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Schizophrenia Outpatients In Yogyakarta: Evidence From Sem-Pls Modeling

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ABSTRACT

Objectives: The purpose of this study is to ascertain the prevalence of DRPs in schizophrenia patients at the PKU Muhammadiyah Hospital Yogyakarta Outpatient Psychiatric Unit by employing PCNE V9.1 and to investigate the correlation between patient characteristics and the prevalence of DRPs.

Materials and Methods: This observational study employed a longitudinal design and successive sampling methodology. This study was conducted at the PKU Muhammadiyah Gamping Hospital in Yogyakarta.103 schizophrenia patients who fulfilled the inclusion criteria constituted the sample size. Additionally, the data was examined with PCNE V9.1, NCC-MERP, and Partial Least Squares Structural Equation Modelling. The model was analysed using Partial Least Squares Structural Equation Modelling (SEM-PLS). Validity was assessed based on factor loading (≥0.40), AVE (≥0.50), and reliability through composite reliability & Cronbach's alpha (≥0.60).

Results: 278 DRPs were identified, with an average of 2.70 DRPs per patient. The most frequent DRP types involved inappropriate drug selection (40.29%), particularly due to drug-drug interactions, followed by adverse drug reactions (34.17%). Risperidone and clozapine were the most implicated drugs. The most common side effects included weight gain and sedation. Most DRPs were classified as causing no harm (56.11%), while 1.08% caused actual patient harm. These findings confirm that patient condition is the primary factor influencing DRP, while sociodemographic did not show significant relationships.

Conclusion: Although most DRPs were classified as causing no harm, regular monitoring remains essential. These findings underscore the critical role of clinical pharmacists in detecting and managing DRPs to improve treatment safety and adherence.

KEYWORDS: Antipsychotics, Drug Related Problems, PCNE V9.1, Schizophrenia

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INTRODUCTION

Schizophrenia is a group of psychotic disorders characterized by typical distortions of one's thought processes, sometimes having the feeling that one is being controlled by other forces, strange visions, perceptual disturbances, abnormal effects integrated with real or actual situations, and autism. Schizophrenia is the most common psychotic disorder. Data shows that there are 21 million people affected by schizophrenia. In Indonesia, in 2018, there were around 400,000 people with schizophrenia, or 1.7 per 1000 population [1]. The Special Province of Yogyakarta ranks second highest in Indonesia, with the number of schizophrenia patients at 10.4% per 1000 households.

Patients with schizophrenia receive therapy for a relatively long period, even for life. It is done to prevent recurrent relapses. There are two patterns of treatment therapy for schizophrenia, namely single and combination. *Combination therapy* consists of two or more antipsychotics called antipsychotic polypharmacy (APP) and is supported by support therapy (non-antipsychotic therapy)[2]. According to Dipiro et al (2020), first-line therapy of schizophrenia is an antipsychotic consisting of first-generation antipsychotics, namely typical, and second-generation antipsychotics, namely atypical [3]. The antipsychotics for schizophrenia aim to reduce symptoms, prevent relapse, and improve the patient's quality of life.

DRPs are defined as events or circumstances that actualize or have the potential to disrupt favourable health outcomes related to

drug therapy. Drug-related issues include medication errors and adverse drug events. Drug-related problems (DRPs) arise from various factors, including inappropriate drug combinations, unsuitable drug forms, and excessively high drug doses, resulting in increased morbidity, mortality, and healthcare costs[4].

In research conducted by Jayakumar et al, as many as 205 cases of DRPs were identified from 102 patients; the highest case was drug interaction, 30.2%, followed by adverse drug effects, 10.2%. Of the total 314 drugs used, risperidone, olanzapine, and lorazepam were found to be the drugs associated with the highest number of DRPs [5]. Similar research at Mutiara Sukma Mental Hospital, NTB Province, in 2020 found that the incidence of DRP was 89.5% with a total of 117 in 105 patients, with the highest case of potential adverse drug effects, which had a percentage of 76.9% with risperidone and lorazepam dominating (moderate severity) and followed by drugs without indications 10.3% [2]. In this case, pharmacists are needed to improve the safety and effectiveness of drug use so that patients can receive optimal therapy.

The possible incidence of Drug Related Problems (DRPs) must be investigated. DRPs also provide advice for secure therapeutic alternatives for patients and an understanding of the harmful consequences of DRPs on individuals. This study focuses on analyzing the relationship between variables that cause drug-related problems and the severity of events on the sociodemographic and condition of patients. These relationships will first be tested using hypotheses so that we can predict which factors most influence drug-related problems in patients with schizophrenia. This research was conducted at PKU Muhammadiyah Gamping Hospital, examining Drug-Related Problems in schizophrenia outpatients using the Pharmaceutical Care Network Europe (PCNE) V9.1 and categorizing the severity of Drug-Related Problems according to the National Coordinating Council for Medication Error Reporting and Prevention. Furthermore, to ascertain the correlation between patient features and the prevalence of DRPs in individuals with schizophrenia.

MATERIALS AND METHODS

A. Study design and participants selection

During one year, this observational study used a longitudinal design in PKU Muhammadiyah Gamping Hospital Yogyakarta. The patient criteria in this study were all outpatient schizophrenia patients who were prescribed single or combined antipsychotics with antipsychotics or non-antipsychotics at PKU Muhammadiyah Gamping Hospital in the period March to June 2023. The participants were patients who were 18-65 years old, had been taking antipsychotic therapy for at least three months, and agreed to be respondents in this study.

B. Data collection

Data was collected in one year through medical records and interviews. The patients were followed up for three months. This study used a consecutive sampling technique based on predetermined inclusion criteria to take the research sample.

C. Classification, Identification, and Assessment of DRPs

The occurrence of Drug Related Problems was assessed utilizing Pharmaceutical Care Network Europe Version 9.1. It evaluated the detrimental effects of medications, inappropriate drug combinations or interactions, the precision of drug indications, adherence to guidelines in medication usage, optimal dosage and frequency of administration, and the correct quantity of drugs for a single indication. Subsequently, an analysis was conducted using Excel to ascertain the percentage of drug-related issues encountered by schizophrenia patients utilizing PCNE V9.1.

The classification of Drug-Related Problems (DRPs) was performed based on severity ratings defined by the National Coordinating Council for Medication Error Reporting and Prevention (NCC-MERP) system. This classification includes four categories organized by the ascending severity of patient outcomes: (1) Conditions or occurrences that may lead to error (no error, subcategory A); (2) Medication errors (MEs) that occurred without causing harm to patients (subcategories B, C, and D); (3) MEs that resulted in patient injury (subcategories E, F, G, and H); (4) MEs that caused a patient's death (subcategory I)[6].

D. Statistical analysis

Data analysis was carried out using SMART-PLS software version 4.0 within the Structural Equation Modeling–Partial Least Squares (SEM-PLS) approach. SEM-PLS incorporates measurement models that evaluate the relationships between indicators and their corresponding latent constructs, with factor loadings used as indicators of construct validity and measurement reliability. Indicators with factor loadings below 0.40 were removed, while those with loadings between 0.40 and 0.70 were retained only when their inclusion did not reduce the average variance extracted (AVE) or composite reliability and when content validity considerations supported their use. A loading value of 0.40 was applied as the minimum validity threshold, accompanied by a significance level of 5%[7].

The reliability of the research instrument was assessed using composite reliability and Cronbach's alpha, which, despite differing calculation methods, both reflect the consistency of latent constructs. A minimum reliability threshold of 0.60 was adopted, with higher values indicating stronger reliability. Composite reliability values greater than 0.70 were considered indicative of satisfactory reliability. Additionally, Cronbach's alpha was examined to evaluate internal consistency, with values exceeding 0.60 signifying acceptable reliability[7]. All validity and reliability analyses were conducted using SEM-PLS with SmartPLS 4 software. The hypothesized relationships tested in this study are presented in the causal model shown in Figure 1,

which was developed based on findings from previous studies and systematic reviews.

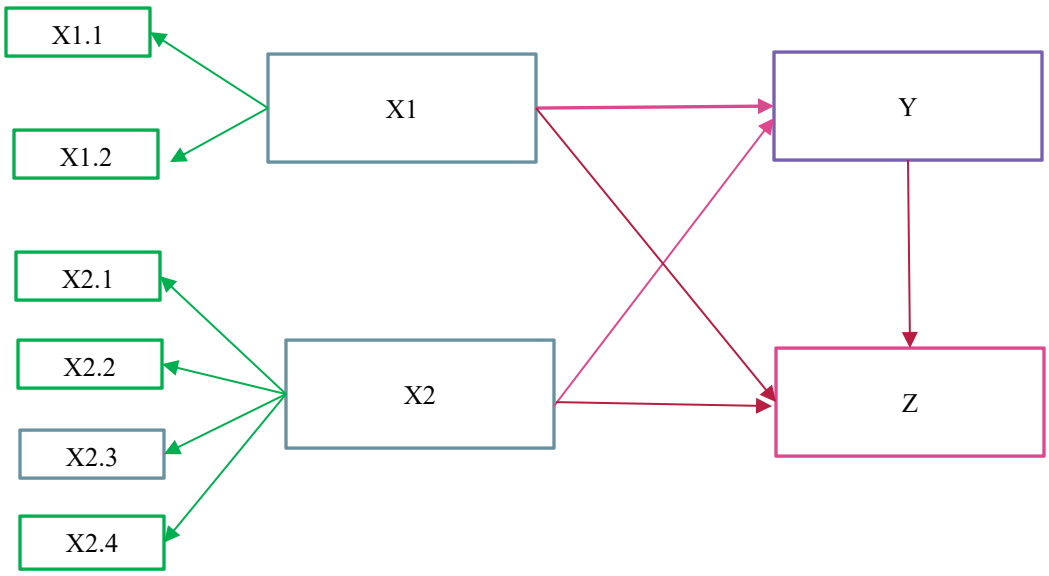

Figure 1. Causal Model

X1: sociodemographic; X1.1: Age; X1.2: occupation
X2: Patient condition; X2.1: diagnosis; X2.2: number of medications; X2.3: duration of therapy; X2.4: Comorbidities
Y: Drug Related Problem based on PCNE V9.1
Z: Severity of Drug-Related Problem based on NCC-MERP

RESULT

During the one-year investigation, 166 patients visited the psychiatry clinic as outpatients. Of them, 43 patients lacking sufficient and comprehensive medical data were excluded, resulting in 103 eligible individuals. The mean age of the patients examined was between 45 and 59 years, with 53.59% being male. Hypertension and Diabetes Mellitus were the predominant comorbidities identified in this investigation. Table 1 delineates the patient features in conjunction with their DRP status.

Table 1. Patient Characteristics

Patient Characteristics	Total (%)	Not experiencing DRP (%)	Experiencing DRP (%)
Number of patients	103	41 (39,80)	62 (60,19)
Gender			
Male	55 (53,39)	20 (36,36)	35 (63,63)
Female	48 (46,60)	21 (43,75)	27 (56,25)
Age Range			
Adolescents (10-19 years old)	5 (4,85)	2 (40)	3 (60)
Mature (20-44 years old)	41 (39,81)	17 (41,46)	24 (58,53)
Pre-elderly (45-59 years old)	45 (43,69)	17 (37,77)	28 (62,22)
Elderly (over 60 years old)	12 (11,65)	5 (41,67)	7 (58,33)
Length of Treatment (years)			
< 5 years	37	20(19,41)	17(16,50)
5-10 years	28	13(12,62)	15(12,62)
>10 years	38	18(17,47)	20(19,41)
Unknown	33 (32,04)	19 (57,57)	14 (42,42)
Amount of Drug			
1-4 drugs	94 (91,26)	37 (39,36)	57 (60,63)
5-8 drugs	9 (8,74)	4 (44,44)	5 (55,55)
Comorbidities			

Hypertension	9 (8,74)	5 (55,55)	4 (44,44)
Diabetes mellitus	5 (4,85)	2 (40)	3 (60)
Hyperlipidaemia	1 (0,97)	0 (0)	1 (100)
Anaemia	1 (0,97)	0 (0)	1 (100)
Gout	1 (0,97)	0 (0)	1 (100)
Chronic Ischemic Heart Disease	2 (1,94)	1 (50)	1 (50)
Glaucoma	1 (0,97)	0 (0)	1 (100)
without comorbidities	83 (80,58)	32 (38,55)	51 (61,44)
Jobs			
Not employed	23 (22,33)	5 (21,73)	18 (78,26)
Casual labourer	22 (21,36)	9 (40,90)	13 (59,09)
Taking care of household	14 (13,59)	4 (28,57)	10 (71,43)
Self-employed	14 (13,59)	8 (57,14)	6 (42,86)
Student/Student	11 (10,86)	5 (45,45)	6 (54,54)
Private Employee	7 (6,80)	5 (71,43)	2 (28,57)
Unknown	9 (8,74)	3 (33,33)	6 (66,67)
Plantation/Farm Labourer	1 (0,97)	0 (0)	1 (100)
Retired	2 (1,94)	2 (100)	0 (0)
Diagnosis			
Schizophrenia (F20)	64 (62,14)	19 (29,69)	45 (70,31)
Residual Schizophrenia (F 20.5)	13 (12,62)	5 (38,46)	8 (61,54)
Paranoid Schizophrenia (F 20.0)	4 (3,88)	1 (25)	3 (75)
Undifferentiated Schizophrenia (F 20.3)	5 (4,85)	0 (0)	5 (100)
Other schizophrenia	17 (16,50)	16 (94,12)	1 (5,88)

Drug-related problems (DRPs) are primarily caused by adverse effects and effectiveness, as per the PCNE V9.1 classification. The greatest concern was "inappropriate drug selection," followed by "adverse effects," "drug efficacy," "drug selection," and "dose selection." Drug selections are the most prevalent factors contributing to drug-related problems (DRP). The findings are displayed in Table 2.

Table 2. DRP Classification Based on PCNE V9.1 and Severity

Drug Related Problem	Number of DRPs	Severity		
		No harm (B, C)	Potential harm (D)	Harm (E)
DRP detected	278			
Cumulative incidence (DRP/patient)	2,70			
Drug Effectiveness				
The therapeutic effect of drugs is not optimal	18 (6,48%)	13 (8,33%)	5 (4,20%)	0 (0%)
Untreated symptoms or indications	7 (2,51%)	0 (0%)	7 (5,88%)	0 (0%)
Drug Safety				
Adverse drug Reactions occur	95 (34,17%)	50 (32,05%)	45 (37,81%)	0 (0%)
Drug selection				
Medication use not according to guidelines/formulary	13 (4,68%)	13 (8,33%)	0 (0%)	0 (0%)
No indication for the drug	1 (0,35%)	1 (0,64%)	0 (0%)	0 (0%)

Inappropriate combinations, e.g., drug-drug, drug-herbal, or drug-supplement	112 (40,29%)	55 (35,25%)	54 (45,38%)	3 (100%)
Duplication of therapeutic groups or inappropriate active ingredients	6 (2,15%)	3 (1,92%)	3 (2,52%)	0 (0%)
Too many drugs prescribed for one indication	6 (2,15%)	3 (1,92%)	3 (2,52%)	0 (0%)
Dose Selection				
Drug dosage is too low	6 (2,15%)	6 (3,85%)	0 (0%)	0 (0%)
Drug dosage is too high	2 (0,72%)	0 (0%)	2 (1,68%)	0 (0%)
Dosing frequency is too low	12 (4,32%)	12 (7,69%)	0 (0%)	0 (0%)
Dosing frequency is too frequent	0	0 (0%)	0 (0%)	0 (0%)
Total	**278**	**156 (56,11%)**	**119 (42,80%)**	**3 (1,08%)**

Figure 2 shows that there are two variables related to drug-related problems, namely X1 and X2. The severity of drug-related problems is also influenced by X1, X2, and Y. Based on the latent structure, several variables, such as X2.1, X2.3, Y2, Y5, Y7, Y8, Y9, and Y10, achieved factor loadings of less than 0.7. Therefore, to correct this, the factors must be removed so that the model achieves a high stability coefficient.

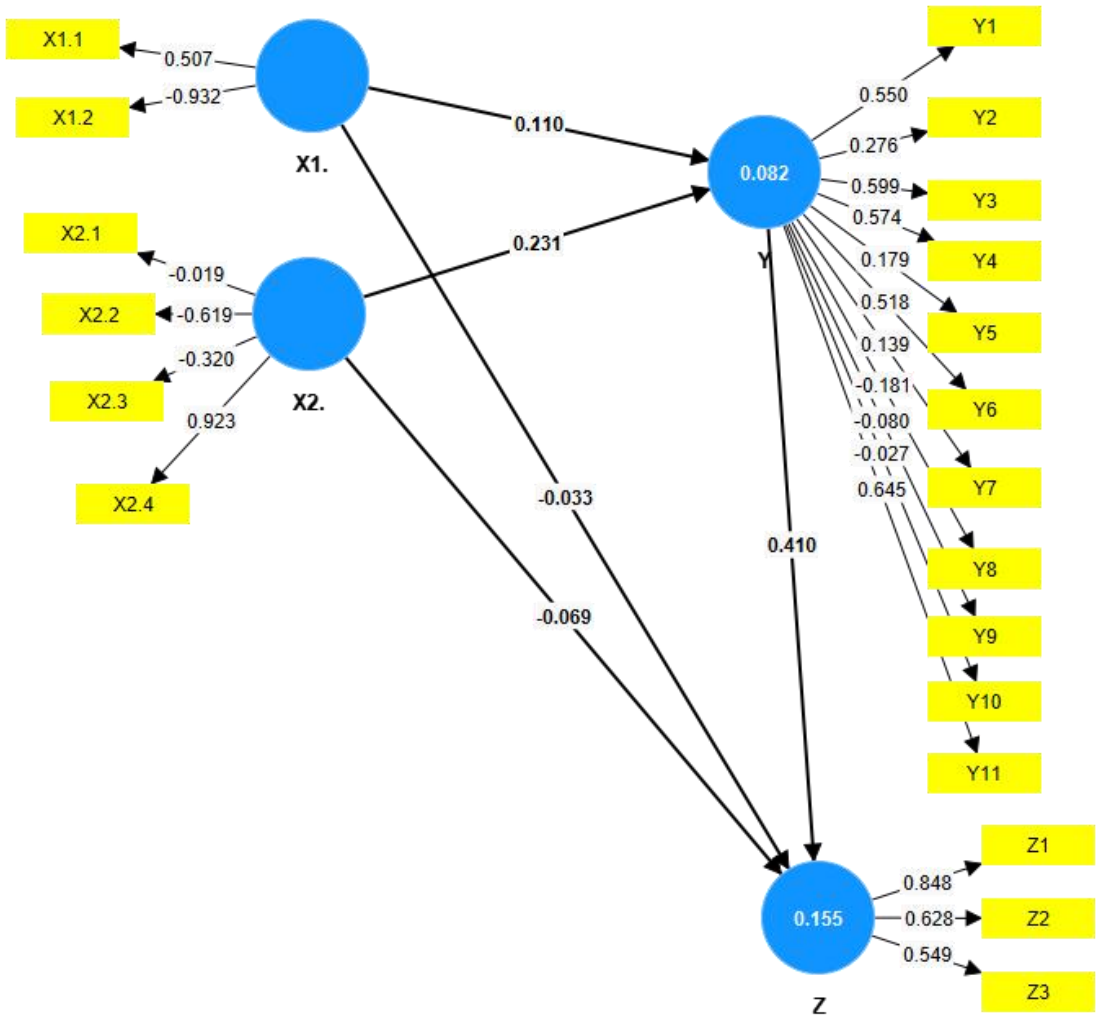

Figure 2. Initial Output Inner Model

X1: sociodemographic; X1.1: Age; X1.2: occupation
X2: Patient condition; X2.1: diagnosis; X2.2: number of medications; X2.3: duration of therapy; X2.4: Comorbidities
Y: Drug Related Problem based on PCNE V9.1
Z: Severity of Drug-Related Problem based on NCC-MERP

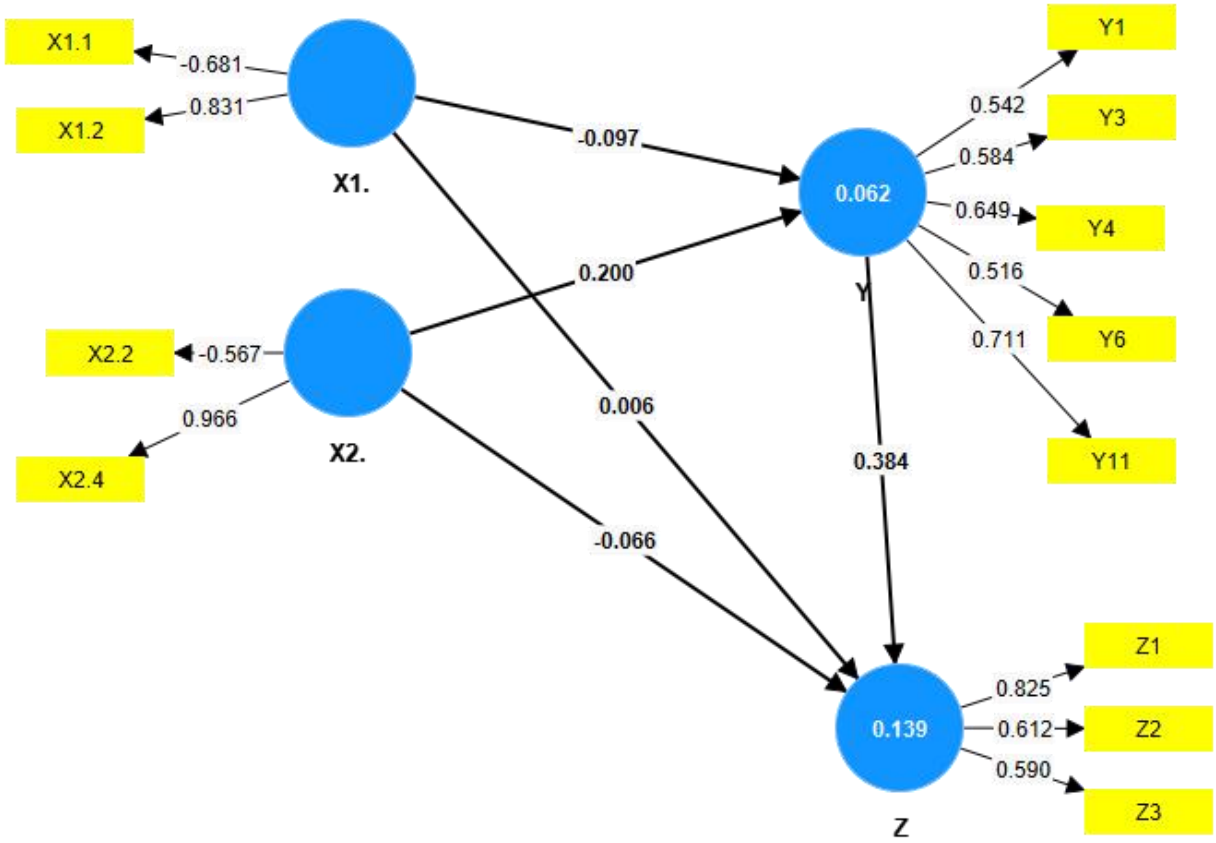

Figure 3. Inner model after removing unsaturated agents.

X1: sociodemographic; X1.1: Age; X1.2: occupation
X2: Patient condition; X2.1: diagnosis; X2.2: number of medications; X2.3: duration of therapy; X2.4: Comorbidities
Y: Drug Related Problem based on PCNE V9.1
Z: Severity of Drug-Related Problem based on NCC-MERP

A. Confirmatory Factor Analysis (CFA)

The measurement results for each construct are presented in Table 2, where individual items were evaluated to determine their respective factor loadings, reflecting the contribution of each item to the construct. Ideally, factor loadings should exceed 0.70; however, items with loadings between 0.40 and 0.70 may still be considered acceptable after further evaluation. This evaluation takes into account their effect on improving the average variance extracted (AVE) and composite reliability. Higher factor loading values indicate stronger construct validity [7]. In addition, factor loadings are required to demonstrate statistical significance, with t-values greater than 1.96 at a 5% significance level[7]. Convergent validity was assessed using AVE, with a minimum threshold of 0.50. A higher AVE value suggests that the latent construct explains a greater proportion of the variance in its indicators, indicating stronger internal consistency among the measured items [7].

Table 2. Analysis of all factors

	Cronbach's alpha	Composite reliability	Average variance extracted (AVE)
Sociodemographic	-0.38	0.287	0.578**
Patient Condition	-1.001	0.974**	0.627**
Drug Related Problem Based On PCNE V9.1	0.563	0.74**	0.366
Severity Of Drug-Related Problem Based On NCC-MERP	0.441	0.72**	0.468

The asterisk (*) shown in the Cronbach's Alpha and Composite Reliability values denotes a high level of significance or strong construct validity. This indicates that the measurements and constructs assessed demonstrate adequate reliability and consistency for use in the present analysis.

Table 3. Factor loading of 13-items

Factor	Items	Factor Loadings
Sociodemographic Related	X1.1	-0.681

	X1.2.	0.831**
Patient Condition Related	X2.2	-0.567
	X2.4.	0.966**
Drug Related Problems -	Y1	0.542
	Y11	0.711**
	Y3	0.584
	Y4	0.649
	Y6	0.516
Severity DRP -	Z1	0.825**
	Z2	0.612
	Z3	0.59

Within the framework of Structural Equation Modeling (SEM), an asterisk (*) associated with factor loadings typically signifies a high level of statistical significance or strong validity. This indicates that the observed variable exerts a substantial influence on the latent construct it represents within the SEM model

B. Sociodemographic-related factor

The composite reliability value for sociodemographic-related factors exceeded 0.70, indicating that the data were appropriate for factor analysis. Two sociodemographic items (X1.1 and X1.2) satisfied the reliability criteria and were therefore retained for subsequent analysis. Overall, all items within the sociodemographic domain were deemed reliable for measuring sociodemographic factors.

C. Patient Condition-related factor

The composite reliability value for patient condition–related factors was also above 0.70, confirming the adequacy of the data for factor analysis. Based on the evaluation of commonality, two items within this construct (X2.1 and X2.3) exhibited very low factor loadings and were consequently excluded from further analysis, as they did not adequately correlate with the other indicators representing the construct. One item (X2.2) demonstrated the lowest acceptable factor loading (0.52) but was retained because factor loadings greater than 0.40 meet the minimum acceptance threshold. In summary, items X2.1 and X2.3 were removed, while the remaining items (X2.2 and X2.4) were considered reliable indicators of patient condition–related factors, as presented in Table 3.

Table 4. Discriminant Validity based on Fornell-Larcker Criteria

Construct	Sociodemographic	Patient Condition	Drug Related Problem Based On PCNE V9.1	Severity Of Drug-Related Problem Based On NCC-MERP
Sociodemographic	0.760			
Patient Condition	-0.309	0.792		
Drug Related Problem Based on PCNE V9.1	-0.159	0.230	0.605	
Severity Of Drug-Related Problem Based On NCC-MERP	-0.034	0.020	0.367	0.684

Table 4 presents the discriminant validity assessment using the Fornell–Larcker criterion. The square root of the Average Variance Extracted (AVE), shown on the diagonal of the matrix, is higher than the correlations between constructs in the corresponding rows and columns. The square root of AVE for the sociodemographic construct was 0.760, patient condition was 0.792, drug-related problems based on PCNE V9.1 was 0.605, and severity of drug-related problems based on NCC-MERP was 0.684. These values exceeded the correlations with other constructs, indicating that each construct measured a distinct concept and that discriminant validity was established according to the Fornell–Larcker criterion.

Table 5. Discriminant Validity based on HTMT

Construct	Sociodemographic	Patient Condition	Drug Related Problem Based On PCNE V9.1	Severity Of Drug-Related Problem Based On NCC-MERP
Sociodemographic				
Patient Condition	0,843			
Drug Related Problem Based On PCNE V9.1	0,555	0,586		

Severity Of Drug-Related Problem Based On NCC-MERP	0,304	0,138	0,680

Table 5 shows the discriminant validity results based on the Heterotrait–Monotrait Ratio (HTMT). All HTMT values between constructs were below the recommended threshold of 0.85. The highest HTMT value was observed between sociodemographic and patient condition constructs (HTMT = 0.843), which remained within the acceptable range. Other HTMT values ranged from 0.138 to 0.680. These findings confirm adequate discriminant validity among all constructs based on the HTMT criterion.

Table 6. Cross Loading Indicators

Indicators	Sociodemographic	Patient Condition	Drug Related Problem Based On PCNE V9.1	Severity Of Drug-Related Problem Based On NCC-MERP
Age	-0.681	0.055	0.095	0.060
Gender	0.831	-0.375	-0.142	-0.001
Number of drugs	0.273	-0.567	-0.081	0.050
Treatment duration	-0.268	0.966	0.238	0.039
Too many drugs prescribed for one indication	0.006	0.210	0.542	0.234
Dosing frequency is too low	-0.086	0.032	0.711	0.279
Side effect	-0.137	0.191	0.584	0.192
Medication use not according to guidelines/formulary	-0.122	0.042	0.649	0.300
Drug interaction	-0.163	0.255	0.516	0.051
No harm	0.004	0.024	0.315	0.825
Potential harm	0.019	-0.012	0.143	0.612

Table 6 presents the cross-loading values for each indicator. The results show that all indicators loaded higher on their respective constructs compared to other constructs. Sociodemographic indicators (age and gender) demonstrated the highest loadings on the sociodemographic construct. Indicators related to patient condition, including number of drugs and treatment duration, showed dominant loadings on the patient condition construct. Drug-related problem indicators based on PCNE V9.1, such as inappropriate dosing frequency, side effects, and drug interactions, loaded highest on the drug-related problem construct. Severity indicators based on the NCC-MERP classification, including no harm and potential harm, demonstrated the highest loadings on the severity construct. Overall, the cross-loading analysis supports the discriminant validity of the measurement model.

D. Structural equation modelling-partial least square (SEM-PLS)

The results of the analysis at the initial validation stage using Confirmatory Factor Analysis (CFA) determined which items were suitable for inclusion in the SEM-PLS modeling. Table 2 shows that of the four primary constructs, sociodemographic, patient condition, drug-related problems (DRP), and severity, only two constructs met the AVE value of greater than 0.50, namely sociodemographic and patient condition. Meanwhile, the DRP and severity constructs were retained because their composite reliability still exceeded 0.70, indicating they were reliable for further analysis. At the CFA stage, several items showed low factor loadings and were subsequently eliminated. Items X2.1 (diagnosis) and X2.3 (duration of therapy) had the lowest loadings and were removed from the patient condition construct. Meanwhile, items with moderate loadings, such as X2.2 (number of medications), were retained because they met the minimum threshold of 0.40. Ultimately, only 13 items were declared valid and entered the SEM-PLS stage (Table 3).

When the SEM-PLS model was simulated (Figures 2 and 3), differences were observed between the valid items in the CFA and the validity results in the structural model. In CFA, all retained items were declared valid based on factor loadings, but in the SEM stage—which considers the relationships between constructs only a few constructs had a significant effect. The SEM-PLS results showed that the patient condition construct was the only factor that significantly influenced drug-related problems (Y). This was reflected in the positive and significant path coefficient value between X2 and Y, indicating that patient conditions, particularly the number of medications and comorbidities, contributed to an increase in drug-related problems. This finding was consistent with the CFA results, in which items related to patient conditions had more substantial factor loadings than those related to other constructs.

Conversely, the sociodemographic construct did not have a significant effect on DRP or severity. Although the age and occupation items met the reliability and validity requirements in CFA, their contribution in the SEM model was not strong enough to influence the outcome variables. Similarly, the DRP construct had no significant relationship with severity in the model. This difference indicates that SEM-PLS assesses items not only based on construct validity but also on their ability to explain the relationship between latent variables. Therefore, the number of "effective" items in the structural model is fewer than the items that passed CFA. Overall, 13 items were retained in the model, consisting of: Sociodemographic: X1.1 (age), X1.2 (occupation), Patient condition: X2.2 (number of medications), X2.4 (comorbidities), Drug-related problems: Y1, Y3, Y4, Y6, Y11, Severity: Z1, Z2, Z3. The reliability test showed that all constructs had a composite reliability >0.70, and Cronbach's alpha was within an acceptable range (>0.6), so all constructs were declared reliable according to the criteria of Ghozali (2016)[8]. The results of the SEM-PLS modeling are presented in Figure 5, which indicates that patient condition is the only

construct with a significant effect. In contrast, the other constructs have no significant impact on the outcome variable.

DISCUSSION

This prospective study was conducted in Indonesia to thoroughly evaluate Drug-Related Problems (DRPs) using the PCNE classification and to identify factors associated with DRPs in psychiatric outpatient units and teaching hospitals in Indonesia. Drug-related problems (DRPs) are common among people with mental illnesses, with an average of 2.70 cumulative DRPs per patient.

In this study, the incidence of DRP was dominated by men, with 6 (60%) DRP events, while women experienced only 4 (56,25%) events. This finding is consistent with the research conducted by Albayrak et al (2022) [9], which also reported a higher incidence of DRP in men than in women. Hormonal changes influence differences in drug pharmacokinetic responses in women [10]. Patients aged between 45-59 have a higher incidence of DRPs (66.7%) compared to other age groups. Older patients are at a greater risk of DRPs due to decreased organ function and age-related changes in pharmacokinetics and pharmacodynamics [11].

The length of treatment for patients who experienced DRP events was primarily more than ten years, accounting for 80,95%. Long-term drug use can increase the risk of DRP. The reason long-term drug use can risk DRP is that long-term drug use often involves multiple medications, which increases the risk of drug interactions and adverse drug reactions. Over time, the use of medicine can decrease tolerance and lead to an increase in dosage, which can result in overdosage or subtherapeutic dosage [12]. Drug selection was the most common type of DRP. The results are different compared to the study in China, where drug safety was the most common DRP[13]. Inappropriate combinations were the major subcategory in the drug selection domain. Drug interactions that occurred in schizophrenia outpatients were 25 patients with actual interactions and 26 patients with potential interactions. The number of interactions found was 112, of which 59 were classified as class C and 53 as class D. The majority of class C interactions were between antipsychotics (risperidone, haloperidol, clozapine, chlorpromazine) with trihexyphenidyl (44 cases), followed by tricyclic depressants (amitriptyline) with trihexyphenidyl and 2 cases were interactions between benzodiazepine (diazepam, clobazam) with antipsychotics (7 case). SSRI antidepressants (Fluoxetine) with trihexyphenidyl 2 cases, Class D interactions were dominated by interactions between risperidone and haloperidol (20 cases). Class D interactions were predominantly between risperidone and haloperidol (20 cases), risperidone and clozapine (12 cases), risperidone and chlorpromazine (8 cases), haloperidol and clozapine (5 cases), clozapine and chlorpromazine (4 cases), haloperidol, and chlorpromazine (4 cases).

The second most common DRP was drug safety, with the subdomain being adverse drug reactions. Adverse drug reactions (ADRs) are events caused by drugs that result in negative effects. The drugs responsible for the adverse events in this case were Risperidone, Diazepam, Clozapine, and Haloperidol. Among these, Risperidone was found to cause the highest side effects, including xerostomia (dry mouth), ocular dystonia (upward eye movements), weakness, weight gain, insomnia, blurred vision, and amenorrhea. Clozapine was the second drug to cause side effects in the adverse event population. The use of Clozapine resulted in drowsiness, blurred vision, and weight gain as side effects. Haloperidol caused drowsiness and weight gain, respectively.

Weight gain was the most common side effect found in this study. Antipsychotics differ in their receptor binding profiles, but all target D2/D3 receptors. D2/D3 antagonists can interfere with the signalling process and lead to weight gain. Other than weight gain, sedation or drowsiness was one of this study's most common side effects. Clozapine has a high affinity for histamine H1 receptors and thus has a higher sedation effect compared to other antipsychotics.

The severity of Drug Related Problems (DRPs) was primarily classified as 'no harm' according to the NCC-MERP B-C classification (56.11%), consistent with findings from many studies. The prevalence of drug-related problems (DRPs) that do not adversely affect patients has been investigated in several hospitals, including tertiary teaching institutions in Thailand and China, resulting in rates of 78.2% and 86.9%, respectively. at alignment with other studies conducted at tertiary teaching hospitals in China, the predominant drug-related problems (DRPs) classified as no harm and possible damage (B-D) constituted between 75% and 89%.[21]. These findings indicate that clinical pharmacists are crucial in recognizing and mitigating drug-related issues prior to their manifestation in patients. This study revealed that 42.80% of cases involved a drug problem necessitating monitoring to avert patient harm or intervention (D), while 1.08% indicated a drug-related issue that negatively impacted the patient, requiring pharmacist intervention (Category E). This study primarily observed the prescribing trend of two antipsychotic medications in conjunction with other pharmaceuticals, including antimuscarinics, antidepressants, and antimanic. Noted The extensive utilization of polypharmacy has led to a significant incidence of drug-related disorders (DRPs) stemming from non-adherence. This non-compliance pertains to insufficient information regarding drug usage, indifference towards medication adherence, and challenges in precise medication management. The counsel provided by clinical pharmacists is crucial for enhancing patient medication adherence and mitigating drug-related problems (DRPs).

Preliminary analysis using CFA shows that of the four constructs, sociodemographic, patient condition, drug-related problems (DRP), and severity, only sociodemographic and patient condition meet the AVE > 0.50 criterion. The DRP and severity constructs were retained because they had composite reliability values > 0.70[7];At this stage, several items were eliminated due to low factor loadings, including X2.1 (diagnosis) and X2.3 (duration of therapy), resulting in a total of 13 items deemed valid for proceeding to SEM-PLS modelling. At the SEM-PLS stage, differences in results were found compared to CFA. Although all items were construct valid in CFA, not all constructs had a significant effect in the structural model. Only the patient condition construct was found to have a significant effect on DRPs, mainly influenced by the number of medications and comorbidities that increase the risk of medication-related problems. This finding aligns with studies indicating that clinical factors are the primary determinants of DRPs [14].

Conversely, the sociodemographic construct did not have a significant effect on DRP or severity, despite the items being valid in the CFA. This shows that SEM-PLS assesses not only construct validity but also the strength of the relationship between latent variables. The DRP construct also did not have a significant relationship with severity in the final model. All constructs had composite reliability greater than 0.70 and Cronbach's alpha greater than 0.60, and were thus deemed reliable. These findings confirm that patient condition is the primary factor influencing DRP, while other factors did not show significant relationships. The findings align with the research by Aldila Satria and Supardi (2021), indicating a correlation between the quantity of drugs or patient condition affecting DRP[15]. By contrast, a study conducted by Octavia et al. (2025) employed structural equation modelling (SEM) using partial least squares (PLS) in related pharmacoepidemiologic research, such as the assessment of determinants of medication adherence, to simultaneously assess interrelationships among multiple latent constructs. This study found that medication problems are influenced by medication regimens or the number of medications, socioeconomic status, and pharmaceutical services. These factors also affect treatment outcomes[16]. This instrument can be used to identify patients at high risk of DRP and can be applied more widely after adjustments for the regional context.

This study has several limitations. First, data collection is only based on medical records and interviews, so the data generated is only based on the medical records of PKU Muhammadiyah Gamping Hospital. The variation in the number of DRPs is manageable due to limited information. Second, due to the limited data, this study could only analyze some PCNE V9.1 categories in the literature review.

CONCLUSION

This research indicates a significant prevalence of Drug-Related Problems (DRPs) among outpatient psychiatric patients in Indonesia, averaging 2.70 DRPs per patient. Most drug-related problems (DRPs) were associated with drug selection, particularly inappropriate drug combinations, as well as side effects like weight gain and sedation, notably from risperidone and clozapine. The primary determinant of the incidence of DRPs was the quantity of medications taken, particularly among patients aged 45-59 years and those receiving long-term therapy. Most DRPs were classified as "no harm"; however, ongoing monitoring is necessary to avert potential serious consequences. The findings highlight the essential function of clinical pharmacists in identifying and addressing drug-related problems to enhance patient safety and adherence to treatment.

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Conflict of interest

No conflict of interest