Evaluation of the psychometric properties of health-related quality of life patient-reported outcome measures for use in people living with HIV and cognitive symptoms

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BACKGROUND

- PLWH with cognitive impairment report poor health-related quality of life (HRQL) and there are domains comprising HRQL which are unique to this population (1,2).
- Prior qualitative and cross-sectional work has identified and validated important domains influencing HRQL in PLWH with cognitive symptoms. These included: Physical function, Cognitive symptoms, Social connectedness, Self-concept, HIV-stigma, Acceptance of and perceived control over cognitive health outcomes, and Physical and mental health and wellbeing (2,3).
- Research and clinical care aiming to target and improve HRQL in this population relies on HRQL patient-reported outcome measures (PROMs) to assess impact; however, for PLWH with cognitive impairment, no illness-specific HRQoL measures exist.
- Instead, researchers and clinicians must select instruments to monitor HRQL, ascertain changes, or current problem areas, without theoretical or empirical evidence regarding which PROMs best capture this outcome.

➢ **This study aimed to examine the psychometric properties of existing PROMs to produce recommendations regarding which PROM/s is best suited to assessing HRQL in this population.**

METHODS

- PLWH with cognitive symptoms based on European AIDS Clinical Society screening guidelines (4) were identified from two HIV clinics in London and Brighton (UK).
- Participants completed four generic or illness-specific (HIV or mild/moderate dementia) quality of life (QoL) or HRQL PROMs. PROMs were selected based on frequency of use in both sites' HIV memory/neurology services. PROMs included were the **WHOQOL-BREF (5), EQ-5D-5L (6), HIVPROM (7) and the DEMQOL (8).**
- We followed the COnsensus-based Standards for the selection of health status Measurement INstruments (COSMIN) (9) recommendations for evaluating measurement properties which included statistical psychometric evaluations: item/scoring distributions, internal reliability (Cronbach's Alpha, α), construct validity (item-domain convergence), convergent and divergent validity (Multitrait Multimethod analysis (10))). Alongside cognitive debriefing exercises with PLWH with cognitive symptoms and expert professionals to assess content validity and face validity.

RESULTS

- 103 PLWH with cognitive symptoms participated (Table 1)
- Statistical psychometric assessments revealed (Table 2):

➢ WHOQOL-BREF, EQ-5D-5L and HIVPROM showed evidence of item skewness and floor/ceiling effects on sub-domain scores, indicating possible item irrelevance in the population

➢ WHOQOL-BREF and DEMQOL showed good internal reliabilities overall and within each sub-domain (α > 0.7). The HIVPROM showed poor internal consistency overall and within the Social and the Relational sub-domains (α < 0.4). Internal reliability is not computable for the EQ-5D-5L as each domain is comprised of only one item.

➢ All domains of the WHOQOL-BREF and DEMQOL showed strong construct validity, insofar as items within each domain correlated highest with their posited domain and not another. The Social construct in the HIVPROM did not demonstrate construct validity, suggesting in PLWH with cognitive symptoms the items within this domain do not represent this construct. This is not computable for the EQ-5D-5L as each domain is comprised of only one item.

➢ The WHOQOL-BREF and DEMQOL performed best on convergent and divergent validity tests, which requires subdomain scores to correlate higher with a score on a conceptually similar independent measure than with conceptually dissimilar same measure subdomains (convergent). Divergent validity posits the opposite to be true.

Table 1. Participant demographics and clinical characteristics

Variable (n)	
Age in years (range) *	58.8 (32-88)
Male (%)	93 (90.3)
Women (%)	10 (9.7)
Race/Ethnicity	
White – British (%)	66 (64.1)
Black – African (%)	11 (10.7)
White – Other (%)	19 (18.4)
Other (%)	7 (6.8)
Sexuality	
MSM (%)	75 (72.8)
Heterosexual (%)	23 (22.3)
Other (%)	5 (4.9)
Relationship Status	
Single (%)	55 (53.4)
In a relationship (%)	16 (15.5)
Married/Civil Partnership (%)	32 (31.1)
Employment	
Full time employed (%)	23 (22.3)
Part-time employed (%)	6 (5.8)
Unemployed (%)	40 (38.8)
Retired (%)	34 (33)
Health variables	
MoCA score (SD) **	17.85 (3.12)
HIV clinical variables	
Years with HIV*	19 (2-36)
Years on ART*	15 (2-31)
VL > 40 copies/ml (%)	5 (5)
On cART (%)	103 (100)

MSM, men who have sex with men; MoCA, Montreal Cognitive Assessment; cART, combination antiretroviral therapy; VL, viral load.
All values are expressed as n, unless otherwise stated. *median (range). **mean (standard deviation)

Table 2. Results from statistical psychometric assessments conducted

	Item Skew (+/- skew)	Sub-domain Floor/ ceiling effects	Internal reliability (Cronbach α) (across PROM whole and sub-domains	Structural construct validity (of posited subdomains)	Convergent/ divergent validity average (difference)
WHOQOL-BREF[5]	5 items +	No	Good (all >0.8)	Yes	0.65/0.43 (0.22)
EQ-5D-5L[6]	1 item -	Yes (mobility, self-care, activities, anxiety/depression)	n/a	n/a	0.54/0.35 (0.19)
HIVPROM[7]	11 items +/-	Yes (relational and informational domains)	Overall and social and relations poor (<0.4)	No *social construct	0.49/0.31 (0.18)
DEMQOL[8]	None	No	Good (all>0.7)	Yes	0.62/0.43 (0.19)

- Cognitive debriefing exercises were conducted with 10 PLWH with cognitive symptoms (8 (80%) were male; median age was 53 years; 7 (70%) White British, 2 (20% Black African) and 5 expert professionals (4 (80%) health professionals; 1 (20%) academic). Participants were asked questions adapted from the COSMIN criteria and rating system for evaluating content validity (Table 3).

➢ Content analysis of the interviews revealed four main themes: Layout and format, ambiguous questions or abstract questions, relevance and comprehensiveness, Implementation/interpretation (professionals only), which were then interpreted based on the COSMIN criteria (Table 3).

➢ Participants described issues with the recall period (EQ-5D-5L, HIVPROM), response options (HIVPROM), and wording of some questions (WHOQOL-BREF, HIVPROM).

➢ None of the PROMs were considered to capture all factors relevant to HRQoL, however, PLWH with cognitive symptoms felt the HIVPROM and DEMQOL captured highly relevant factors albeit with some important omissions.

Table 3. COSMIN criteria and rating system for evaluating the content validity of PROMs

	WHOQOL-BREF	EQ-5D-5L	HIVPROM	DEMQOL
Relevance				
Are the included items relevant for the construct of interest?	✓	✓	✓	✓
Are the included items relevant for the target population of interest?	✓	✓	✓	✓
Are the included items relevant for the context of use of interest?				
Are the response options appropriate?	✓	✓	x	✓
Is the recall period appropriate?	✓	x	x	✓
Comprehensiveness				
Are all key concepts included?	x	x	+	+
Comprehensibility				
Are the PROM instructions understood by the population of interest as intended?	✓	✓	✓	✓
Are the PROM items and response options understood by the population of interest as intended?	x	✓	x	✓
Are the PROM items appropriately worded?	x	✓	x	✓
Do the response options match the questions?	✓	✓	✓	✓

+ indicates items are relevant and important; however, to be fully comprehensive additional items are required

CONCLUSIONS

- **WHOQOL-BREF and DEMQOL perform best in terms of statistical psychometric evaluations.**
- **Face and content validity exercises show preferences towards DEMQOL and HIVPROM, but all measures lack complete comprehensiveness of important domains.**
- **Given that the DEMQOL perform well in both types of assessment this is recommended as the primary measure of HRQoL in PLWH with cognitive symptoms, however, to increase comprehensiveness it should be supplemented with a second PROM. The WHOQOL-BREF may add value in research studies given its strong statistical psychometric properties and availability of comparative data. The HIVPROM may be more suitable to clinical settings or where HIV-related factors are particularly apparent.**

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