A Comparison of Outcomes Among Patients with Schizophrenia in Two Mental Health Systems: A Health State Approach

Gareth M. James, Ph.D.
Marshall School of Business, University of Southern California

Catherine A. Sugar, Ph.D.
Marshall School of Business, University of Southern California

Rani Desai, Ph.D., MPH
Departments of Psychiatry and Epidemiology and Public Health, Yale Medical School and VA Northeast Program Evaluation Center, West Haven, CT

Robert A. Rosenheck, M.D.
Departments of Psychiatry and Epidemiology and Public Health, Yale Medical School and VA Northeast Program Evaluation Center, West Haven, CT

Correspondence Address: Gareth James
University of Southern California
Bridge Hall 401 P
Los Angeles, California 90089-0809
Tel: (213) 740 9696
Fax: (213) 740 7313
Email: gareth@usc.edu

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Complete Author Information

Gareth M. James, Ph.D.

University of Southern California
Bridge Hall 401 P
Los Angeles, California 90089-0809
Tel: (213) 740 9696
Fax: (213) 740 7313
Email: gareth@usc.edu
Expertise: Functional data analysis, classification, cluster analysis

Catherine A. Sugar, Ph.D.

University of Southern California
Bridge Hall 401 R
Los Angeles, California 90089-0809
Tel: (213) 740 7957
Fax: (213) 740 7313
Email: sugar@usc.edu
Expertise: Cluster analysis, functional data analysis, multivariate statistics, biostatistics

Rani Desai, Ph.D., MPH

Associate Professor of Psychiatry and Public Health, Yale Medical School
VA Connecticut Healthcare System
950 Campbell Ave.
West Haven, CT 06516
Tel: (203) 937-3850
Fax: (203) 937-3433
Email: rani.desai@yale.edu
Expertise: Health services research, cost-effectiveness analysis, psychiatry, mental health, service use

Robert A. Rosenheck, M.D.

Director, Northeast Program Evaluation Center
Professor of Psychiatry and Public Health, Yale Medical School
VA Connecticut Healthcare System
950 Campbell Ave.
West Haven, CT 06516
Tel: (203) 937-3850
Fax: (203) 937-3433
Email: robert.rosenheck@yale.edu
Expertise: Health services research, cost-effectiveness analysis, psychiatry, mental health, service use

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Abstract

Objective: To demonstrate a health state modeling approach using clustering and Markov analysis to compare short and long term outcomes among health care populations.

Data Sources/Study Setting: Primary data from a three year observational study of patients treated for schizophrenia at a VA Medical Center (VAMC) and in a Community Mental Health Center (CMHC) in the same urban community.

Study Design: Randomly selected samples of outpatients treated for schizophrenia or schizoaffective disorder were interviewed every six months using standardized psychiatric assessments such as the Positive and Negative Syndrome Scale (PANSS).

Data Collection/Extraction Methods: Items from the PANSS were used to define 7 discrete health states representing different levels of severity and diverse mixtures of psychiatric symptoms. The PANSS positive, negative and general subscale scores were also used in a comparative analysis with conventional mixed-effects regression models.

Principal Findings: Conventional analysis showed that VA patients exhibited increasingly severe symptoms, while CMHC patients remained more stable over the study period. Health state analysis showed few changes among patients in the best and worst health states but VA patients with: a) mild symptoms and hallucinations and b) serious positive and negative symptoms, were more likely to enter a state with severe positive and negative symptoms accompanied by moderate general distress.

Conclusions: Discrete state modeling offers a richer portrait of patient outcomes than standard univariate techniques and may be especially valuable for subgroup analyses. While VA treatment was associated with poorer outcomes than treatment in the CMHC, our observational study did not uncover an explanation for this difference.

Keywords: Schizophrenia, outcomes, health states, cluster analysis, Markov theory.

Introduction

In clinical trials or observational studies of complex diseases such as schizophrenia different aspects of physical and psychological health typically are measured using both disease specific and more general health status instruments consisting of dozens of item responses. Multiple items may be summarized by combining them into continuous scales reflecting symptomatology, functioning or quality of life. Such composite measures are then typically analyzed using a variety of standard univariate statistical techniques such as a mixed models approach (Bryk and Raudenbush 1992)**.** When evaluating complex diseases, such methods are frequently applied to several composite scores. However, this approach potentially ignores important interrelationships between different dimensions of symptomatology or health.

In this paper we aim to demonstrate the advantages of using a multivariate health state modeling approach to harness more of the inherent structural richness in this type of data. Using this approach the patient population is partitioned into a discrete set of health states with each state representing a different level of health. Using a health state model, differences between populations, or treatments, are assessed in terms of the probability of individuals moving from each health state to another over time, rather than in terms of a simple net increase or decrease in the mean on a preset continuous scale. For patients in a given state, members of one population are better off than another if they have a higher probability of moving to superior states. Such a model makes it possible to distinguish more subtle differences between populations that may be hidden when only examining means. For example, two populations may have similar average levels of health but one

may have higher proportions of both very healthy and very unhealthy patients. The standard approach based on comparing means would miss these differences while the health state approach would have no difficulties distinguishing the two populations.

Health state models have several additional advantages. One is that they provide a natural way to estimate long term differences between populations using data from trials that are necessarily of finite duration. Results from Markov chain theory allow one to calculate the long run fraction of individuals residing in each health state for each population and thus compare the populations at equilibrium (Taylor and Karlin 1994). Another potential advantage of health state models is that they facilitate utility estimation. It is relatively straightforward to generate descriptions of the prototypical patients in each state and survey both the general population and patients to estimate the corresponding utilities. These preference weights can be used to express the results of a trial in terms of changes in Quality Adjusted Life Years (QALY), the outcome metric recommended by the US Public Health Service (Gold et al. 1996).

QALY scores can be combined with financial data and long-run distributions to assess the efficiency of investments in health at a societal level.

Using the approach of Sugar et al. 2004 we constructed the health states via cluster analysis rather than by the factorial design traditionally used in health index models such as the Health Utilities Index (Feeny et al. 1995, Feeny et al. 1998), the EQ-5D (Dolan 1997, Kind et al. 1998), or the Quality of Well Being Scale (Andresen et al. 1998, Kaplan and Anderson 1988). It is desirable for patients in the same health state to be as similar as

possible or equivalently to have as little variability as possible over the dimensions of health that describe each patient sub-population. Clustering allows the optimal definition of health states to be derived from the data. As a result, the clinical status of a patient population can often be as accurately represented, in terms of within group variability, with many fewer states than a comparable factorial design. In addition, because it is data–driven, clustering is particularly well suited to capturing complex interrelationships.

This study illustrates the use of health state modeling in an analysis of data from the Connecticut site of the Schizophrenia Care and Assessment Program (SCAP), which followed representative samples of patients with schizophrenia in two different health systems for three years. In particular, we were interested in differences in outcomes between patients treated at a VA medical center and a State-operated community mental health center (CMHC) in the same metropolitan area. To provide an illustration of the advantages of a health state model over a standard mixed effects model we also examine the data using the more traditional approach and compare the results.

Methods

Study design and sampling

The SCAP was a longitudinal study, funded by Eli Lilly, designed to examine health services and outcomes in patients with schizophrenia. It was fielded at both United States sites as well as internationally. The data presented here are only from the Connecticut site of the SCAP study.

Patients were randomly selected from a roster of all patients with a diagnosis of schizophrenia or schizophreniform disorder being treated at either the VA mental health program or the local CMHC. Inclusion criteria included being at least 18 years of age English-speaking, and having the cognitive ability to complete the interview protocol. Patients who were currently enrolled in any medication clinical trial were excluded from the study. Respondents who consented to participate were interviewed at baseline and every six months for three years. Annual assessments included, among other measures, the Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1987), and were conducted by trained interviewers who were certified by SCAP executive staff. Data were collected on 384 patients at baseline and at the end of one, two and three years. The number of subjects with missing data increased over time. Since patients were more likely to be missing complete questionnaires than individual item responses, any subject with missing responses at a particular time point was removed entirely from the analysis of that period. This left data on 80%, 72% and 63% of CMHC patients at the end of years one, two and three respectively and 65%, 49% and 49% of the VA patients. Table 1 provides a breakdown, by patient population, of gender, race and age. There are significant differences in all three variables. The VA population is almost entirely male while the CMHC population is only 59% male. There are many more Caucasian and fewer African-American patients in the VA population and the average age is 7 years higher. These differences highlight the need to control for these variables in any analysis comparing the populations.

<u>Measures</u>

Our analysis focuses on the PANSS. This instrument has 30 items classified into 3 subsections, positive symptoms such as hallucinations, delusions and hostility; negative symptoms such as blunted affect, withdrawal, passivity, and difficulty in abstract thinking; and general emotional disturbances such as anxiety, depression and guilt. The PANSS uses Likert scales to measure severity of symptoms with higher scores indicating greater impairment.

<u>Analyses</u>

Clustering raw questionnaire data produces very unstable health states because of the large number of response items. Dimension reduction techniques allow one to capture the important information in an instrument, while eliminating much of the variability. Hence, a critical first step in constructing any health state model is to identify a smaller set of variables or dimensions of health that capture the information necessary to differentiate among members of the population of interest. We used principal components analysis (Seber 1984) to identify a small number of dimensions that capture the important information in the PANSS.

Next we derived a parsimonious final health state model using k-means clustering (Hartigan and Wong 1978) applied to the variables resulting from the principal components analysis. The k-means algorithm works by partitioning the data space into non-empty, non-overlapping regions so that points in the same cluster are close together while those in different clusters are as widely separated as possible. Specifically, for a

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given number of clusters, k, the algorithm finds the set of centroids that minimizes the *distortion* or sum of squared distances between each observation and its closest cluster center.

The most important issue in implementing k-means clustering is the choice of k, the number of clusters. Ideally there should be as few clusters as possible, both to aid interpretation as well as to increase the accuracy of the estimated health states and longitudinal changes. However, it is important that enough clusters are used to minimize intra-cluster variance so that clinically distinct patients are not grouped together. Cluster profile plots provide a useful tool for selecting the optimal number of clusters by allowing one to visually asses the characteristics of a given health state. For each cluster, one plots the average score for each questionnaire item among all patients falling in that health state. This provides a precise picture of the characteristics of a typical patient in each group. The profile plots can be produced for various values of k. One then chooses the largest k such that all health states have clinically distinct profiles. Note that once the optimal number of clusters has been chosen, cluster profile plots can also be used to create narrative health state descriptions.

After choosing the number of health states and removing patients with missing values we ran the k-means algorithm for the PANSS data to produce the health state model. The observations for all subjects and time combinations were used in the clustering, ensuring that the full range of states encountered over all time periods was included in the model.

<u>Longitudinal Analyses</u>

After constructing the health state model we used it to analyze differences between the VA and CMHC patients over time. First we examined the data cross-sectionally, determining whether patients had different patterns of health state membership at each of the four time points by performing chi-square tests of independence between population membership (VA or CMHC) and health state. Next we examined differences in the patterns of change over time by comparing the "transition matrices" for each population. Transition matrices give the probabilities of a patient moving from any given health state to any other state in a single time period. If the transition matrices for the CMHC and VA populations differ, this indicates that the movement of patients between health states over time is different for the two sets of patients. The i,j th entry of each transition matrix is estimated using the proportion of those patients who reside in state i in one time period who move to state j in the next period. We used a permutation test (Efron and Tibshirani 1993) to check for statistically significant differences between the two transition matrices. The permutation test works by randomly assigning individuals to one of two populations, re-estimating the transition matrices and finally recalculating the difference. This randomized procedure is repeated a large number of times. The observed difference between the true transition matrices is then compared to the randomized differences. If the true difference is larger than most of the randomized ones this provides strong evidence for a difference between the populations. We used this procedure both to test for an overall difference between the transition matrices and to perform individual tests of significance of the differences between each specific transition represented in each of the

two matrices. We controlled for race, gender and age in our randomization procedure to ensure differences were not caused by any of these other factors.

Finally, we used results from Markov chain theory to estimate long run differences between the populations (Taylor and Karlin 1994). Provided that patients' probabilities of movement from one state to another remain fixed over time one can calculate a stationary distribution, i.e. the fraction of patients that will reside in each health state once a state of equilibrium is reached. We used the bootstrap type approach of Sugar et al. 2004 to test for lack of stationarity in the data. A low p-value on this test indicates non-stationary data. We performed separate tests for each time period and each patient population (a total of six tests) and found that the data was consistent with a stationarity assumption at the 5% significance level for all periods and at the 10% level for all but one time period. Hence, we felt confident that stationarity was a reasonable assumption for both populations. We estimated separate stationary distributions for the VA and CMHC populations and checked for long run differences via a permutation test similar to the one used on the transition matrices.

Traditional Mixed Effects Model

A traditional approach for analyzing data of this type involves producing a univariate summary variable, such as the average total PANSS score, and performing a mixed effects analysis with treatment group, time, an interaction effect between time and treatment group and any other covariates as fixed effects; and patient entered as a random effect (Bryk and Raudenbush 1992, Gibbons et al. 1993). One then examines the group

coefficients for differences at baseline and the interaction coefficients for differences in the trajectories of the two groups over time. This analysis may be repeated using several alternative summary variables. To provide a comparison to the health state approach we fit 3 different mixed effects models using, as dependent variables, the means of negative symptom items, positive symptom items and general psychiatric symptoms. In addition to the group (i.e., VA vs. CMHC), time, and group by time interaction variables we also included gender as a fixed effect and patient as a random effect nested within time.

Results

The Health State Model

Principal components analysis identified 4 important dimensions of health on the PANSS. The first three components measured, in order of variability explained, overall mental health, a contrast between negative and positive symptoms, and a contrast between subjective emotional distress and thought disturbances, while the last component did not have a simple interpretation. The components respectively explained 21%, 13%, 10% and 6% of the variability. We opted to use four components because none of the remaining dimensions individually explained a significant amount of the variability, nor did they have any obvious clinical interpretation. In addition, previous studies of patients with schizophrenia have found similar dimensions in the PANSS (Sugar et al. 1998).

Examining cluster profile plots led us to select a model with 7 multidimensional health states. Figure 1 gives the cluster profile plots for the 7 cluster fit. For each cluster we have plotted the average score for each questionnaire item among all patients falling in that health state. The item scores have been centered by subtracting the global mean from

each score. For example, cluster 1 has very low averages over all questions, indicating that patients have relatively few symptoms. In contrast, patients in cluster 7 have severe disorders with high scores on almost all items. The profile plots show clear distinctions among all the clusters, which suggest that there are at least 7 medically interpretable states of health in the total sample. Since no further differentiation was achieved when additional clusters were added, we opted to use 7 states. The states can be characterized as: 1) Mild symptoms in all domains (**MSX**), 2) Mild psychosis with some depressive features (**MPD**), 3) Mild symptoms with hallucinations and poor attention (**MSXHX**), 4) Prominent negative symptoms with mild positive and general symptoms (**PNS**), 5) Serious positive and negative psychotic symptoms with general distress (**SRPNG**), 6) Severe predominantly negative symptoms (**SVPN**) and 7) Severe predominantly positive symptoms (**SVPP**). The health states are ordered from best (1) to worst (7) according to their score on the first principal component which provides a measure of overall mental health. See the appendix for more detailed health state descriptions.

Health State Transitions and Long-term Outcomes

The primary purpose of producing the health state models was to examine differences between the CMHC and VA patients over time. We first performed a cross-sectional analysis to assess whether patients in each group had different distributions across the health states and if so at what times. Figure 2 provides a graphical representation of the distributions at baseline and each follow up period. Chi-square tests of independence indicated highly statistically significant differences between the two populations at all four time points. At baseline there were higher proportions of VA patients in the MSX (1)

and PNS (4) states and a lower proportion in MSXHX (3). However, there was a clear trend of deterioration for the VA population over time while the CMHC population appeared fairly stable with a slightly improving trend. By year 3 the VA population had considerably lower fractions of patients in MPD (2), MSXHX (3), and PNS (4) and many more patients in SRPNG (5) and SVPN (6).

Next we calculated transition probabilities, which describe the likelihood of a patient moving from any one health state to another during a 1 year period. Transition probabilities are given for CMHC patients in Table 2 and for VA patients in Table 3. The difference in transition probabilities between the two populations is provided in Table 4. Differences that are statistically significant at the 5% level are indicated by a bold font. There were some very clear differences between the patient groups. VA patients had significantly higher probabilities of transitioning from some of the better states, MPD (2) and MSXHX (3), into a worse state SRPNG (5). They also had much lower probabilities of remaining in MPD (2) and MSXHX (3), and higher probabilities of remaining in the comparatively bad states of SRPNG (5) and SVPN (6), over a one year period (some of these results are only significant at the 10% level). This accounts for the increasing fraction of VA patients observed in SRPNG (5) over time. VA patients had significantly lower probabilities of transitioning from SRPNG (5) to MSXHX (3) and from SVPP (7) to PNS (4). Finally, they were significantly more likely to move from MSXHX (3) to SVPN (6). Notice that most of the differences appear to relate to states 2 through 6. The two extreme states MSX (1) and SVPP (7) seem to have relatively similar transition structures across the two providers. In summary, the CMHC patients had a higher

likelihood of moving to, and remaining in, the better health states while VA patients had

a higher probability of moving to the worse health states, and were more likely to remain

there. This accounts for the deteriorating trend noted for the VA patients in Figure 2. The

permutation test indicated highly significant evidence of a difference between transition

matrices even after controlling for age, gender and race.

Finally, we calculated the stationary distributions for each population. These distributions

predict the long-run fraction of patients in each health state assuming the transition

probabilities remain constant over time. The results are provided in Table 5 and Figure 2.

The stationary distributions suggest a continuing trend of deterioration in the VA

population and slight improvement in the CMHC population. In the long-run, 78% of

CMHC patients are predicted to reside in MSX (1) through PNS (4) compared to only

36% of VA patients. In addition, only 15% of CMHC patients will reside in SRPNG (5)

and SVPN (6) compared to 55% of VA patients. The long-run fraction in the worst state

of health, SVPP (7), is similar for both populations.

Comparison of the Health State Approach with a Mixed Effects Model

The coefficients, with corresponding test statistics and p-values, for the 3 mixed effects

models we fit to the data are presented in Table 6. We use the results for an average male

patient at baseline as the reference point. Thus, the population coefficients give the

average scores for CMHC and VA patients at the beginning of the study, after adjusting

for gender. The time coefficients give the additional impact above this level for VA

patients in Years 1, 2 and 3. The interaction terms further adjust the results for CMHC

patients. The key information to be derived from these models is the mean score for each group (CMHC and VA) at each time point (baseline and 3 years of follow-up) which are provided in Table 7. Consider for example the negative response model. Here the mean for a typical male VA patient at baseline is 2.77 while the corresponding mean for a typical CMHC patient is 3.01. For a female patient these numbers would be adjusted using the gender coefficient. Notice that CMHC patients begin with a higher mean than VA patients but by the end of year 3 CMHC patients have improved while VA patients have deteriorated. All 3 models exhibit this pattern. In fact, when using general psychiatric symptoms the CMHC patients ended up somewhat better off than VA patients by the end of the study. These results are consistent with the health state model results illustrated in Figure 2.

While the mixed effects models tell a similar tale, overall, to the health state model, they miss many of the finer details. First, the health states model indicates that, while the VA population performs worse overall, the fractions of patients in the best and worst health states, MSX (1) and SVPP (7), are similar for both populations. Upon examining the transition probabilities it is clear that the differences in the populations derives from the fact that CMHC patients are more likely to reside in the better health states, MPD (2), MSXHX (3) and PNS (4), while VA patients are more likely to reside in SRPNG (5) and SVPN (6). Hence the differences are mostly in the center of the populations rather than at the tails. Second, the transition probabilities suggest that VA patients may actually be more likely to remain in MSX (1), once they get there, while CMHC patients tend to move around somewhat among the best four states. Finally, the mixed model approach

provides no reasonable method for extrapolating performance of the populations into the future while the health state approach provides easily interpretable predictions.

Discussion

Health state models have several distinct advantages over traditional univariate approaches to analyzing data for complex diseases such as schizophrenia. First, they provide a convenient framework for performing longitudinal analyses. One can estimate the long run fraction of people in each health state in addition to the cross-sectional distributions of patients during the study period. By performing such analyses on several populations it is easy to compare the differences in both the short and long term. Second, the partitioning of the population into health states leads to a more richly informative analysis of the differences between populations than simply examining mean differences. For example, it may be the case that one population does not dominate the other in terms of overall level of health but that extreme states are more common in one group than the other. Finally, stationary distributions can be combined with a wide variety of outcome variables, such as costs or QALYs, to calculate long-run financial or utility differences between populations. While care is always required when extrapolating beyond the range of the data, this approach allows one to make objective long-term health policy decisions by balancing treatment effectiveness against societal costs on a quantitative basis.

In addition to the general advantages of a health state model, the clustering approach we have taken also allows for a parsimonious multivariate representation of the population. For instance, the model created for this study involves 7 health states whereas a

traditional full factorial design may well easily require 10 times this number of states. This parsimony is critical for subsequent phases of analysis since if the number of states is too great even an extremely large trial would provide insufficient data to estimate the quantities of interest. In addition, because the cluster analysis approach is data driven, the resulting health states can be asymmetrically shaped, capturing important interactions among the characteristics that define the population.

From our study there is clear evidence of the VA patients deteriorating over time while the CMHC patients exhibit small improvements. However, the most significant deterioration in VA patients appears to be caused by fewer patients in the moderate states, MPD (2), MSXHX (3) and PNS (4), and more in SRPNG (5) and SVPN (6), rather than significant changes in the best and worst states, MSX (1) and SVPP (7). The reasons for these differences are not apparent in the available data and could reflect: 1) differences in patient populations not captured by available baseline data, 2) differences in the quality of treatment provided by the two health care systems, or 3) differences in study drop-out rates which were generally greater in the VA sample.

Limitations

The approach described in this paper has several limitations. First, since clustering is data driven, the resulting models may not generalize easily to other populations. For instance, the health state model derived for the VA and CMHC patients may not apply well to other populations of patients with schizophrenia. A second limitation arises from the difficulty of determining the appropriate number of clusters. This generally requires some

degree of clinical judgment, and therefore introduces a subjective component to the analysis. Of course, this is also the case with traditional factorial designs, and is thus not unique to this method. Thirdly, extrapolation of the trial results using stationary distributions requires assuming that the health care processes operating during the study will continue indefinitely. Although this seems reasonable, it may not take into account patient mortality or disease progression. In addition, it may be difficult to identify violations of the Markovian assumption using a relatively small number of time points or subjects. Finally, while the differences between the two populations are statistically significant, it is unclear why VA patients did less well over time than CMHC patients. It is possible that unmeasured baseline differences, or differences in quality of treatment might explain the observed differences in outcomes. However, there is no evidence from these data of differences in either unmeasured baseline characteristics or in service utilization during the subsequent three years that might clarify the meaning of these findings. While there has been substantial emphasis in recent years on outcomes monitoring is health care, generally (Institute of Medicine Committee on Quality 2001), and in mental health care, specifically (Greenberg and Rosenheck 2005) in the absence of detailed data on the population characteristics and the process of treatment such outcomes data are difficult to interpret.

Conclusions

A discrete state, multi-dimensional approach to data analysis has a number of advantages in interpretation of clinical trial or observational study data. It allows a richer understanding of treatment effects, and the projection of long-run outcomes. In addition,

health state modeling can provide a simple framework for elicitations and facilitates the application of cost-effectiveness analyses.

Appendix : Interpretation of health states

1. **Mild symptoms in all domains (psychosis and general symptoms) (MSX).** Patients are in fairly good health overall. They have fewer than average positive, negative and general emotional symptoms.

2. **Mild psychosis with some depressive features (MPD).** Patients have below average positive and negative symptoms except for an above average prevalence of hallucination. Levels of somatic concern, guilt, anxiety and depression are well above average though other general emotional symptoms are better than average.

3. **Mild symptoms with hallucinations and poor attention (MSXHX).** People in this state have high levels of confusion (elevated conceptual disorganization, difficulty with abstract thought, unusual thought content, poor attention, disturbance of volition) but otherwise are fairing better than average (especially with respect to hallucination, negative symptoms, depression and stereotyped thinking).

4. **Prominent negative symptoms with mild positive and general symptoms (PNS).** People in this state are better than average in terms of positive symptoms and general emotional distress, but have high levels of negative symptoms relative to the mean.

5. **Serious positive and negative psychotic symptoms with general distress (SRPNG).** This group is moderately worse off than average in all three PANSS categories,

but particularly exhibits high levels of hallucination, suspiciousness, anxiety, tension and depression.

6. **Severe predominantly negative symptoms (SVPN).** These people are much worse off than average (particularly with respect to negative symptoms and general emotional distress) but are experiencing below average levels of anxiety and guilt.

7. **Severe predominantly positive symptoms (SVPP).** These patients have the most severe positive symptoms, general emotional distress and negative symptoms related to thought processes but are better than average on blunted affect, rapport, spontaneity and motor retardation.

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Figure 1: The cluster profile plot from the final health state model. Each plot provides the average centered scores on each of the 30 PANSS questionnaire items for patients in the corresponding health state. The dashed lines divide the plots into three regions respectively corresponding to positive, negative and general symptoms.
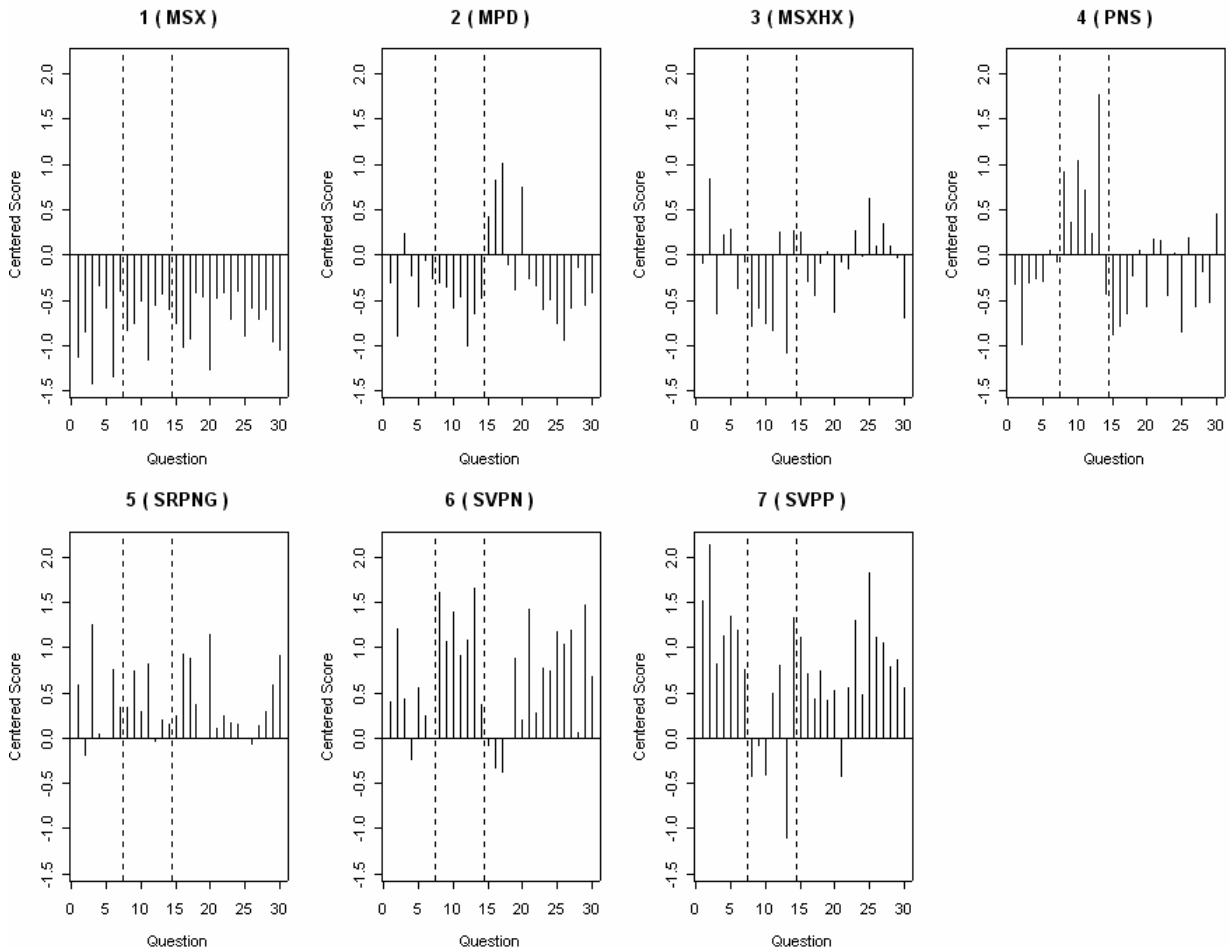
Figure 2: Estimated distributions of CMHC and VA patients over the 7 health states at baseline, the end of years 1, 2 and 3 and in the long run. Differences in the distributions between CMHC and VA patients were highly significant at all five sets of time points with a p-value of 0.011 at baseline and p-values of 0.001 or below at the other time points.
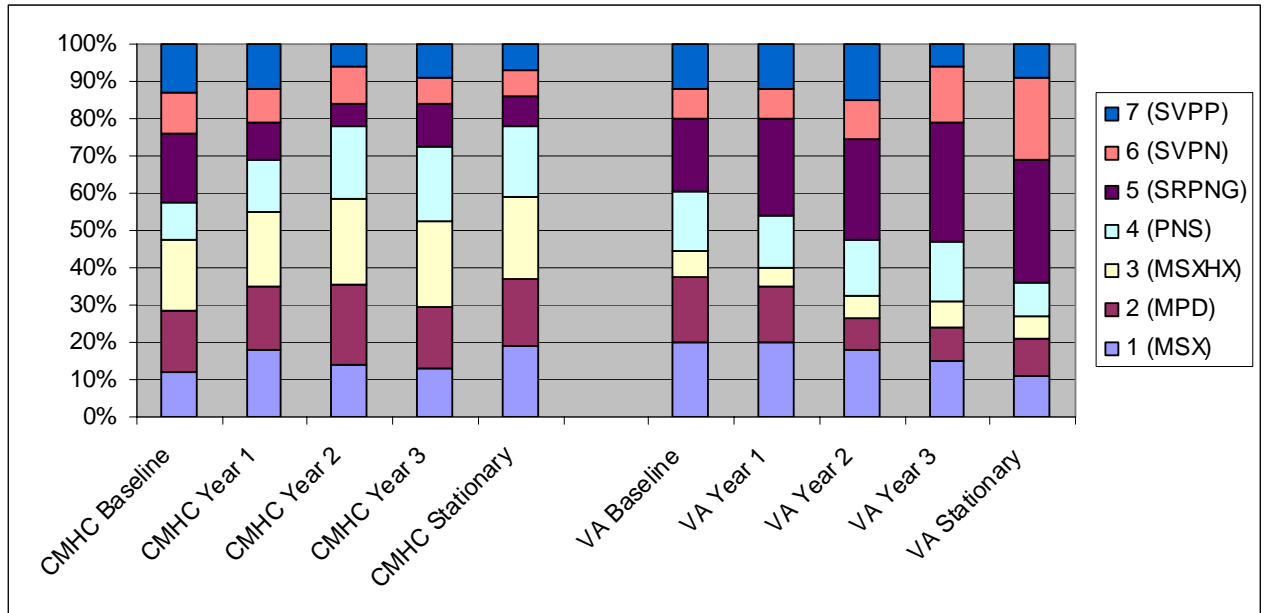
Table 1: Summary statistics on gender, race and age for VA and CMHC populations.

| | Gender | | Race | | | Average |
	Male %	Female %	White %	Black %	Other %	Age
VA	98	2	64	29	7	48.8
CMHC	59	41	49	40	11	41.8

Table 2: Transition probabilities for the CMHC patients.

Transition probabilities for CMHC patients (percentages)		To State						
		1 Mild symptoms in all domains **(MSX)**	2 Mild psychosis with some depressive features **(MPD)**	3 Mild symptoms with hallucinations and poor attention **(MSXHX)**	4 Prominent negative symptoms with mild positive and general symptoms **(PNS)**	5 Serious positive and negative psychotic symptoms with general distress **(PPNG)**	6 Severe predom. negative symptoms **(SVPN)**	7 Severe predom. positive symptoms **(SVPP)**
From State	1 **(MSX)**	44	14	16	21	3	0	2
	2 **(MSD)**	11	56	9	12	8	1	2
	3 **(MSXHX)**	18	10	55	4	5	8	0
	4 **(PNS)**	23	6	8	47	5	5	6
	5 **(PPNG)**	2	15	28	6	36	4	9
	6 **(SVPN)**	2	5	21	12	9	44	7
	7 **(SVPP)**	0	5	0	27	5	9	55

Table 3: Transition probabilities for the VA patients.

Transition probabilities for VA patients (percentages)		To State						
		1 Mild symptoms in all domains **(MSX)**	2 Mild psychosis with some depressive features **(MPD)**	3 Mild symptoms with hallucinations and poor attention **(MSXHX)**	4 Prominent negative symptoms with mild positive and general symptoms **(PNS)**	5 Serious positive and negative psychotic symptoms with general distress **(PPNG)**	6 Severe predom. negative symptoms **(SVPN)**	7 Severe predom. positive symptoms **(SVPP)**
From State	1 **(MSX)**	58	7	7	23	5	0	0
	2 **(MSD)**	9	27	3	15	45	0	0
	3 **(MSXHX)**	7	0	29	7	36	21	0
	4 **(PNS)**	14	14	3	37	14	6	11
	5 **(PPNG)**	2	10	5	2	64	12	5
	6 **(SVPN)**	5	10	5	0	10	71	0
	7 **(SVPP)**	3	0	0	3	14	7	72

Table 4: Differences in the transition probabilities between VA and CMHC patients. Positive numbers indicate higher values for VA patients. Differences that are significant at the 5% level, using the permutation test outlined in Section 2.4, are displayed in bold. In addition the transitions 2→ 2, 4→ 2, 6→ 6 and 7→ 1 are significant at the 10% but not 5% levels.

Differences in transition probabilities between VA and CMHC patients (VA – CMHC)		To State						
		1	2	3	4	5	6	7
		Mild symptoms in all domains **(MSX)**	Mild psychosis with some depressive features **(MPD)**	Mild symptoms with hallucinations and poor attention **(MSXHX)**	Prominent negative symptoms with mild positive and general symptoms **(PNS)**	Serious positive and negative psychotic symptoms with general distress **(PPNG)**	Severe predom. negative symptoms **(SVPN)**	Severe predom. positive symptoms **(SVPP)**
From State	1 **(MSX)**	14	-7	-9	3	1	0	-2
	2 **(MSD)**	-2	-28	-6	3	**38**	-1	-2
	3 **(MSXHX)**	-10	-10	**-26**	3	**30**	**14**	0
	4 **(PNS)**	-8	8	-5	-10	9	1	5
	5 **(PPNG)**	0	-5	**-23**	-4	**28**	8	-4
	6 **(SVPN)**	2	5	-16	-12	0	27	-7
	7 **(SVPP)**	3	-5	0	**-24**	9	-2	18

Table 5: The estimated long run fraction of CMHC and VA patients who will reside in each state.

	Long run stationary percentage of population in each state						
Health States	1 Mild symptoms in all domains **(MSX)**	2 Mild psychosis with some depressive features **(MPD)**	3 Mild symptoms with hallucinations and poor attention **(MSXHX)**	4 Prominent negative symptoms with mild positive and general symptoms **(PNS)**	5 Serious positive and negative psychotic symptoms with general distress **(PPNG)**	6 Severe predom. negative symptoms **(SVPN)**	7 Severe predom. positive symptoms **(SVPP)**
CMHC	19	18	22	19	8	7	7
VA	11	10	6	9	33	22	9

Table 6: Coefficients, test statistics and p-values for the three mixed effects models fit to the data. Race and Age were excluded from the analysis because they were not significant in any of the models. There were 381 degrees of freedom associated with the population and gender test statistics and 719 for the remainder.

Variable	Level	Negative Response			Positive Response			General Response		
		Coef.	t val.	p-value	Coef.	t val.	p-value	Coef.	t val.	p-value
Population	CMHC	3.01	45.33	0.0000	2.97	44.60	0.0000	2.64	55.38	0.0000
	VA	2.77	43.74	0.0000	2.63	41.11	0.0000	2.56	56.18	0.0000
Time	Year 1	0.11	1.74	0.0823	-0.03	-0.55	0.5846	0.12	2.81	0.0051
	Year 2	0.17	2.41	0.0163	0.05	0.87	0.3854	0.18	3.77	0.0002
	Year 3	0.17	2.29	0.0222	0.04	0.70	0.4838	0.18	3.85	0.0001
Interaction	Year 1	-0.17	-2.14	0.0329	-0.16	-2.07	0.0390	-0.19	-3.47	0.0005
Pop vs	Year 2	-0.29	-3.13	0.0018	-0.36	-4.70	0.0000	-0.30	-4.91	0.0000
Time	Year 3	-0.23	-2.47	0.0138	-0.28	-3.68	0.0003	-0.23	-3.74	0.0002
Gender	Female	-0.22	-2.43	0.0157	-0.11	-1.23	0.2182	0.01	0.13	0.8961

Table 7: Mean scores for negative symptoms, positive symptoms and general psychiatric distress for male CMHC and VA patients at baseline and years 1-3 based on the mixed effects models from Table 6. These values could be adjusted for female patients by adding the appropriate gender coefficient.

Time	Negative Response		Positive Response		General Response	
	CMHC	VA	CMHC	VA	CMHC	VA
Baseline	3.01	2.77	2.97	2.63	2.64	2.56
Year 1	2.89	2.88	2.83	2.60	2.57	2.68
Year 2	2.90	2.94	2.67	2.69	2.53	2.74
Year 3	2.94	2.94	2.73	2.68	2.60	2.75
Change (%)	-2.3	6.1	-8.1	1.9	-1.5	7.4