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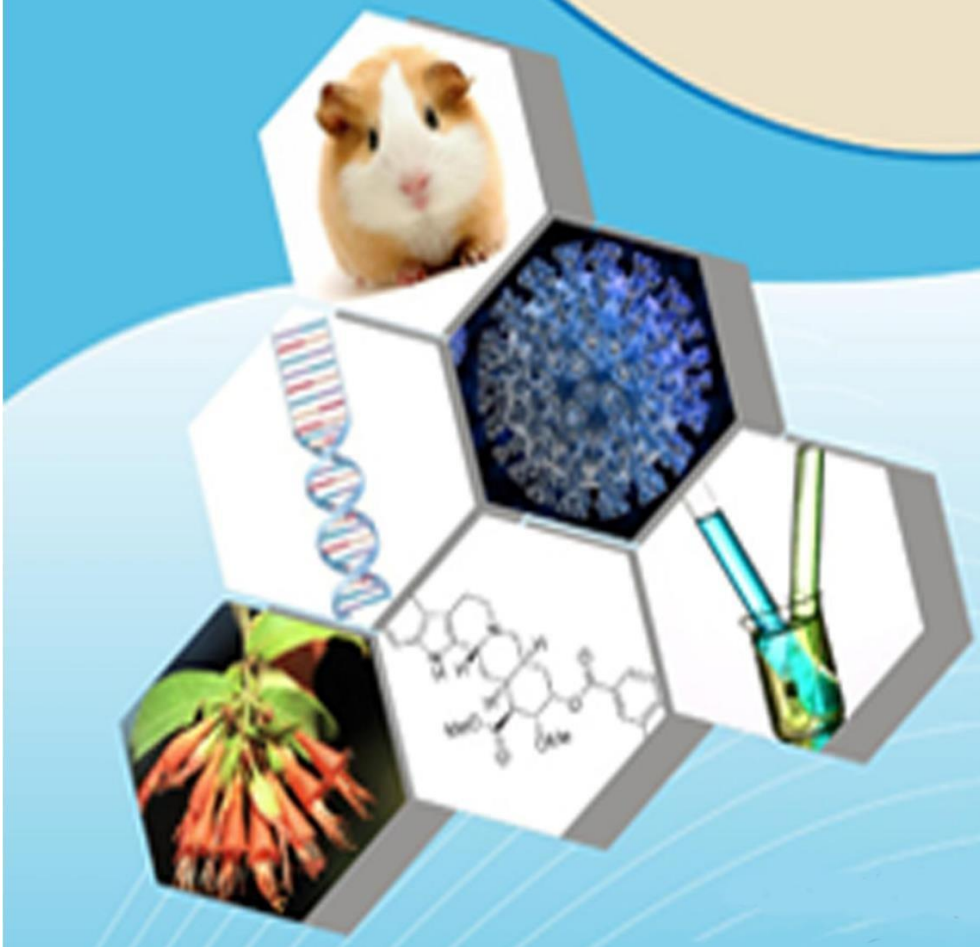

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PHARMACOECONOMIC ANALYSIS OF HIVAIDS MANAGEMENT PHARMACY

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Abstract

Context and Goals: The human immunodeficiency virus (HIV) is becoming more widespread worldwide. Although it has been demonstrated that pharmacist interventions enhance the health outcomes of individuals living with HIV/AIDS (PLWHA), it is unclear how these activities will affect the economy. As a result, our goal is to compile and evaluate the data in a methodical manner about the financial implications of pharmacist care for PLWHA.

Methods: A thorough search of the Cochrane Library, the databases CINAHL Plus, EMBASE, Scopus, and IPA via ProQuest were conducted. The review contained original research assessing the financial impact of pharmacist-managed services for PLWHA.

The Consolidated Health Economic Evaluation Reporting Standard (CHEERS) checklist was used to evaluate the economic studies' quality.

Findings: Four of the 4206 citations that were found through a database search satisfied the eligibility requirements. One study was carried out in a community pharmacy, while three others were carried out in an outpatient hospital environment. Targeted motivational education, pharmaceutical treatment, health screening for opportunistic infections, and specialist referrals were among the "pharmacist-managed services" categories. Two of the four studies that made up the economic evaluation provided full economic evaluations and were deemed to be of average quality. Pharmacist services resulted in cost savings of (51.29 to 165.74 in 2021 USD$) per person per year, 18.5 hours saved per patient annually, and a reduced cost of producing 12 years of quality-adjusted life years as compared to conventional care. Furthermore, the pharmacist service's benefit-to-cost ratio was 2.51:1.

Conclusions: The services run by pharmacists showed the financial sustainability of enhancing the general health outcomes of PLWHAs. To ascertain the long-term cost-effectiveness of these services, however, controlled, high-quality real-world economic studies are necessary, considering the pharmacist's expanding involvement in the health care team overseeing PLWHA.

Keywords: cost-benefit analysis, cost-effectiveness, pharmacoeconomics, pharmacist, pharmaceutical care, HIV/AIDS care

Key Points for decision-makers

- The role of pharmacists in HIV care is expanding, and it is recommended by the World Health Organization and the American Society of Health-System Pharmacists. Therefore, we attempted to find the economic impact of these services.

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- We discovered four such studies, each with minor differences in study intervention, study population, and follow-up duration, making it difficult to generalise their findings.

- Studies have shown that pharmacist interventions have economic benefits; however, future randomised studies to determine the economic benefits, in the long run, are required to strengthen the evidence.

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 HealthSystem 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-

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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 freetext 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.

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

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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 Journal Pre-proof Journal Pre-proof 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 4,204 articles in database searches and two articles in bibliographic searches. After removing duplicate articles remaining 3,409 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 Figure 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 hospitalbased 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-benefit [28] and costeffectiveness 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]. Journal Pre-proof Journal Pre-proof 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

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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 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 $819.74 i.e., 1,028.85 in 2021 US$ 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 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±7.2hr/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 $5,039, i.e., 887.76, 52.41, and 5,502.34 in 2021 US $ respectively. As per study findings HIV specialized clinical pharmacists' interventions stopped 2.75 HIV transmissions and saved Journal Pre-proof Journal Pre-proof 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].

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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 individualised patient-cantered 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 Journal Pre-proof Journal Pre-proof 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 begeneralized 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

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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 Journal Pre-proof Journal Pre-proof 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 impelling 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, programs handled by pharmacists provided PLWHA with a satisfactory return on economic viability. Measuring the financial impact of pharmacist efforts is made easier by the changing roles that pharmacists play in HIV care and the rising costs of medications. In the future, high-quality real-world observational economic studies will be needed to evaluate the long-term cost-effectiveness of pharmacist services in HIV care.

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