

Factors Associated with Readmission Among Individuals with One Previous Episode of Schizophrenia in Southern Thailand: A University Hospital-based Retrospective Study

Jarurin Pitanupong, M.D., Pran Ratanaapiromyakij, M.D., Teerapat Teetharatkul, M.D.

Department of Psychiatry, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

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Abstract:

Objective: Schizophrenia is a chronic disease that has residual symptoms and relapse. The study aims to explore factors associated with readmission from symptom relapse among individuals with schizophrenia.

Material and Methods: Medical records of patients who had their first schizophrenia diagnosis, in the Songklanagarind hospital's inpatient psychiatric unit, were retrospectively reviewed for the period from January 2007 to December 2019. This yielded data outlining demographic information, profiles of schizophrenia, and treatment. Descriptive statistical analysis was utilized to process all data, and factors associated with readmission were investigated using bivariate and multivariate analyses.

Results: Reviewed medical records identified a sample size of 156 individuals with schizophrenia. The majority were male (50.6%), Buddhist (85.9%), unmarried (80.1%), unemployed (50.6%), and living with their families (90.4%). Mean age was 39.2 years. From the 156 patients, they were divided into two groups; the readmission group and the non-readmission group. Readmission was defined as rehospitalization to a psychiatric unit within 5 years after their first schizophrenia diagnosis. Of all of them, 84 (53.8%) featured readmission whereas 72 (46.2%) were non-readmission. The first to fifth readmission rate was 22.4%, 12.8%, 9.6%, 5.1%, 3.8%, respectively. Multivariate analysis indicated that individuals with schizophrenia having stressful life events, non-adherence to medication, prescription changes, and lack of insight were all factors with a statistically significant association to readmission.

Contact: Assoc. Prof. Jarurin Pitanupong, M.D.
Department of Psychiatry, Faculty of Medicine, Prince of Songkla University,
Hat Yai, Songkhla 90110, Thailand.
E-mail: pjarurin@medicine.psu.ac.th

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Conclusion: Stressful life events, adverse events, non-adherence, change the prescription, and lack of insight were related to readmission. Emphasizing multimodality of treatment could be key to successful readmission prevention for individuals with schizophrenia.

Keywords: factor, prevention, readmission, relapse, schizophrenia

Introduction

Schizophrenia is a mental illness affecting about 7 per 1,000 adults globally¹ or approximately 1.0% of the world's population.² In addition, schizophrenia is a long-term debilitating chronic disease that has residual symptoms, including functional impairment, and requires lifelong medical care.¹⁻³ Therefore, biological treatment and psychiatric rehabilitation are necessary to improve patients' quality of life⁴ and lessen the burden for their families.^{5,6}

Historically, the core strategy in the management of schizophrenia has been a combination of medication, ensuring patients gain insight about their condition, and the teaching of essential community-living skills as integrating patients back into society and engaging in employment and other meaningful activities can reduce social stigma.⁷ Although some individuals with schizophrenia can gain insight well, the reality of their condition causes them emotional pain due to social stigmatization. This often leads to them refusing to take their medication, leading to relapse.⁸

Relapse in schizophrenia is broadly defined as the reemergence or the worsening of psychotic symptoms.² Furthermore, this definition can include the aggravation of positive or negative symptoms, readmission, more intensive management, and/or changes in medication.⁸

The previous studies identified that relapse rates varied from 50.0% to 92.0% globally^{9,10}, and most individuals with schizophrenia in treatment relapse within 5 years, and suicide might occur in up to 10.0% of them.³ There is an association between suicidal ideation and the likelihood of relapse with the probability of relapse being 9.1 times

larger than individuals with schizophrenia without suicidal ideation.^{11,12} Additionally, the factors commonly associated with relapse are non-adherence to medication, ranging from 26.0% to 44.0%, as many as two-thirds of patients are at least partially poorly adherent, resulting in an increased risk of hospitalization.^{1,7} However, persistent substance use disorder¹³, poorer premorbid adjustments, co-morbid psychiatric illness¹⁴, co-morbid medical or health-related problems^{15,16}, poverty, unemployment¹³, stressful life events, family' criticism, or low family support^{9,13}, patient-provider relationships or the treatment setting^{17,18}, and aging are also significantly predisposing the risk for relapse and readmission in schizophrenia.¹⁹ In other words, readmission from symptom relapse among individuals with schizophrenia from non-adherence to medication may be due to factors that are related to patients (forgetfulness, anxiety about adverse effects, inadequate knowledge, lack of insight and motivation, and fear of stigma)¹⁹⁻²¹; healthcare (poor patient-health care provider relationship, poor service and access to services, poor staff training)²²; socioeconomic aspects (low level of education, unemployed, cultural and social attitudes, belief systems)⁶; and treatment strategy (poly-pharmacology, complex treatment regimens).²³ In addition, there is some evidence suggesting that drug treatment regimen history, drug administration route, and antipsychotic drug adverse effects can also contribute to schizophrenia relapse.^{24,25} Nowadays, antipsychotic medication plays an effective role regarding symptom control in the management of schizophrenia, but continuous long-term treatment is required to ensure medication adherence, control symptoms, and prevent relapse and its consequences.²⁶

Successive relapse control can reduce the degree and duration of the next remission, worsen disability, and increase refractoriness to future treatment.²⁷ Relapse control and readmission prevention have been a concern and an area of focus for many years in our healthcare setting, Songklanagarind Hospital. Our prior studies of readmission prevention were done aiming to assist in the maintenance of life quality and to lessen the burden and stigma of the families.^{4,5} Additionally, our goals of social de-stigmatization were to boost social or community recognition and positive attitudes towards individuals with schizophrenia.²⁸ As a result, our individuals with schizophrenia have good medication adherence and meaning in life.²⁹ However, some of them still readmit from symptom relapse, even during treatment.² Thus, this study aimed to evaluate the readmission rate among individuals with schizophrenia, within five years, and to identify factors associated with readmission in comparison with a group on non-readmission.

Material and Methods

After being approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC. 63-523-3-4), this retrospective study was conducted at Songklanagarind Hospital, which is an 800-bed university hospital serving as a tertiary referral center in southern Thailand. A review was conducted of all the information in the medical records of 230 individuals with schizophrenia, in regards to the period between January 2007 until December 2015, via the hospital computer system; the inclusion criteria were that patients had a first diagnosis with schizophrenia as per the ICD-10 code F 20.0 to 20.9, they had a diagnosis by a psychiatrist, had medical registration at the psychiatric inpatient unit from January 2007 to December 2019, and their age ranged from 18-60 years old. Meanwhile, individuals with schizophrenia and co-morbidity with mental illness from medical conditions, loss follow up and having diagnosis changes were excluded. The individuals with schizophrenia were divided into two

groups, the readmission group, and the non-readmission group.

The readmission group contained the cases of individuals with schizophrenia who had documented evidence of re-emergence or aggravation of psychotic symptoms or suicide ideation and hospitalization to a psychiatric unit within 5 years after first diagnosed with schizophrenia. Planned hospital admission for a non-related illness or special investigation was not deemed to be a readmission.⁸ Non-readmission was applied to individuals with schizophrenia who did not have a history of readmission within 5 years after the first diagnosis with schizophrenia, had no interrupted periods of the outpatient from symptoms relapse or suicide ideation to the point of hospitalization, and had follow-ups by a psychiatrist at psychiatric outpatient clinic regularly. Therefore, we viewed the information from their first diagnosis with schizophrenia until the next readmission occurred (Figure 1). The factors associated with readmission as well as the protective factors found between the two groups were compared and analyzed.

Data records were reviewed by 5 psychiatrists and a content validity analysis was performed; the content validity index (CVI) score was 0.8. They were composed of 2 parts:

1. Personal and demographic information inquiry consisting of questions related to age, gender, religion, marital status, education level, occupation, patient income, supporting system, health coverage, physical illness, and substance usage.

2. Profile of schizophrenia and treatment information included residual symptoms, insight, stressful life event, suicidal ideation, psychiatric family history, cause of discontinuing antipsychotic drugs due to factors of patient-related or healthcare-related or socio-economically-related, number and duration of readmission, follow-up interval, the regimen of treatment, type and route of drug administration, antipsychotic adverse events, and history of changing type or dose of antipsychotic drugs. Insight of individuals with schizophrenia was evaluated in medical

records retrospectively by coding “poor”, “intellectual” or “true emotional” insight.

Descriptive statistics such as percentage, frequency, proportion, mean, and standard deviation (S.D.) were calculated. In the case that more than 10.0% of data were found to be missing, then this would be classified as a new group. Bivariate and multivariate analyses were utilized to identify factors associated with symptom relapse.

Results

According to the study period, there were 230 individuals who were the first diagnosis with schizophrenia and admitted to the psychiatric inpatient unit. After they were excluded according to study criteria, 156 individuals with schizophrenia were included. Of all of them, 84 (53.8%) reported a relapse of symptoms and readmission within five years after the first diagnosis of schizophrenia, and they formed the readmission group. 72 (46.2%) were in the non-readmission group (Figure 1). The majority of them were male (50.6%), Buddhist (85.9%), unmarried (80.1%), unemployed (50.6%), and staying with family (90.4%). In

regards to all of the participants, their mean age was 39.2 years. In addition, 44 (28.2%) patients, had a history of substance use (Table 1). The most common substances that individuals with schizophrenia used were cigarettes (59.1%), alcohol (29.5%), stimulants (25.0%), marijuana (22.7%), and kratom (11.4%). Additionally, some patients (19.9%) had a physical illness, such as hypertension (32.3%), and diabetes (19.4%).

Of all individuals with schizophrenia in the study, the median interquartile range (IQR) length of patients being symptoms free, prior to readmission was 17 (6.5, 28) months. The first to fifth readmission rate was 22.4%, 12.8%, 9.6%, 5.1%, 3.8%, respectively. Cumulatively, the first to fifth year readmission rate was 22.4%, 35.3%, 44.9%, 50.0%, 53.8%, respectively.

Nevertheless, some individuals with schizophrenia showed residual symptoms (39.1%) and a lack of insight (38.8%). Most residual symptoms were hallucinations (52.5%), delusions (45.9%), and disorganized or catatonic behavior (16.4%). In regards to problems, individuals with schizophrenia were found to be burdensome, they reported

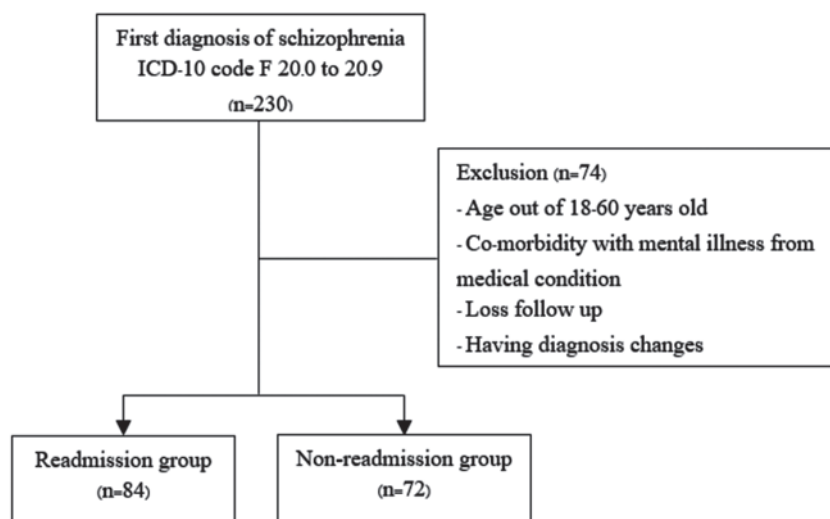


Figure 1 Flowchart of the selection strategy and inclusion/exclusion criteria in the current study.

having stressful life events (32.7%) and suicidal ideation (10.9%) (Table 2). The most common stressful life events that the individuals with schizophrenia identified were relationship problems (47.1%), work stress (27.5%), and the loss of a person significant to them (9.8%).

Table 1 Demographic characteristics (n=156)

Demographic characteristics	Number (%)			Chisq. (df)	p-value
	Total (n=156)	Readmission (n=84)	Non-readmission (n=72)		
Gender				1.62 (1)	0.203
Male	79 (50.6)	47 (56.0)	32 (44.4)		
Female	77 (49.4)	37 (44.0)	40 (55.6)		
Religion				0.09 (1)	0.763
Buddhism	134 (85.9)	71 (84.5)	63 (87.5)		
Others (Islam, Christ, others)	22 (14.1)	13 (15.5)	9 (12.5)		
Marital status*				0.03 (1)	0.859
Single/separated/widowed	125 (80.1)	66 (79.5)	59 (81.9)		
Married	30 (19.2)	17 (20.5)	13 (18.1)		
Education level				11.99 (2)	0.002
High school/diploma or less	57 (36.5)	41 (48.8)	16 (22.2)		
Bachelor's degree or more	46 (29.5)	21 (25)	25 (34.7)		
Not specified	53 (34.0)	22 (26.2)	31 (43.1)		
Occupation				2.16 (2)	0.340
Unemployed/student/monk	79 (50.6)	47 (56)	32 (44.4)		
Self-employed/agricultural work	41 (26.3)	19 (22.6)	22 (30.6)		
Government officer/state enterprise employee/company employee/merchant/personal business	36 (23.1)	18 (21.4)	18 (25.0)		
Patient income				0.91 (1)	0.341
No income	79 (50.6)	46 (54.8)	33 (45.8)		
Yes	77 (49.4)	38 (45.2)	39 (54.2)		
Supporting system**				0.112 ^a	
Stay with family	141 (90.4)	74 (89.2)	67 (97.1)		
Alone	11 (7.1)	9 (10.8)	2 (2.9)		
Health coverage				6.67 (2)	0.036
Civil Servant Medical Benefit Scheme (CSMBS)/Provincial Administrative Organization	19 (12.2)	12 (14.3)	7 (9.7)		
Universal Coverage Scheme (UCS)/Social Security Scheme (SSS)	103 (66.0)	48 (57.1)	55 (76.4)		
Out-of-pocket	34 (21.8)	24 (28.6)	10 (13.9)		
Physical illness				0.53 (1)	0.467
No	125 (80.1)	65 (77.4)	60 (83.3)		
Yes	31 (19.9)	19 (22.6)	12 (16.7)		
Substance usage				0.08 (1)	0.773
No	112 (71.8)	59 (70.2)	53 (73.6)		
Yes	44 (28.2)	25 (29.8)	19 (26.4)		

Note: Substance usage included cigarettes, alcohol, stimulants, marijuana, kratom, opioids.

*There was 1 missing value; **There were 4 missing values.

^ap-value from Fisher's exact test.

Table 2 Schizophrenia characteristics and treatment information (n=156)

Schizophrenia characteristics	Number (%)			Chi2 p-value
	Total (n=156)	Readmission (n=84)	Non- readmission (n=72)	
Residual symptoms				<0.012
No	95 (60.9)	43 (51.2)	52 (72.2)	
Yes	61 (39.1)	41 (48.8)	20 (27.8)	
Insight				<0.001
True emotional	27 (19.4)	7 (8.3)	20 (27.8)	
Intellectual	22 (15.8)	19 (22.6)	3 (4.2)	
Poor	54 (38.8)	51 (60.7)	3 (4.2)	
Not specify	53 (34.0)	7 (8.3)	46 (63.9)	
Stressful life event				<0.001
No	105 (67.3)	37 (44.0)	68 (94.4)	
Yes	51 (32.7)	47 (56.0)	4 (5.6)	
Suicidal ideation				<0.001
No	140 (89.7)	68 (81.0)	72 (100.0)	
Yes	16 (10.3)	16 (19.0)	0 (0.0)	
Having psychiatric family history				0.068
No	116 (74.4)	57 (67.9)	59 (81.9)	
Yes	40 (25.6)	27 (32.1)	13 (18.1)	
History of medical non-adherence				<0.001
No	97 (62.2)	34 (40.5)	63 (87.5)	
Yes	59 (37.8)	50 (59.5)	9 (12.5)	
a) Patient-related				
No	5 (3.2)	5 (6.0)	0 (0.0)	
Yes	54 (34.6)	45 (53.6)	9 (12.5)	
b) Health care-related				
No	55 (35.3)	46 (54.8)	9 (12.5)	
Yes	4 (2.6)	4 (4.8)	0 (0.0)	
c) Socio-economically-related				
No	46 (29.5)	38 (45.2)	8 (11.1)	
Yes	13 (8.3)	12 (14.3)	1 (1.4)	
Amount of type of antipsychotic drugs				0.391
1	87 (55.8)	50 (59.5)	37 (51.4)	
2-4	69 (44.2)	34 (40.5)	35 (48.6)	
Type of antipsychotic				0.295
First generation antipsychotic				
No	101 (64.7)	58 (69.0)	43 (59.7)	
Yes	55 (35.3)	26 (31.0)	29 (40.3)	
Second generation antipsychotic				0.565
No	98 (62.8)	55 (65.5)	43 (59.7)	
Yes	58 (37.2)	29 (34.5)	29 (40.3)	
Combination first & second generation				1
No	127 (81.4)	68 (81.0)	59 (81.9)	
Yes	29 (18.6)	16 (19.0)	13 (18.1)	
Amount of time that administration per day (time)				0.886
1-2	102 (65.4)	54 (64.3)	48 (66.7)	
3-4	54 (34.6)	30 (35.7)	24 (33.3)	
Route of administration				0.363
Oral medication	138 (88.5)	72 (85.7)	66 (91.7)	
Oral medication & long-acting injection	18 (11.5)	12 (14.3)	6 (8.3)	

Table 2 (continued)

Schizophrenia characteristics	Number (%)			Chi2 p-value
	Total (n=156)	Readmission (n=84)	Non- readmission (n=72)	
Adverse events				<0.001
No	100 (64.1)	43 (51.2)	57 (79.2)	
Yes	44 (28.2)	30 (35.7)	14 (19.4)	
Not specify	12 (7.7)	11 (13.1)	1 (1.4)	
History of changing type of medication				0.004
No	138 (88.5)	68 (81.0)	70 (97.2)	
Yes	18 (11.5)	16 (19.0)	2 (2.8)	

According to individuals with schizophrenia in the readmission group, half had residual symptoms (48.8%) and more than half of them reported poor insight (60.7%), having stressful life events (56.0%), and suicidal ideation (19.0%). There was a statistically significant difference in residual symptoms, insight, stressful life events, and suicidal ideation between readmission and non-readmission groups (p -value<0.05) (Table 2).

Treatment information

In regards to all individuals with schizophrenia, their median (IQR) length of hospital stay was 17 (12.8, 25) days. The median (IQR) number of types and amounts in regards to their oral medication prescriptions, tablets, were 3 (2, 5), and 5 (3, 8) respectively. Most of them self-administered tablets 1–2 times per day (65.4%) via the oral route (88.5%). Two-thirds (64.1%) had no adverse effects and demonstrated good medical adherence (62.2%) (Table 2). About half of them (51.3%) had follow-ups by a psychiatrist at an interval of every 1–3 months.

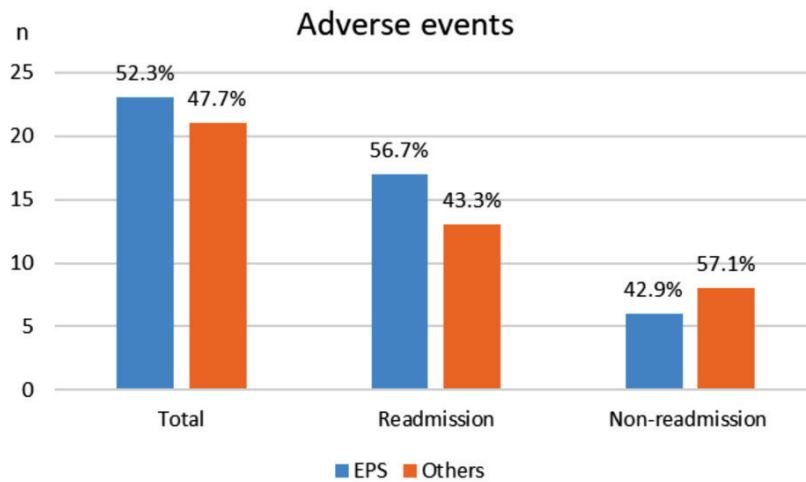
According to the readmission group, two-thirds (59.5%) had a history of medical non-adherence. The most common cause of medical non-adherence was patient-related factors (53.6%) such as; lack of insight (62.2%); anxiety about the adverse events of antipsychotic medication (24.4%), and factors associated with patient's socio-

economic status (14.3%). However, a few patients reported being medical non-adherent due to not having sufficient knowledge, being forgetful, and feeling stigmatized due to having a prescription. There was a statistically significant difference in adverse events, medical non-adherence, and history of change prescription between the readmission and the non-readmission groups (p -value<0.001) (Table 2). Additionally, no statistically significant difference was found regarding the length of hospital stay and between readmission and the non-readmission groups.

Focusing on the adverse events of antipsychotic drugs, individuals with schizophrenia mainly reported no adverse effects (64.1%). Furthermore, more than half of them (55.8%) received second-generation antipsychotic drugs; pure second-generation antipsychotic drugs (37.2%); and/or a combination of first and second-generation antipsychotic drugs (18.6%). There was no statistically significant difference when comparing the use of first or second generation antipsychotics between the readmission or non-readmission groups (Table 2). Extrapyramidal symptoms (EPS) (56.7%) were the most common adverse event among the readmission group. Individuals with schizophrenia who had received first-generation antipsychotics developed EPS more than individuals with schizophrenia taking second-generation antipsychotic drugs (Figure 2 and Figure 3). However, no statistically

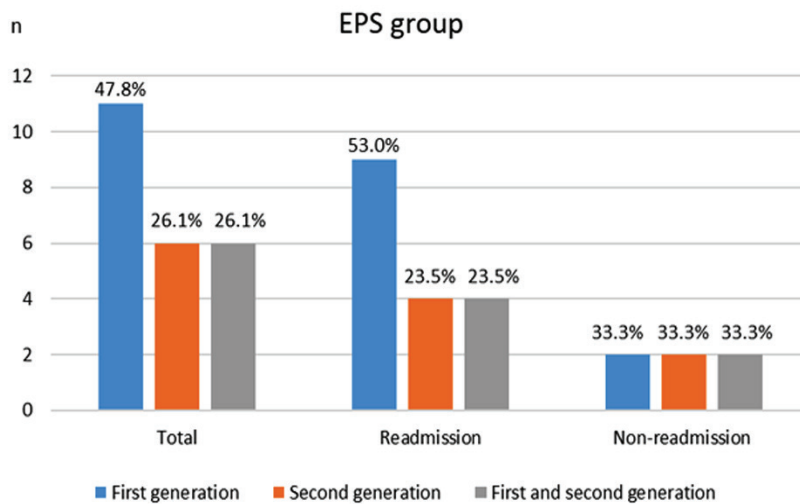
significant difference in EPS between the readmission and the non-readmission group was detected. Viewing this from a different perspective, the adverse event could be related to medication adherence. A statistically significant

association between the group of patients who developed adverse events during treatment and the history of poor drug compliance was detected (p -value<0.001) (Figure 4).



EPS=extrapyramidal symptoms

Figure 2 Comparison of the adverse event of antipsychotic drug between EPS and other adverse effect among readmission and non-readmission group (n=44).



EPS=extrapyramidal symptoms

Figure 3 Comparison of the type of antipsychotic drugs among individuals with schizophrenia who developed EPS (n=23).

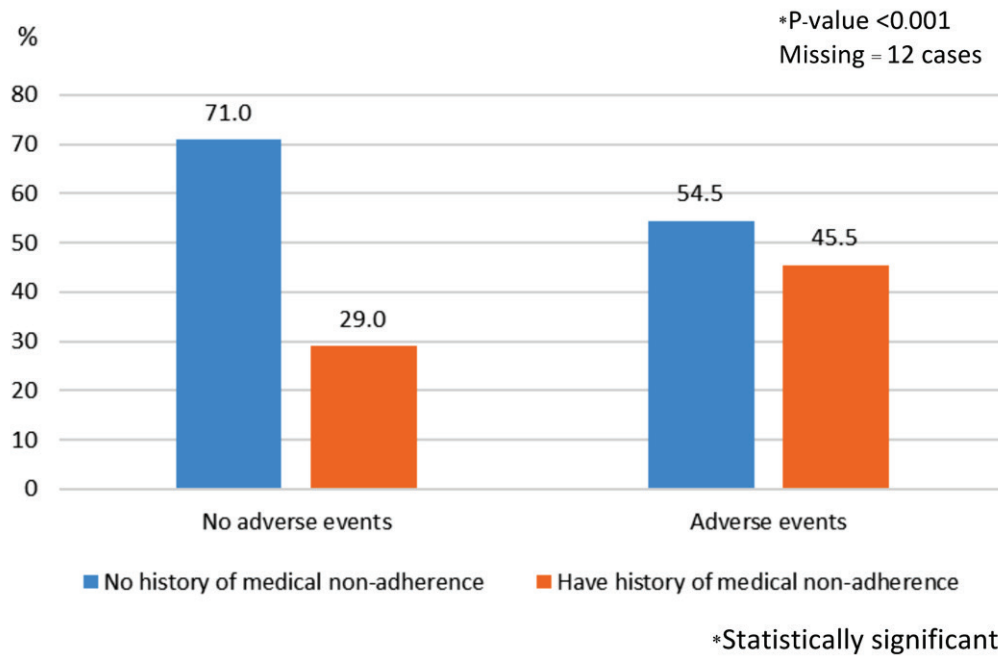


Figure 4 Association between adverse events of antipsychotic drug and history of medical non-adherence (n=156)

Table 3 Factors related to readmission: multivariate analysis

Factors	Crude OR (95%CI)	Adjusted OR (95%CI)	p-value LR-test
Stressful life event			<0.001
No	Reference	Reference	
Yes	21.6 (7.2, 64.6)	23.5 (5.2, 107.2)	
Insight			<0.001
True emotional	Reference	Reference	
Intellectual	18.1 (4.1, 80.4)	10.3 (1.6, 68.6)	
Poor	48.6 (11.4, 206.6)	22.6 (4.1, 123.5)	
Not specify	0.4 (0.1, 1.4)	0.4 (0.1, 1.6)	
History of medical non-adherence			0.021
No	Reference	Reference	
Yes	10.3 (4.5, 23.4)	5.0 (1.3, 19.7)	
History of changing type of medication			0.023
No	Reference	Reference	
Yes	8.2 (1.8, 37.2)	10.9 (1.2, 100.9)	

The association between demographic and schizophrenia characteristics, treatment, and readmission

Multivariate analysis indicated that having stressful life events, medical non-adherence, history of change prescription, and lack of insight were all factors statistically significantly associated with readmission. The individuals with schizophrenia who had stressful life events had a higher rate of readmission than the non-readmission group, the adjusted odds ratio (AOR) was 23.5 and the 95% confidence interval (CI) was 5.2 to 107.1. The same was true when comparing them with those who had medical non-adherence, prescription changes, and poor insight; AOR (95% CI) was 5 (1.3, 19.7), 10.9 (1.2, 100.9), and 22.6 (4.1, 123.5), respectively (Table 3).

Discussion

This survey indicated that the first-year, second-year relapse rate and cumulative relapse rate in five years among individuals with schizophrenia were 22.4%, 12.8%, and 53.8%, respectively. Individuals with schizophrenia from the readmission group reported having a lack of insight (60.7%), stressful life events (56.0%), residual symptoms (48.8%), and suicidal ideation (19.0%). Moreover, two-thirds (59.5%) demonstrated medical non-adherence due to patient-related factors (53.6%) such as lack of insight and experiencing anxiety about the adverse events of antipsychotic drugs as well as due to socio-economic factors (14.3%). The factors with a statistically significant association to readmission were stressful life events, medical non-adherence, prescription changes, and a lack of insight.

Regarding the readmission from symptom relapse, some studies identified that relapse rates vary from 50.0% to 92.0% globally.^{9,10} Our study features a lesser relapse rate vs. the general international levels: much lower than studies in Spain¹⁸ that found rates of relapse were 31.0% after one year and 43.0% at two years. The prior study was

conducted in Taiwan identified the 3-months and one-year readmission rates were 15.2% and 33.3%, respectively.³⁰ These findings may be due to Thai and Asian culture, in general, being more collectivist vs. European and American culture that tends to be more individualistic.³¹ However, it was not easy to consensus the readmission or relapse rate in our country due to the variation of information. One study showed that the relapse rate in Thai individuals with schizophrenia was still high, accounting for 81.9% in the second episode within five years.³² Another study from Northeastern Thailand, Mahasarakham hospital, found the relapse rate of individuals with schizophrenia was 7.3% but also included other psychotic disorders.³³ In one systematic review and meta-analysis of longitudinal studies in individuals with first-episode psychosis, the pooled prevalence of relapse of positive symptoms was 28.0%, 43.0% 54.0% at 1, 1.5–2, and 3 years follow-up.³⁴ In summary, our recent study trended to have a lower relapse rate that needs hospitalization compared to overall data.

To our knowledge, while the majority of Thailand's population are Buddhist, many provinces in the southern region were predominantly Muslim. Therefore, southern peoples' beliefs might differ from those of Thais from the Central and other regions. In our prior study, 90.4% of individuals with schizophrenia stayed with family and it appeared that they had good family support without feeling like a burden in the family⁵ or experiencing stigma in individuals with schizophrenia.⁴ In addition, 73.2% of the caregivers report a non-severe or nil burden as a result of being with individuals with schizophrenia.⁵ This information highlighted that there is a collectivist system in southern Thailand where there is a whole-family sense of duty to care for individuals with schizophrenia and family member. Furthermore, the ability to access our health care system seems easier when compared to other countries.³⁵ Comprehensive psychoeducation appears to be important in aiding relatives and individuals with schizophrenia to

better understand treatment guidelines, potentially reducing readmission from symptom relapse and any burden on the family.

About factors associated with readmission from symptom relapse, our findings support those from previous reports from Australia as non-adherence to medication and psychosocial stressors were commonly noted as clinical precipitants of relapse.³⁶ Furthermore, discontinuing antipsychotic drug therapy increased the risk of relapse by almost 5 times; and it was found that relapse was common after the discontinuation of antipsychotic medication post recovery from the first episode of psychosis.³⁷ Individuals with schizophrenia who wished to discontinue their medication needed to be informed of the high relapse rates and the associated risks. Furthermore, male individuals with schizophrenia who had previous hospital admissions potentially require closer monitoring.³⁸ However, this study identified no statistically significant difference in gender between the readmission and non-readmission groups. The reason for this might be the fact that most individuals with schizophrenia stayed with their family and they equally received the caring from their caretakers.⁵

In addition, this study revealed that psychosocial stressors were a factor noted as a clinical precipitant of readmission. Therefore, psychotherapeutic treatment is potentially an essential component for the treatment of individuals with schizophrenia; aiming to reduce suicidal ideation and the impact of stressful life events, which are both precipitating factors.³⁸

In regards to the adverse effects of antipsychotic drugs associated with medical non-adherence, optimum dosing with the lowest level of adverse effects would be our paramount concern. Even though the type and route of administration of antipsychotic drugs was not a significant factor in our research; the new generation of antipsychotic drugs have shown that they cause fewer adverse events, especially in regards to EPS as compared

with the first generation of drugs. Furthermore, real-world data suggest that long-acting injections tend to reduce the occurrence of EPS and/or neuroleptic malignant syndrome but there is another adverse effect with similar risks to oral antipsychotics.³⁹ According to this information, atypical antipsychotic long-acting injections could be an interesting choice due to reducing the risk of adverse events, medical non-adherence, and any fluctuations of the concentration of the drug in the system of individuals with schizophrenia. If the conventional antipsychotic is necessary, balancing optimum dosing to control symptoms with the least amount of side effects should be considered. A shared decision-making process between physician and patient may be one of the main ways to reduce patient distress or negative attitude.⁴⁰

In southern Thailand, there are about 2,400 individuals with schizophrenia. Of all of them, 520 patients receive caring from Songklanagarind Hospital, which is an 800-bed university hospital serving as a tertiary referral center in southern Thailand, and the rest receive caring from Songkhla Rajanagarindra Psychiatric Hospital, which is a 200-bed psychiatric hospital serving as a referral center in southern Thailand. As per the readmission rate from symptom relapse that was shown in this study, Songklanagarind Hospital has continued creating readmission prevention programs and working through various aspects accentuating the quality of life of individuals with schizophrenia. A previous study identified that most individuals with schizophrenia outpatients at Songklanagarind Hospital had good medication adherence and high scores of meaning in their lives. The presence of a sense of meaning in life and engaging in something that increased their lives to feel meaningful and purposeful could reduce social stigma and promote insight. Therefore, most our individuals with schizophrenia had good medication adherence being associated with their sense of meaning in their lives.²⁹ Additionally, de-stigmatization program

was created by our homestay program to rehabilitate and engage patients by boosting their social skills. This program enables the community and the patient's family to understand the patient's disease, decreasing stigma and making the patient's relationship with society more harmonious.²⁸ Therefore, the individuals with schizophrenia (62.0%) perceived a low level of stigma, and that only 1.8% of them experienced a high level of stigma in our healthcare setting.⁴ Moreover, all our inpatients with a first diagnosis of schizophrenia would engage in a discussion with our staff, aiming to discover positive meaning in their lives; and would participate in our rehabilitation program. Potentially, the reduction of patient-perceived stigma and the boosting of insight could improve their adherence to the pharmacological component of their treatment plans and reduce levels of distress.

Finally, this study was one of the first studies showing that substance use or inadequate knowledge did not increase readmission risk; not corroborating prior reports from Australia.³⁹ This may be because our study had a low sample size in regards to substance use and a relatively small number of patients with insufficient knowledge. Therefore, psychoeducation and co-morbidity prevention for individuals with a first diagnosis of schizophrenia should be highlighted accordingly.

This study had several noteworthy strengths and limitations. To our knowledge, this is the first study that explored the rate of schizophrenia readmission and its associated factors in southern Thailand. Nevertheless, it was a retrospective study reviewing computer medical records which have limitations and the potential of bias. Another drawback was that our data was quantitative, the participants were not young and the sample size restricted to individuals with schizophrenia inpatients only from our hospital instead of including other areas of Thailand. Hence, its findings may not be representative of individuals with schizophrenia throughout the whole of Thailand.

Henceforward, studies are recommended to enclose a larger number of individuals with schizophrenia, with age group and gender differences from other hospitals in Thailand. Therefore, a more comprehensive, multi-centered research study should be performed. Moreover, other studies should retain more qualitative or in-depth methods.

Conclusion

Our results suggest that half of the individuals with schizophrenia were readmitted within 5 years of their first diagnosis of schizophrenia and that the factors heightening the risk of readmission were: stressful life events, medical non-adherence, prescription changes, and lack of insight by the patient. Although our study has some methodological limitations, the results provided interesting information that can inform additional therapeutic intervention strategies. Furthermore, they emphasize the importance of implementing multimodality of treatment such as managing adverse events and reducing the likelihood of relapse by combining optimum dosing, type, and route of antipsychotic drug administration. Furthermore, at the same time, integrating pharmacological strategies with effective psychotherapeutic methods, aiming to reduce stress, gain insight, increase patient perceived life meaning and boost social integration and community acceptance.

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Conflict of interest

No conflicts of interests are declared.

References

1. Higashi K, Medic G, Littlewood KJ, Diez T, Granstrom O, De Hert M. Medication adherence in schizophrenia: factors influencing adherence and consequences of nonadherence, a systematic literature review. *Ther Adv Psychopharmacol* 2013;3:200–18.
2. Kazadi NJB, Moosa MYH, Jeenah FY. Factors associated with relapse in schizophrenia. *S Afr J Psychiatr* 2008;14:52–62.
3. Kaplan G, Casoy J, Zummo J. Impact of long-acting injectable antipsychotics on medication adherence and clinical, functional, and economic outcomes of schizophrenia. *Patient Prefer Adherence* 2013;7:1171–80.
4. Agrasuta T, Pitanupong J. Perceived stigma in patients with schizophrenia and caregivers in Songklanagarind Hospital: cross-sectional study. *Songkla Med J* 2017;35:37–45.
5. Pitanupong J, Rueangwiriyanan C. Caregiver burdens in patients with schizophrenia and related factors. *J Ment Health Thai* 2019;27:95–106.
6. Hong J, Windmeijer F, Novick D, Haro JM, Brown J. The cost of relapse in patients with schizophrenia in the European SOHO (Schizophrenia Outpatient Health Outcomes) study. *Prog Neuropsychopharmacol Biol Psychiatry* 2009;33:835–41.
7. Harrow M, Jobe TH. Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications: a 15-year multifollow-up study. *J Nerv Ment Dis* 2007;195:406–14.
8. Almond S, Knapp M, Francois C, Toumi M, Brugha T. Relapse in schizophrenia: costs, clinical outcomes and quality of life. *Br J Psychiatry* 2004;184:346–51.
9. Csernansky JG, Schuchart EK. Relapse and rehospitalisation rates in patients with schizophrenia: effects of second generation antipsychotics. *CNS Drugs* 2002;16:473–84.
10. Awad AG. Antipsychotic medications: compliance and attitudes towards treatment. *Curr Opin Psychiatry* 2004;17:75–80.
11. Suzuki Y, Yasumura S, Fukao A, Otani K. Associated factors of rehospitalization among schizophrenic patients. *Psychiatry Clin Neurosci* 2003;57:555–61.
12. Siris SG. Depression in schizophrenia: perspective in the era of "Atypical" antipsychotic agents. *Am J Psychiatry* 2000;157:1379–89.
13. San L, Bernardo M, Gomez A, Pena M. Factors associated with relapse in patients with schizophrenia. *Int J Psychiatry Clin Pract* 2013;17:2–9.
14. Chabungbam G, Avasthi A, Sharan P. Sociodemographic and clinical factors associated with relapse in schizophrenia. *Psychiatry Clin Neurosci* 2007;61:587–93.
15. Fenton WS. Comorbid conditions in schizophrenia. *Curr Opin Psychiatry* 2001;14:17–23.
16. Green AI, Canuso CM, Brenner MJ, Wojcik JD. Detection and management of comorbidity in patients with schizophrenia. *Psychiatr Clin North Am* 2003;26:115–39.
17. Berge D, Mane A, Salgado P, Cortizo R, Garnier C, Gomez L, et al. Predictors of relapse and functioning in first-episode psychosis: a two-year follow-up study. *Psychiatr Serv* 2016;67:227–33.
18. Harris MG, Henry LP, Harrigan SM, Purcell R, Schwartz OS, Farrelly SE, et al. The relationship between duration of untreated psychosis and outcome: an eight-year prospective study. *Schizophr Res* 2005;79:85–93.
19. Dolder CR, Lacro JP, Jeste DV. Adherence to antipsychotic and nonpsychiatric medications in middle-aged and older patients with psychotic disorders. *Psychosom Med* 2003;65:156–62.
20. Hudson TJ, Owen RR, Thrush CR, Han X, Pyne JM, Thapa P, et al. A pilot study of barriers to medication adherence in schizophrenia. *J Clin Psychiatry* 2004;65:211–6.
21. Valenstein M, Blow FC, Copeland LA, McCarthy JF, Zeber JE, Gillon L, et al. Poor antipsychotic adherence among patients with schizophrenia: medication and patient factors. *Schizophr Bull* 2004;30:255–64.
22. Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *J Clin Psychiatry* 2002;63:892–909.
23. Suzuki T, Uchida H, Takeuchi H, Nomura K, Tanabe A, Watanabe K, et al. Simplifying psychotropic medication regimen into a single night dosage and reducing the dose for patients with chronic schizophrenia. *Psychopharmacology* 2005;181:566–75.
24. Gaebel W, Schreiner A, Bergmans P, de Arce R, Rouillon F, Cordes J, et al. Relapse prevention in schizophrenia and schizoaffective disorder with risperidone long-acting injectable vs quetiapine: results of a long-term, open-label, randomized clinical trial. *Neuropsychopharmacology* 2010;35:2367–77.
25. Talaslahti T, Alanen HM, Hakko H, Isohanni M, Hakkinen U, Leinonen E. Change in antipsychotic usage pattern and risk

- of relapse in older patients with schizophrenia. *Int J Geriatr Psychiatry* 2013;28:1305–11.
26. Jimenez MA, Priede A, Hetrick SE, Bendall S, Killackey E, Parker AG, et al. Risk factors for relapse following treatment for first episode psychosis: a systematic review and meta-analysis of longitudinal studies. *Schizophr Res* 2012;139:116–28.
 27. Shewangizaw Z, Mukherjee R. Prevalence of relapse and associated factors in patient with schizophrenia at Amanuel mental specialized hospital, Addis Ababa, Ethiopia: institution based cross sectional study. *IJIMS* 2014;2:184–92.
 28. Taengbunngam S, Chincharoensup D, Vitayanont A. Attitudes toward mental illness of psychiatric patients, relatives of psychiatric patients and homeowners from a homestay family camp. *J Psychiatr Assoc Thailand* 2015;60:149–54.
 29. Teetharatkul T, Pitanupong J. Meaning in life and medication adherence among Thai schizophrenic patients. *J Health Sci Med Res* 2022. doi:10.31584/jhsmr.2022864.
 30. Hung YY, Chan HY, Pan YJ. Risk factors for readmission in schizophrenia patients following involuntary admission. *PLoS One* 2017;12:e0186768.
 31. Wolfe MM, Yang PH, Wong EC, Atkinson DR. Design and development of the European American values scale for Asian Americans. *Cultur Divers Ethnic Minor Psychol* 2001;7:274–83.
 32. Phanthunane P, Vos T, Whiteford H, Bertram M, Udomratn P. Schizophrenia in Thailand: prevalence and burden of disease. *Popul Health Metr* 2010;8:1–8.
 33. Anekwit N. Relapse rate of schizophrenia and other psychotic disorders in patients at mahasarakham hospital. *J DMS* 2018; 43:35–9.
 34. Alvarez-Jimenez M, Priede A, Hetrick SE, Bendall S, Killackey E, Parker AG, et al. Risk factors for relapse following treatment for first episode psychosis: a systematic review and meta-analysis of longitudinal studies. *Schizophr Res* 2012;139:116–28.
 35. Roick C, Heider D, Bebbington PE, Angermeyer MC, Azorin JM, Brugha TS, et al. Burden on caregivers of people with schizophrenia: comparison between Germany and Britain. *Br J Psychiatry* 2007;190:333–8.
 36. Brown E, Bedi G, McGorry P, O'Donoghue B. Rates and predictors of relapse in first-episode psychosis: an Australian cohort study. *Schizophr Bull Open* 2020;1. doi:10.1093/schizbullopen/sgaa017.
 37. Capite SD, Upthegrove R, Mallikarjun P. The relapse rate and predictors of relapse in patients with first-episode psychosis following discontinuation of antipsychotic medication. *Early Interv Psychiatry* 2018;12:893–9.
 38. Kreyenbuhl J, Buchanan RW, Dickerson FB, Dixon LB. The Schizophrenia Patient Outcomes Research Team (PORT): updated treatment recommendations 2009. *Schizophr Bull* 2010;36:94–103.
 39. Masakazu H, Hiroyuki K, Akane S, Shigeki Y, Nakao I. Trend survey on adverse event profiles of antipsychotic long-acting injections and oral agents using the Japanese adverse drug event report database. *Psychiatry Res* 2020;291:113249.
 40. Pitanupong J, Karakate A, Tepsuan L, Srirangnant G. Attitudes toward long-acting injectable antipsychotics among schizophrenic patients in southern Thailand: a multihospital-based cross-sectional survey. *Siriraj Med J* 2022. doi:10.33192/Smj.2022.24.