

# Biological, Psychosocial, Therapeutic and Quality Of Life Inequalities between HIV-Positive Men and Women – A Review from a Gender Perspective

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## Abstract

*The proportion of women infected with HIV worldwide has grown in recent years. From a transmission pattern that was once predominantly homosexual men and through intravenous use of drugs, the current pattern has become, to a large extent, heterosexual. Women are more vulnerable to be infected with HIV due to anatomical and psychosocial differences. In spite of this changing gender trend in the HIV pandemic, biological, psychosocial, therapeutic, and quality of life aspects have not been examined in detail in women. Moreover, this lack of investigation has relevance in terms of vertical transmission of the infection to newborns. Herein, we review gender differences in HIV, identifying from a gender perspective the biological and social factors with a greater influence on vulnerability to infection, and, on the other hand, examining gender differences with respect to the use of services, treatment, survival, and quality of life. (AIDS Rev. 2010;12:113-20)*

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## Key words

**HIV. Gender. Psychological factors. Therapeutics. Quality of life.**

## Introduction

The proportion of women infected with HIV worldwide has been growing over recent years. In 1997, women accounted for 41% of those living with HIV, while in 2002, this figure approached 50% and has stayed around the same level since then. In 2008, out of the 33.4 million people living with HIV worldwide, 15.7 million were women<sup>1</sup>.

Changes in the ways in which the virus is transmitted are behind this increased feminization of the disease. From a transmission pattern that was once predominantly homosexual and through intravenous drugs, the

pattern has become, to a large extent, heterosexual<sup>2-4</sup>. In spite of this change in the trend, studies of HIV among women are still much less frequent than those among men. Not only is there less information available about women with HIV, but it is often the case that such information is insufficient, even for the purposes of comparing certain aspects of their disease with that of men<sup>5</sup>.

Although many developed countries have begun to recognize gender issues in their HIV planning processes, there are still great shortages in terms of budgets and policies for tackling this problem. Healthcare systems consider the situation of men and women similar regarding organization and decision making in prevention and treatment. However, clear and significant biological differences (genetic, hormonal, and metabolic), as well as psychosocial or economic differences exist, which have an influence both on vulnerability to infection and on aspects related to the use of healthcare services, such as adhering to treatment, or quality of life<sup>5-8</sup>.

The objective of this paper is to review gender differences in HIV. On the one hand, identifying from a

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gender perspective the biological and social factors, which have an effect on vulnerability to infection with the virus, and on the other hand, examining gender differences with respect to the use of services, treatment, survival, and quality of life in HIV patients.

## Psychosocial aspects

In spite of advances in recent years, there are still economic, social, and cultural factors, which make women the more disadvantaged gender in terms of infection with HIV<sup>2,5</sup>. Women with a low economic and cultural level are especially vulnerable to being infected with HIV, and illegal immigrants are a significant group within this sector of the population. On the one hand, their insecure social situation makes them especially vulnerable to situations where they risk contracting HIV, such as the use of intravenous drugs or engaging in prostitution. On the other hand, their lack of integration into society means that health promotion programs are unlikely to reach these groups, with the result that they have a low knowledge about the use of contraceptive methods or about HIV. Although the results are contradictory, there is evidence suggesting that immigrant women have less knowledge about sexually transmitted diseases (STD) and use contraceptive methods less frequently or inadequately<sup>9</sup>. Additionally, access by this population group to health-care services and to antiretroviral drugs if they do contract the disease is also reduced.

With respect to the vulnerability of women who work as prostitutes, their lack of legal protection and the absence of social support can lead them to feel coerced into having sex and into not using adequate protection methods. There is another problematic belief among the general population, where the existence of a stable relationship can lead to a false sense of security in sexual practices, resulting in not using preventative methods<sup>10</sup>. This is especially harmful for women, who tend to have less casual sexual partners than men<sup>1</sup> before having a stable partner.

One of the most important factors that increase the risk of HIV infection is gender violence. Between 10-50% of women throughout the world admit having been subjected on some occasion to physical abuse<sup>11</sup>. The importance of gender violence in terms of vulnerability to HIV can be observed from many perspectives. Physical abuse is often accompanied by sexual violence with forced intercourse<sup>11</sup>, which can cause cuts in the vagina. If we add to this fact the relationships whereby men perpetrating this abuse have a greater propensity

towards promiscuity, and therefore a greater chance of contracting STD<sup>12</sup>, there is a clear connection between sexual violence against women and an increase in the likelihood of being infected with HIV. On the other hand, the mere threat of violence prevents women from obtaining information on HIV/AIDS, undergoing HIV testing, avoiding transmission from mother to child, negotiating the conditions under which they have sexual relations, and seeking treatment and advice<sup>13</sup>. Additionally, sexual abuse in childhood brings about changes in emotional state, greater psychological morbidity, and lower levels of self-esteem. This increases the risk of being a drug user and of having unprotected sexual relations, heightening the risk of contracting HIV<sup>11,13</sup>. Furthermore, when women admit being HIV-positive they also face the risk of violence and abandonment by their partners, families, and friends<sup>14</sup>.

In the population at large, women display lower levels of self-esteem than men, and double the level of psychological morbidity<sup>15</sup>. The reasons cited range from biological to psychosocial differences. The latter may derive from diverse childhood environments, different roles attributed to men and women, and less favorable economic and social opportunities available to women. These differences become more pronounced in the case of the HIV-positive population<sup>16-19</sup>: in a study, Turner, et al.<sup>20</sup> found that 34% of women with HIV compared to 29% of men with HIV displayed levels of depression ranging from moderate to severe.

The fact that women with HIV are more prone to psychological morbidity brings about important changes in the disease. On the one hand, it affects their social functioning, their welfare, and their quality of life<sup>19</sup>. On the other hand, the presence of psychological morbidity in relation to HIV has been associated with affecting immune system mechanisms: decreased activity of natural killer cells and increased levels of CD8 lymphocytes<sup>21</sup>. These mechanisms lead to an increase in the viral load and acceleration of the infection<sup>18</sup>. If we add to these biological mechanisms the link between the presence of psychological morbidity and an inadequate adherence to antiretroviral drugs<sup>17</sup>, we can see how this is related to a faster development of the disease and, consequently, to an increase in mortality. With this in mind, it is important to implement programs to educate women about confrontation strategies, to teach them to manage factors that affect their mental health, such as stress, which subsequently impact their physical health<sup>16</sup>. Moreover, women living with HIV who have poorer mental health and who undergo psychological treatment and receive both emotional

**Table 1. Factors which may increase the risk of contracting HIV in women**

<b>Social vulnerability</b>	
– Feeling of security in sexual relations with a partner leads women to not use condoms.	
– Immigration	Greater risk of being IDU. Greater risk of becoming a prostitute. Difficulty of access to prevention programs. Lower level of access to healthcare services.
– Prostitution	Lack of legal status leads to impunity in any acts against them: Possible coercion. Relaxation of preventative measures outside of work.
– Gender violence	Sexual violence which frequently accompanies this (cuts, no use of condoms, etc.). Mere threat of violence decreases capacity for negotiation. Link between men who perpetrate violence and sexual promiscuity.  Having suffered violence previously increases situation of risk.  Transmission of HIV increases risk of suffering violence.
<b>Biological vulnerability</b>	
– More extensive exposure zone in women.	
– Semen stays longer in the vagina than vaginal discharge stays in contact with the penis.	
– Higher concentration of viral particles in semen than in vaginal discharge.	
– Greater risk of STD in women, which in turn increases the risk of contracting HIV:	<ul style="list-style-type: none"> <li>• Immunosuppressant effect</li> <li>• Increase of vaginal mucus</li> <li>• Increase in secretions (blood, etc).</li> </ul>

IDU: intravenous drug user; STD: sexually transmitted disease.

support and help in decision making are more inclined to begin antiretroviral treatment<sup>18</sup>.

Social support is another important factor in the course of HIV. It has been observed that it is friends, more than the family, who provide the most support to patients; they are more compassionate with the stigma surrounding this disease and more knowledgeable about the lifestyle<sup>22</sup>. Among HIV patients, benefiting from social support diminishes the effects of stress, improves quality of life, and boosts survival<sup>23</sup>. On the other hand, lack of such support or social isolation has negative repercussions on the progression to AIDS and on death rates<sup>16</sup>.

The results concerning gender differences in terms of social support are inconclusive. Some studies confirm that women have less social support<sup>6,22</sup>, while others find no differences between genders<sup>24</sup>. However, social support protects sufferers from psychological morbidity<sup>25</sup>, especially social support perceived by patients, independent of gender. Social support is very beneficial to women with psychiatric disorders as their quality of life improves and they display less high-risk behavior<sup>8</sup>.

## Biological aspects

Anatomical and histological differences make women more susceptible to infection with HIV. Certain studies show that in heterosexual relationships, the risk of contracting HIV is four times higher in women than in men<sup>26</sup>. There are various reasons for this difference: the length of time semen remains in the vagina is greater than the time vaginal discharge stays in contact with the penis. Also, there is a higher concentration of viral particles in semen compared to vaginal discharge and differences between the sexual mucosal barrier in men and women<sup>27</sup>. The urethra is lined with pseudostratified columnar epithelium, while the vagina and ectocervix are covered by stratified, squamous, non-keratinized epithelial cells. Moreover, the vagina has a greater exposure area to the virus than the penis<sup>27</sup>.

Young women are especially vulnerable because of the changes their bodies undergo during adolescence<sup>2</sup>. According to the literature available, a woman also increases susceptibility to becoming infected or transmitting HIV if she has suffered from vaginal trauma

or from other STD. Sexually transmitted diseases have also an immunosuppressive effect and increase levels of vaginal mucus, making transmission of the virus easier<sup>5</sup>. At the same time, a person with both HIV and other STD is more prone to secreting pus or blood and therefore more likely to transmit HIV to his or her sexual partner. The fact that women more often have untreated STD leads to a greater exposure to and contraction of HIV<sup>28</sup>.

Furthermore, the risk of transmission varies depending on the phase of the infection. A man in the asymptomatic phase is up to five times more likely to transmit HIV to a woman than in the opposite case scenario. In the case of symptomatic phases, no differences have been found in transmission of the disease<sup>5</sup>. Other biological factors, which may increase the risk of HIV transmission in women, are the use of oral contraceptives, postmenopausal sexual relations, and genital mutilation. All of these affect the density of vaginal mucus, making it easier for the virus to incubate<sup>2</sup>.

Concerning the progression of the disease, hormones play a vital role. Increased levels of estrogen produce a rise in the replication of HIV<sup>5</sup>. As such, the viral load varies according to the stage of the menstrual cycle, being lower in the early stages when the predominant hormone is progesterone (the follicular to the luteal phase)<sup>29</sup>. In addition, certain complications arising from infection with HIV only occur, or occur more frequently, in women. The most important among these are gynecological complications arising from HIV, especially cervical carcinoma. For this disease to develop, a woman must be infected with the human papillomavirus (HPV). In the case of having HIV, coinfection with HPV is more frequent and persistent<sup>30</sup>.

## Prevention

With respect to primary prevention methods for HIV, work has been done in two main areas: investigation into barrier methods during sexual contact and information. Much work has been carried out on the use and distribution of the male condom, which has benefited from important support and financing. However, an insufficiency can be observed in terms of investigating methods of protection specific to women, these being scarce and lacking sufficient funding. On the one hand, the female condom continues to be an expensive, not widespread option, and as a result many women do not know about it<sup>1</sup>. On the other hand, in spite of advances made in the study of microbicides, with several clinical trials in progress and promising

results<sup>31</sup>, it does not seem that the applicability of these drugs is immediately imminent. At the same time, more and more studies are revealing a lower incidence of the transmission or acquisition of HIV in circumcised males<sup>32,33</sup>. There seems to be a clear agreement on benefits, both for men and for their sexual partners, but this possibility has not yet been suggested as a new preventative measure<sup>34</sup>. Today, the only reliable method available is the male condom, and the role of the woman depends on her ability to negotiate with the man, putting her at a disadvantage.

In any case, there are prevention strategies for serodiscordant couples (such as counseling programs) with encouraging results<sup>35</sup>, yet the risk of transmission is not completely eliminated. In this line, as a consequence of the widespread use of HAART in most developed countries, another way to prevent heterosexual transmission has been identified: to ensure undetectable plasma HIV RNA in the index partner<sup>36</sup>. Moreover, this fact provides an opportunity for pregnancy in heterosexual couples and several studies have indicated that natural conception could now be considered a possible alternative for HIV-serodiscordant couples<sup>37,38</sup>.

With respect to information about HIV, in certain cultures or societies where premarital sexual relations (especially for women) continue to be frowned upon, paradoxically the rate of infection with HIV increases. The reason for this is that by making sex a taboo subject, nobody is allowed to speak or ask about it, and many young people remain ill-informed on the subject<sup>39</sup>. To counteract this, there is need for properly structured sex education to be incorporated into education programs, rather than only being available upon request. Promotion of the use of condoms should be accompanied by programs specific to each gender. Lack of education, coupled with lack of social or family support, paves the way for greater ignorance of methods for preventing the disease and contributes to a greater risk of infection with HIV<sup>40</sup>.

Up to now, the prevailing campaigns, based on an ABC strategy (A for Abstinence, B for Be Faithful, and C for Condoms) have shown controversial results. This strategy seems to play an important role in reducing the prevalence of HIV in countries like Uganda<sup>41</sup>. The ABC elements are crucial to reducing HIV incidence, although the emphasis placed on individual elements needs to vary according to the target population<sup>42,43</sup>. There remains a considerable distance between what is being advertised in the prevention campaigns in order to educate women and preparing men to accept the information.

Interventions should be aimed at women, but also at men, and within the latter group, they should focus on the idea that violence against women and sexual promiscuity are founded on a false idea of masculinity. An effort must be made to eliminate the preconceptions and attitudes, which have traditionally linked “success” to men who have sexual relationships and control over women<sup>12,39</sup>. Interventions must also be aimed at women, equipping them with the power to have better control over decisions about their life and health. This has been called “empowerment of women”, and it is a resource for fighting against vulnerability, facilitating their acquisition of skills for negotiating and for decision making, and providing them with access to information, economic resources, education, and healthcare services.

## Use of services

In terms of the use of healthcare services by HIV patients depending on gender, studies have been carried out in different areas showing contradictory results. Among these, several demonstrate that women with HIV receive less medical care in external consultations and spend less time in hospital than men. These results are found both in studies that precede the introduction of HAART<sup>44</sup>, and in others carried out afterwards<sup>7,45</sup>. The main explanation for this lesser use of services is that in the presence of a similar progression of the infection, women wait longer before seeking medical attention<sup>46</sup>.

However, a larger number of published works observe a higher use of outpatient care and a greater number of admissions both to hospitals and to Intensive Care Units (ICU) among women with HIV<sup>47,48</sup>. In this respect, some authors indicate that when women have identical possibilities of access to healthcare services (for example in hospital or in prison), they make use of them more frequently<sup>46,49</sup>. This greater use of healthcare services by women could be attributed to various factors. On the one hand, to a greater frequency of complications in women arising from HAART<sup>49</sup>, and on the other, as a result of the care required during pregnancy, obstetric tests, and the associated symptomatology<sup>23</sup>.

A third group of published works compares the use of healthcare services by men and women with HIV<sup>50,51</sup>. Women, in spite of having specific needs, were quite slow to join care plans provided by different healthcare systems. It would seem that today, in the most developed countries, making adjustments for variables such as ethnic differences or having health insurance, there

is no difference between genders in terms of access to healthcare services<sup>51</sup>. In any case, it appears necessary to continue investigating the qualitative and quantitative differences that exist in this respect.

If we focus on the carrying out of tests for the detection of HIV, there are few studies that determine the frequency with which men and women undergo testing. Among those studies available, there is a tendency to deal with overall figures, not taking into account that for a large part of the history of HIV, homosexual men and intravenous drug users (predominantly men) were the main groups affected, and as a result, these groups were most likely to undergo these tests<sup>3</sup>. In fact, it does appear that until approximately the year 2000 it was women who least frequently underwent testing. The reasons for that may be a diminished sense of vulnerability to the disease, possible difficulties in terms of access, or embarrassment<sup>4</sup>. Since that time, it appears that it is women who take the tests more frequently, both in Europe and in the USA<sup>3,4,52</sup>. However, the rates of infection for women in these countries continue to be significantly lower than the infection rates for men<sup>4</sup>. The change in transmission patterns seems to have raised awareness among women of the risk of contracting the disease.

## Treatment

Antiretroviral treatment has decreased not only the incidence of opportunistic diseases but also the number of cases of AIDS, especially since the introduction of HAART<sup>17,22</sup>. Even when there is specific data available on the effectiveness and the negative side effects of HAART in women, these have not been studied in sufficient depth<sup>49</sup>. Studies that analyze the differences between genders in relation to HAART have yielded contradictory results. In terms of beginning treatment, in some cases they show no difference<sup>21,69,53</sup>. Nevertheless, some other studies suggest that it is men, especially homosexual men, who begin treatment sooner<sup>46,54</sup>. At the same time, different studies indicate a lower prescription for women<sup>48</sup>. Women can experience various complications when it comes to starting treatment, such as a low level of social support, or the high cost of treatment in conjunction with the low income of women in certain contexts. Moreover, beginning treatment can lead many women to find their spending power reduced, as well as their quality of life, which endangers much of the responsibility that they bear in caring for their families, and this can cause them to refuse treatment<sup>20,21,54,69</sup>. Certain factors can



**Table 2. Factors which may exacerbate HIV disease progression in women**

<b>Psychosocial factors</b>	
– Higher psychological morbidity	Effect on social functioning, wellbeing and quality of life. Immune system mechanisms affected. Lower adherence to HAART.
<b>Biological factors</b>	
– Estrogen increases viral replication. – Affected more by other diseases (mainly gynecological).	
<b>Factors related to HAART</b>	
– High cost of treatment. – Higher CD4 levels. – Lower adherence to HAART. – More frequent drug-related toxicity.	

HAART: highly active antiretroviral therapy.

affect the choice of antiretroviral drugs by women: some of these drugs, such as nelfinavir or ritonavir, decrease the effectiveness of oral contraceptives; others, such as efavirenz, are not recommended during pregnancy<sup>55</sup>.

With respect to the response to HAART in these patients, levels of CD4 and plasma viral load are especially important as they are the main predictors of the progression to AIDS and death. Studies show that women display higher levels of CD4<sup>23,56,57</sup> and a lower plasma viral load<sup>56,58</sup>. This latter difference decreases as the disease progresses and disappears altogether in the final stage. As such, many studies indicate that there are no differences based on gender in the speed of progression to AIDS and death, even though women have a lower viral load than men at the beginning of the infection. This is due to the fact that the viral load increases more rapidly in women throughout the course of the disease<sup>56,58-60</sup>. Although this mechanism has not been fully proven, it is considered that it may be due to the dynamic variations of HIV between genders or to hormonal differences, such as the tumor necrosis factor, the aforementioned hormonal mechanism. In any case, this should be a key factor to be taken into account in guides to treatment, which usually recommend beginning treatment when there is a low level of CD4 lymphocytes ( $< 350$  cells/mm<sup>3</sup>) and a high level of viral load<sup>61</sup>. However, what has been demonstrated in women is an increased likelihood to interrupt HAART due to higher toxicity<sup>54,57</sup>.

Concerning adherence to antiretroviral treatment, various factors contribute to women adhering less to

treatment. The notion that their privacy is threatened when they have to take medications in public, disruption of their daily routine and their nutritional habits, being continually reminded that they are ill by having to take medications<sup>62</sup>, and rejection of the negative side effects of the medication, such as lipodystrophy and hypotrophy, changes which affect women's bodies<sup>21,57,69</sup>. In addition to this, psychological morbidity, which is more frequent in women, is associated with inadequate adherence<sup>20</sup>. This morbidity is linked to a lower motivation for personal care, decreased cognitive ability, and a reduction in their competence to follow the complex HAART instructions, which are all essential for correct medical monitoring<sup>62</sup>.

## Quality of life

With the introduction of HAART, HIV has become a chronic disease. As such, patient evaluation can no longer be limited to their survival or the appearance of complications, but should also include patient wellbeing. Because of this, in research into HIV, health-related quality of life (HRQoL) has become a lot more relevant. However, the majority of the many studies carried out in the last few years have focused on population groups mainly composed of men, with a low female representation. In addition to this, very few of these have focused on analyzing gender differences.

Of the studies reviewed, the majority of these are consistent in indicating a better quality of life for HIV-positive men than for women. Women display worse quality of life, even in circumstances where the opposite

might be expected; for example, when they are in a less advanced phase of the disease than men, or when they are younger<sup>6</sup>. In the different areas which make up the HRQoL components, women score lower in the areas of social functioning, mental health, and in satisfaction with life. They also experience more physical limitations, higher levels of depression, and lower self-esteem<sup>6,63,64</sup>. On the other hand, men enjoy greater levels of wellbeing and social support, although they show lower levels of general health<sup>63,64</sup>. In addition to this, studying the subject in greater depth, psychological morbidity, age, and social support have been identified as three of the main factors related to a lower quality of life in women living with HIV<sup>65,66</sup>.

Only two studies did not find a lower quality of life among women<sup>65,67</sup>. The differences between the results can be attributed to the use of different measurement tools. Interestingly, the only study reviewed which did not find differences favoring one gender or the other was also the only one that used the MOS-HIV tool, considered the most accurate instrument for measuring the quality of life<sup>68</sup> of HIV patients.

What is clear is that given the importance currently attributed to the quality of life experienced by HIV sufferers, it is necessary to continue investigating not only the differences between the quality of life enjoyed by men and women, but also the specific characteristics of these.

## Conclusions

Women have not been sufficiently studied in relation to HIV, and it is the intention of this article not just to demonstrate this, but also to suggest those areas where this has been more common. In many chronic diseases, the existence of gender differences has been extensively studied, such as in cardiovascular diseases and cancer. This fact makes it all the more conspicuous that in a pathological condition such as HIV, these differences have not been closely studied, even when their serological state plays a crucial role in newborn children. Although it was discovered in the early years of the disease that women were also affected, the scientific community has been very slow to recognize women as a specific at-risk group. Currently, in spite of a greater awareness and increased effort, and for all that a significant number of new cases of HIV are recorded among women in heterosexual relationships, the stereotype still exists that it is largely a disease which affects homosexual men, and which only affects women who work as prostitutes or who use

intravenous drugs. All of this contributes to a delay in the recognition of HIV as a disease that affects women. Therefore, consequent delays occur in the investigation into what specific measures could prevent them from contracting HIV, into which factors make them especially vulnerable to it or into treatment, care requirements, or quality of life in relation to the infection. Perhaps this deficit of attention from the scientific world, as well as on a social and political level, has led to increased infection among women. And it is precisely this increase that has caused institutions to take measures to address this trend and to bring it into the public eye. However, the specific nature of HIV/AIDS as a disease that affects women is neither recognized as a problem by healthcare institutions across the board, nor has it been flagged as a priority in terms of public health policy.

As this article has shown, there are certain aspects of the disease that affect women in a particular way, and to address these, lines of investigation must be opened and set as a priority, just as it has been done for other populations, such as intravenous drug users and homosexual men.

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