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Review article

HIV-related care for transgender people: A systematic review of studies from around the world



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ABSTRACT

Rationale: Transgender people face unique challenges, such as structural, interpersonal, and individual vulnerabilities to chronic diseases. Stigma and prejudice may hamper their access to health care and prevent their inclusion in the labor market, as well as cause exposition to violence. Labor market exclusion contributes to engagement in survival sex work, which increases HIV infection vulnerability. HIV continuum of care combines HIV prevention (including antiretroviral pre-exposure prophylaxis (PrEP), antiretroviral post-exposure prophylaxis (PEP) and HIV testing) with linkage to care (that is, initiating, maintaining and monitoring antiretroviral therapy). Currently, many studies evaluate the access barriers and facilitators to HIV care for transgender people.

Objective: The present systematic review aimed to provide a clear summary of the current literature on HIV-related care for transgender men, transgender women and gender diverse people.

Method: Inclusion criteria were peer-reviewed quantitative studies, published through April 04, 2018, concerning transgender women, transgender men and gender diverse people and HIV-related care, which was any intervention aiming to prevent, treat or alleviate the impact of HIV on these populations.

Results: From 6,585 references, 62 articles were included: Three articles had results on PEP, 18 on PrEP, 29 on HIV-testing, 17 on access to health care, and 13 on adherence to treatment.

Conclusions: The present study is the first systematic review evaluating HIV-related care for transgender people. Data collection is still scarce regarding transgender men and gender diverse people. Worldwide, testing for HIV infection does not necessarily enable access to the HIV continuum of care for transgender populations or even guarantee awareness of HIV seropositivity.

1. Introduction

Transgender is an umbrella term that refers to individuals whose sex assigned at birth diverges from their current gender identity. Transgender identity can be used with this connotation in the academic context, and many communities adopt the term. However, gender identity and expression vary across the world and are often culturally defined. Transgender people face unique challenges related to stigma (White et al., 2015). A narrative review assessing empirical reports about HIV among transgender women points out transphobia, moderated by social support and access to gender-affirming care, as responsible for maladaptive coping strategies that may lead to HIV infection (Jaspal et al., 2018). Whereas transgender women exhibit the

pooled HIV prevalence, worldwide, of 19.1% (Baral et al., 2013), gender diverse people and transgender men showed HIV infection estimates ranging from 0 to 4.3% depending on the sample (Reisner and Murchison, 2016; Herbst et al., 2008). Even though transgender men and gender variant people have documented HIV risk factors, to date, data collection is still scarce regarding these populations (Reisner and Murchison, 2016).

The HIV prevention and care continuum, or HIV care cascade, encompasses HIV testing, prevention, treatment and care services provided for people at risk of acquiring HIV infection and people living with HIV infection (WHO, 2016a,b). HIV prevention and care continuum combine prevention (including HIV testing, antiretroviral preexposure prophylaxis (PrEP) and antiretroviral post-exposure

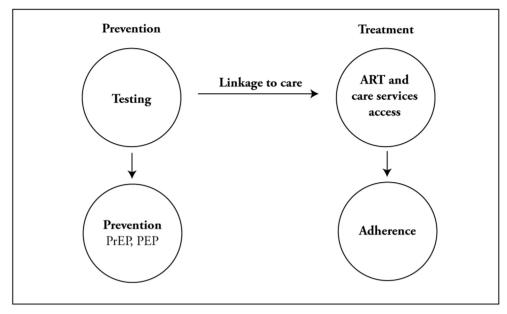
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HIV care continuum

Fig. 1. HIV care continuum.

prophylaxis (PEP)) and linkage to care (WHO, 2016a,b). The HIV prevention continuum refers to the linkage of HIV-uninfected persons to prevention services and adherence to prevention interventions with repeated HIV testing to monitor for HIV acquisition (McNairy and El-Sadr, 2014), whereas care linkage and retention focus on initiating, maintaining and monitoring antiretroviral therapy (ART) (Gardner et al., 2011; WHO, 2016a,b). (See Fig. 1).

HIV testing every three months is recommended for specific populations, such as transgender women (WHO, 2013). The main barriers to HIV testing among transgender women occurs at institutional, societal and individual-levels. Institutional and societal aspects include homelessness (Andrinopoulos et al., 2014), health care provider mistreatment (Costa et al., 2016; Logie et al., 2017; Woodford et al., 2016), confidentiality breaches (Lippman et al., 2016; Logie et al., 2017; Wirtz et al., 2017; Woodford et al., 2016), and HIV-related stigma (Andrinopoulos et al., 2014; Lippman et al., 2016; Logie et al., 2017; Pal et al., 2016; Wirtz et al., 2017; Woodford et al., 2016). Barriers to HIV testing at the individual-level might include alcohol use (Bao et al., 2016), post-traumatic stress symptoms (Bao et al., 2016), lack of education related to HIV (Pal et al., 2016), cost (Frye et al., 2015; Lippman et al., 2016; Pal et al., 2016), and internalized homophobia (Andrinopoulos et al., 2014). None of the previous studies on barriers to HIV testing explicitly discussed transgender men or gender diverse persons.

The HIV prevention continuum also includes PEP use and, more recently, PrEP, as well as reducing the viral load for preventing HIV transmission (TasP). PEP consists of a 27-day regimen of antiretroviral medication taken after exposure to HIV. Many barriers have been reported concerning human utilization, outside of work, and labor (Cohen et al., 2013a,b). These barriers include difficulty in gaining timely access to health services, an inadequacy of risk perception, and insufficiency of adherence to PEP due to adverse events (Cohen et al., 2013a,b). Even though PEP has been available since the 1990s, limited awareness has been shown among transgender women (Costa et al., 2018; Liu et al., 2008; Mehta et al., 2011).

PrEP consists of the daily use of one or more antiretroviral drugs by seronegative individuals to prevent HIV infection (Jiang et al., 2014). PrEP has shown to be an effective strategy in at least five placebocontrolled trials that included the most vulnerable populations (Jiang et al., 2014). The effectiveness of PrEP is, however, dependent on uptake, acceptability, and adherence (Yang et al., 2013). Regarding transgender populations, many recent articles concerning PrEP awareness and uptake, as well as adherence to treatment, have been published. Briefly, these studies showed diminished awareness and many particularities that may act as barriers to adherence to treatment for transgender people, such as concern about interactions with hormone treatment and health services distrust (Deutsch et al., 2015; Eaton et al., 2017a, 2017b; Garnett et al., 2018; Hoagland et al., 2017a, b; Kuhns et al., 2016; Oldenburg et al., 2016; Rael et al., 2018; Uthappa et al., 2018; Wang et al., 2017; Wood et al., 2017; Yang et al., 2013; Zalazar et al., 2016).

Finally, treatment as prevention (TasP) is based on the finding that people living with HIV with total and constant suppression of the viral plasma count for at least six months are no longer considered to be potential sources of HIV transmission (Attia et al., 2009). Viral suppression is achieved through adherent use of ART. Therefore, the challenges of TasP are evident: Not all individuals living with HIV are diagnosed and, even if they are tested for HIV and receive the results and treatment accordingly, some of them may experience side effects from using ART, and many are simply not going to use ART assiduously (Kuchenbecker, 2015). Nevertheless, TasP has not yet been evaluated in key populations, such as transgender women (Cohen et al., 2013a,b).

Adherence is the crucial point of HIV care linkage. There are many complex factors associated with non-adherence (Ahmed et al., 2018). Adherence depends on patient characteristics but also on medication side effects and interpersonal relations (Ahmed et al., 2018). For example, depression has been strongly associated with noncompliance (DiMatteo et al., 2000), as well as poor patient-provider relationships (Johnson et al., 2006). As mentioned above, transgender people face unique challenges in accessing health services such as bad experiences with health providers, fear of mistreatment, and lack of provider knowledge (Costa et al., 2016; Woodford et al., 2016). These difficulties may also affect HIV-related care, especially adherence to ART.

2. Theoretical framework: vulnerability and human rights framework

The vulnerability and human rights frameworks are the theoretical models that informed this review (Ayres et al., 2011). Vulnerability analyses involve three dimensions: individual, social, and

programmatic. The individual dimension of vulnerability does not ignore the biological aspects but considers the psychosocial aspects such as the amount of information that people may have regarding prevention. This dimension also considers individuals as the citizen-rights holder. The social dimension of the vulnerability is comprised of the intersectionality of aspects such as gender, race, migratory status, social class, sexual orientation, generation, as well as, religious beliefs, and others. Finally, the programmatic dimension of vulnerability considers health care policies and institutions, analyzing the way they may reduce or increase the vulnerability conditions of individuals and groups in their territories.

Fundamental to this vulnerability is a human rights perspective (Gruskin and Tarantola, 2004). The analysis of human rights violations or protections addresses contexts that boost or compensate inequities in health. This framework recognizes that HIV infection occurs at the individual-level but emphasizes the institutional and societal factors that create greater or lesser vulnerability to risk-behaviors (Ayres, 1997; Ayres et al., 2000, 2012). For example, the non-guarantee of fundamental rights, such as the possibility of administrative change of names in civil registries, impacts on the social level, since health care professionals and services will take less account of the correct nominal treatment of transgender people, which will ultimately impact on the individual-level, causing anticipation of discrimination and avoidance to those health care services, thus having less access to prevention and care. A recent meta-analysis identified these aspects and their complex interaction among HIV-risk transgender populations (Poteat et al., 2015).

3. Objectives

The UNAIDS Fast-track commitments to end AIDS by 2030 established as the first concern to successfully integrate people living with HIV into health care in order to suppress their viral load, improve their health, and reduce their risk of transmitting HIV infection (UNAIDS, 2014). To that end, they presented 90/90/90 goals: by 2020, 90% of all people living with HIV should know their HIV status, 90% of all the persons diagnosed HIV infection should continuously receive ART, and 90% of all people receiving ART should have viral suppression (UNAIDS, 2014). Currently, worldwide, numerous studies are assessing the multiple steps of the HIV continuum of care for transgender people, particularly for transgender women. The present systematic review seeks to summarize the literature on HIV-related care for transgender people to advise future interventions, health surveillance, and public health policies and help to promote health equity.

4. Method

4.1. Protocol and registration

The present systematic review followed PRISMA recommendations (Moher et al., 2009) and also satisfied the AMSTAR 2 (Shea et al., 2017); see supplementary material for both checklists. The review was registered online on International Prospective Register of Systematic Reviews (PROSPERO 2017 CRD42017071213).

4.2. Eligibility criteria

The included articles presented research data on transgender people and HIV-related care. For this review, HIV-related care was considered to encompass all interventions aiming to prevent, treat or alleviate the impact of HIV on transgender persons. It included studies focusing on HIV-negative transgender persons such as PEP, PrEP and HIV testing – as well as articles concerning the access to linkage to care for HIVpositive transgender people – that is, access to health providers and adherence to treatment. Inclusion criteria were as follows: (a) have transgender women, transgender men or gender variant persons as participants; (b) analyze at least one form of HIV/AIDS-related care – that is, PEP, PrEP, treatment as prevention, HIV testing, barriers or facilitators to health care assistance and adherence to ART; (c) be a quantitative research article; (d) have been written in English, French, Spanish or Portuguese; and (e) be an indexed peer-reviewed article.

In contrast, the exclusion criteria were as follows: (a) includes incomplete or ambiguous methods; (b) is not a complete article, that is, a poster or abstract; (c) is not available for downloading; (d) does not present results of a direct evaluation of HIV/AIDS-related care for transgender people, for example, an analysis of government programs; and (e) does not present any result exclusively concerning transgender women, transgender men or gender variant persons. It is noteworthy that articles concerning condom use, rectal microbicides, and HIV vaccine were not included in the string search and, if selected, were excluded during the screening process. Even though condom use, rectal microbicides and HIV vaccine are prevention strategies and, therefore, could be considered HIV/AIDS-related care, the review included only strategies already available for population use. Furthermore, approaches, such as condom and rectal microbicides use, which are strongly dependent on individual characteristics, were not included.

4.3. Study selection

All references were extracted to Mendeley or EndNote software on April 04, 2018. The articles' organization, as well as the studies' inclusion and exclusion, was carried out in these programs. During the database search, the following articles were found in each database: PubMed (n = 1,336), Scopus (n = 1,276), EBSCO (n = 1,502), Global Health (n = 937), PsycINFO (n = 154), Web of Science (n = 1,131), and POPLine (n = 249). In total, 6,585 articles were found. (For search strings, see the Electronic Supplementary Material.)

After 3,407 duplicates were removed, the 3,178 remaining articles had their titles and abstracts screened by three independent reviewers (AMVF, GZ, and MF). Any discrepancy was resolved through discussion among the three reviewers (AMVF, GZ, and MF). After applying the inclusion criteria, the full text was retrieved and independently assessed for eligibility by three independent reviewers (AMVF, GZ, and MF). At this point, the exclusion criteria were applied (See Fig. 2 and, for additional information, see a list containing all screened articles in the Electronic Supplementary Material.).

4.4. Data collection process

A standardized, pre-piloted form was used to extract data from the included studies to assess study quality and evidence synthesis. Three reviewers independently collected data and unified views after joint reading.

4.5. Risk of bias

Risk of bias was assessed for the 62 included articles according to Sanderson and collaborators (2007) (See Table S5 in the Electronic Supplementary Material.).

5. Results

5.1. Study characteristics

Three articles included information on PEP; 17 articles on PrEP; 27 articles, on HIV-testing; 17 articles on access to health care; and 13 articles on adherence to treatment. More than half (46) were published during or after 2015, and only three articles were published before 2010 (see Fig. 3). All three articles published before 2010 are from the US (Harawa and Bingham, 2009; Holstad et al., 2006; Melendez et al., 2006). In fact, 30 of the 62 (48.4%) selected articles have samples collected in the US. The other 32 articles included samples from Brazil,

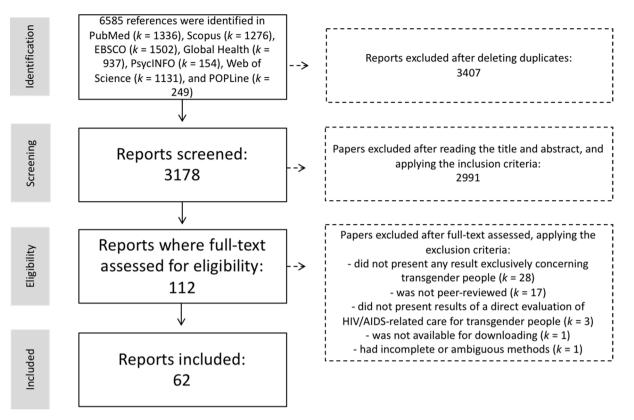


Fig. 2. Flow of reports into the systematic review.

Peru, Thailand, Indonesia, Vietnam, China, United Kingdom, Jamaica, El Salvador, India, Myanmar, Argentina, Puerto Rico, and Portugal. See Fig. 4.

The articles were classified in two main categories as follows: prevention continuum or health care assistance for HIV-negative transgender people (PEP, PrEP and HIV testing) and linkage to care or health care assistance for transgender people living with HIV (access to medical assistance and adherence to treatment).

5.2. Health care assistance for HIV-negative transgender people: HIV prevention continuum

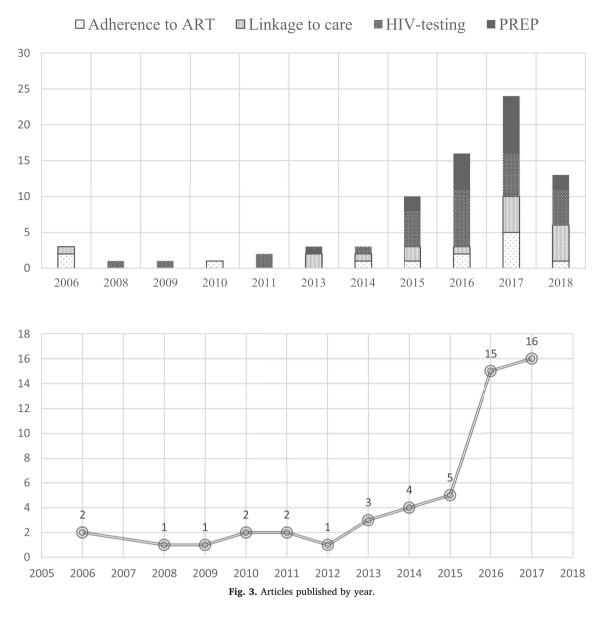
PEP. In Brazil, a study including transgender adults from Sao Paulo and Rio Grande do Sul verified that 71% of them did not know what PEP was, 26.5% were familiar with it but had never used it, and only 2.6% had already used it (Costa et al., 2018). When considering adult transgender women from Rio de Janeiro PEP awareness and willingness was almost 70% (Hoagland et al., 2017a,b). In the US, a study including 121 transgender youth verified that five young transgender women have already used PEP (4.1%).

PrEP. Results concerning PrEP awareness and interest were divergent. In a sample of 107 adult transgender women, from Thailand, 66% of them had prior knowledge of PrEP and PrEP acceptability was 37% among these respondents (Yang et al., 2013). In contrast, only 13.1% of 168 adult transgender women, from Vietnam, were aware of PrEP, and after hearing about the uses and efficacy of PrEP, 79.2% of 168 HIV-uninfected transgender women reported being interested in taking PrEP (Oldenburg et al., 2016). More recent studies presented a higher PrEP awareness: 57.1% of 56 adult Brazilian transgender women (Hoagland et al., 2017a,b) and 42.6% of 54 US transgender women (Eaton et al., 2017b) were aware of PrEP; even considering transgender youth PrEP awareness: 42.7% of 67 US young transgender women (Wilson et al., 2016) and 64% of 25 US young transgender women were aware of PrEP (Wood et al., 2017). Interest in using PrEP varied from

8.3% of six adult transgender women from the US (Eaton et al., 2017a) to 89.3% of 56 adult transgender women from Brazil (Hoagland et al., 2017a,b). The prevalence of actual use of PrEP is relatively low, especially concerning transgender youth: 1.5% of 67 US young transgender women (Wilson et al., 2016), 5% of 180 US young transgender women (Kuhns et al., 2016), and 8.2% of 181 US transgender youth (Reisner et al., 2017a). Only one study, by Reisner and collaborators (2017a,b), assessed PrEP among transgender men: None had ever used PrEP (Reisner et al., 2017a). See Table 1 and for a summary of all included publications addressing PrEP see Table S1 in the Electronic Supplementary Material.

The included studies showed different barriers to PrEP awareness, interest, and use. Among the reasons for not being interested in using PrEP, adult transgender women, from the US and Thailand, were especially worried about the interactions between PrEP and their other medications (Wilson et al., 2016; Yang et al., 2013). Adult transgender women, from the US and China, were also concerned about the possibility of side effects affecting their daily life (Rael et al., 2018) and that their male sex partner would consider the use of PrEP as a symbol of distrust (Wang et al., 2017; Wilson et al., 2016). Previous experience of discrimination by health care workers was also associated with diminished odds of willingness to use PrEP among adult transgender women from Argentina (Zalazar et al., 2016). Furthermore, many transgender women, from US, who were not interested in using PrEP associated PrEP with "promiscuous" behavior and reported that the Centers for Disease Control and Prevention (CDC), as well as the drug industry, cannot be trusted to tell gay communities the truth about PrEP (Eaton et al., 2017a).

Another critical barrier to PrEP use is adherence. The iPrEX trial was a randomized control trial (RCT) to evaluate the efficacy of PrEP. Deutsch and collaborators (2015) analyzed the iPrEX data to determine differences in PrEP efficacy for adult transgender women relative to cisgender men who have sex with men and examined factors associated with efficacy and patterns of PrEP use (Deutsch et al., 2015). Among the



286 US transgender women included in the RCT, only 33 obtained protective drug concentrations – that is, the remaining 253 transgender women were not sufficiently adherent to use more than four pills per week. Consequently, HIV seroconversion was similar between PrEP and placebo groups: 11 transgender women participants in the intervention group seroconverted compared to 10 transgender women in the placebo group. None of the transgender women who became infected had detectable drug levels at the time of seroconversion. Therefore, the lack of protection was a result of low adherence to PrEP. A Brazilian cohort also analyzed adherence to PrEP, during 48 weeks follow up (Grinsztejn et al., 2018), and found higher levels of adherence than was reported by adult transgender women in the iPrEX trial (Deutsch et al., 2015). More precisely, the Brazil-based study found that of the 25 transgender women enrolled in the trial 12 had protective drug concentrations at week 48 (Grinsztejn et al., 2018).

HIV testing. Brazil, China, Thailand and Vietnam presented the lower percentages with 27.0% (Castro et al., 2016), 34.6% (Best et al., 2015), 43.6% (Chariyalertsak et al., 2011) and 43.9% (Oldenburg et al., 2016) respectively of transgender women that ever tested in the past. It is noteworthy that, when evaluating transgender youth, the US also exhibited low percentages, with 41% of 111 US transgender youth that have ever been tested (Fisher et al., 2017). (See Table 2).

Five studies included and provided separated results for transgender

men and gender diverse people (Chen et al., 2011; Costa et al., 2018; Fisher et al., 2017, Reisner et al., 2017a,b, Schulden et al., 2008). Considering the US studies, 69% of 59 North American transgender men have tested in the last 12 months (Chen et al., 2011), while 26.7% of 25 young transgender men and 48% of 42 adult transgender men have ever tested (Fisher et al., 2017, Schulden et al., 2008). From Brazil, 50.6% of 156 transgender men and 52% of 50 gender diverse people had been tested in the past (Costa et al., 2018).

Only three articles considered the possibility of being tested but not actually receiving the results (Chariyalertsak et al., 2011; Lee et al., 2015; Prabawanti et al., 2015). Prabawanti and collaborators (2015) verified that 90.4% of 209 Indonesian *waria* had been tested for HIV, but only 64.6% had collected the results. Lee and collaborators showed that among men who have sex with men and transgender women, from Peru, 12.9% of ever-testers reported not returning for their results. Providing STI and HIV test services in the same place and releasing the results on the same day were indicated as factors that could improve attitudes toward HIV testing, and the likelihood of collecting the results (Prabawanti et al., 2015).

Numerous studies evaluated facilitators and barriers to HIV testing. Among the reasons to test, most Brazilian transgender women were tested in public services for "curiosity", as well as for "feeling at risk" (Pinheiro et al., 2016). Only 8% of them were tested because of a

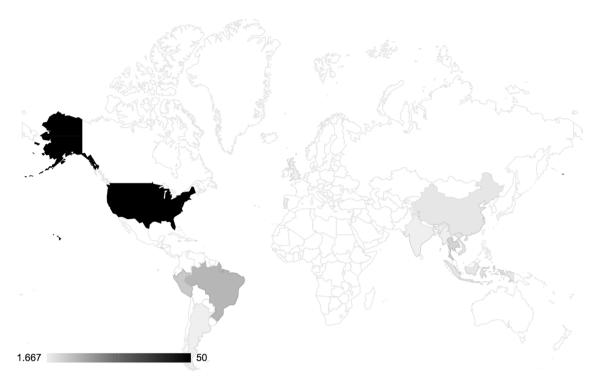


Fig. 4. US samples represented 50% of the total sample; two articles are not represented because these studies examined samples from many different countries.

doctor's recommendation (Pinheiro et al., 2016). Sociodemographic factors associated with avoiding HIV testing include younger in age (< 18 years), being single, and reporting no religious affiliation (Andrinopoulos et al., 2014; Bao et al., 2016; Pinheiro et al., 2016; Reisner et al., 2017a). Avoidance due to concerns over anonymity and expected prejudice were also reported (Costa et al., 2018). Accordingly, transgender women from Thailand who reported higher total HIV-related stigma had lower odds of being tested for HIV (Logie et al., 2016). Eight-five percent of US transgender women were receptive to the idea of peer-delivered HIV testing (Veronese et al., 2018).

5.3. Health care assistance for transgender people living with HIV: linkage to care

Access to HIV-related care. This category included HIV related health services use, health-seeking behaviors after HIV diagnosis and factors associated with lower access to HIV-related care, mainly represented by the number of medical consultations, use of ART and HIV virologic suppression.

Adult transgender women living with HIV had a significantly higher risk of presenting late for HIV care compared to other people living with HIV in Thailand (Koirala et al., 2017). In Indonesia, 78.5% were linked to HIV care within three months after receiving their HIV diagnosis, and this figure did not differ between men who have sex with men and transgender women (i.e., known as waria in Indonesia); however, men who have sex with men were more likely to have at least one health care visit every three months (73%) than waria (59%) (Nugroho et al., 2017). Considering adult transgender women who have initiated ART, the lower percentage is from Peru, where only 37% of transgender women sex workers are using ART (Degtyar et al., 2018), and the higher is from Brazil, with 82.1% of transgender women using ART (Costa et al., 2018) (see Table 3). As reported, transgender women from Peru exhibited lower access to care when compared to heterosexual, gay and bisexual samples (Silva-Santisteban et al., 2013). Only one study found divergent results: No discrepancies were seen between transgender women and cisgender persons concerning HIV-related health status, the mean number of visits to a health care worker, and health security

coverage (Melendez et al., 2006). It is noteworthy that the mean number of meetings with primary care providers in the past three months was 3.9 among transgender women versus 3.4 among cisgender persons, which is high and probably related to the place of recruitment (Melendez et al., 2006). US samples were collected in outpatient clinics and community organizations for patients who are HIV-positive (For additional information, see Tables S3 and S4 in the Supplementary Materials.).

Among the reasons to present late for HIV care, previous experiences of discrimination were highlighted. Transgender women living with HIV, from the UK, more frequently avoided care and felt refused treatment, in STI clinics, when compared to cisgender people (Hibbert et al., 2018). In Brazil, 48.7% of transgender women living with HIV reported some discrimination in the health care context. Black racial identity, low income (less than 160 USD) and unstable housing were associated with significantly lower odds of viral suppression (Jalil et al., 2017).

Adherence to ART. In general, adherence to ART was lower among transgender women compared to cisgender women and, accordingly, US transgender women were less likely to achieve viral suppression (Baguso et al., 2016; Kalichman et al., 2017; Mizuno et al., 2015). (See Table S4 in the Supplementary Materials).

Only one study exhibited results on transgender men receiving HIVrelated medical care (Lemons et al., 2018). Although they represent only 11% of the included US transgender people living with HIV, they showed unmet health care needs: 41% were not virally suppressed in their last test, and 40% had not maintained viral suppression in the last year (Lemons et al., 2018).

Multiple studies assessed facilitators and barriers to ART adherence. The main factor associated with inferior adherence to ART was fewer positive provider interactions (Sevelius et al., 2010). In comparison to other respondents, US adult transgender women disclosed significantly fewer positive interactions with their health care providers (Sevelius et al., 2010). Concern for ART and hormonal therapy interactions were also listed as an important reason for not taking ART, hormonal therapy, or both among US transgender women (Braun et al., 2017b). Furthermore, among US transgender women, lower dose adherence was

Table 1 PrEP awareness, inter	rest, histor	Table 1 PrEP awareness, interest, history of use and adherence.					
Reference	Country	Sampling method	Quality rating	Awareness	Interest	Ever take	Adherence
Deutsch et al. (2015)	SU	Clinic-based recruitment	+ + +	I	I	I	88.5% of 339 transgender women did not presented adherence to treatment enough to use more than four pills
Eaton et al. (2017a)	SU	Gay Pride events	+ + +	I	8.3% of 6 transgender	I	per week -
Eaton et al. (2017b)	SU	Gay Pride events	+ + +	42.6% of 54 transgender	мошеп –	I	I
Grinsztejn et al. (2018)	Brazil	Respondent-driven sampling	++++	-	I	I	48% of 25 transgender women had not protective drug concentrations at work 48
Hoagland et al., 2017a.b	Brazil	Respondent-driven sampling	+++	57.1% of 56 transgender women	89.3% of 56 transgender women	I	
Kuhns et al. (2015)	SU	Convenience sampling grounded in community-based participatory research principles	+++++	30.6% of 180 transgender women	68.9% of 180 young transgender women	5% of 180 young transgender women	
Oldenburg et al.	Vietnam	Social networks	+ +	13.1% of 168 transgender women	79.2% of 168 transgender women	I	1
Rael et al. (2018)	SU	Community-based recruitment and venue- based annroach	+++	96.3% of 28 transgender women		22.2% of 28 transgender women	1
Reisner et al. (2017)	SU	Clinic-based recruitment	+++		I	8.2% of 181 transgender	
Wang et al. (2017)	China	Clinic-based recruitment	++++	I	61.2% of 183 transgender		1
Wilson et al. (2016)	SU	Not described (secondary data analysis)	+	42.7% of 67 young transgender women	wonnen 73.9% of young transgender women	1.5% of 67 young transcender women	I
Wood et al. (2017)	SU	Clinical and community-based organizations	+++++	64% of 25 young transgender women			
Yang et al. (2013)	Thailand	Venue-day-time sampling	+ + +	66% of 107 of transgender women	37% of 107 transgender women	I	I
<i>Notes.</i> 0 = no risk of	f bias; 1 =	Notes. 0 = no risk of bias; 1 = risk of bias; + + + low risk of bias; + + moderate risk of bias; + high risk of bias.	moderate ri	sk of bias; + high risk of	bias.		

Reference	Country	Sampling method	Quality rating	Tested for HIV in the past?
Bao et al. (2016)	Vietnam	Snowball	++++	59.3% of 204 Vietnamese transgender women have tested in the past.
Best et al. (2015)	China	Internet based	+++++	34.6% of 52 Chinese transgender women have tested in the past.
Bustamante et al. (2015)	Peru	Clinic-based recruitment	+	78% of 45 transgender women from Peru tested in the past.
Castro et al. (2016)	Brazil	Community-based	+++++	27.0% of 37 Brazilian transgender women have tested in the past.
Chariyalertsak et al. (2011)	Thailand	Clinic-based	+	43.6% of 140 Thai transgender women have tested in the past.
Chen et al. (2011)	SU	Chart review	+	69% of 59 North American transgender men have tested in the last 12 months.
Costa et al. (2018)	Brazil	Clinic and Internet based	+++	From Brazil, 72.7% of 334 transgender women, 50.6% of 156 transgender men and 52% of 50 GDP had been tested in
				the past.
Degtyar et al. (2018)	Peru	Sex work venues	+++++	84% of 181 transgender women sex worker from Peru, tested in the past, and 44% in the last 6 months.
Denson et al. (2017)	SU	Respondent driven sampling	+++	58% black and Latin US transgender women had tested for HIV in the last 12 months.
Fisher et al. (2017)	SU	Internet based	+++	41% of 111 US transgender youth had been tested.
Gama et al. (2017)	Portugal	Sex work venues	+++	97.6% of 125 TW, involved on sex worker, from Portugal tested in the past.
Harawa and Bingham, 2009	SU	Venue based sampling and community-based	+++	91.0% of 128 US transgender women sex worker have tested in the past.
		organizations		
Jalil et al. (2017)	Brazil	Respondent driven sampling	+++++	89.2% of 345 transgender women, from Brazil, have tested in the past.
Lee et al. (2015)	Peru	Snowball	+++++	89.4% of 208 transgender women from Peru tested in the past.
Logie et al. (2016)	Jamaica	Snowball	+++++	75.7% of 137 transgender women from Jamaica have tested in the past.
Oldenburg et al. (2016)	Vietnam	Social networks	+++	43.9% of 168 transgender women from Vietnam tested in the last 12 months.
Pinheiro junior et al. (2015)	Brazil	Internet-based	++++	69% of 304 Brazilian transgender women tested in the past.
Porsch et al. (2016)	SU	Snowball	+	64% of 113 transgender men, transgender women and gender diverse people, from US, were tested for HIV in the last
				12 months.
Prabawanti et al. (2015)	Indonesia	Cluster sampling	++++++	90.4% of 206 warias from Indonesia tested in the past.
Reisner et al., 2017a,b	SU	Clinic-based recruitment	++++	92.3% of 181 transgender youth had been tested for HIV in their lifetime.
Scheim et al. (2016)	Global	Internet-based	+++++	91.1% of 69 transgender men, who have sex with men, from many countries, reported that their last HIV test result was
				negative.
Schulden et al. (2008)	SU	Venue based sampling and community-based	++++	54% of 299 US transgender women and 48% of 20 transgender men reported having been tested for HIV in the past
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Notes. 0 = no risk of bias; 1 = risk of bias; + + + low risk of bias; + + moderate risk of bias; + high risk of bias.

Reference	Country	Sampling method	Quality rating	Initiated art	Adherence to art
Costa et al. (2018)	Brazil	Clinic and Internet based	++++++	82.1% of 39 transgender women living with HIV and older than 18 year reported using ART.	
Baguso et al. (2016)	SU	Secondary data analysis	+ + +		TW had lower adherence to ART compared to cisgender males and females and were less likely to achieve viral suppression.
Degtyar et al. (2018)	Peru	Sex work venues	+ + +	37% of transgender women involved in sex work are using ART comparing with 77% of male sex workers.	-
Denson et al. (2017)	SU	Respondent driven sampling	++++	75% of 44 transgender women living with HIV were on ART.	1
Dowshen et al. (2016)	SU	Secondary analysis	+ +	1	Young transgender women reported suboptimal ART adherence when compared to young cisgender people (51% vs. 30%).
Holstad et al. (2006).	SU	Clinic-based	+ +	1	Transgender persons had the lowest mean adherence score (77.8%).
Lemons et al. (2018)	SU	Chart review	+	1	83% reported being 100% dose adherent during the past 3 days. About 69% had an undetectable viral load at their most recent test, and 60% had maintained undetectable viral loads over the previous 12 months.
Melendez et al. (2006)	SU	Convenience sampling	+ +	Fewer TW (59%) than control subject (82%) of 59 transgender women living with HIV reported currently taking ART.	
Mizuno et al. (2017)	SU	Chart review	+ +	· ·	80.5% of transgender women self-reported dose adherence to ART.
Mizuno et al. (2015)	SU	Chart review	+	1	Transgender women were significantly less likely than cisgender men to report 100% dose adherence (78% vs. 87%), and less likely to achieve sustained viral suppression (51% vs. 61%).
Reisner et al., 2017a,b	SU	Clinic-based recruitment	+ +	83.9% of 56 transgender women living with HIV, aged between 16- and 24-years old initiated ART, of which 85.1% were still currently taking ART.	62.5% self-reported being adherent to their ART medications last weekend and 55.0% reported being adherent over the last week. Only 57.1% knew their viral load, of which 65.6% were virologic suppressed.
Sevelius et al. (2010)	SU	Community agencies and health care clinics that served HIV-infected clients.	+ +	1	Transgender women were less likely to report 90% or higher adherence rates.
Sevelius et al. (2014)	SU	Street outreach, venue-based sampling, and snowball sampling	+ +	1	About a third of transgender women reported excellent adherence to ART and over 20% reported having a detectable viral load at last assessment.
Santos et al. (2014)	SU	Respondent driven sampling	+ + +	65% of 123 transgender women living with HIV, with more than 18-years old were currently on ART.	1
Yehia et al. (2013)	SU	Chart review	+ +	76% of 264 transgender women living with HIV and transgender men living with HIV. older than 18 year received ART.	1

Notes. 0 = no risk of bias; 1 = risk of bias; + + + low risk of bias; + + moderate risk of bias; + high risk of bias.

associated to a younger age, not having health insurance coverage, depression, lower self-efficacy to take medication as prescribed, and having more than one daily ART dose (Mizuno et al., 2015). Accordingly, also among US transgender women, ART adherence was related to older age, abstinence from alcohol, positive gender affirmation, and adherence to hormonal therapy (Sevelius et al., 2014).

6. Discussion

Considering the 90/90/90 goals established by UNAIDS Fast-track commitments to end AIDS by 2030, it is clear that, although there are significantly cross-cultural variations, worldwide transgender people are not sufficiently engaged in each stage of the HIV prevention and care continuum. The present discussion evaluates important topics on HIV prevention continuum (including PrEP and HIV testing) and linkage to HIV-related care (briefly commenting on access to health and adherence to treatment). In sequence, five critical topics that should receive special attention in future research are presented: transgender youth, health care provider interactions, transgender sexual diversity, transgender men and gender diverse people, and cultural nuances.

6.1. Health care assistance for HIV-Negative transgender women: HIV prevention continuum

PrEP. Levels of PrEP awareness, interest, and use varied significantly depending on the study. Two main reasons can justify the differences among articles and the first concerns cross-cultural variations. That is, countries that have PrEP available for many years will exhibit higher awareness. Accordingly, US studies showed higher awareness than, for example, Vietnam articles (Eaton et al., 2017b; Oldenburg et al., 2016). Second, the studies used different methodologies and definitions to evaluate PrEP awareness, acceptability, and interest. For example, Yang and collaborators (2013) evaluated acceptability by asking if PrEP was 50% effective in preventing HIV infection and how likely respondents were to use PrEP as an HIV prevention method (Yang et al., 2013). In contrast, Oldenburg and collaborators (2016) developed the concept of PrEP readiness, which included having heard of, being interested in taking, and believing that PrEP is efficacious. They explained to participants that PrEP was a medication capable of reducing the risk of HIV infection by up to 92% (Oldenburg et al., 2016). It is not surprising that the results were divergent (See Table S1 in the Supplementary Materials.).

The second reason is as follows: Even if PrEP awareness was high among transgender people, being aware is not enough for true adherence to daily tablets. Instead, one must have interest in using PrEP and have enough money to pay for it, as well as have reported sexual risk practices in the last six months. In countries where this technology is available, many transgender women are not interested in using PrEP, mostly because they fear interactions between PrEP and their other medications, particularly hormonal therapy (Deutsch et al., 2015; Yang et al., 2013). Another factor, reported among North American transgender women, is distrust of health services, including both the CDC and the pharmaceutical industries (Eaton et al., 2017a; Reisner et al., 2017b), and previous experience of discrimination by health care workers, described among Latin American transgender women (Zalazar et al., 2016). Considering that a high proportion of transgender women avoid health services (43.9% of 249 Brazilian transgender women), fearing exposure to violence (Costa et al., 2016; Socías et al., 2014), it is plausible that they also hesitate to adhere to treatments that are not as highly desired and have not shown as clear results as feminizing and masculinizing hormone therapy (Sevelius et al., 2010). Finally, economic marginalization is a significant impediment to the monthly acquisition of PrEP for countries whose governments do not offer it in public health services.

HIV testing. In Brazil, few transgender women reported having an HIV test recommended by a doctor among their reasons for testing

(Pinheiro Júnior et al., 2016). Therefore, it is not surprising that posttest counseling is frequently not included (Wirtz et al., 2017), and it was not reported by almost all articles in the present review.

Regarding facilitators and barriers to HIV testing, HIV testing was more frequent among transgender women, from developing countries, who reported risk behaviors, such as those who did not use condoms (Lee et al., 2015) and transgender women who would have the PrEP indication (Oldenburg et al., 2016). The association between risk behaviors and HIV testing is well established among men who have sex with men (Phillips et al., 2013). However, among transgender women, it is still controversial: Transgender women from Brazil who did not use a condom during their last sexual intercourse and reported risky silicone injection or use of alcohol and other drugs during sex were less likely to have ever been tested (Pinheiro Júnior et al., 2016). A closer look at these apparently divergent results reveals that perhaps the most important difference between the samples is age. Whereas Lee and collaborators (2015) included transgender women from Peru who were at least 18-years old; their ages varied from 23- to 35-years (median 29), Pinheiro and collaborators (2016) included transgender women, from Brazil who were at least 14-years old, with 25.8% of their sample younger than 18-years old. In fact, never-testers in the sample of Lee and collaborators were significantly younger than ever-testers (p < 0.001). In accordance with this finding, 49.9% of transgender women younger than 18-years old from the Pinheiro Junior sample had never been tested (p < 0.001). Therefore, it is possible that transgender youth endure multilevel barriers to HIV testing (e.g., stigma, cost, no local provider) that are aggravated by their young age, and the impact of being exposed to risk behaviors can only be seen in older samples. This apparent lack of care for HIV infection is probably justified by social vulnerabilities that may be aggravated during youth, including previous experiences with health care discrimination and societal and family rejection.

The differences in the prevalence of HIV testing may have been related to sampling strategies. Some studies recruited participants who were already engaged in HIV-related research studies (Bustamante et al., 2017; Lee et al., 2015). The recruitment methodology was predominately convenience sampling, including participants who attended STIs clinics (Bustamante et al., 2017; Chariyalertsak et al., 2011) and members of an NGO (Pinheiro et al., 2016). In contrast, the lower prevalence of HIV testing may also be justified by recruitment strategies that may have reached more vulnerable populations. For example, Castro and collaborators (2016), which verified that only one third of Brazilian transgender women have been tested in the past, analyzed HIV rapid tests offered at a mobile testing unit located in front of a popular LGBT venue and at the site of Arco-Íris Group, a well-known LGBT NGO (Castro et al., 2016). Furthermore, cross-cultural variations may also be responsible for the differences found in HIV testing prevalence. For example, since anticipated HIV stigma has been reported as an HIV testing barrier, regions where transgender populations are more frequently victimized may exhibit a lower HIV testing prevalence (Costa et al., 2018; Gamarel et al., 2018; Golub and Gamarel, 2013; Logie et al., 2016).

The repeated invitations for HIV testing, especially for vulnerable populations, may assume a coercive tone (WHO, 2014a,b). Communitybased testing, as well as rapid HIV testing and peer-delivered HIV testing, without counseling and with difficult linkage to treatment, can be treacherous by offering a diagnosis that is potentially fatal and certainly stigmatizing without providing survival-enabling alternatives. The HIV self-test, in which transgender women could test themselves at home or with friends, in spite of having well documented benefits (such as mitigate fear of stigma and privacy concerns), presents the same problems, aggravated by the need for confirmatory testing (Bustamante et al., 2017; Lee et al., 2015; Volk et al., 2016). Unfortunately, for populations in such a vulnerable position, HIV testing does not guarantee serostatus awareness; and HIV seropositivity awareness does not assure linkage to care. The ideal manner of testing for transgender people that endure situations of extreme vulnerability is through primary care professionals who can provide culturally competent care and are available to offer and explain the importance of HIV testing, as well as to promise assistance in the event of a positive outcome. Nevertheless, transgender people that would be able to access confirmatory testing and, in case of a positive result, to access medical treatment, may benefit the most by having a range of options available to them.

6.2. Health care assistance for transgender women living with HIV: linkage to care

Almost all included articles reported that transgender women had the lowest mean adherence score compared to cisgender men and women (see Table 3) (Baguso et al., 2016; Dowshen et al., 2016; Holstad et al., 2006; Kalichman et al., 2017; Melendez et al., 2006; Mizuno et al., 2015; Sevelius et al., 2010). It has been suggested that transgender women tend to prioritize hormone therapy at the expense of HIV-related care (Braun et al., 2017a), probably because hormonal therapy improves the quality of life (da Silva et al., 2016), lowers suicidal ideation (Bauer et al., 2015), and ameliorates depressive symptoms (White and Reisner, 2016). Another possible justification for transgender women to use hormonal therapy exclusively is that HIV care physicians may have little knowledge about drug-drug interactions, and, therefore, discourage transgender women from using both medications. In fact, it is plausible to imagine that, after investing so much money and time to obtain hormone therapy, the possibility of ART-related drugs reducing estrogen serum concentrations would be highly undesirable (Robinson et al., 2012). Furthermore, hormone therapy could cause transgender people to have a more complex side effect profile from ART use (Sevelius et al., 2010), including hyperlipidemia, weight gain, and cardiovascular disease. Despite these possible adverse effects and undesirable results, studies evaluating interactions between ART and hormonal therapy have been focused on cisgender women using oral contraceptives; thus, data demonstrating adverse effects of using both hormones and ART medications among transgender people are limited. Bearing in mind that hormonal treatment and ART use are vital for transgender people living with HIV, efforts are needed to ensure their uptake.

A possible solution to encourage HIV-positive transgender women to adhere to ART is to provide the follow-up of hormone therapy along with ART (Reisner et al., 2016, 2017b). Reisner and collaborators, through a series of focus groups with transgender women and health care professionals, evaluated barriers and facilitators to implementing a model of care that integrates HIV services with gender-affirming hormone therapy in Peru and found high levels of perceived acceptability among both transgender women and health providers (Reisner et al., 2016). Barriers and facilitators to integrating HIV services with genderaffirming hormone therapy will vary according to the country studied. In countries where social stigma towards transgender identity is widespread, transgender people may be forced to hide and, consequently, may lack access to gender-affirming hormone therapy (Winter 2009). Therefore, future studies should explore interactions between ART and hormonal therapy in transgender women, from different countries, in order to guide clinical decision making.

6.3. Areas for future research

Transgender Youth. Only six of the 62 included articles evaluated HIV-related care among transgender youth (Castro et al., 2016; Dowshen et al., 2016; Fisher et al., 2017; Reisner et al., 2017a,b; Wilson et al., 2016; Kuhns et al., 2016; Wood et al., 2017). Transgender youth exhibited a low prevalence of PrEP uptake (Reisner et al., 2017a,b). Additionally, transgender youth, compared to cisgender youth, presented lower ART adherence (Dowshen et al., 2016). Finally, transgender youth showed a lower likelihood for linkage and retention to HIV-related care (Castro et al., 2016).

Currently, adolescents aged 15- to 24-years old represent the only age range in which the prevalence of HIV infection is still rising (WHO, 2016a,b). Worldwide, poverty is repeatedly associated with HIV, as is survival sex and homelessness (Rotheram-Borus et al., 2018). Almost 70% of young transgender women reported a history of survival sex. When comparing to cisgender youth living with HIV, transgender youth living with HIV presented low educational achievement (42.0% vs. 13.0%) and were more frequently unemployed (25.0% vs. 19.0%) (Dowshen et al., 2016). Even though transgender youth are a key population for HIV prevention, few studies have explicitly explored HIV-prevention continuum and linkage to care among transgender youth. Accordingly, a global systematic review assessing research gaps suggested that young transgender populations access to HIV-related care should be further explored (MacCarthy et al., 2017).

Health Provider Interactions. All stages of the HIV-related continuum depend substantially on health professionals. Indeed, a recent systematic review exploring barriers and facilitators for transgender people accessing HIV services identified lack of knowledge among healthcare providers as one of the most important m ain barriers (Uhrig et al., 2019). Nevertheless, only a few articles considered health providers and patients' interactions among the barriers and facilitators to HIV-related care. The researchers that assessed health providers and patients' interactions verified that the lack of adherence among transgender women to both HIV testing and treatment had been associated with negative provider interactions (Logie et al., 2017; Woodford et al., 2016).

Two main factors should be considered and potentially modified. First, most health professionals do not receive adequate training to provide culturally competent care to members of transgender and gender-diverse patient populations (Poteat et al., 2013; Reisner et al., 2017b; White et al., 2017). Second, professionals who specialize in working with transgender individuals also suffer from and anticipate discrimination (Reisner et al., 2017b). Extracurricular courses and training, as well as curricular modification within health courses, should cover the basic needs (such as social terminology) and the specific needs (for example, guidelines for providing gender-affirming medical care) of transgender individuals. Thus, health professionals can assume a more active role in engaging these individuals in health assistance.

Transgender People Sexual Diversity. It is curious that only a few articles explicitly addressed participants' sexual orientation. For example, Pinheiro Júnior and collaborators included transgender women who reported having anal or oral sex in the previous year; however, since sexual orientation and partner' gender and sex were not asked, the sample might have included transgender women who have anal or oral sex with, for example, transgender men or cisgender women, using objects or fingers. A factor that may explain this lack of attention is that in diverse contexts gender identities and sexual orientations mingle culturally. For example, in some Latin American countries, such as Brazil, travestis can be socially perceived an extremely effeminate cisgender gay man, meaning that gender roles overlap with sexual orientation in these cultures (Costa et al., 2013). Therefore, investigating the sexual orientation of transgendered people in these contexts can pose great challenges in collecting this information as distinct categories.

Even though a primary driver of HIV infection in transgender women seems to be the very high transmission probability of receptive anal intercourse (Baggaley et al., 2010; Beyrer et al., 2012), it is essential to also consider the sexual orientation of transgender people (Bauer and Scheim, 2013). Transgender women who have sex with women and transgender men who have sex with men may anticipate stigma not only for being transgender but also because of their sexual minority identity and/or behavior, further aggravating their access to health services (Golub and Gamarel, 2013; Scheim et al., 2016; Starks et al., 2013). It is also possible that transgender women who have sex with women do not have a greater risk for HIV infection, but still suffer from stigmatization toward HIV infection and insistence on repeated HIV testing. Therefore, new studies should include questions concerning gender identity and expression, and sex assigned at birth, as well as, sexual behavior and, finally, sexual orientation.

Transgender Men and Gender Diverse People. A 2016 review of HIV and STI biobehavioral risks in transgender men found 25 peer-reviewed papers that addressed transgender men, corresponding to 18 quantitative and seven qualitative studies (Reisner and Murchison, 2016). Only 10 of them had laboratory-confirmed HIV serology, with HIV seropositivity between 0% and 4.3% among transgender men. Clearly, there are limited data for HIV risks including these groups. It seems that transgender men have a low risk of contracting STIs when compared with transgender women and men who have sex with men. but not necessarily when compared with cisgender men and women (Stephens et al., 2011). It is noteworthy that transgender men and gender diverse people may identify as gay and have exclusively or predominantly receptive anal sex with men, thus being at higher risk for contracting STIs. Future studies, therefore, should focus on transgender men and gender diverse people's facilitators and barriers to accessing health care services, in particular, STI-related care.

Cultural Nuances. Although the current review presents a global perspective of HIV-related health, cultural diversity among transgender populations must be considered, mainly because they may explain some of the discrepancies found. For example, in Rio de Janeiro, a study evaluating community-based HIV testing offered in a popular LGBT venue and, after working hours, at the site of a Brazilian well-known LGBT NGO, verified that only 27.0% of transgender people had been previously tested for HIV (Castro et al., 2016). In contrast, another study from Southern Brazil included transgender people recruited from a hospital and web-based cross-sectional survey and found that 63.7% of participants had already been tested for HIV infection at least once in their lifetime (Costa et al., 2018). It is possible that the clinic-based sampling mostly selected transsexual persons, whereas the communitybased sample primarily encompassed Travesti individuals. Travesti is a Latin American term that refers to persons who perform feminine roles and appearances without necessarily altering all of their physical characteristics and, therefore, usually do not seek health assistance for gender-affirming care (Vartabedian, 2016). Travesti status is associated with social stigma, as well as low socioeconomic status, psychological adversity and social exclusion, related to survival sex work (Martins et al., 2013). Therefore, a sample composed of Travesti persons probably would present lower HIV testing prevalence when compared to a sample comprising transsexual participants.

6.4. Limitations

The present review presents some limitations. First, although the present review has the ambition to overview studies from across the globe, almost half of the included reports have samples collected in the US; thus, generalizations should be made cautiously. Second, several studies that addressed primarily prevalence or incidence of HIV, mostly from the 1990s, could discuss indirectly HIV-related care and are not part of this manuscript. Therefore, a new review with a more historical outlook could incorporate that literature. Third, choosing the most appropriate terminology for researching transgender populations, due to the enormous variations of concepts used to describe transgender identity by researchers and by the communities, was a challenge. All terms suggested by Lee and collaborators and by MeSH terms were included (Lee et al., 2016) but new studies could adopt different approaches. Finally, a large number of studies concerning HIV-related care for transgender people are constantly being published; therefore, keeping the systematic review up to date was a challenge.

7. Conclusions

Considering a global perspective for the implementation of effective

care for transgender people, we can establish some guidelines based on the vulnerability and human rights framework (Winter et al., 2016). Improving an understanding of legal and social policies that impact on vulnerability, and on the effectiveness of health programs for this population, is fundamental. In this sense, the self-determined gender, in legal documents and elsewhere, is essential. Also, laws and policies protecting against discrimination on the basis of gender identity, gender expression, or bodily diversity are critical. Accordingly, a systematic review found correlations between human rights for sexual minorities and improvement on indicators of HIV prevention, such as reduction in unprotected anal intercourse and enhance in HIV testing (Anderson and Kanters, 2015). Without the recognition of gender diversity at the programmatic level, to guarantee fundamental human rights, there will be no recognition of this diversity in the training of health care professionals. In turn, professionals' attitudes will affect the quality of care and resulting health outcomes among transgender people.

Worldwide, testing for HIV infection does not enable access to the HIV continuum of care for transgender women or even guarantee awareness of HIV seropositivity. Belief in quick solutions or "magic pills" (Mayer & Zanoni, 2013; Radix and Golub, 2015), such as PrEP, suggests a shallow comprehension of HIV infection among populations as vulnerable as transgender women. Finally, the full diversity of transgender people populations, including transgender youth, should be further considered in future studies, interventions, health surveillance, and public health policies.

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Appendix A. Supplementary data

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