Prevalence and reasons of loss to follow-up in HIV clinics: a systematic review of current evidence

SeyedAhmad SeyedAlinaghi¹, Amirali Karimi², Alireza Barzegary³, Zahra Pashaei¹, Ghazal Zargari⁴, Shaghayegh Kianzad⁴, Mehrzad MohsseniPour¹, Pegah Mirzapour¹, Amirata Fakhfouri³, Esmaeil Mehraeen⁵, Omid Dadras⁶

¹Iranian Research Center for HIV/AIDS, Iranian Institute for Reduction of High-Risk Behaviors, Tehran University of Medical Sciences, Tehran, Iran

²School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

³School of Medicine, Islamic Azad University, Tehran, Iran

⁴School of Medicine, Iran University of Medical Sciences, Tehran, Iran

⁵Department of Health Information Technology, Khalkhal University of Medical Sciences, Khalkhal, Iran

⁶School of Public Health, Walailak University, Nakhon Si Thammarat, Thailand

Abstract

Introduction: Loss to follow-up (LTFU) slows the progress in reaching the goals of human immunodeficiency virus (HIV) prevention and treatment. Therefore, it is important to understand the causes behind this phenomena. Herein, we aimed to systematically review the prevalence of LTFU among people living with HIV and the reasons behind this event.

Material and methods: A systematic search was conducted with key words applied in online databases, including PubMed, Web of Science, Scopus, UpToDate, and Science Direct, from January 2015 to March 2021. Most relevant papers were retrieved and screened in two phases against inclusion criteria, based on their title/abstract and their full texts, and eligible records were included in the review.

Results: In this systematic review, 54 studies were included. Unfavorable socio-demographic and supportive status, distance to facility, age, gender, challenges related to antiretroviral therapy initiation and its' side effects, and CD4+ counts were among the most common reasons cited for LTFU in HIV clinics.

Conclusions: LTFU remains a major factor halting the progress in the prevention and treatment of HIV. Great efforts are still needed to address this issue, especially in populations and regions with higher LTFU incidence. Accessibility of receiving care should be increased to encourage patients to continue their treatments. Upcoming follow-up studies are needed to re-evaluate the progress and to report future challenges and limitations.

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Key words: AIDS, follow-up, HIV, HIV clinic, human immunodeficiency virus, loss to follow-up.

Introduction

Human immunodeficiency virus (HIV) is a global health concern, with a total of 32.7 (24.8-42.2) million deaths since

Address for correspondence: Esmaeil Mehraeen, Department of Health Information Technology,

Khalkhal University of Medical Sciences, Khalkhal, Iran, e-mail: es.mehraeen@gmail.com

its' emergence to the end of 2019, with 690,000 of deaths occurring in 2019 [1]. In 2019, an estimated 38.0 (31.6-44.5) million people were living with HIV, while 26 (25.1-26.2) million

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According to the WHO's 2019 estimates, 7.1 million people living with HIV (PLHIV) are not aware of their disease status [1]. Unfortunately, even among the patients who are aware of their clinical status, a high percentage have no or delayed access to treatment [5-7]. WHO proposed the goal of 90-90-90, to ensure 90% of the patients are aware of their disease, 90% among them receive sustained ART, and 90% of these patients achieve undetectable viral suppression [8]. Nevertheless, loss to follow-up (LTFU) is a serious obstacle toward achieving this goal [5, 9-11]. Of the patients attending their first clinical visit in a study, 21.7% did not come back to the clinic, and only 20.4% completed the ideal established care [5]. Several studies also mentioned different rates of LTFU that might be influenced by the difference in LTFU definition and the country of study [5, 9-11]. The impact of regular follow-up is substantial, as even patients returning to care after LTFU might be five times more likely to die from the disease [12]. Patients' LTFU increases morbidity and mortality of PLHIV, and worsens their clinical status [13-23]. Some groups of patients might face lower rates of adequate follow-up. Male gender, younger patients, white race patients (compared to Hispanics), and patients with CD4+ T cells higher than 50 cells/mm³ had lower rates of ideal follow-up visits [5, 9].

Debates still exist surrounding the possible causes of LTFU among PLHIV. Social, psychological, economic, and political deficiencies are some of the proposed causes of LTFU in HIV service providing centers [24-26]. Nevertheless, the need to identify and review these reasons still exists. In this systematic review, we aimed to address the prevalence of LTFU among PLHIV and the reasons behind this adverse event, guiding future policies on preventing LTFU.

Material and methods

Data sources

This study was a systematic review of current evidence conducted in 2021. The authors tried to investigate the prevalence and reasons of loss to follow-up in HIV clinics. Our study was consistent with preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist to ensure the reliability and validity of reported results. We retrieved all the relevant papers and reports published in English from January 2015 to March 2021 through a systematic search, using key words in the online databases of PubMed (Medline), Web of Science, Scopus, UpToDate, and Science Direct. The literature search was done using key words in combination with the following search strategy: "HIV" OR "AIDS" OR "human immunodeficiency virus" [Title/abstract]; "Follow-up" OR "loss to follow-up" OR "reason" OR "HIV clinics" [Title/abstract].

Study selection

Most relevant studies by titles and abstracts were selected by three independent investigators. Full texts were reviewed for eligibility criteria. Exclusion criteria were as follows: review articles, reports, editorial, commentaries, opinions, or any studies with no original data; ongoing projects; duplicated results in databases; no access to full-text document.

Data extraction

Data extraction forms were used, including information on the authors, year of publication, country, study population, age, gender, and reasons for LTFU. These information were extracted by two independent investigators, and the collected data were utilized to construct the results section.

Results

The search included 964 potentially relevant studies. After removing duplicates, 688 articles remained. Titles and abstracts were assessed by three reviewers who eliminated 397 articles. Then, 291 articles entered full text screening process, and full texts of these studies were read. Finally, 237 articles that did not meet inclusion criteria were removed, and 54 were retained (Figure 1).

The included studies were conducted in 20 countries. Six studies were from Kenya [27-32], six studies from South Africa [33-38], five studies each from the USA [39-43] and Ethiopia [44-48], four studies each from Nigeria [24, 49-51] and India [52-55], three each from China [56-58], Malawi [59-61], and Uganda [62-64], two each from Tanzania [65, 66], Mozambique [67, 68], and Brazil [69, 70], and one study each from the Netherlands [71], United Kingdom [72], Myanmar [73], sub-Saharan Africa [74], West Africa [75], Congo [76], Mali [77], Australia [78], and Cameroon [79]. All studies' quality were evaluated as good or fair [80]. Most of the studies assessed LTFU in adults (n = 17), fourteen in PLHIV, nine studies in children, four studies in adolescents (range, 10-24 years old), three studies in infants, two studies in each groups of women, men who have sex with men (MSM), and mother-infant pair, and one study in sex workers (Table 1).

Socio-demographic and supportive status, distance to facility, age, CD4+ counts, ART, and gender were some of the reasons discussed in the included records. Lack of support, inadequate supervision, poverty, and poor attitude toward ART benefits were the most common reasons for LTFU. According to the studies, age was also an important factor, as adolescents had higher levels of LTFU than other age groups. In all analyzes, older adolescents were at particular risk. Gender was also examined, and men were the most at risk group for mortality and LTFU, as in eight studies, being male were considered a related factor to LTFU [30, 32, 35, 38, 41, 66, 68, 74]. On the other hand, one study reported that being female was the associated factor [71].



Figure 1. PRISMA flow diagram of the selection process

Discussion

One of the biggest problems for PLHIV is that they do not properly follow the treatment guidelines and taking action to prevent the progress of the disease. In this review article, we surveyed different studies to find the most important reasons associated with LTFU. HIV/AIDS is a chronic disease that needs long-term treatment to control the disease and reduce viral load; thus, patients experience a better quality of life, and transmission of the disease to others would be limited. The Joint United Nations Programme on HIV/AIDS (UNAIDS) follow a strategy called '90-90-90', and the treatment target is that by 2020, 90% of all PLHIV know their HIV status, 90% of patients have access to antiretroviral therapy (ART), and 90% of patients receiving ART have an undetectable viral load [81]. However, currently, only 81% know about their HIV status, 2 out of 3 people are on ART, and only 59% of PLHIV receiving ART are virally suppressed. Different studies showed a significant number of patients that do not continue their treatment. LTFU is a big problem because it has negative effects both on individuals and society. In this review article, several reasons for ART discontinuation were observed in included studies. Socio-demographic and supportive characteristics, distance to facility, age, gender, ART initiation, and CD4+ counts were among the most common reasons.

PLHIV who are receiving ART, showed LTFU rates between 5% to 53% [82]. There are multiple problems including socio-demographic issues. Different studies have reported social and economic issues, such as poverty, lack of social support, and community level stigma as important factors in not receiving proper HIV care [61]. Another important factor is the long distance to a medical facility; one of the major problems for patients living far from medical centers is transportation [24, 60, 77]. In most of the studies reviewed, there was no difference between genders. Although in a few, male gender was mentioned as one of the possible risk factors for discontinuation of treatment, which could be due to delays in testing and lack of social support [35, 68]. In general, there was no significant relationship between a specific age group and LTFU in most of the studies. Although, one study revealed people who were initiating ART at an older age were more likely to discontinue their treatment [34]. Also, according to some studies, adolescents and young adults were at higher risk of LTFU compared to both younger children under 10 and adults older than 45 [83]. In children and adolescents, growth retardation due to ART has been cited as one of the important reasons for discontinuation of treatment [83]. In one study in children under two years of age, the child's nutritional status and side effects of starting treatment, such as diarrhea, were cited as potential reasons for treatment discontinuation [42]. Some other physical factors, including being underweight (BMI \leq 18), have also been mentioned as predisposing factor for LTFU [47, 49, 74].

Pregnant mothers infected with HIV and their infants have been one of the most important at-risk groups studied in many surveys. Many mothers discontinue their treatment during and after pregnancy [67]. However, according to the results, the continuation of ART during pregnancy reduces the risk of infection in exposed infants [33]. Hospitalized exposed infants (HEIs) are usually at risk for LTFU due to lack of appropriate methods to prevent mother-to-child

	Other	Seeking nPEP in HIV treatment services as opposed to VCT	HIV-positive patients to fully benefit from ART, need to know their HIV status, be productively engaged in HIV care, start ART in a timely fashion, and adhere to their ART regimen on a long-term basis	Pregnant women Care associated with lower SES	Easy and unavailable transfer	Younger adolescents and children had similar LTFU rates	Understanding pattems and determinants of both disengagement and re-engagement with care, and the role of migration as important for improving the retention of individuals within HIV care pathway	Same-day ART increased the risk of LTFU, but same-day patients experienced slightly lower mortality
	Gender	I	1	Gender-specific risk factors also compromise program retention	I	Females at higher risk of LTFU compared with males	1	Males at highest risk of mortality and LTFU
	ART	1	Poor attitude toward ART benefits	Among women of child-bearing age, counseling and strategies for sustaining continuity of HIV care during and after pregnancy, and engagement in ART and PMTCT are of particular importance	1	1	1	Same-day ART increased the risk of LTFU
	CD4+ count	I	Test-and-treat ART for HIV- infected people by considering level of CD4+ cells	1	1	1	1	1
	Age	1	1	1	1	Adolescents at higher risk of mortality and LTFU, as compared to children aged 0-9 years	1	1
	Distance to facility	I	1	1	I	I	1	I
	Socio-demographic and supportive characteristics	Increased social vulnerability	1	Lack of social support	No patient-centered system; gaps in therapy	1	Continuity of care to assess the potential impact of public health	Same-day patients may require additional counseling and inter- ventions to improve retention in care
C44.	population	Women	РІНІЛ	ИНИ	PLHIV	Adolescents (age, 10-19 years) and children (age, 0-9 years)	РЦНІХ	РГНІЛ
and had the	of publication	2019, Brazil	2016, China	2015, USA	2016, USA	2019, The Netherlands	2018, UK	2020, USA
Flood and and	(reference)	Grangeiro [69]	Gu [56]	Gwynn [39]	Hickey [40]	Jerene [71]	Jose [72]	Joseph Davey [41]

Table 1. Identified reasons of loss to follow-up in HIV clinics

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Table 1. Cont.

	Other	Maintenance optimization should be a priority in care	Loss to follow-up of caregivers and their HIV-exposed infants had an impact on the elimination of HIV interventions. Caregivers' use traditional medicine that con- tinues to significantly contribute to HIV-exposed infants' loss to follow-up; hence, hampering HIV elimination targets in Kenya	The risk of loss to follow-up in- creases with time, and was higher among patients who started ART within seven days following HIV diagnosis, higher among patients without a telephone set, lower among patients with at least pri- mary education, and lower among patients with BMI ≥ 30	1	1
	Gender	1	1	1	1	1
IS	ART	Longer ART refills or home/ community ART delivery for stable patients living far from the clinic	1	1	Life-long ART provision to HIV- positive pregnant women was shown to reduce exposed infants' LTFU, death, and transmission rate (unfavorable outcomes) in this setting	1
Reaso	CD4+ count	1	1	1	1	1
	Age	1	Hospitalized HIV- exposed infants (HEIs)	Lower among patients aged ≥ 25 years	High proportion of HIV-infected mothers and infants exposed to LTFU	1
	Distance to facility	Patients living away from clinic	1	1	1	1
	Socio-demographic and supportive characteristics	Insufficient social support	Caregivers' intrinsic, inter-personal, community, and health system factors; early HIV testing among mothers, disclosure support, health education, and partner's involvement	1	Inadequate care support for mothers and infants	High-rate of HEIs LTFU was associated with delayed linkage to postnatal care, poor prophylaxis adherence, non-EBF
Study	population	PLHIV	Children	Children	HIV-infected: women with infants, pregnant women, and postpartum women with infants	Infants
Date and place	of publication	2020, Tanzania	2018, Kenya	2020, Uganda	2017, Myanmar	2020, Mozambique
First author	(reference)	Kalinjuma [65]	Kigen [27]	Kiwanuka [62]	Kyaw [73]	Lain [67]

Prevalence and reasons of loss to follow-up in HIV clinics: a systematic review of current evidence

	author erence) ena Zingoni	Date and place of publication 2020, South Africa	Study population PLHIV	Socio-demographic and supportive characteristics Inadequate HIV care and control	Distance to facility	- Age	CD4+ count -	ART ART Lack of ongoing physician training support for the im-	Gender	Other Patient retention in care was a drawback in HIV prevention and control
	1ick [42]	2015, USA	Children	1	1	Age ≤ 2	I	Receiving ART at hospitals	I	Diarrhea at enrolment and poor underlying nutritional status were important predictors for LTFU in HIV-infected children
nick [42] 2015, USA Children – – Age ≤ 2 – Receiving ART at – Diarrhea at enrolment and poor underlying nutritional status were important predictors for LTFU in HIV-infected children	52]	2018, India	PLHIV	Gap between diagnosis and treatment	I	I	I	1	I	1
lick[42] 2015, USA Children - Beceiving ART at - Diarrhea at enrolment and poor	53]	2016, India	PLHIV	1	I	I	I	Lack of cost optimization of ART	I	Lack of optimization of intervention costs were associated with LTFU
ick [42]2015, USAChildren-Age ≤ 2 -Receiving ART at-Diarrhea at enrolment and poor underlying nutritional status were important predictors for LTFU in HIV-infected children52]2018, IndiaPLHVGap betweenDiarrhea at enrolment and poor hospitals52]2018, IndiaPLHVGap between53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]5016, IndiaPLHV </td <td>n [24]</td> <td>2019, Nigeria</td> <td>PLHIV</td> <td>1</td> <td>Difficult access to health care facilities</td> <td>1</td> <td>1</td> <td>1</td> <td>1</td> <td>Lack of support Bad/dangerous/expensive roads, long working hours</td>	n [24]	2019, Nigeria	PLHIV	1	Difficult access to health care facilities	1	1	1	1	Lack of support Bad/dangerous/expensive roads, long working hours
ick [42]2015, USAChildren-Age ≤ 2 -Receiving ART at-Diarrhea at enrolment and poor underlying nutritional status52]2018, IndiaPLHIVGap betweenDiarrhea at enrolment and poor underlying nutritional status52]2018, IndiaPLHIVGap between53]2016, IndiaPLHIVGap between53]2016, IndiaPLHIV53]2016, IndiaPLHIV53]2016, IndiaPLHIV53]2016, IndiaPLHIV53]2016, IndiaPLHIV <t< td=""><td>[49]</td><td>2017, Nigeria</td><td>Adults</td><td>I</td><td>I</td><td>I</td><td>1</td><td>1</td><td>I</td><td>Being underweight, WHO stages III and IV at baseline, and male gender were associated with LTFU</td></t<>	[49]	2017, Nigeria	Adults	I	I	I	1	1	I	Being underweight, WHO stages III and IV at baseline, and male gender were associated with LTFU
ick [42]2015, USAChildren- $ Age \leq 2$ -Receiving ART at-Dimeta at enoment and poor52]2018, IndiaPLHVGap betweenDimetant predictors for were important predictors for52]2018, IndiaPLHVGap between53]2016, IndiaPLHVGap between53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV53]2016, IndiaPLHV <td< td=""><td>13]</td><td>2015, USA</td><td>Adolescents</td><td>I</td><td>I</td><td>I</td><td>I</td><td>No ART prescribed</td><td>I</td><td>Youth were at high-risk of falling out of care</td></td<>	13]	2015, USA	Adolescents	I	I	I	I	No ART prescribed	I	Youth were at high-risk of falling out of care
ick [42] 2015, USA Children - Age ≤ 2 - Receiving AKT at - Interhase at routionment and optionment and optionment and potiation in the status is user important predictors for Underlying nutritional status 52] 2018, India PLHV Gap between - - Neoptials Vere important predictors for Underlying nutritional status 53] 2016, India PLHV Gap between - - - Interventional status 53] 2016, India PLHV Gap between - - - Inderlying nutritional status 53] 2016, India PLHV Gap between -	li [76]	2017, Congo	PLHIV	Living outside of the city, patients who attained secondary or higher education level	I	I	1	1	1	Not sharing their HIV status was associated with LTFU. Individuals with a higher level of education were at greater risk of LTFU
ivit - - Age 5.2 - Receiving AFT at hoot montent and our meritying nutritional status were important predictors for LIFU in HV-infected children 521 2018, India PLHV Gap between - - Nospitals - Individual status were important predictors for LIFU in HV-infected children 521 2018, India PLHV Gap between - - - - - Individual status were important predictors for LIFU in HV-infected children 531 2018, India PLHV Gap between -	[0	2015, Nigeria	PLHIV	Unemployment, poor functional status	I	1	Higher CD4+ counts	1	1	Earlier WHO clinical stage, pregnant women dropped out of treatment at similarly high-rates as non-pregnant women and men
ick [12] 2015, USA Childrea - Age ≤ 2 - Receiving ArT at 0 to thorphy or attronom status version positions or transmiss and the position status version version status versi version status version status versi versi version status versi v	3g [28]	2017, Kenya	Adults	I	I	I	I	I	I	Rates were lowest in Central Africa and highest in East Africa
indefinition indefinion indefinition indefinition <td>a [63]</td> <td>2020, Uganda</td> <td>Infants</td> <td>Distance from home to hospital</td> <td>I</td> <td>I</td> <td>I</td> <td>I</td> <td>I</td> <td>Mother's age was associated with LTFU</td>	a [63]	2020, Uganda	Infants	Distance from home to hospital	I	I	I	I	I	Mother's age was associated with LTFU

Table 1. Cont.

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Table 1. Cont.

	Other	WHO clinical stage IV and patients aged above 45 years had a lower risk of LTFU as compared to those aged 15-28 years	1	Advanced HIV disease, an initial Hb < 12 g/dl, BMI < 18 kg/m² were associated with LTFU	Shorter travel distance was associated with lower LTFU for both transfers and non-transfers	WHO clinical stage IV, no cell phone, malnutrition, unemployment, substance use, sub-optimal adherence were associated with LTFU	More advanced HIV disease, lower BMI were shown as reasons for LTFU	WHO stage 1 or 2, missed clinic visits, mortality may have been an unlikely reason for LTFU	Patients with a higher current CD4+ cell count were less likely to be LTFU	Unaccounted for deaths and rapid progression of HIV among children were associated with LTFU	Patients who were enrolled earlier in the program (2008 and 2009)	WHO stage III/IV, history of regimen substitution, history of TB treatment, children with HIV were associated with LTFU	Substance abuser, jobless, not receiving isoniazid prophylaxis, and underweight were associated with LTFU
	Gender	1	I	Male	1	1	Male	1	I	I	1	1	I
ns	ART	No IPT prophylaxis	I	1	1	Patients who do not take INH prophylaxis	1	1	Year of ART initiation	'Silent' transfers to other ART centers	1	Poor/fair level of ART adherence	Sub-optimal adherence
Reason	CD4+ count	1	1	Initial CD4+ cell count < 100 cells/μl	1	1	Hemoglobin, and CD4+ count at cART initiation	1	Lower current CD4+ cell count	1	I	1	CD4+ count of 201-349 cells/µl
	Age	Age category, 15-28 years	1	Aged > 60 years	I	1	I	Older age at ART initiation	Age at ART initiation: ≤ 30 years	I	I	1	1
	Distance to facility	I	Distance from home to care centers	1	Distance to care	1	I	1	I	I	I	I	I
	Socio-demographic and supportive characteristics	1	I	I	I	1	I	I	I	I	I	1	1
Study	population	Adults	PLHIV	Adults who initiated ART	Adult and pediatric patients	Adults	Adults	Children	Adults	Children	Adults	Children	569 adults
Date and place	of publication	2018, Ethiopia	2019, Mali	2018, sub-Saharan Africa	2017, Malawi	2020, Ethiopia	2015, Mozambique	2018, South Africa	2017, Australia	2017, India	2015, Nigeria	2020, Ethiopia	2019, Ethiopia
First author	(reference)	Assemie [44]	Balde [77]	Bernard [74]	Bilinski [59]	Birhanu [45]	Blevins [68]	Chandiwana [34]	De La Mata [78]	Devi [54]	Eguzo [51]	FisihaKassa [46]	Mekonnen [47]

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First author	Date and place	Study				Keaso	SU		
(reterence)	of publication	population	Socio-demographic and supportive characteristics	Distance to facility	Age	CD4+ count	ART	Gender	Other
Mpinganjira [60]	2020, Malawi	19 mother- infant pairs	Poverty	Long distance to health facilities	I	1	ART side effects, perceived good health after taking ART	1	Adoption of other alternative HIV treatment options, lack of support, community-level stigma were associated with LTFU
Mulongeni [35]	2019, South Africa	6,137 TB/HIV adolescents (10-24 years old)	I	1	Age groups: 20-24 years and 15-19 years	CD4+ count 200- 349, and CD4+ count ≥ 500 cells/µl	I	Male	Re-treatment of TB was associated with LTFU
Nimkar [55]	2018, India	402 adolescents (10-19 years old)	1	1	Age, ≥ 15 years	1	I	1	Factors associated with mortality, WHO stage II and IV, and CD4+ count of 100 cells were associated with LTFU
Ojwang [29]	2016, Kenya	924 adolescents (15-21 years old)	1	1	I	CD4+ cell count ≥ 350 cells/µl	Not being on antiretroviral therapy	1	Those who were pregnant and did not disclose HIV infection status were more likely to become LTFU
Onoya [36]	2017, South Africa	6,306 women	Secondary school, unemployment	1	1	1	Patients who conceived on ART	1	Notably, having received at least 7 months of antenatal ART compared with 3 or less months was associated with a lower risk of becoming LTFU
Opio [64]	2019, Uganda	646 adults	Normal weight	1	I	1	1	1	Receiving HIV care from hospitals, no telephone contact, stigmatization, and long waiting times were the prominent reasons for LTFU
Papavarnavas [37]	2017, South Africa	264 adults	1	I	Age: 0.6 per 10-year increase	1	Time from exposure to receiving PEP of more than 24 hours	1	Healthcare workers category of doctor was associated with LTFU
Saumu [30]	2019, Kenya	261 children	I	1	I	I	Not on ART	Male	Low caregiver level of education was associated with LTFU
Sidze [79]	2015, Cameroon	4,104 infants	In HIV-exposed in- fants, young maternal age, and in HIV-un- exposed infants, low maternal education level and housewife/ unemployed mothers	1	1	1	In HIV-exposed infants, the absence of antiretroviral treatment for prophylaxis	1	In HIV-exposed infants, emergency caesarean section, and in HIV-unexposed infants, young maternal age were predictors of LTFU
Silva [70]	2017, Brazil	1,197 MSM	Monthly income per capita of more than six or less than one Brazi- lian minimum wage	1	Age group: 21-30 years old	1	1	1	Report of bisexual practice, inconsistent use of condoms for receptive anal sex were predictors of becoming LTFU

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Table	

	Other	Low hemoglobin level was significantly associated with LTFU	Severe immunodeficiency and underweight were independent predictors of mortality	FSWs who had a history of more than 3 years' duration of sex work at enrollment, who were older than 25 years of age, and whose HSV-2 status was positive were associated with a lower risk of LTFU	1	Not receiving cotrimoxazole and isoniazid preventive therapy, and ambulatory functional status were associated with LTFU	35-year-olds and females had lower risk of LTFU	1	1	Patients who were LTFU had a higher mean CD4+ count over time than those who were not LTFU anization
	Gender	Male	I	1	1	1	1	1	Male	Male 40 – World Health Org
8	ART	I	1	1	1	Taking AZT-3TC- NVP medication at the start of ART	At ART initiation, poor adherence to clinical appointments	1	1	– Landreiter – – – – – – – – – – – – – – – – – – –
Reason	CD4+ count	Low CD4+ count	1	1	1	1	1	1	1	CD4+ count at baseline < 200 vs. > 350 cells/μl nan immunodeficiency vir
	Age	Younger age	I	1	1	Age group 15-30 years	I	1	Between 20 and 35 years old's	Age (per 5 year increase) to follow-up, HIV – hun
	Distance to facility	I	I	1	1	1	Receiving HIV care in rural facilities	Residence outside the immediate clinic catchment area	I	– – erapy, LTFU – loss
	Socio-demographic and supportive characteristics	Extremes of weight	1	Single/divorced/ widowed, whose census registration was in another city	Official residency in provinces other than Nanjing, lower level of education, small social network size	Daily laborer	1	Disordered alcohol use, tertiary or higher education level	Being single or divorced, BMI of less than 18.5 kg/m ²	Employment status, after TB treatment men, ART – antiretroviral th
Study	population	450 adults	525 children	1,158 female sex worker	410 adults	531 adults	10,812 adults	179 MSM	23,890 adults	642 PLHIV who have sex with
Date and place	of publication	2017, Tanzania	2018, West Africa	2016, China	2015, China	2020, Ethiopia	2018, Malawi	2020, Kenya	2020, Kenya	2016, South Africa ith HIV, MSM – men
First author	(reference)	Siril [66]	Steiniche [75]	Su [57]	Tang [58]	Teshale [48]	Tweya [61]	Wahome [31]	Wekesa [32]	Yende-Zuma [38]

transmission (PMTCT). Adherence to proper postnatal prophylaxis, early diagnostic HIV testing of infants, and proper education and support with mother's partner involvement reduced the risk of mother-to-child transmission [42, 52].

According to the results of the studies, the highest rate of LTFU was in the first 6 months of treatment. This shows the importance of proper education to continue ART treatment [53]. Patients who start ART within seven days after HIV diagnosis were more likely to be at risk for LTFU. In general, same-day patients were at higher risk for LTFU, but the mortality rate was slightly lower in this group [24, 49]. According to the results, the number of baseline CD4+ cells did not play a role in LTFU; however, it seems that higher CD4+ cells during treatment was effective in reducing the risk of LTFU [43, 50, 76]. Some of patients were not responding to ART, they experienced different types of side effects, some of them were getting tired of using life-long drugs, and they started to not taking the drugs anymore [84-89]. One study showed the reason for higher rates of LTFU was that patients can only receive ART in hospitals [90].

Considering that this article was a systematic review, the limitations of the research go back to the limitations of the references, from which the required data was collected. In these studies, the reasons for HIV patients' loss to follow-up have been evaluated. Since most of these factors should be taken from patients' reports, the lack of cooperation of patients in explaining the reasons for termination of treatment has been one of the most important limitations mentioned in these articles [24]. Also, the lack of complete documentation of information about main indicators of patients' health status was one of the most important limitations mentioned in the references [69]. Although, due to the lack of a national follow-up system in many countries, the possibility that patients continued on treatment in another clinic or under other insurance coverage, has been raised. Of course, efforts have been made to follow-up the condition of patients more accurately before confirming the cessation of their treatment by clinic staff [43]. In addition, changes in treatment strategies and guidelines for eligible patients to initiate ART within the time frame of some studies may have distorted the results [60]. Finally, it should be noted that since the data of this study was collected indirectly, errors in sampling and reporting the results of the initial studies may also affected the results used.

Conclusions

LTFU remains a major factor halting the progress of the prevention and treatment of HIV. Several strategies reduced LTFU rates among PLHIV in recent years; however, great efforts are still needed to address this issue, especially in populations and regions with higher LTFU incidences. These measures might also take into account the stage of treatment, as patients in their first six months of receiving ART might have higher rates of LTFU. Accessibility of receiving care should be increased to encourage the patients to continue their treatment. Upcoming follow-up studies are needed to re-evaluate the progress and report future challenges and shortcomings.

Conflict of interest

The authors declare no conflict of interest.

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