Congresso Nazionale
AGGIORNAMENTI INFETTIVOLOGICI:
HIV, EPATITI & …..
Firenze, 15-17 Gennaio 2024
Centro Congressi Hotel Albani

La qualità della vita come end-point

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Disclosure:

A. Cingolani served as consultant for ViiV Healthcare, Gilead, Bristol Meyer Squibb, Janssen

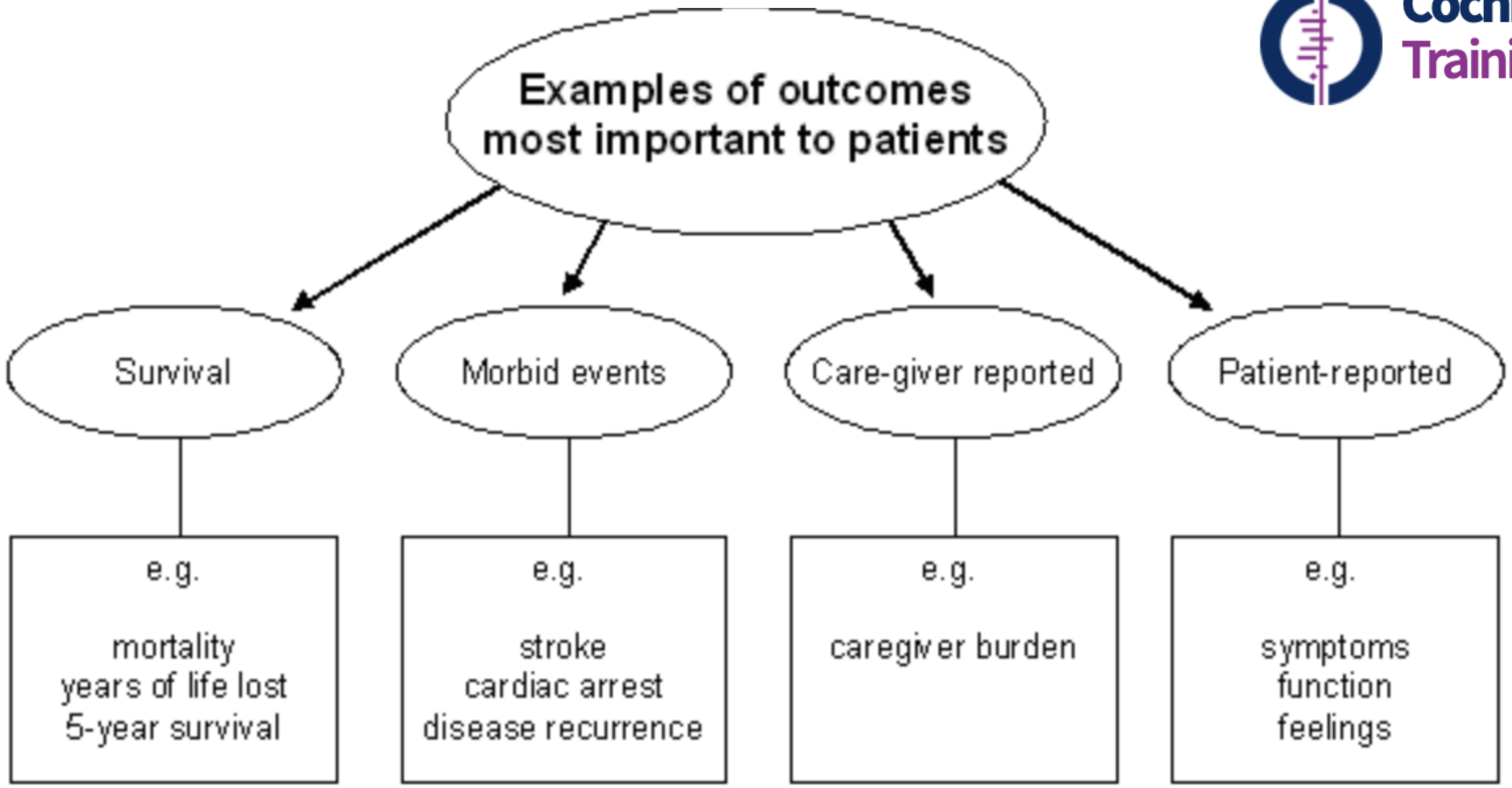
HR-QoL and HIV

- ART has changed HIV to a chronic condition but **PLWH c**ontinue to have substantially **lower HRQoL than the general population** (even virological suppressed and immunologically stable PLWH)
- Evidence suggests that in addition to the underlying infection, social circumstances, relationship issues, comorbidities and stigma may **impact on HRQoL** in PLWH
- **Improving quality of life is central to the care and support of PLWH.**
- **Present and future of PLWH care** passes towards the **ability to collect individual's perception of HRQoL**, using patient reported outcomes (**PROs**)

Could QoL be considered an outcome?

Cochrane Training

Trusted evidence.
Informed decisions.
Better health.



Johnston BC, Patrick DL, Devji T, Maxwell LJ, Bingham III CO, Beaton D, Boers M, Briel M, Busse JW, Carrasco-Labra A, Christensen R, da Costa BR, El Dib R, Lyddiatt A, Ostelo RW, Shea B, Singh J, Terwee CB, Williamson PR, Gagnier JJ, Tugwell P, Guyatt GH. Chapter 18: Patient-reported outcomes. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.4 (updated August 2023). Cochrane, 2023. Available from www.training.cochrane.org/handbook.

How to measure QoL: Patient reported outcomes (PRO)

Symptoms
QoL, HR-QoL
Satisfaction with Care
Treatment adherence

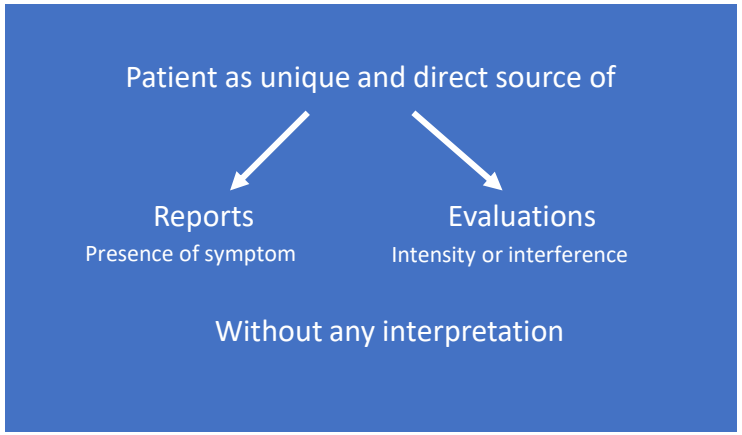
- The condition of health at a given point of time
- Health: A multi-dimensional concept[2]
  - **Not** only the absence of diseases or illness
  - **But** physical, mental, and social well-being

A PRO is a measurement of any aspect of a patient's health status that comes directly from the patient without the interpretation by physicians or anyone else[1]

- Measurement implies a tool with known characteristics in terms of validity[3]
- Validity is not a yes/no attribute but implies the availability of a comprehensive set of information and data

Validity
Reliability
Responsiveness
Interpretability

- Conceptual framework
- Item generation
- Scaling, scoring
- Item reduction
- Reproducibility
- Content validity
- Construct validity
- Discriminant validity
- Convergent validity
- Responsiveness
- Cultural adaptation



1. Apolone G, *Health Qual Life Outcomes*. 2003;1:3; 2. Pollard B, et al. *Health Qual Life Outcomes*. 2007;5:14; 3. Medical News Today 2017. Available at: https://www.medicalnewstoday.com/articles/150999.php (Last accessed June 2019).

Checklist for describing and assessing PROMs in clinical trials.

1. What were the PROMs assessing?
1.1. What concepts or constructs were the PROMs used in the study assessing?
1.2. What rationale (if any) for selection of concepts or constructs did the authors provide?
1.3. Were patients involved in the development (e.g. focus groups, surveys) of PROMs?
2. Omissions
2.1 Were there any important aspects of patient's health (e.g. symptoms, function, perceptions) or quality of life (e.g. overall evaluation, satisfaction with life) that were not reported in this study? A search for 'Core Outcome Sets' for condition would be helpful (see Section 18.4.1).
3. What were the measurement strategies?
3.1. Did investigators use instruments that yield a single indicator or index number, or a profile, or a battery of instruments?
3.2. Did investigators use specific or generic measures, or both?
4. Did the instruments work in the way they were supposed to work – validity?
4.1. Was evidence of prior validation for use in the current population presented?
5. Did the instruments work in the way they were supposed to work – responsiveness?
5.1 Are the PROMs able to detect important change in patient status, even if those changes are small?
6. Can you make the magnitude of effect (if any) understandable to readers – interpretability?
6.1 If the intervention has had an apparent impact on a PROM, can you provide users with a sense of whether that effect is trivial, small but important, moderate, or large?

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Patrick and Erickson, a Users' Guide to the Medical Literature, CDC guidance for evaluation of community preventive services, and criteria used by the Medical Outcomes Trust (Patrick 1993, Guyatt 1997, Zaza 2000, Lohr 2002).

JAMA | Special Communication

Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols
The SPIRIT-PRO Extension

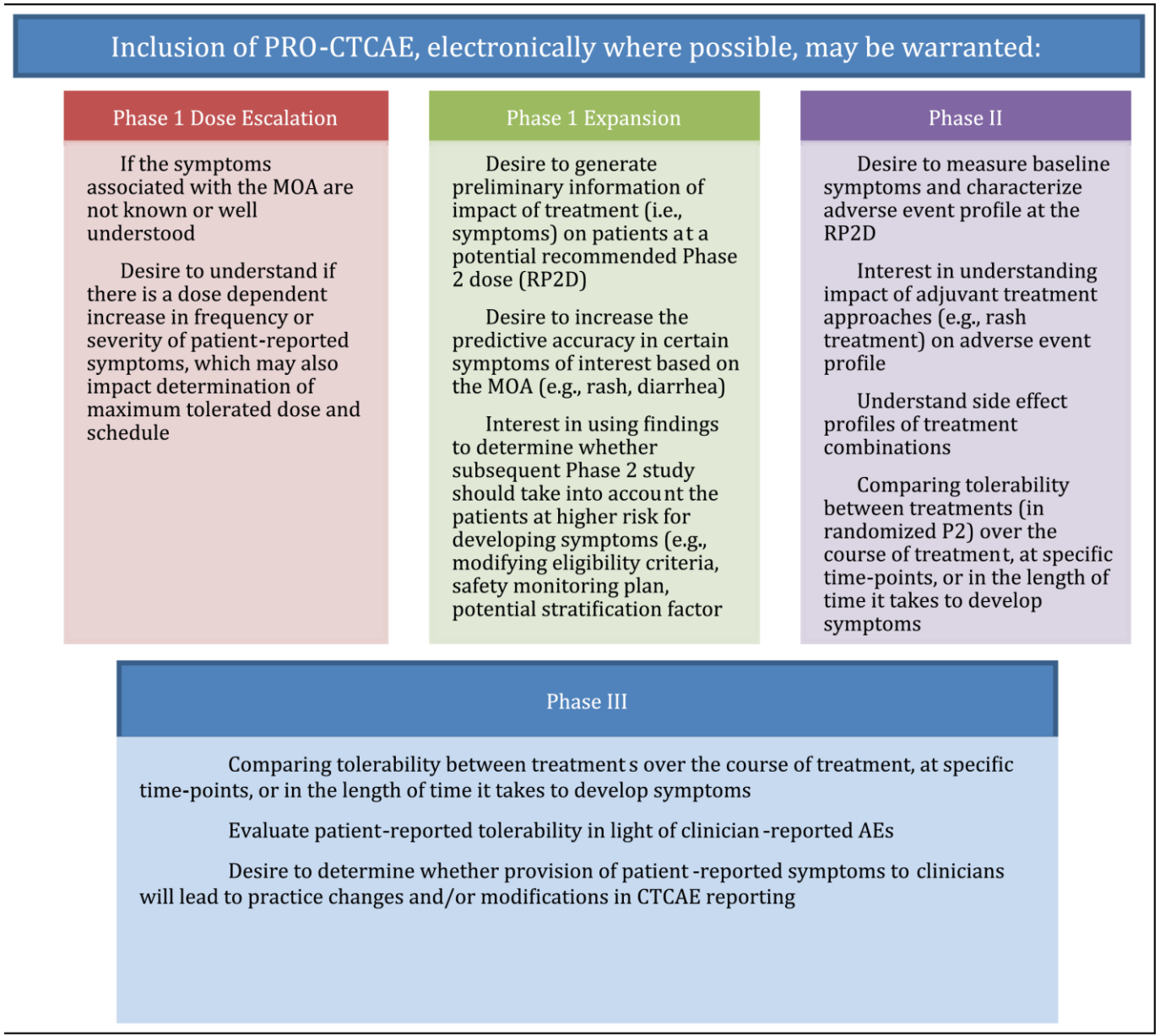
Melanie Calvert, PhD; Derek Kyte, PhD; Rebecca Mercieca-Bebber, PhD; Anita Slade, PhD; An-Wen Chan, MD, DPhil; Madeleine T. King, PhD; and the SPIRIT-PRO Group

Special Communication

February 6, 2018

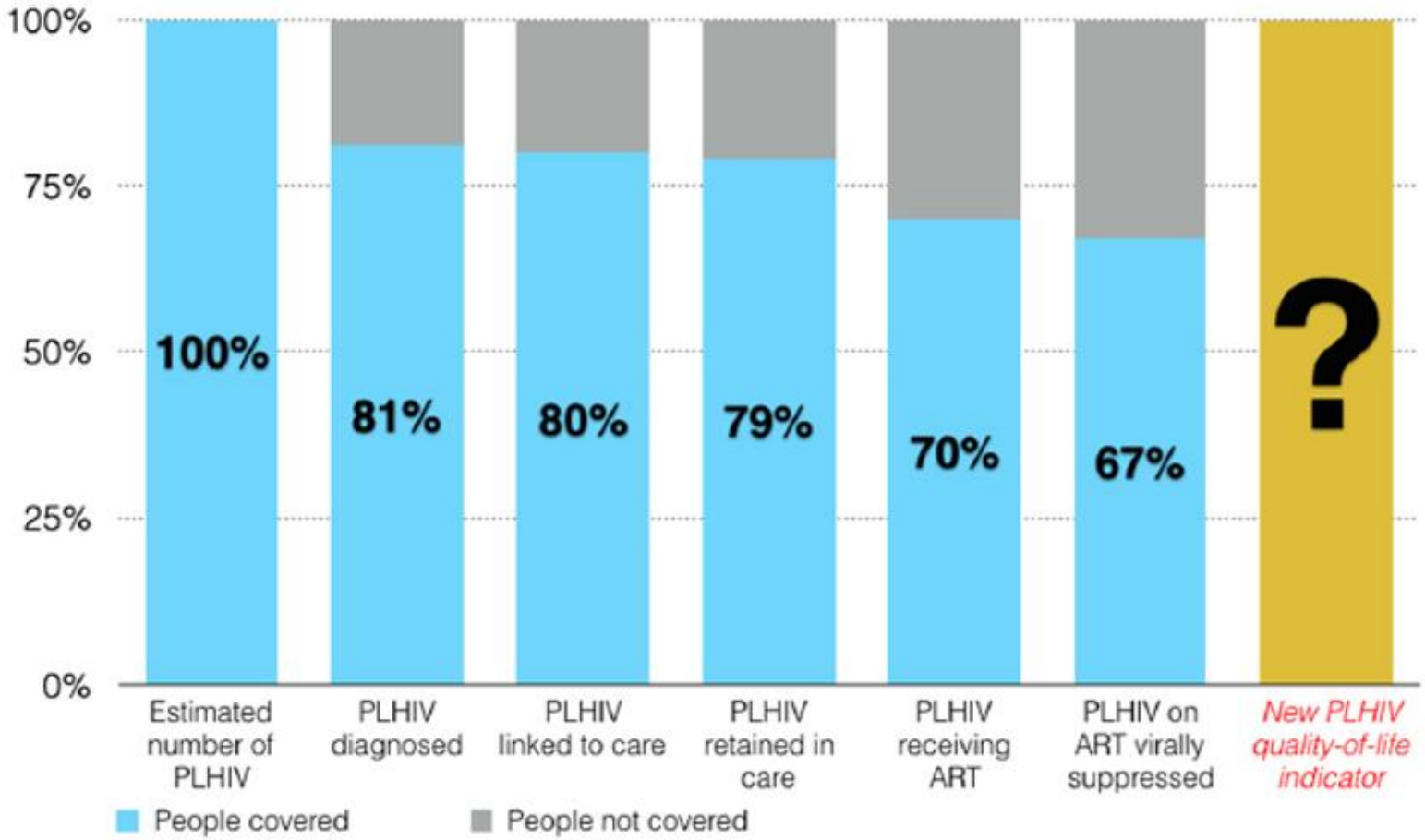
Section/Topic	Item	CONSORT 2010 Statement Checklist Item	PRO-Specific Extensions Are Prefaced by the letter *P*
		Title and Abstract	
	1a	Identification as a randomized trial in the title	
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[3]	P1b: The PRO should be identified in the abstract as a primary or secondary outcome
		Introduction	
Background and objectives	2a	Scientific background and explanation of rationale	Including background and rationale for PRO assessment
	2b	Specific objectives or hypotheses	P2b: The PRO hypothesis should be stated and relevant domains identified, if applicable
		Methods	
Trial design	3a	Description of trial design (such as parallel, factorial), including allocation ratio	
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	Not PRO-specific, unless the PROs were used in eligibility or stratification criteria
	4b	Settings and locations where the data were collected	
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	
Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	P6a: Evidence of PRO instrument validity and reliability should be provided or cited if available including the person completing the PRO and methods of data collection (paper, telephone, electronic, other)
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	Not required for PRO unless it is a primary study outcome
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
		Results	
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	The number of PRO outcome data at baseline and at subsequent time points should be made transparent
	13b	For each group, losses and exclusions after randomization, together with reasons	
Recruitment	14a	Dates defining the periods of recruitment and follow-up	
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Including baseline PRO data when collected
Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Required for PRO results
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, the estimated effect size, and its precision (such as 95% confidence interval)	For multidimensional PRO results from each domain and time point
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
		Results	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory	Including PRO analyses, where relevant
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
		Discussion	
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	P20/21: PRO–specific limitations and implications for generalizability and clinical practice
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	PRO data should be interpreted in relation to clinical outcomes including survival data, where relevant

Recommendations on whether to include Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events in clinical trials (PRO-CTCAE Working Group)



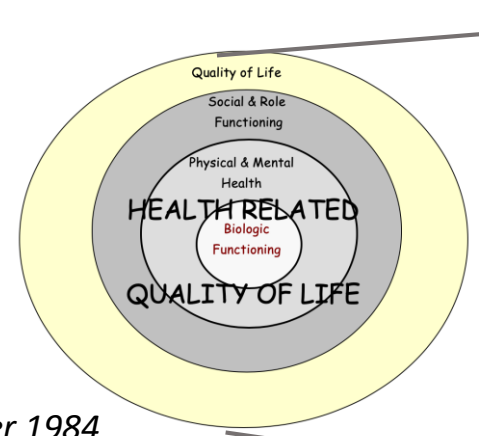
Trask, Clin Trials 2018

Qol . The need of a unique definition as end point

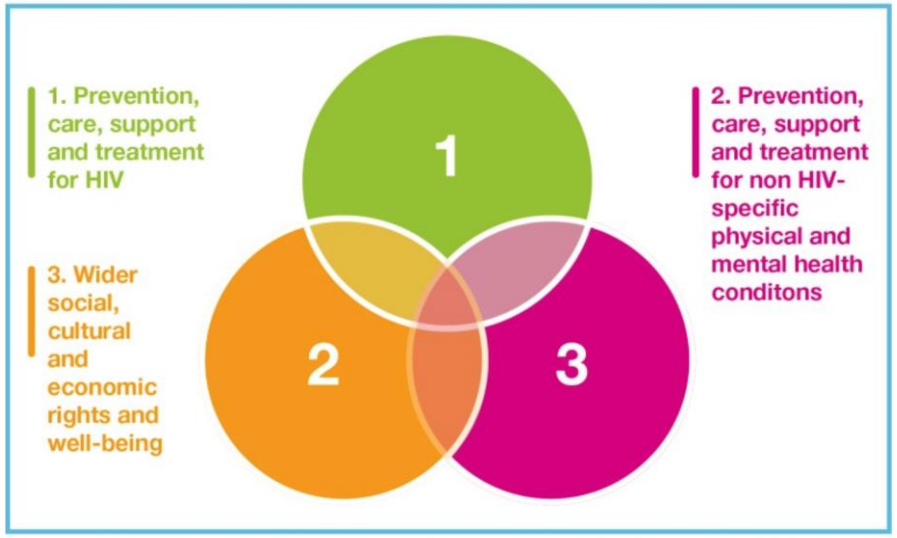


*Adapted from Philipp Kohler, Axel J. Schmidt, Matthias Cavassini, Hansjakob Furrer, Alexandra Calmy, Manuel Battegay, *et al.* The HIV care cascade in Switzerland: reaching the UNAIDS/WHO targets for patients diagnosed with HIV. *AIDS* 2015; 18: 2509-2515

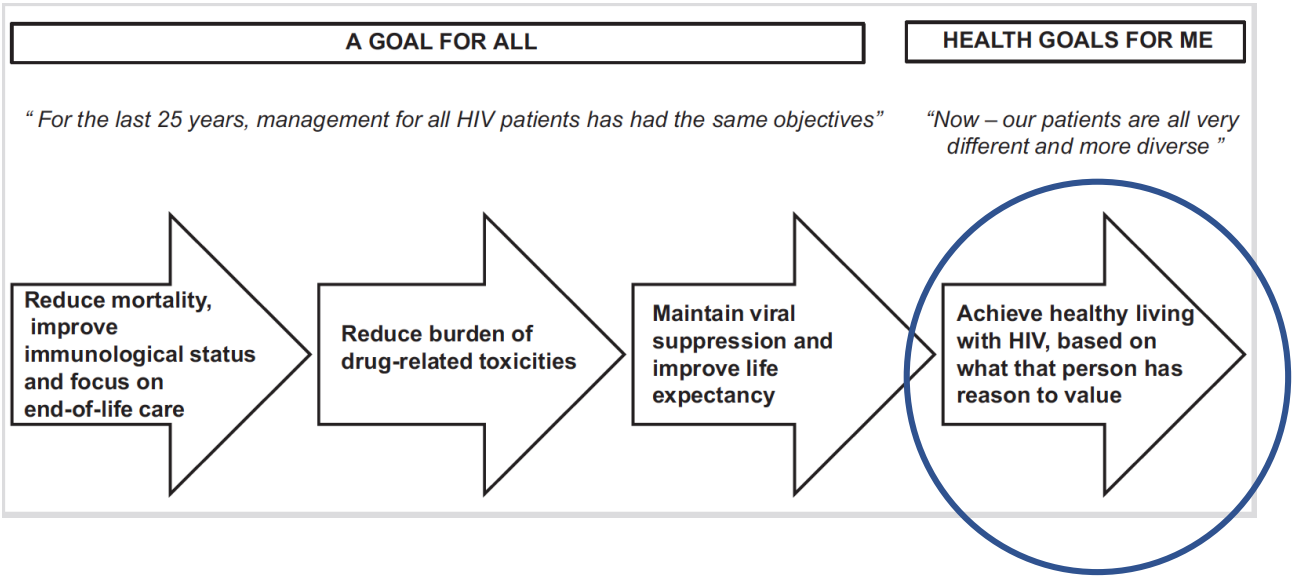
QoL. The challenge of a unique definition as end point



Ware, Cancer 1984



FRONTLINE AIDS



G. Guaraldi, AIDS Rev 2019

QoL as end point in cohort studies

HIV treatment and disease burden (H-TDB) : role of treatment satisfaction

On line anonymous survey on 531 pts

Objectives

- To investigate the potential correlates of disease burden from the point of view of PLHIV.
- To correlate the disease burden with the overall self-reported health status.

	OR	p	95%CI		aOR*	p	95%CI	
Age (per 10 years older)	0.68	<0.001	0.56	0.84	0.70	0.002	0.55	0.87
Current HIV-RNA								
<50 cps/mL	1.00				1.00			
>=50 cps/mL	2.04	0.104	0.86	4.83	1.96	0.174	0.74	5.20
unknown	2.13	0.047	1.01	4.51	1.29	0.606	0.49	3.37
Current Regimen (R)								
2 ARV R STR or MTR	1.00				1.00			
3 ARV R STR (w/o booster)	1.54	0.128	0.88	2.70	1.57	0.227	0.75	3.31
3 ARV R MTR or 3 ARV R STR w booster	2.07	0.033	1.06	4.05	1.44	0.234	0.79	2.62
Unknwon	4.41	0.001	1.82	10.69	3.20	0.031	1.11	9.24
Treatment Satisfaction								
Yes, fully	1.00				1.00			
Yes, but can be improved	3.17	<0.001	1.93	5.21	2.39	0.001	1.40	4.09
No, I've some issues	7.27	<0.001	2.50	21.14	3.51	0.043	1.04	11.80
I would like to have a more sincere dialogue with my ID physician (vs. No)	3.97	<0.001	2.30	6.87	2.75	0.001	1.49	5.05
>1 daily assumption of all the drugs	1.10	0.720	0.67	1.80				
Polypharmacy, >=5 drugs/die	1.06	0.846	0.60	1.87				
Other comorbidities	1.14	0.585	0.71	1.83				
Overall Health, per 1 point lower (1-5 scale)	2.05	<0.001	1.59	2.63	1.75	<0.001	1.32	2.32

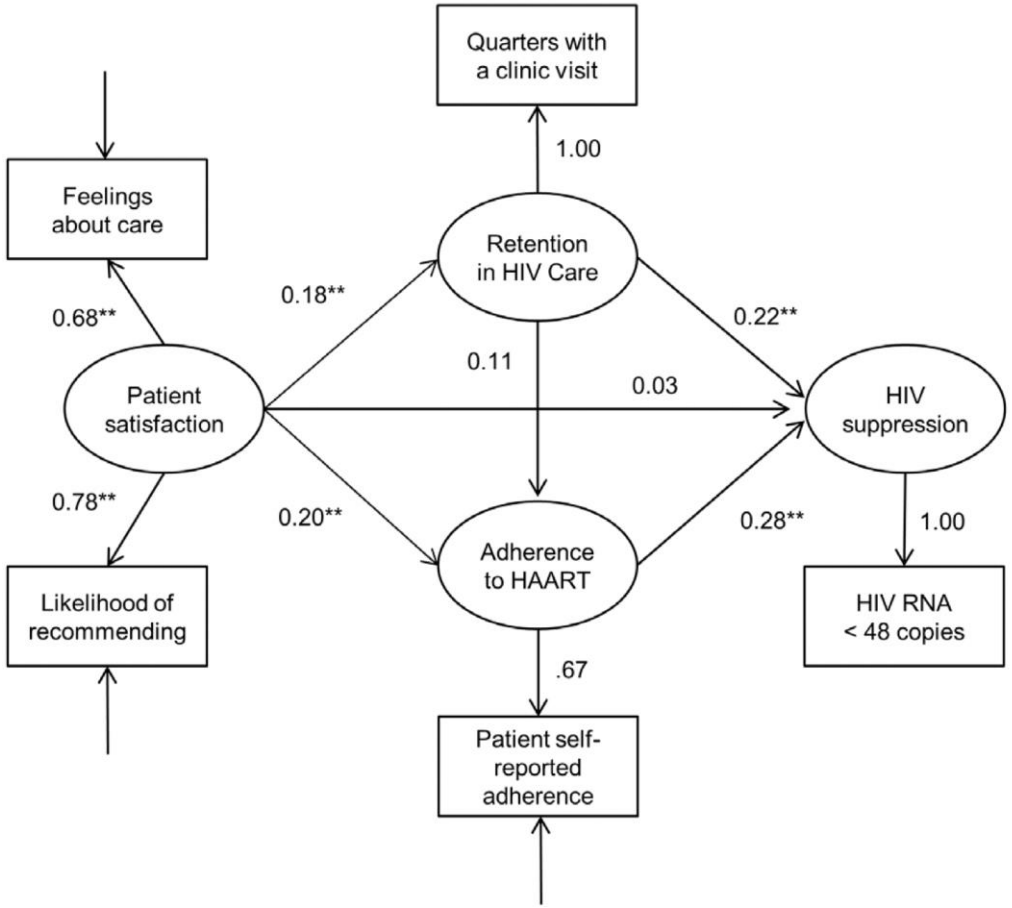
*Adjusted for overall Health status, dialogue with ID, treatment satisfaction, current reported ART, current reported HIV-RNA and age

Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Cingolani et al, J Clin Med 2022

Patient satisfaction may have direct effects on retention in HIV care and adherence to HAART.

	B[a]	β	p
Baseline Model[b]			
Structural Model			
Retention in Care→Adherence to HAART	.147 (.062)	.147	.02
Retention in Care→HIV Suppression	.220 (.049)	.220	<.001
Adherence to HAART→HIV Suppression	.287 (.061)	.287	<.001
Patient Satisfaction Model[c]			
Measurement Model			
Patient Satisfaction→Feelings about care	1.000	.680	NA[d]
Patient Satisfaction→Recommend Clinic	1.149	.778	<.001
Structural Model			
Patient Satisfaction→Retention in Care	.266 (.094)	.181	<.001
Patient Satisfaction→Adherence to HAART	.298 (.115)	.203	<.001
Patient Satisfaction→HIV Suppression	.047 (.089)	.032	.60
Retention in Care→Adherence to HAART	.110 (.063)	.110	.08
Retention in Care→HIV Suppression	.215 (.050)	.215	<.001
Adherence to HAART→HIV Suppression	.280 (.062)	.280	<.001



Dang, PlosOne 2013

Role of social support and loneliness are crucial at different steps of continuum of HIV care

Internalised HIV-stigma, loneliness, depressive symptoms and sleep quality in people living with HIV

Erin M. Fekete[a]*, Stacey L. Williams[b] and Matthew D. Skinta[c]

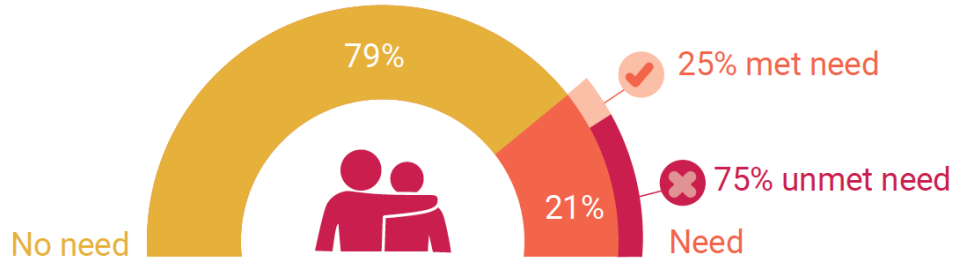
[a]*School of Psychological Sciences, University of Indianapolis, Indianapolis, IN, USA;* [b]*Department of Psychology, East Tennessee State University, Johnson City, TN, USA;* [c]*Pacific Graduate School of Psychology, Palo Alto University, Palo Alto, CA, USA*

Loneliness in Older Adults Living with HIV

Meredith Greene[1], Nancy A. Hessol[2,3], Carla Perissinotto[1], Roland Zept[3], Amanda Hutton Parrott[3], Cameron Foreman[4], Robert Whirry[5], Monica Gandhi[6], Malcolm John[3]

[1]Division of Geriatrics, Department of Medicine, University of California San Francisco, 3333 California St. Suite 380, San Francisco, CA 94143-1260, USA

PEER SUPPORT AND CONTACT WITH OTHER PEOPLE WITH HIV



Help addressing loneliness and isolation

Supportive relationships, social networks and social interaction with other people who have HIV are all important for our well-being and quality of life. Talking about HIV and how it affects us can be pivotal to overcoming challenges.

But feelings of isolation and loneliness were commonly reported by 1 in 5 (20%) people with HIV. Of all the services examined, this had the greatest area of unmet need – 75% of people who needed help dealing with loneliness and isolation did not receive it. Feelings of loneliness and isolation were equally common across all ages, ethnicities, genders and areas of residence and similarly this need was mostly unmet for everyone.

1 in 5 people living with HIV reported feelings of isolation and loneliness

Positive Voices
the national survey of people living with HIV

Successful aging in PLWH: role of social determinants of health

- Positive Brain Health Now (BHN) cohort. People ≥ 50 years (n = 513) were classified as aging successfully if they were at or above norms on 7 or 8 of 8 health-related quality of life domains from the RAND-36.

- 73 (14·2%) met criteria for successful aging at entry and did not change status over time.
- The most influential factor was loneliness which split the sample into two groups with the prevalence of successful aging 28·4% in the "almost never" lonely compared to 4·6% in the "sometimes/often" lonely group. Other influential factors were feeling safe, social network, motivation, stigma, and socioeconomic status.
- The nine variables important to classifying successful aging had a predictive accuracy of 0.862.
- Self-reported cognition but not cognitive test performance improved this accuracy to 0.895.
- The two groups defined by successful aging status did not differ or age, sex or viral load, nadir and current

Construct	Question	Relative Importance*	$N^{\#}$	$\%^{\#}$
Resilience	Do you find yourself feeling lonely?	1	208	40.7
Resilience	How safe do you feel in your daily life?	0.811	340	67.3
Comorbidity	Having arthritis or lung disease	0.699	337	65.7
Resilience	How much do you fear the future?	0.679	124	24.4
Social network	Time with someone who does not live with you	0.622	222	43.5
Lifestyle	Physically active past 6 months	0.612	144	28.2
Lifestyle	Current smoker	0.604	133	26.3
Resilience	To what extent do you feel your life to be meaningful?	0.601	412	81.3
Motivation	Interested in learning new things	0.524	293	57.7
SES	Enough money to meet your needs	0.475	261	51.3
SES	University education	0.474	172	33.9
Social network	Someone to trust and can confide in	0.460	458	89.5
Resilience	Bothered by people blaming you for your HIV status	0.426	346	68.2
Resilience	Worry about death	0.406	219	43.3
Social network	Number of people know well enough to visit within their homes	0.357	280	54.6
Environment	Healthy physical environment	0.208	361	71.6
Environment	Satisfied with conditions of living place	0.174	200	39.1
Motivation	Plans and goals for the future	0.123	170	34.1

Mayo et al, Qual Life Res 2022

Impact of loneliness on HRQoL in older HIV-infected patients

"Silver Project", UCSF-affiliated HIV clinics, survey on 356 PLWH>50 y (2012-2014)
58% reported at least some symptoms of loneliness (mild 24%, moderate 22%, severe 12%)

Association of loneliness symptoms and poor or fair Health Related Quality of Life (HRQoL)

	N with poor/fair health	Unadjusted PR (95% CI)	Adjusted[a] PR (95% CI)
Loneliness[b] (per 5 point increase)		**1.36 (1.13–1.63)**	1.06 (0.85–1.33)
Age[c]		0.98 (0.94–1.01)	
Male sex at birth[c]	91	0.95 (0.55–1.63)	
Non-white race[c]	52	1.34 (0.92–1.97)	
Latino ethnicity	17	1.67 (0.99–2.81)	
Annual income			
< $10,000	41	**2.58 (1.50–4.45)**	**1.85 (1.05–3.28)**
$10,000–20,000	39	**1.98 (1.15–3.43)**	1.60 (0.90–2.84)
≥ $20,001 (reference)	19	1.0	1.0
VACS index[d]		1.07 (0.96–1.19)	1.03 (0.92–1.16)
Length of time with HIV (years)[e]		1.07 (0.94–1.23)	
Depressive symptoms by PHQ-9[f]			
None (reference)	19	1.0	1.0
Mild	30	**2.57 (1.45–4.56)**	**2.19 (1.17–4.12)**
Mod	31	**5.15 (2.91–9.12)**	**4.18 (2.14–8.16)**
Severe	24	**4.84 (2.65–8.84)**	**4.34 (2.13–8.85)**
Education			
< High school	15	2.06 (0.97–4.41)	
High school	21	**2.14 (1.05–4.35)**	
Some college/college degree	58	1.87 (1.0–3.47)	
Some graduate/graduate degree (reference)	12	1.0	
Cognitive impairment[g]	41	1.23 (0.83–1.81)	
At risk alcohol and/or drug use[h]	38	1.30 (0.87–1.94)	
Low physical social support[i] (0–12)	64	**1.54 (1.04–2.27)**	

Greene, AIDS Behav 2017

Mobile app e-QoL of Icona and collected PROs

Conceived by Professor Mauro Moroni
Fondazione Icona

- PROs collected:

1. **EQ-5D-5L**, measure of current health status
2. **PHQ-9**, Depression screening
3. **GAD-7**, Generalized Anxiety screening
4. **Adherence questionnaire**, ART adherence
5. **AUDIT-C**, measure of alcohol misuse
6. **HIVDQoL**, measure QoL and impact of HIV
7. **HIVSRQ,** measure presence and grading of symptoms
8. **HIVTSQ**, measure treatment satisfaction of ART
9. **W-BQ16**. measure of psycho-physical well-being

ICONA PLWH included

Icona PLWH to whom the app has been offered (4.4%) and completed at least 1 questionnaire are:

- Younger
- ART-experienced but with shorter history of HIV
- MSM
- With higher education

	No questionaire N=2709 (95.6%)		At least 1 questionaire completed N=126 (4.4%)		p
Sex, Female	452	16.7	14	11.1	0.099
Age, median (IQR)	48	39-56	45	36-53	
<40	700	26	39	30.95	0.036
40-49	782	29	46	36.51	
50-59	768	28.35	23	18.25	
60+	459	16.94	18	14.29	
Years from HIV diagnosis	7.6	3.1-12.4	4.3	1.9-11.0	0.004
ART-naive	250	9.2	4	3.2	0.02
Years from ART-start	6.9	3.8-10.7	4.4	2.0-9.6	<0.001
Ethnicity, Caucasiam	2,348	86.67	116	92.06	0.080
Italian	2199	81.2	107	84.9	0.291
Mode of Transmission					<0.001
Hetero	853	31.49	22	17.46	
IDU	180	6.64	5	3.97	
MSM	1,468	54.19	93	73.81	
Other/Unknown	208	7.68	6	4.76	
Nadir CD4	290	151-432	305	197-447	0.426
AIDS	388	14.3	16	12.7	0.61
CD4 cell count, cells/mmc	703	505-946	656	519-918	0.384
CD4<200 cells/mmc	142	5.3	4	3.2	0.299
HIVRNA<50 copies/ml	2321	87.8	110	87.3	0.872
HIVRNA<50 cps/ml among ART-exp	2309	93.9	110	90.2	0.097
Education, University	478	24.4	41	40.6	<0.001
Job status, Not Occupied	256	9.4	8	6.3	0.242
HBsAg pos	125	5.2	4	3.3	0.364
HCVAb pos	288	11.3	8	6.7	0.117
2DR-INSTI based regimen	522	19.3	35	27.8	0.019

Italian Cohort I. C O. N A. Naive Antiretrovirals

Conceived by Professor Mauro Moroni

Fondazione Icona

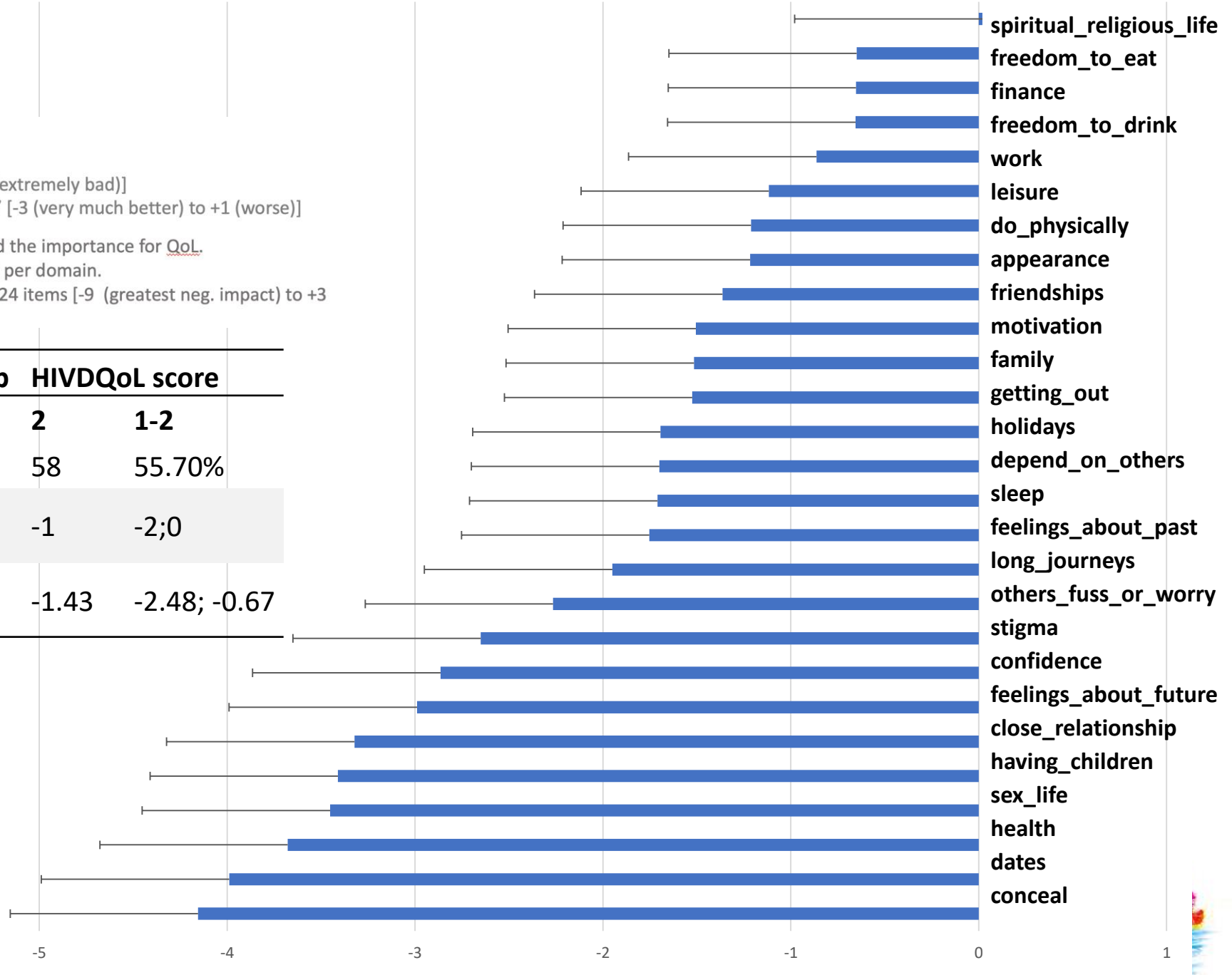
HIV-weighted impact on QoL

Conceived by Professor Mauro Moroni
Fondazione Icona

Measure of QoL

- Overview items:
  - Generic QoL 'My QoL in this period is' [+3 (excellent) to -3 (extremely bad)]
  - HIV-dependent QoL *('If I did not have HIV, my QoL would be'* [-3 (very much better) to +1 (worse)]
- 26 domain specific items measuring the impact of HIV on each and the importance for QoL.
- Weighted impact (WI) scores are calculated (*impact x importance*) per domain.
- Average weighted impact score (AWI) can also be calculated from 24 items [-9 (greatest neg. impact) to +3 (greatest pos. impact)]

	N. Resp	HIVDQoL score	
HIVDQOL, general QoL, median (IQR)	**104**	**2**	**1-2**
Very Good (+2) or Optimal (+3), n(%)		58	55.70%
HIVDQoL HIV dependent, median (IQR)	104	-1	-2;0
HIVDQoL HIV Averege Weighted Impact, median (IQR)	103	-1.43	-2.48; -0.67



PHQ-9 (Patient Health Questionnaire-9)

	N responses	PHQ-9 score	
PHQ-9 score, median (IQR)	**79**	**6**	**(3-9)**
No Depression, n(%)		28	(35.4%)
Mild Depression, n(%)		34	(43.0%)
Moderate Depression, n(%)		3	(16.5%)
Severe Depression, n(%)		4	(5.0%)

21.5%

- 9-items tool to assess the degree of **depression**
- 4 levels responses [0-3]. Total score 0-27 pts

Score interpretation

>=10 pts: 88% specificity and sensibility detecting major depressive disorder

GAD-7 (General Anxiety Disorder-7)

	N. responses	GAD-7 score	
GAD7 score, median (IQR)	75	6	(3-7)
Minimal Anxiety <5, n(%)		31	(41.3%)
Mild Anxiety 5-9, n(%)		33	(44.0%)
Moderate Anxiety 10-14, n(%)		6	(8.0%)
Severe Anxiety >14, n(%)		5	(6.7%)

14.7%

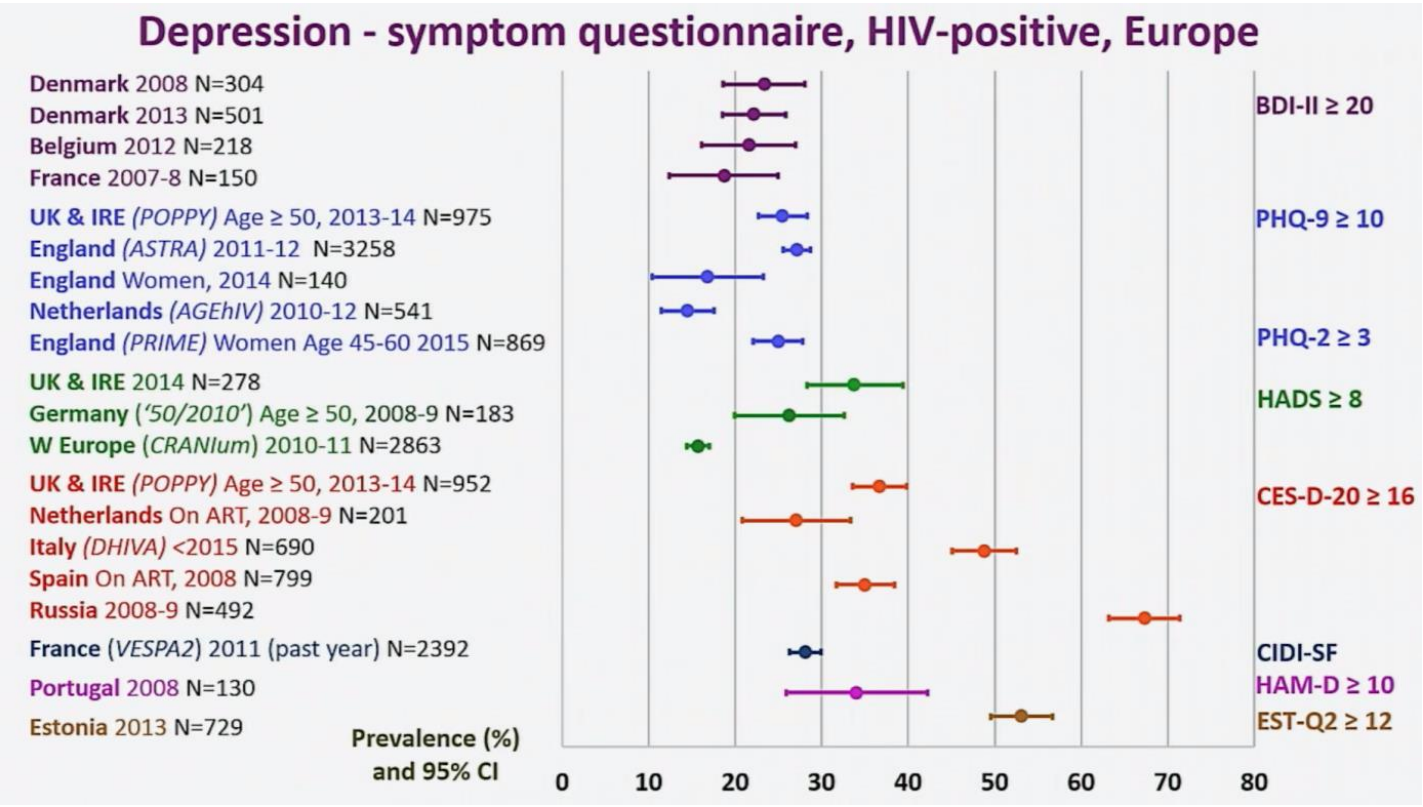
- 7-items tool to assess the **general anxiety disorder**
- 4 levels responses [0-3]. Total score 0-21 pts

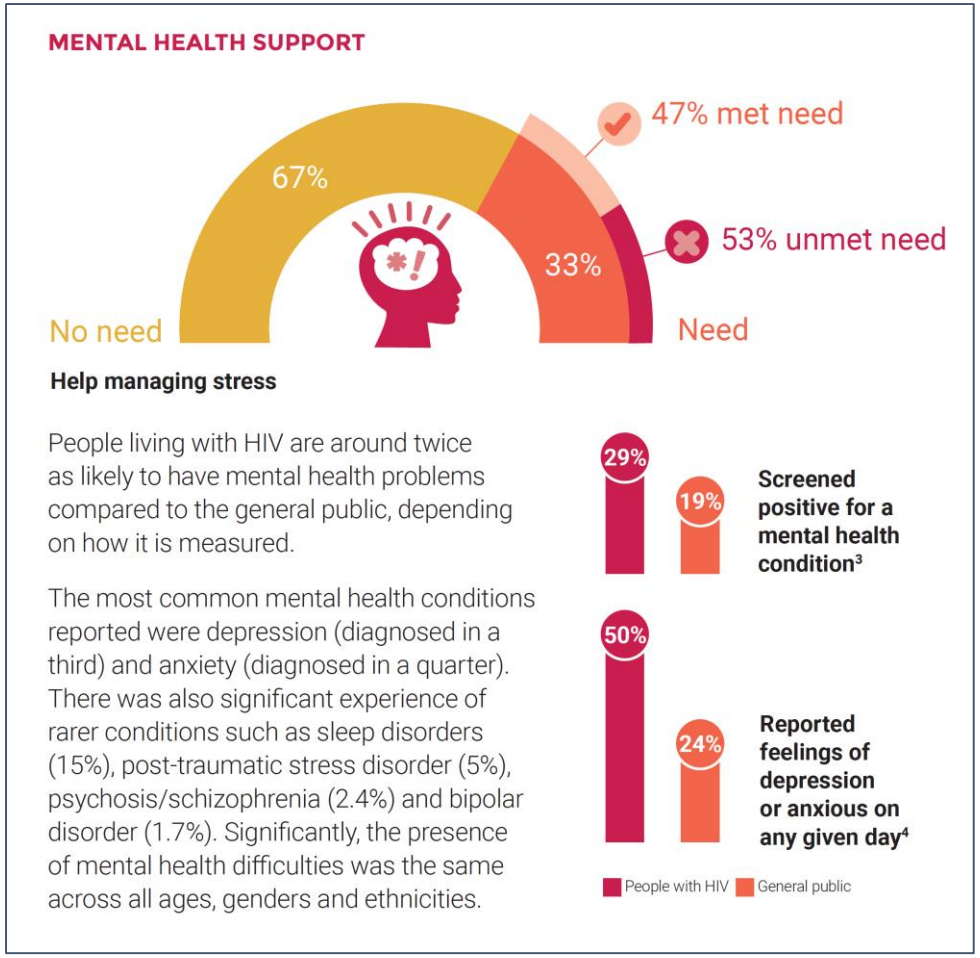
Score interpretation

>=10 pts: 89% sensitivity 82% and sensibility detecting GAD

Mental health issues rates and PLHIV needs in Europe

Moderate/severe depression in ICONA eQol





F. Lampe, HIVGlasgow 2018

Positive Voices
the national survey of people living with HIV

- Strong negative correlation between GAD and Depression measures and well-being, QoL, health status
- Positive correlation with negative WB and symptoms rating

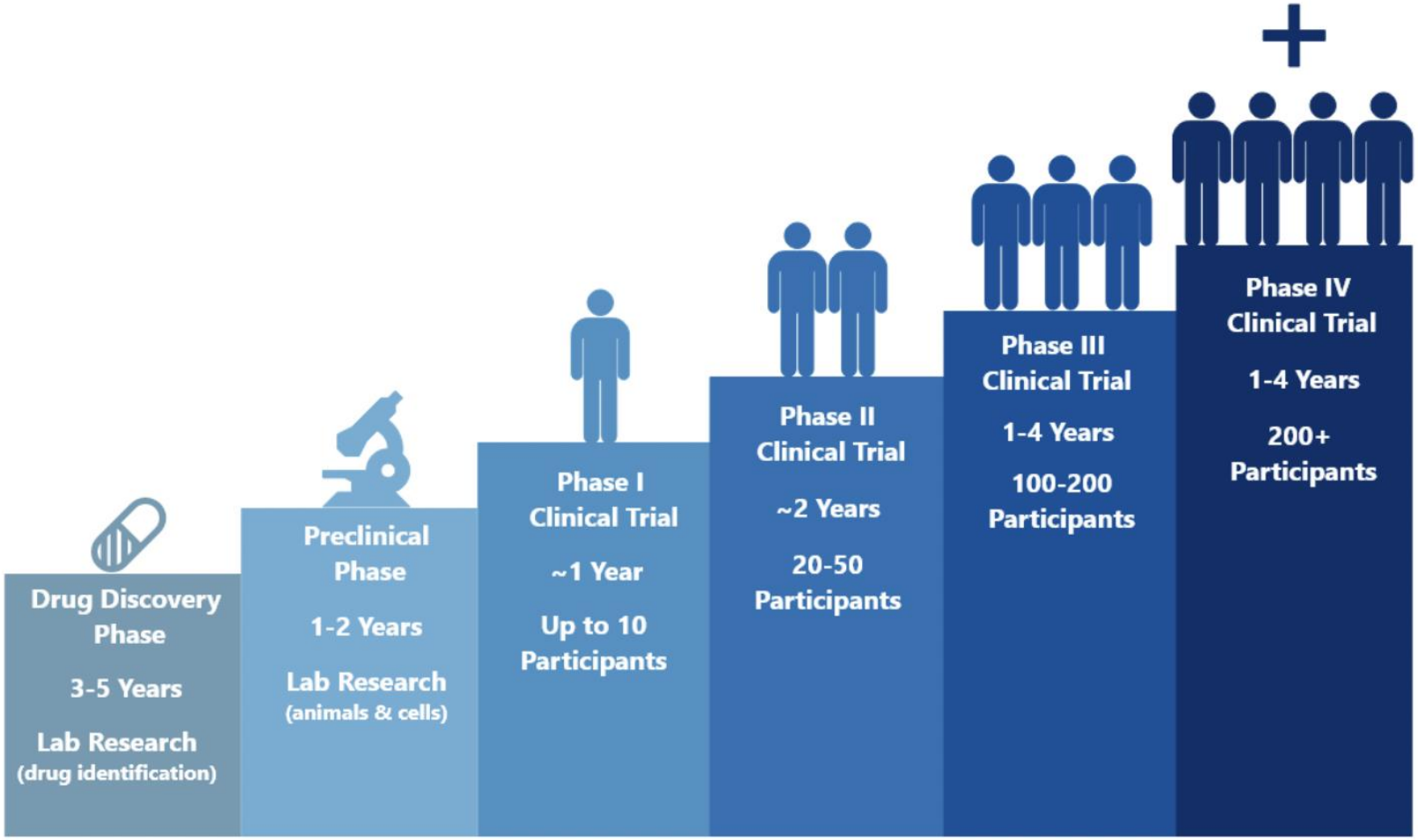
Mental Health is an important aspect of PLWH care

Conceived by Professor Mauro Moroni
Fondazione Icona

	EQ-5D-3L VAS	HIVDQoL QoL	HIVDQoL QoL-HIV	HIVDQoL AWI	WBQ16 General	WBQ16 Energy	WBQ16 Neg WB	WBQ16 Pos WB	WBQ16 Stress	PHQ9 score	GAD7 score	HIVTSQs score	HIVSRQ overview
EQ-5D-3L VAS	1												
HIVDQoL QoL	0.406*	1											
HIVDQoL QoL-HIV	0.290*	0.258*	1										
HIVDQoL AWI	0.426*	0.337*	0.706*	1									
WBQ16 General	0.538*	0.618*	0.473*	0.615*	1								
WBQ16 Energy	0.399*	0.586*	0.452*	0.504*	0.845*	1							
WBQ16 Neg WB	-0.458*	-0.531*	-0.392*	-0.500*	-0.826*	-0.625*	1						
WBQ16 Pos WB	0.511*	0.585*	0.351*	0.480*	0.817*	0.674*	-0.591*	1					
WBQ16 Stress	-0.458*	-0.416*	-0.419*	-0.537*	-0.780*	-0.543*	0.566*	-0.469*	1				
PHQ9 score	-0.444*	-0.600*	-0.294*	-0.446*	-0.760*	-0.740*	0.674*	-0.620*	0.524*	1			
GAD7 score	-0.340*	-0.571*	-0.374*	-0.311*	-0.739*	-0.660*	0.654*	-0.538*	0.645*	0.777*	1		
HIVTSQs score	0.398*	0.326*	0.255*	0.225	0.405*	0.384*	-0.349*	0.323*	-0.355*	-0.3863*	-0.357*	1	
HIVSRQ overview	-0.379*	-0.580*	-0.262*	-0.431*	-0.596*	-0.555*	0.591*	-0.389*	0.367*	0.719*	0.576*	-0.341*	1

ρ

1.000
0.900
0.800 — Strong pos correlation
0.700
0.600
0.500
0.400 — Moderate pos correlation
0.300
0.200
0.100
0.000
-0.100
-0.200
-0.300
-0.400
-0.500
-0.600
-0.700 — Moderate neg correlation
-0.800
-0.900
-1.000 — Strong neg correlation



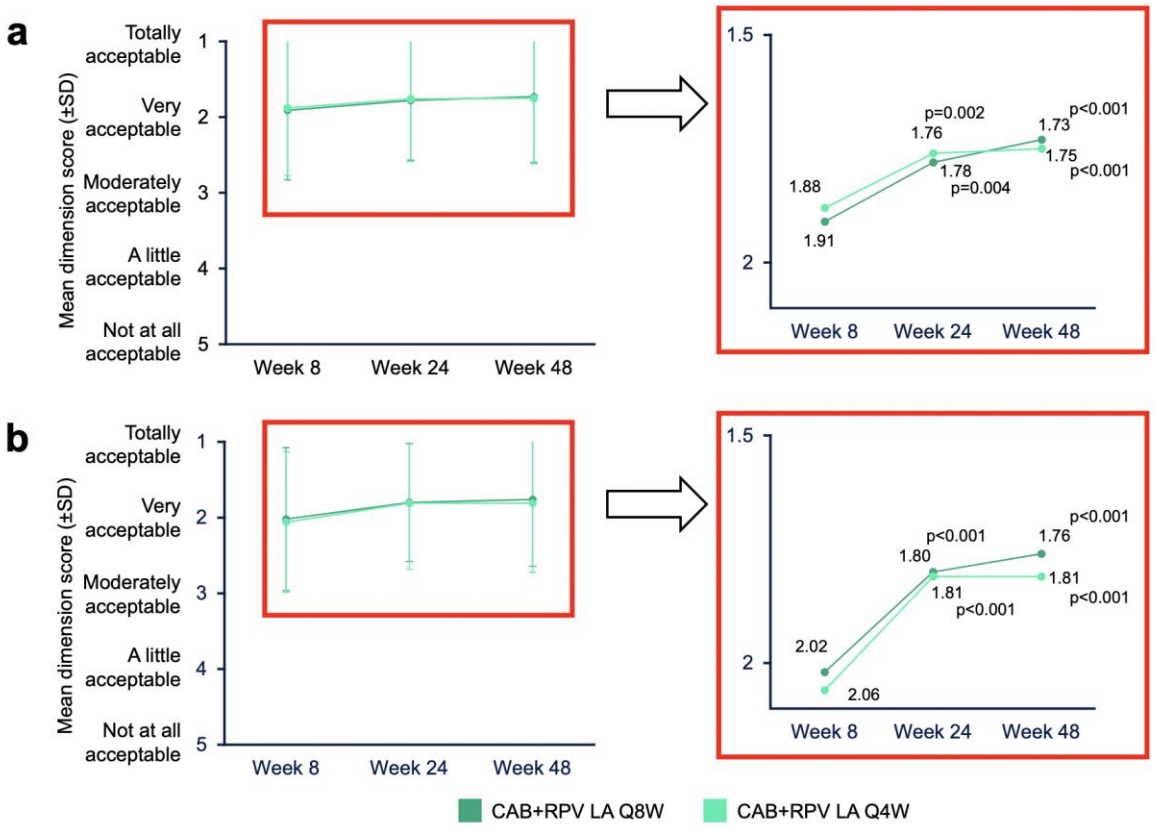
Qol as end point in clinical trials

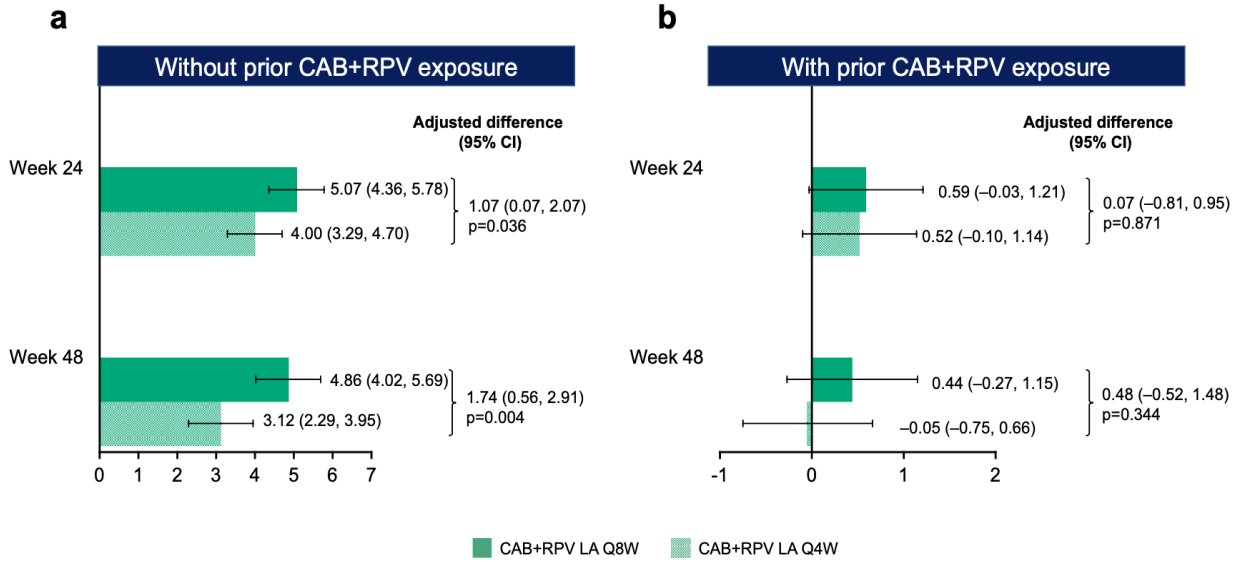
PROs in Phase III trials of LA CAB+RPV : A paradigm of QoL as and point

PRO Dimensions	PRO instrument	Endpoint	Score range
Tolerability and acceptability of IM injections	Perception of Injection questionnaire (PIN)*	Tolerability and acceptability related to ISRs (21 questions)	1–5
Treatment acceptance	Chronic Treatment Acceptance (ACCEPT®)*	Acceptance of treatment, defined as the balance between treatment advantages and disadvantages (only general treatment acceptance included – 3 questions)	0–100
Treatment satisfaction and preference	HIV Treatment Satisfaction Questionnaire (HIVTSQ)*	Satisfaction with treatment (12 questions)	0–66 (HIVTSQs)
	Preference for HIV Treatment†	ATLAS and FLAIR: Preference for CAB + RPV LA compared to CAR (1 question) ATLAS-2M: Preference for the Q4W vs Q8W regimen (3 questions)	N/A
Health status and QoL	Short Form Health Survey (SF-12®)	Health status measure (12 questions)	0–100 (mental and physical scores)

- ***These PRO instruments have been adapted for the program; †These PRO instruments have been developed by ViiV
CAR, current antiretroviral regimen; **HIVTSQs,** HIV Treatment Satisfaction Questionnaire (Status); **IM,** intramuscular
N/A, not applicable; **PIN,** Perception of Injection questionnaire; **Q4W,** every 4 weeks; **Q8W,** every 8 weeks

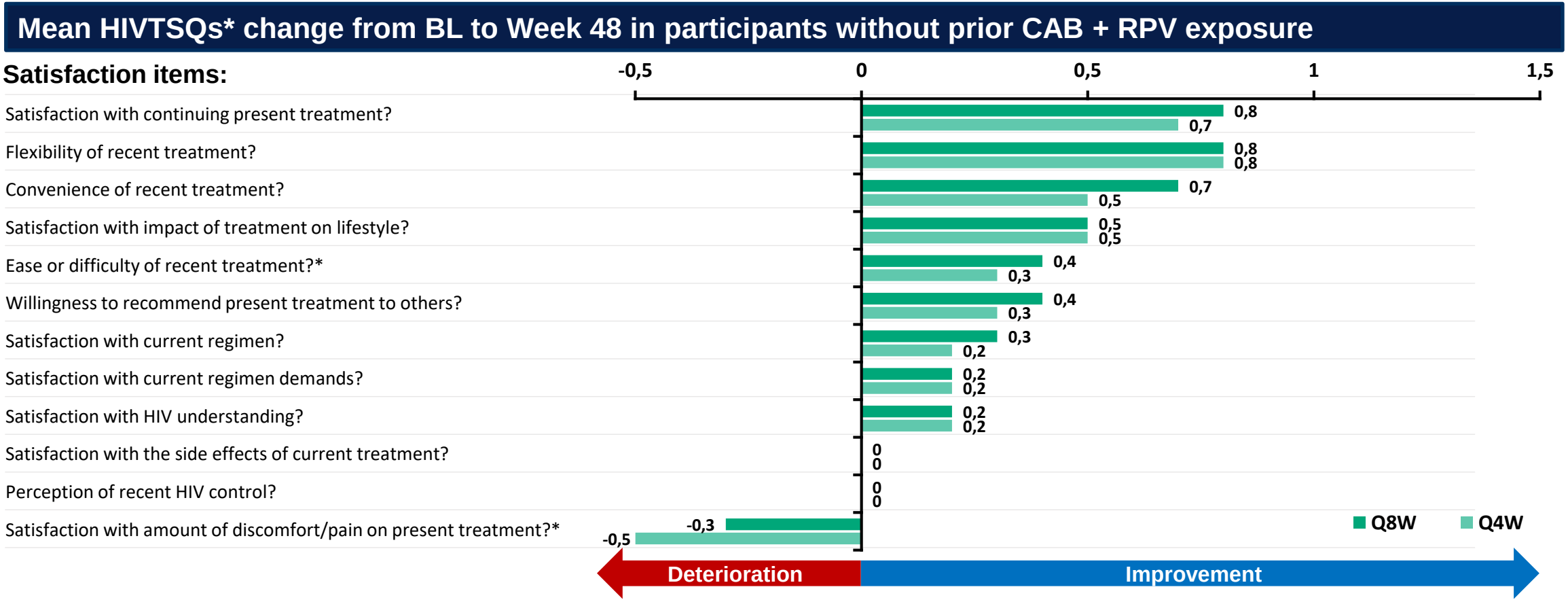
High treatment satisfaction and acceptance, irrespective of prior CAB + RPV exposure, with most participants preferring Q8W dosing over both the Q4W regimen and their previous daily oral regimen.





Chounta et al, The Patient - Patient-Centered Outcomes Research (2021)

ATLAS-2M: Q8W participants showed equal or greater scores on all treatment satisfaction items versus Q4W



In participants without prior CAB + RPV exposure, satisfaction improved from BL to Week 48 in nine of the 12 individual items

- ***HIVTSQ was adapted to include two additional questions relating to injectable treatment

Chounta et al, The Patient - Patient-Centered Outcomes Research (2021)

The role of patient-reported outcomes in reimbursement decisions and drug innovation in Italy

Association between use of PROs/PROMs in the European Public Assessment Reports (EPARs) from EMA of drugs authorized between 2017 and 2021.

Uso dei PROs/PROMs per classi di rimborsabilità aifa

PRO/PROM	Rimborsati			Classe C	In Attesa/Assenza di rimborso	Totale EPAR
	Totale	Classe A*	Classe H*			
Sì	105 (49,8%)	*37 (45,7%)*	*68 (52,3%)*	8 (44,4%)	84 (48,3%)	197 (48,9%)
No	106 (50,2%)	*44 (54,3%)*	*62 (47,7%)*	10 (55,6%)	90 (51,7%)	206 (51,1%)
Totale	211 (100%)	*81 (100%)*	*130 (100%)*	18 (100%)	174 (100%)	403 (100%)

Associazione tra riconoscimento di innovatività, designazione di status di orfano ed uso di PROs/PROMs

Innovatività	OR	SE	p-value	[95% CI]	
Utilizzo di PRO/ PROM	2,16	0,81	0,039	1,04	4,49
Status di orfano	11,56	4,08	0,000	5,79	23,08

Malandrini et al, Glob Reg Health Technol Assess 2023

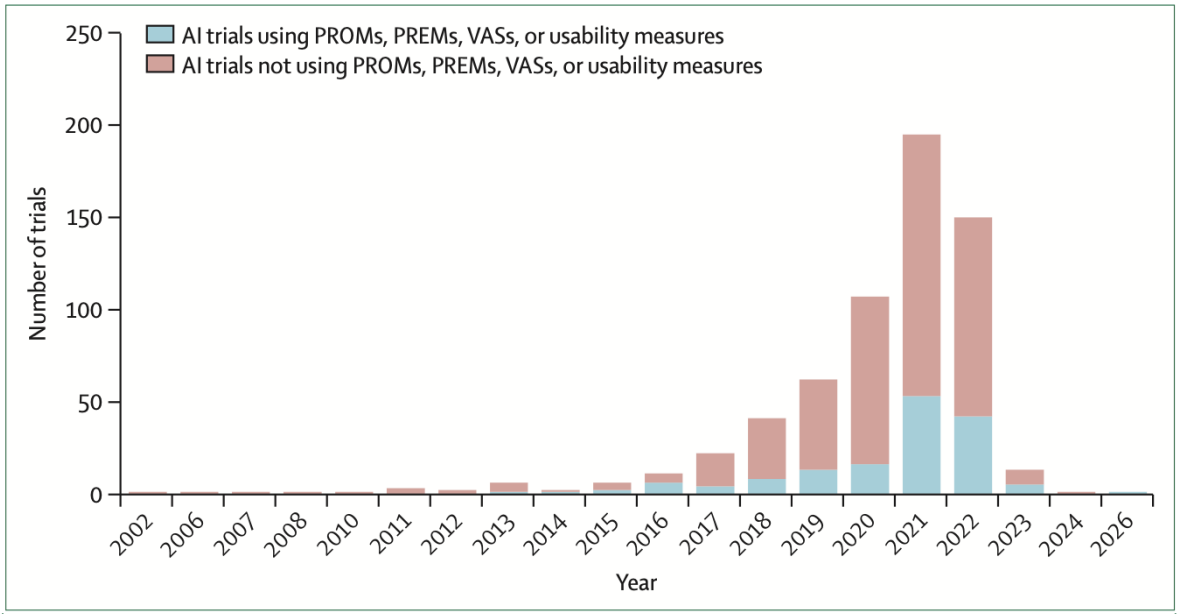
The role of patient-reported outcome measures in trials of artificial intelligence health technologies: a systematic evaluation of ClinicalTrials.gov records (1997–2022)

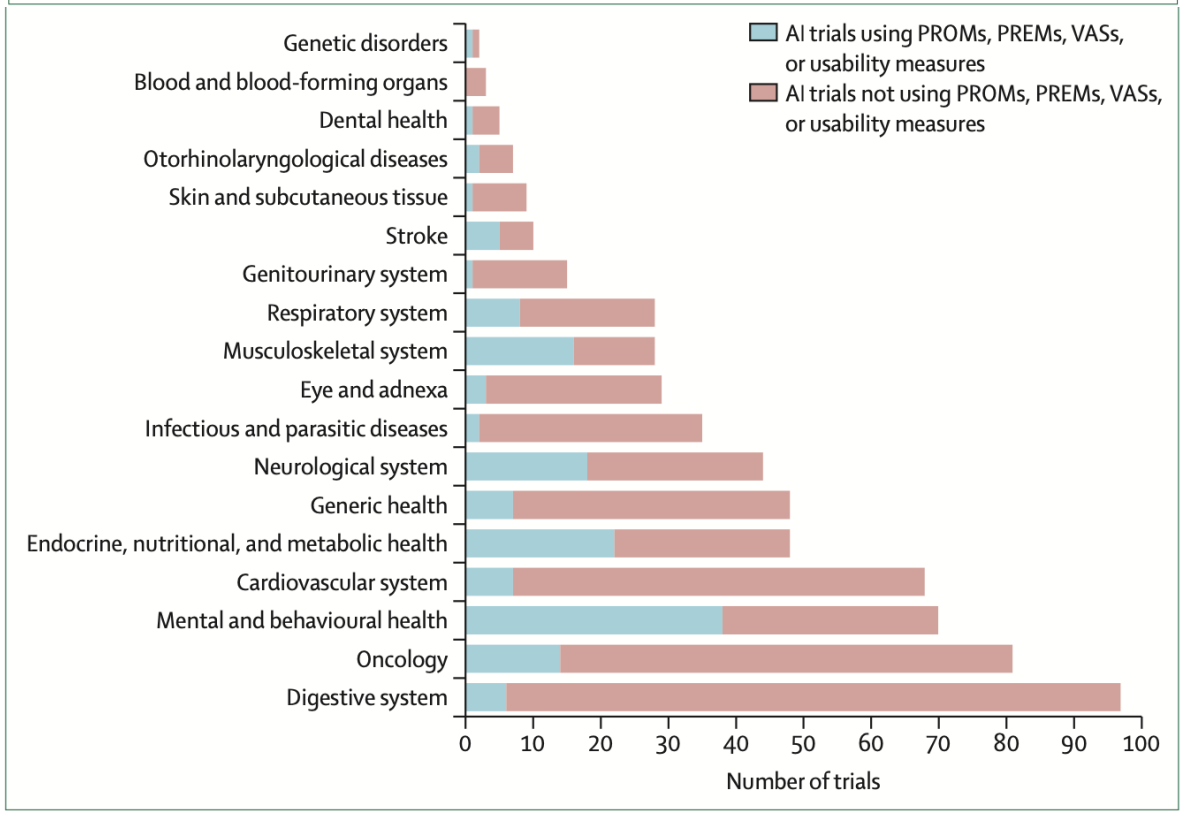
FJ Pearce, and MJ Calvert

Lancet Digit health 2023

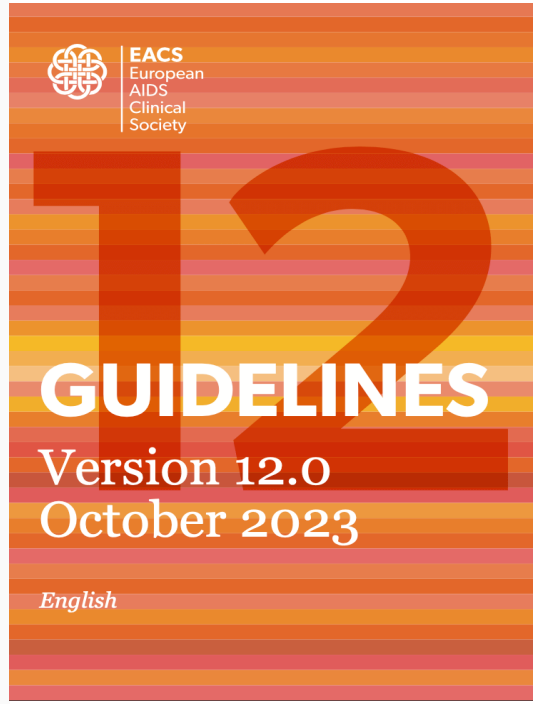
	Trials (n=627)	Trials that used at least one PROM, PREM, VAS, or usability measure
Role of artificial intelligence		
Diagnosis	217	12 (6%)
Treatment	183	90 (49%)
Monitoring or supportive care	64	32 (50%)
Prevention	66	11 (17%)
Screening	76	5 (7%)
Other	21	2 (10%)
Intended use population		
Patients	176	95 (54%)
Health-care provider	395	31 (8%)
Patients and health-care provider	56	26 (46%)

PREM=patient-reported experience measure. PROM=patient-reported outcome measure. VAS=visual analogue scale.





Use of Patient Reported Outcome Measures (PROMs) in HIV Clinical Care



The use of Patient Reported Outcome Measures (PROMs) in HIV Clinical Care

Patient reported outcome measures (PROMs) are being increasingly used in clinical care to directly measure patient symptomatology and quality of life. EACS guidelines recommend utilization of PROM tools annually in every individual to facilitate the dialogue between care providers and the patient, improve patient and physicians' awareness of their own health, introduce patient-centered care and to empower patients in this conversation.

What to collect?

PROMs pertain multidimensional domains including (but not limited to): physical, mental and sexual health, pain, stigma, family/community support, social isolation, loneliness, food security, housing, financial and migration status.
Domains should be chosen according to local and regional requirements, age, socio-economic background and environmental characteristics in consultation with local patient representatives.

How to choose PROMs?

Prioritize PROMs which are:

- designed and validated for a specific outcome(i)
- available in multiple languages
- short and concise (consider using computer adaptive testing if available)
- formulated in understandable way
- are supported by local guidelines or healthcare providers
- validated in people with HIV (if available)

Who should be assessed?

All persons with HIV in particular prior to or during a healthcare encounter with a care provider including telemedicine encounters. Whichever approach is chosen the purpose of collecting PROMs is to evaluate them. Therefore, PROM results should always be discussed.

How to collect?

PROMs are generally self-completed questionnaires (EACS guideline recommend some screening tools for anxiety, depression and sexual function). In addition, a widely used and important PROM are those to assess Health Related Quality of Life (HRQoL) for example EQ-5D-5L or SF36 or HIV specific PROMs for HRQoL (for example WHOQoL).

Ideally PROMs should be integrated within electronic patients records and collected using electronic tools, including websites, tablets or apps. However, people with technological or language barriers may have higher burdens of unmet needs and may require assistance to complete PROMs.

Patient reported outcome assessment must be inclusive and equitable

Patient-reported outcomes are increasingly collected in clinical trials and in routine clinical practice, but strategies must be taken to include underserved groups to avoid increasing health disparities.

Melanie J. Calvert, Samantha Cruz Rivera, Ameeta Retzer, Sarah E. Hughes, Lisa Campbell, Barbara Molony-Oates, Olalekan Lee Aiyegbusi, Angela M. Stover, Roger Wilson, Christel McMullan, Nicola E. Anderson, Grace M. Turner, Elin Haf Davies, Rav Verdi, Galina Velikova, Paul Kamudoni, Syed Muslim, Adrian Gheorghe, Daniel O'Connor, Xiaoxuan Liu, Albert W. Wu and Alastair K. Denniston

Nat Med, 2022

Considerations	Actions
Diversity	
Consider how individuals from all relevant demographics within the target population (including those of differing age, sex, pregnant women, sexual orientation, race, ethnicity, level of education and socioeconomic status) can be included[16].	Involve individuals that are representative of the target population in the identification of key concepts to measure, the development and selection of PROs, the co-design of PRO systems, and data collection. Assess whether PRO measures perform consistently across groups (for example, based on measurement equivalence or differential item functioning).
Clinical characteristics	
Consider the type and severity of disease, the range of symptoms and functional impacts, comorbidities and physical and cognitive disabilities[16].	When heterogeneity in disease symptoms, signs and impacts exists, assess concepts that are most important to a broad range of patients. Minimize functional impacts that may limit a patient's ability to complete PROs (for example, issue of dexterity). Use accessible formats that address the needs of the target population. Allow proxy completion (someone to report the participant's outcomes on their behalf as though they are the patient) for individuals who are unable to complete PROs, for example, due to cognitive impairment. Please note regulatory requirements regarding the use of proxies.
Cultural needs and languages	
Include individuals from relevant cultures and languages within the target population to ensure that results are generalizable. People from distinct cultures may describe their symptoms differently and may have different values or preferences[16].	Be aware of cultural values and preferences, including whether key concepts of interest are appropriately captured via the PRO, and whether data collection is sensitive to the needs of those within the target population. Use validated translations and culturally validated PROs developed in accordance with internationa guidance[19]. Provide translators or interpreters for interviewer-led completion.
Literacy and health literacy	
Include individuals with all levels of reading, writing and problem-solving abilities, where possible[16].	Format PROs to adhere to accessibility principles including Easy-read versions, large font sizes and ample white space Allow flexibility for patients to choose where to complete PROs and to request assistance from people they know or professionals. Clearly convey the purpose and benefit of PROs to both patients and professionals by reducing intimidation and frustration caused by form filling in general. Ensure that content and training is easy to understand for participants with different literacy levels and educational experience by conducting relevant readability assessments (for example, Flesch–Kincaid grade level or SMOG (simple measure of gobbledygook) index score).
Digital inclusion	
Consider ways to promote digital inclusion.	Provide alternative modes of delivery (for example, bring your own device, provision of device, web completion or voice response systems that do not require internet access, phone calls from staff or in-person PRO completion in clinic). Offer hardcopy for those without smartphones or internet access. Provide training and support to patients and staff.
Regulatory engagement	
Meet with the regulator early during drug development, ask questions and seek advice regarding patient and public engagement, and arrange a regulatory or scientific advice meeting.	Discuss inclusivity in the context of the disease being investigated. Discuss potential barriers to inclusivity and discuss possible regulatory enablers, such as adoption regulatory guidance that details approaches to increased enrolment of underserved population[20] an legislation requirements to deliver and support this. Use regulatory agency patient engagement tools and resources (for example, Medicines and Healthcare Products Regulatory Agency Innovative Licensing Pathway Patient Tools and US Food ar Drug Administration patient-focused drug discovery guidance).

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