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Enhancing the responsiveness of HIV healthcare services in Spain to address long-term well-being

Trenton Michael White

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Enhancing the responsiveness of HIV healthcare services in Spain to address long-term well-being

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Abbreviations and Acronyms

AIDS – Acquired immunodeficiency syndrome

ART – Antiretroviral therapy (or antiretroviral treatment)

CCAA – Autonomous communities

CD4 – Cluster of differentiation 4 receptor

CVD – Cardiovascular disease

ECDC – European Centre for Disease Prevention and Control

EHR – Electronic health record

EU/EEA – European Union and European Economic Area

HIV – Human immunodeficiency virus

HCV – Hepatitis C virus

HRQoL – Health-related quality of life

MSM – Men who have sex with men

PLHIV – People living with HIV

PREM – Patient-reported experience measures

PROM – Patient-reported outcome measures

PWID – People who inject drugs

WHO – World Health Organization

List of articles in the thesis

Thesis in compendium of publications format.

The thesis consists of two objectives and three articles:

White T. M. Fuster-RuizdeApodaca M.J., Iniesta C., Prats-Silvestre C., Lazarus J.V., Izquierdo R., and Jarrín I. Network analysis to prioritize issues for intervention to improve the health-related quality of life of people with HIV in Spain. *HIV Med,* 2024, Online ahead of print.

- *HIV Medicine.* Journal Citation Report Impact Factor: 2.8 (2023); Scimago Journal Rank: Q1 Infectious Diseases (2023) and Q1 Health Policy (2023)

White T. M., Gresle A.-S., Roqueta J., Pine C. and Lazarus J. V. Co-creation of patient-centered metrics for long-term well-being involving people with HIV and HIV care providers. *AIDS Patient Care and STDs,* 2024, Accepted.

- *AIDS Patient Care and STDs.* Journal Citation Report Impact Factor: 3.4 (2023); Scimago and Web of Science Journal Rank: Q1 Infectious Diseases (2023) and Q1 Public Health, Environmental and Occupational Health (2023)

White T. M. Fuster-RuizdeApodaca M.J., Iniesta C., Prats-Silvestre C., Díaz A., Baberá A., and Lazarus J.V. Examining the Capacity and Feasibility to Monitor the Long-Term Well-Being of People with HIV in Spain. *PLOS ONE,* 2024, Under review.

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Thesis summary

HIV continues to be a major public health issue in Europe, including Spain. In 2014, UNAIDS introduced the 90-90-90 national targets, aiming that 90% of people living with HIV (PLHIV) know their HIV status, 90% of those diagnosed with HIV to be taking antiretroviral therapy (ART), and 90% of those on ART to be virally suppressed. This sequence of targets defined by specific national goals has helped drive advancements in policy, research, and service delivery, contributing to declines in mortality from HIV-related causes. These targets also highlight an important aspect of HIV prevention, as achieving viral suppression prevents onward transmission. Spain met the third target in 2021, with 73% of all PLHIV having achieved viral suppression.

Despite advancements in antiretroviral therapy (ART) and improved life expectancy, PLHIV in Spain and elsewhere report health-related quality of life (HRQoL) that can be substantially improved, especially in some dimensions and areas, and substantial burdensome symptoms compared with the general population. Further, evidence demonstrates accelerated ageing and greater multimorbidity among this population, which may further impair HRQoL. In all countries, PLHIV report stigma and discrimination, which can impact their health and well-being through avoiding services and treatment or through psychosocial pathways that increase anxiety and depression.

The advent of a national long-term well-being metric, similar to the 90-90-90 targets, may encourage countries to address issues beyond viral suppression in routine HIV care. Enhancing the monitoring capabilities in Spain such that they collect multimorbidity and HRQoL data may contribute to the health system's ability to address issues beyond viral suppression. Factors most acutely impacting the HRQoL of PLHIV, such as psychological distress and material deprivation, if monitored by the sub-national and national health information systems in Spain may provide healthcare providers with additional knowledge to intervene on burdensome issues. Addressing these factors through integrated and patient-centered care approaches with monitoring via standardized data collection may enhance HRQoL and long-term well-being for PLHIV in Spain.

Resum de tesi

El VIH continua sent un problema de salut pública important a Europa, inclosa Espanya. L'any 2014, el programa conjunt de les Nacions Unides sobre el VIH/SIDA (ONUSIDA) va introduir els objectius nacionals 90-90-90, amb l'objectiu que el 90% de les persones que viuen amb VIH (PVVIH) coneguin el seu estat serològic, el 90% de les persones diagnosticades amb VIH rebin teràpia antiretroviral (TAR) i el 90% de les persones en TAR aconsegueixin la supressió viral. Aquesta seqüència d'objectius, definida per metes nacionals específiques, ha contribuït a impulsar avenços en polítiques, recerca i prestació de serveis, contribuint a la disminució de la mortalitat per causes relacionades amb el VIH. Aquests objectius també subratllen un aspecte important de la prevenció del VIH, ja que aconseguir la supressió viral prevé la transmissió del virus. Espanya va assolir el tercer objectiu l'any 2021, amb el 73% de totes les PVVIH havent aconseguit la supressió viral.

Malgrat els avenços en la teràpia antiretroviral (TAR) i la millora de l'esperança de vida de les PVVIH, aquestes, tant a Espanya com a altres indrets, manifesten que la seva qualitat de vida relacionada amb la salut (*health-related quality of life,* HRQoL) es pot millorar substancialment, especialment en algunes dimensions i àrees concretes. Les PVVIH pateixen símptomes significativament més complexos en comparació amb la població general. A més, l'evidència entre les persones que envelleixen amb VIH demostra un envelliment accelerat i una major multimorbilitat en aquesta població, la qual cosa pot afectar encara més la seva HRQoL. En tots els països, les PVVIH denuncien l’estigma i la discriminació que pateixen, i que poden afectar la seva salut i benestar, ja que els porta a evitar l’ús de serveis i tractaments, o bé mitjançant vies psicosocials que augmenten l'ansietat i la depressió.

L'adopció d'un indicador nacional de benestar a llarg termini, similar als objectius 90-90-90, pot incentivar els països a abordar els problemes que pateixen les PVVIH, més enllà de la supressió viral gestionada en l'atenció rutinària del VIH. Millorar les capacitats de monitoratge a Espanya de manera que es recullin dades sobre multimorbilitat i HRQoL pot contribuir a la capacitat del sistema de salut per abordar aquests problemes. Si aquells factors que més impacten en la HRQoL de les PVVIH, com el malestar psicològic i la privació material, són monitoritzats pels sistemes

d'informació sanitària subnacionals i nacionals d'Espanya, aquests poden proporcionar als professionals de la salut un valuós coneixement addicional que els permeti intervenir en la gestió dels problemes que pateixen les PVVIH. Així doncs, abordar aquests factors a través d’una atenció integrada i centrada en el pacient, amb un monitoratge basat en la recollida estandarditzada de dades, pot millorar la HRQoL de les PVVIH a Espanya.

Introduction

The human immunodeficiency virus (HIV) targets cluster of differentiation-4 (CD4) lymphocytes, inhibiting immune system defense, and if left untreated can lead to acquired immune deficiency syndrome (AIDS), which makes it easier for other opportunistic diseases, such as cancer and pneumonia, to evade immune defenses.[1] Since the beginning of the HIV and AIDS epidemic in the early 1980s, an estimated 85.6 [65.0–113.0] million people have contracted HIV and 40.4 [32.9–51.3] million have died from it. An estimated 39 [33.1–45.7] million people were living with HIV (PLHIV) at the end of 2023 worldwide.[2]

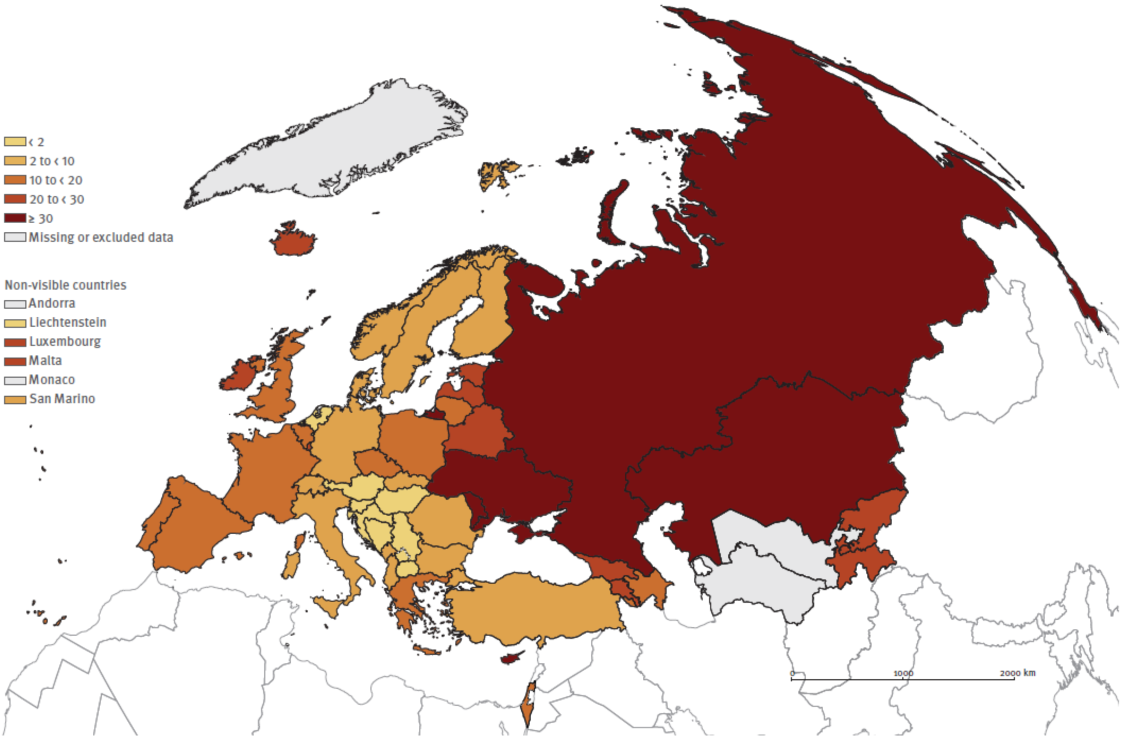
Though no cure exists, HIV can be effectively treated with antiretroviral therapy (ART), a combination of antiviral agents which disrupt the replication of the virus in the body, aiming to suppress the viral load, with viral suppression most commonly defined as having fewer than 200 copies of the virus per milliliter of blood.[3] Since the introduction of highly-active ART in 1996, early mortality due to HIV and AIDS has fallen drastically, with life expectancy of virally-suppressed PLHIV nearly equal to their seronegative counterparts.[4] In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set targets for each country that by 2020, 90% of people living with HIV know their status, 90% of those who know their status are receiving treatment, and 90% of those receiving treatment have suppressed viral loads.[5] In 2021, these 90-90-90 targets were updated to 95-95-95, reflecting 95% for each metric by 2025.[6] Despite clinical and public health advancements in HIV, PLHIV experience worse physical and mental health outcomes compared to HIV-negative comparison groups, including advanced ageing and greater multimorbidity for chronic illnesses like cardiovascular, renal, liver and bone diseases as well as cancers, anxiety and depression, even when viral suppression is achieved.[7–10]

Epidemiology of HIV in Europe

HIV continues to pose a major public health concern in Europe, with an estimated 2.4 million people having been diagnosed with HIV in the WHO European region since the start of the pandemic.[11] In 2022, the year of the latest available full data, 110,486 new HIV diagnoses were reported across 49 countries in the WHO European Region, with an incidence rate of approximately 12.4 per 100,000 population.[11] This marks a slight increase compared to 2021 (4.2%) but a significant decrease from the rate in 2019 (-20.5%), just prior to the COVID-19 pandemic. Notably, HIV and AIDS surveillance data for 2022 represents a year that saw increases in population movements within and to Europe as well as the recovery of health and HIV surveillance services following the COVID-19 pandemic.[12]

The epidemiology of HIV in Europe is shaped by a range of factors, including geographical disparities, modes of transmission, age distribution, and access to care. Europe experiences a heterogeneous epidemic, with eastern European countries typically reporting higher incidence rates compared with western European countries.[11] The Russian Federation reported the highest incidence rate in 2022 of 38.4 per 100,000 people (**Figure 1**).[11]

Figure 1. HIV diagnoses per 100,000 population, 2022

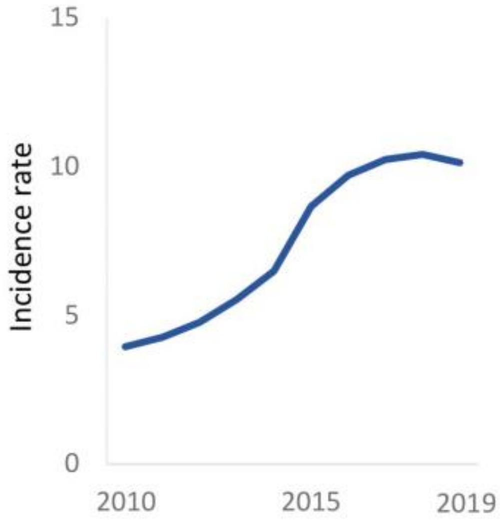


Source: European Centre for Disease Prevention and Control/WHO Regional Office for Europe. HIV/AIDS Surveillance in Europe 2023 – 2022 Data (2023).

Heterosexual transmission and injecting drug use are the most prevalent modes of transmission in eastern Europe. The age distribution of PLHIV in Europe is dependent on the mode of transmission, with younger individuals more frequently diagnosed with HIV through sexual transmission, while older individuals are more commonly diagnosed with injecting drug use reported as the mode of transmission.[11] Incidence remains disproportionately high among key populations such as men who have sex with men (MSM), people who inject drugs (PWID), and migrants from high-prevalence countries, regardless of region. In the combined EU/EEA, 33.3% of the 110,486 reported HIV diagnoses in 2022 were among MSM, and an estimated 26.7% were among migrants originating outside of the country in which they received their diagnosis.[11] Stigma, socioeconomic disparities, and varying health policy implementations across borders persist as significant barriers to effectively controlling the epidemic, particularly for vulnerable and key populations.[13,14] Disparities in access to testing and care still exist, particularly among populations such as PWID and migrants from low- and middle-income countries.[15–18] This issue is most acute in eastern Europe but remains a public health challenge across the continent. Screening practices for HIV among migrants and refugees vary across Member States, with only three countries, France, Greece and the United Kingdom, in the WHO European Region that have HIV policies in alignment with WHO and ECDC guidelines.[19] Nine countries have national policies that discriminate against PLHIV through the restriction of movement and/or confidential and voluntary testing, contradicting WHO and ECDC guidelines.[19]

HIV prevention in Europe remains a multifaceted challenge. In 2015, clinical trials in France (IPERGAY)[20] and the United Kingdom (PROUD)[21] demonstrated a high protective efficacy for pre-exposure prophylaxis (PrEP), or the use of a combination of tenofovir disoproxil and emtricitabine, two ART drugs, in preventing the transmission of HIV. HIV prevention, including PrEP and expanded testing, have been instrumental in reducing new infections in primarily western European countries, like Austria, Belgium, Denmark, Estonia, the Netherlands, Norway, and the UK, which have reported declines in year-on-year HIV incidence for a majority of the years 2016-2022.[11] Yet, the European region overall has experienced increasing incidence since 2010, with countries such as Ukraine and the Russian Federation accounting for the greatest burden and countries like Portugal and Spain experiencing increasing incidence from 2010-2018 and decreasing incidence thereafter (**Figure 2**).[22]

Figure 2. HIV Incidence in Spain, 2010-2019



Source: Govender, R. D., Hashim, M. J., Khan, M. A., Mustafa, H. & Khan, G. Global Epidemiology of HIV/AIDS: A Resurgence in North America and Europe. *J Epidemiol Glob Health* 11, 296–301 (2021).

Several barriers hinder the widespread implementation of PrEP, including high costs, low awareness among medical professionals and people at risk, challenges in adherence, and limited accessibility.[23] Further, the European Centre for Disease Prevention and Control (ECDC) highlights late diagnosis, social stigma, and insufficient political support for services (e.g., needle exchange programs, opioid substitution therapy, comprehensive sex education) as barriers to HIV prevention.[11]

Epidemiology of HIV in Spain

In 2021, an estimated 148,631 PLHIV (95%CI 136,436 - 162,307) lived in Spain, or 0.31% of the population.[24] In 2022, 2,956 new cases of HIV were reported, leading to a preliminary incidence rate of 6.23 per 100,000 people, which, after adjustment for delayed notification, is projected to be 7.71 per 100,000 people for 2022.[25] The demographic profile of these cases predominantly includes men (85.7%), with a median age of 36 years.[25] The epidemiology of HIV in Spain is influenced by population characteristics, health seeking behavior, socio-economic status, cultural beliefs and perceptions towards HIV and AIDS. In 2021, the autonomous community of Catalonia, with a population of approximately 7.7 million people, reported 345 new HIV diagnoses.[24,26] The autonomous community of Madrid, with a population of approximately 6.8 million people, reported 451 cases.[24,26] Andalusia, with approximately 8.5 million people, recorded 501 diagnoses, while Valencia, with a population of about 5 million inhabitants, recorded 455 cases.[24,26] These regions with higher population densities than the other communities and are more urbanized, which may serve as a focus for HIV transmission dynamics, for example higher levels of mobility, demographic and socio-economic diversities, and other cultural factors that affect people's perception towards health and utilization of prevention services.[27–30] Additionally, access to health care services, including HIV testing, counseling, and treatment, varies across regions, affecting HIV prevention and management.[31,32]

Among specific population groups, MSM continue to be the most affected by HIV with the highest rate of new diagnoses each year since the collection of this data in 2013, underscoring persistent challenges in curbing transmission despite targeted public health interventions.[25] In 2022, MSM accounted for 55.0% of all new cases, compared with 24.5% heterosexual transmission and 1.9% through injection drug use.[25] Almost half (46.5%) of the new diagnoses were among migrants born outside of Spain, up from 38.6% in 2021,[33] with a significant proportion (48.6% in 2022) of these being diagnosed at a late stage, defined as presenting with fewer than 350 CD4 cells/mm^3 at the time of diagnosis.[24,25]

In 2021, an estimated 92.5% of all PLHIV in Spain were aware of their status, demonstrating effective efforts in diagnosis and awareness.[24] An estimated 96.6% of those diagnosed were receiving ART.[24] Among those on treatment, 90.4% have achieved viral suppression.[24] Since the first evaluation of the HIV care continuum in 2013, the number of diagnosed HIV cases has increased by 12.8%, and there has been a corresponding rise in the numbers receiving treatment (11.0%) and achieving viral suppression (10.9%), highlighting the efficacy of Spain's public health and prevention interventions in HIV during this time.[24] Spain met the ambitious 90-90-90 targets set by UNAIDS for 2020 in 2021, with 73% of all PLHIV in Spain having achieved viral suppression.[24] Current targets aim for countries to achieve viral suppression among 86% of all PLHIV by 2025.[34,35]

Challenges in Long-Term Health and Well-Being Beyond Viral Suppression

PLHIV face substantial health challenges beyond viral suppression, including a high burden of multimorbidity and associated polypharmacy, which requires managing multiple chronic conditions that may be exacerbated by HIV or its treatment, or may be exacerbated by exogenous factors that disproportionately impact key populations (i.e., men who have sex with men, sex workers, transgender people, and people who inject drugs).[36] Stigma and discrimination within healthcare settings and within society persist, negatively impacting the mental and physical HRQoL for PLHIV. These health factors, as well as early aging and burdensome symptoms experienced by PLHIV negatively influences HRQoL for PLHIV. Addressing these challenges requires an integrated, person-centered approach in health systems that focuses not only on treating HIV but also on improving the long-term well-being and quality of life of PLHIV.[37,38]

Multimorbidity Among PLHIV

Multimorbidity, understood to refer to the coexistence of two or more chronic health conditions within an individual, may encompass a broad spectrum of conditions, including mental health problems and chronic burdensome symptoms.[39] PLHIV are at greater risk than the general population for concurrently having one or multiple comorbidities, with mental health issues such as depression and anxiety being commonly reported.[40,41] Even in settings with widespread access to ART, PLHIV have a higher burden of multimorbidity in the long-term than the general population, with several common non-communicable diseases contributing to substantially to the extra disease burden.[42,43] A large meta-analysis of studies published 1990-2015 found that PLHIV are at twice the risk of having a cardiovascular disease compared with their seronegative counterparts.[44] In a large cohort study from the United States, PLHIV were at significantly higher risk than other people for cardiovascular disease, chronic kidney disease, and osteoporotic fractures.[45] Similarly in Europe, PLHIV are most commonly hospitalized for respiratory diseases, mental health issues, renal diseases, heart diseases, kidney disorders, and liver problems.[46]

Globally, cardiovascular diseases (CVD) like atherosclerosis and hypertension are common among PLHIV,[44,47] while this population is more susceptible to myocardial infarction, stroke, and heart failure, compared to those without HIV.[48] Prevalence for CVDs in Spanish national samples ranged from 4.7% in 2019 to 52.7% in 2020.[49–51] Hypertension prevalence estimates for national samples ranged from 8.5% in 2023[9] to 28.6% in 2021[52] and were 66.7% in 2021 in a sample (n=30) from Aragon[53] and 85.5% in 2022 in a sample of PLHIV with advanced kidney disease (n=3090) from Catalonia.[54] Ischemic heart disease was estimated at 1% in a national sample (n=4798) in 2023.[55]

Bone diseases, including osteoporosis and low bone mineral density, further compound the health challenges faced by PLHIV, with older populations showing a higher prevalence of osteoarthritis. The national *VIH y AdvanCedHIV* (VACH) cohort in 2019 reported a 2.8% prevalence of bone disease and 11.1% osteoporosis.[50] Osteoporosis was also reported in 14.7% of a national sample of women with HIV in 2021,[56] as well as 10%[57] and 7%[58] of samples of PLHIV in Madrid in 2018 and 6%[59] in another Madrid-based sample in 2014. Low bone mineral density was reported among 4.1% of vertically-infected children in Madrid in 2017,[60] 22.8% of ART-naïve-HIV-infected men aged 21-50 in Madrid in 2021,[61] and 61% of a sample of PLHIV from Madrid in 2020.[62] Other bone diseases reported in the literature for Spain include osteoarthritis and asymptomatic vertebral fracture, with prevalence estimates of 21.2%[63] and 20%,[58] respectively, of samples of PLHIV over age 50 in Madrid. Prevalence for renal disease was estimated to be 0.4% and 5.9% in national samples in 2023 and 2019, respectively.[50,55]

Respiratory conditions like chronic obstructive pulmonary disease (COPD) and cases of recurrent infections are also prevalent among PLHIV, influenced by immune suppression and high rates of smoking among some key populations.[64,65] Respiratory problems may include shortness of breath, persistent cough, and reduced exercise tolerance, which in combination and over time reduces quality of life and interferes with one's ability to perform daily tasks.[64,65] The estimated prevalence for any chronic lung disease among a random national sample of PLHIV in Spain was 8.1% in 2020 [49] and 13% among a sample of PLHIV over age 50 in 2018.[51] COPD was estimated to be 10.9% among PLHIV over the age of 50 in Madrid in 2023.[63]

Key causes of liver disease in PLHIV include hepatitis B (HBV) and C (HCV) infections, which can progress to cirrhosis and liver cancer if untreated.[66] Despite advances in curing HCV and suppressing HBV, liver disease remains a leading cause of morbidity and mortality in this population. Other contributing factors include alcohol and drug use, psychiatric conditions, and socioeconomic barriers that hinder disease management and treatment access.[66] National samples of PLHIV estimate 1.5% chronic HCV co-infection in 2022,[67] 2.2% active HCV co-infection in 2022,[67] and previous HCV infections among 23.9% in 2021,[56] 57% in 2018,[51] and 37.7% in 2016.[68] Liver cirrhosis was estimated among 5.4% of PLHIV in 2022[67] and 32.1% in 2016.[68] Previous HCV infection was estimated among 46.4% of adults in 2022,[69] 43.6% in 2019,[70] and 45% in 2014,[59] while 0% prevalence was estimated in a sample of youth living with HIV in 2022.[71] Chronic HCV infection was estimated among 18.9% of PLHIV in Andalusia in 2015 and 21% of those with chronic HCV infection had an advanced liver fibrosis stage of four.[72] Among diseases affecting the liver, diabetes and other metabolic illnesses among PLHIV signal an additional layer of complexity in managing HIV. Prevalence estimates for diabetes among PLHIV from 2.5%-19.9% in national samples,[50–52,55,56,73,74] and one study reported a prevalence of 43.3% in Aragon,[53] while four studies in Madrid ranged from 4% to 16%.[63,70,75,76] Steatosis was estimated among 30.5% of PLHIV in a national sample in 2023.[55] Steatosis was estimated to be 41% in 2019, and significant steatosis to be 29% in 2018, in samples in Catalonia.[77,78] Metabolic dysfunction-associated steatotic liver disease (MASLD) and MASH have also emerged as significant concerns, potentially exacerbated by ART-related weight gain and metabolic syndrome.[66] MASLD was estimated at 28.9% among 38 children and adolescents with HIV from Madrid in 2022.[79] MASLD was prevalent among 30.5% of the Spanish national Cohort of the AIDS Research Network (CoRIS).[55] Comparatively, the estimated pooled prevalence of MASLD among PLHIV in high and middle-income countries is 38%.[8]

Moreover, PLHIV have higher incidences of 30 out of 40 types of non-AIDS-defining cancers (NADCs) examined, including particularly increased incidence for all 20 infection-related NADCs and cancers associated with human papillomavirus (HPV) infection such as cervical, anal, and other anogenital cancers.[80] A 2023 study of PLHIV in Spain over age 50 estimated the current prevalence of any cancer type to be 6.9% while the prevalence of any history of cancer was 7.4%. Lung cancer was estimated to be prevalent among 3.6% of adults in 2021.[81] High-grade anal squamous intraepithelial lesions were prevalent among 15.3% of biopsies among MSM in 2021 and 29% in 2014.[82]

The psychosocial symptoms reported by PLHIV can have a profound impact on their overall well-being and quality of life. Mental health comorbidities such as anxiety, depression, and substance use disorder are commonly reported by PLHIV and can affect adherence to ART and overall health outcomes.[83] Adolescents with HIV face unique challenges, including environmental stressors and mental health difficulties, which are closely linked to ART nonadherence and may require targeted interventions.[84] Aging PLHIV often encounter compounded psychosocial challenges, including HIV-related stigma, loss of social networks, and cognitive impairments, which can exacerbate the deterioration of health and well-being.[85,86] Effective retention in HIV care may be hindered by mental health issues, emphasizing the necessity of integrated mental health services to improve retention and health outcomes.[83,87]

Key populations at higher risk for HIV also may experience stigma and discrimination independent of their serostatus that may impact their psychosocial well-being. For example, men who have sex with men (MSM) may experience stigma and discrimination related to their sexual orientation, which can exacerbate psychosocial symptoms such as depression and anxiety.[36] People who inject drugs (PWID), also at high risk for HIV, may experience stigma and discrimination related to their drug use.[36] Sex workers report experiencing stigma and discrimination related to their profession.[36] Any members of these groups may experience feelings of internalized stigma and anxiety both unrelated to and compounded by their serostatus, which may result in social isolation and symptoms of depression or anxiety.[14]

In Spain, burdensome mental health problems are commonly reported by PLHIV, as 26.7% of participants in a 2021 study based in Aragon reported having a mental health disorder.[53] In Catalonia in 2023, 21.42% of participants in one study reported depressive symptoms,[88] whereas a separate study in 2017 estimated clinical depression to be prevalent among 4% of participants and anxiety prevalence to be 7%.[89] A 2023 Madrid-based study estimated that 9.2% of participants over age 50 have one or more psychiatric disorders.[63] Anxiety was estimated to be experienced by 13.9% of Madrid-based youth living with HIV in 2022,[71] and 21.3% among people of any age in 2020.[90] Likewise, bipolar disorder prevalence was estimated among 11.3% of adults with HIV in Madrid in 2020, while an estimate for delusional disorder prevalence was 6.3%.[90] Mental health services are integrated within the primary care system in Spain, and PLHIV have access to mental health services through their primary care and HIV care providers, who can refer them to specialized mental health services as needed.[91] Mental health support for PLHIV in Spain nominally includes counseling, psychotherapy, and psychiatric services.[35] However, the mental health system in Spain, which is predominantly situated within primary care, faces substantial challenges, such as a shortage of specialists and limited resources, with some aspects of the responsiveness of such services frequently rated as poor by patients.[92] While mental health patients often perceive good responsiveness in terms of dignity, confidentiality, and communication, the demand for mental health services often outstrips the capacity of primary care providers, leading to longer wait times and reduced quality in areas such as autonomy and choice of provider, especially in urban areas, where the pressure on primary care services is particularly acute, and for economically disadvantaged populations who experience poorer responsiveness overall.[92]

Other problems and symptomologies related to multimorbidity, such as frailty, polypharmacy, sexual health issues, sleep quality and vitamin deficiencies are reported by PLHIV in Spain, further illustrating the diverse and complex healthcare needs of this population.[59,61,71] Frailty was estimated among 6% and 15.4% of PLHIV over age 50 in Madrid in 2023 and 2017, respectively; prefrailty was estimated among 52.7% and 52.1% of PLHIV over age 50 in Madrid in 2023 and 2017, respectively.[63,93]

The landscape of multimorbidity among PLHIV in Spain paints a picture of complex interrelated health challenges that extend beyond HIV management. The prevalence and variance in comorbid conditions across different regions underscore the need for holistic, patient-centered care approaches that integrate various medical specialties. As PLHIV live longer, addressing these multifaceted health needs becomes paramount to improving their health outcomes and long-term well-being, calling for a reorientation of healthcare systems towards more integrated care models tailored to the unique needs of PLHIV.[94,95]

Despite early research implying that PLHIV with higher numbers of comorbidities, including depression, suffer from a poorer quality of life,[10,96–98] national health systems are not always equipped to address multimorbidity in a responsive, patient-centered way that considers their HRQoL.[95] The link between comorbidities and HRQoL is particularly notable given that PLHIV have a higher burden of multimorbidity than the general population, with several common non-communicable diseases contributing significantly to their disease burden.[42,43] Preliminary research has also found that among PLHIV, a higher number of comorbidities is correlated with lower quality of life.[96,97,99,100] Health systems in Europe and throughout the world remain unprepared to address the challenge of managing the long-term health of PLHIV and few, if any, national surveillance systems collect comorbidity data for PLHIV.[101] While not all comorbidities among PLHIV are directly related to HIV, the higher prevalence among this population and the fact that comorbidities are often not diagnosed even when PLHIV are in care make this a priority issue to address.

Stigma and Discrimination

Stigma and discrimination are routinely reported by PLHIV as contributing substantially to lower quality of life, lower treatment adherence, and poorer health outcomes, such as anxiety and depression.[14,102–106] Yet, research on these topics remains inconclusive in part because of a lack of a consensus on how to measure them.[107,108] Types of HIV-related stigma include public stigma, i.e., negative perceptions and behaviors towards PLHIV by the general public, perceived external stigma (i.e., how individuals think society views them), internalized stigma (i.e., how they view themselves due to societal attitudes), enacted stigma (i.e., actual discriminatory actions or behaviors experienced by people due to their HIV status), institutional stigma (i.e., discriminatory policies and practices within organizations that hinder rights and/or services for PLHIV), and intersectional stigma (i.e., the compounded effect of multiple stigmas experienced at the intersection of HIV status with other social identities like race, gender, or sexuality).[109–112] While the negative effects of stigma and discrimination on well-being are important from a public health standpoint, HIV-related discrimination would be equally objectionable even in the absence of such evidence, as it constitutes a violation of human rights.[113] For example, HIV-related discrimination has been linked to negative outcomes such as avoidance of health services, medication non-adherence, and viral non-suppression.[114–116] The persistence of HIV-related discrimination in healthcare settings has led UNAIDS to include the following target in its 2021–2026 strategy: “90% of people living with HIV and key populations report no discrimination in the health sector.”[117]

In Spain, the stigma related to HIV and AIDS remains a significant psychosocial issue, manifesting through both personal and societal attitudes that can lead to discrimination and social exclusion.[106,118,119] The stigmatization process involves multiple layers, including individual prejudices and structural facilitators that intersect with overlapping stigmas such as gender, poverty, migration, and sexual orientation.[120] Data since 2008 demonstrate that although there has been a slight decrease in the discomfort and negative feelings towards PLHIV, substantial misconceptions about the transmission of the virus,[121] indicating an ongoing need for improved public education and awareness campaigns to address these misconceptions and, ultimately, reduce stigma. A majority of PLHIV in Spain rank stigma and discrimination as the most burdensome issues impacting mental health and overall quality of life.[119,122] Among 119 Spanish and Latin American residents, resilience to stigma has been significantly influenced by factors such as lower rumination and internalized stigma, and higher emotional expression, positive thinking, and past resilience.[123]

Legal and policy discrimination against PLHIV continue to be documented across high-, middle-, and low-income countries.[108,124–129] and it continues to exist in healthcare settings,[101,130] as well as in travel restrictions[131] and other forms worldwide.[132] Such institutionalized discrimination can exacerbate the stigma and discrimination experienced by individuals. PLHIV in the United States report that the criminalization of HIV transmission, exposure, and non-disclosure contributes to felt social stigma, and they often do not trust the judicial system to deal with them fairly.[133] Countries that require HIV testing to obtain long-term visas usually refuse entry or deport those testing positive, and these laws affect vulnerable populations like asylum seekers and migrant workers disproportionately.[134] Some countries continue to enact discriminatory laws and policies that target populations merely at risk for HIV,[132] for instance by banning blood donations from people who inject drugs, who are sex workers, and men who have sex with men, though these laws are changing.[135,136] Many countries continue to criminalize key populations (e.g. men who have sex with men, sex workers, transgender people, and people who inject drugs) who are particularly vulnerable to HIV and frequently lack adequate access to services.[125,136] In 2016, the

WHO Global Health Sector Strategy on HIV recognized discrimination as detrimental to the well-being of PLHIV.[137]

In Spain, access to HIV care among undocumented immigrants is influenced by discriminatory policies, with regions like Galicia and Valencia demonstrating lower levels due to more restrictive healthcare policies, compared with other regions, such as Andalucía, that provide greater than national policies that generally restrict healthcare services for undocumented immigrants.[31] Each autonomous community has the authority to plan, finance, and manage healthcare services within its jurisdiction, including for hospitals, primary care centers, and mental health services.[91] While the central government retains a role in coordinating national health policy and ensuring overall equity, healthcare is primarily funded through general taxation with the allocation of resources varying substantially between regions due to differences in resource availability and political priorities at the local and regional levels.[91] Further, Spanish legal judgments on HIV transmission between 1981 and 2016 often reflected stigmatizing views, including attributions of blame and responsibility to PLHIV.[138] Nonetheless, Spain has committed to end institutional discrimination and to mitigate interpersonal HIV-related stigma.[139]

Early Ageing among PLHIV

Early or accelerated ageing among PLHIV has contributed to an increased risk of age-associated non-communicable comorbidities at a younger age compared to the seronegative population.[43,140–143] Persistent immune activation, or chronic inflammation, even in the presence of effective ART can contribute to early ageing. Ongoing viral replication, albeit at low levels, along with dysregulated immune responses, contribute to a state of chronic inflammation.[143–145] This inflammation is implicated in the pathogenesis of several non-AIDS-related comorbidities, such as cardiovascular disease, kidney disease, and neurocognitive disorders, which are prevalent in the ageing population of PLHIV. These conditions often appear 10 to 15 years earlier in HIV-positive individuals than in the general population.[10,43,50] Neurocognitive disorders affect a significant proportion of PLHIV and manifest with features similar to those of neurodegenerative diseases associated with ageing, even among those with suppressed viral loads, likely due to ongoing low-level inflammation and direct viral effects of ART on neural tissues.[146] Apart from comorbidities, early ageing also contributes to burdensome clinical manifestations like frailty.[43,58,93] Symptoms of functional decline, such as slower walking speeds, weaker grip strength, and neurocognitive impairment, progress faster in PLHIV compared to those without the virus.[147] Factors such as reduced muscle mass and bone density have been linked to these declines in physical function among older adults with HIV.[147]

Furthermore, social determinants of health, such as stigma and socioeconomic disparities, can exacerbate the ageing process in PLHIV, who often face higher levels of stress and mental health issues, which can also contribute to accelerated ageing.[43,148] Some behavioral risk factors such as smoking, substance use, and poor diet are disproportionately higher among some populations living with HIV.[149–151] These factors can exacerbate the risk of developing comorbid conditions and can independently accelerate the ageing process.[152–155] Substance use, including high-risk alcohol consumption and drug dependence, emerges as another significant concern within the PLHIV community in Spain. Variations in substance use prevalence across different regions reflect the complexity in managing HIV and substance use disorders. Current injecting drug use was reported in a 2020 sample (n=80) in Madrid estimating a 0.9% prevalence among PLHIV[90] and a 2020 sample (n=297 men with “normal” cytology) in Catalonia estimating a 2% prevalence among PLHIV.[156]

Health-Related Quality of Life (HRQoL) of PLHIV

Several determinants, both related and unrelated to the virus, influence the HRQoL of PLHIV. The impact of clinical markers such as CD4 cells/mm3 and HIV viral load has a well-established association with lower overall HRQoL score[157–159] and self-perception of health for specific HRQoL domains like physical and mental health status.[160,161] Detectable HIV viral load has been linked to worse general HRQoL and physical health status, while improvements in HIV viral load have been found to impact positively on HRQoL.[160,162,163] The evidence suggests that poor clinical outcomes can result in diminished HRQoL, and there is additional evidence showing the predictive capacity of HRQoL on clinical outcomes. For example, both physical and mental HRQoL dimensions' scores were predictive of all-cause hospitalization, emergency department utilization, and hospital discharge rates of PLHIV in the United States.[164,165] In the Netherlands, higher patient-reported HRQoL outcomes in physical domains predicted survival among PLHIV receiving ART.[166] Similarly, higher baseline depressive symptoms, hopelessness, and avoidant coping, measurable aspects of the mental health domain of HRQoL, predicted greater viral load increases and a significant linear decrease in CD4 cell count over a four-year period.[167] These findings suggest that improving the health status of PLHIV could lead to enhanced HRQoL but also that improving HRQoL is central to addressing the long-term health of PLHIV. This is prescient because emerging challenges related to the ageing process in PLHIV,[95] make clear that self-reported HRQoL offers a clear relationship to clinical markers and considers factors experienced by the patient that are not often measured in care settings, such as life satisfaction, patient empowerment, the impacts of stigma, and burdensome symptoms or pains.[168] Moreover, HRQoL has demonstrated some acceptability in monitoring health system performance.[169] Measuring HRQoL in clinical practice could provide highly useful information for physicians about the problems that undermine the HRQoL of their patients. Addressing modifiable factors that influence HRQoL has the potential to benefit both PLHIV health outcomes and also the efficiency of health systems.

Patient- or Person-Reported Outcome and Experience Measures

Patient-reported outcome measures (PROMs) focus specifically on the patient's perspective regarding their health condition and treatment effects, capturing symptoms, functioning, and well-being in the context of care provision.[170] PROMs offer an assessment by which individuals can self-report their symptoms and quality of life. In the context of HIV care and science, PROMs are often used to evaluate the effectiveness of medical treatments, to measure HRQoL, and to gain a deeper understanding of the impact of aspects of the disease and care on patients' lives.[168,170]

PROMs can take various forms, including questionnaires, interviews, and diaries. They can assess a range of outcomes commonly reported as burdensome by PLHIV, including physical symptoms, psychological well-being, social functioning, and treatment adherence. The use of PROMs in HIV care and science provides valuable information that complements objective measures of disease progression and treatment response. PROMs are an important tool in patient-centered care as they provide patients with a voice in the evaluation of their treatment and allow for a more comprehensive understanding of the disease experience.[168] Additionally, the use of PROMs in clinical trials can help ensure that treatments are effective and tolerable for patients, and can inform the development of new treatments that better address patients' needs. PROMs play a crucial role in improving the quality of care and advancing the science of HIV treatment.[168] They provide valuable insights into the patient experience and can inform the development of more effective and patient-centered treatments.[168]

PROMs in HIV research provide valuable insights into the impact of the disease on an individual's quality of life. PROMs may be disease-specific, such as the POZ Quality of Life (POZQOL) scale or the World Health Organization’s Quality of Life tool for HIV (WHOQOL-HIV),[171] or generic, such as the EuroQol five-dimension five-level scale (EQ-5D-5L).[172] These tools can be used to track changes in quality of life over time, compare the health status of different populations, and inform treatment decisions and public health policies. A 2021 study in Spain reported a summary averaged PozQoL score of 3.5 on a scale from 0.0 to 5.0, indicating a moderate to high perceived quality of life among participants.[173] Factors that were significantly associated with lower PozQoL scores included poor self-rated health, having been diagnosed with a mental health condition, and not having enough money for basic needs.[173] These factors point to the significant impact of health perceptions, mental health status, and financial stability on the quality of life. The health concerns sub-scale received the lowest average score, 2.9 of 5.0, suggesting that health worries are a prominent issue affecting the quality of life for PLHIV in Spain.[173]

EQ-5D-5L is a general health status measurement tool that can be used to assess the impact of various health conditions, including HIV, on an individual's quality of life.[172] The scale measures five dimensions of well-being: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.[172] The same 2021 POZQOL study also estimated a mean EQ-5D-5L utility score of 0.88 among PLHIV, slightly lower than the general population score of 0.91.[173] The most affected EQ-5D-5L domain among PLHIV was anxiety/depression, where 38% reported problems compared to 15% in the general population.[173] Older age, poor self-rated health, and the presence of a mental health condition were identified as significant predictors of lower EQ-5D-5L utility scores.[173]

The World Health Organization's Quality of Life - HIV Brief Version (WHO-QOL-HIV-Bref) is a short form of the WHOQOL-HIV instrument.[171] The abbreviated scale measures six domains of well-being: physical health, psychological health, level of independence, social relationships, environment, and spirituality. Its validation in Spain revealed a relatively high average score for the physical health domain, 15.5 out of 20, suggesting that the physical well-being related to symptoms, energy, sleep, and pain is generally managed effectively among the participants.[119] Psychological health scored an average of 14.9 out of 20, indicating a moderately good perception of psychological well-being, including aspects like mood, positive feelings, and self-esteem, although there is room for improvement, especially in managing negative feelings.[119] The score for the level of independence domain was also 15.5 out of 20.[119] This score reflects a reasonable level of autonomy in daily activities and medication management, suggesting that many individuals feel capable of managing their day-to-day life. The social relationships domain had an average score of 15.0 out of 20.[119] This score points to generally satisfactory social interactions and support but highlights potential issues in items related to sexual satisfaction and deeper personal relationships.[119] The environment domain scored an average of 15.3 out of 20, reflecting generally positive perceptions about safety, physical surroundings, and access to medical services, though financial resource constraints were a notable concern. Spirituality presented the lowest average score of 14.5 out of 20, indicating some challenges in addressing existential and spiritual concerns.[119]

Patient-reported experience measures (PREMs) are tools used to gather information about a patient's overall experience with healthcare services.[170] They focus on the quality of care from the patient's perspective, capturing aspects such as communication with healthcare providers, understanding of medical information, and the perceived level of respect and empathy shown during their care.[170] PREMs are valuable for assessing and improving patient satisfaction and the effectiveness of healthcare delivery. A broader perspective of PREMs may also encompass social, psychological, and general life satisfaction factors that affect an individual's well-being, aiming to capture a comprehensive view of their quality of life.[170] Of the 47 quality of care indicators developed and validated by the AIDS Study Group (GeSIDA) of the Spanish Society of Infectious Diseases and Clinical Microbiology, established in 2010, four relate to patient satisfaction.[174] On these, participants (n=334) scored 9.04 out of 10, indicating a high level of patient satisfaction with healthcare services in 2010.[175]

Current HIV and AIDS Monitoring Indicators for Countries

The HIV “continuum of care” has served as a primary model for monitoring progress on national HIV and AIDS responses.[176] In 2014, UNAIDS set (inter)national targets for the three main stages of the care continuum: that 90 percent of people living with HIV know their status; 90% who know their status receive antiretroviral therapy (ART); and 90% of those on ART achieve viral suppression.[5] These data are reported to UNAIDS via ad-hoc country progress reports. In Spain, the report is prepared by the Ministry of Health, Social Services and Equality and the subdivisions of the *Secretaría General de Sanidad Dirección General de Salud Pública, Calidad e Innovación Subdirección General de Promoción de la Salud y Epidemiología.* The current strategic plan of Spain, from 2021-2030, aligns with the UNAIDS 2030 targets by emphasizing prevention, early diagnosis, and treatment, promoting equity and community involvement.[35] The strategic plan also highlights the importance of early detection of comorbidities and modifiable risk factors among PLHIV and emphasizes the integration of chronic care approaches in managing HIV without setting explicit targets or activities.[35]

The UNAIDS global strategy for the period 2022-2030 sets the overarching goal to end AIDS by 2030.[177] Specific indicators include the UNAIDS 95-95-95 targets aiming for the following by the year 2025: 95% of all people living with HIV will know their HIV status; 95% of all people diagnosed with HIV will receive sustained ART; and 95% of all people receiving antiretroviral therapy will have viral suppression.[34] These targets are designed to maximize the prevention benefits of ART and bring the HIV pandemic under control by reducing the rate of new infections and improving the health of those living with HIV. Importantly, UNAIDS also recognizes the importance of countries measuring stigma, discrimination, and patient-centered approaches to HIV care, including integrated health services for sexually transmitted and viral infections, differentiated service delivery to meet patient needs (e.g., longer refill prescriptions, fewer in-person visits), and achieving a good health-related quality of life at all stages of the HIV care continuum.[34]

The WHO Global Health Sector Strategy for HIV and sexually transmitted infections set targets for measuring national progress to end AIDS as a public health threat by 2030: reduce the global number of new HIV infections to 335,000 annually from 1.5 million in 2020 and to decrease HIV-related deaths to below 240,000 annually from 680,000 in 2020.[177] Related milestones include reducing the number of people living with HIV dying from tuberculosis, hepatitis B, and hepatitis C, aiming for a reduction to 55,000 annually by 2030 from 210,000 in 2020. While, there is an emphasis on addressing comorbidities among the broader health needs of PLHIV, aligning with recent calls that HIV care not solely focus on suppressing the virus but also aim to enhance overall health and well-being, the strategy does not propose or set targets beyond viral suppression, such as (health-related) quality of life nor co- or multimorbidity prevalence. This emphasis expands on the previous WHO global health sector strategy on HIV, 2016-2021, which recommended “monitoring the health consequences of HIV epidemics, including common HIV coinfections and other comorbidities," among calling on Member States to commit to an ambitious reporting agenda of 50 indicators,[178] without any measuring issues beyond viral suppression.

The Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia has been the central mechanism guiding HIV monitoring in the European region since 2004. It identified 33 actions for governments to lead in HIV treatment, care, and prevention.[179] The European Centre for Disease Prevention and Control (ECDC) monitors country progress, biannually from 2008-2018 and annually since 2018, using a combination of a country questionnaire, country consultations, and surveillance data from ECDC and UNAIDS.[180] Since 2020, the country questionnaire has included two items on national monitoring for HRQoL and another item reporting the top five causes of morbidity among PLHIV,[181] though Spain has never reported these data.[182]

HIV Monitoring in Spain

Spain has achieved the three 90 targets in 2021; 92.5% of the estimated 148,631 PLHIV in Spain knew their status, 96.6% of those were on ART, and 90.4% of those on ART had achieved viral suppression.[24] These data indicate that 80.8% of all PLHIV in Spain have achieved viral suppression. Data to report these metrics are collected through Spain's epidemiological surveillance network (*Red de Vigilancia Epidemiológica,* RENAVE), established in 1995, which is managed by the Institute of Health Carlos III (ISCIII) under authorities provided by Law 14/1986.[183] In the decentralized national health system (*Sistema Nacional de Salud*, SNS), the autonomous communities (*Comunidades Autónomas*, CCAA) are competent for the provision of health services, while the central government maintains competencies for regulating its structure and general coordination. Regional health authorities manage operational planning, resource allocation, and health service provisions at the local level, guided by the national Ministry of Health.[91] Management for the SNS is coordinated through its Interterritorial Council of Health (*Consejo Interterritorial del Sistema Nacional de Salud*), which approves the list of Mandatory Notifiable Diseases (*Enfermedades de Declaración Obligatoria*, EDO).[184] These data are reported by the public health departments of CCAA to the ISCIII National Epidemiology Centre (*Centro Nacional de Epidemiología*, CNE). To operationalize this reporting, the *Subdirección General de Información Sanitaria* of the Ministry of Health, responsible for managing the information system for the SNS[185] and established by the Law 16/2003,[186] manages a Statistical Portal, by which the reporting of key indicators such as the EDO list and several disease registries can be conducted.[187] As a competency of the CCAA, regional public health departments collect this data from primary sources, including surveys of hospitals and health centers, and secondary sources, such as antiretroviral prescribing patterns.[91,188] The EDO was amended in 2010 such that HIV be notified by a special system (*Sistema de información sobre nuevos diagnósticos de VIH*, SINIVIH).[189] Currently, the SINIVIH covers most of the Spanish population, apart from *Comunidad Valenciana*, which for technical reasons has not been able to incorporate its data into the national database.[189] Both at the national and autonomous level, HIV and AIDS registries must contain homogeneous data on cases, deaths, testing, and mode of transmission, but indicators beyond viral suppression, such as those measuring multimorbidity or quality of life, are not mandated nor collected.[184,190] Consolidated HIV data are reported in two annual public reports, the *Vigilancia Epidemiológica del VIH y SIDA en España*[25] and *Vigilancia Epidemiológica de las Infecciones de Transmisión Sexual en España*.[191]

Clinical guidelines govern HIV clinical practice by establishing uniform standards of evidence-based care, and in Spain are established by the AIDS Study Group (GeSIDA) of the Spanish Society of Infectious Diseases and Clinical Microbiology.[192] Current guidelines, recommend annual clinical monitoring for co-infection of tuberculosis,[193] hepatitis B,[194] hepatitis C,[194,195] and opportunistic or AIDS-defining infections,[196] as well as chronic conditions such as kidney and bone diseases,[197] and neurocognitive diseases.[198] With these guidelines, which apply to clinical surveillance, only AIDS-defining infections are reported in the annual epidemiological surveillance report for HIV.[25]

The European AIDS Clinical Society (EACS) guidelines emphasize managing comorbidities, enhancing long-term well-being, and improving quality of life for HIV patients by integrating comprehensive care that includes physical, psychological, and social aspects.[199] They also stress the importance of incorporating patient-reported outcomes towards improved overall patient satisfaction and treatment adherence.[199] Among clinical care providers surveyed in Europe showed high levels of consensus with the EACS guidelines on comorbidities in aging PLHIV.[200] Nonetheless, significant gaps were noted, for example in standardized assessments for frailty and menopause, which are increasingly recognized as crucial for optimizing care in ageing PLHIV.[56,63,93,200,201]

Healthcare institutions, in Spain and elsewhere, implement clinical guidelines into practice trough clinical protocols and standard operating procedures, which may involve, for example, updating electronic health records (EHR) systems to include the latest recommendations and providing clinicians with decision support tools. The absence of long-term well-being recommendations and suggested metrics for their monitoring represents a significant gap in the clinical management of HIV, which potentially limits the implementation of interventions that could improve health and quality of life.

HIV Cohorts in Spain

CoRIS is a large, ongoing observational cohort study of people living with HIV in Spain.[202] The cohort, established in 2004, includes over 27,000 PLHIV who receive care in 48 centres from 14 of 17 Autonomous Regions in the Spanish public healthcare system.[202]

The PISCIS cohort is a multicentric longitudinal study of HIV-positive patients over 16 years of age who have been seen at one of the 18 participating hospitals across Catalonia and the Balearic Islands since January 1998, regardless of their stage of disease or level of immunosuppression.[203] The cohort's main objectives are the clinical-epidemiological surveillance of patients receiving HIV care, evaluation and monitoring of the response, and conducting research to address emerging clinical and epidemiological questions. From 1998 to 2016, 22,198 people were enrolled.[203] A majority, 60.3%, were new diagnoses. At enrollment, 15.4% of the patients were diagnosed with AIDS, and the overall mortality rate for the cohort stood at 8.8%.

Additionally, during the study period, 5.1% of those followed developed AIDS. The cohort predominantly consisted of males (79.5%) within the 25–44-year age group (74.6%). Key transmission groups included men who have sex with men (MSM) and persons who inject drugs (PWID). Immigrants constituted 33.0% of the cohort and 36.1% of new diagnoses.[203]

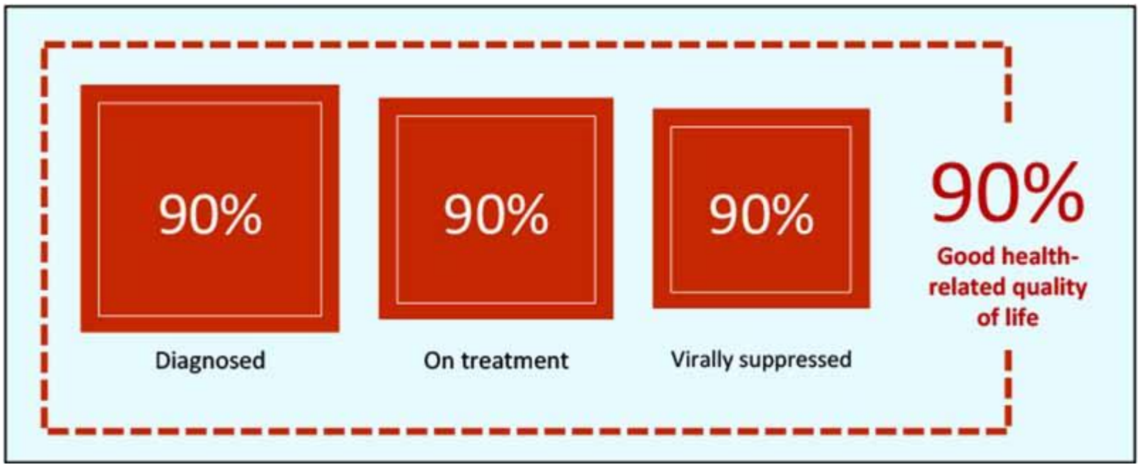
The *VIH y AdvanCedHIV* (VACH) cohort consists of predominantly middle-aged men who acquired HIV via sexual or parenteral routes.[73] Sociodemographic factors significantly impact treatment adherence and study follow-up, with higher loss rates among immigrants, intravenous drug users, and those who are unemployed.[70] As recently as 2020, the cohort exhibited high rates of cardiovascular risk factors like hyperlipidemia and hypertension, indicating a need for comprehensive cardiovascular risk management.[74]

The GEMES study in Spain aimed to estimate HIV seroconversion dates among cohorts of hemophiliacs who likely acquired the infection through contaminated blood products during the late 1970s and early 1980s.[204] This study involved 632 hemophiliacs identified as HIV-positive between 1983 and 1985 and described and validated methods for imputing HIV seroconversion dates using two main approaches: one based on the expected value of the estimated distribution and another using the geometric mean of five random samples from the estimated distribution. These methods were evaluated against mid-point seroconversion dates and their efficacy in estimating AIDS-free time and survival rates. The findings indicated no significant differences in the AIDS-free time and survival estimates across the different methods, demonstrating that both imputation approaches provided reliable estimates of HIV seroconversion dates.[204] This capability is particularly useful for enhancing epidemiological analyses and understanding of disease progression in hemophiliac populations, where exact seroconversion dates are often unknown.[204]

Towards a Metric for Long-Term Well-Being Beyond Viral Suppression in HIV Care

In European countries, the monitoring of long-term well-being in HIV care necessitates an integrative approach that transcends traditional HIV clinical outcomes to include HRQoL metrics, management of multimorbidity and early ageing, and consideration of the social determinants of health. This approach aligns with the UNAIDS 90-90-90 targets and a "Fourth 90" metric proposed in 2016 by Lazarus, et al, which focuses on ensuring good HRQoL of PLHIV. It was first suggested as a target that 90% of those achieving viral suppression achieve good HRQoL[37] and later revised to include all PLHIV (**Figure 3**).[95] To align with the current global targets, a similar indicator may be referred to as a long-term well-being metric. In 2023, Lazarus et al. proposed that a comprehensive framework for long-term success should emphasize five key outcome pillars: sustained undetectable viral load, minimal impact of treatment and clinical monitoring, optimized health-related quality of life, lifelong integration of healthcare, and freedom from stigma and discrimination.[205] This framework aims to address the multifaceted needs of PLHIV by integrating person-centered healthcare approaches, reducing the treatment burden, and eliminating societal and structural barriers to improve overall well-being and quality of life, and it could be operationalized by addressing multimorbidity (and common chronic comorbidities), mental health, experienced stigma, and overall HRQoL through integrated, person-centered care approaches.[206]

Figure 3. The "Fourth 90" proposed revision to the UNAIDS 90-90-90 targets



Source: Lazarus JV, Safreed-Harmon K, Barton SE, Costagliola D, Dedes N, del Amo Valero J, et al. Beyond viral suppression of HIV - the new quality of life frontier. BMC Med [Internet]. 2016 [cited 2020 Mar 11];14(1):94.

Comprehensive HRQoL assessment tools are essential for capturing the multifaceted impacts of HIV on individuals' lives, including mental health, stigma, and social support. The management of multimorbidity, including routine screening for common co-infections and non-communicable diseases, calls for integrated care models that address both HIV and other chronic conditions concurrently, towards an holistic approach to patient care. The provision of mental health services, facilitated by routine screenings and access to mental health care, is crucial in addressing the psychological aspects of living with HIV. Additionally, addressing the social determinants of health through robust support systems and community engagement is vital for improving the overall well-being of PLHIV. As the PLHIV population ages, geriatric HIV care and longitudinal studies on ageing with HIV become increasingly important, necessitating adaptations in care models to meet these emerging needs.[215] The successful implementation of these strategies depends on standardized data collection protocols, integration of health information systems, and the support of policies and funding mechanisms that prioritize the comprehensive care of PLHIV. Realizing a long-term well-being metric, such as a Fourth 95, would necessitate a paradigm shift in HIV care towards a more patient-centered approach that not only involves managing viral replication to reach viral suppression, but also prioritizing mental health, social support, and the integrated management of comorbidities in clinical care.

Hypothesis

Monitoring long-term well-being for people living with HIV can be improved in Spain.

Objectives

This thesis seeks to identify opportunities for health systems to better respond to the long-term well-being needs of people living with HIV and will aim to:

1. Examine long-term well-being monitoring capabilities among the subnational and national health information systems of Spain in order to improve surveillance and inform healthcare for people living with HIV.
2. Identify factors that affect health-related quality of life using a novel, validated clinic screening tool for use in people living with HIV.

Material, methods, and results

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ORIGINAL ARTICLE

Network analysis to prioritize issues for intervention to improve the health-related quality of life of people with HIV in Spain

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Abstract

Objectives: The objective is to assess the interconnectedness of a network of health-related quality of life (HRQoL) variables among people with HIV (PHIV) to identify key areas for which clinical interventions could improve HRQoL for this population.

Methods: Between 2021 and 2023, we carried out a cross-sectional study within the Spanish CoRIS cohort. We conducted a weighted and undirected network analysis, which examines complex patterns of relationships and interconnections between variables, to assess a network of eight HRQoL dimensions from the validated Clinic Screening Tool for HIV (CST-HIV): anticipated stigma, psychological distress, sexuality, social support, material deprivation, sleep and fatigue, cognitive problems and physical symptoms.

Results: A total of 347 participants, predominantly male (93.1%), currently working (79.0%), self-reported homosexual (72.6%) and college-educated (53.9%), were included in the study. Psychological distress showed the highest centrality in the network, indicating its strong connections with sleep and fatigue, cognitive problems and social support within the HRQoL network.

Conclusions: Psychological distress, sleep and fatigue, cognitive issues and social support were identified as key factors in an HRQoL network, indicating that interventions focused on these areas could significantly enhance overall well-being.

KEYWORDS
health-related quality of life, long-term well-being, network analysis, patient-report outcome measures, Spain

INTRODUCTION

Maintaining good health-related quality of life (HRQoL) is a central component of long-term care for people with HIV (PHIV) beyond achieving viral suppression [1]. HRQoL encompasses physical, psychological and social dimensions of well-being, all of which can be significantly impacted by living with HIV. Addressing HRQoL is crucial because it affects overall health outcomes, adherence to treatment and the ability to engage in daily activities and social roles. Therefore, improving HRQoL should be an integral goal of HIV care, alongside clinical management of the virus. Several problems strongly impact PHIV's HRQoL, but these are usually unknown or underdiagnosed by healthcare professionals (HCPs) [2]. These health-related problems persist despite the success of many health systems in identifying PHIV and engaging them in long-term care, for example in Spain where an estimated 80% of all PHIV have achieved viral suppression [3]. To help HCPs identify these problems in clinical practice and consequently take action to address them, Fuster-RuizdeApodaca et al. developed a Clinic Screening Tool (CST-HIV) to efficiently identify health-related issues undermining the HRQoL of PHIV during routine clinical care, allowing for timely and targeted interventions. It includes eight dimensions affecting HRQoL and was validated in Spain (Figure 1) [4].

The prevalence of any problem does not equate to its ability to influence HRQoL. These problems are interconnected, and often there is no causal direction between them. Instead, these problems are interrelated in various ways. Some issues, such as cognitive problems, difficulties with memory, attention and decision-making, or burdensome physical symptoms and issues in sleeping commonly reported by PHIV, directly impact daily functioning and overall well-being and can become more problematic as one ages [5, 6]. Anticipated stigma refers to the expectation of discrimination or prejudice due to one's HIV status and can lead to increased stress and social isolation, adversely affecting mental health and potentially discouraging people from seeking treatment or disclosing their status to others [7]. Psychological distress encompasses anxiety, depression and stress, which are prevalent among PHIV and can diminish HRQoL by affecting emotional and social well-being [8, 9]. Issues related to sexuality, including changes in sexual function, fear of transmitting the virus to others, and anticipated or experienced stigma, can significantly impact relationships and self-esteem [10]. Material deprivation, including lack of access to basic needs, financial resources and healthcare, is a foundational challenge to the rest of the CST domains that disadvantages many PHIV [11]. Social support from friends, family and community members can buffer the negative impacts of HIV on HRQoL through emotional, informational and practical assistance [12].

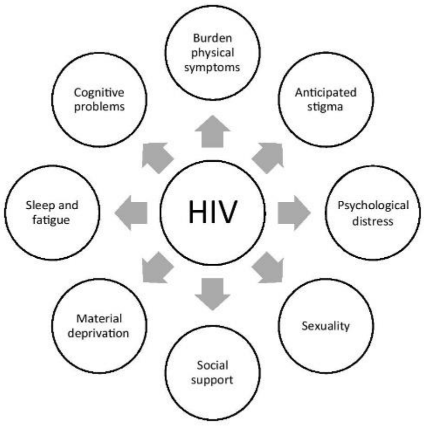

FIGURE 1 HIV-related problems that undermine health-related quality of life [Clinic Screening Tool for HIV (CST-HIV) dimensions].

Diagnosing and improving the HRQoL of PHIV involves identifying the problems that affect them. The development of the CST-HIV and its initial validation showed that all eight dimensions included in the CST-HIV had a negative direct impact on HRQoL [4]. Yet, these dimensions are interrelated and their degree of influence on each other is not well understood [7, 9, 13, 14]. HIV treatment and care may be improved through modifications of this network by applying interventions targeting the strongest factors. The present analysis aims to utilize a network analysis approach to better understand the interrelationships between the dimensions of the CST-HIV and to identify key areas for intervention. Because the CST-HIV was designed to detect issues affecting HRQoL, this study can elucidate the complex network of relationships between these dimensions, offering deeper insights into the underlying structure of HRQoL issues in PHIV.

METHODS

Study design

We designed a cross-sectional study within the Spanish CoRIS cohort. CoRIS is an open, multicentre and prospective cohort of HIV-positive adults, naïve to antiretroviral treatment at study entry, recruited since January 2004 from any of the 48 centres from 14 of 17 autonomous regions in the Spanish public healthcare system, which has been described in detail elsewhere [15]. A total of 17 CoRIS centres participated in this study.

Participants and sample size

Eligible participants were any HIV-positive adults in a CoRIS-participating centre and who attended their outpatient clinic between June 2021 and June 2023. For a network analysis of eight dimensions using 24 items, we defined the network structure as an 8 × 8 model matrix with a target sensitivity of 0.6, a probability of 0.8 and 95% confidence intervals, we estimate that approximately 300 participants were sufficient to achieve the desired sensitivity stability and accuracy of the network [16].

Variables

We designed a self-administered questionnaire to collect information on sociodemographic characteristics (i.e. age, duration of infection, sex, gender, marital status, sexual orientation, country of origin, level of education, work situation, housing, home monthly income, personal monthly income), health data (i.e. HIV transmission route, years since diagnosis) and the CST-HIV. The CST-HIV is a short measure to screen eight problems undermining the HRQoL of PHIV [4]. The CST-HIV was developed following established instrument development procedures, including a literature review, focus group discussions with HIV care providers and PHIV, and a pilot study to analyse psychometric properties [13]. The tool includes eight dimensions: anticipated stigma, emotional distress, sexuality, social support, material deprivation, sleep/fatigue, cognitive problems and physical symptoms. Each dimension is measured through three items, resulting in a 24-item scale. All items use a five-point scale with a total score in each dimension ranging from 1 to 15. Negative items are reverse-coded for scoring, such that higher scores indicate greater problem severity within the dimension. The validation of the CST-HIV occurred in the Spanish CoRIS cohort [4].

Procedures

Healthcare providers explained the aims of the study to the eligible patients and offered them the opportunity to participate. Those who agreed were provided an informed consent form. Once consent was obtained via signature, each recruitee was provided a link to download the mobile application through which they could answer the online version of the questionnaire with a unique login that allowed each person to return to their responses at their convenience. The mobile app was specifically designed for this study, and the average time to complete the questionnaire was 14 min. In-person recruitment through healthcare providers continued until the minimum sample size of $n = 300$ was exceeded. Data collection occurred between June 2021 and June 2023.

Data analysis

We first calculated mean scores for each CST-HIV dimension and conducted Pearson correlation analyses to explore the associations between these dimensions. We then conducted a weighted and undirected network analysis [17]. The network model, which has its basis in psychopathology, seeks to analyse the dynamic, sometimes causal, interactions between symptoms and signs [18]. In this case, the problems affecting HRQoL are in a complex dynamic system and influence each other. This analysis allows us to see the pattern of relationships between these problems by placing the most relevant nodes in the centre of the network through an iterative procedure, while the weakest nodes are placed at the periphery. The following measures are available to analyse the network structure: distance and length of the shortest path, centrality, connectivity and clustering. Centrality measures allow the node's relative importance within the network to be analysed in terms of the pattern of connections. Not all nodes are equally important. A node is central if it has many connections. A node is peripheral – it is on the outside of the network – if it has few connections. To assess whether a node is central, and therefore influential, in the network, this analysis considers (a) degree centrality (i.e. the number of connections, or 'edges' of a node), (b) strength centrality, (c) closeness centrality, and (d) betweenness centrality. Nodes with more connections are more central in a network, and more central nodes are potentially more critical than less central nodes. Node strength is considered the most important index of centrality, indicating which nodes are the most influential in a network. Closeness measures how close a node is to all other nodes, indicating efficiency within the network. Betweenness represents the centrality of the node vis-à-vis other nodes, acting as a 'bridge' between two nodes. Nodes with high centrality may be the most clinically relevant intervention targets, as these central nodes are associated with most of the interrelationships in the network [17]. The edges represent bidirectional partial correlations between nodes (i.e. the CST-HIV dimensions).

Partial correlations were used to investigate edges that can provide evidence of possible direct relationships between dimensions [18]. Partial correlations statistically control all other dimensions in the network, resulting only in the information about the relationship between two dimensions that remains after applying such a statistical control [19].

We next investigated the stability of this network using bootstrapping, a resampling technique to generate 1000 iterations by randomly dropping increasing percentages of data points from the original dataset. We also analysed whether the network stability differed as a function of the sociodemographic profile of the participants using a two-stage cluster analysis. This analysis allows the creation of models of clusters based on both categorical and continuous variables [20]. We introduced in the analysis the main sociodemographic variables (i.e. sex, age, sexual orientation, level of education and household income). Schwarz's Bayesian criteria, useful and objective selection criteria because they avoid arbitrariness compared with traditional clustering techniques, determined the number of clusters [21], which resulted in two clusters: cluster 1 consisted predominantly of homosexual men with higher socioeconomic profiles; and cluster 2 consisted predominantly of heterosexual and bisexual men and all women, regardless of sexual orientation and those with lower socioeconomic profiles. Next, we then conducted a network analysis within each of the obtained clusters to compare these to the full sample. We used IBM SPSS v. 27 for the cluster analysis and JASP 0.18.1 for their visualization.

Ethics

The CoRIS cohort was approved by the Clinical Research Ethics Committee of the Gregorio Marañon General University Hospital. All patients agreed to participate in CoRIS by signing an informed consent form. This particular study was approved by the Carlos III Health Institute Ethics Committee (no. CEI PI 94_2019-v2).

RESULTS

Sample

Our sample of 347 participants, divided into two clusters, cluster 1 ($n = 90$) and cluster 2 ($n = 257$), had an average age of 43.4 years (Table 1). Age ranged from 19 to 81 years, with cluster 1 being slightly older on average (45.5 years) than cluster 2 (42.7 years). The duration of infection averages 9.7 years, with cluster 1 having a longer mean duration (12.5 years) than cluster 2 (10.0 years). The majority of participants are male (93.1%) and identify as men (90.2%), with greater gender and sex diversity in cluster 1. Most participants are either married or single, with a majority identifying as homosexual (72.6%). Cluster 1 has a higher proportion of heterosexual and bisexual participants compared with cluster 2, which has almost exclusively homosexual participants. A large portion originates from Spain (71.8%) and has a university degree (53.9%). Most are employed (79.0%) and live independently (77.5%). Monthly incomes vary widely, with most falling between 901 and 3000 euros. HIV transmission is primarily through sexual intercourse (85.0%), with cluster 1 showing more diversity in transmission routes, including injection materials and unknown routes.

CST-HIV dimensions mean scores

The most affected CST-HIV dimension reported was anticipated stigma, followed by sleep and fatigue (Figure 2). Sexuality and psychological distress also exceeded the mean range of responses.

Correlations between the dimensions of the CST-HIV

All dimensions of the CST-HIV had significant correlations (Table 2). The largest were the associations between psychological distress with sleep and fatigue, cognitive problems and bothersome physical symptoms. Sleep and fatigue were most strongly correlated with cognitive problems and physical symptoms.

Network analysis

The network analysis demonstrated a high density of connections (Figure 3). Yet, not all nodes were equally important, with some occupying a peripheral position, such as anticipated stigma and sexuality, and psychological distress occupying a central role.

Figure 4 shows the standardized values for all network nodes' strength, closeness and betweenness. As can be seen, the dimension that had the highest centrality index in all three indexes (i.e. betweenness, closeness and strength) was psychological distress. This node has the highest number of relationships and therefore has the capacity to influence the rest of the nodes significantly (Data S1).

TABLE 1 Characteristics of the participants.

			Sample ($n = 347$)		**Cluster 1 ($n = 90$)**		**Cluster 2 ($n = 257$)**	
ID	**Variable**	**Category**	**%***	***n***	**%***	***n***	**%***	***n***
1	Age (years)	Mean (SD)	43.4 (10.6)*	347	45.5 (12.5)*	90	42.7 (9.8)*	257
		Minimum	19.0*	-	19.0*	-	22.0*	-
		Maximum	81.0*	-	75.0*	-	81.0*	-
2	Duration of infection (years)	Mean (SD)	9.7 (6.9)*	347	12.5 (1.0)*	88	10.0 (0.3)*	257
		Minimum	0.0*	-	1.0*	-	1.0*	-
		Maximum	41.0*	-	42.0*	-	29.0*	-
3	Sex	Female	6.9	24	26.7	24	0.0	0
		Male	93.1	323	73.3	66	100	257
4	Gender	Woman	9.2	32	31.1	28	1.6	4
		Man	90.2	313	67.8	61	98.1	252
		Other	0.6	2	1.1	1	0.4	1
5	Marital status	Married or with a partner	42.4	147	41.1	37	42.8	110
		Divorced or separated	8.1	28	12.2	11	6.6	17
		Single	47.8	166	43.3	39	49.4	127
		Widowed	1.7	6	3.3	3	1.2	3
6	Sexual orientation	Heterosexual	13.3	46	51.1	46	0.0	0
		Homosexual	72.6	0	0.0	0	98.1	252
		Bisexual	8.9	31	34.4	31	0.0	0
		Other	1.4	0	0.0	0	1.9	5
		Prefer not to answer	3.7	13	14.4	13	0.0	0
7	Country of origin	Spain	71.8	249	73.3	66	71.2	183
		Other	28.2	98	26.7	24	28.8	74
8	Level of education	No education	0.9	3	1.1	1	0.8	2
		Elementary school	8.1	28	8.9	8	7.8	20
		High school	35.4	123	32.3	29	36.6	94
		University degree	53.9	187	55.6	50	53.3	137
		Other	1.7	6	2.2	2	1.6	4
9	Work situation	Working	79.0	274	72.2	65	81.3	209
		Retired	4.9	17	7.8	7	3.9	10
		Unemployed	8.9	31	12.2	11	7.8	20
		Student	3.2	11	3.3	3	3.1	8
		Others	4.0	14	4.4	4	3.9	10
10	Housing	On your own (owned, inherited or rented home)	77.5	269	74.4	67	78.6	202
		At home with family	8.4	29	12.2	11	7.0	18
		Shared home	11.8	41	10.0	9	12.5	32
		Someone else's home	1.4	5	3.3	3	0.8	2
		Shelter/institution	0.3	1	0.0	0	0.4	1
		Other	0.6	2	0.0	0	0.8	2
11	Home monthly income (€)	None	1.4	5	1.1	1	1.6	4
		≤300	2.6	9	3.3	3	2.3	6
		301–600	3.7	13	11.1	10	1.2	3

(Continues)

TABLE 1 (Continued)

ID	Variable	Category	Sample ($n = 347$) %*	n	Cluster 1 ($n = 90$) %*	n	Cluster 2 ($n = 257$) %*	n
		601–900	5.2	18	8.9	8	3.9	10
		901–1.200	13.3	46	8.9	8	14.8	38
		1201–1800	17.6	61	11.1	10	19.8	51
		1801–2400	15.9	55	16.7	15	15.6	40
		2401–3000	13.3	46	14.4	13	12.8	33
		3001–4500	13.8	48	14.4	13	13.6	35
		4501–6000	6.3	22	6.7	6	6.2	16
		No answer	6.9	24	3.3	3	8.2	21
12	HIV transmission route	Sexual intercourse	85.0	295	66.7	60	91.4	235
		Sharing injection materials	1.4	5	4.4	4	0.4	1
		Blood transfusion	0.6	2	2.2	2	0.0	0
		Unknown	11.8	41	23.3	21	7.8	20
		Other	1.2	4	3.3	3	0.4	1

Note: *N* does not sum to 347 for all variable items as not all questionnaires were completed in full.
Abbreviations: IQR, interquartile range; M, mean; SD, standard deviation.
*Values with asterisks represent non-percentage values (i.e. age and duration of infection in years).

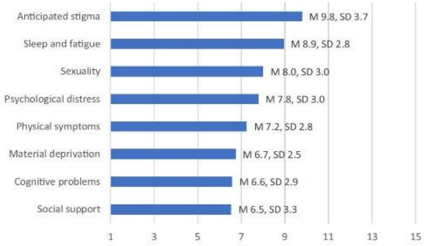

FIGURE 2 Mean scores in the dimensions of the Clinic Screening Tool for HIV (CST-HIV). The range is 1–15 points, where higher scores represent a greater degree of the health-related quality of life (HRQoL) problem measured by the dimension. M, mean; SD, standard deviation.

The dimensions that had the most connections (i.e. strength centrality) were, first, psychological distress, followed by sleep and fatigue, and the cognitive dimension. When considering closeness centrality, it was observed that psychological distress, the cognitive dimension, sleep and fatigue, and social support were the closest dimensions. Regarding betweenness centrality, psychological distress, cognitive problems and social support were found to be the most interrelated. In the metric expected influence (which considers negative associations among nodes), it was observed that the dimensions of psychological distress, sleep and fatigue, and cognitive problems were the ones with the highest values.

Stability analyses

In the bootstrapping analysis, all three centrality measures (i.e. betweenness, closeness, strength) maintain a high correlation with the original sample when more than 30% of the data are used (Figure 5). This suggests these measures are quite stable and reliable when a large portion of the data is available. Below 30%, the correlation for betweenness drops significantly and shows more variability, as indicated by the wider shaded area, suggesting it becomes less stable as the sample size decreases; closeness and strength remain relatively stable but start to show some decline and increased variability as well.

The two-stage cluster analysis classified the participants into two groups. Cluster 1 ($n = 90$) included nearly 80% of the women in the sample, all heterosexual and bisexual respondents, those with lower levels of education and household income. Cluster 1 was labelled as 'PHIV with a vulnerable socioeconomic profile'. Cluster 2 ($n = 257$) included all homosexual male participants, with a younger profile and higher levels of education and income than cluster 1 (Table 1). Cluster 2 was labelled as 'homosexual PHIV with a good socioeconomic profile'.

The cluster network analysis revealed that psychological distress was the main central node with multiple

TABLE 2 Correlations between the Clinic Screening Tool for HIV (CST-HIV) dimensions.

CST-HIV dimension	AS	PD	SEX	SS	MD	S&F	CP	PhyS
AS	-							
PD	0.324**	-						
SEX	0.311**	0.368**	-					
SS	0.234**	0.385**	0.309**	-				
MD	0.109*	0.343**	0.186**	0.385**	-			
S&F	0.186**	0.601**	0.296**	0.273**	0.321**	-		
CP	0.188**	0.578**	0.261**	0.206**	0.328**	0.487**	-	
PhyS	0.131*	0.402**	0.210**	0.202**	0.351**	0.426**	0.443**	-

Abbreviations: AS, anticipated stigma; CP, cognitive problems; MD, material deprivation; PD, psychological distress; PhyS, physical symptoms; S&F, sleep and fatigue; SEX, sexuality; SS, social support.

**$p < 0.01$.*$p < 0.05$.

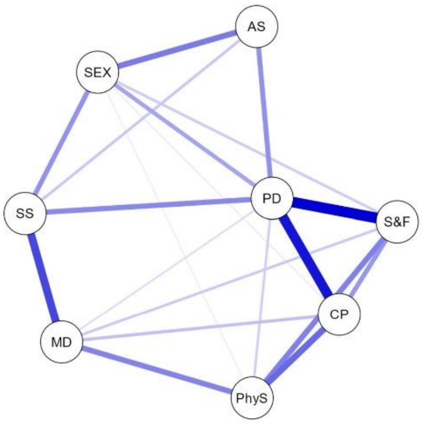

FIGURE 3 Health-related quality of life (HRQoL) network analysis of the Clinic Screening Tool for HIV (CST-HIV) dimensions. All associations were positive (i.e. blue lines). Thicker, darker lines indicate stronger associations than do thinner, lighter ones. AS, anticipated stigma; CP, cognitive problems; MD, material deprivation; PD, psychological distress; PhyS, physical symptoms; S&F, sleep and fatigue; SEX, sexuality; SS, social support.

strong connections to other nodes (i.e. material deprivation, sleep and fatigue, and physical symptoms) in these two networks, as in the full sample (Figure 6). This suggests that psychological factors are a central aspect of this sample's network, irrespective of cluster categorization factors. There were stronger associations between nodes related to symptoms such as sleep and fatigue, cognitive problems, and physical symptoms with social-related nodes such as material deprivation, social support or lack of sexual satisfaction. However, in cluster 2 the association of psychological distress with cognitive problems emerged as stronger than in cluster 1. Similarly, the association of material deprivation with lack of social support emerged as stronger in cluster 2 than in cluster 1.

The cluster network analysis shows that cluster 1 has higher centrality values for physical symptoms, sleep and fatigue, social support and anticipated stigma, while cluster 2 has higher values for cognitive problems, material deprivation and sex (Figure 7). Both clusters display similar, and the highest, values for psychological distress across all centrality measures.

DISCUSSION

This study has shown that the most prevalent HRQoL problems among 347 PHIV in Spain were anticipated stigma followed by sleep and fatigue, sexuality and psychological distress. However, the most relevant knowledge to prioritize interventions to improve HRQoL is to know the pattern of interrelationships between its dimensions, and this network analysis found that the most central dimensions, measured by the CST-HIV, were, in order of descending centrality, psychological distress, sleep and fatigue, cognitive problems and social support.

The dimensions that had the most connections (i.e. strength) were, first, psychological distress, followed by sleep and fatigue and cognitive problems. Intervening in these dimensions would amount to changing many of the relationships in the network, affecting the problem network comprehensively. When considering closeness, it was observed that psychological distress, cognitive dimension, sleep and fatigue, and social support were the most closely related dimensions, implying that interventions in these dimensions can result in indirect changes across the problem network. In other words, it may be

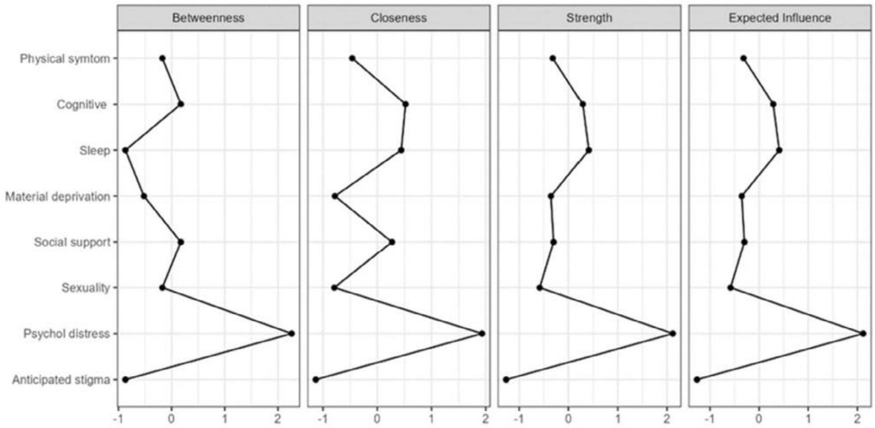

FIGURE 4 Centrality measures of each node in the network analysis. *Z*-scores are presented on the *x*-axis for each centrality measure.

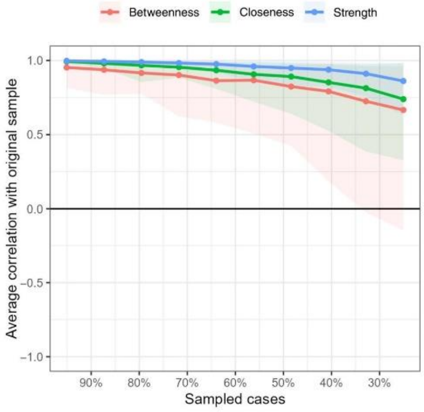

FIGURE 5 Bootstrapping analysis. Lines demonstrate centrality measures (betweenness in red, closeness in green, strength in blue) of the original sample beginning at 100%, and sampled cases decreasing to 30%, with shaded areas indicating confidence intervals.

quicker to change the network by intervening in these centrally strong dimensions rather than in those that are more peripheral. Psychological distress among PHIV encompasses a broad spectrum of emotional and psychological challenges that significantly impact their quality of life and can manifest in various forms, such as anxiety, depression and post-traumatic stress disorder (PTSD). Psychological distress is often influenced by factors such as stigma, social support, overall physical health and sleep [22]. However, it is important to note that the pattern of relationships between these nodes is much stronger in the cluster of PHIV with a vulnerable socioeconomic profile. These results are consistent with evidence showing that the social determinants of health, and in particular socioeconomic status, have an important impact on the health and quality of life of people with HIV [23–25]. Nevertheless, the association between material deprivation and social support emerged with higher strength in the cluster of homosexual PHIV with good socioeconomic profile. It is possible that the leisure culture of this group is more affected by the lack of economic resources in ways that inhibit the establishment of a strong social network, but more investigation is needed.

Moreover, in cluster 2, predominantly homosexual PHIV with a good socioeconomic profile, we observed a stronger association between psychological distress and cognitive problems than in cluster 1. Cognitive impairments, particularly in memory, may contribute to higher levels of self-stigma, and thereby be a critical mediating factor in the relationship with HRQoL among men living with HIV who have sex with men [14]. Self-stigma acts as a mediator of psychological well-being, social relationships and physical health through which perceived public stigma and experienced stigma detrimentally impact HRQoL, while social support can protect against this negative mediating effect [26]. The prevalence of sleep disturbances and fatigue among PHIV has been well documented, including a 2016 study reporting that over 50% of PHIV experience some form of neurocognitive impairment that is often exacerbated by sleep problems and fatigue [27]. Sleep disturbance across all stages of

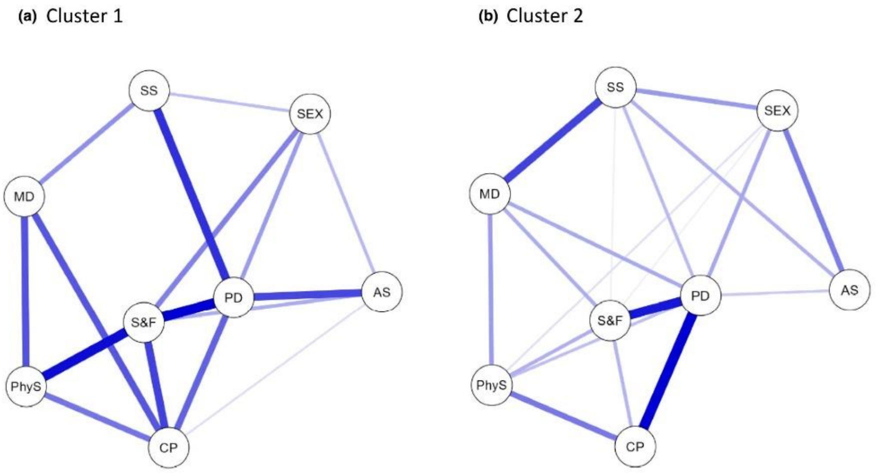

FIGURE 6 Cluster network analyses. AS, anticipated stigma; CP, cognitive problems; MD, material deprivation; PD, psychological distress; PhyS, physical symptoms; S&F, sleep and fatigue; SEX, sexuality; SS, social support.

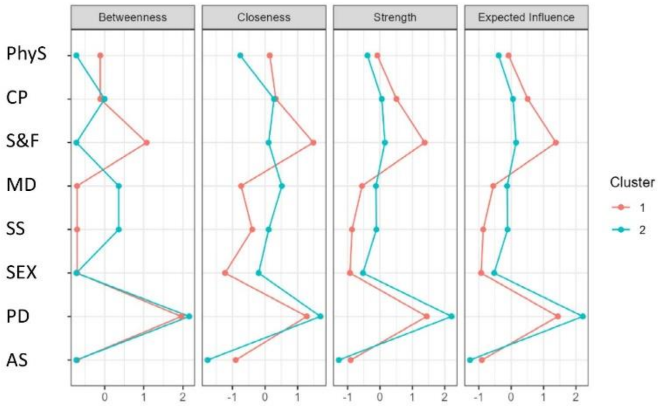

FIGURE 7 Comparison of centrality measures of each node between clusters. AS, anticipated stigma; CP, cognitive problems; MD, material deprivation; PD, psychological distress; PhyS, physical symptoms; S&F, sleep and fatigue; SEX, sexuality; SS, social support.

HIV-related illness contribute to chronic fatigue and reduced physical and social functioning [28]. These findings align with the present study's results, where sleep and fatigue were significant dimensions. However, it was the cluster of PHIV with a more vulnerable socioeconomic profile that presented the higher centrality index in sleep and fatigue. This may not only be related to their increased psychological and social vulnerability, but may also be attributed to an older age and the likelihood of experiencing greater comorbidities and associated greater physical health burdens [29]. Therefore, intervening in these problems, mainly psychological distress, would increase the probability of decreasing the rest of the problems measured by the dimensions of the CST-HIV.

The results also indicate the importance that material deprivation, a dimension of social exclusion, has on PHIV's HRQoL. Despite material deprivation not emerging as one of the central dimensions in the network analysis, it is essential to note the high degree of association it showed with social support and psychological distress. Therefore, by intervening in these variables, for example through referral and follow-up to appropriate services, clinicians may improve the material deprivation dimension that negatively harms HRQoL.

Our findings underscore the value of the CST-HIV as a comprehensive screening tool for identifying key HRQoL issues in PHIV in Spain. Compared with standard tools that focus on specific areas such as psychological distress, anxiety, depression and sleep disorders [30], the CST-HIV provides a more holistic assessment by integrating multiple dimensions of HRQoL into a single instrument. This comprehensive approach not only simplifies the screening process for healthcare providers but also ensures that a broader range of issues is identified and addressed. Unlike standard tools and clinical interviews that may require multiple assessments and considerable time, the CST-HIV offers an efficient and targeted way to identify the most pressing HRQoL concerns in clinical practice. PHIV in Spain commonly report high levels of psychological distress, sleep/fatigue and social support deficiencies [13, 31–36]. These findings highlight the critical need for effective screening and intervention strategies to address these pervasive issues. Enhancing social support through peer support programmes and community-based interventions has demonstrated the ability to improve mental health outcomes among PHIV [37]. Such evidence-based interventions, when addressed in routine HIV care, may have the potential to substantially improve HRQoL for PHIV by identifying the most impactful HRQoL dimensions within an HRQoL problem network.

Among the main limitations of this study is the possible lack of generalizability of the results. This is due to the profile of the participants in this study, which differs from the sociodemographic characteristics of the population with HIV in Spain. This difference could be due to several reasons. On the one hand, the CoRIS cohort started in 2004, after the onset of cases in Spain and the introduction of highly active antiretroviral therapy (ART) in 1996, and therefore is composed of younger participants with a shorter duration of infection compared with all PHIV in Spain [38]. There may have been biases in the selection or willingness to participate in this study as a more favourable sociodemographic and economic profile predominates than in other studies. However, the interrelationship between the nodes (HRQoL problems) in a complex network of problems, as is the case here, is expected to change over time depending on individual and social evolution. We were able to obtain health data on HIV transmission route and duration of infection, but not for other clinical variables such as CD4 T-cell count and duration on ART due to missing data for the period of analysis, which may have introduced a selection bias. However, we could analyse and compare the network interrelationships between two groups clustered by differences in their sociodemographic profiles. Although the group with the lower socioeconomic profile was smaller, the commonalities in strength and centrality between the nodes of the network highlight the urgent need to address the problems measured by the CST [4]. The present study has shown that the most prevalent HRQoL problems among the 347 participants in Spain were anticipated stigma, followed by sleep and fatigue, sexuality and psychological distress. However, the findings are based on a specific cohort predominantly composed of men who have sex with men, who are employed and have a relatively high educational level. Therefore, while the network analysis provides valuable insights into the interrelationships between different HRQoL dimensions, caution must be exercised when generalizing these results to the broader population of PHIV, including women, heterosexual men and those from different socioeconomic backgrounds. The use of an electronic format for data collection may also have introduced selection bias. Individuals with limited access to the internet or lower digital literacy may have been less likely to participate. To mitigate this bias, we provided support through NGOs and clinical sites to assist participants in completing the online questionnaire within their outpatient clinic. In any case, given that the CST-HIV is an instrument designed to assist in clinical practice, it is recommended that in each cohort of patients, the interrelationship between the problems be analysed to know which interventions to prioritize according to the different contexts and profiles of PHIV within a community of care. Future research should investigate the network in larger samples powered for sociodemographic and clinical characteristics, as well as in localized samples at the level of the autonomous communities.

CONCLUSION

Among a sample of predominantly men living with HIV in Spain who have sex with men, the most central issues affecting HRQoL were psychological distress, sleep and fatigue, cognitive problems and social support, with psychological distress and cognitive issues being particularly pivotal in influencing the overall problem network. Interventions targeting these central dimensions are likely to have a broader impact on improving HRQoL. Moreover, despite a better socioeconomic status of participants compared with earlier studies, material deprivation and psychological distress strongly influence HRQoL, highlighting the importance of addressing these areas in clinical practice where possible. Moreover, we have found differences between two groups with differences in their sociodemographic profile that provides important clues for intervention in each one. The study underscores the value of a tailored approach in the care of people living with HIV, suggesting that interventions should be prioritized based on the interrelationship of problems specific to different community profiles and contexts within the care continuum.

AUTHOR CONTRIBUTIONS

M.J.F.-R. conceptualized and designed the study and oversaw its administration. T.M.W., C.I. and C.P.-S. collected and analyzed the data. All authors contributed to the interpretation of results. I.J. and R.I. provided critical revisions of the manuscript. T.M.W. and C.I. drafted the initial manuscript. All authors reviewed, edited, and approved the final version of the manuscript for submission.

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CONFLICT OF INTEREST STATEMENT

MJF-R and CI are members of the Spanish Interdisciplinary AIDS Society (SEISIDA) Executive Board. SEISIDA has received grants from Gilead, Janssen, MSD and ViiV, outside of the submitted work. MJF-R has provided consultancy services to Gilead, Janssen, MSD, ViiV and Theratechnologies, and has received payments for lectures or educational presentations from Gilead, Janssen, MSD and ViiV, outside of the submitted work. JVL reports grants and speaker fees from Gilead Sciences, and MSD and speaker fees from AbbVie, Echosens, GSK, Moderna, Novo Nordisk and ViiV, outside of the submitted work, and an institutional grant to ISGlobal from Gilead Sciences for other work packages of the comprehensive study of which the present research is a part. All other authors report no conflicts of interest.

DATA AVAILABILITY STATEMENT

All relevant data are available for download at www.doi.org/10.5281/zenodo.10939952.

ETHICS STATEMENT

The Ethics Committee of the Instituto de Salud Carlos III (ISCIII) approved procedures on 15-01-2020 (no. CEI PI 94_2019-v2).

PATIENT CONSENT STATEMENT

All study participants provided written informed consent.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Presented materials are authors' own.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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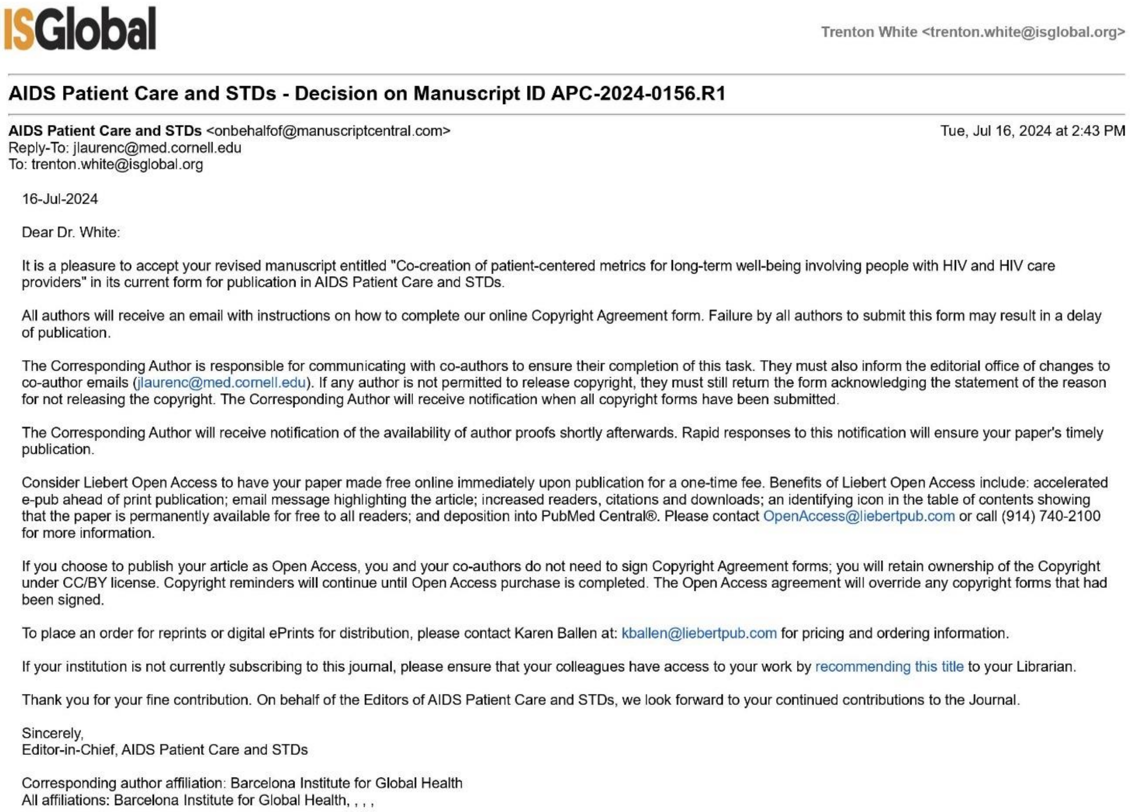

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AIDS Patient Care and STDs - Decision on Manuscript ID APC-2024-0156.R1

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Tue, Jul 16, 2024 at 2:43 PM

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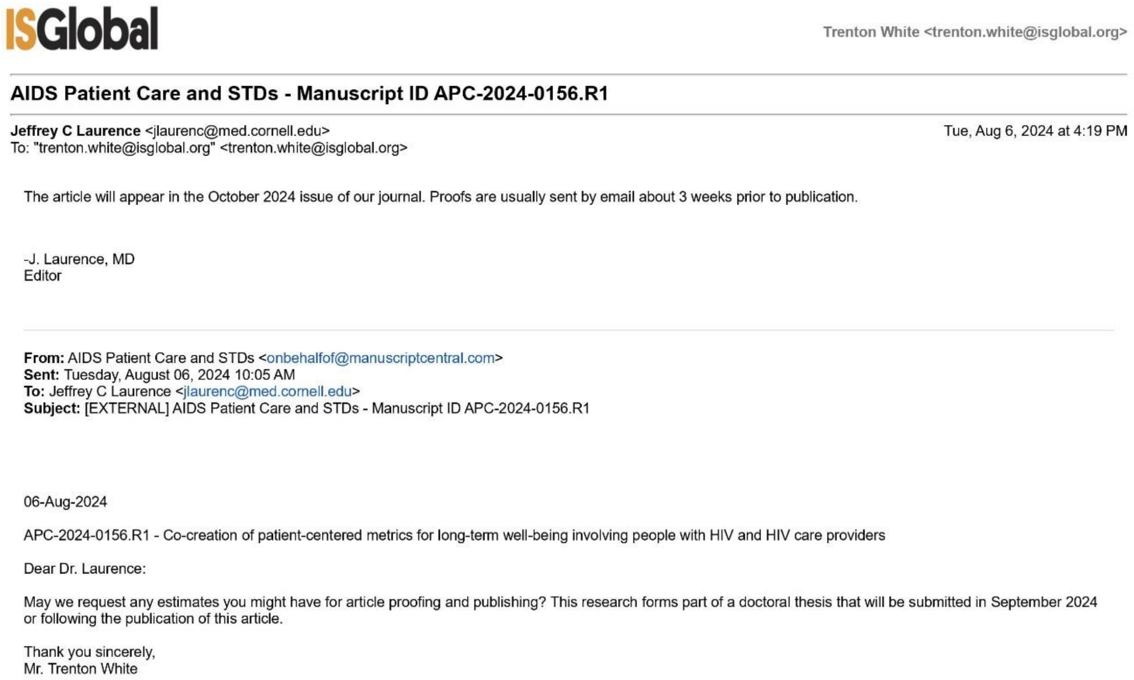

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06-Aug-2024

APC-2024-0156.R1 - Co-creation of patient-centered metrics for long-term well-being involving people with HIV and HIV care providers

Dear Dr. Laurence:

May we request any estimates you might have for article proofing and publishing? This research forms part of a doctoral thesis that will be submitted in September 2024 or following the publication of this article.

Thank you sincerely,
Mr. Trenton White

AIDS Patient Care and STDs

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Co-creation of patient-centered metrics for long-term well-being involving people with HIV and HIV care providers

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Co-creation of patient-centered metrics for long-term well-being involving people with HIV and HIV care providers

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Short title: Patient-Centered HIV Well-Being Metrics

Keywords: patient-reported outcomes, health-related quality of life, HIV, ageing, community health

Abstract

Achieving viral suppression alone does not fully resolve the multifaceted health challenges faced by people with HIV (PWH), such as early ageing, multimorbidity, and low health-related quality of life (HRQoL). This co-creation pilot study to investigate patient-centered metrics for long-term well-being involved the development of a knowledge attitudes and practices (KAP) survey through focus groups and its implementation among HIV care providers in Barcelona, Spain, in 2024. A collaborative approach of involving PWH from the community was essential in ensuring the relevance of the identified issues. The results underscored the importance of monitoring comorbidities such as mental health issues, cardiovascular diseases, and neurological disorders, alongside the use of patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs). The findings highlighted several barriers to implementing PROMs, including time constraints, patient health literacy, and technical issues. Overall, the study emphasizes the need for health systems in Barcelona, Spain to integrate PROMs and PREMs into routine HIV care to enhance patient-centered care and address the comprehensive well-being of PWH.

Introduction

In 2014, the Joint United Nations Programme on HIV and AIDS (UNAIDS) introduced the "90–90–90" targets: diagnose 90% of people with HIV (PWH), provide antiretroviral therapy (ART) to 90% of those diagnosed and achieve viral suppression in 90% of those on ART.[1] Although ART access is widespread, it is not accessible to all PWH in all settings, and these targets do not address major challenges facing PWH even once viral suppression is achieved, such as a high burden of multimorbidity and concomitant polypharmacy, which typically increases with age, and ongoing HIV-related stigma and discrimination.[2,3] These, and other factors, can worsen PWH's health-related quality of life (HRQoL), which is lower than the general population's in some settings,[4] yet health systems have been slow to reorient themselves to the challenge of promoting better HRQoL in PWH.[5]

PWH still often face major health challenges and experience poor HRQoL, even when they respond well to ART.[4] For instance, virally suppressed PWH have high rates of multimorbidity and related burdensome health issues, such as polypharmacy and frailty,[6–8] and face HIV-related discrimination.[9] Lower HRQoL scores have predicted all-cause hospitalization,[10] mortality, emergency department utilization and hospital discharge rates among PWH in the United States.[11] Increased life expectancy due to ART presents health systems with a new challenge in managing comorbidities associated with long-term survival, as psychosocial factors may outweigh medical factors in determining HRQoL.[12] Yet, health systems are largely unprepared to manage the breadth of burdensome problems of increasingly aging PWH.[2,5,13]

Person-centeredness, or prioritizing the values, needs and preferences of patients, has become the third pillar of healthcare quality, in addition to effectiveness and safety.[14,15] There is a strong association between positive patient experience and the quality of care.[16–18] Therefore, understanding and giving priority to the patient experience is integral to achieve patient involvement and people-centered collaborative healthcare. Patient-reported outcome measures are means to retrieve information on patient experience and provide high-value evidence that is useful for informing healthcare service governance decision-making, clinical care delivery and health research.[19,20]

By focusing on viral suppression as the end goal of HIV care, the public health science that drives health system decisions lacks the framework and tools needed to adequately study the full health and wellbeing of a cadre of people already engaged in care. Without extending HIV monitoring to issues beyond viral suppression, the diminished HRQoL of PWH cannot be adequately investigated, let alone addressed. This study aims to co-define with PWH receiving care in Barcelona, Spain, important patient-reported issues to monitor beyond viral suppression.

Methods

Study Design

This pilot study employed a co-production patient-centered collaborative research design, consisting of three main phases. In the first phase, local HIV partner associations and PWH underwent training to engage as co-researchers in defining research questions and methods. This training aimed to empower participants and ensure that the research is aligned with their needs and values. The second phase involved the co-creation of a knowledge, attitudes, and practices (KAP) survey. This survey, developed through focus group discussions with community collaborators who were HIV-positive focused on key elements of long-term well-being, including comorbidities, patient-reported outcome measures (PROMs), and patient-reported experience measures (PREMs). The final phase included the implementation and analysis of the KAP survey completed by healthcare providers in Barcelona-area hospitals. The results were jointly analyzed in a focus group open to participating healthcare providers and community collaborators. Together, these participants co-created a community well-being informational brochure for PWH.

Participants

Participants in the PODER study included HIV-positive community collaborators and medical professionals from hospitals in the Barcelona metropolitan area. Recruitment for community collaborators was conducted through Gais Positius, a local LGBTQ+ organization. Community collaborators must have been HIV-positive adults receiving or eligible for HIV care in Barcelona, Spain. Three individuals were recruited from the community. Medical professionals were recruited through the professional networks of the researchers by email invitation to the heads of infectious disease clinics at Hospital del Mar, Hospital Clinic, Hospital San Pau, and Hospital Val d'Hebron; participants must have currently been providing healthcare to PWH in the Barcelona metropolitan area at the time of recruitment. Ten healthcare providers were recruited. This inclusion criterion ensured that participants had relevant experience and insights into the challenges and needs of HIV care, both from the patient and provider perspectives.

Data Collection

Data collection involved community-based focus groups and the administration of the co-created KAP survey via Qualtrics, a secure online platform that ensures anonymity and compliance with General Data Protection Regulation (GDPR) rules.

The community focus groups were designed to elicit patient-centric issues and/or metrics crucial for monitoring long-term well-being among PWH beyond viral suppression. These focus groups, held on December 19, 2023, January 16, 2024, and February 13, 2024, involved active participation from PWH community members. The discussions led to the co-creation of a comprehensive survey that incorporated these elements, ensuring that the issues developed were truly reflective of the patient population's needs and priorities. The collaborative nature of this process underscored the value of engaging PWH in research to create more relevant and effective health monitoring tools.

The KAP survey included items on various aspects of HIV care, such as the management of comorbidities, and the use of PROMs and PREMs, derived from the focus group discussions. Participants provided their responses to items related to their experiences and practices in HIV care. Two focus groups were held, on May 27 and 28, 2024, to review the survey results with respondents.

Statistical Analysis

Descriptive statistics, including frequencies and means, were used to analyze the survey responses and provide a summary of the data, thereby highlighting key trends and insights into the current state of HIV care in Barcelona.

Results

Participants emphasized the significance of monitoring various comorbidities such as mental health issues, cardiovascular diseases, neurological disorders, substance use problems, cancers, bone diseases, kidney diseases, pulmonary diseases, liver diseases, and diabetes (Table 1). They noted that these conditions often coexist with HIV and significantly impact the quality of life (QoL) of PWH. Participants also stressed the need for PROMs and PREMs to capture the broader aspects of health and well-being beyond viral suppression (Table 2). PROMs were identified as essential tools for understanding the impact of HIV and its treatment on patients' overall health and daily functioning. PREMs were highlighted for their role in assessing patients' experiences with healthcare services, including aspects such as time management, quality of contact, participation in decision-making, accessibility to healthcare professionals, and respect for patient values.

Table 1. Key Comorbidities Identified by Participants

Comorbidity	Description
Mental Health Issues	Includes depression, anxiety, and other mental health conditions
Cardiovascular Diseases	Heart-related conditions such as hypertension, heart disease
Neurological Disorders	Conditions affecting the nervous system, including neurodegenerative diseases
Substance Use Problems	Issues related to the use of drugs, alcohol, or other substances
Cancers	Various forms of cancer, which may be more prevalent or develop differently in PWH
Bone Diseases	Includes osteoporosis and other bone-related conditions
Kidney Diseases	Chronic kidney disease and other renal issues
Pulmonary Diseases	Respiratory conditions, including chronic obstructive pulmonary disease (COPD)
Liver Diseases	Liver conditions, including viral hepatitis and cirrhosis
Diabetes	Metabolic disorder characterized by high blood sugar levels

Table 2: Essential PROM and PREM Issues for Monitoring Health and Well-Being

Issue	Description	Measure Type
Physical Symptoms	Tracking symptoms like pain, fatigue, and other physical health issues	PROM
Cognitive Problems	Monitoring issues such as memory loss and concentration difficulties	PROM
Emotional Distress	Assessing levels of stress, anxiety, and depression	PROM
Sexual Health	Evaluating sexual function and related issues	PROM
Social Support	Understanding the support systems available to patients	PROM

Material Deprivation	Assessing issues like housing and financial resources	PROM
Sleep/Fatigue	Monitoring sleep quality and levels of fatigue	PROM
Time Management	Evaluating the efficiency and timeliness of care received	PREM
Quality of Contact	Assessing the quality of interactions between patients and healthcare providers	PREM
Participation in Decision-Making	Understanding the extent to which patients are involved in their care decisions	PREM
Accessibility to Healthcare Professionals	Evaluating ease of access to necessary healthcare services	PREM
Respect for Patient Values	Ensuring that care respects patients' personal values and preferences	PREM
Pain Management	Assessing how effectively pain is managed within the care setting	PREM
Emotional Support	Evaluating the emotional support provided by healthcare services	PREM

Of the ten healthcare providers invited to participate, five completed the KAP survey. The survey revealed that PROMs and PREMs are considered crucial for personalized HIV care, with 80% of respondents agreeing or strongly agreeing that PROMs contribute positively to the care of PWH (Table 3). However, several challenges were identified in implementing PROMs, including time constraints (60%), patient health literacy (40%), and technical issues related to data management (30%). These barriers highlight the need for improved systems and training to effectively use PROMs in routine care.

Table 3: Knowledge, Attitudes, and Practices (KAP) Survey Results

Survey Item	**Responses (n=5)**
PROMs (Patient-Reported Outcome Measures)	
PROMs contribute positively to the personalized care of PWH.	Strongly Agree (50%), Agree (30%), Neutral (10%), Disagree (5%), Strongly Disagree (5%)
Challenges faced in using PROMs (select all that apply):	Time constraints (60%), Patient health literacy (40%), Technical data management issues (30%), Data privacy issues (20%), Cost constraints (15%), Interpretation and actionability of results (25%)
Do you collect any of the following PROMs from PWH in your practice?	Physical symptoms (88%), Cognitive problems (75%), Anticipated stigma (50%), Emotional distress (82%), Sexuality (70%), Social support (78%), Material deprivation (65%), Sleep/fatigue (72%)
PREMs (Patient-Reported Experience Measures) (n=5)	
PREMs are crucial in enhancing the quality of HIV care	Strongly Agree (55%), Agree (30%), Neutral (10%), Disagree (3%), Strongly Disagree (2%)
Do you use feedback from PREMs to initiate changes in your practice or approach towards the care of PWH?	Frequently (70%), Somewhat frequently (20%), Rarely (7%), Never (3%)

Does your hospital have mechanisms for people living with HIV to report any experience of stigma and discrimination in healthcare settings?	Yes (70%), No (10%), Don't know (20%)
Coordination of Care (n=5)	
How do you rate the overall coordination between hospital departments in managing comorbidities of patients with HIV?	1 (lowest) to 5 (highest) - Average Rating: 2.8
Efficiency in sharing patient information	1 (lowest) to 5 (highest) - Average Rating: 2.8
Timeliness of consultations between departments	1 (lowest) to 5 (highest) - Average Rating: 2.8
Effectiveness of joint care planning	1 (lowest) to 5 (highest) - Average Rating: 2.6
Clarity of communication among departments	1 (lowest) to 5 (highest) - Average Rating: 2.8
Coordination in the management of comorbidities	1 (lowest) to 5 (highest) - Average Rating: 2.8

Regarding the coordination of care, KAP survey respondents rated the overall coordination between hospital departments as moderate, with an average score of 2.8 out of 5. Specific aspects such as the efficiency of sharing patient information and the effectiveness of joint care planning received similar ratings, indicating room for improvement. Additionally, 70% of respondents reported having mechanisms in place for PWH to report experiences of stigma and discrimination in healthcare settings, though 20% were unaware of such mechanisms.

The co-created well-being informational brochure for PWH is presented in **Supplemental Material 1**.

Discussion

These findings underscore the need for comprehensive person-centered HIV care that extends beyond achieving viral suppression to also include patient-reported metrics. PROMs identified by participants in this study included physical symptoms, cognitive problems, emotional distress, sexual health, social support, material deprivation, and sleep and fatigue. PREMs identified included time management, quality of contact, participation in decision-making, accessibility to healthcare professionals, respect for patient values, pain management, and emotional support. Integrating PROMs and PREMs into routine HIV care can provide valuable insights into patient experiences and outcomes, and may inform better healthcare practices and policies. However, addressing barriers such as time constraints, patient health literacy, and technical issues is crucial for the effective use of these measures.[5,20] The moderate ratings for care coordination between hospital departments highlight the necessity for enhanced communication and collaboration to manage comorbidities effectively. Furthermore, addressing stigma and discrimination remains a priority to ensure equitable and respectful care for all PWH.[4] There was consensus among focus group participants of the benefit of integrated care models, such as those found in multi-disciplinary clinics, to effectively manage multimorbidity and polypharmacy,[21] thereby enhancing patient outcomes.

Key elements of patient-centered care include empathy, respect, and effective communication, which foster a strong patient-provider relationship and shared decision-making.[16,22] Nevertheless, targeted interventions, such as training for providers in communication and continuity of care, have shown promise in improving outcomes like viral suppression and patient satisfaction.[22] HRQoL measurement for PWH is mainly limited to clinical trials and ART adherence, and is rarely used in routine clinical practice for issues beyond viral suppression.[23] The clinical use of quality-of-life (QoL) assessments that primarily focus on ART adherence, while crucial, is insufficient for achieving health parity with the general population.[23,24] Self-reported QoL or HRQoL captures patient experiences like life satisfaction, empowerment, and stigma impact, often overlooked in care settings, yet influential on health outcomes.[20]

In Spain, studies have shown that while ART significantly improves clinical outcomes, there is a critical need to address the quality of care perceived by patients. For instance, the perception of outpatient care at the HIV unit of Hospital Clínic in Barcelona was generally positive, but areas such as the physical environment and waiting times were identified for improvement.[25] Additionally, adherence to quality care indicators has been shown to correlate with high patient satisfaction, although this adherence does not always align perfectly with patient-reported satisfaction.[26] Our findings align with those from other studies in Spain highlighting the persistent challenges PWH face, including stigma, psychological distress, and physical symptoms.[27] For instance, PROMs are essential for understanding how HIV and its treatment affect patients' overall health and daily functioning, while PREMs assess patients' experiences with healthcare services, emphasizing the importance of time management, quality of contact, and participation in decision-making.[27] These measures are vital for patient-centered care, as they provide insights into patient experiences that are not typically captured by clinical outcomes alone. The development and validation of a clinic screening tool for HIV (CST-HIV) has identified burdensome health-related issues affecting both clinical and psychosocial aspects of HIV care.[28] Self-reported measures highlight issues such as stigma, empowerment, and life satisfaction, which are pivotal for the long-term health and well-being of PWH.[26] This suggests that while clinical indicators are important, capturing patient experiences through PROM and PREM tools is essential for truly patient-centered care.

Challenges in the implementation of PROMs and PREMs include varied design methodologies of scales and instruments, which may make it difficult to compare PWH populations, cultural resistance, inadequate IT infrastructure, high implementation costs, competing priorities, staff skill gaps, skepticism about data reliability, patient burden, and issues with instrument length and sensitivity.[29] Any of these challenges may hinder health system decision-making based on quality data. The use of telehealth in HIV care can address some of these challenges by reducing stigma-related delays and improving access to care (e.g., flexible virtual appointments), patient satisfaction with care, and use of patient-reported measures (e.g., symptoms or burdensome health issues).[30] To maximize these benefits, ensuring privacy, providing low-cost technological resources, enhancing technology proficiency through training, and adopting hybrid approaches to maintain strong clinician-patient relationships are crucial.[30]

Limitations of this study include selection bias in both the PWH recruited by Gais Positius and healthcare providers recruited by hospital infectious disease department heads. Additionally, both samples were small and had insufficient sizes to power statistical analysis. Future research should focus on developing and validating HRQoL assessment tools tailored to the specific needs of aging PWH populations. Such tools can help health systems better understand and address the diverse factors influencing the well-being of PWH, ultimately leading to improved health outcomes and quality of life. The engagement of healthcare providers and the HIV community in designing and implementing PROMs and PREMs in routine care can enhance our understanding of the long-term health needs of ageing with HIV.

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Author contributions

JVL oversaw the study design and implementation. TMW, A-SG, and CP oversaw data collection and analysis. JR contributed to the study design and participant recruitment. All authors contributed equally to manuscript drafting and editing.

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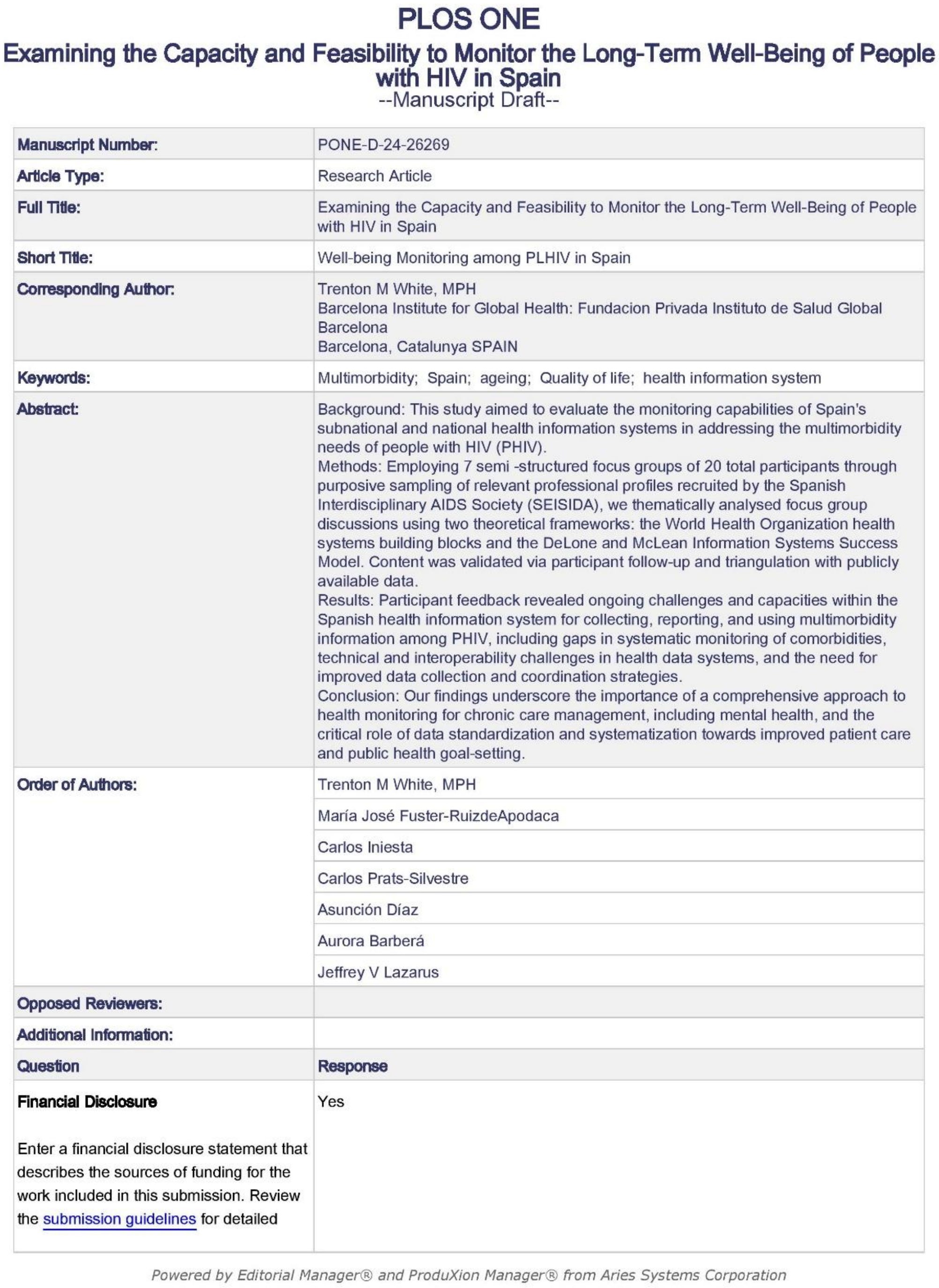

PLOS ONE

Examining the Capacity and Feasibility to Monitor the Long-Term Well-Being of People with HIV in Spain

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Keywords:	Multimorbidity; Spain; ageing; Quality of life; health information system
Abstract:	Background: This study aimed to evaluate the monitoring capabilities of Spain's subnational and national health information systems in addressing the multimorbidity needs of people with HIV (PHIV). Methods: Employing 7 semi -structured focus groups of 20 total participants through purposive sampling of relevant professional profiles recruited by the Spanish Interdisciplinary AIDS Society (SEISIDA), we thematically analysed focus group discussions using two theoretical frameworks: the World Health Organization health systems building blocks and the DeLone and McLean Information Systems Success Model. Content was validated via participant follow-up and triangulation with publicly available data. Results: Participant feedback revealed ongoing challenges and capacities within the Spanish health information system for collecting, reporting, and using multimorbidity information among PHIV, including gaps in systematic monitoring of comorbidities, technical and interoperability challenges in health data systems, and the need for improved data collection and coordination strategies. Conclusion: Our findings underscore the importance of a comprehensive approach to health monitoring for chronic care management, including mental health, and the critical role of data standardization and systematization towards improved patient care and public health goal-setting.
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Title: Examining the Capacity and Feasibility to Monitor the Long-Term Well-Being of People with HIV in Spain

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Abstract
Background: This study aimed to evaluate the monitoring capabilities of Spain's subnational and national health information systems in addressing the multimorbidity needs of people with HIV (PHIV).
Methods: Employing 7 semi -structured focus groups of 20 total participants through purposive sampling of relevant professional profiles recruited by the Spanish Interdisciplinary AIDS Society (SEISIDA), we thematically analysed focus group discussions using two theoretical frameworks: the World Health Organization health systems building blocks and the DeLone and McLean Information Systems Success Model. Content was validated via participant follow-up and triangulation with publicly available data.
Results: Participant feedback revealed ongoing challenges and capacities within the Spanish health information system for collecting, reporting, and using multimorbidity information among PHIV, including gaps in systematic monitoring of comorbidities, technical and interoperability challenges in health data systems, and the need for improved data collection and coordination strategies.
Conclusion: Our findings underscore the importance of a comprehensive approach to health monitoring for chronic care management, including mental health, and the critical role of data standardization and systematization towards improved patient care and public health goal-setting.

Keywords: Multimorbidity; Spain; ageing; quality of life; health information system

Examining the Capacity and Feasibility to Monitor the Long-Term Well-Being of People with HIV in Spain

Introduction

The global advancement in HIV treatment, particularly through widespread access to antiretroviral therapy (ART), has significantly improved the life expectancies of people with HIV (PHIV) to nearly match those of the HIV-negative population [1]. Yet, PHIV continue to report lower health-related quality of life (HRQoL) [2–4] and have more comorbidities than their seronegative counterparts, for example, cardiovascular disease, chronic kidney disease, and osteoporosis, which are commonly associated with older age in the general population, as well as other infectious diseases such as hepatitis B and hepatitis C [5–7]. Many health systems continue to employ HIV care models that focus predominantly on achieving viral suppression and protecting against opportunistic infections without necessarily focusing on ageing-related issues and long-term well-being, including multimorbidity and HRQoL [8,9].

The HIV "continuum of care" has served as a primary model for monitoring progress in national HIV/AIDS responses since the early 2000s [10]. The Joint United Nations Programme on HIV/AIDS (UNAIDS) targets, the "three 90s" (2014-2020) and "three 95s" (2020-2030) [11], are country targets that have considered three main stages of the care continuum: percentage of PHIV who are diagnosed, who receive ART, and who achieve viral suppression. In 2021, Spain achieved each of the three 90 targets: 92.5%, 96.6% and 90.4%, respectively, with an estimated 80.8% of all PHIV in Spain having reached viral suppression [12]. A Fourth 90 target was proposed in 2016 by HIV researchers suggesting that all PHIV, regardless of viral suppression, should enjoy good HRQoL [13]. The Fourth 90 emphasizes the importance of not just controlling the virus to undetectable levels but also ensuring that PHIV have a high quality of life and acknowledges the comprehensive well-being of persons. The current World Health Organization (WHO) global strategy for HIV (2022-2030) recognizes the importance of countries measuring stigma, discrimination, and patient-centred approaches to HIV care that achieve a good HRQoL at all stages of the HIV care continuum [14].

Spain's 17 regional autonomous regions are competent for health system management, including service delivery and the collection of public health and epidemiological data, while the central government maintains competencies for general coordination of public health information [15]. In Spain's decentralized health system, management of the national health system is coordinated through the Interterritorial Council, which establishes the list of Mandatory Notifiable Diseases [16]. Notification of the epidemiological surveillance for HIV is to occur every three months for new cases and annually for routine monitoring thereafter by the regional surveillance systems to the National Epidemiology Centre. The General Subdirectorate of Health Information of the Ministry of Health is responsible for managing the health information system, which includes the reporting of key indicators through the management of disease registries, and currently does not report indicators for long-term well-being, including multimorbidity and HRQoL [17,18]. Health information system functions are funded centrally through general public taxes, while this funding is managed and allocated at the autonomous community level [15].

Developing national monitoring indicators and strategies for issues beyond the 95-95-95 targets will require deeper understanding of the capacity of and feasibility of health information systems to collect multimorbidity and other well-being data among PHIV. This study aims to examine monitoring capabilities in the subnational and national health information systems of Spain for long-term well-being of PHIV.

Materials and Methods

Study design and setting

A purposive key informant qualitative study adhering to the Standards for Reporting Qualitative Research (SRQR) [19] was conducted in seven autonomous communities, which were selected for having the highest incidence of new HIV diagnoses in Spain [20]. The seven autonomous regions comprise 72% of Spain's population [21]. Semi-structured focus groups (n=7) were held virtually from 19 June to 24 November 2023 among 20 total participants (Table 1) using Microsoft Teams, which allowed for verbatim transcription in Spanish.

Table 1. Focus group dates and participant (n=20) profiles

Region of Spain	Date of Focus Group	Participant Profiles		
		Assistance	Information System	Public Health
Andalucia	19 June 2023	3	1	0
Aragon	20 June 2023	2	1	1
Basque country	8 November 2023	1	1	0
Catalonia	19 July 2023	1	1	1
Galicia	22 November 2023	2	1	0
Madrid	24 November 2023	1	1	0
Valencia	24 November 2023	1	1	0

Participant recruitment

Participants were recruited through purposive sampling from the authors' professional networks from 14 June 2023 to 21 July 2023, targeting three specific groups: assistance professionals involved in care provision, public health experts, and specialists in healthcare information systems. This approach was designed to gain a comprehensive view of the multimorbidity monitoring process across various healthcare sectors.

Data collection

A quorum of three participants was set for each focus group, where possible, to have sufficient representation to support, question, and resolve any discrepancies that may arise in real-time among individual participants. All focus groups were conducted and recorded in a private Microsoft Teams meeting, with a combination of three researchers from ISGlobal and SEISIDA to direct the focus group using a semi-structured guide, probe unclear statements, and ensure recording quality. The focus group guide (S1 Appendix) was designed to facilitate in-depth discussions on the practical data collection, management, reporting, and use of PHIV encountered by the professional profiles of the participants in alignment with the research aim [19,22]. Video recordings were transcribed using the Microsoft Teams transcription feature, and both the recordings and transcriptions were saved in password-protected files accessible only to the researchers for subsequent analysis.

The semi-structured guide ensured that each session adhered to a predefined set of topics, maintaining consistency across different regions to gather comprehensive and comparable data. The open-ended questions allowed participants to express their thoughts and experiences in their region. A critical aspect discussed at the beginning of each focus group was the history of the Fourth 90, a concept in HIV care focusing on the quality of life for PHIV that emphasizes the importance of going beyond the traditional goals of diagnosis, treatment, and viral suppression [13].

Data analysis

Transcriptions were thematically analysed to facilitate a comprehensive examination of patterns within the data, which aligned with the study's theoretical frameworks and permitted an in-depth understanding of the focus group discussions in relation to the study aim [23]. The coding process was conducted in two stages, beginning with the first researcher performing thematic coding by labeling and categorizing key concepts after an initial immersion in the transcripts. This approach facilitated a comprehensive understanding and identification of emergent patterns and themes. In the second stage, coding was performed to classify the extracted text using a thematic analysis within two theoretical frameworks: the six WHO health systems building blocks (i.e., service delivery, health workforce, health information system, access to essential medicines and technologies, financing, and governance) and the six dimensions of the DeLone and McLean Health Information Systems Success Model (i.e., system quality, information quality, service quality, use, user satisfaction, and net benefits) within the health information system building block (S2 Appendix) [19,22]. The researchers characterized the overarching themes that were captured in the coded segments of the focus group discussions, ensuring these characterizations were both reflective of the data and linked to the study aim.

To ensure the validity and reliability of the analysis, several strategies were employed. A two-step coding refinement process was implemented, complemented by a verification system where a second researcher reviewed the coding, thematic development, and findings to maintain objectivity. Discrepancies were resolved by a senior researcher. Participant validation involved sharing key themes and interpretations with focus group participants. Additionally, triangulation with public data from the Ministry of Health and regional health bodies was used to corroborate the findings.

Ethical statement

This study was conducted in full compliance with ethical standards for research involving human participants after approval by the Comité de Ética de la Investigación con medicamentos (CEIm) of Hospital Clinic in Barcelona (HCB/2022/0934) in 2023. Informed consent was verbally obtained from all participants, witnessed by their peers and three researchers, and recorded via Microsoft Teams video conferencing after receiving comprehensive information about the study's purpose, procedures, potential risks, and benefits, and their rights as study subjects.

Results

From among 138 coded segments of transcribed focus group text, our analysis revealed substantial capacities and challenges within the Spanish health system to collect, report and use multimorbidity information among PHIV (Fig 1).

Fig 1. Thematic summary of focus group segments coded by theoretical framework domains

Fig 1 Legend: The outer ring represents the distribution of the 138 segments coded by building blocks of the Health Systems Strengthening (HSS) framework. Within the Health Information System building block, the inner ring represents the dimensions system quality, information quality, service quality, use, user satisfaction, and net benefits of the DeLone and McLean model.

Leadership and Governance

Despite frequent discussions on the importance of comorbidities among HIV and infectious disease professionals, participants identified a lack of their integration into systematic monitoring, except for some co-infections like tuberculosis, hepatitis B, and C. HIV and AIDS surveillance systems at both national and autonomous levels are expected to include homogeneous indicators based on case data, deaths, testing, and transmission modes. However, there is no central mandate for indicators measuring multimorbidity or quality of life. Furthermore, participants noted a lack of standardized tools, questionnaires, and guidelines for collecting such data, emphasizing the absence of systematic quality-of-life data collection in healthcare settings, despite ongoing efforts to enhance patient-centered care.

Financing

Several participants indicated that the best methods to collect multimorbidity data might be through clinical trials, cohort studies, or other primary data collection methods, suggesting a reliance on external monitoring and potentially inconsistent financial sources. They also highlighted the need for additional personnel to develop new reporting and surveillance systems or to review medical records, underscoring significant budgetary requirements.

Service Delivery

Participants identified multiple challenges in managing comorbidities across chronic conditions, emphasizing the necessity for improved tools and standardized methods, such as a consensus visual form to assess quality of life uniformly across healthcare facilities. They also stressed the need for enhanced training for primary care physicians to better manage specific comorbidities, including diabetes, cardiovascular diseases, mental health, and oncological issues. Despite acknowledging the importance of comorbidities in chronic disease management, participants noted difficulties in systematically incorporating these insights into current monitoring practices.

Health Workforce

Healthcare professionals expressed a strong interest in improving care conditions and protocols while recognizing the existing workloads of these professionals, suggesting that any data collection or intervention strategies should be designed with the intent to minimize additional burdens. Limitations of insufficient staffing, multiplicity of systems used in hospitals, and workload in HIV consultations were identified as potentially impacting the capacity to effectively manage and analyse new data from among PHIV.

Access to Essential Medicines and Technologies

Participants discussed the fragmented nature of ART dissemination tracking across autonomous regions, highlighting the challenges due to multiple HIV case recording systems and the reporting of ART and PrEP prescriptions by hospital pharmacies and laboratories without the ability to integrate with other patient data, including epidemiological and diagnostic information. Moreover, some participants saw a potential role for pharmacies in reporting comorbidity treatments, suggesting a shift towards more integrated data collection and management systems. Despite these proposals, including integrated screening and testing services to identify common comorbidities, participants remained uncertain about the impact on the workload of hospital laboratories and information management staff.

Health Information (DeLone and McLean Model)

a. System Quality

Participants noted the use of clinical records to collect data from patients through consultations. Yet the lack of integration of data collection methods for surveillance purposes with clinical practice was identified as a system quality issue. Participants expressed the need for better integration, for example using electronic notifications to remind or prompt physicians and nurses and automated systems to retrieve desired information. The difficulty to cross-reference patient data (e.g., HIV with diabetes) was often acknowledged, attributed sometimes to the lack of systematized collection methods.

Participants noted the fragmentation in hospital and primary care systems, where many chronic health issues are managed, poses challenges to integrating databases. They identified the need for better coordination between clinical and administrative IT departments across regions to create unified systems. The desire for structured, automated data collection was apparent, with suggestions to merge this with existing electronic systems or use regular surveys and cohort studies for specific health conditions. Additionally, two participants questioned the suitability of public health information systems for monitoring, suggesting that primary research via clinical cohorts might be more effective.

b. Information Quality

Participants revealed a lack of systematic and coded data collection for multimorbidity information, with each hospital having its own database(s), which are often not interoperable between hospitals. This would indicate a technical challenge in obtaining coherent and homogeneous information through any potential standardized system for data collection beyond that which is currently collected through quarterly and annual epidemiologic reporting. There is a notable lack of standardization for data collection at the clinical level, leading to potential inconsistencies in data collection and reporting from reviews of clinical notes. This is compounded by the diverse systems used by different entities, which may hinder effective data integration and analysis.

c. Service Quality

The potential impact of multimorbidity monitoring on health service quality identified the previously discussed staffing and resource constraints, as well as the lack of integration and interoperability between information management systems, as preventing the use of multimorbidity information to inform public health efforts, such policy planning, at the population level. The use of electronic clinical record notes represents compatibility with healthcare professionals' workflow and health service delivery. Yet, the repeated emphasis on systematizing data collection and ensuring its clinical relevance reflects the necessity to make data collection purposeful and improvement-driven. Participant assessment of a need for clear criteria on what data should be collected (e.g., which chronic conditions or HRQoL measures) underscore the need for comprehensive health information management to improve services.

d. Use

Participants highlighted several challenges, including resource constraints, staff reductions, and the complexities of shifting from passive to active HIV case notification systems. They pointed out critical interoperability issues among hospital data systems, which hinder effective data consolidation and standardization, affecting the use of health information systems across different healthcare settings. This limitation impacts the effective use and collection of patient multimorbidity data. Additionally, technical shortcomings, such as the absence of a structured policy framework for multimorbidity and quality-of-life data collection, along with the reliance on clinicians for case reporting, obstruct the practical use of data in patient care and public health initiatives.

e. User Satisfaction

Despite the identified challenges, an underlying motivation and recognition of the importance of improving system quality was evident among the participants and their impressions of their immediate colleagues. Participants discuss their motivation to address these issues and participate in the development of new plans in improving data collection and integration.

f. Net Benefits

Within this domain emphasizing the health information system's impact on health, seven segments of text were relevant. The aspirational nature of plans for multimorbidity management is evident. The emphasis on the need for systematic and coded data collection of comorbidities underscores a broader goal rather than a concrete plan. These aspirations indicate a desire to improve health monitoring such that it improves service delivery for chronic care management, including mental health.

Discussion

This study set out to examine monitoring capabilities on the long-term well-being of PHIV in the Spanish health information system. Healthcare professionals highlight a substantial gap in the systematic monitoring and integration of comorbidity data in HIV care, which if available could help Spain set national targets beyond viral suppression. They also note the absence of standardized tools for data collection and quality-of-life assessments and suggest enhancing data integration through electronic notifications, automated systems, and better inter-organizational coordination, emphasizing the need for structured, automated collection methods that can simultaneously improve person-centred care and relieve health workforce resource burdens.

HIV-related data collected within regional health systems must be reported according to surveillance protocols set centrally by RENAVE [24]. Data may be obtained through primary (e.g., surveys, diagnoses) or secondary sources (e.g., antiretroviral provision). Aside from incident positive cases, the autonomous regions may elect to collect other data related to each case, but in practice, such systematic collection does not occur for information related to long-term well-being beyond viral suppression, such as multimorbidity or health-related quality of life, according to participants and public reports [24,25]. Objective 4 of the strategic plan 2021-2030 for the prevention and control of HIV and sexually-transmitted infections in Spain, focuses on enhancing the quality of life for PHIV and those at risk of acquiring it [26]. Specifically, it aims to monitor and incorporate quality of life measurements into clinical practice, promote psychosocial health in PHIV, eliminate social and legal barriers, and reduce the stigma associated with HIV.

Identified barriers to multimorbidity data collection, monitoring, and use included a lack of a systematic process for collecting information on comorbidities in existing reporting systems. Participants suggested that a single monitoring program managed by RENAVE that encompasses all PHIV and facilitates consistent and unified data collection would allow for more comprehensive and coherent data to be obtained. Implementing such a program could streamline the data collection process and improve the overall quality of data for analysis and decision-making purposes. Yet, a technical barrier raised by participants included the heterogeneity of comorbidity data that is currently recorded in patient clinical records without an existing mechanism to systematically extract and taxonomise such data.

Clinical guidelines inform HIV clinical practice by establishing uniform standards of evidence-based care, and in Spain are established by the AIDS Study Group (GeSIDA) of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). Of the current guidelines, six recommend monitoring for co-infection of tuberculosis, hepatitis B, hepatitis C, opportunistic or AIDS-defining infections [27–31]. Participants reported that information on these illnesses are collected by hospitals and, following data quality control procedures, reported in aggregate by the regional disease surveillance entities. Yet, some GeSIDA guidelines also recommend the clinical monitoring of health and well-being indicators beyond viral suppression, for example for kidney and bone diseases [32], neurocognitive morbidity [33] and quality of life [34], which have yet to been systematically monitored by information systems covering PHIV. Our results indicate that these data may be, and often are, recorded by individual physicians in a patient's clinical record, but are not collated within hospitals or within any region's health information system. In October 2022, Seville, Spain, was the venue for a global conference of Fast-Track Cities, where the Seville Declaration was endorsed, which emphasizes the critical role local community organizations play in addressing HIV in key urban populations [35], a topic that was not raised in our focus groups, which could indicate a lack of awareness among participants or their perception of a lack of relevance to this topic.

A European study of health information managers in six countries (i.e., Estonia, Italy, the Netherlands, Slovenia, Sweden, and Turkey) regarding their ability to monitor national responses to the HIV epidemic similarly found gaps in the systematic tracking of comorbidities such as bone loss, cardiovascular disease, and neurocognitive disorders, with three of six respondents reporting no monitoring of these aspects [36]. Participants raised the prospective that HIV cohorts can serve as data collection and monitoring mechanisms for issues beyond viral suppression. Sweden has implemented a national HIV registry, InfCareHIV, that covers greater than 99% of PHIV in the country and collects information beyond viral suppression, including long-term comorbidities and patient-reported outcome and experience measures [37]. Similarly, the Netherlands employs a monitoring system through its open national cohort that integrates data from all healthcare settings to monitor comorbidities and healthcare utilisation patterns for greater than 99% of PHIV [38].

Our findings also demonstrate the need for technical and policy improvements to realize the systematic monitoring of comorbidities among specific disease cohorts. There is a clear need for policy frameworks and technical solutions that facilitate the integration of multimorbidity data into health information systems. Such integration could benefit the ability of healthcare providers to offer more holistic and patient-centred care or for policymakers to address health-related quality-of-life concerns at the population level. Furthermore, our results emphasize the role of leadership and governance in driving improvements in health information systems. Effective management and coordination at both national and regional levels are crucial for the successful implementation of standardized and interoperable health data systems. By focusing on multimorbidity and quality of life, alongside traditional HIV care metrics, health systems can provide more comprehensive and effective care, ultimately improving the health outcomes and quality of life for PHIV.

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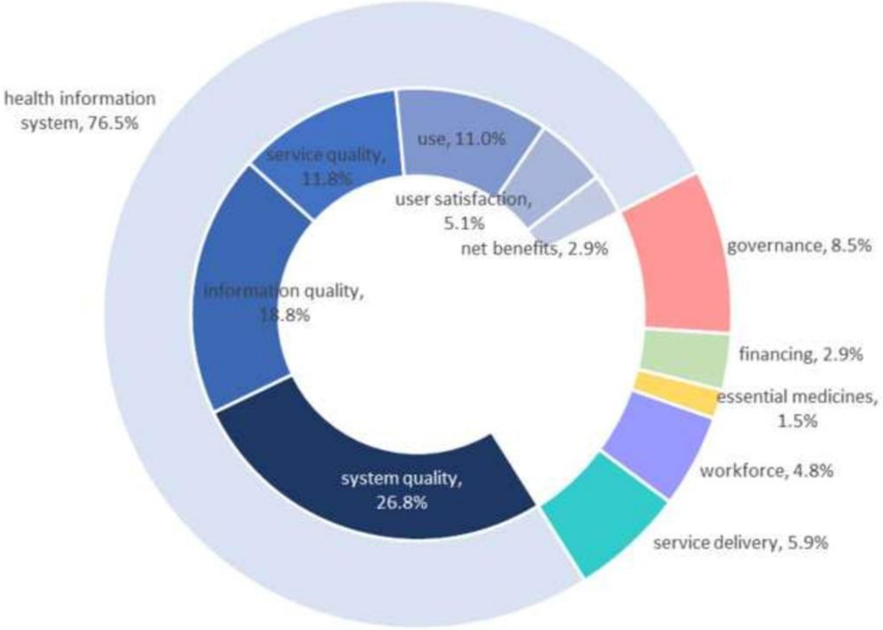
Supporting Information
S1 Appendix. Focus group guide
S2 Appendix. Description of theoretical analytical frameworks


health information system, 76.5%
service quality, 11.8%
use, 11.0%
user satisfaction, 5.1%
net benefits, 2.9%
information quality, 18.8%
system quality, 26.8%
governance, 8.5%
financing, 2.9%
essential medicines, 1.5%
workforce, 4.8%
service delivery, 5.9%

Discussion

This doctorate identified opportunities for the decentralized health system of Spain to better respond to the long-term well-being needs of people living with HIV (PLHIV) by improving surveillance of multimorbidity and factors affecting HRQoL in this population. Improved monitoring of these issues at a population level can further enhance the public health of PLHIV by, first, encouraging their collection at the individual level for people who are already engaged in care, and, second, informing policies and decision-making at the health system level. No autonomous community currently reports the prevalence nor incidence of common comorbidities (with the exceptions of tuberculosis and viral hepatitis, which have been international targets since the Dublin Declaration for HIV Monitoring in 2008),[179] nor patient-reported metrics of well-being, like HRQoL, to the national health system surveillance authorities. Further, these data may or may not be collected for all people with HIV during routine clinical care. Data on comorbidities, such as clinical biomarkers or previous diagnoses, are directed by clinical guidelines and may be collected in the electronic health records of patients. Therefore, these data remain accessible to and known only by healthcare providers, without aggregation to the autonomous community or national levels, outside of ad-hoc primary research, and would require proactive investigation by one's healthcare provider on case-by-case bases to review. Similarly, while HRQoL has been investigated among PLHIV in care in Spain through ad-hoc primary research, nor are these data routinely collected in healthcare settings to inform care, much less aggregated in national metrics to inform health system policy. Moreover, the lack of data implies that there are not normative clinical thresholds or cut-off points which can provide accurate information about the level of (health-related) quality of life nor its related facets to guide decisions for intervention. Research on patient-reported outcomes indicate that psychological distress, material deprivation, and social support are three critical factors that influence the overall HRQoL among PLHIV in the nationwide CoRIS cohort of Spain.[207] Striving to incorporate multimorbidity and HRQoL metrics into the national HIV surveillance system may encourage the longitudinal monitoring of such data and its use in improving long-term well-being outcomes for PLHIV in care.

The healthcare system of Spain has made substantial strides in identifying and treating HIV cases, achieving the 90-90-90 UNAIDS targets in 2021.[24] Despite successes in life expectancy, excess mortality remains higher among PLHIV than the general population, due to HIV-related and non-HIV-related causes.[208] PLHIV continue to report low health-related quality of life (HRQoL), often borne from mental health and psychosocial challenges as well as ageing-related burdensome symptoms, which can impact daily functioning and well-being.[93,122,209] Further, PLHIV, especially those 50 years of age or older, face HIV-related and ageing-related comorbidity challenges that are currently not fully addressed at the population level.[40,148,210]

Core outcomes for person-centered care in PLHIV can include a broad range of health and quality-of-life issues, necessitating comprehensive assessment methods.[211] Key aspects of patient-centered care involve demonstrating empathy, showing respect, and maintaining effective communication, which can help build a robust relationship between patients and providers, enabling shared decisionmaking.[212,213] This approach aligns with global strategies by WHO and UNAIDS, which advocate for measuring patient-centered outcomes and addressing comorbidities to improve the overall well-being of PLHIV.[214] The WHO global strategy for HIV 2022-2030 underlines the significance of countries' capacity to assess stigma, discrimination, and patient-centered approaches to HIV care that result in a good HRQoL at all stages of the HIV care continuum without directly setting targets.[177]

Therefore, there is a need for health systems to adopt a holistic, patient-centered approach to care that aligns with these global strategies. Such an approach goes beyond viral suppression and entails addressing the complex interplay of social, psychological, and physical factors that affect the long-term health and well-being of PLHIV in their care.[95,215] A focus beyond viral suppression in HIV treatment highlights the need to address various health challenges that persist even when viral load is controlled, and is understood to consider factors such as multimorbidity and health-related quality of life.[38,214] Even with effective ART, residual and chronic inflammation remains a concern that can exacerbate other health issues impacting HRQoL and necessitating real-time adherence monitoring to mitigate systemic inflammation and improve patient-reported outcomes.[216] In 2020, Horberg et al. advocated broadening the scope of metrics for HIV patient care to include measures beyond traditional HIV care continuum benchmarks, like viral suppression, proposing process quality metrics (e.g., pneumococcal and influenza vaccination, ART medication fills) and outcome quality metrics (e.g., achieving HIV RNA levels below 200/mL, maintaining normal blood pressure and BMI, no hospitalization or emergency department visit) for use in HIV research and practice.[217] While such process and quality metrics would make available some data on the physical health status of PLHIV in care beyond viral suppression, they alone would not provide indications of well-being in a holistic nor patient-centered way among this population. To enable such an approach, health systems in Spain and elsewhere would benefit from indicators to monitor trends in multimorbidity and HRQoL among PLHIV.

The concept of a Fourth 90 metric,[35] or long-term well-being metric, to align with current global targets, can have a crucial role in shaping future modifications in health information systems.[37] This concept emphasizes the importance of the role of health systems not only achieving viral suppression but also ensuring that PLHIV enjoy a good quality of life. For health systems to operationalize such an approach could entail monitoring well-being issues over the long-term that influence quality of life. Yet, health systems typically do not have the authority, let alone capacity, to address all quality of life issues. Rather, being responsible for maintaining and improving the health status of the populations they serve, health systems may be responsive to health-related quality of life (HRQoL). For example, incorporating HRQoL and multimorbidity indicators into health information systems may satisfy a measurement for this target, but would necessitate a paradigm shift towards more comprehensive and patient-centered care models across health systems. PLHIV in Spain and their healthcare providers report a desire for more person-centered metrics in HIV care, for example, patient-reported outcome (PROM) and patient-reported experience measures (PREM).[218] By systematically collecting and analyzing data on HRQoL and multimorbidity, healthcare providers can gain a better understanding of the broader health challenges faced by

PLHIV, enabling more tailored and effective interventions. The successful implementation of these strategies depends on standardized data collection protocols, enhanced inter-regional coordination, and the integration of health information systems.

Robust multimorbidity monitoring can enable data-driven decision-making in healthcare policy and practice.[219] For example, accurate and up-to-date data on the prevalence and impact of various comorbidities among PLHIV can inform the allocation of resources, the design of targeted interventions, and the development of public health strategies. Such data are critical for patient-centered healthcare services to meet the specific needs of PLHIV. Yet, Spain's healthcare system, decentralized across its 17 autonomous communities, presents both capacities and challenges in monitoring the long-term well-being of PLHIV, particularly in addressing multimorbidity. The decentralized structure of Spain's healthcare system may impact the uniformity and comprehensiveness of health data collection in healthcare settings. Each autonomous community is responsible for managing its healthcare services, including the collection of public health and epidemiological data.[91] This autonomy can lead to variations in how health data is collected, reported, and utilized across the regions. The lack of standardized protocols for data collection on multimorbidity and HRQoL among PLHIV creates inconsistencies in the available data, making it challenging to form a comprehensive national picture of well-being among PLHIV as they age.[220] The technical and interoperability challenges between different regional health data systems may further exacerbate these inconsistencies, hindering effective data integration and analysis.[220] For example, apart from tuberculosis and viral hepatitis B and C, comorbidity data are not routinely or systematically reported by the health system for PLHIV in care in Spain.[218,220] The health system in Spain must also overcome barriers to the implementation of long-term well-being measures, such as time limitations, patient health literacy, and technical challenges to effectively utilize these measures.[228] For example, healthcare providers and PLHIV have reported the need for improved communication and collaboration to manage comorbidities more efficiently.[218,221]

In addition to these obstacles, there is no central mandate for indicators beyond viral suppression, for example those that measure multimorbidity or HRQoL.[220] Further, the lack of standardized tools for data collection underscores an urgent need for integrated care models that can consider ageing-related issues and multimorbidity as part of HIV management.[94] This lack of systematic monitoring may limit the ability to provide holistic and patient-centered care that addresses the diverse health needs of PLHIV beyond viral suppression. For example, without consistent and comprehensive data on the various comorbidities that PLHIV may experience, healthcare providers may not fully understand the broader. Similarly, policymakers may lack the necessary information to allocate health system resources efficiently. From a public health perspective, the lack of routine monitoring of long-term well-being issues, such as multimorbidity and HRQoL, represents a missed opportunity to identify early signs of non-HIV-related health issues among a largely linked-to-care population, which would allow for timely intervention and potentially mitigate the severity or progression of burdensome issues.

Therefore, researchers and others in the HIV community in Spain have relied on ad-hoc primary research studies to estimate aspects of long-term well-being and early ageing, including frailty and pre-frailty,[63,93] polypharmacy,[49,222,223] cognitive decline,[224] psychological distress,[71,90] and various mental,[88,89] metabolic,[50,52,55,74,225] renal,[50,55] cardiovascular,[49,50] and other types of comorbid conditions.[63] For example, the Clinic Screening Tool for HIV (CST-HIV), developed and validated among PLHIV in Spain, contributes to understanding long-term well-being by providing a standardized approach to collecting and assessing a wide range of health indicators specific to and self-reported by PLHIV, including information on physical, mental, and social well-being.[226] This information can be assessed and used by HIV physicians to address problems in routine care that negatively impact HRQoL.[207] By incorporating a standardized, validated set of existing patient-reported measures into a shortened questionnaire, the CST-HIV can facilitate consistent data collection across different regions and healthcare settings, helping to address any disparities emerging in the decentralized system and allowing for targeted interventions that more effectively manage long-term health and well-being in PLHIV. Yet, currently this information is not routinely collected in HIV care and therefore healthcare providers are not readily able to intervene on the factors that most affect HRQoL and well-being.

Preliminary national data collected in 2022 from the ECDC indicate that 10 of 55 countries that report via the Dublin Declaration monitoring system provided national HRQoL assessments, including Spain for the first time.[227] The data from Spain come from a 2021 questionnaire among a convenience sample in the CoRIS cohort asking one item, "In last 12 months, would you say that your health has been..?", with five possible responses ranging from “very good” to “very bad”. The preliminary report does not provide a point estimate for this item for all PLHIV, nor estimates disaggregated by gender, age, socioeconomic status, or key population status. Further, while this item captures an overall metric for health satisfaction, it does not capture overall well-being, nor specific domains of well-being nor HRQoL, despite primary research indicating there is variance in well-being by domain, by sociodemographic factors, and over time.[119,226]

Key dimensions of HRQoL of PLHIV in Spain, such as psychological distress, material deprivation, and social support, indicate a need to focus on these issues in HIV care, especially given their predilection to influence overall HRQoL and other HRQoL factors such as sleep, fatigue, and cognitive problems.[207,218] Psychological distress, encompassing anxiety, depression, and stress, directly influence other HRQoL problem issues, such as sleep and fatigue, cognitive problems, and social support.[207,228,229] For example, HIV-related distress, may be linked to higher levels of avoidant, or maladaptive, coping and lower levels of cognitive coping, suggesting that neurocognitive deficits may lead to greater reliance on avoidant coping, which exacerbates a cycle of psychological distress.[230] Interventions targeting psychological distress are likely to have a broader impact on other interconnected issues, thereby improving overall well-being, for example improvements in sleep quality,[231] cognitive functioning,[230] and the capacity to maintain social support networks,[232] whereas social isolation negatively impacts psychological and psychosocial well-being.[228] Material deprivation, which refers to a lack of financial resources for basic needs, is not often assessed in medical research in

PLHIV, and may significantly influence psychological distress, exacerbating feelings of anxiety and depression, and in turn negatively affect other aspects of HRQoL and health status.[233] Its indirect yet powerful impact underscores the need for comprehensive interventions that address both the economic and psychological needs of PLHIV to improve their overall quality of life.

The lack of standardized tools and heterogeneous data collection practices across different autonomous communities can be mitigated by developing and implementing uniform protocols and tools for data collection nationwide, facilitated by the Carlos III Institute of Health (ISCIII) and the General Subdirectorate of Health Information. Future research implementing standardized quality-of-life assessment tools across all regions can ensure consistent data collection, which is recommended in the 2021-2030 "Strategic Plan for the Prevention and Control of HIV and other Sexually Transmitted Infections in Spain."[35] The CST-HIV is an existing tool that could be adopted in routine clinical practice as a standardized approach to identifying and addressing the multifaceted issues affecting HRQoL among PLHIV. A standardized approach to the collection of patient-reported measures for well-being may enable timely intervention, addressing problems before they escalate and improving overall patient outcomes. In turn, such data may be used to monitor these issues among PLHIV in a systematic manner, for example through their incorporation into electronic health records (EHR) or national monitoring surveys, rather than ad-hoc primary research which may or may not focus on long-term well-being as a primary outcome of interest. This approach could enable healthcare providers and policymakers to capture comprehensive data on HRQoL and identify key areas requiring intervention over time.

Similarly, the management of comorbidities among PLHIV in Spain faces ongoing challenges, although efforts have been made to improve the integration and quality of HIV services with other healthcare services.[221,234–236] Accurate recording and systematic collection of comorbidity data enhances the quality and consistency of health information.[237] While there is currently a weak body of evidence supporting the effectiveness of integrated management of comorbidities over individual, parallel diseases or conditions,[238] there is increasing recognition of its importance within the HIV medical community[37,210,214,217,220,239] and beyond[240,241] to address burdens faced by people with multiple chronic conditions. The integration of comorbidity data collection in robust data infrastructures, such as clinical data registries and EHRs can permit the analysis of aggregate data that may enable the identification of patterns of multimorbidity in this chronic care population as well as the earlier diagnosis or prevention of other chronic conditions, related and unrelated to HIV.[242–244] Further, the integration of comorbidity data, such as diagnoses, with machine learning and artificial intelligence tools may enhance this ability.[245] Establishing a unified monitoring program for comorbidities among PLHIV, a population that is predominantly linked to regular care in Spain, collected from autonomous communities via the RENAVE or SINIVIH systems can promote the analysis of these data to inform health policy and planning. PLHIV and HIV care providers agree that integrated care models, such as multi-disciplinary clinics, hold advantages for monitoring and managing multimorbidity and its related burdensome health issues, such as polypharmacy and, among ageing PLHIV, frailty.[218] Effective multimorbidity monitoring may help optimize treatment plans and, through better coordinated and more comprehensive care strategies, reduce the strain on healthcare resources.[237,245,246]

Stigma and discrimination remain significant barriers reported by PLHIV to effective HIV care.[218,247] HIV stigma refers to negative attitudes and beliefs about PLHIV, which can lead to discrimination.[14] This discrimination can manifest in various ways, such as being denied healthcare services, employment, or housing, and experiencing judgmental attitudes and harassment from others. While these behaviors can deter individuals from getting tested or sharing their HIV status, inhibiting HIV prevention efforts, discrimination can also impact routine HIV care by discouraging individuals from engaging in necessary medical care, for HIV or otherwise, thereby impacting their long-term health and well-being.[106] Experienced and internalized stigma, or self-stigma that occurs when individuals internalize negative stereotypes, both may produce feelings of shame, fear, and isolation in some PLHIV, which can lead to poorer mental health and psychosocial outcomes.[108] Some PLHIV may take direct actions that lead to missing or delaying medication, such as concealing or hiding medications to avoid HIV status disclosure, or actions that indirectly affect adherence such as avoiding social support or information that could aid in treatment adherence.[106] Apart from HIV treatment adherence, people ageing with HIV face compounded stigmas from both HIV and age-related discrimination, which represents a unique, intersectional oppression system that can result in traumatic experiences and adversely impact their quality of life.[248] PLHIV may avoid healthcare utilization if they have previously experienced or anticipate discrimination in healthcare settings, which are missed opportunities to monitor long-term health measures and possibly prevent the progression of other chronic diseases.[248,249]

While there is a lack of well-designed intervention studies specifically documenting stigma reduction and its direct impact on HRQoL, current evidence suggests that interventions that meaningfully involve PLHIV in their design and implementation and which address the complexities of intersectional stigma tend to be more effective in this regard.[108] A 2022 review of 69 frameworks with 50 measures of HIV-related stigma found that most existing frameworks incorporate broad socio-ecological factors.[112] Frameworks incorporating broad socio-ecological factors typically encompass multiple domains of stigma, such as internalized stigma, experienced stigma and discrimination in healthcare settings. These frameworks often emphasize the complexity of stigma by highlighting intersecting stigmas at various socio-ecological levels, including individual (e.g., self-stigma), interpersonal (e.g., fear of disclosure, prejudicial language and behavior), community (e.g., cultural norms of social networks), organizational/institutional (e.g., healthcare practices, workplace policies), policy/societal level (e.g., legal frameworks, media representation).[112] In contrast, studies focusing on specific domains in healthcare tend to have more detailed measures, often capturing beliefs and practices among health workers, and experiences of PLHIV as clients, but they vary widely in their scope and specificity, making comparability across different settings challenging.[112] Among 502 PLHIV surveyed in Spain in 2024, approximately one-fourth reported previously experiencing stigmatization in a healthcare setting, which was significantly associated with lower HRQoL.[247] HIV stigma in healthcare settings can be driven by factors such as lack of education, religious beliefs, and workplace culture, and it is important for health systems to recognize that improved HIV knowledge alone does not necessarily reduce stigmatizing attitudes.[249] While some healthcare facilities have mechanisms for PLHIV to report experiences of stigma or discrimination, not all do, nor are patients and healthcare providers always aware of them.[218,220] Addressing HIV stigma and discrimination is crucial for improving long-term health and well-being outcomes, including quality of life, for PLHIV.

This thesis provides valuable insights but has several limitations. Firstly, the sampling methods in the supporting studies may introduce biases. The network analysis included a relatively small number (n=371) of predominantly socioeconomically well MSM, which could limit the generalizability of the findings to the diverse demographic and socio-economic profiles of all PLHIV in Spain. The focus group discussion participants informing the capacity of the health system to monitor on well-being issues was similarly small (n=21) and did not include representatives from central bodies within the health information system, only those from regional bodies. Relatedly, the regional coverage of these studies predominantly focuses on urban and better-resourced regions of Spain, potentially overlooking experiences of small regions. Rural populations often face different challenges and barriers to accessing healthcare and support services compared to their urban counterparts.[250–253] Additionally, the thesis lacks quantitative data on the long-term evolution of HRQoL to assess the stability of the findings over time. While qualitative insights are valuable, the absence of robust quantitative data limits the ability to make strong, evidence-based recommendations for policy and practice. This gap highlights the need for future research to incorporate quantitative assessments to provide a more comprehensive understanding of the long-term impacts of HIV and associated comorbidities on HRQoL. Future research should focus on conducting longitudinal studies that track the HRQoL of PLHIV over extended periods, evaluating the effectiveness of targeted interventions, expanding regional coverage to include small and rural communities, and integrating mixed-methods approaches to combine qualitative and quantitative data. These steps will help to ensure a more holistic and representative understanding of the issues affecting PLHIV in Spain, ultimately leading to improved care and support for this population.

Conclusions

1. The lack of standardized tools for health-related quality-of-life assessments in Spain limits the ability of health information systems at the subnational and national levels to monitor long-term well-being among people living with HIV.
2. The absence of the systematic collection of comorbidity data from healthcare facilities by subnational and national health information systems limits the capacity of these systems to monitor important health factors affecting long-term well-being.
3. Technical and interoperability challenges in the subnational health information systems of Spain's decentralized healthcare system complicate efforts to achieve a comprehensive national understanding of the long-term well-being challenges faced by people living with HIV.
4. The development of standardized data collection protocols for patient-reported outcome and experience measures, improvements in inter-regional coordination, and implementation of comprehensive, multidisciplinary care models for people living with HIV can contribute to improved monitoring capacities for long-term well-being metrics.
5. Psychological distress is a central dimension affecting the health-related quality of life of people living with HIV in Spain, impacting other factors such as sleep, fatigue, and cognitive problems, which highlights its importance as a critical metric in interventions to improve long-term well-being.
6. Material deprivation significantly impacts health-related quality of life of PLHIV in Spain through its associations with psychological distress and social support, which highlights the need for socio-economic metrics to comprehensively address the long-term well-being among this population.

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