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## Factors associated with erectile dysfunction among men living with HIV: a systematic review

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### ABSTRACT

Erectile dysfunction (ED) is more prevalent among men with HIV than HIV negative men. This study systematically reviewed quantitative studies published since 1997 which sampled men with HIV to examine factors associated with ED. Searches on PsycINFO, Medline, Scopus, Embase and Cinahl databases produced 5552 records, and 14 studies met inclusion criteria. Two researchers independently extracted data and assessed the quality studies using standardized criteria. Age and depression were found to be significantly associated with ED. Importantly, factors unique to HIV emerged as consistently significant across studies, including time on antiretroviral medication and protease inhibitor medication use. However, these relate to organic cause factors associated with ED only. Only four studies examined social factors with inconsistent findings. There was a paucity of research related to psychosocial factors associated with ED. This systematic review used a broad search strategy employed across multiple data-bases, however, it is limited by the over-representation of treatment centre based studies conducted in high-income nations. Future research should examine psychosocial factors, such as undue fear of transmission of HIV or fear of rejection by a sexual partner and develop a psychosocial model of sexual difficulties with HIV, from which casual hypotheses can be derived and tested.

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### KEYWORDS

HIV; erectile dysfunction;  
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Sexual difficulties are experienced by roughly half of people living with HIV (PLWH) (Collazos, 2007). Estimates suggest HIV positive men are 2.3 times more likely than HIV negative men to experience erectile dysfunction (ED) (Santi, Brigante, Zona, Guaraldi, & Rochira, 2014; Shindel, Horberg, Smith, & Breyer, 2011). Moreover, an association has been found between ED and reduced adherence to medication (Trotta et al., 2008). There is strong evidence that early commencement and adherence to medication results in better health outcomes for PLWH (Lundgren et al., 2015), which contributes to the increasingly equal life expectancy estimates for HIV positive and HIV negative people (Nakagawa, May, & Phillips, 2013; Teeraananchai, Kerr, Amin, Ruxrungtham, & Law, 2017). Moreover, when adherence to HIV medication results in sustained viral suppression, HIV cannot be transmitted sexually to another person (Bavinton et al., 2018; Rodger et al., 2016; Rodger et al., 2018). Therefore, by effectively managing ED, and thereby promoting adherence to medication, health professionals

can not only promote the length and quality of life of PLWH in their care, but also potentially prevent new acquisitions of HIV.

In order to more effectively address ED in HIV care, greater understanding is required of which factors (demographic, medical and psychosocial) result in greater prevalence and greater odds of ED among men with HIV. Past reviews relevant to this topic have focused on prevalence, diagnosis, pathogenesis and treatment (Crum, Furtek, Olson, Amling, & Wallace, 2005; Santi et al., 2014; Scanavino, 2011). In 2011 as part of a review with such a focus, Scanavino (2011) did review what was termed “mental factors”, however, CD4 cell levels, viral load and CDC stage were reported under “mental factors” and there was no review of demographic factors which have been examined in past research. This 2011 review focused on medical factors, and there have been significant changes in HIV care in the past eight years. Therefore, our aim was to conduct a systematic review of published research which sampled people with HIV and used statistical methods to examine

factors associated with ED in HIV care, since 1997 (the introduction of combination therapy).

## Method

### Search strategy and selection criteria

The search strategy for this systematic review was developed by three authors (BH, DM, IJ) in consultation with a university librarian. The terms HIV AND erectile dysfunction AND factors (as well as synonyms of these terms and closely related terms) were searched on PsycINFO, Medline, Scopus, Embase and Cinahl using both free text and controlled vocabulary (i.e., MeSH terms). See Appendix 1 for the full electronic search strategy used for Ovid databases. References lists were screened for additional relevant studies.

### Study selection

Authors BH and DM independently reviewed the title and abstract and then full-text articles and applied the eligibility criteria. Eligibility criteria were: an HIV-positive sample or sub-sample recruited since 1997 (after the introduction of combination therapy), which used statistical methods to investigate factors associated with ED. Studies were excluded if they fit the following criteria: reviews, conference proceedings, brief reports, non-peer reviewed work, qualitative research methods only, not written in the English language, and studies making direct comparison between PLWH and other clinical groups without reporting factors relevant to PLWH only.

### Data extraction, data analysis and quality assessment

The Joanna Briggs Institute standardised data extraction and critical appraisal tools (JBI, 2017) were used to extract data on populations, study methods, specific objectives and significant and non-significant findings relevant to the review question. Data were extracted by two researchers (BH and DM), and then checked by a research assistant to ensure accuracy. Significant and non-significant study findings were grouped together by similarity and then compared and synthesised. This resulted in a synthesis organised under four thematic headings. Two researchers also independently applied the Joanna Briggs Institute standardised checklist for analytical cross-sectional studies (JBI, 2017) to assess the quality of included studies. This checklist has eight questions (e.g., were confounding factors identified?) to which “yes”, “no” can be given in response. Scoring 1

for yes and 0 for no allowed calculation of a percentage score. The researchers discussed any disagreements in quality scoring until agreement was reached, or a third reviewer was involved to reach agreement.

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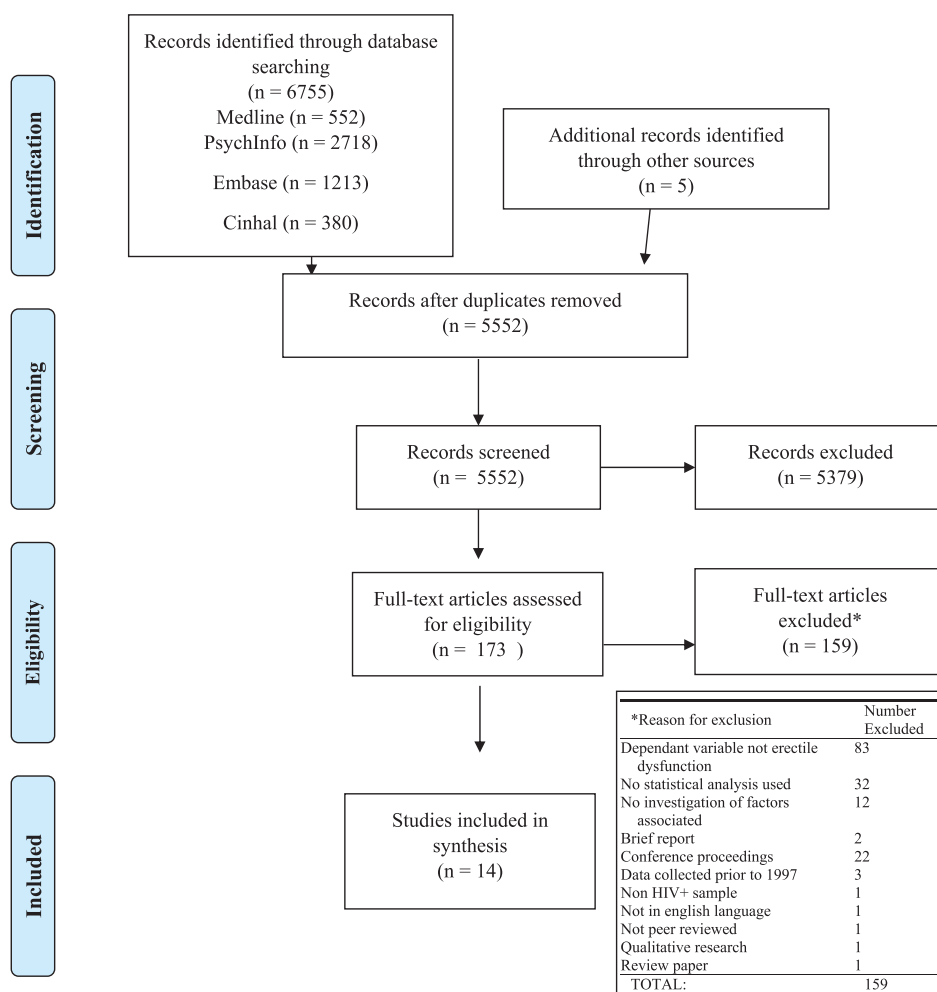
France Recherche Nord & Sud Sida-HIV Hépatites had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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## Results

5552 records were screened and 14 studies met the selection criteria (see Figure 1). Of these 14 studies, four did not report the sexual orientation of their sample, eight sampled all sexual orientations, and two sampled men who have sex with men only. All but one of the studies were conducted in HIV treatment centres. The exception to this Vansintejan, Janssen, Van De Vijver, Vandevoorde, and Devroey (2013) used a community sample recruited via the internet. All studies employed convenience sampling methods. Study samples ranged from 72 to 4064 participants. Nine studies were conducted in European countries, three in the USA, one in Mexico and one in Malaysia. Six studies were published in the '00s and ten in the '10s. All studies employed cross-sectional analytic designs. Most studies ( $n = 11$ ) reported analysing data using regression analyses. The exceptions were studies that used structural equation modelling (Hart et al., 2015), analysis of variance (Perez, Moreno, Navarro, Santos, & Palacios, 2013), and a study that described performing a “multivariate analysis” but it was unclear which multivariate analysis had been performed (De Ryck, Van Laeken, Apers, & Colebunders, 2013). The average rating of quality of included studies was 68%, two scores were rated 50% in quality and one 25% (see Table 1).

Twelve of the 14 studies used the validated International Index of Erectile Function, in either its full 15-item version (IIEF-15) (Rosen, Cappelleri, & Gendrano, 2002) ( $n = 6$ ) or shorter 5-item version (IIEF-SF5) (Rosen, Cappelleri, Smith, Lipsky, & Pena, 1999) ( $n = 5$ ), and one study employed the version designed to assess erectile function among men who have sex with men (Coyne et al., 2010) (IIEF-MSM) ( $n = 1$ ). These twelve studies which used the IIEF used established clinical cut-offs (Cappelleri, Rosen, Smith, Mishra, & Osterloh, 1999; Rosen et al., 1999) to assign



**Figure 1.** Flowchart of study selection.

participants to ED or no ED groups for analysis. Three studies used non-validated yes/no questions to ascertain whether participants were experiencing ED (Crum-Cianflone et al., 2007; Sollima et al., 2001), or took a single frequency question from the IIEF to measure the frequency of ED (Wang et al., 2013) (See Table 2).

The factors associated with ED were synthesised under thematic headings: (i) demographic factors, (ii) HIV parameters and treatment-related factors (e.g., viral load, CD4 count, anti-retroviral drug regimen), (iii) other non-HIV health-related factors, and (iv) psychosocial factors. Table 3 summarises the number of studies concluding for or against the relevance of each factor.

### Demographic factors

Four demographic factors were examined in the included studies. Yet, only age was consistently investigated across studies and the weight of evidence (7 out of 11 studies)

suggests it is significantly associated with ED. Other significant demographic ED factors were low education (Aghahowa, Ching, Hoo, & Omar, 2017) and identifying as homosexual (Sollima et al., 2001). Household income was not significant (Aghahowa et al., 2017).

Regarding age, six of these studies found age to be associated with ED (Crum-Cianflone et al., 2007; De Ryck et al., 2013; Fumaz et al., 2017; Guaraldi et al., 2012; Moreno-Pérez et al., 2010; Perez et al., 2013), while four did not (Aghahowa et al., 2017; Ende, Lo Re Iii, DiNubile, & Mounzer, 2006; Romero-Velez et al., 2014; Vansintejan et al., 2013). In another study, older age was significantly associated with greater frequency of ED (Wang et al., 2013). Close inspection of the measures of central tendency reported by these studies suggests a trend toward age being slightly higher in studies which found age to be significantly associated (42.8), than in those which found age to be non-significant (39.8). Age is therefore associated with ED in studies with older samples, and not in younger samples.

**Table 1.** Characteristics of included studies ( $n = 14$ ).

Study	<i>n</i>	Gender	Location	Sample age	Ethnicity	Study start to end date	Quality rating %
Aghahowa et al. (2017)	220	Males 63.6% reported sex with male as mode of transmission	Kuala Lumpur, Malaysia	Mean = 37.9 ± 9.9	Malay 32.6% Chinese 56.9% Indian 7.3% Others 3.2%	April 2015 to January 2016	87.5
Asboe et al. (2007)	668	Males 73% MSM	“Europe”	Missing: 11 < 35: 173 36–40: 170 41–46: 166 > 46: 148	European	April 2000 to May 2002	100
Crum-Cianflone et al. (2007)	300	Males [Sexual orientation not reported]	San Diego, California, USA	Mean = 39 (19–72)	61% were Caucasian; 24%, African American; 9%, Hispanic; and 5% other	September 2004 to May 2005	62.5
De Ryck et al. (2013)	244	Males [Sexual orientation not reported]	Antwerp, Belgium	Median = 46, IQR 39–52	Not reported. Conducted in Belgium	March 2011 to July 2011	62.5
Ende et al. (2006)	118	Males 52% homosexual, 29% heterosexual, 18% bisexual	Philadelphia, Pennsylvania, USA	Median = 41 (28–67)	53% African American, 36% Caucasian, 9% Hispanic, and 2% Asian	July to August 2004	75
Fumaz et al. (2017)	501	Males 75.8% MSM	Barcelona, Spain	Median = 42 (IQR 35, 48)	Not reported. 73.3% born in Spain. 26.7% not born in Spain.	November 2013 to March 2014	62.5
Guaraldi et al. (2012)	133	Males [Sexual orientation not reported]	Modena, Italy	No ED: mean = 47 ED: mean = 50	Not specified	September 2009 to July 2010	75
Hart et al. (2015)	1363	Males 100% MSM	Baltimore, Washington, DC, Chicago, Los Angeles, and Pittsburgh – USA	HIV + MSM group mean 47.3, SD = 8.9	HIV + MSM group: White 76.2% Black 13% Hispanic 8.6% Other 2.1%	October 2006 to September 2007	87.5
Moreno-Pérez et al. (2010)	619 HIV+ 744 HIV– 90	Males 75.6% MSM, 4.8% bisexual, 19.5% heterosexual	Alicante, Spain	Mean = 42 (SD = 8.2)	“All were white”	Unclear	50
Perez et al. (2013)	158	Males [No sexual orientation info reported]	Malaga, Spain	Mean = 46	Not reported	April 2011 to July 2011	75
Romero-Velez et al. (2014)	109	Males 70.6% MSM	Salvador Zubirán, Mexico City	Mean = 39.9	Not reported. Conducted in Mexico City	January 2008 to December 2008	50
Sollima et al. (2001)	334	Males 22% MSM	Italy	Mean = 36	Not specified	March 1999 to March 2000	62.5
Vansintejan et al. (2013)	72	Male 100% MSM	Belgium	Mean = 41, SD = 10, 18–88	Not reported. Conducted in Belgium	April 2008 to December 2008	25
Wang et al. (2013)	4064	Males 40–52% MSM [Reported for each sub-group]	Basel, Bern, Geneva, Lausanne, St Gallen, Ticino and Zurich – Switzerland	Not reported for whole sample Yes to “often” experiencing ED: median = 53 IQR 46–60 No to “often” experiencing ED: median = 46 IQR 40–52	Not reported Swiss Cohort Study ethnicity published elsewhere	December 2009 to November 2010	87.5

**Table 2.** How included studies measured erectile dysfunction.

Study	How erectile dysfunction (ED) was measured (+ validated, – non-validated)
Aghahowa et al. (2017)	IIEF-15 – Malay Version (+)
Asboe et al. (2007)	IIEF-15 (+)
Crum-Cianflone et al. (2007)	IIEF-15 (+) <b>OR</b> participant said yes to question about inability to obtain or maintain erection (-)
De Ryck et al. (2013)	IIEF-SF5 (+)
Ende et al. (2006)	IIEF-SF5 (+)
Fumaz et al. (2017)	IIEF-SF5 (+)
Guaraldi et al. (2012)	IIEF-15 (+)
Hart et al. (2015)	IIEF-MSM (+)
Moreno-Pérez et al. (2010)	IIEF-15 (+)
Perez et al. (2013)	IIEF-SF5 (+)
Romero-Velez et al. (2014)	IIEF-15 (+)
Sollima et al. (2001)	Question asked: Are you experiencing erectile dysfunction? (-) (*IIEF used to characterise sample only)
Vansintejan et al. (2013)	IIEF-SF5 (+)
Wang et al. (2013)	<b>Frequency of ED was measured</b> Single question on frequency of ED taken from IIEF (-)
<b>Questionnaire</b>	<b>Short description</b>
International Index Erectile Dysfunction (IIEF-15) Rosen (1997)	The IIEF-15 is a 15-item questionnaire which measures five domains (erectile function, orgasm function, sexual desire, intercourse satisfaction, and overall satisfaction). It possible to calculate a clinical cut-off for the erectile function domain to designate individuals as having or not having erectile dysfunction, and all included studies which used the IIEF-15 did so for their analysis
International Index Erectile Dysfunction – Abridged Version (IIEF-SF5) Rosen et al. (1999)	The IIEF-SF5 is a 5-item questionnaire which includes four of the six questions from the IIEF-15 which comprise the erectile function domain (Qs 2, 4, 5, 15) and one question from the intercourse satisfaction domain (Q7). The IIEF-5 was designed as an aid to making a diagnosis of erectile dysfunction.
International Index Erectile Dysfunction – for MSM (IIEF-MSM) Coyne et al. (2010)	Questions 2 and 4 of the IIEF-15 which are identical to questions 2 and 3 in the IIEF-5, make reference to being an insertive partner during sex. The IIEF-MSM is a 22-item validated version of the IIEF-15 with altered wording and additional questions to better assess sexual function between MSM.

### HIV parameters and treatment-related factors

Eleven studies considered whether HIV parameters and treatment-related factors are associated with ED. Six out of eight studies found no significant relationship between ED and CD4, which supports the conclusion that CD4 is not associated with ED. Length of time on antiretroviral therapy appeared to only relate to severe and frequent reports of ED, rather than to milder symptoms of ED. While most studies did not find the type of medication to be associated with ED, there was limited evidence that protease inhibitors are associated with ED in studies that examined this medication type specifically. One study suggested that lipodystrophy is significantly associated. Time since diagnosis and disease progression factors were not meaningful factors.

Although CD4 parameters were found to be non-significant factors in six studies (Aghahowa et al., 2017; Ende et al., 2006; Fumaz et al., 2017; Moreno-Pérez et al., 2010; Perez et al., 2013), two studies found higher CD4 counts to be associated with better erectile function (Crum-Cianflone et al., 2007; Sollima et al., 2001), as did lower viral load (Sollima et al., 2001). Importantly, the two latter studies that found significant effects both used a non-validated measure of erectile function, and were published in the 00s (2001 and 2007). In contrast, all papers reporting a non-significant relationship between CD4 and ED employed the standardised IIEF-SF5 (Aghahowa et al., 2017; Ende et al., 2006; Fumaz

et al., 2017; Perez et al., 2013) or IIEF-15 (Moreno-Pérez et al., 2010), and all except one (Ende et al., 2006) were published in the 10s.

Regarding cumulative effects of anti-retroviral medications, two studies found longer time on antiretroviral medication generally to be associated with ED (Asboe et al., 2007; Wang et al., 2013). Yet three studies did not find any association between the length of time on antiretroviral medication and ED (Crum-Cianflone et al., 2007; Ende et al., 2006; Guaraldi et al., 2012). All three studies assessed ED using the IIEF-SF5 (Ende et al., 2006) or IIEF-15 (Crum-Cianflone et al., 2007; Guaraldi et al., 2012). Two studies found longer use of antiretroviral medication to be associated with ED (Asboe et al., 2007; Wang et al., 2013), however, each study measured ED differently. One only assessed factors of moderate to severe ED as classified by the IIEF-15 (and excluded those with normal to mild symptoms from analysis) (Asboe et al., 2007), while the second used a single question on frequency of ED as the outcome measure (Wang et al., 2013). The three studies that found no relationship all measured ED using the IIEF-SF5 (Ende et al., 2006) or IIEF-15 (Crum-Cianflone et al., 2007; Guaraldi et al., 2012).

Two studies found antiretroviral type used as a general variable not to be associated with ED (Fumaz et al., 2017; Moreno-Pérez et al., 2010). Similarly, protease inhibitor treatment as a general variable was not

**Table 3.** Summary of study conclusions.

Factor	Number studies concluded relevant ✓	Number studies concluded not relevant ×	Total number of studies investigating this factor
<i>- Demographic</i>			
Age	7	4	11
Low education	1	0	1
Identifying homosexual	1	0	1
Household income	0	1	1
<i>- HIV parameters and treatment related</i>			
CD4	3	6	8
Viral load	1	0	1
Length time on antiretrovirals	2	3	5
Antiretroviral type (general)	0	2	2
Protease inhibitor use (general)	0	1	1
Indinavir (specifically)	1	0	1
Longer time on protease inhibitors (generally)	1	0	1
Time since diagnosis	0	3	3
Advanced stage of HIV	0	1	1
History of opportunistic infections	0	1	1
Lipodystrophy	1	0	1
<i>- Other non-HIV health-related factors</i>			
Intravenous drug use	1	0	1
Dyslipidaemia	1	1	2
ED medication	1	0	1
Low frequency masturbation	1	0	1
Low frequency sex with partner	1	0	1
Drug and alcohol use	0	2	2
Tabaco smoking	0	1	1
Other health issues	0	1	1
Hypertension	0	2	2
Cardiovascular risk	0	1	1
HCV co-infection	0	1	1
Testosterone levels	0	2	2
Hypogonadism	0	2	2
Physical health	0	1	1
Sedentary lifestyle	0	1	1
BMI	0	1	1
Diabetes	0	1	1
Atherosclerosis parameters	0	1	1
<i>- Psychosocial factors</i>			
Anxiety	2	0	2
Depression	4	2	6
Low social support	0	1	1
Satisfaction with facial appearance	1	0	1
No steady relationship	1	0	1

Note: Factors examined, and number of studies that concluded on its relevance to erectile dysfunction.

significantly associated with ED in one study (Romero-Velez et al., 2014). Yet, another study assessing the use of indinavir type protease inhibitor medication found a relationship with ED (Sollima et al., 2001), and another found longer time on protease inhibitor medications specifically (Moreno-Pérez et al., 2010) to be significant. Three studies examined “time since diagnosis” and also found no significant relationship (Fumaz et al., 2017; Guaraldi et al., 2012; Moreno-Pérez et al., 2010). HIV disease progression factors including: advanced stage of HIV illness (Moreno-Pérez et al., 2010; Perez et al., 2013) and history of opportunistic infections (Ende et al., 2006) were also found to be non-significant factors. Lipodystrophy was significantly associated with ED in a study conducted in Spain (Moreno-Pérez et al., 2010).

### Other non-HIV health-related factors

Nine studies investigated whether general health factors were associated with ED, yet no factors emerged as consistently significant. Intravenous drug use was found significant in one study (Sollima et al., 2001). Dyslipidaemia was assessed in two studies, and found to be associated with ED in one study (Romero-Velez et al., 2014), but not the other (Perez et al., 2013). We can discern no meaningful difference between these studies to explain these contradictory findings. Another study reported that use of ED medication was associated with ED (Vansintejan et al., 2013), which is a self-evident finding. The same study reported low frequency of both masturbation and sex with partner as factors associated with ED (Vansintejan et al., 2013). A number of non-HIV general health-related factors examined and found not to be significant factors of ED were: drug and alcohol use (Moreno-Pérez et al., 2010; Perez et al., 2013), tobacco smoking (Guaraldi et al., 2012), having other health issues (Fumaz et al., 2017), hypertension (Aghahowa et al., 2017; Perez et al., 2013), cardiovascular risk (De Ryck et al., 2013), hepatitis C co-infection (Fumaz et al., 2017), testosterone levels (Ende et al., 2006; Moreno-Pérez et al., 2010), hypogonadism (Moreno-Pérez et al., 2010; Perez et al., 2013), physical health (Aghahowa et al., 2017), sedentary lifestyle (Moreno-Pérez et al., 2010), BMI (Guaraldi et al., 2012), diabetes (Guaraldi et al., 2012) and atherosclerosis parameters (Guaraldi et al., 2012).

### Psychosocial factors

Nine studies considered whether at least one psychosocial factor was associated with ED. The evidence for psychological distress related factors is somewhat mixed, yet five out of seven studies found these factors

to be associated with ED. Social and relational factors have been investigated less frequently (three studies) than psychological factors (seven studies), therefore drawing any conclusions on these would be premature.

Regarding psychological distress related factors, two papers found anxiety to be associated with ED (Fumaz et al., 2017; Perez et al., 2013). Depression was found to be associated with ED in four (Crum-Cianflone et al., 2007; Hart et al., 2015; Moreno-Pérez et al., 2010; Wang et al., 2013) out of six studies (Perez et al., 2013; Romero-Velez et al., 2014) that examined this. There were no major discernible differences between these studies to explain these contrary findings. Of the two studies which found no relationship between depression and ED, one only included men with asymptomatic HIV (Perez et al., 2013) and the second sample comprised men on antiretroviral medications only (Romero-Velez et al., 2014). Moreover, two of the studies did not report the sexual orientation of their sample (Crum-Cianflone et al., 2007; Perez et al., 2013), which makes the comparison between studies difficult.

Regarding relational factors, low social support was not found to be significantly associated in a Spanish study (Fumaz et al., 2017). Another study conducted in an Italian metabolic clinic found satisfaction with facial appearance to be significantly associated with ED (Guaraldi et al., 2012). One community-based study conducted in Belgium found relational factors such as taking a more passive sex role, and not having a steady relationship to be associated with ED (Vansintjean et al., 2013).

## Discussion

The aim of this work was to systematically review published research on factors associated with ED among men with HIV. Age was associated with ED more often than not (6 vs 4 studies). The four studies that did not find a significant effect had slightly younger aged samples. We conclude that CD4 was not significantly associated with ED as a greater number of studies found no relationship compared to studies which did find a relationship (6 studies vs 2). The former were more validly conducted (used validated measurement tools). Of note, they were also more recently published which means newer HIV medications were likely examined. Length of time on antiretroviral viral medication seems to be significantly associated with more clinically significant (more severe and more frequent) experiences of ED. Yet, the cause of this association may be due to age, rather than length of time on treatment per se, and therefore longitudinal or multivariate research is required to tease apart the relationship between these factors. Some evidence suggests that protease inhibitor

treatment is significantly associated with ED. The vast majority of non-HIV general health-related factors examined were not significant. Depression was significantly associated more often than not (4 studies vs 2), two additional studies found anxiety to be a significant factor. Only three studies considered social and relational factors, there was some suggestion that satisfaction with facial appearance, taking a passive sexual role and not having a regular sexual partner are associated with ED. The direction of causality is particularly unclear with these latter two factors. For example, do those who take a passive sexual role experience greater ED, or do those who experience ED consequently adopt a more passive sexual role.

Age and depression are well-established factors associated with ED among the general population (Corona et al., 2010; Feldman, Goldstein, Hatzichristou, Krane, & McKinlay, 1994). As expected, we conclude that these factors are relevant also to PLWH. Yet in order to understand why men with HIV are 2.3 times more likely to experience ED (Shindel et al., 2011), further examination of those factors that are unique to living with HIV is required. Namely, this systematic review concludes that CD4 is not relevant, nor is type of anti-retroviral treatment, however, length of time on antiretroviral treatment and the use of protease inhibitors appear to be significant. This is the limit of our conclusions based on available evidence, yet this is highly unlikely to be the full story of why men with HIV are at greater risk of ED.

That psychosocial factors are relevant to ED is well established in the general population (Yafi et al., 2016). Yet, this review finds a distinct lack of research on social and relational factors, and anxiety relevant to men with HIV. It seems likely that anxiety, which is relevant to ED regardless of HIV status (Jannini, McCabe, Salonia, Montorsi, & Sachs, 2010), is particularly relevant to men with HIV given that disclosure of HIV status, fear of rejection by a sexual partner and fear of transmission of HIV are additional anxiety-based experiences unique to HIV. It is also likely that the cause of ED among PLWH is multi-factorial with contributions from organic and psycho-social factors, however, the studies included in this review did not employ HIV-specific theories and models to guide their research, and we are aware of no HIV-specific models of ED to guide further research in this topic. Such a model is sorely needed. Given that it is largely unknown which additional HIV-specific factors are relevant, qualitative methods to explore and develop theory are warranted. A model developed through qualitative research of the experience of sexual difficulties with HIV would be an appropriate starting point to conduct further quantitative research



on this topic. Future regression analyses of factors associated with ED should hold those factors relevant to the general population (e.g., age and general health) constant, and then explore which HIV-specific factors are associated with sexual difficulties over and above these non-HIV factors.

The strength of this systematic review lies in the well-developed, broad search strategy employed across multiple data-bases. Regarding the limitations of included studies, we conducted a power analysis using G\*Power 3.1.9.2 (Faul, Erdfelder, Lang, & Buchner, 2007) which suggested that required sample size to effect at least small effects using Regression analysis with four independent variables was 98. Two studies had sample sizes below this, such that they likely did not have appropriate statistical power to detect associations with small effect sizes. Many studies also dichotomised the erectile dysfunction outcome variable into a “yes/no” variable such that relevant sub-diagnostic erectile difficulties were lost in their analysis. Future studies should include appropriate justification for dichotomising a previously continuous variable. Moreover, most studies gave no theoretical justification for the independent variables they chose to investigate. If these studies tested all available data for potential significant effects (rather than only those for which an association with erectile dysfunction was theoretically grounded), this would increase the potential for type I error and increase the possibility of false-positive results. This systematic review is further limited by the potential for measurement error inherent in the widespread use of the IIEF-15 and IIEF-SF5 which assumes all men are penetrative sexual partners and therefore does not effectively measure ED among MSM. Research conducted in high-income nations with convenience samples recruited from HIV treatment centres forms the vast majority of the included studies. Further research conducted in developing nations, and community-based recruitment research is required to more accurately reflect the experiences of PLWH. The conclusions of this systematic review are therefore limited to the experience of erectile dysfunction above a diagnostic threshold of PLWH in high-income nations who are accessing treatment centres.

A narrative synthesis of study findings was deemed the most fitting way to report the results of this review. We decided not to pool data and conduct a meta-analysis for a number of reasons. Most factors were investigated in 1 or 2 studies, in such cases presenting these studies in a narrative synthesis only was the clearest way of presenting these results. Of the five factors investigated in three or more studies, CD4, length of time on antiretroviral and time since diagnosis were found not to be relevant to erectile dysfunction in the narrative synthesis.

For age and depression, there was heterogeneity in terms of participant demographics (including varied reporting of sexuality) and the methods for measuring erectile dysfunction meaning narrative synthesis only was again the clearest way of presenting these results. In clinical practice health professionals should therefore pay attention to those non-HIV factors consistently found to be associated with ED of men with HIV (age and depression), as well as factors unique to HIV (time on HIV treatment and protease inhibitor treatment). There is currently very little research on the role of anxiety and relational factors, such as undue fear of transmission of HIV or undue fear of rejection by a sexual partner to guide clinical practice. It is only by examining such HIV-specific experiences that health professionals can address the increased risk of ED among men with HIV. In so doing, health professionals can promote three key outcomes: increase quality of life with HIV, and increase length of life with HIV and prevent new acquisitions of the virus through greater adherence to medication. By achieving these three outcomes, we can end the impact of HIV on our societies.

## Conclusion

This systematic review concludes that age, depression, time on antiretroviral medication and protease inhibitor medication use are factors relevant to ED of PLWH. There is a dearth of research on psychosocial factors, and of theoretical models of sexual difficulties with HIV, which are appropriate avenues for future research.

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




















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## Appendix 1. Search terms used with OVID databases

<input type="checkbox"/> # ▲ Searches	Results	Type	Actions	Annotations
<input type="checkbox"/> 1 exp HIV/	93835	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 2 HIV.ti.ab.	260116	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 3 human immunodeficiency virus.ti.ab.	75997	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 4 1 or 2 or 3	263847	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 5 exp Sexual Dysfunctions, Psychological/	24651	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 6 exp Sexual Dysfunction, Physiological/	27962	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 7 exp Erectile Dysfunction/	17931	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 8 exp Premature Ejaculation/	321	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 9 exp Dyspareunia/	1922	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 10 sexual function*.mp.	10847	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 11 sexual dysfunction*.mp.	16683	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 12 (sexual adj5 difficulties).mp.	826	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 13 (sexual adj5 concerns).mp.	958	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 14 psychosexual.mp.	5314	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 15 erectile dysfunction.mp.	20968	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 16 dyspareunia.mp.	3840	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 17 sexual malfunction.mp.	7	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 18 sexual disorder.mp.	172	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 19 sexual desire disorder.mp.	374	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 20 sexual arousal disorder.mp.	137	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 21 premature ejaculation.mp.	1308	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 22 retarded ejaculation.mp.	48	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 23 early ejaculation.mp.	29	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
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<input type="checkbox"/> 25 orgasm* disorder.mp.	100	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>
<input type="checkbox"/> 26 anorgasmia.mp.	227	Advanced	<a href="#">Display Results</a> <a href="#">More ▾</a>	<input type="checkbox"/>

<input type="checkbox"/>	27	sexual pain disorder.mp.	26	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	28	vaginismus.mp.	344	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	29	vaginal dryness.mp.	784	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	30	vulvodynia.mp.	642	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	31	vulvar vestibulitis.mp.	308	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
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<input type="checkbox"/>	33	sexual dissatisfaction.mp.	175	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	34	impotence.mp.	6515	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	35	sexual avoidance.mp.	25	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	36	"avoidance of sex".mp.	30	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	37	intimacy.mp.	3000	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	38	sexual intimacy.mp.	209	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	39	sexual relationship.mp.	843	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	40	sexual satisfaction.mp.	1747	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	41	sexual wellbeing.mp.	35	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	42	sex life.mp.	1041	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
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<input type="checkbox"/>	44	sexual interaction.mp.	285	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	45	5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44	56734	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	46	exp Risk Factors/	728496	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
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<input type="checkbox"/>	50	correlat*.mp.	1449592	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
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<input type="checkbox"/>	54	predict*.mp.	1191398	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
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<input type="checkbox"/>	56	associat*.mp.	3449487	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	57	46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56	8114487	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	58	limit 57 to yrs="1980 -Current"	7547222	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
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<input type="checkbox"/>	61	59 or 60	788805	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	62	4 and 45 and 57	871	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	
<input type="checkbox"/>	63	(62 and 58) not 61	552	Advanced	<a href="#">Display Results</a>	<a href="#">More ▾</a>	