Clinical Schizophrenia & Related Psychoses

A Systematic Review on the Impact of Clinical Pharmacist Interventions in Patients with Mental Health Disorders

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Abstract

Introduction: Mental disorders are one of the most significant public health challenges and major cause of disability and overall global burden of diseases. They often receive multiple medications associated with their comorbid conditions and mental illness increasing the risk for drug related problems leading to increased risk of hospitalization, morbidity, mortality and healthcare expenditure.

Aims/Objectives: The aim of this systematic review is to evaluate the impact of clinical pharmacist involvement in psychiatric settings in patients with mental disorders.

Methodology: A literature search was undertaken using three electronic databases (PubMed, Scopus and Google Scholar) with full text by using the following search terms; 'clinical pharmacist' or 'mental health pharmacist', in combination with 'psychiatry', 'psychiatric' or 'mental illness' and 'drug related problems' or 'interventions'. Studies published between January 2010 to December 2019 and references identified within the studies were included. Case studies and series were excluded.

Results: Fifteen studies met the inclusion criteria, out of which forteen studies were carried out in inpatient health care settings and one within an outpatient assertive community treatment (ACT) team. Of the total studies, nine studies were prospective while six were retrospective study design in nature. Only six studies utilized control or comparison groups with three comprised of randomized and one non-randomized, one pre-post study design and one 'before-and-after' study intervention measures corresponding to evidence level of II, III-2 and III-3 respectively. The outcome evaluation measures showed that four studies reported clinical outcome, three were economic outcomes and two studies reported both clinical and humanistic outcome. The remaining six studies focused on impact evaluation measures.

Conclusion: Multiple studies highlighted the positive impact of various services provided by the clinical pharmacist in psychiatric settings with respect to different outcome measures. However, the quality and measured outcomes of most of these studies vary greatly suggesting a need for additional well –designed randomized controlled trials assessing the various outcomes in patients with psychiatric disorders.

Keywords: Clinical pharmacist• psychiatry• Interventions• outcomes

Introduction

Mental health disorders or psychiatric illness is one of the most important public health challenges and major cause of disability and overall global burden of diseases following diabetes, cardiovascular disease and oncology. Mental health is a state of psychological, emotional and social well-being in which every person realizes his or her own abilities, manages the normal stress of life, work effectively and is able to make a contribution to his or her community [1,2]. Psychiatric disorders affects individual's mental health that often includes combination of troubled thoughts, emotions, behavior and relationships with others. These features include disorders that cause a high burden of disease such as anxiety disorders, affective disorders, schizophrenia, dementia, substance use disorders, intellectual disabilities, and developmental and behavioral disorders with onset usually occurring in childhood and adolescence, including autism [3].

It is estimated that 450 million people overall in the world suffers from some kind of mental or brain disorder at any given time, including behavioral and substance abuse disorders causing 7% of all global burden of disease as measured in disability adjusted life years (DALYs) and 19% of all years living with disability [4]. Depression leads the major cause of disability in the world, and suicide was the tenth leading cause of death in 2015. Major Depressive Disorder (MDD) is the fourth cause of disability around

the world and is estimated to be the second leading cause of disability by 2020. It is expected that the number of people with mental and neurological disorders continuous to rise steeply to 15% of DALYs lost by the year 2020. Individuals who are at increased risk of developing mental disorders include people with serious or chronic physical illnesses, children and adolescents, whose rearing has been disrupted, people living with low socio economic status or in pressed conditions, the unemployed, female victims of violence and abuse, and disregarded elderly persons [5,6].

Mental health conditions can lead to negative health outcomes, early death, human rights violations, and economic loss both nationally and globally. They can also have serious impact on physical health and are associated with the prevalence, progression, and outcome of some of the most common chronic diseases, including diabetes mellitus, cardiovascular disease, and cancer. Mental health disorders can have detrimental and long-lasting effects—including high psychological and socio - economic costs for the people affected with the disorders and also for their families, institutions, workstations, and communities [1,2,7].

Breathtaking development in neurosciences, genetics, psychosocial therapy, drug therapy, and sociocultural disciplines including the cognitive behavioral therapy with prompt and productive interventions for all types of mental health problems offers a great opportunity for people with psychological disorders and their families to lead a filled and productive

life [8]. Psychiatry practice is a multidisciplinary field that demands different healthcare professionals to collaboratively work together towards achieving better patient care. Antipsychotic medications offer variety of challenges to clinicians because of the enormous potential for drug interactions, therapeutic drug monitoring requirements and medication non-adherence. In addition, individuals diagnosed with mental disorders often receive multiple medications to manage their mental illness and associated comorbid conditions that put them at risk for drug related problems, frequent visits and hospitalization, increased healthcare expenditure and negative therapeutic outcome [9,10,11]. Involvement of clinical pharmacist in the psychiatric health care team helps in identification and prevention of drug related problems (DRPs) through prompt interventions can reduce psychiatric burn outs and there by achieving better therapeutic outcome [12,13]. So the present study aims to systematically review the impact of pharmacist interventions in a psychiatric multidisciplinary team in patients with mental disorders.

Methods

A comprehensive literature searches of published articles analyzing the impact of psychiatric pharmacist interventions in the management of patients with mental health disorders was undertaken by using the three electronic databases (PubMed, Scopus and Google Scholar). Studies published between February 2010 to February 2020 were included in the search criteria. The key search terms include "pharmacist" or "clinical pharmacist" or "psychiatric pharmacist" in association with "psychiatry" or "psychiatric" or "mental health" or "mental illness" or "mental disorders" or "affective disorder" or "bipolar disorder" along with "drug related problems" or "interventions" were used to develop the search string. The studies were restricted to English publications. We also manually searched the reference lists of all included articles to find any additional appropriate eligible studies. The reviewers carefully screened titles and abstract independently, reviewed free full-text of articles for further assessment and inclusion and confirmed the final eligible records. Discrepancy between reviewers over inclusion of article were resolved by discussion or by consulting the third reviewer and attained consensus. A systematic review of the included studies was undertaken and the flow chart of the selection of the studies for the review is shown in the Figure 1.

Inclusion criteria

Eligible studies met the following criteria were included in the study. Study design consisting of clinical trials, cohort studies, case-control studies evaluating the impact of pharmacist in patients with mental disorders and their care.

Exclusion criteria

Articles published as review, case reports, case series, editorials, letters, comments, abstracts, poster presentations and meta-analysis were excluded from the study.

Data analysis

Data were qualitatively summarized based on study design, classification of drug problems, and the recommendation provided by the pharmacists. Mean and standard deviations were used to summarize the age, number of patients and acceptance rate of recommendations included in the studies.

The included studies were provided with a level of evidence based on the outcome of the study, study design and its appropriateness to assess the effect of an intervention according to Australia's National Health and Medical Research Council's hierarchy of clinical evidence (NHMRC)4 (Table 1). In order to include in the classification for the level of evidence, the interventional studies must have comparison between intervention to control. Achieving a level of evidence - 1 indicates the highest quality of evidence supporting the intervention.

Stature	Study design
I	A systematic review of randomized controlled trials
II	A randomized controlled trial
III-1	A pseudorandomized controlled trial
III-2	A comparative study with concurrent controls
	Non-randomized experimental trial
	Cohort study
	Case-control study
	Interrupted time series with a control group
III-3	A comparative study without concurrent controls
	Historical control study
	Two or more single arm study
	Interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test / post-test outcomes

Table 1. National Health and Medical Research Council's hierarchy of clinical evidence.

The study findings were also categorized according to their impact or outcome evaluation measures. Impact evaluation is associated with the immediate effects of the study whereas outcome evaluation focuses on the long term beneficial effects of the study. These outcome evaluation is further classified as economic, clinical, humanistic model of outcome (ECHO) assessment based on the outcome achieved from the pharmacist interventions. Study results showing changes or improvement in the patient care were classified as clinical outcome, changes in quality of life or functional status as humanistic outcomes and economic changes to the patient directly or the healthcare system as a result of pharmacist interventions were grouped as having an economic outcome.

Results

A total of 114 articles were screened through the various database searches and 46 studies were excluded after the preliminary screening for titles and abstracts. Of the remaining 68 articles, fifteen studies were found to be appropriate and met the inclusion criteria after removing the duplicates and secondary screening with full text for analysis on the impact of psychiatric pharmacist involvement in patients with mental disorders. Manual searching from the reference lists of the included articles found four additional studies for inclusion.

A total of 1986 patients with psychiatric illness were included in the study. The mean age of the study participants was found to be 54.53 ± 22.39 ranging from 2.5 – 95 years (Figure 1). Among the 15 studies, ten studies have used the various types of classification to categorize the different types of drug related problems identified during the study. These classification of drug related problems includes Cipolle, Pharmaceutical care Network Europe (PCNE), Hepler – strand classification, DOCUMENT system of classification, Third Consensus of Granada DRP classification and Slovenian classification (DRP – SLO – VI). The remaining five studies did not specify the classification of drug related problems. A total of 3611 interventions and or recommendations were performed by the clinical pharmacist of which 2714 suggestions were accepted and lead to change in drug therapy. The mean percentage of the pharmacist interventions accepted by the clinicians in the studies reviewed was found to be 75.08 ± 20.41 ranging from 29 – 100. The summary of the included studies in the systematic review is presented in the Table 2.
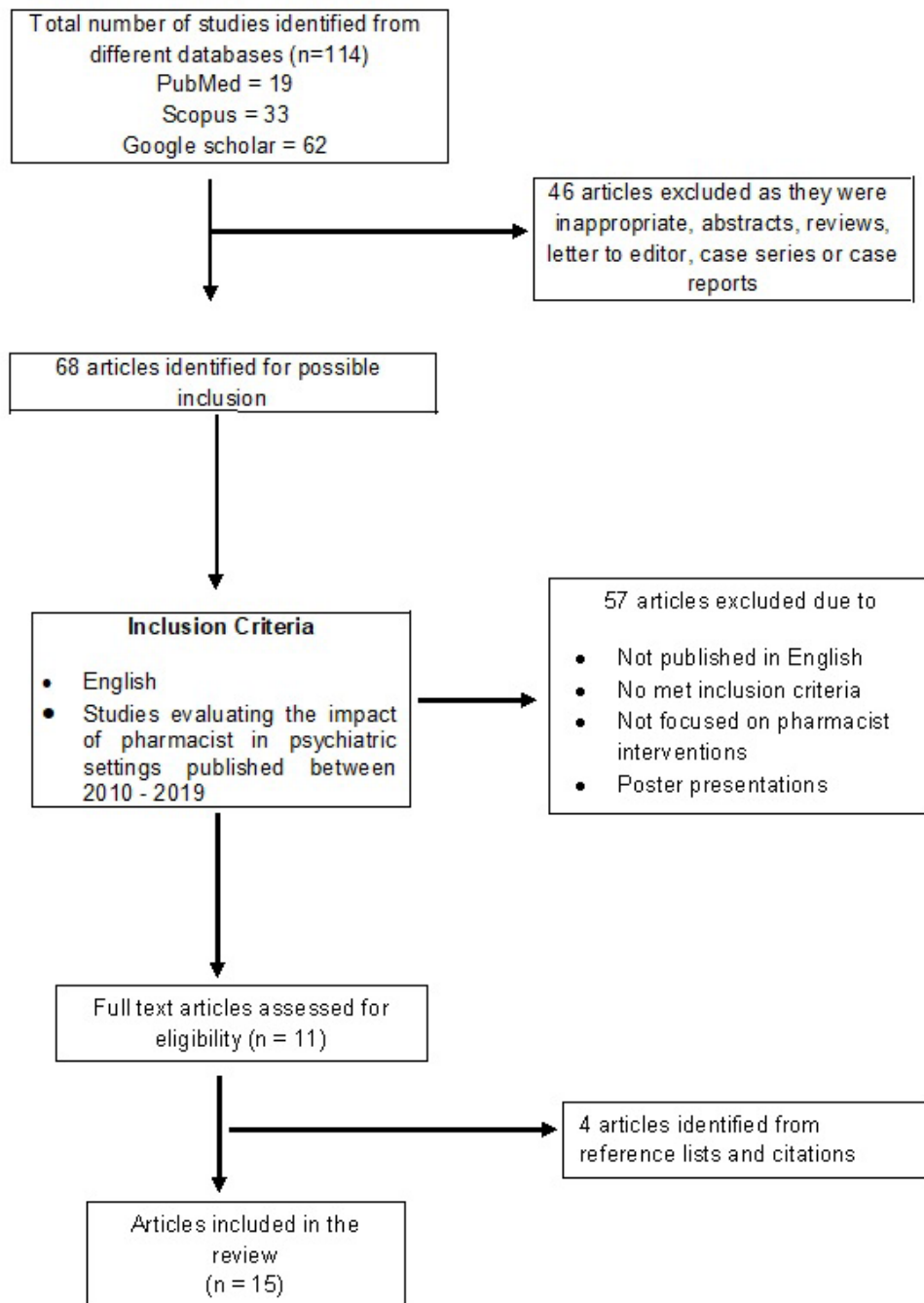
Total number of studies identified from
different databases (n=114)
PubMed = 19
Scopus = 33
Google scholar = 62

46 articles excluded as they were
inappropriate, abstracts, reviews,
letter to editor, case series or case
reports

68 articles identified for possible
inclusion

Inclusion Criteria

- English
- Studies evaluating the impact of pharmacist in psychiatric settings published between 2010 - 2019

57 articles excluded due to

- Not published in English
- No met inclusion criteria
- Not focused on pharmacist interventions
- Poster presentations

Full text articles assessed for
eligibility (n = 11)

4 articles identified from
reference lists and citations

Articles included in the
review
(n = 15)

Figure 1. Flow chart of selection of studies for review.

Study description	Value
Publication year	2010-2019
Prospective	8
Retrospective	6
Cross-sectional survey with semi structured interview	1
Age	
Mean (range)	54.53 ± 22.39 (2.5-95)
Number of patients	1986
Drug related problem classification	(n=14)
Cipolle	3
Pharmaceutical Care Network Europe (PCNE)	3
Hepler-strand	1
Document system	1
Slovenian (DRP-SLO-VI)	1
Third Consensus of Granada	1
Not Specified	5
Interventions	
Recommended	3611
Accepted	2714
Percentage mean (range)	75.08 ± 20.41 (29-100)

Table 2. Summary of the included studies.

A total of fifteen studies fulfilling the inclusion criteria with eight prospective (randomized control clinical trial, non-randomized, before and after study), six retrospectives and one cross-section semi structured survey study designs were included in the review. Fourteen studies were carried out in hospital settings or healthcare centers while one study was carried out in a community based Assertive Community Treatment (ACT) team. All the studies evaluated the impact of clinical pharmacist involvement in patients diagnosed with a psychiatric disorder. Eight of these studies involved patients diagnosed with any psychiatric illness or mental disorders admitted in the hospital. The remaining seven studies includes children with autistic or developmental disorder, patients with bipolar or depression disorder and patients with schizophrenia or insomnia or dementia or cognitive impairment. Elderly patients with psychiatric illness were also formed the sample in two studies. The summary of the studies evaluating the impact of pharmacist interventions in patients with mental health disorders is presented in the Table 3.

Clinical pharmacist activities

All the studies included in this review evaluated the clinical pharmacist interventions in ensuring the safety and effective use of medications by reviewing the patient drug therapy, monitoring of laboratory parameters and assessing the clinical progress of the patients. Among the total studies included in the review, five studies have mainly focused on the impact of pharmacist interventions in the medication therapy management services by identifying and resolving drug related problems. These studies include both prospective and retrospective study designs where clinical pharmacist interventions were carried out with or without control or comparison group for a period of 6 – 12 months and their acceptance rate was reported. The above mentioned studies highlights the impact of clinical pharmacist services in an investigative format and did not evaluated the outcome achievements.

Among the drug related problems identified in the various studies, improper / inappropriate drug selection (8 of 15) was the most common followed by adverse drug reactions (5 of 15). The other drug related problems reported in the studies were patient non - compliance, lack of therapeutic drug monitoring, unnecessary drug therapy and sub therapeutic dose or over dose. Pharmacist interventions/recommendations to the healthcare providers commonly involved discontinuation of the drug therapy, monitoring of laboratory parameters, changing drug therapy, dosage adjustments and patient education/counselling.

Level of evidence

Among the total fifteen studies reviewed, six studies were controlled clinical trial study design compared patients who received interventions to a group who did not receive interventions. Of these six studies, three studies exercised randomized controlled trial study design indicating a level of evidence II whereas the other three studies were a non-randomized, open, controlled study, pre and post study and before and after study signifying a level of evidence III-A and III-B respectively. The remaining nine studies reviewed did not include control group in their study and cannot provide a level of evidence.

Outcome evaluation

Evaluation measures were carried out for nine of the total 15 studies reviewed to assess the outcomes with respect to the clinical pharmacist interventions. These studies include both prospective and retrospective study design and clinical outcomes alone were reported in 4 studies while economic outcomes were investigated in 3 studies. Two studies have reported both clinical and humanistic outcomes achieved as a result of clinical pharmacist interventions. The remaining six studies focused mainly on direct impact of clinical pharmacist activities such as the implementation and acceptance rate of interventions instead of measuring economic, clinical or humanistic outcomes. Even though the studies are quite interesting, evaluation could not be done in line with the type of outcome.

S.no	Author, year of study	I Study design and duration	Study population and sample size	Level of evidence	Classification of drug related problems	Results	Evaluation measure
1	Stuhec et al. 2019	Retrospective cohort study; 12 months	Elderly patients with psychiatric illness (Schizophrenia, insomnia, dementia etc); N=49	-	NR	49.9% of the suggested interventions were accepted by the clinicians. Decrease in mean number of medications from 15.4 to 12.0 per patient (p<0.05). Improved adherence to antipsychotic treatment guidelines (p=0.041, β=1.477, R2=0.123).	Impact; Outcome-Clinical
2	Alshahrani et al, 2019	I Prospective study; 15 months	Patients with psychiatric illness; N=420	--	NR	Pharmacist identified drug related problems and conducted clinical interventions of which 54.13% were accepted by the clinicians.	Impact
3	I Stuhec et al, 2019	I Prospective non-randomized pre-post study; 12 months	Elderly patients with mental health problems; N=24	III-3	I DRP-SLO-VI	The mean number of medications before the intervention was 12.2 ± 3.1 per patient and decreased to 10.3 ± 3.0 medications per patient (p<0.05). Collaborative approach with a clinical pharmacist led to a decrease of drug related problems, potential drug-drug interactions and potential inappropriate medications and an improvement in the patients quality of life (p<0.05).	Impact; Outcome-Clinical and Humanistic
4	I Parihar et al, 2019	Prospective study; 6 months	Patients with Bipolar disorders; N=286	--	I PCNE	72.5% of clinical pharmacist interventions were accepted by the psychiatrist.	Impact
5	Shashikala et al, 2018	Prospective study; 6 months	I Patients with psychiatry disorders; N=120	--	CIPOLLE	52.4% of the clinical pharmacist's suggested recommendations were accepted and implemented.	Impact
6	I Pfister et al, 2017	Retrospective randomized controlled study; 24 months	I Elderly patients with dementia or cognitive impairment; N=442	II	CIPOLLE	Clinical pharmacist identified drug related problems in 66% of participants in the intervention group. Drug related problems were more common among patients with polypharmacy and people with earlier stroke. 82% of the suggested recommendations by the clinical pharmacist were accepted by the physician in charge.	Impact
7	Wongpakaran et al, 2016	Prospective, randomized open-label study; 2 months	I Patients with autistic disorder, Asperger's syndrome or a pervasive developmental disorder; N=50	II	HEPLER-STRAND	Number of drug related problems (DRPs) identified in the intervention group was found to be 17 (0.68 DRPs per patient) and control group was found to be 63 (2.52 DRPs per patients) which was not significantly different at the end of week 8. However, the total number of patients who resolved at least one DRP was 13 (52%) in the intervention group and 4(16%) in the control group demonstrated significant difference (p=0.016) by week 8. The acceptance rate of interventions to psychiatrist was 90.1% in the intervention group and 88.9% in the control group which was not significantly different between both groups (p>0.05). In terms of disruptive behaviors, mean Aberrant Behavior Checklist-Irritability (ABC-1) scores improved in the intervention group more than in the control group (9.8 ± 5.6 vs. 17.7 ± 7.9; p<0.001).	Impact; Outcome-Clinical

Table 3. Studies evaluating the impact of pharmacist in patients with psychiatric disorders.

8	Gunterus et al, 2016	Retrospective chart review; 12 months	Patients with psychiatric disorders; N=200	--	NR	Clinical pharmacist interventions were associated with 92.5% acceptance arte. Two hundred clinical pharmacist interventions were associated with $6760.19 medication cost saving and $62806.67 cost avoidance.	Impact; Outcome-Economic
9	Ilickovic et al, 2016	I Prospective intervention pre & post study; 6 months	Patients with schizophrenia; N=99	III-2	PCNE	50% of the clinical pharmacist interventions were accepted and implemented by the physicians. Total number of medications per patient was significantly reduced from 4.2 ± 1.5 to 3.9 ± 1.6 in the intervention group (p=0.002) after the pharmacist interventions as compared to the control group (4.0 ± 0.9 to 3.9 ± 0.9, p=0.320).	Impact; Outcome-Clinical
10	Wolf et al, 2015	Prospective non-randomized controlled trial; 15 months	Patients with psychiatric illness; N=265	III-2	PCNE	Pharmacist interventions had led to a reduced Medication Appropriateness Index (MAI) score by 1.4 points per patient (95% CI: 0.8-2.0, p<0.001) at discharge and 1.3 points (95%CI: 0.7-1.9, p<0.001) at follow up compared with control. Number of unsolved drug related problems in the intervention group was 1.8 (95%CI: 1.5-2.1) less than control. 88.6% of pharmacist recommendations were accepted by the ward staff.	Impact; Outcome-Clinical
11	Marques et al, 2014	Prospective randomized controlled trial; 6 months	Patients with depressive disorder; N=48	II	THIRD CONSENSUS OF GRANADA DRP CLASSIFICATION	Comparison of the effects of usual treatment (Control group) and pharmaceutical care (Intervention group) on depressive symptoms showed a statistically significant difference between groups with a median reduction in Beck Depression Inventory score of 2.5 points in the CG and 13.5 points in the IG.	Impact; Outcome-Clinical
12	Richardson et al, 2014	Cross-sectional survey and semi-structured interviews; 2 months	Pharmacists working primarily in mental health	--	DOCUMENT	91.8% of the mental health pharmacist recommendations were implemented by the psychiatrists.	Impact
13	Cobb CD, 2014	Retrospective chart review; 6 months	Patients with psychiatric disorders; N=154	--	CIPOLLE	861 drug therapy problems were identified and resolved by the pharmacists.4A total net cost avoidance was estimated 5 to be $90,484.00 with a mean savings of $586.55 per patient. A cost saving of $30,467 was determined as a net result of two hospitalizations and two emergency department visits and remaining $60,017 was due to estimated net drug cost savings.	Impact; Outcome-Economic
14	Campbell et al, 2011	Retrospective chart review; 12 months	Patients with psychiatric disorders; N=320	--	NR	97% of the student pharmacist recommendations were accepted by the physicians. Estimated cost avoidance from the interventions made by the student pharmacist was between $6000-$24,000.	Impact; Outcome-Economic
15	Gable et al, 2010	Retrospective chart review; 3 months	Patients with psychiatric diagnosis; N=29	--	NR	All the interventions made by the psychiatric pharmacy specialist were accepted and implemented by the psychiatrists.	Impact

Discussion

Pharmacotherapy remains the cornerstone for the management of psychiatric illness and these medications have complex mechanisms of action as well as extensive adverse effect profile and multiple drug interactions. Practicing clinical pharmacy specialist plays a very important role in optimizing medication use and patient care by assessment, monitoring patient response, identifying and resolving drug related problems by recommending appropriate interventions [14,15].

Our systematic literature search identified 15 studies that were published between February 2010 and February 2020 analyzing the impact of clinical pharmacist's interventions in patients with mental disorders in various settings. However, the quality of the studies and its reporting varied significantly, both in practice settings and the types of interventions in which clinical pharmacists were involved. Sixty percentage studies included patients with all psychiatric disorders while the remaining studies focused on specific psychiatric illness such as Schizophrenia, bipolar disorder or major depressive disorder, dementia or cognitive impairment and autism spectrum disorder. All these studies varied considerably in size, study design and measurement of outcomes. Considering the quality of studies, only six of the 14 studies utilized the control group and the definition and the classification adopted to categorize the drug related problems is not specified in few studies.

This review shows that clinical pharmacist plays a very important role in the medication therapy management service of patients with mental health disorders. The role was well supported with the studies reviewed focusing on pharmacist reviewing treatment charts including past and present medications, laboratory parameters, clinical progress of the patients, interacting with the psychiatrists at the prescribing level and providing counseling and health education to improve the medication adherence that will ultimately promotes better quality of life. The different drug related problems identified in the various studies and the recommendation by the clinical pharmacist indicates that their role and involvement as a member of mental healthcare team is highly valuable and has clinical relevance [12,13,16,17]. Three studies have assessed the pharmacist led changes in the total number of medications per patient before and after the pharmacist interventions treated with polypharmacy anti-psychotics as statistically significant. One of these studies also assessed the collaborative care approach involving a clinical pharmacist that has led to improvement in the treatment adherence guidelines in the management of psychiatric disorders. Studies also identified that clinical pharmacist focused collaborative care may help to reduce potentially inappropriate medications in patients on polypharmacy with psychiatric illness and thereby improving the quality of care [18,19,20]. A non – randomized controlled clinical trial assessed the pharmacist led drug therapy reviews to identify and resolve drug related problems by providing recommendations resulted in reduction in medication appropriateness index scores and number of unsolved drug related problems in the intervention group when compared with the controlled group in patients with psychiatry illness [21].

The potential severity and actual risk for patient harm of the identified drug related problems has been evaluated in two of the 14 studies reviewed. In one study the potential severity of the identified drug related problem were 'moderate' in nature where as in another study the actual risk for patient harm of the identified drug related problems categorized as 'potential adverse drug events' – defined as an error that had the potential for patient harm but did not contribute to patient harm during the study period [9,21].

Improper or inappropriate drug selection related to drug duplication, drug interaction and wrong drug selection is the most common drug related problems identified in the reviewed studies [9,16,17,18,22]. This might be because of lack of adherence to the treatment guidelines or evidence based medicines. Evidence based medicine practice is elementary to clinical pharmacists in ensuring the safe and effective use of medications in patients with mental disorders. Most often in patients with mental disorders the evidence based treatment is suboptimal and psychiatrist were non-adherence to the treatment guidelines. Adverse drug reaction, patient non-compliance and lack of laboratory monitoring or drug level monitoring are the other common drug related problems identified in the various studies [12,22,23,24]. It is well known that patients with mental illness are prescribed with polypharmacy associated with their comorbid conditions leading to increased risk of adverse drug reactions and potential drug – drug interactions. So it is very important to pay attention to the patient characteristics and drugs while prescribing, especially with narrow therapeutic index and highly alert medications which might can increase the risk of adverse reactions and clinical drug interactions leading to frequent hospitalization and increased healthcare expenditure. A study reported that pharmacist intervention has led to reduction in the number of frequent visits to emergency department in patients receiving five or less medications on admission as compared to those prescribed with five or more drugs [21]. Psychiatric medications in comparison to their medications needs a close attention and monitoring for their pharmacokinetic (therapeutic drug monitoring) and pharmacodynamics (signs of adverse reactions) parameters and also to optimize the dose to avoid drug toxicity in patients with mental health disorders. Poor medication adherence in patients with psychiatric illness are well documented in the literature [14]. Patients should be educated or counselled on managing the medications by setting up a pill boxes and understanding the drug side effects and recognizing the symptoms as they do occur is vital to adherence which will help to improve positive treatment perceptions. This is most important in patients who are prescribed with polypharmacy or complex drug therapy regimen where adherence is vital in achieving better therapeutic outcome. The most important recommendations or interventions proposed by clinical pharmacist identified in two – third of the reviewed studies were discontinuation of the medication, dose adjustment and drug initiation. The most common reason for medication discontinuation were polypharmacy, drug duplication and drug use without indication.

In order to assess the benefits of clinical pharmacy services in patients with mental disorders, a variety of study designs were employed and each provided with a level of clinical evidence ranging from 1-4 according to the NHMRC hierarchy of clinical evidence. Only six of the total studies reviewed were shown to have benefit from clinical pharmacy services and were assigned a level of evidence as compared to other studies evaluating the role of pharmacist in mental health disorders [16,18,19,21,22,23]. It is also important that even studies with lower levels of evidence can also provide support for an intervention as effectively as randomized controlled trials. Wongparakan carried out a randomized controlled trial to evaluate the impact of pharmacist intervention in identifying and resolving drug related problems among children with autism spectrum disorder corresponding a level of evidence –II where as Stuhec et al [19, 22] utilized a non-randomized pre-post study design to determinate the impact of clinical pharmacist interventions on quality of life and improvement in the pharmacotherapy in elderly patients before and after the interventions. The later stands for a moderate level of evidence III-3. However, it cannot conclude that Wongparakan et al supports the role of clinical pharmacist to a greater extent than Stuhec et al. just because they carried out a randomized control trial which has higher level of evidence. The remaining nine studies neither followed randomization nor included a control or comparison group for the intervention demonstrating that the role of clinical pharmacist did not aim to describe a correlation between clinical pharmacy activities and outcomes. The bias in these studies are uncontrolled and therefore cannot assigned a level of evidence.

There were nine studies that measured both the impact and outcomes resulting from clinical pharmacist interventions in patients with mental disorders [18-26]. Of these, clinical outcomes alone have been achieved in four studies where clinical changes along with reduction in overall psychiatric symptoms and improvement in the quality of drug therapy were identified as a result of pharmacist interventions [18,20,21,23]. These studies also focused heavily on improving prescribing practice by adhering to the treatment guidelines and providing counseling to improve the medication adherence in patients with mental disorders there by

resolving drug related problems. Three studies evaluated the economic benefit of clinical pharmacist services to determine the financial benefits of interventions in acute psychiatric hospital settings [24-26]. These studies showed a significant cost savings and cost avoidance from $ 6760.19 up to $ 90,484.00 after the clinical pharmacist chart review and implementation of interventions. Two studies that measured both clinical and humanistic outcomes showed a statistically significant as a result of clinical pharmacist interventions with one study showing a significant improvement in the quality of life in elderly patients with mental disorders and the another study showed a decrease in the number of drug related problems there by reducing severity of disruptive behavioral symptoms among children with autism spectrum disorder [19,22]. The study findings evaluating economic outcomes identified pharmacist interventions resulted in cost savings are promising as there is an ongoing search for ways to reduce healthcare expenditure. However, these studies compared actual costs with the projected yearly cost without a control group. So further studies employing larger sample sizes with a randomized control clinical trial should be carried out which will give a more accurate estimate of the cost savings resulting from the pharmacist interventions. The great difference in rating scales used by the various studies examined in this review manifest the possible need for a more uniform, standardized and consistent among the rating scales that will be able to assess the clinical outcomes.

Conclusion

Numerous studies published over the last ten years highlights the inevitable role of clinical pharmacist in providing various services in the management of patients with psychiatric disorders. A clinical pharmacist collaborative pharmaceutical care approach is an effective tool in identifying and preventing drug related problems that will enhance the drug therapy and helps in improving clinical, economic and humanistic outcomes. However, the quality and measured outcomes in most of the studies vary greatly and there is a need for additional well –designed randomized controlled trials assessing the various outcomes in patients with psychiatric disorders.

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References

1. World Health Organization. "Fact Sheets on Sustainable development goals: Health targets." *Mental Health* (2020).

2. Ghebreyesus TA. "The WHO Special Initiative for Mental Health (2019-2023): Universal Health Coverage for Mental Health." (2020).

3. World Health Organization. "Comprehensive Mental Health Action Plan." (2020).

4. Richardson, Tom E, Claire L O'Reilly, and Timothy F Chen. "A Comprehensive Review of the Impact of Clinical Pharmacy Services on Patient Outcomes in Mental Health." *Int J Clin Pharm* 36(2014): 222-232.

5. Mohiuddin, Abdul Kader. "Psychiatric Pharmacy: New Role of Pharmacists in Mental Health." *J Psychiatry Mental Disord* 4(2019): 1010.

6. Goldstone, Lisa W, Bethany A DiPaula, Joshua Caballero, and Susie H Park, et al. "Improving Medication-Related Outcomes for Patients with Psychiatric and Neurologic Disorders: Value of Psychiatric Pharmacists as Part of the Health Care Team." *Ment Health Clin* 5(2015): 1-28.

7. Chavez, Benjamin, and Emily Kosirog. Impact on an Integrated Psychiatric Pharmacy Service in a Primary Care Clinic. Ment Health Clin 9(2019): 269-274.

8. World Health Organization. "Mental Health. A call for action by World Health Ministers." (2020).

9. Richardson, Tom E, Claire L O'Reilly, and Timothy F Chen. "Drug-Related Problems and the Clinical Role of Pharmacists in Inpatient Mental Health: an Insight into Practice in Australia." *Int J Clin Pharm* 2014(36):1077-1086.

10. Larco, Jonathan P, and Dilip V Jeste. "Physical Co-Morbidity and Polypharmacy in Older Psychiatric Patients." *Biol Psychiatry* 36(1994): 146-152.

11. Mann, Eva, Burkhard Haastert, Birgit Böhmdorfer, and Thomas Frühwald, et al. "Prevalence and Associations of Potentially Inappropriate Prescriptions in Austrian Nursing Home Residents: Secondary Analysis of a Cross-Sectional Study." *Wien Klin Wochenschr* 125(2013): 180-188.

12. Shashikala C Wali, Madiwalayya S Ganachari, Ashish Singh Parihar, and Sourabh B Sonawale. "Impact of clinical pharmacist in the monitoring of drug-related problems in psychiatry patients at tertiary care teaching hospital." *Int J Pharm Sci Res* 9(2018): 819-823.

13. Sultan M. Alshahrani, Shady Abosamra, and M Khobrani. "Implementation of clinical pharmacy service in a tertiary psychiatric hospital in Aseer region, Saudi Arabia: 15 experience." *Biomed Res* 5(2019): 716-720.

14. Gable, Kelly N, and Mary Janet Stunson. "Clinical pharmacist interventions on an assertive community treatment team." *Community Ment Health J* 46(2010): 351-355.

15. Lucca, Jisha M, Jintu Kurian, Madhan Ramesh, and Dushad Ram. "Appraisal of Clinical Pharmacy Services in Mental Helath Unit of a South Indian Tertiary Care Hospital." *World J Pharm Pharm Sci* 3(2014): 780-791.

16. Pfister, Bettina, Jeanette Jonsson, and Maria Gustafsson. "Drug-Related Problems and Medication Reviews among Old People with Dementia." *BMC Pharmacol Toxicol* 28(2017): 52.

17. Singh, Parihar Ashish, S. Ganachari Madiwalayya, and V. Tekkalaki Bheemsain. "Clinical Pharmacist Assessment of Monitoring and Resolving the Drug-Related Problems in Bipolar Disorder Patients: A Prospective, Observational Study at Tertiary Care Teaching Hospital." *IJPSR* 10(2019): 2790-2796.

18. Ilickovic, Ivana M, Slobodan M Jankovic, Aleksandar Tomcuk, and Jovo Djedovic. "Pharmaceutical care in a long-stay psychiatric hospital." *Eur J Hosp Pharm* 23(2016): 177-181.

19. Stuhec, Matej, Nika Bratović, and Aleš Mrhar. "Impact of clinical pharmacist's interventions on pharmacotherapy management in elderly patients on polypharmacy with mental health problems including quality of life: A prospective non-randomized study." *Sci Rep* 9(2019): 16856.

20. Stuhec, Matej, and Katja Gorenc. "Positive Impact of Clinical Pharmacist Interventions on Antipsychotic use in Patients on Excessive Polypharmacy Evidenced in a Retrospective Cohort Study." *Global Psychiatry* 2(2019): 155-163.

21. Wolf, Carolin, Anne Pauly, Andreas Mayr, and Teja Grömer, et al. "Pharmacist-Led Medication Reviews to Identify and Collaboratively Resolve Drug-Related Problems in Psychiatry: A Controlled, Clinical Trial." *PLOSOne* 10(2015): e0142011.

22. Rewadee, Jenraumjit, Thanarat Suansanae, Tan-Khum T, and Kraivichian C, et al. "Impact of Providing Psychiatry Specialty Pharmacist Intervention on Reducing Drug-Related Problems among Children with Autism Spectrum

Disorder related to Disruptive Behavioural Symptoms: A Prospective Randomized Open-label Study. " *J Clin Pharm Ther* 42(2017):329-36.

23. Marques, Luciene Alves Moreira, Galduróz JCF, Fernandes MR, and Beijo LA, et al. "Drug-Related Problems, Drug-Related Negative Clinical outcomes and Pharmacist Interventions in Outpatients with Depressive disorder." *J Sci Res Phar* 3(2014): 26-30.

24. Cobb, Carla D. "Optimizing Medication use with a Pharmacist-Provided Comprehensive Medication Management Service for Patients with Psychiatric Disorders." *Pharmacotherapy* 34(2014):1336-40.

25. Campbell, Austin R, Leigh Anne Nelson, Ellie Elliott, and Robin Hieber, et al. "Analysis of Cost Avoidance from Pharmacy Students' Clinical Interventions at a Psychiatric Hospital." *Am J Pharm Educ* 75(2011):8.

26. Gunterus, Alicia, Shruti Lopchuk, Christina Dunn, Ronald Floyd, and Brad Normandin. "Quantitative and Economic Analysis of Clinical Pharmacist Interventions during Rounds in an Acute Care Psychiatric Hospital." *Ment Health Clin* 6(2016):242– 247.