

The Impact of The Clinical Pharmacist-Led Interventions in Turkey

Türkiye'de Klinik Eczacı Tarafından Yapılan Müdahalelerin Etkisi

Emre Kara¹, Burcu Kelleci¹, Mesut Sancar², Kutay Demirkan¹

¹Department of Clinical Pharmacy, Hacettepe University Faculty of Pharmacy, Ankara, Turkey

²Department Of Clinical Pharmacy, Marmara University Faculty of Pharmacy, Istanbul, Turkey

Corresponding Author

Emre Kara

emrekara@hacettepe.edu.tr

orcid.org/0000-0002-7034-4787

05060512443

17.05.2020

05.07.2020

ABSTRACT

Background: Detecting drug-related problems (DRPs) is important in pharmaceutical care in terms of better treatment outcomes. Clinical pharmacists-led comprehensive medication management plays a crucial role in the rational use of drugs by preventing, identifying, and resolving DRPs.

Objectives: In this narrative review, it is aimed to determine the effect of interventions performed by the clinical pharmacist in Turkey on patients' outcomes.

Materials and Methods: A systematic literature search was performed on the PubMed, Google Scholar, EMBASE, Cochrane Library and Turkish databases (ULAKBIM, Dergipark). The main categories were "clinical pharmacist", "intervention" and "Turkey". Two reviewers reviewed each article independently. Two independent reviewers screened all records and extracted data; disagreements were resolved through consensus. Randomized controlled studies, pre to post-intervention comparison studies, and cross-sectional studies which including pharmacists-led interventions were included.

Results: This review included 15 articles evaluating clinical pharmacist interventions. Ten studies (66.7%) focused on DRPs and pharmacist interventions to these problems, while the remaining 5 (33.3%) studies focused on patient education and adherence issues. Studies were conducted in oncology (33.3%), geriatrics (20.0%), chest diseases (13.3%), psychiatry (6.7%), cardiology (6.7%) and infectious diseases (6.7%) clinics. When outcomes of studies are reviewed, most of the interventions were made at the prescriber level followed by drug level and patient level. Problems were solved in 54.2%-93.2% of DRPs and adherence, patient knowledge or skills were improved in most of the studies.

Conclusions: Most of the included studies carried out within the scope of a postgraduate or doctorate thesis and yet various of positive outcomes such as prevention of side effects, increase in quality of life and decrease in length of hospital stay were observed with the high

acceptance rates of interventions which indicate that other healthcare workers are ready to collaborate with the clinical pharmacists in Turkey.

Keywords: clinical pharmacy, drug-related problems, pharmaceutical care, clinical pharmacist, Turkey

ÖZ

Giriş: İlaçla ilgili problemlerin saptanması, farmasötik bakım kapsamında daha iyi tedavi sonuçlarının sağlanması açısından önemlidir. Klinik eczacı tarafından yapılan kapsamlı ilaç yönetimi, ilaçla ilgili problemleri önleyerek, tanımlayarak ve çözerek ilaçların rasyonel kullanımında önemli bir rol oynamaktadır.

Amaç: Bu derlemede, Türkiye'de klinik eczacı tarafından yapılan müdahalelerin hasta sonuçları üzerindeki etkisinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Sistematik bir literatür taraması PubMed, Google Akademik, EMBASE, Cochrane Kütüphanesi ve Türk veri tabanlarında (ULAKBİM, Dergipark) yapılmıştır. Ana kategoriler “klinik eczacı”, “müdahale” ve “Türkiye” olarak belirlenmiştir. İki araştırmacı her makaleyi bağımsız olarak gözden geçirmiştir. İki bağımsız araştırmacı ise tüm kayıtları taradı ve verileri çıkartmış; anlaşmazlıklar fikir birliği ile çözülmüştür. Eczacılar tarafından yapılan müdahaleleri içeren randomize kontrollü çalışmalar, müdahale öncesi ve sonrası karşılaştırma çalışmaları ve kesitsel çalışmalar dahil edilmiştir.

Bulgular: Bu derlemeye, klinik eczacı müdahalelerini değerlendiren 15 makale dahil edilmiştir. On çalışma (%66,7) ilaçla ilgili problemler ve bu problemlere eczacı müdahalelerine odaklanırken, geri kalan 5 (%33,3) çalışma hasta eğitimi ve uyunç konularına odaklanmıştır. Çalışmalar, onkoloji (%33,3), geriatri (%20,0), göğüs hastalıkları (%13,3), psikiyatri (%6,7), kardiyoloji (%6,7) ve enfeksiyon hastalıkları (%6,7) kliniklerinde yapılmıştır. Çalışmaların sonuçları incelendiğinde, müdahalelerin çoğu hekim düzeyinde, daha sonrası ise ilaç düzeyi ve hasta düzeyinde yapılmıştır. İlaç ilişkili problemlerin %54,2-93,2'sinde problem çözülmüştür ve çalışmaların çoğunda uyunç, hasta bilgisi veya becerileri geliştirilmiştir.

Sonuçlar: Çalışmaların çoğunluğu yüksek lisans veya doktora tezi kapsamında yapılmıştır. Müdahalelerin yüksek kabul oranlarının yanı sıra, yan etkilerin önlenmesi, yaşam kalitesinde artış ve hastanede kalış süresinde azalma gibi çeşitli olumlu sonuçlar gözlenmiştir. Bu sonuçlar Türkiye'deki diğer sağlık çalışanlarının klinik eczacılarla iş birliği yapmaya hazır olduklarını göstermektedir.

Anahtar Kelimeler: klinik eczacılık, ilaçla ilgili problemler, farmasötik bakım, klinik eczacı, Türkiye

Introduction

Drug-related problem (DRP) has been defined as “an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes” (1, 2). Detecting of DRPs is important in pharmaceutical care because DRPs are related to treatment outcomes. To identify and resolve DRPs in terms of rational drug use, clinical pharmacists-led comprehensive medication management plays a crucial role (2, 3).

Clinical pharmacists beyond the many other duties primarily provide pharmaceutical care to improve treatment adherence and decrease DRPs (4-6). The quality of care could be improved by pharmaceutical care services in many diseases like hypertension (7), asthma (8), hyperlipidemia (9), and diabetes (10). The first step in pharmaceutical care services is identifying patient's pharmaceutical care needs and the second step is developing an

individualized pharmaceutical care plan, regards to the patient's knowledge, attitudes, and motivation. The third step is evaluating the outcomes of the pharmaceutical care plan. Finally, the fourth and fifth steps consist of implementing the care plan and continuous monitoring, respectively (11).

Clinical pharmacy services including pharmaceutical care have been developed in the United States of America in the 1960s. It has been changed over time in terms of concept and variety of practices (12). It has been linked to appropriate prescribing, prevent or reduce DRPs, adverse drug events, quality of life (QoL), medication errors, and cost (13-18). According to the International Pharmaceutical Federation (FIP) consensus report in 2009, clinical pharmacy services should be global. Thus, it has been established in many developed countries (19). More importantly, it has been emerging in many developing countries including Turkey (20). Clinical pharmacy service is a relatively new and developing concept in Turkey (21). The first discussions started in 1986 (22). It has been performing since 1991 and started at Marmara University with opening the first postgraduate education program. In 1994 clinical pharmacy as a course was part of undergraduate education at Hacettepe University. In 1997 Ankara University has been established the interdisciplinary clinical pharmacy postgraduate education program. In 1998 to promote clinical pharmacy in Turkey "The Society of Clinical Pharmacy, KED" was established. Since 2003 many continuing education programs were organized by both TKED and the "Turkish Pharmacists' Association Academy of Pharmacy" on clinical pharmacy and pharmaceutical care (21). In Turkey, the first Department of Clinical Pharmacy was established at Hacettepe University in 2013, thereafter at Marmara University and Inonu University (23). Although clinical pharmacy was established as a subdivision at Marmara University many years ago (1995) and allowed to open a department throughout Turkey in 2013, it still operates as a subdivision under the pharmacology department in some universities due to its insufficient academic staff. Furthermore, in 2014 with the approval of the Grand National Assembly of Turkey, clinical pharmacy becomes a legal specialty supported by 'Law on pharmacies and pharmacy'. According to this law, pharmacists may take a special exam once a year and according to the scores of this exam, a limited number of them may start the 3-year post-graduate clinical pharmacy specialty education in selected universities (24).

As it is mentioned above, as a member of the multidisciplinary and interdisciplinary team, the clinical pharmacist has a significant role in improving the treatment, patients' outcomes, and QoL. The positive impact of clinical pharmacists-led interventions on patients' outcomes in terms of reduced hospital visits and mortality was reported in other countries (25, 26).

Another impact of clinical pharmacists is on the pharmacoeconomic parameters. Studies shows that there is a proven evidence of the economic benefits of clinical pharmacy services via reducing the total healthcare costs in various health related areas (13,14).

It is important to show nationwide results from a developing science to emphasize weak and strong sides and guide to complete education. In this review, it is aimed to present the impact of interventions performed by the clinical pharmacist in Turkey on patients' outcomes. We believe that this paper will be useful to show an inside view of what has been done since the implementation of the clinical pharmacy program in Turkey and lead to more powerful studies in the future.

Methods

A systematic literature search (up to 20th of February, 2020) was performed according to PICOS formatting on the PubMed, Google Scholar, EMBASE, Cochrane Library, Turkish databases (ULAKBIM, Dergipark). “clinical pharmacist”, “intervention” and “Turkey” headings were used with “AND” and “OR” operators. Two reviewers (EK and BKC) reviewed each article independently. The searching strategy of PubMed was as following: (((“pharmacists”[MeSH Terms] OR “pharmacists”[All Fields]) OR (“clinical”[All Fields] AND “pharmacist”[All Fields])) OR “clinical pharmacist”[All Fields]) AND (“Turkey”[MeSH Terms] OR “Turkey”[All Fields]).

The general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement were used. Two independent researchers screened records and extracted the data and disagreements were resolved through consensus. Extracted data and quality assessment variables were presented in tables with a narrative description. Randomized controlled studies, pre- to post-intervention comparison studies, and cross-sectional studies which including pharmacists-led interventions were included. Even though abstracts, letters, and case reports were also read and evaluated, articles with no-full-text, conference reports, reviews, editorials, letters, or case reports were excluded. Articles referring to other countries than Turkey were excluded. First author’s name, publication year, study design, the type of clinical pharmacist-led interventions, patients’ age, patients’ outcomes, and the acceptance rate of interventions were evaluated. The first author (EK) extracted the data and another review author (BKC) did the double-checking. If there was any conflict, another author (MS or KD) made the final decision.

To prevent bias in individual studies every researcher extracted data other than their study. Data extraction was undertaken by one reviewer using a tailored data extraction framework, developed to explicit data extraction elements related directly to the review question for the qualitative studies. All of the extractions were checked by a second reviewer. No additional analyses were made to combine the data.

Results

This review included 15 articles out of 94 publications evaluating clinical pharmacist interventions in Turkey (Figure 1). The oldest article included in this review was published in 2007 and the latest in 2020. The distribution of publishing years of articles is given in Graphic 1. The majority of the articles were published in Science Citation Index-Expanded (SCI-E) indexed journals that were ranked in the third quartile (Q3) and fourth quartile (Q4). The characteristics of the journals in which the articles were published are listed in Table 1. The study design of 2 (13.3%) of the 13 articles included were retrospective, while the remaining 13 (86.7%) were prospective. Ten studies (86.7%) focused on DRPs and pharmacist interventions to these problems, while the remaining 5 (33.3%) studies focused on patient education and adherence issues. Different versions of The Pharmaceutical Care Network Europe (PCNE) drug-related problem classification system was used in 7 (46.7%) of the studies. Different tools were used in other studies such as Beers' criteria, Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) criteria, Screening Tool to Alert doctors to the Right Treatment (START) criteria and National Cancer Institute Common Toxicology Criteria for Adverse Effects (NCI-CTCAE) version 4.

Studies were conducted in oncology (n=5, 33.3%), geriatrics (n=3, 20.0%), chest disease (n=2, 13.3%), psychiatry (n=1, 6.7%), cardiology (n=1, 6.7%) and infectious diseases (n=1, 6.7%) clinics and in a community pharmacy (n=2, 13.3%). The studies were conducted in the inpatient (n=6, 40.0%), outpatient (n=7, 46.7%) and community pharmacy (n=2, 13.3%) settings. The characteristics of the studies, patients and interventions are listed as Table 2. The duration of the studies is between 3 to 11 months, the number of patients in the studies is between 25 and 186, and the average age of the patients included in the studies are between 33 and 80 years.

When outcomes of the studies were reviewed, most of the interventions made at the prescriber level followed by drug level and patient level. Problems are solved in a median of 86% (54.2%-93.2%) of drug-related problems and adherence, patient knowledge or skills were improved in these studies (Table 2).

Discussion

According to our knowledge, our study is the first study that reviewed the studies in the field of clinical pharmacy in Turkey. Clinical pharmacy services in Turkey still has not entered into routine practice. It is thought that it will become a routine practice by 2023 (24). The majority of the studies included in this review are the studies carried out within the scope of a postgraduate thesis. Therefore, almost all of these studies are the studies where clinical pharmacy services are offered for the first time to the clinicians or patients. Due to the clinical pharmacist is still not a routine member of the interdisciplinary team; these studies could not be able to address all of the identified pharmaceutical care needs and for the same reason the duration of studies is limited to a few months.

In China, it was determined that appropriate prescribing and patient's knowledge about medications were enhanced with the implementation of clinical pharmacy practices both in inpatient and outpatient settings (43). Rotta et al. overviewed 49 systematic reviews between 2000-2010. They found that clinical pharmacy practices were focused on certain chronic diseases like blood pressure and glucose control. Due to the variability of methods, interventions about medication adherence and prescription appropriateness caused inconclusive results. (44).

The findings of decreased adverse drug effects, improved appropriate prescribing, shortened length of stay (LoS), and reduced costs that were reported in many other studies from outside of Turkey (13, 18, 42). The outcomes of the interventions are beneficial in terms of visualizing clinical pharmacy activities and better results in patients. Positive outcomes were observed such as reduction or prevention of side effects, improvement in QoL, and reduction in LoS in the hospital with the high acceptance rates of interventions by the physicians which indicate that despite the obstacles that faced the implementation of clinical pharmacy services, other healthcare professionals are ready to collaborate with the clinical pharmacists in Turkey. Pehlivanlı et al. reviewed 46 articles published between 2006-2016 on the role of the clinical pharmacist. They found that the studies were mostly related to cardiovascular diseases (13%), adverse drug events (11%), and infectious diseases (9%). The studies evaluated are generally prospective, observational, or interventional studies (45). In Turkey, there are also studies conducted within the scope of clinical pharmacy but without pharmacist intervention such as Sancar et al. evaluated adverse effects and compliance of patients with major depression using antidepressants. In 56 patients, side effects such as dizziness, dry mouth, increased sleep were found to be the most common, and 73.2% of the patients were found to have low compliance with the treatment. In addition to the routine service they receive from the outpatient clinic, it is concluded that educating and monitoring the side effects and compliance by pharmacists will contribute to preventing possible DRPs (46). In another study, the appropriateness of drug treatment was evaluated and requirements of pharmaceutical care were identified in geriatric patients. A low level of knowledge about drug usage was detected in patients and they have rarely been informed about appropriate drug use (47). Okuyan et al. aimed to evaluate the knowledge and attitudes of type 2 diabetic patients regarding the use of a disposable insulin pen. As a result of this study, missing or improper usage of the disposable insulin pen was observed in hospitalized patients (48). The Patient Risk Score (PRS) was used by Aras et al. to evaluate the risk of febrile neutropenia (FN) and to assess granulocyte colony-stimulating factors use and its side effects in an outpatient clinic. They found that inadequately or unnecessarily treatments should be evaluated for the risk of FN in each chemotherapy cycle, also a routine risk assessment can be implemented (49). Abunahlah et al. conducted a study in the internal medicine wards to identify DRPs in a teaching and research hospital in Istanbul, Turkey. In this study, 163 DRPs were determined by using the PCNE classification V7.0 in 100 patients that used a total of 808 drugs. According to the results they found that age, LoS in hospital, number of drugs, renal impairment and inflammation were in

correlated with the causes of DRPs and age, number of drugs, LoS in hospital, kidney dysfunction, liver failure, diagnosis, and comorbidities were correlated with the number of DRPs (50).

Another concern is appropriate measures for pharmacists' service effectiveness.

Hospitalization, mortality, or outpatient visits should be used for evaluation of effectiveness endpoints; however, extended duration of follow-up periods is needed to demonstrate a potential input for these endpoints. Thus, intermediate or surrogate indicators could be used to evaluate the short-term effects of interventions. Short-term evaluation methods of the included studies were also shown in this review.

American College of Clinical Pharmacy (ACCP) is defining that the clinical pharmacists are a primary source of scientifically valid information and advice regarding the safe, appropriate, cost-effective use of medications and optimizing medication therapy with the philosophy of pharmaceutical care. They routinely provide updated knowledge that contributes to improved health and QoL to patients and healthcare professionals (51). Consistent with the definition of ACCP also in Turkey clinical pharmacists are contributing many research projects not only in the clinical pharmacy field but also in various health-related fields. They provide an undebatable knowledge to other healthcare professionals. Due to these publications were out of the scope of this study, they were not discussed.

As clinical pharmacy is a relatively new and specific field, most of the journals in this field remain Q3 or Q4 quartiles since the articles are not as categorized as other pharmaceutical and health sciences. The main limitations of the studies assessed in this review were their study setting (one hospital) and the study size (small groups) (28, 29, 32, 34). Other limitations were retrospective evaluations of pharmacist interventions (29, 38) and having no control group for comparisons (28). Controlled and prospective studies are also available within the scope of the thesis or project, which is currently finished or in progress in Turkey, and some of them have been submitted for publication. A significant expansion in the number of publications is expected due to the increase in the number of both graduates and specialist program graduates trained in the field of clinical pharmacy in recent years.

The limitations of this review were even though a literature search was conducted on different databases, the possibility of omitted or overlooked studies might exist. PRISMA checklist items could not be fully followed because the studies included in this review are not homogeneous and the available number of studies are few. Further studies are needed to assess the impact of clinical pharmacist intervention on health expenditure in Turkey by using cost-effectiveness or cost-benefit analysis methods.

Conclusion

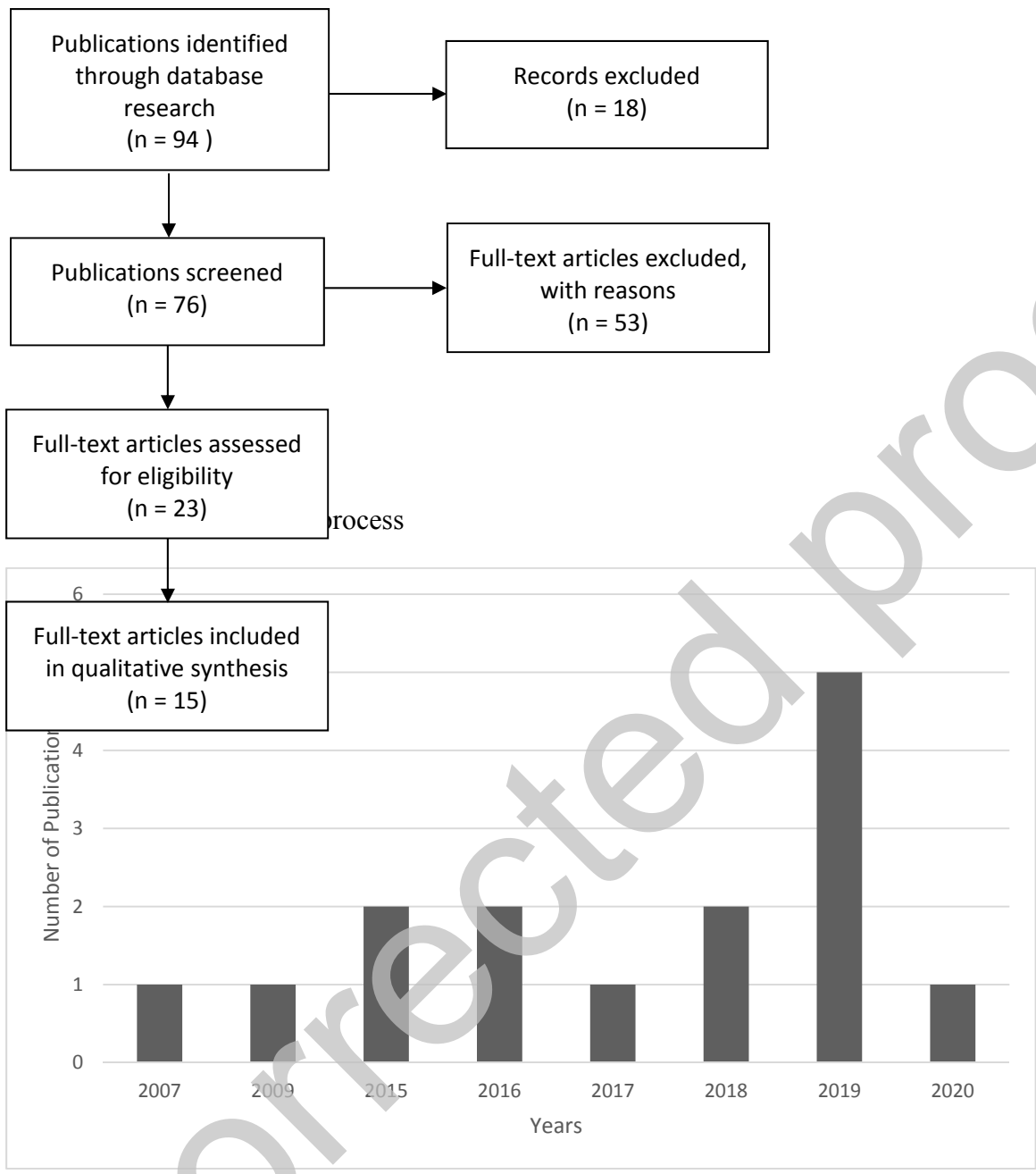
In conclusion, there is a growing experience of clinical pharmacy in Turkey however a clear definition of clinical pharmacy services, implementation to the routine healthcare team, and standardized methods that assess the impact of these services on patient health-related outcomes are still needed. It is shown that even with the institutional effort, clinical pharmacy services can make a strong contribution to the Turkish healthcare system but for providing a trustworthy and sustainable service further governmental and educational support should develop.

References

1. van den Bemt PM, Egberts TC, de Jong-van den Berg LT, Brouwers JR. Drug-related problems in hospitalised patients. *Drug Saf*. 2000;22(4):321-33.
2. Schlienger RG, Fedson DS, Jick SS, Jick H, Meier CR. Statins and the risk of pneumonia: a population-based, nested case-control study. *Pharmacotherapy*. 2007;27(3):325-32.
3. Viktil KK, Blix HS. The impact of clinical pharmacists on drug-related problems and clinical outcomes. *Basic Clin Pharmacol Toxicol*. 2008;102(3):275-80.
4. Ellis SL, Billups SJ, Malone DC, Carter BL, Covey D, Mason B, et al. Types of interventions made by clinical pharmacists in the IMPROVE study. *Impact of Managed Pharmaceutical Care on Resource Utilization and Outcomes in Veterans Affairs Medical Centers*. *Pharmacotherapy*. 2000;20(4):429-35.
5. Schumock GT, Michaud J, Guenette AJ. Re-engineering: an opportunity to advance clinical practice in a community hospital. *Am J Health Syst Pharm*. 1999;56(19):1945-9.
6. Gourley DR, Gourley GA, Solomon DK, Portner TS, Bass GE, Holt JM, et al. Development, implementation, and evaluation of a multicenter pharmaceutical care outcomes study. *J Am Pharm Assoc (Wash)*. 1998;38(5):567-73.
7. Garcao JA, Cabrita J. Evaluation of a pharmaceutical care program for hypertensive patients in rural Portugal. *J Am Pharm Assoc (Wash)*. 2002;42(6):858-64.
8. Gonzalez-Martin G, Joo I, Sanchez I. Evaluation of the impact of a pharmaceutical care program in children with asthma. *Patient Educ Couns*. 2003;49(1):13-8.
9. Paulos CP, Nygren CE, Celedon C, Carcamo CA. Impact of a pharmaceutical care program in a community pharmacy on patients with dyslipidemia. *Ann Pharmacother*. 2005;39(5):939-43.
10. Anaya JP, Rivera JO, Lawson K, Garcia J, Luna J, Jr., Ortiz M. Evaluation of pharmacist-managed diabetes mellitus under a collaborative drug therapy agreement. *Am J Health Syst Pharm*. 2008;65(19):1841-5.
11. Strand LM, Guerrero RM, Nickman NA, Morley PC. Integrated patient-specific model of pharmacy practice. *Am J Hosp Pharm*. 1990;47(3):550-4.
12. Biles JA. The doctor of pharmacy. *JAMA*. 1983;249(9):1157-60.
13. Schumock GT, Butler MG, Meek PD, Vermeulen LC, Arondekar BV, Bauman JL, et al. Evidence of the economic benefit of clinical pharmacy services: 1996-2000. *Pharmacotherapy*. 2003;23(1):113-32.
14. Bond CA, Raehl CL, Franke T. Clinical pharmacy services, pharmacy staffing, and the total cost of care in United States hospitals. *Pharmacotherapy*. 2000;20(6):609-21.
15. Bond CA, Raehl CL. Clinical pharmacy services, pharmacy staffing, and hospital mortality rates. *Pharmacotherapy*. 2007;27(4):481-93.
16. Kaboli PJ, Hoth AB, McClimon BJ, Schnipper JL. Clinical pharmacists and inpatient medical care: a systematic review. *Arch Intern Med*. 2006;166(9):955-64.
17. Pickard AS, Hung SY. An update on evidence of clinical pharmacy services' impact on health-related quality of life. *Ann Pharmacother*. 2006;40(9):1623-34.
18. De Rijdt T, Willems L, Simoens S. Economic effects of clinical pharmacy interventions: a literature review. *Am J Health Syst Pharm*. 2008;65(12):1161-72.
19. Pedersen CA, Schneider PJ, Santell JP. ASHP national survey of pharmacy practice in hospital settings: prescribing and transcribing--2001. *Am J Health Syst Pharm*. 2001;58(23):2251-66.
20. 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 Syst Rev*. 2013(2):CD010398.

21. Sancar M, Okuyan B, Apikoglu-Rabus S, Izzettin F. Opinion and knowledge towards pharmaceutical care of the pharmacists participated in clinical pharmacy and pharmaceutical care continuing education program. *Turkish J Pharmaceutical Sci.* 2013;10(2):245-54.
22. Ustel I. Klinik Eczacılık Eğitimi. *FABAD J Pharm Sci.* 1986;11:270-7.
23. Aypar E, Sancar M, Izzettin FV. [New period in pharmacy: place in health system and clinical pharmacy]. *SD Sağlık Düşüncesi ve Tıp Kültürü Dergisi* 2014;30:48-51.
24. Resmi Gazete (14.11.2014/29175), 6566 sayılı Eczacılar ve Eczaneler Hakkında Kanun ile Bazı Kanun ve Kanun Hükmünde Kararnamelerde Değişiklik Yapılmasına Dair Kanun; 2014. p.3-7. .
25. Dawoud DM, Smyth M, Ashe J, Strong T, Wonderling D, Hill J, et al. Effectiveness and cost effectiveness of pharmacist input at the ward level: a systematic review and meta-analysis. *Res Social Adm Pharm.* 2019;15(10):1212-22.
26. Rodrigues CR, Harrington AR, Murdock N, Holmes JT, Borzadek EZ, Calabro K, et al. Effect of pharmacy-supported transition-of-care interventions on 30-day readmissions: a systematic review and meta-analysis. *Ann Pharmacother.* 2017;51(10):866-89.
27. Umar RM, Apikoglu-Rabus S, Yumuk PF. Significance of a clinical pharmacist-led comprehensive medication management program for hospitalized oncology patients. *Int J Clin Pharm.* 2020.
28. Kucuk E, Bayraktar-Ekincioglu A, Erman M, Kilickap S. Drug-related problems with targeted/immunotherapies at an oncology outpatient clinic. *J Oncol Pharm Pract.* 2020;26(3):595-602.
29. Ertuna E, Arun MZ, Ay S, Kocak FOK, Gokdemir B, Ispirli G. Evaluation of pharmacist interventions and commonly used medications in the geriatric ward of a teaching hospital in Turkey: a retrospective study. *Clin Interv Aging.* 2019;14:587-600.
30. Yalcin N, Ak S, Gurel SC, Celiker A. Compliance in schizophrenia spectrum disorders: the role of clinical pharmacist. *Int Clin Psychopharmacol.* 2019;34(6):298-304.
31. Izzettin FV, Celik S, Acar RD, Tezcan S, Aksoy N, Bektay MY, et al. The role of the clinical pharmacist in patient education and monitoring of patients under warfarin treatment. *Journal of Research in Pharmacy.* 2019;23(6):1057-163.
32. Kara E, Inkaya AC, Aydin Hakli D, Demirkan K, Unal S. Polypharmacy and drug-related problems among people living with HIV/AIDS: a single-center experience. *Turk J Med Sci.* 2019;49(1):222-9.
33. Paksoy C, Özkan Ö, Ustaalioglu BB, Sancar M, Demirtunç R, Izzettin FV, et al. Evaluation of potentially inappropriate medication utilization in elderly patients with cancer at outpatient oncology unit. *Journal of Oncology Pharmacy Practice.* 2018;25(6):1321-7.
34. Tecen-Yucel K, Bayraktar-Ekincioglu A, Kilickap S, Erman M. Clinical pharmacy practices in oncology patients treated with tyrosine kinase inhibitors. *International Journal of Hematology and Oncology.* 2018;28(4):053-60.
35. Izzettin FV, Al-taie A, Sancar M, Aliustaoğlu M. Influence of pharmacist recommendations for chemotherapy-related problems in diabetic cancer patients. *Marmara Pharmaceutical Journal.* 2017;21(3):603-11.
36. Tezcan S, İzzettin FV, Sancar M, Turhal NS, Yumuk PF. Role of clinical oncology pharmacist in determination of pharmaceutical care needs in patients with colorectal cancer. *European Journal of Hospital Pharmacy.* 2018;25(e1):e17-e20.
37. Apikoglu-Rabus S, Yesilyaprak G, Izzettin FV. Drug-related problems and pharmacist interventions in a cohort of patients with asthma and chronic obstructive pulmonary disease. *Respir Med.* 2016;120:109-15.
38. Selcuk A, Sancar M, Okuyan B, Demirtunc R, Izzettin FV. The potential role of clinical pharmacists in elderly patients during hospital admission. *Pharmazie.* 2015;70(8):559-62.

39. Sancar M, Sirinoglu Y, Okuyan B, Karagoz T, Izzettin FV. The effect of pharmacist-led education on inhaler use skills in hospitalised patients with chronic obstructive pulmonary disease. *Eur J Hosp Pharm*. 2015;22(6):366-8.
40. Turnacilar M, Sancar M, Apikoglu-Rabus S, Hursitoglu M, Izzettin FV. Improvement of diabetes indices of care by a short pharmaceutical care program. *Pharmacy World Sci*. 2009;31(6):689.
41. Clark PM, Karagoz T, Apikoglu-Rabus S, Izzettin FV. Effect of pharmacist-led patient education on adherence to tuberculosis treatment. *American Journal of Health-System Pharmacy*. 2007;64(5):497-505.
42. Schumock GT, Meek PD, Ploetz PA, Vermeulen LC. Economic evaluations of clinical pharmacy services--1988-1995. The Publications Committee of the American College of Clinical Pharmacy. *Pharmacotherapy*. 1996;16(6):1188-208.
43. Penm J, Li Y, Zhai S, Hu Y, Chaar B, Moles R. The impact of clinical pharmacy services in China on the quality use of medicines: a systematic review in context of China's current healthcare reform. *Health policy and planning*. 2014;29(7):849-72.
44. Rotta I, Salgado TM, Silva ML, Correr CJ, Fernandez-Llimos F. Effectiveness of clinical pharmacy services: an overview of systematic reviews (2000-2010). *International journal of clinical pharmacy*. 2015;37(5):687-97.
45. Pehlivanli A, Akyol B, Ozcelikay G. Evaluation of studies between 2006-2016 years contributions related to treatment of clinical pharmacists (In Turkish). *Turkiye Klinikleri Journal of Health Sciences*. 2018;3(2):95-112.
46. Sancar M, Duzgun E, Okuyan B, Deniz S, Caliskan M, Coskun K, et al. Determination of side effects and medication adherence in major depression patients utilized antidepressants (In Turkish). *Marmara Pharmaceutical Journal*. 2017;21(1).
47. Sancar M, Mutlu BY, Okuyan B, Izzettin FV. Determination of geriatric patients' drug profile and identify their pharmaceutical care requirements by determining potential risk factors. *European Geriatric Medicine*. 2011;2(5):280-3.
48. Okuyan B, Saglam B, Emre E, Demirtunc R, Izzettin F, et al. Attitude and Knowledge of Hospitalized Patients with Type 2 Diabetes Mellitus Towards Disposable Insulin Pens Utilization. *Marmara Pharmaceutical Journal*. 2014;18(3):159-63.
49. Aras E, Bayraktar-Ekincioglu A, Kilickap S. Risk assessment of febrile neutropenia and evaluation of G-CSF use in patients with cancer: a real-life study. *Supportive Care in Cancer*. 2020;28(2):691-9.
50. Abunahlah N, Elawaisi A, Velibeyoglu FM, Sancar M. Drug related problems identified by clinical pharmacist at the Internal Medicine Ward in Turkey. *Int J Clin Pharm*. 2018;40(2):360-7.
51. American College of Clinical P. The definition of clinical pharmacy. *Pharmacotherapy*. 2008;28(6):816-7.



Graphic 1. Distribution of publishing years of articles

Table 1. The characteristics of the journals in which the articles were published

Journal name	First author and year	Indexing	Impact factor	Quartiles
International Journal of Clinical Pharmacy (formerly Pharmacy World & Science)	Umar R. M. (2020)	SCI-expanded	1.941 (5-years)	Q4
Journal of Oncology Pharmacy Practice	Kucuk E. (2019)	SCI-expanded	1.826 (2018)	Q3
Clinical Interventions in Aging	Ertuna E. (2019)	SCI-expanded	3.195 (5-years)	Q3
International Clinical Psychopharmacology	Yalcin N. (2019)	SCI-expanded	2.169 (5-years)	Q4
Journal of Research in Pharmacy (formerly Marmara Pharmaceutical Journal)	Izzettin F. V. (2019)	Emerging-SCI	0.14 (2018)	-
Turkish Journal of Medical Sciences	Kara E. (2019)	SCI-expanded	0.698 (5-years)	Q4
Journal of Oncology Pharmacy Practice	Paksoy C. (2018)	SCI-expanded	1.826 (2018)	Q3
UHOD - Uluslararası Hematoloji-Onkoloji Dergisi	Tecen Yucel K. (2018)	SCI-expanded	1.667 (5-years)	Q4
Marmara Pharmaceutical Journal	Izzettin F. V. (2017)	Emerging-SCI	0.14 (2018)	-
European Journal of Hospital Pharmacy-Science and Practice	Tezcan S. (2016)	SCI-expanded	0.661 (5-years)	Q4
Respiratory Medicine	Apikoglu-Rabus S. (2016)	SCI-expanded	3.702 (5-years)	Q2
Pharmazie	Selcuk A. (2015)	SCI-expanded	1.004 (5-years)	Q4
European Journal of Hospital Pharmacy-Science and Practice	Sancar M. (2015)	SCI-expanded	0.661 (5-years)	Q4

Pharmacy World & Science	Turnacilar M. (2009)	SCI-expanded	1.429 (5-years)	Q3
American Journal of Health- System Pharmacy	Clark P. M. (2007)	SCI-expanded	2.427 (5-years)	Q3

*SCI: Science citation index

Uncorrected proof

Table 2. The characteristics of the studies, patients, and interventions

First Author and Design	Title	Population and Monitoring time	Age of Population	Clinical Pharmacist Interventions	Major Outcomes
Umar R. M. (2020) (27) Prospective, study	Significance of a clinical pharmacist-led comprehensive medication management program for hospitalized oncology patients	137 oncology patients 5 months	58 ± 14.60	Identification and classification of DRPs were performed by using the PCNE classification V6.2.	A total of 481 DRPs were identified in 114 patients. The majority (69%, n=332) of interventions were made at the prescriber level, while 29.3% (n=141) interventions were made at the drug level, most of which included beginning a new medication (11.4%, n=55) or stopping a medication (9.6%, n=46). The vast majority (n=437; 90.9%) of the problems were solved.
Kucuk E. (2019) (28) Descriptive, prospective study	Drug-related problems with targeted/ immunotherapies at an oncology outpatient clinic	54 oncology patients in the outpatient setting 3 months	57 ± 11.98	DRPs were identified by a clinical pharmacist in patients receiving targeted chemotherapy and/or immunotherapy. PCNE classification v.7 was used.	During the study period, a total of 105 DRPs (1.94 per patient, 0.38 per consultation) were identified. A total of 149 planned interventions were recorded by the clinical pharmacist of which 8 (5%) were at the prescriber-level, 23 (15%) were at drug-level, 92 (62%) were at patient-level, and 14 (9%) were other interventions or activities. As a result, 68 (65%) out of 105 DRPs were resolved.
Ertuna E. (2019) (29) Retrospective study	Evaluation of pharmacist interventions and commonly used medications in the geriatric ward of a teaching hospital in Turkey: a retrospective study	91 geriatric patients Weekly order review for 8 months	80 ± 0.46	Problems were classified according to the PCNE classification system v8.02. PIM use was determined by using Beers and STOPP/START criteria.	329 possible DRPs were detected in 156 orders. 282 (85.71%) interventions were proposed to the prescribers and on 47 (14.28%) occasions, the prescriber was only informed or the intervention was discussed with the prescriber. The acceptance rate of pharmacist interventions was 85.41% (n=281) and 38 (11.55%) of the proposed interventions were rejected by the physician.

Yalcin N. (2019) (30) Prospective study	Compliance in schizophrenia spectrum disorders: the role of clinical pharmacist	40 schizophrenia spectrum disorders patients 10 months, during hospitalization and 4–6 weeks following discharge	33 ± 10.99	PANSS, ROMI, UKU, SAS, BARS were used.	23 (57.5%) patients were showed poor compliance at the first interview, while only 7 (17.5%) patients were recorded with poor compliance at the second interview after drug education (average total MARS scores of the first and second interviews were, respectively, 6.6 (2.23) and 8.6 (1.29); (p<0.001). According to ROMI, the number of patients who wanted to use medication was detected 35 (87.5%) during the first intervention and 39 (97.5%) during the second intervention.
Izzettin F. V. (2019) (31) Prospective, cross-sectional randomized study	The role of the clinical pharmacist in patient education and monitoring of patients under warfarin treatment	25 patients diagnosed with venous thromboembolism or prosthetic valve replacement in a cardiology clinic 3 months	53 ± 2.18	Pre- and post-test to evaluate the level of knowledge of the patients on oral anticoagulant. The quality of life was measured by SF-36 and the DASS tests were applied.	After three months of the study, the SF-36 Physical Component Score and SF-36 Mental Component Score were increased and results were statistically significant. The number of correct answers of the patients in the pre-test was increased and results were statistically significant after three months of the study (p<0.001). Total DASS scores, DASS “limitations” scores, DASS “burdens” scores, and DASS “positive effects” scores were improved (p<0.05).

Kara E. (2019) (32) Prospective, cross-sectional study	Polypharmacy and drug-related problems among people living with HIV/AIDS: a single-center experience	186 PLWHA in an infectious disease outpatient clinic 40 ± 13.1 11 months	Followed by pharmacist interview with PLWHA, the official recommendation was offered to the attending physician and the participants, which encompassed treatment, drug interactions, side effects. PCNE Classification v7.0 was used.	Fifty-eight DRPs were found in 45 patients. Twenty-nine (50%) of the interventions were made to the physicians alone, 25 (43%) to the patients alone, and 4 were made to both the physicians and the patients. Twenty-nine (50%) interventions involved comorbidities or co-medications and 19 (32.8%) of these involved antiretroviral drugs. In this study, 93.2% of the interventions were accepted by the physicians.
Paksoy C. (2018) (33) Prospective study	Evaluation of potentially inappropriate medication utilization in elderly patients with cancer at outpatient oncology unit	114 elderly patients oncology outpatient clinic 71.78 ± 5.50 4 months	Medication review to determine PIMs and POMs made by using STOPP/START criteria.	In 94.73% of the patients, polypharmacy was detected. STOPP criteria were applied to a total of 114 patients and 20 PIM uses in 18 patients were found and interventions were accepted by clinicians. According to the START criteria, a total of 221 medication omissions in 112 patients was found and interventions were accepted by clinicians. The number of non-cancer medications and the total number of medications was statistically high according to the presence of STOPP criteria (p<0.001).
Tecen Yucel K. (2018) (34) Descriptive, cross-sectional, prospective study	Clinical Pharmacy Practices in Oncology Patients Treated with Tyrosine Kinase Inhibitors	55 medical oncology outpatient clinic patients 60 (range 28-79) 3 months	TKI-related adverse effects were monitored and evaluated by using the NCI-CTCAE version 4.	A total of 92 interactions were detected and 54 (58.7%) were evaluated as clinically significant which required intervention. A total of 32 recommendations for the management of adverse effects were provided by a clinical pharmacist and 29 (90.6%) were accepted by consultant physicians. Clinically significant improvements in patients were observed in criteria related to dry

					skin, diarrhea, fatigue, infection, hematuria, acute kidney injury, vomiting, salivary duct inflammation, and alanine aminotransferase levels between the 1st and the 2nd visits.
Izzettin F. V. (2017) (35)	Influence of Pharmacist Recommendations for Chemotherapy-Related Problems in Diabetic Cancer Patients	50 diabetic patients with a new diagnosis of diverse types of cancers 8 months	61 ± 8.99	The assessment of DRPs was based on PCNE classification V6.2	In this study, 69.57% (n=80) of the DRPs were solved due to recommendations by the clinical pharmacist. After clinical pharmacist recommendations and provision of patient education, a significant decrease in the occurrence (1st vs. 2nd readings) and severity (mild vs. moderate) of adverse drug effects was observed as a mild urinary frequency (p=0.0001) and mild vomiting (p=0.0001).
Tezcan S. (2016) (36)	Role of clinical oncology pharmacist in the determination of pharmaceutical care needs in patients with colorectal cancer	36 colon cancer patients in the outpatient chemotherapy unit 5 months, during three chemotherapy courses	58 ± 12.86	The symptom-based quality-of-life questionnaires were administered before the first and after the third course of chemotherapy. Potential DRPs were recorded.	DRPs decreased within the third course of chemotherapy compared with the first course after interventions. A total of 147 recommendations were given and of those, 52.4% (n=77) were non-pharmacological and 47.6% (n=70) were pharmacological. One hundred and forty-four (98%) recommendations were followed by patients. Of the recommendations followed, 91.7% (n=132) were succeeded to solve the DRP, while 8.3% (n=12) were failed to solve the problem.

Apikoglu-Rabus S. (2016) (37) Prospective Study	Drug-related problems and pharmacist interventions in a cohort of patients with asthma and chronic obstructive pulmonary disease	44 patients with asthma and 37 patients with chronic obstructive pulmonary disease 6 months	Asthma patients: 52.4 ± 11.9 COPD patients: 65.9 ± 10.5	DRPs were identified at the initial visit using the Turkish version of the PCNE Classification scheme for Drug-Related Problems v6.2. In addition, MMAS was used.	Only five patients with asthma (11.4%) and four patients with COPD (10.8%) were highly adherent with their medication regimen. Fifty-nine DRPs were identified for 44 patients with asthma, of which 93% were manifested and 7% were potential. A majority of these problems (98%) were identified by the pharmacist. A total of 134 causes were identified for 59 problems. Sixty were identified for 37 patients with COPD, with 88% of the problems manifested, while 12% were potential. A majority (95%) of these problems were identified by the pharmacist. A total of 128 causes were identified for 60 problems. A total of 84 interventions were provided for the patients with asthma and 95 interventions were provided for the patients with COPD. Most of the interventions were made at the patient level (81% at asthma patients and 80% at COPD patients). Almost half of the problems were solved (54.2% at asthma patients and 63.3% at COPD patients).
Selcuk A. (2015) (38) Retrospective study	The potential role of clinical pharmacists in elderly patients during hospital admission	133 hospitalized elderly patients 4 months, weekly participation in the ward	77 ± 8.12	Medication discrepancies were determined and divided between intended and unintended discrepancies. All DRPs were determined regarding home and hospital medications according to PCNE classification, v.6.2.	The utilization of high alert medications was seen in 77.4 % of the patients. The PIM was found in 19.5% of elderly patients. A total of 394 medication discrepancies were detected and classified as either intended or unintended discrepancies. The clinical pharmacist was presented a total of 396 recommendations to the physician on the ward and the physicians were accepted 85.6% of them.
Sancar M. (2015) (39) Prospective, Pre- and post-intervention study	The effect of pharmacist-led education on inhaler use skills in hospitalized patients with chronic	41 hospitalized patients with COPD 9 months, clinic visit was arranged for a month later from hospital	64 ± 11.78	The clinical pharmacists used verbal instruction and printed and demonstration materials to educate patients on the correct methods for using each inhaler device according to GOLD guideline.	Patients' inhaler administration skills were found to be improved by pharmacist-led education (p<0.05). Statistically significant improvement in patient inhaler use skills was obtained for every scored item except removing the cap before starting to use inhalers following pharmacist-led education. The improvement in appropriate inhaler device usage techniques following pharmacist-led

	obstructive pulmonary disease	discharge (2 days/week)			education was also determined when evaluating patients' attitudes towards different types of inhalers. An increase in the rate of mouth rinsing after corticosteroid inhalation was observed following pharmacist-led training (38.2% vs 91.2%).
Turnacilar M. (2009) (40)	Improvement of diabetes indices of care by short pharmaceutical care (PC) program	43 patients with type 2 diabetics visiting community pharmacies 7 months retrospective.	62. ± 1.50	Retrospective data of the past 3 months was collected using a standard self-administered questionnaire.	Nine (20.9%) patients used to perform SMBG before PC; this number increased to 13 (30.2%) patients after PC (p<0.05). After PC this number increased to 95.3% (p<0.001). During the PC period, two out of twelve smoking patients quit smoking and reported being smoke-free until the end of the PC period. The barriers to adherence were identified and managed in two patients.

Clark P. M. (2007) (41)	Effect of pharmacist-led patient education on adherence to tuberculosis treatment	154 hospitalized, newly diagnosed tuberculosis (TB) patients.	Newly diagnosed TB patients: 38 ± 14.0	In the first interview, patients' health beliefs and knowledge of their current drugs and doses were assessed through an interviewer-assisted questionnaire. The clinical pharmacist was provided standard oral and written patient education to the patients in the education group shortly before discharge.	The effect of pharmacist-directed patient education in terms of improving visit attendance was statistically significant ($p < 0.05$). The number of patients who attended all of the scheduled visits was higher in the education group than in the No-education group (53.6% versus 29.3%, respectively). The beneficial effect of patient education on the positive isoniazid test result percentage was statistically significant ($p = 0.001$). The drug-related issues were again similar for newly diagnosed TB and MDR-TB patients.
Prospective, randomized, case-control study		8 months, two months during inpatient clinics, and six months after discharge.	Multi-drug resistant (MDR) TB patients: 43 ± 2.50		

*PIM: Potentially inadequate medication, STOPP: Screening tool of older people's prescriptions, START: screening tool to alert to right treatment, PANSS: Positive and Negative Syndrome Scale, MARS: Medication Adherence Rating Scale, ROMI: The Rating of Medication Influences, UKU: Udvalg for Kliniske Undersogelser, SAS: Simpson-Angus, Abnormal Involuntary Movement Scale, BARS: Barnes Akathisia Rating Scale, SF-36: Short Form 36, DASS: Depression Anxiety Stress Scales, HIV: human immunodeficiency virus, AIDS: acquired immunodeficiency syndrome, PLWHA: people living with HIV/AIDS, POM: potential prescribing omission, TKI: tyrosine kinase inhibitors, NCI: National Cancer Institute, CTCAE: Common Terminology Criteria for Adverse Events, COPD: Chronic obstructive pulmonary disease, MMAS: Morisky Medication Adherence Scale, GOLD: The Global Initiative for Chronic Obstructive Lung Disease