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Effectiveness of clinical pharmacist interventions in optimizing pharmacotherapy for somatic comorbidities in serious mental illness: A clinical audit

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ABSTRACT

Background: Clinical pharmacists significantly improve pharmacotherapy outcomes. Patients with serious mental illness (SMI) represent a group particularly vulnerable to medication mismanagement, potentially benefiting from pharmaceutical care targeting medication appropriateness.

Objective: This study aimed to assess the prevalence of inappropriate medication for somatic comorbidities in SMI patients and to evaluate the impact of clinical pharmacist-led interventions.

Methods: A pre-post intervention audit involving clinical pharmacist intervention was conducted on SMI patients with somatic comorbidities in a psychiatric clinic in Greece. A comprehensive medication review was undertaken by a clinical pharmacist. The Medicines Appropriateness Index (MAI) and Assessment of Underutilization of medication (AOU) instruments were used to gauge pharmacotherapy appropriateness before and after intervention. Physician acceptance rates and clinical significance were also noted. Statistical analysis employed descriptive and inferential methods, with a significance level set at $\alpha = 0.05$.

Results: A total of 58 patients were reviewed. Most patients (75.86%) were being inappropriately treated at baseline, versus 15.52% post-intervention. The pharmacist proposed 107 interventions of which 104 (97.2%) were physician-accepted. Changes in MAI and AOU identified improved medication appropriateness post-intervention [$\chi^2 = 33.029$, $p < 0.005$]. Pharmacist interventions resulted in more (52.1%, $n = 25$), less (16.7%, $n = 8$) and no changes (31.2%, $n = 15$) in the total number of prescribed medicines [median difference:1, $p < 0.005$]. From 49 medication initiation recommendations, the most prescribed medicines were statins for primary or secondary prevention ($n = 21$, 42.8%), aspirin for primary or secondary prevention ($n = 9$, 18.36%) and metformin ($n = 4$, 8.2%).

Conclusion: SMI patients had a high prevalence of physical comorbidities, mainly cardiovascular disease, and a high ratio of inappropriate medication treatment. Intervention by a clinical pharmacist significantly improved medication appropriateness and led to the adoption of a new standard of care, to be checked with re-auditing.

Introduction

Serious mental illness (SMI), which encompasses conditions like schizophrenia, bipolar disorder, and severe depression, significantly impacts mental health.[1] Individuals with SMI exhibit increased morbidity and mortality rates compared to the general population.[2–6] This disparity is further heightened by a higher prevalence of somatic comorbidities, including cardiovascular disorders (CVD), COPD, cancers, diabetes, and liver diseases in those with SMI.[6] Notably, 74% of SMI patients who died in psychiatric settings had comorbidities like hypertension, diabetes, and CVD.[5] These somatic illnesses, particularly CVD, play a major role in the elevated mortality rates within this group.[2,5]

Healthcare access inequalities and utilization barriers contribute significantly to these adverse outcomes.[2] An interesting observation is that individuals with SMI and concurrent somatic disorders are more likely to be hospitalized than those with the same somatic conditions alone.[6] Respiratory disorders and CVD are the leading causes of mortality in psychiatric hospitals,[5] highlighting the need for improved pharmacotherapy management to optimize disease outcomes in SMI.[6]

Inappropriate or suboptimal treatment is a common issue in SMI.[7,8] Under-diagnosis and under-treatment of somatic comorbidities in these

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patients are well-documented.[9,10] Factors contributing to this include problematic interdisciplinary collaboration between psychiatric and non-psychiatric clinicians, compounded by stigma, prejudice, and communication challenges.[2] The lack of preparedness among psychiatric clinicians for treating somatic illnesses and unfamiliarity with psychiatric conditions among non-psychiatric clinicians further exacerbates the issue.[2] Patient-related challenges such as disease unawareness, medication non-adherence, need for support, and financial barriers also impede effective care.[2] Therefore, enhancing interdisciplinary cooperation among healthcare professionals is essential for providing comprehensive care to SMI patients, including screening and treatment for conditions like CVD and diabetes. Additionally, it has been observed that SMI patients often receive fewer medications for somatic disorders compared to those without mental illness.[11] These factors underscore the critical role of clinical pharmacists in optimizing pharmacotherapy for this vulnerable population.[1]

Evidence strongly supports the involvement of clinical pharmacists in hospitalized patient care, demonstrating significant positive clinical outcomes.[1,12–14] Pharmacists are pivotal in optimizing medication therapy for psychiatric patients.[14] Their roles encompass pharmaceutical care, medication therapy management (MTM), identifying and addressing drug-related problems (DRP), reducing polypharmacy, and various interventions to enhance healthcare suitability and decrease health disparities in SMI.[1,14] Crucially, the clinical pharmacist-patient relationship is key to maximizing treatment efficacy and minimizing adverse events through strategies that empower patients and increase adherence. A common issue in SMI care is the exclusion of patients from discussions about their medication, leading to uninformed and potentially harmful self-directed pharmacotherapy decisions.[14] This can result in serious adverse events and a cascade of negative health and socioeconomic outcomes.[14] Hence, activating the clinical pharmacist-patient relationship within an integrated, multidisciplinary somatic healthcare framework in SMI settings is of utmost importance.[2] The pharmacist-led care service actively involves patients in decision-making, which evidence shows can optimize clinical outcomes.[14] In Greece, mental illness, including SMI, requires dedicated attention and improvement from healthcare professionals, with significant gaps in care.[15–17] Epidemiological studies indicate a rising trend in psychiatric diseases within the Greek population, accompanied by high rates of somatic co-morbidity.[5,18,19] A substantial proportion, around one third of the Greek population, may experience mental illness in their lifetime, leading to a considerable socioeconomic burden.[19] This trend could be attributed to the growing elderly population in Greece.[19] Notably, respiratory and cardiovascular diseases are primary causes of death in psychiatric hospital settings.[5] Discrimination against individuals with mental illness, coupled with reluctance and stigma among Greek workers and healthcare professionals, complicates patient care, often leading to inappropriate therapy, undertreatment, misdiagnosis, and adverse events.[7,16,20] Integrating clinical pharmacists into healthcare teams for SMI patients can bridge the gap between somatic and psychiatric care, enhancing the quality of pharmacotherapy and reducing risks for this vulnerable group.[2] However, in Greece, the role of the clinical pharmacist is still in its infancy, with limited exploration and implementation to date.

To the best of our knowledge, no studies have yet investigated the impact of clinical pharmacist interventions on medication appropriateness and underutilization in the Greek context. Considering the identified gaps in the care of SMI patients with somatic comorbidities, particularly in the Greek healthcare system, this study aims to:

Evaluate the Impact of Clinical Pharmacist Interventions: We intend to assess how clinical pharmacist-led pharmaceutical care interventions influence the appropriateness of pharmacotherapy for somatic comorbidities in SMI patients. This includes examining medication selection, dosing, adherence, and overall management.

Analyze Medication Appropriateness and Utilization: The study will investigate medication underutilization and appropriateness in SMI patients, using tools such as the Medicines Appropriateness Index (MAI) and the Assessment of Underutilization of Medication (AOU).

Methods

Ethical approval

Our study was conducted as a clinical audit rather than traditional research. Clinical audits are designed to improve patient outcomes by systematically reviewing clinical practices, comparing them to established standards of care and implementing necessary changes. As such, they differ from research studies in that they are meant to evaluate existing practices and seek ways to improve them within the framework of routine clinical practice.

In line with standard practice for clinical audits, ethical approval and informed consent were not required for our study. Despite this, ethical approval was sought from the clinic's Ethics Committee, but a waiver was issued instead.

Study population and setting

The clinical audit took place in “Agia Aikaterini,” a private mental health hospital in Greece with a capacity of 191 beds. The facility operates a single inpatient pharmacy, managed by a hospital pharmacist, catering exclusively to inpatients. In this setting, prescribing and treatment decisions are solely made by the attending physician, with no clinical pharmacist involvement. Medications are dispensed daily by the hospital pharmacist.

Inclusion criteria

The audit encompassed all inpatients at ‘Agia Aikaterini’ who met the specific criteria over a four-month period. This timeframe was selected to provide a comprehensive snapshot of patient data, ensuring a robust sample for the clinical audit. Eligibility required the presence of SMI and at least one concurrent somatic disorder. SMI was defined per the criteria of a non-organic psychosis diagnosis, ongoing treatment for a minimum of two years, and a score of 50 or less on the Global Assessment of Functioning (GAF) scale.[21] Non-organic psychosis diagnoses were classified according to the 10th revision of the International Classification of Diseases (ICD-10), as detailed in Table 1. The GAF scale measures functional ability, with scores of 50 or below indicating significant impairment in social or occupational functioning.

The clinical pharmacist utilized the Electronic Medical Records (EMR) system to identify potential participants, and a clinical psychologist assessed each subject's GAF score to determine eligibility. The medication review process, conducted as part of the audit, was completed within a matter of days. Recommendations derived from this review were communicated collectively to the attending physician for all patients at once, thereby eliminating the possibility of intervention spill-over effects among the specific patient population.

Table 1
ICD-10 codes for the diagnosis criterion.

ICD-10 code	Description
F20	Schizophrenia
F21	Schizotypal disorder
F22	Persistent delusional disorders
F24	Induced delusional disorder
F25	Schizoaffective disorders
F28	Other nonorganic psychotic disorders
F29	Unspecified nonorganic psychosis
F30	Manic episode
F31	Bipolar affective disorder
F32.3	Severe depressive episode with psychotic symptoms
F33.3	Recurrent depressive disorder, current episode severe with psychotic symptoms

Development of the data collection tool

A comprehensive data collection tool was meticulously developed, undergoing both pretesting and pilot testing to ensure effective data capture for the clinical audit. This tool was utilized by the clinical pharmacist for data collection, medication reviews, medication therapy management, and documentation. DRPs and pharmacist recommendations were systematically communicated to the treating physician.

Structure of the tool

The data collection form, both pretested and pilot-tested, comprised five key sections (as detailed in Table 2). Section 1 focused on gathering all relevant patient clinical and demographic data. Sections 2 and 3 were designed to assess the appropriateness of pharmacotherapy before and after the clinical pharmacist's intervention. This assessment employed slightly modified versions of the MAI and the AOU tools.

Table 2
Data collected and documented during the clinical audit.

Section 1: Patient clinical and demographic history	
• Demographic data	
• Mental and physical diagnoses	
• Clinical laboratory test results	
• Current and past medication history	
• Allergies and adverse events	
Section 2*: Modified[a] MAI instrument	
Criterion	Relative weight
• Appropriateness of drug indication	3
• Appropriateness of treatment duration	3
• Effectiveness of prescribed medicine for the condition	2
• Dosage appropriateness	2
• Presence of clinically significant drug-disease interactions	2
• Presence of clinically significant drug-drug interactions	2
• Medication price economics among alternatives	1 1
• Presence of avoidable medication duplications	1
• Practicality of directions	1 1
Section 3*: Modified[b] AOU instrument	
• The presence of an omission of a needed drug per each active and confirmed ICD-10 diagnosis per patient.	
• Details of the drug needed and recommendations of the clinical pharmacist when relevant.	
Section 4: DRPs and clinical pharmacist interventions	
• List of all clinical pharmacist identified DRPs	
• List of all clinical pharmacist recommendations	
• Physician acceptance per recommendation	
• Total number of interventions approved or rejected	
• Drug costs per patient per day before and after the intervention.	
Section 5: Importance evaluation of clinical pharmacist intervention Each intervention was classified under one of the following grades by 2 independent raters[26]:	
• Grade 1: Intervention is detrimental for patient well-being	
• Grade 2: Intervention has no significance to patient care	
• Grade 3: Significant intervention but does not reflect into improved patient care	
• Grade 4: Significant intervention that leads to improved patient care	
• Grade 5: Very significant intervention that prevents major organ failure or adverse event of similar importance.	
• Grade 6: Potentially mortality-preventing intervention	

MAI: Medicines Appropriateness Index.
AOU: Assessment of Underutilization of medication.
DRP: Drug-related problems.
* Items were captured twice per patient per intervention, before and after receiving clinical pharmacist interventions.
[a] Correct directions criteria omitted due to evaluation within institutional setting.
[b] ICD-10 codes were used, US-specific "Veteran affairs drug class code" was omitted.

Modifications to MAI and AOU instruments

The original MAI, typically consisting of 10 criteria with a weighting scheme for summated scoring per drug,[22] was adapted for this study. In the context of institutional care, the criterion evaluating correct directions was excluded, leading to a modified 9-question MAI with a maximum score of 16 points per drug. The AOU instrument[23] underwent modifications where ICD-10 codes replaced ICD-9, and the "Veteran Affairs drug class code" was omitted, as it is relevant only for studies in the United States. The clinical pharmacist calculated summated MAI and AOU scores for each patient at baseline and post-intervention.

Documentation of DRPs and recommendations

Section 4 enabled the documentation of identified DRPs, associated clinical pharmacist recommendations, and the physician's acceptance of these recommendations. A DRP was defined as every instance where the MAI and/or AOU scores were above 0, which indicated either a potentially inappropriately used or a potentially inappropriately omitted medication.

Rating the importance of recommendations

Section 5 involved evaluating the significance of the recommendations. A random sample of 15 patients, selected using a "random sequence generator",[24] was assessed by three independent raters: a Professor of Clinical Pharmacology (Rater A), a General Practitioner (Rater B), and the clinical pharmacist (Rater C). The importance of the recommendations was graded accordingly [Section 5; Table 2]. Table 2 provides a summary of the items included in each section of the data collection form.

Statistical analysis

Descriptive and inferential statistics were conducted using SPSS v.20 (IBM Corp.). Two-sided significance level alpha = 0.05 was applied.

Normality testing and medication appropriateness

The Shapiro-Wilk's test was used to assess the normality of the data. Medication treatments were deemed appropriate if both the MAI and AOU scores were zero. Any other score indicated inappropriate medication use.

Comparative analysis methods

To compare the proportion of inappropriate medication treatments before and after the intervention, McNemar's test with continuity correction was utilized.[25,26] The Wilcoxon Signed Rank Test was applied to assess changes in the number of medications prescribed for somatic comorbidities per patient and to evaluate the median cost differences pre- and post-intervention.

Exploratory analysis

Chi-square tests were conducted to explore associations between variables such as gender, age group, GAF score, mental diagnosis, presence of somatic disease, and baseline medication appropriateness. The Sign Test with continuity correction was used to compare the differences in MAI and AOU scores before and after the intervention.

Intervention self-assessment and reliability testing

The clinical pharmacist conducted a self-assessment of all interventions using a 6-item Likert scale (detailed in Table 2, Section 5).[27] To determine the inter-rater reliability, Krippendorff's Alpha statistic

was used.[28] This statistic was chosen due to its ability to handle weighted ordinal variables and to accommodate ratings from multiple raters. Additionally, percentage agreement calculations were performed for all ratings and specifically between the two independent raters.

Results

Demographic and clinical characteristics

Out of 235 screened patients, 58 met the inclusion criteria, with ages ranging from 32 to 90 years and body weights from 43 to 160 kg (75% ≤ 89 kg). Their GAF scores varied from 11 to 50, with 75% scoring below 34. The female to male ratio was approximately 2:1. The patients presented with 25 different somatic illnesses (Table 4), primarily essential hypertension (48.3%), type 2 diabetes (20.7%), and iron deficiency anemia (19%). The illnesses were categorized into six major groups: CVD (75.9%), diabetes (20.7%), lipidaemia (8.6%), cancer (breast cancer exclusively in women), gastrointestinal diseases (17.2%), and others (37.9% including anemia, hyperuricemia, hypothyroidism, etc.). CVD, including hypertension, was the most prevalent (75.9%). Schizophrenia (F20) was the most common mental diagnosis with no gender bias, while other mental health conditions were predominantly found in women. No association was found between gender and CVD [$\chi2 = 0.002$, $p = 0.965$], or age and somatic diseases [$\chi2 = 1.148$, $p = 0.563$]. A significant association existed between gender and diabetes [$\chi2 = 5.089$, $p = 0.024$]. Tables 3 and 4 summarize these demographic and clinical characteristics.

Medication appropriateness before and after intervention

Prior to the clinical pharmacist intervention, 75.86% ($n = 44$) of patients received inappropriate medication. The median MAI score was 2 (range 0–20), and for AOU, it was 0 (range 0–3). The interventions included medication initiation, replacement, cessation, dosage/timing changes, specialist referrals, and weight reduction suggestions (Fig. 1). Post-intervention, the MAI range narrowed to 0–3 and the AOU range to 0–1, with medians of 0. Table 5 details these changes. Nine patients (15.52%) continued receiving potentially inappropriate medications post-audit (Fig. 2). There was significant reduction in the proportion of inappropriate medication treatments [$\chi2 = 33.029$, $p < 0.005$]. The total number of prescribed medications for somatic comorbidities increased by 23.28%, with a median post-intervention difference of 1 ($z = 3.039$, $p < 0.005$). The intervention led to an increase in the total number of prescribed medications in 52.1% of cases ($n = 25$), a decrease in 16.7% ($n = 8$), and no change in 31.2% ($n = 15$), with a median difference of 1 ($p < 0.005$). The most common new prescriptions were statins, aspirin, and metformin. Medicines stopped were proton pump inhibitors (2 cases), iron sulfate (2 cases), antiplatelets (2 cases), antidiabetics (1 case) and spironolactone (1 case). We believe this result to be a normal variation of the multiple types of interventions, since no trend was identified among the 8 patients who were receiving fewer medicines post-audit.

Clinical significance of interventions

The clinical pharmacist classified 67.3% of interventions as Grade 4, 14% as Grade 5, and 18.7% as Grade 3, with none in grades 1, 2, or 6 (Table 6). There was low agreement among the raters (Krippendorff's Alpha $\alpha = 0.19$, Table 7). Rater A rated most interventions as Grade 4, while Rater B provided a broader range of ratings, including one intervention as harmful. The percentage agreement between raters A and B was approximately 53.49%, with complete agreement observed in 23 out of 43 instances. This indicates a moderate level of agreement in their assessments. When the clinical pharmacist's self-ratings are included in the calculation, the percentage agreement decreases to 32.56%, corresponding to agreement in 14 out of 43 instances.

Discussion

This clinical audit aimed to investigate the incidence of inappropriate medication use in SMI patients with physical disorders and the impact of clinical pharmacist interventions on medication appropriateness. Our findings reveal that a significant majority of SMI patients with comorbidities were prescribed potentially inappropriate medications, as

Table 3
Sample characteristics, sub-grouped by mental ICD-10 code and gender.

	Overall	F20	F22	F25	F31	F32.3	F33.3
	N = 58	*N* = 33	N = 9	N = 1	N = 9	N = 5	N = 1
Age in years, Mean ± SD	61.4 ± 12.8	57.03 ± 12.6	72.1 ± 8.5	55*	63.2 ± 10.6	68.6 ± 14.5	64*
Gender, N (%)							
Female	37 (63.8)	16 (48.5)	7 (77.8)	1 (100.0)	7 (77.8)	5 (100.0)	1 (100.0)
Male	21 (36.2)	17 (51.5)	2 (22.2)	0 (0.0)	2 (22.2)	0 (0.0)	0 (0.0)
Weight in kg							
Female, Median [IQR]	71.0 [17]	71.0 [21]	70.0 [32]	60*	72.0 [25])	60.0 [15]	75*
Male, Mean ± SD	84.8 ± 20.9	83.9 ± 22.6	95.5 ± 13.4	–	82.0 ± 9.9	–	–
GAF score, Median [IQR]							
Female	25.0 [13]	21.0 [8]	21.0 [10]	49*	45.0 [28]	30.0 [7]	50*
Male	22.0 [13]	21.0 [10]	42.5 [–]	–	26.0 [–]	–	–
Number of somatic diagnoses, Median [IQR]							
Female	2 [1]	1.5 [1]	2 [0.5]	2 [0]	2 [2]	1 [1]	1 [0]
Male	2 [1]	1 [1]	2.5 [0.5]	–	2.5 [0.5]	–	–
Number of medicines for somatic diagnoses pre-audit, Median [IQR]							
Female	2 [2]	2.5 [2.25]	2 [1]	2 [0]	2 [3]	1 [1]	1 [0]
Male	2 [1]	2 [1]	4 [2]	–	3 [1]	–	–

F20: Schizophrenia, F22: Persistent delusional disorders, F25: Schizoaffective disorders, F31: Bipolar affective disorder, F32.3: Severe depressive episode with psychotic symptoms, F33.3: Recurrent depressive disorder, current episode severe with psychotic symptoms.

* There is only one case in this subgroup. M: Mean, SD: Standard Deviation, IQR: Interquartile range.

Table 4
Prevalence of somatic diseases sub-grouped by gender and age.

ICD-10 code	Somatic illness description	n(%)						Total n (%)
		Female			Male			
		30–50 years	50–65 years	>65 years	30–50 years	50–65 years	>65 years	
C50	Malignant neoplasm of breast	1(1.7)	1(1.7)	–	–	–	–	2(3.4)
D50	Iron deficiency anemia	–	4(6.9)	2(3.4)	–	4(6.9)	1(1.7)	11(19)
E03	Other hypothyroidism	–	–	2(3.4)	1(1.7)	–	–	3(5.2)
E05	Thyrotoxicosis	–	1(1.7)	–	–	–	–	1(1.7)
E11	Non-insulin-dependent diabetes mellitus)	1(1.7)	8(13.8)	2(3.4)	–	–	1(1.7)	12(20.7)
E78	Disorders of lipoprotein metabolism and other lipidemias	1(1.7)	–	2(3.4)	1(1.7)	–	1(1.7)	5 (8.6)
E79.0	Hyperuricemia without signs of inflammatory arthritis and tophaceous disease	–	–	2(3.4)	1(1.7)	1(1.7)	–	4(6.9)
G40	Epilepsy	–	–	–	–	1(1.7)	–	1(1.7)
I10	Essential hypertension	1(1.7)	11(19)	7(12.1)	4(6.9)	4(6.9)	1(1.7)	28(48.3)
I20	Angina pectoris	–	1(1.7)	–	–	2(3.4)	–	3(5.2)
I25	Chronic ischaemic heart disease	–	2(3.4)	3(5.2)	–	1(1.7)	–	6(10.3)
I49	Other cardiac arrhythmias	1(1.7)	–	–	1(1.7)	1(1.7)	1(1.7)	4(6.9)
I50	Heart failure	–	1(1.7)	1(1.7)	–	1(1.7)	–	3(5.2)
I77.1	Stricture of artery	1(1.7)	–	–	–	–	–	1(1.7)
I79.2	Peripheral angiopathy in diseases classified elsewhere	–	–	1(1.7)	–	–	–	1(1.7)
I80	Phlebitis and thrombophlebitis	–	–	–	–	1(1.7)	–	1(1.7)
I87.2	Venous insufficiency (chronic, peripheral)	1(1.7)	–	–	–	–	–	1(1.7)
K20	Esophagitis	–	1(1.7)	1(1.7)	–	–	–	2(3.4)
K21	Gastro-esophageal reflux disease	1(1.7)	–	–	1(1.7)	–	–	2(3.4)
K26	Duodenal ulcer	–	–	–	–	1(1.7)	–	1(1.7)
K29	Gastritis and duodenitis	–	–	1(1.7)	1(1.7)	1(1.7)		3(5.2)
K58	Irritable bowel syndrome	–	–	1(1.7)	–	–	–	1(1.7)
L93.1	Subacute cutaneous lupus erythematosus	–	–	–	–	1(1.7)	–	1(1.7)
M10	Gout	–	–	–	1(1.7)	–	–	1(1.7)
K51.0	Ulcerative (chronic) enterocolitis	1(1.7)	–	–	–	–	–	1(1.7)

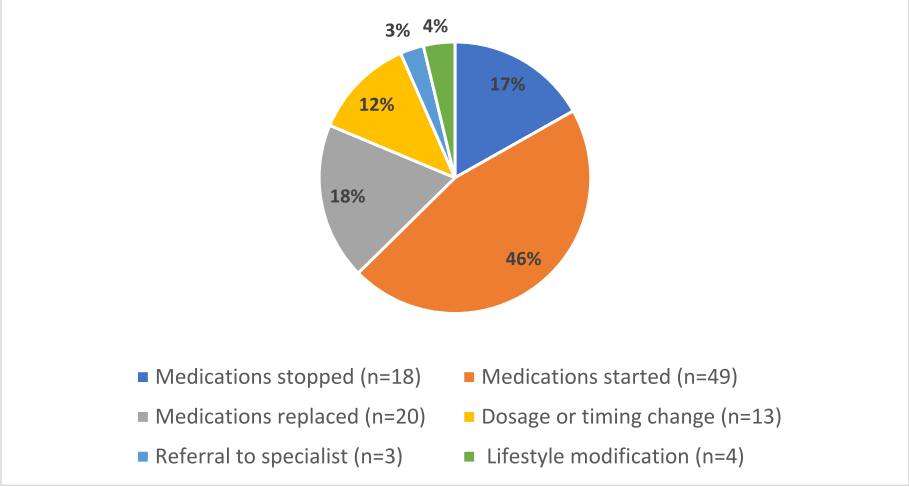

Fig. 1. Types of clinical pharmacist interventions (n = 107) proposed for 48 patients.

determined by the MAI and AOU instruments. Post-intervention, the percentage of patients receiving inappropriate treatments decreased notably to 15.52%. This improvement underscores the potential value of clinical pharmacist interventions within interdisciplinary healthcare teams, particularly in settings similar to ours.

Despite the overall success in reducing inappropriate medication use, a subset of patients (15.52%) continued to receive treatments deemed inappropriate post-intervention. This persistence can be attributed to several factors. In most cases, patient or physician preference to continue certain medications over their less expensive alternatives led to MAI scores above zero, resulting in these treatments being categorized as inappropriate, despite their clinical suitability. This highlights the challenges in balancing cost considerations with patient and physician preferences. Additionally, one specific instance involved a significant drug-drug interaction; the treatment regimen remained unchanged due to the patient's stable condition and ongoing close monitoring, reflecting the complex decision-making process in managing SMI patients. Other cases were related to a hesitancy to introduce new medications for conditions potentially not adequately addressed and the necessity of continuing off-label medication use due to the lack of suitable alternatives. These scenarios underscore the intricate considerations and challenges in optimizing medication management for SMI patients, illustrating the balance required between achieving ideal pharmacotherapy outcomes and adhering to the practicalities of individual patient care.

Regarding the pharmacist-physician relationship, it is important to clarify the nature of their interaction within the context of this study. Both the clinical pharmacist and the physicians involved were full-time

Table 5
Pharmacotherapy characteristics and appropriateness indices pre- and post clinical pharmacist intervention.

	Pre-intervention	Post-intervention	*P*-value
Appropriateness Measure for all patients, median [IQR], N = 58			
MAI score	2.0 [5]	0 [0]	<0.001*
AOU score	0 [1]	0 [0]	<0.001*
Appropriateness Measures for patients with proposed interventions, median, N = 48			
MAI score	2.5	0	<0.001*
AOU score	1	0	<0.001*
Number of medications for somatic disorders, Median [IQR], *N* = 48			
	2 [3]	3 [3]	0.002**

IQR: Interquartile range.
* Related samples sign test.
** Related samples Wilcoxon signed rank test.

colleagues working in the same institution. Their professional relationship was characterized primarily by routine, daily interactions that are typical of colleagues in a clinical setting. This study did not involve any extraordinary collaboration or interaction beyond what is commonly observed among healthcare professionals in a hospital environment. Therefore, the high acceptance rate of the pharmacist's recommendations is reflective of the merit of the recommendations themselves rather than any special interpersonal influence or existing collaboration beyond the usual professional working relationship.

This is the first study in Greece assessing medication appropriateness pre- and post-clinical pharmacist intervention in SMI patients with somatic comorbidities. It uniquely evaluates the impact of clinical pharmacist interventions on medication appropriateness in this group within the Greek healthcare setting, utilizing both MAI and AOU tools.

This study highlights the prevalence of inappropriate pharmacotherapy in SMI, underscoring the importance of multi-disciplinary treatment approaches for somatic comorbidities. In our sample, 76% of patients were identified as receiving inappropriate treatment, based on the MAI and AOU assessments. Notably, 40% were under-medicated for their conditions, aligning with existing research indicating undertreatment in SMI patients. The co-occurrence of positive MAI and AOU scores pre-clinical pharmacist intervention may indicate the severity of treatment inappropriateness. Supporting this, a meta-analysis[11] suggests that SMI patients typically receive fewer medications for physical diagnoses compared to the general population. Our study corroborates this, finding 43% of patients required 1 to 3 additional medications for their physical conditions, as per clinical guidelines. Coupled with the high MAI scores for current medications, 44 patients (75.86% of the sample) were inappropriately treated for their somatic comorbidities. Unfortunately, comparative data on medication appropriateness in the Greek general population is unavailable.

The likely reasons for this discrepancy in treatment include unequal access to healthcare, potential discrimination by non-mental health healthcare providers, non-adherence to clinical guidelines, psychiatrists' limitations in managing physical health, and patients' challenges in seeking care for comorbidities. Furthermore, a general lack of emphasis on medication appropriateness in healthcare may contribute.

Clinical pharmacists, now integral to multidisciplinary healthcare teams in SMI,[29,30] have demonstrated their value. Our study aligns with findings by Grimes et al.,[31] Somers et al.,[32] and Burnett et al.,[33] showing significant MAI score reductions post-clinical pharmacist intervention. A notable issue in our study was uncontrolled hypertension, prevalent among over half of the SMI patients with comorbid physical disorders, primarily CVD and diabetes. Hypertension, a major CVD risk factor, has

Table 6
Clinical pharmacist's self-rating of all interventions (*n* = 107) for clinical significance.

Significance category	n (%)
Intervention is detrimental for patient well-being (Grade 1)	0(0)
Intervention has no significance to patient care (Grade 2)	0(0)
Significant intervention but does not reflect into improved patient care (Grade 3)	0(0)
Intervention which is significant but does not lead to an improvement in patient care (Grade 3)	20 (18.7)
Intervention is significant and results in an improvement in patient care (Grade 4)	72 (67.3)
Intervention is very significant and prevents a major organ failure or adverse reaction of similar importance (Grade 5)	15 (14.0)
Potentially mortality-preventing intervention (Grade 6)	0(0)

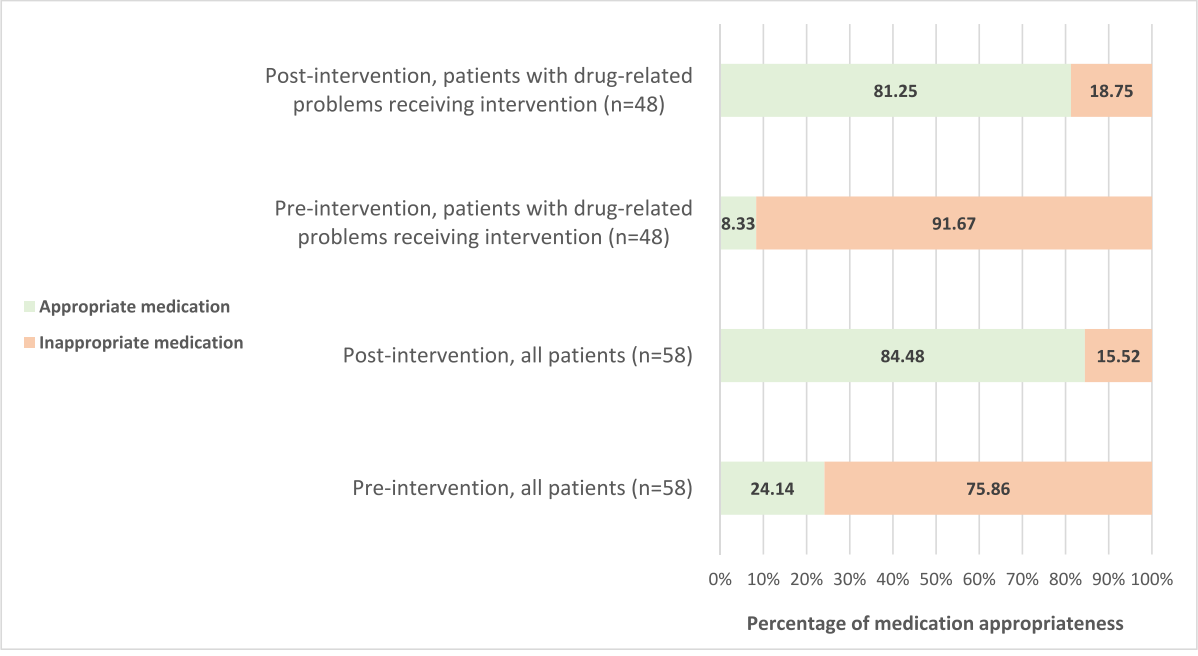

Fig. 2. Medication appropriateness pre- and post- clinical pharmacist interventions.

Table 7
Clinical significance ratings of random sample of interventions (42 interventions for 15 patients) in the random sample by all raters.

Clinical pharmacist	Rater A[a]	Rater B[b]
n(%)	n(%)	n(%)
Grade 1: Intervention which is detrimental to the patient's well being		
0 (0)	0(0)	1 (2.4)
Grade 2: Intervention has no significance to patient care		
0(0)	0(0)	0(0)
Grade 3: Intervention which is significant but does not lead to an improvement in patient care		
11 (26.2)	4 (9.5)	3 (7.1)
Grade 4: Intervention is significant and results in an improvement in patient care		
26 (61.9)	38 (90.5)	26(61.9)
Grade 5: Intervention is very significant and prevents a major organ failure or adverse reaction of similar importance		
5 (11.9)	0 (0)	9(21.5)
Grade 6: Intervention is potentially life-saving		
0 (0)	0 (0)	3 (7.1)

[a] Rater A: Professor of Clinical Pharmacology.
[b] Rater B: General Practitioner.

seen improved outcomes through MTM and other clinical pharmacy activities, particularly in hypertension management.[34]

The active engagement of pharmacists in treatment decisions significantly improves pharmacotherapy appropriateness, diminishes adverse drug events, and elevates clinical outcomes.[29] Substantial evidence upholds the efficacy of clinical pharmacist-led interventions in chronic SMI management,[30] both independently and as part of multidisciplinary teams. A systematic review, analyzing 37 diverse studies, corroborates the positive impact of pharmacist interventions on SMI clinical outcomes.[30] In SMI settings, pharmacists commonly engage in counselling, medication review, and providing recommendations to clinicians, with key actions including reducing polypharmacy, enhancing laboratory monitoring, and modifying drug orders.[29] Polypharmacy often emerges as the primary reason for medication discontinuation.[29] Together with our findings, these insights confirm the significant benefits of integrating pharmacists into healthcare teams, markedly improving healthcare efficiency and clinical outcomes.[34]

Our study also highlights the feasibility of pharmacist-led interventions in SMI, evidenced by high physician acceptance rates, paralleling findings from other psychiatric clinical environments.[29] The noted discrepancies in inter-rater agreement may stem from the diverse professional backgrounds of the raters and their differing interpretations of clinical significance. The self-assessment by the clinical pharmacist, despite introducing a potential bias, was a deliberate methodological choice aimed at leveraging the audit for professional reflection and development. This process provided an opportunity to critically evaluate the effectiveness of interventions and identify areas for improvement, enriching the overall understanding of the interventions' impact.

While equal quality healthcare is a fundamental right, the strenuous and time-intensive nature of these processes suggests a need to prioritize those in urgent need, especially in contexts like Greece where pharmacist staffing in hospitals and clinics is often limited. Implementing exclusive clinical pharmacy services, though ideal, may be impractical and unsustainable. Nonetheless, the heightened morbidity and mortality in SMI patients necessitates such prioritization.

Furthermore, this study emphasizes the necessity for detailed and accurate documentation in healthcare. Our findings indicate that enhancements in EMR, such as adding BMI measurements and smoking status, are essential for a more precise assessment of CVD risk factors, aiding in the optimization of medication treatment decisions.

The study, however, has limitations. Diagnoses were sourced from EMR and, given the common under-diagnosis of somatic comorbidities in SMI, some patients might have been excluded due to missing somatic diagnoses. The stringent inclusion criteria led to a small sample size. Furthermore, due to the study's short duration, clinical endpoints regarding safety and efficacy could not be assessed. Future research addressing these limitations is needed.

It is also essential to acknowledge that this audit was conducted in the context of a single clinical pharmacist's involvement, reflective of the staffing realities in many clinical settings, especially those with limited resources. This setup inherently limits the generalizability of our findings but provides critical insights into the feasibility and impact of clinical pharmacist interventions in similar contexts. The nature of clinical audits, focusing on immediate application and improvement within a specific setting, further confines the broad applicability of our results. However, it offers valuable lessons on enhancing medication management practices.

Besides the small sample size, there are additional reasons why our results should not be generalized. Clinical audits, by design, cannot produce broadly generalizable conclusions since they are confined by the context of their specific clinical setting. Thus, our study confirmed our initial hypothesis regarding the high prevalence of somatic comorbidities in our SMI patients, as well as significant potential problems with medication appropriateness for those comorbidities; however, it should only be used as a starting point for hypothesis testing by others in similar clinical settings. Furthermore, since clinical audits that employ implicit criteria rely heavily on the experience and clinical judgement of the assessor, any metrics that describe the interventions should also not be generalized.

Future research should include more clinical audits in similar settings, as well as traditional research studies, such as randomized controlled trials comparing MAI/AOU scores and relevant clinical outcomes between standard care and pharmacist-enhanced care groups A broader patient base, longer study durations, and varied settings are needed for more conclusive results. Additionally, to draw generalizable conclusions about the impact of clinical pharmacist interventions on SMI patient health, randomized trials or prospective observational studies comparing clinical outcomes between standard treatment and clinical pharmacist-enhanced care are essential.

Conclusion

Our clinical audit revealed a high prevalence of somatic comorbidities and often inappropriate medication treatments in SMI patients, emphasizing the necessity for targeted medication management. Clinical pharmacist interventions significantly reduced inappropriate treatments, demonstrating their potential in improving patient care within our psychiatric clinic. However, the specific context and design of our study limit the generalizability of these results.

To address these issues, we've formulated an action plan focusing on comprehensive screening, timely diagnosis of common comorbidities, and regular medication reviews to ensure treatment appropriateness, with a goal to set a minimum accepted medication appropriateness standard at 20% based on MAI and AOU scores. *Re*-auditing will be crucial for ongoing evaluation and enhancement of our approach.

The need for further research is evident to broaden the applicability and deepen the understanding of clinical pharmacist interventions in diverse psychiatric care settings, thereby improving outcomes for SMI patients with comorbidities.

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Author contribution

Diamantis Klimentidis conducted all phases of this research starting from conceptualization followed by data collection, data analysis and manuscript writing.

CRediT authorship contribution statement

Diamantis Klimentidis: Writing – review & editing, Writing – original draft, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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