What are the current factors that impact on health-related quality of life (HRQOL) for women living with HIV?

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Abstract

Since the start of the HIV epidemic, care has often had a strong focus on quality of life. In the early days this was in part due to the limited treatment options available for people living with HIV alongside the strong humanistic desire of those working in the specialty to provide optimum care. Advances in HIV treatments has led to care having more of a medical focus with national and international targets concentrating on the prevention of new infections. Despite medical progress, the impact of being diagnosed and living with the HIV has a significant impact for many people, across all aspects of their life. Factors that impact on health-related quality of life for women living with HIV are often poorly understood and under-explored in health care settings.

Keywords

HIV, Quality of life, Women, Biopsychosocial Model

Introduction

Whilst we have seen decades of continual advancements in the understanding and treatment of HIV; the impact of being diagnosed and living with the condition still has a significant impact on many, across all aspects of their life. It would appear that the central focus of the HIV epidemic has largely been around the needs of men, with the needs of women and young girls living with HIV remaining an afterthought, and one that is still only considered within the existing framework of knowledge around men’s needs, rather than everybody living with HIV. As the care paradigm of HIV continues to evolve health care providers are urged to consider the needs of women living with HIV when delivering services.

In 2014, UNAIDS launched its ambitious global targets of 90-90-90; aiming to ensure that by 2020: (1) 90% of those living with HIV worldwide are aware of their status (2) that 90% of those who know they are living with HIV are on treatment, and (3) that 90% of those on treatment are virally suppressed
(UNAIDS, 2014). The overall goal behind these targets is to keep progressing towards end of HIV, as the more people living with HIV that are virally suppressed, the lower new infection rates will be.

There have since been calls from the scientific community to add a 4th 90: “that 90 % of people with viral load suppression have good health-related quality of life” (Lazarus et al, 2016). Sadly, to date this call has yet to be answered, as focus remains on preventing new infections.

**What do we mean by Quality-of-Life and Health Related Quality of Life?**

The terms quality of life (QoL), health-related quality of life (HRQoL) and health status are frequently used interchangeably within the literature (Karimi and Brazier 2016). However, there is very little consistency in how these concepts differ from one another. It is unlikely that a universal definition will be reached with regards to Quality of Life. Therefore, a more pragmatic approach has been suggested where researchers and clinicians (a) clearly define what they mean by QoL within their work, (b) specify what factors they consider contributing to this definition of QoL within the population they study and/or care for, and (c) measure these factors accordingly (Farquar 1995; Post 2014; Croston and Bourne 2021)

HRQoL in HIV has previously been defined as: understanding of an individual’s whole person well-being in relation to the biological, psychological and social sequelae of living with HIV. (Croston and Bourne, 2021). This definition is based on the WHO definition of health (2020), and the long-standing recognition that a diagnosis of HIV has an impact on psychological and social factors both directly and independently of biological factors.

This definition will be used to highlight some of the unique biological, social and psychological issues, which may impact on the QoL of women living with HIV. In this article we consider the term Women to be an inclusive term to represent all individuals who identify as a woman all or part of the time. When specifically referring to women who were assigned female gender at birth, we use the term cis-women. When talking about women who were assigned a different gender at birth, we use the term
trans-women. In addition to this, some of the issues raised here may be relevant to individuals who do not identify as women but were assigned female gender at birth. We acknowledge that in writing this article, we may get things wrong in terms of the way we use our language around gender and identity; and we very much welcome discussion, correction and education on this.

Currently within the UK 1 in 3 of those infected with HIV are cis women, with a quarter of new infections being reported in this group (PHE 2020). There is very limited data available about the prevalence of HIV amongst trans individuals. 2017 was the first time Public Health England reported figures on the number of transgender and non-binary individuals living with HIV in the UK. 113 trans-women and gender diverse individuals accessed HIV care that year. The paucity of information about the number of transwomen living with HIV in the UK is itself indicative that we do not know enough about the needs of this particular group of women. It is unfortunately not surprising given that there is no reliable estimate of how many transgender individuals currently live in the UK, as gender identity has been limited to binary options in previous versions of the national census. However, speculative estimates suggest somewhere between 200,000 – 500,000 transgender individuals currently live in the UK (Government Equalities Office 2018). Given that globally it is estimated that as many as 1 in 5 transwomen may be living with HIV (Baral et al. 2013); this would heavily imply that the reported number of trans-women reported to be accessing HIV care in the UK is massive under-representative of the true number of trans-women living with HIV.

A high proportion of all women diagnosed with HIV have been diagnosed late and on average they have been living undiagnosed for between 3-5 years. (Umeh et al 2011) This suggested that there needs to be more awareness with regards to women’s vulnerability and risk to acquiring HIV amongst healthcare professionals and then the subsequent health needs related to receiving a late diagnosis. There is also evidence of gender differences regarding HIV treatment and HIV-related health outcomes.
In addition to this, Women living with HIV have reported high levels of unmet need relating to social and welfare issues, and report significant levels of psychological distress (Public Health England 2020, Terence Higgins Trust 2017).

Within the UK, a significant proportion of women living with HIV are over the age of 50 and will require healthcare services to consider what care they will need as they age with HIV. Alongside this is the need to future proof services to meet the complex needs of women living with HIV. There is a wealth of evidence indicating that at present, services are not necessarily designed to meet the needs of women living with HIV (Terence Higgins Trust 2017). It is hoped that by exploring the key biopsychosocial factors that impact on the HRQoL of women living with HIV will be the first step in creating a good clinical practice guideline or tool, which will enable services to proactively establish services that meet the needs of women.

**Biological Factors in HIV care for Women**

There are a number of sex and gender differences that are relevant both to the treatment of HIV and long-term consequences of living with HIV. Cis-women typically have lower viral loads (VL) and higher CD4 counts early on in HIV infection. Over time however, cis-women display a faster disease progression than men given the same VL. In clinical settings this information may not always be at the forefront of healthcare professional’s mind when making decisions about care (Anderson 2005).

**Pharmacokinetics**

There have also been noted differences in antiretroviral therapy (ART) drug absorption and disposition between men and cis-women (Umeh et al. 2011; Mirochnick et al. 2015). In a comprehensive review of sex differences in HIV treatments, Floridia et al (2008) proposed that pharmacokinetic differences in ART may be attributable to differences in P450 enzyme system, but the overall sentiment within this area of research is that much more research is needed to understand differences in pharmacokinetics within ART. With regards to side effects of ART, cis-women are at higher risk of a
number of adverse side effects including an increased risk for: Pancreatitis, Gastrointestinal intolerance and metabolic disorders, Hepatic Steatosis, Lactic Acidosis, fat accumulation, triglyceride, Non- Nucleoside Reverse Transcript Inhibitors (NNRTI) associated rash and hepatotoxicity, and PI-associated diabetes (Mirochnick et al. 2015). They are also more likely to have decreased fat atrophy and Bone Mineral Density (Anderson 2005). This potentially places women at a greater risk of co-morbidities and health complaints as a result of the natural ageing process.

**Menopause and Cardiovascular Disease (CVD)**

Another major sex-specific issue in HIV is the menopause. In the UK, normative data suggests that most cis-women become menopausal between 45 and 55, with the average mean age being 51. Early menopause is defined as ≥12 consecutive months of amenorrhoea due to natural causes at ≤45 years. Premature menopause is defined as ≥12 consecutive months of amenorrhoea due to natural causes at ≤40 years. There is considerable data that has shown that premature and early menopause are associated with a number of serious negative outcomes. Jacobsen et al. (2003) followed a very large cohort of Norwegian Women (19,731) over a 37-Year period. They found that an early natural menopausal age increased the risk of premature aging and death. In addition to this, premature and early menopause are associated with the development of comorbidities such as osteoporosis (Santoro et al. 2009) and CVD. In Europe, evidence shows that women are at a higher risk of death from CVD than men (51% compared to 42% respectively, Nicholson et al. 2014). However, it appears to be women who are post-menopausal that are at most risk. A large cohort study found the incidence rate of CVD in post-menopausal cis-women was double that of pre-menopausal cis-women, and that this risk applied to both naturally occurring and surgically-induced menopause (Gordon et al. 1978).

Recent research has confirmed that post-menopausal cis-women living with HIV are just as much at risk as a general population. The POPPY study (Bagkeris et al 2018) assessed the risk of CVD in cis-women
living with HIV aged ≥50 years (n=86), compared to age-matched cis-women who were HIV-negative (n=109). 83% (n=163) of the women in the study were defined as post-menopausal. Similar CVD risk factors seen among HIV-positive and age-matched HIV-negative cis-women. What was most concerning however, was that a substantial number of women with high CVD risk and/or hypertension were not receiving medication for these conditions. The authors reported that 79% of patients in the study were eligible for lipid lowering drugs, and 56% were eligible for anti-hypertensives; but they were not receiving this medication.

Widening the lens from physical health outcomes, cis-women who experience premature and early menopause also report increased levels of depression and anxiety, poorer sleep, reduced libido, and overall lower quality of life (Royal College of Nursing, 2019). Interestingly all these factors can and have been reported to co-occur independently of the menopause, significantly impacting on women’s QoL. However there appears to be little evidence that explores the accumulating issues such as lack of sleep, psychological distress, lower libido etc alongside women’s QoL. The Prime study recently reported that 10,350 women living with HIV aged between 45 and 56 (potentially menopausal age) attended HIV care in the UK; a five-fold increase over ten years. The data showed a high prevalence of somatic (hot flushes, muscle and joint pains and sleep disturbances 89%), urogenital (vaginal dryness, sexual problems 68%), and psychological (anxiety, depression 78%) symptoms in women living with HIV aged 45-60, which for many could be linked to menopausal changes.

**Case base example:**

Juliet is a 43-year cis-woman who has been attending the clinic for nearly 20 years. Her 19-year-old daughter who is also living with HIV is planning to leave for university. Juliet comes into clinic to get her annual blood tests and doesn’t look her usual self; in that she usually dresses up for her visits and instead she is wearing no make-up and her hair doesn’t look in good shape. When the nurse is alone with Juliet, she asks her how she is doing, Juliet avoids eye contact and then reports that she has not been doing ok. Rebecca’s university is over 150 miles away and is concerned that she won’t
get to see her apart from during school holidays. Juliet’s husband died over 12 years ago and whilst there are some parts of her that would like another relationship there are also parts of her that feels apprehensive. Rebecca’s eyes begin to well up as she explains that she has no sexual desire and feels very low in mood. All these factors are affecting her sleep.

There is mixed evidence as to whether a diagnosis of HIV and/or its treatment has an impact on the cause of menopause in cis-women. In a systematic review of HIV and menopause, Imai and colleagues (2103) found some evidence that cis-women living with HIV entered the menopause earlier than cis-women without a diagnosis of HIV; However, there are also studies that have failed to find any significant difference in the onset of menopause in these two populations. Cetjin and colleagues (2006) also found that a large number of cis-women in their study were not actually menopausal despite having symptoms such as extended amenorrhea; which indicates that transition into menopause could be missed. The study highlights the importance that cis-women need to know if they are menopausal so as to monitor for increased co-morbidities such reduced bone density, take necessary steps mitigate their increased risk of CVD, and so they can also make lifestyle changes such as stop birth control which can often be burdensome and expensive. Furthermore, bleeding after menopause can be a symptom of other serious illnesses, so knowing if menopause has occurred or not helps to identify and investigate unexplained bleeding quicker.

A last biological consideration is the use of Hormone Replacement Therapy (HRT). HRT can be prescribed to cis-women to mitigate the negative symptoms associated with menopause which can have considerable impact on cis women HRQoL, and HRT would therefore be of significant benefit to these cis-women. There is evidence that HRT is linked with increased CVD risk, thus advice is to give lowest dose for shortest time possible (Grady and Sawaya, 2005). Despite the known benefits of HRT, Adanay et al. (2016) noted in their comprehensive review paper that HRT appeared to be underutilised
for menopausal cis-women living with HIV. They suspected this was due to potential concerns about possible drug interactions between HRT and ART. There is, however, no research into this area on which to make these decisions which may have a significant impact on a large number of women’s HRQoL. Conversely, many trans-women use hormone therapy in the long-term as an important part of their gender-affirming therapy; and therefore, it must be assumed many trans-women living with HIV will be on hormone therapy. So here we have a worrying dilemma: are we under-utilizing HRT in cis-women where it could be used more to offer relief from distressing menopausal symptoms, or are we not recognising, monitoring and managing the increased risk of potentially harmful HRT x ART drug interactions which could be affecting trans-women?

What is clear when we consider biological factors related to HRQoL in women is there are still a lot of unknown answers, because we are only just starting to ask the questions relevant to the aging population of cis-women and the long-time marginalised trans-women, who are accessing HIV services.

**Psychological factors in HIV care from Women**

Whilst levels of psychological distress and difficulties are higher for the whole population of individuals living with HIV compared to the HIV negative population (e.g Chaponda et al. 2018); there is also evidence that women living with HIV suffer with increased levels of psychological distress compared to men living with HIV.

**Common Mental Health Disorders**

Waldron and colleagues (2021) recent review of the unique and unmet needs of women living with HIV offers an excellent and timely summary of psychological distress experienced by cis-women living with HIV. The authors’ preface their review by noting that in the general population; it is well documented that cis-women report higher rates of common psychological disorders (Breslau and Anthony 2007; Breslau et al. 1997; McClean and Anthony 2009; Noble 2005).
Cis-women living with HIV are more likely to be depressed than HIV-negative cis-women, and they report increased symptom severity (Morisson et al. 2002). This is also true when comparing prevalence severity of depression (e.g. Ickovics et al. 2001) of Cis-women living with HIV to men living with HIV. Similarly, evidence shows a higher prevalence of anxiety in women living with HIV when compared to HIV-negative cis-women (Morisson et al. 2002) and men living with HIV (Gaynes et al. 2008).

There is strong and consistent evidence that people living with HIV experience higher rates of trauma compared to the general population (LeGrand et al. 2015). Unsurprisingly, women living with HIV appear to be even more disproportionally affected by trauma. For example, women living with HIV who were accessing care at a hospital in Togo; just over 63% reported experiencing physical violence in their lifetime, and just under 70% reported having experienced sexual violence (Burgos-Soto et al. 2014) A large-scale meta-analysis of women living with HIV in western countries found that 30% of women in the sample had recently experienced post-traumatic stress disorder, which is five times higher than the women in the general population (Machtinger et al. 2012). Furthermore, the lifetime prevalence of experiencing abuse was extremely high (61.1%-71.1%, dependent on type of abuse reported).

Information about the psychological well-being of trans-women living with HIV is sparse. Within the general population, transgender individuals are more likely to experience psychological distress compared to their cis-gender counterparts (Tan et al. 2020); however, the depth and breadth of research is lacking compared to the relative wealth of data on the mental health of cis-gender individuals in the general population. A recent publication (Jaspal et al. 2018) reporting data for the first time on trans and gender-diverse people accessing HIV care in England found that they were significantly more likely to be under psychiatric care compared to cis-gender individuals accessing HIV services (11% vs 4%).
**Suicide and Suicidality**

There are also important research findings specific to cis-women and transgender women when it comes to suicidal thoughts and behaviours. Traditionally suicide risk may be something clinicians, and the general population, associate more frequently with males. It is true men are far more likely to die by suicide completion than women (Freeman et al. 2017); and in the UK suicide is the leading cause of death of men under 45 years. What this mask, however, is the fact that women are more likely to attempt suicide, think about suicide, and self-injure (Schrijvers et al. 2012). The literature around women living with HIV and suicidality shows that cis-women living with HIV may be more likely to attempt suicide than their male counterparts (Komiti et al. 2004); and that the period immediately after diagnosis may be a period of significantly increased risk.

In addition to this, there is also consistent evidence that prevalence of suicidal ideation and attempts in transgender individuals is extremely high (Virupaksha et al. 2016), and a least one study reported that death by suicide is one of the leading causes of mortality in trans-women. Again, specific information considering suicidal thoughts and behaviours in trans-women living with HIV is extremely lacking, so it is hard to provide any useful overview within this paper.

**Perinatal and postnatal mental health**

Pregnancy and the postpartum period is a time where cis-women are at increased risk of psychiatric disorder (Vesga-Lopez et al. 2008). A meta-analytic study found that cis-women living with HIV had a significantly higher odds ratio of antenatal and postnatal depressive symptoms than HIV negative women (Zhu et al. 2019). Moreover, research has also found that women with lower CD4 counts (<200) were more likely to be depressed during the perinatal period that those with higher CD4 counts 500;( Kapetanovic et al. 2009).
Within clinical practice it is paramount that people providing care for women living with HIV are aware of the psychological impact HIV has on overall HRQoL. When placing this in the context of our biopsychosocial model of HRQoL in HIV; we are reminded of the impact psychological factors can have on biological factors. Reduced psychological well-being has been shown to have deleterious effects of physical outcomes in healthcare (Naylor et al. 2012) and HIV is no exception. Studies that show that for cis-women living with HIV, depression is related to increased mortality, depression and anxiety have both been linked with disease progression, depression and trauma symptoms are related to lower ART adherence, and finally trauma is associated with higher-risk of acquisition and transmission of HIV (Waldron et al. 2021).

Social factors

The distinction between psychological and social factors can sometimes be confusing as they are often inextricably linked; a point that we will explore further in the next section. Psychological factors can be thought of as the individual’s level phenomena, processes and outcomes that are specific to the person. Social factors are wider societal processes, norms, values, systems and phenomena that are not specific to individuals, but that impact on individuals living within these social factors. As individual members of any given society or social group, we have a responsibility as to the societal factors which uphold, consciously or unconsciously, and to those that we challenge.

Stigma and Discrimination

It is a lamentable and unacceptable fact that a diagnosis of HIV still carries considerable stigma for people living with this condition. Studies which explore the experiences of cis- and trans-women living with HIV have shown that women may experience higher levels of both social and internal stigma. For example, there is evidence that cis-women are dealt a double blow of blame and negative judgement when it comes to HIV acquisitions and transmissions – women living with HIV are more likely to be given labels such as “immoral” and promiscuous” than men; and also women are blamed for being “dirty” and “tempting” as the cause of men acquiring HIV (Visser 2012; 2013; Rice et al. 2015). In a
review of the literature, Paudel and Baral (2015) noted that HIV stigma in cis-women is associated with rejection from family, friends and society, feelings of loss and uncertainty and psychological difficulties including depression, anxiety and suicidal ideation. Many trans-women experience daily stigma and discrimination in the form of gender identity discrimination, transphobia, violence; which also leads isolation and increased psychological distress (Magno et al. 2019). Whilst there was plenty of research into how these experiences increase trans-women’s risk in relation to acquiring HIV, it was harder to find any research with discussed the experiences of trans-women already living with HIV.

**Gender-based and intimate partner violence**

Gender-based violence and intimate partner violence are both known risk factors for HIV acquisition for women. When it involves sexual violence, there is a direct pathway in that rape is likely to be condomless (Campbell et al. 2013); and women are more likely to suffer vaginal or anal tears (McClean et al. 2011), which further increases transmission risk. In addition to this, women who are currently in violent relationships, or have previously experienced either type of violence, are less likely to be able to negotiate condom use and safe sex in current relationships (Wingood and DiClemente 2000). Gender-based and intimate partner violence also indirectly increases the risk of HIV acquisition, as women who experience such violence are more likely to experience a range of psychological and social difficulties as a result, which also increase their risk of acquiring HIV (UNAIDS 2019).

In addition to this, there is also evidence that women living with HIV are more likely to experience gender-based violence and intimate partner violence than women without HIV (Gielen et al. 2000).

**Poverty, lack of education and high risk and transactional sex or sex work.**

Both Cis- and trans- women are disproportionately affected by poverty and a lack of access to education, which are both well-established risk factors for acquiring HIV (AVERT, 2019). Women living in the poorest conditions may have little options when it comes to work and relationships; and are therefore more likely to engage in higher risk sex work, and to have to stay in violent relationships.
HIV infection is higher in both cis- and trans-women working in sex work due to repeated risk of exposure through sex, multiple sexual partners, higher risk sex acts and higher incidence of condomless sex either through increased risk of rape, or through not being able to negotiate safe sex (Evens et al. 2019).

Research has shown that in cis-women, there is a strong link between education and HIV risk. Girls who have no access to education have double the risk of acquiring HIV compared to their schooled counterparts. A UNAIDS study in Botswana demonstrated that every additional year of education reduced a girl’s risk of acquiring HIV by 11.6% (UNAIDS, 2019). Trans-women are also at high risk of not completing their education due to a range of factors such as facing discrimination and bullying at school and being thrown out of their homes (Magno et al. 2019).

**Health inequalities**

It is well documented that cis- and trans-women have less access to healthcare and/or attend healthcare setting less (PHE 2020). This increases their risk of acquiring HIV due to lack of testing in higher risk populations, and less access to preventative measures such as condoms and PReP (Invisible no longer 2017) reduced access to healthcare also has obvious implications for women living with HIV, in that it means they cannot readily access ART and be monitored for HIV progression and the development of AIDS-related infections. All of this equates to delayed diagnoses, health complications associated with advanced HIV, and increased rates of mortality.

All of the social factors mentioned so far in this paper are associated with poorer access and engagement with healthcare for women (AVERT 2019, 2020). Moreover, when women living with HIV do access healthcare, they often experience discrimination and stigma which affects the quality of their care and the likelihood or returning for further care (Wagner et al. 2016; Magno et al. 2019); which has obviously worrying implications regarding worse outcomes including unnecessary deaths.
Discussion

The biopsychosocial model of HRQOL in women living with HIV presented here helps create awareness and understanding of the many factors that impact on the dynamics that contribute to the risk of women acquiring HIV, how women experience a diagnosis of HIV, and also how a diagnosis of HIV impacts on their lives. It is key to understand, however, they way in which these factors layer on top of each other to create a condition that is more than just the sums of its parts. It is essential to understand how each factor impacts on other factors within any given context for any given individual.

An intersectional approach to understanding HIV and women

One way to do this, is to build a person-centered understanding using an intersectional approach. The concept of Intersectionality was first developed by the black feminist scholar and lawyer Kimberlé Crenshaw (1989). It refers to the way individuals are subjected to and experience multiple acts of oppression, stigma and disadvantage due to being a member of more than one marginalized group; for example, being female, being non-white, being LGBQT, being an asylum seeker, being homeless or being disabled. It is inherent to the theory that these labels are largely based on socially constructed power dynamics, rather than objective biological differences, and that this results in the creation and upholding of a broad spectrum of inequality (Mullings and Schulz, 2006). For the purpose of this paper, we can make a simplified and reductionist example to illustrate Crenshaw’s ascertain that “not all inequality is equal”. As has been made evident in this review, a diagnosis of HIV may result in many negative consequences for women. However, the way in which it impacts on, and is experienced by, a black, cisgender woman, with a secure job, in a monogamous relationship, with close family, in an affluent country with free healthcare; will be different to that of a black, transgender single woman who has a limited support network, no steady stream of income in a country where healthcare is sparse. It is not within the scope of this paper to fully explain and consider the nuances of intersectional theory, however Ciaola and colleagues (2014) offer an accessible description of the
theory, and a nuanced explanation of how it can be applied to understand the experiences and needs of women living with HIV.

Conclusion

This article is not an exhaustive review of the literature, rather it is a current overview of what we know in relation to the HRQoL factors that affect women living with HIV. Rather it is intended to be an opportunity to acknowledge that a person-centred approach is needed to understand the unique way a person’s life experiences will impact on how they live with HIV; with a particular focus on women as they represent over half the population of individuals living with HIV (though these stats only refer to cis-women, so the true figures are higher when including trans-women), they are often at higher risk due to structural inequality; and yet remain under-represented and included in research and policy. This is particularly true of trans-women. The purpose of this paper was to be inclusive of all women, yet we are mindful that our attempts to include the needs of transwomen may appear a tokenistic addition. This was never our intention rather a reflection on what is currently explored and understood about the needs of this group of women, or rather the lack thereof.

More research is needed to be inclusive of women and focus on their needs. Healthcare professionals in clinical practice must understand women’s needs within the context of their experiences by being more proactively aware of their biological, psychological, and social experiences and needs; and how these interact within the context of their HIV diagnosis if they are to provide effective care.

Reflective Questions

1. What does Quality of life and Health Related Quality of life mean to you?

2. How is your service designed to meet the needs of women living with HIV?

3. What do you think are the key challenges women living with HIV will experience as a result of the ageing process?
References


