



Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop

The economic impact of pharmacist care for people living with HIV/AIDS: A systematic review



Ali Ahmed, PharmD, M.Phil^{a,*}, Juman Abdulelah Dujaili, PhD^{a,*}, Furqan Khurshid Hashmi^b, Ahmed Awaisu, PhD^c, Nathorn Chaiyakunapruk, PhD^{a,d}, Syed Shahzad Hasan, PhD^e

^a School of Pharmacy, Monash University, Jalan Lagoon Selatan, Bandar Sunway, 47500 Subang Jaya, Selangor, Malaysia

^b University College of Pharmacy, University of Punjab, Allama Iqbal Campus, 54000, Lahore, Pakistan

^c College of Pharmacy, QU Health, Qatar University, P.O. Box 2713, Doha, Qatar

^d College of Pharmacy, University of Utah, Salt Lake City, UT, USA

^e Department of Pharmacy, School of Applied Sciences, University of Huddersfield, UK

ARTICLE INFO

Article history:

Received 27 May 2021

Received in revised form 14 August 2021

Accepted 29 August 2021

Keywords:

Pharmacist

Pharmaceutical care

HIV/AIDS care

Pharmacoeconomics

Cost-benefit

Cost-effectiveness

ABSTRACT

Background and objective: There is an increase in the global prevalence of the human immunodeficiency virus (HIV). While it has been proven that pharmacist interventions improve the health outcomes of people living with HIV/AIDS (PLWHA), the economic impact of these initiatives is uncertain. Consequently, we aim to systematically review and synthesize the evidence surrounding the economic impact of pharmacist care in PLWHA.

Methods: PubMed, EMBASE, Scopus, IPA via ProQuest, the Cochrane Library, and the CINAHL Plus databases were systematically searched. Original studies evaluating the economic effect of pharmacist-managed services for PLWHA were included in the review. The quality of the economic studies was assessed using the Consolidated Health Economic Evaluation Reporting Standard (CHEERS) checklist.

Results: A search of databases yielded 4206 citations, four of which met the eligibility criteria. Three studies were conducted in a hospital-based outpatient facility, while one study was conducted in a community pharmacy setting. The types of “pharmacist-managed services” included targeted motivational education, pharmaceutical care, health screening for opportunistic infections, and referral to specialists. Two of the four economic evaluation studies had complete economic analyses and were rated as moderate in quality. In comparison with usual care, pharmacist services led to cost savings of (51.29 to 165.74 in 2021 USD\$) per person per year, saving 18.5 h per patient per year, and a lower cost of generating 12 years of quality-adjusted life years. In addition, the benefit-to-cost ratio of the pharmacist service was 2.51:1.

Conclusions: The pharmacist-managed services demonstrated the benefits of improving overall PLWHA health outcomes in economic viability. However, future real world controlled, high-quality economic studies are required to determine the long-term cost-effectiveness of these services, given the pharmacist's growing role in the health care team managing PLWHA.

Contents

1. Introduction	2
2. Methods	2
2.1. Eligibility criteria	2
2.2. Information sources	2
2.3. Data extraction and synthesis	2
2.4. Quality assessment	2
3. Results	3
4. Discussion	6
4.1. Limitations	6
5. Conclusion	6

* Corresponding authors.

E-mail addresses: ali.ahmed@monash.edu (A. Ahmed), Juman.Dujaili@monash.edu (J.A. Dujaili), furqan.pharmacy@pu.edu.pk (F.K. Hashmi), aaawaisu@qu.edu.qa (A. Awaisu), nathorn.chaiyakunapruk@monash.edu (N. Chaiyakunapruk), S.Hasan@hud.ac.uk (S.S. Hasan).

<http://dx.doi.org/10.1016/j.rcsop.2021.100066>

2667-2766/© 2021 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Funding	8
Ethics approval	8
Appendix A. Supplementary data	8
References	8

1. Introduction

As of 2020, approximately 37.7 million people globally are living with the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS).¹ Of these, more than 50% are from low-and middle-income countries (LMICs).² The socioeconomic burden of HIV/AIDS is notable because of the significant strain and cost incurred on people living with HIV/AIDS (PLWHA), their relatives, and the community.³ Between 2000 and 2015, \$562.6 billion was spent on HIV/AIDS, and, in 2015 alone, \$48.9 billion was spent on HIV/AIDS prevention, care, and treatment worldwide.⁴ Furthermore, between 2000 and 2016, HIV/AIDS prevention investment increased by 519.6%, from \$596 million to \$3 billion.⁵ On the other hand, AIDS-related deaths have decreased by 39% since 2010, owing primarily to the introduction of highly active antiretroviral therapy (HAART) in the early 2000s.¹ The end of the AIDS threat by 2030 and the achievement of UNAIDS 95–95–95 targets will largely depend on the effectiveness of the current antiretroviral therapy (ART), which will contribute to viral suppression, reduction in the spread of the virus, and prevention of AIDS-related deaths.^{6–8}

ART plays a crucial role in HIV prevention and management,^{9,10} and pharmacists play an invaluable role in maintaining the continuity and safety of their use.^{11,12} Pharmacists offer high-quality, patient-oriented medication therapy management services for PLWHA.^{13,14} Pharmacist interventions could mitigate medication errors, improve medication literacy skills and adherence.^{15,16} With pharmacist care, PLWHA could control their condition and better health outcomes.^{14,17} Consequently, the use of healthcare facilities and resources, such as clinic and emergency room admissions, could be decreased, thereby lowering increased health spending.^{16,18} A meta-analysis conducted by Ahmed et al. in 2021 (including evidence from inception to June 2020) showed that the availability of pharmaceutical services to PLWHA was correlated with statistically meaningful increases in adherence to medication and had a beneficial influence on viral suppression.¹² Other studies have also reported pharmacists' positive effects on patients' CD4 T lymphocyte counts, viral loads, and ART adherence.^{11,15,19,20} The American Society of Health-System Pharmacists (ASHP) now considers pharmacy services an essential component of HIV care.^{12,21,22} However, previous systematic reviews evaluating pharmacist interventions did not focus on economic consequences or directly targeted PLWHA health outcomes.^{11,12,23} As a result, we plan to conduct a systematic review of the literature to assess the economic outcomes of pharmacist care for PLWHA.

2. Methods

We registered the systematic review on PROSPERO (CRD42020173057) and followed the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) guidelines for reporting the findings.²⁴

2.1. Eligibility criteria

The studies were included if they were: (1) original research publication; (2) analysing pharmacist-managed services in PLWHA; (3) document an economic assessment; (4) written in English; and (5) available in full text. However, workshop materials published guidelines, case reports, editorials, opinions, letters to editors, commentaries, correspondences, news articles, qualitative studies and conference abstracts were excluded if not available in full-text form.

2.2. Information sources

The following electronic databases were searched: PubMed, EMBASE, Scopus, international pharmaceutical abstracts (IPA) via ProQuest, the Cochrane Library, and the CINAHL Plus. Three categories of keywords, i.e., pharmacist managed services (e.g., 'pharmacists'), HIV (e.g., 'AIDS'), and economic assessment ('economics') describing the key components of the research question, were used with variations from inception to 23 February 2021. Both free-text keywords and headings unique to the databases were used (e.g., MESH and Emtree) (Supplementary Table S1).

Bibliographies of relevant documents were searched manually to identify any additional records that were not found from the electronic searches. Two authors independently screened the titles and abstracts of all the documents listed. The full-text of potentially eligible titles/abstracts was retrieved for a full review by two independent reviewers. Any discrepancies between the two reviewers were resolved through discussion and consensus. A third independent reviewer was consulted when an agreement was not reached.

2.3. Data extraction and synthesis

Information extracted from the included studies includes author(s), study objectives, study design, comparison type, research setting, the country of study, inclusion and exclusion criteria, study duration, sample size, intervention (i.e., pharmacist services), control group(s), perspective(s), cost year, program costs, economic outcomes, significant statistical results, benefit-to-cost ratio, currency, and type of economic assessment. The comparison styles included pre-post, and inter-group comparisons. Control groups were categorized as parallel control for cross-group comparisons and historical self-control for pre-post comparisons. Study settings were classified as hospital-based outpatients or community pharmacies. The research perspectives were categorized as the patient, provider, or societal.²⁵ Finally, equivalents were provided for all currency values in 2021 USD, considering inflation and currency changes for each study.²⁶

In the current systematic review, program costs include the costs of implementing and sustaining pharmacy-managed project or programs (e.g., pharmacist salary time, incentives, office supplies, equipment's, facility space, and utility costs). On the other hand, economic outcomes include costs incurred with or without services (e.g., medication costs), cost reductions, per-case costs saved, and others. For example, the benefits-to-cost ratio, i.e., economic benefits per dollar spent on pharmacist-managed services, was established where appropriate, dividing service economic benefits by delivery cost for the same period. Furthermore, if the cost year was not explicitly stated in the research, the year of study completion was used.

2.4. Quality assessment

The type of economic assessment was classified as suggested by Drummond et al.²⁵ based on the number of alternatives and whether the costs and intervention outcomes were analysed. Specifically, studies with two or more options (e.g., intervention group versus control group or historical control group) were considered as 'analysis' whereas those without control group were 'description.' A partial economic assessment may include a cost description, a cost analysis, a description of the outcome and an evaluation of the outcome. The full economic evaluation includes all cost and outcomes components, and studies can be further classified as cost-effectiveness, cost-benefit, and cost-utility analysis. The quality evaluation

of the economic studies was carried out using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 24-item checklist.²⁷

3. Results

We found 4204 articles in database searches and two articles in bibliographic searches. After removing duplicate articles remaining 3409 were screened for titles and abstracts. Finally, 48 articles were identified for the full-text review; 44 articles were excluded for the reasons listed in Fig. 1, and four papers were included for the qualitative assessment.

Table 1 summarises the characteristics of the included studies. A study was conducted in the USA, Mexico, Spain, and Brazil.^{15,28-30} Three studies were conducted in a hospital-based outpatient facility,^{15,28,29} while one study was conducted in a community pharmacy setting.³⁰ In addition, three studies were prospective, single group, pre-post trials,^{15,29,30} while the one study was a prospective, parallel controlled study.²⁸ The minimum sample size was 28, and the maximum sample size was 279. Two studies have a sample size of less than 50,^{10,19} while two studies have greater than 100.^{28,30} The duration of the two studies was six months,^{15,29} while the rest were conducted over 12 months.^{28,30} The pharmacist managed interventions utilized in the studies can be divided into five types: targeted education for adherence ($n = 4$)^{15,28-30}; pharmaceutical care (e.g., medicine review, modification, and recommendations for other health care providers) ($n = 4$)^{15,28-30}; health screening and laboratory services ($n = 2$)^{15,30}; referral to specialists ($n = 2$)^{15,30}; motivational interviewing for adherence ($n = 1$).¹⁵

Table 2 summarises the economic characteristics and other outcomes of the included studies. Two studies reported partial economic assessments, i.e., outcome and cost description,^{15,29} while two studies measured the full economic evaluation, i.e., cost-benefit²⁸ and cost-effectiveness analysis.³⁰ One study was carried out from a provider perspective,²⁸ one from a patient perspective,²⁹ one from a societal perspective,¹⁵ and one from both provider and societal perspective.³⁰

The program's costs include labor costs, and other costs, i.e., office (light, space rent), pharmacist training, and sustaining costs of pharmacist-managed services.^{15,28-30} Carnevale et al. reported that additional daily investment in intervention group US\$1.45, 1.09, 2.13, 4.35, 1.09, and 0.87 i.e., 2.30, 1.73, 3.38, 6.90, 1.38 in 2021 US \$ of would be required for each additional outcome of viral load < 50 copies/ml, absence of co-infection, CD4 + >200, 350, and 500 cells/mm³, and optimal immune response, respectively. The intervention group generated annual savings of US\$ 32.33 per patient, i.e., 51.29 in 2021 US\$ per year i.e., associated with appointments, laboratory tests, and hospitalizations. In addition, the intervention group reported a benefit-to-cost ratio of 2.51:1 compared to standard care.²⁸

According to Dilworth et al., the true mean cost of the 5-visit intervention was \$819.74 i.e., 1028.85 in 2021 US\$ per patient. This total includes \$139.24 i.e., 174.4 in 2021 US\$ in patient costs and \$680.50 i.e., 853.19 in 2021 US\$ in clinic costs. Compensation for pharmacists' time (\$528.86 i.e., 663.73 in 2021 US\$ per patient, on average) accounted for 78% of the clinic's total cost for each patient who completed the adherence intervention. As per transmission rate modelling analysis, the adherence intervention prevented approximately 0.134 secondary HIV infections among

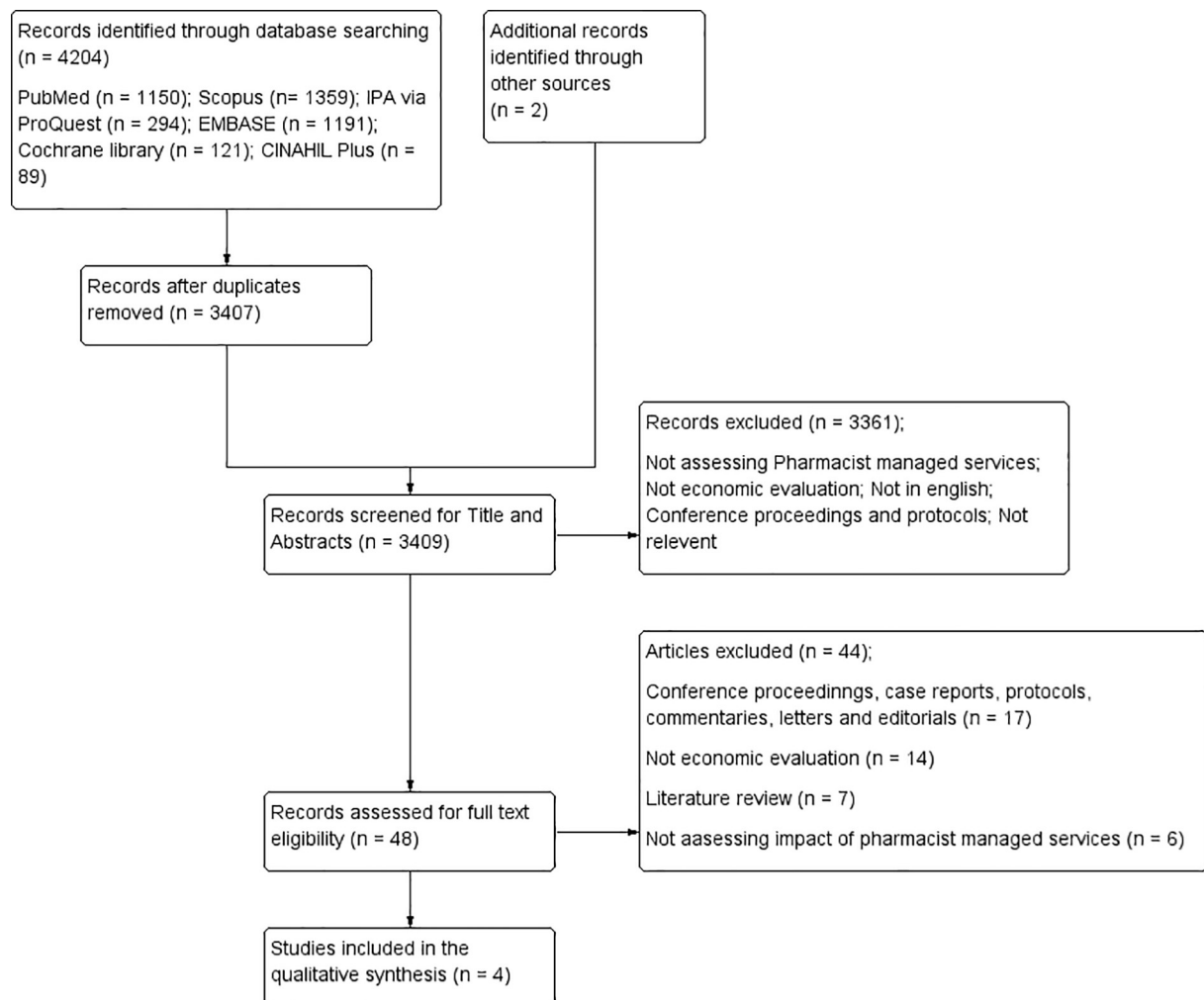


Fig. 1. PRISMA Flow chart of the search method and screening results.

Table 1
Characteristics of the included studies.

Authors (Publication year)	Study objective, Study setting and Country	Study design, type of comparison, sample size, and study period	Inclusion and exclusion criteria	Intervention (pharmacist role) and control
Carnevale, R. C. (2015)	<ul style="list-style-type: none"> To evaluate the clinical and economic impact of pharmaceutical care on HIV-infected patients. Hospital-based outpatients. Brazil 	<ul style="list-style-type: none"> ambispective, controlled study Between groups comparison 102 participants (51 participants in each intervention and control group) 12 months 	<ul style="list-style-type: none"> Outpatients diagnosed with HIV/AIDS aged 18–60 years with BMI below 30 kg/m² and receiving ART were included. Psychiatric, pregnant, and patients unable to return for follow-up were excluded. 	<ul style="list-style-type: none"> Pharmacists provided pharmaceutical services by PWDT method. Guided patients about adherence. Monitor problems with dosage, drug-drug and drug-food interactions, side effects, and adverse reactions, Suggesting medication changes to physicians when needed. The clinical pharmacy team did not follow the control group, and its data were collected through a review of medical charts encompassing the same period.
Dilworth, T. J. (2018)	<ul style="list-style-type: none"> To determine the clinical and economic effects of a pharmacist-administered ART adherence clinic for patients living with HIV Pharmacist-led ART adherence clinic at THS Mexico 	<ul style="list-style-type: none"> Prospective cohort study Pre-post comparison 28 patients enrolled but 16 attended all the follow-ups. 6 months 	<ul style="list-style-type: none"> THS Adherence clinic included patients if they were (a) referred to the clinic by their PCPs for medication adherence concerns between December 1, 2011, and June 1, 2013; (b) aged 18 years; (c) without HIV dementia as determined by their PCPs; (d) consented to participation in the study; (e) were able to read and understand English. 	<ul style="list-style-type: none"> Pharmacists provided medication adherence and disease state education with motivational interviewing techniques. Screening for opportunistic infection, Medication reconciliation, adherence barriers; ART side effects, drug interactions; patient CD4 counts and HIV viral loads. Ordering laboratory tests, immunizations, and providing recommendations to the physician; developing patient ART regimens with the PCPs; and making referrals to specialists.
Margusino et al. (2019)	<ul style="list-style-type: none"> To describe HIV patient candidates for the teleconsultation pharmaceutical care -home drug delivery (TcPhC-HDD) protocol, the implementation phases required, and the care circuit and subsequently to evaluate the clinical, economic, and patient-perceived quality results postimplementation. Hospital outpatients Spain 	<ul style="list-style-type: none"> Cohort observational. pre-post comparison 38 participants 6 months at least follow up 	<ul style="list-style-type: none"> Adult HIV outpatients included if adherent to ART; at least 6 months of follow-up in the HIU and HPS before inclusion; stable patients with chronic controlled infection objectified by two negative viral loads in consecutive determinations. Patients excluded with change in ART due to virologic failure or adverse effects; breach of appointment during the last year in outpatient hospital pharmacy or medical clinic without scheduling a replacement; concomitant treatment with other HD-medicines or H-medicines that require face-to-face consultation in HPS. 	<ul style="list-style-type: none"> Pharmacist did Bi-monthly telematic consultation Pharmaceutical care by clinical interviews to assess treatment, clinical variables monitoring, adherence evaluation, pharmacological interactions, adverse effects monitoring and maintaining records of activity.
Shresta R. K. (2020)	<ul style="list-style-type: none"> To assess the costs and cost-effectiveness of the patient-centred HIV care model (PCHCM), an evidence-informed structural intervention that integrates community-based pharmacists with primary medical providers to improve rates of HIV viral suppression. Community-based HIV-specialized pharmacies USA 	<ul style="list-style-type: none"> Prospective cohort study Pre-post comparison 279 participants from all three project sites 12 months 	<ul style="list-style-type: none"> Patients aged 18 years who were on or planning to start ART and who met the eligibility criteria (e.g., agreed to follow-up clinic and pharmacy visits, were willing to use project pharmacies to fill prescriptions, had an unmet immunological or virologic goal, failed a previous ART regimen) were enrolled in the project. Three of the 10 project sites (Albany, GA, Chicago, IL, Kansas City, MO), which reported complete cost data, were included in the cost and cost-effectiveness analyses. 	<ul style="list-style-type: none"> Pharmacists with training on HIV treatment and prevention, stigma, and cultural competency, offered individualized adherence support. Did initial comprehensive medication therapy review and subsequent quarterly targeted or comprehensive reviews depending upon the clinical need. Monitored prescription patterns and tracked clinical and laboratory test results to assess treatment response and to identify potential therapy-related adverse events. The project pharmacists worked directly with their partnered clinics to develop action plans to address any identified therapy-related problems. Plans were formulated in person (eg, “morning huddle” face-to-face meetings between the pharmacists and clinic providers) or by phone, fax, or email. Medical providers, pharmacists, and patients then collaborated to implement the action plans, and progress was reviewed at subsequent project visits.

HIV/AIDS: Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome, BMI: body mass index, ART: Antiretroviral therapy/treatment, PWDT: Pharmacist's Workup of Drug Therapy, HIU: Hospital Immunodeficiency Unit. HPS: hospital pharmacy services. HD: hospital diagnosis. H: hospital use. THS: Truman Health Services. PCPs: Primary care providers.

Table 2
Economic findings of the included studies.

Authors (publication year), type of economic evaluation, perspective, cost year and currency	Programme costs and economic outcomes	Economic results
<ul style="list-style-type: none"> Carnevale, R. C. (2015) CBA Provider 2012 US Dollar 	<ul style="list-style-type: none"> Programme costs Costs of appointments, laboratory tests, procedures, hospitalizations, total cost, and total cost without procedures. Economic outcomes Direct medical cost. Cost savings 	<ul style="list-style-type: none"> Intervention group showed better clinical outcomes and generated lower spending (not to procedures). An additional health care system daily investment of US\$1.45, 1.09, 2.13, 4.35, 1.09, and 0.87 i.e., 2.30, 1.73, 3.38, 6.90, 1.38 in 2021 US \$ would be required for each additional outcome of viral load < 50 copies/ml, absence of co-infection, CD4+ >200, 350, and 500 cells/mm³, and optimal immune response, respectively. Intervention group spent less per day on appointments, laboratory tests, and hospitalizations, but spent more on procedures and in total than the control group. The intervention group annually generated savings per patient of \$3.20, i.e., 5.08 in 2021\$ associated with appointments, \$23.19, i.e., 36.79 in 2021 \$ with laboratory tests, and \$5.94, i.e., 9.42 in 2021 \$ with hospitalizations. The intervention group also generated additional annual costs per patient of \$50.60, i.e., 80.28 in 2021 \$ associated with procedures, \$12.88 i.e., 20.44 in 2021 \$ with pharmaceutical appointments, and \$31.13, i.e., 49.39 in 2021 \$ with total costs. However, the difference in costs between the groups was not statistically significant. The stark contrast in the costs associated with procedures was caused by two hip surgeries performed on patients from the intervention group, which together added \$1916.09, i.e., 3039.79 in 2021 \$ to the total expenses. The BC ratio was 2.51:1. The intervention was highly cost-saving, with a return of \$2.96, i.e., 3.63\$ in 2021 in future medical care savings for each dollar spent on the adherence intervention. The total cost of the intervention was \$16,811 i.e., 21,092 (\$1051 i.e., 1318 in 2021 \$ per patient), which was less than the future savings in averted HIV-related medical care expenditures (\$49,702 i.e., 62,360.68 in 2021 \$). The corresponding savings in averted future HIV-related medical care expenditures and lost QALYs were \$49,702, i.e., 54,337.3 in 2021 \$ and 0.772, respectively” The true mean cost of the 5-visit intervention was \$819.74 i.e., 1028.85 in 2021 US\$ per patient. This total includes \$139.24 i.e., 174.4 in 2021 US\$ in patient costs and \$680.50 i.e., 853.19 in 2021 US\$ in clinic costs. Compensation for pharmacists' time (\$528.86 i.e., 663.73 in 2021 US\$ per patient, on average) accounted for 78% of the clinic's total cost for each patient who completed the adherence intervention. The economic evaluation revealed 137 ± 23 euro, i.e., 165.74 in 2021 US \$ patient/year costs-saved and 18.5 ± 7.2 h/patient/year working time gained. Patient-perceived quality average score was >9.4 out of 10 in all items; the most valued factors were the saving of direct costs and reconciliation with work commitments (45%), and the least valued attributes were making the payment for the shipment and having to adjust to a telephone appointment (41%). PCHCM annual intervention cost for the 3 project sites was \$226,741 i.e., 247,590.20 in 2021 US \$ this cost was composed of the annual clinic cost of \$74,043 i.e., 80,851.372021 US\$ and the annual pharmacy cost of \$152,698 i.e., 166,738.832021 US\$ The average cost per patient, cost per patient visit, and incremental cost per patient virally suppressed were \$813, \$48, and \$5039, i.e., 887.76, 52.41, and 5502.34 in 2021 US \$ respectively. The intervention averted 2.75 HIV transmissions and saved 12.22 QALYs and nearly \$1.28, i.e., 1.40 million in 2021 US \$ in lifetime HIV treatment costs. The intervention was cost-saving overall and at each project site.
<ul style="list-style-type: none"> Dilworth, T. J. (2018) Cost analysis Societal 2015 US dollars 	<ul style="list-style-type: none"> Programme cost Net cost of patient time and travel expenses, as well as costs incurred by the adherence clinic to implement the intervention. Economic analyses were conducted on an intention-to-treat basis and therefore included costs (but no benefits) for the 12 patients who failed to complete the intervention. Economic outcomes Direct and indirect medical cost. Cost saving 	
<ul style="list-style-type: none"> Margusino et al. (2019) Outcome analysis (Cost minimization analysis) Patient 2017 Euros 	<ul style="list-style-type: none"> Programme costs Not reported Economic outcomes Direct costs avoided from the patient's perspective (cost-minimization study assuming the same final clinical results—costs of public or private transportation that the patient would have had to incur to go to the HPS consultation less the costs actually paid by the patient to the company responsible for drug home delivery) Indirect costs (lost work hours avoided by the avoidance of the need to travel the hospital in active patients). 	
<ul style="list-style-type: none"> Shrestha R. K. (2020) Cost analysis, cost-effectiveness analysis Provider and societal perspective 2016 US dollars 	<ul style="list-style-type: none"> Programme cost Labour (salaries), non-labour (office supplies, durable material and equipment, facility space, and utilities) participant time, transportation Economic outcomes The annual total intervention cost per patient and cost per patient visit were calculated and reported for all 3 sites combined (ie, “overall” costs), by the project site, and separately for the clinics and pharmacies 	

CBA: cost benefit analysis, PCHCM: patient-centred HIV care model, QALYs: Quality-adjusted life years, \$; dollars.

sexual partners of PLWHA who completed the full 6-month assessment intervention. The prevention of future HIV-related medical care costs saved \$49,702, i.e., 62,360.68 in 2021 \$, and lost 0.772 QALYs. It was a very cost-effective intervention, with a \$2.96, i.e., 3.63\$ in 2021 return on investment in future medical savings for every dollar invested.¹⁵

PLWHA travel every month or every two months to the clinic for face-to-face consultation and drug dispensing represents an important expense that the patient bears and is the cause of a loss of relevant productivity throughout the year. However, the study results demonstrate a clear benefit to patients. Margusino et al. patient perspective revealed that pharmacist teleconsultation saved 137 ± 23 Euro patient/year, i.e., 165.74 in 2021 US \$ cost and 18.5 ± 7.2 h/patient/year time gained.²⁹

Shrestha et al. reported that interventions such as the patient-centered HIV care model PCHCM (that broadly facilitates viral suppression (and thus prevents HIV transmission) are required to end the HIV epidemic in the United States. The average cost per patient cost per patient visit, and incremental cost per patient virally suppressed were \$813, \$48, and \$5039, i.e., 887.76, 52.41, and 5502.34 in 2021 US \$ respectively. As per study findings HIV specialized clinical pharmacists' interventions stopped 2.75 HIV transmissions and saved 12.22 QALYs and almost \$1.28 million, i.e., 1.40 million in 2021 US\$ in living expenses for HIV care.³⁰ In addition, studies have shown that pharmacist interventions have increased pharmacist intervention costs and reduced future medical costs (e.g., laboratory tests, appointments, hospitalization, and emergency visits costs), compensating for the increased cost of drugs.

Based on the CHEERS checklist (Table 3), all the four economic evaluations have fulfilled item 1 as the titles suggest that the studies have been an economic evaluation. All reviews have completed point 2, except for Carnevale et al., which was completed partially because the study perspective was not summarised.²⁸ No discounts were applied in all the studies because the duration of the studies was not more than one year. In item 19 of the CHEERS checklist, Dilworth et al. and Margusino et al. did not report any incremental analysis and consequences of alternatives.^{15,29} Model-based structural uncertainties and input parameter delays were fully explained by Carnevale et al. and partially explained by Shrestha et al..^{28,30} Carnevale et al. partially reported the differences in baseline subgroup differences and variability in intervention effects.²⁸

4. Discussion

This systemic review described and examined studies investigating the economic impact of pharmacist-managed services for PLWHA. Although pharmacist interventions have become more expensive as programme costs have risen, the overall impact of these interventions on improving PLWHA is far more significant, either directly or indirectly, than the cost of the intervention itself. Interventions had a positive impact on adherence to ART, viral load suppression, immune system improvement, avoiding opportunistic infections, laboratory costs, hospitalization, emergency hospital visits in intervention groups. Further, these interventions were also meaningful in reducing the HIV transmission to HIV-negative partners and improving QALYs. This result could have been linked to improved HIV management through improved drug monitoring, contributing to a general decrease in overall healthcare costs. Studies show that pharmacist-managed programs resulted in cost-saving, demonstrating pharmacists' important role in HIV/AIDS management.

Pharmacists' role in healthcare has expanded from drug dispensing and distribution to individualized patient-centered care, such as pharmacotherapy supervision and personalized education.³¹⁻³⁴ The presence of pharmacists as a member of the HIV/AIDS healthcare management teams is likely to be sustained and gradually extended, especially following the recommendations of the World Health Organization (WHO) and the ASHP, each of which promotes the integration of pharmacists into a multidisciplinary team to improve PLWHA health outcomes.^{6,22}

This review included one study conducted in a community pharmacy setting and three studies conducted in hospital outpatient settings. This was consistent with the related reviews of the pharmacist-managed services

for diabetes and hypertension, which recognized that the pharmacist had increased pharmacotherapy services in outpatient settings.^{18,31} One theory may be that pharmacists are readily available and willing to provide prompt guidance on medications in outpatient settings, particularly for people who are on outpatient treatment for chronic diseases such as HIV/AIDS. The results in these studies will enable pharmacist managers to justify the budgetary benefit of pharmacist-managed programs and expand such services in ambulatory conditions, given the increasing recognition of pharmacists' contribution to the optimal use of medicine in chronic diseases. The results from studies conducted in the USA, Mexico, Spain, and Brazil cannot be generalized to other countries due to variations in pharmacist skills and services performed.

There are a few limitations to mention. First, half of the included studies were full economic studies similar to a review conducted in an economic evaluation of pharmacist services in patients living with diabetes.³¹ To encourage decision-makers to optimise the allocation of limited healthcare resources, full economic evaluations should be conducted and reported based on defined parameters, considering both cost and outcomes. Secondly, most research is from a provider's perspective, although only one study took a patient's perspective. In comparison, none of the studies found whether participants were insured because non-insured individuals appear to have low wages. Non-insured patients have fewer prescribed drugs and doctor's office visits but more emergency room visits, suggesting inadequate HIV treatment contributing to a substantial economic burden. Thus, potential research could be undertaken to examine the economic effect of pharmacist initiatives on such a perspective of uninsured individuals.

Third, two studies have investigated indirect costs, which account for a significant portion of the overall cost of HIV treatment.^{15,29} Bam et al. reported that cumulative total days missed in a monthly cycle due to HIV/AIDS were 3.5 days lost.³⁵ As pharmacist-managed programs may increase individuals' health outcomes and productivity, the existing literature may not have entirely grasped these services' economic effects. Fourth, the uncertainty underlying the key point calculations and the cost and outcome expectations must be considered so differences in parameter values may not lead to different results and conclusions. Potential economic estimates of pharmacist interventions may employ one-way, multi-way, and probabilistic sensitivity testing and non-parametric bootstrapping to calculate discrepancies in estimates. Finally, establishing a causal link between pharmacist-managed services and their economic effects could use a study approach by using a concurrent control group and introducing randomization to reduce bias. Policymakers can find more solid and compelling evidence from future, randomized, controlled, large sample-sized trials.

4.1. Limitations

There are some limitations associated with the present study. First, though a systematic search technique has been used to find qualifying studies, not all papers matching the inclusion requirements have likely been included. Secondly, this research is prejudiced by publication bias, and only certain reports that have been published could reflect the findings, and non-significant results may not have been published. Thirdly, no attempt was made to contact the authors of the studies examined to request information not reported; consequently, reporting bias could have been present. Finally, we did not include conference abstracts or dissertations that were not available in full text, so there may have been publication bias.

5. Conclusion

In conclusion, there was a good return in economic viability on programs run by pharmacists managed services in PLWHA. The evolving roles of pharmacists in HIV care and increases in medication costs promote the measurement of the economic effects of pharmacist initiatives. To assess the long-term cost-effectiveness of pharmacist services in HIV care, high-quality real-world observational, economic studies will be required in the future.

Table 3
Quality assessment of included studies using the Consolidated Health Economic Evaluation Reporting Standards checklist.

Carnevale et al. (2015) ²⁸	Dilworth et al. (2018) ¹⁵	Margusino et al. (2019) ²⁹	Shrestha et al. (2020) ³⁰
1. Identify the study as an economic evaluation or use more specific terms such as 'cost-effectiveness analysis', and describe the interventions compared.			
*1	1	1	e48
2. Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses) and conclusions.			
1, Partially ^a	1	1	e48
3. Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.			
2	165–166	1, 2	e48, e49
4. Describe characteristics of the base case population and subgroups analysed, including why they were chosen.			
2	166	2, 3	e49
5. State relevant aspects of the system(s) in which the decision(s) need(s) to be made.			
2, 3	166	2, 3	e49, e50
6. Describe the perspective of the study and relate this to the costs being evaluated.			
3	166	3	e50
7. Describe the interventions or strategies being compared and state why they were chosen.			
3	166	3	e49, e50
8. State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.			
2	166	3	e50
9. Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.			
NA ^b	NA ^b	NA ^b	NA ^b
10. Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.			
3	166	3	e50
11a. Single study-based estimates: describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.			
3	NA	3	e49
11b. Synthesis-based estimates: describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.			
NA	NA	NA	NA
12. If applicable, describe the population and methods used to elicit preferences for outcomes.			
NA	NA	NA	NA
13a. Single study-based economic evaluation: describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.			
3	167	3	e50
13b. Model-based economic evaluation: describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.			
NA	NA	NA	NA
14. Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.			
3	167	NA	e50
15. Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.			
NA	NA	NA	NA
16. Describe all structural or other assumptions underpinning the decision-analytical model.			
NA	NA	NA	NA
17. Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.			
3	167	3	e50
18. Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.			
3, 4	167, 168, 169	3, 5	e50, e51
19. For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.			
4, 5, 7	168, 169 ^c	5 ^c	e50, e51
20a. Single study-based economic evaluation: describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).			
NA	168	NA	NA
20b. Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.			
4	NA	NA	e52 ^d
21. If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information			
4, 5, 7	NA	NA	NA
22. Summarize key study findings and describe how they support the conclusions reached. Discuss limitations and the generalizability of the findings and how the findings fit with current knowledge.			
5, 7, 8	169, 170	5, 6, 7	e51, e52, e53
23. Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.			
8	171	7	E49
24. Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.			
8	171	7	e53

References

- Carnevale, R.C., et al., Cost analysis of pharmaceutical care provided to HIV-infected patients: An ambispective controlled study. *DARU, Journal of Pharmaceutical Sciences*, 2015. 23(1).
- Dilworth, T.J., et al., Clinical and economic effects of a pharmacist-administered antiretroviral therapy adherence clinic for patients living with HIV. *Journal of Managed Care and Specialty Pharmacy*, 2018. 24(2): p. 165–172.
- Margusino-Framiñán, L., et al., Teleconsultation for the Pharmaceutical Care of HIV Outpatients in Receipt of Home Antiretrovirals Delivery: Clinical, Economic, and Patient-Perceived Quality Analysis. *Telemed J E Health*, 2019. 25(5): p. 399–406.
- Shrestha, R.K., et al., Costs and Cost-Effectiveness of the Patient-Centered HIV Care Model: A Collaboration Between Community-Based Pharmacists and Primary Medical Providers. *Journal of acquired immune deficiency syndromes (1999)*, 2020. 85(3): p. e48–e54.

* Page numbers listed, N/A; not applied.

^a Perspective not stated.

^b Study duration was not greater than 12 months.

^c An incremental analysis of costs and consequences of alternatives was not performed.

^d Partially explained uncertainties related to model.

Funding

We received no funding for this project.

Ethics approval

Not required.

Declaration of Competing Interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rcsop.2021.100066>.

References

- UNAIDS. *Global HIV & AIDS statistics 2020 fact sheet*. AIDS-related deaths 2020 [cited 2021 08 July]; Available from: <https://www.unaids.org/en/resources/fact-sheet>.
- WHO. HIV/AIDS Key facts. [cited 2020 28 December]; Available from: [https://www.who.int/news-room/fact-sheets/detail/hiv-aids#:~:text=There%20were%20an%20estimated%2038.0,lifelong%20antiretroviral%20therapy%20\(ART\)%2020](https://www.who.int/news-room/fact-sheets/detail/hiv-aids#:~:text=There%20were%20an%20estimated%2038.0,lifelong%20antiretroviral%20therapy%20(ART)%2020).
- Burns R, et al. "I saw it as a second chance": a qualitative exploration of experiences of treatment failure and regimen change among people living with HIV on second-and third-line antiretroviral therapy in Kenya, Malawi and Mozambique. *Global Public Health* 2019;14(8):1112–1124.
- Dieleman JL, et al. Spending on health and HIV/AIDS: domestic health spending and development assistance in 188 countries, 1995–2015. *Lancet* 2018;391(10132):1799–1829.
- Haakenstad A, et al. Potential for additional government spending on HIV/AIDS in 137 low-income and middle-income countries: an economic modelling study. *The Lancet HIV* 2019;6(6):e382–e395.
- Organization, W.H. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach*. World Health Organization. 2016.
- Ahmed A, et al. Health-related quality of life and its predictors among adults living with HIV/AIDS and receiving antiretroviral therapy in Pakistan. *Qual Life Res* 2021;1-12.
- Ahmed A, et al. Concerns of HIV-positive migrant workers in COVID-19 pandemic: A call for action. *J Glob Health* 2020;10(2).
- Fauci AS, Lane HC. Four decades of HIV/AIDS—much accomplished, much to do. *N Engl J Med* 2020;383(1):1–4.
- Ahmed A, et al. Translation and cross-cultural adaptation of WHOQOL-HIV Bref among people living with HIV/AIDS in Pakistan. *Health Qual Life Outcomes* 2021;19(1):1–11.
- Saberi P, et al. The impact of HIV clinical pharmacists on HIV treatment outcomes: a systematic review. *Pat Pref Adher* 2012;6:297.
- Ahmed A, et al. Effect of pharmacist care on clinical outcomes among people living with HIV/AIDS: a systematic review and meta-analysis. *Res Soc Adm Pharm* 2021. <https://doi.org/10.1016/j.sapharm.2021.07.020> S1551-7411(21)00278-3; Epub ahead of print. PMID: 34353754.
- McNicholl IR, et al. A pharmacist-led program to evaluate and reduce polypharmacy and potentially inappropriate prescribing in older HIV-positive patients. *Pharmacotherapy* 2017;37(12):1498–1506.
- Barnes E, et al. The effect of an integrated health system specialty pharmacy on HIV antiretroviral therapy adherence, viral suppression, and CD4 count in an outpatient infectious disease clinic. *J Manag Care Spec Pharm* 2020;26(2):95–102.
- Dilworth TJ, et al. Clinical and economic effects of a pharmacist-administered antiretroviral therapy adherence clinic for patients living with HIV. *J Manag Care Spec Pharm* 2018;24(2):165–172.
- Cocohoba J. *THE PHARMACIST'S ROLE IN HIV CARE. Fundamentals of HIV MedicineCME ed.* 2021:2021.
- Scott-Sheldon LA, et al. Mindfulness-based interventions for adults living with HIV/AIDS: a systematic review and meta-analysis. *AIDS Behav* 2019;23(1):60–75.
- Touchette DR, et al. Economic evaluations of clinical pharmacy services: 2006–2010. *Pharmacotherapy* 2014;34(8):771–793.
- Farmer EK, et al. The pharmacist's expanding role in HIV pre-exposure prophylaxis. *AIDS Patient Care STDs* 2019;33(5):207–213.
- Chiampas TD, Biagi MJ, Badowski ME. Impact of an HIV-trained clinical pharmacist intervention on error rates of antiretroviral and opportunistic infection medications in the inpatient setting. *Pharm Pract (Granada)* 2019;17(3).
- Dalton K, Byrne S. Role of the pharmacist in reducing healthcare costs: current insights. *Integr Pharm Res Pract* 2017;6:37.
- Schafer JJ, et al. ASHP guidelines on pharmacist involvement in HIV care. *Am J Health Syst Pharm* 2016;73(7):468–494.
- Rocha B, et al. Pharmaceutical interventions in antiretroviral therapy: systematic review and meta-analysis of randomized clinical trials. *J Clin Pharm Ther* 2015;40(3):251–258.
- Moher D, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6(7), e1000097.
- Drummond MF, et al. *Methods for the economic evaluation of health care programmes*. Oxford university press. 2015.
- Turner HC, et al. Adjusting for inflation and currency changes within health economic studies. *Value Health* 2019;22(9):1026–1032.
- Husereau D, et al. Consolidated health economic evaluation reporting standards (CHEERS)—explanation and elaboration: a report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. *Value Health* 2013;16(2): 231–250.
- Carnevale RC, et al. Cost analysis of pharmaceutical care provided to HIV-infected patients: an ambispective controlled study. *DARU J Pharm Sci* 2015;23(1):13.
- Margusino-Framiñán L, et al. Teleconsultation for the pharmaceutical care of HIV outpatients in receipt of home antiretrovirals delivery: clinical, economic, and patient-perceived quality analysis. *Telemed e-Health* 2019;25(5):399–406.
- Shrestha RK, et al. Costs and cost-effectiveness of the patient-centered HIV care model: a collaboration between community-based pharmacists and primary medical providers. *JAIDS J Acq Immune Def Synd* 2020;85(3):e48–e54.
- Wang Y, Yeo Q, Ko Y. Economic evaluations of pharmacist-managed services in people with diabetes mellitus: a systematic review. *Diabet Med* 2016;33(4):421–427.
- Ahmed A, et al. Bridging the gap for clinical pharmacist in developing countries like Pakistan. *J Coll Physicians Surg Pak* 2018;28:229–232.
- Mohiuddin AK. *The Role of the Pharmacist in Patient Care: Achieving High Quality, Cost-Effective and Accessible Healthcare through a Team-Based, Patient-Centered Approach*. Universal-Publishers. 2020.
- Ahmed A, et al. *The Effect of Pharmacist Services on Patient Health Outcomes in a Low Middle-Income Country: A Systematic Review*. 2021.
- Bam K, et al. Strengthening adherence to anti retroviral therapy (ART) monitoring and support: operation research to identify barriers and facilitators in Nepal. *BMC Health Serv Res* 2015;15(1):188.