10 Years On: How Has Incorporation of Health-related Quality of Life (HRQoL) in HIV Research Changed Since the Proposal of the '4th 90' Target?

Poster P468

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Key Takeaways

- **The number of health-related quality of life (HRQoL)-related interventional and observational studies reported in recent HIV literature has increased since the '4th 90' target was proposed by Lazarus et al. in 2016,[1] with more HIV-specific QoL and HRQoL instruments being introduced and utilised over time**
- **We observed many social media posts from the HIV community referring to HRQoL or associated terms, suggesting the increased interest in HRQoL is also reflected in public discourse**
- **Despite evidence of the increasing prominence of HRQoL in HIV clinical research and community discussions, incorporation of HRQoL into clinical guidelines, care pathways and routine clinical care is limited, and its application in clinical practice is likely to be highly variable**
- **HRQoL is broad and influenced by many factors, which may be beyond the scope of guidelines and clinical care alone. Defining the HIV and treatment-related aspects of HRQoL that care can directly influence may offer a practical route to recognising these as additional markers of treatment success in routine care**

Plain Language Summary

- Following the introduction of the Joint United Nations Programme on HIV/AIDS 90-90-90 treatment targets in 2016, a paper suggested that another target should be considered, known as the '4th 90', to recognise the importance of health-related quality of life (HRQoL)[1]
- In our analysis, we looked at whether the scientific reporting and public opinion of HRQoL related to HIV treatment have changed since the 4th 90 target was proposed
- We found that HRQoL is measured in scientific papers more recently (2024–2026) than it was before the 4th 90 target was proposed (2014–2016), and that people are discussing HRQoL online. However, mention of HRQoL in HIV management guidelines is limited
- It is important that there is guidance on how to measure and improve HRQoL outcomes so they can become part of routine care for people with HIV

Introduction

- The World Health Organization (WHO) constitution broadly defines 'health' as "…a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity"[2]
- In 2016, the WHO adopted a new Global Health Sector Strategy on HIV for 2016–2021, including the Joint United Nations Programme on HIV/AIDS (UNAIDS) '90-90-90' targets in which 90% people with HIV are diagnosed, 90% of those diagnosed are on treatment, and 90% of those who are receiving treatment are virally suppressed[3,4]; however, a QoL-related target was not included
- Shortly following publication of these targets, Lazarus et al. proposed that a '4th 90' target should be considered, in which 90% of virally suppressed people achieve good HRQoL,[1] to support the end of the HIV epidemic
- When the UNAIDS targets were updated to '95-95-95'[5], the proposed 4th 90 target was not incorporated; despite increasing recognition of the importance of HRQoL outcomes in people with HIV, its incorporation into clinical practice is unclear
- In our analysis, we examined:
  - How the integration of HRQoL and related concepts have changed in scientific literature from the period before the 4th 90 target was proposed (2014–2016) versus the last two years (2024–2026);
  - Whether there is engagement with HRQoL outcomes in the HIV community; and
  - What guidance clinical HIV guidelines include for reporting HRQoL outcomes

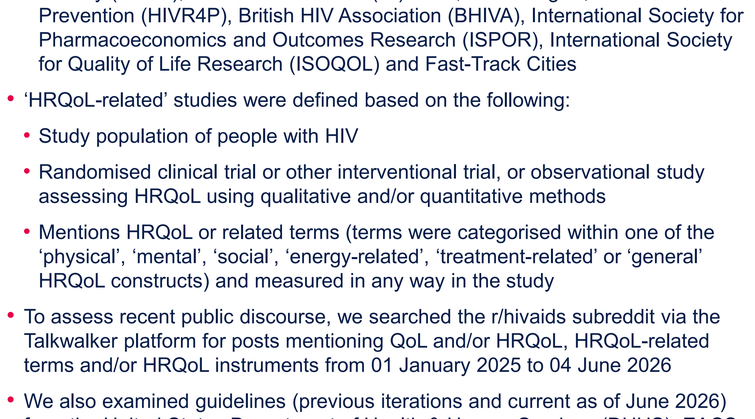
Methods

- We conducted a pragmatic literature review of congress and journal article abstracts via PubMed, Embase and selected congresses between 01 June 2014 and 31 May 2016 ('Period 1'), and 01 May 2024 and 30 April 2026 ('Period 2')
  - PubMed and Embase article results were reviewed for any duplicates, with the PubMed record prioritised over Embase
  - Congresses included International AIDS Society (IAS), AIDS, Conference on Retroviruses and Opportunistic Infections (CROI), European AIDS Clinical Society (EACS), Infectious Diseases (ID)Week, HIV Glasgow, HIV Research for Prevention (HIVR4P), British HIV Association (BHIVA), International Society for Pharmacoeconomics and Outcomes Research (ISPOR), International Society for Quality of Life Research (ISOQOL) and Fast-Track Cities
- 'HRQoL-related' studies were defined based on the following:
  - Study population of people with HIV
  - Randomised clinical trial or other interventional trial, or observational study assessing HRQoL using qualitative and/or quantitative methods
  - Mentions HRQoL or related terms (terms were categorised within one of the 'physical', 'mental', 'social', 'energy-related', 'treatment-related' or 'general' HRQoL constructs) and measured in any way in the study
- To assess recent public discourse, we searched the r/hivaids subreddit via the Talkwalker platform for posts mentioning QoL and/or HRQoL, HRQoL-related terms and/or HRQoL instruments from 01 January 2025 to 04 June 2026
- We also examined guidelines (previous iterations and current as of June 2026) from the United States Department of Health & Human Services (DHHS), EACS, IAS-USA and WHO for HRQoL-related recommendations
  - DHHS: September 2025 only; EACS: October 2017 through to October 2025; IAS-USA: July 2016 through to December 2024; WHO: July 2021 through to December 2025

Results

- We observed 4,052 independent literature results; following screening for HRQoL-related studies, 707 abstracts were included for the analysis (**Figure 1**)

Figure 1. Flow Chart of Screening Results



Analysis of HRQoL-related Studies

- Reporting of HRQoL-related studies almost tripled between Period 1 (June 2014 to May 2016) and Period 2 (May 2024 to April 2026; n=179 vs n=528; difference of +195%; **Table 1**)
  - In an ad-hoc analysis of complete-year comparisons (2015 vs 2025), the number of HRQoL-related studies increased from 87 (2015) to 317 (2025; difference of +264%)
- Most HRQoL-related studies were non-industry supported (Period 1: n=172/179 [96%]; Period 2: n=489/528 [93%]) and observational (Period 1: n=100/179 [56%]; Period 2: n=381/528 [72%]; **Table 1**)
- Increases were observed across all regions, with the largest in Europe (Period 1: n=16; Period 2: n=73; difference of +356%) and Africa (Period 1: n=46; Period 2: n=170; difference of +270%; **Table 1**)
- Reporting across all HRQoL constructs increased, with the largest increase observed in 'Treatment-related' constructs (Period 1: n=23; Period 2: n=128; difference of +457%; **Table 1**)
  - 'Mental', with associated terms including anxiety, depression and stress, was the highest reported construct in HRQoL-related studies across both periods (Period 1: n=98/179 [55%]; Period 2: n=330/528 [63%]; **Table 1**)

Table 1. Analysis of HRQoL-related Studies Reported in Literature from Period 1 (June 2014 to May 2016) versus Period 2 (May 2024 to April 2026)

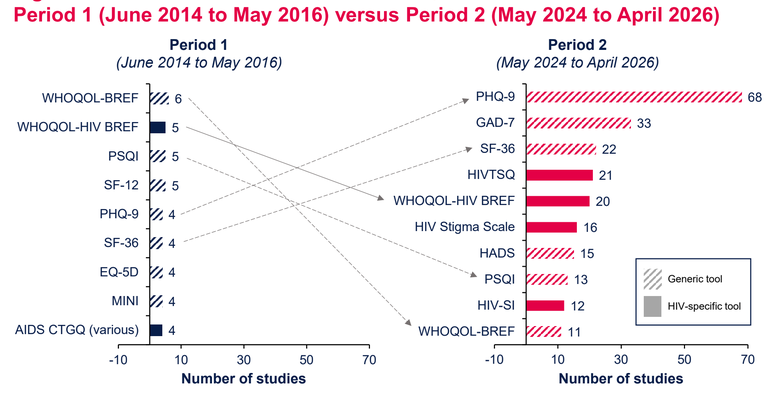
	Period 1 *(Jun 2014 to May 2016)*	Period 2 *(May 2024 to Apr 2026)*	Difference, n (%)
HRQoL-related studies, n	179	528	+349 (195)
Study type, n			
Observational	100	381	+281 (281)
Randomised controlled trial	56	118	+62 (111)
Other controlled trial	23	29	+6 (26)
Industry supported, n	7	39	+32 (457)
Randomised controlled trial/ other controlled trial	6	13	+7 (117)
Observational	1	26	+25 (2,500)
Region, n*			
Africa	46	170	+124 (270)
Americas	28	92	+64 (229)
Asia-Pacific	27	90	+63 (233)
Europe	16	73	+57 (356)
Unknown	62	124	+62 (100)
HRQoL construct reported, n*			
Mental	98	330	+232 (237)
Social	48	189	+141 (294)
General	57	166	+109 (191)
Treatment-related	23	128	+105 (457)
Energy-related	29	55	+26 (90)
Physical	16	31	+15 (94)
QoL or HRQoL instrument, n*			
HIV-specific, validated	19	93	+74 (389)
Generic, validated	77	235	+158 (205)
Unvalidated or Unknown	99	253	+154 (156)
HRQoL mention, n			
In abstract (excl. conclusions)	178	524	+346 (194)
In conclusions	144	465	+321 (223)

*Studies may include multiple regions, constructs and/or HRQoL instruments
HRQoL, health-related quality of life; QoL, quality of life

Use of QoL and HRQoL Instruments in HRQoL-related Studies

- The use of validated HIV-specific and generic instruments increased from Period 1 to Period 2 by 389% and 205% respectively, with unvalidated tools increasing by 156% (**Table 1**)
  - The most used instruments in recent literature were the Patient Health Questionnaire-9 (PHQ-9), the Generalised Anxiety Disorder-7 (GAD-7) tool and the Short Form-36 (SF-36) survey, and the most used HIV-specific tools were the HIV Treatment Satisfaction Questionnaire (HIVTSQ), WHO QoL-HIV Brief Questionnaire (WHOQOL-HIV BREF) and HIV Stigma Scale (**Figure 2**)

Figure 2. Most Used Validated QoL and HRQoL Instruments in Literature in Period 1 (June 2014 to May 2016) versus Period 2 (May 2024 to April 2026)

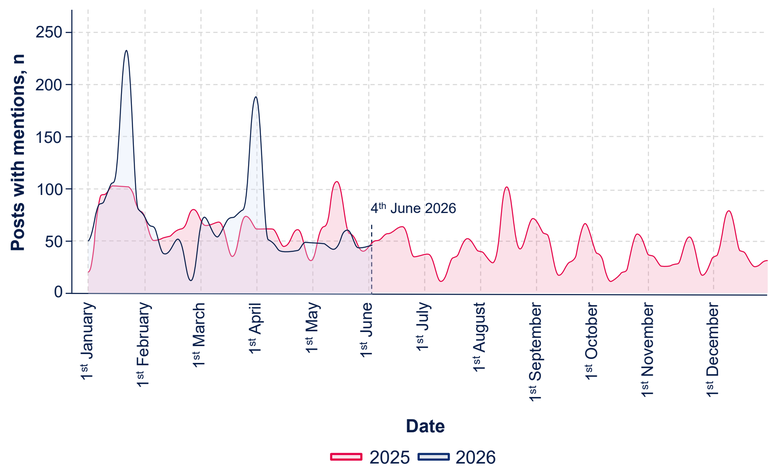


Overall, 371 studies reported the use of validated instruments (Period 1: n=86; Period 2: n=285). Of these studies, 112 used HIV-specific instruments, 312 used generic instruments, and 53 used both. The charts display the most frequently used instruments in each time period, applying minimum thresholds of four studies for Period 1 and 11 studies for Period 2; thresholds were based on the natural distribution of studies within each time period, resulting in ~10 instruments displayed per period.
AIDS CTGQ, AIDS Clinical Trial Group Questionnaire; GAD-7, Generalised Anxiety Disorder-7; HADS, Hospital Anxiety and Depression Scale; HIV-SI, HIV Symptom Index; HIVTSQ, HIV Treatment Satisfaction Questionnaire; HRQoL, health-related quality of life; MINI, Mini-International Neuropsychiatric Interview; PHQ-9, Patient Health Questionnaire-9; PSQI, Pittsburgh Sleep Quality Index; SF-12/36, Short Form-12/36; WHOQOL-BREF, World Health Organization Quality of Life – Brief Questionnaire; WHOQOL-HIV BREF; World Health Organization Quality of Life – HIV Brief Questionnaire

Public Discourse of QoL

- The pre-defined subreddit search identified 4,303 posts in 2025 and 2026 referring to HRQoL or associated terms (**Figure 3**)
  - There were 2,675 posts in 2025 and 1,628 posts in 2026 (up to 04 June 2026)
  - Posts in the first 5 months of 2026 reached 59% of the total 2025 volume

Figure 3. Number of Posts Mentioning QoL and/or HRQoL, HRQoL-related Terms and/or HRQoL Instruments in the Subreddit r/hivaids



Mention of HRQoL in Clinical Guidelines

- Reference to QoL and/or HRQoL in current HIV clinical guidelines is limited
- EACS guidelines introduced a section for patient-reported outcome measures (PROMs) in 2023,[6] and updated in 2025[7]
  - The current EACS guidelines provide guidance on what data to collect, recommendations for HIV-specific (e.g. HIV Symptom Index [HIV-SI], HIV Stigma Scale, WHOQOL-HIV BREF) and non-specific tools, and how PROMs should be used to improve clinical care[7]
- The most recent iterations of the DHHS, IAS-USA and WHO guidelines (as of June 2026) have little or no direct mention of QoL and/or HRQoL or PROMs[8–10]

Conclusions

- The number of HRQoL-related HIV studies reported in literature has increased nearly three-fold since the 4th 90 target was proposed, with interest also reflected in public discourse
  - The large representation of independent, observational studies may reflect progress in integrating HRQoL into clinical practice
- The use of HIV-specific validated instruments in interventional and observational studies has increased over time
  - In Period 2, frequent reporting of PHQ9 and GAD7 may indicate the recent importance of assessing mental health, while the introduction of the HIV Stigma Scale reflects the growing recognition of stigma
  - HIVTSQ was the most frequently used HIV-specific tool in the current period, suggesting that treatment satisfaction is increasingly important in modern care
- However, the incorporation of QoL and/or HRQoL in guidelines remains limited, and as a subjective, multidimensional outcome, its application in clinical practice is variable
  - Unvalidated tool use increased over time, despite the availability of HIV-specific tools, highlighting the need for guidance on appropriate tool selection
- It is essential that HRQoL as a non-virological marker of treatment success is not only recognised and incorporated into clinical guidelines, but that HRQoL measurement, and sufficient time to do so, becomes part of routine practice, to support effective person-centred care and efforts to end the HIV epidemic

Study Limitations

- Reviewing titles and abstracts only may have excluded insights reported in full publications
- Comparing two selected periods may have missed developments between them, and Talkwalker data were available only from 2025, limiting the assessment of long-term trends
- Assigning each HRQoL term to a single construct rather than multiple may have led to misclassification

Acknowledgments: This study was funded by ViiV Healthcare. Editorial assistance and graphic design support for this poster were provided under the direction of the authors by Ashfield MedComms, an Inizio Company, and funded by ViiV Healthcare

References: 1. Lazarus JV, et al. BMC Med 2016;14:94; **2.** WHO. Constitution of the World Health Organization. 1946; **3.** WHO. Draft global health sector strategies: HIV, 2016–2021; **4.** UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic; **5.** UNAIDS. Understanding measures of progress towards the 95–95–95 HIV testing, treatment and viral suppression targets; **6.** EACS. EACS Guidelines, Version 12.0. October 2023; **7.** EACS. EACS Guidelines, Version 13.0. October 2025; **8.** DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV. September 2025; **9.** Gandhi RT, et al. JAMA 2025;333:609–628; **10.** WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. July 2021

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