

The Effect of Pharmacist Services on Patient Health Outcomes in a Low Middle-income Country: a Systematic Review

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Abstract

Background: The pharmacist's role is shifting from dispensing to bedside care, resulting in better patient health outcomes. However, pharmacist services on healthcare utilization in low- and middle-income countries such as Pakistan are unclear. As a result, we intend to conduct a systematic review of pharmacists' roles in improving Pakistani patients' health outcomes.

Methods: We searched PubMed, Scopus, EMBASE, CINAHL, and Cochrane Library for relevant articles published from inception to February 2021. Original studies investigating the therapeutic, humanistic, safety, and economic impact of pharmacists in Pakistani patients (hospitalized or outpatients) were selected. Two reviewers independently assessed the bias in studies, and mutual consensus resolved discrepancies.

Results: The literature search found 751 articles from which ten studies were included; seven were randomized controlled trials (RCTs), and three were observational studies. Three RCTs included were having a low risk of bias (ROB), two RCTs were having an unclear ROB, while two RCTs were having high ROB. Pharmacist interventions comprised one or more components like provision of education about the disease, medication adherence counselling, medication therapy management, and consultation with a physician regarding change of prescription. In most studies, pharmacists provided therapeutic care, followed by humanistic and safety outcomes with significant improvements. Intervention effect on cost-effectiveness and long-term outcomes were unclear.

Conclusions: Positive but not always statistically significant pharmacist effects on therapeutic, humanistic, and safety outcomes have been reported. Therefore, the results favour adding on the benefit of pharmacist services but lack evidence of economic feasibility and long-term impact of pharmacist interventions.

Background

Since 1990, with pharmaceutical care introduction, pharmacists' careers have evolved from single dispensary positions to patient-oriented health care [1, 2]. Pharmacists are sufficiently empowered to play a vital role in pharmaceutical care [3, 4]. However, pharmacists' role in developing countries is gradually moving towards direct cooperation with other health professionals [5, 6]. In the meantime, they remain primarily responsible for the production, distribution, and dispensing of medicines [3, 7].

To improve pharmacy services across the country, the Federal Government of Pakistan has established a regulatory body, the Drug Regulatory Authority of Pakistan (DRAP) Act 2012 [8]. Under the DRAP Act 2012, pharmacy services include pharmacy services that range from existing basic services (i.e., dispensing, procurement, storage, distribution of therapeutic products and counselling) to enhanced drug services (pharmaceutical care, pharmacovigilance, pharmacoepidemiology, pharmaco-economic and drug management services) at all levels [9]. The pharmacy curriculum underwent a transition from four years of Bachelor of Pharmacy to five years of Doctor of Pharmacy degree in 2004 by the Higher Education Commission (HEC) of Pakistan [10]. Currently, 21 public sector and 25 private sector universities are offering Pharm D degrees to more than 3000 pharmacists each year [11]. Moreover, as of 2019, the number of community pharmacies in Pakistan has also increased to more than 40,000 [12]. In 2014, to strengthen pharmacists' expertise in clinical roles, HEC introduces the Department of Pharmacy Practice in Pakistan's private and public sector universities [13]. As a result, studies have begun to highlight potential clinical pharmacy progress, including further bedside activities, patient consultation, and therapy optimization in Pakistan [14–16].

The inclusion of pharmacy workers in primary care has been seen as an effective means of improving patient health outcomes [17, 18]. Published literature reviews of the effects and outcomes of pharmacists' interventions in the United States and west showed various outcomes, health care settings, and disease states could benefit through pharmacists' direct care [19–23]. Pande et al. systematically reviewed the impact of pharmacist interventions on patient outcomes, health service utilization and costs in low-and middle-income countries in 2013 [24]. Pande et al. concluded that the pharmacist's services positively impact treatment outcomes such as hyperglycaemia and systolic/diastolic blood pressure (BP), the control of cholesterol, and the quality of life of chronic diseases such as asthma, diabetes, and hypertension [24]. However, the authors were uncertain about the implications of a lack of evidence on health services and costs. All the studies used in the review were from middle-income countries such as South East Asia, Africa and Eastern Europe. These results were heterogeneous as each study measured different outcomes with different clinical conditions using different measurement methods, which requires careful interpretation. As a result, the results may not apply to countries with varying healthcare systems, such as Pakistan, which has recently been classified as one by the World Bank, with low, middle incomes in southern Asia. The real impact of clinical pharmacists and, therefore, the use of services is not well established in Pakistan. There may be a lack of knowledge of clinical pharmacists' added benefits and drivers to support the practice among stakeholders and service users. The objective of this systematic review is therefore to synthesise the therapeutic, safety, humanistic and cost-effective consequences of pharmacist intervention compared to standard treatments without the involvement of pharmacists in direct patient care in Pakistani population.

Methods

Scope of review: eligibility criteria

This systematic review was conducted following the Cochrane Handbook for Systematic Reviews of the Intervention Guidelines [25], and the reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [26]. Studies were included if they were 1) randomized controlled trials (RCTs), pre-post, follow up; 2) involved pharmacist intervention either alone or in a multidisciplinary team 3); measuring any health outcome (humanistic, safety, economic and therapeutic effects); 4) conducted among outpatients or inpatients in the hospital or community pharmacy settings; 5) had a control or comparison group (with healthcare professionals other than a pharmacist); 6) published in a peer-reviewed journal in English language only and available in full-text.

Information sources

We used a population, intervention, comparator, and outcome (PICO) search strategy to identify relevant records from PubMed, Scopus, OVIDEmbase, CINAHL Plus, and Cochrane Libraries. The initial search was done on 14 February 2021, and follow-up searches were done on 28 February 2021

Database searching

The search strategy identified original research on the effect of pharmacists' interventions on therapeutic, safety, humanistic and cost-effective consequences of pharmacist intervention compared to standard treatments without the involvement of pharmacists in direct patient care in Pakistani Population. An extensive literature search was carried out using different search term combinations. The search terms used were Pharmacist OR Pharmacy OR "Clinical Pharmacy" OR PharmD OR "Pharmacist-led") AND (Adherence OR "Health outcomes" OR "Medication management" OR "Patient outcomes" OR outcome OR "Quality of life" OR "clinical outcome" OR Pharmacovigilance OR Economics OR "drug interactions" AND "drug safety") AND (Pakistan OR Pakistani). Due to each database's technical differences and limitations, the search mechanism in each database has been subsequently adapted and slightly modified. Case reports, expert opinions, systematic reviews, letters to editors, comments, correspondence, news articles and qualitative studies were excluded from the study. Conference abstracts were excluded from the study if they were not available in full text and non-English studies.

Data extraction

The titles and abstracts of all the studies collected were examined separately by two authors, AA and MS. The full-text screening was carried out independently by the reviewers for each potential research, and the differences were resolved by consensus. If a discrepancy remained, a third reviewer (MT) helped to develop a mutual agreement. Using a standardized extraction form, the AA extracted the data independently after selecting the eligible studies. The extracted data were checked for accuracy and consistency by the second author (MS). Article details (objective, year of publication and first authors), study design, country of study, sample size and study characteristics (age, follow-up duration, pharmacist intervention, intervention strategy, control group, intervention group, type of outcome measure, main health outcomes) were extracted.

Risk of bias

Two reviewers (AA and MS) independently assessed the quality of RCTs using the Cochrane Risk of Bias Tool (ROB.2) [27]. The mutual consensus resolved discrepancies. In non-RCTs, a Risk of Bias in non-Randomized Intervention Studies (ROBINS-I) tool was used for quality evaluation [28]. These studies have been assessed as being of low risk (if no bias), unclear risk (if any doubts affect results), and high risk (if bias has affected the results severely).

Results

Study Selection

After an initial literature search, a total of 751 research items were identified. As depicted in the PRISMA flow diagram, 44 duplicate records were removed (Figure 1). Following the exclusion of 662 citations found to be irrelevant to the primary research question based on title and abstract view, 45 full-text publications were retrieved and evaluated for eligibility. Thirty five studies were excluded due to following reasons: Editorial/letter to editor = (n=5), study protocol = (n=1), review articles = (n=1), conference paper / proceedings = (n=7), commentary/short report = (n=4), qualitative studies (n=6), not met inclusion criteria = (n=11). Ten studies were selected for analysis.

Study Characteristics

All ten studies chosen for review were conducted between 2013 and 2020 and included 2931 people over the age of 18. Outpatients were included in eight studies [29-36], while inpatients were included in two [37, 38]. Studies included patients of different chronic diseases such as diabetes (2), hypertension (2), tuberculosis (1), chronic kidney disease (1), human immune deficiency virus (1), hepatitis C infection (1), cancer (1), and pharmacovigilance (1).

Of 10 studies, seven were randomized clinical trials (RCTs) [29-35], and three were observational studies [36-38]. Therapeutic outcomes were studied in nine studies [29-36, 38], six studies reported humanistic outcomes [29, 31-33, 35, 36], and two studies discussed safety outcomes [33, 37]. None of the studies reported economic results.

Pharmacist provided a variety of interventions broadly classified into six categories 1) Provision of education regarding disease stages with booklets; 2) exploring adherence barriers and motivational interviewing to improve adherence; 3) lifestyle modification guidance; 4) pharmaceutical care consisting of pharmacovigilance, drug-drug interactions, drug-food interactions; 5) interacting with the physician to change the drug regimen 6) maintain patient follow up care. Detailed characteristics of individual studies and their outcomes are shown in Table 1.

Three RCTs included were having a low ROB [31, 33, 34], two RCTs were having an unclear ROB [29, 32], while two RCTs were having a high ROB [30, 35]. The most common reasons for bias were problems in randomization of participants, measurement of outcomes, and handling of missing data. One observational study had an unclear risk [38], while two had a high ROB [36, 37] due to bias in outcome measurement and handling of missing data. Details of Bias in each study are shown in Figures 2 and 3.

Impact of Clinical pharmacist intervention on patient outcomes

Table 2 summarized the patients' outcomes and the impact of pharmacist intervention on therapeutic, safety, humanistic, and economic outcomes.

Therapeutic outcomes

Saleem et al detected significant reduction in mean SBP (mean difference: IG=8.4 vs CG=0.2; P=0.004) and DBP (mean difference: IG=6.6 vs. CG=0.4 ; P=0.009) in intervention group compared to control group [31].

Amer et al. reported that pharmacist-led educational intervention significantly improved hypertension as SBP (IG:131.81 vs. CG:137.91) and DBP (IG:83.75 vs. CG:87.77) was considerably lower in the intervention group compared to the control group (P<0.001) [32].

Similar findings were reported by Javaid et al. that participants in intervention arm had better improvement in SBP (mean difference= IG: -21.1 vs. CG: +6.1; P<0.001) and DBP (mean difference= IG: -7 vs. CG: +4; P<0.001) than control arm [34].

Samtia et al. reported that there was no statistical difference in mean fasting blood glucose (mean difference: -11.95; P=0.116) and HbA1C level (mean difference: -0.43; P=0.112) between the intervention group and control group at five months follow-up [29]. Kokhar et al. also reported similar findings as there was no change in fasting and random blood glucose level at baseline and follow-up [36].

On the contrary to these findings, Javaid et al. reported that at follow-up, participants in the intervention arm 10.9 ± 1.7 vs. 7.7 ± 0.9) had better improvement in HbA1C level compared to the control arm (10.3 ± 1.3 vs. 9.7 ± 1.3) [P<0.001] [34].

Samtia et al. reported that pharmacist-led intervention had significantly reduced BMI (mean difference: -1.87; P=0.014) and waist circumference (mean difference: -1.27; P=0.002) of diabetic patients between the control and intervention group [29].

Kaukab et al. studied the impact of pharmacist education and socioeconomic support on the depression status among drug-resistant tuberculosis patients. At ten months follow-up, the study revealed that patients who received education and support had significant improvement in depression symptoms than the control group [30].

Aziz et al. reported that clinical pharmacists performed 2649 interventions in phase 1 and 3064 interventions in phase 2, with 2411 (91%) interventions in phase 1 and 2757 (90%) interventions in phase 2 being accepted by related consultants in cancer patients [38].

Safety outcomes

Khan et al. reported that clinical pharmacists investigated the 373 profiles and identified 147 drug-related problems, of which 41.5% (n=61) were related to adverse drug reactions. To solve these problems, 161 recommendations were made by a clinical pharmacist, of which 139 (86.33%) successfully solved the issues [37].

Ali et al. evaluated the frequency of adverse drug events and reported that fewer patients in the pharmaceutical care group (8.2%) had experienced adverse drug events than the usual care group (10.5%) [33].

Humanistic outcomes

Samtia et al. reported that the intervention group had shown improved compliance (p=0.003) compared to the control group. Study evidencing that pharmacist lead intervention also results in improved knowledge regarding sensory changes (p<0.001), self-monitoring of blood glucose level (p=0.001), and knowledge regarding exercise (p<0.001) [29].

Saleem et al. observed at follow-up there was a significant improvement in adherence (-1.8 vs. 3.2; p<0.001) and disease-related knowledge (7.5 vs. 10.2; p<0.001) among participants who received intervention [31].

Similar results were reported by Amer et al. that hypertensive patients who received the educational intervention had improved adherence (IG: 5.89 vs. CG:3.89; p<0.001) and disease-related knowledge score (IG: 18.18 vs. CG:13.31; P<0.001) compared to patients in the control group [32].

Ali et al. revealed that patients in the pharmaceutical care group had better (88.6%) adherence than patients in the usual care group (77.9%) (p<0.001) [33]. Chatha et al. also observed that educational intervention significantly improved the medication adherence among HIV patients as a proportion of patients who never missed their medication was increased up to 36% in the intervention group compared to only a 3% change in the usual care group [35].

Kokhar et al. evaluated the medication adherence and knowledge scores among CKD patients. At follow-up, a significant improvement was observed in medication adherence (p=0.042) and knowledge scores (p=0.022) of participants in the intervention group compared to the control group [36].

Interestingly Saleem et al. reported that at follow up the quality of life was significantly reduced (42.2 vs. 39.6; p<0.001) in the intervention group [31].

Amer et al. reported that after the educational intervention, the participants had significantly improved HRQoL score (IG: 0.73 vs. CG: .689; p<0.001) and VAS score (IG: 69.43 vs. CG:64.29; p<0.001) compared to the control group [32].

Ali et al. reported that HRQoL was significantly improved in both the usual care and pharmaceutical care groups, but no statistically significant change was observed between them. While there was a significant difference in VAS score between both groups at follow-up as patients in the pharmaceutical care group had higher scores than the usual care group (P<0.001) [33].

Discussion

To the best of the authors' knowledge, this is the first systematic review to include widespread evidence of pharmacists' role in Southern Asia, particularly in a low-medium-income country like Pakistan. Clinical pharmacy education in Pakistan is evolving, but still at the root level, and the value of these services for

patients and healthcare systems is not well understood. To endorse changes in practice, policymakers must understand pharmacist benefit add-ons for patients and health systems. This review highlights potential consequences for pharmacists in better disease management and patient outcomes and likely drivers of future professional development and research for decision-makers and scientists.

There was variation in health outcome measurements as well as heterogeneity in pharmacist interventions. Provision of simple education was the most common intervention by the pharmacist. Few studies evaluated complete pharmaceutical care follow-up, which included optimizing medication therapy, monitoring disease progression, assessing adherence, identifying and resolving drug-related problems, and maintaining manual records for each patient. Interventions were delivered (for example, at outpatient departments or inpatient departments), frequency of intervention range from 2 to 6 times during follow up (range 2 to 10 months), length of pharmacist intervention sessions (First session range 15 to 60min, follow up sessions range from 10 to 45min) reported in the studies.

The reviewed studies included were of moderate quality, demonstrating methodological heterogeneity, versatility in the measurement of outcomes, reporting of selected outcomes, and adequacy of power of studies with differential interventions. Nonetheless, clinical pharmacists played an important role in identifying and addressing therapy-related issues in chronic diseases (diabetes, Hepatitis C, CKD, hypertension, tuberculosis, and HIV) and pharmacovigilance in neonatal care. These findings are comparable with the study conducted in a similar Jordanian LMIC setting [3]. However, we could not find any research that evaluated the cost-effectiveness of pharmacist intervention. Similarly, a Cochrane review also reported limited evidence of the cost of pharmacist interventions [24]. Likewise, minimal safety evidence was generated and reported from the growing literature from the UK, the USA, and European countries [20, 39–41].

Implications for Practice and research

Clinical pharmacy services are emerging and are feasible in the Pakistan context. Pharmacists interact with patient consultations and medication therapy management. However, acceptance of their clinical roles by other healthcare workers is challenging [9, 10]. There should be multidisciplinary group discussions to advance clinical pharmacy services in Pakistan. There is no professional body that certifies the pharmacist specialities, like the board of pharmacy specialities (BPS) of America certifies pharmacists in specialized services [42]. Govt of Pakistan should start initiatives like forming a council at a state level to begin clinical residency and certification program to strengthen pharmacist to take better responsibility for patient pharmaceutical care. Moreover, govt should start continuous education programs like in the UK 30 hours of continuous professional development are necessary to complete per year [43].

There was little evidence of pharmacist intervention in terms of safety outcomes, and no study assessing the cost-effectiveness of pharmacist interventions was discovered. Future research should focus on the safety and cost-effectiveness of pharmacist interventions to further develop pharmacist roles. In the future, adequately powered randomized studies with standardized outcome measurements, longer intervention duration, and equal baseline between groups will be required. Research is also needed on the time, frequency, and content of pharmacist interventions to improve clinical outcomes [44]. Furthermore, this study concludes essential insight for future research focusing on a tailored intervention and cost of delivering future cost-effective interventions. The result will be beneficial for the policymakers to choose pharmacist interventions based on the availability of their resources.

Limitations

First, to avoid bias, only peer-reviewed published studies were included in this review; unpublished studies were not included. Second, we found one or a maximum of two studies for each outcome, so it was practically impossible to apply meta-analysis due to variation in follow-up and differences in intervention content. Third, only evidence from Pakistan was included; Other data from neighbouring countries were not included due to different healthcare systems.

Conclusion

The review underlined the role of the clinical pharmacist services in improving patient outcomes and medication therapy management. Pharmacist interventions showed a positive impact on therapeutic, humanistic, and safety outcomes. However, much remains to be understood in safety, cost, and long-term intervention impact. Future studies must be more rigorous in terms of evaluating multidimensional and long-term outcomes. Evidence of Costs-effectiveness must also be sought to allow informed decision-making and allocation of resources.

Abbreviations

DRAP Drug Regulatory Authority of Pakistan

HEC Higher Education Commission

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PICO Population, intervention, comparator, and outcome

ROB Risk of Bias

ROBINS Risk of Bias in non-Randomized Intervention Studies

RCTs Randomized clinical trials

Declarations

Authors' contributions

AA conceived the idea; AA, MS did databases searches, data extraction, risk of bias assessment, data analysis, write up of first draft of paper; MT, data extraction, risk of bias; AQB, JD, SSH reviewed the first draft, did changes in the draft, proof read the manuscript revisions. All authors approved the final version of manuscript.

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Ethics approval and consent to participate

Not required as its review article.

Consent for publication

Not applicable.

Availability of data and materials

All data is presented within the manuscript.

Competing/conflict of interest

We declare no Competing/conflict of interest.

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References

1. Jaber D, Aburuz S, Hammad EA, El-Refae H, Basheti IA: **Patients' attitude and willingness to pay for pharmaceutical care: An international message from a developing country.** *Research in Social and Administrative Pharmacy* 2019, **15**(9):1177-1182.
2. Hepler CD, Strand LM: **Opportunities and responsibilities in pharmaceutical care.** *American journal of hospital pharmacy* 1990, **47**(3):533-543.
3. Hammad EA, Qudah RA, Akour AA: **The impact of clinical pharmacists in improving Jordanian patients' health outcomes.** *Saudi medical journal* 2017, **38**(11):1077.
4. Milosavljevic A, Aspden T, Harrison J: **Community pharmacist-led interventions and their impact on patients' medication adherence and other health outcomes: a systematic review.** *International Journal of Pharmacy Practice* 2018, **26**(5):387-397.
5. Katoue MG, Schwinghammer TL: **Competency-based education in pharmacy: A review of its development, applications, and challenges.** *Journal of evaluation in clinical practice* 2020, **26**(4):1114-1123.
6. Ilardo ML, Speciale A: **The community pharmacist: perceived barriers and patient-centered care communication.** *International journal of environmental research and public health* 2020, **17**(2):536.
7. Babar Z-U-D: **Ten recommendations to improve pharmacy practice in low and middle-income countries (LMICs).** *Journal of Pharmaceutical Policy and Practice* 2021, **14**:1-5.
8. Atif M, Ahmad M, Saleem Q, Curley L, Qamar-uz-Zaman M: **Pharmaceutical policy in Pakistan.** In: *Pharmaceutical Policy in Countries with Developing Healthcare Systems.* edn.: Springer; 2017: 25-44.
9. Atif M, Razzaq W, Mushtaq I, Malik I, Razzaq M, Scahill S, Babar Z-U-D: **Pharmacy services beyond the basics: a qualitative study to explore perspectives of pharmacists towards basic and enhanced pharmacy services in Pakistan.** *International journal of environmental research and public health* 2020, **17**(7):2379.
10. Ahmed A, Tanveer M, Siddiqui A, Khan GM: **Bridging the gap for clinical pharmacist in developing countries like Pakistan.** *J Coll Physicians Surg Pak* 2018, **28**:229-232.
11. **Pakistan Pharmacy council** [<https://www.pharmacycouncil.org.pk/PI.php>]
12. Reporter W: **95 per cent pharmacies in Pakistan are run without a pharmacist.** In: *Gulf news.* World asia news: Online website; 2019.
13. Hashmi FK, Saleem F: **Pharmacy practice in Pakistan: The Catch-22 continues.** *Research in social & administrative pharmacy: RSAP* 2018, **14**(2):213.
14. Khan N, McGarry K, Naqvi AA, Iqbal MS, Haider Z: **Pharmacists' viewpoint towards their professional role in healthcare system: a survey of hospital settings of Pakistan.** *BMC health services research* 2020, **20**(1):1-15.
15. Malik I, Atif M, Scahill SL: **Pharmacy Practice and Policy Research in Pakistan: A Review of Literature Between 2014 and 2019.** *Global Pharmaceutical Policy* 2020:139-175.

16. Atif M, Malik I, Asif M, Qamar-Uz-Zaman M, Ahmad N, Scahill S: **Drug safety in Pakistan**. In: *Drug Safety in Developing Countries*. edn.: Elsevier; 2020: 287-325.
17. McNab D, Bowie P, Ross A, MacWalter G, Ryan M, Morrison J: **Systematic review and meta-analysis of the effectiveness of pharmacist-led medication reconciliation in the community after hospital discharge**. *BMJ quality & safety* 2018, **27**(4):308-320.
18. Naseralallah LM, Hussain TA, Jaam M, Pawluk SA: **Impact of pharmacist interventions on medication errors in hospitalized pediatric patients: A systematic review and meta-analysis**. *International journal of clinical pharmacy* 2020:1-16.
19. Newman TV, San-Juan-Rodriguez A, Parekh N, Swart EC, Klein-Fedyshin M, Shrank WH, Hernandez I: **Impact of community pharmacist-led interventions in chronic disease management on clinical, utilization, and economic outcomes: An umbrella review**. *Research in Social and Administrative Pharmacy* 2020.
20. Imfeld-Isenegger TL, Soares IB, Makovec UN, Horvat N, Kos M, van Mil F, Costa FA, Hersberger KE: **Community pharmacist-led medication review procedures across Europe: Characterization, implementation and remuneration**. *Research in Social and Administrative Pharmacy* 2020, **16**(8):1057-1066.
21. Crawford ND, Myers S, Young H, Klepser D, Tung E: **The Role of Pharmacies in the HIV Prevention and Care Continuums: A Systematic Review**. *AIDS and Behavior* 2021:1-10.
22. Qin S-b, Zhang X-y, Fu Y, Nie X-y, Liu J, Shi L-w, Cui Y-m: **The impact of the clinical pharmacist-led interventions in China: A systematic review and Meta-Analysis**. *International journal of clinical pharmacy* 2020, **42**(2):366-377.
23. Lin G, Huang R, Zhang J, Li G, Chen L, Xi X: **Clinical and economic outcomes of hospital pharmaceutical care: a systematic review and meta-analysis**. *BMC health services research* 2020, **20**:1-14.
24. Pande S, Hiller JE, Nkansah N, Bero L: **The effect of pharmacist-provided non-dispensing services on patient outcomes, health service utilisation and costs in low-and middle-income countries**. *Cochrane Database of Systematic Reviews* 2013(2).
25. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA: **Cochrane handbook for systematic reviews of interventions**: John Wiley & Sons; 2019.
26. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P: **Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement**. *PLoS medicine* 2009, **6**(7):e1000097.
27. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM: **RoB 2: a revised tool for assessing risk of bias in randomised trials**. *bmj* 2019, **366**.
28. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I: **ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions**. *bmj* 2016, **355**.
29. Samtia AM, Rasool MF, Ranjha NM, Usman F, Javed I: **A multifactorial intervention to enhance adherence to medications and disease-related knowledge in type 2 diabetic patients in Southern Punjab, Pakistan**. *Tropical Journal of Pharmaceutical Research* 2013, **12**(5):851-856.
30. Kaukab I, Nasir B, Abrar MA, Muneer S, Kanwal N, Shah SN, AHMAD S, MURTAZA G: **Effect of pharmacist-led patient education on management of depression in drug resistance tuberculosis patients using cycloserine. A prospective study**. *Lat Am J Pharm* 2015, **34**:1403-1410.
31. Saleem F, Hassali MA, Shafie AA, Ul Haq N, Farooqui M, Aljadhay H, Ahmad FUD: **Pharmacist intervention in improving hypertension-related knowledge, treatment medication adherence and health-related quality of life: a non-clinical randomized controlled trial**. *Health Expectations* 2015, **18**(5):1270-1281.
32. Amer M, Rahman NU, Nazir R, Ur S, Raza A, Riaz H, Sultana M, Sadeeqa S: **Impact of pharmacist's intervention on disease related knowledge, medication adherence, HRQoL and control of blood pressure among hypertensive patients**. *Pakistan journal of pharmaceutical sciences* 2018.
33. Ali S, Ali M, Paudyal V, Rasheed F, Ullah S, Haque S, Ur-Rehman T: **A randomized controlled trial to assess the impact of clinical pharmacy interventions on treatment outcomes, health related quality of life and medication adherence among hepatitis C patients**. *Patient preference and adherence* 2019, **13**:2089.
34. Javaid Z, Imtiaz U, Khalid I, Saeed H, Khan RQ, Islam M, Saleem Z, Sohail MF, Danish Z, Batool F: **A randomized control trial of primary care-based management of type 2 diabetes by a pharmacist in Pakistan**. *BMC health services research* 2019, **19**(1):1-13.
35. Chatha ZF, Rashid U, Olsen S, ud Din F, Khan A, Nawaz K, Gan SH, Khan GM: **Pharmacist-led counselling intervention to improve antiretroviral drug adherence in Pakistan: a randomized controlled trial**. *BMC infectious diseases* 2020, **20**(1):1-10.
36. Khokhar A, Khan YH, Mallhi TH, Khan HM, Alotaibi NH, Alzarea AI, Bokharee N: **Effectiveness of pharmacist intervention model for chronic kidney disease patients; a prospective comparative study**. *International journal of clinical pharmacy* 2020:1-10.
37. Khan MU, Ahmad A: **The impact of clinical pharmacists' interventions on drug related problems in a teaching based hospital**. *Int J Pharm Clin Res* 2014, **63**(63):276-280.
38. Aziz MT, Rehman TU, Qureshi S, Andleeb S: **Effects of multidisciplinary teams and an integrated follow-up electronic system on clinical pharmacist interventions in a cancer hospital**. *International journal of clinical pharmacy* 2017, **39**(6):1175-1184.
39. Stewart D, Whittlesea C, Dhital R, Newbould L, McCambridge J: **Community pharmacist led medication reviews in the UK: a scoping review of the medicines use review and the new medicine service literatures**. *Research in Social and Administrative Pharmacy* 2020, **16**(2):111-122.
40. Bonetti AF, Reis WC, Lombardi NF, Mendes AM, Netto HP, Rotta I, Fernandez-Llimos F, Pontarolo R: **Pharmacist-led discharge medication counselling: A scoping review**. *Journal of evaluation in clinical practice* 2018, **24**(3):570-579.
41. Silva RdOS, Macêdo LA, Santos GAd, Aguiar PM, de Lyra DP: **Pharmacist-participated medication review in different practice settings: service or intervention? An overview of systematic reviews**. *PloS one* 2019, **14**(1):e0210312.
42. Joseph T, Hale GM, Moreau C: **Training pharmacy residents as transitions of care specialists: a United States perspective**. *International Journal of Clinical Pharmacy* 2021:1-3.
43. Britain RPSoG: **Medicines, ethics and practice 39: the professional guide for pharmacists**: Pharmaceutical Press; 2015.

44. Presley B, Groot W, Pavlova M: **Pharmacy-led interventions to improve medication adherence among adults with diabetes: A systematic review and meta-analysis.** *Research in Social and Administrative Pharmacy* 2019, **15**(9):1057-1067.

Tables

Table 1: Detailed characteristics of studies included in the review

Author (Year)	Objective	Study design	Sample size	Mean age	Follow up	Setting	Patients' description	Pharmacist intervention	Outcome: Thera
Samtia et al. 2013	Pharmacist led interventions on glycaemic control, medication adherence, disease knowledge, and lifestyle modifications among patients with diabetes	RCT	N = 348 Inter = 178 Control = 170	IG = 46.1 CG = 42.3	5 months, 5 follow ups after every month	Outpatient settings of Nishtar Hospital Multan and DHQ Hospital Layyah	Diabetic patients who were receiving oral hypoglycaemic medication from at least the last 6 months and were having a BMI of more than 25 were included in this study. Patients solely on insulin therapy were not included.	Patients in the intervention group received pre-defined specialised care, i.e., education regarding the disease, adherence, dietary restrictions, self-monitoring of blood glucose, fasting blood glucose and guide patients about control of HBA1c, smoking cessation and exercise impact on glucose control. Also provide education regarding sensory changes, including foot examination	✓
Khan et al. 2014	To check the impact of academic clinical pharmacists in reducing drug-related problems	prospective, observational, and interventional study	N = 373	NR	3 months	Inpatients of 250 bedded teaching-based hospital, located in Karachi	Inpatients of neonatal intensive care unit, Female surgical ward, male surgical ward, post-natal ward, cardiac ward, and medical ward.	Pharmacist on daily basis, monitored all aspects of patients' drug therapy along with the past medical history, laboratory reports and practitioner's notes. The identified drug-related problems were then discussed with the pharmacist team members, and with the development of consensus interventions were conveyed to the respective physician along with the best possible approach to rectify drug-related problem	×
Kaukab et al. 2015	To analyse the effect of pharmacist individual counselling on depression in MDR-TB patients to improve depressive symptoms	RCT	N = 70 IG = 35 CG = 35	NR	10 months	Tuberculosis department of Nishtar Hospital, Multan, Pakistan	Outpatients drug resistance tuberculosis	Pharmacist provided educational intervention with economic help, e.g. monthly food basket (Ghee, flour, milk, sugar, tea, and all cereals). Two-way transportation fares free lab facilities, free medical check-up and free of cost medicines for whole month.	✓
Saleem et al., 2015	to assess the impact of an educational intervention provided to hypertensive patients through hospital pharmacists to improve their knowledge on hypertension,	RCT	N = 385 IG = 193 CG = 192	39 ± 6.5	9 months, 3 follow up visits; first visit 15min, later visits of 10min	the study was carried out in the cardiac units of Sandeman Provincial Hospital (SPH) and Bolan Medical Complex Hospital (BMCH) located in Quetta	Outpatients of Patients aged 18 or over with an established medical diagnosis of hypertension, familiarity with Urdu (the national language of Pakistan) and	Pharmacist provided health education about hypertension (nature, management, treatment and recommended diet and lifestyle modification), medication adherence and its	✓

	their adherence to the medication prescribed and their health-related quality of life.						on antihypertensive medication for the last 6 months.	importance in pharmacotherapy and HRQoL (conceptualisation and importance in treatment outcomes for hypertensive patients). The pharmacist also provided a pocket-sized educational book on hypertension, information leaflets and medication adherence cards (all in Urdu) during the counselling process	
Aziz et al. 2017	aimed to describe and evaluate rejected interventions (RIVs) with a particular emphasis on their correctness. Second, to compare two methods to improve the acceptance rate: a computerised electronic prompt of RIVs and a multidisciplinary team (MDT) approach.	Observational, follow up	NA	NA	6 months Phase 1: 3 months Phase 2: 3 months	Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH&RC)	In patents of different cancer types	Three clinical pharmacists reviewed RIVs one by one based on the outcome of laboratory tests related to the patient's clinical condition, physician decisions, comorbidities and concurrent drug therapy. Pharmacists discussed the issue with the prescriber and re-initiated the intervention, or the prescriber amended the order accordingly. FIVs that were later accepted were also recorded. A comparison of the acceptance rate after the computerised prompt alert was also analysed.	√
Amer et al. 2018	To evaluate the effect of pharmacist educational intervention to the patients of hypertension to improve knowledge, adherence to medicines, blood pressure control and HRQoL	RCT	N = 394 IG = 192 CG = 192	NA	9 months with 3 follow ups	Polyclinic hospital of Islamabad	Outpatients visiting the cardiology section of the hospital	Pharmacist conducted a thorough interview of patients at each visit. Pharmacist identified leading causes of lack to adherence towards medication adherence and provided disease-related education to the patient (hypertension-related information, lifestyle education, medication counselling tips to increase knowledge about hypertension, adherence to medication and HRQo1). A printed booklet (in Urdu language) of hypertension-related educational material was	√

								provided to the patients.	
Ali et al. 2019	To evaluate the impact of clinical pharmacy interventions on treatment outcomes, HRQoL, and medication adherence among hepatitis C patients.	RCT	N = 931 IG = 465 CG = 466	42.35	3 months, three follow up visits,	Gastroenterology outpatient department of SIMS, Lahore and the PIMS Islamabad	Confirmed HCV-positive patients aged ≥ 18 years who presented to the gastroenterology department or HCV clinic during the study period were eligible for inclusion in the study.	Clinical pharmacist-provided individualised patient care, including direct patient monitoring, provision of medication diary, education on lifestyle modifications, and counselling on the appropriate use of HCV medication. Clinical pharmacy services continued until treatment completion.	✓
Javaid et al. 2019	To demonstrate the pharmacist-led improvements in glycaemic, blood pressure and lipid controls in type 2 diabetes mellitus (T2DM) patients	RCT	N = 244 IG = 123 CG = 121	50.92	9 months with 3 follow-ups; 15-30 min	primary care facility, Murad clinic Shalamar link road, Lahore, under the supervision of a general practitioner	Un-controlled T2DM patients (HbA1c > 8%) were provided with information on the trial conduct and operational procedures by the research pharmacist	Pharmacist performed PWDT, CORE, PRIME, non-adherence, adverse drug reactions, monitoring and screening of patients at each follow-up.	✓
Chatha et al. 2020	To investigate pharmacist-led intervention can increase adherence to antiretroviral therapy (ART) for people living with HIV	RCT	N = 66 IG = 33 CG = 33	IG = 36.18 CG = 31.39	2 months, two follow ups of 30min duration	ART centre, Pakistan institute of medical sciences	HIV positive, > 18 years of age, taking ART for > 3 months and not enrolled in another treatment adherence program. The exclusion criteria were: having incomplete baseline blood test, pregnancy, or a cognitive impairment that may prevent engagement with the intervention.	Pharmacist provided counselling was tailored to each social factor focused on personal barriers to taking medication and was aimed at helping participants understand their medication-taking behaviours while acknowledging the actions needed to maintain a high level of adherence, also included advice on the potential negative impact of diet and supplementary herbs or medicines on the effectiveness of ART	✓
Khokhar et al. 2020	To evaluate the impact of pharmacist-led intervention among pre-dialysis CKD patients to improve disease knowledge, adherence, body composition and physiological profile of CKD patients.	Pre-post prospective	N = 120 IG = 60 CG = 60	55.88 ± 13.83	3 months; 45min first session	Nephrology outpatient department, National Institute of Kidney Diseases, Sheikh Zayed Hospital, Lahore	All patients with an established diagnosis of CKD stage 2 to 4 (GFR between 15- 89 ml/min per 1.73 m2) according to K/DOQI guidelines of the National Kidney Foundation (NKF) were enrolled in the study.	Pharmacist provided information about the disease, dietary recommendations, counselling to improve medication adherence along with telephonic follow-up	✓

FIVs = Follow on interventions, RIVs = rejected interventions, HRQoL = Health Related Quality of Life, SIMS = Services, Institute of Medical Sciences, PIMS = Pakistan Institute of Medical Sciences, PWDT = Pharmacist's work up of drug therapy, CORE = Condition, Outcome, Regime, Evaluation, PRIME = Problem, Risk, Interaction, Mismatch, Efficacy

Table 2: Summary of the clinical pharmacist effect on patients' outcomes.

Authors	Therapeutic	Safety	Humanistic	Economic
Samtia 2013	FBS* HbA1C* Waist Circumference*	-	Compliance (+)	-
Khan et al. 2014		DRP		
Kaukab et al.	Depression (+)	-	-	-
Saleem et al., 2015	SBP (+) DBP (+)		Knowledge (+) Adherence (+) EQ5D (+) EQ-VAS (+)	-
Aziz et al. 2017				
Amer et al. 2018	SBP (+) DBP (+)		Knowledge (+) Adherence (+) EQ5D (+) EQ-VAS (+)	
Ali et al. 2019	SVR 12 (+)	ADE (+) DDI (+)	Adherence (+)	
Javaid et al. 2019	Waist* BMI (+) HbA1C (+) SBP (+) DBP (+)	-	-	-
Chatha et al. 2020	CD4 Cell Count (+)		Adherence (+)	
Khokhar et al. 2020	CBC* RFT* Blood Glucose* Electrolytes*		Knowledge (+) Adherence (+)	

*No significant (P>0.05) difference between intervention and control group, += significant (P<0.05) effect in favor of intervention group, SVR 12 = sustained virological response at 12 weeks, ADE= adverse drug event, CBC=Complete Blood count, RFT= renal function test, BMI= Body mass index, SBP= Systolic blood pressure, DBP= Diastolic blood pressure

Figures

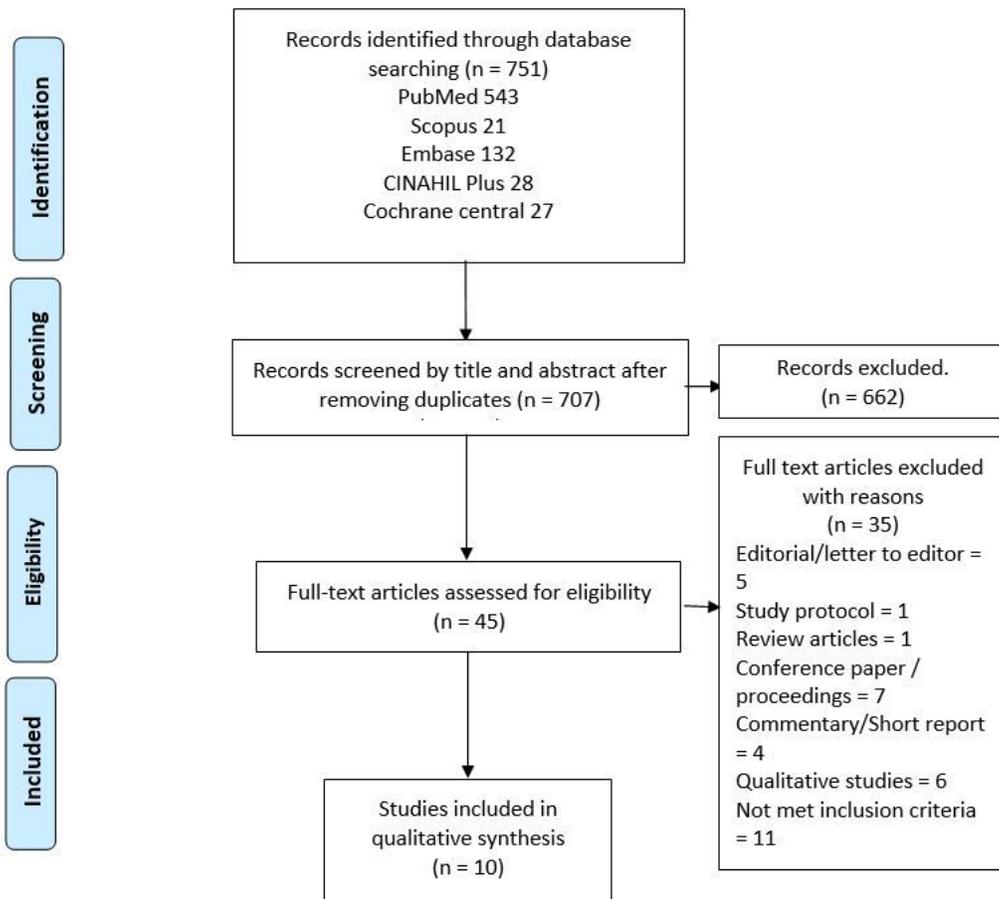


Figure 1

PRISMA flow diagram of included studies

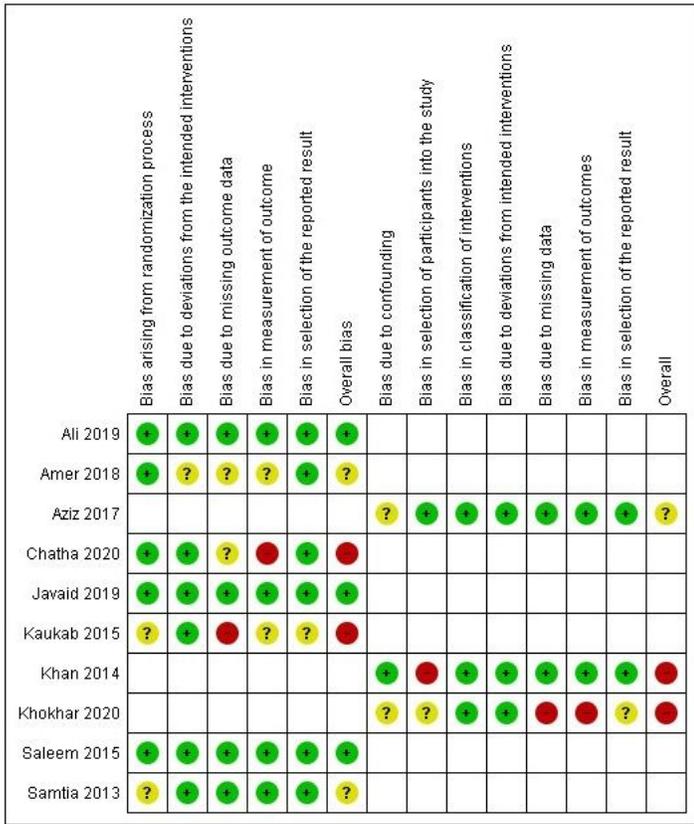


Figure 2

Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

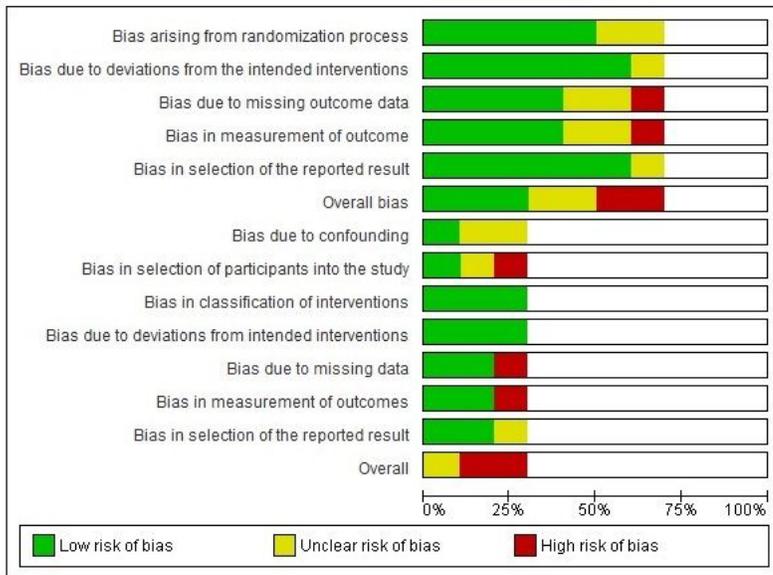


Figure 3

Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.