Pharmacist-led interventions for people living with severe and persistent mental illness: a systematic review

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Abstract

Objective

People living with severe and persistent mental illness (SPMI) experience poorer physical health, often due to medication and preventable lifestyle factors, and exacerbated by barriers to accessing healthcare services. Pharmacists are well-positioned to improve the physical and mental health of this population. However, little is known about pharmacists' current practices when providing services to this population nor the impact of pharmacist-led interventions on consumer health outcomes. We undertook a systematic review to identify, describe and assess the effectiveness of pharmacist-led interventions for supporting people living with SPMI and the impact on consumer outcomes.

Methods

MEDLINE, Embase, PsycINFO, CINAHL, Web of Science, Scopus, Cochrane Library, International Pharmaceutical Abstracts and ProQuest Dissertations and Theses were searched between January 1990 – April 2020. Full-text studies exploring pharmacist-led interventions in any setting for people living with SPMI were included. A risk of bias assessment was conducted.

Results

A total of 37 studies were included. More than half of the pharmacist interventions were multifaceted. The most common components of pharmacist-led interventions included education and/or patient counselling, providing recommendations to healthcare professionals and conducting medication reviews. Multifaceted interventions demonstrated improvements in clinical outcomes, whereas single interventions focused mostly on consumer-reported outcomes. The methodological quality of included

studies was moderate-to-high risk of bias and there was considerable heterogeneity in the study design, interventions described, and outcomes reported.

Conclusions

There is evidence that pharmacist-led interventions improve consumer-reported and clinical outcomes for people living with SPMI. Pharmacists are capable and have a role in supporting people living with SPMI, either individually or as interprofessional collaborators with other healthcare professionals. Future research should attempt to better understand which particular intervention components have the greatest impact and also evaluate the implementation and long-term sustainability of such interventions.

Key words

severe and persistent mental illness; mental health; pharmacist intervention; systematic review

Introduction

Severe and persistent mental illness (SPMI), including (but not limited to) schizophrenia and other psychotic disorders, bipolar disorder, and severe and recurrent major depression, refers to any mental illness that negatively impacts a person's relationships, educational achievements and occupational performance (Carey and Carey, 1999). It also contributes to a significant burden of US\$148 billion dollars to the US economy annually (Carey and Carey, 1999). People living with SPMI have up to 25 years lower life expectancy than the general population (Royal Australian New Zealand College of Psychiatrists, 2016), mainly due to modifiable lifestyle factors such as smoking, physical inactivity, and unhealthy diet (World Health Organization, 2018), side effects of antipsychotic medications (World Health Organization, 2018), and compounded by stress intrinsic to living with a mental illness (Liu et al., 2017). As a result, this population experiences a significantly higher incidence of comorbid preventable chronic diseases including type 2 diabetes, cardiovascular and respiratory diseases (World Health Organization, 2014). There is evidence that inequality in healthcare access and provision contributes to these comorbid physical illnesses being under-recognised and sub-optimally treated among people living with SPMI, leading to poor overall physical and mental health (Lawrence and Kisely, 2010; De Hert et al., 2011).

Given the personal, social, and economic impacts of untreated and undertreated SPMI, involving primary healthcare professionals to ensure adequate support for this population is essential. In general, consumers are 1.5 to 10 times more likely to see their pharmacist than they see primary care physicians (Tsuyuki et al., 2018). Over the past decade, pharmacists have demonstrated their capability to improve health outcomes by educating consumers about psychotropic medication to improve adherence (Kyle,

2018), and providing medication information, either individually or collaboratively as integral members of the healthcare team (Davis et al., 2020).

Treatment for more severe mental health conditions, such as schizophrenia has historically relied on pharmacological approaches (Lally and MacCabe, 2015). However, recent studies have started to recognise the need for ongoing routine management and monitoring by healthcare professionals (Whiteford et al., 2017). Evidence exists around the role of the pharmacist to lead screening and risk assessment and conduct medication reviews to ensure quality use of medicines for a broad range of mental health conditions (Rubio-Valera et al., 2014). Mental health professionals including physicians and nurses have also been shown to have positive perceptions and expectations from pharmacists to help manage medication side effects and improve quality of care (Eltorki et al., 2019). However, there is still a lack of understanding as to how specific pharmacist-led interventions may impact health outcomes among people living with SPMI. A Cochrane review revealed that pharmacist-led services may be more cost-effective and can produce similar positive effects on patient health and physical function, in comparison to doctor-led services (de Barra et al., 2018). Another review conducted by Sud et al. explored pharmacists' involvement as part of a multidisciplinary team in supporting people living with severe mental illness (Sud et al., 2021). It focused specifically on pharmacists' involvement in the management of cardiometabolic risk and metabolic syndrome and showed that pharmacists could significantly improve cardiometabolic screening rates (Sud et al., 2021). To the best of our knowledge, no previous reviews have ever focused on exploring the overall evidence relating to pharmacist-led interventions for people living with SPMI. Therefore, this systematic review aimed to identify, describe and assess the effectiveness of pharmacist-led interventions for supporting people living with SPMI and all the associated impact on consumer and pharmacist-reported outcomes. Specifically, this review was guided by the following research questions:

1. How have pharmacists been involved in supporting people living with SPMI?
2. What is the nature, extent and outcome of pharmacist-led intervention for people living with SPMI?
3. What type of education and training is developed for and provided to pharmacists prior to their involvement in interventions for people living with SPMI?
4. What are the barriers to and facilitators of pharmacists' involvement in supporting people living with SPMI?

Methods

This review was guided by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guideline (Moher et al., 2009). The protocol was registered in PROSPERO, an international prospective register of systematic reviews (CRD42020170711) (El-Den et al., 2020a).

Search strategy and selection criteria

Potentially relevant publications published between January 1, 1990 through to April 1, 2020 were identified by searching the following databases: MEDLINE, Embase (Ovid), PsycINFO, CINAHL, Web of Science, Scopus, Cochrane Library, International Pharmaceutical Abstracts and ProQuest Dissertations and Theses. In addition, reference lists of relevant reviews were screened for any potentially relevant individual studies. The year 1990 was chosen as it aligned with the introduction of second generation antipsychotics (Tamminga, 2000), and a global shift towards community-based mental healthcare (Robson, 2008; Mechanic, 2007; Mental Health Council of Australia, 2005).

The following search terms or subject headings (and related concepts, depending on the database) were used:

Concept 1: *pharmacist* OR *pharmacy*; AND

Concept 2: *severe and persistent mental disorders* OR *severe and persistent mental illnesses* OR *schizophrenia spectrum and other psychotic disorders* OR *bipolar and related disorders* OR *substance related disorders* OR *depressive disorders* OR *anxiety disorders*.

Study selection and data extraction

Search results were downloaded into EndNote X9, duplicates were removed automatically and manually. One reviewer (RN) was involved in removing duplicates and screening titles. Two reviewers (RN and VS) independently screened studies by abstract and then by full-text for potentially eligible studies, in Covidence (Covidence systematic review software). Any discrepancies were discussed with COR and SE until consensus was reached. The following data were extracted where possible as per the terminology used in the study: author(s), year, country, study aim, setting, sample size, study population, study design, intervention(s), consumer- or pharmacist/clinician-reported outcomes or other outcomes related to pharmacists' intervention(s). Due to a significant degree of heterogeneity between intervention and outcome measures, a meta-analysis was not deemed suitable.

Inclusion/exclusion criteria

The inclusion criteria were formulated using the PICOS (Participant, Intervention, Comparison, Outcome and Study) design (Moher et al., 2009). Studies were included if they met the following criteria:

Participants

The study population involved people living with SPMI. SPMI refers to any mental illness that has a continuous and significant lifelong impact on a person's relationships, social functioning, education, and livelihood. It includes (but not limited to) schizophrenia, bipolar disorder, any psychotic illness (e.g. schizoaffective disorder, psychotic depression) and moderate-to-severe depression or anxiety.

- a. For studies with a mixed population of participants, including people living with SPMI, the studies were included if the outcome(s) pertaining to pharmacist-led intervention(s) for people living with SPMI could be extracted.
- b. For studies that did not report on a definitive diagnosis, the studies were included if it had a detailed description of illness severity and the authors were satisfied that it meets the definition of SPMI mentioned above. For example, a study that included participants in a psychiatric hospital receiving antipsychotic treatment would be eligible for inclusion.
- c. For studies that included people living with SPMI also experiencing a comorbid substance-use disorder, the outcomes relating to both the SPMI and the substance-use disorder will be reported.

Intervention

"Pharmacist-led intervention" in this review refers to any service or contribution made by the pharmacist for people living with SPMI. For study inclusion, the intervention had to be delivered by pharmacists, working either individually or as part of a multidisciplinary healthcare team, in any healthcare setting, including but not limited to hospitals, community pharmacies and outpatient settings.

- a. For studies with a mixed population of healthcare professionals, if the outcome(s) relating to the intervention(s) delivered by the pharmacist could be extracted then the study was included.

Comparator and Outcome

As per the aforementioned definition of a pharmacist-led intervention, studies were included with or without a comparator group. Any outcomes attributable to pharmacist involvement such as consumer or pharmacist-reported outcomes were included.

Study design

All primary research published in English was considered for inclusion, regardless of study design.

The following types of studies were excluded:

- a. Studies that only included people living with a substance-use disorder (e.g., opioid, tobacco, alcohol). Pharmacist-led intervention(s) (e.g., naloxone dispensing, smoking cessation therapy, alcohol misuse screening) for people living with substance-use disorders have been established and explored previously through published reviews of the literature (Mdege and Chindove, 2014; Greenhalgh et al., 2016; Saba et al., 2014; Watson and Blenkinsopp, 2009; Nielsen and Van Hout, 2016; Thakur et al., 2020);
- b. Studies conducted in educational settings such as a university. For example, a study conducted in a university classroom setting was excluded as the aim of this review was to explore the role of pharmacists in practice healthcare settings;
- c. Non-primary research publications, such as conference abstracts, case reports, editorials, and letters.

Risk of bias

The risk of bias was assessed using the Cochrane risk-of-bias tool for randomised trials (RoB 2) (Higgins et al., 2016) and Risk Of Bias In Non-randomised Studies - of Interventions (ROBINS-I) (Sterne et al., 2016). The risk of bias assessment was conducted primarily by RN, in consultation with SE and COR.

Randomised Controlled Trials (RCTs) were assessed according to the following RoB 2 domains:

randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of reported result (Higgins et al., 2016). The ROBINS-I tool assesses the risk of bias in non-RCTs across seven domains: bias due to confounding, bias in the selection of participants, bias in the classification of the intervention, bias due to deviation from intended intervention(s), bias due to missing data, bias in measurement of outcome, and bias in selection of reported results (Sterne et al., 2016). Each risk of bias item was rated as either low, some concerns/moderate or serious/high risk of bias.

Results

The literature search yielded a total of 9264 potentially relevant studies. After the removal of 2222 duplicates, 7042 studies were considered for inclusion. Three hundred and forty-two studies were identified as non-primary articles, and the remaining 6700 studies were screened by title (5287 removed based on titles) and then abstract. Thirty-three studies met the inclusion and exclusion criteria and were included in the review. Further screening for potentially relevant studies in the reference lists of literature reviews resulted in four additional studies, resulting in 37 included studies. Figure 1 outlines this process and the search results.

Fig. 1 PRISMA flow diagram showing process of study selection for inclusion in systematic review

Study characteristics

As described in Table 1 and 2, studies were conducted in various countries worldwide, with the majority conducted in North America (n=11) and Asia (n=11). Ten of the 37 studies were RCTs and 27 were non-RCTs, of which 15 employed pre/post intervention single (n=8) or two-group (n=7) study designs and 12 employed post-intervention single-group study designs.

Twenty studies were conducted in hospitals (n=20), with only two in community pharmacies (n=2). In relation to diagnosis, most studies included only people living with schizophrenia (n=12), followed by bipolar disorder (n=5) and severe depression (n=3). Twelve studies included mixed SPMI populations, whereby participants had dual or multiple diagnoses.

The sample size of included studies ranged from 10 to 648 participants. Study duration was reported in 33 studies, ranging from one month to 10 years. Of these, 14 studies had a duration of six months or less. Twelve studies mentioned a follow-up period that ranged from two weeks to 12 months, of which eight studies had a follow-up period of six months or less.

Pharmacist-led intervention components

Pharmacist-led interventions were broadly classified into the following groups: education or patient counselling, recommendations to healthcare professionals, medication review, clinical assessments and monitoring and reminders. These are discussed further below:

Education and/or patient counselling

Seventeen studies involved interventions whereby pharmacists provided consumers education and/or patient counselling, either through face to face or telephone support. These interventions were delivered by the pharmacist individually or as a group and focused on medication and disease state information and lifestyle modification recommendations, discussing the importance of medication adherence, and providing advice on how to manage medication side effects. Educational and counselling materials were developed based on published information such as consumer information leaflets (Mishra et al., 2017a; Mishra et al., 2017b) or information derived from the US pharmacopeia (Kaukab et al., 2015) or guidelines from the American Society of Hospital Pharmacists (Greco, 1994).

Medication review

Eighteen studies involved a pharmacist-led medication review service as part of the intervention. Components of the medication review services included comprehensive medication history taking and

medication regimen review. Half of the medication reviews (n=9) were conducted in hospitals, and only four were conducted in community settings such as a community mental health team.

Clinical assessments and monitoring

Pharmacists conducted clinical assessments and monitoring for people living with SPMI in 15 studies. These assessments and monitoring helped identify adverse drug reactions (n=5), medication-related problems such as reducing antipsychotic polypharmacy (n=7), drug efficacy and appropriateness (n=3), and symptom/illness related issues (n=3).

Recommendations to healthcare professionals

Eighteen studies involved pharmacists providing recommendations or feedback to other healthcare professionals. All recommendations or feedback provided were after medication reviews and clinical assessments and monitoring conducted by pharmacists. Pharmacological recommendations provided to prescribers were all medication-related, whereby pharmacists made dose adjustments and suggested alternative medication recommendations to optimise treatment or reduce antipsychotic polypharmacy. Other recommendations involved requesting laboratory tests (Dorevitch and Perl, 1996), and monitoring for various parameters such as any changes in glucose and lipid profile (Diefenderfer et al., 2014).

Reminders

Reminders were provided to both consumers and healthcare professionals. Reminders were given to consumers to improve medication adherence through mailing medication refill reminders and packing dose administration aids (Stip et al., 2013; Valenstein et al., 2011). On the other hand, doctors were

provided reminders for metabolic monitoring and assessments of antipsychotic adverse effects by a pharmacist-driven antipsychotic monitoring database (Diefenderfer et al., 2014).

Intervention design

Single or multifaceted interventions

Twenty-four studies employed more than one intervention (multifaceted interventions), whereas 13 studies involved a single pharmacist-led intervention (shown in Table 2 and 1, respectively). Of the 24 multifaceted intervention studies, two studies described the range and types of pharmacist-led interventions conducted (Gable and Stunson, 2010; Rees et al., 1997). Gable et al. reviewed all the interventions a clinical pharmacist made and showed that medication management was the most frequent intervention performed (Gable and Stunson, 2010). Rees et al. documented the consumer-pharmacist interactions and found that almost half of the community pharmacist interactions with people with schizophrenia involved counselling about medication adverse effects (Rees et al., 1997).

Single intervention: Of the thirteen studies that employed a single intervention, nine were education and/or patient counselling interventions, two involved clinical assessments and monitoring, one involved medication reviews, and one study involved adherence reminder messages. The majority of studies (n=9) relied solely on consumer-reported measures to evaluate outcomes such as medication adherence, consumer knowledge, and quality of life (QOL). Only one study evaluated outcomes such as medication adherence and adverse effect through scales such as the Medication Adherence Rating Scale, Abnormal Involuntary Movement Scale and Barnes Akathisia Rating Scale that were completed by both the consumer and clinician (Yalcin et al., 2019).

Multifaceted interventions: The 15 studies involving multifaceted pharmacist-led interventions included a combination of components such as providing recommendations to other healthcare professionals, medication reviews, and performing assessments and monitoring. Nine studies involved interventions focusing on education and/or patient counselling and other components such as performing clinical assessments and monitoring, providing feedback or conducting medication reviews. Details of the outcomes reported are presented in Table 1 and 2. In terms of the effectiveness of the interventions, 10 studies showed significant improvement in medication adherence, QOL, antipsychotic polypharmacy and dose, disease or symptoms severity, adverse effects, hospitalisation and relapse rate.

Outcome measurement

Consumers and pharmacists/clinicians were involved in the evaluation of various outcomes, which included medication adherence, QOL, clinical, medication-related outcomes, medical practitioners' acceptance rate of pharmacists' recommendations and other healthcare outcomes such as healthcare service utilisation. Table 1 and 2 provide detailed presentations of all study outcome(s) and their statistical significance. The outcome measures reported in more than five studies are reported below:

Consumer-reported outcomes

Medication adherence: A total of 10 studies measured medication adherence as an outcome. The tools used to assess adherence varied; eight studies relied solely on validated self-reported adherence tools, and two used objective adherence measures such as pharmacy records and drug concentration. Seven of the eight studies using self-reported measures showed significant improvement(s) in at least one measure or domain of adherence. Only two included studies involved multiple adherence measures

(Stip et al., 2013; Valenstein et al., 2011). Stip et al. reported a lack of concordance between clinician-reported and self-reported adherence (Stip et al., 2013). Valenstein et al. assessed changes in adherence using objective and subjective measures, namely self-reported and pharmacy data, and found significant improvements in both (Valenstein et al., 2011).

Quality of life: Six studies investigated changes in consumers' QOL. Different tools were used to assess QOL, but half of the studies (n=3) used the WHO Quality of Life-BREF assessment and all showed significant QOL improvement (Mishra et al., 2017a; Mishra et al., 2017b; Singh et al., 2017).

Clinical outcomes

A range of clinical outcome measures were reported in 11 studies. Most common reported outcomes included symptom/illness severity (n=6), depression symptoms (n=5), presence, number and severity of adverse effects (n=4), and cognition (n=3). All studies (n=4) showed significant improvement in the number or severity of adverse effects (Canales et al., 2001; Dorevitch et al., 1993; Lupu et al., 2017; Yalcin et al., 2019). Various tools were used to assess changes in clinical outcomes, for example depression symptoms were commonly assessed by the Hamilton Depression Rating Scale or Beck Depression Inventory, and studies mostly used the Positive and Negative Syndrome Scale, Brief Psychiatric Rating Scale, or Clinical Global Impression scale to assess symptom severity.

Medication-related outcomes

Of the eight studies that reported on a medication-related outcome, seven described reduction in the use of antipsychotics (n=4), anti-Parkinson (n=1), and anticholinergic (n=2) medications. However, only three of the seven studies showed significant reductions in at least one type of medication use (Hashimoto and Tensho, 2016a; Hazra et al., 2011; Sathienluckana et al., 2018).

Medical practitioners' acceptance rate of pharmacists' recommendations

Seven studies reported on medical practitioners' acceptance rate of pharmacists' recommendations. All recommendations made were related to pharmacotherapy changes such as dose adjustments and changing or discontinuing inappropriate medications. Parihar et al. had the lowest acceptance rates of 52.7% (Parihar et al., 2019) whereas Canales et al. reported the highest (94%) (Canales et al., 2001). Two studies demonstrated a 100% acceptance rate for specific recommendations relating to preventing unnecessary drug therapy among consumers living with schizophrenia (Sathienluckana et al., 2018), and medication adjustments, laboratory monitoring, continuity of medications, and adverse events among consumers living with a diagnosis of SPMI (Gable and Stunson, 2010).

Healthcare service utilisation

The use of healthcare services was reported in five studies. More than half (n=3) were related to hospitalisation, of which two studies showed significant reduction in hospitalisation and length of stay (Battig et al., 2020; Salazar-Ospina et al., 2017).

Pharmacists' qualifications and training provided for intervention delivery

The details of pharmacists' qualifications and/or the training provided to pharmacists prior to their delivery of interventions were reported in eight studies. Two studies included board certified psychiatric pharmacists (Gable and Stunson, 2010; Tallian et al., 2012). Six provided descriptions of the intervention training provided, and all the intervention training content varied and the personnel delivering the intervention were different (Gisev et al., 2006; Ilickovic et al., 2016; Marques et al., 2013; Salazar-Ospina et al., 2017; Sathienluckana et al., 2018; Stoner et al., 2000). For example, some pharmacists received training by psychiatrists to prepare them to support people living with SPMI (Salazar-Ospina et al.,

2017), whereas in the study by Gisev et al., training was delivered by a multidisciplinary team including specialist pharmacists, consumer educators, a psychologist, a mental health nurse and a psychiatrist (Gisev et al., 2006). Training duration was reported in only two studies, which ranged from eight to 57 hours of training.

Risk of bias

RCTs

Figure 2 shows the results of the RoB-2 risk of bias assessments conducted for 10 RCTs. Eight had a high risk of bias, and the other two had some concerns. All RCTs had at least some concerns due to the nature of the intervention resulting in difficulty in blinding consumers and pharmacists. Six RCTs were assessed to have a high risk of bias relating to the 'measurement of the outcome' as they relied on self-report measures with non-blinded participants (Ahamad et al., 2019; Kaukab et al., 2015; Marques et al., 2013; Mishra et al., 2017a; Mishra et al., 2017b; Singh et al., 2017). Although there were 10 RCTs included in this review, only two specified the randomisation technique, and were rated as having low risk of bias in the randomisation process (Ahamad et al., 2019; Singh et al., 2017). The randomisation process of the other eight RCTs was not reported, potentially introducing selection bias. One RCT had a high risk of bias in the randomisation process, as there were significant differences in baseline symptom severity (Kaukab et al., 2015).

Non-RCTs

Figure 3 shows the results of the ROBINS-I risk of bias assessment conducted for pre/post and post-intervention studies. Of the 27 non-RCT studies included in this systematic review, 20 had high risk, and

seven had moderate risk of bias. All post-intervention study designs were assessed as moderate-high in the 'bias due to confounding' category as they lacked a control group, thereby increasing the chance of confounding. All except one study had low risk of 'bias due to deviations from intended interventions' (Dorevitch et al., 1993). The study by Dorevitch et al. was assessed as high risk since the authors stated changes to hospitalisation criteria over the study period could have affected intervention delivery (Dorevitch et al., 1993).

	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Ahamad et al, 2019 (Ahamad et al., 2019)	+	?	+	-	+	-
Kaukab et al, 2015 (Kaukab et al., 2015)	-	?	+	-	-	-
Marques et al, 2013 (Marques et al., 2013)	?	?	+	-	+	-
Mishra et al, 2017 (Mishra et al., 2017a)	?	?	+	-	+	-
Mishra et al, 2017 (Mishra et al., 2017b)	?	?	+	-	+	-
Salazar-Ospina et al. 2017 (Salazar-Ospina et al., 2017)	?	?	+	?	+	?
Sathienluckana et al, 2018 (Sathienluckana et al., 2018)	?	?	-	?	+	-
Singh et al, 2017(Singh et al., 2017)	+	?	+	-	+	-
Stip et al, 2013 (Stip et al., 2013)	?	?	-	+	-	-
Valenstein et al, 2011 (Valenstein et al., 2011)	?	?	+	?	+	?

Fig. 2 Risk of bias of randomised controlled trials using RoB 2 tool (Higgins et al., 2016)

Note: +, - and ? show low, high risk of bias or some concerns, respectively

	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall quality assessment
Aburamadan et al, 2018 (Aburamadan et al., 2018)	?	+	—	+	+	?	+	—
Battig et al, 2020 (Battig et al., 2020)	+	+	+	+	+	?	+	?
Canales et al, 2001 (Canales et al., 2001)	?	+	+	+	+	—	—	—
Diefenderfer et al, 2013 (Diefenderfer et al., 2014)	?	—	+	+	—	?	—	—
Dorevitch et al, 1993 (Dorevitch et al., 1993)	—	?	—	—	+	—	?	—
Dorevitch and Perl, 1996 (Dorevitch and Perl, 1996)	?	+	—	+	+	+	+	—
Drivenes, 2016 (Drivenes et al., 2016)	+	?	?	+	+	?	?	?
Fleming et al, 2020 (Fleming et al., 2020)	?	+	+	+	+	?	+	?
Gable and Stunson, 2009 (Gable and Stunson, 2010)	+	—	+	+	+	?	—	—
Gisev et al, 2006 (Gisev et al., 2006)	+	+	+	+	?	+	+	?
Greco, 1994 (Greco, 1994)	—	+	+	+	—	—	+	—
Hashimoto and Tensho, 2016 (Hashimoto and Tensho, 2016b)	?	+	+	+	+	—	?	—
Hashimoto and Tensho, 2016 (Hashimoto and Tensho, 2016a)	+	—	+	+	—	?	—	—
Hazra et al, 2011 (Hazra et al., 2011)	—	+	—	+	+	+	—	—
Ilickovic et al, 2016 (Ilickovic et al., 2016)	+	+	+	+	+	?	+	?
Kjeldsen et al, 2013 (Kjeldsen et al., 2013)	—	+	+	+	+	?	+	—

Kavanagh et al, 2003 (Kavanagh et al., 2003)	+	?	+	+	+	-	?	-
Lin et al, 2019 (Lin et al., 2019)	-	+	?	+	+	+	?	-
Lupu et al, 2017 (Lupu et al., 2017)	?	-	+	+	?	?	+	-
Murata et al, 2012 (Murata et al., 2012)	+	-	+	+	+	-	+	-
Parihar et al, 2019 (Parihar et al., 2019)	-	+	+	+	+	?	-	-
Raynsford et al, 2020 (Raynsford et al., 2020)	+	-	?	+	+	+	+	-
Razali and Yahya, 1997 (Razali and Yahya, 1997)	?	?	-	+	?	?	+	-
Rees et al, 1997 (Rees et al., 1997)	+	+	?	+	-	?	+	-
Stoner et al, 2000 (Stoner et al., 2000)	?	+	?	+	+	?	+	?
Tallian, K.B., et al., 2012 (Tallian et al., 2012)	+	+	+	+	+	+	?	?
Yalcin et al, 2019 (Yalcin et al., 2019)	+	+	+	+	-	+	-	-

Fig. 3 Risk of bias of nonrandomised controlled trials using ROBINS-I tool (Sterne et al., 2016)

Note: +, - and ? show low, serious or moderate risk of bias, respectively

Discussion

This review provides a comprehensive overview of the literature pertaining to the effectiveness and demonstrated the potential value of pharmacist-led interventions for people living with SPMI. This review aimed to explore pharmacists' involvement, outcomes of pharmacist-led intervention(s) of supporting people, education and training for pharmacists prior to delivering the intervention(s) and barriers and facilitators for pharmacist-led intervention. The review's research questions are explored in detail below.

Pharmacists' involvement in supporting people living with SPMI

Pharmacists have demonstrated the ability to provide a wide range of services in a variety of healthcare settings to people living with SPMI. Findings from this review suggest most pharmacist-led interventions involve a component of consumer education and/or patient medication counselling, regardless of whether the intervention was single or multifaceted. While no included studies conducted a cost-effectiveness analysis of pharmacist-led educational intervention for SPMI, other studies have suggested that one reason for this may be the relatively easy implementation and cost-effectiveness of educational interventions (Milosavljevic et al., 2018). Educational interventions alone have been shown to be effective in the current literature, and the findings of this review align with this suggesting that pharmacist-led educational interventions improve medication adherence, levels of knowledge and QOL in people living with SPMI (Hätönen et al., 2008; Yeni et al., 2018; Amer et al., 2018). This systematic review found that multifaceted interventions with a larger number of elements were more successful in improving both medication adherence and clinical outcomes when compared to pharmacist-led single interventions. This may be due to

several reasons, including reporting bias and the nature of multifaceted interventions. It is identified in this review that studies employing multifaceted interventions were more likely to report on both consumer- and clinician-reported outcomes, whereas single interventions focused on reporting consumer-reported outcomes. The lack of consistency in the intervention design, as well as outcome measures rendered it difficult for the authors to conduct comparisons of the effectiveness of the interventions. However, it is also arguable the multifaceted approach that involves multiple components is more likely to address the complex health issues that people living with SPMI experience (Ostler and Ackerson, 2008).

An example of this multifaceted approach was the Dader method, which was used in two studies (Marques et al., 2013; Salazar-Ospina et al., 2017). The pharmacists first conducted a pharmaceutical interview to assess consumers' health problems. Next, consumers and prescribers were informed about any medication-related problems identified, and then education and recommendations were provided to consumers and prescribers, respectively. Another multifaceted approach is involving pharmacists in clozapine clinics to help monitoring and adverse events (Maryan et al., 2019). While none were included in this review as they did not meet the inclusion criteria, previous studies have explored how pharmacists could help overcome the barriers to clozapine use and the potential of pharmacists in clozapine monitoring and assessments was acknowledged (Kelly and Love, 2019; Maryan et al., 2019). Nevertheless, similar to previous studies exploring pharmacist-led multifaceted interventions, it is not known which component are specifically responsible for outcome improvements (Milosavljevic et al., 2018). There is a need to explore what components of multifaceted pharmacist-led interventions are most effective, feasible and acceptable. Further research is required to definitively determine if a multifaceted intervention is more effective than a single intervention, and which elements and combinations are most effective.

Outcomes of pharmacist-led intervention(s)

Furthermore, findings from this systematic review suggest that pharmacist-led interventions do lead to significant improvements across a broad range of health outcomes, including medication adherence, QOL, and reduce disease progression, symptom or illness severity, hospitalisations and antipsychotic polypharmacy. Pharmacists' recommendations were generally well-accepted by medical practitioners, with up to 100% acceptance rate for medication-related or monitoring recommendations (Gable and Stunson, 2010; Sathienluckana et al., 2018). Despite these positive effects on consumer health outcomes, the heterogeneity in the outcomes reported did not allow for more targeted analyses to explore the pooled effects in terms of the benefit to consumers. While consumer-reported measures were the most common method used to evaluate outcomes, studies used a variety of measures including consumer, pharmacist or clinician-reported outcomes. It is interesting to note that the reliability of using consumer self-reported measures to assess QOL in people living with psychiatric disorders has been questioned previously (Revicki et al., 2014). Consumer-reported outcomes often poorly correlate with clinical or performance-related outcomes (Johnston et al., 2019), and the ability of people living with severe mental illness to self-assess their own health have been questioned (Milosavljevic et al., 2018). However, recent emerging evidence suggests the importance of consumer involvement in the assessment of treatment outcomes, particularly in the field of psychiatry (Deshpande et al., 2011; Sartorius, 2014). Specifically, it is important for consumers to assess their own QOL and the clinicians' views should be used as a proxy to rate QOL (Sartorius, 2014). Therefore, it is recommended that future intervention studies include both consumer-reported and clinician/pharmacist-reported outcomes to assess the overall health and functioning of people living with SPMI (Sartorius, 2014).

Education and training provided prior to pharmacists' intervention

This systematic review also identified that standardised training was not provided to pharmacists in the studies included in this systematic review. The authors recommend the delivery of standardised training such as Mental Health First Aid training should be provided to pharmacists prior to the intervention delivery to increase their confidence in working with people living with SPMI (El-Den et al., 2020b; O'Reilly et al., 2019; O'Reilly et al., 2011), and to allow for comparisons across studies.

Barriers and facilitators of pharmacist-led interventions

None of the studies included in this systematic review specifically reported on barriers or facilitators to implementing a pharmacist-led intervention for people living with SPMI. Other studies demonstrated that common barriers to implementing pharmacy mental health interventions included consumer- and pharmacist-related factors such as pharmacists' attitudes and beliefs, and also social and healthcare system-related factors such as stigma and the lack of privacy in community pharmacy settings (Aaltonen et al., 2010). The majority of studies identified in this review were conducted in hospital settings and one important barrier to consider is the transferability of effective interventions identified in this review from inpatient hospital settings to community pharmacy settings. Community-based treatment has the potential to provide better clinical outcomes (Hoult et al., 1983), and have demonstrated higher consumer satisfaction compared to treatment in a psychiatric hospital (Hoult et al., 1983). The lack of access to clinical information in the community pharmacy may explain the limited community based interventions (Blalock et al., 2013). Another reason for the majority of studies occurring in hospital settings may be related to time constraints, in that the successful implementation of pharmacist-led services for people living with SPMI in community

settings will require appointment-based consultation (Tallian et al., 2012). Community pharmacies traditionally do not have the capacity in terms of staffing, infrastructure and reimbursement to deliver appointment-based consultations; however, the introduction and expansion of pharmacist-led interventions such as depression screening clinics has shed light to the potential of pharmacist-led services in the area of mental health (O'Reilly et al., 2015). More pharmacies are starting to have private consult rooms, which will allow consumers to comfortably talk about their mental health. Nonetheless, the literature pertaining to community pharmacy-led interventions for people living with SPMI is largely lacking and there is a need for further research in this space and overcome other barriers such as time, stigma and the lack of awareness of the pharmacists' role (O'Reilly et al., 2015). As suggested in previous research, there is a need for future research to evaluate the effectiveness of these interventions in community settings (Bell et al., 2005).

Strengths and limitations of the review and future directions

The current review was conducted with strong methodological rigour, in line with PRISMA guidelines and following a pre-registered protocol. A broad search strategy was applied to nine databases to capture an extensive amount of available literature. The screening process was undertaken by two independent reviewers who determined each study's eligibility. A quality assessment of the studies was also conducted using validated tools such as the Cochrane the Risk of Bias assessments (RoB 2 and ROBINS-I).

However, these results should be interpreted with caution. Despite conducting a comprehensive search, only studies from the designated databases published in English were included, thus introducing a level of publication and selection bias. Nonetheless, given that an initial 6700 studies were screened, it is unlikely that this systematic review did not include any relevant publications that met the inclusion and exclusion

criteria. In addition, the studies identified demonstrated considerable heterogeneity among participant groups, type of outcome(s) measured, length of intervention, intervention components, intervention delivery and pharmacists' qualification and training prior to intervention delivery. The lack of well-designed RCTs and high degree of heterogeneity in this review suggests that there are potentially important differences that need to be accounted for and standardized across studies to allow for accurate comparisons. Most studies had a short follow-up period of less than six months and only a limited number of studies that have study durations of up to a year. Previous literature exploring pharmacist-led interventions to improve antidepressant adherence recommends that the duration of the intervention and follow-up period should be at least two years in order to assess intervention effectiveness (Al-Jumah and Qureshi, 2012). In this study, it is unclear whether reported improvements were sustained beyond the study duration. To demonstrate whether pharmacist-led interventions lead to significant, sustained effects on consumers' health outcomes there is a need for future studies to conduct methodologically robust RCTs with large sample sizes, across multiple settings, for longer durations and longer follow-up periods to assess the long-term impacts.

Conclusion

Overall, this systematic review has shown the positive outcomes of pharmacist-led interventions for people living with SPMI and has highlighted a number of significant gaps in the current literature regarding pharmacist-led interventions for people living with SPMI. Future research should attempt to better

understand which specific intervention components have the greatest impact and evaluate the long-term sustainability of such interventions.

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Author contributions

RN, SE-D, SSM, AJW and COR designed the review. RN carried out the database search. RN and VS conducted the screening. RN collected and analysed the data. RN prepared the first draft of the manuscript. COR, SE-D, SSM, AJW, VS, JC and HR contributed to and reviewed the manuscript. RN, COR and SE-D worked to finalise the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Declaration of interest

None.

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Table 1. Description of single pharmacist-led intervention studies

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcomes	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
Aburamadan et al, 2018,(Aburamadan et al., 2018) United Arab Emirates	Observe and record the incidence, pattern, nature, and management of ADRs	Hospital	N=170, psychotic disorder	Post intervention study (single group)	Monitoring and assessment of ADRs	-	51 ADRs identified; 28 (54.9%) had no medication changes, 17 (33.3%) withheld suspected drug, 6 (11.8%) managed by an altered antipsychotic dose	-
Ahamad et al, 2019,(Ahamad et al., 2019) India	Assess the effectiveness of the collaborative approach involving clinical pharmacist-psychiatrist towards the medication adherence	Hospital	IG=30, CG=30, schizophrenia	RCT	Provided pharmaceutical information to families and carers	MMAS-8 Domain 2, 3, 6 improved for IG * MMAS-8 Domain 1,5,7,8 improved for IG (NS) Medication adherence at follow-up IG>CG; IG=26, CG=9 (SNR)	-	-
Gisev et al, 2006,(Gisev	Assess and discuss the pattern of	Community mental	N=56, SPMI	Post-intervention study	Reviewed drug charts, obtained community	-	28 (50%) took ≥2 psychiatric drugs from the same	-

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcomes	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
et al., 2006) Australia	psychiatric drug use among a sample of patients receiving case management for long term or persistent bipolar mood disorders or psychotic illnesses	health service		(single group)	pharmacy dispensing records		<p>class, 23 (41%) received antipsychotic polypharmacy</p> <p>26 (46%) were taking antipsychotics at higher than recommended doses</p> <p>37 (66%) experienced DDIs; 24 (43%) had ≥1 major DDIs, 11 (20%) had ≥1 moderate DDIs, 2 (4%) had ≥1 minor DDIs</p>	
Greco, 1994,(Greco, 1994) USA	Effect of medication compliance if a pharmacist educates about medication and its use	Community mental health centre	N=29, chronic schizophrenia	Pre/post intervention study (single group)	Group educational sessions and weekly individual counselling (MedEd)	Morisky scale improved pre- to post-intervention, 2.20 to 2.75 *	-	-

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcomes	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
Hashimoto and Tensho, 2016,(Hashimoto and Tensho, 2016b) Japan	Investigated the effects of education on awareness of the adverse effects of their medication for patients with schizophrenia	Hospital	N=87, schizophrenia	Pre/post intervention study (single group)	Education about potential adverse effects	24 (27.6%) were aware of adverse effects of pre-intervention 3 (0.034%) were unaware of adverse effects pre- and post-intervention 60 (69.0%) were unaware of adverse events pre-intervention, but were aware post intervention *	-	-
Kaukab et al, 2015,(Kaukab et al., 2015) Pakistan	Analyse effect of individual counselling on score of depression, to investigate that pharmacist can manage depressive symptoms by	Hospital	IG=13, CG=35, severe depression	RCT	Counselling and participants received socio-economic help	Reduction in the number of participants with severe depression (measured based on BDI Scale) post-intervention in IG and CG, IG=13 (37.1%) to 0 (0%), CG=35		-

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer- reported outcomes	Pharmacist/clinician- reported outcomes	Other outcomes of care related to pharmacist- led intervention(s)
	providing health education regarding dose of medicines, related side effects, and to highlight the importance of pharmacist in Pakistan and enhance the interaction of pharmacist with patients					(100%) to 30 (85.7%) (SNR)		
Kavanagh et al, 2003,(Kavanagh et al., 2003) London	Explore the effectiveness of a medication education group on knowledge about drug treatment, insight and treatment adherence	Hospital	IG=15, CG=15, psychotic disorders	Pre/post intervention study (two group)	Provided information sessions	Knowledge increased for IG, 8.33 pre- to 13.07 post-intervention, CG remained similar * IG insight increased, CG decreased *	-	-

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcomes	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
						Compliance between IG and CG (NS)		
Lin et al, 2019,(Lin et al., 2019) USA	Examine the effect of a pharmacist-administered LAIA program in a supermarket-based community pharmacy on medication adherence rate	Community pharmacy	N=641, participants receiving LAIA	Post intervention study (single group)	Assessment to confirm appropriateness of LAIA, review potential adverse events, inform prescriber about missed/complete d appointments, administer LAIA	-	78% adherent to LAIA	-
Mishra et al, 2017,(Mishra et al., 2017a) India	Compare the impact of pharmacist-psychiatrist collaborative patient education with that of treatment by psychiatrist alone	Outpatient department in tertiary care setting	IG=38, CG=35, BPAD	RCT	Patient education using patient information leaflets, carer counselling	Medication adherence improved for IG, IG=1.87, CG=0.59 * QOL improved for IG, IG=20.57, CG=10.96 *	-	-
Mishra et al, 2017,(Mishra et al., 2017b) India	Assess the impact of pharmacist-led	Outpatient department	IG=13, CG=10, schizophrenia	RCT	Patient education using patient information	Medication adherence	-	-

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcomes	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
a et al., 2017b) India	collaborative patient care along with psychiatrist on medication adherence and QOL	in tertiary care setting			leaflets, counselling	improved for IG, IG=1.75, CG=0.7 * QOL improved for IG, IG=24.17, CG=16.12 *		
Singh et al, 2017,(Singh et al., 2017) India	Measure the effect of PC on various domain of the QOL of the patients with bipolar disorder through WHO-QOL-BREF	Hospital	IG=134, CG=13, bipolar disorder	RCT	Medication-related, psycho-, lifestyle modification education using patient information leaflets and booklets to patient and family	WHO-QOL-BREF improved significantly in all follow-up visit, e.g., 3 rd follow up visit IG=56.27, CG=49.11 *	-	-
Stip et al, 2013, (Stip et al., 2013) Canada	Test if smart pill dispenser DoPill® will improve antipsychotic adherence ratio of schizophrenic patients	Hospital	IG=26, CG=21, schizophrenia	RCT	DoPill® sends signal to pharmacist when person has a missed dose	Medication adherence improved based on clinician rating, IG=92.6 in pre- to 96.3 post intervention * Medication adherence improved based	-	-

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcomes	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
						on self-report, IG=95.9 in pre- to 99 post-intervention (NS)		
Yalcin et al, 2019,(Yalcin et al., 2019) Turkey	Evaluates the causes of noncompliance in patients with schizophrenia spectrum disorders and the effect clinical pharmacists may have on improving medication compliance	Outpatient mental health	N=40, schizophrenia, schizoaffective disorder-unspecified, schizotypal disorder, and acute schizophrenia-like psychotic disorder	Pre/post intervention study (single group)	Drug education, provide patients both a printed text (brochure) and an oral training to increase compliance with prescribed medication	Decrease patients with poor compliance, 23 (57.5%) in pre- and 7 (17.5%) post-intervention MARS improved from pre- to post intervention, 6.6 to 8.6 *	SAS improved from pre- to post intervention, 1.15 to 0.35 * BARS improved from pre- to post intervention, 0.78 to 0.58 (NS) AIMS improved from pre- to post intervention, 0.43 to 0.07 *	
ADR, adverse drug reaction; IG, intervention group; CG, control group; RCT, randomised controlled trial; MMAS-8, Eight-item Morisky Medication Adherence Scale; NS, non-significant; SNR, significance not reported; SPMI, severe and persistent mental illness; DDI, drug-drug interaction; BDI, Beck Depression Inventory; LAIA, antipsychotic long acting injection; BPAD, bipolar affective disorder; QOL, quality of life; WHO-QOL-BREF, World Health Organisation Quality of Life; MARS, Medication Adherence Rating Scale; SAS, Simpson-Angus Scale; BARS, Barnes Akathisia Rating Scale; AIMS, Abnormal Involuntary Movement Scale * $P < 0.05$.								

Table 2. Description of multifaceted pharmacist-led intervention studies

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
Battig et al, 2020,(Battig et al., 2020) German y	Assess the effect of a pharmacogenetics-guided drug therapy on the length of hospitalisation, severity of depression, and number of antidepressant switches	Hospital	IG=49, CG=94, major depressive disorder, single episode or recurrent, severe without psychotic features	Pre/post intervention study (two group)	Interpreted results of genetic testing, recommended a drug	Greater improvement rate for BDI-II for IG, IG=-0.626, CG=-0.38 *	Greater improvement rate for GAF for IG, IG=0.685, CG=0.39 (NS)	Reduction in length of hospital stay for IG after correction, IG=36.3, CG=46.6 * Longer time to starting antidepressant therapy for IG, IG=15.3, CG=8.1 *
Canales et al, 2001,(Canales et al., 2001) USA	Determine the effects of a psychiatric pharmacist on clinical outcomes	Hospital	IG=45, CG=48, SMI with Axis I and II diagnosis	Pre/post intervention study (two group)	Weekly education classes, monitoring for adverse drug reactions, performing baseline assessments and weekly reviews, provide pharmacological recommendation, review drug administration daily	Higher clinic visit compliance in IG, IG=54%, CG=46% (NS) Lehman QOL interview	BPRS improved for IG, IG=32.4, CG=14.6 * CGI improved for IG, IG=32.7, CG=11.8 * HAM-D improved for IG, IG=55.0, CG=25.8 *	Medication cost per patient, IG=\$252.14, CG=\$150.59 (NS) Cost-effectiveness ratio, IG=\$10,596.80, CG=\$35,536.62 (cost \$2.48 more per patient to achieve a successful outcome) 158/168 (94%) recommendations made by a pharmacist were accepted

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
						IG; CG (NS) Positive patient satisfaction in IG, not analysed in CG due to low response rate	MMSE improved for IG, IG=14.1, CG=9.2 (NS) AIMS improved for IG, IG=3.5, CG=-0.9 * BARS IG=27.0, CG=-6.8 * SAS IG=21.9, CG=-6.5 *	
Diefenderfer et al, 2013,(Diefenderfer et al., 2014) USA	Evaluate the effectiveness of a pharmacist-driven TD monitoring database to meet facility policy goals	Hospital	IG=57, CG=34, participants receiving ≥1 antipsychotic with an inpatient stay at a psychiatric hospital	Pre/post intervention study (single group)	TD assessment, provide reminders for monitoring	-	-	Compliance with facility monitoring policy improved for IG, IG=38 subjects (66.7%); CG=1 subject (2.9%) *
Dorevitch et al, 1993,(Dorevitch	Report on our experience of a psychiatric clinical pharmacist acting	Outpatient clinic	N=14, schizophrenia	Pre/post intervention study (single group)	Educate and counsel; assess patient response, perform informal		No. of side-effects per patient decreased, 27 (1.92%) pre- to 6	Hospitalisation due to noncompliance decreased, from 4 patients pre- to 1 patient post intervention (SNR)

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
et al., 1993) Israel	in a primary care function under the supervision of a psychiatrist to monitor medication				mental status assessment, monitor patient for EPSE/TD; schedule next appointment; enter medication recommendation into chart		(0.42%) post-intervention * No. of anti-Parkinson medication decreased, from 12 (84%) pre- to 7 (50%) post-intervention (SNR)	Intervention resulted in a potential saving of \$58200 for 582 fewer days spent in hospital
Dorevitch and Perl, 1996,(Dorevitch and Perl, 1996) Israel	Describes the nature of physician-initiated psychopharmacology consultations and interventions by a clinical pharmacist and examines the impact of these interventions on global patient outcome	Hospital	N=191, schizophrenia, affective disorder, mixed and other diagnosis	Post-intervention study (single group)	Assess the nature of the problem, follow up consultation with psychiatrist, document recommendation into patient's chart, review patient's chart	-	-	229 recommendations were made, 203 (88.2%) recommendations adopted, 26 (11.8%) not followed Pharmacist recommendations involved, 130 (57.6%) adding a new or discontinuing a current drug, 67 (29.3%) were increasing or decreasing the dose, 21 (9.2%) were requesting laboratory test or monitoring various parameters, 9 (3.9%) were changing dose schedule
Drivene s, 2016,(D	Describe the drug therapy and follow-up in	Outpatient hospital	N=77, schizophrenia, schizoaffective	Post-intervention study	Follow-up, suggestions for improvement, assess	-	-	68 DRPs in 51 patients, of which 54 (79%) were concurred by psychiatrist

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer -reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
rivenes et al., 2016) Norway	patients and to investigate the potential for improvement of drug therapy through specific recommendations from a consultant pharmacist		e disorders, delusional disorders	(single group)	medical reviews, comments about DRPs were forwarded to psychiatrist for evaluation			Most frequent DRP identified was “lack of monitoring”
Fleming et al, 2020,(Fleming et al., 2020) England	Examine the feasibility of reducing LAI frequency with service user consent	Community mental health team/unit	N=30; people on LAI	Post-intervention study (single group)	Discuss findings and propose action plan to reduce LAI frequency, rationalise psychotropic medication, interview with nurse to capture their view, review electronic patient review for any deterioration that occurred	-	-	No reduction in dose frequency in 11 service users Reduction in LAI frequency was theoretically possible 19 service users, reduction occurred in 8/19, no change in LAI frequency in 11 Dose reduced after medication review in 9 service users, overall LAI dose reduced in 6, oral dose reduced in 3
Gable and Stunson, 2009,(G	Demonstrate the role of a pharmacist on an ACT	Assertive community treatment team	N=34, at least one active Axis I DSM-IV diagnosis of SPMI	Post-intervention study (single group)	-	-	-	341 recommendations were made, of which 80 (medication adjustments, labs, continuity of medication and adverse events) had 100% acceptance rate

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
able and Stunson, 2010) USA	team by reviewing the recommendations and interventions a clinical pharmacist made							Medication management (170) was the most common intervention performed, followed by mental health assessment (54) and medication adjustments (48)
Hashimoto and Tensho, 2016,(Hashimoto and Tensho, 2016a) Japan	Evaluate the usefulness of pharmacist intervention on physician prescribing	Hospital	N=52, schizophrenia	Pre/post intervention study (single group)	Recommendations to optimize and simplify prescription (e.g. discuss polypharmacy, excessive antipsychotic dose; gradual tapering, discontinuation of concurrent medication); examine patients' medical histories	-	<p>Decrease in antipsychotic dose, from 982.6 pre- to 857.6 post-intervention *</p> <p>Decrease in no. of antipsychotics, from 2.0 pre- to 2.0 post-intervention *</p> <p>Rate of concurrent medication use including anti-Parkinson (NS), benzodiazepine (NS) and mood stabiliser (NS)</p>	<p>Cost per day of all medicine decreased, from \$10.33 pre- to \$8.76 post-intervention *</p> <p>Antipsychotics cost decreased, from \$8.04 pre- to \$6.48 post-intervention *</p> <p>Psychotropic agents cost decreased, from \$9.42 pre- to \$7.68 post-intervention *</p> <p>Lower seclusion room use, from 23 pre- to 15 post intervention *</p>

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
Hazra et al, 2011,(Hazra et al., 2011) Canada	Examine effects of active interventions on physician's prescribing of antipsychotic polypharmacy	Hospital	N=648, schizophrenia	Pre/post intervention study (single group)	Team educational sessions on polypharmacy, monitor antipsychotic polypharmacy, follow-up with doctor if multiple antipsychotic use detected; review individual prescription	-	Prevalence of antipsychotic polypharmacy decreased, from 118 (18.3%) pre- to 51 (6.6%) post-intervention * Use of three antipsychotic combinations decreased, from 5.3% pre- to 0% post -intervention (SNR)	-
Ilickovic et al, 2016,(Ilickovic et al., 2016) Montenegro	Perform and document medication review by a clinical pharmacist, reveal DRPs, develop PC interventions, communicate them to the relevant physicians, and assess their	Hospital	IG=49, CG=80, schizophrenia	Pre/post intervention study (two group)	Provide recommendations to physicians, perform medication review		No. of prescribed drugs per patient reduced, from 4.2 pre- to 3.4 post-intervention * Total daily dose of antipsychotics reduced, from 603.9 pre- to 618.0 (NS)	91 interventions accepted and implemented, 36 were not implemented

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
	acceptance and outcomes							
Kjeldsen et al, 2013,(Kjeldsen et al., 2013) Denmark	Evaluate the effect of outreach visit by clinical pharmacists to support the implementation of screening of MeS	Hospital	IG=112, CG=93, schizophrenia, affective disorder	Pre/post intervention study (two group)	Discuss recommendations with other HCP; review patient electronic record focusing on risk medications	-	-	Use of screening sheet improved in IG, IG=81%, CG=36% * Documentation of screening measures in medical charts improved in IG, IG=76%, CG=22% * Screening increased in IG, led to increased identification of MeS, IG=45%, CG=10% *
Lupu et al, 2017,(Lupu et al., 2017) USA	Improve clinical outcomes and QOL in patients prescribed anticholinergic medications by reducing side effects and medication burden	Outpatient psychiatric Clinic	N=29, SMI	Pre/post intervention study (single group)	Medication and disease state education; follow-up assessment; medication use recommendations; provide comprehensive medication management	Anticholinergic burden on QOL improved, from 5 pre- to 3 post-intervention *	Medication changes were clinically appropriate for 19, 13 had >1 anticholinergic medication discontinued, 6 had dose decreased ACB improved, from 7 pre- to 5 post-intervention *	-

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
							PASS improved, from 29 pre- to 14 post-intervention *	
							Memory recall score improved, from 4 pre- to 5 post-intervention *	
Marques et al, 2013,(Marques et al., 2013) Brazil	Assess the effectiveness of PC via pharmacotherapy follow up according to the Dáder Method	Outpatient clinic of hospital	IG=5, CG=5, severe depression	RCT	Dáder method; conduct interviews and pharmacotherapy-related problems were identified, educational lectures	Severe depression, 80% reduction in IG, 60% reduction in CG (SNR) High patient satisfaction in IG	-	-
Murata et al, 2012,(Murata et al., 2012) Japan	Examine the efficacy of pharmacist adherence instruction on antidepressant adherence	Hospital	N=19, bipolar depression	Pre/post intervention study (two group)	Pharmacist adherence instruction using a short information leaflet; monitor side effects and drug efficacy	DAI-10 improved, from 6 pre- to 2 post-intervention *	-	

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
Parihar et al, 2019,(Parihar et al., 2019) India	Identify, resolve and report and percentage of DRP	Hospital	N=286, bipolar disorder	Post intervention study (single arm)	Assess and monitor DRP; provide intervention to resolve DRP	-	-	91 interventions proposed, 66 (72.5%) accepted, 25 (27.4%) were not accepted by the prescriber
Raynsford et al, 2020,(Raynsford et al., 2020) UK	Explore the gaps in service provision relating to medicines and determine whether a specialist pharmacy team could provide useful input for patients on the SMI register	GP surgeries	N=197, SMI	Post-intervention study (single arm)	Raise concerns and discuss with healthcare professionals, resolve concerns, review medication	-	-	104 pharmacist interventions, clarifying discharge information in 12 (11.5%), reviewing high dose and multiple antipsychotic prescribing in 18 (17.3%), correcting errors in 10 (9.6%), investigating adherence issues in 16 (15.4%), following up missing health checks in 22 (21.2%), answering queries from staff in 23 (22.1%), other causes 3 (2.9%) interventions
Razali and Yahya, 1997,(Razali and Yahya, 1997)	Assess the effectiveness of a family-based intervention program	Hospital	IG=85, CG=80, schizophrenia	Pre/post intervention study two group)	Carer education, counsel patient and carer, recommend changes to dose frequency		Lower relapse rate in IG, IG=11 (13%), CG=23 (29%) *	

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
Malaysia								
Rees et al, 1997,(Rees et al., 1997)	Monitor specific interactions community pharmacists had with patients, their carers and other health professionals, in order to identify in detail the nature of the involvement of community pharmacists in the management of patients with schizophrenia	Community pharmacy	N=285, schizophrenia or taking antipsychotic	Post intervention study (single group)	Patient and carer counselling; solve problem about supply and administration of medicine; identify prescription error and drug misuse from patient medical record; supply prescription aid	-	-	39 pharmacists recorded 426 interactions with 285 patients 82 clinical interventions were made
England								
Salazar-Ospina et al, 2017,(Salazar-Ospina et al., 2017)	Assess the effectiveness of a pharmaceutical intervention using the Dader Method	Outpatient psychiatric clinic	IG=38, CG=43, bipolar disorder-I	RCT	Dader method, pharmaceutical interview, DRP assessment, suggest necessary interventions and patient education	-	HAM-D improved in IG, IG=0.88, CG=2.15 * Mania symptoms did not change over time (NS)	Hospitalisation rate improved in IG, IG=1, CG=16 hospitalisation * No. of emergency service consultations reduced in IG, IG=5 (17.9%), CG=23 (82.1%) * Unscheduled outpatient visits, IG<CG *

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
Colombia							CGI improved in IG, IG=1.3, CG=1.6 *	
Sathienlueckana et al, 2018, (Sathienlueckana et al., 2018) Thailand	Evaluate the impact of pharmacist intervention on cognitive functions in patients with schizophrenia by focusing on anticholinergic discontinuation	Outpatient department	IG=13, CG: 17, schizophrenia	RCT	Identify DRPs, conduct treatment plans, resolve DRPs and suggest pharmacological management, review medication history		<p>WCST perseverative errors improved in IG, IG= -11.62, CG= -2.14 *</p> <p>BPRS improved in IG, IG=24.69, CG=36.35 *</p> <p>No difference in WMS (short delay free recall trial), IG=6.31, CG=6.24 (NS)</p> <p>No difference in TMT A and B between IG and CG (NS)</p> <p>No. of DRPs reduced in IG by 85.19%, 9.76% in CG</p>	Pharmacist in IG made 28 interventions (acceptance rate: 92.86%), psychiatrist in CG made 4 interventions

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
							Anticholinergic use reduced from 12 to 0 in IG, remained at 15 in CG (SNR)	
Stoner et al, 2000,(Stoner et al., 2000) USA	Assess the presence, severity, and management of extrapyramidal symptoms in patients treated with antipsychotics	Hospital	N=83, axis I mental disorder	Post intervention study (single arm)	Assess antipsychotic induced movement disorders and severity; recommendation regarding dosage and treatment; drug evaluations	-	-	130 (54%) recommendations were made, 107 (82%) were accepted and followed, 23 (18%) were refused by physician, psychiatrist or patient 99 (93%) of evaluations had positive clinical outcome (complete or partial resolution of EPS), 8 (7%) had no improvement or worsening side effect/clinical feature
Tallian et al, 2012,(Tallian et al., 2012) USA	Describe a needs assessment, practice description, practice innovation and reimbursement of a psychiatric pharmacist medication therapy management	Outpatient psychiatric service clinic	N=68, SMI (major depressive disorder, schizophrenia, schizoaffective disorder, substance abuse, anxiety disorder, bipolar disorder)	Post-intervention study (single arm)	Provide medication management; develop pharmacotherapy and psychosocial treatment plan; review progress and response to pharmacological and nonpharmacological therapies	-	-	Pharmacists spent on average 26 minutes per patient per visit with a total mean contact time of 174 minutes per patient and mean documentation time of 80 minutes per patient Cost of the service was \$84542.80 at a contractual rate of \$4.82 per minute

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer-reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
	clinic with related challenges and opportunities							
Valenstein et al, 2011,(Valenstein et al., 2011) USA	Assess the effectiveness of this pharmacy-based intervention, Meds-Help, in improving antipsychotic adherence among patients with SMI Examine the effects of the intervention on patients' psychiatric symptoms, QOL, and satisfaction with health services	Outpatient psychiatric service clinic	IG=58, CG=60, SMI	RCT	Medication and packaging education session; notify doctor if prescription not filled; review patient prescription medication and treatment indication; mail reminders before scheduled refill date	MPRs improved in IG, mean difference was 6 and 12 months was 0.26 and 0.25 * CAM improved in IG, IG=50%, CG 17% were adherent at 6 months * and 12 months (NS)	No difference in PANSS at 12 months, IG=55.3, CG=57.1 (NS) No difference in QWB at 12 months, IG=0.60, CG=0.61 (NS)	Intervention was acceptable with 74% of intervention patients completing the full 12-month intervention

Author, year, country	Study aim	Setting	Sample size, population	Study design	Interventions	Consumer -reported outcome	Pharmacist/clinician-reported outcomes	Other outcomes of care related to pharmacist-led intervention(s)
						No difference in CSQ-8 at 12 months, IG=26.4, CG=27.0 (NS)		
IG, intervention group; CG, control group; BDI-II, Becks Depression Inventory II; GAF, Global Assessment of Functioning Scale; NS, non-significant; SMI, severe mental illness; QOL, quality of life; BPRS, Brief Psychiatric Rating Scale; CGI, Clinical Global Impression; HAM-D, Hamilton Psychiatric Rating Scale for depression; MMSE, Mini-Mental State Exam; AIMS, Abnormal Involuntary Movement Scale; BARS, Barnes Akathisia Rating Scale; SAS, Simpson-Angus Scale; TD, tardive dyskinesia; EPSE, extrapyramidal side effects; SNR, significance not reported; DPR, drug related problem; LAI, antipsychotic long acting injection; ACT, Assertive Community Treatment; SPMI, severe and persistent mental illness; PC, pharmaceutical care; HCP, healthcare professionals; MeS, metabolic syndrome; ACB, Anticholinergic Cognitive Burden; PASS, Pittsburgh Anticholinergic Symptom Scale; RCT, randomised controlled trial; DAI-10, Drug Attitude Inventory; GP, general practice; WCST, Wisconsin Card Sorting Test; WMS, Wechsler Memory Scale; TMT, Trial making Test; EPS, extrapyramidal symptoms; MPRs, medication possession ratios; CAM, composite adherence measure; CSQ-8, Client Satisfaction Questionnaires; PANSS, Positive and Negative Symptom Scales; QWB, Quality of Well-being Scales * $P < 0.05$.								