UNIVERSITAT DE BARCELONA

Development and Validation of a Clinic Screening Tool to Improve Clinical Management of Symptoms and Health-related Concerns in People Living with HIV in Spain

Kelly Safreed Harmon

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Development and Validation of a Clinic Screening Tool to Improve Clinical Management of Symptoms and Health-related Concerns in People Living with HIV in Spain

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Table of Contents

List of Tables **7**

Glossary **9**

Articles Included in the Thesis **11**

1. Summary **13**

2. Resumen **19**

3. Introduction **25**

4. Hypotheses **33**

5. Objectives **35**

6. Materials and methods and results **37**

ARTICLE 1 39

ARTICLE 2 51

ARTICLE 3 67

ARTICLE 4 87

7. Discussion **111**

8. Conclusions **119**

9. References **121**

List of Tables

Table 1. HIV epidemiology in study countries 37

Table 2. A comparison of the HIV Clinic Screening Tool (CST-HIV), the Positive Outcomes PROM and the Short-Form HIV Disability Questionnaire (SF-HDQ) 112

Glossary

ART	antiretroviral therapy
CST-HIV	HIV Clinic Screening Tool
HRQoL	health-related quality of life
PLHIV	people living with HIV
PROM	patient-reported outcome measure
SF-HDQ	Short-form HIV Disability Questionnaire

Articles Included in the Thesis

This thesis is presented as a compendium of three published articles which address five objectives. It also includes a fourth article which is under peer review.

ARTICLE 1

Ability to monitor national responses to the HIV epidemic 'beyond viral suppression': findings from six European countries

Kelly Safreed-Harmon, Meaghan Kall, Jane Anderson, Natasha Azzopardi-Muscat, Georg M. N. Behrens, Antonella d'Arminio Monforte, Udi Davidovich, Teymur Noori and Jeffrey V Lazarus on behalf of the HIV Outcomes Beyond Viral Suppression Study Group

Frontiers in Public Health. 2020;8:36.
Impact factor (JCR, 2020): 3.709
Quartile (JCR, 2020): 2

ARTICLE 2

Assessing quality of life in people with HIV in Spain: psychometric testing of the Spanish version of WHOQOL-HIV-BREF

María José Fuster-RuizdeApodaca, Ana Laguia, Kelly Safreed-Harmon, Jeffrey V Lazarus, Santiago Cenoz and Julia del Amo

Health and Quality of Life Outcomes. 2019;17:144.
Impact factor (JCR, 2019): 2.344
Quartile (JCR, 2019): 2

ARTICLE 3

Development of a clinic screening tool to identify burdensome health-related issues affecting people living with HIV in Spain

María José Fuster-RuizdeApodaca, Kelly Safreed-Harmon, Marta Pastor, Ana Laguia, Denise Naniche and Jeffrey V Lazarus

Frontiers in Psychology. 2021;12:681058.
Impact factor (JCR, 2020): 2.990
Quartile (JCR, 2020): 2

ARTICLE 4

Problems undermining the health-related quality of life of people living with HIV in Spain: a qualitative study to inform the development of a novel clinic screening tool

Kelly Safreed-Harmon, María José Fuster-RuizdeApodaca, Marta Pastor and Jeffrey V Lazarus

Under peer review

1. Summary

Introduction

Almost 38 million people were living with HIV at the end of 2020, 73% of whom were estimated to be receiving antiretroviral therapy (ART). The face of HIV has changed greatly since the first highly effective ART regimens were introduced in 1996, and PLHIV who initiate ART at a sufficiently early disease stage have a near-normal life expectancy. Yet their lives are markedly different in some ways from the lives of people without HIV. The prevalence of multimorbidity is higher in PLHIV than in the general population, with a wide range of infectious and noninfectious conditions contributing to the multimorbidity burden. PLHIV report being troubled by uncertainty about the future, and have high levels of depression and anxiety. Furthermore, even among PLHIV who have responded well to ART, some studies have documented poorer health-related quality of life (HRQoL) in comparison to that of the general population. PLHIV also report experiencing a high symptom burden, social isolation and multiple forms of HIV-related stigma.

Improving the health and HRQoL of PLHIV in the context of high uptake of ART is the ultimate goal of the group of studies presented in the following thesis, which describes the development and piloting of a novel patient-reported outcome measure (PROM) for use in HIV clinical care in Spain. This work is timely because of the pressing need to rethink conventional approaches to HIV care in Spain and many other countries. From the mid-1990s onward, healthcare providers and public health experts have emphasised the importance of using ART to reduce viremia in PLHIV, while giving less attention to other health-related issues in this population. However, with growing awareness of the high burden and health effects of these other issues, it has become clear that conventional criteria for assessing the effectiveness of HIV care in terms of viral load outcomes and HIV-related mortality are insufficient. There are growing calls by researchers, PLHIV and other stakeholders for the HIV community to recognise the quality of life of PLHIV as a major healthcare concern. This changing paradigm is reflected in the UNAIDS Global AIDS Strategy for 2021–2026, which addresses "optimizing quality of life and well-being across the life-course".

Integrating people-centred healthcare principles and standards into clinical practice is an essential strategy for improving the HRQoL of PLHIV who are engaged in care. Taking a people-centred approach entails giving attention to the health-related issues that matter to individual PLHIV rather than merely focusing on how to halt HIV disease progression. There must be effective communication between patients and healthcare providers in order for patients' needs and preferences to meaningfully inform their interactions with health systems.

Various research findings call into question whether HIV care providers sufficiently understand their patients' concerns. Studies have documented providers' lack of awareness of clinically important symptoms in PLHIV patient populations, and PLHIV have reported communication barriers with their providers. There is also evidence that HIV care providers and PLHIV may not be in agreement about healthcare priorities.

At the time of this writing, various stakeholders had published recommendations and guidance regarding the health-related needs of PLHIV beyond viral suppression, and the World Health Organization's draft 2022–2030 strategy on HIV calls on countries to "address chronic care needs of adults and children living with HIV". Clinical tools are needed to support healthcare providers in implementing this vision.

PROMs can make an important contribution to the next chapter of HIV care by providing a structured mechanism for PLHIV to directly express health-related concerns to healthcare providers. PROMs may address a wide range of health-related issues and may be administered via interview, paper-based forms, or digital devices such as touch-screen tablets. Historically, they have had a more prominent role in research than in clinical practice. In recent years, there has been increasing interest in the potential for PROMs to contribute to clinical management across different healthcare fields, in part because of greater awareness of the principles of people-centred healthcare. When PROMS are used effectively in clinical practice, benefits may include greater provider awareness of health issues, improved patient-provider communication, more effective symptom management, and better health and HRQoL outcomes.

There is currently an unmet need for short broadly focused PROMs that can give healthcare providers a convenient means of identifying disparate health-related challenges commonly experienced by PLHIV. The general objective of the body of research presented in this thesis is to design and pilot a PROM instrument that can be used in routine clinical practice to identify issues undermining the health-related quality of life of PLHIV in Spain, thus aiding health systems in responding more effectively to the long-term needs of this population beyond antiretroviral therapy.

Methods

The research presented in this thesis is based on three studies, which are presented in four articles. The first study was a policy survey that collected data from one expert in each of six European countries to investigate health system capacity to monitor aspects of healthcare such as mental health and psychosocial services. Findings are reported in *Article 1*. The second study used an observational cross-sectional ex-post-facto study design to validate the Spanish version of WHOQOL-HIV-BREF, a widely used HIV-specific HRQoL PROM, and to explore the HRQoL of Spanish PLHIV. Findings are reported in *Article 2*. The third study focused on the development of the CST-HIV in accordance with standard instrument development procedures. Findings from the first two phases of the study process, a literature review and a qualitative investigation of PLHIV and healthcare provider perceptions of issues that undermine the well-being of PLHIV in Spain, are reported in *Article 3.* Findings from the latter phases, including a Spanish pilot study assessing the psychometric properties of the new instrument, are reported in *Article 4*.

Results

The first article reports on a policy survey that investigated the national monitoring of HIV care issues in six European countries: Estonia, Italy, the Netherlands, Slovenia, Sweden and Turkey. The survey was administered in April–June 2018, with one purposively selected expert in each country providing information about health system monitoring capacity in relation to issues such as comorbidities, HRQoL, psychosocial services, and HIV-related discrimination in healthcare settings. According to respondents, only two countries (Slovenia and Sweden) had the capacity to monitor indicators addressing the screening, diagnosis and treatment of anxiety and depression. None of the respondents reported the use of national-level indicators to monitor the provision of psychosocial services. Respondents from three countries (the Netherlands, Slovenia and Sweden) indicated that their national monitoring systems had the capacity to report on the HRQoL of PLHIV.

The second article reports on the validation of WHOQOL-HIV-BREF in a nationally representative sample of PLHIV in Spain (N=1,462) and on the HRQoL of this population. Data were collected between October 2016 and April 2017. Psychometric testing demonstrated that the Spanish version of the instrument has adequate construct, convergent and concurrent validity. Female study participants and heterosexual study participants had poorer HRQoL in comparison to their counterparts, as did people with low socioeconomic status, people who had been living with HIV for a longer period of time, and people older than 50.

The third article reports on the literature review findings and focus group discussion findings that informed the early development of the CST-HIV. The literature review documented high prevalence of symptoms such as sleep-related problems, fatigue, and pain in PLHIV populations, and also identified studies that showed symptom burden and other issues such as social support, emotional health and material security to be associated with HRQoL in PLHIV. An analysis of data from the focus group discussions, two with HIV service providers (N=8 per group) and two with PLHIV (N=8 and N=7), identified a number of broad categories of issues impacting the HRQoL of PLHIV. The issues emphasised the most by both categories of focus group participants were social problems including HIV-related stigma and discrimination, sleep-related problems, fatigue, pain, and emotional distress.

The fourth article reports on the entire CST-HIV instrument development process, including the definition of domains, development of potential items, expert assessment of items, cognitive debriefing interviews with eight PLHIV, and validation of the instrument in a cohort of 226 PLHIV in Spain. The eight domains chosen for the initial pilot instrument were anticipated stigma, emotional distress, sexuality, social support, material deprivation, sleep/fatigue, cognitive problems, and physical symptoms. Pilot findings confirmed the suitability of these domains, and led to the selection of three items per domain from among the 40 items used in the pilot instrument. The resulting 24-item instrument met standards for content, face, construct, convergent and concurrent validity.

Discussion and conclusions

The results of this thesis contribute to ongoing efforts to reorient HIV care to address the wide-ranging physical, emotional and social issues that challenge people who are living with HIV on a long-term basis. The PROM developed through this research, the CST-HIV, shows adequate preliminary validity and is currently undergoing additional validation to strengthen the evidence supporting its use in routine clinical care. To our knowledge, it is one of only three short validated instruments developed specifically to support HIV care providers in identifying a wide range of health-related issues that affect the well-being of PLHIV, and the only such instrument developed in Spain.

The CST-HIV was developed through a methodologically rigorous process that closely followed best practices for instrument development. It displayed good psychometric properties in pilot testing, as well as evidence of convergent and concurrent validity. Its brevity and simplicity allow for rapid completion by clinic patients and easy assessment of data by healthcare workers. In light of these considerations, the research team anticipates that the CST-HIV has the potential to meaningfully inform HIV care in Spain, and perhaps also in other countries with similar social, cultural, epidemiological and health system contexts. Methodologically rigorous studies are needed to assess how the use of the CST-HIV affects specific dimensions of the clinical experience such as patient-provider communication, clinical decision-making, and health and HRQoL outcomes.

Commonalities and differences can be observed when the CST-HIV is compared to two other short, broadly focused PROMS developed to support the clinical care of PLHIV: the Positive Outcomes PROM, developed in England and Ireland, and the Short-Form HIV Disability Questionnaire, developed in Canada. It is not known how differences among PLHIV and healthcare providers in Spain and these other settings might be reflected in differences across the CST-HIV and these other two instruments. Thus, an open question that should inform future research and practice in this area is whether one instrument or another might be a better "fit" with the self-defined needs of PLHIV and healthcare providers in other countries.

In sum, the CST-HIV is a promising new tool for improving healthcare for PLHIV in Spain. Its relevance for HIV care in other countries should be explored. Researchers must engage with policy-makers and affected communities to maximise the potential for PROMs of this nature to contribute to advancing the multidimensional health and HRQoL of PLHIV, consistent with the World Health Organization's vision of health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".

2. Resumen

Introducción

Casi 38 millones de personas vivían con VIH a finales del 2020, de los cuales se estima que el 73% estaban recibiendo terapia antirretroviral (TAR). El panorama del VIH ha cambiado enormemente desde que se introdujeron los primeros, altamente efectivos regímenes de TAR en 1996 y las personas con VIH que inician TAR en una etapa suficientemente temprana de la enfermedad tienen una esperanza de vida casi normal. Sin embargo, sus vidas son notablemente diferentes de alguna manera en comparación con las personas sin VIH. La prevalencia de multimorbilidad es mayor en personas con VIH que en la población general, con una amplia gama de enfermedades infecciosas y no infecciosas que contribuyen a la carga de multimorbilidad. Las personas con VIH reportan que se preocupan por la incertidumbre sobre el futuro y tienen altos niveles de depresión y ansiedad. Además, incluso entre las personas con VIH que han respondido bien al TAR, algunos estudios han documentado una peor calidad de vida relacionada con la salud (CVRS) en comparación con la población general. Las personas con VIH también reportan sentir una alta carga de síntomas, aislamiento social y múltiples formas de estigma relacionado con vivir con VIH.

Mejorar la salud y CVRS de personas con VIH en un contexto de alta captación de TAR es el objetivo final del grupo de estudios presentados en la siguiente tesis, la cual describe el desarrollo y pilotaje de una nueva medida de resultado reportado por el paciente (por sus siglas en inglés, PROM - patient-reported outcome measure) para su uso en la atención clínica del VIH en España. Este trabajo es oportuno debido a la necesidad apremiante de repensar el abordaje convencional de la atención del VIH en España y muchos otros países. A partir de mediados de la década de los 90, los proveedores de atención médica y expertos en salud pública han enfatizado la importancia de usar el TAR para reducir la viremia en personas con VIH, prestando menos atención a otros temas relacionados con la salud en esta población. Sin embargo, debido a la conciencia creciente sobre las altas cargas y los efectos de salud de estas otras cuestiones, ha quedado claro que los criterios convencionales para evaluar la efectividad de la atención del VIH en términos únicamente en resultados de carga viral y mortalidad relacionada con el VIH son insuficientes. Hay llamadas crecientes a reconocer la calidad de vida de las personas con VIH como una preocupación importante de atención médica por parte de investigadores, personas viviendo con VIH y otras partes interesadas en la comunidad del VIH. Este paradigma cambiante se refleja en la Estrategia Mundial sobre el Sida 2021-2026 del Programa Conjunto de las Naciones Unidas sobre el VIH/Sida (ONUSIDA), que aborda "optimizar la calidad de vida y el bienestar a lo largo del curso de la vida".

La integración de estos principios y estándares de atención médica centrados en las personas en la práctica clínica es una estrategia esencial para mejorar la CVRS de personas con VIH que están recibiendo cuidado. Un abordaje centrado en la persona conlleva prestar atención a las cuestiones relacionadas con la salud que son importantes para una persona viviendo con VIH en lugar de simplemente centrarse en cómo detener la progresión de la enfermedad del VIH. Debe haber comunicación efectiva entre pacientes y proveedores de atención médica para que las necesidades y preferencias de los pacientes informen de manera significativa sus interacciones con los sistemas de salud.

Varios hallazgos de investigación cuestionan si los proveedores de atención del VIH comprenden suficientemente las preocupaciones de sus pacientes. Varios estudios han documentado la falta de conocimiento de los proveedores de los síntomas clínicamente importantes en las poblaciones de pacientes con VIH y personas con VIH han reportado barreras de comunicación con sus proveedores. También hay evidencia de que los proveedores de atención del VIH y las personas con VIH pueden no estar de acuerdo sobre las prioridades de atención médica.

En el momento de esta escritura, varias partes interesadas habían publicado recomendaciones y guías con respecto a las necesidades relacionadas con la salud de las personas con VIH, más allá de la supresión viral, y el borrador de la estrategia del 2022-2030 de la Organización Mundial de la Salud (OMS) sobre el VIH llama a que los países "aborden las necesidades de atención crónica de los adultos y niños que viven con VIH". Se necesitan herramientas clínicas para apoyar a los proveedores de atención médica en la implementación de esta visión.

Los PROMs pueden contribuir importantemente en el siguiente capítulo de atención del VIH al proporcionar un mecanismo estructurado para que las personas con VIH puedan expresar directamente sus preocupaciones relacionadas con la salud a los proveedores de atención médica. Los PROMs pueden abordar una amplia gama de problemas relacionados con la salud y pueden administrarse a través de entrevistas, formularios de papel o dispositivos digitales, como tabletas de pantalla táctil. Históricamente, los PROMs han tenido un papel más prominente en la investigación que en la práctica clínica. En los últimos años, ha habido un interés creciente en el potencial de la contribución de los PROMs en la gestión clínica en diferentes campos de atención médica, en parte debido a una mayor conciencia de los principios de la atención médica centrada en las personas. Cuando los PROMs se utilizan de manera efectiva en la práctica clínica, los beneficios pueden incluir un mayor conocimiento delos problemas de salud por parte del proveedor, una mejor comunicación entre el proveedor y el paciente, una gestión más efectiva de los síntomas y mejora en los resultados de salud y CVRS.

En la actualidad existe una necesidad insatisfecha de PROMs cortas y ampliamente enfocadas que puedan dar a los proveedores de servicios de salud un medio conveniente para identificar los diferentes desafíos relacionados con la salud que comúnmente experimentan las personas que viven con VIH. El objetivo general del cuerpo de investigación presentado en esta tesis es diseñar y pilotar un instrumento de PROM que se pueda usar en la práctica clínica rutinaria para identificar problemas que socavan la CVRS de personas con VIH en España, lo que ayudará a los sistemas de salud al responder más efectivamente a las necesidades a largo plazo de esta población, más allá del TAR.

Métodos

La investigación presentada en esta tesis se basa en tres estudios que se presentan en cuatro artículos. El primer estudio fue una encuesta de políticas que recopiló datos de un experto en cada uno de los seis países europeos para investigar la capacidad del sistema de salud para monitorear los aspectos de la atención médica, como la salud mental y los servicios psicosociales. Los hallazgos están reportados en el *Artículo 1*. El segundo estudio utilizó un diseño de estudio ex post facto transversal observacional para validar la versión española del "WHOQoL-HIV-BREF", un PROM de CVRS específico para el VIH ampliamente utilizado, y para explorar la CVRS de personas con VIH de España. Los hallazgos están reportados en el *Artículo 2*. El tercer estudio se centró en el desarrollo del PROM "CST-VIH" de acuerdo con los procedimientos de desarrollo de instrumentos estándar. Los hallazgos de las dos primeras fases del proceso de estudio, una revisión de la literatura y una investigación cualitativa de las percepciones de personas con VIH y proveedores de atención médica sobre problemas que socavan el bienestar de personas con VIH en España, están reportados en el *Artículo 3*. Los hallazgos de las últimas fases, incluyendo un estudio piloto español que evalúa las propiedades psicométricas del nuevo instrumento, están reportados en el *Artículo 4*.

Resultados

El primer artículo se trata de una encuesta de políticas que investigó el monitoreo nacional de los problemas de atención del VIH en seis países europeos: Estonia, Italia, Holanda, Eslovenia, Suecia y Turquía. La encuesta se administró de abril a junio del 2018, con un experto seleccionado a propósito en cada país que proporciono información sobre la capacidad de monitoreo del sistema de salud en relación con temas como las comorbilidades, la CVRS, los servicios psicosociales y la discriminación relacionada con el VIH en entornos de atención médica. Según los encuestados, solo dos países (Eslovenia y Suecia) tenían la capacidad de monitorear los indicadores que abordan el cribado, diagnóstico y tratamiento de la ansiedad y depresión. Ninguno de los encuestados report el uso de indicadores a nivel nacional para monitorear la provisión de servicios psicosociales. Los encuestados de tres países (Holanda, Eslovenia y Suecia) indicaron que sus sistemas de monitoreo nacional tenían la capacidad para reportar sobre la CVRS de personas con VIH.

El segundo artículo informa sobre la validación del WHOQoL-HIV-BREF en una muestra representativa a nivel nacional de personas con VIH en España (n = 1,462) y la CVRS de esta población. Los datos se recopilaron entre octubre del 2016 y abril del 2017. Pruebas psicométricas demostraron que la versión española del instrumento tiene una construcción adecuada y una validez convergente y concurrente. Las mujeres que participaron en el estudio y los participantes heterosexuales tuvieron una peor CVRS en comparación con sus contrapartes, al igual que las personas de estrato socioeconómico bajo, las personas que habían estado viviendo con VIH durante un período de tiempo más largo y las personas mayores de 50 años.

El tercer artículo trata sobre todo el proceso de desarrollo de instrumentos CST-VIH, incluida la definición de dominios, el desarrollo de ítems potenciales, la evaluación experta de los ítems, los interrogatorios cognitivos con ocho personas con VIH y la validación del instrumento en una cohorte de 226 personas con VIH en España. Los ocho dominios elegidos para el instrumento piloto inicial fueron el estigma anticipado, la angustia emocional, la sexualidad, el apoyo social, la privación material, el sueño/fatiga, los problemas cognitivos y los síntomas físicos. Los hallazgos del piloto confirmaron la idoneidad de estos dominios, y llevaron a la selección de tres ítems por dominio entre los 40 elementos utilizados en el instrumento piloto. El instrumento resultante de 24 elementos cumplió con los estándares para el contenido, la cara, la construcción y la validez convergente y concurrente.

El cuarto artículo informa sobre los hallazgos de la revisión de la literatura y los hallazgos de las discusiones de los grupos de enfoque que informaron el desarrollo temprano del CST-VIH. La revisión de la literatura documentó la alta prevalencia de síntomas, como los problemas relacionados con el sueño, la fatiga y el dolor en las poblaciones de personas con VIH, y también identifico estudios que demostraron que la carga de síntomas y otros asuntos, como el apoyo social, la salud emocional y la seguridad material se asocian con la CVRS en personas con VIH. Un análisis de los datos de las discusiones de los grupos de enfoque, dos con proveedores de servicios de VIH (n = 8 por grupo) y dos con personas con VIH (n = 8 y n = 7), identificó una serie de categorías amplias de problemas que afectan la CVRS de personas con VIH. Las cuestiones más destacadas por ambas categorías de participantes de los grupos de enfoque fueron problemas sociales, incluido el estigma y la discriminación relacionados con el VIH, los problemas relacionados con el sueño, la fatiga, el dolor y la angustia emocional.

Discusión y conclusiones

Los resultados de esta tesis contribuyen a los esfuerzos en curso para reorientar la atención del VIH con el fin abordar la amplia gama de problemas físicos, emocionales y sociales que desafían a las personas que viven con VIH a largo plazo. El PROM desarrollado a través de esta investigación, el CST-VIH, demuestra una validez preliminar adecuada y actualmente está siendo validada más allá para fortalecer la evidencia que respalde su uso en la atención clínica rutinaria. Hasta donde sabemos, este es uno de los tres instrumentos concisos y validados, desarrollados específicamente para ayudar a los proveedores de atención del VIH en la identificación de una amplia gama de problemas relacionados con la salud que afectan al bienestar de las personas con VIH y el único instrumento de este tipo desarrollado en España.

El CST-VIH se desarrolló a través de un proceso metodológicamente riguroso que siguió de cerca las mejores prácticas para el desarrollo del instrumento. Este demostró buenas propiedades psicométricas en las pruebas piloto, así como validez convergente y concurrente. Su brevedad y simplicidad permiten la finalización rápida por pacientes en las clínicas y una fácil evaluación de los datos por parte de los trabajadores de la salud. A la luz de estas consideraciones, el equipo de investigación anticipa que el CST-VIH tiene el potencial de informar significativamente la atención del VIH en España y quizás también en otros países con contextos similares, epidemiológicos y de salud. Se necesitan estudios metodológicamente rigurosos para evaluar cómo el uso del CST-VIH afecta las dimensiones específicas de la experiencia clínica, como la comunicación entre el proveedor y el paciente, la toma de decisiones clínicas y los resultados de salud y CVRS.

Se pueden observar similitudes y diferencias cuando el CST-VIH se compara con otros dos PROMs concisos y ampliamente enfocados desarrollados para respaldar la atención clínica de personas con VIH: el PROM “Positive Outcomes” (“Resultados Positivos”), desarrollado en Inglaterra e Irlanda, y el “Short-Form HIV Disability Questionnaire” (“Cuestionario Corto de Discapacidad del VIH”), desarrollado en Canadá. Aún no se sabe cómo las diferencias entre las personas con VIH y los proveedores de atención médica en España y estos otros entornos pueden reflejarse en las diferencias en el CST-VIH y estos otros dos instrumentos.

Por lo tanto, una pregunta abierta que debe informar a futuras investigaciones y prácticas en esta área es si un instrumento u otro podría encajar mejor con las necesidades autodefinidas de las personas con VIH y los proveedores de atención médica en otros países.

En resumen, el CST-VIH es una nueva herramienta prometedora para mejorar la atención médica para las personas con VIH en España. Se debe explorar su relevancia dentro de la atención del VIH en otros países. Los investigadores deben interactuar con los responsables de la formulación de políticas y las comunidades afectadas para maximizar el potencial de los PROMs de este tipo, para contribuir a promover la salud multidimensional y CVRS de las personas con VIH, lo cual es consistente con la visión de la salud de la OMS como “un estado de completo bienestar físico, mental y social, y no solamente la ausencia de afecciones o enfermedades”.

3. Introduction

As the global HIV pandemic enters its fifth decade, there is growing recognition that the healthcare needs of people living with HIV (PLHIV) extend well beyond the need for antiretroviral therapy (ART). The face of HIV has changed greatly since the first highly effective ART regimens were introduced in 1996, and PLHIV who initiate ART at a sufficiently early disease stage have a near-normal life expectancy.[1] Yet their lives are markedly different in some ways from the lives of people without HIV. The prevalence of multimorbidity is higher in PLHIV than in the general population,[2] with a wide range of infectious and noninfectious conditions contributing to the multimorbidity burden.[3] PLHIV report being troubled by uncertainty about the future,[4,5] and have high levels of depression and anxiety.[6] Furthermore, even among PLHIV who have responded well to ART, some studies have documented poorer health-related quality of life (HRQoL) in comparison to that of the general population.[7–9]

The scale of the HIV pandemic suggests that these issues may be affecting large in-care populations worldwide. Almost 38 million people were living with HIV at the end of 2020, 73% of whom were estimated to be receiving antiretroviral therapy. New cases of HIV infection have been decreasing in recent years, but at a slow pace. An estimated 1.5 million people acquired HIV in 2020, a further indication that the long-term health-related needs of PLHIV will continue to require considerable health system resources well into the future.[10]

Improving the health and HRQoL of PLHIV in the context of high uptake of ART is the ultimate goal of the group of studies presented in the following thesis. As a preface to the studies, the first section of this chapter describes common burdensome health-related issues experienced by PLHIV. The second section explores how health systems might manage the long-term care of PLHIV more effectively through people-centred health services. The third section discusses the role of patient-reported outcome measures (PROMs) in people-centred health services and the need for new PROMs such as the one we have developed.

Burdensome health-related issues experienced by people living with HIV

A wide range of issues may negatively affect the HRQoL of PLHIV. The following overview focuses on issues that are relevant for PLHIV in high-income settings where ART is widely used, as is the case in Spain, where 85% of the country’s 150,000 PLHIV are taking ART.[11]

Comorbidities

PLHIV have a greater burden of non-HIV-related comorbidities than the general population, including infectious diseases, noncommunicable diseases, and psychiatric disorders. Studies have observed higher prevalence of hepatitis B virus, hepatitis C virus, lipid disorders, diabetes, and cardiovascular, kidney and bone disease among PLHIV in comparison to people without HIV.[2,3,12–14] For example, in a German claims database analysis that compared PLHIV to non-HIV-infected controls matched on the basis of age, gender and socioeconomic variables, PLHIV had significantly higher prevalence of hepatitis B virus (5.9% vs. 0.3%), hepatitis C virus (8.8% vs. 0.3%), cardiovascular disease (12.8% vs. 10.4%), chronic kidney disease (4.3% vs. 2.4%), and bone fractures due to osteoporosis (6.4% vs. 2.1%).[12] The excess multimorbidity burden in PLHIV is thought to be driven by multiple factors, including side-effects of ART and health-related behaviours such as smoking and drug use. Additionally, HIV may continue to damage the immune system even in the context of viral suppression.[15]

Psychiatric conditions contribute greatly to the multimorbidity burden in PLHIV and have complex health implications. PLHIV have much higher prevalence of depression, anxiety and post-traumatic stress disorder than the general population, and are at higher risk of dying from suicide.[6,16–18] In a 2014 systematic review, the estimated point prevalence for depression among PLHIV was 33%.[6] This contrasts with an estimated point prevalence of less than 5% in the general population.[19] Depression in PLHIV has been associated with missed HIV care appointments, antiretroviral nonadherence, virological failure, decreased social capital, increased sexual risk-taking and increased all-cause mortality.[20–24] Anxiety in PLHIV has been associated with missed HIV care appointments, hazardous alcohol consumption, greater use of emergency or urgent care facilities, and more overnight hospitalizations.[25,26]

Symptoms

Although the typical symptom profile for PLHIV who are taking ART has changed in some ways from the pre-ART and early ART eras, the symptom burden remains quite high.[27–30] Symptoms may be caused by HIV disease itself or by other factors such as HIV treatment or comorbid conditions.[27] A higher symptom burden has been associated with low ART adherence, viral rebound, poor self-reported health, poor HRQoL, and suicidal ideation.[31–36]

Pain, sleep-related problems and fatigue are among the symptoms most widely reported in PLHIV populations with high levels of viral suppression.[28,29,37–39] An analysis of the prevalence of pain in PLHIV in the POPPY study cohort in the United Kingdom and Ireland found that 67% of PLHIV (N=1,325) reported experiencing aches and pains in the previous month.[40] The POPPY study cohort also investigated three types of sleep disorders (insomnia, sleep apnea and restless legs syndrome) and found that 36% of PLHIV (N=321) had at least one of these disorders. Insomnia was the most common, and PLHIV were five times more likely to experience insomnia than were HIV-negative controls.[41] As in the general population, sleep problems and pain often co-occur in PLHIV.[42] Sleep problems also commonly co-occur with fatigue in PLHIV, although fatigue may also have causes unrelated to poor sleep quality.[43]

Gastrointestinal problems such as diarrhoea, nausea, vomiting and loss of appetite are also common among PLHIV. The use of newer ART regimens with better side-effect profiles has reduced the burden of gastrointestinal problems, but HIV itself damages the gastrointestinal tract and may account for the persistence of symptoms, even when ART treatment is effective.[30] Fat loss and fat accumulation, like gastrointestinal problems, are less common in the modern ART era but remain issues of concern. In a 2013–2014 cross-sectional study of the symptom burden in virally suppressed German PLHIV (N=698), 22% of study participants reported bothersome changes in body appearance.[37]

Sexuality

PLHIV have higher prevalence of sexual dysfunction than HIV-negative people, and also report lower levels of sexual satisfaction.[44–46] Depression has frequently been associated with sexual dysfunction in studies of PLHIV.[44] Common sexual difficulties among PLHIV include loss of libido, erectile dysfunction in men, and vaginal dryness and difficulty reaching orgasm in women.[46–48] PLHIV face notable challenges in relation to psychological and interpersonal dimensions of sexuality. Anxiety about transmitting HIV to potential sexual partners is common, as are concerns about disclosing one's HIV-positive status and being rejected by sexual partners.[45,47] HIV-related stigma and discrimination may greatly undermine sexual well-being.[44,45,49] In a study in the United Kingdom, 27% of gay men and 9% of heterosexual men living with HIV reported experiencing HIV-related sexual rejection.[50]

HIV-related stigma and discrimination

Despite longstanding efforts to challenge negative beliefs about HIV, it remains a highly stigmatised disease. The many forms of HIV-related stigma, including discriminatory actions, affect the health and well-being of PLHIV through multiple pathways. Studies have found that PLHIV who experienced HIV-related stigma were less likely to be adherent to ART or to access or use health and social services.[51] HIV-related stigma also has been associated with poorer physical health and higher risk of depression and anxiety among PLHIV.[51] HIV-related stigma may further affect PLHIV through indirect pathways such as loss of income resulting from workplace discrimination.[52] HIV-related stigma is associated with social isolation, which in turn is associated with poor health outcomes.[53–56] Numerous studies have shown HIV-related stigma to predict poor HRQoL outcomes among PLHIV.[57,58]

Social isolation

Social isolation appears to be common in PLHIV populations, and studies have documented higher prevalence of social isolation among PLHIV in comparison to their counterparts without HIV.[53,59,60] Factors contributing to social isolation in PLHIV include HIV-related stigma, physical limitations, self-consciousness about body fat changes, mental health challenges, material insecurity, and the deaths of social network members.[53,60–65] While social isolation is frequently highlighted as a challenge facing older PLHIV, at least one study has found it to be more prevalent in younger PLHIV in comparison to older PLHIV,[60] perhaps reflecting variations in the dynamics of social isolation across different cultures, settings and populations.

In the general population, social isolation predicts mortality and morbidity,[66] and there is some evidence that this trend prevails in PLHIV populations.[53] A 2020 longitudinal cohort of 936 Canadian PLHIV found a significant association between social isolation and all-cause mortality.[62] Current efforts to reduce social isolation in PLHIV may be inadequate: a 2017 survey of a nationally representative sample of PLHIV in England and Wales found that 21% of respondents expressed a need for help dealing with loneliness and isolation, and that three-quarters of these individuals characterized their need as unmet.[67]

The imperative to make health services for people living with HIV more people-centred

The ongoing high burden of multimorbidity, symptoms, and psychological and social stressors experienced by PLHIV, including those who are stable on ART, calls into question whether clinical HIV care has an overly narrow focus. From the mid-1990s onward, healthcare providers and public health experts have emphasised the importance of using ART to reduce viremia in PLHIV, while giving less attention to other health-related issues in this population. This approach has been reflected in and reinforced by key targets in the global HIV response, most notably the “90-90-90” target introduced by UNAIDS in 2014, calling for 90% of all people living with HIV to be diagnosed, 90% of those diagnosed to receive ART, and 90% of those receiving ART to be virally suppressed.[68] Although many countries did not meet the target by the designated deadline of 2020, efforts to do so resulted in great progress, and UNAIDS has established 2021–2025 targets that similarly envision performance levels of 95% at each of the three critical points in the treatment cascade.[69]

Meanwhile, as the success of ART has enabled more people to live for many years with controlled HIV, the complexity of the non-HIV-specific needs of PLHIV has become more apparent.[70,71] PLHIV ageing into the later decades of life must contend with ageing-associated health challenges, including common chronic comorbidities such as cardiovascular disease and osteoporosis. The prevention of comorbidities and management of multimorbidity in PLHIV may be complicated by issues such as long-term effects of ART, interactions between ART and other types of medications, high prevalence of behavioural risk factors for some chronic diseases, and disparities relating to socioeconomic status, sexual orientation, and other social determinants of health.[72] In this context, conventional criteria for assessing the effectiveness of HIV care in terms of viral load outcomes and HIV-related mortality are insufficient.[73–75] There are growing calls by researchers, PLHIV and other stakeholders for the HIV community to recognise the quality of life of PLHIV as a major healthcare concern.[76–79] This changing paradigm is reflected in the UNAIDS Global AIDS Strategy for 2021–2026, which addresses “optimizing quality of life and well-being across the life-course”.[69]

There is a strong rationale for healthcare providers to seek to ameliorate problems that undermine the HRQoL of PLHIV. A 2008 observational cohort study reported that poor HRQoL predicted all-cause hospitalisation in PLHIV,[80] while other research has found HRQoL to predict survival in PLHIV.[81] Similar findings have been reported in other patient populations such as elderly outpatient primary care patients, people undergoing hemodialysis, and people with cancer, type 2 diabetes, and chronic obstructive pulmonary disorder.[82–86] While evidence of this nature points to the potential health benefits of addressing modifiable determinants of HRQoL, it is also important to recognise the intrinsic value of HRQoL itself. The Constitution of the World Health Organization, adopted in 1946, famously defines health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”.[87] From this perspective, it is not sufficient for HIV service delivery to evolve in ways that merely promote better HIV-specific outcomes in PLHIV. Optimizing HRQoL – which is typically measured using validated instruments that reflect WHO’s broad definition of health[88] – must also be a key objective.

Integrating people-centred healthcare principles and standards into clinical practice is an essential strategy for improving the HRQoL of PLHIV who are engaged in care. The World Health Organization defines people-centred care as “an approach to care that consciously adopts individuals’, carers’, families’ and communities’ perspectives as participants in, and beneficiaries of, trusted health systems that are organised around the comprehensive needs of people rather than individual diseases, and respect social preferences”.[89] The provision of people-centred care has multiple dimensions, such as engaging patients in shared decision-making with healthcare providers, simplifying patient navigation of care pathways, offering services at times that are convenient to patients, and being respectful of patients' cultural and personal values.[90,91]

In the context of HIV care, taking a people-centred approach entails giving attention to the health-related issues that matter to individual PLHIV rather than merely focusing on how to halt HIV disease progression. Hence, issues as disparate as insomnia, sexual dysfunction and HIV-related stigma all may warrant attention in clinic visits, and providers of people-centred HIV care should be prepared to offer screening, referral and health education about these and other health-related challenges that are widespread in PLHIV populations. There must be effective communication between patients and healthcare providers in order for patients' needs and preferences to meaningfully inform their interactions with health systems. A hallmark of people-centred care is that patients and their families feel listened to and understood.[90]

Various research findings call into question whether HIV care providers sufficiently understand their patients' concerns. In a US study cohort of 751 PLHIV, nine self-reported symptoms were significantly associated with clinical outcomes, and yet the study participants' healthcare providers had low agreement beyond chance about the presence of any of the nine symptoms in their patients.[92] Another US study found that providers frequently did not identify depressive symptoms that were self-reported by PLHIV, and also were unaware of many self-reported cases of current drug use.[93] PLHIV may encounter difficulties communicating with healthcare providers. Only 35% of PLHIV in a Portuguese study population reported having no communication barriers with their healthcare providers.[94] Patients' discomfort in discussing sensitive personal information is likely to contribute to communication challenges, as reflected in research suggesting that electronic surveys elicit more accurate self-reporting in comparison to face-to-face interviews when people are asked questions about their sexual history or their engagement in drug use.[95,96] Furthermore, patients and healthcare providers may have discrepant priorities. A study in which both PLHIV and their healthcare providers were asked to rank patient healthcare priorities found disagreement about the importance of issues such as fatigue, substance use and HIV stigma.[97] A large qualitative study in the United Kingdom and Ireland found that HIV professionals preferred to focus clinical consultations on HIV treatment and physical outcomes while giving less attention to patients' other concerns, including psychological and social concerns.[64]

The policy environment in which healthcare providers are working has the potential to greatly influence how clinical care is delivered. Perhaps the most prominent example of this in the HIV field is the ubiquity of the UNAIDS "90-90-90" testing and treatment targets from 2014 to 2020, and the accompanying efforts by healthcare providers worldwide to address barriers to viral suppression such as poor adherence to ART and disengagement from clinical care.[98,99] At the time of this writing, various stakeholders had published recommendations and guidance regarding the health-related needs of PLHIV beyond viral suppression,[73,75,77,79,100] and the World Health Organization's draft 2022–2030 strategy on HIV calls on countries to "address chronic care needs of adults and children living with HIV".[101] A more specific global policy framework relating to this body of concerns appears to be lacking. Nonetheless, some national health systems have begun to emphasise quality-of-life dimensions of HIV care.[102,103] Clinical tools are needed to support healthcare providers in implementing this vision.

The role of patient-reported outcome measures in clinical care

Patient-reported outcome measures provide a mechanism for PLHIV to directly share their health-related concerns with their healthcare providers. One widely cited source defines a patient-reported outcome as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else".[104] In this study, a patient-reported outcome *measure* is understood to be an instrument that is used to collect patient-reported outcome data.

PROMs typically are formulated as questionnaires with items that have fixed response options. PROMs may be administered by clinical or non-clinical personnel through multiple channels including interviews, paper-based forms, and digital devices such as touch-screen tablets. Some PROMs are suitable for use across various patient populations to assess issues such as sleep quality, pain, alcohol consumption, self-efficacy, social support, and HRQoL. Other PROMs have been developed to elicit information about these and other issues from patients in particular healthcare fields such as oncology, mental health, diabetes and chronic kidney disease.[105] A 2017 review of HIV-specific PROMS identified 117 validated instruments, which the authors grouped into 12 categories: HRQoL, healthcare-related views and experiences, psychological challenges, symptoms, psychological resources, HIV self-management, HIV-related stigma, body appearance, disability, social support, and sexual and reproductive health.[106]

Historically, PROMs have had a more prominent role in research than in clinical practice. In recent years, there has been increasing interest in the potential for PROMs to contribute to clinical management across different healthcare fields, in part because of greater awareness of the principles of people-centred healthcare.[107–110] Models for integrating PROMs into clinical practice often call for one or more PROM instruments to be administered to a patient preceding the consultation, with responses then made available for healthcare providers to consider in the course of attending to the patient.

The question of how the use of PROMs may improve healthcare delivery processes and patient outcomes has been addressed in numerous studies, with a wide range of findings reported. A 2021 Cochrane Systematic Review identified 116 randomised studies that examined the impact of providing feedback from PROMs to healthcare providers, patients or both groups.[111] The studies were conducted in the context of care for diverse conditions such as cancer, epilepsy, rheumatoid arthritis, mental health conditions, diabetes and chronic heart failure, as well as primary healthcare and emergency care. A series of meta-analyses of specific intervention outcome measures found the strongest evidence of impact for diagnosis and notation (moderate improvements, 21 studies randomising 7,223 patients), patient-provider communication (moderate improvements, 5 studies randomising 658 patients), disease control (small improvements, 14 studies randomising 2,806 patients), and quality of life (small improvements, 11 studies randomising 2,687 patients). For other intervention outcome measures such as referrals, hospital admissions, social functioning, pain, fatigue, and physical and mental functioning, either the use of PROMs was associated with little or no effect or else the evidence was of insufficient quality to draw conclusions. The review authors expressed the opinion that there is adequate evidence to recommend the use of PROMs in clinical practice, but noted that the impact of PROMs is currently difficult to assess because of shortcomings in the evidence base. Similarly, a 2020 systematic review of the impact of PROMs use in cancer care presented encouraging findings but called attention to the need for better evidence.[110] Many of the 22 studies that met review criteria lacked sufficient power to detect significant differences in outcomes of interest. Some positive associations were observed between PROMs feedback and patient-provider communication, symptom control, and health-related quality of life.

Although there appears to be interest in the use of PROMs in HIV clinical care, little evidence has been published specifically regarding the impact of PROMs use on healthcare delivery or on health outcomes in PLHIV patient populations. There were no studies from the HIV field among the 116 studies that met review criteria for the aforementioned Cochrane Systematic Review, which presented findings from literature searches conducted in October 2020.[111] A non-peer-reviewed 2020 evidence synthesis addressing the impact of administering PROMs in HIV clinical care drew favorable conclusions about the potential benefits of PROMs use, but relied heavily on evidence from patient populations with other conditions, particularly those with cancer, to supplement the scant HIV-specific evidence.[112]

According to the evidence synthesis, a small number of studies conducted in the HIV field demonstrate that PROMs may increase provider awareness of symptoms and patient-provider communication.[112] There are also at least two studies providing evidence of a positive impact on care delivery. Crane *et al* found that the introduction of PROMs data collection into routine HIV care was associated with a significant increase in provider action (discussion, prescription or referral) in response to inadequate adherence. Furthermore, there was also a significant increase in provider action to address depression.[113] Jabour *et al* compared a PLHIV patient cohort whose substance use and mental health screening results were shared with HIV care providers to a historic control cohort from the same HIV clinic population. They found that the sharing of results was associated with a significantly higher proportion of patients receiving action plans from providers to address substance use and mental health issues.[114]

Researchers assessing the feasibility and acceptability of using PROMs in clinical practice have strongly cautioned that the collection of PROM data should not disrupt the workflow of the clinic or impose a significant time burden on healthcare providers or patients.[109,112,115] These requirements argue against administering a series of lengthy PROMs that discretely address different issues such as symptoms, psychological challenges and social support. In HIV care, there is currently an unmet need for short broadly focused PROMs that can give providers a convenient means of identifying the disparate health-related issues that commonly undermine the well-being of PLHIV. Researchers have reported on the development of two such instruments in recent years, with one informed by qualitative research in the United Kingdom and Ireland, and the other informed by qualitative research in Canada.[116,117] It is not known to what extent these instruments capture the health-related concerns of PLHIV in countries with different social, cultural, epidemiological and health system dynamics.

4. Hypotheses

The hypotheses of this thesis are as follows:

1. The high burden of physical and mental health issues and other challenges to the well-being of PLHIV in settings with high ART coverage are not being sufficiently addressed by health systems.
2. Healthcare providers may have opportunities to deliver more effective care and help PLHIV achieve better health and HRQoL outcomes if they have more information about specific burdensome issues experienced by individual patients.
3. Patient-reported outcome measures can facilitate communication between healthcare providers and patients, and their use may potentially contribute to improving health and HRQoL outcomes.
4. The development of short, broadly focused PROMs for use in HIV clinical care may assist healthcare providers and health systems in broadening the focus of HIV care and addressing patients’ needs in a more people-centred manner.

5. Objectives

General objective

The general objective of the body of research presented in this thesis is to design and pilot a patient-reported outcome measure (PROM) that can be used in routine clinical practice to identify diverse issues undermining the health-related quality of life of PLHIV in Spain, thus aiding health systems in responding more effectively to the long-term needs of this population beyond antiretroviral therapy.

Specific objectives

This thesis has the following additional specific objectives:

1. Explore the extent to which European health systems are prepared to monitor the broader health-related needs and HRQoL of PLHIV.
2. Use a validated Spanish version of WHOQOL-HIV-BREF to identify ways in which the HRQoL of Spanish PLHIV is compromised.
3. Gather and analyse qualitative data to determine which health-related issues are perceived to be the most burdensome by PLHIV and healthcare providers in Spain.
4. Define the domains of the novel HIV clinic screening tool (CST-HIV) and develop items for the pilot version of this PROM.
5. Conduct a pilot study to assess the construct and criterion validity and psychometric properties of the CST-HIV.

6. Materials and methods and results

Research setting

The first study was conducted in six European countries with highly varying HIV epidemics: Estonia, Italy, the Netherlands, Slovenia, Sweden and Turkey (Table 1). The second, third and fourth studies were conducted in Spain, which has an adult (aged 15-49) HIV prevalence rate of 0.4% and an estimated adult HIV population of 150,000.[11] More than four-fifths of adult PLHIV in Spain are men, the majority of them men who have sex with men.[11] There were 2,698 new cases of HIV infection reported in Spain in 2019, with people aged 40 and older accounting for more than one-third of cases.[118] An estimated 85% of PLHIV in Spain are taking ART, and an estimated 77% of PLHIV are virally suppressed.[119] In keeping with the general trend in countries with high ART coverage, people who have had their HIV diagnosis for 15 years or longer comprise an increasingly large proportion of the PLHIV population in Spain. Almost half of PLHIV who engaged with the national health system in 2019 were in this demographic category.[120] Among the full 2019 national health system cohort, 68% of PLHIV described their health as good or very good, while 13% described their health as bad or very bad.

Table 1. HIV epidemiology in study countries (Article 1)

	Estonia	**Italy**	**The Netherlands**	**Slovenia**	**Sweden**	**Turkey**
Estimated number of adults (aged 15 and older) living with HIV, 2020[a]	7,100	140,000	24,000	810	NA	NA
Estimated adult HIV prevalence (aged 15 and older), 2020 (%)[a]	0.7	0.3	0.2	0	NA	NA
Estimated % people living with HIV who are taking antiretroviral therapy, 2020[b]	65	90	85	80	89	NA
Estimated % of people living with HIV who are virally suppressed, 2020[b]	NA	78	82	77	86	NA
New HIV diagnoses in 2019[c]	178	2,531	563	34	449	3,229
Most common known transmission route for new HIV infections, 2019 (%)[c]	HS (44)	HS (42)	MSM (59)	MSM (59)	HS (45)	NA

a. UNAIDS[11]
b. European Centre for Disease Prevention and Control[119]
c. European Centre for Disease Prevention and Control/WHO Regional Office for Europe[121]
HS = heterosexual sex, MSM = sex between men who have sex with men, NA = not available.

ARTICLE 1

Ability to monitor national responses to the HIV epidemic 'beyond viral suppression': findings from six European countries

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This article addresses specific objective 1: *Explore the extent to which European health systems are prepared to monitor the broader health-related needs and HRQoL of PLHIV.*

Resumen

Objetivo: Dado que cada vez más personas que viven con el VIH envejecen hasta sus 50 años y más en entornos donde el tratamiento antirretroviral está ampliamente disponible, las comorbilidades no relacionadas con el con el sida y la calidad de vida relacionada con la salud (CVRS) se están convirtiendo en grandes desafíos. Se necesita información sobre si los programas nacionales de seguimiento del VIH han evolucionado para reflejar el enfoque cambiante de la atención del VIH.

Métodos: Creamos una encuesta en inglés de 56 artículos para evaluar si los sistemas de salud informan sobre temas comunes relacionados con la salud para las personas con VIH, incluidas las comorbilidades de salud física y mental, la CVRS, las necesidades psicosociales y los deseos de fertilidad. Un experto se identificó por muestreo intencional en cada uno de los seis países (Estonia, Italia, Países Bajos, Eslovenia, Suecia y Turquía) y se le pidió que participara en la encuesta.

Resultados: Tres encuestados informaron de que los actuales sistemas de seguimiento en sus países no controlan ninguno de los cuatro aspectos especificados de 10 comorbilidades, incluyendo la pérdida ósea, las enfermedades cardiovasculares y los trastornos neurocognitivos. Dos encuestados declararon que sus países potencialmente pueden informar sobre las principales causas de la admisión hospitalaria entre personas con VIH, y cinco en los principales casos de muerte. En tres países, los encuestados informaron que había la capacidad de informar sobre el CVRS de personas con VIH. En dos países, los encuestados proporcionaron datos sobre el porcentaje de personas con VIH a las que se les denegaron los servicios de salud por su condición de seropositivas en los últimos 12 meses.

Conclusiones: Este estudio identificó áreas para potenciales mejoras de monitoreo del VIH en seis países europeos en relación con las comorbilidades, la CVRS, la discriminación dentro de

los sistemas de salud y otros temas asociados con la naturaleza cambiante de la epidemia del VIH. También indicó que algunos países actualmente monitorean o tienen la capacidad de monitorear algunos de estos problemas. Hay oportunidades para los sistemas de información de salud en los países europeos para ampliar el alcance de su monitoreo del VIH para apoyar la toma de decisiones sobre cómo se pueden satisfacer las necesidades de las personas que viven con el VIH.

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Ability to Monitor National Responses to the HIV Epidemic "Beyond Viral Suppression": Findings From Six European Countries

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Objective: With more people living with HIV (PLHIV) ageing into their 50s and beyond in settings where antiretroviral therapy is widely available, non-AIDS comorbidities and health-related quality of life (HRQoL) are becoming major challenges. Information is needed about whether national HIV monitoring programmes have evolved to reflect the changing focus of HIV care.

Methods: We created a 56-item English-language survey to assess whether health systems report on common health-related issues for people with HIV including physical and mental health comorbidities, HRQoL, psychosocial needs, and fertility desires. One expert was identified via purposive sampling in each of six countries (Estonia, Italy, the Netherlands, Slovenia, Sweden, and Turkey) and was asked to participate in the survey.

Results: Three respondents reported that the current monitoring systems in their countries do not monitor any of four specified aspects of 10 comorbidities including bone loss, cardiovascular disease, and neurocognitive disorders. Two respondents stated that their countries potentially can report on leading causes of hospital admission among PLHIV, and five on leading cases of death. In three countries, respondents reported that there was the ability to report on the HRQoL of PLHIV. In two countries, respondents provided data on the percentage of PLHIV denied health services because of HIV status in the past 12 months.

Conclusions: This study identified areas for potential HIV monitoring improvements in six European countries in relation to comorbidities, HRQoL, discrimination within health systems, and other issues associated with the changing nature of the HIV epidemic.

It also indicated that some countries either currently monitor or have the ability to monitor some of these issues. There are opportunities for health information systems in European countries to expand the scope of their HIV monitoring in order to support decision-making about how the long-term health-related needs of PLHIV can best be met.

Keywords: comorbidity, Europe, health-related quality of life, HIV, indicator, monitoring

INTRODUCTION

Effective health policy-making and health system management require up-to-date information about people's health-related needs and about health system performance in response to those needs (1). Furthermore, the public reporting of such information promotes accountability by enabling stakeholders to assess the extent to which governments are meeting their health-related obligations (2). In the HIV field, many national governments participate in regional and global monitoring initiatives that require standardised reporting on selected indicators while also collecting data on additional indicators for national monitoring purposes. Decisions about which indicators to include in monitoring can greatly shape national HIV responses since evidence of the need for specific services and commodities can be a major factor in determining how health system resources are allocated.

The highly effective antiretroviral therapy (ART) regimens introduced in the late 1990s have transformed HIV into a manageable long-term condition in the sense that the life expectancy of people who initiate ART at an early stage of infection is close to that of the general population (3). However, as more people living with HIV (PLHIV) age into their 50s and beyond, additional threats to their health and well-being are emerging (4, 5). For multiple reasons, including HIV-mediated chronic inflammation as well as lifestyle factors, PLHIV have higher levels of multimorbidity than the general population (6–8). The disease burden associated with comorbidities is an increasingly prominent concern in HIV clinical care in settings where ART is widely available. A 2018 review found that PLHIV are twice as likely as HIV-negative people to develop cardiovascular disease, and that the global burden of HIV-associated cardiovascular disease has increased three-fold from 1990 to 2015 (9). PLHIV likewise have a higher prevalence of depression, which is underdiagnosed in this population (10). Common causes of hospitalisation among PLHIV in Europe include cardiovascular, respiratory, renal, liver, and psychiatric conditions (11).

In 2014, UNAIDS called for international action on an ambitious three-part target: by 2020, 90% of PLHIV were to know their HIV status, 90% of those diagnosed were to be receiving ART, and 90% of those receiving ART were to be virally suppressed (12). The "90-90-90" target has spurred many countries to concentrate resources on increasing diagnosis of HIV and reducing the proportions of diagnosed individuals who do not initiate treatment and do not achieve viral suppression. Meanwhile, there is a dearth of high-level policy guidance addressing what else countries should strive to achieve with regard to the growing number of PLHIV who are likely to live for many years into the future. A "fourth 90" target addressing the health-related quality of life (HRQoL) of PLHIV has been proposed [**Figure 1**; (5, 13)], but no consensus has emerged regarding how HRQoL should be defined in this context or how progress toward such a target should be measured.

European countries are experiencing the changing HIV care paradigm ahead of many other countries, and European health systems have the opportunity to set an instructive example by adapting their HIV services to reflect a model of care that is suitable for long-term conditions. However, little is known about whether national HIV monitoring programmes in Europe have evolved in accordance with changing needs. Without the right information, health systems will be limited in their efforts to meet new HIV-related health challenges. This study assesses the ability of health systems in six European countries to report on indicators that can speak to the health and psychosocial needs of people who are living with HIV on a long-term basis.

METHODS

Study Instrument

We identified common health-related issues for people with controlled HIV using an iterative process of desk research and consultation with an expert panel. For the literature review, we used PubMed to identify relevant English-language publications, using the term "HIV" in combination with terms such as "comorbidity," "Europe," "epidemiology," and "health-related quality of life." We prioritised review articles and large longitudinal cohort studies published after 2010 but did not exclude other sources. We also examined relevant clinical guidelines such as those published by the European AIDS Clinical Society as well as key gray literature sources that were located through internet searches. The expert panel members who advised on the selection of relevant health-related issues to be addressed in the study included European researchers, clinicians, epidemiologists, policymakers, industry representatives, and civil society stakeholders including PLHIV.

We created a 56-item English-language survey to investigate the readiness of national health systems to report on the chosen health-related issues as part of their routine HIV monitoring (**Supplementary File**). The survey was organised into seven thematic sections: HIV clinical management, comorbidities, health-related quality of life, psychosocial services, discrimination within health systems, preconception

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Abbreviations: ART, antiretroviral therapy; ECDC, European Centre for Disease Prevention and Control; HRQoL, health-related quality of life; NCDs, non-communicable diseases; PLHIV, people living with HIV; WHO, World Health Organization.

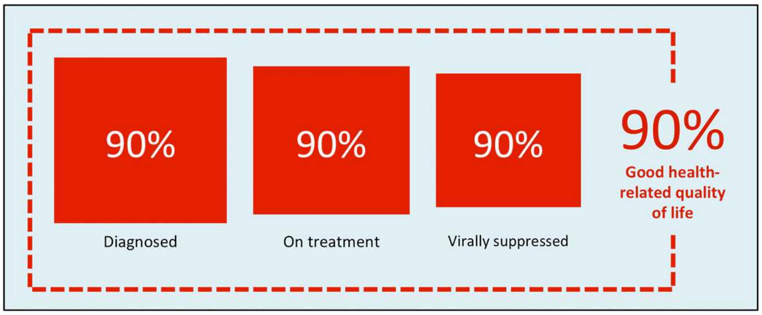

FIGURE 1 | A proposed "fourth 90" target for health-related quality of life [source: Safreed-Harmon et al. (13)].

planning, and general issues. A number of survey items asked about specific indicators in these areas, instructing respondents to characterise national reporting on these issues by choosing one of four possible responses: (a) national HIV monitoring does include reporting on such an indicator; (b) national HIV monitoring systems collect data that would allow for reporting on such an indicator; (c) national HIV monitoring systems could be easily modified to collect data that would allow for reporting on such an indicator; or (d) national HIV monitoring systems could not be easily modified to collect data that would allow for reporting on such an indicator. In order to keep the survey short enough for respondents to be willing to complete all items, we largely restricted the content to questions such as these about reporting capacity rather than about the actual data being reported. However, some items requested data, e.g., respondents were asked to report leading causes of hospital admission and death among PLHIV and to report the percentage of PLHIV denied health services because of their HIV status.

The survey underwent multiple rounds of revision in response to input from co-authors regarding the topics addressed as well as the structure of the survey questions. Four co-authors reviewed it for clarity and ease of navigation before it was finalised.

Study Sample

The study group's nine members, who include experts in monitoring, policy, and health system responses to HIV in Europe, were consulted regarding the selection of study countries. The objective was to construct a geographically diverse sample that also included countries with diverse health systems and different levels of robustness in their national HIV monitoring activities. Through this process, Estonia, Italy, the Netherlands, Slovenia, Sweden, and Turkey were selected as study countries. We then identified one expert to serve as the respondent in each country via purposive sampling, drawing on multiple co-authors' networks of contacts in the countries of interest to select this person. The objective was to choose the respondents with the most comprehensive knowledge of their countries' national HIV monitoring mechanisms and resources. There were no other eligibility criteria, and the experts identified included both individuals working directly for government agencies as well as individuals working closely with those agencies. These experts were encouraged to collaborate with other experts in their country to present a comprehensive response.

Data Collection and Analysis

The survey was administered from 20 April to 30 June 2018 using a Microsoft Word survey document. After data-cleaning, we compiled findings in Microsoft Excel and performed descriptive analyses. For reporting purposes, findings were organised into two domains: (1) ability to report on indicators of interest; and (2) data for selected indicators. In the first domain, a country was considered to be able to report on a specified indicator if the respondent reported that either: (a) national HIV monitoring does include reporting on such an indicator; (b) national HIV monitoring systems collect data that would allow for reporting on such an indicator; or (c) national HIV monitoring systems could be easily modified to collect data that would allow for reporting on such an indicator. We classified a country as not able to report if the respondent reported that national HIV monitoring systems were not currently able and could not be easily modified to collect data that would allow for reporting on such an indicator. Findings relating to comorbidities, health-related quality of life, psychosocial services, discrimination within health systems, and fertility desires are presented in terms of the two domains previously named: reporting ability and data for selected indicators.

RESULTS

Participating Study Countries

All six national monitoring experts who were approached about the survey completed it for a 100% response rate. **Table 1** describes the HIV epidemiology of the countries included.

Reporting Ability

Regarding ability to report on comorbidities, respondents in three countries (Estonia, Italy, and Turkey) reported that the countries could not monitor any of the four specified aspects (testing/screening offer, uptake, diagnosis, or treatment) of 12 of the 17 comorbidities (**Table 2**). The comorbidities reported to be most comprehensively monitored by study countries were drug dependence, hepatitis B virus, hepatitis C virus, and tuberculosis. The comorbidities reported to be least comprehensively monitored were anxiety, chronic pain syndrome and depression, all of which could only

TABLE 1 | HIV epidemiology in study countries.

	Estonia	Italy	The Netherlands	Slovenia	Sweden	Turkey
European area[a]	East	West	West	Centre	West	Centre
Estimated number of people living with HIV	11,000[b]	127,000[b]	22,900[b]	970[c]	7,700[b]	Unknown
Antiretroviral therapy coverage among people diagnosed with HIV[b]	40%	88%	88%	91%	95%	Unknown
New HIV diagnoses in 2016[a]	229	3,451	745	58	429	2,438

[a] *European Centre for Disease Prevention and Control/WHO Regional Office for Europe (14).*
[b] *European Centre for Disease Prevention and Control (15).*
[c] *UNAIDS (16).*

TABLE 2 | Reported ability of six* European countries to report on indicators for comorbidity screening/testing, diagnosis and treatment in PLHIV.

	Indicators addressing whether PLHIV are offered screening/testing for specified comorbidities	**Indicators addressing whether PLHIV are screened/tested for specified comorbidities**	**Indicators addressing whether PLHIV are diagnosed with specified comorbidities**	**Indicators addressing whether PLHIV are treated for specified comorbidities**
Alcohol dependence	SVN SWE	SVN SWE	NLD SVN SWE	SVN SWE
Anxiety	SVN SWE	SVN SWE	SVN SWE	SVN SWE
Bone loss	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE
Cardiovascular disease	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE
Chronic pain syndrome	SVN SWE	SVN SWE	SVN SWE	SVN SWE
Depression	SVN SWE	SVN SWE	SVN SWE	SVN SWE
Drug dependence	EST SVN SWE	EST SVN SWE	EST ITA NLD SVN SWE	EST SVN SWE
Hepatitis B virus	EST SVN SWE NLD	EST NLD SVN SWE	EST NLD SVN SWE	NLD SVN SWE
Hepatitis C virus	EST NLD SVN SWE	EST NLD SVN SWE	EST NLD SVN SWE	NLD SVN SWE
Liver disease other than chronic viral hepatitis	SVN SWE	NLD SVN SWE	NLD SVN SWE	SVN SWE
Neurocognitive disorders	SVN SWE	NLD SVN SWE	NLD SVN SWE	SVN SWE
Non-AIDS malignancies	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE
Renal disease	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE
Respiratory disease	SVN SWE	NLD SVN SWE	NLD SVN SWE	SVN SWE
Sexual dysfunction	SVN SWE	NLD SVN SWE	NLD SVN SWE	NLD SVN SWE
Sexually transmitted infections	EST SVN SWE	NLD SVN SWE	NLD SVN SWE	SVN SWE
Tuberculosis	EST NLD SVN SWE	EST ITA NLD SVN SWE	EST ITA NLD SVN SWE	EST ITA NLD SVN SWE

EST, Estonia; ITA, Italy; NLD, The Netherlands; SVN, Slovenia; SWE, Sweden.
* *Turkey was not able to monitor any aspect of any of the comorbidities listed.*

be monitored by Slovenia and Sweden. There were no comorbidities that all six countries were reported to be able to monitor.

According to respondents, two countries had the ability to report on leading causes of hospital admission among PLHIV, while five had the ability to report on leading causes of death (**Table 3**). Respondents indicated that three countries had the ability to report on the health-related quality of life of PLHIV. Two countries were reported to be able to make modifications to report on the percentage of PLHIV who want to have children, and one, to be able to make modifications to report on the percentage of PLHIV who have an unmet need for preconception planning services.

Respondents were asked to list up to three indicators used at the national level for monitoring psychosocial service provision (e.g., housing, employment, social support), but none of the respondents reported any psychosocial indicators. Three respondents indicated in comments that no such indicators were used at the national level in their countries. The respondent from Sweden noted that while there was not regular data collection for psychosocial indicators, the Public Health Agency of Sweden had conducted a survey on this

TABLE 3 | Reported ability of six European countries to report on causes of hospital admission, causes of death, health-related quality of life, and fertility desires in PLHIV (*N* = 6 countries).

	Currently reported			**Data available**		**Could be modified**			**Could not be modified**			
Leading causes of hospital admission among PLHIV				NLD			SWE			EST TUR	ITA	SVN
Leading causes of death among PLHIV	NLD	SVN					EST	ITA	SWE	TUR		
Health-related quality of life among PLHIV	SWE						NLD	SVN		EST	ITA	TUR
Percentage of PLHIV who want to have children							SVN	SWE		EST TUR	ITA	NLD
Percentage of PLHIV who have an unmet need for preconception planning services							SVN			EST TUR	ITA SWE	NLD

Currently reported = National HIV monitoring includes reporting on such an indicator.
Data available = National HIV monitoring systems collect data that would allow for reporting on such an indicator.
Could be modified = National HIV monitoring systems could be easily modified to collect data that would allow for reporting on such an indicator.
Could not be modified = National HIV monitoring systems could not be easily modified to collect data that would allow for reporting on such an indicator.
EST, Estonia; ITA, Italy; NLD, The Netherlands; SVN, Slovenia; SWE, Sweden; TUR, Turkey.

issue and planned to repeat the survey approximately every five years.

Indicator Data

Respondent reporting on the five leading causes of hospital admission and five leading causes of death among PLHIV are shown in **Table 4**. Respondents in five countries could not report on leading causes of hospital admission, and information for the sixth country, Sweden, reflected the respondent's estimates. In comments from two countries, respondents indicated that data for reporting on this indicator existed: Italy was said to have a national hospital admissions database from which HIV records could be extracted, and the Netherlands was said to have uncoded free text collected in HIV surveillance reports. Respondents in a larger number of countries were able to report data on leading causes of death.

Respondents in two countries provided data on the percentage of PLHIV who had been denied health services because of their HIV status in the past 12 months; respondents from the remaining four countries were unable to do so (**Table 5**).

DISCUSSION

This study in six European countries assessed aspects of health system monitoring that are considered relevant to the care of PLHIV on a long-term basis. Based on input from respondents who are regarded as top HIV monitoring experts in their countries, it found that a number of countries cannot report on indicators for many major comorbidities in PLHIV populations, including highly prevalent comorbidities such as cardiovascular disease and depression. It also identified large monitoring gaps in relation to health-related quality of life, fertility desires, psychosocial services, and discrimination within health systems.

There are multiple processes for monitoring progress against HIV in Europe, with most countries reporting to UNAIDS, the World Health Organization (WHO) and the European Centre for Disease Prevention and Control (ECDC) in addition to conducting further national-level monitoring to inform in-country decision-making. UNAIDS and ECDC reporting influence country-level monitoring activities in Europe, while at the same time, decisions about which indicators to include in multi-country monitoring activities are influenced by what is known about countries' reporting ability. The reported lack of ability of study countries to monitor some issues addressed in our survey suggests a need for country-level stakeholders to re-assess their HIV monitoring priorities as well as a need for regional stakeholders to provide technical support in this area. The reported lack of ability to monitor many comorbidities is particularly disquieting in light of modelling research that indicates that the large comorbidity burden among PLHIV will continue to increase in the coming years (18).

In the interest of capturing as much information as possible, we sought to learn about the monitoring of each comorbidity included in our study in four domains spanning the diagnosis and treatment spectrum: whether PLHIV are offered screening/testing, whether they are screened/tested, whether they are diagnosed and whether they are treated. Three or more countries had the ability to report on all four domains for some comorbidities. While this is a welcome finding, the methodological decision to ask survey respondents to report in terms of the four domains is not meant to imply that health systems should be asked to monitor all four of them. Where health systems do not currently have robust reporting processes in place, a better use of resources would be to focus on collecting data at one stage of the diagnostic process for each comorbidity of interest, e.g., whether PLHIV are screened for cardiovascular disease and whether PLHIV who have been diagnosed with drug dependence receive treatment.

The health-related quality of life of PLHIV has long been a matter of interest for researchers (19), practitioners and community stakeholders, but there is little published information about how this issue has been monitored by health systems.

TABLE 4 | Leading causes of hospital admission and death among PLHIV in six European countries as reported by respondents[a].

	Estonia	Italy	The Netherlands	Slovenia	Sweden	Turkey
Hospital admissions[b]						
1	–	–	–	–	80% late HIV diagnosis	–
2	–	–	–	–	15% ageing-related comorbidities	–
3	–	–	–	–	5% issues related to drug addiction	–
4	–	–	–	–	–	–
5	–	–	–	–	–	–
Year data collected					2017	
Deaths[c]						
1	–	24% chronic viral hepatitis	25% non-AIDS malignancies	There are only 1 to 5 deaths per year: they are in very late presenters: opportunistic infections, lymphomas and also suicides[d]	Very few deaths. I believe it was 10 during 2017. No specific pattern[d]	–
2	–	11% non-Hodgkin lymphoma	15% cardiovascular disease			–
3	–	12% septicemia	11% AIDS			–
4	–	16% pneumonia	8% non-AIDS infections			–
5	–	10% heart disease	8% lung disease			–
Year data collected		2006–2010	2016[c]			

[a] *Since respondents were asked to report the proportions of hospital admissions and deaths attributable to the top five causes as percentages of total hospital admissions and deaths, percentages may not sum to 100%.*

[b] *Reporting for Sweden reflects estimates.*

[c] *For The Netherlands, reporting was incomplete at the time the survey was submitted and cause of death was unknown for 12% of deaths.*

[d] *Verbatim transcription from survey response.*

"–" indicates that no data were reported.

Furthermore, we are not aware of any expert guidance on the use of HRQoL indicators in national HIV monitoring. In 2018, the Dublin Declaration questionnaire (20) included an item about HRQoL for the first time, asking respondent countries to report on whether or not they included HRQoL in their HIV monitoring. Only five of 48 responding countries answered that they did so (personal communication, European Centre for Disease Prevention and Control to Jeffrey V. Lazarus, 5 June 2018). In light of this finding, it is notable that one of the six countries in our study currently carries out reporting on the HRQoL of PLHIV and two more countries said they were able to easily modify their current monitoring systems to carry out such reporting. It may be that there is widespread readiness to incorporate HRQoL into HIV monitoring in the European region, and this is perhaps an opportune time for stakeholders to identify best practices for health information systems to adopt in this regard.

On the other hand, there was little evident capacity to monitor HIV-related discrimination within health systems, which is cause for concern in light of the persistence of such discrimination (21–24) and the impact that it has on the health and well-being of PLHIV (25–27). In 2017, UNAIDS introduced a new indicator for countries to report on in 2018: "Percentage of people living with HIV who report experiences of HIV-related discrimination in health-care settings" (28). This indicator was drawn from an item in the widely used People Living with HIV Stigma Index, a survey developed by a coalition of civil society organisations in collaboration with UNAIDS (29). Our results point to a significant monitoring gap, and in light of the link between HIV-related stigma and poor health outcomes (30), stakeholders are advised to consider whether the Stigma Index indicator selected by UNAIDS should also be added to European regional reporting, which would further encourage national health systems to take up the indicator and collect robust monitoring data.

TABLE 5 | Discrimination against PLHIV within health systems in six European countries.

Of all PLHIV, what percentage report being denied health services (including dental care) because of HIV status in past 12 months?[a]

Estonia	Italy	The Netherlands	Slovenia	Sweden	Turkey
–	–	–	10%[b]	–	20%[c]

[a] *Adapted from an indicator in the People Living with HIV Stigma Index (GNP+, ICW, UNAIDS); http://www.stigmaindex.org.*

[b] *Source of data unknown.*

[c] *Respondent indicated that data were collected in 2011 and were published in Gökengin et al. (17).*

"–" indicates that no data were reported.

Given the high level of collaboration and coordination among many European countries in the response to HIV, the use of standardized "fourth 90" HIV care indicators across multiple countries would be beneficial to researchers, policy-makers, and other stakeholders. The optimal way for European countries to choose such indicators would be through a coordinated process that yields recommendations for a small number of new indicators to be used by national governments. In seeking consensus on indicators, stakeholders should consider how to minimise the reporting burden for countries and align data collection with current country-level monitoring activities, particularly in regard to comorbidity monitoring options. With such a large number of comorbidities contributing to the disease burden in PLHIV, the objective should not be to capture information about numerous comorbidities but rather to choose some comorbidities and other indicators as proxies for how health systems are managing comorbidity care in PLHIV overall. Such a process should take into account the possible need to harmonise definitions of some comorbidities such as alcohol dependence and sexual dysfunction.

Efforts to strengthen this aspect of the HIV response might benefit from consideration of lessons emerging from the evolving response to non-communicable diseases (NCDs) since in some regards the HIV and NCD epidemics are challenging health systems in similar ways (31). In a landmark 2018 report on health system responses to NCDs, action points identified by the WHO Regional Office for Europe encompassed issues such as multidisciplinary primary care, people-centred care, and service integration and coordination (32). In the coming years, strategies for monitoring progress on issues such as these are likely to become increasingly relevant to stakeholders in the HIV field.

This study has multiple limitations. The collection of data from only six of the 53 countries in the WHO European Region limits the representativeness of study findings, and a larger number of countries would need to be surveyed to acquire an evidence base for making recommendations about indicators that should be incorporated into national HIV monitoring throughout the region. The recruitment of survey respondents who are regarded as top HIV monitoring experts in their countries may have resulted in selection bias if this strategy led to a lack of representation of countries with HIV monitoring systems that are not sufficiently advanced for any one individual to be regarded as an expert in this area. In study countries where more than one person might be considered suitably knowledgeable about the issues of interest, our choice of experts might be biased by unknown variables. Since only one expert was asked to respond to the survey in each study country, findings directly reflect any gaps in the knowledge of these individuals regarding HIV monitoring in their countries.

The accuracy of the information reported by the survey respondents was not confirmed by other sources, and it may reflect errors or biases on the part of respondents. Biases among respondents also may have influenced some of the estimates and explanations provided in response to survey items that requested data. Country data for leading causes of hospitalisation and death among PLHIV and for discrimination within health systems were not collected using standardised methodologies and definitions. Hence, it is not possible to make meaningful cross-country comparisons. The survey item that asked for the percentage of PLHIV who report being denied health services did not elaborate criteria for what constitutes denial of health services, and thus the outcome measure could have been interpreted in multiple ways.

CONCLUSIONS

Findings from our study indicate that although the existing gaps may be considerable, there are opportunities for health information systems in European countries to expand the scope of their HIV monitoring in order to support decision-making about how the long-term health-related needs of PLHIV can best be met. Scaling up this survey to involve a larger number of European countries would provide stronger evidence regarding how to build on monitoring activities and resources that are already in place. Studies of HIV monitoring capacity are also needed in other regions, including Africa and Asia, where low- and middle-income countries with widespread access to HIV treatment are beginning to face HIV care challenges that similarly call for integrated and people-centred health system responses (31, 33). The larger goals of reorienting monitoring systems to better address the chronic care dimensions of HIV should be to transform HIV care into a more holistic undertaking and to help guide the integration of health system responses to HIV and to other chronic diseases.

DATA AVAILABILITY STATEMENT

The survey questionnaire and full dataset are available upon request from the authors.

AUTHOR CONTRIBUTIONS

JL and KS-H had the idea for this study and developed the study instrument with input from MK and the other co-authors. All authors reviewed and approved the final draft of the article.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2020.00036/full#supplementary-material

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ARTICLE 2

Assessing quality of life in people with HIV in Spain: psychometric testing of the Spanish version of WHOQOL-HIV-BREF

María José Fuster-RuizdeApodaca, Ana Laguia, Kelly Safreed-Harmon, Jeffrey V. Lazarus, Santiago Cenoz and Julia del Amo

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This article addresses specific objective 2: *Use a validated Spanish version of WHOQOL-HIV-BREF to identify ways in which the HRQoL of Spanish PLHIV is compromised.*

Resumen

Antecedentes: la evaluación de la calidad de vida relacionada con la salud (CVRS) en personas que viven con VIH se ha vuelto crucial para la práctica basada en la evidencia. Los objetivos de este estudio son analizar las propiedades psicométricas y la evidencia de la validez de la versión en español de WHOQOL-VIH-BREF en una muestra de personas con VIH en España y para examinar las facetas y dimensiones de CVRS más deterioradas e identificar las personas con VIH que muestran el perfil más vulnerable.

Métodos: Un total de 1462 personas con VIH participó en un estudio ex-post-facto de sección transversal observacional. Los datos se recopilaron en 33 sitios españoles a través de una encuesta en línea. Además de medir CVRS, el estudio usó otras herramientas para medir la adherencia al tratamiento (versión CEAT-VIH 2.0), el bienestar psicológico (GHQ-12) y el estigma relacionado con el VIH (HSSS). El análisis factorial de confirmación alfa, el primer y segundo orden de Cronbach (CFA), el coeficiente de Pearson y la ANOVA de ida, se utilizaron para evaluar la confiabilidad, construir validez y validez concurrente y conocida, respectivamente. Se analizaron las diferencias de acuerdo con los perfiles sociodemográficos y epidemiológicos de los participantes.

Resultados: CFAs de primer y segundo orden confirmó una estructura de primer orden de seis dominios de la versión en español de Whoqol-VIH-BREF y un factor de segundo orden relacionado con la CVRS general con un ajuste aceptable a los datos, aunque algunos cambios menores lo mejorarían. La estructura de seis dominios mostró una consistencia interna aceptable (el alfa de Cronbach desde .61 a .81). Se encontraron importantes correlaciones moderadas a grandes entre los dominios y la CVRS general, la adherencia, el bienestar psicológico y la autoimagen negativa. Se encontraron diferencias significativas de acuerdo con el recuento de células CD4+ autoinformadas de los participantes en varias facetas y dominios CVRS. Ser mujer, heterosexual, tener bajos estados socioeconómicos y educativos, haber adquirido el VIH a través de una inyección insegura y vivir más años con VIH, se

relacionaron con un CVRS más pobre. Personas con VIH mayores de 50 años presentó puntuaciones más bajas en 19 facetas CVRS.

Conclusiones: Este estudio demuestra que la versión en español del Whoqol-HIV-BREF es un instrumento válido. También presenta los datos más recientes sobre CVRS en personas con VIH en España con la muestra más grande hasta la fecha.

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RESEARCH

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Assessing quality of life in people with HIV in Spain: psychometric testing of the Spanish version of WHOQOL-HIV-BREF

Maria Jose Fuster-RuizdeApodaca[1,2], Ana Laguía[2*], Kelly Safreed-Harmon[3], Jeffrey V. Lazarus[3], Santiago Cenoz[4] and Julia del Amo[5,6]

Abstract

Background: The assessment of health-related quality of life (HRQoL) in people living with HIV (PLHIV) has become crucial to evidence-based practice. The goals of this study are to analyze the psychometric properties and evidence of the validity of the Spanish version of WHOQOL-HIV-BREF in a sample of PLHIV in Spain and to examine the more impaired HRQoL facets and dimensions and identify the PLHIV who show the most vulnerable profile.

Methods: A total of 1462 PLHIV participated in an observational cross-sectional ex-post-facto study. Data were collected at 33 Spanish sites through an online survey. In addition to measuring HRQoL, the study used other tools to measure treatment adherence (CEAT-VIH 2.0 version), psychological well-being (GHQ-12) and HIV-related stigma (HSSS). Cronbach's alpha, first- and second-order confirmatory factor analysis (CFA), the Pearson coefficient and one-way ANOVA were used to evaluate reliability, construct validity and concurrent and known-group validity, respectively. Differences according to the socio-demographic and epidemiological profiles of participants were analyzed.

Results: First- and second-order CFAs confirmed a six-domain first-order structure of the Spanish version of WHOQOL-HIV-BREF and one second-order factor related to overall HRQoL with an acceptable fit to the data, although some minor changes would improve it. The six-domain structure showed an acceptable internal consistency (Cronbach's alpha ranged from .61 to .81). Significant moderate to large correlations between domains and overall HRQoL, adherence, psychological well-being and negative self-image were found. Significant differences were found according to participants' self-reported CD4+ cell count in several HRQoL facets and domains. Being female, heterosexual, having low socio-economic and educational statuses, having acquired HIV through an unsafe injection and living more years with HIV were related to poorer HRQoL. PLHIV older than 50 presented lower scores in 19 HRQoL facets.

Conclusions: This study demonstrates that the Spanish version of the WHOQOL-HIV-BREF is a valid instrument. It also presents the most recent data about HRQoL in PLHIV in Spain with the largest sample to date.

Keywords: HIV, Health-related quality of life, WHOQOL-HIV-BREF

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Background

An estimated 36.7 million people are living with HIV worldwide [1]. Spain has an estimated 145,000 people living with HIV (PLHIV) [2], and there were 3353 new HIV diagnoses in 2016 [3]. While AIDS cases have declined in Spain in recent years with the use of effective antiretroviral therapy (ART) regimens, late diagnosis remains a problem. In more than one-quarter of new diagnoses in 2016, the person diagnosed had a CD4 cell count of less than 200, indicating advanced disease [3].

Improvements in ART have resulted in increased life expectancy for many PLHIV. Nonetheless, HIV infection and its related problems still have a notable impact on health-related quality of life (HRQoL), even in people who are virally suppressed as a result of taking ART [4]. Helping PLHIV achieve good outcomes in regard to their HRQoL requires understanding its determinants in this population. Studies have identified a number of factors that are consistently associated with HRQoL among PLHIV, including ageing, immunological status, the presence of symptoms, treatment adherence, depression, social support, employment and HIV-related stigma [5, 6].

In this context, the precise assessment of HRQoL with a valid measure has become crucial to the improvement of quality of life of PLHIV [7]. Additionally, HRQoL assessment has a major role in evaluating intervention outcomes [8]. Several instruments, both generic and HIV-specific, have been used to measure HRQoL in PLHIV. Generic instruments such as the widely used EQ-5D and SF-36 have the advantage of yielding findings that can be compared to HRQoL findings for the general population. However, HIV-specific instruments have shown greater sensitivity than generic ones [9]. WHOQOL-HIV-BREF [8] is considered to be one of the most promising of the HIV-specific instruments because of its psychometric properties, relevance to PLHIV and cross-cultural validity [9].

WHOQOL-HIV-BREF is the short version of WHOQOL-HIV [7]. Both instruments contain facets (individual components) of the generic WHOQOL measure [10] as well as HIV-specific facets. WHOQOL-HIV-BREF includes 29 items covering six domains: physical, psychological, level of independence, social, environmental and spiritual. There is also a two-item general facet.

The generic WHOQOL instrument has been validated in Spain [11]. However, there are no studies reporting the use of WHOQOL-HIV-BREF with Spanish PLHIV. This study aimed to assess the psychometric properties and evidence of the validity of the Spanish version of WHOQOL-HIV-BREF in a large sample of people with HIV in Spain. Furthermore, it aimed to determine which HRQoL facets and dimensions are most impaired and which groups of PLHIV are more vulnerable to these outcomes.

Methods

Study population and procedures

An observational cross-sectional ex-post-facto study was conducted in which 1462 PLHIV participated. They were recruited by convenience sampling. The general inclusion criteria were positive HIV diagnosis, being at least 18 years old, on antiretroviral therapy (ART) for at least one year, and not having any severe psychiatric or cognitive disorder. Data were collected between October 2016 and April 2017.

An online survey was designed using the Qualtrics survey platform (available at: www.qualtrics.com). Qualtrics is a private online survey development platform that allows the creation of surveys which can be accessed through a link. In the present study, our survey was self-administered with the support of tablet computers. Service providers from 33 service delivery points across Spain (hospitals and NGOs) collaborated in the participants' recruitment and data collection. During their medical consultations or when attending various services, the collaborating service providers explained the goals of the study to the participants, requesting their participation and obtaining their informed consent. The rate of refusal to participate in the study varied across centers, ranging from 0 to 18%, with an average around 7%. The main reasons argued for the refusal were not having enough time, the survey length or lack of skills to use tablets. Participants were compensated with 15 euros.

The Ethics Committee of the Hospital Clínico of Valencia approved the research protocol in March 2016. All study procedures were conducted in accordance with the 1964 Helsinki Declaration (revised in 1996) [12].

Measures

WHOQOL-HIV-BREF

WHOQOL-HIV-BREF has 31 items covering six domains: physical health; psychological health; level of independence; social relationship; environmental health; and spirituality, religion and personal beliefs (SRPB) [8]. Responses to all items are given on a 5-point scale. Items that ask about negative perceptions and experiences, such as "How much do you fear the future?" are reverse-coded for scoring. Thus, higher scores for all items indicate better quality of life. The average score for each domain is multiplied by four, yielding domain scores that range from 4 to 20 [13].

Several studies have examined the validity and psychometric properties of WHOQOL-HIV-BREF in different languages and countries. (A summary of these studies is presented in Additional file 1). They have found the instrument to have good psychometric properties and have also found evidence of its validity. The Spiritual, Religion and Personal Beliefs domain (SRPB) is the one that exhibited the lowest reliability (under .70) and discriminative power in most of the studies [8, 14–18], although it is the domain which contains more HIV-specific items measuring existential concerns relating to HIV.

Because WHOQOL-BREF has been validated in a Spanish study population [19], only the translation of the HIV-specific items was needed (see Additional file 2). The HIV-specific items collect information about the bother caused by physical problems related to HIV infection, HIV-related stigma, and fears related to the future and to death ("How much are you bothered by any physical problems related to your HIV infection?," "To what extent are you bothered by people blaming you for your HIV status?," "How much do you fear the future?," "How much do you worry about death?," and "To what extent do you feel accepted by the people you know?"). These items were extracted from five HIV facets of the WHOQOL-HIV long form and then integrated with the WHOQOL-BREF to complete the 31-item WHOQOL-HIV BREF [8]. They were translated following the criteria of the International Test Commission [20]. A backward translation was performed by two expert translators. In addition, a person with HIV reviewed the translation.

Questionnaire to evaluate the adherence to HIV therapy (CEAT-VIH 2.0 version)

The validated Spanish version of the Questionnaire to Evaluate the Adherence to HIV Therapy (CEAT-VIH 2.0 version) [21–23] was used. This scale is comprised of 17 items rated on a 5-point scale. Negative items were reverse-coded. A composite of all items (total score) was calculated, with higher the scores indicating higher treatment adherence. A systematic review of the psychometric properties of the CEAT-VIH including 20 studies revealed an adequate internal consistency as well as no floor or ceiling effects [23]. Additionally, evidence of validity comprised criterion-related validity (e.g., HIV viral load, length of time with continuous undetectable HIV viral load, days of missed doses, number of pills per day, and adherence assessed by the pharmacist or physician); responsiveness, sensitivity, and specificity; and patterns of convergence and divergence (e.g., negative mood, depression, anxiety and stress were negatively associated with CEAT-VIH scores whereas positive correlations with CEAT-VIH scores were found for perceived social support and quality of life outcomes).

General Health Questionnaire (GHQ-12)

The validated Spanish version of the General Health Questionnaire (GHQ-12) was used [24]. Items are rated on a 4-point scale, with higher scores indicating better psychological health. In previous studies, this scale has shown adequate reliability and validity in the Spanish general population [24].

HIV-related stigma

Five items of the Negative Self-image dimension and three items of the Disclosure Concerns dimension of the Spanish HIV Stigma Scale (HSSS) were used [25]. These items were selected for having higher validity constructs in the validation study of the scale. A previous study in Spain revealed that this scale shows good internal consistency and good construct validity, including content and criterion validity [25]. The items are rated on a 4-point scale.

Self-reported questions related to health status such years living with HIV, lymphocyte CD4 count and viral load copies were included in the survey. Moreover, the questionnaire also measured socio-demographic information.

Data analysis

Completing most items of the online questionnaire in the Qualtrics survey platform was programmed to be compulsory. Only items related to some sensitive characteristics of the participants were allowed to be skipped. Thus, there were no missing values in the tools used to measure the variables under analysis.

To test the construct validity, first-order confirmatory factor analysis (CFA) was used to assess the fit of the Spanish version of the WHOQOL-HIV-BREF to the six-dimension original structure (Model 1, [8]). Next, second-order CFA was performed to determine whether the six first-order factors could be explained by a higher-order latent factor associated with HRQoL. Previous studies showed that one of the items of the SRPB dimension presented a low facet-domain correlation [18] or factor loading [14, 17] and was saturated in the psychological domain rather than in the existential domain when exploratory factor analysis (EFA) was conducted [16]. Thus, we tested an alternative model (Model 2) allowing one of the items of the SRPB dimension—feelings of personal meaning—to load in the Psychological Health latent dimension. The robust unweighted least square method was used because the items in the scale did not meet the assumption of normality. Goodness of fit was evaluated using the goodness of fit index (GFI), the adjusted goodness of fit index (AGFI), the comparative fit index (CFI), the standardized root mean square residual (SRMR) and the standardized root mean square error of approximation (RMSEA). Also, the consistent Akaike information criterion (CAIC) was used to compare the alternative models. According to Hu and Bentler [26], the models are considered to have a good fit when the goodness of fit indexes (GFI and AGFI) and CFI > .90, RMSEA < .08 and SRMR <.08. The reliability of each domain was assessed using Cronbach's α coefficient.

Pearson's correlation analysis between domain scores and the general health dimension of WHOQOL-HIV-BREF was performed for convergent validity. To assess concurrent validity, we examine the association between domain scores and the criterion variables measured. We expected to find positive correlations between domain scores and CEAT-VIH and GHQ-12. We also expected to find negative correlations between domain scores and HIV-related stigma dimensions.

Known-group validity was used to assess the capacity of WHOQOL-HIV-BREF to discriminate among subgroups of participants according to their immunological (CD4 count) and virological (viral load copies) status. It was expected that participants with higher CD4 count and undetectable viral load would have higher HRQoL domain scores.

Finally, differences according to the socio-demographic and epidemiological profiles of study participants were analyzed. For the sake of simplicity and clarity, only differences in the domains were assessed in most of the characteristics of the participants, and only *p*-values are shown. However, differences in all HRQoL facets were tested according to age and sex. It was done because of the current relevance of analyzing HRQoL in aging PLHIV and the UNAIDS recommendations about disaggregation of data according to relevant socio-demographic characteristics [27]. To test differences by age, a cut-off point of 49 years (≤ 49 vs. ≥ 50 years) was established. T-test and one-way variance analysis were used for these analyses.

Regarding the data analysis software, LISREL (LInear Structural RELations) 8.7 program and its companion preprocessor program PRELIS for Windows were used for the CFAs. LISREL is an application for structural equation modeling developed by K. G. Jöreskog and D. Sörborm [28]. PRELIS is an application for data manipulation, data transformation, data generation, computing moment matrices and imputation by matching. A widely used program for statistical analysis in social science, IBM SPSS Statistics 22 [29], was selected for the remaining analyses.

Results

Sample characteristics

Socio-demographic and health data of the participants are shown in Table 1. The epidemiological profile found was concordant with Spanish epidemiological data for PLHIV [3].

WHOQOL-HIV-BREF scores

The descriptive statistics of each item and domain are displayed in Table 2. The mean scores of the WHOQOL-

Table 1 Sociodemographic and clinical characteristics of the participants ($N = 1462$)

Sociodemographic and clinical variables	%
Gender	
Males	79.3
Females	19.3
Transsexual	1.4
Age, years, mean (*M* ± *SD*)	45.0 ± 10.2
Education level	
No studies	3.9
Elementary School	26.2
High School	33.1
University degree	30
Other	6.8
Work situation	
Working (full time)	33.9
Working (part-time)	10.8
Unemployed	18.2
Retired/impaired	16.4
Other	20.7
Monthly incomes	
None	13.3
< 1000 €	37.7
1001 €–1500 €	29.3
1501 €–2000 €	7.5
> 2000 €	12.2
Sexual behavior	
Heterosexual	39.7
Homosexual	52.8
Bisexual	4.2
Others	1.9
No answer	1.3
Transmission route	
Sexual intercourse	68.2
Sharing injection materials	18.6
Unknown (various concomitant practices)	10.2
Other	3
CD4 cell count, cells/mm^3	
< 200	4.8
201–400	10.5
> 400	68.1
Unknown	16.6
Duration of infection, years, mean (*M* ± *SD*)	13.8 ± 9.6
Years taking antiretroviral therapy (*M* ± *SD*)	11.3 ± 8.3
Undetectable plasma viral load	90.4

Note: Data in percentages unless otherwise stated

Table 2 Descriptive statistics and reliability of the domains and items (*N* = 1462)

Domains and items	Mean (± *SD*)	Skewness	Kurtosis	Corrected item-domain correlation	Cronbach's α if item is deleted
Overall QoL/General Health (α = .77)	14.9 ± 3.6				
How would you rate your QoL?	3.6 ± 1.06	−.40	−.63	.63	
How satisfied are you with your health?	3.8 ± .93	−.94	.78	.63	
Physical health (α = .73)	15.5 ± 3.2				
Pain and discomfort[a]	3.9 ± 1.1	−.87	−.39	.58	.64
Symptoms of HIV[a]	4.2 ± 1.0	−1.2	.55	.54	.66
Energy and fatigue	3.9 ± .97	−.77	.05	.56	.65
Sleep and rest	3.3 ± 1.1	−.38	−.79	.43	.73
Psychological health (α = .81)	14.9 ± 3.0				
Positive feelings	3.9 ± 1.0	−.92	.29	.66	.75
Concentration ability	3.5 ± .96	−.52	−.40	.46	.81
Bodily image self-acceptance	3.9 ± .96	−.91	.49	.52	.79
Self-satisfaction	3.8 ± 1.0	−.82	.16	.73	.73
Negative feelings[a]	3.3 ± 1.0	−.11	−.71	.61	.77
Level of Independence (α = .67)	15.5 ± 3.2				
Dependence on medication[a]	3.4 ± 1.5	−.39	−1.3	.29	.79
Mobility	4.4 ± .81	− 1.6	2.9	.46	.62
Activities of daily living	3.9 ± .96	−.81	.25	.64	.51
Work capacity	3.7 ± 1.1	−.83	−.01	.60	.51
Social relations (α = .75)	15.0 ± 3.2				
Social inclusion	4.1 ± .91	−1.1	1.3	.51	.71
Personal relationships	3.7 ± 1.0	−.73	−.03	.63	.64
Sexual satisfaction	3.2 ± 1.2	−.37	−.95	.46	.75
Social support	3.9 ± 1.0	−.96	.38	.61	.65
Environmental health (α = .81)	15.3 ± 2.5				
Physical safety and security	3.7 ± .96	−.64	−.05	.54	.79
Physical environment	3.9 ± .90	−.93	.87	.57	.79
Financial resources	3.0 ± 1.0	−.24	−.64	.51	.79
Information for daily living	4.1 ± .84	−.90	.93	.56	.79
Participation in leisure activities	3.7 ± 1.0	−.68	−.23	.61	.78
Home environment	3.9 ± 1.0	−1.0	.82	.62	.78
Accessibility of health services	4.2 ± .80	− 1.0	1.1	.46	.80
Transport	3.8 ± 1.0	−.83	.29	.38	.81
Spirituality/Personal beliefs (α = .61)	14.5 ± 3.5				
Personal life meaning	4.0 ± 1.0	−1.0	.49	.24	.63
Forgiveness and blame[a]	3.3 ± 1.6	−.33	−1.4	.32	.62
Concerns about the future[a]	3.4 ± 1.2	−.36	−.88	.57	.40
Death and dying[a]	3.7 ± 1.2	−.66	−.57	.47	.48

[a] Reversed items recoded

HIV-BREF domains were calculated according to the WHOQOL-HIV Instrument Users Manual [30].

The skewness and kurtosis coefficients of most items ranged from – 1.00 to 1.00. Some of them showed somewhat higher coefficients, but coefficients of less than 1.5 can also be considered adequate [31]. The item showing highest kurtosis (2.9) was the one measuring mobility.

The facets showing the lowest scores were *financial resources, sexual satisfaction, sleep and rest, negative feelings,* and *forgiveness and blame*. Across domains, Physical Health and Level of Independence showed the highest scores while the SRPB domain presented the lowest score.

Validity of the Spanish version of the WHOQOL-HIV-BREF

Construct validity

The results of the first-order CFA confirmed the six-domain factor structure with an acceptable fit to the data (Table 3). The results of the second-order CFA confirmed the six first-order dimensions and one second-order factor related to overall HRQoL, also with acceptable model fit statistics. Most of the standardized loadings were higher than 0.5, the level considered adequate [32]. However, lower loadings were found in the facet *dependence on medication* in the Level of Independence domain; the facet *transport* in the Environmental Health domain; and the facets *forgiveness and blame* and *death and dying* in the Spirituality.

Results of the alternative model tested (Model 2) showed a high standardized loading for the item *religion, spirituality and personal beliefs* in the Psychological Health domain. Furthermore, the remaining three items – *forgiveness and blame, concerns about the future and death and dying*—showed higher loadings in the SRPB latent factor than in Model 1 (Table 3). Moreover, both first-order and second-order Model 2 showed a substantial improvement in fit indexes. However, results of the second-order model showed that the SRPB latent factor was the one with the lowest loading in the high second-order latent factor related to HRQoL (Table 3).

Internal consistency

Results of the different reliability coefficients were calculated. These showed that internal consistency was acceptable for most HRQoL dimensions (Table 4). However, the SRPB domain showed the lowest reliability coefficient. The Level of Independence domain showed an alpha below expectations (< .70). Nevertheless, the Omega coefficient (ω) showed an adequate value (.80), because it is between .70 and .90 [33]. The Omega coefficient, unlike the alpha coefficient, works with factorial loads and it makes calculations more stable [34].

Convergent and concurrent validity

Positive and moderate to large correlations were found between all domains and the General Health one that indicated a good convergent validity. Religion and Personal Beliefs domains (Table 3). The results of the covariances among the first-order factors are presented in Table 5.

Regarding concurrent validity, positive correlations were found between all HRQoL dimensions and ART adherence and psychological well-being. Moreover, negative correlations were found between HRQoL dimensions and negative self-image. However, there was a moderate negative correlation with disclosure concerns when correlated with the SRPB dimension (Table 5).

Known-group validity

Significant differences were found according to participants' self-reported CD4+ T cell count in several HRQoL facets and domains (Table 6). The higher the CD4+ T cell count, the higher the HRQoL scores. However, the effect sizes of the differences were small. The highest ones were found in the facets measuring *participation in leisure activities, financial resources, sexual satisfaction, symptoms of HIV,* and *overall perception of health.*

Some differences according to virological status were also found. Those with undetectable viral load presented significantly higher scores in the facets measuring *satisfaction with their own health*, *pain and discomfort*, *sexual satisfaction* and *concerns about the future*, as well as marginally higher scores in facets related to *symptoms of HIV* and *participation in leisure activities*.

Differences in HRQoL according to the characteristics of the participants

Women showed significantly lower scores than men in several HRQoL facets (see Additional file 3 for further detail). However, higher effect sizes were found in *sexual satisfaction* (Cohen's $d = 0.64$), *bodily image self-acceptance* (Cohen's $d = 0.53$), *participation in leisure activities* (Cohen's $d = 0.49$), *pain and discomfort* (Cohen's $d = 0.44$), and *energy and fatigue* (Cohen's $d = 0.43$).

Regarding age, PLHIV older than 50 also presented lower scores in several HRQoL facets. The greater differences were found in the items measuring *sexual satisfaction* and *work capacity* (Cohen's $d = 0.47$ and 0.37, respectively). Nevertheless, older PLHIV showed higher scores in the three HIV-specific items from the SRPB domain (*forgiveness and blame, concerns about the future, death and dying)* although the effect sizes of these differences were small (Cohen's $d = -0.13$, -0.11 and -0.10, respectively).

The scores in all facets and the statistics assessing the differences can be found in the supplementary material (Additional file 3). Differences according to the other socio-demographic characteristics revealed lower scores in heterosexuals than homosexuals in all domains ($p < .0001$) except in the SRPB domain. Bisexuals presented significant lower scores than homosexuals in General Health ($p < .0001$), Physical Health ($p < .0001$), Level of Independence ($p < .0001$), Social Relationships ($p < .001$), and Environmental Health ($p < .0001$).

Moreover, the higher the level of education, the higher the scores in all HRQoL domains ($p < .0001$) except in

Table 3 Standardized estimations for the six-domain first-order and HRQoL second-order structure Confirmatory Factor Analysis (CFA) model

	First Order (λ)		Second Order (γ)	
Domains and items	Model 1	Model 2	Model 1	Model 2
Physical health			.92	.93
Pain and discomfort[a]	.62	.63		
Symptoms of HIV[a]	.60	.60		
Energy and fatigue	.88	.88		
Sleep and rest	.65	.65		
Psychological health			.97	.94
Positive feelings	.84	.85		
Concentration ability	.57	.57		
Bodily image self-acceptance	.67	.68		
Self-satisfaction	.86	.87		
Negative feelings[a]	.69	.70		
Religion, spirituality and personal beliefs (personal life meaning)	–	.81		
Level of Independence			.94	.94
Dependence on medication[a]	.38	.39		
Mobility	.73	.73		
Activities of daily living	.87	.87		
Work capacity	.81	.81		
Social relations			.91	.91
Social inclusion	.70	.70		
Personal relationships	.81	.81		
Sexual satisfaction	.65	.65		
Social support	.71	.71		
Environmental health			.92	.92
Physical safety and security	.82	.81		
Physical environment	.69	.69		
Financial resources	.56	.56		
Information for daily living	.69	.69		
Participation in leisure activities	.74	.74		
Home environment	.71	.71		
Accessibility of health services	.51	.51		
Transport	.40	.40		
Spirituality/Personal beliefs			.86	.50
Religion, spirituality and personal beliefs (personal life meaning)	.89	–		
Forgiveness and blame[a]	.36	.56		
Concerns about the future[a]	.51	.87		
Death and dying[a]	.35	.60		
SB-χ2 (Satorra-Bentler Chi-square)	3210.71	2691.78	3435.87	2906.40
Degrees of freedom	362	362	370	370
p	< .001	< .001	< .001	< .001
RMSEA (IC 90%)	0.073 (0.071; 0.076)	0.066 (0.064; 0.069)	0.075 (0.073; 0.078)	0.068 (0.066; 0.071)
SRMR	0.064	0.058	0.068	0.062
GFI	0.98	0.98	0.98	0.98

Table 3 Standardized estimations for the six-domain first-order and HRQoL second-order structure Confirmatory Factor Analysis (CFA) model *(Continued)*

	First Order (λ)		Second Order (γ)	
Domains and items	Model 1	Model 2	Model 1	Model 2
AGFI	0.97	0.98	0.97	0.98
CFI	0.97	0.97	0.97	0.97
NFI	0.97	0.97	0.97	0.97
CAIC	3815.70	3296.77	3974.56	3445.10

Notes: $N = 1462$. Estimation of the robust unweighted least squares. SB-χ^2: Satorra-Bentler Chi-square. *df*: degrees of freedom. Model 1: dimensions according to the original scale. Model 2: allowing the item *religion, spirituality and personal beliefs* (feeling that life is meaningful) to load in the Psychological Health domain instead of the SRPB domain

[a] Reversed items recoded

All factor loadings $p < .05$

the SRPB domain. Besides, positive correlations were found between participants' incomes and all dimensions of HRQoL (ranging from $r = .11$ in the SRPB domain to $r = .36$ in the Environmental Health domain; $p < .01$).

Furthermore, participants who acquired HIV infection through the injection route presented the lower scores in HRQoL domains ($p < .0001$) except in the SRPB domain.

Finally, negative correlations were found between most HRQoL dimensions (except the SRPB domain) and years since diagnosis (ranging from $r = -15$ in the Social Relationship domain to $r = -.27$ in Physical domain; $p < .01$).

Discussion

This study assessed the validity of the Spanish version of WHOQOL-HIV-BREF. It also described HRQoL in PLHIV living in Spain and the more vulnerable profiles.

Regarding its validity, the instrument showed acceptable construct validity although some minor changes could improve it. The SRPB domain showed the lowest reliability. In line with other studies [17, 18], the item *religion, spirituality and personal beliefs* (feeling that life is meaningful), was the one with the lowest item-domain correlation. Some authors have suggested including this item in the Psychological Health domain [16, 35]. The results of the present study support this modification.

The instrument also showed concurrent validity. In line with findings from other studies [17, 36], all of its dimensions were positively related to ART adherence and psychological well-being. At the same time, all of the HRQoL dimensions were negatively related to negative self-image, and the SRPB domain was the unique dimension that was significantly and negatively related to disclosure concerns. People who have a stigmatized condition may find some advantages in concealing the condition, but concealment may also result in mental strain and poorer psychological well-being [37, 38]. Thus, the results of this highlighted the relevance of the SRBP HIV-specific items, despite the low discriminant capability of this dimension.

The instrument was able to discriminate according to self-reported immunological and virological statuses in several HRQoL facets. This finding is in line with evidence from other studies [8, 14, 39, 40], although not all studies have had the same finding [15, 17].

The present study also described the HRQoL of PLHIV in Spain. Financial resources and sexual satisfaction were the most impaired facets. Both facets were found to be related to HRQoL in a previous Spanish study, but financial problems showed in that study the highest correlation [6]. Sociodemographic data collected from our participants revealed that they were in a precarious financial situation, and it could be damaging their HRQoL. Although Physical Health was one of the

Table 4 Reliability coefficients of the domains of the WHOQOL-HIV-BREF

Dimensions	Cronbach's alpha	Spearman-Brown (ρ)	Guttman Split-half	MCDonald's composite score (ω)	Intraclass correlation [IC]
Overall QoL/General Health	.77	.775	.772		.77 [.747, .794]
Physical health	.73	.662	.660	.786	.734 [.711, .756]
Psychological health	.81	.842	.827	.851	.812 [.796, .827]
Level of Independence	.67	.638	.638	.803	.678 [.650, .704]
Social relations	.75	.785	.779	.810	.749 [.728, .770]
Environmental health	.81	.809	.809	.851	.816 [.801, .830]
Spirituality/Personal beliefs	.61	.547	.545	.623	.61 [.579, .644]

Table 5 Covariances (ϕ) between the Spanish WHOQOL-HIV-BREF dimensions and correlations between these dimensions and criterion variables

	Covariances (ϕ)							Pearson's Correlations (*r*)			
	PHY	PSY	IND	SR	EH	SRPB	GH	ART Adherence (α = .78)	Psychological Well-being (α = .91)	Negative Self-Image (α = .80)	Disclosure Concerns (α = .82)
PHY	1	.90	.96	.75	.83	.81	.67**	.44**	.63**	−.33**	−.04
PSY		1	.87	.89	.86	.95	.66**	.42**	.74**	−.44**	−.07*
IND			1	.79	.89	.74	.61**	.36**	.58**	−.31**	.00
SR				1	.90	.81	.56**	.39**	.57**	−.33**	−.07*
EH					1	.72	.65**	.47**	.57**	−.33**	−.01
SRPB						1	.41**	.29**	.53**	−.55**	−.30**
GH							1	.44**	.58**	−.29**	−.02

Notes: GH = General Health, PHY = Physical Domain, PSY = Psychological Domain, IND = Level of Independence Domain, SR = Social Relations Domain, EH = Environmental Health Domain, SRPB = Spirituality, Religion and Personal Beliefs Domain. α = Cronbach's alpha reliability coefficient
N = 1462. ** *p* < .01. * *p* < .05

domains with higher scores, the facet related to sleep and rest had one of the lowest facet scores. This result was also found in other studies conducted in other countries [8, 14, 17, 41]. Also, HIV-specific existential concerns and negative feelings were among the most affected HRQoL facets. HIV-specific existential concerns included in the WHOQOL-HIV-BREF are related to stigma and concerns about the future and death. Research showed that there are prejudices towards PLHIV in Spain [42] and that both enacted and internalized stigma were related to poor HRQoL [6, 37]. Furthermore, research also showed that emotional loneliness, HIV-related stress and depressive mood were negatively related to HRQoL of PLHIV in Spain [6]. Stigma, depression, anxiety and other variables not measured in the present study such as comorbidities, social support, family situation or lifestyle are found to be determinants of PLHIV's HRQoL [5]. All these variables might explain the concerns and negative feelings of the participants in the present study. Correlations found between psychological well-being, HIV-related stigma and HRQoL dimensions in this study support it.

Moreover, our results suggest that specific subgroups of PLHIV in Spain are particularly vulnerable to poor health-related quality of life for HRQoL. We found lower HRQoL scores for people who had been living with HIV for a longer time, in older people and in heterosexuals. Although incidence of heterosexual transmission of HIV has been decreasing in Spain in recent years, people whose HIV infection is attributed to this mode of transmission are estimated to constitute one-third of all PLHIV nationally [43]. Furthermore, Spain is estimated to have large proportions of PLHIV who are older than 50 years (46%) and who were diagnosed with HIV more than 15 years ago (49%) [43]. Older age and a longer period of time living with HIV are both associated with higher prevalence of non-HIV-related comorbidities such as diabetes and chronic kidney disease [44, 45]. The long-term management of multiple comorbidities, in turn, gives rise to high levels of polypharmacy [46]. Comborbidities and polypharmacy both have the potential to undermine HRQoL [47].

According to our findings, acquiring HIV through injection drug use is another factor associated with poorer HRQoL. While HIV transmission via the sharing of unsterile injection drug equipment is decreasing in Spain, 31% of PLHIV are estimated to belong to this transmission category [43]. We also found lower socioeconomic and educational status to be related to poorer HRQoL, and women in our study had lower HRQoL than their male counterparts. The role of aging should be considered in terms of how it specifically affects the HRQoL of women living with HIV, and it is notable that some of the most impaired HRQoL facets found in the present research might be exacerbated by menopause [48, 49].

Our study findings lead us to propose that initiatives to improve the HRQoL of PLHIV might have the greatest impact if they target specific populations and take into account both structural, psychosocial, and biomedical drivers of poor HRQoL. Interventions that can improve HRQoL through mechanisms such as social support and self-empowerment may have far-reaching consequences for individual PLHIV and for health systems. A recent longitudinal study found that both physical and mental HRQoL dimensions' scores were predictive of all-cause hospitalization in a cohort of PLHIV, suggesting that improving HRQoL in this population can result in better health outcomes [50].

The main limitation of our study derives from its cross-sectional nature. Another limitation is the self-

Table 6 Known-group comparisons of the WHOQOL-HIV-BREF scores

	CD4+ T cells					Viral load (copies mm^3)			
	< 200 (*N* = 70)	201–400 (*N* = 153)	> 400 (*n* = 996)			Undetectable (*n* = 1321)	Detectable (*n* = 87)		Cohen's *d*
Domains and items	Mean ± SD	Mean ± SD	Mean ± SD	*p*-Value	η^2	Mean ± SD	Mean ± SD	*p*-Value	
Overall QoL/General Health	13.8 ± 3.8	14.1 ± 3.7	15.2 ± 3.5	.000	0.014	15.1 ± 3.5	14.2 ± 4.2	.128	0.253
How would you rate your QoL?	3.3 ± 1.2	3.4 ± 1.1	3.7 ± 1.0	.000	0.012	3.7 ± 1.1	3.5 ± 1.2	.279	0.180
How satisfied are you with your health?	3.7 ± 1.1	3.7 ± 1.0	3.9 ± 0.9	.002	0.010	3.9 ± 0.9	3.6 ± 1.1	.050	0.328
Physical health	14.7 ± 3.5	15.0 ± 3.2	15.6 ± 3.2	.004	0.008	15.6 ± 3.2	14.8 ± 3.7	.084	0.247
Pain and discomfort[a]	3.8 ± 1.3	3.9 ± 1.2	4.0 ± 1.2	.312	0.002	4.0 ± 1.2	3.8 ± 1.3	.069	0.165
Symptoms of HIV[a]	3.9 ± 1.2	4.1 ± 1.2	4.3 ± 1.1	.001	0.014	4.3 ± 1.1	4.0 ± 1.1	.078	0.272
Energy and fatigue	3.7 ± 1.1	3.8 ± 0.9	4.0 ± 1.0	.044	0.005	3.9 ± 1.0	3.9 ± 1.0	.511	0
Sleep and rest	3.3 ± 1.2	3.3 ± 1.1	3.4 ± 1.2	.190	0.002	3.4 ± 1.1	3.2 ± 1.3	.143	0.179
Psychological health	14.8 ± 3.2	14.7 ± 2.9	15.1 ± 3.0	.322	0.001	15.0 ± 3.0	14.8 ± 3.3	.633	0.066
Positive feelings	3.8 ± 1.2	3.8 ± 1.0	4.0 ± 1.0	.019	0.001	4.0 ± 1.0	3.9 ± 1.2	.575	0.009
Concentration ability	3.7 ± 0.8	3.5 ± 1.0	3.6 ± 1.0	.326	0.002	3.6 ± 1.0	3.6 ± 1.0	.708	0
Bodily image self-acceptance	4.0 ± 1.1	3.9 ± 1.0	4.0 ± 1.0	.781	0.000	4.0 ± 0.9	4.0 ± 1.0	.833	0
Self-satisfaction	3.9 ± 1.2	3.8 ± 1.0	3.9 ± 1.0	.695	0.000	3.9 ± 1.0	3.8 ± 1.1	.396	0.099
Negative feelings[a]	3.1 ± 1.1	3.4 ± 1.0	3.3 ± 1.1	.139	0.004	3.4 ± 1.1	3.2 ± 1.1	.134	0.181
Level of Independence	14.8 ± 3.5	14.7 ± 3.1	15.7 ± 3.1	.000	0.011	15.6 ± 3.1	15.3 ± 3.4	.478	0.096
Dependence on medication[a]	3.1 ± 1.5	3.1 ± 1.4	3.5 ± 1.5	.003	0.009	3.4 ± 1.5	3.3 ± 1.5	.440	0.066
Mobility	4.4 ± 0.9	4.4 ± 0.8	4.5 ± 0.8	.081	0.003	4.5 ± 0.8	4.5 ± 0.8	.969	0
Activities of daily living	3.7 ± 1.1	3.7 ± 0.9	4.0 ± 0.9	.004	0.007	3.9 ± 0.9	3.8 ± 1.0	.457	0.110
Work capacity	3.6 ± 1.3	3.6 ± 1.2	3.8 ± 1.1	.082	0.003	3.8 ± 1.1	3.7 ± 1.2	.520	0.090
Social relations	14.5 ± 3.9	14.6 ± 3.1	15.1 ± 3.1	.075		15.1 ± 3.2	14.4 ± 3.7	.081	0.216
Social inclusion	4.1 ± 1.0	4.2 ± 0.9	4.1 ± 0.9	.985	0.000	4.2 ± 0.9	4.0 ± 1.0	.161	0.220
Personal relationships	3.7 ± 1.2	3.8 ± 1.0	3.8 ± 1.0	.942	0.000	3.8 ± 1.0	3.8 ± 1.2	.822	0
Sexual satisfaction	2.8 ± 1.5	2.9 ± 1.3	3.3 ± 1.3	.000	0.013	3.3 ± 1.3	2.9 ± 1.4	.003	0.306
Social support	3.8 ± 1.3	3.8 ± 1.0	4.0 ± 1.0	.308	0.001	3.9 ± 1.0	3.7 ± 1.2	.111	0.197
Environmental health	14.7 ± 2.9	15.0 ± 2.3	15.5 ± 2.4	.005	0.003	15.4 ± 2.5	15.0 ± 2.7	.244	0.159
Physical safety and security	3.6 ± 1.1	3.7 ± 0.9	3.8 ± 0.9	.196	0.003	3.8 ± 0.9	3.6 ± 1.0	.306	0.220
Physical environment	3.8 ± 1.0	3.9 ± 0.9	4.0 ± 0.9	.279	0.002	4.0 ± 0.9	3.8 ± 1.1	.145	0.218
Financial resources	2.7 ± 1.1	3.0 ± 1.0	3.2 ± 1.1	.000	0.015	3.1 ± 1.1	3.0 ± 1.2	.241	0.090
Information for daily living	4.0 ± 1.0	4.1 ± 0.8	4.1 ± 0.8	.681	0.001	4.1 ± 0.8	4.1 ± 0.9	.754	0
Participation in leisure activities	3.5 ± 1.3	3.5 ± 1.1	3.9 ± 1.0	.000	0.019	3.8 ± 1.1	3.6 ± 1.2	.081	0.180
Home environment	3.9 ± 1.2	3.9 ± 1.0	4.0 ± 1.0	.374	0.001	4.0 ± 1.0	3.9 ± 1.1	.353	0.099
Accessibility of health services	4.4 ± 0.8	4.1 ± 0.9	4.2 ± 0.8	.111	0.003	4.2 ± 0.8	4.3 ± 0.9	.538	−0.124
Transport	3.7 ± 1.2	3.9 ± 1.0	3.9 ± 1.0	.337	0.002	3.9 ± 1.0	3.9 ± 1.0	.562	0
SRPB	14.0 ± 3.4	14.9 ± 3.3	14.5 ± 3.5	.209	0.002	14.6 ± 3.5	14.1 ± 3.7	.213	0.142
Personal life meaning	4.0 ± 1.2	4.0 ± 1.0	4.1 ± 1.0	.451	0.001	4.1 ± 1.0	4.1 ± 1.1	.926	0
Forgiveness and blame[a]	2.8 ± 1.7	3.7 ± 1.5	3.3 ± 1.6	.001	0.010	3.3 ± 1.6	3.3 ± 1.6	.974	0

Table 6 Known-group comparisons of the WHOQOL-HIV-BREF scores *(Continued)*

	CD4+ T cells					Viral load (copies mm^3)			
	< 200 (*N* = 70)	201–400 (*N* = 153)	> 400 (*n* = 996)			Undetectable (*n* = 1321)	Detectable (*n* = 87)		Cohen's *d*
Domains and items	Mean ± SD	Mean ± SD	Mean ± SD	*p*-Value	η^2	Mean ± SD	Mean ± SD	*p*-Value	
Concerns about the future[a]	3.5 ± 1.3	3.5 ± 1.2	3.4 ± 1.3	.771	0.000	3.5 ± 1.2	3.2 ± 1.4	.024	0.247
Death and dying[a]	3.7 ± 1.4	3.8 ± 1.2	3.7 ± 1.2	.685	0.000	3.7 ± 1.2	3.5 ± 1.4	.283	0.164

Notes: *SRPB* Spirituality, Religion and Personal Beliefs. η^2 = F-test effect size. Cohen's *d* = t-test effect size. Near to 4% (*N* = 54) of the participants stated not knowing their viral load copies, and 16.6% (*N* = 243) stated being unsure of the amount of CD4 + T cells

[a] Reversed items recoded

reported nature of health-related variables measured, since people may not correctly recall information such as their viral load level. The large sample size of our study led to many findings of statistically significant differences between groups. Although we reported the effect sizes, the cross-sectional nature of our study did not allow us to test how such differences have an impact on clinical outcomes. Thus, future longitudinal studies should be conducted analyzing data collected from clinical records. This would allow for assessment of the predictive validity of the instrument and thus would provide stronger evidence than the findings of the present study, as well as showing which facets and dimensions of HRQoL have the most substantial impact on clinical outcomes. Such evidence also could be used to guide interventions to address the needs of the most vulnerable populations in regard to the issues that are having the greatest negative effect on their health and HRQoL. In addition, the heterogeneity of PLHIV and the differences found point to the need to analyze scale invariances across sex, age and other relevant characteristics. Also, our study has the limitation that the population was recruited by convenience sampling. This affects the representativeness of the sample. However, the large sample size of our study could offset this limitation, as demonstrated by the finding that the characteristics of our participants were concordant with Spanish epidemiological data for PLHIV. Finally, our study did not include PLHIV having any severe psychiatric or cognitive disorder. This was because survey respondents were required to have sufficient cognitive capacity to answer the questionnaires [51]. However, there is a need to implement strategies to facilitate the participation of PLHIV who suffer from those disorders because they may be underrepresented in quality-of-life assessments, and their needs and experiences may not be taken into account in interventions to improve quality of life.

Conclusions

This study demonstrates the validity and reliability of the Spanish version of WHOQOL-HIV-BREF. It also provides evidence about HRQoL in PLHIV in Spain by using the largest study sample to date. Long-term survivors, older adults, and women are key populations to address in order to improve HRQoL. Monitoring of HRQoL and taking steps to help patients with poor HRQoL can result in better overall health outcomes.

Additional files

Additional file 1: Studies that have made adaptations and validations of the WHOQOL-HIV-BREF. (DOCX 33 kb)

Additional file 2: Spanish translation of the HIV-specific items of the WHOQOL-HIV-BREF. (DOCX 14 kb)

Additional file 3: Known-group comparisons of the WHOQOL-HIV-BREF scores. (DOCX 26 kb)

Abbreviations

AIDS: Acquired Immune Deficiency Syndrome; ART: Antiretroviral Therapy; HIV: Human Immunodeficiency Virus; HRQoL: Health-Related Quality of Life; PLHIV: People Living with HIV; SRPB: Spirituality, Religion and Personal Beliefs domain

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Authors' contributions

MJF-RdA was the main analyst and writer of the manuscript. AL contributed by reviewing other studies, elaborating tables and improving the writing of the paper. KSH, JVL, JdA and SC contributed by reviewing other studies and improving the writing of the paper and the discussion of its findings. All authors have read and approved the final manuscript.

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Availability of data and materials
The datasets collected and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate
The Ethics Committee of the Hospital Clínico of Valencia approved the research protocol. The participants were informed of the objectives of the study and written informed consent was obtained.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

ARTICLE 3

Development of a clinic screening tool to identify burdensome health-related issues affecting people living with HIV in Spain

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This article addresses specific objectives 3, 4 and 5:

- *Gather and analyse qualitative data to determine which health-related issues are perceived to be the most burdensome by PLHIV and healthcare providers in Spain.*
- *Define the domains of the novel HIV clinic screening tool (CST-HIV) and develop items for the pilot version of this PROM.*
- *Conduct a pilot study to assess the construct and criterion validity and psychometric properties of the CST-HIV.*

Resumen

Antecedentes: numerosos problemas relacionados con la salud continúan socavando la calidad de vida de la salud (CVRS) de las personas que viven con el VIH. Desarrollamos una herramienta de detección de clínicas (CST-HIV) con el fin de identificar estos problemas en la atención clínica especializada de rutina en España.

Métodos: utilizamos los siguientes procedimientos establecidos de desarrollo de instrumentos: (1) una revisión de la literatura; (2) Cuatro discusiones de grupos focales (DGF), dos que convocaron a 16 proveedores expertos en atención al VIH, y dos que convocaron a 15 personas con VIH; (3) priorización, selección y definición de construcciones (problemas relacionados con la salud) para incluir en el CST-HIV y la redacción del grupo de artículos iniciales; y (4) un estudio piloto para analizar las propiedades psicométricas y la validez de los artículos y determinar cuáles se mantendrían en el CST-HIV final. Los guiones de las entrevistas FGD incorporaron un ejercicio para priorizar los problemas de salud que se percibían cómo los que más afectaban a la CVRS. El cuestionario en línea utilizado para el estudio piloto incluyó el grupo de artículos CST-HIV y medidas validadas de cada constructo.

Resultados: identificamos 68 artículos que informaron sobre factores asociados con la CVRS de personas con VIH. Los problemas más molestos relacionados con la salud que se identificaron en los DGF estaban relacionados con el estigma, la vulnerabilidad socioeconómica, el sueño / fatiga, el dolor, los cambios corporales, la angustia emocional y la sexualidad. Sobre la base de la revisión de la literatura y los hallazgos de DGF, seleccionamos y definimos las siguientes construcciones para incluir en el CST-HIV inicial: estigma anticipado, angustia emocional, sexualidad, apoyo social, privación material, sueño/fatiga, problemas cognitivos y síntomas físicos. Dos investigadores escribieron de seis a ocho artículos para cada constructo. A continuación, 18 expertos calificaron 47 artículos basados en su claridad, relevancia y representatividad. Las pruebas piloto se llevaron a cabo con 226 personas con VIH en España. Retuvimos 24 artículos basados en criterios empíricos que mostraron propiedades psicométricas adecuadas. El análisis factorial de confirmación confirmó la estructura de ocho factores con un buen ajuste a los datos (RSEA = 0.035, AGFI = 0.97, CFI = 0.99). Encontramos fuertes correlaciones positivas entre las ocho dimensiones del instrumento y las medidas validadas de las mismas construcciones. Asimismo, encontramos asociaciones negativas entre las dimensiones del CST-HIV y la CVRS.

Conclusión: El CST-HIV es una herramienta prometedora para su uso en la atención clínica de rutina para identificar y abordar de manera eficiente los problemas relacionados con la salud que socavan la CVRS de personas con VIH.

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Development of a Clinic Screening Tool to Identify Burdensome Health-Related Issues Affecting People Living With HIV in Spain

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Background: Numerous health-related issues continue to undermine the health and health-related quality of life (HRQoL) of people living with HIV (PLHIV). We developed a clinic screening tool (CST-HIV) for the purpose of identifying these issues in routine specialist clinical care in Spain.

Methods: We used the following established instrument development procedures: (1) a literature review; (2) four focus group discussions (FGDs), two that convened 16 expert HIV care providers, and two that convened 15 PLHIV; (3) prioritisation, selection and definition of constructs (health-related issues) to include in the CST-HIV and drafting of initial item pool; and (4) a pilot study to analyse psychometric properties and validity of items and to determine which to retain in the final CST-HIV. The FGD interview scripts incorporated an exercise to prioritise the health-related issues perceived to have the greatest negative effect on HRQoL. The online questionnaire used for the pilot study included the pool of CST-HIV items and validated measures of each construct.

Results: We identified 68 articles that reported on factors associated with the HRQoL of PLHIV. The most burdensome health-related issues identified in the FGDs related to stigma, socioeconomic vulnerability, sleep/fatigue, pain, body changes, emotional distress, and sexuality. Based on the literature review and FGD findings, we selected and defined the following constructs to include in the initial CST-HIV: anticipated stigma, emotional distress, sexuality, social support, material deprivation, sleep/fatigue, cognitive problems, and physical symptoms. Two researchers wrote six to eight items for each construct. Next, 18 experts rated 47 items based on their clarity, relevance, and representativeness. Pilot testing was carried out with 226 PLHIV in Spain. We retained 24 items based on empirical criteria that showed adequate psychometric properties. Confirmatory factor analysis confirmed the eight-factor structure with a good fit to the data (RMSEA = 0.035, AGFI = 0.97, CFI = 0.99). We found strong positive

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correlations between the instrument's eight dimensions and validated measures of the same constructs. Likewise, we found negative associations between the dimensions of the CST-HIV and HRQoL.

Conclusion: The CST-HIV is a promising tool for use in routine clinical care to efficiently identify and address health-related issues undermining the HRQoL of PLHIV.

Keywords: HIV, patient-reported outcome measure (PROM), health-related quality of life, symptom assessment, health measurement instrument, psychometrics, Spain

INTRODUCTION

Widespread access to antiretroviral therapy (ART) has enabled many people living with HIV (PLHIV) to control their infection on a long-term basis. The life expectancy of PLHIV now approaches that of the general population in resource-rich settings and has greatly increased in resource-poor settings as well (Antiretroviral Therapy Cohort Collaboration, 2017; Teeraananchai et al., 2017). However, numerous issues undermine the well-being of PLHIV, including PLHIV who are stable on ART.

Multimorbidity is more prevalent among PLHIV than members of the general population, with commonly occurring comorbidities including mental health disorders and ageing-related non-communicable diseases such as cardiovascular, liver and kidney disease (Chuah et al., 2017; Maciel et al., 2018; Smit et al., 2015). PLHIV have a high burden of symptoms of ill health such as pain, fatigue and gastrointestinal problems (Harding et al., 2010; Wilson et al., 2016; Ibarra-Barrueta et al., 2019). They furthermore face an array of challenges to their psychosocial and material well-being (Bristowe et al., 2019; Public Health England, 2020). HIV-related stigma and discrimination have far-reaching ramifications in terms of mental health, medication adherence, health-seeking behaviour, social relationships, employment and other areas of people's lives (Sweeney and Vanable, 2016; Wagener et al., 2017; Ikeda et al., 2019). PLHIV also must grapple with the emotional and practical demands of living with a complex chronic health condition that requires lifelong ongoing treatment.

In this context, it is notable that a large study in the United Kingdom found poorer health-related quality of life (HRQoL) outcomes among PLHIV than among the general population (Miners et al., 2014). This difference persisted even for the subgroup of PLHIV who were virally suppressed. Other research has found poor HRQoL outcomes in PLHIV populations to be associated with a wide range of factors, including pain, insomnia, mental health disorders and HIV-related stigma (Degroote et al., 2014; Sabin et al., 2018; Andersson et al., 2020; Kunisaki et al., 2021).

People living with HIV who have responded well to ART typically are advised to see their healthcare providers for clinical monitoring two to four times per year. These routine clinic visits present an important window of opportunity for healthcare providers to identify and address some of the problems that can contribute to poor HRQoL. However, PLHIV often encounter communication barriers with their healthcare providers and may not feel that providers are responsive to their healthcare priorities (Antunes et al., 2020; Fredericksen et al., 2020a; Okoli et al., 2020). Furthermore, providers may overlook important symptoms (Edelman et al., 2011).

In recent years, the World Health Organization (WHO) and many health systems increasingly have promoted person-centred care, which WHO describes as being "organised around the comprehensive needs of people rather than individual diseases" (McCormack et al., 2015; World Health Organization (WHO), 2016). One means of promoting good communication about people's healthcare needs is to ask patients to complete surveys known as patient-reported outcome measures (PROMs) (Wheat et al., 2018; Fredericksen et al., 2020b). There are validated PROMs focusing on numerous aspects of health and well-being, including generic PROMs designed for all patient populations as well as PROMS that reflect the concerns of patients with specific diseases and conditions including HIV.

A 2017 review of HIV-specific PROMs identified 117 validated instruments for measuring patients' perceptions of their health and related issues in areas such as medication adherence, symptoms, psychological challenges, HIV-related stigma, social support, and sexual and reproductive health (Engler et al., 2017). Because these instruments typically focus on narrow topics, it would be necessary to use multiple instruments to learn about different aspects of a patient's well-being. The time-intensive nature of such an approach points to a need for broadly focused PROMs that are short enough to be easily integrated into routine clinic visits, enabling healthcare providers to quickly determine which of many potential health-related problems should be addressed in these visits. Despite the contribution that this type of PROM could make to routine clinical care, this remains an area under development. The only such instrument that we are aware of in the HIV field is currently being developed by Bristowe et al. (2019, 2020), with the content of the instrument guided by qualitative research involving PLHIV and other key stakeholders in England and Ireland.

The present study is part of a broader research project to improve the HRQoL and the long-term health of PLHIV in Spain and Italy. It constitutes the first stage of the research, and its aim is to develop a brief Spanish clinic screening tool (CST-HIV) that can be used in routine clinical care to identify problems that undermine the HRQoL of PLHIV. This paper reports the process of developing the instrument to ensure its content and face validity, describes the psychometric properties of the instrument, and presents the evidence of construct and criterion validity that we obtained when we piloted the instrument.

MATERIALS AND METHODS

Study Design

This study comprised several steps, including a literature review, a qualitative study, an item design process, a cognitive debriefing study, and a pilot cross-sectional *ex post-facto* study to analyse the psychometric properties of the initial version of the CST-HIV. **Table 1** summarises the research design, procedures and participants involved. All of these steps will be detailed in the following sections.

Participants

A total of 31 persons participated in the qualitative study to identify the initial dimensions of the CST-HIV. Sixteen of them were expert service providers from diverse disciplines (physicians, nurses, psychiatrists, psychologists, and staff of non-governmental organisations [NGOs]). The remaining 15 were PLHIV. Six of the experts and also six of the PLHIV were cis-women. Among PLHIV, one transgender woman also participated. The other participants were cis-men.

A total of 18 multidisciplinary experts from diverse disciplines and areas of expertise, three of whom were PLHIV, participated in the expert assessment and inter-rater process to develop the initial pool of items.

Eight PLHIV, five men and three women, participated in the cognitive debriefing of the CST-HIV items. Next, we conducted the pilot study investigating the item pool's psychometric properties in a sample of 226 PLHIV from different regions of Spain. The sample size was determined in accordance with the sample size requirements for carrying out confirmatory factor analysis (Bentler and Chou, 1987). Since these requirements call for 10 participants per item, and we anticipated that the final number of CST-HIV items would be between 21 and 24, our target sample size was between 210 and 240 PLHIV. The inclusion criteria were having an HIV-positive diagnosis, being at least 18 years old, and not having any severe psychiatric or cognitive disorders. Excluding people with such disorders is standard in studies in which participants complete self-administered surveys since the presence of such disorders could affect one's cognitive capacity to understand questions and provide reliable responses.

TABLE 1 | Summary of research design.

Steps		Procedures	Participants involved
Step 1	Literature review	Identification of initial domains	Authors
Step 2	Qualitative study with focus groups	Identification of initial domains	*N* = 15 PLHIV *N* = 16 experts *N* = 31 Total
Step 3	Development of initial pool of items	Definition of constructs and drafting of items	*N* = 3
		Expert assessment and inter-rater process	*N* = 18
		Cognitive debriefing	*N* = 8
Step 4	Pilot study	Assessment of psychometric properties and validity of items	*N* = 226

PLHIV, people living with HIV.

Table 2 shows the sociodemographic and clinical characteristics of pilot study participants. Most of them were male and homosexual, and the most commonly reported mode of HIV infection was sexual intercourse. The mean age was 44. Approximately one-third of the participants had a university degree, and 39% were employed. Sixty-eight percent reported having a personal monthly income of €900 or less. The immunological and virological HIV status of most participants were good.

Procedure

This research took place from April 2019 to October 2020. The Ethics Committee of the Hospital Clínic of Barcelona, Spain, approved all research procedures. Participants in all phases signed informed consent forms before data collection began.

The HIV Clinic Screening Tool (CST-HIV) was developed through the following well-established methodological steps (Eignor, 2001; Revicki et al., 2007).

Firstly, we conducted an exploratory literature review to obtain information about issues that undermine the well-being of PLHIV and to identify themes that would warrant further exploration in focus group discussions (FGDs). We identified English-language peer-reviewed articles and conference abstracts indexed in PubMed using search strings that addressed two major lines of research: HIV symptom burden and predictors of HRQoL in PLHIV. We used appropriate selection criteria to identify the studies of greatest relevance to our study (e.g., studies reporting on adult PLHIV who are taking ART and studies reporting on the symptom burden in PLHIV from 2010 onward, in recognition that the symptom profile has changed in accordance with ART improvements). We used Scopus and ResearchGate to identify articles that cited a key source about the widely used HIV Symptom Index (Justice et al., 2001). Selected references were compiled in tables to identify evidence regarding burdensome symptoms and predictors of HRQoL in PLHIV.

Drawing on literature review findings, we conducted a qualitative study using the FGD methodology to obtain the perspectives of PLHIV and other key informants regarding the most burdensome health-related problems facing PLHIV. We carried out four FGDs. Two of them enrolled HIV service providers (n = 8 per FGD), and the other two enrolled PLHIV (n = 8 and n = 7). Participants in the service provider FGDs were selected via purposive sampling to ensure the representation of different types of providers such as physicians, nurses, psychiatrists, psychologists, and NGO staff. Service providers worked in Barcelona, Bilbao, Madrid, Seville, and Valencia. Participants in the PLHIV FGDs were selected via purposive sampling to ensure diverse epidemiological profiles in terms of age, sex, sexual orientation, and drug use history. One PLHIV FGD was comprised of clients of an NGO providing HIV services in Barcelona, and the other PLHIV FGD was comprised of patients at the HIV outpatient clinic of a large Barcelona university hospital. FGDs took place in April and May 2019, with each one lasting approximately two hours. Facilitators used

TABLE 2 | Characteristics of pilot study participants (*N* = 226).

Sociodemographic and clinical variables	% (*n*)
Age, mean (*M* ± *SD*)	43.81 ± 11.15
Gender	
Male	75.7 (171)
Female	21.7 (49)
Transgender	1.3 (3)
Other	1.3 (3)
Sexual orientation	
Heterosexual	41.2 (93)
Homosexual	54.9 (124)
Bisexual	2.2 (5)
Other	1.3 (3)
No answer	0.4 (1)
Education level	
No education	2.2 (5)
Elementary school	19.9 (45)
High school	44.2 (100)
University degree	32.3 (73)
Other	1.3 (3)
Work situation	
Working	38.9 (88)
Unemployed	28.3 (64)
Retired/on disability	21.2 (48)
Other	11.5 (26)
Personal monthly income	
None	12.8 (29)
≤ 300 €	13.7 (31)
301–600 €	17.3 (39)
601–900 €	24.3 (55)
901–1200 €	13.7 (31)
1201–1800 €	11.9 (27)
1801–2400 €	3.1 (7)
2401–3000 €	0.4 (1)
3001–4500 €	0.9 (2)
No answer	1.8 (4)
Housing	
Own home (rent or own)	56.6 (128)
Family home	12.8 (29)
Shared home	16.8 (38)
Someone else's home	1.3 (3)
Shelter/institution	6.6 (15)
Other	5.8 (13)
HIV transmission route	
Sexual intercourse	78.3 (177)
Sharing injection materials	10.6 (24)
Unknown	8.8 (20)
Other	2.2 (5)
CD4 cell count, cells/mm^3	
≤ 200	7.5 (17)
201–400	7.1 (16)
> 400	53.5 (121)
Unknown	31.9 (72)
Duration of infection, years, mean (*M* ± *SD*)	14.18 ± 10.47
Undetectable plasma viral load	92.5 (209)

Data in percentages unless otherwise stated.

semi-structured scripts with open-ended questions and prompts to guide the discussions.

The next step in the development of the CST-HIV consisted of developing a pool of potential items. Based on findings from the FGDs and the literature reviews, three members of the research team selected the most prevalent and burdensome health-related problems undermining the HRQoL of PLHIV. Also, they defined the constructs (the health-related problems) after deliberation (Nunnally and Bernstein, 1994). Items were developed to measure each construct, following psychometric recommendations (Osterlind, 1989; Haladyna et al., 2002), and the response format for the items was decided. A team of 18 multidisciplinary experts rated the items based on their clarity, relevance and representativeness. Based on the experts' ratings and comments, items were selected and reworded as appropriate to create the initial item pool. A cognitive debriefing study was then carried out, in which eight PLHIV rated the understandability of the items. These participants were members of the NGO collaborators in the research.

Finally, we conducted a pilot study to assess the initial items' psychometric properties and to select those that would be part of the final CST-HIV. We recruited participants through NGO collaborators, and we asked those who agreed to participate to complete an online questionnaire using Qualtrics[1], a private online survey development platform.

Measures

For the qualitative study, we designed a semi-structured FGD script addressing two central questions: (1) "In your opinion, what are the health-related problems that have the most significant negative effect on the quality of life of PLHIV?"; and (2) "Among the problems that you have identified, what do you think are the most important ones to include in a short diagnostic questionnaire?" All FGD participants were also asked to carry out a prioritisation exercise in which they selected what they believed to be the most burdensome issues from among all issues identified during the discussions.

The online questionnaire used for the pilot study included the 40 items selected after the inter-rater process. We selected brief instruments to measure preliminary evidence of the convergent validity of each CST-HIV dimension. We chose instruments according to their psychometric properties, validity, and availability of cut-off points. When a Spanish version of an instrument was available, we used it. When it was not, we conducted a backward translation of the instrument. The questionnaire included the following instruments:

Anticipated Stigma

The factors of disclosure concerns and public stigma of the Spanish Stigma Scale measured through 13 items were used (Fuster-RuizdeApodaca et al., 2015). Results of the Spanish adaptation of the instrument indicated that these two factors could be grouped in a latent second-order dimension related to internalised stigma (Fuster-RuizdeApodaca et al., 2015). The scale is rated on a four-point response format (*1 = strongly*

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[1] www.qualtrics.com

disagree, 4 = strongly agree), with higher scores indicating greater concerns.

Emotional Distress

We used the Patient Health Questionnaire-4 (PHQ-4) (Kroenke et al., 2009) and the Spanish version of the Hospital Anxiety and Depression Scale (HADS) (Tejero et al., 1986). The PHQ-4 is a validated ultra-brief screening tool that has a two-factor structure, one containing two anxiety items (GAD-2) and the other containing two depression items (PHQ-2). Responses are scored from 0 (*not at all*) to 3 (*nearly every day*). The total score on this measure ranges from 0 to 12. The HADS is a 14-item, self-reporting screening scale that contains two seven-item Likert scales, one for anxiety and one for depression. Each item is answered by the patient on a four-point (0–3) response category, and thus the possible scores range from 0 to 21 for anxiety and 0 to 21 for depression.

Sexuality

We used the PROMIS V2.0 Satisfaction with Sex Life scale (Weinfurt et al., 2015), which is part of the modular and customisable PROMIS Sexual Function and Satisfaction 2.0 measures that assess multiple components of sexual functioning. The Satisfaction with Sex Life module assesses how satisfying and pleasurable the person regards his or her sexual activities, with no constraints on how the person defines "sex life". Items are gender-non-specific. Higher scores indicate more satisfying sexual experiences.

Social Support

The Duke-UNC Functional Social Support Questionnaire was selected (Broadhead et al., 1988). It is an 11-item scale measuring two dimensions of social support: confidant support and affective support. Items have a five-point Likert format response. Higher scores indicate higher social support.

Material Deprivation

We used the Social Exclusion Index for Health Surveys (SEI-HS) (Van Bergen et al., 2017). This instrument contains 17 items that measure four dimensions: (1) social participation; (2) normative integration; (3) material deprivation; and (4) access to basic social rights.

Sleep Problems

We used the Spanish version of the Insomnia Severity Index (ISI) (Bastien et al., 2001; Fernandez-Mendoza et al., 2012). This seven-item index is a reliable measure for evaluating perceived sleep difficulties. Each item is rated on a 5-point Likert scale (*0 = no problem, 4 = very severe problem*), yielding a total score ranging from 0 to 28.

Fatigue

We used the seven-item version of the Fatigue Severity Scale (FSS), which has demonstrated good psychometric properties in PLHIV (Lerdal et al., 2011). Each item is rated on a seven-point Likert-scale (*1 = strongly disagree, 7 = strongly agree*). The mean score is used to estimate fatigue severity.

Cognitive Problems

The Neuro-QoL V2.0 Cognitive Function measure was used for cognitive assessment (Lai et al., 2014). This eight-item scale measures both cognitive function concerns and abilities.

HRQoL

We used the HIV-specific WHOQoL-HIV-BREF measure that has been validated in Spanish (Fuster-RuizdeApodaca et al., 2019). The instrument has 31 items covering six domains: physical health; psychological health; level of independence; environmental health; social relationships; and spirituality, religion and personal beliefs (SRPB). It additionally has a general health dimension assessing one's overall perception of one's health and HRQoL. All items use a five-point scale. Negative items are reverse-coded for scoring. Thus, higher scores for all items indicate better HRQoL.

We also used the generic HRQoL measure EQ-5D-5L, which has five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Responses are provided on a five-point scale ranging from "no problems" to "extreme problems" (Herdman et al., 2011).

The online questionnaire also included a section that requested health and sociodemographic data.

Data Analysis

To analyse the qualitative data, we performed directed content analysis (Mayring, 2000) using MAXQDA 12 software. The FGDs were transcribed, reviewed for accuracy, and coded. Inductive and deductive coding were used to identify relevant concepts, and an analysis of these concepts led to the identification of key categories and subcategories of health-related problems. We also performed a quantitative analysis of the qualitative data to determine the number of times each code and category was used. Two analysts discussed and agreed on the data categorisation, with inconsistencies resolved by consensus. Following the coding of the FGD content, all research team members reviewed and approved the final categorisation of data.

To analyse the content validity of the initial pool of items evaluated in the inter-rater process, we calculated the Osterlind Index (Osterlind, 1989) for the items' representativeness and relevance scores. Representativeness and relevance items had a three-point ordinal response (high, medium, low). There is no clear criterion regarding a cut-off point for this index; some use 0.5 and others 0.75 depending on the objective. We used a strict criterion in most dimensions, selecting items with an Osterlind Index of up to 0.75.

In the pilot study, we assessed the psychometric properties of the initial CST-HIV item pool based on empirical criteria. We assessed the floor and ceiling effects, the internal consistency, the reliability, and the validity index of each dimension (Kline, 2013). Most items in the online questionnaire in the Qualtrics survey platform were programmed for compulsory completion. Thus, there were no missing values in the variables collected.

Next, to test the construct validity, first-order confirmatory factor analysis (CFA) was used to assess the retained CST-HIV items' fit with the theoretical proposed structure. Due to the ordinal nature of our data and the sample size, we chose the robust unweighted least-squares extraction method (ULS) (Batista-Foguet and Coenders, 2000; Holgado-Tello et al., 2009; Holgado–Tello et al., 2010). Although the weighted least squares method also could be used, we did not use it because of the instability of its inverse matrix when the models have more than ten variables or a moderate sample size (Holgado-Tello et al., 2018; Holgado-Tello et al., 2009; Satorra, 1990). The goodness of fit was evaluated using several absolute and relative fit indices, including the goodness of fit index (GFI), the adjusted goodness of fit index (AGFI), the comparative fit index (CFI), the standardised root mean square residual (SRMR) and the standardised root mean square error of approximation (RMSEA). A model is considered to have a good fit when the goodness of fit indices (GFI and AGFI) and CFI are greater than 0.90, RMSEA is lower than 0.08, and SRMR is lower than 0.08 (Hu and Bentler, 1995).

We then calculated reliability and construct statistics of the CST-HIV including the Cronbach's alpha coefficient to assess internal consistency, the average extracted variance (AVE) to assess convergent validity, and the Jöreskog rho (Omega) to assess construct reliability (Fornell and Larcker, 2016). Cronbach's alpha coefficients between 0.70 and 0.90 are adequate, and between 0.60 and 0.70 are acceptable (Kline, 2013). AVE values greater than 0.50 indicate convergent validity, and Omega coefficients between 0.70 and 0.90 are considered to represent acceptable construct reliability (Campo-Arias and Oviedo, 2008), although in some circumstances, values higher than 0.65 can be accepted (Katz, 2006).

Convergent and concurrent validity were analysed by calculating the Pearson correlation between each CST-HIV dimension and the validated instruments used to measure the constructs and HRQoL. We expected each dimension to correlate positively with its convergent criterion measure and negatively with HRQoL.

Regarding the data analysis software, LISREL (LInear Structural RELations) 8.7 and its companion preprocessor programme PRELIS for Windows were used for the CFAs (Jöreskog and Sörbom, 1996). IBM SPSS Statistics 22 (IBM Corp, 2013) was used for the remaining analyses.

RESULTS

Step One – Identification of Dimensions to Include in the CST-HIV: Literature Review

The literature review on the HIV symptom burden identified five articles and two conference abstracts that were relevant to the current study. The symptoms that were most commonly reported to be highly prevalent in PLHIV were sleep-related problems, fatigue, and muscle/joint pain (Erdbeer et al., 2014; McGowan et al., 2014; Wilson et al., 2016; Schnall et al., 2018; Cioe et al., 2019; Ibarra-Barrueta et al., 2019; Schnall et al., 2019). Other highly prevalent symptoms observed in some studies included anxiety, depression, sexual dysfunction, changes in body appearance, and gastrointestinal problems (Erdbeer et al., 2014; Wilson et al., 2016; Schnall et al., 2018; Ibarra-Barrueta et al., 2019).

The HRQoL literature review identified a large body of relevant research on factors associated with HRQoL outcomes in PLHIV, including a 2014 review article (Degroote et al., 2014). We analysed the findings of the review article and 68 additional articles that reported on more recent studies. We observed that one of the factors most commonly reported to be associated with positive HRQoL outcomes in PLHIV is social support (Bekele et al., 2013; Emlet et al., 2013; Slater et al., 2013; Dalmida et al., 2015; George et al., 2016; Nideröst and Imhof, 2016; den Daas et al., 2019). Two factors associated with negative HRQoL outcomes in many studies are depression and material insecurity (e.g., unemployment, financial problems, unmet needs for food and housing) (Douab et al., 2014; Dalmida et al., 2015; Ballester-Arnal et al., 2016; George et al., 2016; Nideröst and Imhof, 2016; Catalan et al., 2017; Logie et al., 2018; Sok et al., 2018; Olson et al., 2019). Other factors associated with negative HRQoL outcomes in some studies included comorbidity, stigma and HIV disclosure concerns (Emlet et al., 2013; Slater et al., 2013; Fekete et al., 2016; George et al., 2016; Nideröst and Imhof, 2016; Logie et al., 2018; Reinius et al., 2018). A high symptom burden was also associated with negative HRQoL outcomes, as were specific symptoms such as body disfigurement, memory difficulties and sexual functioning (Ballester-Arnal et al., 2016; George et al., 2016; Brandt et al., 2017; den Daas et al., 2019; Olson et al., 2019).

Step Two – A Qualitative Study With Focus Groups to Identify the Most Burdensome Health-Related Problems Undermining HRQoL in PLHIV

Focus group discussion participants identified many issues that impact the HRQoL of PLHIV. The issue raised most frequently by both PLHIV and healthcare providers was stigma/discrimination (n = 150 segments coded), with people commenting far more on this issue than on physical symptoms or emotional problems. The category of physical symptoms was the second-most frequently discussed (n = 83 segments coded). The physical symptom noted most often was sleep problems. Other physical symptoms that were frequently mentioned included fatigue, pain, body fat changes, and neurocognitive problems. Both PLHIV and healthcare providers emphasised the importance of psychological well-being (n = 67 segments coded). They often commented on emotional distress in general terms rather than naming specific disorders, although depression and anxiety were mentioned numerous times. Healthcare providers, and to a lesser extent PLHIV, called attention to sexuality-related problems such as lack of libido, sexually transmitted infections and general sexual dissatisfaction. When PLHIV addressed sexuality-related problems, they often linked these problems to their perceptions about HIV-related stigma.

Step Three – Development of Potential CST-HIV Items

The initial item pool was developed through the following steps:

(a) Selection and definition of the constructs to include in the CST-HIV. A theoretical conceptualisation of the selected health-related problems undermining HRQoL was carried out, taking into account the content analysis of the FGDs and the literature review. A total of eight constructs were selected: anticipated stigma, emotional distress, sexuality, social support, material deprivation, sleep/fatigue, cognitive problems, and physical symptoms. Three members of the research team wrote independent definitions for the constructs. They then met to reach agreement about definitions and about the essential components that should be included in the instrument.

(b) Development and writing of items. First, we conducted a review of validated instruments measuring the constructs selected for inclusion in the CST-HIV. The same three researchers selected the items that most closely represented the components of each construct. Drawing on these items and the definitions of constructs, two Spanish researchers adapted or wrote six to eight items for each construct. Psychometric recommendations for the development of items were followed (Nunnally and Bernstein, 1994), with the following criteria taken into account: clarity (i.e., items should be written in short, simple and intelligible sentences, and should avoid excessive generality); relevance (i.e., content should be clearly related to the construct); and representativeness (i.e., items should be representative of the construct). This process yielded an initial pool of 47 items.

(c) Expert assessment and inter-rater process. The 18 participating experts rated the items based on their clarity, relevance and representativeness. They also assessed whether the items required modification, and provided further input in comments. This process led to the elimination of seven items. Sixteen other items were modified in response to suggestions from experts. The item pool to be evaluated in the pilot study was comprised of 40 items. **Table 3** shows the items and their Osterlind Index scores for representativeness/relevance. All of the experts agreed on the five-point response format that was proposed for the items.

(d) Cognitive debriefing interview. Eight PLHIV completed a questionnaire containing the selected items, then reported to a member of the research team about possible difficulties in understanding the questionnaire. The items were generally regarded as relevant, accessible, and easy to understand and answer.

Step Four – A Pilot Study to Analyse the Psychometric Properties of the CST-HIV Items

The pilot study enrolled 226 PLHIV. Data collection was carried out with the collaboration of NGOs from the following Spanish cities: Alicante, Barcelona, Bilbao, Madrid, Malaga, and Seville.

Assessment and Selection of the Items

Because our goal was to create a brief instrument that was feasible to use in clinical practice, we had previously decided that no more than three items should be selected for each construct. Any item was eliminated because of ceiling or floor effects. We considered each item's reliability and validity indices to select the three items that would maximise the reliability and representation of each construct. **Table 3** presents all piloted items, indicating their psychometric properties and the retained items. The Spanish wording of items is provided in **Supplementary Table 1**.

Construct Validity: Confirmatory Factor Analysis Results

The Confirmatory Factor Analysis (CFA) results confirmed the eight-factor structure with a good fit to the data. All of the standardised loadings were higher than 0.5, the level considered adequate (Green, 1978). The results of the fully standardised solution including fit indices of the model are displayed in **Table 4**. **Table 5** reports the covariance among factors. The highest covariance was found between the physical symptoms dimension and three other dimensions: emotional distress, sleep/fatigue, and cognitive problems.

Internal Consistency

Despite the low number of items, most of the dimensions presented an alpha index of close to or $\geq$ 0.70, with the notable exception of the physical symptoms dimension (**Table 6**). However, since the number of items is crucial for Cronbach's alpha, values lower than 0.70 for scales with only two or three items may not be considered an indicator of low consistency. As can be seen in **Table 6**, estimates of reliability were higher using the Jöreskog rho (omega) coefficient because the Cronbach's alpha underestimates reliability in ordinal data (Bentler, 2009). Omega is based on the loadings rather than the correlations between the observed variables.

Regarding validity, we calculated the Average Variance Extracted (AVE) values for all variables. All of them except for physical symptoms were above the critical threshold of 0.50, indicating good convergent validity. The AVE measures the amount of variance that is captured by the construct in relation to the amount of variance due to measurement error (Fornell and Larcker, 2016); thus, an AVE value greater than 0.50 indicates that the variance captured by the construct is larger than the amount of variance due to measurement error.

Convergent and Concurrent Validity

We found high positive correlations between the CST-HIV dimensions and the validated measures of the same constructs (**Table 7**). Also, we found correlations in the expected direction between each CST-HIV dimension and the validated instruments used to assess the convergent validity of the other CST-HIV dimensions.

We found negative associations between the eight dimensions of the CST-HIV and the dimensions of HRQoL measured using the disease-specific instrument WHOQOL-HIV-BREF. As can be seen in **Table 8**, most of the correlations were moderate to high. We also found negative associations between most of the

TABLE 3 | Psychometric properties of the initial pool of items of the CST-HIV.

CST-HIV dimensions and items	Osterlind Index (representativeness/ relevance)	Mean ± SD	Skewness	Kurtosis	Corrected item-domain correlation	Cronbach's α if item is deleted	Reliability Index	Validity Index
Anticipated Stigma[a] ($\alpha = 0.877$)								
During the past month, to what extent have you been worried...								
S1... about telling someone you have HIV?[1]	0.94/1.00	2.62 ± 1.51	0.40	−1.30	0.694	0.859	1.04	0.84
S3... about people judging you if they learn you have HIV?[1]	1.00/0.94	2.95 ± 1.45	0.06	−1.39	0.824	0.807	1.19	0.98
S4... about the idea that you can't find a partner because you have HIV?	0.94/0.94	2.66 ± 1.43	0.32	−1.24	0.618	0.886	0.89	0.74
S5m... about people rejecting you for having HIV?[1,2]	1.00/1.00	2.86 ± 1.43	0.12	−1.33	0.815	0.812	1.16	0.97
Emotional distress[b] ($\alpha = 0.901$)								
During the past month, how often...								
E1m... have you had negative feelings? (for example, sadness, despair, low spirits, or anxiety?[2])	1.00/1.00	3.04 ± 1.01	−0.35	−0.76	0.789	0.872	0.79	0.64
E2m... have you felt anxiety?[1]	0.88/0.89	2.94 ± 1.11	−0.33	−0.82	0.800	0.869	0.88	0.75
E3m... have you felt sadness or discouraged?[1,2]	0.88/0.83	2.95 ± 1.06	−0.33	−0.85	0.825	0.866	0.86	0.67
E5... have you felt fearful of the future?[1]	0.76/0.83	3.01 ± 1.24	−0.09	−0.99	0.744	0.881	0.92	0.69
E6m... have you been concerned for your future because of having HIV?[2]	0.81/0.88	2.74 ± 1.33	0.14	−1.19	0.647	0.907	0.86	0.66
Sexuality[a] ($\alpha = 0.734$)								
During the past month...								
Sx1m... how satisfied have you felt with your sex life?[1,2,3]	0.82/0.94	3.03 ± 1.21	−0.23	−0.96	0.310	0.736	0.37	0.88
Sx2... has your sex drive or interest in sex decreased?[1]	1.00/1.00	2.72 ± 1.26	0.02	−1.10	0.380	0.720	0.48	0.52
Sx3m... how difficult has it been to start an intimate or sexual relationship with a new partner?[2]	0.88/0.94	2.83 ± 1.47	0.10	−1.37	0.510	0.685	0.75	0.48
Sx4m... how fearful have you been of being rejected by a sexual partner for having HIV?[2]	0.94/0.94	2.96 ± 1.52	0.04	−1.46	0.616	0.649	0.94	0.29
Sx5... how worried have you been about transmitting HIV to a sexual partner?	1.00/1.00	2.84 ± 1.66	0.14	−1.64	0.458	0.700	0.76	0.06
Sx6... has HIV negatively affected your sex life?[1]	0.94/0.94	2.52 ± 1.33	0.39	−1.03	0.572	0.670	0.76	0.50
Social Support[b] ($\alpha = 0.837$)								
During the past month, how often...								
SS1m... have you had people around you whom you can lean on in case of need?[1,2,3]	0.88/0.82	3.62 ± 1.18	−0.39	−0.85	0.699	0.787	0.82	0.61
SS2... have you had someone you trust to speak to about your problems?[1,3]	1.00/1.00	3.61 ± 1.21	−0.45	−0.75	0.657	0.800	0.79	0.58
SS3... have people made you feel loved?[1,2]	0.82/0.89	3.83 ± 1.08	−0.67	−0.27	0.739	0.777	0.80	0.63
SS4... have you felt isolated from other people?	1.00/1.00	2.49 ± 1.01	0.13	−0.81	0.486	0.843	0.49	0.48
SS6... have you felt alone?	0.82/0.83	2.83 ± 1.15	−0.10	−0.89	0.622	0.809	0.71	0.55
Material deprivation[a] ($\alpha = 0.774$)								
During the past month...								
Ex1... how concerned have you been about your economic situation?	0.94/0.89	3.45 ± 1.31	−0.44	0.96	0.580	0.720	0.76	0.46
Ex3... have you had enough money to meet your needs?[1]	0.94/0.94	3.01 ± 1.01	−0.03	−0.80	0.646	0.703	0.65	0.58
Ex4m... how satisfied have you been with the quality of the place where you live?[1,2,3]	0.47/0.61	3.52 ± 1.10	−0.49	−0.48	0.344	0.792	0.38	0.60

(Continued)

TABLE 3 | Continued

CST-HIV dimensions and items	Osterlind Index (representativeness/relevance)	Mean ± SD	Skewness	Kurtosis	Corrected item-domain correlation	Cronbach's α if item is deleted	Reliability Index	Validity Index
Ex5m. . . have you had money for leisure activities?[1,2,3]	0.47/0.72	2.71 ± 1.21	0.15	−0.97	0.717	0.672	0.87	0.75
Ex6m. . . how worried have you been about keeping your home in the short term?[2]	0.88/0.88	2.81 ± 1.39	0.12	−1.26	0.483	0.759	0.66	0.44
Sleep and fatigue[a] ($\alpha = 0.827$)								
During the past month. . .								
SF1. . . have you had sleep problems?[1]	1.00/1.00	3.12 ± 1.31	−0.20	−1.04	0.571	0.815	0.75	0.89
SF3. . . have you had enough energy to do the things you would like to?[3]	1.00/0.94	3.22 ± 1.06	−0.16	−0.73	0.586	0.803	0.62	0.40
SF5m. . . have you had enough energy for your daily life activities?[2,3]	0.94/0.94	3.29 ± 0.97	−0.08	−0.62	0.627	0.794	0.61	0.44
SF7. . . how satisfied have you felt with the quality of your sleep?[1,3]	0.94/0.94	2.89 ± 1.14	0.01	−0.82	0.698	0.770	0.79	0.65
SF8. . . how tired have you felt?[1]	0.88/0.94	3.30 ± 1.01	−0.17	−0.42	0.663	0.782	0.67	0.54
Cognitive problems[a] ($\alpha = 0.924$)								
During the past month. . .								
CG1. . . do you feel you've lost memory or capacity to focus or to organise yourself?	0.94/1.00	2.80 ± 1.22	0.09	−0.96	0.769	0.911	0.93	0.71
CG2m. . . how difficult has it been for you to remember things?[2]	1.00/1.00	2.77 ± 1.13	0.09	−0.73	0.822	0.905	0.93	0.71
CG3. . . how difficult has it been for you to make decisions?	0.88/0.89	2.71 ± 1.14	0.03	−0.96	0.737	0.916	0.84	0.71
CG4. . . have you had difficulty thinking clearly?[1]	0.88/0.89	2.55 ± 1.15	0.23	−0.94	0.795	0.908	0.91	0.76
CG7. . . have you had difficulty paying attention?[1]	0.65/0.67	2.65 ± 1.17	0.12	−0.96	0.836	0.902	0.98	0.76
CG8 . . . do you think that it has been harder for you to learn new things?[1]	1.00/1.00	2.62 ± 1.22	0.24	−1.05	0.729	0.917	0.89	0.79
Physical symptoms[a] ($\alpha = 0.729$)								
During the past month. . .								
PS1m. . . have you experienced unpleasant body changes such as fat accumulation, weight gain, or weight loss?[1,2]	0.94/0.89	2.68 ± 1.26	0.19	−1.01	0.550	0.649	0.69	0.49
PS2. . . how worried have you been about experiencing future body changes?	0.76/0.78	3.11 ± 1.27	−0.22	−1.04	0.586	0.627	0.74	0.49
PS3. . . have you felt pain somewhere in your body? (for example, headache, joint pain, muscle cramps)[1]	0.89/1.00	3.04 ± 1.20	−0.24	−0.84	0.504	0.677	0.60	0.66
PS5. . . have you suffered digestive problems? (stomach pain, flatulence, diarrhea, nausea, or vomiting)[1]	0.94/0.89	2.62 ± 1.31	0.26	−1.13	0.440	0.715	0.58	0.58

[1] *Item selected for final CST-HIV.*
[2] *Item slightly reworded after inter-judgement process.*
[3] *Reverse item.*
[a] *Response category labels: 1, None; 2, Slightly; 3, Somewhat; 4, Quite; 5, Extremely.*
[b] *Response category labels: 1, Never; 2, Rarely; 3, Sometimes; 4, Frequently; 5, Always.*

CST-HIV dimensions and the generic measure of HRQoL EQ-5D-5L, with the exception of the anticipated stigma and sexuality dimensions (**Table 7**).

CST-HIV Scores

Table 5 reports the CST-HIV dimension scores. These were calculated by adding the values corresponding to each response after recoding the positive items. Thus, higher scores indicate a higher burden in the construct measured in the dimension. All scores were higher than the theoretical mean of the scale except for social support ($M = 6.95$, $SD = 3.10$), although that score was close to it. The highest score was found in the sleep/fatigue dimension ($M = 9.52$, $SD = 2.97$), followed by emotional distress ($M = 8.90$, $SD = 3.03$) and material deprivation ($M = 8.76$, $SD = 2.80$).

TABLE 4 | Standardised estimations for the first-order confirmatory factor analysis model.

CST-HIV dimensions and items	Lambda (λ)
Anticipated stigma	
S1	0.70
S3	0.97
S5m	0.98
Emotional distress	
E2m	0.90
E3m	0.93
E5	0.79
Sexuality	
Sx1m[a]	0.57
Sx2	0.76
Sx6	0.82
Social support	
SS1m[a]	0.83
SS2[a]	0.85
SS3	0.93
Material deprivation	
Ex3[a]	0.71
Ex4m[a]	0.61
Ex5m[a]	0.97
Sleep and fatigue	
SF1	0.75
SF7[a]	0.72
SF8	0.88
Cognitive problems	
CG4	0.94
CG7	0.89
CG8	0.79
Physical symptoms	
PS1m	0.60
PS3	0.69
PS5	0.62
SB-χ*2*	285.09
Degrees of freedom	224
p	0.0036
RMSEA [90% CI]	0.035 (0.021;0.046)
SRMR	0.053
GFI	0.98
AGFI	0.97
CFI	0.99
NFI	0.96

N = 226. Estimation of the robust unweighted least squares. SB-χ^2, Satorra-Bentler chi-square; RMSEA, root mean square error of approximation; CI, confidence interval; SRMR, standardised root mean square residual; GFI, goodness of fit index; AGFI, adjusted goodness of fit index; CFI, comparative fit index; NFI, normed fit index.

[a] Reversed items recoded.

All factor loadings $p < 0.05$.

DISCUSSION

The present paper described the development and psychometric properties of a clinic screening tool to facilitate the rapid identification of problems that undermine the HRQoL of PLHIV in Spain. The results indicate that this new measure could be useful for achieving the intended objective. The CST-HIV showed adequate psychometric properties and evidence of content, face, construct and criterion validity. Although this preliminary evidence of validity should be confirmed in a broad validation study, the results enable us to state that a new brief PROM to identify burdensome problems experienced by PLHIV in routine clinical care is now available.

This new instrument has several strengths. It was developed following a robust methodological process that used both qualitative and quantitative data, in accordance with best practices for ensuring content validity (Pedrosa et al., 2014). The selection of the instrument's content was based on a relevant literature review and on the findings of a qualitative study that included PLHIV and multidisciplinary experts. These procedures allowed us to learn firsthand and from multiple perspectives the problems that undermine the HRQoL of PLHIV in Spain. Findings guided us in determining which issues to prioritise for inclusion in the CST-HIV. The selected issues – anticipated stigma, emotional distress, sexuality, social support, material deprivation, sleep/fatigue, cognitive problems, and physical symptoms – are consistent with research findings about social, psychological, and symptom issues prevalent in Spain (Muñoz-Moreno et al., 2013; Fuster-RuizdeApodaca et al., 2015; Fuster-RuizdeApodaca et al., 2019).

The selected issues are quite similar to those chosen for inclusion in a recent PROM developed by Bristowe et al. (2020) and colleagues on the basis of research conducted in England and Ireland. Those authors have reported the content and face validity of their new instrument. They defined six initial dimensions – physical, cognitive, psychological, welfare, social/relational, and information – and their final version of the instrument is comprised of 23 items. Many of the items are similar to CST-HIV items. However, the other instrument includes some issues that were not considered high priorities by our study participants. These issues included information needs, conception and contraception issues, immigration problems, and alcohol and drug use. Most of these issues also arose during our FGDs, but were not emphasised to the same degree as other issues that we selected for inclusion in our CST-HIV. Several reasons could explain this, such as differences in the epidemiological and socioeconomic profiles of PLHIV whose experiences informed instrument development, differences in the nature of the health-related issues that impose the greatest burden in different settings, and cultural differences that affect how these issues are conceptualised by PLHIV and service providers (Regnault and Herdman, 2015; Nobre et al., 2016). A potential avenue of future research is to explore whether new CST-HIV modules might be developed to add dimensions that are relevant to PLHIV in Spain if this can be done without making the length of the instrument overly burdensome.

After we defined the constructs and drafted the items in accordance with psychometric recommendations, we conducted an inter-judgement process with the participation of 18 multidisciplinary experts, including PLHIV. This

TABLE 5 | Descriptive statistics and covariances (ϕ) between the CST-HIV dimensions

			Covariances (ϕ)							
CST-HIV dimensions	**M**	**SD**	**STG**	**EMD**	**SEX**	**SS**	**MAD**	**SF**	**CG**	**PHYS**
Anticipated stigma	8.43	4.00	1							
Emotional distress	8.90	3.03	0.48	1						
Sexuality	8.21	3.00	0.32	0.55	1					
Social support	6.95	3.10	0.34	0.29	0.39	1				
Material deprivation	8.76	2.80	0.26	0.38	0.40	0.52	1			
Sleep and fatigue	9.52	2.97	0.25	0.67	0.37	0.22	0.36	1		
Cognitive problems	7.82	3.17	0.19	0.63	0.30	0.23	0.26	0.59	1	
Physical symptoms	8.34	2.87	0.23	0.71	0.29	0.22	0.36	0.83	0.78	1

Overall scores for each dimension, comprised by three items, ranged from 3 to 15. M, mean; SD, standard deviation; STG, anticipated stigma; EMD, emotional distress; SEX, sexuality; SS, social support; MAD, material deprivation; SF, sleep and fatigue; CG, cognitive problems; PHYS, physical symptoms.

process guided us to select and reword items with consideration for clarity, relevance and representativeness. Furthermore, we conducted cognitive debriefing interviews that allowed us to test the face validity of the instrument. According to the previous procedures, the CST-HIV seems to be relevant to, and representative of, the targeted constructs that it is designed to measure, and it is subjectively viewed as covering the concepts that it purports to measure.

The pilot study results enabled us to select a 24-item scale considering both the reliability and validity indices of the items. We were able to estimate the validity indices because our study, despite its pilot nature, included convergent measures for each CST-HIV dimension. We selected three items per dimension, ensuring that both consistency and representation of the construct were fulfilled.

This study also provided preliminary evidence of the validity of the internal structure of the instrument. The results confirmed the eight-factor structure that was theoretically proposed. These factors were related to each other with different magnitudes. The highest covariances were found between the physical symptoms dimension and the dimensions of emotional distress, sleep/fatigue, and cognitive problems. Several studies have found relationships between these issues (Muñoz-Moreno et al., 2014; Tedaldi et al., 2015; Uebelacker et al., 2015; Allavena et al., 2016; Redman et al., 2018; Ren et al., 2018; Nogueira et al., 2019; Sabin et al., 2020). The size of the covariances suggests that these four dimensions could be grouped in a second-order latent dimension that encompasses physical, emotional and cognitive concerns. A second validation study is planned using a larger sample, and in that study it will be feasible to analyse the instrument's potential second-order structure.

The results showed that most CST-HIV dimensions presented adequate-to-good internal consistency and construct validity. The physical symptoms dimension was the one that showed the lowest internal consistency and construct validity. This result was not surprising because the dimension included three different physical symptoms, with each measured through one item (body changes, pain, and gastrointestinal problems). We decided not to eliminate the dimension for several reasons. The reliability and validity coefficients were not far from the values considered adequate (Bentler, 2009). Moreover, the construct is theoretically relevant. Several studies have shown that the symptoms included in the dimension are prevalent and burdensome (Edelman et al., 2011; Erdbeer et al., 2014; Wilson et al., 2016; Schnall et al., 2018; Ibarra-Barrueta et al., 2019). Additionally, the size of the correlations found between this dimension and other constructs such as HRQoL and psychological well-being endorse its relevance.

This study also provided preliminary evidence of criterion validity of the CST-HIV. We found high correlations between its dimensions and the measures of the convergent constructs. Furthermore, most dimensions presented moderate-to-high correlations with the HRQoL dimensions, providing evidence of concurrent validity. The anticipated stigma dimension was the one that presented the lowest correlations with the criterion measures. The anticipated stigma dimension includes items measuring HIV disclosure concerns and anticipatory fear of being rejected. Previous research on multiple dimensions of stigma has found that the disclosure concerns dimension was less correlated with HRQoL than other dimensions (Franke et al., 2010; Fuster-RuizdeApodaca et al., 2015). A potential explanation for this finding is the mediating role of other variables such as self-efficacy or coping strategies on the negative impact of some stigma dimensions on HRQoL (Fuster-RuizdeApodaca

TABLE 6 | Construct and reliability statistics of the CST-HIV dimensions.

CST-HIV dimension	Cronbach's alpha	Average variance extracted	Jöreskog rho (omega)
Anticipated stigma	0.800	0.797	0.920
Emotional distress	0.866	0.766	0.907
Sexuality	0.698	0.525	0.764
Social support	0.869	0.759	0.904
Material deprivation	0.765	0.606	0.816
Sleep and fatigue	0.800	0.618	0.828
Cognitive problems	0.874	0.767	0.907
Physical symptoms	0.627	0.407	0.672

TABLE 7 | Correlations between the CST-HIV dimensions and the criterion variables.

	Criterion measures											
CST-HIV dimension	**SSS**	**HADS-A**	**HADS-D**	**PHQ-4**	**PROMIS-SEX**	**DUKE-AC**	**DUKE-AA**	**SEI-HS**	**ISI**	**FSS**	**PROMIS-NQ**	**EQ-5D-5L**
STG	**0.63****	0.33**	0.19**	0.29**	−0.09	−0.15*	−0.19**	0.21**	0.19*	0.16*	0.12	0.09
EMD	0.35**	**0.74****	**0.59****	**0.71****	−0.32**	−0.32**	−0.36**	0.41**	0.54**	0.42**	0.50**	0.47**
SEX	0.23**	0.34**	0.33**	0.33**	**−0.64****	−0.28**	−0.29**	0.35**	0.19**	0.22**	0.20**	0.11
SS	0.23**	0.33**	0.49**	0.28**	−0.38**	**−0.59****	**−0.64****	0.55**	0.16*	0.11	0.19**	0.27**
MAD	0.22**	0.41**	0.42**	0.37**	−0.30**	−0.36**	−0.42**	**0.72****	0.33**	0.19**	0.31**	0.34**
SF	0.19**	0.63**	0.45**	0.52**	−0.30**	−0.25**	−0.28**	−0.32**	**0.71****	**0.36****	0.41**	0.46**
CG	0.10	0.63**	0.54**	0.58**	−0.26**	−0.33**	−0.32**	0.53**	0.46**	0.46**	**0.71****	0.46**
PHYS	0.13	0.59**	0.49**	0.56**	−0.19**	−0.22**	−0.25**	0.31**	0.52**	0.43**	0.52**	**0.52****

CST dimensions: STG, anticipated stigma; EMD, emotional distress; SEX, sexuality; SS, social support; MAD, material deprivation; SF, sleep and fatigue; CG, cognitive problems; PHYS, physical symptoms. Criterion variables: SSS, Spanish Stigma Scale; HADS-A, Hospital Anxiety and Depression Scale–Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale–Depression Subscale; PHQ-4, Patient Health Questionnaire-4; PROMIS-SEX, PROMIS V2.0 Satisfaction with Sex Life; Duke-AC, Duke-confidential support dimension; Duke-AA, Duke-affective support dimension; SEI-HS, Social Exclusion Index for Health Surveys; ISI, Insomnia Severity Index; FSS, Fatigue Severity Scale; PROMIS-NQ, PROMIS Neuro-QoL V2.0 Cognitive Function; EQ-5D-5L, generic health-related quality of life.
Correlations in bold: correlations with specific criterion variables.
**p < 0.05, **p < 0.001.*

TABLE 8 | Correlations between the CST-HIV dimensions and dimensions of health-related quality of life (WHOQOL-HIV-BREF).

	HRQoL dimensions						
CST-HIV dimensions	**General health**	**Physical health**	**Psychological health**	**Level of independence**	**Social relationships**	**Environmental health**	**SRPB**
Anticipated stigma	−0.18**	−0.25**	−0.27**	−0.17**	−0.27**	−0.28**	−0.52**
Emotional distress	−0.54**	-0.57**	−0.66**	−0.49**	−0.47**	−0.46**	−0.69**
Sexuality	−0.35**	−0.27**	−0.33**	−0.25**	−0.47**	−0.36**	−0.37**
Social support	−0.34**	−0.23**	−0.37**	−0.28**	−0.65**	−0.51**	−0.24**
Material deprivation	−0.46**	−0.33**	−0.35**	−0.42**	−0.44**	−0.68**	−0.27**
Sleep and fatigue	−0.51**	−0.62**	−0.54**	−0.48**	−0.37**	−0.39**	−0.48**
Cognitive problems	−0.47**	−0.58**	−0.64**	−0.57**	−0.42**	−0.44**	−0.49**
Physical symptoms	−0.44**	−0.59**	−0.52**	−0.52**	−0.29**	−0.42**	−0.41**

*HRQoL, health-related quality of life; SRPB, spirituality, religion, and personal beliefs. **p < 0.001.*

et al., 2015). Although most correlations were small, the anticipated stigma dimension showed a high correlation with the HRQoL domain for spirituality, religion and personal beliefs. This domain of the WHOQOL-HIV-BREF is the one that includes HIV-specific items assessing existential issues and concerns. A previous Spanish study found that the SRPB domain was the unique WHOQOL-HIV-BREF dimension significantly and negatively associated with disclosure concerns (Fuster-RuizdeApodaca et al., 2019). Thus, our current finding provides additional evidence about the relationship between stigma and HIV-specific existential concerns such as those related to fearing the future or feeling that one's life is meaningful. Correlations found between each CST-HIV dimension and HRQoL point to the relevance of the scale for both theory and intervention.

The present study showed that the scores obtained in most of the CST-HIV dimensions were higher than the theoretical mean of the scale, indicating a relevant burden in these dimensions. The highest scores were found in the sleep/fatigue dimension, followed by emotional distress and material deprivation. These results are consistent with a 2019 Spanish HRQoL study in a cohort of 1462 PLHIV who were demographically similar to the overall Spanish PLHIV population. In that study, sleep was the facet most impaired in the physical health HRQoL dimension, and the psychological HRQoL dimension was one of the most impaired dimensions. The financial resources facet had the lowest score of all facets (Fuster-RuizdeApodaca et al., 2019).

This study had several limitations. We conducted an exploratory but not systematic literature review. Further, our priority in designing the CST-HIV was to keep it brief in order to ensure the feasibility of integrating it into clinical practice. This forced us to prioritise the most prevalent and relevant problems according to our content validity sources. Other potentially relevant health-related issues that negatively impact the HRQoL of PLHIV may have been omitted. It is also possible that the most burdensome problems may change over time in accordance with changing factors such as improvements in ART and simplified ART dosing schedules. To offset these limitations, we recommend collecting HRQoL data periodically to assess whether other dimensions will emerge as more burdensome. The desired brevity of the measure led us to choose only three items in each dimension. This could result in low levels of reliability and low construct validity scores in some dimensions. It might also have an impact on the predictive validity of the tool. We plan to test it further in subsequent studies, and we anticipate that by defining risk cut-off points for the scores on all dimensions, we will be able to provide guidance to healthcare providers regarding when findings should be followed up with the administration of other validated PROMs to further investigate specific issues of concern. Moreover, PLHIV are a heterogeneous group, and there are specific sub-groups particularly vulnerable to poor HRQoL (Degroote et al., 2014; Fuster-RuizdeApodaca et al., 2019). Thus, we should analyse the scale invariance as a function of relevant sociodemographic or epidemiological characteristics. This would allow for the generalisation of the model (Vandenberg and Lance, 2000). Moreover, this scale was developed and tested in the Spanish context. Thus, the scale and its factor structure should be tested in samples from other cultures to investigate its applicability in different contexts. As a first step, we will perform the cross-cultural adaptation of the CST-HIV to another European country (Italy).

Despite these limitations, we can conclude that we have a new brief instrument to screen eight significant problems that undermine HRQoL and contribute to poor health outcomes in PLHIV. The CST-HIV appears to have good psychometric properties and good preliminary evidence of validity. We anticipate that our next validity study results will strengthen the present evidence, recommending its use in clinical care in Spain. In addition to conducting the CST-HIV validation study, our other planned research will involve assessing the usefulness, efficacy, feasibility, and acceptability of integrating the CST-HIV and related PROMs into clinical practice.

The use of PROMs has been associated with improvements in clinical care and in health outcomes in fields such as mental health and oncology, and there are unrealised opportunities for the HIV field to integrate PROMs into clinical care in ways that will benefit patients (Fredericksen et al., 2020b; Kall et al., 2020). This new instrument is particularly timely in light of growing interest in the objective of improving HRQoL in PLHIV (Lazarus et al., 2016; Guaraldi et al., 2019). Our research findings are novel because few studies focus on brief screening PROMs that cover the range of biological, psychological and social issues that impair the HRQoL of PLHIV, and the present study is unique in Spain. The clinical care challenges presented by the COVID-19 pandemic underscore the importance of implementing tools that will help PLHIV and their healthcare providers make the best use of limited consultation time (Guaraldi et al., 2020). Using the CST-HIV to gather information about patients' symptoms, concerns, and experiences in advance of clinical appointments could help determine individual consultation models, resulting in greater patient satisfaction and better health outcomes.

DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: Figshare repository [https://doi.org/10.6084/m9.figshare.14216162].

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of the Hospital Clínic of Barcelona. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

KS-H and MJFR conceptualised the study, prepared the focus group scripts, and prepared the first draft of the manuscript. KS-H, MJFR, and JL jointly acquired funding for the study and organised the focus group discussions. MJFR formulated the study design. KS-H conducted literature reviews. MJFR moderated the focus groups with assistance from JL. MJFR conducted the pilot study and was the main analyst with the support of AL. MJFR performed the qualitative analysis of focus group data and reported on results. KS-H, MJFR, and MP contributed to the interpretation of results and participated in the development of the pool of items. MJFR, MP, and DN were involved in the inter-judgement process. All authors participated in revising the manuscript and all authors approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2021.681058/full#supplementary-material

The Spanish Clinic Screening Tool (CST-HIV) items are presented in both Spanish and English in **Supplementary Table 1**.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

ARTICLE 4

Problems undermining the health-related quality of life of people living with HIV in Spain: a qualitative study to inform the development of a novel clinic screening tool

Kelly Safreed-Harmon, María José Fuster-RuizdeApodaca, Marta Pastor and Jeffrey V. Lazarus

Under peer review

This article addresses specific objective 3: *Gather and analyse qualitative data to determine which health-related issues are perceived to be the most burdensome by PLHIV and healthcare providers in Spain.*

Resumen

Antecedentes: En entornos con una alta cobertura de la terapia antirretroviral, numerosos problemas relacionados con la salud continúan socavando la calidad de vida relacionada con la salud (CVRS) de las personas que viven con el VIH. Como parte de un estudio más grande para desarrollar y validar las nuevas medidas de resultado informadas por el paciente, realizamos una investigación cualitativa para aprender qué problemas se perciben como los más molestos.

Métodos: Tras una revisión de la literatura sobre el tema de interés, realizamos cuatro grupos focales (DGF) en España con los participantes seleccionados por muestreo intencional. Dos grupos de enfoque convocaron a 16 proveedores de servicios de VIH expertos, y dos convocaron a 15 personas con VIH con diversos perfiles epidemiológicos. Los grupos de enfoque siguieron los guiones de entrevistas semiestructurados e incorporaron un ejercicio para priorizar los problemas más críticos relacionados con la salud entre los nombrados en las discusiones. El análisis de contenido se realizó utilizando MaxQDA 12.

Resultados: El análisis de los datos de DGF identificó varias categorías generales de problemas que afectan la calidad de vida relacionada con la salud de la personas con VIH, y los problemas más frecuentemente mencionados se encuentran en las categorías de problemas sociales, síntomas físicos, problemas psicológicos y problemas relacionados con la sexualidad. Dentro de la categoría de problemas sociales, el estigma / discriminación fue, con mucho, el problema que se planteó con más frecuencia. En el ejercicio de priorización, el estigma/discriminación también se clasificó como el tema más molesto, tanto por los proveedores de salud como por las personas con VIH. Dentro de la categoría de síntomas físicos, los problemas nombrados con mayor frecuencia fueron los problemas relacionados con el sueño, la fatiga, el dolor físico y los cambios en la grasa corporal. Respecto a los problemas psicológicos, los participantes de DGF más comúnmente hablaban de angustia emocional en términos generales. Cuando las personas comentaron trastornos específicos, los que mencionan con mayor frecuencia fueron la depresión y la ansiedad. En el ejercicio de priorización, tanto los proveedores de servicios como las personas con VIH clasificaron el bienestar psicológico como el segundo problema más importante después del estigma. Los problemas relacionados con la sexualidad que se informaron incluyeron la falta de libido, las

infecciones de transmisión sexual, los problemas hormonales y la insatisfacción sexual general.

Conclusiones: diversos problemas relacionados con la salud socavan el CVRS de personas con VIH. El estigma relacionado con el VIH y el bienestar psicológico siguen siendo importantes desafíos. Identificar y abordar con precisión estos problemas en la atención clínica de rutina puede ayudar a personas con VIH a disfrutar de un mejor CVRS y puede apoyar el envejecimiento saludable en estas poblaciones.

Problems undermining the health-related quality of life of people living with HIV in Spain: a qualitative study to inform the development of a novel clinic screening tool

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Abstract

Background: In settings with high antiretroviral therapy (ART) coverage, numerous health-related issues continue to undermine the health and health-related quality of life (HRQoL) of people living with HIV (PLHIV). As part of a larger study to develop and validate a new patient-reported outcome measures, we conducted qualitative research to learn which issues are perceived as most burdensome.

Methods: Following a literature review on the topic of interest, we conducted four focus groups in Spain with participants selected by purposive sampling. Two focus groups convened 16 expert HIV service providers, and two convened 15 PLHIV with diverse epidemiological profiles. Focus groups followed semi-structured interview scripts and incorporated an exercise to prioritize the most critical health-related issues among those named in the discussions. Content analysis was conducted using MAXQDA 12.

Results: The analysis of FGD data identified several broad categories of issues impacting the health-related quality of life of PLHIV, with the most frequently named issues falling within the categories of social problems; physical symptoms; psychological problems; and sexuality-related problems. Within the category of social problems, stigma/discrimination was by far the issue raised the most frequently. In the prioritisation exercise, stigma/discrimination was also ranked as the most burdensome issue by both health providers and PLHIV. Within the physical symptoms category, the issues named most frequently were sleep-related problems, fatigue, physical pain and body fat changes. Regarding psychological problems, FGD participants most commonly spoke of emotional distress in general terms. When people commented about specific disorders, the ones most frequently mentioned were depression and anxiety. In the prioritisation exercise, both service providers and PLHIV ranked psychological well-being as the second-most important issue following stigma. Sexuality-related problems that were reported included lack of libido, sexually transmitted infections, hormonal problems and general sexual dissatisfaction.

Conclusions: Various health-related issues undermine the HRQoL of PLHIV. HIV-related stigma and psychological well-being remain major challenges. Accurately identifying and addressing these issues in routine clinical care can help PLHIV enjoy better HRQoL and can support healthy aging in this populations.

Keywords: health-related quality of life, HIV, symptoms, patient-reported outcome measures, qualitative research, Spain

Introduction

Following the introduction of the first highly effective antiretroviral therapy (ART) regimens in 1996, the widespread use of ART has transformed HIV care [1,2]. ART suppresses viral replication and thus prevents HIV from destroying the immune system. More than two-thirds of the world's 38 million PLHIV are now taking ART, and its effect on survival is reflected in the 39% decline in HIV-related deaths from 2010 to 2019 [3]. For people who initiate ART sufficiently early in the course of infection, life expectancy is almost that of the general population [4].

Health systems are increasingly focusing on the question of how to meet the health needs of large numbers of PLHIV who are stable on ART. Viral suppression has conventionally been regarded as a key marker of the success of HIV care, but as more people live with controlled HIV for many years, there is recognition that health-related quality of life (HRQoL) warrants greater consideration[5]. A large British study found that virally suppressed PLHIV had significantly lower HRQoL scores than a representative sample of the general population, and other studies have documented similar gaps [6–8].

These outcomes likely reflect the burden of living with HIV on a long-term basis. HIV remains a highly stigmatised disease, and discrimination and other manifestations of stigma contribute to the social isolation and mental health problems that are commonly reported by PLHIV [9–12]. Periodic disability as well as stigma and discrimination have limited the employment opportunities of many PLHIV, with consequences for their material well-being and long-term financial security [13,14]. Although high adherence to ART typically controls HIV infection, PLHIV often experience bothersome physical symptoms such as pain, fatigue and gastrointestinal distress [15–18]. Furthermore, PLHIV have a greater multimorbidity burden than the general population, with comorbidities occurring at younger ages [2]. They are at elevated risk of some comorbidities including depression, hepatitis C virus, diabetes, cardiovascular disease, and chronic kidney disease [2,19–21].

The World Health Organization defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [22]. From this standpoint, healthcare for PLHIV should promote good HRQoL outcomes rather than merely addressing HIV on a biomedical level. Furthermore, poorer HRQoL has been observed to predict hospitalisation, while better HRQoL is associated with a lower mortality risk, suggesting that efforts to influence modifiable determinants of HRQoL may have important health benefits [23–26].

In order to help PLHIV experience better HRQoL outcomes, clinical healthcare providers must have the capacity to recognise problems that might be resolved or mitigated through interventions and referrals. Time constraints and communication barriers can impede their efforts to understand their patients' needs. Patient-reported outcome measures (PROMs) offer a means of capturing information about a wide range of issues that can affect HRQoL. Administering PROMs as part of routine clinical care can lead to the recognition of problems that might have otherwise been overlooked [27]. More than 100 HIV-specific PROMs have been validated [28], and there are many other non-disease-specific PROMs that providers might also consider administering to PLHIV. However, most of these instruments focus on particular aspects of health and well-being, and patients would need to be asked to complete separate instruments in order for providers to learn about disparate issues such as physical symptoms, mental health and social functioning. Hence this is not an efficient way to screen for the large number of issues that potentially warrant attention in routine clinic visits.

This study is part of a larger study conducted for the purpose of developing a short broadly focused PROM for use in HIV clinical care in Spain [29]. It is envisioned that the PROM will assist healthcare providers in identifying issues that are negatively affecting the HRQoL of PLHIV, thus providing opportunities to address these issues through interventions and referrals. Here, we report on the first phase of instrument development. The overall objective in this phase was to identify the most burdensome health-related issues experienced by PLHIV in order to determine which issues should be addressed by the PROM. Specific objectives were to: (a) conduct a literature review that would inform qualitative data collection and subsequent phases of instrument development; and (b) obtain qualitative evidence from PLHIV and HIV service providers. This work was intended to provide the conceptual basis for the new instrument.

Methods

In accordance with established methodologies for questionnaire development [30], our study employed a four-step process: (1) a literature review; (2) a qualitative study using data from key informants; (3) item pool development; and (4) pilot testing. The first two steps are reported in this article. Data collection and analysis for these two steps took place in January–November 2019. Ethical approval for the study was obtained from the research ethics committee of Hospital Clínic Barcelona in 2019, and all study participants provided written informed consent.

Literature review

We conducted an exploratory literature review to obtain information about issues that undermine the well-being of PLHIV and to identify themes that would warrant further exploration in focus group discussions (FGDs). We searched PubMed using search strings that addressed two major lines of research: the symptom burden in PLHIV and predictors of HRQoL in PLHIV. The search strings employed both general descriptors and MeSH terms (Annex 1). We also searched PubMed for articles relating to HIV symptom screening tools and the use of HIV-specific PROs in clinical practice. We reviewed the references cited in key articles to identify further relevant sources of information, as well as incorporating other sources known to research team members through prior work. We used Scopus and ResearchGate to identify articles that cited the widely used HIV Symptom Index as a key source and considered the relevance of those articles as well [31].

We restricted the selection of articles and abstracts relating to the symptom burden in PLHIV to English-language peer-reviewed articles that reported on adult PLHIV who live in high-income countries and are taking ART. We prioritised articles reporting on the symptom burden in PLHIV from 2010 onward, in recognition that the symptom profile has changed in accordance with ART improvements, and performed full-text reviews of all relevant articles. The HRQoL search in PubMed identified a very large number of records for peer-reviewed articles, including a 2014 narrative review article reporting on HRQoL in PLHIV in high-income countries [32]. We thus modified our search to identify articles published from 2013 onward in order to supplement the findings of the review article.

Qualitative study

For the qualitative study we conducted focus group discussions (FGDs) to obtain the perspectives of PLHIV and other key informants regarding the most burdensome health-related problems facing PLHIV. The methodologies for data collection and analysis followed standard qualitative research procedures [33].

Two FGDs enrolled HIV service providers (N=8 per FGD) and two FGDs enrolled PLHIV (N=8 and N=7). Participants in the service provider FGDs were selected via purposive sampling to ensure the representation of different types of providers such as physicians, nurses, psychiatrists, psychologists and NGO representatives. Service providers worked in the metropolitan areas of Madrid, Barcelona, Bilbao, Sevilla and Valencia. Participants in the PLHIV FGDs were selected via purposive sampling to ensure diverse epidemiological profiles in terms of age, sex, sexual orientation, and history of drug use. One PLHIV FGD was comprised of clients of a nongovernmental organisation providing HIV services in Barcelona, and the other PLHIV FGD was comprised of patients at the HIV outpatient clinic of a large Barcelona university hospital.

FGDs took place in April and May 2019, with each one lasting approximately two hours. All focus groups were conducted in Spanish. Facilitators used semi-structured focus group scripts with open-ended questions and prompts to guide the discussions. The scripts asked FGD participants to address two central questions: (1) In your opinion, what are the health-related problems that have the greatest negative effect on the quality of life of PLHIV? and (2) Among the problems that you have identified, what do you think are the most important ones to include in a short diagnostic questionnaire? All focus group participants were also asked to carry out a prioritisation exercise in which they selected what they believed to be the most burdensome issues from among all issues identified during the discussions.

We performed a qualitative analysis through a directed content analysis of the FGD transcripts [34] assisted by the qualitative analysis software MAXQDA 12. For this purpose, FGDs were recorded, transcribed literally, reviewed for accuracy, and coded. Inductive and deductive coding were used to identify relevant concepts, and an analysis of these concepts led to the identification of key categories and subcategories of health-related problems. There was also a quantitative analysis of the qualitative data to determine the number of times each code and category was used. Three research team members who were experts in HIV-related public health and psychosocial issues, two of whom had community-level experience working with PLHIV, assessed the methodological and theoretical quality of core categories and subcategories [35].

Illustrative quotations for key themes were translated into English for reporting purposes.

Results

Literature review

The literature review identified seven studies that met inclusion criteria regarding the symptom burden in relevant PLHIV populations [16,36–41]. Three types of symptoms were reported to be common across many of these studies: sleep-related symptoms, fatigue/energy-related symptoms, and muscle/joint pain. Other symptoms noted to be common in a smaller number of studies included anxiety/fear, sadness/depression, peripheral neuropathy, sexual dysfunction, changes in body appearance, and gastrointestinal symptoms.

We assessed the published research on predictors of HRQoL in PLHIV by utilising the aforementioned 2014 narrative review article on this topic and identifying original research articles published after the search period in the 2014 review. Forty-nine studies met the inclusion criteria for the 2014 review [32]. Additionally, our literature search identified 68 more recent studies reporting on factors associated with HRQoL in PLHIV (Figure 1). Examples of relevant findings from the review article and the more recent studies are presented in Table 1. Numerous studies identified social support as a predictor of positive HRQoL outcomes. Physical and emotional health concerns, including symptoms, comorbidity, and depression, were often found to predict negative HRQoL outcomes. Other notable predictors of negative HRQoL outcomes included stigma, HIV disclosure concerns, and material insecurity (e.g., unemployment, financial problems, unmet needs for food and housing).

Figure 1. Literature review process to identify factors affecting health-related quality of life

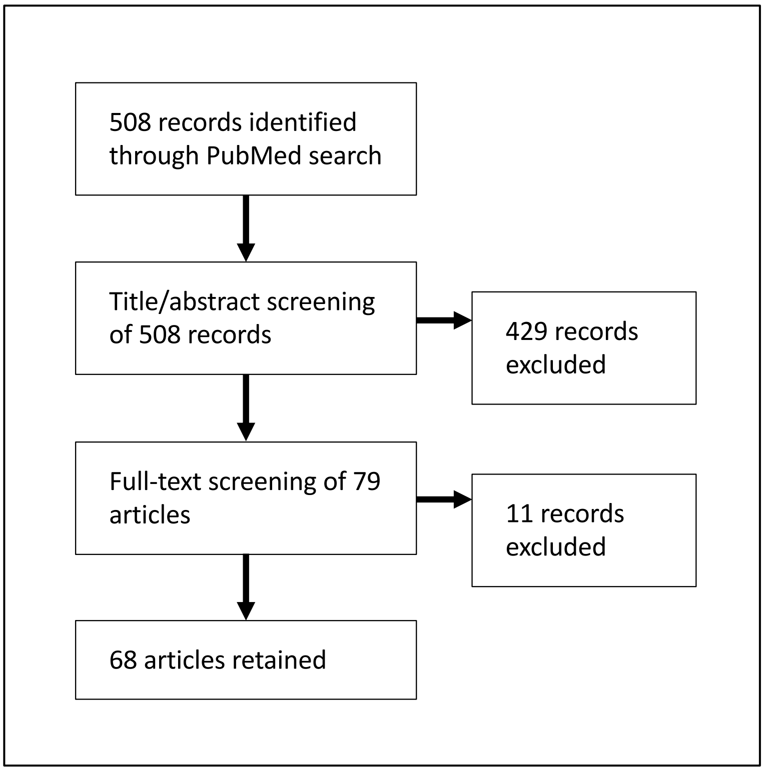

Table 1. Selected examples of study findings on factors associated with positive and negative health-related quality-of-life outcomes

Factors associated with health-related quality-of-life outcomes	Year	Source	Instrument
Factors associated with positive outcomes			
Social support	2013	Bekele [42]	MOS-HIV
	2015	Dalmida [43]	SF-36
	2014	DeGroote [32]	N/A
	2019	den Daas [44]	SF-12
	2013	Emlet [45]	SF-8
	2016	George [46]	MOS-HIV
	2016	Niderost [47]	WHOQOL-HIV-Bref
	2013	Slater [48]	HAT-QoL
Factors associated with negative outcomes			
Comorbidity	2014	DeGroote [32]	N/A
	2013	Emlet [45]	SF-8
	2016	George [46]	MOS-HIV
	2016	Niderost [47]	WHOQOL-HIV-Bref
	2013	Slater [48]	HAT-QoL
Depression	2016	Ballester-Arnal [49]	MOS-HIV
	2017	Catalan [50]	WHOQOL-HIV Bref
	2015	Dalmida [43]	SF-36
	2014	DeGroote [32]	N/A
	2019	Olson [51]	FAHI

High symptom burden or presence of specific symptoms (e.g., body disfigurement, memory difficulties, sexual functioning)	2016	Ballester-Arnal [49]	MOS-HIV
	2017	Brandt [52]	WHOQOL-HIV-Bref
	2014	DeGroote [32]	N/A
	2019	den Daas [44]	SF-12
	2016	George [46]	MOS-HIV
	2019	Olson [51]	FAHI
Stigma	2018	Reinius [53]	Swed-Qual
	2013	Slater [48]	HAT-QoL
HIV disclosure concerns	2016	Fekete [54]	HAT-QoL
	2018	Logie [55]	SF-12
Material insecurity (e.g., unemployment, financial problems, unmet needs for food and housing)	2016	Ballester-Arnal [49]	MOS-HIV
	2014	DeGroote [32]	N/A
	2014	Douab [56]	SF-12
	2016	George [46]	MOS-HIV
	2018	Logie [55]	SF-12
	2016	Niderost [47]	WHOQOL-HIV-Bref
	2018	Sok [57]	MOS-HIV

Qualitative study

Among service providers who participated in FGDs (N=16), ten were men and six were women. The service providers included four HIV physicians, one psychiatrist, two psychologists, four nurses, one social worker, and four peers with diverse professional expertise. Among PLHIV who participated in FGDs (N=15), eight were men, half of them men who have sex with men. Six were heterosexual cis women, and one was a transgender woman. Three PLHIV were immigrants, four were long-term survivors (diagnosed with HIV before 1996), and six were people who acquired HIV through injection drug use.

The analysis of focus group data identified several broad categories of issues impacting the health-related quality of life of PLHIV, with the most frequently mentioned issues falling into four categories: social problems; physical symptoms; psychological/emotional problems; and sexuality-related problems. Table 2 displays the categories and sub-categories identified, indicating the number of coded segments in each one, along with illustrative examples of segments.

Table 2. Issues impacting health-related quality of life of people living with HIV: anlysis of focus group data

Category	Number of coded segments	Sub-category	Number of coded sub-category segments*	Illustrative example
Social problems	191	Anticipated stigma	150	I fear being rejected by my relatives. My mother has never rejected me and nor has my father, ever, but I do fear rejection by my relatives because they … they would never ever understand. [PLHIV Focus Group, Barcelona, woman]
		Socioeconomic vulnerability	22	For these people, the biggest thing is their financial uncertainty. Some people live with very little money, extremely little, with pensions that get regularly reviewed. The infection becoming chronic, and the improvement of their physical health also have an impact on the reviewing of those pensions. In the past, if you had a pension, whatever it was, they never changed it, and that provided a certain future stability for that person. Now, that stability does not exist, and people feel vulnerable in that sense. [Experts Focus Group, Barcelona, physician]
Physical symptoms	83	Sleep-related problems	28	There is another aspect that has always worried me in those patients and that is, for instance, from what I've been told, a certain emotional instability and lack of sleep, sleep disturbance, lack of rest.… They wake up, especially [when newly diagnosed with HIV], … they have told me that they wake up often; they are concerned; they don't rest well. [Experts Focus Group, Madrid, physician]
		Fatigue	17	My main problem is tiredness. I have very severe chronic fatigue.... I had larynx cancer in 2012, and after radiotherapy, my energy levels never went back up.… My current struggle is to have a good quality of life and to rest. The company [where I work] has moved its headquarters to Sant Joan Despí, so I need to catch a train at six in the morning and I get back home at four in the afternoon. Then I lie down in bed like a mummy after lunch to rest, because I can't … I can't manage this pace. [PLHIV Focus Group, Barcelona, woman]

Category	**Number of coded segments**	**Sub-category**	**Number of coded sub-category segments***	**Illustrative example**
		Physical pain	14	Persistent chronic pain. I think that we should assess and thoroughly detail what type of pain, whether articular or muscular or.… To talk about it in terms of the degree of pain perceived by every single person. However, general pain is something that is often brought up at doctor’s appointments. [Experts Focus Group, Madrid, physician]
		Body fat changes	10	There is still a group of people who are survivors of a different era.… They may have body changes and, I am not sure if this is subjective, [but] women feel that it affects them more than men.… That is the feeling I have from the consultations. Another prevalent problem in some cases, more and more prevalent, is the uncontrolled weight gain, you know? Sometimes, for good reason, there are many totally unusual diets … high caloric intake, carbonated drinks… [Experts Focus Group, Barcelona, physician]
Psychological problems	67	General emotional distress	43	One patient said to me: “It’s not only physical. It’s not just that my feet hurt because I have neuropathy. It’s that I haven’t developed myself. My soul hurts. I don’t have a job like everyone else, nor a pension. I feel old.... I don’t really have anything.”
		Anxiety/ depression	24	You can’t sleep, sometimes you panic, you know? That feeling that when I go to bed: *Ahh!* [Inhaling.] I feel like I suffocate. And then it’s like if you wake up: *Ahh!* [Inhaling.] And it is, it is horrible. It’s horrible. [PLHIV Focus Group, Barcelona, man]
		Fear of the future	14	An issue, mostly among people who are growing old, is concern about the future. Because if, on top of that, you have financial issues and social issues, the concern about the future and the uncertainty about what is going to happen to you … impacts a lot on the quality of life of people with HIV. [Expert Focus Group, Barcelona, psychologist]
Sexuality-related problems	38	Lack of libido	9	Sexual health issues. Not only sexually transmitted infections … but also issues related to the loss of libido. Especially for women. It’s a very important issue that affects their quality of life. [Expert Focus Group, Barcelona, nurse]

Category	**Number of coded segments**	**Sub-category**	**Number of coded sub-category segments***	**Illustrative example**
		Sexuality and HIV-related stigma	5	For years now, I’ve given up on sexual issues, only … focusing on masturbation. Because I also had that feeling of guilt, right? I said, “If I like someone, they want me … I also want them, but I feel bad, right? How am I supposed to tell them?” [PLHIV Focus Group Barcelona, man]

* Segments could be coded in more than one subcategory depending on the content. Thus, the number of segments coded in each category does not necessary correspond to the sum of the segments coded in that subcategory. Not all subcategories are reported in this table.

Social problems

Within the category of social problems, stigma was by far the issue raised the most frequently (Table 2). In the FGD prioritisation exercise, stigma/discrimination was ranked as the most burdensome issue by both service providers and PLHIV.

While a number of different aspects of stigma and discrimination were discussed, many of these related to the concept of anticipated stigma, i.e., the belief that one's HIV-positive status would elicit negative responses in other people. Anticipated stigma was reported to have important implications for many PLHIV in regard to social and intimate relationships. Among other concerns, a number of PLHIV focus group participants emphasised the effects of anticipated stigma on their romantic and sexual lives. Self-stigma often was noted to be part of the dynamic when these issues were discussed. Service providers called attention to the interconnected nature of public stigma, self-stigma, and a broad range of other challenges that PLHIV experience.

Another social problem, socioeconomic vulnerability, was identified as a high priority by service providers, but not by PLHIV. Service providers noted both the immediate financial challenges facing PLHIV and also the concerns that some PLHIV expressed about not being able to accumulate the financial resources that they will need in later life. Service providers reported having the perception that some PLHIV patients may be experiencing financial difficulties although this issue is seldom discussed explicitly in clinic visits. One service provider also called into question the stereotype that PLHIV who belong to the MSM community are financially secure.

Physical symptoms

Within the physical symptoms category, the issues named most frequently were sleep-related problems and fatigue (Table 2). PLHIV spoke about these issues being a prominent part of their lives. It was also observed that sleep-related problems were not being resolved satisfactorily.

Physical pain also was frequently mentioned by both PLHIV and service providers. Physical pain was identified as a cause of sleep problems. One PLHIV focus group participant, for example, reported being awakened several times per night by shoulder pain.

PLHIV and service providers also noted concerns about body fat changes such as lipoatrophy and weight gain. Multiple PLHIV focus group participants reported that body fat changes had been emotionally distressing. One service provider expressed the view that improvements in ART have meant that only a very small proportion of PLHIV continue to suffer from body fat changes. Another service provider, however, called for continuing attention to this issue.

Psychological problems

In the category of psychological problems, FGD participants most commonly spoke of emotional distress in general terms rather than naming specific disorders. When people commented about specific disorders, the ones most frequently mentioned were depression and anxiety. Fear of the future was identified as an issue negatively affecting the emotional health of some PLHIV. In the prioritisation exercise, both service providers and PLHIV ranked psychological well-being as the second-most important issue following stigma. The burden of mental health challenges experienced by PLHIV was emphasised in all focus group discussions. One service provider called for emotional well-being to be viewed as more than the absence of conditions such as depression and anxiety. Service providers noted that the aging experience may bring on further mental health challenges.

Sexuality-related problems

Focus group participants mentioned sexuality-related problems considerably fewer times than they mentioned other issues such as stigma and physical symptoms (Table 2), but sexuality-related problems were ranked as the third-most burdensome issue in the prioritisation exercise. More service providers than PLHIV identified this as a high-priority issue. Service providers also talked about sexuality-related problems more than PLHIV did in the focus group discussions. Comments from service providers as well as PLHIV touched on a wide range of concerns, including lack of libido, sexually transmitted infections, hormonal problems, and general sexual dissatisfaction. When PLHIV spoke about sexuality, their concerns often encompassed the issue of HIV-related stigma.

Discussion

This article describes the qualitative research phase of the development of a novel PROM that is intended to help healthcare providers identify burdensome health-related problems experienced by PLHIV in routine clinical care. The literature review and focus group findings identified a range of issues that should be considered as potential topics for inclusion in this PROM. These issues span the domains of physical, emotional and social well-being, reflecting the complexity of living with HIV as a long-term chronic condition. Findings provide preliminary evidence of the content validity of the planned instrument, thus meeting key criteria in the instrument development process [58,59].

Many of the specific issues identified by focus group participants as important factors negatively affecting the HRQoL of PLHIV correlate with key findings in the scientific literature. For example, studies have indicated that half or more of PLHIV experienced pain in recent months [60], and pain is undertreated in PLHIV [61,62]. PLHIV are five times more likely than HIV-negative people to suffer from insomnia, which often remains undiagnosed [63]. A systematic review of depression in PLHIV reported an estimated point prevalence of 33%, which appears to be much higher than the prevalence of depression in the general population [64][65]. Anxiety and sexuality-related problems are also more prevalent in PLHIV than in the general population [64,66]. Half of PLHIV are thought to experience sexuality-related problems, and these problems are often not recognised by physicians [66,67].

A striking finding of our qualitative research was the strong emphasis that focus group participants placed on the role of stigma and discrimination in reducing health-related quality-of-life. Not only was stigma/discrimination the highest-ranked issue when PLHIV and service providers were asked to identify the issues that they believed to be most burdensome, but it was also addressed far more often than any other issue in the focus group discussions. This finding is consistent with a large body of evidence showing that experiences of HIV-related stigma are common and distressing among PLHIV worldwide [3,64,68]. HIV-related stigma takes multiple forms, including anticipated stigma, internalised stigma and enacted stigma (i.e., manifestations of stereotyping, prejudice or discrimination) [69]. HIV-related stigma is associated with multiple health outcomes of concern, including lower ART adherence, lower usage of health and social services, poorer physical health, and worse HRQoL outcomes [70,71]. The existence of evidence-based interventions that can mitigate some of the negative effects of HIV-related stigma, as well as evidence-based interventions that can reduce HIV-related stigma itself [72], provides a strong rationale for healthcare providers to seek to identify PLHIV who are experiencing stigma. These patients may benefit from screening for associated problems and from referral to a range of health and psychosocial services.

As focus group participants themselves suggested, many of the issues that undermine HRQoL in PLHIV may be interrelated. For example, pain and sleep problems are often found to co-occur [73], and both of these issues are associated with depression in PLHIV [60,74]. Associations also have been observed between HIV-related stigma and sexuality-related problems [75], and between both of these issues and depression [66,70]. While it is difficult to determine the cause-effect relationship in many of these associations, we speculate that successfully addressing some of these issues in clinical care may reduce the burden of other related issues. Thus, a PROM such as the one that we are developing may assist healthcare providers in identifying multiple pathways through which various factors affecting the HRQoL of PLHIV can be influenced.

This study has a number of limitations. The literature review that constituted the first stage of the instrument development process was not systematic, thus possibly reducing the number of relevant studies identified. Participants in the service provider FGDs were recruited from among the professional networks of the researchers who led this study, and unknown biases may have influenced their selection. Participants in the PLHIV FGDs were recruited from among clients at a Barcelona-based NGO and patients at a large Barcelona university hospital. Although purposive sampling ensured sociodemographic diversity in both of the PLHIV FGDs, the PLHIV who participated in this study might not be representative of PLHIV in other settings in Spain in regard to the health-related issues that they identified as most burdensome. PLHIV might have felt reluctant to discuss some sensitive personal matters in a group setting, and thus the PLHIV focus group findings might not accurately convey the extent of the burden imposed by issues such as problematic drug and alcohol use, financial hardship and sexuality-related problems. Given the heterogeneity of the Spanish PLHIV population [76], conducting a larger number of focus groups may have yielded more information, particularly in relation to intersectional issues faced by many PLHIV.

Conclusion

Various health-related issues undermine the HRQoL of PLHIV. This qualitative study found that HIV-related stigma and psychological well-being remain major challenges. Some of the issues identified by our participants could now represent a greater challenge to PLHIV than when we conducted this study. For example, material deprivation and social support could have worsened during the COVID-19 pandemic. Accurately identifying and addressing these issues in routine clinical care may help PLHIV enjoy better HRQoL as well as supporting healthy aging in this population.

Abbreviations

ART = antiretroviral therapy
FDGs = focus group discussions
HRQoL = health-related quality of life
PLHIV = people living with HIV
PROMs = patient-reported outcome measures

DECLARATIONS

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Availability of data and materials

All relevant data are within the paper. Anonymized literal transcripts of interviews may be requested from the authors.

Authors’ contributions

KS-H and MJF-R conceptualised the study. JVL, KS-H and MJF-R jointly acquired funding for the study. MJF-R formulated the study design. KS-H conducted literature reviews. KS-H, MJF-R and JVL organised the focus group discussions, and KS-H and MJF-R prepared the focus group scripts. MJF-R moderated the focus groups with assistance from JVL. MJF-R performed the qualitative analysis of focus group data and reported on results. KS-H, MJF-R and MP contributed to the interpretation of results. KS-H and MJF-R prepared the first draft of the manuscript. All authors participated in revising the manuscript and all authors approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee of the Hospital Clínic of Barcelona, Spain, approved all research procedures in 2019. All study participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

MJF-R and MP 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 AbbVie and MSD, outside of the submitted work, speaker fees from Gilead Sciences and ViiV, and an institutional grant from Gilead Sciences for this study.

Annex 1. Search strings used in literature search

Symptom burden in people living with HIV

(((HIV OR AIDS) AND "symptom burden")) AND ("2010"[Date - Publication] : "3000"[Date - Publication])

(((HIV OR AIDS) AND symptom list)) AND ("2000"[Date - Publication] : "3000"[Date - Publication])

((symptom cluster*[Title]) AND (((HIV[Mesh] OR "Acquired Immunodeficiency Syndrome"[Mesh] OR HIV OR AIDS)))) AND ("2010/01/01"[Date - Publication] : "3000"[Date - Publication])

Health-related quality of life in people living with HIV

((“quality of life”[Title]) OR (quality-of-life[Title]) OR (QOL[Title]) OR (“health-related quality of life”[Title]) OR (“health-related quality-of-life”[Title]) OR (HRQOL[Title]) OR (“life quality”[Title])) AND ((HIV[Title]) OR (“human immunodeficiency virus”[Title]) OR (“acquired immunedeficiency syndrome”[Title]) OR (“acquired immune deficiency syndrome”[Title]) OR (AIDS[Title]) OR (“people living with HIV” [title]) OR (PLWHIV[Title]) OR (PLWH[Title]) OR (PLHIV[Title]) OR (HIV[Mesh]) OR (“Acquired Immunodeficiency Syndrome”[Mesh])) AND (“2013"[Date - Publication] : “3000”[Date - Publication])

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7. Discussion

The results of this thesis contribute to ongoing efforts to reorient HIV care to address the wide-ranging physical, emotional and social issues that challenge people who are living with HIV on a long-term basis. The PROM developed through this research, known as the HIV Clinic Screening Tool (CST-HIV), shows adequate preliminary validity and is currently undergoing additional validation to strengthen the evidence supporting its use in routine clinical care. The PROM contains 24 items: three per domain for eight domains defined as anticipated stigma, emotional distress, sexuality, social support, material deprivation, sleep/fatigue, cognitive problems, and physical symptoms (Annex 1). To our knowledge, it is one of only three short validated instruments developed specifically to support HIV care providers in identifying a wide range of health-related issues that affect the well-being of PLHIV,[116,122] and the only such instrument developed in Spain.

How the HIV Clinic Screening Tool contributes to advancing the use of patient-reported outcome measures in HIV clinical care

The HIV Clinic Screening Tool was developed through a methodologically rigorous process that closely followed best practices for instrument development.[123,124] Key strengths of the CST-HIV are that it displayed good psychometric properties in pilot testing, as well as evidence of convergent and concurrent validity. Its brevity and simplicity allow for rapid completion by clinic patients and easy assessment of data by healthcare workers. The CST-HIV reflects the participation of PLHIV in focus group discussions, expert assessment of proposed instrument items, and cognitive debriefing interviews. Furthermore, the researcher who guided the instrument development process is a person openly living with HIV, and another member of the research team has been engaged in providing mental health and social services to PLHIV in Spain for more than two decades. The full instrument development process, including the selection of constructs and development of items, was highly informed by direct information and observation about the health-related needs and priorities of PLHIV. In this manner, the CST-HIV meets one of the essential criteria for the use of PROMs in clinical practice: for PROMs to optimally contribute to people-centred healthcare, they must address issues that patients themselves perceive to be important.[64,125,126] In light of these considerations, the research team anticipates that the CST-HIV has the potential to meaningfully inform HIV care in Spain, and perhaps also in other countries with similar social, cultural, epidemiological and health system contexts.

Commonalities and differences can be observed when the CST-HIV is compared to two other short, broadly focused PROMS developed to support the clinical care of PLHIV: the Positive Outcomes PROM and the Short-Form HIV Disability Questionnaire (SF-HDQ).[116,117] The framing of the SF-HDQ in terms of disability may seem to imply a narrower purpose for this instrument compared to the two others, but in fact the developers of the SF-HDQ based their work on a highly comprehensive definition of HIV-associated disability as "a combination of physical, cognitive, mental and emotional symptoms and impairments; difficulties carrying out day-to-day activities; challenges to social inclusion; and uncertainty about future health."[127] This focus overlaps considerably with the focus of the CST-HIV and Positive Outcomes PROM, and key features of all three instruments are summarised in Table 2.

All three instruments include domains that address physical, emotional and social well-being. The CST-HIV and SF-HDQ have domains for cognitive issues, while in the Positive Outcomes PROM, cognitive issues are addressed in an item about memory/concentration in the physical domain. (Individual items are not reported in Table 2.) The CST-HIV is the only one of the three instruments with specific domains for sleep/fatigue, material deprivation, sexuality, and anticipated stigma. The other instruments address facets of these issues: the SF-HDQ, for example, has an item about the respondent's ability to "maintain safe and stable housing," and the Positive Outcomes PROM has an item about HIV disclosure. The Positive Outcomes PROM is the only instrument with items about information needs (1 item), drug/alcohol use (1 item), immigration concerns (1 item) or contraception concerns (1 item). Other variations can be observed in the selection of items. For example, the Positive Outcomes PROM and the SF-HDQ, unlike the CST-HIV, have items asking about ability to perform usual activities (1 item and 3 items, respectively).

Table 2. A comparison of the HIV Clinic Screening Tool (CST-HIV), the Positive Outcomes PROM[64,117,122] and the Short-Form HIV Disability Questionnaire (SF-HDQ)[116,128]

	CST-HIV	**Positive Outcomes**	**SF-HDQ**
Total # items (total # domains)	24 items (8 domains)	23 items (6 domains)[a]	35 items (6 domains)
Domain content *(# items per domain)*	• Anticipated stigma *(3)* • Emotional distress *(3)* • Sexuality *(3)* • Social support *(3)* • Material deprivation *(3)* • Sleep/fatigue *(3)* • Cognitive problems *(3)* • Physical symptoms *(3)*	• Global assessment (general health and well-being) *(1)* • Information *(1)* • Physical *(5)* • Psychological *(5)* • Social *(6)* • Relational *(4)*	• Physical *(10)* • Cognitive *(3)* • Mental/emotional *(5)* • Uncertainty *(5)* • Day-to-day activities *(5)* • Social inclusion *(7)*
Item scoring	5-point Likert scale	5-point Likert scale	5-point ordinal response scale for presence/ severity of disability and binary (yes/no) response scale for episodic nature of disability
Language in which instrument was developed	Spanish	English	English
Setting(s) in which qualitative data informing selection of domains were obtained *(date qualitative data were obtained)*	Spain *(2019)*	United Kingdom, Ireland *(~2018)*	Canada *(~ 2008)*

Sources of qualitative data	• 2 focus group discussions with HIV service providers (N=8, N=8) • 2 focus group discussions with PLHIV (N=8, N=7)	• Interviews with PLHIV (N=28) • Interviews with HIV service providers (N=21) • Interviews with HIV commissioners (N=8)	• 4 focus group discussions with PLHIV (N=23 total participants) • Interviews with PLHIV (N=15)
Setting(s) in which psychometric properties of instrument were initially assessed	Spain	Belgium, Croatia, Portugal, Spain, United Kingdom	Canada, Ireland

PLHIV = people living with HIV

[a] Instrument contains 22 items in 6 domains plus 1 free-text item inviting comment on main problems/concerns)

To the extent that the CST-HIV, the Positive Outcomes PROM and the SF-HDQ differ in terms of the focus of domains and items, various factors may account for this, such as methodological differences in their development processes and researcher biases favoring the emphasis of some issues over others. An additional possibility is that HIV-related care priorities may vary across cultures, as discussed in the next section.

Are different patient-reported outcome measures needed in different cultures?

Due to the resource-intensive nature of developing new PROMs, researchers and healthcare providers may consider the suitability of existing PROMs for addressing their objectives. If a PROM if interest was developed and validated in a different language from that of the patient population, then it is strongly advisable to not merely translate the instrument but instead to undergo a more extensive cross-cultural adaptation process.[129] Cross-cultural adaptations of PROMs are quite commonly performed across many healthcare fields, but some researchers have expressed concern about methodological standards for this work.[129–132] One aspect of cross-cultural adaptation that appears to receive insufficient attention is conceptual equivalence, which encompasses consideration of both the meaning and the relevance of the content of a PROM to members of the culture for which it is being adapted.[129,133] That is, in addition to being understandable to members of the target culture, items in the PROM must also address issues that are considered to be important.

The introduction of the CST-HIV presents an opportunity to explore the issue of whether stakeholders in different cultures may have different perceptions about the relevance of various factors associated with the well-being of PLHIV. The qualitative data that guided the selection of domains for the Positive Outcomes PROM were gathered from interview participants in the United Kingdom and Ireland, while the qualitative data that informed the theoretical framework for the SF-HDQ were gathered from focus group participants in Canada.[64,128] It is not known how social, cultural, epidemiological or health system differences between Spain and these other countries might be reflected in differences across the CST-HIV, the Positive Outcomes PROM and the SF-HDQ. Reasons for some of the apparent variations in health priorities can be hypothesised on the basis of how issues of interest manifest differently in different settings.

For example, attention to immigration concerns in the Positive Outcomes PROM but not the CST-HIV may reflect variations in HIV epidemic dynamics. The most recently available data indicate that 52% of annual new HIV infections in the United Kingdom are diagnosed in foreign-born people, as are 71% of annual new HIV infections in Ireland.[134,135] In contrast, only 36% of annual new HIV infections in Spain are diagnosed in foreign-born people.[118] Thus the Positive Outcomes item addressing immigration – "Over the past four weeks, have you been worried about your immigration status?"[117] – might seem more important to stakeholders in the former two countries than those in Spain.

Additionally, the Positive Outcomes PROM includes items about contraception and becoming a parent, [117] neither of which is addressed in the CST-HIV. While both issues are potentially of interest to both men and women, it is possible that women may more frequently have concerns around these issues than men do. If this is the case, then perhaps the prioritisation of these issues by stakeholders in the United Kingdom and Ireland but not stakeholders in Spain is related to the composition of the PLHIV populations of the three countries. In the United Kingdom, 31% of diagnosed cases of HIV infection are in women, and in Ireland, an estimated 35% of PLHIV are women.[136,137] In Spain, in contrast, an estimated 18% of PLHIV are women.[137]

Material security, which is addressed in different ways in the CST, the Positive Outcomes PROM and the SF-HDQ, is another issue that may be perceived differently across cultures. In a comparative analysis of the self-reported HRQoL of PLHIV in Finland and Portugal, there was a statistically significant relationship between environmental aspects of HRQoL and overall HRQoL in the Portuguese cohort but not the Finnish cohort.[138] The study's authors speculated that higher unemployment levels in Portugal may have contributed to the observed difference. This finding raises the question of whether economic factors might influence PLHIV and healthcare provider perceptions of whether and how material security should be addressed in a short, broadly focused PROM intended for use in HIV clinical care.

Cultural norms regarding alcohol consumption may be another factor informing the health-related priorities of PLHIV and healthcare providers. Researchers have called attention to wide variation in cultural norms regarding alcohol consumption, even among Western European countries.[139,140] Furthermore, it has been proposed that cultural norms also influence perceptions about the incidence and prevalence of alcohol dependence and alcohol use disorders, even when standardised instruments are being used to assess these issues.[140] Interestingly, prevalence of alcohol dependence is estimated to be higher in both England (6.9%) and Ireland (4.2%) than in Spain (0.7%), and the Positive Outcomes PROM includes an item about alcohol use whereas the CST-HIV does not.[141]

Taken together, these observations caution against assuming that the CST-HIV and other short, broadly-focused PROMs designed for use in HIV clinical care are equally relevant across different national settings. At this relatively early stage in the exploration of how PROMs might contribute to HIV clinical care, developing a new PROM in Spain with the same general purpose as that of two existing instruments developed in other countries (the United Kingdom and Ireland for the Positive Outcomes PROM, and Canada for the SF-SDQ) provides an important opportunity to explore whether there is significant variation across countries in the health-related concerns of PLHIV. An open question that should inform future research and practice in this area is whether one instrument or another might be a better "fit" with the self-defined needs of PLHIV and healthcare providers outside of the country or countries where these instruments were developed.

In carrying out the cross-cultural adaptation of an instrument, the research team may conduct desk research to choose the instrument and then ask an expert panel to assess how the content of the instrument is likely to resonate with stakeholders in the target culture. Alternately, a more comprehensive approach is to first conduct qualitative research in the target culture, then use the findings to help guide instrument selection. A rigorous application of this approach can be observed in the cross-cultural adaptation of an HRQoL instrument by researchers seeking to assess HRQoL in polio survivors in Nigeria.[142] The research team began by conducting a qualitative study to determine how polio survivors in Nigeria conceptualised the key domains of their health-related quality of life. Findings were systematically mapped against the content of all candidate PROMs that the research team identified, and the PROM that most fully reflected the qualitative research participants' concerns was chosen to be carried forward in the cross-cultural adaptation process. Such a methodology may be relevant in helping to determine how the CST-HIV and other short broadly-focused HIV clinic screening tools can contribute to HIV clinical care in diverse national settings.

Assessing the value of using patient-reported outcome measures in clinical practice

A key premise of this thesis is that the effective use of suitable PROMs in HIV clinical care can improve the health and HRQoL of PLHIV. Thus, it is important to reflect on the strengths and weaknesses of the existing evidence base regarding this proposed causal relationship and to consider the justification for promoting the use of the CST-HIV in spite of current evidence gaps.

As noted in the introduction to this thesis, there is a paucity of published evidence from the HIV field regarding the impact of PROMs use in clinical care, although two studies examining the issue found PROMs use to be associated with positive changes in care processes.[113,114] Considerably more research has been published about the impact of PROMs use in other healthcare fields, particularly oncology, and findings from these studies provide indirect support for the use of PROMs in HIV clinical practice. Extrapolating from other healthcare fields is not ideal in light of the great variation in health-related challenges experienced by different patient populations. Nonetheless, evidence of the potential benefits of PROMs use in clinical practice, including evidence from a large systematic review, is sufficiently promising to warrant further investigation of the role of PROMs in routine care.[111]

One possible explanation for the lack of more conclusive evidence is that methodologically rigorous studies may be difficult to undertake.[143] In a review of PROMs use in clinical care, Porter *et al* called attention to widespread methodological weaknesses in the evidence base and also suggested that researchers need greater clarity about the causal pathways through which PROMs are theorised to act on patient health outcomes.[144] Even when a well-designed study of the impact of PROMs use on patient care and patient outcomes is performed, it cannot be expected to find improvements in health and HRQoL outcomes unless the PROM intervention speaks to the needs of patients and their healthcare providers. That is, the PROM or PROMs that patients are asked to complete must effectively target modifiable factors adversely affecting their health and well-being, while at the same time, healthcare providers must be able to easily administer PROMs to patients and act on the results. Choosing a PROM that is not fit for purpose could undercut any benefits of collecting PROMs information from patients, while institutionalizing the clinical use of PROMs in an ineffective manner could prevent healthcare providers from responding appropriately to this information.

Researchers have identified a number of challenges associated with the effective implementation of PROMs in clinical practice, such as a lack of clear guidance on how PROMs should be administered and insufficient training on how to interpret the results.[115,145] Some of these challenges may conceivably limit the effectiveness of PROM interventions. For example, a study in a group of primary healthcare clinics in the United States compared eight intervention clinics to six control clinics to see if the use of PROMs in intervention clinics was associated with more medical record notation of patient fall risk or urinary incontinence.[146] Only slightly more reports of these issues were found in the medical records for the intervention arm. Interviews with 16 physicians who participated in the intervention arm indicated that multiple issues hindered effective PROMs use. Physicians reported that the brevity of clinic sessions prevented them from carefully reviewing the large amount of data generated from the 46-item PROM that was administered to patients, and some said that they did not even look at PROM findings. Problems with the electronic interface for accessing PROMs data also discouraged some physicians from making use of this information during clinic visits.

In sum, integrating PROMs into routine clinical care is not a simple undertaking, nor is the rigorous assessment of their impact. However, these considerations do not obviate the need for stronger evidence. As researchers, healthcare providers and health service administrators continue to explore the benefits of using PROMs in clinical practice, greater attention is needed to the existing literature regarding how to implement PROMs interventions and how the impact of using PROMs can be most effectively measured.[111,147,148]

The policy environment for broadening the focus of HIV care

The widespread uptake of people-centred healthcare practices depends on more than the availability of scientific evidence that identifies the potential value of these practices. Healthcare providers and managers need to feel motivated to accept changes in how clinical care is delivered, particularly when they face the prospect of having new tasks added to clinical consultations and administrative processes. Population-level data can help to make the case for why HIV care providers should be attentive to a range of issues that do not directly relate to the goals of achieving and maintaining viral suppression. Thus, the first article in this thesis reports on a survey conducted to determine whether national health systems in six European countries are monitoring other important issues for PLHIV.

As previously noted, the CST-HIV has eight domains that are considered to be highly relevant to the HRQoL of PLHIV. The six-country monitoring survey, conducted prior to the development of the PROM, asked about issues that are pertinent to a number of these domains, including emotional distress, social support and material deprivation. It also asked if HRQoL itself is monitored. Findings suggest varying capacity to monitor these issues across the six study countries: Estonia, Italy, the Netherlands, Slovenia, Sweden and Turkey. Only two countries (Slovenia and Sweden) were reported to have the capacity to monitor indicators addressing the screening, diagnosis and treatment of anxiety and depression. None of the respondents reported the use of national-level indicators to monitor the provision of psychosocial services. Respondents from three countries (the Netherlands, Slovenia and Sweden) indicated that their national monitoring systems had the capacity to report on the HRQoL of PLHIV. Two weaknesses of the monitoring survey were the small number of countries surveyed and the sampling strategy, which relied on one purposively selected individual in each country to answer survey questions. It is not possible to draw firm conclusions from the results that were obtained, although results suggest that health system monitoring of healthcare for PLHIV may have had a narrow focus in some study countries at the time the survey was administered in the first half of 2018.

The larger lesson to be drawn in the context of this thesis is that research does not by default align with the priorities of national health systems, and that it is therefore not realistic to expect research to influence policy simply through the publication of findings in scientific journals. The disconnect between public health research and policy is in fact regarded as a widespread problem.[149] In the words of one commentator, "Policies and practices are often enacted either in apparent ignorance of the evidence or even in direct opposition to it. The examples are numerous, with the experience of a single country, the United Kingdom, justifying an entire book filled with examples tellingly titled 'The blunders of our governments.' "[150,151]

Thus, it is not sufficient to develop a PROM that identifies issues undermining the HRQoL of PLHIV if the policy environment does not encourage healthcare providers to recognise the value of such an instrument. Although it is beyond the scope of this thesis to address how the gap between public health research and policy might be reduced, this author contends that public health research can have a stronger impact when researchers develop greater policy literacy and engage in processes to communicate key evidence-based conclusions in language that policy-makers can easily understand. An example of the latter activity is the 2021 "Consensus statement on the role of health systems in advancing the long-term well-being of people living with HIV", developed through a Delphi process that this author helped to lead.[75]

8. Conclusions

This thesis has reported on the development and preliminary validation of the HIV clinic screening tool, a novel patient-reported outcome measure for advancing the health and HRQoL of PLHIV in Spain, while additionally exploring the policy context for providing people-centred HIV care. The following conclusions are submitted:

1. Consistent with the evidence base relating to the well-being of PLHIV in settings with widespread uptake of antiretroviral therapy, PLHIV in Spain face numerous barriers to enjoying good health-related quality of life. These include physical, psychological and social challenges.
2. In this study, PLHIV and healthcare providers indicated that high-priority health-related issues that should be addressed by a clinic screening tool include physical symptoms, emotional distress, socioeconomic vulnerability, and HIV-related stigma and discrimination.
3. Study participants' insights coupled with literature review findings led to the definition of eight constructs for inclusion in the CST-HIV: anticipated stigma, emotional distress, sexuality, social support, material deprivation, sleep/fatigue, cognitive problems, and physical symptoms.
4. In pilot testing, the CST-HIV demonstrated the adequacy of the proposed eight-factor structure and also demonstrated preliminary evidence of construct, convergent and concurrent validity.
5. The CST-HIV should undergo further study to explore its measurement properties and its potential contributions to routine outpatient HIV care in Spain.
6. Differences between the CST and the Positive Outcomes PROM, which is based on formative research conducted in the United Kingdom and Ireland, raise the question of whether issues such as immigration concerns, contraception and alcohol consumption may be prioritised differently by stakeholders in different cultures.
7. The relevance of the CST-HIV for HIV care in other countries should be investigated, taking into account the potential for social, cultural, epidemiological and health system factors to shape stakeholders' priorities.
8. Shortcomings in how PROMs are integrated into clinical practice may limit their possible value, and thus the CST-HIV should be implemented by healthcare providers in accordance with established best practices for the use of PROMs in clinical care.
9. Methodologically rigorous studies are needed to assess how the use of the CST-HIV affects specific dimensions of the clinical experience such as patient-provider communication, clinical decision-making, and health and HRQoL outcomes.
10. Researchers must engage with policy-makers and affected communities to maximise the potential for PROMs such as the CST-HIV to contribute to advancing the multidimensional health and HRQoL of PLHIV, consistent with the World Health Organization's vision of health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".[87]

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3 January 2022

I, Kelly Safreed Harmon, declare that all work carried out for my doctoral thesis, “**Development and validation of a clinic screening tool to improve clinical management of symptoms and health-related concerns in people living with HIV in Spain**,” presented to fulfil the doctoral degree requirements of the Barcelona Institute for Global Health and the Doctoral Program in Medicine and Translational Research, Faculty of Medicine, University of Barcelona, complies fully with good research practices and ethical codes, including those governing the participation of human subjects in research.

This thesis does not contain plagiarism, and I consent to all procedures to verify its originality.

Cordially,

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9 January 2022

We, Jeffrey V Lazarus and Denise Naniche, co-directors of Kelly Safreed Harmon's doctoral thesis, "**Development and validation of a clinic screening tool to improve clinical management of symptoms and health-related concerns in people living with HIV in Spain**," presented to fulfil the doctoral degree requirements of the Barcelona Institute for Global Health and the Doctoral Program in Medicine and Translational Research, Faculty of Medicine, University of Barcelona, attest that the thesis complies fully with good research practices and ethical codes, including those governing the participation of human subjects in research. To our knowledge, the thesis does not contain plagiarism.

Cordially,

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