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Falls in people living with HIV: a scoping review

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ABSTRACT

Objectives Recent research has indicated seemingly increased propensity for falls and accelerated bone demineralisation in people living with HIV (PLWH). We aim to map out the extent and nature of existing research relating to falls in PLWH and describe the relationship between bone demineralisation and falls in PLWH.

Methods A scoping review was done following Arksey & O'Malley's methodological framework and recommendations from Joanna Briggs Institute. Four databases were searched until October 2019 for peer-reviewed studies available in English reporting on the definition, prevalence, assessment, risk factors and interventions for falls in PLWH as well as information on bone demineralisation linked to falls in PLWH. Narrative reviews were excluded. Two reviewers independently performed the extraction using a predesigned Excel sheet. A descriptive analysis of extracted information was done.

Results Fourteen studies on falls in older PLWH were identified, with all but one study conducted in high-income countries. Prevalence of falls in PLWH ranged from 12% to 41%. Variable assessment tools/tests were used to assess potential risk factors, but it remains to be determined which are more predictive and appropriate for use among PLWH. Considerable agreement existed for risk factors regarding use of medications while evidence regarding functional and cognitive impairments were variable. Few studies compared risk factors for falls in PLWH with those in age-matched and sex-matched seronegative population. There is currently no evidence for interventions to prevent or reduce falls risk in PLWH.

Conclusion More research is needed on falls in younger cohorts of PLWH and in sub-Saharan Africa where HIV is most prevalent and more robust clades exist. More studies need to report on data in seronegative controls to determine risk factors unique to PLWH. More intervention studies targeted at falls prevention and promotion of bone health are required. Quality clinical practice guidelines highlighting validated assessment tools and outcome measures need to be developed.

Strengths and limitations of this study

► The scoping review design enables a comprehensive mapping of the breadth of evidence on falls in people living with HIV.
► The absence of methodological quality appraisal limits the strength of this review to recommend the proposed assessment and intervention strategies.
► Much of the evidence came from prospective cohort studies which are prone to selection bias and bias from lost to follow-up.
► Antecedent-consequent bias occurs in the included cross-sectional studies (level III evidence) making it difficult to determine causal relationships.
► While convenient, limiting our studies to the English language may have resulted in omission of some studies and more likely those in low-income and middle-income country.

INTRODUCTION

Falls are an emerging concern among people living with HIV (PLWH) because of the adverse effects on their health outcomes,[1] and is currently being increasingly investigated. Improved access to combinations of antiretroviral therapy (cART) has increased the number and life expectancy of PLWH and reduced the incidence of human immune deficiency virus (HIV) infections.[2] However, antiretroviral (ARV) drug-associated neurotoxicity remains a challenge even after the advent of cART,[3] and has contributed to other negative side effects such as bone demineralisation, more so in low-income and middle-income countries (LMICs) including sub-Saharan Africa.[4] The seemingly increased propensity for falls and accelerated bone demineralisation in PLWH compounds their risk of fractures,[5] which has been reported to be at least twice that of HIV-seronegative controls in one recent meta-analysis.[6] Mobility may be impacted in the short and longer term at younger-than-expected ages, and ultimately, affect quality of life (QoL).[7] The benefits of life-saving ARV medications may be overshadowed if PLWH suffer from excess morbidity, such as falls, fractures and functional impairments.[5] Rehabilitation specialists have an increasingly notable role to play in the reconceptualisation of HIV care into a rehabilitation framework so that PLWH not only live longer but also have improved QoL.[8]

Several studies have established that PLWH lose bone at an accelerated rate compared with age matched, seronegative controls, often also being diagnosed with low bone mineral density (BMD) at a younger age.[9]

PLWH on ART with low BMD are at threefold higher risk of osteoporosis which translates into clinically relevant risk of low-energy trauma fractures.[10] These fractures can have significant impact on daily function and can lead to increased disability. Reductions in BMD observed in PLWH are related to HIV infection itself, the relative high prevalence of traditional and behavioural risk factors for low BMD; as well as exposure to ART.[11]

Research on falls to date has been most extensive in older adults of the general population, with high-quality data supporting multifactorial risk assessments and screening to identify those at risk of falling. In this population, several fall risk factors or predictors have been identified, including sedative use, cognitive impairment, lower limb disability, balance and gait impairment.[12] Results of a Cochrane review on fall prevention interventions in community-dwelling older adults supported group and home-exercise programmes and home safety interventions in reducing falls,[13] while another review[14] found strong evidence for using standardised tests (five times sit-to-stand (STS) test; gait speed assessment) to predict falls. It has also been recommended that BMD measurements be assessed in fallers as useful indicator of fracture risk.[15]

Falls have not been characterised in PLWH until fairly recently; the first study assessing fall prevalence and risk factors being published in the USA in 2012.[16] To date, published reviews of the scanty literature have been narrative in nature, lacking in methodological rigour and analytical evaluation of the available evidence.[17] Whereas the complex interplay between BMD, HIV-1 and ART have been widely investigated (including scoping and systematic reviews),[10 18] it seems that such data have not been adequately investigated in relation to falls in PLWH. The aim of this scoping review was thus to map the extent and nature of existing peer-reviewed research relating to falls in PLWH; specifically, in terms of describing fall definitions, assessments, epidemiology, risk factors or predictors and prevention interventions. A secondary aim was to describe the relationship between bone demineralisation and falls in PLWH noted in the fall-related articles. It was envisaged that the scoping review would provide insight into the breadth of evidence regarding falls in PLWH and identify areas for further research, in addition to forming the basis for knowledge translation research for rehabilitation specialists to conform to evidence-informed practice in their care of PLWH.

METHODS

A scoping review was conducted according to the methodological framework developed by Arksey and O'Malley.[19] Corresponding guidance developed by Peters *et al* and Joanna Briggs Institute[20] was also considered. An a priori protocol was developed as part of the first author's (MYC) Master's thesis proposal to guide the review (see online supplemental file 1). Reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Review checklist (see online supplemental file 2).[21]

Patient and public involvement

The sixth optional step of the methodological framework for scoping reviews involves consultation with stakeholders.[19] Though not included in this study, PLWH should be consulted when developing clinical practice guidelines. A patient-centred approach is important by considering their concerns and involving them in the decision-making process of their treatment.[1]

Search strategy

A comprehensive search of published research reports was conducted during May to June 2019. Four computerised databases (PubMed, Google Scholar, Scopus and CINAHL [EBSCO]) were accessed. An initial search of PubMed using key terms and medical subject headings (MeSH), followed by analysis of words used in titles and abstracts or index terms that described eligible articles. The search terms used included: "HIV-1", "HIV infection", "accidental falls", "fall risk", "fall assessment" and "fall prevention". Varying combinations of the identified terms were used in searching the remaining databases after refining keywords and/or subject headings specific to each relevant database. Separate search terms for bone demineralisation were not included. Instead, a manual search of reference to bone demineralisation in the identified articles on falls in PLWH was done to fulfil our secondary objective; a narrative review[10] on bone demineralisation in PLWH has been conducted. The full search strategy is included in the online supplemental file 3. Reference lists of key articles identified in the primary search were explored to identify additional relevant evidence that may have been missed during the initial database search (pearling). Key authors were contacted to identify additional sources. The search was rerun in October 2019 to ensure inclusion of recently published papers.

Identifying the research question

The research question was 'What peer-reviewed evidence exists regarding falls in PLWH, particularly fall definitions, assessments, epidemiology, risk factors or predictors and interventions?'

Study selection

All searches were saved into Mendeley and duplicates removed. Two reviewers (MYC and KB) independently assessed the titles and abstracts for eligibility using predetermined criteria. Further review of potentially eligible full texts was done. Any differences in opinion during the selection process were resolved by discussion, or consultation of a third reviewer (QL) if required.

Eligibility criteria
Population

Any articles focusing on PLWH, regardless of ART use were included. Comparative data from seronegative controls were considered. No other limitations based on population characteristics (including age, gender or ethnicity) were applied.

Concept

Any studies containing any information on accidental falls in PLWH as an outcome were included. This included information on definition, prevalence, risk factors or predictors, assessments and interventions. The comprehensive, non-exclusive definition of accidental falls recommended by Hauer et al[22] was used; 'an unexpected event in which the participant comes to rest on the ground, floor or lower level'.[23] Any information about loss of BMD linked to falls in PLWH was extracted from the retrieved articles.

Context

All sources of evidence pertaining to any contextual setting were eligible for inclusion.

Type of evidence sources

Articles were eligible if they were peer-reviewed primary research studies or systematic reviews. Although the scoping review does not include a formal assessment of methodological quality appraisal, we aimed to answer our research question using evidence carried out in a trustworthy and robust manner, which is ensured by the peer-review process. Narrative reviews were excluded due to the repetition of information from the already included studies with limited evidence synthesis. However, the reference lists of the identified narrative reviews were checked to ensure that all eligible studies were accessed. Full texts had to be available in English due to limited resources for translation. No date limits were applied to obtain information from both the pre-cART and post-cART eras.

Data charting

All reviewers discussed the information that was to be extracted from the studies prior to data charting to ensure consistency and clarity. A data extraction sheet was developed in Excel and two randomly selected studies piloted. No modifications were required therefore summaries of data from the remaining included studies were extracted and arranged according to study design by two independent reviewers (MYC and KB). Extracted data included first author, publication year, country, sample demographics, fall definition, fall prevalence, methods of fall risk assessment, risk factors or predictors of falls, interventions and recommendations from the studies. Any information regarding bone demineralisation in relation to falls in PLWH was also extracted. One key author was contacted regarding their analysis of risk factors for falls in one study,[24] in which clarification on use of proportional odds was given. Extracted data were discussed by all reviewers for consistency and consensus.

Quality appraisal

As this was a scoping review in which the aim is to identify gaps in existing evidence, methodological quality was not assessed.

Data analysis

A summary of extracted information was tabulated according to the predetermined categories (fall definition, epidemiology, risk factors, assessment and interventions) and a descriptive analysis was conducted. The findings from the included studies were presented narratively.

RESULTS
Selection of studies

The initial database search yielded 4072 hits. Considering time constraints and that the hits from other databases were low, we followed methodology recommended by Bramer et al[25] and used the first 200 references as sorted in the relevance ranking for Google Scholar. Two articles were retrieved via pearling of reference lists of key articles. After screening 274 records by title and abstract, 32 full-text articles were retrieved; 14 proved eligible for analysis (see PRISMA flow chart in online supplemental file 4).

Study characteristics

The identified studies were published between December 2012 and August 2019 with 11 studies (79%) being published in the last 5 years. Only one study[26] was conducted in an LMIC, while the rest were conducted in high-income countries, mostly from the USA (n=12; 85.7%). Six studies (43%) used longitudinal prospective cohort design,[16 24 27–30] four studies (29%) used cross-sectional design,[26 31–33] one study was a secondary analysis of data from a longitudinal prospective cohort study,[34] one study was a longitudinal retrospective analysis of patient databases,[35] while another used qualitative methods.[1] One systematic review was also included.[36] Four studies (29%)[24 27 30 32] had samples consisting of both PLWH and HIV-seronegative participants (SNP). Six studies (43%)[16 27–29 31 33] had participants who were mostly or only men, ranging from 81% to 100%, while two studies (14%)[30 32] included only women. The age means or medians of the study populations were between 48 and 61 years. The percentage of PLWH who were on ART varied from 61% to 100%. Table 1 summarises study characteristics including recommendations regarding fall-risk assessment and interventions and future research. These are to be considered with caution considering that a formal quality appraisal of included studies was not done. Table 2 further summarises the studies' sample characteristics.

Definition of 'fall'

Despite slight variations in terminology, all fall definitions included components of the falls being 'unintentional/unexpected' and 'coming to a lower level'. The most comprehensive definition of a fall was that used in three studies (21%)[27 30 32]; using descriptions a patient would understand ('slip or trip'), including falls resulting in furniture contact but excluding falls from major medical events (eg, stroke) or overwhelming external hazard (eg,

Table 1 Summary of study characteristics

Study	Country	Study design	Aim	Eligibility criteria	Recommendations from the studies:[a] assessment;[b] intervention;[c] future research
Berner et al 2017[36]	Various	Systematic review	To synthesise the evidence of objective impairments of gait and balance associated with HIV-1 infection, and to emphasise those which could contribute to increased fall risk	Definition, prevalence, risk factors, assessment.	Ascertain 5STS (determined as most valid clinical test to screen for gait deviation impairments in a clinical setting) as predictive of falls in PLWH.[c] Explore knowledge among South African physiotherapists and first contact primary healthcare workers that fall risk may be increased in PLWH.[c]
Erlandson et al 2012[16]	USA	Longitudinal prospective cohort study	To determine incidence of and risk factors for falls in PLWH	Definition, prevalence, risk factors, assessment, intervention.	Falls risk should be routinely assessed as part of care of PLWH.[a] Validate fall prevention interventions that effectively reduce falls in older adults of general population for effectiveness in PLWH.[c]
Erlandson et al 2016[24]	USA	Longitudinal prospective cohort study	To (1) compare fall rates in PLWH or adults at risk for HIV, (2) determine if HIV infection is an independent fall risk, and (3) determine other fall risk factors potentially unique to HIV.	Definition, prevalence, risk factors, assessment, intervention.	During subjective assessments assess for complaints of lightheadedness, dizziness, feeling off-balance.[a] Investigate safety and efficacy of multifactorial fall reduction interventions (used successfully in older adults) in PLWH.[c]
Erlandson et al 2019[27]	USA	Longitudinal prospective cohort study	To identify fall risk factors among men with and without HIV	Definition, prevalence, risk factors, assessment, intervention.	Collecting real-time fall characteristics for example, circumstances, cause and injury can help identify high priority areas for interventions in falls-risk reduction by identifying falls with poor outcomes.[a] Focus on physical activity, ART adherence, and transfer to non-efavirenz ART regimens.[b]
Greene et al 2015[31]	USA	Cross-sectional study	To describe geriatric syndromes in older PLWH aged ≥50 with undetectable VL.	Definition, assessment, prevalence, intervention.	Comorbidities that put one at high risk of falls should be identified and treated.[b]
John et al 2016[33]	USA	Cross-sectional study	To perform geriatric assessments in older PLWH in San Francisco and examine the association with age and the Veterans Ageing Cohort Study (VACS) index scores	Prevalence, assessment, intervention.	Recommended the VACS Index score for assessment of functional impairment in PLWH.[a] Specified peripheral neuropathy as a comorbidity that should be assessed and treated.[b]
Kim et al 2018[34]	USA	Secondary analysis of longitudinal study data	To determine whether polypharmacy is associated with falls and fractures among PLWH and substance dependence or injection drug use	Definition, prevalence, risk factors, assessment, intervention	Prescribers should avoid over prescription of non-ARV medications, especially sedating medications.[b]
Richert et al 2014[29]	France	Longitudinal prospective cohort study	To assess changes in locomotor function in PLWH and to evaluate the determinants of variations in lower limb muscle performance	Prevalence, risk factors, assessment, intervention	Evaluation of efficacy of physical exercise in prevention of falls among PLWH.[c] Investigate the extent to which poor locomotor function contributes to fracture risk in PLWH.[c]

Continued

Table 1 Continued

Study	Country	Study design	Aim	Eligibility criteria	Recommendations from the studies:[a] assessment;[b] intervention;[c] future research
Ruiz et al 2013[35]	USA	Longitudinal retrospective review	To investigate fall incidence and risk factors in PLWH	Definition, incidence, risk factors.	Larger studies are needed to properly characterise falls in PLWH.[c] As PLWH age more, fall risk evaluations may be needed.[b]
Sharma et al 2016[32]	USA	Cross-sectional study	To determine fall frequency and risk factors among middle-aged women with HIV and HIV- controls.	Definition, prevalence, risk factors, assessment, intervention.	Identify modifiable risk factors for falls including CNS-active medications and substance abuse which can be targeted as areas of fall prevention.[b] Longitudinal studies to determine if incidence and consequences for falls will be greater in women living with HIV than seronegative women.[c]
Sharma et al 2018[30]	USA	Longitudinal prospective cohort study	To determine the longitudinal occurrence and risk factors for falls in women with HIV and explore associations with cognition	Definition, prevalence, risk factors, assessment, intervention	Identify underlying mechanism of falls in PLWH in order to identify effective intervention strategies.[c]
Ssonko et al 2018[26]	Uganda	Cross-sectional study	To determine polypharmacy prevalence, associated factors and whether polypharmacy was associated with adverse effects among older PLWH on ART	Risk factors, assessment	Considering the limitations of their study design, the association between polypharmacy and falls in PLWH may need to be explored further.[c]
Tassiopoulos et al 2017[28]	USA	Longitudinal prospective multicohort study	To examine associations between frailty and fall risk among PLWH	Definition, prevalence, risk factors, assessment, intervention	Assessment and careful consideration should be given to PLWH presenting with peripheral neuropathy.[a]
Womack et al 2018[1]	USA	Qualitative study	To understand perceptions of HIV+ individuals who had fallen regarding what caused their falls, prevention strategies that they used, and the impact of falls on their lives	Risk factors, intervention	Develop interventions that are specific to needs and concerns of PLWH; multidisciplinary approach should be considered.[c]

ART, antiretroviral therapy; ARV, antiretroviral; PLWH, people living with HIV; 5STS, 5 times sit-to-stand.

hit by truck or pushed). Four studies (29%)[24 31 34 35] did not excluded falls resulting from acute medical events or external forces in their definition; of these, only one study[34] provided motivation for their inclusion of falls caused by external hazard. In determining whether polypharmacy was associated with falls in PLWH, some medications could increase falls due to both external and non-external causes. Half of the studies[1 27 28 30–32 34] distinguished injurious falls from non-injurious (benign) falls by determining falls that resulted in participants requiring medical attention or resulting in fractures. Six studies (43%)[16 24 27 28 30 32] defined a recurrent faller as having more than one fall in the previous year. Three studies (21%)[1 26 29] did not report on their definition of a fall.

Epidemiology of falls

Ten studies (71%) reported on prevalence of falls in PLWH (table 3). The first prevalence study on falls in PLWH reported that 30% of middle-aged PLWH (45–65

years) sustained at least one fall in the previous year and that 18% sustained two or more falls.[16] Subsequent studies reported frequencies for any fall ranging from 12% to 41%. Only one study[35] reported on the incidence of falls (16×1000 patients/year) that occurred in the previous year from a retrospective review of PLWH's medical records. Four studies reported on recurrent falls ranging from 7% to 25%.[16 24 28 32]

Differences in fall rates between PLWH and the seronegative controls were found to be insignificant in the four studies that included seronegative participants,[24 27 30 32] even after adjusting for covariables including age.

Time period of recall of falls

Eight studies (57%) assessed falls retrospectively using self-reported history of falls within a specified period.[16 24 28 29 31–34 37] Of these, five studies used a recall period comprising the prior 12 months[16 24 29 31 33 34] and three studies used the prior 6 months.[28 30 32] Only one

Table 2 Summary of sample characteristics

Study	Description of sample	PLWH									SNP			
		n	Age (years) Median (IQR)	Male (%)	Female (%)	Time since HIV diagnosis (years) Median (IQR)	On ARV (%)	PLWH with VL <LDL% (plasma HIV-1-RNA)	Current CD4+ count (cells/µL)	Nadir CD4+ count (cells/µL)	n	Age (years) Median (IQR)	Male (%)	Female (%)
Erlandson et al 2012[16]	PLWH aged 45–65 years, receiving ART from academic hospital's infectious diseases clinic.	359	52±0.3*	85	NR	NR	100	95% (<200 c/mL)	594±16*	NR				
Erlandson et al 2016[24]	PLWH and SNP (men and women) from the Hearing and Balance Substudy of MACS and WIHS.	233	49.7 (43;55)	NR	47	NR	69	69% (<200 c/mL)	534†	NR	303	54.9 (48;62)	NR	18
Erlandson et al 2019[27]	PLWH and SNP men aged 50 to 75 years from the Bone Strength Substudy of the MACS.	279	61.1 (55.6;64.2)	100	0	NR	100	91% (<50c/mL)	NR	36% (<200) 73% (>500)	379	62.4 (58.5;66.8)	100	0
Greene et al 2015[31]	PLWH from SCOPE cohort aged ≥50 years, on ART with VL <LDL.	155	57 (54;62)	94	NR	21(16;24)	100	NR	567 (398;752)	174 (51;327)				
John et al 2016[33]	Older PLWH aged ≥50 years at two San Francisco-based HIV clinics.	359	57	85	12.5	NR	100	82% (<40c/mL)	52% (>500)	NR				
Kim et al 2018[34]	PLWH with substance dependence or injection drug use, from Boston ARCH Cohort study.	250	50 (44;56)	62	NR	NR	88	72% (<200 c/mL)	NR	NR				
Richert et al 2014[29]	Adult PLWH from the ANRS CO3 Aquitane Cohort from six public hospitals in south-western France.	178	48 (43;56)	81	NR	12(6;18)	89	84% (<500c/mL)	506 (340;715)	245 (151;371)				
Ruiz et al 2013[35]	Patient records of PLWH from an academic urban HIV clinic with history of fall in prior 12 months.	32	48.19†	25	75	9.38†	NR	31 379 c/mL†	342.2†	NR				
Sharma et al 2016[32]	PLWH and SNP from WIHS with available falls data.	1 412	48†	0	100	NR	87.8	65.4% (<20c/mL)	589 (385;808)	274 (146;462)	650	NR	NR	NR
Sharma et al 2018[30]	PLWH and SNP from WIHS with available falls data and attending semi-annual study visits.	1 816	48.9 (42.8;54.6)	0	100	NR	88.3	63.4% (<20c/mL)	588 (385;781)	280 (161;411)	566	47.1 (39.9;53.8)	NR	NR
Ssonko et al 2018[26]	PLWH aged ≥50 years attending an outpatient HIV/AIDS care centre.	411	NR but aged 50 and over.	41.8	58.2	NR	93	NR	NR	NR				
Tassiopoulos et al 2017[28]	PLWH (men and women) aged ≥40 years from the ACTG.	967	51(46;56)	81.1	18.9	NR	100	NR	NR	NR				

Table 2 Continued

| Study | Description of sample | PLWH | | | | | | | | | | SNP | | | |
		n	Age (years) Median (IQR)	Male (%)	Female (%)	Time since HIV diagnosis (years) Median (IQR)	On ARV (%)	PLWH with VL <LDL% (plasma HIV-1-RNA)	Current CD4+ count (cells/µL)	Nadir CD4+ count (cells/µL)		n	Age (years) Median (IQR)	Male (%)	Female (%)
Womack et al 2018[1]	PLWH (men and women) from an HIV primary care clinic.	21	55±6*	43	57	19 (1,33)	NR	NR	NR	NR					

NB. One study by Berner et al[36] is excluded from this table due to being a systematic review design.

*Mean±SD.

†Mean.

ACTG, AIDS clinical trials group; ANRS, Agence Nationale de Recherches sur le Sida et les Hépatites Virales; ARCH, Alcohol Research Collaboration on HIV/AIDS; ART, antiretroviral therapy; MACS, Multi-center AIDS Cohort Study; NR, not reported; PLWH, people living with HIV; SCOPE, Observational Study of the Consequences of the Protease Inhibitor Era; SNP, seronegative participants; VL<LDL, viral load less than lowest detectable level; WIHS, Women's Interagency HIV Study.

study collected real-time (within 24 hours) fall reports prospectively over a 2-year period.[27]

Assessment of falls and risk factors
Measures for assessing falls and risk factors
Comprehensive medical assessments were done to evaluate specific risk factors for falling as part of a postfall assessment in five studies,[16 24 27 30 32] or as part of an overall geriatric assessment in two studies.[31 33] Falls were also assessed as an outcome in three studies[26 28 34] which sought to determine association between falls and specific risk factors such as frailty and polypharmacy.

All but two studies[35 36] subjectively assessed fall history. Five studies[24 27 28 30 32] used a self-reporting questionnaire. Review of patient databases were also done to verify medications, comorbidities and obtained laboratory data on HIV-specific markers including CD4+ count and viral load. Various standardised assessment tools and objective tests were used across studies to assess falls and related factors during both the subjective and objective assessments (table 4).

Risk factors for falls in PLWH
Five longitudinal studies,[16 24 27 30 35] one cross-sectional study[32] and one qualitative study[1] had the primary objective of determining fall risk factors among PLWH. Seven studies[16 24 27 28 30 32 34] provided ORs regarding the associations between risk factors and falls in PLWH. ORs, for the risk factors that were significantly associated with falls (any fall, single fall and recurrent falls) in PLWH (p≤0.05) were plotted in figure 1 (a meta-analysis could not be done due to the heterogeneity of included studies).[38]

Polypharmacy and medications
Nine studies (64%) reported on polypharmacy as a risk factor for falls in PLWH; six studies (43%)[16 24 30 32 34 35] reported significant associations (figure 1). Additionally, participants in one qualitative study[1] reported use of multiple medications as a cause for their falls. Two studies (14%)[26 27] reported polypharmacy as not significantly associated with falls.

Five studies (36%)[16 27 30 32 34] reported significant associations between different medications and falls (figure 1). Insignificant odds were reported for each additional non-sedating or opioid drugs (OR1.31; 95% CI 0.64 to 2.67).[34] Four studies reported protective odds ratios (PORs) for HAART use[24 27 30 32] especially current protease inhibitor (PI) drug use (POR 0.40; 95% CI 0.2 to 0.81; p=0.011).[24] Longer duration on ART was protective of injurious fall (OR 0.41; 95% CI 0.23 to 0.74; p=0.014) in one study.[27]

Physical function and cognitive impairments
Six studies[16 24 27 28 30 32] proved significant associations between falls and functional and cognitive impairments (figure 1). One study[29] did not provide ORs but reported significant association between any fall and poor STS (p=0.01) and 6 min walk distance (6MWD) tests (p<10⁻²), with the timed-up-and-go test (TUGT) being marginally significant (p=0.05).

Table 3 Summary of fall prevalence reported in included studies

Study	Method of fall history collection	Time frame assessed for falls	PLWH No of participants (n)	Overall fall prevalence (%)	Prevalence for single fall (%)	Prevalence for recurrent falls (%)	SNP No of participants (n)	Overall fall prevalence (%)	Prevalence for single fall (%)	Prevalence for recurrent falls (%)
Berner et al 2017*[36]										
Erlandson et al 2012[16]	Retrospective recall	1 year	359	30	12 (F=14%)	18 (F=26%)				
Erlandson et al 2016[24]	Retrospective recall	1 year	303	24	11	13	233	18	9	9
Erlandson et al 2019[27]	Prospective reporting tool (within 24 hours).	2 years	279	41	21	20	379	39	22	17
Greene et al 2015[31]	Retrospective recall	1 year	155	25.8	NR	NR				
John et al 2016[33]	Retrospective recall	1 year	359	40.7 (50–59 years.=38.5%) (60–80 years.=45.5%)	NR	NR				
Kim et al 2018[34]	Retrospective recall	1 year	250	16 (M=51%)	NR	NR				
Richert et al 2014[29]	Retrospective recall	1 year	178	12	NR	NR				
Ruiz et al 2013†[35]	Retrospective review of patient databases.	1 year	2000							
Sharma et al 2016[32]	Retrospective recall	6 months	1412	18.6	9.2	9.4	650	18.3	8.3	10
Sharma et al 2018[30]	Retrospective recall	6 months	1816	41	15.5	25.4	566	42	18	24
Ssonko et al 2018*[26]	Retrospective recall	12 months	411							
Tassiopoulos et al 2017[28]	Retrospective recall	6 months	967	18	11 (M=80.2%; F=19.8%)	7 (M=72.1%; F=27.9%)				
Womack et al 2019*[1]	Retrospective recall	2 years	21							

Assessment of falls and risk factors.
Measures for assessing falls and risk factors.
*Prevalence not reported.
†Incidence reported.
F, female; M, male; NR, not reported; PLWH, people living with HIV; SNP, seronegative participants.

Table 4 Summary of assessments tests/tools for falls and related factors used in included studies

Key area	Test/tool	Berner et al 2017[36]	Erlandson et al 2012[16]	Erlandson et al 2016[24]	Erlandson et al 2019[27]	Kim et al 2018[34]	Richert et al 2014[29]	Ruiz et al 2013[35]	Sharma et al 2016[32]	Sharma et al 2018[30]	Ssonko et al 2018[26]	Tassiopoulos et al 2017[28]	Womack et al 2019[1]
Subjective assessment													
Subjective history	History of falls*	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓
	Fear of falling								✓				
	Cause of falls			✓	✓								✓
	Resulting injury or fractures		✓	✓	✓	✓			✓	✓		✓	✓
	Review of medications and polypharmacy	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
	Review of chronic diseases and comorbidities	✓	✓		✓	✓†	✓	✓	✓	✓	✓†	✓	✓
	History of alcohol, smoking and illicit substance abuse		✓		✓	✓			✓	✓		✓	
	Subjective cognitive complaints								✓	✓			
	Environmental hazard assessment (assessed subjectively)	Lighting, wet/slippery surface, uneven surface, obstacle, step/curb, pets.				✓								
HIV-specific variables	Duration of infection	✓			✓		✓	✓					✓
	ART use		✓		✓	✓	✓		✓	✓	✓		
Objective assessment													
Vitals	Orthostatic blood pressure				✓	✓			✓	✓			
Sensation	120 Hz tuning fork				✓				✓				
Laboratory testing	Haemoglobin, CD4 T cell count, HIV-1 RNA viral load, cholesterol.	✓	✓		✓	✓		✓	✓	✓			

Continued

Table 4 Continued

Key area	Test/tool	Berner et al 2017[36]	Erlandson et al 2012[16]	Erlandson et al 2016[24]	Erlandson et al 2019[27]	Kim et al 2018[34]	Richert et al 2014[29]	Ruiz et al 2013[35]	Sharma et al 2016[32]	Sharma et al 2018[30]	Ssonko et al 2018[26]	Tassiopoulos et al 2017[28]	Womack et al 2019[1]
Standardised objective tests													
Balance	Berg Balance Scale	✓											
	Tandem stand	✓	✓										
	Single leg stand	✓		✓	✓								
	Forward reach	✓			✓								
	Timed Up and Go Test	✓					✓						
	The Five Times Sit to Stand (5STS)	✓	✓		‡		✓						
	Dynamic posturography	✓											
Gait	4 m walk (fast or preferred)		✓	✓	✓								
	400 m walk		✓										
	Six-minute walk distance		✓				✓						
Standardised Questionnaires/Scores													
Mental health and cognitive capacity	Depression (CES-D)			✓	✓				✓	✓			
	Cognitive impairment										✓§	✓¶	
Physical function	Functional impairment (VACS Index Score)		✓										
	Balance (ABC survey)				✓								
	Physical activity			✓**	✓††								
	Frailty (Fried Frailty Scores)		✓		✓						✓‡‡	✓	
Debilitating Pain	Pain Scale		✓										

Continued

Table 4 Continued

Key area	Test/tool	Berner et al 2017[36]	Erlandson et al 2012[16]	Erlandson et al 2016[24]	Erlandson et al 2019[27]	Kim et al 2018[34]	Richert et al 2014[29]	Ruiz et al 2013[35]	Sharma et al 2016[32]	Sharma et al 2018[30]	Ssonko et al 2018[26]	Tassiopoulos et al 2017[28]	Womack et al 2019[1]

*NB. Two cross-sectional studies by Greene et al, John et al[31 33] measured falls as part of geriatric assessments. Any other risk factors measured were not linked to falls as causality could not be claimed, hence the studies were excluded from this table. Both studies had assessed history of falls through subjective report.

†CCI.

‡Modified 10STS.

§FMMSE.

¶IA5001 Neuroscreen.

**SF survey.

††IPAC.

‡‡Used a 40-item questionnaire.

ABC, Activities-Specific Balance Confidence; CCI, Charlson Comorbidity Index; CES-D, Center for Epidemiological Studies-Depression; FMMSE, Folstein's Mini Mental State Examination; IPAC, International Physical Activity Questionnaire; SF, Short Form; VACS, Veterans Aging Cohort Study.

One study[28] reported insignificant association between single falls and weak grip strength (aOR 1.38; 95% CI 0.82 to 2.34) and gait speed (aOR 0.61; 95% CI 0.36 to 1.01). One study[27] also reported insignificant ORs for poor balance measurements. Although three studies[26 30 32] showed significant association between cognitive impairments and falls in PLWH, one of these studies[30] found that the results were attenuated after adjusting for comorbid illness. Another study[28] reported neurocognitive impairments in 29.4% of recurrent fallers vs 14.1% of non-fallers.

Comorbidities and chronic diseases

All but two[29 36] of the identified studies assessed comorbidities and chronic diseases in their participants. Two studies[16 35] reported significant association between falls and multimorbidity.

Four studies[16 27 30 32] found significant association between falls and specified chronic diseases; neuropathy being cited in all four studies. Another study[28] identified peripheral neuropathy as a potential confounder for the association between falls and frailty in PLWH. In one qualitative study,[1] PLWH reported peripheral neuropathy in addition to opportunistic infections, spinal stenosis, arthritis, stroke, hepatic encephalopathy as being causes of their falls. Only one study[24] failed to find an association between peripheral neuropathy and falls and attributed it to their relatively younger cohort being potentially better able to compensate for neuropathies or possibly less sensitive tests being used to determine peripheral neuropathy. In three studies each, diabetes[16 30 32] and depressive symptoms[27 30 32] were also frequently cited as risk factors for falls in PLWH.

Behavioural factors

Six studies[1 16 24 27 30 32] assessed behavioural risk factors for falls in PLWH; four studies reported significant odds ratios (figure 1). In one qualitative study[1] participants reported substance abuse as a cause of their falls. One study[27] reported protective odds for greater physical activity and falls with fractures (OR 0.23; 95% CI 0.08 to 0.72; p=0.011).

Demographic factors

Significant ORs were reported for older age[30 32] (aOR 1.29; 95% CI 1.11 to 1.49),[30] (aOR 2.00; 95% CI 1.11 to 3.59 age ≥60 vs.<39),[32] white race (OR 1.39; 95% CI 1.08 to 1.78; p=0.011)[30] and being female (OR 2.5; 95 CI 1.3 to 4.8).[16] However two studies[16 24] found that age was not a significant predictor of falls (OR 1.0; 95 CI 0.96 to 1.1; p≥0.30),[16] (OR 1.32; 95 CI 0.9 to 1.92; p=0.14).[24]

HIV-related variables

Ten out of the 14 included studies (71%) assessed viral load in their participants; one study reported on persons with higher HIV-1 RNA viral loads having greater fall frequencies.[24] Four studies[16 30 32 35] found no association between current or nadir CD4+ cell count and falls.
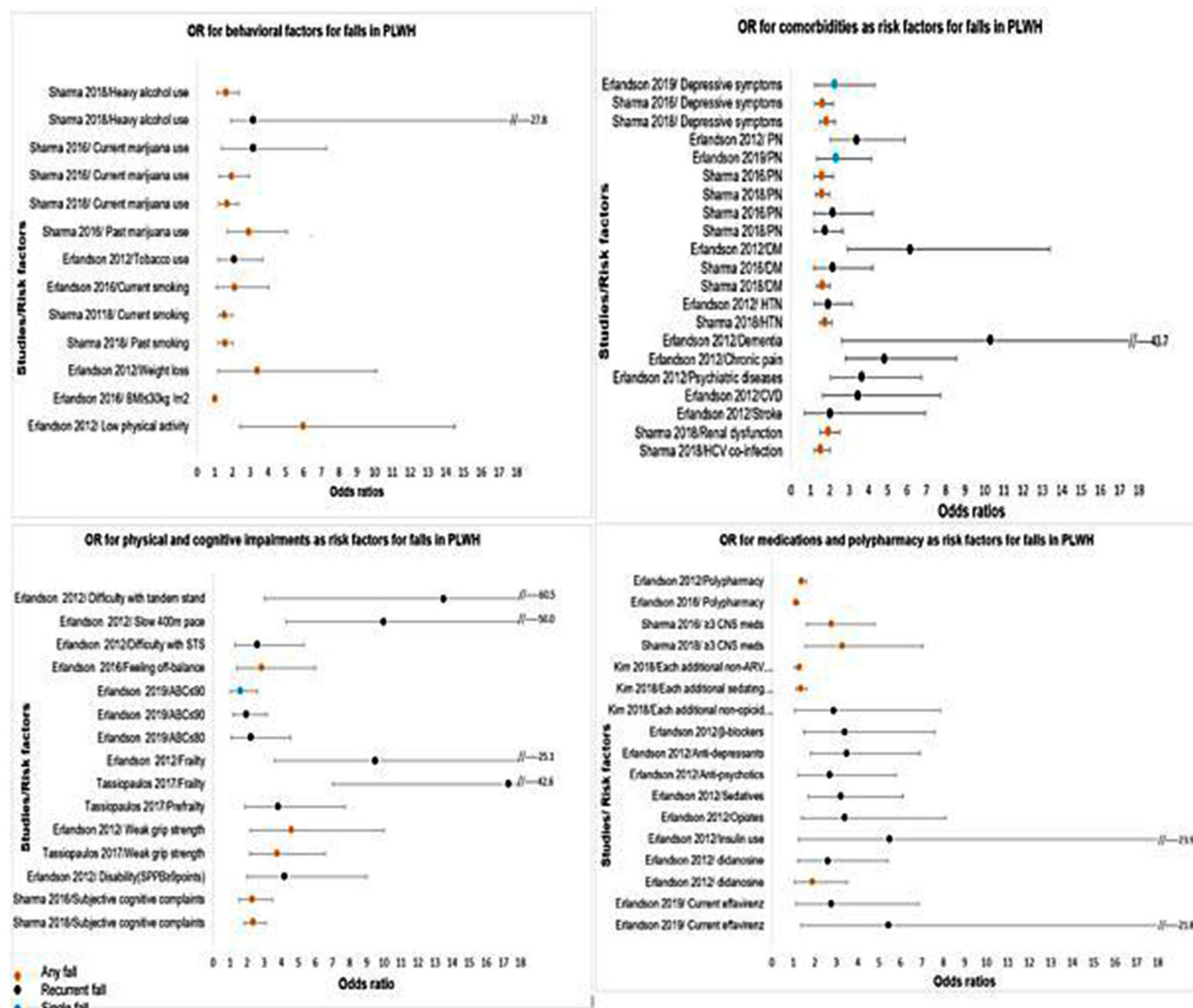
Figure 1 ORs for risk factors significantly associated with falls in PLWH. NB. These forest plots are not a meta-analysis, which was impeded by the heterogeneity of the studies.[38] ABC, Activities-Specific Balance Confidence Scale; CNS, central nervous system; DM, diabetes mellitus; HTN, hypertension; PLWH, people living with HIV; PN, peripheral neuropathy; SPPB, short physical performance battery.

Clinical AIDS diagnosis was also not associated with falls in two longitudinal studies.[24 30]

Comparison of risk factors for falls between PLWH and seronegative population

Of the four studies including seronegative controls, two studies[27 30] compared risk factors for falls between the groups. One study[27] found falls in relation to pets to be more significant among PLWH while use of illicit substances was more commonly associated with falls among SNP. Sharma *et al*[30] found similar risk factors between the groups: depressive symptoms (aOR 1.70; 95% CI 1.33 to 2.16; p=0.0001 for PLWH; aOR 1.61; 95% CI 1.12 to 2.32; p=0.01 for SNP) and peripheral neuropathy (aOR 1.44; 95% CI 1.12 to 1.84; p=0.004 for PLWH; aOR 1.63; 95% CI 1.10 to 2.41; p=0.015 for SNP). This study also found subjective cognitive complaints and

hypertension to be significantly associated with falls in SNP.

Intervention for fall prevention

No intervention studies were found. However, many recommendations were found among studies regarding potentially effective falls prevention strategies for PLWH—these are listed in table 1 under the section 'Recommendations from the studies: Interventions'.

BMD and fall-related fractures

BMD was not reported in any of the studies. Rather, data were mostly presented in the context of fall-related fractures. Five studies[27 28 30 32 34] reported a prevalence of fall-related fractures ranging from 3.8% to 8%. Three of these studies had controls; one study[32] showing a markedly higher prevalence of fall-related fractures in

postmenopausal SNP (9.2% SNP vs 3.8% PLWH) while two studies[27 30] showed similar (6%) or slightly higher (4.7% PLWH vs 3.1% SNP) prevalence in PLWH. One qualitative study[1] reported that five out of 21 participants (23.8%) sustained fall-related fractures.

Although not statistically significant, one study[27] reported that diabetes medications (OR 3.19, 95% CI 0.94 to 10.88), p=0.064) and detectable HIV-1 RNA viral load (OR 4.48, 95 CI 0.77 to 25.99, p=0.094) were associated with an increased risk of fall-related fractures, while high physical activity was found to be protective (OR 0.23, 95% CI 0.08to 0.72), p=0.011).

DISCUSSION

We present the results of our scoping review of 13 primary studies and one systematic review reporting on falls in PLWH. There is indication of increasing awareness of falls as a concern in PLWH considering the recency of published articles. All but three of the fourteen included studies were based in the USA which may affect the generalisability of results to other contexts especially sub-Saharan Africa where most and more robust clades of HIV infection exist. However, we were able to present a comprehensive map of the breadth of evidence available regarding falls and bone demineralisation in PLWH.

Definition

The studies that reported their definition of fall had two homogeneous components: being unexpected or unintentional and coming to rest on a lower level. However, definitions used in the studies were varied with some excluding falls from disease-related causes and external forces. It is possible that by making such exclusions, falls relevant to this population were missed. One Cochrane review[22] of case definitions of falls recommended a standardised, non-exclusive fall definition; 'an unexpected event in which the participant comes to rest on the ground, floor or lower level' and for patients to understand, terminology such as 'slipped, tripped or losing balance' should be used to describe falls.[22] Using a standardised definition in future studies will enhance generalisability in comparing prevalence statistics between countries and studies.

Epidemiology of falls in PLWH

The prevalence of falls in PLWH was found to approximate that of their seronegative counterparts.[24 27 30 32] In these studies, middle age and older participants were included. Therefore, factors related to ageing may have influenced the prevalence of falls in the seronegative participants as well. One Ph.D. thesis[39] showed that falls were a problem in a relatively younger cohort of PLWH (median age of 36.61 years) living in a rural district of South Africa. A higher prevalence of falls in PLWH compared with the SNP was reported (34% PLWH vs 16% SNP; p=0.038). The prevalence of falls among younger PLWH may be useful in determining whether higher risk of falls occurs earlier in their life course when compared with age-matched seronegative counterparts.

All studies were conducted in HIC where participants had access to good healthcare and effective health promotion strategies.[40] For example, lower rates reported by Erlandson et al[24] and Sharma et al[32] were attributed to volunteer bias of participants with access to healthcare agreeing to participate in the study, indicating how better adherence and access to treatment can result in better fall outcomes in PLWH. However, the higher burden of risk factors which are mediating variables of falls and ageing in PLWH (including coexisting comorbidities, opportunistic infections, malnutrition and poor ART compliance),[41] may indicate that the situation could be very different in LMIC settings. The risk profiles of participants in in LMIC with lower socioeconomic factors and suboptimal health systems may differ considerably. It could be that strains of HIV-1 Clade C virus, epidemic in southern Africa, are more robust and having a greater effect on the CNS.[42 43] Perhaps this phenomenon should be investigated in LMIC settings.

The prevalence of falls reported in the studies included in this review could have been compromised by the possible recall bias in reporting falls retrospectively. Varying time intervals over which participants were asked to recall their falls were used with varied prevalence rates being reported. The optimal time period to obtain accurate recall of fall history remains to be determined, although the 1-year recall period seems to be more precise.[44 45] Even so, researchers reportedly favour prospective recall methods considering that participants may forget or underreport their falls.[45] Only one of the included studies[27] collected falls data prospectively and reported a relatively higher prevalence rate of 41% compared with all but one studies which used a 1-year recall period and reported rates below 30%. More studies collecting fall data prospectively may be useful in determining fall prevalence. Advancements in technology could see sensors and computerised interactive response technology being used to record falls more accurately and prospectively.

Assessment

Most included studies screened for falls risk using the approach used in the general population by checking fall frequency and context in the previous year,[46] but varied questionnaires were used. This resulted in some studies omitting important details such as fear of falling, duration of HIV infection, characteristics, and cause of falls. One narrative review[44] of assessment of falls in PLWH recommended that the same assessments used in geriatrics be applied to PLWH, and incorporating HIV-related factors.

Although standardised tools were used appropriately, they were often varied. For example, while some studies used the Fried Score to assess frailty,[16 27 28] one study used a different questionnaire.[26] Controversy also existed regarding the use of the VACS Index score, already validated for use among PLWH, to assess physical function.

Common balance and gait assessment tools used in a few of the studies included the Berg Balance Scale, Functional Reach Test, TUGT and 6MWD, but it remains unclear which tool is the most predictive. Some of the tests are time-consuming and tedious and may not be suitable to PLWH or to LIC settings which are commonly understaffed. Validation of specific assessments tailored to PLWH and the African context are needed.

Additionally, none of the included studies reported on assessment of osteoporosis risk as recommended in high-quality clinical practice guidelines for falls-risk management such as National Institute for Health and Care Excellence, American Geriatrics Society and British Geriatrics Society.[47] This is very important for fragility fracture prevention in PLWH because of their high risk of reduced BMD, which also further predisposes them to falls.[5] Assessment of visual impairments, a significant predictor of falls in the older general population,[48] was also omitted in the included studies. Yet high prevalence of HIV-associated ocular disease have been reported in PLWH.[49]

While a falls risk assessment is individualised, there is need for clinical practice guidelines which indicate the risk factors to be assessed and which tools/scores are more predictive and more appropriate for use among PLWH. Local consensus processes may be done to agree on which measures to use for PLWH and knowledge translation strategies such as use of opinion leaders, printed materials and interactive education sessions to increase use of standardised tests may be implemented.[50]

Risk factors

Very few studies compared whether risk factors for falls in PLWH were similar to risk factors for age and sex-matched seronegative populations. However, the trend in the available studies indicated that most risk factors for falls in PLWH were not associated with falls in SNP. More studies are needed to make a comparison of risk factors for falls in PLWH and SNP to determine risk factors unique to PLWH.

The body of evidence is consistent for most risk factors for falls in PLWH. More precise estimates of relatively higher ORs, ranging between 2 and 4, indicate more affirmative evidence for use of medications as risk factors for falls in PLWH (figure 1). The burden of comorbidities including cardiovascular diseases and mental health disorders in PLWH has been well described.[51] Multimorbidity associated with chronic pain, disability and poor health-related QoL may require that PLWH take multiple drugs. Drug–drug interactions and potential side effects of these medications may result in further decline in physical function and falls.[52] While encouraging adherence to ART, it is important for physicians to continuously review patients' medications and avoid overprescribing.

Although the ORs were lower than for medications (mostly ranging between 1 and 2), considerable overlap also existed for risk factors regarding chronic diseases such as depression, diabetes and neuropathies

which have been found to be higher in this population (figure 1).[53] Sakabumi et al[54] supported the latter because PLWH with peripheral neuropathy were more susceptible to balance problems than HIV-uninfected persons.

Evidence for functional and cognitive impairments as risk factors for falls in PLWH was variable. ORs from studies claiming balance impairments and frailty to be strong predictors of falls among PLWH had wide CI ranges indicating low precision possibly due to small sample size (figure 1). Some studies failed to find significant association; for example, one study came to a contradictory conclusion that frailty should not be investigated as a risk factor for falls in PLWH.[35] However, this study appeared overambitious in its claims considering it had not been designed to evaluate frailty as a risk factor for falls. More studies involving larger sample sizes are needed to determine whether balance and cognitive impairments are indeed risk factors for falls in PLWH.

Although HIV serostatus was not found to be predictive of falls, risk factors unique to this population included non-adherence to ART and use of specific ART regimens such as efavirenz, didanosine and ritonavir-boosted proteases inhibitors. Controversy seems to exist regarding detectable viral load as a risk factor for falls in PLWH. One recent study[27] reported a novel finding that detectable viral load was associated with recurrent falls in women living with HIV whereas four previous studies had found no association between detectable viral loads and falls.[16 30 32 35] This raises the importance of healthcare providers being proficient in encouraging early diagnosis and ART adherence among PLWH. On the other hand, the risk factor of nadir CD4+ T cell count is no longer relevant since recent WHO HIV/AIDS guidelines[55] recommend that ART start at time of diagnosis.

Interventions

The review found that there is currently no evidence for interventions to prevent or reduce fall risk in PLWH. One study recommended that the safety and efficacy of multifactorial fall reduction interventions in PLWH be investigated.[24] Multifactorial interventions address the identified modifiable risk factors and involve a multidisciplinary approach. However, new evidence suggests that these multifactorial interventions may not be effective, proposing multiple component interventions (a combination of interventions regardless of identified risk factors, most combinations involving an exercise programme) as an alternative.[56]

Only one study, not included in the review, was found in which exergaming, a virtual reality based exercise programme was reported to improve balance and thus reduce fear of fall and fall risk in PLWH.[57] More research to determine optimal exercise programmes to promote bone health and modify fall related risk factors, thereby reducing risk of fall-related fractures is needed.

STRENGTHS AND LIMITATIONS

The absence of methodological quality appraisal limits the strength of this review to recommend the proposed assessment and intervention strategies. Indeed, much of the evidence came from prospective cohort studies which are prone to selection bias and bias from lost to follow-up. Antecedent-consequent bias occurs in cross-sectional studies (level III evidence) making it difficult to determine causal relationships.[58] The generalisability of included study results is to be applied with caution considering that most studies were based in one HIC country. While convenient, limiting our studies to the English language may have resulted in omission of some studies and more likely those in LMIC. However, we provided a comprehensive and encompassing review of emerging peer-reviewed literature on falls in PLWH and demonstrated a scarcity of high-level evidence regarding assessment and intervention strategies for falls reduction among PLWH. This provides grounds for future high-quality research and preliminary material for further investigation by health researchers especially in Africa.

RECOMMENDATIONS FOR FUTURE RESEARCH

More studies are required on younger cohorts living with HIV in LMIC settings especially sub-Saharan Africa where most and more robust clades of HIV infection exist.

More research is needed to determine the effect of reduced BMD on risk of falls in PLWH. It has been determined that PLWH may be at higher risk of bone demineralisation[10] and falls but no studies have linked these two phenomena.

Interventions to reduce and prevent falls in PLWH is still an area lacking research. Targeted interventions should also promote bone health to address the risk of fall-related fractures in PLWH.

More studies reporting on data in the seronegative controls are needed to determine whether indeed falls are a problem in PLWH. It could be that the risk factors and consequences for falls in PLWH are in fact the same for the general population.

CONCLUSION

The scoping review provided a comprehensive and encompassing review of emerging literature on falls in PLWH and demonstrated a scarcity of high-level evidence regarding assessment and intervention strategies for falls reduction among younger cohorts of PLWH. This provides grounds for future high-quality research and preliminary material for further investigation by health researchers especially in sub- Saharan Africa where HIV is endemic. Future next steps include development of quality clinical practice guidelines for falls assessment and prevention in PLWH or inclusion in current HIV guidelines, implementation of knowledge-translation strategies to aid healthcare providers in evidence-informed practice. This will contribute to improved health outcomes and QoL for PLWH as well as reduce the burden on healthcare systems.

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