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Review Paper

Prescription drug diversion among people living with HIV: a systematic scoping review

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ABSTRACT

Objectives: Globally, people living with HIV (PLWH) are at greater risk for various infections and chronic pain, therefore, vulnerable to prescription drug diversion which might negatively impact HIV care. The study purpose is to gather evidence on prescription drug diversion among PLWH.

Study design: This is a systematic scoping review.

Methods: Arksey and O'Malley's framework and recommendation by Levac et al. were used to guide this study. Literature was searched in PubMed, Google Scholar, EBSCOhost (Academic Search Complete, MEDLINE and Newspaper Source) and Open Access Theses and Dissertations. Studies reporting evidence of prescription drug diversion from January 1996 to July 2017 were included. Thematic content analysis was performed to summarize data on the prevalence.

Results: Twenty-nine studies were eligible for data synthesis. Twenty-six studies were conducted in the United States of America (USA), one study in France and two multi-country studies; one study in Kenya and Uganda and the other study in Botswana, Kenya, Malawi, South Africa; Zimbabwe, India, Thailand, Brazil and the USA. Research evidence shows high prevalence of prescription drug diversion for analgesics and antiretroviral drugs; meanwhile, stimulants and erectile dysfunction drugs were the least diverted drugs among PLWH. There is a research gap in low- to middle-income countries (LMICs) investigating prescription drug diversion among PLWH.

Conclusion: Our findings reveal that diversion of various prescription drug classes among PWLH exists. There is lack of research in LMICs. We recommend research in LMICs where there is high HIV prevalence.

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Introduction

Although human immunodeficiency virus (HIV) infection is currently regarded as a chronic condition, optimum HIV care serves as a critical requirement to achieve viral suppression. Prescription drug diversion might serve as one of the barriers for HIV care and management.[1,2] Prescription drug diversion is an illegal distribution of controlled drugs from a rightful owner to the illegitimate owner.[1,2] This event can occur at any stage such as at the pharmaceutical company, during transportation, in the healthcare provider's office, at the pharmacy, at the patient level and others.[1,2] In addition, other sources have defined drug diversion as the illegal exchange and non-medical use of pharmaceutics.[3] However, the term diversion incorporates numerous events such as recreational, misuse, abuse, illicit, selling, trading, sharing, giving away, stealing, loosing drugs, fraudulent prescriptions and also doctor or pharmacy shopping which will be taken into consideration in this review.[1–3] Globally, about 54 million people confirmed to non-medical use of prescription drugs at least once in their lifetime.[4] Approximately 50% of prescribed drugs to patients are either taken incorrectly or not taken at all.[5] In response to these phenomena, the American Society of Health-System Pharmacist guidelines on preventing diversion of controlled substances are put in place because drug diversion compromises patients' safety, endangers the diverter and also leads to substantial liability risk to the affected organization.[6] In South Africa (SA), a National Drug Master Plan 2013–2017 had been developed and implemented with the aim of addressing drug diversion, misuse and abuse challenges.[7] In addition, there has been a National Drug Policy implemented since 1996.[8,9] However global estimates of the extent of prescription drug diversion among people living with HIV (PLWH) are premature, despite the growing public health problem.

Literature has reported that PLWH often present with chronic illnesses that often require prescription drugs in addition to antiretroviral therapy (ART) to manage opportunistic infections and side-effects.[10,11] One of the common illnesses is chronic pain,[10,11] which affects more than 50% of PLWH.[10] Currently, opioids, the most addictive analgesics, are the most commonly used drug among PLWH.[10] Understanding the extent of prescription medication diversion forms the principal step in addressing this problem among PLWH, therefore assisting clinicians/physicians to balance the need to treat legitimate symptoms with the risks for diversion and also evidence to inform practice, policymaking and research. The primary aim of this review is to gather evidence on prescription drug diversion among PLWH.

Methods

Study design

The review protocol was registered in PROSPERO with registration number: CRD42017074076 and is available online.[12]

A systematic scoping review of both published and unpublished literature was chosen as the best method to gather and map existing literature reporting evidence of prescription drug diversion among PLWH. This review was guided by Arksey and O'Malley,[13] a six-stage scoping review framework. The framework comprised of the following sections: (i) identifying the research question, (ii) identifying relevant studies, (iii) study selection, (iv) charting the data, (v) collating, summarizing and reporting the results and (vi) consultation exercise (not included in this study).[13] This review also included quality assessment stage recommended by Levac et. al.[14] To address the review question, the population, intervention, comparison, outcome framework was used for determining the eligibility of the studies (Table 1). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were adhered to when presenting this review.

Search strategy

For this review, a systematic literature search was conducted from August to December 2017. Eligible studies were sourced through the following search engines: PubMed, Google Scholar, EBSCOhost (Academic Search Complete, MEDLINE and Newspaper Source) as well as Open Access Theses and Dissertations. The following keywords were used during the search: people living with HIV; prescription; drug; diversion; misuse and abuse. Boolean terms (AND and OR) were used to separate the keywords.

Eligibility criteria

Selection of eligible studies was guided by the eligibility criteria presented below. Studies were regarded as eligible if they met all of the inclusion criteria.

Inclusion criteria

- Studies on prescription drug diversion among PLWH
- Evidence from January 1996 to 31 July 2017

Table 1 – Framework for determining eligibility of the research question.

Population	Intervention	Comparison	Outcomes
People living with HIV	Prescription drug diversion	Not applicable	Prevalence

HIV, human immunodeficiency virus.

- Study design: quantitative, qualitative, mixed methods, randomized controlled trial, cohort study, case–control study and cross-sectional study
- Prescriptions drugs classes: sedatives, analgesics, stimulants, Z-drugs, anaesthetic, antiretroviral drugs and any other prescription drugs

Exclusion criteria

- Evidence of prescription drug diversion among people not living with HIV
- Studies before January 1996 and after July 2017
- Review articles, animal research and test-tube laboratory research. However, the reference list from review articles was hand searched for additional eligible studies
- Drugs such as cocaine, heroin, methamphetamine, cannabis and ecstasy

Selection procedure

Study selection occurred in three stages. First, a single reviewer (B.C.) searched for studies through the selected search engines by using the following keywords (PLWH, prescription, drug, diversion, misuse and abuse) with the use of Boolean terms (AND and OR). The reviewer (B.C.) screened all retrieved titles and decided on their eligibility based on the inclusion and exclusion criteria. Some titles were not excluded at the title screening stage but rather carried to the abstract screening stage if the reviewer was unsure about their eligibility. All selected titles were exported to a clean EndNote library file to be used for the next step. Second, two reviewers (B.C. and Z.S.) worked independently to perform abstract screening of all saved studies in EndNote with the use of a structured Google form based on the inclusion and exclusion criteria. Discrepancies from abstract screening were resolved by discussion until an agreement was reached. Third, two reviewers (B.C. and N.T.) independently screened all remaining studies by full text for eligibility for data extraction. A structured Google form based on the inclusion and exclusion criteria was also used. Discrepancies during the full-text screening stage were resolved by a third reviewer (Z.S.). Kappa statistics calculation was performed to determine the degree of agreement between reviewers at full-text screening by using STATA 13 software.

Quality assessment

The Mixed Methods Appraisal Tool (MMAT) was used to evaluate the methodology of both qualitative and quantitative studies, therefore allowing us to evaluate the overall quality (risk of bias) of all the included records.[15] All included studies were assessed on whether the research question was clear, and the collected data addressed the research question. For qualitative studies, the following were further assessed: whether the sources of data and the process for analyzing qualitative data were relevant to address the research question and how the research findings relate to the context and researcher's influence. For quantitative studies randomized controlled (trials), the following were further assessed: whether there was a clear description of the randomization and allocation concealment, if the complete outcome data was 80% or above and the withdrawal rate was below 20%. For quantitative descriptive studies, the following were also assessed: whether the sampling strategy was relevant to address the research question, whether the sample was representative of the population studied, whether the measures were appropriate and if the response rate was 60% or above. The overall percentage quality score (risk of bias) was calculated for all included records. The scores were presented using descriptors such as poor quality (25%), fair quality (50%), average quality (75%) and good quality (100%). Two reviewers (B.C. and Z.S.) independently performed each quality assessment. Differences in ratings were resolved through discussion until consensus was reached.

Data extraction

One reviewer (B.C.) extracted the following fields to create Table 2 which presents characteristics to the selected studies: author and year, aim of the study, country and geographic setting, data collection year, study design, sample size of females, sample size of males and number of PLWH, average age or age range and prevalence results.

Collating and summarizing the findings

Thematic content analysis was conducted using themes. In this review, thematic analysis was conducted to report the prevalence of prescription drug diversion among PLWH.

Results

Screening results

The review screening results are presented on Fig. 1 and explained in detail in this section. Records search resulted in a total of 825 potentially eligible studies (723 records obtained from PubMed, Google Scholar and EBSCO Host databases; 11 additional records identified through review articles and 91 records obtained from Open Access Theses and Dissertation). After removal of 320 duplicates, 505 records remained and forwarded to abstract screening. Two reviewers (B.C. and Z.S.) screened 505 abstracts with guidance from the eligibility criteria, and 448 records were excluded because they did not meet the eligibility criteria. Therefore, the remaining 57 records were regarded as eligible for full-text screening. Furthermore, two reviewers (B.C. and N.T.) performed full-text screening with guidance from the eligibility criteria; 31 records were excluded, and 25 records were deemed eligible and included for data extraction and analysis.

Degree of agreement was calculated after full-text screening. There was 66.67% agreement versus 49.89% expected by chance which constitutes moderate agreement (Kappa statistic = 0.34, P-value<0.05). McNemar's Chi-squared statistic suggests that there is not a statistically significant difference in the proportions of yes/no answers by the reviewer with P-value >0.05. A hand search through all

Table 2 – Characteristics of the included studies.

Author and year	Aim of the study	Country, location	Data collection year	Study design	No. of females	No. of males	No. of PLWH or %	Age/yrs	Prevalence results
Tsao et al. (2007)[47]	To test the predictive and concurrent associations among pain, aberrant use of prescription analgesics, the use of these medications specifically for pain and history of problem drug use.	United States of America Metropolitan areas and clusters of rural counties	January 1996 to January 1998	Prospective, longitudinal study	Not stated	Majority of participants were male (77%)	100%	18 yrs and older	**At time 1**: aberrant opiate use was reported by 9% among participants with no drug problem history and 23% among participants with drug problem history. **At time 2:** aberrant opiate use was reported by 9% among participants with no drug problem history and 18% amaong participants with drug problem history. **At time 3:** aberrant opiate use was reported by 3% among participants with no drug problem history and 7% among participants with drug problem history.
Vlahov et al. (2007)[48]	To identify the frequency and correlates of 'street methadone' use among a population of injection drug users (IDUs) recruited and followed semiannually in Baltimore, Maryland	United States of America Baltimore, Maryland	February 1988 to June 2004	Prospective, longitudinal study	N = 114	N = 210	N = 108	N = 493, aged 18 yrs and older N = 169, aged less than 40 yrs N = 165, aged 40–59 yrs N = 3, aged 60 yrs and older	N = 493 reported use of street methadone (4.0/100 person-year; 95% confidence interval (CI) = 3.6, 4.2). Of those on HAART), N = 17 used street methadone; of these, N = 9 had withdrawal, and all nine were using heroin.
Kelly et al. (2010)[73]	To examine the prevalence of lifetime and recent non-medical Rx drug use in an urban community-based sample of MSM. To examine the differences in the prevalence of recent non-medical Rx drug use between different groups of MSM—groups based on age, HIV status, sexual identity and race/ethnicity. To examine the associations between various factors and lifetime non-medical Rx drug use as well as recent non-medical Rx drug use.	United States of America Four large GLB community events in New York City	2006 to 2007	Cross-sectional study	N/A	N/A	11.7%	Average age 34.60 yrs	49.2% used a prescription drug recreationally during their lifetimes. 33.6% used a prescription drug recreationally within the past three months. 16.3% recently used prescription drugs. Commonly used drugs: • Sleep aids (16.3%) • Erectile dysfunction medications (15.2%) • Pain killers (11.5%) • Sedatives (8.3%) • Stimulants (4.7%)

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Table 2 – (*continued*)

Author and year	Aim of the study	Country, location	Data collection year	Study design	No. of females	No. of males	No. of PLWH or %	Age/yrs	Prevalence results
Mansergh et al. (2010)[49]	To examine recent use and sharing of ART medications for the purposes of PrEP and PEP among high-risk substance-using MSM.	United States of America Chicago, Los Angeles, New York City and San Francisco	2006 to 2008	Prospective, longitudinal study	N/A	N/A	N = 557 55%	22%, aged 18–29 yrs 35%, aged 30–39 yrs 43%, aged 40 yrs and older	PrEP (was used by 2% (9 of 454) of HIV-negative participants in the past 6 months. 2.5% (17 of 557) of HIV-positive participants gave their sex partners PrEP to use. 4% (24 of 557) of HIV-positive participants gave their HIV-negative sex partners 4% (18 of 454) PEP to use.
Tsao et al. (2010)[27]	To examine sex differences in the experience of pain and the misuse of prescription analgesics in a nationally representative sample of HIV + persons using a prospective, longitudinal design.	United States of America Nationally representative probability sample	Time 1: January 1996 to April 1997 Time 2: December 1996 to July 1997 Time 3: August 1997 to January 1998	Prospective, longitudinal study	N = 664	N = 1603	100%	Females: aged 36.25 yrs Males: aged 39.57 yrs	Compared with men, women reported a significantly higher correlation between pain-specific analgesic use at time 2 and opioid misuse at time 3 (0.15 vs 0.07). Younger men were more likely than younger women to report opioid misuse at time 2 (-0.14 vs-0.02). Women reported more pain at times 1 and 2, whereas the men reported greater opioid misuse at all time periods.
Hansen et al. (2011)[72]	To characterize prevalence and factors associated with aberrant opioid analgesic behaviours in a cohort of HIV-infected individuals who are at high risk for opioid analgesic misuse	United States of America San Francisco	September 2007 to June 2008	Cross-section study	N = 76 (28.1%)	N = 173 (64.1%) Transgender (men to women) N = 21 (7.8%)	N = 270 100%	N = 63, aged 27–44 yrs N = 65 aged 45–48 yrs N = 65, aged 49–53 yrs N = 67, aged 54–82 yrs N = 75, aged 83 yrs and older	73.3% (N = 198) reported a lifetime history of at least one aberrant behaviour. 37.4% (N = 101) reported a history of aberrant behaviour within 90 days. 18.5% (N = 50) reported major aberrant behaviour.
Mansergh et al. (2011)[50]	To report on demographic factors associated with ART use for prophylaxis purposes prior to known efficacy	United States of America Chicago, Los Angeles, New York city and San Francisco	Not mentioned	Prospective, longitudinal study	0	N = 1011 100%	N = 557 55%	22%, aged 18–29 yrs 35%, aged 30–39 yrs 43%, aged 40 yrs and older	HIV-positive men with less education were more likely to report sharing ART with sex partners for the purpose of PrEP (6% vs 1%) and PEP (8% vs 2%) in the past 6 months.

Roux et al. (2011)[51]	To identify the correlates of non-medical use of opioids during opioid maintenance treatment	France The study took place in several settings	6-month intervals	Prospective, longitudinal study	HIV positive, receiving opioid maintenance treatment N = 72 (30.6%) were women	HIV positive, receiving opioid maintenance treatment N = 163 (69.4%) were men	HIV positive, receiving opioid maintenance treatment N = 235 (100%)	HIV positive, receiving opioid maintenance treatment median (IQR) age was 34 [31−37] yrs	Among all treatment visits, non-medical use of opioids was found in 439 (41.6%) visits for N = 196 (83%) of individual patient.
Vijayaraghavan et al. (2011)[74]	To determine the concordance and discordance of primary care providers' (PCPs') judgements about prescription opioid misuse and illicit substance use compared with patients' self-reports	United States of America San Francisco	September 2007 to June 2008	Prospective, longitudinal study	Not clear	Not clear	N = 105 Prescribed an opioid analgesic by PCPs in the past year.	Not clear	N = 21 (20.0%) self-reported getting high, altering the route or selling prescription opioids in the past year. PCPs estimated that half (49.5%) of the patients got high, altered the route or sold opioid analgesics in the past year. The sensitivity of PCPs' opinions of their patients misusing opioid analgesics in the past year was 61.9% (95% CI 38.4%−81.9%), and the specificity was 53.6% (95% CI 42.4% −64.5%). PCPs did not identify 38.1% (8/21) of patients who reported misusing opioid analgesics and misidentified 46.4% (39/84).
Robinson-Papp et al. (2012)[52]	To determine whether the risk factors described among chronic pain patients would also be associated with problematic use in HIV-infected individuals, using both urine toxicology and psychiatric interview to define outcomes. To examine the role of some factors specifically pertinent to HIV namely adherence to antiretrovirals (ARVs), CD4+ count, plasma HIV viral load (VL) and burden of comorbid illnesses	United States of America	Patients were evaluated at three to six month intervals until the time of death	Prospective, longitudinal study	43%	57%	N = 173 (41%)	Average age, 47 yrs	64% of participants had problematic opioid use. Among past substance users, 67% had problematic use. Most common substance of abuse was as follows: • Cocaine (42%), • Cannabis (26%), • Non-prescribed opiates (26%), • Alcohol (11%), • Sedatives (11%). • Stimulants and hallucinogens were used by one patient each.
Fogel et al. (2013)[71]	To describe a post hoc analysis of unreported ARV drug use in the HPTN 052 trial.	Africa (Botswana, Kenya, Malawi, South Africa and Zimbabwe); Asia (India and Thailand) and the Americas (Brazil and United States)	Follow-up visit samples	Randomised control trial	Not mentioned	Not mentioned	N = 209 (11.9%) of the 1763 participants were tested.	Not mentioned	ARV drugs were detected in participants who were not receiving study-administered treatment during follow.

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Table 2 – (*continued*)

Author and year	Aim of the study	Country, location	Data collection year	Study design	No. of females	No. of males	No. of PLWH or %	Age/yrs	Prevalence results
Genberg et al. (2013)[53]	We characterize the prevalence, correlates and reasons for street-obtained buprenorphine use in an ongoing community-based cohort of former or current IDUs in Baltimore, Maryland	United States of America Baltimore, Maryland	June 2008 to October 2008	Prospective, longitudinal study	Not clear	65	N = 602 (analytical sample) 30% HIV positive	Median age 50 yrs (45 –54 yrs)	The prevalence of recent street-obtained buprenorphine use was 9% (n = 53/602). 74% (n = 446) reported having seen buprenorphine (in any form) sold on the street. 23% reported obtaining buprenorphine from the street and 13% from a friend.
Surratt et al. (2013)[54]	To examine factors that affect vulnerability to ARV diversion among highly marginalized HIV-positive individuals.	United States of America South Florida	2010 to 2012	Mixed methods study Data reported for the qualitative study	Not mentioned	59.4%	N = 503 (100%)	Median age 46 yrs	Diverters reported a median of 7 lifetime episodes of ARV diversion
Vijayaraghavan et al. (2013)[55]	To examine rates of and factors associated with opioid analgesic misuse	United States of America San Francisco Community-based field site	Data collection period to mentioned but data were collected quarterly for 2 yrs	Prospective, longitudinal study	Not mentioned	71.9%	N = 296 (100%)	Not mentioned	71.9% reported any misuse. 53.4% reported major misuse.
Jeevanjee et al. (2014)[56]	To examine whether pain, opioid analgesic use and opioid analgesic misuse were associated with self-reported ARV adherence in a cohort of HIV-infected indigent adults.	United States of America Tenderloin Clinical Research Center (TCRC)	September 2007 to June 2008	Prospective, longitudinal study	Not mentioned	N = 189 (73.3%)	N = 258 Pain participants (on ARVs) 100%	Average age, 48 yrs	20.5% reported opioid analgesic misuse in the preceding 90 days.
Kurtz et al. (2014)[57]	To describe the diversion of ARVs among a highly vulnerable sample of HIV-positive substance-using men who have sex with men (MSM)	United States of America South Florida	November 2008 to October 2011	Randomized clinical trial	N/A	100%	42.4%	Average age, 38.9 yrs	27.0% (N = 51) reported having ever sold and/or traded their ARVs. 19.0% reported having sold and/or traded their ARVs in the past year.
Levi-Minzi et al. (2014)[58]	To examine the demographic, mental health, behavioural, contextual and HIV care–related correlates of specific internalized HIV stigma domains among a sample of socioeconomically disadvantaged substance abusing PLWHA. To examine the predisposing factors of HIV-related stigma among a vulnerable, indigent sample of PLWH	United States of America South Florida	2010 to 2012	Mixed methods study	N = 204 (40.6%)	N = 299 (59.4%)	N = 503 (100%)	Mean age 46.07 yrs N = 252 (50.1%), 46 yrs and below N = 251 (49.9%) 47 yrs and older	Nearly 50% of the sample reported recent ARV diversion.
O'Grady et al. (2014)[59]	To examine these factors (diverted medications, diversion motivation and medication recipients) in an exploratory South Florida study	United States of America South Florida	2010 to 2012	Mixed methods study	74 (29.5%)	Not mentioned	N = 503 (100%)	Mean age 45.9 yrs	80% reported recently selling their ARVs to pill brokers (selling an average of seven times).

Vijayaraghavan et al. (2014)[60]	To examine rates of and factors associated with non-medical use of benzodiazepines, muscle relaxants and prescription stimulants.	United States of America San Francisco	September 2007 to June 2008	Prospective, longitudinal study	Not mentioned	71.9%	N = 296 HIV positive	Average age 49.4 yrs	**At the enrolment visit:** 28.7% reported a lifetime history of non-medical use of benzodiazepines. Non-medically used drugs: • 14.9% used muscle relaxants. • 9.5% used stimulants. • 54.4% used prescription opioid analgesic. **Over the study interval:** Misused drug: • 25.3% used benzodiazepines. • 115% used muscle relaxants. • 6.1% used stimulants. **During the study interval**: • 53.4% reported opioid analgesic misuse. **Over the study duration**: N = 30 (41.7%) reported nonmedical use of benzodiazepines. N = 16 (22.2%) reported non-medical use of muscle relaxants. N = 8 (11.1%) reported non-medical use of prescription stimulants.
Aden et al. (2015)[61]	To assess the impact of illicit drug use on health utility among opioid-dependent HIV patients.	United States of America 9 cities (Baltimore, New York City, Chicago, Miami, New Haven, Providence, Portland, San Francisco and Tucson)	2004 to 2009	Prospective, longitudinal study	N = 101 (33%)	N = 206 (67%)	60%	At baseline N = 20 (3%), aged less than 30 yrs N = 49 (16%), aged 30 −39 yrs N = 144 (47), aged 40 −49 yrs N = 104 (34%), aged 50 yrs and older	Patients frequently reported substance use in the past 30 days, including reporting illicit opioid use at 57% of visits.

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Table 2 – (*continued*)

Author and year	Aim of the study	Country, location	Data collection year	Study design	No. of females	No. of males	No. of PLWH or %	Age/yrs	Prevalence results
Newville et al. (2015)[62]	To evaluate self-reported prescription medication misuse in a community sample of HIV-infected patients prescribed ART, based on substance use, psychiatric and quality of life indicators.	United States of America HIV primary care clinic at San Francisco General Hospital Medical Center (SFGH).	March 2012 to May 2012	Cross-sectional design	N = 76 (26%) And N = 19 (6%) transgender.	N = 200 (68%)	N = 295 (100%)	Average age, 47.5 yrs	N = 32 (11%) reported past month misuse of prescription medications. • N = 13 (41%) misused opiates/ analgesics. • N = 12 (38%) misused sedatives, hypnotics, or tranquilizers. • N = 6 misused methadone. • N = 6 (19%) misused barbiturates.
Surratt et al. (2015)[63]	To examine risky social networks and housing instability as key elements of the disordered neighbourhood environment that may mediate individual ARV diversion and adherence behaviours. To test a multiple mediation model to examine the direct and indirect effects of neighbourhood disorder on diversion-related non-adherence to ARVs	United States of America Urban South Florida	2010 to 2012	Mixed method study	Not clear	Not clear	N = 503 (100%)	Average age 46.1 yrs and had been living with HIV for 13.3 yrs on average	29.8% reported non-adherence because of diversion of their ARV medications in the past 90 days.
Surratt et al. (2015)[64]	To examine the prevalence of food and housing insecurity among substance using HIV-positive patients in South Florida and explore the association of food and housing insecurity with psychological distress and poor behavioural coping strategies, including ARV non-adherence and ARV diversion	United States of America South Florida	2010 to 2012	Mixed methods study	Not mentioned	FH insecure N = 129 (59.2%) FH Secure N = 170 (59.6%)	N = 503 (100%)	FH insecure N = 218, average age, 45.8 yrs FH Secure N = 285, average age, 46.3 yrs	Nearly 60% endorsing diversion of their ARV medications in the past three months
Tsuyuki et al. (2015)[65]	To examine ARV illicit market dynamics and describe the health and social risk profiles, as well as the motivations, of those who buy diverted ARVs	United States of America South Florida	November 2009 and July 2011	Mixed methods study	Not mentioned	59%	N = 44 (100%)	Average age, 45.8 yrs old	41% accessed the illicit marketplace for ARVs.
Tsuyuki et al. (2015)[65]	To identify individual-level factors that are associated with ARV diversion and poor adherence in a vulnerable population of people living with HIV	United States of America South Florida	2010 and 2012	Mixed methods study	Not mentioned	62%	N = 503 (100%)	Average age, 46.2 yrs	48% recently diverted their ARVs
Wixson (2015)[67]	To estimate the prevalence of potentially problematic benzodiazepine use in a commercially insured population of HIV-infected adults and determine if HIV infection is associated with an increased risk of potentially problematic benzodiazepine use	United States of America 50 states and the District of Columbia	January 2007 to December 2009	Prospective, longitudinal study	Not mentioned	N = 2886 (84%)	N = 3447 (0.41%)	Average age, 44.1 yrs	At least one indicator of potentially problematic benzodiazepine use was found in 45% of HIV-infected patients and 31% of uninfected patients. Long-term continuous use exceeding 120 days duration was observed in 28% of HIV-infected patients compared with 16% of uninfected patients.

Turner et al. (2016)[68]	To characterize the prevalence of both medical and non-medical prescription drug use among HIV-positive patients attending either an urban, academic medical centre or community-based AIDS service organization.	United States of America Large, urban academic medical centre (hereafter called hospital clinic) Community-based AIDS service organization that provides HIV medical care and support services (hereafter called community clinic).	November 2014 and April 2015 in the hospital clinic. July and August 2015 in the community clinic	Cross-sectional study	N = 24 (9%)	N = 230 (91%)	N = 254 (100%)	N = 10, aged18-24 yrs N = 31, aged 25–29 yrs N = 59, aged 30–39 yrs N = 60, aged 40–49 yrs N = 76, aged 50–59 yrs N = 18, aged 40 yrs and older	At both clinics, 11% reported non-medical use of prescription opioids in the last year. 8% reporting non-medical use of antianxiety medication in the past year in the hospital clinic and 10% reporting non-medical use at the community clinic. 7% of participants reported for non-medical use of prescription sedatives in the past year in the hospital. 12% of participants for non-medical uses of prescription sedatives in the community clinic. 9% use non-medically of erectile dysfunction medications in the past year similar for both clinics. Use of stimulants in the past year was rare and similar in both sites. Use of antipsychotic medications was rarely reported by participants at the hospital clinic but was much more frequent at the community clinic. 27% of participants reported non-medical use in the past year of any prescription drug. 14% of respondents reported non-medical use in the past month of at least one prescription medication.
Shiau et al. (2017)[69]	To investigate the association between legal and illegal drug use and HIV infection in a nationally representative sample of adults in the United States	United States of America National survey	Public use data files (2005–2014)	Cross-sectional study	N = 141	N = 407	N = 548 (0.19%)	N = 126, aged 18–25 yrs N = 84, aged 26–34 yrs N = 241, aged 35–49 yrs N = 97, aged 50 yrs and older	A higher proportion of the HIV-infected group reported ever use of substances including hallucinogens, non-medical psychotherapeutics and any illegal drug use compared with the HIV-uninfected group. • 49.2% ever used hallucinogen • 42.7% ever used inhalant • 47.4%.ever used non-medical psychotherapeutic Ever use of any illegal drug use was 4 times higher in HIV-infected participants compared with HIV-uninfected participants Past year substances use was significantly higher among those with HIV infection than those without HIV infection.

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Table 2 – (continued)

Author and year	Aim of the study	Country, location	Data collection year	Study design	No. of females	No. of males	No. of PLWH or %	Age/yrs	Prevalence results
Thomson et al. (2017)[70]	To assess the extent to which PrEP sharing occurred within a large cohort of HIV-1 serodiscordant couples enrolled in an efficacy trial in Africa.	Kenya and Uganda 9 clinical research sites in Kenya and Uganda	2008–2013	Randomised control trial Phase III, randomized, double-blind, placebo-controlled, 3-arm clinical trial of daily oral PrEP	Not clear	Not clear	Not clear	Not clear	Eight instances of HIV-1–infected partners using study medication (PrEP) was self-reported from 7 couples across 155,875 study visits (8/155,875, <0.01%).

HIV, human immunodeficiency virus; PLWH, people living with HIV; PrEP, preexposure prophylaxis; PEP. postexposure prophylaxis; AIDS, acquired immunodeficiency syndrome; ART, antiretroviral therapy; HAART, highly active antiretroviral therapy; IQR, interquartile range; HPTN, HIV Prevention Trials Network; FH, food and housing.

reference lists of the 25 included studies was conducted, and an additional four records were eligible to be included for data extraction. To conclude, the screening stage resulted into 29 records included for data extraction.

After full-text screening, 32 records[1,16–46] were excluded and deemed unsuitable for answering the research question posed in this study. They were excluded because of the following reasons: (1) records that had PLWH but lacked relevance specifically to prescription drugs diversion to address the review aim (n = 29);[1,16–36,38–40,42–44,46] (2) records that were not specific to any prescription drugs (n = 2);[37,41] and (3) records that in their study findings prescription drug diversion was not reported (n = 1).[45]

Characteristics of included studies

The characteristics of the identified studies are presented in Table 2. Twenty-five studies[27,47–70] of the 505 reviewed records were eligible for data extraction because they enabled us to gather evidence on prevalence of prescription drugs among PLWH. Through hand search of the reference lists of the 25 selected studies, an additional four studies[71–74] were also eligible for data extraction. Therefore, in total, 29 studies were included for data extraction.[27,47–74] All included studies were published between the period of January 1996 to July 2017. All studies had PLWH except for one study[74] which interviewed primary care providers' regarding judgements of opioid analgesic misuse in a community-based cohort of HIV-infected people. Of these included studies, 26 studies were conducted in the United States of America (USA),[27,47–50,52–69,74] one study was conducted in France[51] and two other studies were conducted in multicountries; one study in Kenya and Uganda[70] and the other study in Botswana, Kenya, Malawi, South Africa, Zimbabwe, India, Thailand, Brazil and USA.[71]

Study designs of the 29 included studies were as follows: 14 studies were prospective, longitudinal cohort studies;[27,47–51,53,55,56,60,61,67,74] five studies were cross-sectional studies;[62,68,69,72,73] three studies were randomized controlled trial study design;[57,70,71] and seven studies were mixed methods studies[54,58,59,63–66] (see Fig. 2).

Quality of evidence from included studies

From the 29 included studies that went through methodological quality assessment, 11 studies scored the good quality score of 100%,[47,54,58–60,63–67,69] seven studies scored average score of 75%,[48,52,53,61,72–74] ten studies scored a fair score of 50%[27,49–51,55–57,62,68,70] and only one study was scored a poor score of 25%[71] because the methodology regarding the trial was not explained in detail.

Summary of the findings: the prevalence of prescription drug diversion among PLWH

The prevalence of prescription drug diversion was found in 29 studies.[27,47–74] In this study, the prevalence of prescription drug diversion was reported according to the prescription drug type, and Fig. 3 represents the number of studies that reported the prevalence of drug diversion. Here, the summary

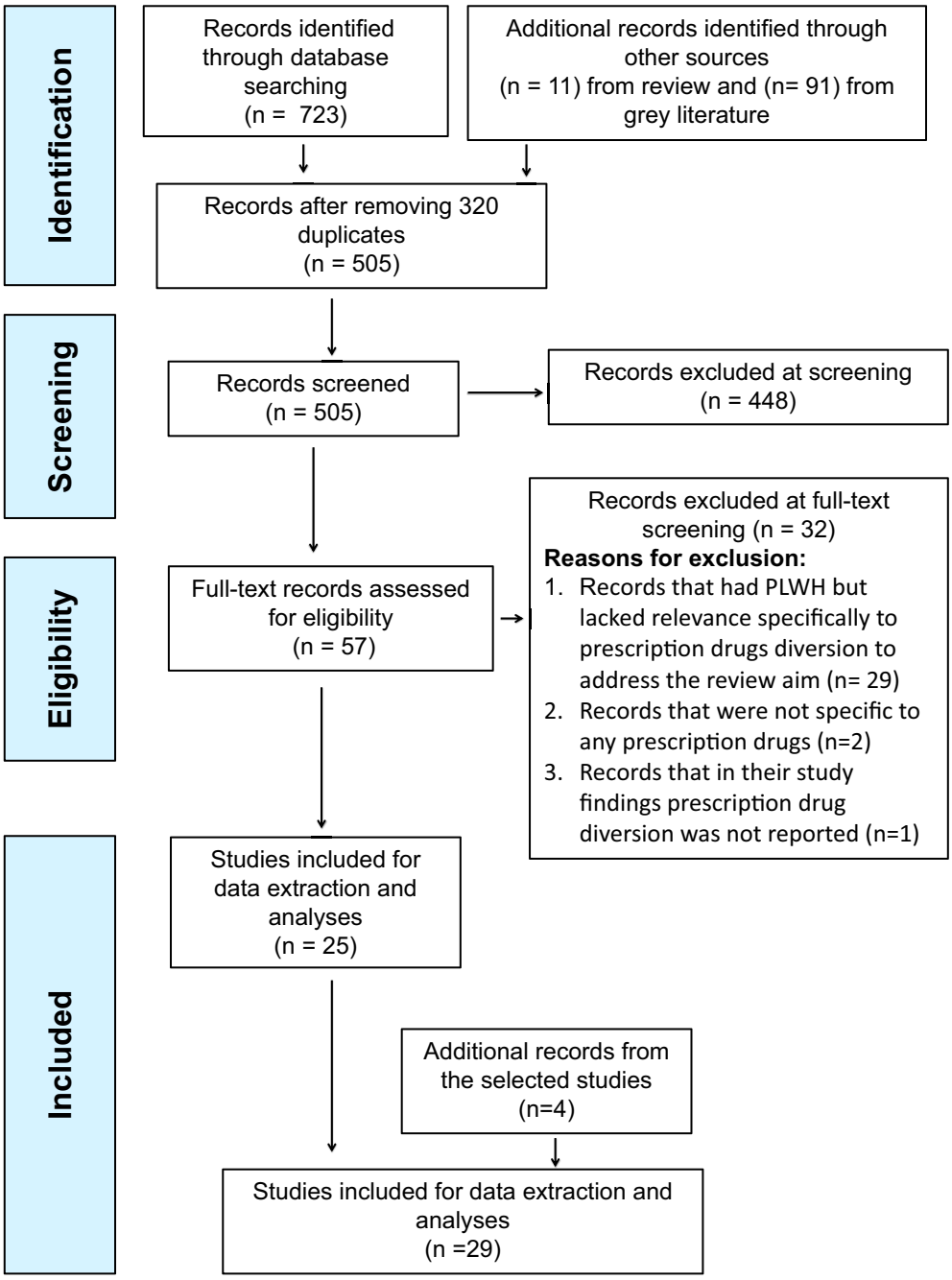

Fig. 1 – Literature search and selection of studies. PLWH, people living with HIV.

of findings were presented under the themes for the prevalence of analgesics drug diversion, ARV drug diversion, psychoactive drug diversion, sedative drug diversion, stimulant drug diversion, erectile dysfunction drug diversion.

Prevalence of analgesic drug diversion

Fourteen studies reported the diversion of analgesics among PLWH from the age of 18 years and older.[27,47,51–53,55,56,60–62,67,68,72,73] The prevalence of aberrant opiate use among PLWH in the USA was reported for time 1 (January 1996 to April 1997), time 2 (December 1996 to July 1997) and time 3 (August 1997 to January 1998).[27,47] The prevalence of aberrant opiate use among PLWH with drug use history versus no drug use history for time 1, time 2 and time 3 was 23%, 43% and 18% versus 9%, 32% and 9%, respectively.[27,47] From the data collected between September 2007 to June 2008, 73.3% PLWH reported at least one aberrant behaviour for opioids; meanwhile, 37.4% reported a history of aberrant behaviour within 90 days.[72] In addition, from the same cohort, 71.9% PLWH reported any

Prospective, longitudinal cohort	14
Mixed methods	7
Cross-sectional	5
Randomized controlled trial	3

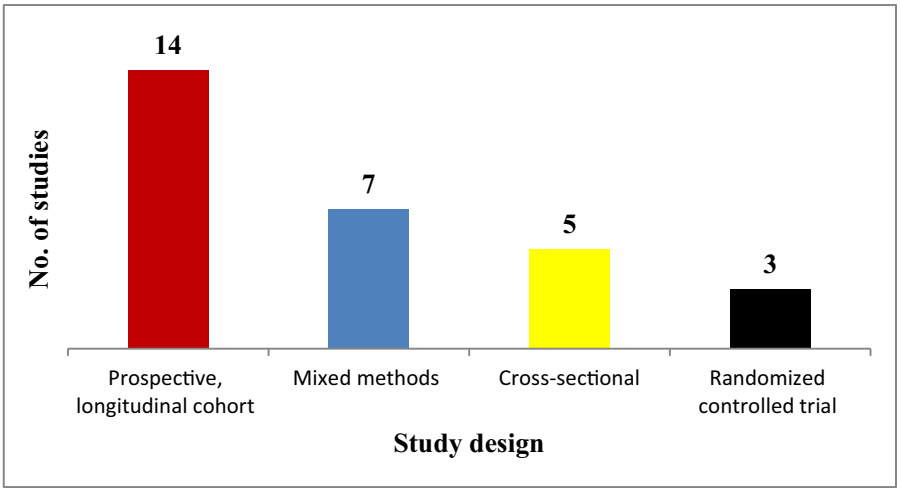

Fig. 2 – Distribution of study designs for the included studies (N = 28).

opioid analgesic misuse. while 53.4% reported major misuse.[55] Furthermore, from the same cohort, 20.5% reported opioid misuse in the past 90 days.[56] Between 1995 and 1996, PLWH in France reported non-medical use of opioids in 41.6% of visits for 196 individual patients.[51] Another observation was that during the study interval, 53.4% reported opioid analgesic misuse nearly of similar rate as lifetime misuse (54.4%).[60]

	Column1
Analgesics	14
ARVs	11
Psychoactive drugs	4
Sedatives	4
Stimulants	2
Erectile dysfunction	2

To resize chart data range, drag lower right corner of range.

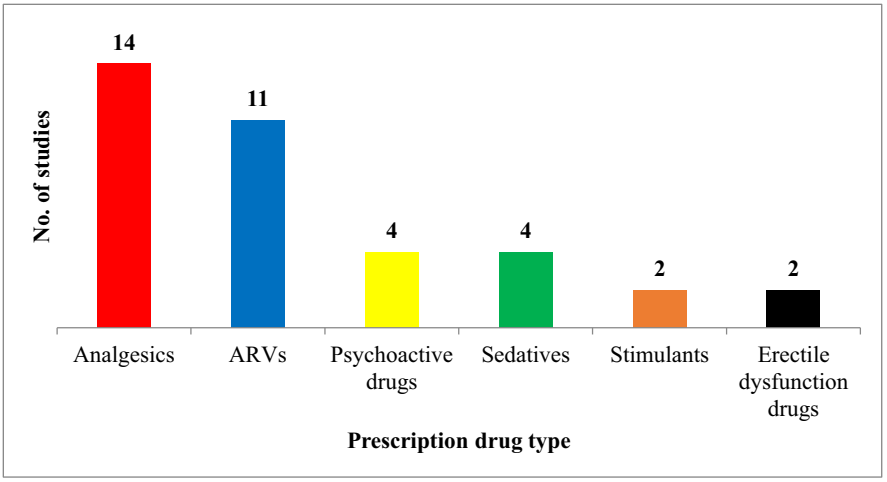

Fig. 3 – The number of studies reporting prevalence according to prescription drug type. ARV, antiretroviral drug.

From nine US cities (Baltimore, New York City, Chicago, Miami, New Haven, Providence, Portland, San Francisco and Tucson) between 2004 and 2009, 57% illicit opioid use was reported.[61] In the data collected from a cohort study established in 1998, 64% reported problematic opioid use.[52] In 2008, recent street-obtained buprenorphine use was reported by nine percent PLWH and 74% reported having seen buprenorphine (in any form) sold on the street, while two percent reported using to get high.[53] Additional from the same cohort, street methadone use was reported by 493 people (16.59%).[48]

Data from January 2007 to December 2009 reported at least one indicator of potentially problematic benzodiazepine use in 45% of HIV-infected patients.[67] Twenty-eight percent had a long-term continuous use of benzodiazepine exceeding 120 days duration compared with 16% of HIV-uninfected patients.[67] During 2006 and 2007, 11% of men who have sex with men (MSM) living with HIV reported non-medical use of pain killers at least once in their lifetime and in the past 90 days and the prevalence was 49.2% and 33.6%, respectively.[73] In addition, 13% of MSM used pain killers recreationally.[73] During March and May 2012, 11% of prescription medications misuse (41% opiates/analgesics) was reported in the past month.[62] The prevalence of using a prescription medication that they were not prescribed to them was reported at 75% among PLWH.[62] During 2014–2015, non-medical use of prescription opioids was reported at 11% for both hospital and community clinic in the past 12 months.[68] Furthermore, non-medical use of any prescription in the last 12 months and past month was 27% and 14%, respectively.[68]

Although opioids were the most prevalent drugs diverted since 1995, there is still limited research in LMICs with high HIV prevalence.

Prevalence of ARV drug diversion

Eleven studies reported ARV drug diversion among PLWH aged 18 years and older.[49,50,54,57–59,63–66,70] During 2006–2008, MSM in Chicago, Los Angeles, New York City and San Francisco reported recent use and sharing of ART medications for the purposes of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP).[49] HIV-positive men with less education reported sharing ART (6% for PrEP and 8% for PEP) with their sex partners in the prior 6 months.[50] During a randomized control trial in 2008–2013 conducted in Kenya and Uganda, 7 couples of HIV-1–infected partners across 155,875 study visits reported eight instances where HIV-1–infected partners found using study PrEP medication.[70]

Data drawn from a mixed-methods study among 503 indigent, substance-abusing PLWH in South Florida between 2010 and 2012 mentioned that ARV drug diverters reported a median of seven episodes or ARV drug diversion in their lifetime.[54] Drawing from the same data, about 50% of participants reported recent ARV diversion.[58,66] About 79.1% of PLWH were prescribed ARV medication, and from that, 27.0% reported having ever sold and/or traded their ARVs medication and 19.0% had diverted in the past year.[57] Similarly, from the people who were prescribed ARVs, about 29.8% of them reported ART non-adherence because they diverted their ARV medications in the past 90 days.[63] Nearly 60% of participants with food/housing insecurity endorsed diverting their ARV medications in the past 90 days.[64] Some participants (41%) obtained ARVs from illegal marketplace, and some participants (25%) reported misusing prescription medications that they were prescribed.[65] About 37.4% reported a history of aberrant behaviour within 90 days, while others reported buying ARVs from the illicit marketplace at least once in the prior six months, and some participants mentioned having access to illicit ARVs through friends, street acquaintances and pharmacy contacts.[65] Results from similar data reported 80% of participants who recently sold their ARVs to pill brokers, and the study participants sold at about an average of seven times.[59] Participants who reported selling ARVs were 11% (were asked by a stranger), 40% (were asked by an acquaintance), 24% (were asked by friend/family), 20% (heard someone talking about it) and 5% (were asked by someone).[59]

It is evident that ARV diversion exists in the USA and in other countries; however, there is limited research in LMICs with high HIV burden and shortage of ARVs supply.

Prevalence of psychoactive drug diversion

Four studies reported on non-medical use of psychoactive drugs among PLWH aged 18 years and older.[60,68,69,73] Between September 2007 and June 2008, non-medical use of benzodiazepines was reported at 28.7% and 25.3% for lifetime history and over the study interval, respectively.[60] Data obtained from 2005 to 2014 reported 47.4% non-medical use of psychotherapeutics.[69] During 2006 and 2007, 11% of MSM living with HIV reported 28.4% non-medical use of sleep aids in the past 90 days.[73] During 2014–2015, non-medical use of antianxiety medications was reported at 8% and 10% at the hospital and community clinic, respectively, in the past 12 months.[68]

There is lack of research on psychoactive drug diversion in other countries beside USA among PLWH.

Prevalence of sedative drug diversion

Four studies reported on non-medical use of sedatives among PLWH aged 18 years and older.[60,62,68,73] During 2006 and 2007, MSM living with HIV reported 13.2% recreational use of sedatives.[73] Between September 2007 and June 2008, non-medical use of muscle relaxants was reported at 14.9% and 11.5% for lifetime history and over the study interval, respectively.[60] Between March and May 2012, 38% reported misuse of sedatives/hypnotics/tranquilizer and 19% reported barbiturates misuse in the past month.[62] During 2014–2015, non-medical use of prescription sedatives was reported at 7% and 12% at the hospital and community clinic, respectively, in the past 12 months.[68]

There was limited research on diversion of sedatives, even though MSM living with HIV were studied.

Prevalence of stimulant drug diversion

Two studies reported on non-medical use of stimulants among PLWH aged 18 years and older.[60,73] During 2006 and 2007, MSM living with HIV reported 5.8% recreational use of stimulants.[73] Between 2007 and 2008, lifetime history and over the study interval non-medical use of prescription stimulants was reported at 9.5% and 6.1%, respectively.[60]

There is dearth of research among college students who are living with HIV because they are the most vulnerable group to divert stimulants.

Prevalence of erectile dysfunction drug diversion

Two studies reported on non-medical use of erectile dysfunctional drugs.[68,73] During 2006 and 2007, MSM living with HIV reported 25.3% non-medical use of erectile dysfunctional medications in the past 90 days.[73] In 2014–2015, non-medical use of erectile dysfunctional medications was reported at 9% in the past 12 months for the hospital clinic and community clinic.[68]

There is limited research on diversion of erectile dysfunctional drugs among older adults living with HIV.

Discussion

In this study, we reviewed evidence on the prevalence of prescription drug diversion among PLWH and also revealed research gaps to guide future research. Our study findings show that prescription drug diversion existed as early as 1995 among PLWH aged 18 years and older. In this review, the prevalence of diversion for analgesics and ARVs was high, followed by psychoactive drugs, sedatives and erectile dysfunction drugs, and the least diverted drugs were stimulants. The key finding for our review was the lack geographic coverage of data on prescription drug diversion among PLWH. This highlights a need for research in LMICs with high HIV burden. The study findings were of significance and addressing these threats will assist LMICs to achieve Goal 3 of the Sustainable Development Goals that states that "by 2030, end the epidemics of AIDS …" and also "to strengthen the prevention and treatment of substance abuse …".[75]

Our trend of findings were in agreement with literature which reports pain medications as the common non-medically used drugs and stimulants as the least non-medically used drugs among general population.[76–78] Although the trend of misuse is similar between PLWH and the general population, the burden of prescription drug diversion is significantly higher in PLWH. Evidence has shown that PLWH engage in different kinds of diversion such as selling of their own prescription drugs to others,[57,64,66,72,74] exchanging their prescription drugs for sex or illicit drugs,[55,65,74] stealing prescription drugs from pharmacies and healthcare facilities,[74] forging prescriptions,[74] borrowing opioid analgesics from others,[72] sharing of prescription medications,[72,74] consuming street drugs to enhance effects of opioid analgesics[55,72] and some altering the route of administration (snorted, crushed, injected, smoked, licked or dissolved opioids).[72,74] Evidence has shown that the motive for PLWH to engage in drug diversion was mostly due to financial hardships[1,59] and some with the motive of getting high.[72,74]

Despite the development and implementation of regulations, policies and guidelines such as the American Society of Health-System Pharmacist guidelines,[79] the Medicines Control Council[9,80] and the National Drug Policy[9,80] to regulate medicines and diversion literature still document drug diversion. Evidence shows poor implementation of regulations, policies and guidelines related to the distribution of medicines from the supplier to the consumer in the health system as drivers for the continuous drug diversion.[81-87] Urgent interventions are imperative to halt the spread and avoid the consequences related to drug diversion such as addiction and dependency as well as the development of drug-resistant strains for tuberculosis, HIV and some bacterial infections which could be preventable. Case studies, frequent audits and advanced technology are needed to monitor and evaluate the implementation of policies and guidelines related to prescribing and dispensing of controlled medicines. Lack of regulatory policies and strict enforcement of prescribing policies accompanying medicines has also led to easy access of prescription drugs through over the counter in most pharmacies, therefore perpetuating corruption in the health system. Finally, interventions that will bring awareness and improve consumer knowledge and attitude toward medicine use and potential risks are warranted to be a joint intervention between the healthcare providers, the pharmacists and the public.

Implications for practice

It would be wise for the Department of Health to put more effort in ensuring that physicians, healthcare providers and pharmacists comply with the National Drug Policy and reinforce the importance of medication misuse assessment on patients. The following interventions might serve as a way forward to address drug diversion: (1) training is needed among health providers for appropriate implementation of regulations, policies and guidelines regarding good prescribing and dispensing rational; (2) specialized training to assist health providers to screen, identify and monitor vulnerable people and to be able to provide appropriate referrals; (3) integrated surveillance between prescribers and dispensers would be essential to strengthen the health system with closed monitoring to enable prompt response when diversion is suspected; and (4) education campaigns are needed to address and advance consumer knowledge, awareness and attitude toward medication use.

Strengths and limitations

We believe that the scoping review methodology used was comprehensive to perform the extensive search for relevant studies. Additionally, degree of agreement between two reviewers was computed and it was found that there was no significant difference between responses from the two reviewers. MMAT[15] was used to perform quality appraisal for all selected studies to assess biased. Finally, four search engines were used to search for studies. Nevertheless, there were some limitations to our review such as: (1)comparisons across selected studies was not done due to difference in the measures, time period and age (some reported as average, median, different age ranges); (2) it was noticed that some studies reported data from the same primary study and some studies recruited participants from the same cohort. Four studies recruited PLWH into the pain study from the same cohort, Research in Access to Care in the Homeless.[56,60,72,74] Two studies were from the same cohort, The AIDS Link to Intravenous Experiences study.[48,53] Eight studies[54,57–59,63–66] reported data from the same mixed methods primary study (the RISE study). Therefore, this reduces the overall number of unique studies conducted.

Recommendations for future research

The majority of the reviewed studies were conducted in the urban areas of the USA where prescriptions drugs are easily accessible. However, evidence shows that there is high HIV prevalence and barriers to achieving viral suppression result from poor ART adherence. PLWH are vulnerable to prescription drug diversion because they have easy access to a variety of prescription drugs to treat the wide spectrum of HIV-related illnesses and HIV treatment side-effects. Our findings have shown that research is needed in LMICs with high HIV prevalence. We recommend an systematic review as one of the follow-up studies because there are randomized control trials and cross-sectional studies.

Conclusion

Our findings show that diversion of various prescription drug classes among PWLH exists. There is lack of research investigating the prevalence of prescription drug diversion among PLWH in LMICs which are faced with high HIV pandemic. Primary studies investigating prescription drug diversion among PLWH are needed in countries with high HIV burden. Urgent collaborative interventions to halt prescription drug diversion among PLWH are needed.

Author statements

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Competing interests

None declared.

Consent for publication

Not applicable.

Availability of data and materials

All the data analyzed and reported in this paper was from published literature.

Author contributions

B.C. and T.P.M-.T conceptualised and designed the study. B.C. prepared the first manuscript draft which was reviewed by T.P.M-.T several times until ready for submission. Z.S. contributed to abstract screening, contributed in resolving discrepancies at full-text screening and also quality assessment. N.F.T. contributed to full-text screening of the included studies.

REFERENCES

1. Inciardi JA, Surratt HL, Kurtz SP, Cicero TJ. Mechanisms of prescription drug diversion among drug-involved club- and street-based populations. *Pain Med* 2007;**8**:171–83.
2. Inciardi JA, Surratt HL, Kurtz SP, Burke JJ. The diversion of prescription drugs by health care workers in Cincinnati, Ohio. *Subst Use Misuse* 2006;**41**:255–64.
3. Wood D. Drug diversion. *Aust Prescr* 2015;**38**:164–6.
4. National Institute on Drug Abuse (NIDA). *Misuse of prescription drugs*. 2016.
5. Brown MT, Bussell JK. Medication adherence: WHO cares? *Mayo Clin Proc* 2011;**86**:304–14.
6. ASHP Guidelines on preventing diversion of controlled substances [https://doi.org/10.2146/ajhp160919]. (Acces Date: 05 August 2017).
7. Development DoS. *National drug master plan 2013–2017*. Government Printers Pretoria; 2013.
8. McCann TV, Renzaho A, Mugavin J, Lubman DI. Stigma of mental illness and substance misuse in sub-Saharan African migrants: a qualitative study. *Int J Ment Health Nurs* 2018;**27**:956–65.
9. Zuma ND. South Africa's new national drug policy. *J Public Health Policy* 1997;**18**:98–105.
10. Liu B, Liu X, Tang SJ. Interactions of opioids and HIV infection in the pathogenesis of chronic pain. *Front Microbiol* 2016;**7**:103.
11. Parker R, Stein DJ, Jelsma J. Pain in people living with HIV/AIDS: a systematic review. *J Int AIDS Soc* 2014;**17**.
12. http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017074076.
13. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;**8**:19–32.
14. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci* 2010;**5**:69.
15. Pluye P, Robert E, Cargo M, Bartlett G, O'Cathain A, Griffiths F, et al. *Proposal: a mixed methods appraisal tool for systematic mixed studies reviews*. Montréal: McGill University; 2011. p. 1–8.
16. Stein MD, Rich JD, Maksad J, Chen MH, Hu P, Sobota M, et al. Adherence to antiretroviral therapy among HIV-infected methadone patients: effect of ongoing illicit drug use. *Am J Drug Alcohol Abuse* 2000;**26**:195–205.
17. Martini M, Recchia E, Nasta P, Castanotto D, Chiaffarino F, Parazzini F, et al. Illicit drug use: can it predict adherence to antiretroviral therapy? *Eur J Epidemiol* 2004;**19**:585–7.
18. Cunningham CO, Sohler NL, Berg KM, Shapiro S, Heller D. Type of substance use and access to HIV-related health care. *AIDS Patient Care STDS* 2006;**20**:399–407.
19. Peretti-Watel P, Spire B, Lert F, Obadia Y. Drug use patterns and adherence to treatment among HIV-positive patients: evidence from a large sample of French outpatients (ANRS-EN12-VESPA 2003). *Drug Alcohol Depend* 2006;**82**(Suppl 1):S71–9.
20. Hinkin CH, Barclay TR, Castellon SA, Levine AJ, Durvasula RS, Marion SD, et al. Drug use and medication adherence among HIV-1 infected individuals. *AIDS Behav* 2007;**11**:185–94.

21. Raffa JD, Grebely J, Tossonian H, Wong T, Viljoen M, Khara M, et al. The impact of ongoing illicit drug use on methadone adherence in illicit drug users receiving treatment for HIV in a directly observed therapy program. *Drug Alcohol Depend* 2007;**89**:306–9.
22. Korthuis PT, Zephyrin LC, Fleishman JA, Saha S, Josephs JS, McGrath MM, et al. Health-related quality of life in HIV-infected patients: the role of substance use. *AIDS Patient Care STDS* 2008;**22**:859–67.
23. Baum MK, Rafie C, Lai S, Sales S, Page B, Campa A. Crack-cocaine use accelerates HIV disease progression in a cohort of HIV-positive drug users. *J Acquir Immune Defic Syndr* 2009;**50**:93–9.
24. Marquez C, Mitchell SJ, Hare CB, John M, Klausner JD. Methamphetamine use, sexual activity, patient-provider communication, and medication adherence among HIV-infected patients in care, San Francisco 2004-2006. *AIDS Care* 2009;**21**:575–82.
25. Mellins CA, Havens JF, McDonnell C, Lichtenstein C, Uldall K, Chesney M, et al. Adherence to antiretroviral medications and medical care in HIV-infected adults diagnosed with mental and substance abuse disorders. *AIDS Care* 2009;**21**:168–77.
26. Wang YG, Swick TJ, Carter LP, Thorpy MJ, Benowitz NL. Safety overview of postmarketing and clinical experience of sodium oxybate (Xyrem): abuse, misuse, dependence, and diversion. *J Clin Sleep Med* 2009;**5**:365–71.
27. Tsao JC, Stein JA, Dobalian A. Sex differences in pain and misuse of prescription analgesics among persons with HIV. *Pain Med* 2010;**11**:815–24.
28. Brion JM, Rose CD, Nicholas PK, Sloane R, Corless IB, Lindgren TG, et al. Unhealthy substance-use behaviors as symptom-related self-care in persons with HIV/AIDS. *Nurs Health Sci* 2011;**13**:16–26.
29. Sullivan LE, Botsko M, Cunningham CO, O'Connor PG, Hersh D, Mitty J, et al. The impact of cocaine use on outcomes in HIV-infected patients receiving buprenorphine/naloxone. *J Acquir Immune Defic Syndr* 2011;**56**(Suppl 1):S54–61.
30. Korthuis PT, Fiellin DA, McGinnis KA, Skanderson M, Justice AC, Gordon AJ, et al. Unhealthy alcohol and illicit drug use are associated with decreased quality of HIV care. *J Acquir Immune Defic Syndr* 2012;**61**:171–8.
31. Moore DJ, Blackstone K, Woods SP, Ellis RJ, Atkinson JH, Heaton RK, et al. Methamphetamine use and neuropsychiatric factors are associated with antiretroviral non-adherence. *AIDS Care* 2012;**24**:1504–13.
32. Nishijima T, Gatanaga H, Komatsu H, Takano M, Ogane M, Ikeda K, et al. High prevalence of illicit drug use in men who have sex with men with HIV-1 infection in Japan. *PLoS One* 2013;**8**. e81960.
33. Rasbach DA, Desruisseau AJ, Kipp AM, Stinnette S, Kheshti A, Shepherd BE, et al. Active cocaine use is associated with lack of HIV-1 virologic suppression independent of nonadherence to antiretroviral therapy: use of a rapid screening tool during routine clinic visits. *AIDS Care* 2013;**25**:109–17.
34. Duncan A, VanDevanter N, Ahmed R, Burrell-Piggott T, Furr-Holden CD. The role of substance use in adherence to HIV medication and medical appointments. *J Assoc Nurses AIDS Care* 2014;**25**:262–8.
35. Azar P, Wood E, Nguyen P, Luma M, Montaner J, Kerr T, et al. Drug use patterns associated with risk of non-adherence to antiretroviral therapy among HIV-positive illicit drug users in a Canadian setting: a longitudinal analysis. *BMC Infect Dis* 2015;**15**:193.
36. Fleetwood CD. *Barriers to nutrition counseling with a registered dietitian (RD) and its association with dietary intake, nutrition status, disease outcomes and substance abuse in people living with HIV (PLWH)*. 2015.
37. Joseph B, Kerr T, Puskas CM, Montaner J, Wood E, Milloy MJ. Factors linked to transitions in adherence to antiretroviral therapy among HIV-infected illicit drug users in a Canadian setting. *AIDS Care* 2015;**27**:1128–36.
38. Lappalainen L, Nolan S, Dobrer S, Puscas C, Montaner J, Ahamad K, et al. Dose-response relationship between methadone dose and adherence to antiretroviral therapy among HIV-positive people who use illicit opioids. *Addiction (Abingdon, England)* 2015;**110**:1330–9.
39. De Boni RB, Shepherd BE, Grinsztejn B, Cesar C, Cortes C, Padgett D, et al. Substance use and adherence among people living with HIV/AIDS receiving cART in Latin America. *AIDS Behav* 2016;**20**:2692–9.
40. Lake S, Kerr T, Buxton J, Guillemi S, Parashar S, Montaner J, et al. Prescription opioid injection among HIV-positive people who inject drugs in a Canadian setting. *AIDS Behav* 2016;**20**:2941–9.
41. Ompad DC, Giobazolia TT, Barton SC, Halkitis SN, Boone CA, Halkitis PN, et al. Drug use among HIV+ adults aged 50 and older: findings from the GOLD II study. *AIDS Care* 2016;**28**:1373–7.
42. Flores J, Liang Y, Ketchum NS, Turner BJ, Bullock D, Villarreal R, Potter JS, Taylor BS. Prescription Opioid Use is Associated with Virologic Failure in People Living with HIV. *AIDS and Behavior* 2018 Apr 1;**22**(4):1323–8.
43. Garin N, Zurita B, Velasco C, Feliu A, Gutierrez M, Masip M, et al. Prevalence and clinical impact of recreational drug consumption in people living with HIV on treatment: a cross-sectional study. *BMJ Open* 2017;**7**. e014105.
44. Hayashi K, Wakabayashi C, Ikushima Y, Tarui M. High prevalence of quasi-legal psychoactive substance use among male patients in HIV care in Japan: a cross-sectional study. *Subst Abus Treat Prev Policy* 2017;**12**:11.
45. Nolan S, Walley AY, Heeren TC, Patts GJ, Ventura AS, Sullivan MM, et al. HIV-infected individuals who use alcohol and other drugs, and virologic suppression. *AIDS Care* 2017;**29**:1129–36.
46. Noorhasan M, Drozd DR, Grunfeld C, Merrill JO, Burkholder GA, Mugavero MJ, Willig JH, Willig AL, Cropsey KL, Mayer KH, Blashill A. Associations between at-risk alcohol use, substance use, and smoking with lipohypertrophy and lipoatrophy among patients living with HIV. *AIDS Res Hum Retrovir* 2017 Jun 1;**33**(6):534–45.
47. Tsao JCI, Stein JA, Dobalian A. Pain, problem drug use history, and aberrant analgesic use behaviors in persons living with HIV. *Pain* 2007;**133**:128–37.
48. Vlahov D, O'Driscoll P, Mehta SH, Ompad DC, Gern R, Galai N, et al. Risk factors for methadone outside treatment programs: implications for HIV treatment among injection drug users. *Addiction* 2007;**102**:771–7.
49. Mansergh G, Koblin BA, Colfax GN, McKirnan DJ, Flores SA, Hudson SM. Preefficacy use and sharing of antiretroviral medications to prevent sexually-transmitted HIV infection among US men who have sex with men. *J Acquir Immune Defic Syndr* 1999;**55**(2010):e14–6.
50. Mansergh G, Koblin B, Colfax GN, Flores SA, Hudson SM. 'Less education' is associated with use and sharing of antiretroviral medications for prophylaxis of HIV infection by US men who have sex with men. *Sex Transm Infect* 2011;**87**:510.
51. Roux P, Carrieri PM, Cohen J, Ravaux I, Spire B, Gossop M, et al. Non-medical use of opioids among HIV-infected opioid dependent individuals on opioid maintenance treatment: the need for a more comprehensive approach. *Harm Reduct J* 2011;**8**:31.
52. Robinson-Papp J, Elliott K, Simpson DM, Morgello S. Problematic prescription opioid use in an HIV-infected cohort: the importance of universal toxicology testing. *J Acquir Immune Defic Syndr* 2012;**61**:187–93.
53. Genberg BL, Gillespie M, Schuster CR, Johanson CE, Astemborski J, Kirk GD, et al. Prevalence and correlates of

street-obtained buprenorphine use among current and former injectors in Baltimore, Maryland. *Addict Behav* 2013;**38**:2868–73.
54. Surratt HL, Kurtz SP, Cicero TJ, O'Grady C, Levi-Minzi MA. Antiretroviral medication diversion among HIV-positive substance abusers in South Florida. *Am J Public Health* 2013;**103**:1026–8.
55. Vijayaraghavan M, Penko J, Bangsberg DR, Miaskowski C, Kushel MB. Opioid analgesic misuse in a community-based cohort of HIV-infected indigent adults. *JAMA Intern Med* 2013;**173**:235–7.
56. Jeevanjee S, Penko J, Guzman D, Miaskowski C, Bangsberg DR, Kushel MB. Opioid analgesic misuse is associated with incomplete antiretroviral adherence in a cohort of HIV-infected indigent adults in San Francisco. *AIDS Behav* 2014;**18**:1352–8.
57. Kurtz SP, Buttram ME, Surratt HL. Vulnerable infected populations and street markets for ARVs: potential implications for PrEP rollout in the USA. *AIDS Care* 2014;**26**:411–5.
58. Levi-Minzi MA, Surratt HL. HIV stigma among substance abusing people living with HIV/AIDS: implications for HIV treatment. *AIDS Patient Care STDS* 2014;**28**:442–51.
59. O'Grady CL, Kurtz SP, Surratt HL. Antiretroviral medication diversion in South Florida: prescription types and motivations. *Drug Alcohol Depend* 2014;**140**:e164.
60. Vijayaraghavan M, Freitas D, Bangsberg DR, Miaskowski C, Kushel MB. Non-medical use of non-opioid psychotherapeutic medications in a community-based cohort of HIV-infected indigent adults. *Drug Alcohol Depend* 2014;**143**:263–7.
61. Aden B, Dunning A, Nosyk B, Wittenberg E, Bray JW, Schackman BR. Impact of illicit drug use on health-related quality of life in opioid-dependent patients undergoing HIV treatment. *J Acquir Immune Defic Syndr* 2015;**70**:304–10.
62. Newville H, Roley J, Sorensen JL. Prescription medication misuse among HIV-infected individuals taking antiretroviral therapy. *J Subst Abus Treat* 2015;**48**:56–61.
63. Surratt HL, Kurtz SP, Levi-Minzi MA, Chen M. Environmental influences on HIV medication adherence: the role of neighborhood disorder. *Am J Public Health* 2015;**105**:1660–6.
64. Surratt HL, O'Grady CL, Levi-Minzi MA, Kurtz SP. Medication adherence challenges among HIV positive substance abusers: the role of food and housing insecurity. *AIDS Care* 2015;**27**:307–14.
65. Tsuyuki K, Surratt HL. Antiretroviral drug diversion links social vulnerability to poor medication adherence in substance abusing populations. *AIDS Behav* 2015;**19**:869–81.
66. Tsuyuki K, Surratt HL, Levi-Minzi MA, O'Grady CL, Kurtz SP. The demand for antiretroviral drugs in the illicit marketplace: implications for HIV disease management among vulnerable populations. *AIDS Behav* 2015;**19**:857–68.
67. Wixson SE. *Medication misadventures: the case of benzodiazepines*. University of Kentucky; 2015.
68. Turner AN, Maierhofer C, Funderburg NT, Snyder B, Small K, Clark J, et al. High levels of self-reported prescription opioid use by HIV-positive individuals. *AIDS Care* 2016;**28**:1559–65.
69. Shiau S, Arpadi SM, Yin MT, Martins SS. Patterns of drug use and HIV infection among adults in a nationally representative sample. *Addict Behav* 2017;**68**:39–44.
70. Thomson KA, Haberer JE, Marzinke MA, Mujugira A, Hendrix CW, Celum C, et al. Brief report: medication sharing is rare among African HIV-1 serodiscordant couples enrolled in an efficacy trial of oral pre-exposure prophylaxis (PrEP) for HIV-1 prevention. *J Acquir Immune Defic Syndr* 2017;**75**:184–9.
71. Fogel JM, Wang L, Parsons TL, Ou S-S, Piwowar-Manning E, Chen Y, et al. Undisclosed antiretroviral drug use in a multinational clinical trial (HIV Prevention Trials Network 052). *J Infect Dis* 2013;**208**:1624–8.
72. Hansen L, Penko J, Guzman D, Bangsberg DR, Miaskowski C, Kushel MB. Aberrant behaviors with prescription opioids and problem drug use history in a community-based cohort of HIV-infected individuals. *J Pain Symptom Manag* 2011;**42**:893–902.
73. Kelly BC, Parsons JT. Prevalence and predictors of non-medical prescription drug use among men who have sex with men. *Addict Behav* 2010;**35**:312–7.
74. Vijayaraghavan M, Penko J, Guzman D, Miaskowski C, Kushel MB. Primary care providers' judgments of opioid analgesic misuse in a community-based cohort of HIV-infected indigent adults. *J Gen Intern Med* 2011;**26**:412–8.
75. Arnsten JH, Demas PA, Farzadegan H, Grant RW, Gourevitch MN, Chang CJ, et al. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. *Clin Infect Dis* 2001;**33**:1417–23.
76. Ghandour LA, El Sayed DS, Martins SS. Prevalence and patterns of commonly abused psychoactive prescription drugs in a sample of university students from Lebanon: an opportunity for cross-cultural comparisons. *Drug Alcohol Depend* 2012;**121**:110–7.
77. Cassidy TA, Varughese S, Russo L, Budman SH, Eaton TA, Butler SF. Nonmedical use and diversion of ADHD stimulants among US Adults ages 18-49: a national internet survey. *J Atten Disord* 2015;**19**:630–40.
78. Cassidy TA, McNaughton EC, Varughese S, Russo L, Zulueta M, Butler SF. Nonmedical use of prescription ADHD stimulant medications among adults in a substance abuse treatment population: early findings from the NAVIPPRO surveillance system. *J Atten Disord* 2015;**19**:275–83.
79. ASHP Guidelines on preventing diversion of controlled substances [https://doi.org/10.2146/ajhp160919]. 05 August 2017.
80. National drug policy for South Africa [http://apps.who.int/medicinedocs/documents/s17744en/s17744en.pdf]. Accessed 03 August 2017.
81. Dada S, Harker Burnhams N, Van Hout MC, Parry CD. Codeine misuse and dependence in South Africa–learning from substance abuse treatment admissions. *S Afr Med J* 2015;**105**:776–9.
82. Carney T, Wells J, Bergin M, Dada S, Foley M, McGuiness P, et al. A comparative exploration of community pharmacists' views on the nature and management of over-the-counter (OTC) and prescription codeine misuse in three regulatory regimes: Ireland, South Africa and the United Kingdom. *Int J Ment Health Addict* 2016;**14**:351–69.
83. Foley M, Carney T, Rich E, Dada S, Mburu C, Parry C. A study of medical professionals' perspectives on medicines containing codeine in South Africa. *S Afr J Psychiatry* 2018;**24**:1162.
84. Wang XM, Zhou XD, Hesketh T. Massive misuse of antibiotics by university students in China: a cross-sectional survey. *Lancet* 2016;**388**(Suppl 1):S94.
85. Peng D, Wang X, Xu Y, Sun C, Zhou X. Antibiotic misuse among university students in developed and less developed regions of China: a cross-sectional survey. *Glob Health Action* 2018;**11**:1.
86. Van Hout MC, Rich E, Dada S, Bergin M. "Codeine is my helper": misuse of and dependence on codeine-containing medicines in South Africa. *Qual Health Res* 2017;**27**:341–50.
87. Wang X, Peng D, Wang W, Xu Y, Zhou X, Hesketh T. Massive misuse of antibiotics by university students in all regions of China: implications for national policy. *Int J Antimicrob Agents* 2017;**50**:441–6.