Contents available at **PubMed**
www.aidsreviews.com

PERMANYER

AIDS Rev. 2019;21:195-210

The Role of the Clinical Pharmacist in the Management of People Living with HIV in the Modern Antiretroviral Era

Lucas A. Hill[1], Craig Ballard[1], and Edward R. Cachay[2]*

[1]Department of Pharmacy, Owen Clinic; [2]Department of Medicine, Division of Infectious Diseases, University of California, San Diego, California

Abstract

As the HIV epidemic has evolved, so too has the role of the clinical pharmacist (CP) in the management of people living with HIV (PLWH). The modern antiretroviral therapy (ART) era has resulted in PLWH living normal life spans with resulting increased comorbidities. CPs have long been a part of the multidisciplinary management of ART. However, with the changing demographics of PLWH and health-care system dynamics, CPs have had the opportunity to expand their role. This includes involvement in managing increasing comorbidities with expanding and more complicated medication regimens, drug interaction monitoring, and optimizing transitions of care, all while recognizing and addressing barriers to successful HIV and hepatitis C virus (HCV) treatment. In addition, with the expansion of HIV prevention and pre-exposure prophylaxis (PrEP) services, CPs have the opportunity to be involved in HIV prevention. This study summarizes the literature evaluating the impact of CPs in the management of PLWH in the era of modern ART. We conducted a literature search to identify studies that assessed the CP role in HIV clinical practice since 2006. The identified studies were grouped into two categories. The first was HIV related outcomes, including interventions on regimen selection, adherence, regimen optimization, and management of treatment failure. The second group of studies pertained to aging and vulnerable populations, including management of comorbidities, transitions of care, medication-assisted treatment, hepatitis C, and HIV screening and PrEP. We concluded that the evidence supports the expanding role of CPs to positively impact a variety of aspects related to the care of PLWH. **(AIDS Rev. 2019;21:195-210)**

Corresponding author: Lucas A. Hill, luhill@ucsd.edu

Key words

Clinical pharmacist. Antiretroviral therapy. HIV. Aging. Comorbidities.

Introduction

The introduction of modern antiretroviral therapy (ART), starting with the protease inhibitor (PI) class in the mid-1990s, has transformed HIV into a chronic disease state that with treatment allows patients to live essentially normal life spans[1]. There has been a dramatic transformation in the safety, tolerability, efficacy,

Correspondence to:
*Lucas A. Hill
University of California, San Diego
Owen Clinic
4168 Front St.
PC. 92103 San Diego, California
E-mail: luhill@ucsd.edu

Received in original form: 01-07-2019
Accepted in final form: 25-08-2019
DOI: 10.24875/AIDSRev.19000089

and general ease of administration of ART. We now have five major classes of antiretrovirals (ARV) available globally (nucleos(t)ide reverse transcriptase inhibitors [NRTI], non-NRTI, integrase strand transfer inhibitors, PI, and entry inhibitors) as well as ten single-tablet regimens available making it possible to find effective, easy to take medications for the majority of our patients[2].

With the success of ART people living with HIV (PLWH) are living longer, and 45% of PLWH were greater than or equal to 50 years of age at the end of 2015 in the USA[3]. Aging PLWH face increased prevalence of medical comorbidities such as cardiovascular, renal, bone, diabetes, obesity, and hyperlipidemia that is often associated with the use of multiple medications (polypharmacy)[4]. Thus, current successful care of PLWH relies on multidisciplinary teamwork integrated within the medical home model of care that differs slightly depending on the health-care system. Tantamount to medical management is recognizing barriers to care that is prevalent among PLWH such as social isolation, mental illness, alcohol, and illegal substance use that could adversely impact engagement in care[5]. In a rapidly evolving health-care system, medical providers increasingly rely on the mutual support of the clinical pharmacists (CPs) as a part of the multidisciplinary team management.

CPs have been an essential component of caring for PLWH since the beginning of the epidemic and have favorably influenced clinical outcomes in a variety of settings[6-8]. Nevertheless, the role of CPs in the modern ART era can vary widely depending on the health system and country of practice. CPs are directly involved with patient disease state education, medication side effect monitoring, adherence counseling and monitoring, and selection or optimization of ART in complex PLWH and multidrug resistance. With the aging population, CPs can have a larger impact on managing polypharmacy associated with an increased number of comorbidities. CPs can contribute to reduce pill burden including deprescribing, and focus on fidelity verification of inadvertent iatrogenic interactions that can result in adverse clinical outcomes[9,10]. CPs also assist in the transitions of care aspects from home to hospital and vice versa. Further, CPs have has an active role in the treatment of hepatitis C in PLWH in the era of direct-acting antivirals (DAA) and participate actively in HIV prevention including pre-exposure prophylaxis (PrEP). Herein, in this review, we aim to describe the role that the CP has played in the management of PLWH in the modern ART era as well as a discussion of the future direction of clinical pharmacy in caring for PLWH, particularly with the aging population of PLWH.

Methods

A literature search was performed using PubMed and Cochrane Library to identify available literature reporting pharmacist involvement in the care of PLWH. The search was limited to articles published and including interventions from 2006 to present to limit studies to the "modern ART era." We chose the period of 2006-2008 for defining the start of the modern ART era as it coincides with the approval in the United States of the first complete single-tablet regimen, and it was when most clinical guidelines started reviewing and changing recommendations to initiate ART at higher CD4+ T-cell counts[11-13]. There were no specific requirements of study size or design given the limited number of available studies. The references of identified studies were also reviewed to ascertain any additional literature available. Studies were excluded if they were not written in English as the primary language or did not discuss interventions made specifically by a pharmacist. Studies were grouped into categories of HIV related interventions and impact on virologic outcomes (12), aging and vulnerable populations (2), pharmacist role in comorbidities (2), medication reconciliation and transitions of care (9), and HIV prevention including PrEP (5). Table 1 includes a summary of studies directly related to HIV treatment outcomes. Table 2 includes a summary of studies related to the management of comorbidities, medication reconciliation and transitions of care, and HIV screening and PrEP.

HIV-related interventions and impact on virologic outcomes

Treatment initiation and regimen selection

When choosing initial ART, general considerations include regimen potency, potential adverse effects, potential drug interactions, the genetic barrier to resistance, patient comorbidities, and compatibility with the patient's lifestyle[2]. The study conducted by Nevo et al. illustrates that the beneficial role of CPs in the selection of initial ART regimens and the favorable impact CP participation can have on outcomes for treatment of HIV-infected naïve patients[14]. The study compared two groups of patients, those re-

Table 1. Impact of pharmacists on HIV-related outcomes

Study	Country of origin	Population	Intervention	Outcome	Comment
Nevo et al.[14] (2015)	United States	– ART naïve – 819 patients in intervention group versus 436 in the control group	Treatment initiation: CP based ART initiation versus initiation by PCP	– CP group had higher likelihood of achieving viral suppression during the first 2 years (HR 1.37) – CP group remained on initial regimen significantly longer than control group (100 vs. 44 months)	– CP group with more frequent monitoring which was controlled for – Did not control for patient complexity, however CP group had higher viral loads and lower CD4 counts
Henderson et al.[19] (2011)	United States	28 patients on ART with poor adherence	Adherence: referral to pharmacist based adherence clinic	– Increase from 7% to 32% having 95% or greater PDC – Overall increase in mean adherence from 60% to 81% – Increase in proportion with undetectable viral load	– Increase in proportion with undetectable viral load and changes in CD4 count not significant – Small sample size
McPherson-Baker et al.[20] (2010)	United States	21 patients on ART received intervention compared to 21 patients who continued the standard of care	Adherence: referral to pharmacist based adherence clinic in non-adherent patients	– CP intervention resulted in 29% improvement in compliance to refills – Intervention group with significant improvement in adherence to clinic appointments – Intervention group with lower rates of hospitalizations and opportunistic infections	Small sample size
Krummenacher et al.[21] (2011)	Switzerland	104 patients on ART with non-adherence	Adherence: referral to pharmacist adherence clinic for motivational interviewing	– ART adjusted in 45% of subjects – Increase in viral load suppression from 20.2% to 74% post-intervention	High proportion of women (59%) and black ethnicity (42%)
Dilworth et al.[22] (2018)	United States	– 28 patients currently off ART of which 64.3% were treatment naïve – 16 patients completed the intervention	Adherence: referral to CP for adherence counseling with ongoing monitoring by pharmacist for 6 months	– Significant increase in median CD4 count from 298 to 454 cells/mm^3 – Median viral load decreased from 48,000 copies/mL to all being undetectable – Return of $3 savings for every $1 spent based on avoidance of new infections	– 78% with mental illness and 28.6% with substance abuse – Did not specifically address adherence measures

(Continues)

Table 1. Impact of pharmacists on HIV-related outcomes *(Continued)*

Study	Country of origin	Population	Intervention	Outcome	Comment
Hirsch et al.[23] (2011)	United States	2234 Medicaid beneficiaries, 628 attended an MTM service at community pharmacy	Adherence: HIV community pharmacies providing MTM services to Medicaid beneficiaries	– Patients who attended MTM services had 22-27% higher adherence rates compared to the control group – Fewer regimen changes in the MTM group –Attending MTM services carried OR of 2.74 for improved adherence	– Non ART medication costs higher in the MTM group, but inpatient costs were lower – Large cohort with a comparator group
Cocohoba et al.[24] (2012)	United States	783 women (82% HIV positive) of whom 30% received counseling (WIHS cohort)	Adherence: pharmacist counseling at community pharmacy	– AIDS and greater number of years of infection associated with counseling – Trend for those that received counseling to be more adherent and have higher CD4 count	– Only study focusing specifically on women with a relatively large sample size – Outcomes were not statistically significant
Ma et al.[25] (2010)	United States	75 patients (78.7% men, 40% non-white) on ART with 6 months before intervention as control phase and 6 months after intervention as study phase	Regimen optimization: pharmacist assessment and change in ARV regimens based on non-response, toxicities, or reduction in pill burden. Also adherence counseling	– Significant reduction in mean pill quantity from 7.2 to 5.4 pills/days. – Significant reduction in mean dosing frequency from 2.0 to 1.5 times/days. – Significant improvement in mean CD4 count and those with undetectable viral load post-intervention (63% vs. 96%)	– Regimen changes reviewed with ID physician before change – Short follow-up time
Lee et al.[26] (2018)	United States	57 patients on TDF regimen that were switched to a TAF regimen	Regimen optimization: pharmacist provided education on the benefits of switching from TDF to TAF	– 91% were able to identify increased renal safety of TAF – 73% able to identify increased bone safety of TAF	– Single site with small number of participants – Did not assess any virologic outcomes
Molino et al.[27] (2016)	Brazil	96 patients on ART with 50% in intervention group paired by gender and CD4 count	Regimen optimization: – review by CP for DRP – Development of care plan by CP to address DRP	– 5.02 DRP identified per patient initially with a 38.4% reduction to 3.09 DRP/ patient after 1 year – Most common DRP related to med. safety – Greater increase in CD4 count in the intervention group – No difference in viral load changes	– Did not comment specifically on DRP directly related to ART

(Continues)

Table 1. Impact of pharmacists on HIV-related outcomes *(Continued)*

Study	Country of origin	Population	Intervention	Outcome	Comment
Byrd et al.[28] (2019)	United States	– 765 patients on ART of which 421 were in the adherence analysis and 649 in the viral suppression analysis – 73% male and 43% were non-white	Regimen optimization: – Pharmacist conducted MTM in a community pharmacy – Clinical information shared between pharmacy and clinic with collaborative medication action planning	– No change in adherence rates after the intervention – Overall viral suppression significantly improved from 75% to 86% – Improved viral suppression rates in younger and minority patients – Significant improvement in sustained viral suppression from 65% to 80%	– Large cohort with good outcomes using collaboration with community pharmacy and outpatient clinics – Lack of change in adherence with improvement in viral suppression likely indicates regimen optimization
Dong et al.[30] (2017)	United States	32 patients on ART with undetectable viral loads, the majority due to resistance or toxicities	Management of treatment failure: clinical consultation center made up of physician and CP consulted by board of prisons pharmacists on difficult HIV cases	– 4 of 32 recommendations were not accepted – Regimen change recommended in 87.5% of cases with suspected virologic failure – Reduction in viral load of at least 0.5 log achieved in 89% and complete viral suppression in 64%	– BOP pharmacists able to work successfully with clinical consultation center to manage difficult cases – Lack of specifics for the role of the CP

ART: antiretroviral therapy; CP: clinical pharmacist; PCP: primary care physician; MTM: medication therapy management; PDC: proportion of days covered; OR: odds ratio. ARV: antiretroviral; ID: infectious diseases; TDF: tenofovir disoproxil fumarate; TAF: tenofovir alafenamide; DRP: drug-related problems.

ferred to the clinic-based HIV pharmacist for initiation of ART (n = 819) versus those initiated on treatment by their primary care provider (n = 436). Patients who initiated treatment with the HIV pharmacist had a higher likelihood of achieving viral suppression during the first 2 years after ART initiation (HR 1.37, $p < 0.0001$), and this positive effect persisted after controlling for the frequency of viral load monitoring. In addition, patients in the pharmacist initiation group remained on their initial regimen longer than the control group (100 months vs. 44 months). Of note, there could be some unmeasured confounders such as a higher prevalence of more complex medical comorbidities or ongoing barriers to care that affect engagement in those patients whose ART was initiated by their HIV providers. The study also showed that individuals in the pharmacist group had more frequent viral load monitoring, suggesting that patients in this group may have had more frequent interactions for education, support, counseling on adherence, and monitoring of adverse effects. This study highlights the contribution of CPs in consolidating patient engagement and retention in care following ART initiation. More recently, there is a movement to more rapidly initiate ART in patients who are newly diagnosed. Supporters of this strategy argue that more rapid ART initiation leads to faster viral load suppression, which is beneficial from both the patient and public health perspective[15,16]. Rapid ART initiation may result in a reduction in the size of the HIV reservoir in those recently infected and may increase engagement in care[17,18]. However, what is missing from the literature is the role that CPs can play in more rapid ART initiation. To successfully scale up this initiative will take a team-based approach and a partnership between physicians and other members of the patient's care team. CPs can be an important part of this team given their accessibility, expertise in regimen selection and adherence counseling, ability to provide disease state education, and ability to assist in medication acquisition.

Adherence

One of the widely known benefits of involving CPs in ART initiation is the positive impact they have on patient's adherence to ART therapy. Henderson et al. evaluated the impact of a pharmacist-based adherence clinic in which providers referred patients with adherence problems[19]. Of the 28 patients enrolled in the study, only 7% had 95% or greater adherence

Table 2. Role of pharmacist in the management of comorbidities, transitions of care, and HIV prevention

Study	Country of origin	Population	Intervention	Outcome	Comment
Cope et al.[31] (2015)	United States	140 patients with HIV, 90 in the intervention group, and 50 in the control group	Management of comorbidities: – Interv-ention group managed by team of CP and medical provider versus control group managed only by individual provider – Evaluated patients specifically with pharmacist interventions	– No change between groups in systolic BP, diastolic BP, or Hgb A1C. – Significant reduction in LDL on the intervention group – More patients in intervention group appropriately prescribed aspirin	– Fewer drug interactions in the intervention group but not significant when controlling for baseline factors – Did not control for mental illness or socioeconomic status
McNicholl et al.[36] (2017)	United States	– 248 PLWH over the age of 50 – High frequency of comorbidities	Deprescribing: CP evaluated potentially inappropriate prescribing using STOPP and Beers Criteria as well as drug interactions	– Potentially inappropriate prescribing in 54% and 63% using STOPP and Beers criteria – 69% had at least one medication discontinued and 10% six or more medications discontinued	– Only study focusing on pharmacist intervention specifically in PLWH over the age of 50
Olea et al.[47] (2018)	United States	153 HIV/HCV coinfected patients treated for HCV	HIV/HCV coinfection: CP part of multidisciplinary team, involved in regimen selection, medication and disease state education, and treatment monitoring	Primary role of the pharmacist identified as prior authorization completion, medication counseling, and drug interaction screening	– Descriptive study only – CP used collaborative practice protocol
Cachay et al.[39] (2013)	United States	359 HIV/HCV coinfected patients of which 196 were treated in HIV primary care model and 163 in subspecialty model	HIV/HCV coinfection: transition from using hepatology based model of HCV treatment to multi-disciplinary team based approach, including CP, in HIV primary care model to deliver HCV treatment	– Significantly greater number of patients treated in primary care model (43) versus hepatology model (26) – Similar SVR rates between the two models	– Treatment was during the interferon era before availability of DAA – Demonstrates ability of multidisciplinary primary care based approach to more effectively initiate HCV treatment
Shea et al.[53] (2018)	United States	– Hospitalized patients with HIV – Preintervention group of 126 admissions and post-intervention of 108 admissions	Transitions of care: CP performed prospective audits of ART including medication reconciliation, review of dosing, regimen, administration and drug interactions.	Significant reduction in ART medication errors from 67.5% to 13% post-intervention	– Potential temporal bias – Computerized order entry initiated simultaneously to intervention
Billedo et al.[54] (2016)	United States	185 admissions of PLWH evaluated during the intervention period compared to 252 during control period	Transitions of care: as part of ART stewardship program CP performed daily laboratory and medication reviews	Significant increase in drug interactions that were intervened on at admission (80% vs. 98%) and during hospitalization (43% vs. 95%)	ART stewardship program was available 24/7 at tertiary care hospital

(Continues)

Table 2. Role of pharmacist in the management of comorbidities, transitions of care, and HIV prevention *(Continued)*

Study	Country of origin	Population	Intervention	Outcome	Comment
Lauzevis et al.[55] (2013)	France	– PLWH admitted to the hospital – 35 patients with 56 admissions during control versus 43 patients with 77 admissions during the intervention	Transitions of care: CP worked with an infectious disease physician to review all ART prescriptions for potential errors	– Increase in the number of medication errors identified from 39.3% to 42.9% – Intervention allowed for 36% of errors to be corrected	– Small sample size – Intervention was a combination of pharmacist and infectious disease physician
Carcelero et al.[56] (2011)	Spain	Review of 189 PLWH consisting of 247 admissions	Transitions of care: CP reviewed ART prescriptions for drug interactions, performed medication reconciliation, and monitored for dose adjustments	– 60 ARV problems identified in 41 patients – 92% of pharmacist interventions were accepted	– Observational study – Also evaluated predictors of errors
Eginger et al.[57] (2013)	United States	86 patients admitted to hospital with HIV, AIDS, or OI	Transitions of care: review of all medication records by CP to identify and intervene on ARV or OI medication errors	– 210 combined ARV or OI medication errors identified – At least one medication error in 54.7% of patients – 94.7% of correctable errors were fixed	Observational study only
Sanders et al.[58] (2014)	United States	– PLWH admitted on ART – 162 admissions in the control group and 110 admissions in the intervention group	Transitions of care: development of antimicrobial stewardship that included daily review of ARV prescriptions by CP	– Significant reduction of medication errors from 50% pre-intervention to 34% post-intervention – Significant reduction in major drug interactions and incomplete regimens	Primary part of the intervention was medication review by CP
Liedtke et al.[59] (2016)	United States	330 admissions in 184 PLWH with 177 admissions during the intervention	Transitions of care: implementation of daily review of ART prescriptions by HIV pharmacist	– Significant decrease of 73.9% in the number of errors after the intervention	Observational retrospective study
Chiampas et al.[60] (2015)	United States	344 PLWH admitted to the hospital of which 49% had a CP on service	Transitions of care: CP present on some of the services managing patients admitted with HIV	– 190 errors in 132 patients with 24% corrected within the median time of 36 h – No difference in number of errors with or without a pharmacist on service	– Pharmacists did not have specific training in caring for PLWH – Pharmacists not specifically focused on admitted patients with HIV

(Continues)

Table 2. Role of pharmacist in the management of comorbidities, transitions of care, and HIV prevention *(Continued)*

Study	Country of origin	Population	Intervention	Outcome	Comment
Seden et al.[61] (2013)	United Kingdom	200 PLWH being seen in outpatient HIV clinic	Medication reconciliation: pharmacist screening for drug interactions and completion of medication reconciliation before physician appointment	– DDI identified in 58% of patients – Survey with 103 physician responses in which 61.2% reported being notified of something they did not know	Only study reporting impact of medication reconciliation in an outpatient setting
Tung et al.[62] (2018)	United States	695 HIV-negative patients eligible for PrEP	HIV prevention and screening – Pharmacist managed PrEP clinic in which PrEP was initiated and monitored in a community pharmacy setting	– 695 patients initiated on PrEP over 3 year period – No seroconversions – 90% of patients with mean proportion days covered of 80% – 25% dropout rate	Only example of PrEP initiation in a community pharmacy setting using collaborative practice protocol
Weidle et al.[65] (2014)	United States	Testing of HIV-negative patients	HIV prevention and screening implementation of HIV testing in 21 community pharmacy locations using rapid point-of-care oral fluid tests	– 21 sites (18 community pharmacies) administered 1540 HIV tests over 2 years period – 1.6% of results were preliminary positive	– Majority of sites used in-store staff to conduct testing – Rural and urban setting
Darin et al.[66] (2015)	United States	Testing of HIV-negative patients	HIV prevention and screening: implementation of HIV testing in 2 independent retail pharmacies using rapid HIV tests	– 69 HIV tests performed with one reactive test (1.5%) – First HIV test for 42% of participants	– Included 59.4% women and 53.6% non-white patients
Sherman et al.[67] (2014)	United States	Testing of HIV-negative patients in the public hospital system	HIV prevention and screening: addition of two part-time CP to perform POCT for HIV at outpatient clinic	– Of 164 POCT conducted pharmacists performed 2.4% – 6% of tests were positive – Pharmacist testing identified 28.6% of those with positive tests	–Testing site also treated HIV-positive patients
Amesty et al.[68] (2015)	United States	HIV testing of patients using pharmacies participating in needle-exchange programs	HIV prevention and screening: rapid HIV testing using oral fluid in two community pharmacies providing needle exchange services in community at high risk of HIV	– 233 tests conducted – Females, higher number of sex partners, injection drug use, and more frequent testing were more likely to accept pharmacy testing	Population tested mostly ethnic and racial minorities

(Continues)

Table 2. Role of pharmacist in the management of comorbidities, transitions of care, and HIV prevention *(Continued)*

Study	Country of origin	Population	Intervention	Outcome	Comment
Lecher et al.[69] (2015)	United States	Testing of HIV-negative patients in community pharmacies and retail clinics	HIV prevention and screening: six sites trained staff to perform POC HIV testing in community pharmacy setting and evaluated cost-effectiveness	– 939 tests performed over 12 months – 17 reactive tests – Average cost per person tested estimated to be $47.21 with recurrent costs of $32.17/person – Determined to be cost effective	– Urban and rural setting – Various ownership structures for the pharmacies
Collins et al.[70] (2018)	United States	Testing of HIV-negative patients in chain retail pharmacy setting	HIV prevention and screening: Retail pharmacy stores located in low-income areas or areas with a higher proportion of minorities conducted POC HIV testing	– 3630 tests conducted – 0.8% of results were reactive – 84.6% who had confirmatory testing were linked to care – Mean cost per person was $41.79	– Successful implementation of HIV testing in large retail chain pharmacy

CP: clinical pharmacist; BP: blood pressure; PLWH: people living with HIV; HCV: hepatitis C virus; ART: antiretroviral therapy; OI: opportunistic infections; ARV: antiretroviral; DDI: drug-drug interaction; PrEP: pre-exposure prophylaxis; POCT: point of care testing.

based on the proportion of days covered (PDC) before referral to a pharmacist-based clinic. The proportion of patients with > 95% PDC increased to 32% after the CP intervention ($p = 0.01$) which consisted of five visits over 6 months focused on reasons for non-adherence and potential strategies to overcome these barriers. Overall, CP participation lead to an increase in mean adherence from 60% at baseline to 81% after the intervention ($p < 0.0001$). Henderson et al. also demonstrated an increase in the proportion of patients with an undetectable viral load after the CP intervention (58% vs. 73%), but this was not statistically significant. A similar study conducted at the Veterans Administration evaluated the impact of monthly adherence counseling by CPs among 42 patients with adherence challenges. Half received counseling by the CP ($n = 21$), and the other half did not receive additional counseling[20]. Intervention by the CP resulted in significant improvement in compliance with medication refills (29% improvement) and adherence to clinic appointments. Patients counseled by the CP had lower rates of hospitalizations than those who did not receive additional counseling (mean 0.33 vs. 1.05, $p < 0.05$). Finally, Krummenacher et al. reported on a pharmacist-run adherence clinic in which 104 patients with non-adherence were referred for motivational interviewing and monitoring with medication event monitoring system caps[21]. The study observed a high adherence rate of 83% among the participants but due to study design pre- or post-intervention adherence comparisons could not be made. Overall, there was a significant improvement in viral load suppression (20.2% vs. 74%) and an increase in CD4 counts when comparing entrance to the intervention versus at the end of the intervention. Further, it seems that CP participation in patient adherence counseling is a cost-effective approach for delivering care to PLWH. Dilworth et al. estimated the cost benefits on the differential increased proportion of patients who achieved undetectable HIV viral load when receiving CP counseling[22]. They estimated that patients who received CP counseling at the time of ART initiation would produce a return of $3 for every $1 spent on the intervention based on the reduction in risk of HIV transmission in viremic patients. Although most studies documenting the beneficial role of CPs in monitoring ART adherence were relatively small and conducted in outpatient clinic settings, there are some large community-based observations as well. Hirsch et al. assessed that the impact community pharmacies could have on adherence to

ARVs and outcomes[23]. The study evaluated 2234 Medicaid beneficiaries of which 628 patients at one point attended an HIV pharmacy that was conducting medication therapy management (MTM) services over 4 years. Those that attended the MTM services had adherence rates 22-27% higher than the control group based on pharmacy fill data ($p < 0.001$). The patients who accessed MTM services were also less likely to change their ARV regimens. Rates of opportunistic infections were similar between the two groups. Using adjusted logistic regression analysis, Hirsch et al. demonstrated that the most important factor for improved adherence was attending one of the pharmacies with MTM services (odds ratio [OR] 2.74, 95% confidence interval [CI] 2.44-3.10). Finally, another study describes the beneficial impact that community pharmacists had on counseling women with HIV[24]. The study identified 30% of 783 women (82% with HIV) who received counseling from a community pharmacist. There was a favorable trend among those that received counseling in that they were more likely to be adherent (OR 1.23, 95%CI 0.7-2.18) and also have higher CD4 cell counts (+43 cells/mm^3, 95% CI 17.7-104.3). Altogether, these studies highlight the positive impact pharmacists have on adherence to ARVs. Improvements in adherence are likely derived from the ability for pharmacists to have more time to focus on conversations pertaining to individual patient's perceived barriers to adherence and strategies to overcome these barriers. Also, there is likely a benefit due to the ability for pharmacists to spend time on disease state education in those with low health literacy, in combination with a detailed knowledge of drug-drug, drug-food, and drug-disease state interactions.

Regimen optimization

The success of ART depends on regimen optimization to reduce pill burden and dosing frequency, reduce side effects, and address drug interactions. CPs can assist in the optimization of ART therapy either through recommendations to the prescribing physician or through direct ART regimen adjustments using a collaborative practice protocol. Ma et al. described the impact of recommendations made by CPs for adjustment of ART regimens in 75 patients from 2006 to 2008[25]. Reasons for recommending ART change included virologic failure, toxicities, regimen complexity, non-adherence, and prevention of toxicities. After CP intervention, the number of pills patients took decreased from a mean of 7.2 to 5.4 pills/days ($p < 0.001$) and mean dosing frequency decreased from 2.0 to 1.5 times/days ($p < 0.001$). There was also a significant increase in ARV adherence. The study demonstrated a significant improvement in mean CD4 count pre versus post-intervention (423 vs. 491 cells/mm^3, $p < 0.001$) as well as the percentage of those with undetectable viral load post-intervention (63% vs. 96%, $p < 0.001$). More recently, Lee et al. reported the favorable impact of CP education on a pharmacist-led protocol to switch patients from a tenofovir disoproxil fumarate (TDF) based regimen to a tenofovir alafenamide (TAF)-based regimen[26]. Fifty-seven patients completed a follow-up survey, and 91% of them were able to correctly identify the increased renal safety of TAF versus TDF. In addition, 73% identified the decreased bone toxicity of TAF versus TDF. Hence, CP education is not only perceived but is also effective for patient knowledge. Finally, a study from Brazil compared 96 patients, 43 in each group, in which one group CPs participated in the care of patients, and the other did not[27]. Participation of the CP resulted in a 38.4% reduction in drug-related problems (DRP), although characterization of the specific DRP and their relationships with ART regimens was limited. The group of patients where a CP participated in their care had significant improvements in their CD4 count with no difference in viral load outcomes between the two groups. CP impact on regimen optimization has also been described in the community pharmacy setting. Byrd et al. described the impact of community pharmacists providing MTM services within a patient-centered HIV care model that integrated community HIV trained pharmacists with primary care providers[28]. They evaluated adherence, measured by PDC, and viral suppression rates pre- and post-intervention by a pharmacist. Adherence rates did not change after pharmacist intervention; however, overall viral suppression improved from 75% to 86% ($p < 0.001$) including in groups typically with lower rates of viral suppression such as younger patients and minority patients. Given the lack of improved adherence with significant changes in viral suppression, the authors identified regimen optimization based on drug interactions, side effects, and other medication-related barriers as the likely reason for the improvement in viral suppression rates. In 2019, with HIV care in the outpatient setting becoming more longitudinal management of different primary care needs, HIV medical

providers have more time constraints to address patient's needs related to ART. CPs are important health allies that can spend more time on ART optimization outside of the regular PCP visits. Collaborative practice protocols or a licensed pharmacist clinician, as is available in the state of New Mexico in the USA and is used to provide care to PLWH, can be implemented to allow pharmacists to order medications or laboratory studies increasing the impact pharmacists can have in collaborating in the care of PLWH[29].

Management of treatment failure

In many academic centers, the CP is an essential member of a cadre of HIV professionals involved in making decisions in the setting of virologic failure and drug resistance. However, scarce published data describe these services. Dong et al. described the impact of the Bureau of Corrections HIV CP consultants in conjunction with the Clinician Consultation Center in management of difficult HIV resistance cases[30]. They summarized 32 cases from 2010 to 2012 in which an antiretroviral regimen change was made in 87.5% of the cases with a favorable viral load response, described as at least a 0.5 log reduction in viral load, in 89% and complete virologic suppression in 64% of cases. CPs have the ability to spend time assessing a patient with virologic failure, discussing reasons for failure, and providing education on new antiretroviral regimens and should be considered as a valuable service to the multidisciplinary management of these patients.

Aging and vulnerable populations

Using access to USA federal-sponsored healthcare plans, Gallant et al. compared the presence of comorbidities from 2003 to 2013 in over 64,000 PLWH and demonstrated significant increases in the percentage of patients with hypertension, hyperlipidemia, obesity, and endocrine disease over time[4]. Over the same time, there were also significant increases in the proportion of patients with deep vein thrombosis, hepatitis C, thyroid disease, renal impairment, and liver disease in PLWH as compared to HIV negative controls. Cope et al. performed a retrospective study specifically to evaluate the impact of CP collaboration on the management of comorbidities in PLWH[31]. They compared 96 patients who were managed using an interdisciplinary team that included CPs with 50 patients managed solely by their PCP. The interdisciplinary team resulted in significant improvement in LDL cholesterol (–8.8 vs. +8.4, $p = 0.014$) as well as significantly more patients prescribed aspirin if indicated in the intervention group. However, there was no significant difference between the two groups in systolic or diastolic blood pressure or hemoglobin A1C.

Polypharmacy is more common in PLWH as compared to similar-aged HIV-uninfected people and contributes to an increase in DRP including increased drug interactions[9,10]. Drug-drug interactions (DDIs) with ARVs are complex and include pharmacokinetic and pharmacodynamic interactions that may potentially lead to increased toxicities or potential treatment failure[32]. In addition, the negative consequences of polypharmacy in older adults have been well documented to include an impact on the performance of daily activities and increased risk of falls[33,34]. More specific to PLWH, polypharmacy has been identified as a significant predictor of non-adherence to ART[35]. As highlighted by McNicholl et al., CPs effectively help to identify potentially inappropriate prescribing in aging PLWH[36]. They studied 248 HIV patients age 50 years and older who were evaluated by a pharmacist using Beers Criteria and STOPP Criteria to assess potentially inappropriate prescribing. The studied group had a high prevalence of comorbidities including hypertension (56%), depression (52%), asthma/COPD (48%), dyslipidemia (39%), coronary artery disease (27%), and diabetes mellitus (22%). The mean number of non-ARV medications was 11.6. A review by a CP identified potentially inappropriate prescribing in 54% and 63% of patients using the STOPP and Beers Criteria, respectively. The pharmacist review resulted in 69% of patients having at least one medication discontinued and 10% having six or more medications discontinued. The likelihood of meeting STOPP or Beers Criteria significantly increased when six or more medications were being prescribed. This signals the importance of increasing awareness among busy medical providers regarding the impact of polypharmacy and the need to consider deprescribing in older adults. More importantly, this highlights the collaborative role CPs bring to the team to focus on the prevention of iatrogenic adverse clinical outcomes including working with physicians to identify and correct potentially harmful drug interactions.

Additional vulnerable populations that require special attention include those with ongoing substance

use, mental illness, and unstable housing as these syndemics contribute to non-adherence to ART and worse HIV-related outcomes[37,38]. Although several of the adherence studies mentioned above described the frequency of substance abuse and mental illness in their studied populations, there is very limited data demonstrating the beneficial impact pharmacists can have on these specific populations[19,21,23]. In our institution, patients with ongoing mental illness, unstable housing and ongoing drug use, and who were treated with an interferon-based regimen for HCV received an intense and frequent monitoring protocol where the CP was a core component of patient follow-up. We showed that having CPs involved in monitoring these vulnerable groups had similar HIV and HCV virologic outcomes compared to sub-specialty groups that often exclude these vulnerable populations[39]. Our strategy remains even in the DAA era as described below. As ART continues to improve, actual virologic failure will become less frequent with social barriers presenting as the primary challenge to successful treatment, and CPs must be prepared to address many of the social issues that contribute to unsuccessful treatment with ART.

Pharmacist role in other comorbidities

Opioid dependence and medication-assisted treatment (MAT)

The ongoing opioid epidemic in the United States demands significant attention, and the HIV infected population is also significantly affected by this epidemic. PLWH are more likely to receive opioids and at higher doses as compared to uninfected individuals with estimates of 21-53% of PLWH receiving opioid prescriptions at any time point[40]. There is increased support of CPs in multidisciplinary MAT programs. DiPaula and Menachery described a pilot program in which a CP and physicians collaborated in an integrated manner to provide outpatient opioid substitution maintenance therapy to low-income patients[41]. The pilot program included 12 patients; all patients were retained at 6 months and 73% at 12 months. The CP's role included obtaining a medical, psychiatric, and substance abuse history as well as providing adherence counseling and completing a treatment contract. The pilot program demonstrated high adherence rates to buprenorphine therapy, with 98% of urine toxicology screens positive for buprenorphine and 88% positive for buprenorphine but negative for opioids indicating successful MAT. CPs need to be aware of the potential role in many scaling-up efforts to widely implement MAT programs and be prepared and trained accordingly. CPs can assist in various aspects including adherence counseling, medication acquisition including facilitating transition to long-acting formulations, and laboratory and diversion monitoring.

Hepatitis C coinfection

Although 25% of PLWH in the United States are coinfected with HCV, historically HCV treatment uptake remained low, reflecting not only the sub-optimal efficacy and toxicity of former treatments but also the complexity of the population that needs to be treated[42]. Our team was one of the first to describe the clinical benefits of a co-managed HIV/HCV model of care using medical providers and CPs within an HIV clinic before the advent of DAA[39]. We showed that using a comanaged CP HCV team; our HCV virologic outcomes not only improved in the era of sub-optimal interferon but also achieved an overall improvement in engagement in HIV care for a group of vulnerable patients with ongoing barriers to care. Nevertheless, with the introduction of DAA and interferon-free regimens starting in 2014, the participation of CPs in HCV treatment groups across the different models of care in the USA is well described[43-45]. The role of the CP in the treatment of monoinfected HCV patients in the DAA era includes successful treatment delivered by a pharmacist-run HCV clinic as well as pharmacists as part of a multidisciplinary team[46]. In the DAA era the CP has contributed with a more unique role when treating HCV among PLWH, as illustrated in the study of Olea et al.[47] Medical providers often rely on CPs for the management of complex drug interactions between ARV and DAA[48]. Further, the heterogeneous health-care system in the USA and elevated cost of DAA obligated CPs to participate in vital roles related to DAA medication acquisition. Although DAA treatments are shorter, and better tolerated, than prior interferon-containing regimens, the higher prevalence of active drug abuse and mental illness had resulted in an increased no show of PLWH in need of DAA therapy[49]. Hence, the CP is increasingly involved in a new role of outreach methods and facilitating patients' access aimed to increase HCV linkage to HCV care to our PLWH who need it the most[49,50]. One potential model of HCV care delivery is through community pharmacies that provide daily opioid substitu-

tion therapy (OST) in which patients can get screened and treated using pharmacist-led care teams. Radly et al. described successful screening for HCV using dried blood spot testing of patients enrolled in OST at community pharmacies in Scotland and improved linkage to assessment for HCV treatment as compared to the conventional pathway[51]. HCV treatment provided in this model will also be evaluated and presents a method of optimizing interactions with a patient population in high need of HCV treatment using community pharmacies[52].

Transitions of care and medication reconciliation

An important impact pharmacists have on caring for PLWH is improving transitions of care from the outpatient to inpatient setting or vice versa. CPs can reduce medication errors as well as perform medication reconciliation to ensure patients are continued on chronic medications when hospitalized but in an accurate and safe manner. Shea et al. recently reported on an approach using pharmacists to perform prospective audits on ART in PLWH who were hospitalized. The review included medication reconciliation and verification of dosing, regimen, appropriate administration, and screening for drug interactions[53]. The study compared a pre-intervention group of 126 admissions from May 2010 to October 2010 and a post-intervention group of 108 admissions from May 2014 to October 2014. They observed a significant reduction in antiretroviral medication errors from 67.5% of patients to 13% after the intervention ($p < 0.001$), and these reductions in errors included incorrect/incomplete regimens, incorrect dosages, renal dose adjustments, incorrect administration, and drug interactions with incorrect administration being the most frequent error pre-intervention. The use of ritonavir was the only significant predictor of errors pre-intervention. It was noted that the post-intervention group had significantly fewer PI-based regimens used; however, post-intervention ritonavir use was no longer a predictor of medication errors likely demonstrating the impact of the intervention. Noteworthy, computerized order entry was also initiated at the same time as the pharmacist intervention. Several other studies report similar findings in a reduction in medication errors in either antiretroviral prescribing or opportunistic infections prophylaxis and are included in table 2[54-59]. One study showed no benefit of CPs in this setting. The study found no significant difference in the frequency of errors with or without a CP present on the service but the study design had shortcomings that limit its conclusions[60]. Among them, none of the pharmacists had specific training in caring for PLWH nor were they focused specifically on this population of patients. What appears to be missing from the literature is the role pharmacists can play in the discharge process of PLWH to not only reduce prescribing errors but also resolve medication access issues during the transition from hospital to home. Medication reconciliation is also an important contribution of CPs in the outpatient setting. Seden et al. described a pharmacist screening of 200 patients before their physician appointments in which medication reconciliation was performed as well as DDI screening and adherence assessment[61]. Of these 200 patients, 103 physician responses were obtained regarding the utility of the pharmacist screening. Physicians reported that one or more component of the consultation told them something they did not know in 61.2% of the cases, including 37.9% of the consultations related to DDI checks. The benefit of the CP consultation was greater in patients who were taking two or more concomitant medications, demonstrating the need to focus on patients taking a high number of medications.

HIV prevention and PrEP

Pharmacists have the opportunity also to be heavily involved in HIV prevention, testing, and providing PrEP. One innovative model of care is described by Tung et al.[62] In the study; Tung et al. described a pharmacist-managed PrEP clinic in a community pharmacy setting, in which PrEP was initiated in 695 patients over 3 years with 74% of them starting medication the same day as their first appointment. The pharmacists provided PrEP services under a collaborative practice protocol. There were no HIV seroconversions, and patients had good adherence with 90% of patients having a mean PDC > 80%. Importantly, retention rates (19% lost to follow-up, and 25% dropout rate) were as good as or better than other reports of retention in PrEP services, which is a real challenge in providing successful PrEP services[63,64]. There are several studies (Table 2) that report successful HIV testing performed by pharmacists, most in the community pharmacy setting, including in marginalized populations such as minorities and low-income groups[65-68]. These testing interventions by pharmacists were well accepted and also appeared to be cost-effective[69,70]. CPs contributes to PrEP services in various ways from assisting with

medication acquisition and reduction in costs, counseling and education, adherence monitoring, and recommendations on treatment and prevention of other sexually transmitted infections (STIs), which is one of the most important aspects of providing PrEP services given the increasing rates of STIs[71].

Medication access and cost

CPs are advocates for the welfare of their patients, both between the patient and provider but also the patient and their insurance company. As health-care systems become more consumed with cost containment measures, medication access for PLWH likely will become more difficult. In a health-care system like the United States, pharmacists in all settings must be well versed in many aspects of insurance coverage to be able to assist their patients in being able to access all of their required medications. A significant amount of resources is involved in the prior authorization process for all medication classes, and PLWH are no exception[72]. Pharmacists can use their clinical and medication knowledge to advocate for coverage of the optimal medication regimens for their patients and assist in justifying coverage. In rapidly evolving health-care systems that increasingly are productivity and revenue driven, increased time spent on drug access adds to medical provider pressures and adds to burn out. CPs act as allies to execute these tasks as CPs know the various medication patient assistance programs, copay programs, and foundations available for financial support to help reduce prohibitive costs of medications to patients. This medication access issue does not only apply to ARVs but also to many aspects of caring for PLWH or those at risk of HIV including access to PrEP, hepatitis C treatment, MAT treatment, and medications for various comorbidities that are becoming more common among PLWH.

Conclusion

As the success of ART has continued to evolve and PLWH are living longer, so has evolved the role of CPs in the care of PLWH. CP participation in multidisciplinary teams of care continues to influence favorable clinical outcomes in the inpatient and outpatient setting.

Pharmacists are well positioned to perform medication reconciliation, screen for drug interactions, and potentially recommend deprescribing particularly in older patients. Medication access will also continue to be an evolving issue for PLWH and success of medication therapy relies on having access, with CPs in a key position to assist patients in a variety of ways. Finally, with ongoing efforts to expand the use of PrEP, primarily to key populations who are at higher risk but not accessing PrEP services, CPs will be an important resource to increase access to PrEP services as part of multidisciplinary approaches tailored to the individual's needs of different medical systems and regions.

References

1. Broder S. The development of antiretroviral therapy and its impact on the HIV-1/AIDS pandemic. Antiviral Res. 2010;85:1-8.
2. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available from: http://www.aidsinfo.nih.ogv/contentfiles/lvguidelines/AdultandAdolescentGL.pdf.
3. HIV among People Aged 50 and Older. Center for Disease Control and Prevention. Available from: http://www.cdc.gov/hiv/group/age/olderamericans/index.html.
4. Gallant J, Hsue PY, Shreay S, Meyer N. Comorbidities among US patients with prevalent HIV infection-A trend analysis. J Infect Dis. 2017; 216:1525-33.
5. Cachay ER, Hill L, Wyles D, Colwell B, Ballard C, Torriani F, et al. The hepatitis C cascade of care among HIV infected patients: a call to address ongoing barriers to care. PLoS One. 2014;9:e102883.
6. Crawford NS. Organizing pharmacists to help fight AIDS. Am Pharm. 1991;NS31:44-7.
7. Noormohamed SE, Ferguson K. Pharmacists' role in preventing and treating HIV infection. Am Pharm. 1993;NS33:38-44.
8. Foisy MM, Tseng A, Blaikie N. Pharmacists' provision of continuity of care to patients with human immunodeficiency virus infection. Am J Health Syst Pharm. 1996;53:1013-7.
9. Greene M, Steinman MA, McNicholl IR, Valcour V. Polypharmacy, drug-drug interactions, and potentially inappropriate medications in older adults with human immunodeficiency virus infection. J Am Geriatr Soc. 2014;62:447-53.
10. Gimeno-Gracia M, Crusells-Canales MJ, Armesto-Gómez FJ, Compaired-Turlán V, Rabanaque-Hernández MJ. Polypharmacy in older adults with human immunodeficiency virus infection compared with the general population. Clin Interv Aging. 2016;11:1149-57.
11. Roul H, Mary-Krause M, Ghosn J, Delaugerre C, Pialoux G, Cuzin L, et al. CD4+ cell count recovery after combined antiretroviral therapy in the modern combined antiretroviral therapy era. AIDS. 2018; 32:2605-14.
12. Besson C, Lancar R, Prevot S, Algarte-Genin M, Delobel P, Bonnet F, et al. Outcomes for HIV-associated diffuse large B-cell lymphoma in the modern combined antiretroviral therapy era. AIDS. 2017;31:2493-501.
13. Eholié SP, Badje A, Kouame GM, N'takpe JB, Moh R, Danel C, et al. Antiretroviral treatment regardless of CD4 count: the universal answer to a contextual question. AIDS Res Ther. 2016;13:27.
14. Nevo ON, Lesko CR, Colwell B, Ballard C, Cole SR, Mathews WC, et al. Outcomes of pharmacist-assisted management of antiretroviral therapy in patients with HIV infection: a risk-adjusted analysis. Am J Health Syst Pharm. 2015;72:1463-70.
15. Pilcher CD, Ospina-Norvell C, Dasgupta A, Jones D, Hartogensis W, Torres S, et al. The effect of same-day observed initiation of antiretroviral therapy on HIV viral load and treatment outcomes in a US public health setting. J Acquir Immune Defic Syndr. 2017;74:44-51.
16. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365:493-505.
17. Jain V, Hartogensis W, Bacchetti P, Hunt PW, Hatano H, Sinclair E, et al. Antiretroviral therapy initiated within 6 months of HIV infection is associated with lower T-cell activation and smaller HIV reservoir size. J Infect Dis. 2013;208:1202-11.
18. Ananworanich J, Chomont N, Eller LA, Kroon E, Tovanabutra S, Bose M, et al. HIV DNA set point is rapidly established in acute HIV infection and dramatically reduced by early ART. EBioMedicine. 2016;11:68-72.

19. Henderson KC, Hindman J, Johnson SC, Valuck RJ, Kiser JJ. Assessing the effectiveness of pharmacy-based adherence interventions on antiretroviral adherence in persons with HIV. AIDS Patient Care STDS. 2011;25:221-8.
20. McPherson-Baker S, Malow RM, Penedo F, Jones DL, Schneiderman N, Klimas NG, et al. Enhancing adherence to combination antiretroviral therapy in non-adherent HIV-positive men. AIDS Care. 2000;12:399-404.
21. Krummenacher I, Cavassini M, Bugnon O, Schneider MP. An interdisciplinary HIV-adherence program combining motivational interviewing and electronic antiretroviral drug monitoring. AIDS Care. 2011;23:550-61.
22. Dilworth TJ, Klein PW, Mercier RC, Borrego ME, Jakeman B, Pinkerton SD, 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;24:165-72.
23. Hirsch JD, Gonzales M, Rosenquist A, Miller TA, Gilmer TP, Best BM, et al. Antiretroviral therapy adherence, medication use, and health care costs during 3 years of a community pharmacy medication therapy management program for medi-cal beneficiaries with HIV/AIDS. J Manag Care Pharm. 2011;17:213-23.
24. Cocohoba JM, Althoff KN, Cohen M, Hu H, Cunningham CO, Sharma A, et al. Pharmacist counseling in a cohort of women with HIV and women at risk for HIV. Patient Prefer Adherence. 2012;6:457-63.
25. Ma A, Chen DM, Chau FM, Saberi P. Improving adherence and clinical outcomes through an HIV pharmacist's interventions. AIDS Care. 2010; 22:1189-94.
26. Lee SS, Havens JP, Sayles HR, O'Neill JL, Podany AT, Swindells S, et al. A pharmacist-led medication switch protocol in an academic HIV clinic: patient knowledge and satisfaction. BMC Infect Dis. 2018;18:310.
27. Molino CG, Carnevale RC, Rodrigues AT, Moriel P, Mazzola PG. HIV pharmaceutical care in primary healthcare: improvement in CD4 count and reduction in drug-related problems. Saudi Pharm J. 2017;25:724-33.
28. Byrd KK, Hou JG, Bush T, Hazen R, Kirkham H, Delpino A, et al. Adherence and viral suppression among participants of the patient-centered HIV care model project-a collaboration between community-based pharmacists and HIV clinical providers. Clin Infect Dis. 2019:ciz276.
29. Ryan KL, Jakeman B, Conklin J, Pineda LJ, Deming P, Mercier RC, et al. Treatment of patients with HIV or hepatitis C by pharmacist clinicians in a patient-centered medical home. Am J Health Syst Pharm. 2019;76:821-8.
30. Dong BJ, Williams MR, Bingham JT, Tokumoto J, Allen JD. Outcome of challenging HIV case consultations provided via teleconference by the clinician consultation center to the federal bureau of prisons. J Am Pharm Assoc (2003). 2017;57:516-9.
31. Cope R, Berkowitz L, Arcebido R, Yeh JY, Trustman N, Cha A, et al. Evaluating the effects of an interdisciplinary practice model with pharmacist collaboration on HIV patient co-morbidities. AIDS Patient Care STDS. 2015;29:445-53.
32. Jiménez-Nácher I, Alvarez E, Morello J, Rodriguez-Nóvoa S, de Andrés S, Soriano V, et al. Approaches for understanding and predicting drug interactions in human immunodeficiency virus-infected patients. Expert Opin Drug Metab Toxicol. 2011;7:457-77.
33. Crentsil V, Ricks MO, Xue QL, Fried LP. A pharmacoepidemiologic study of community-dwelling, disabled older women: factors associated with medication use. Am J Geriatr Pharmacother. 2010;8:215-24.
34. Fletcher PC, Berg K, Dalby DM, Hirdes JP. Risk factors for falling among community-based seniors. J Patient Saf. 2009;5:61-6.
35. Cantudo-Cuenca MR, Jiménez-Galán R, Almeida-Gonzalez CV, Morillo-Verdugo R. Concurrent use of comedications reduces adherence to antiretroviral therapy among HIV-infected patients. J Manag Care Spec Pharm. 2014;20:844-50.
36. McNicholl IR, Gandhi M, Hare CB, Greene M, Pierluissi E. A pharmacist-led program to evaluate and reduce polypharmacy and potentially inappropriate prescribing in older HIV-positive patients. Pharmacotherapy. 2017;37:1498-506.
37. Chander G, Himelhoch S, Moore RD. Substance abuse and psychiatric disorders in HIV-positive patients: epidemiology and impact on antiretroviral therapy. Drugs. 2006;66:769-89.
38. Aidala AA, Wilson MG, Shubert V, Gogolishvili D, Globerman J, Rueda S, et al. Housing status, medical care, and health outcomes among people living with HIV/AIDS: a systematic review. Am J Public Health. 2016;106:e1-23.
39. Cachay ER, Hill L, Ballard C, Colwell B, Torriani F, Wyles D, et al. Increasing hepatitis C treatment uptake among HIV-infected patients using an HIV primary care model. AIDS Res Ther. 2013;10:9.
40. Cunningham CO. Opioids and HIV infection: from pain management to addiction treatment. Top Antivir Med. 2018;25:143-6.
41. DiPaula BA, Menachery E. Physician-pharmacist collaborative care model for buprenorphine-maintained opioid-dependent patients. J Am Pharm Assoc (2003). 2015;55:187-92.
42. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Department of Health and Human Services. Available from: http://www.aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/345/hcv.
43. Wyles DL, Ruane PJ, Sulkowski MS, Dieterich D, Luetkemeyer A, Morgan TR, et al. Daclatasvir plus sofosbuvir for HCV in patients coinfected with HIV-1. N Engl J Med. 2015;373:714-25.
44. Naggie S, Cooper C, Saag M, Workowski K, Ruane P, Towner WJ, et al. Ledipasvir and sofosbuvir for HCV in patients coinfected with HIV-1. N Engl J Med. 2015;373:705-13.
45. Wyles D, Brau N, Kottilil S, Daar ES, Ruane P, Workowski K, et al. Sofosbuvir and velpatasvir for the treatment of hepatitis C virus in patients coinfected with human immunodeficiency virus type 1: an open-label, phase 3 study. Clin Infect Dis. 2017;65:6-12.
46. Naidjate SS, Zullo AR, Dapaah-Afriyie R, Hersey ML, Marshall BD, Winkler RM, et al. Comparative effectiveness of pharmacist care delivery models for hepatitis C clinics. Am J Health Syst Pharm. 2019;76:646-53.
47. Olea A Jr., Grochowski J, Luetkemeyer AF, Robb V, Saberi P. Role of a clinical pharmacist as part of a multidisciplinary care team in the treatment of HCV in patients living with HIV/HCV coinfection. Integr Pharm Res Pract. 2018;7:105-11.
48. Soriano V, Labarga P, Fernandez-Montero JV, Mendoza C, Benítez-Gutiérrez L, Peña JM, et al. Drug interactions in HIV-infected patients treated for hepatitis C. Expert Opin Drug Metab Toxicol. 2017;13:807-16.
49. Cachay ER, Mena A, Morano L, Benitez L, Maida I, Ballard C, et al. Predictors of hepatitis C treatment failure after using direct-acting antivirals in people living with human immunodeficiency virus. Open Forum Infect Dis. 2019;6:ofz070.
50. Cachay ER, Hill L, Torriani F, Ballard C, Grelotti D, Aquino A, et al. Predictors of missed hepatitis C intake appointments and failure to establish hepatitis C care among patients living with HIV. Open Forum Infect Dis. 2018;5:ofy173.
51. Radley A, Tait J, Dillon JF. DOT-C: a cluster randomised feasibility trial evaluating directly observed anti-HCV therapy in a population receiving opioid substitute therapy from community pharmacy. Int J Drug Policy. 2017;47:126-36.
52. Radley A, de Bruin M, Inglis SK, Donnan PT, Dillon JF. Clinical effectiveness of pharmacy-led versus conventionally delivered antiviral treatment for hepatitis C in patients receiving opioid substitution therapy: a study protocol for a pragmatic cluster randomised trial. BMJ Open. 2018;8:e021443.
53. Shea KM, Hobbs AL, Shumake JD, Templet DJ, Padilla-Tolentino E, Mondy KE, et al. Impact of an antiretroviral stewardship strategy on medication error rates. Am J Health Syst Pharm. 2018;75:876-85.
54. Billedo JA, Berkowitz LB, Cha A. Evaluating the impact of a pharmacist-led antiretroviral stewardship program on reducing drug interactions in HIV-infected patients. J Int Assoc Provid AIDS Care. 2016;15:84-8.
55. Lauzevis S, Chaix F, Lazzerini C. Evaluation of a strategy aimed at reducing errors in antiretroviral prescriptions for hospitalized HIV-infected patients. Med Mal Infect. 2013;43:391-7.
56. Carcelero E, Tuset M, Martin M, De Lazzari E, Codina C, Miró J, et al. Evaluation of antiretroviral-related errors and interventions by the clinical pharmacist in hospitalized HIV-infected patients. HIV Med. 2011;12:494-9.
57. Eginger KH, Yarborough LL, Inge LD, Basile SA, Floresca D, Aaronson PM, et al. Medication errors in HIV-infected hospitalized patients: a pharmacist's impact. Ann Pharmacother. 2013;47:953-60.
58. Sanders J, Pallotta A, Bauer S, Sekeres J, Davis R, Taege A, et al. Antimicrobial stewardship program to reduce antiretroviral medication errors in hospitalized patients with human immunodeficiency virus infection. Infect Control Hosp Epidemiol. 2014;35:272-7.
59. Liedtke MD, Tomlin CR, Skrepnek GH, Farmer KC, Johnson PN, Rathbun RC, et al. HIV pharmacist's impact on inpatient antiretroviral errors. HIV Med. 2016;17:717-23.
60. Chiampas TD, Kim H, Badowski M. Evaluation of the occurrence and type of antiretroviral and opportunistic infection medication errors within the inpatient setting. Pharm Pract (Granada). 2015;13:512.
61. Seden K, Bradley M, Miller AR, Beadsworth MB, Khoo SH. The clinical utility of HIV outpatient pharmacist prescreening to reduce medication error and assess adherence. Int J STD AIDS. 2013;24:237-41.
62. Tung EL, Thomas A, Eichner A, Shalit P. Implementation of a community pharmacy-based pre-exposure prophylaxis service: a novel model for pre-exposure prophylaxis care. Sex Health. 2018;15:556-61.
63. Dombrowski JC, Golden MR, Barbee LA, Khosropour CM. Patient disengagement from an HIV preexposure prophylaxis program in a sexually transmitted disease clinic. Sex Transm Dis. 2018;45:e62-4.
64. Hojilla JC, Vlahov D, Crouch PC, Dawson-Rose C, Freeborn K, Carrico A, et al. HIV pre-exposure prophylaxis (PrEP) uptake and retention among men who have sex with men in a community-based sexual health clinic. AIDS Behav. 2018;22:1096-9.
65. Weidle PJ, Lecher S, Botts LW, Jones L, Spach DH, Alvarez J, et al. HIV testing in community pharmacies and retail clinics: a model to expand access to screening for HIV infection. J Am Pharm Assoc (2003). 2014; 54:486-92.
66. Darin KM, Klepser ME, Klepser DE, Klepser SA, Reeves A, Young M, et al. Pharmacist-provided rapid HIV testing in two community pharmacies. J Am Pharm Assoc (2003). 2015;55:81-8.

67. Sherman EM, Elrod S, Allen D, Eckardt P. Pharmacist testers in multidisciplinary health care team expand HIV point-of-care testing program. J Pharm Pract. 2014;27:578-81.
68. Amesty S, Crawford ND, Nandi V, Perez-Figueroa R, Rivera A, Sutton M, et al. Evaluation of pharmacy-based HIV testing in a high-risk new york city community. AIDS Patient Care STDS. 2015;29:437-44.
69. Lecher SL, Shrestha RK, Botts LW, Alvarez J, Moore JH Jr., Thomas V, et al. Cost analysis of a novel HIV testing strategy in community pharmacies and retail clinics. J Am Pharm Assoc (2003). 2015;55:488-92.
70. Collins B, Bronson H, Elamin F, Yerkes L, Martin E. The "No wrong door" approach to HIV testing: results from a statewide retail pharmacy-based HIV testing program in virginia, 2014-2016. Public Health Rep. 2018;133:34S-42.
71. Soriano V, Romero JD. Rebound in sexually transmitted infections following the success of antiretrovirals for HIV/AIDS. AIDS Rev. 2018;20:187-204.
72. Raper JL, Willig JH, Lin HY, Allison JJ, Broner MB, Mugavero MJ, et al. Uncompensated medical provider costs associated with prior authorization for prescription medications in an HIV clinic. Clin Infect Dis. 2010;51:718-24.