Tropical Medicine and International Health doi:10.1111/tmi.12449

VOLUME 20 NO 4 PP 411–429 APRIL 2015

Systematic Review

The relationship between HIV and prevalence of disabilities in sub-Saharan Africa: systematic review (FA)*

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Abstract

OBJECTIVE To systematically review evidence on the prevalence and risk of disabilities among children and adults living with HIV in sub-Saharan Africa.

METHODS Articles were identified from 1980 to June 2013 through searching seven electronic databases. Epidemiological studies conducted in sub-Saharan Africa that explored the association between HIV status and general disability or specific impairments, with or without an HIV-uninfected comparison group, were eligible for inclusion.

RESULTS Of 12 867 records initially identified, 61 papers were deemed eligible for inclusion. The prevalence of disability was high across age groups, impairment types and study locations. Furthermore, 73% of studies using an HIV- comparator found significantly lower levels of functioning in people living with HIV (PLHIV). By disability type, the results were as follows: (i) for studies measuring physical impairments (n = 14), median prevalence of limitations in mobility and motor function among PLHIV was 25.0% (95% CI: 21.8–28.2%). Five of eight comparator studies found significantly reduced functioning among PLHIV; for arthritis, two of three studies which used an HIV- comparison group found significantly increased prevalence among PLHIV; (ii) for sensory impairment studies (n = 17), median prevalence of visual impairment was 11.2% (95%CI: 9.5–13.1%) and hearing impairment was 24.1% (95%CI: 19.2–29.0%) in PLHIV. Significantly increased prevalence among PLHIV was found in one of four (vision) and three of three studies (hearing) with comparators; (iii) for cognitive impairment in adults (n = 30), median prevalence for dementia was 25.3% (95% CI: 22.0–28.6%) and 40.9% (95% CI: 37.7–44.1%) for general cognitive impairment. Across all types of cognitive impairment, twelve of fourteen studies found a significant detrimental effect of HIV infection; (iv) for developmental delay in children with HIV (n = 20), median prevalence of motor delay was 67.7% (95% CI: 62.2–73.2%). All nine studies that included a comparator found a significant difference between PLHIV and controls; for cognitive development and global delay, a significant detrimental effect of HIV was found in five of six and one of two studies, respectively. In the nine cohort studies comparing vertically infected and uninfected children, eight showed a significant gap in development over time in children with HIV. Finally, fifteen of thirty-one (48%) studies found a statistically significant dose–response relationship between indicators of disease progression (CD4 or WHO stage) and disability.

CONCLUSIONS HIV is widespread in sub-Saharan Africa and the evidence suggests that it is linked to disabilities, affecting a range of body structures and functions. More research is needed to better understand the implications of HIV-related disability for individuals, their families as well as those working in the fields of disability and HIV so that appropriate interventions can be developed.

keywords HIV, disabilities, sub-Saharan Africa, prevalence

*Free full access from www.tmih.com.

Introduction

Since HIV first came to international attention in the 1980s, its devastating effects have been felt worldwide. To date, 75 million people have been infected and 36 million have died from AIDS-related causes [1]. However, the advent of antiretroviral therapy (ART) has changed the prognosis from invariable death to a lifelong, but manageable, chronic condition [2], with a near-normal life expectancy [3].

While ART reduces the risk of death and of developing serious opportunistic infections, evidence from high-income countries (HICs) suggests that many people living with HIV (PLHIV) face new or worsening experiences of disability [4, 5]. Disability can be characterised as dysfunction at the level of body functions or structures (impairments), the individual's ability to execute a task or action (activity limitations) and the individual's involvement in life situations within society (participation restrictions), as described by WHO's International Classification of Functioning, Disability and Health (ICF) [6]. Environmental and personal contextual factors may act to mitigate or exacerbate disability [6].

The link between HIV and disability is thought to be due to the direct action of HIV, its secondary conditions and/or side effects of medications used for treatment, which may lead to impairments in a wide range of areas such as cognition, vision, hearing, mental health and musculoskeletal functioning [7]. Many PLHIV then encounter activity limitations (e.g. in self-care, mobility) and participation restrictions (e.g. employment, schooling) due to these impairments, especially when combined with modifiers such as poor access to care and rehabilitation and stigmatisation [6, 8].

Research from high-income countries (HICs) has begun to explore the link between HIV and disability. For example, a systematic review of neurocognitive development in children found a detrimental effect of HIV in 36 of 41 (88%) of HIC-based studies [9]. A further Canadian survey showed that 80% of participants reported disablement within the past month that they attributed to their HIV status [10]. In another US-based study, PLHIV had higher levels of physical disability than matched HIV-negative controls [11].

Although there is a general dearth in research on HIV-related disability, the data from low- and middle-income countries (LMICs) are particularly sparse. The epicentre of the HIV pandemic is in sub-Saharan Africa, which, although home to slightly over 10% of the world's population, comprises 72% of all new infections [12]. Progress is being made in this region though, as today 56% of those eligible for ART are receiving treatment [13, 14]. If patterns mirror experiences in HICs, PLHIV in Africa will live longer, but face the challenges associated with the development of disability [4].

Key contextual differences between sub-Saharan Africa and HICs will likely lead to unique challenges for tackling HIV-related disability. The absolute numbers and prevalence of PLHIV and disability will be far higher in Africa than in other parts of the world [4]. Furthermore, compounding factors often encountered by PLHIV in this region could further increase risk and severity of disablement. For example, malnutrition, higher exposure to opportunistic infections (OIs) and irregular access to ART could all increase the odds of developing impairments or exacerbating existing ones [4, 15]. Shortages in health resources and social supports, particularly in the area of rehabilitation, will limit management strategies, leading to further participation and activity constraints [16, 17]. Additionally, the implications of HIV-related disability in children have little precedent from HICs as paediatric HIV infection is rare in these settings due to rigorous enforcement of interventions to prevent mother-to-child transmission of HIV [18].

Given these gaps, a systematic review was conducted to compile evidence on the magnitude and scope of HIV-related disabilities in sub-Saharan Africa to contribute towards establishing programmatic, policy and research priorities. Specifically, this review aims to report prevalence of disabilities in PLHIV and to investigate the association of HIV with disability.

Methods

Search strategy

Seven electronic databases, EMBASE, PubMed, Medline, Global Health, Web of Knowledge, Academic Search Complete and Africa Wide Information, were searched in June 2013. Search terms for HIV/AIDS and disability in Africa were identified through MeSH as well as from those used for systematic reviews on similar topics. Terms for both general disability and specific impairments were employed to capture the range of possible forms of disablement resulting from HIV/AIDS. Filters to retrieve only English-language texts were set and the date of publication was restricted from 1980 to June 2013 as HIV/AIDS was recognised in the early 1980s.

Inclusion/exclusion criteria

Papers were included if they addressed HIV/AIDS and disability in Africa. In this review, HIV/AIDS and disability were considered respectively the exposure and

outcome under investigation; thus, papers exploring the reverse relationship, i.e. disability as a risk factor for HIV infection, were excluded in the final sample.

A study with any epidemiological design was eligible for inclusion (survey, case–control, cohort, trials). Given the expectation that there would be a dearth of information, studies with and without comparison groups were included and no restrictions concerning population characteristics (other than HIV seropositivity in some portion of the sample) or study size were applied.

Disability was defined broadly, in line with WHO's International Classification of Functioning, Disability and Health (ICF) definition [6]. Studies investigating depression and/or anxiety following HIV diagnosis were excluded as this review focused on downstream development of disability.

Study selection

Articles were screened by one reviewer (LMB), first by titles, then by abstract and finally by full text to determine eligibility in the final sample. In the event of indecision, the screener asked for a second opinion. Furthermore, 100 randomly selected abstracts were dually reviewed to check for agreement.

Data extraction

Data from the final sample were collated using an extraction table. Entries were grouped by disability type (vision, hearing, locomotor – mobility/motor function and arthritis, cognition in adults, developmental delay and general dysfunction).

Odds of disability or difference in mean score on assessments between HIV-infected and uninfected groups were the primary measures of HIV association with disability. For studies without a comparison group, the prevalence of disability in PLHIV was recorded.

Meta-analysis was not used to pool results, due to the lack of standardised outcome measures and heterogeneity in study designs. Studies using a comparison group were analysed separately from those without. The median prevalence estimate was calculated for each category of disability. We did this by ranking the studies in the category by prevalence, and reporting the prevalence and 95% confidence intervals (CI) of the median study in that category. Studies that either were based in hospital units for the impairment in question (e.g. studies on arthritis where patients were recruited from rheumatology departments) or focused on only severe forms of impairment (e.g. blindness within visual impairment) were excluded in determining the median. In the event that two studies formed the median, the two measures of prevalence were averaged, weighting it to take account of the sample sizes. Evidence of a dose–response relationship between indicators of disease progression (CD4 count or WHO stage) and disability was either obtained from analyses presented by study authors or self-calculated from disaggregated but unanalysed data included within the paper.

Quality assessment

Quality assessment of the final sample of studies was conducted using a modified version of the quality assessment tool for systematic reviews of observational studies (QATSO) [19]. Criteria included the following: (i) two measures on representativeness of sampling method (use of probability sampling to select study participants, population-based recruitment), (ii) objectivity of measurement of HIV, (iii) validated disability measurement, (iv) acceptable response rate (60% of higher) and (v) control for confounding in studies with a comparison group. Table 1 presents the criteria used in assessing studies; quality criteria not fulfilled by each individual study are reported in Tables 2–6.

Results

The search yielded 12 867 papers. After 5236 duplicates were removed, the remainder was screened, leading to the rejection of 6190 records by title and a further 1350

Table 1 Quality of papers assessed in systematic review

Quality variable	Quality variable criteria	Number of papers	Percent
Sampling	1. Non-probability	47	77
	Probability (+1)	14	23
	2. Not population based	56	92
	Population based (+1)	5	8
Objectivity of HIV measurement	3. Self-reported	0	0
	Clinical records/laboratory tests (+1)	61	100
Objectivity of disability measurement	4. Non-validated assessment tool	0	0
	Validated assessment tool, clinical evaluation (+1)	61	100
Response rate	5. Not reported or below 60%	48	79
	Reported and over 60% (+1)	13	21
Control for confounding	6. No	4	7
	Yes (+1)	13	54
	N/A	24	39

Table 2 Summary of studies examining HIV and sensory impairments

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV-control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of dose response relationship	QATSO criteria not fulfilled
Vision											
Emina and Odjimogho, 2010 [33]	Nigeria	CC	Adults	40	40	a. Reduced vision (CE) b. Visual acuity scores (CE)	a. 25%, b. –	a. 7.5% b. –	a. OR = 4.11, $P = 0.03$ b. $P < 0.05$	Yes	1, 2, 5
Morgan *et al.*, 1998 [34]	Uganda	CS	Adults	105	133	Low vision (CE)	3.8%	6.8%	ns	–	–
Padhani *et al.*, 2000 [35]	Tanzania	CC	Children	62	47	Abnormal visual acuity (CE)	9.7%	6.4%	ns	–	1, 2, 4, 5
Scholten *et al.*, 2011 [36]	Uganda	CS	Adults	199	311	Poor vision (CE)	–	–	ns	–	–
Assefa *et al.*, 2006 [37]	Ethiopia	CS	Adults	125	–	Blindness (CE)	5.6%	–	–	–	1, 2, 5
Govender *et al.*, 2011 [38]	South Africa	CS	Children, infants	78	–	Visual impairment (CE)	16%	–	–	–	2, 5
Osahon and Onunu, 2007 [39]	Nigeria	CS	Adults	526	–	1. Reduced vision (CE) 2. Bilateral blindness (CE)	a. 2.3% b. 0.4%	–	–	–	1, 2, 5
Otiti-Sengeri *et al.*, 2010 [40]	Uganda	CS	Adults	1212	–	Visual impairment (CE)	11%	–	–	Yes*	1, 2
Giorgis *et al.*, 2007 [41]	Ethiopia	CS	Adults	186	–	Blindness (CE)	17%	–	–	Yes*	1, 2, 5
Hearing											
Ongulo and Oburra, 2010 [42]	Kenya	CC	Adults	194	124	Hearing loss (CE)	34%	8.1%	OR = 5.74, $P < 0.0001$	Yes*	1, 2, 5
Taipale *et al.*, 2011 [43]	Angola	CC	Children	78	78	Hearing loss (CE) a. Overall b. Bilateral	a. 26% b. 13%	a. 15% b. 1%	a. ns b. OR = 11.32, $P = 0.005$	–	1, 2, 5
van der Westhuizen *et al.*, 2013 [44]	South Africa	CS	Adults	200	184	Hearing loss (CE)	43%	6%	OR = 11.86, $P < 0.0001$	ns	1, 2, 5
Christopher *et al.*, 2013 [45]	Uganda	CS	Children	370	–	Hearing loss (CE)	33%	–	–	Yes*	1, 2, 5
Govender *et al.*, 2011 [38]	South Africa	CS	Children, infants	78	–	Hearing impairment (CE)	6%	–	–	–	2, 5
Khoza and Ross, 2002 [46]	South Africa	CS	Adults	150	–	Hearing loss (CE)	23%	–	–	Yes*	1, 2, 5
Khoza-Shangase, 2011 [47]	South Africa	CS	Adults	150	–	Hearing loss (severe) (CE)	10% (2%)	–	–	–	1, 2, 5

Table 2 (*Continued*)

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV- control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of dose response relationship	QATSO criteria not fulfilled
Tshifularo *et al.*, 2013 [48]	South Africa	CS	All ages	153	–	Sensory-neural hearing loss (CE)	14%	–	–	–	1, 2, 5

Study design abbreviations: CS, cross-sectional; CC, case control; Means of assessment abbreviations: CE, clinical evaluation; QATSO criteria: 1, probability sampling; 2, population-based; 3, HIV measure is objective; 4, disability assessment tool validated; 5, response rate reported and over 60% and 6, some control for confounding (if applicable).
†Unless otherwise stated, comparisons are HIV+ to all HIV- (including seroreverters).
*Statistically significant ($P < 0.05$); ns, non-significant ($P > 0.05$).

by abstract. The full texts of 91 records were then reviewed. After 29 articles were deemed ineligible, 3 untraceable and an additional 2 sources found through reference lists of other included articles, a final sample of 61 studies was attained (Figure 1).

The 61 studies included in the final sample are summarised in Tables 1–5. Findings are categorised by disability type. Articles examining multiple disabilities were subdivided by outcomes, and thus, some studies are repeated in different categories.

From the quality assessment, certain criteria were notably lacking in the majority of studies (Table 1). Namely, most studies were not population-based (56 of 61, 92%) and instead focussed on clinic-based populations. In addition, most studies did not use probability sampling strategies (47 of 61, 77%). The majority of studies (48 of 61, 79%) did not report response rates. Studies consistently showed strengths in terms of using validated methods to measure both HIV and disability, and control for confounding.

Prevalence and risk of disability in PLHIV

The prevalence of disability was high across age groups, impairment types and study locations. Furthermore, 73% of studies using an HIV- comparator found significantly lower levels of functioning in PLHIV.

For visual impairments studies, excluding blindness, the median prevalence in PLHIV was 11.2% (95% CI: 9.5–13.1%) (Table 2). When a HIV- comparator was used, only one of four studies demonstrated significantly more visual impairment among PLHIV. Median prevalence among studies of hearing loss in PLHIV was 24.1% (95% CI: 19.2–29.0%). All three studies using a HIV- control group found a significantly higher prevalence of hearing impairment among PLHIV.

The median prevalence for studies on mobility and motor limitations in PLHIV was 25.0% (95% CI: 21.8–28.22%) (Table 3). Limitations in mobility and motor function were significantly more common in PLHIV compared to their HIV- counterparts for five of eight studies. As half of the studies on arthritis recruited patients from rheumatology departments, median prevalence was not calculated. Two of the three studies with an HIV- comparator found significantly elevated odds of arthritis in PLHIV.

Studies utilised a wide range of assessment tools and definitions to measure cognitive impairment (Table 4). Among these studies, the median prevalence for dementia in PLHIV was 25.3% (95% CI: 22.0–28.6%). The sole study utilising an HIV- comparator found significantly increased prevalence in PLHIV. For overall cognitive impairment, median prevalence in PLHIV among the

Table 3 Summary of studies examining HIV and locomotor impairments

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV-control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of dose response relationship	QATSO criteria not fulfilled
Mobility and motor function											
Clifford *et al.*, 2007 [49]	Ethiopia	CS	Adults	73	87	Motor function (IHDS, NP)	–	–	ns	–	1, 5
Hestad *et al.*, 2012 [23]	Zambia	CS	Adults	38	42	Motor function (NP)	–	–	ns	–	1, 2, 5
Holguin *et al.*, 2011 [50]	Zambia	CS	Adults	86	57	Motor function (NP) a. Motor speed b. Gross motor c. Fine motor	–	–	a. $P > 0.05$ b. $P = 0.002$ c. $P = 0.001$	–	1, 2, 5
Howlett *et al.*, 1989 [51]	Tanzania	CS	Adults	135	53	Psychomotor retardation (CE)	24%	5.5%	OR = 5.178, $P = 0.004$	–	1, 2, 5
Lawler *et al.*, 2011 [52]	Botswana	CS	Adults	60	70	Psychomotor slowing (Trail Making Test A)	–	–	$P = 0.01$	–	1, 2, 5
Odiase *et al.*, 2007 [53]	Nigeria	CC	Adults	192	96	Psychomotor slowing (FePsy test battery)	–	–	$P < 0.05$	Yes*	2
Perriens *et al.*, 1992 [54]	Zaire (DRC)	CS	Adults	104	92	a. Difficulty walking (MH) b. Psychomotor slowing (CE)	a. 39% b. 13%	a. 25% b. 6%	a. OR = 1.93, $P = 0.05$ b. ns	Yes*	1, 2, 4
Robertson *et al.*, 2007 [55]	Uganda	CC	Adults	110	100	Motor function (NP)	–	–	ns	–	1, 2, 5
Myezwa *et al.*, 2009 [56]	South Africa	CS	All ages	80	–	Mobility impairments (ICF Checklist) a. Overall b. Severe	a. 56% b. 16%	–	–	–	1, 2
van As *et al.*, 2009 [57]	South Africa	CS	Adults	45	–	a.Neuromusculoskeletal and movement-related impairment (ICF Checklist) b. Mobility limitation	27% 40%	– –	– –	– –	1, 2, 5
Arthritis											
Bileckot *et al.*, 1998 [27]	Republic of Congo	CS	Adolescents, adults	39	132	Arthritis (CE)	82%	55%	OR = 3.81, $P = 0.002$	Yes	1, 2, 4, 5

Table 3 (*Continued*)

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV- control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of dose response relationship	QATSO criteria not fulfilled
Blanche *et al.*, 1993 [28]	Rwanda	CS	Adolescents, adults	52	20	Arthritis (CE)	72%	28%	OR = 6.33, $P < 0.001$	–	1, 2, 4, 5
Saraux *et al.*, 1997 [58]	Rwanda	CS	Adults	1850	1170	Septic arthritis (CE)	0.5%	0.3%	ns	–	1, 2, 5
Kaddu-Mukasa *et al.*, 2011 [59]	Uganda	CS	Adults	300	–	Arthritis (CE)	4.7%	–	–	ns	1, 2

Study design abbreviations: CS, cross-sectional; CC, case control; Means of assessment abbreviations: CE, clinical evaluation; NP, neuropsychological test battery; MH, medical history; ICF, International Classification of Functioning, Disability and Health; IHDS, International HIV Dementia Scale; QATSO criteria: 1, probability sampling; 2, population-based; 3, HIV measure is objective; 4, disability assessment tool validated; 5, response rate reported and over 60% and 6, some control for confounding (if applicable).

†Unless otherwise stated, comparisons are HIV+ to all HIV- (including seroreverters).

*Statistically significant ($P < 0.05$); ns, non-significant ($P > 0.05$).

studies was 40.9% (95% CI: 37.7–44.1%) and significance of association with HIV was found in four of six studies. By cognition subcategories, PLHIV experienced significantly lower scores than HIV- comparators in executive functioning (3 of 3), memory (3 of 7) and attention (3 of 4).

Association between developmental delay and HIV status appears highly significant (Table 5). For motor development, median prevalence of delay was 67.7 (95% CI: 62.2–73.2%) among the studies, and all nine studies with a comparator found significantly poorer functioning among PLHIV than controls. Cognitive development was significantly poorer among PLHIV in at least one measure for five of six studies, while global delay was significantly more frequent among PLHIV in one of two studies.

Cohort studies are useful to track the progression of development over time. From this perspective, the gap in development between children living with HIV and their HIV- counterparts remained significant in all five studies of motor development, in three of four for cognitive development and in the sole study for global delay.

Of the two studies that used broad measures of general disability, one found significantly lower prevalence among PLHIV (Table 6).

Finally, 15 of 31 (48%) studies found a statistically significant relationship between disease progression and disability. Evidence of dose response was lowest for cognitive impairments, as only six of seventeen studies (35%) found significant evidence of higher prevalence of impairment with worsening disease.

Discussion

Results from this review indicate that HIV is associated with disability and consequently that HIV-related disability is common across sub-Saharan Africa, affecting individuals of all ages and a wide range of body functions/structures. Prevalence of disability among PLHIV was high for all categories. Furthermore, 27 of 37 studies (73%) using a HIV- comparator found significantly lower levels of functioning in PLHIV across a range of impairment types. Developmental delay stands out as most strongly linked to HIV, with prevalence as high as 78% in children with HIV and significance of effect present in 15 of 17 studies with comparators. Only one study found an inverse relationship [20]. However, the authors commented that this higher functional ability among PLHIV than controls may be explained by their enhanced health care received as part of their ART treatment.

Of the 31 studies that disaggregated findings by disease status, 15 (48%) found a statistically significant dose-response relationship between worsening disease and

Table 4 Summary of studies examining HIV and cognitive impairments in adults

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV- control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Dementia											
Howlett *et al.*, 1989 [51]	Tanzania	CS	Adults	135	53	Dementia (CE)	19%	6%	OR = 3.98, $P = 0.02$	ns	1, 2, 5
Isezuo *et al.*, 2009 [60]	Nigeria	CS	Adults	322	–	AIDS dementia complex (MH)	3.7%	–	–	–	1, 2, 5
Joska *et al.*, 2011 [61]	South Africa	CS	Adults	170	–	HIV dementia (CE)	25%	–	–	ns	2
Modi *et al.*, 2007 [62]	South Africa	CS	Adults	506	–	HIV-associated dementia (CE)	38%	–	–	Yes	1, 2, 5
Nakku *et al.*, 2013 [63]	Uganda	CS	Adults	680	–	Probable dementia (IHDS)	64%	–	–	Yes*	1, 2
Patel *et al.*, 2010 [64]	Malawi	CS	Adults	179	–	HIV-associated dementia (IHDS)	14%	–	–	ns	2
Wong *et al.*, 2007 [65]	Uganda	CS	Adults	78	–	HIV dementia (NP)	31%	–	–	ns	1, 2, 5
General cognition											
Choi *et al.*, 2011 [66]	Guinea-Bissau	CS	Adults	22	45	HAND (IHDS)	23%	11%	*Crude*: ns *Adjusted* ns	ns	-
Clifford *et al.*, 2007 [49]	Ethiopia	CS	Adults	73	87	Neurocognitive function (IHDS)	–	–	ns	–	1, 5
Kanmogne *et al.*, 2010 [67]	Cameroon	CS	Adults	44	44	Overall cognitive function (NP)	–	–	$P < 0.05$	Yes*	1, 2, 5
Nakasujja *et al.*, 2010 [68]	Uganda	Cohort, 6 month	Adults	102	25	Cognitive impairment (NP) a. At baseline b. Improvement over time	a. 69% b. –	a. 16% b. –	a. Adjusted OR = 8.88, $P < 0.001$ b. $P < 0.001$	–	1, 2, 5
Nakasujja *et al.*, 2012 [69]	Uganda	Cohort, 6 month	Adults	156	322	Severe cognitive impairment (NP) a. At baseline b. Overall	a. 65% b. –	a. 49% b. –	a. OR = 1.88, $P = 0.002$ b. *Crude*: OR = 1.88, $P = 0.002$; *Adjusted*: OR = 1.85, $P = 0.014$	–	1, 2, 5
Salawu *et al.*, 2008 [70]	Nigeria	CS	Adults	60	60	Cognitive function (NP) a. Impairment b. Overall scoring differences	a. 57% b. –	a. 13% b. –	a. OR = 8.5, $P < 0.0001$ b. $P = 0.011$	ns	1, 2, 5

Table 4 (*Continued*)

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV-control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Imam, 2007 [71]	Nigeria	CS	Adolescent, adults	202	–	Cognitive impairment (CE)	12%	–	–	ns	1, 2, 5
Joska *et al.*, 2010 [72]	South Africa	CS	Adults	536	–	HAND (IHDS)	24%	–	–	–	1, 2, 5
Joska *et al.*, 2011 [61]	South Africa	CS	Adults	170	–	Mild neurocognitive disorder (CE)	42%	–	–	–	2
Lawler *et al.*, 2010 [73]	Botswana	CS	Adults	120	–	Neurocognitive impairment (IHDS)	38%	–	–	ns	2
Lawler *et al.*, 2011 [52]	Botswana	CS	Adults	60	–	Cognitive impairment (NP)	37%	–	–	ns	1, 2, 5
Myezwa *et al.*, 2009 [56]	South Africa	CS	All ages	80	–	Impairment in mental functions (ICF) a. Overall b. Severe	a. 73% b. 19%	–	–	–	1, 2
Njamnshi *et al.*, 2009 [74]	Cameroon	CS	Adults	185	–	HAND (IHDS)	22%	–	–	Yes*	1, 2, 5
van As *et al.*, 2009 [57]	South Africa	CS	Adults	45	–	Impairments in mental functions (ICF)	69%	–	–	–	1, 2, 5
Cognition subcategories											
Hestad *et al.*, 2012 [23]	Zambia	CS	Adults	38	42	Neuropsychological performance (NP) a. Overall b. Verbal fluency c. Working memory d. Information processing speed e. Executive functions	–	–	a. $P = 0.004$ b. $P = 0.017$ c. ns d. $P = 0.001$ e. $P = 0.026$	ns	1, 2, 5
Holguin *et al.*, 2011 [50]	Zambia	CS	Adults	86	57	Neurocognitive function (NP): a. HAND b. Sustained attention and sequencing c. Memory recall d. Executive function	–	–	a. ns b. $P = 0.02$ c. ns d. $P < 0.001$	–	1, 2, 5

Table 4 (*Continued*)

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV-control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Jacqueline *et al.*, 2012 [75]	South Africa	CS	Adults	128	32	Poor prospective memory (NP)	60%	28%	OR = 3.86, $P = 0.001$	–	2
Odiase *et al.*, 2007 [53]	Nigeria	CC	Adults	192	96	a. Significant memory impairment (Recognition Memory Test) b. Impaired sustained attention (FePsy test battery)	–	–	a. HIV+ symptomatic to HIV- $P < 0.05$ b. $P < 0.001$	Yes*	2
Perriens *et al.*, 1992 [54]	Zaire (DRC)	CS	Adults	104	92	a. Concentration problems (MH) b. Memory problems (MH)	a. 21% b. 16%	a. 6% b. 7%	a. OR = 3.70, $P = 0.010$ b. ns	Yes*	1, 2, 4
Robertson *et al.*, 2007 [55]	Uganda	CS	Adults	110	100	Neuropsychological performance (NP) a. Overall b. Executive functioning c. Verbal learning/memory d. Attention	–	–	a. $P < 0.001$ b. $P < 0.0001$ c. $P < 0.0001$ d. $P < 0.005$	–	1, 2, 5
Spies *et al.*, 2012 [76]	South Africa	CS	Adults, with and without childhood trauma	83	47	a. Learning and delayed recall (Hopkins Verbal Learning test) b. Delay in attention and working memory (Paced Auditory Serial Addition) c. Language (NP)	–	–	a. $P < 0.01$ b. ns c. ns	–	1, 2, 5

Table 4 (*Continued*)

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV- control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Mupawose and Broom, 2010 [77]	South Africa	CS	Adults	16	–	Cognitive deficits (NP) a. Overall (severe) b. Memory (severe) c. Executive functions (severe) d. Language (severe) e. Visual spatial (severe)	a. 88%(13%) b. 81% (13%) c. 81% (19%) d. 50% (31%) e. 75% (0%)	–	–	–	1, 2, 5

SR, seroreverters; Study design abbreviations: CS,cross-sectional; CC, case control; HAND, HIV-associated Neurocognitive Disorders; Means of assessment abbreviations: CE, clinical evaluation; NP, neuropsychological test battery; MH, medical history; IHDS, International HIV Dementia Scale, International Classification of Functioning, Disability and Health; QATSO criteria: 1, probability sampling; 2, population-based, 3, HIV measure is objective, 4, disability assessment tool validated, 5, response rate reported and over 60% and 6, some control for confounding (if applicable).

†Unless otherwise stated, comparisons are HIV+ to all HIV- (including seroreverters).

*Statistically significant ($P < 0.05$); ns, non-significant ($P > 0.05$).

Table 5 Summary of studies examining HIV and developmental delay

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV- control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Motor development											
Abubakar *et al.*, 2009 [15]	Kenya	CS	Children	31	319 (+17 SR)	a. Psychomotor development (NP) b. Locomotor development (NP)	–	–	a. $P < 0.001$ b. $P < 0.05$	Yes*	1, 2, 5
Boivin *et al.*, 1995 [78]	Zaire (DRC)	Cohort, 18 month	Infants	14	16 (+20 SR)	Motor development (Early Childhood Screening Profiles)	–	–	$P < 0.05$	–	1, 2, 5
Drotar *et al.*, 1997 [79]	Uganda	Cohort, 12 month	Infants	79	116 (+241 SR)	Abnormal motor development (BSID) a. At baseline (6 months) b. At study end (24 months)	a. 16% b. 23%	a. 6.3% b. 1.6%	a. OR = 2.74, $P = 0.015$ b. OR = 19.17, $P < 0.0001$	–	2
Ferguson and Jelsma, 2009 [80]	South Africa	CS	Children	51	35	Significant motor delay (BSID)	67%	5.7%	OR = 33.0, $P < 0.00001$	–	1, 2, 5
Jelsma *et al.*, 2011 [81]	South Africa	CC	Children	23	21	Motor development (Peabody Development Motor Scale)	–	–	$P < 0.001$	–	1, 2, 5
McDonald *et al.*, 2013 [24]	Tanzania	Cohort, 18 month	Infants	31	280 SR	Psychomotor development scores (BSID)	–	–	$P = 0.0001$	–	2, 5
Msellati *et al.*, 1993 [82]	Rwanda	Cohort, 2 year	Infants	50	218 (+168 SR)	Motor development (questionnaire, CE) a. Gross motor b. Fine motor	a. – b. –	a. – b. –	a. $P < 0.002$ b. Only significant at 6 and 12 months	–	1, 2, 5
Ruel *et al.*, 2012 [83]	Uganda	CC	Children	93	106	Motor proficiency scores (Bruininks-Oseretsky Test)	–	–	$P = 0.003$	Yes*	1, 2, 5
Shead *et al.*, 2010 [84]	South Africa	Cohort, 6 month	Children	16	24	Psychomotor development scores (BSID) a. At baseline b. At follow-up	–	–	a. $P = 0.00$ b. $P = 0.00$	–	1, 2, 5

Table 5 (*Continued*)

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV-control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Baillieu and Potterton, 2008 [85]	South Africa	CS	Infants	40	–	Significantly delayed motor development (BSID)	78%	–	–	–	1, 2, 5
Cognitive development											
Bagenda *et al.*, 2006 [86]	Uganda	Cohort	Children	28	37 (+42 SR)	Cognitive impairment (KABC, WRAT3)	–	–	ns	–	2
Boivin *et al.*, 1995 [78]	Zaire (DRC)	Cohort, 18 month	Infants	14	16 (+20 SR)	Cognitive development (DDST, KABC)	–	–	a. $P < 0.001$	–	1, 2, 5
Drotar *et al.*, 1997 [79]	Uganda	Cohort, 12 month	Infants	79	116 (+241 SR)	Abnormal mental development (BSID) a. At baseline (6 months) b. At study end (24 months)	a. 16% b. 3%	a. 5.3% b. 0.9%	a. OR = 3.25, $P = 0.005$ b. ns	–	2
McDonald *et al.*, 2013 [24]	Tanzania	Cohort, 18 month	Infants	31	280 SR	Mental development (BSID)	–	–	$P = 0.03$	–	2
Ruel *et al.*, 2012 [83]	Uganda	CC	Children	93	106	Cognitive functioning (KABC)	–	–	$P = 0.024$	ns	1, 2, 5
Shead *et al.*, 2010 [84]	South Africa	Cohort, 6–8 month	Children	16	24	Mental development (BSID) a. At baseline b. At follow-up	–	–	a. $P = 0.00$ b. $P = 0.00$	–	1, 2, 5
Baillieu and Potterton, 2008 [85]	South Africa	CS	Infants	40	–	Significantly delayed mental development (BSID)	70%	–	–	–	1, 2, 5
Global development											
Kandawasvika *et al.*, 2011 [87]	Zimbabwe	Cohort, 1 year	Infants	65	287 (+188 SR)	High risk of neurodevelopmental impairment (BSID)	17%	9%	OR = 2.1, $P = 0.05$, aOR = ns	–	1, 2

Table 5 (*Continued*)

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV- control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV-	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Msellati *et al.*, 1993 [82]	Rwanda	Cohort, 2 year	Infants	50	218 (+168 SR)	Neurodevelopment delay (questionnaire, CE)	15–40%	0–5%	a. 0.001 < $P < 0.006$	Yes*	1, 2, 5
Govender *et al.*, 2011 [38]	South Africa	CS	Children infants	78	–	Developmental delay (NP)	49%	–	–	–	2, 5

SR,seroreverters; Study design abbreviations: CS, cross-sectional, CC, case control; Means of assessment abbreviations: CE, clinical evaluation; NP, neuropsychological test battery; BSID, Bayley Scales of Infant Development; KABC, Kaufman Assessment Battery for Children; DDST, Denver Developmental Screening Test; WRAT3, Wide Range Achievement Test; QATSO criteria: 1, probability sampling; 2, population-based; 3, HIV measure is objective; 4, disability assessment tool validated; 5, response rate reported and over 60 and; 6, some control for confounding (if applicable).

†Unless otherwise stated, comparisons are HIV+ to all HIV- (including seroreverters).

*Statistically significant ($P < 0.05$); ns, non-significant ($P > 0.05$).

impairment. Evidence of dose response was least apparent for studies on cognitive impairment as only 6 of 17 studies (35%) found significant differences by disease status. This finding is mirrored in the experience in high-income countries in the post-ART era, where severe forms of cognitive impairment appear to be on the decline, but prevalence of mild impairment is largely unchanged and may even be increasing [21, 22]. Consequently, while ART treatment may lower risk and severity, disability may still be part of the lived experience for many PLHIV. However, more research is needed to address this question.

There is some evidence of biological mechanisms underlying links between HIV and disabilities. The direct action of HIV, its secondary conditions and side effects of medications used for their treatment can affect numerous body systems, and consequently, the resulting damage may result in short-term, fluctuating or permanent dysfunction and disability [4]. For example, studies from North America and Europe indicate that HIV-related neuronal damage leads to structural and functional changes in the brain of about 30–50% of PLHIV [23, 24], which could lead to a wide range of impairments; cytomegalovirus retinitis, an OI affecting the eyes, is implicated in 90% of HIV-related blindness in HICs [25, 26]. While additional research is needed to elucidate further details on these and other pathways through which HIV may lead to disability - particularly in LMIC settings– there is biological plausibility to reinforce the findings of this review.

Several limitations should be taken into account when interpreting the findings of this systematic review. Importantly, as the majority of studies were not population-based and used non-probability sampling, the results they present are not necessarily representative of all PLHIV. Many of the studies were clinic based, which affect the generalisability of the results. For instance, both the Bileckot and Blanche studies on arthritis recruited subjects from rheumatology departments and thus are not indicative of prevalence in the broader population of PLHIV [27, 28]. Similarly, median prevalence for each category or subcategory of disability should be interpreted with caution, given the wide range of different definitions, severities and methods of assessing a specific type of disability between studies. Furthermore, outcomes are not disaggregated by factors such as ART status of participants, which may impact upon prevalence for certain types of disability. Disability is also a potential risk factor for HIV [29, 30], and so it is possible that the observed associations could be due to reverse causality. Although studies which clearly focused on disability as a risk factor for HIV were excluded from analysis, within studies, it is

Table 6 Summary of studies examining HIV and general disability

Author, year	Study location	Study design	Age group	PLHIV (*n*)	HIV- control (*n*)	Disability measured (means of assessment)	Measure of prevalence in HIV+	Measure of prevalence in HIV−	Measure of HIV effect†	Evidence of Dose response relationship	QATSO criteria not fulfilled
Nyirenda *et al.*, 2012 [20]	South Africa	CS	Adults	203	119	Functional ability (WHODAS)	–	–	$P < 0.001$ (inverse)	–	–
Scholten *et al.*, 2011 [36]	Uganda	CS	Adults	199	311	Problems in functioning and disability (WHODAS)	–	–	ns	–	–

CS, cross-sectional; CE, clinical evaluation; WHODAS, WHO Disability Assessment Schedule; QATSO criteria: 1, probability sampling; 2, population-based; 3, HIV measure is objective; 4, disability assessment tool validated; 5, response rate reported and over 60% and 6, some control for confounding (if applicable).
†Unless otherwise stated, comparisons are HIV+ to all HIV- (including seroreverters).
ns, non-significant ($P > 0.05$).

often difficult to determine whether HIV infection preceded development of an impairment in all participants. However, an effect of HIV on disability remained when cohort studies with vertically infected children were employed. Finally, as search terms focused on impairments and general disability, with no terms specifically targeting activity limitations or participation restrictions, the full range of disability arising from HIV may not have been captured.

Even with these limitations, evidence from this review indicates an overwhelming need to address HIV-related disability, from both a research and policy perspective.

Experiences from HICs indicate that treating and managing HIV-related disabilities may present unique challenges for both individuals and healthcare providers. First, as HIV-related impairments can have an unpredictable course – with temporary, episodic or permanent presentation – goals for rehabilitation, treatment plans and expectations need continual adjustments to account for changes in status [5, 31]. Second, impairments are often multisystemic, requiring a diverse range of treatments and supports [5, 16]. Finally, PLHIV may be unwilling to self-identify as having a disability due to fear of added discrimination, which limits care-seeking behaviour [5, 16]

Prevention and management of HIV-related disability thus will require inputs and coordination from both rehabilitation and HIV care providers. Early detection, prompt initiation and consistent adherence to ART and prevention/effective treatment of OIs can reduce the risk of developing or exacerbating disability. Meanwhile, rehabilitation can improve level of functioning, prevent deterioration of condition and find adaptations to mitigate activity and participation restrictions. As resources are limited in most settings in sub-Saharan Africa, development of effective, low-cost interventions is a priority. Currently, it is unclear to what extent HIV-related disability is included in the strategies of those working in the fields of HIV or disability/rehabilitation in the region.

Further epidemiological and operational research is needed to better guide policy decisions. Given some of the limitations of this review, more studies on HIV-related disabilities would be useful, particularly those using HIV- comparators, population-based samples, cohort designs and comprehensive adjustment for potential confounding. Additionally, as most included studies only measured a single type of impairment, the use of more comprehensive measures could elucidate the multisystemic nature of HIV-related disability. Research is also needed to gain a better understanding of the social and biological impact of HIV-related disability over the life course, as age will be a compounding factor in the development and management of disabilities as PLHIV live longer on ART.

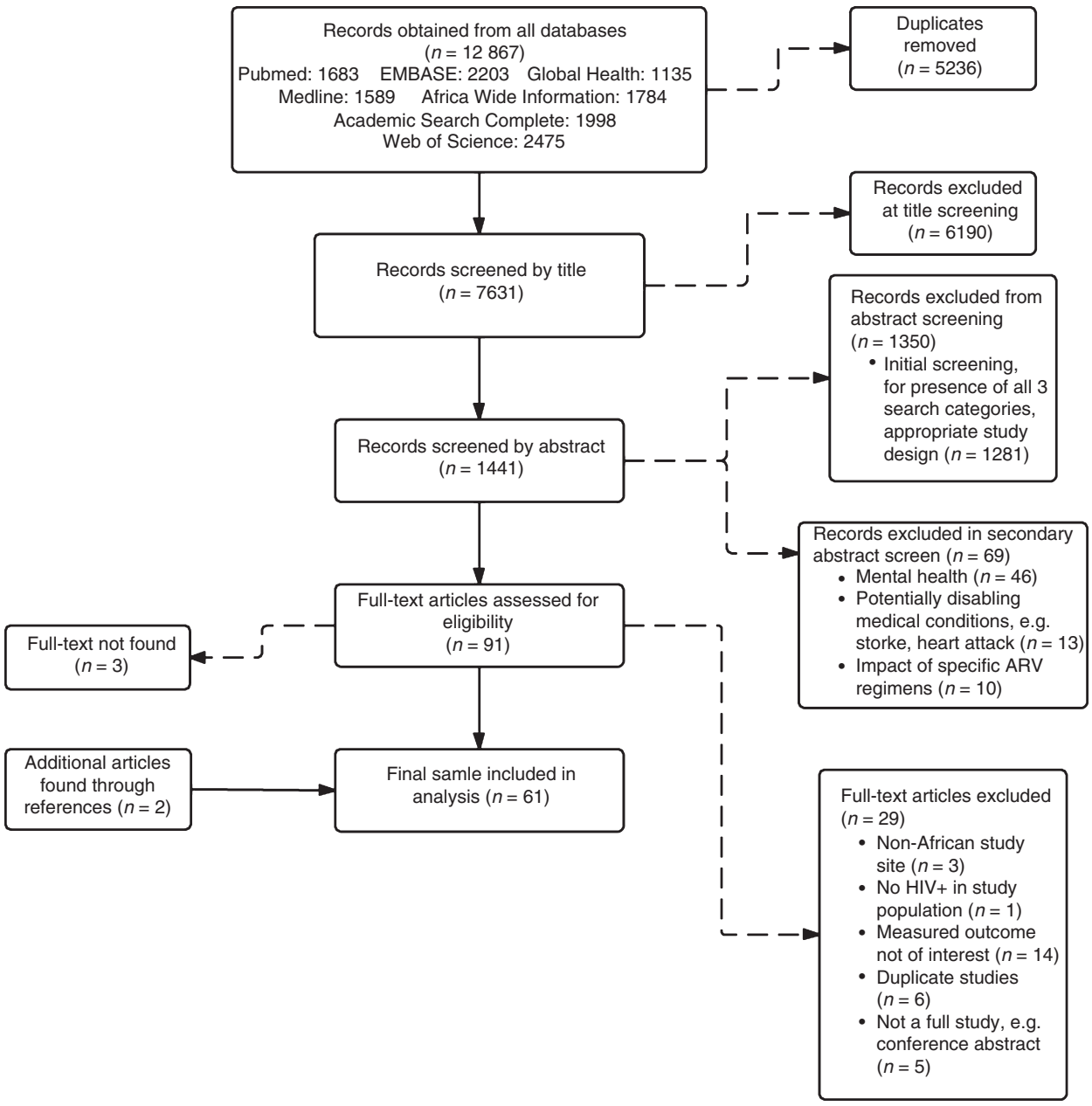

Figure 1 Flowchart of search results.

Policy and research will need to give special attention to the situation of children living with HIV. There is an urgent need to scale up early access to ART among children: currently, only 34% of eligible children are receiving ART, whereas 64% of adults do [14]. While evidence from HICs indicates that ART adherence can lead to many benefits, including significant resolution of impairments, many children are not able to regain full functioning, particularly if the initial damage was extensive [32]. Thus, more research is needed to determine the best treatment strategies for preventing and mitigating disabilities.

Conclusion

HIV-related disability remains an underexplored public health and development concern, particularly in

sub-Saharan Africa where the burden of HIV is highest. Although more research is needed to fill in gaps in knowledge, this review indicates that HIV is strongly linked to disability, and HIV-related disability is common in this region. As HIV control efforts progress through their fourth decade, incorporating disability prevention and rehabilitation interventions alongside standard treatment strategies will be necessary to adapt to the changing experiences of PLHIV.

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