
Aripiprazole	3.97	74.32	3.89	72.32	73.32
Olanzapine	3.15	53.70	3.23	55.82	54.76
Olanzapine-fluoxetine combination	3.14	53.57	3.19	54.84	54.21
Risperidone	3.53	63.36	3.63	65.73	64.55
Quetiapine fumarate	3.57	64.35	3.65	66.16	65.26
Ziprasidone	3.63	65.77	3.77	69.27	67.52
Anticonvulsants					
Carbamazepine IR	3.14	53.45	3.17	54.13	53.79
Carbamazepine IR (brand)	3.14	53.45	3.17	54.13	53.79
Carbamazepine ER	3.16	54.09	3.35	58.77	56.43
Carbamazepine ER (brand)	3.16	54.09	3.35	58.77	56.43
Valproic acid/divalproex sodium IR	3.45	61.30	3.17	54.35	57.83
Valproic acid/divalproex sodium IR (brand)	3.45	61.30	3.17	54.35	57.83
Valproic acid/divalproex sodium MR	3.60	65.00	3.58	64.47	64.74
Valproic acid/divalproex sodium ER	3.60	65.00	3.66	66.45	65.72
Gabapentin	4.06	76.51	4.07	76.72	76.62
Gabapentin (brand)	4.06	76.51	4.07	76.72	76.62
Lamotrigine	3.34	58.41	3.91	72.84	65.63
Oxcarbazepine	3.50	62.61	3.70	67.57	65.09
Topiramate	3.32	58.04	3.14	53.54	55.79

ER indicates extended release; IR, immediate release; MR, modified release; *U_{st}*, weighted safety and tolerability utility score.

^aBased on 5-point Likert-type scale, where 1 indicates unsafe or very poorly tolerated and 5 indicates very safe or very well tolerated.

■ **Appendix Table 3.** Raw Factor Scores (*f*) and Utility Factor Scores (*u*) for Dosing Frequency, Monitoring Burden, and Cost Values Among 116 Survey Respondents^a

Medication	<i>f</i> _{dosing}	<i>u</i> _{dosing}	<i>f</i> _{monitoring}	<i>u</i> _{monitoring}	<i>f</i> _{cost}	<i>u</i> _{cost}
Lithium carbonate						
Lithium	80.00	71.43	1.88	21.98	4.54	88.38
Lithium (brand)	80.00	71.43	1.88	21.98	3.63	65.77
Antipsychotics						
Aripiprazole	90.00	85.71	3.55	63.84	1.40	9.91
Olanzapine	80.00	71.43	2.56	39.01	1.28	7.02
Olanzapine-fluoxetine combination	90.00	85.71	2.56	39.02	1.24	6.02
Risperidone	80.00	71.43	3.02	50.43	1.75	18.64
Quetiapine fumarate	80.00	71.43	2.97	49.35	1.52	12.94
Ziprasidone	70.00	57.14	3.15	53.64	1.60	15.05
Anticonvulsants						
Carbamazepine IR	60.00	42.86	2.10	27.59	4.25	81.25
Carbamazepine IR (brand)	60.00	42.86	2.10	27.59	2.93	48.27
Carbamazepine ER	70.00	57.14	2.10	27.59	3.78	69.55
Carbamazepine ER (brand)	70.00	57.14	2.10	27.59	2.37	34.16
Valproic acid/divalproex sodium IR	70.00	57.14	2.31	32.76	4.12	78.01
Valproic acid/divalproex sodium IR (brand)	70.00	57.14	2.31	32.76	3.24	56.07
Valproic acid/divalproex sodium MR	80.00	71.43	2.31	32.76	2.50	37.39
Valproic acid/divalproex sodium ER	90.00	85.71	2.31	32.76	2.33	33.33
Gabapentin	40.00	14.29	4.22	80.43	3.75	68.81
Gabapentin (brand)	40.00	14.29	4.22	80.43	2.36	34.05
Lamotrigine	90.00	85.71	3.20	54.96	2.11	27.70
Oxcarbazepine	80.00	71.43	3.23	55.75	2.18	29.55
Topiramate	80.00	71.43	3.63	65.79	2.06	26.58

ER indicates extended release; IR, immediate release; MR, modified release.

^aDosing scores based on 0 to 100 scale, where 90 indicates once daily and 40 indicates 3 to 4 times daily. Monitoring and cost scores based on 5-point Likert-type scale, where 1 indicates very high monitoring burden or very expensive and 5 indicates very low monitoring burden or very inexpensive.