



ORIGINAL ARTICLE

Cost-effectiveness of therapeutic interventions in schizophrenia



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Decision tree

Abstract

Background: Various studies have reported that a decision-tree analysis is useful to evaluate different treatment strategies in real clinical practice.

Objective: The main aim of this study was to research the clinical decisions regarding the treatment of patients who were diagnosed with schizophrenia.

Method: Cost-effectiveness study of three different interventions to treat patients with schizophrenia were studied. Interventions were divided into the following categories: a) day hospital (psycho-educational treatment + psychiatric consultation + psychopharmacological treatment); b) therapy adherence clinic (psychopharmacological treatment with depot antipsychotic medication + psychiatric consultation); c) outpatient psychiatric care (psychopharmacological treatment + psychiatric consultation). For this purpose decision tree model was designed and three outcomes were measured (therapeutic compliance, non-compliance and rehospitalization). TreeAge software was used in order to estimate outcome probabilities and sensitivity analysis, distribution Beta for probabilities and Gamma for cost of interventions. **Results:** The probability of therapeutic compliance and average semestral cost of therapy adherence clinic, outpatient psychiatric care and day hospital are 0.594, 0.284, 2.393, and mean cost intervention US\$ 2145.6, US\$ 700.2 and US\$ 1412.1 respectively (IC95%), according to Montecarlo analysis.

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Conclusions: According to the results, the clinical decision to treat patients in therapy adherence clinic improved therapeutic compliance, but the cost of treatment was higher. There were extra costs and risks to society and patient that are associated with therapeutic non-compliance. It is less expensive for the health care system to provide the patients outpatient psychiatric care, but perhaps in the long-term outpatient psychiatric care is more costly for the patient, their family, and society. According to the many important limitations of this study, further studies are needed to reject/confirm these strategies to be included in real clinical practice.

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Background

Schizophrenia (SCH) is a chronic mental disorder, which may start in childhood. This implies high direct and indirect costs of the disease in patient's life. Worldwide, the lifetime prevalence of schizophrenia is about 0.3–0.7%.¹ In Mexico, estimated lifetime prevalence is 0.7%.²

The lack of therapeutic compliance in SCH increases the risk of relapse. This implies a greater number of relapses, suicides, serious self-inflicted wounds, and an increase in the demand of outpatient psychiatric care and hospitalizations, which increase the overall costs of the disease. The term 'therapeutic compliance' refers to when the patient follows the physician's recommended treatment, and 'non-compliance' refers to when there is a difference between what is recommended by the physician and what is taken by the patient. These terms have replaced the term 'adherence', in order to emphasize the role of the patient.³ Evidence indicates that compliance reduces the risk of relapse; however, some reports show that the rate of therapeutic non-compliance is between 20% and 89%, with an average of 50%.⁴ The rates of therapeutic non-compliance in controlled situations is reduced to 11–33%, and rises up to 37–57% in uncontrolled situations.⁵ Another report shows that only 20% of patients with good therapeutic adherence had relapses, compared to 42% of patients who demonstrated poor treatment, which also resulted in more prolonged hospitalization periods.⁶ In the CATIE study of 18 months, treatment discontinuation was 74% in the first phase. In that study, patients treated with second-generation antipsychotics had better adherence to treatment, but there was no statistically significant difference when compared to perphenazine.⁷ The risk of rehospitalization is directly linked to therapeutic non-compliance: interruptions in the treatment increase the risk of rehospitalization, with an odds ratio (OR) of 1.98 when treatment is interrupted from 1 to 10 days, 2.81 OR with interruptions of 11–30 days, and 3.96 OR with periods longer than 30 days.⁸

Studies have reported that a decision-tree analysis is useful to evaluate different treatment strategies based on results, probabilities and costs.^{9,10} Thus, a decision tree analysis reported an increase in the cost of olanzapine compared to haloperidol (\$3424.6 USD) in patients who had shown improvement, and \$13801.2 USD to prevent relapse in patients. In that study, improvement was evaluated using the BPRS (Brief Psychiatric Rating Scale).¹¹ In

Slovenian decision tree analysis in duration of 12 months, where different treatment strategies were used for acute SCH, treatment with risperidone was less expensive, while olanzapine and risperidone were more cost-effective, even more than aripiprazole, paliperidone and quetiapine. The price of treatment per year were as follows: €6812 for risperidone, €7509 for quetiapine, €7295 for olanzapine, €8229 for aripiprazole and €8044 for paliperidone in 2011.¹²

The main aim of the present study was to develop a decision tree model based on the three different alternatives for treatment of patients diagnosed with schizophrenia in a public hospital, and to evaluate options in terms of cost and therapeutic compliance.

Methods

A cost-effectiveness study; diagnosis was performed by psychiatrists. The selected patients met the criteria for schizophrenia according to the International Classification of Diseases (ICD-10). To maximize the reliability of the data, only the diagnosis of schizophrenia (F20) was considered. Other psychoses such as schizotypal disorder (F21), persistent delusional disorder (F22), acute psychotic disorder (F23), induced delusional disorder (F24) and schizoaffective disorder (F25) were excluded, because these disorders have a different clinical course to schizophrenia and consequently the demand for health services is different. This investigation was approved by The Ethics and Research Committee of the hospital, which is regulated by the Mexican Health Law.

Services types and therapeutic interventions.

In the Psychiatric Hospital "Fray Bernardino Álvarez" there are three interventions to treat patients with SCH; these alternatives are: a) day Hospital (psycho-educational treatment + psychiatric consultation + psychopharmacological treatment); b) therapy adherence clinic (psychopharmacological treatment with depot antipsychotic medication + psychiatric consultation); c) outpatient psychiatric care (psychopharmacological treatment + psychiatric consultation). Each alternative was used as single branch in the final model structure.

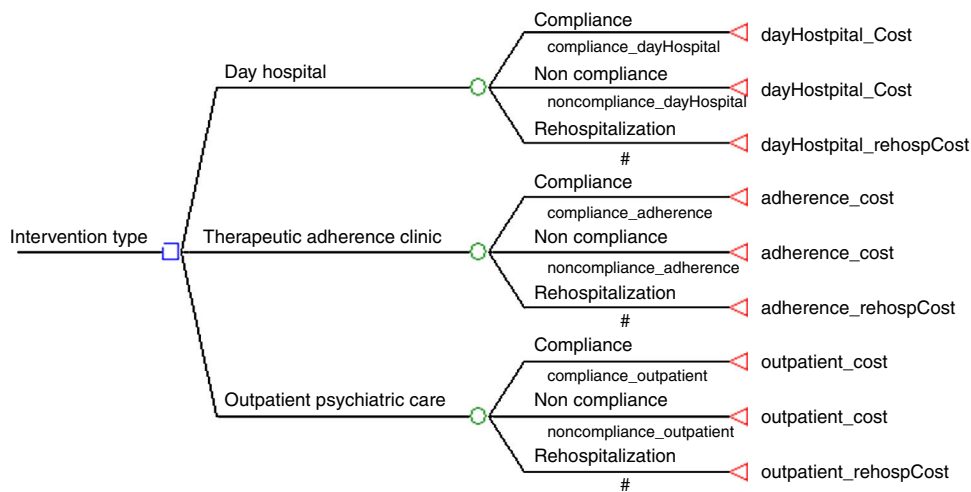


Figure 1 Decision tree model: between each frame 6 months period.

Model structure

A study was designed according to a decision tree model, consisting of four phases, the first frame (time 0) is the clinical decision to send the patient to one of the following ambulatory psychiatric services of the hospital (see Fig. 1): outpatient psychiatric care, day hospital or therapy adherence clinic. In the following semester, there are three possible courses or branches: therapeutic compliance, therapeutic non-compliance, and rehospitalization. The probability of incidence was determined for each event. The final frame is the probability of incidence for events chained in each branch.

When a patient required hospitalization, it was due to a dramatic increase in the psychotic symptoms. Therapeutic non-compliance refers to when there is difference between what is recommend and what the patient takes or when the patient stopped attending consultation and there was no notification of transfer. The treatment continuity was confirmed by the existence of medical notes taken during each scheduled appointment.

The probability of the initial decision to refer a patient to one of the ambulatory services was determined as follows: In average each year, 3672 patients were hospitalized, of which 1474 were diagnosed with schizophrenia. In an average of 18 months, 85 patients were sent to therapy adherence clinic, 53 to day hospital and 600 to outpatient psychiatric care. Thus, the probability to send to outpatient psychiatric care is 0.813, to day hospital 0.071 and to therapy adherence clinic 0.115. The probability of therapeutic compliance, therapeutic non-compliance or rehospitalization was obtained from the same descriptive study. TreeAge software was used for results calculation.

Sensitivity analysis

Sensitivity analysis investigates how uncertainty in the input parameters of the model can affect the results and therefore the conclusions or decision-making, based on the strategies are evaluated.

In this paper, given the nature of the model inputs, probabilistic sensitivity analysis was performed using a beta distribution for the estimated probabilities, from semestral measurements and gamma distribution for the estimated costs for intervention, with a standard deviation of 10%. One thousand simulations Monte Carlo analysis was performed. This analysis can incorporate variability in the results and generate confidence intervals for each intervention, in order to verify if the results are robust to variations of input parameters of the final decision model.

For the construction of the distribution of costs, the total cost calculated over the period of 18 months, this value considered as the mean of the distribution and a standard deviation of 10% of the average. TreeAge software was used for sensitivity analysis.

Costs

The health system in Mexico is comprised of two sectors: public and private. The public sector provides care to two types of users: 1) patients that receive social security (funded by employers, workers and federal government), representing 48.3 million people; and 2) patients without social security (funded by the federal government, local governments and payment of user input), and this sector represents about 58 million people.¹³ The hospital where this study was performed serves people without social security. It has developed programs which support patients by providing part of the drug treatment, hence the importance of the study.

Regarding costs, government reports from the State Health Department show that the monthly costs for psychiatric treatment range from \$53.83MX to \$2073.38MX per person treated, depending on the medication, either haloperidol or clozapine, respectively.¹⁴ It has been reported that the average annual cost for schizophrenia is US\$ 92.85, based on the total annual budget allocated to the treatment of this disorder.¹⁵ In the present study we used the costs reported in a previous study of the analysis of direct and indirect costs of healthcare.¹⁶ Table 1, shows the costs used in the model. These costs are in U.S. dollars, at the

Table 1 Attention costs in psychiatric hospital.

	Cost/day attention	Semestral average attention cost	Average cost per hospitalization
Outpatient psychiatric care	US\$ 9.17	US\$ 21.90	US\$ 2780.21
Therapeutic adherence clinic	US\$ 65.33	US\$ 490.03	US\$ 1631.57
Day hospital	US\$ 32.78	US\$ 770.37	US\$ 1124.36

exchange rate of October 31, 2015: \$16.50 Mexican pesos to 1 U.S. dollar.

Analysis: TreeAge software was used in order to estimate outcome probabilities and sensitivity analysis and we used determinant *p*-value using ANOVA in Stata V13.

Results

The probabilities of each result (therapeutic compliance, non-compliance, and rehospitalization), for each intervention are shown in column 3, [Table 2](#). In the case of outpatient psychiatric care, the individual probability of therapeutic non-compliance (0.481) was greater than compliance (0.284). This is contrary to what was observed in the therapy adherence clinic, where the probability of therapeutic compliance was almost doubled compared to outpatient care (0.594 versus 0.284), and the probabilities of non-compliance and rehospitalization were low (0.191 and 0.19). These results influence the total probability simply by the fact that there was a greater initial probability to send the patient to outpatient psychiatric care.

In order to identify the most effective alternative, that is, the one that minimizes or reduces the risk of therapeutic non-compliance or rehospitalization and maximizes the continuation of the treatment. The result of the beta distribution estimated from the semestral measurements and gamma distribution for the estimated costs for intervention with a standard deviation of 10%, see [Table 2](#).

The model was simulated 1000 times and using a Monte Carlo analysis. The average cost per procedure was obtained, and the results are shown in [Table 3](#). According to the results, the strategy that on average is less expensive is the outpatient psychiatric care. We found significant (*p*-value <0.00) differences among the three interventions. Therapeutic adherence clinic is the option that maximizes compliance, but the cost of this intervention is very high for the public health system of Mexico.

Finally incremental cost-effectiveness ratio (ICER) between day hospital and out psychiatric care was US\$ 4302.2 to each semester added with option more effectiveness (day hospital) respect out psychiatric care. On the other hand, ICER between therapeutic adherence clinic and out psychiatric care was US\$ 2415.83 to each semester

Table 2 Distribution *beta* and *gama* of analysis sensibility.

Intervention	Outcome	Estimate probability of measures semestral	Distribution β for probabilistic analysis	Semestral cost	Distribution α of total cost ^b (18 months) for probabilistic sensitivity analysis
Day hospital	Therapeutic compliance	0.393	$\alpha = 242.8, \beta = 375$	US\$ 490.03	Gamma $\alpha = 100.8, \lambda = 0.069$
	Therapeutic non-compliance	0.474	$\alpha = 210.4, \beta = 233.4$	US\$ 490.03	Gamma $\alpha = 100.8, \lambda = 0.069$
	Rehospitalization	0.107	Complement	US\$ 1124.36 ^a	Gamma $\alpha = 100, \lambda = 0.088$
Therapeutic adherence clinic	Therapeutic compliance	0.594	$\alpha = 162.4, \beta = 111$	US\$ 770.37	Gamma $\alpha = 100.76, \lambda = 0.044$
	Therapeutic non compliance	0.191	$\alpha = 323.6, \beta = 1370$	US\$ 770.37	Gamma $\alpha = 100.76, \lambda = 0.044$
	Rehospitalization	0.19	Complement	US\$ 1631.57 ^a	Gamma $\alpha = 100, \lambda = 0.061$
Outpatient psychiatric care	Therapeutic compliance	0.284	$\alpha = 286.4, \beta = 722$	US\$ 21.09	Gamma $\alpha = 102.12, \lambda = 1.62$
	Therapeutic non-compliance	0.481	$\alpha = 207, \beta = 224$	US\$ 21.09	Gamma $\alpha = 102.12, \lambda = 1.62$
	Rehospitalization	0.179	Complement	US\$ 2780.21 ^a	Gamma $\alpha = 100, \lambda = 0.035$

^a Cost incurred once in 18 months.

^b 3% discount rate for the third semester.

Table 3 Cost of each intervention by montecarlo analysis.

Intervention	Mean of cost for intervention	IC 95%*
Day hospital	US\$ 1412.1	US\$ (1171.1–1680.3)
Therapeutic adherence clinic	US\$ 2145.6	US\$ (1801.1–2521.6)
Outpatient psychiatric care	US\$ 700.2	US\$ (520.2–902.9)

We found significant (p -value <0.00) differences among the three interventions using ANOVA.

added with option more effectiveness (therapeutic adherence clinic).

Conclusions

After 18 months of taking the decision to send the patient to one of the treatment alternatives, the decision to send the patient to day hospital and outpatient psychiatric care have a far smaller probability of therapeutic compliance, compared to that of therapy adherence clinic. Low therapeutic compliance represents higher costs for the health system due to the clinical and social deterioration of the patient, as well as the high costs incurred due to rehospitalization. The greater probability of therapeutic compliance in therapeutic adherence clinic compared to day hospital is perhaps surprising, since the patient in day hospital treatment was provided with psychopharmacological, psycho-educational and psychiatric treatment, and a better outcome might have been expected.

So, the alternative of therapy adherence clinic had greater therapeutic compliance, most likely because the psychopharmacological treatment is based on depot antipsychotic medication, therefore the oral forms of antipsychotics (such as clozapine, olanzapine and risperidone) were not excluded within this alternative. In this aspect, different cost-effectiveness studies support the idea that treatment with depot antipsychotic medication increases the rate of therapy adherence^{17,18} and reduced days of hospitalization.¹⁹ However, that is options not reduce the cost for the health systems, due to its higher cost compared to oral medications.

Add the results of the present study indicate that more studies are necessary in order to evaluate the cost-effectiveness of the strategies of treatment in mental health programs in México, including both forms of antipsychotic, oral and depot medication. Although there is a previous study carried out in Mexico, which measured the effectiveness in terms of Disability Adjusted Life Years (DALYs), in which found that the best option was psychosocial treatment plus atypical antipsychotic medication,²⁰ that study only was a theoretical approach.

Highlighting the fact that there are extra costs and risks to society and to the patient that are associated with therapeutic non-compliance, in our opinion increase number of patients receiving free treatment, maybe is less expensive for the health care system and reduce in the long-term costly for the patient, his family, and society; future studies should examine these aspects.

In this study the best clinical intervention, according to the constructed decision tree model is the therapy adherence clinic because it increases therapeutic compliance.

However, the cost is very high for the health system of México compared to the other alternatives. Finally, the decision tree is a valid method for evaluation of the decision-making process in the treatment of schizophrenia, in countries with similar health systems to that of Mexico.

Some limitations of this study are that were not included control group and pharmacological costs, in the future, other studies should evaluate it. Whereas the strategy of providing the medication to the patient as it is the case in the clinic of therapeutic adherence, result in minor probability of hospitalization, add the studies should cover every possibility of existing medicines to treatment of SCH and to make studies cost-effectiveness. In order to have the best option to treatment of the SCH.

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Conflict of interest

The authors report no competing interests.

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