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Hospitalization and cost after switching from atypical to typical antipsychotics in schizophrenia patients in Thailand

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Background: Several clinical practice guidelines suggest using atypical over typical antipsychotics in patients diagnosed with schizophrenia. Nevertheless, cost-containment policy urged restricting usage of atypical antipsychotics and switching from atypical to typical antipsychotics.

Objective: This study aimed to evaluate clinical and economic impacts of switching from atypical to typical antipsychotics in schizophrenia patients in Thailand.

Methods: From October 2010 through September 2013, a retrospective cohort study was performed utilizing electronic database of two tertiary hospitals. Schizophrenia patients aged 18 years or older and being treated with atypical antipsychotics were included. Patients were classified as atypical antipsychotic switching group if they switched to typical antipsychotics after 180 days of continual atypical antipsychotics therapy. Outcomes were schizophrenia-related hospitalization and total health care cost. Logistic and Poisson regression were used to evaluate the risk of hospitalization, and generalized linear model with gamma distribution was used to determine the health care cost. All analyses were adjusted by employing propensity score and multivariable analyses. All cost estimates were adjusted according to 2013 consumer price index and converted to US$ at an exchange rate of 32.85 Thai bahts/US$.

Results: A total of 2,354 patients were included. Of them, 166 (7.1%) patients switched to typical antipsychotics. The adjusted odds ratio for schizophrenia-related hospitalization in atypical antipsychotic switching group was 1.87 (95% confidence interval [CI] 1.23–2.83). The adjusted incidence rate ratio was 2.44 (95% CI 1.57–3.79) for schizophrenia-related hospitalizations. The average total health care cost was lower in patients with antipsychotic switching (–$64; 95% CI –$459 to $332).

Conclusion: Switching from atypical to typical antipsychotics is associated with an increased risk of schizophrenia-related hospitalization. Nonetheless, association with average total health care cost was not observed. These findings can be of use as a part of evidence in executing prospective cost-containment policy.

Keywords: antipsychotic switching, schizophrenia, hospitalization, cost, atypical antipsychotics, typical antipsychotics

Introduction

Schizophrenia is one of the most debilitating mental disorders with high disability rate.[1] The global prevalence of schizophrenia is ~1%.[2] Since 2004, it has been ranked as the fifth and sixth cause of health-related morbidity among males and females, respectively, worldwide.[3] Schizophrenia is significantly associated with humanistic[4] and economic burdens internationally, especially in Asia.[5,6]

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Antipsychotics are mainstay for management of patients diagnosed with schizophrenia.[7] American Psychiatric Association Practice Guidelines 2004[8] and its 2009 update,[9] the 2005 International Psychopharmacology Algorithm Project,[10] and the 2006 Texas Medication Algorithm Project[11] have recommended atypical antipsychotics as drugs of choice given that they exert an optimal efficacy[12,13] and improved safety/tolerability profile,[14] compared to those of typical antipsychotics. In developing countries such as Thailand, national clinical practice guideline allows the usage of both typical and atypical antipsychotics as recommended therapy.[15] As of currently, all typical (eg, haloperidol, chlorpromazine) and only some atypical (eg, risperidone, clozapine) antipsychotics have been included in the National List of Essential Medicines,[16] which is a standard coverage for beneficiaries in all main public health sectors in Thailand.

Due to the increasing health expenditures and budget constraints, cost-containment strategies have been implemented in most developed[17] and developing countries[18] to efficiently ensure expenditure control. The advocacy to use typical antipsychotics for new cases as well as switching of atypical to typical antipsychotics has been proposed as a potential cost-containment policy for schizophrenia management in Thailand. Still, clinicians and professional health care organizations voiced their concerns regarding the potential implications of such policy. Therefore, there is an urgent need to understand potential impacts of the antipsychotic switching policy on both clinical and economic aspects. This study aims to determine the effects of switching from atypical to typical antipsychotics on hospitalization and health care cost in Thailand. We hypothesized that schizophrenia patients who switched from atypical to typical antipsychotics had higher risk for hospitalization and higher costs than those who continued on atypical antipsychotics.

Methods

Setting and data sources

A retrospective cohort study using electronic databases from university-based hospital and a tertiary psychiatric hospital in Bangkok, Thailand, was undertaken. The inpatient and outpatient database, and pharmacy and financial database were analyzed. Patients' demographic characteristics (eg, age, sex, insurance) and diagnostics code (International Classification of Disease version 10 [ICD-10]) were extracted from inpatient and outpatient databases. In Thailand, health coverage schemes[19] consisted of the Civil Servant Medical Benefit Scheme for government employees and state enterprise employees, the Social Security Scheme and Workman's Compensation Fund for private sector employees, the Universal Coverage Scheme and fee exemption for the poor and underprivileged, and others such as private insurance and out-of-pocket payments for patients who are uninsured. Information on drug's name, amount of drug prescribed, and treatment regimen were extracted from pharmacy database from October 2010 to September 2013. Information on date of payment, type of payment, and medical charges (medication, medical service, laboratory charge, and other

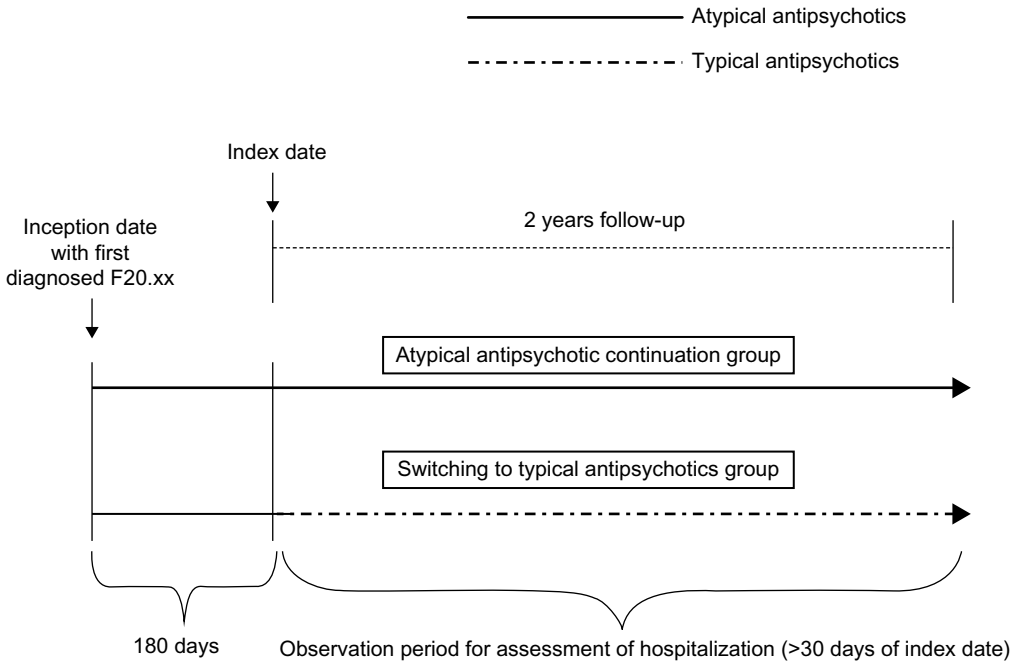


Figure 1 Selection of cohort for evaluation of hospitalization and duration.

charges) were extracted from financial database. The study protocol was submitted to, and approved by, the Ethical Review Committees of both Ramathibodi Hospital and Somdet Choapraya Institute of Psychiatry in accordance with the Declaration of Helsinki. As this study is retrospective, the Ethical Review Committees deemed written informed consent is not required.

Patient selection and study period

Patients who visited outpatient departments in one of the university hospitals and one of the tertiary psychiatric hospitals in Bangkok metropolitan area and met the following inclusion criteria were included in the study: 1) diagnosed as schizophrenia (defined by ICD-10: F20.xx) during the period from October 2010 through April 2011; 2) aged 18 years or older; 3) received atypical antipsychotics (clozapine, olanzapine, quetiapine, aripiprazole, risperidone, paliperidone) at least 180 days before the date of switching to typical antipsychotics (index date) or not switching to typical antipsychotics or other atypical antipsychotics. Typical antipsychotics – both oral and parenteral dosage forms – comprise haloperidol, thioridazine, trifluoperazine, fluphenazine, perphenazine, zuclopenthixol, flupenthixol, and pimozide. Patients receiving a combination of atypical and typical antipsychotics during our study period were excluded. Patient data during the period of 180 days prior to the index date were used to determine propensity score and follow outcomes of interest of adult schizophrenia patients up to 2 years. Patients were categorized into two cohorts as follows: 1) atypical antipsychotic switching to typical antipsychotics group and 2) atypical antipsychotic continuation group by the index date defined as the date of switching from atypical to typical antipsychotics in the former cohort and the first date after continuation of atypical antipsychotics for 180 days in the latter cohort. The selection of cohort was shown in Figure 1.

Outcomes of interest

Schizophrenia-related hospitalization according to ICD-10 (F20.xx) was selected as a primary outcome. The secondary outcomes were all-cause hospitalization, health care resource utilization, and related health care costs. All-cause hospitalization was described as any hospitalization that can be categorized by ICD-10 during the 2-year study period. Health care resource utilizations were measured in terms of number of outpatient visits, number of inpatient visits, and length of hospitalization. Total health care cost included outpatient- and inpatient-related costs and was not limited to the medication costs. Both total health care cost and medication costs were calculated from charges using a cost-to-charge ratio among Thailand University hospital which appeared to be 0.73.[20]

Statistical analysis

The baseline sociodemographic and clinical characteristics of patients were summarized using descriptive statistics and were compared using chi-square or Fisher's exact tests (for categorical variables) or nonparametric Wilcoxon rank-sum test (for numerical variables).

Primary analyses were conducted on patients in atypical antipsychotic continuation group and compared with atypical antipsychotic switching group. We performed sensitivity analyses on patients switching from atypical antipsychotics to other atypical antipsychotics to explore the consistency of the effect of atypical antipsychotic drugs class.

A multivariate logistic regression was used to determine associations of antipsychotic switching with schizophrenia-related and all-cause hospitalizations with the use of conditional logistic regression models for matched analysis, while a multivariate Poisson regression was used to determine associations of antipsychotic switching with schizophrenia-related and all-cause hospitalization rates. A multivariate generalized linear model with log-link function and gamma distribution was used to determine total health care cost, pharmacy cost, outpatient cost, and inpatient cost. The health care cost was converted to 2013 value using consumer price index[21] and was subsequently converted to US$ according to an exchange rate of 32.85 Thai bahts/US$.[22] Propensity score (PS) was calculated and used to adjust baseline characteristics imbalance between the two groups. For this purpose, logistic regression model was initially developed to estimate a propensity score for each patient based on baseline covariates including age, sex, health insurance, occupation, Charlson comorbidity index score, number of previous hospitalizations, and concomitant psychotropic medications (anticholinergics, antidepressants, mood stabilizers, and benzodiazepines). The propensity score was later applied as a matching variable to pair patients who switched antipsychotics to patients who continued on atypical antipsychotics using 1:1 nearest neighbor matching technique. The propensity score was also applied as a covariate in different analyses. Statistical analysis was performed using STATA version 12. The statistical significant level was set at $P<0.05$ in a two-sided test.

Results

Patient characteristics

As shown in Figure 2, a total of 20,910 patients were identified; however, only 2,354 patients met our inclusion criteria. Applying a propensity score matching technique, the number

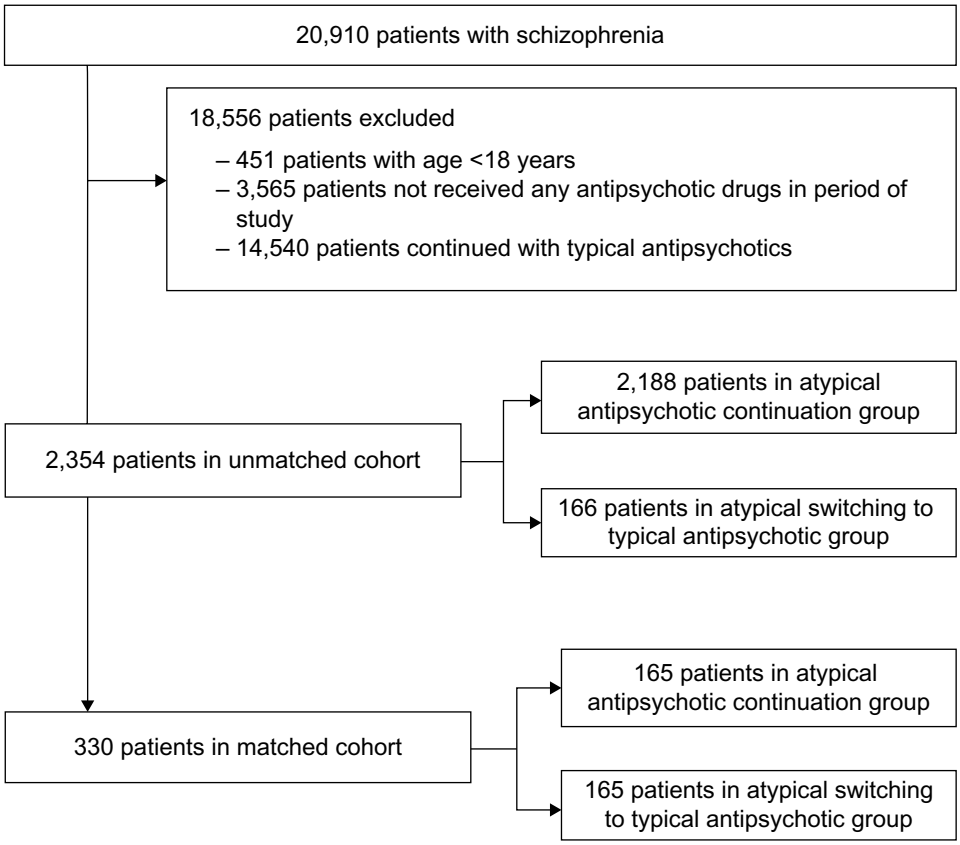


Figure 2 A study flow chart.

of patients included in a matched cohort was 330 patients (165 patients for each group).

Patient demographics are shown in Table 1. The unmatched analysis of two groups yielded significant differences in age with a higher mean in atypical antipsychotics continuation, the average age was 42.8±13.6 years. Percentages of male were similar in both the groups. For matched cohort, there were no significant differences in any baseline characteristics between the two groups except for occupation.

Effects of antipsychotic switching on schizophrenia-related and all-cause hospitalizations

For unmatched cohort, the unadjusted odds ratios (OR) for schizophrenia-related and all-cause hospitalizations within 2-year follow-up between antipsychotic switching and antipsychotic continuation groups were 2.49 (95% CI 1.70–3.66) and 2.25 (95% CI 1.54–3.29), respectively. Based on a multivariable logistic regression analysis, the adjusted OR was 1.87 (95% CI 1.23–2.83) and 1.77 (95% CI, 1.17–2.68), respectively. Based on the PS-matched cohort, all observed hospitalizations were schizophrenia-related hospitalizations. The adjusted OR for schizophrenia-related hospitalizations within 2-year follow-up period was 4.62 (95% CI 0.99–21.62). In sensitivity analyses using atypical antipsychotic switching to other atypical antipsychotics as comparator, the outcomes result was similar to that obtained for primary analyses (Table 2).

Based on multivariable Poisson regression analyses within unmatched cohort, the PS-adjusted incidence rate ratios for schizophrenia hospitalization and all-cause hospitalizations within 2 years were 2.44 (95% CI 1.57–3.79) and 2.89 (95% CI 2.16–3.86), respectively. For PS-matched cohort, the adjusted incidence rate ratios for schizophrenia hospitalization and all-cause hospitalizations were 2.18 (95% CI 1.34–3.56) and 2.34 (95% CI 1.66–3.31), respectively. The results of the sensitivity analyses also show similar incidence rate ratios (Table 3).

Resource utilization during the follow-up period

The number of outpatient visits, inpatient visits, and length of stays were significantly higher in atypical antipsychotic switching group for unmatched cohort. However, in matched

Table 1 Baseline characteristics

Characteristics	Unmatched cohort (N=2,354)			Matched cohort (N=330)		
	Atypical antipsychotic continuation (N=2,188)	Atypical antipsychotic switching (N=166)	*P*-value	Atypical antipsychotic continuation (N=165)	Atypical antipsychotic switching (N=165)	*P*-value
Demographic variables						
Age, mean (SD), years	42.8 (13.6)	39.2 (13.4)	0.001	39.1 (11.9)	39.3 (13.4)	0.85
Sex						
Female, n (%)	1,113 (50.9)	77 (46.4)	0.27	75 (45.5)	77 (46.7)	0.83
Socioeconomic variables, N (%)						
Marital status						
Married	944 (43.1)	75 (45.2)	0.61	73 (44.2)	74 (44.9)	0.91
Unmarried	1,244 (56.9)	91 (54.8)		92 (55.8)	91 (55.1)	
Religion						
Buddhist	2,124 (97.1)	162 (97.6)	0.70	162 (98.2)	161 (97.6)	0.70
Christian	27 (1.2)	3 (1.8)	0.53	2 (1.2)	3 (1.8)	0.65
Muslim	37 (1.7)	1 (0.6)	0.28	1 (0.6)	1 (0.6)	1.00
Occupation						
Government officer	138 (6.3)	8 (4.8)	0.44	4 (2.5)	8 (5.0)	0.24
Housewife	555 (25.4)	30 (18.1)	0.04	43 (26.1)	30 (18.2)	0.09
Self-employed	139 (6.4)	11 (6.6)	0.89	11 (6.7)	11 (6.7)	1.00
Student	467 (21.3)	55 (33.1)	<0.001	36 (21.8)	54 (32.7)	0.03
Blue collar	149 (6.8)	13 (7.8)	0.62	13 (7.9)	13 (7.9)	1.00
Farmer	9 (0.4)	2 (1.2)	0.15	0	2 (1.2)	0.16
Unemployed	8 (0.4)	0	0.44	0	0	N/A
Unknown	723 (33.0)	47 (28.3)	0.21	58 (35.0)	47(28.5)	0.19
Health coverage						
UC	1,131 (51.7)	109 (65.7)	0.001	116 (68.3)	108 (64.6)	0.35
SSS	112 (5.1)	8 (4.8)	0.87	10 (6.1)	8 (4.9)	0.48
CSMBS	285 (13.0)	17 (10.2)	0.30	11 (6.7)	17 (10.3)	0.24
Others	660 (30.2)	32 (19.3)	0.003	28 (17.0)	32 (19.4)	0.57
Concomitant medications						
Antidepressants	779 (35.6)	65 (39.2)	0.36	62 (37.6)	65 (39.4)	0.73
Mood stabilizers	506 (23.1)	53 (31.9)	0.01	46 (27.9)	52 (31.5)	0.47
Benzodiazepines	1,304 (59.6)	143 (86.1)	<0.001	141 (85.5)	142 (86.1)	0.88
Anticholinergics	1,481 (67.7)	149 (89.8)	<0.001	147 (89.1)	148 (89.7)	0.86
Charlson index score						
0	1,931 (88.3)	145 (87.4)	0.73	145 (88.2)	145 (88.2)	1.00
1	178 (8.1)	18 (10.8)	0.22	18 (10.9)	17 (10.3)	0.86
≥2	79 (3.6)	3 (1.8)	0.22	2 (1.2)	3 (1.8)	0.65
Number of previous hospitalizations[a]						
0	2,028 (92.7)	156 (94.0)	0.54	157 (95.2)	156 (94.6)	0.80
1	143 (6.5)	7 (4.2)	0.24	6 (3.6)	7 (4.2)	0.78
≥2	17 (0.8)	3 (1.8)	0.07	2 (1.2)	2 (1.2)	1.00

Note: [a]Number of hospitalization in inclusion period (180 days).
Abbreviations: UC, Universal Coverage Scheme; SSS, Social Security Scheme; CSMBS, Civil Servant Medical Benefit scheme; NA, not available.

cohort, there was no significant difference between atypical antipsychotic switching and continuation groups (Table 4).

Health care cost utilization during the follow-up period

The adjusted differences in total health care cost for unmatched and matched cohort were –$64 (95% CI –$459 to $332) and –$222 (95% CI –$713 to $268), respectively. When inpatient and outpatient costs were analyzed separately, there were no significant differences between the antipsychotic switching and continuation groups. In sensitivity analyses, outpatients health care cost in atypical antipsychotic switching to typical antipsychotics was lower than that observed for atypical antipsychotic switching to other atypical antipsychotics in unmatched cohort with a difference of $1,226 ($510–$1,942) for total outpatient cost and $1,208

Table 2 Logistic regression analysis of hospitalization between atypical antipsychotic switching to typical antipsychotics and atypical antipsychotic continuation groups

Outcomes measure	Unadjusted model		Adjusted model[a]	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic continuation: unmatched cohort (N=2,354)				
Schizophrenia-related hospitalization	3.13 (2.11–4.63)	<0.001	2.23 (1.45–3.45)	<0.001
All-cause hospitalization	2.72 (1.84–4.01)	<0.001	1.98 (1.29–3.06)	0.002
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic continuation: matched cohort (N=330)				
Schizophrenia-related hospitalization	4.28 (0.92–19.85)	0.06	4.28 (0.92–19.85)	0.06
All-cause hospitalization	4.28 (0.92–19.85)	0.06	4.28 (0.92–19.85)	0.06
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic switching to other atypical antipsychotics: unmatched cohort (N=452)				
Schizophrenia-related hospitalization	1.64 (1.02–2.66)	0.04	2.35 (1.34–4.11)	0.01
All-cause hospitalization	1.49 (0.93–2.38)	<0.001	2.00 (1.16–3.48)	0.007
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic switching to other atypical antipsychotics: matched cohort (N=310)				
Schizophrenia-related hospitalization	2.58 (0.26–25.20)	0.42	2.58 (0.26–25.20)	0.42
All-cause hospitalization	2.58 (0.26–25.20)	0.42	2.58 (0.26–25.20)	0.42

Notes: [a]Adjusted for age, sex, marital status, religion, health coverage, concomitant medication, Charlson index score, propensity score.
Abbreviation: CI, confidence interval.

Table 3 Poisson regression analysis between atypical antipsychotic switching to typical antipsychotics and atypical antipsychotic continuation groups

Outcomes measure	Unadjusted model		Adjusted model[a]	
	Incidence rate ratio (95% CI)	*P*-value	Incidence rate ratio (95% CI)	*P*-value
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic continuation: unmatched cohort (N=2,354)				
Schizophrenia-related hospitalization	4.08 (2.91–5.71)	<0.001	2.56 (1.79–3.66)	<0.001
All-cause hospitalization	3.79 (2.86–5.04)	<0.001	2.96 (2.19–3.99)	<0.001
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic continuation: matched cohort (N=330)				
Schizophrenia-related hospitalization	2.50 (1.54–4.06)	<0.001	3.18 (1.84–5.50)	<0.001
All-cause hospitalization	2.46 (1.64–3.72)	<0.001	2.73 (1.73–4.31)	<0.001
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic switching to other atypical antipsychotics: unmatched cohort (N=452)				
Schizophrenia-related hospitalization	2.61 (1.72–3.96)	<0.001	3.21 (2.03–5.09)	<0.001
All-cause hospitalization	3.01 (2.09–4.33)	<0.001	3.74 (2.52–5.58)	<0.001
Atypical antipsychotic switching to typical antipsychotics vs atypical antipsychotic switching to other atypical antipsychotics: matched cohort (N=310)				
Schizophrenia-related hospitalization	3.09 (1.82–5.27)	<0.001	3.39 (1.94–5.90)	<0.001
All-cause hospitalization	3.56 (2.19–5.79)	<0.001	3.94 (2.37–6.56)	<0.001

Notes: [a]Incidence rate ratio based on negative binomial or Poisson regression model, adjusted for time to switching and other covariates (sex, age, health coverage, previous hospitalization, Charlson index score, concomitant medication, propensity score).
Abbreviation: CI, confidence interval.

Table 4 Resource utilization of atypical antipsychotic continuation and switching to typical antipsychotics

Health resource utilization	AAP continuation	AAP switching	Difference	*P*-value
	Mean ± SD	Mean ± SD		
Unmatched cohort (N=2,354)				
Outpatient visits (times)	4.22±3.19	5.07± 5.27	−0.85 (−1.39 to −0.31)	0.002
Inpatient visits (times)	0.55±1.23	1.32±1.83	−0.77 (−0.98 to −0.57)	<0.001
Length of stay (days)	22.91±65.93	62.66±124.58	−39.75 (−51.24 to −28.26)	<0.001
Matched cohort (N=330)				
Outpatient visits (times)	4.52±3.73	5.07±5.28	−0.56 (−1.54 to 0.43)	0.27
Inpatient visits (times)	0.89±1.73	1.26±1.67	−0.37 (−0.74 to −0.001)	0.05
Length of stay (days)	33.39±79.27	59.92±119.83	−26.52 (−48.53 to −4.52)	0.02

Abbreviations: SD, standard deviation; AAP, atypical antipsychotics.

($541–$1,875) for outpatient medication cost, but there was no significant difference for other outpatient costs and the results were similar to the matched cohort (Table 5).

Discussion

To our knowledge, this is the first study to determine the effects of antipsychotic switching from atypical to typical antipsychotics in schizophrenia patients on hospitalization and health care cost. The results demonstrated that patients who switched from atypical antipsychotics to typical antipsychotics had an increased risk of schizophrenia-related and all-cause hospitalizations than patients who continued taking atypical antipsychotics. However, total health care costs are similar between the two groups. These findings warrant policy makers and stakeholders to carefully implement the atypical to typical antipsychotic switching program.

Our study discovered higher rate of concomitant psychotropic drugs usage in atypical antipsychotic switching group

Table 5 Health care cost between atypical antipsychotic continuation and switching to typical antipsychotics

Health care cost[a]	Unadjusted model		Adjusted model[b]	
	Difference	*P*-value	Difference	*P*-value
Atypical antipsychotic continuation vs atypical antipsychotic switching to typical antipsychotics: unmatched cohort (N=2,354)				
Total direct medical cost	26 (–740 to 793)	0.95	–64 (–459 to 332)	0.75
Outpatient health care cost				
Total medical outpatient cost	–265 (–878 to 347)	0.40	–147 (–519 to 194)	0.40
Outpatient medication cost	–379 (–969 to 210)	0.21	–200 (–510 to 108)	0.20
Other outpatient costs	73 (–23 to 170)	0.14	28 (–44 to 101)	0.45
Inpatient health care cost				
Total medical inpatient cost	753 (330 to 1,176)	<0.001	601 (–490 to 1,692)	0.28
Inpatient medication cost	44 (–40 to 129)	0.31	38 (–90 to 166)	0.56
Other inpatient costs	705 (336 to 1,073)	<0.001	628 (–363 to 1,621)	0.21
Atypical antipsychotic continuation vs atypical antipsychotic switching to typical antipsychotics: matched cohort (N=330)				
Total direct medical cost	144 (–602 to 892)	0.70	–223 (–713 to 268)	0.37
Outpatient health care cost				
Total medical outpatient cost	–19 (–662 to 623)	0.95	–239 (–652 to 174)	0.26
Outpatient medication cost	–59 (–635 to 516)	0.84	–72 (–346 to 201)	0.60
Other outpatient costs	33 (–219 to 285)	0.80	5 (–94 to 105)	0.91
Inpatient health care cost				
Total medical inpatient cost	674 (–5 to 1,353)	0.052	536 (–353 to 1,425)	0.24
Inpatient medication cost	49 (–29 to 126)	0.22	–15 (–90 to 61)	0.71
Other inpatient costs	625 (–15 to 1,265)	0.056	715 (–259 to 1,688)	0.15
Atypical antipsychotic switching within class vs atypical antipsychotic switching to typical antipsychotics: unmatched cohort (N=452)				
Total direct medical cost	73 (–493 to 639)	0.80	192 (–479 to 864)	0.58
Outpatient health care cost				
Total medical outpatient cost	–948 (–1,696 to –199)	0.013	–1,226 (–1,942 to –510)	0.001
Outpatient medication cost	–1,014 (–1,734 to –293)	0.006	–1,208 (–1,875 to –541)	<0.001
Other outpatient costs	40 (–161 to 241)	0.70	–27 (–165 to 110)	0.70
Inpatient health care cost				
Total medical inpatient cost	33 (–492 to 558)	0.90	202 (–831 to 124)	0.70
Inpatient medication cost	–58 (–167 to 50)	0.29	–466 (–1,803 to 870)	0.49
Other inpatient costs	84 (–374 to 542)	0.72	244 (–876 to 136)	0.67
Atypical antipsychotic switching within class vs atypical antipsychotic switching to typical antipsychotics: matched cohort (N=310)				
Total direct medical cost	229 (–296 to 754)	0.39	183 (–490 to 857)	0.59
Outpatient health care cost				
Total medical outpatient cost	–702 (–1,527 to 121)	0.10	–1,133 (–1,919 to –347)	0.005
Outpatient medication cost	–741 (–1,519 to 38)	0.06	–1,121 (–1,987 to –455)	0.002
Other outpatient costs	33 (–225 to 291)	0.80	–6 (–100 to 88)	0.90
Inpatient health care cost				
Total medical inpatient cost	197 (–255 to 649)	0.39	258 (–1,612 to 2,129)	0.79
Inpatient medication cost	9 (–45 to 63)	0.74	86 (–1,193 to 1366)	0.89
Other inpatient costs	188 (–227 to 602)	0.38	404 (–251 to 332)	0.79

Notes: [a]$1 =32.85 Thai Baht; [b]adjusted for age, sex, marital status, health coverage, concomitant medication, Charlson index score, and number of previous hospitalizations.

as compared to that of atypical antipsychotic continuation group. With reference to CATIE trial, the overall concomitant psychotropic drugs usage was found in 82%[23] of all treated patients. However, when redefined according to our study criteria by each agent – for instance, antidepressants – the proportion of use of antidepressants was found to be ~38% in this study, but the proportion of use of other agents such as mood stabilizers was found be to be higher in our study than that observed in CATIE trial. The predictors for utilization of multiple concomitant psychotropic medications in CATIE trial were anxiety or depression, being female, and taking atypical antipsychotics. The other possible reason for usage of concomitant medications may relate to the lack of efficacy.[24]

Although, there was no study evaluating the effect of atypical switching to typical antipsychotics, there were several studies comparing the effect of both classes on the risk of hospitalization in schizophrenia patients.[25–27] These studies revealed that atypical antipsychotic was associated with a lower or equal risk of hospitalization compared to typical antipsychotics.[26,28] Also, in geriatric patients, studies showed a lower risk of hospitalization in patients using atypical antipsychotics than in patients using typical antipsychotics.[29,30]

Our study addressed a key message differently from what has been quoted by the previous studies.[31–33] Most studies compared the effect of antipsychotic switching from typical to atypical antipsychotics;[34] in contrast, our study addressed this issue in the opposite way. Despite the question being answered differently, the risk of hospitalization in patients receiving typical antipsychotics was higher than that in patients receiving atypical antipsychotics. The increased risk of hospitalization is hypothesized to be due to disease relapse among the patients who switched to typical antipsychotics. A previous study[34] indicated that atypical antipsychotics show superiority in relapse prevention compared to typical antipsychotics, which could lead to lower hospitalization rate.[32,35]

Our study elucidated that the total health care cost in atypical antipsychotic continuation group may be lower than that of atypical antipsychotic switching group due to a lower cost of hospitalization. This probably means that the lower cost of hospitalization in the atypical antipsychotic continuation group is not sufficient to offset higher medication cost. Our findings are consistent with a finding from a previous study that cost-containment policy focusing on reducing drug expenditures on chronically mentally ill patients results in unintended outcomes such as an increase in hospitalization and nursing home admission, and use of emergency mental health services.[36]

The strengths of our study should be highlighted. First, we used databases from different settings (both university and psychiatric hospitals) to increase generalizability of our findings to wider schizophrenia patients seen in the mental health system in Thailand. Second, we measured outcomes longitudinally using 2-year follow-up period to capture outcomes in a natural course of schizophrenia as chronic mental illness since hospitalization is a proxy of relapse of disease.[37] Third, we used a state-of-art approach such as propensity score method to minimize residual confounding in our adjusted and matched analyses. The use of propensity score matching can help achieve balance between the covariates of the two groups. Therefore, the findings can be considered to mimic the outcomes observed by randomized control trials (RCTs).[38]

Several limitations deserve discussion. First, according to a limitation of the hospital databases, information on reasons for antipsychotic switching, disease severity, and some socioeconomic information such as educational level and patient income were not available. Second, we did not take into account patient's adherence to antipsychotics, which was considered an important factor affecting hospitalization. It was clearly shown that partial nonadherence was directly associated with an increased hospitalization.[39] Third, because of the retrospective nature of the database analysis, our outcomes might not be completely captured as patients might be hospitalized in other health care facilities. Our findings might be underestimated in terms of the rate of hospitalization. Fourth, we could not separate cost analysis between generic and brand antipsychotics, and this may affect the total health care cost and medication cost because of the higher price of branded atypical antipsychotics.

Our findings have both clinical and policy implications that should be considered. Our study showed that switching from atypical antipsychotic to typical antipsychotic significantly increased the risk of hospitalization, approximately two times, without a difference in the total health care cost. These findings may caution clinicians to reconsider adverse effects of switching from atypical to typical antipsychotics, before switching the antipsychotics, in clinical practice and policy makers to carefully consider the potential impact of atypical to typical antipsychotic switching policy program before implementing the policy program at the national level.

Conclusion

In this study, we found an increased risk and rate of hospitalizations and increased health care resource utilization

in patients who switched from atypical antipsychotics to typical antipsychotics. However, health care cost was not significantly different between the two groups. Policy makers could potentially adapt these findings in developing prospective policies and practice guidelines for treatment in schizophrenia where resources are limited to achieve both clinical efficacy and cost-containment outcomes.

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Disclosure

The authors report no conflicts of interest in this work.

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