I PROs nella pratica clinica: un nuovo punto di vista

Sergio Lo Caputo
Malattie Infettive
Università di Foggia

PRO (patient reported outcome)

- A **patient-reported outcome** (**PRO**) is a health outcome directly reported by the patient who experienced it. It stands in contrast to an outcome reported by someone else, such as a physician-reported outcome, a nurse-reported outcome, and so on.
- PRO methods, such as questionnaires, are used in clinical trials or other clinical settings, to help better understand a treatment's efficacy or effectiveness.
- The use of digitized PROs, or electronic patient-reported outcomes (ePROs), is on the rise in today's health research setting.

Unconventional outcomes: definitions -I

- Patient Reported Outcomes (PROs): any report of the status of the patient's health that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else (e.g. symptoms, functioning, or a more global assessment of the effect of the disease on health and functioning from the patient's perspective).

- PRO Measures (PROMs) are standardized, validated questionnaires that are completed by patients to catch their perceptions of their health status, perceived level of impairment, disability, and health-related quality of life. They allow the efficacy of a clinical intervention to be measured from the patients' perspective.

- PROMs can be classified as *generic or disease or treatment specific*. The generic tools measure a variety of aspects of a broad range of medical conditions, allowing for the overall evaluation of care, quality of life, and cost effectiveness of interventions. The disease specific PROMs allow individual aspects of a condition and their impact on outcome to be examined and, similarly the treatment specific ones on a treatment.

Unconventional outcomes: definitions - II

- PREMs gather information on patients' self-evaluation of their experience whilst receiving care. They are an indicator of the quality of patient care, although do not measure it directly. PREMs are most commonly in the form of questionnaires.

- In contrast to PROMs, PREMs do not look at the outcomes of care, but the impact of the process of the care on the patient's experience (e.g. communication and timeliness of assistance).

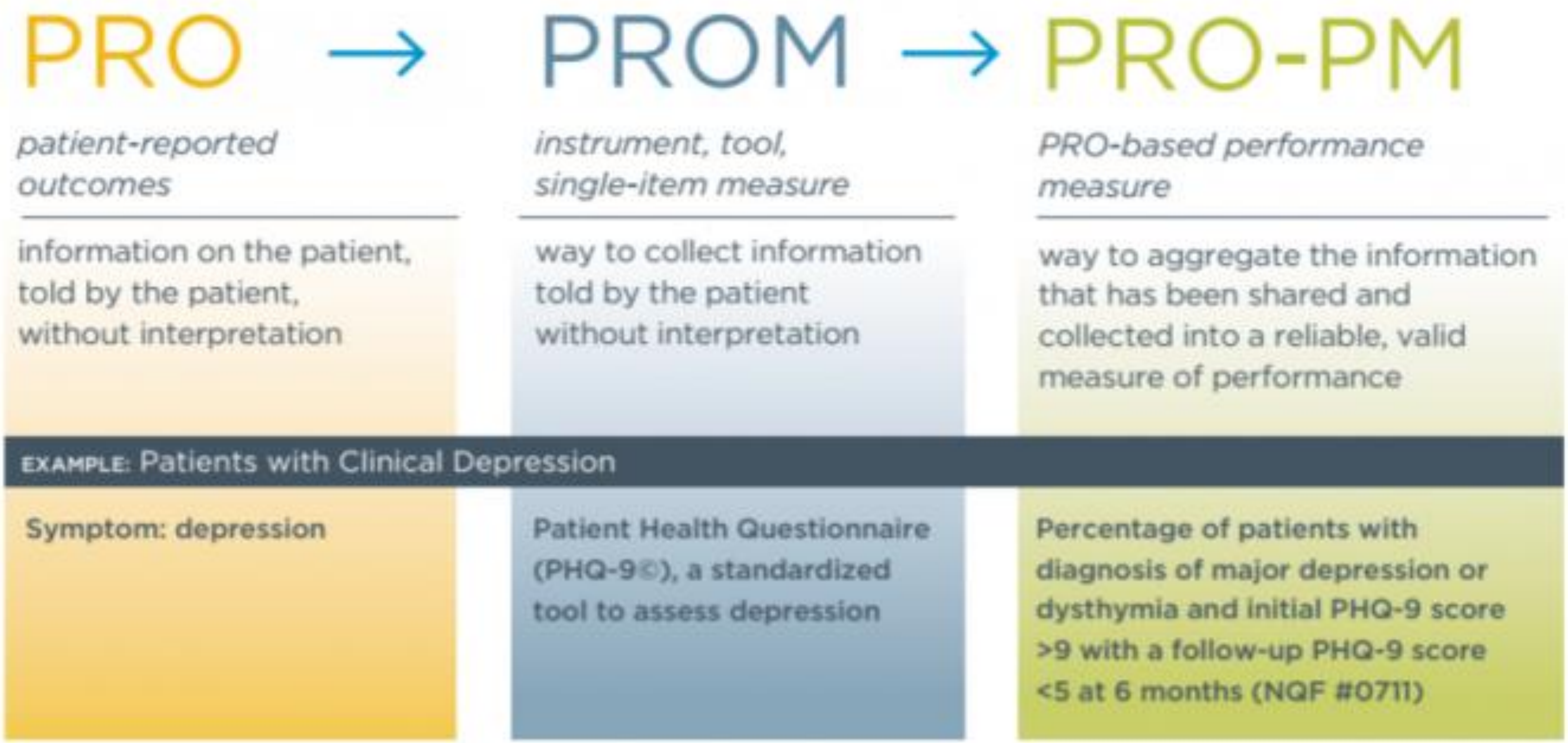
- PREMs can be classified as either relational or functional. Relational PREMs identify the patients experience of their relationships during treatment (e.g. did patients feel listened to?). Functional PREMs examine more practical issues, such as the facilities available. The CARE measure, a relational questionnaire, is an example of a PREMs tool.

The most commonly used PRO questionnaires assess one of the following constructs

- Symptoms (impairments) and other aspects of well-being
- Functioning (disability)
- Health status
- General health perceptions
- Quality of life (QoL)
- Health related quality of life (HRQoL)
- Reports and Ratings of health care

It is essential that a PRO instrument satisfy certain development, psychometric and scaling standards if it is to provide useful information Specifically, measures should have a sound theoretical basis and should be relevant to the patient group with which they are to be used

FIGURE 1. NQF FRAMEWORK: PRO TO NQF-ENDORSED PRO-PM



PRO →	PROM →	PRO-PM
patient-reported outcomes	*instrument, tool, single-item measure*	*PRO-based performance measure*
information on the patient, told by the patient, without interpretation	way to collect information told by the patient without interpretation	way to aggregate the information that has been shared and collected into a reliable, valid measure of performance
EXAMPLE: Patients with Clinical Depression		
Symptom: depression	**Patient Health Questionnaire (PHQ-9©), a standardized tool to assess depression**	**Percentage of patients with diagnosis of major depression or dysthymia and initial PHQ-9 score >9 with a follow-up PHQ-9 score <5 at 6 months (NQF #0711)**

Patient’s reported outcomes: Definition

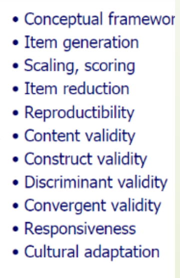
Symptoms
QoL, HR-QoL
Satisfaction with Care
Treatment adherence

- The condition of health at a given point of time
- Health: a multi-dimensional concept
  - **Not** merely the absence of diseases or infirmity
  - **But** a 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 patients** without the interpretation by physicians or anyone else

- Measurement implies a tool with known characteristics in terms of validity
- Validity is not a yes/not attribute but it implies the availability of a comprehensive set of information and data

Validity
Reliability
Responsiveness
Interpretability



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

Patient as unique and direct source of

Reports
Presence of Symptom

Evaluations
Intensity or Interference

Without any interpretations

Modified from G. Apolone

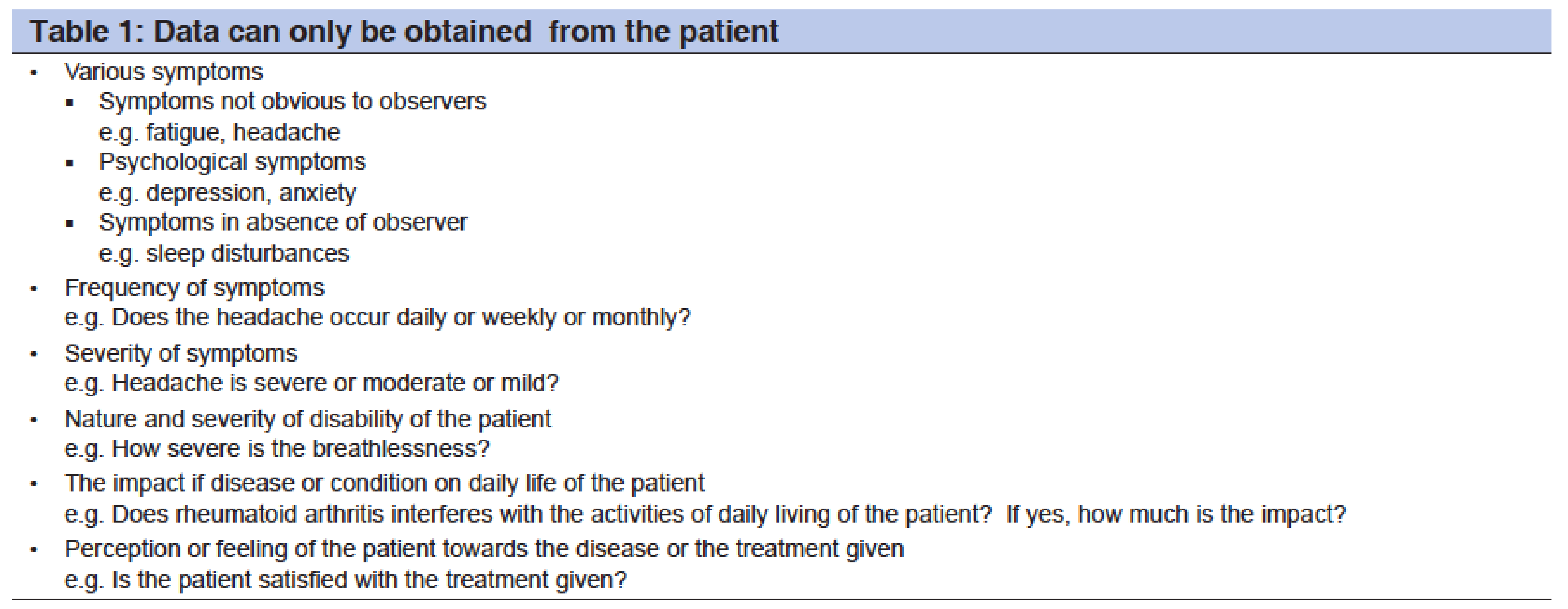
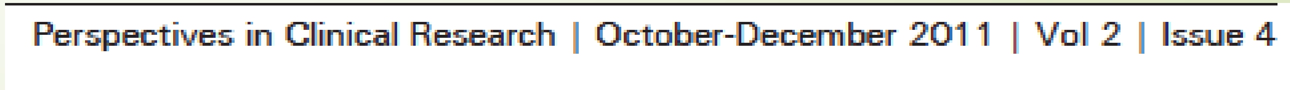


Table 1: Data can only be obtained from the patient

- Various symptoms
  - Symptoms not obvious to observers
    e.g. fatigue, headache
  - Psychological symptoms
    e.g. depression, anxiety
  - Symptoms in absence of observer
    e.g. sleep disturbances
- Frequency of symptoms
  e.g. Does the headache occur daily or weekly or monthly?
- Severity of symptoms
  e.g. Headache is severe or moderate or mild?
- Nature and severity of disability of the patient
  e.g. How severe is the breathlessness?
- The impact if disease or condition on daily life of the patient
  e.g. Does rheumatoid arthritis interferes with the activities of daily living of the patient? If yes, how much is the impact?
- Perception or feeling of the patient towards the disease or the treatment given
  e.g. Is the patient satisfied with the treatment given?



Perspectives in Clinical Research | October-December 2011 | Vol 2 | Issue 4

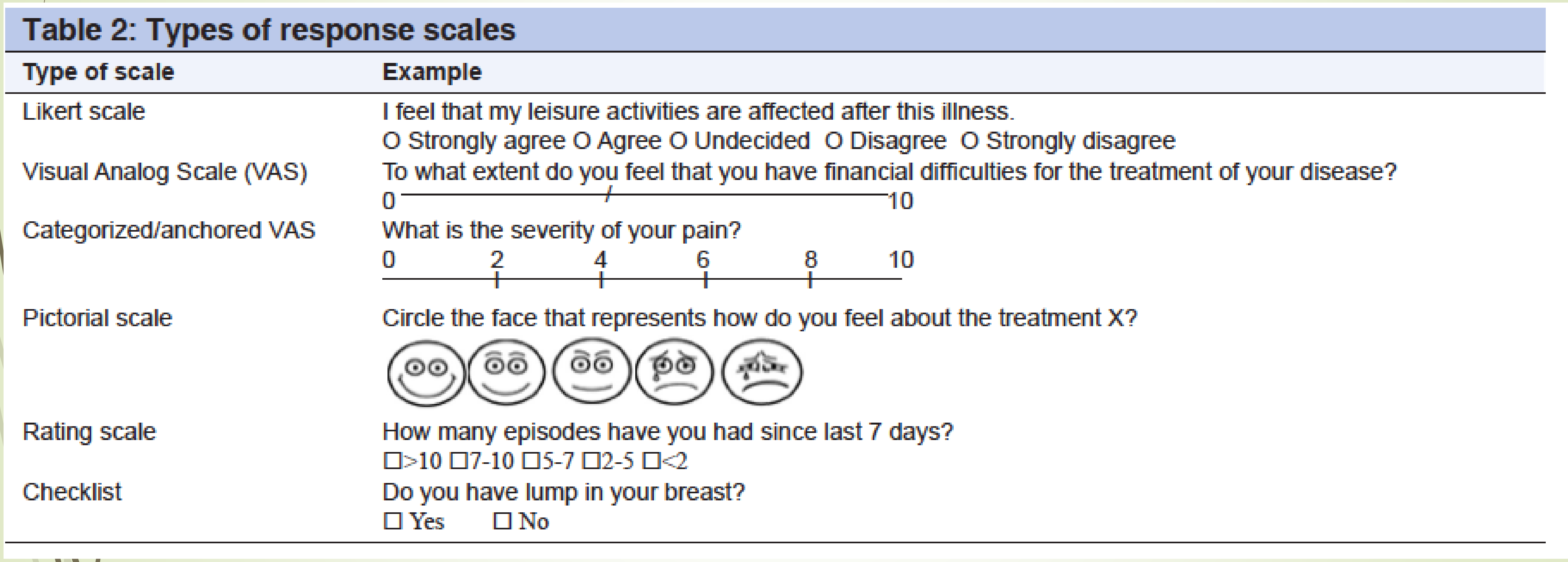
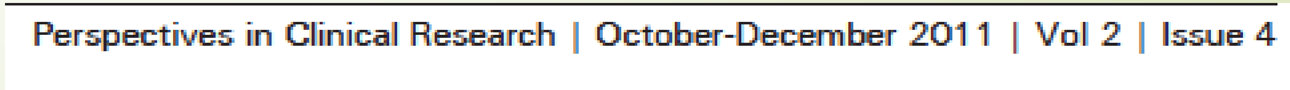


Table 2: Types of response scales

Type of scale	Example
Likert scale	I feel that my leisure activities are affected after this illness. O Strongly agree O Agree O Undecided O Disagree O Strongly disagree
Visual Analog Scale (VAS)	To what extent do you feel that you have financial difficulties for the treatment of your disease? 0 10
Categorized/anchored VAS	What is the severity of your pain? 0 2 4 6 8 10
Pictorial scale	Circle the face that represents how do you feel about the treatment X?
Rating scale	How many episodes have you had since last 7 days? ☐>10 ☐7-10 ☐5-7 ☐2-5 ☐<2
Checklist	Do you have lump in your breast? ☐ Yes ☐ No



Perspectives in Clinical Research | October-December 2011 | Vol 2 | Issue 4

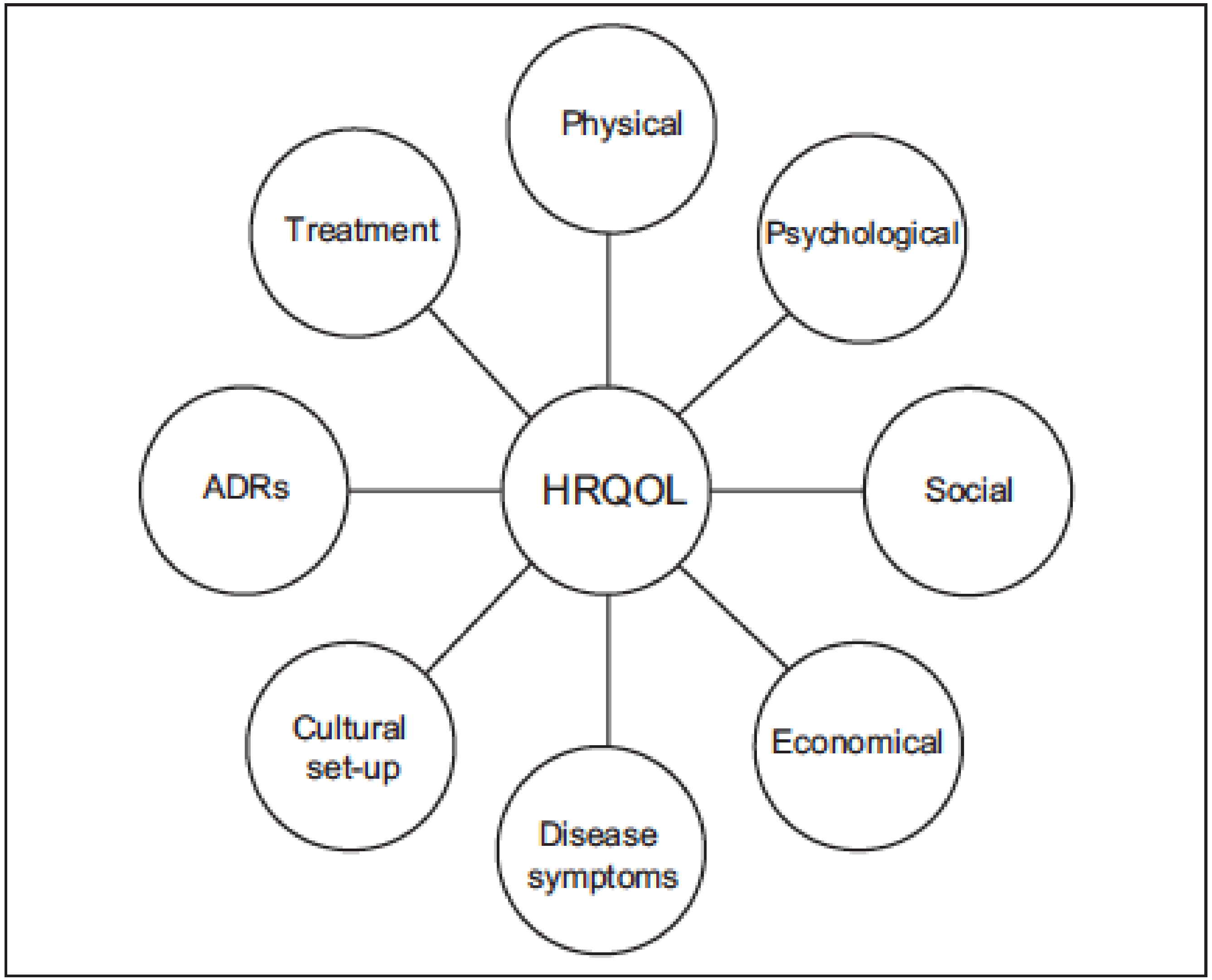
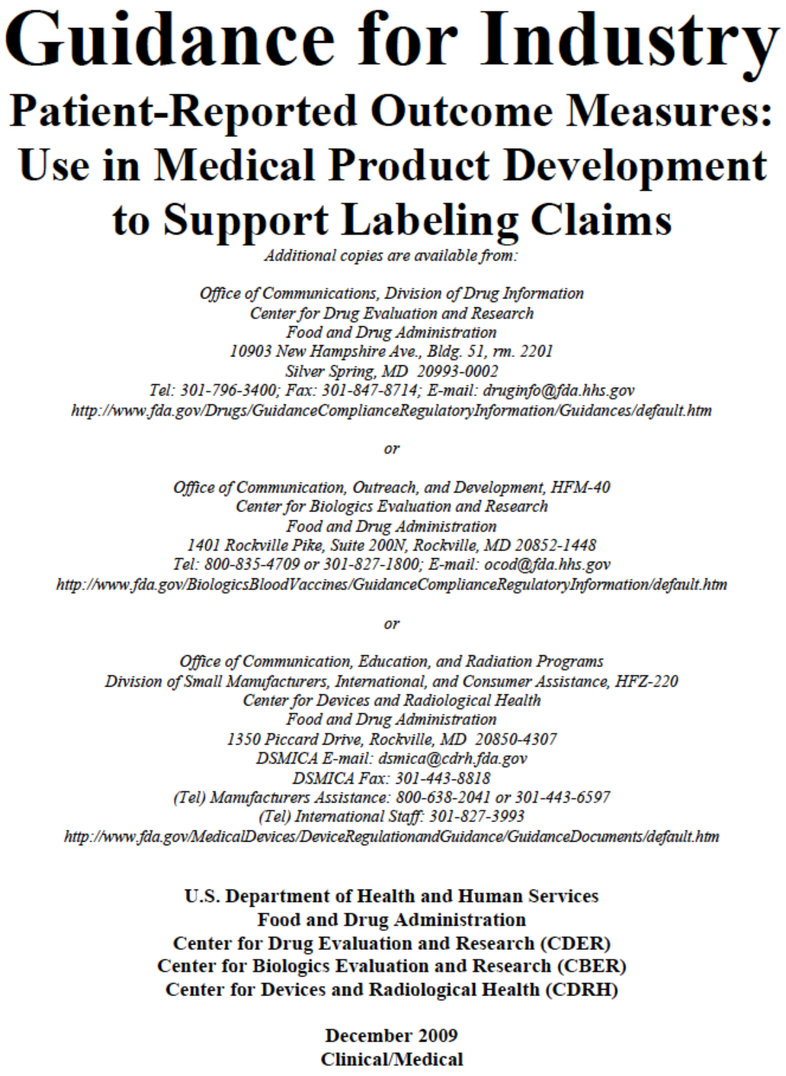


Figure 3: Factors affecting health related quality of life

Perspectives in Clinical Research | October-December 2011 | Vol 2 | Issue 4

Patient’s reported outcomes could be used at regulatory level



Guidance for Industry

Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 51, rm. 2201
Silver Spring, MD 20993-0002
Tel: 301-796-3400; Fax: 301-847-8714; E-mail: druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

or

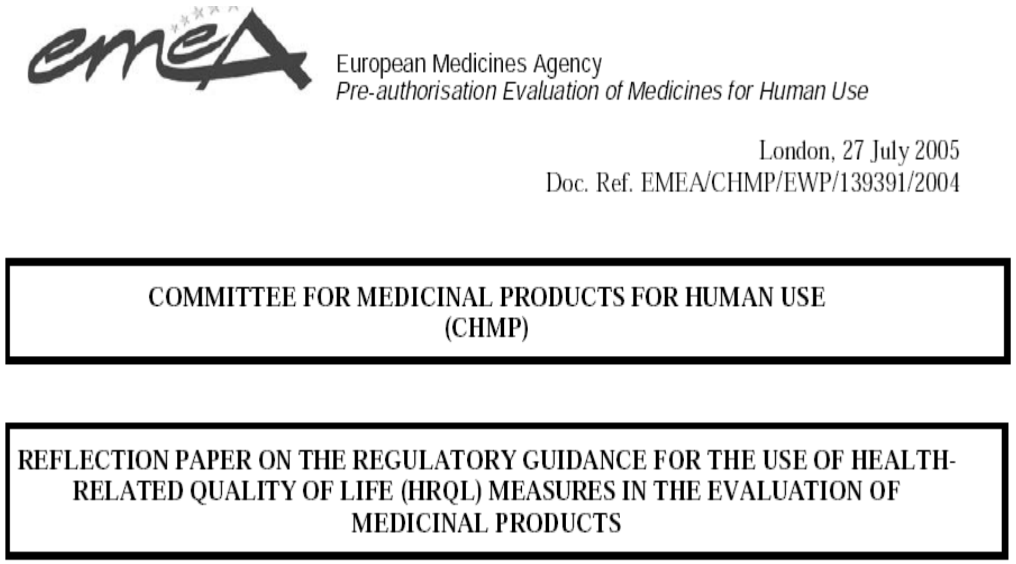
Office of Communication, Outreach, and Development, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448
Tel: 800-835-4709 or 301-827-1800; E-mail: ocod@fda.hhs.gov
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm

or

Office of Communication, Education, and Radiation Programs
Division of Small Manufacturers, International, and Consumer Assistance, HFZ-220
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, Rockville, MD 20850-4307
DSMICA E-mail: dsmica@cdrh.fda.gov
DSMICA Fax: 301-443-8818
(Tel) Manufacturers Assistance: 800-638-2041 or 301-443-6597
(Tel) International Staff: 301-827-3993
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2009
Clinical/Medical

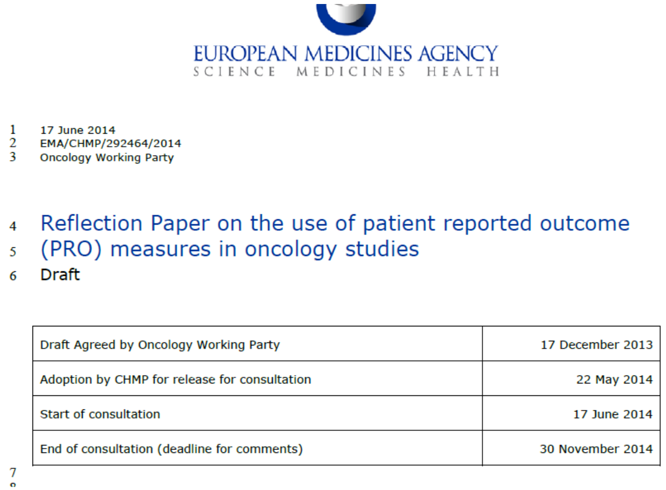


European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

London, 27 July 2005
Doc. Ref. EMEA/CHMP/EWP/139391/2004

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

REFLECTION PAPER ON THE REGULATORY GUIDANCE FOR THE USE OF HEALTH-RELATED QUALITY OF LIFE (HRQL) MEASURES IN THE EVALUATION OF MEDICINAL PRODUCTS



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 June 2014
EMA/CHMP/292464/2014
Oncology Working Party

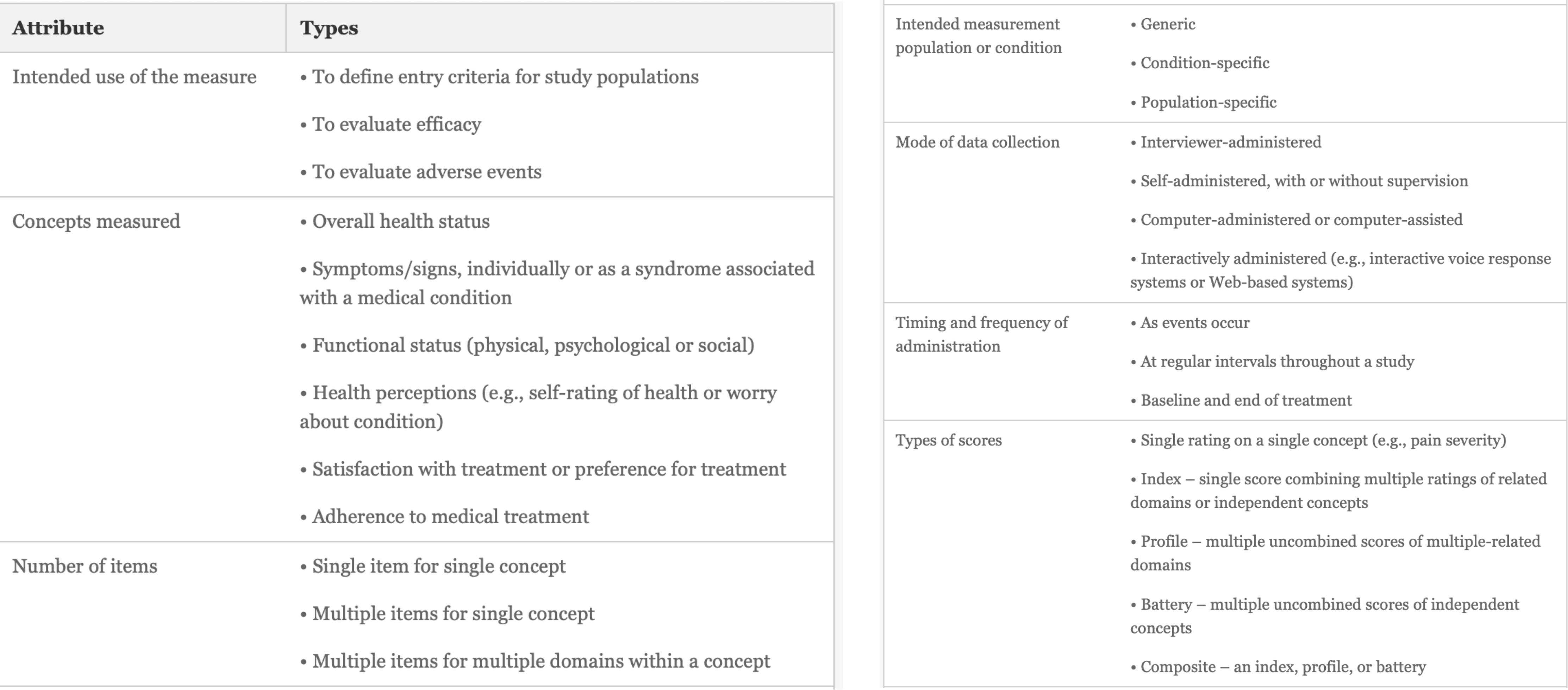
Reflection Paper on the use of patient reported outcome (PRO) measures in oncology studies

Draft

Draft Agreed by Oncology Working Party	17 December 2013
Adoption by CHMP for release for consultation	22 May 2014
Start of consultation	17 June 2014
End of consultation (deadline for comments)	30 November 2014

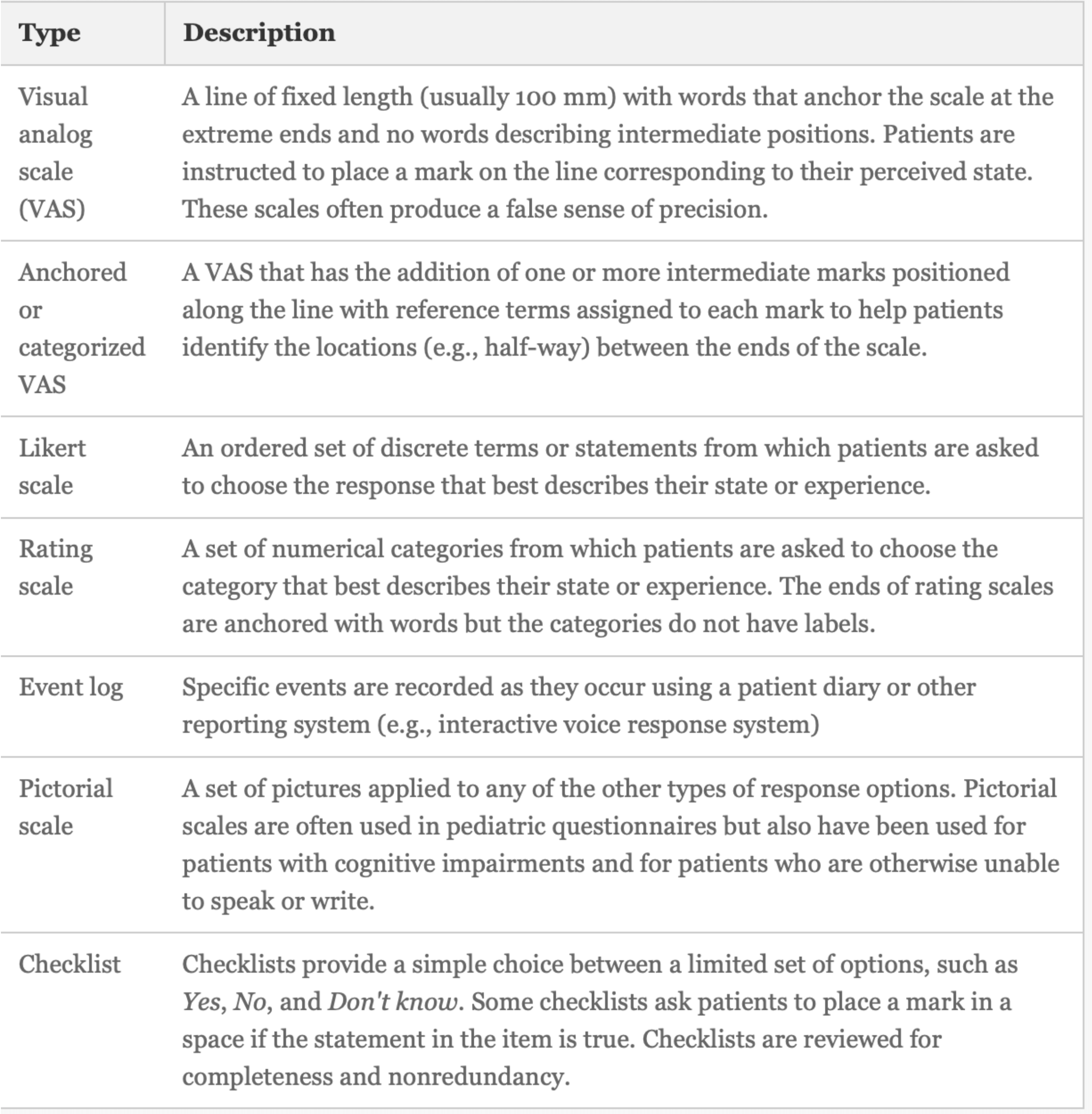
Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance

Taxonomy of PROs Used in Clinical Trials



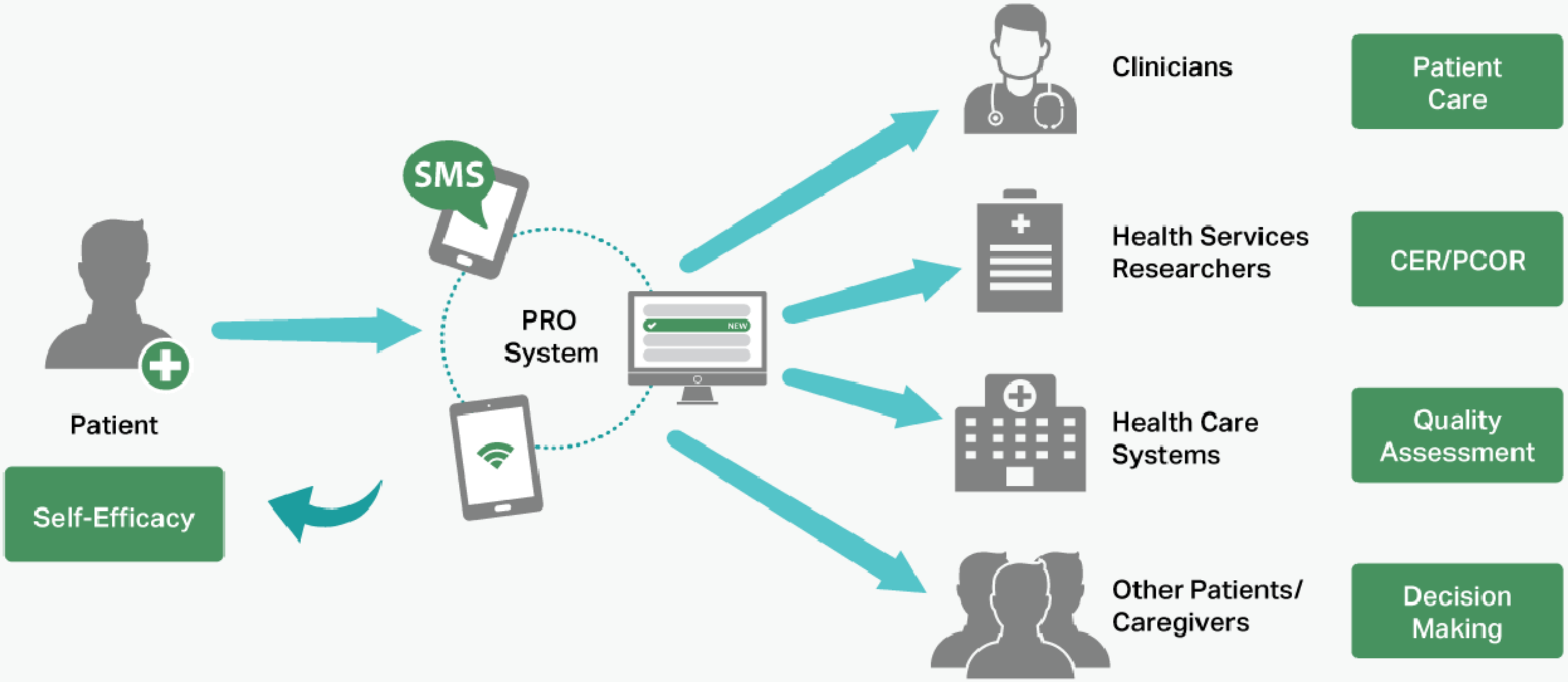
Attribute	**Types**
Intended use of the measure	• To define entry criteria for study populations • To evaluate efficacy • To evaluate adverse events
Concepts measured	• Overall health status • Symptoms/signs, individually or as a syndrome associated with a medical condition • Functional status (physical, psychological or social) • Health perceptions (e.g., self-rating of health or worry about condition) • Satisfaction with treatment or preference for treatment • Adherence to medical treatment
Number of items	• Single item for single concept • Multiple items for single concept • Multiple items for multiple domains within a concept
Intended measurement population or condition	• Generic • Condition-specific • Population-specific
Mode of data collection	• Interviewer-administered • Self-administered, with or without supervision • Computer-administered or computer-assisted • Interactively administered (e.g., interactive voice response systems or Web-based systems)
Timing and frequency of administration	• As events occur • At regular intervals throughout a study • Baseline and end of treatment
Types of scores	• Single rating on a single concept (e.g., pain severity) • Index – single score combining multiple ratings of related domains or independent concepts • Profile – multiple uncombined scores of multiple-related domains • Battery – multiple uncombined scores of independent concepts • Composite – an index, profile, or battery

Type of response options



Type	Description
Visual analog scale (VAS)	A line of fixed length (usually 100 mm) with words that anchor the scale at the extreme ends and no words describing intermediate positions. Patients are instructed to place a mark on the line corresponding to their perceived state. These scales often produce a false sense of precision.
Anchored or categorized VAS	A VAS that has the addition of one or more intermediate marks positioned along the line with reference terms assigned to each mark to help patients identify the locations (e.g., half-way) between the ends of the scale.
Likert scale	An ordered set of discrete terms or statements from which patients are asked to choose the response that best describes their state or experience.
Rating scale	A set of numerical categories from which patients are asked to choose the category that best describes their state or experience. The ends of rating scales are anchored with words but the categories do not have labels.
Event log	Specific events are recorded as they occur using a patient diary or other reporting system (e.g., interactive voice response system)
Pictorial scale	A set of pictures applied to any of the other types of response options. Pictorial scales are often used in pediatric questionnaires but also have been used for patients with cognitive impairments and for patients who are otherwise unable to speak or write.
Checklist	Checklists provide a simple choice between a limited set of options, such as *Yes*, *No*, and *Don't know*. Some checklists ask patients to place a mark in a space if the statement in the item is true. Checklists are reviewed for completeness and nonredundancy.

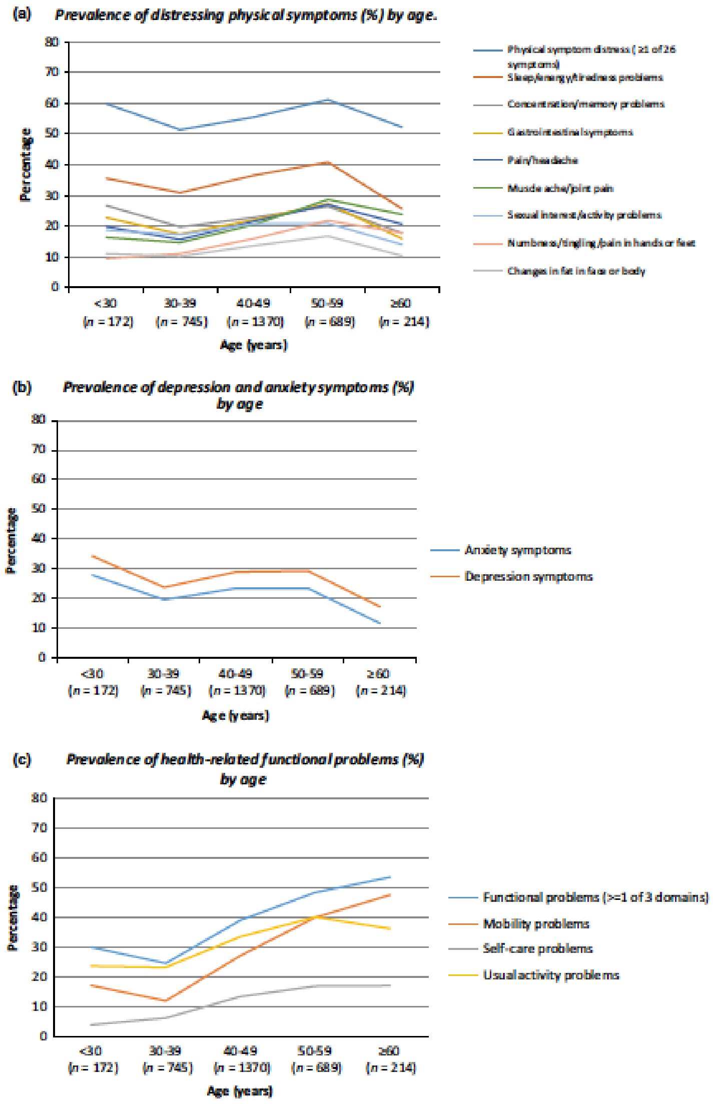
Figure 1. Potential uses of patient-reported data collected during routine cancer care



Source: Dr. Ethan Basch.

The patient-reported outcome measure's conceptual framework of barriers to antiretroviral therapy adherence (revised from Engler et al 2018

Longer time with HIV, rather than age, contributes to psycological morbidity and lower QoL: Results from ASTRA study

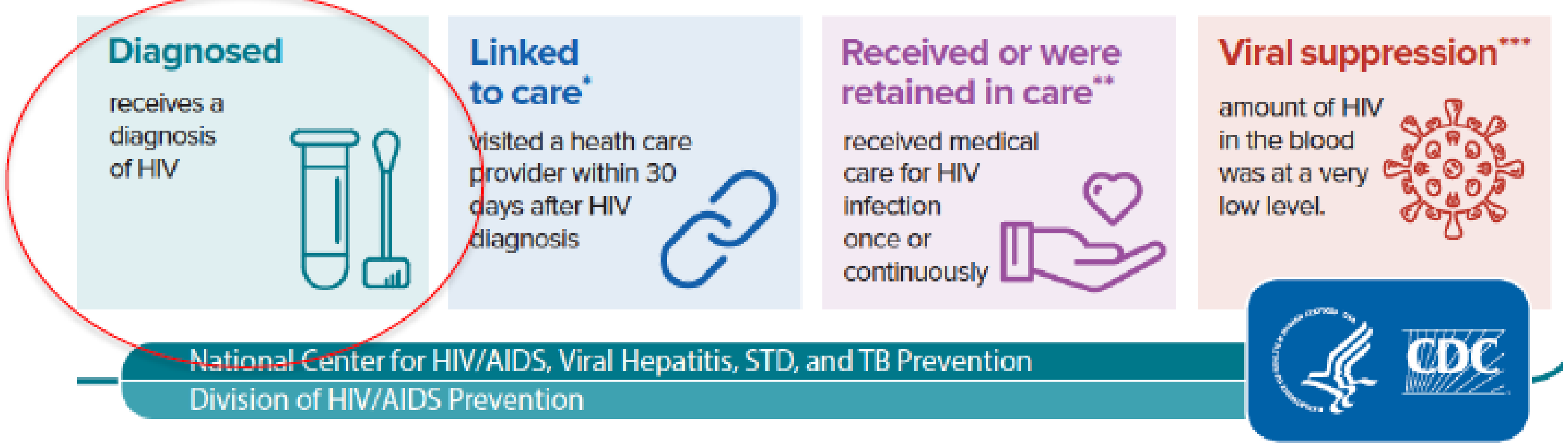


Trend in prevalence by age

	AOR	95%CI	p
Physical symptoms	0.96	0.89-1.04	0.36
Depression	0.86	0.79-0.94	0.001
Anxiety	0.85	0.77-0.94	0.001
Functional problem	1.28	1.17-1.39	<0.001

Longer time with HIV infection was strongly and independently associated with a higher prevalence of symptoms, anxiety, functional problems (P<0.001 for trend)

McGowan, HIV med 2017



Diagnosed
receives a diagnosis of HIV

Linked to care*
visited a heath care provider within 30 days after HIV diagnosis

Received or were retained in care**
received medical care for HIV infection once or continuously

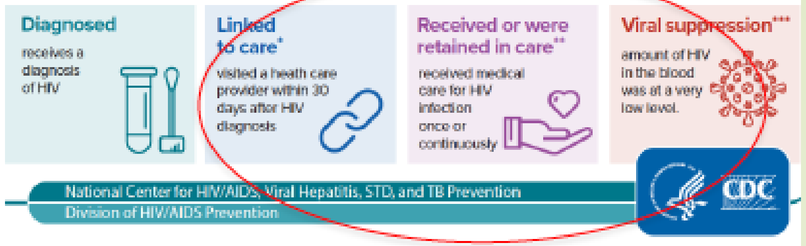
Viral suppression***
amount of HIV in the blood was at a very low level.

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of HIV/AIDS Prevention

MH and HIV testing: still a missed opportunities

- Rates of HIV Testing Among Adults With Severe Mental Illness Receiving Care in Community Mental Health Settings is persistently inadequate. *Mangurian, Psychiatric services 2017*
- Half of individuals in MH settings who engaged in HIV risk behavior were not tested. *Meade AIDS and behavior 2005*
- Lack of interventions for promoting HIV testing among individuals with an SMI who are those at higher risk of risky sexual behaviors. *Senn, Psychological medicine 2009;*

Greater chronicity of depression increased the likelihood of failure at multiple points along the HIV care continuum


Diagnosed
receives a diagnosis of HIV

Linked to care*
visited a heath care provider within 30 days after HIV diagnosis

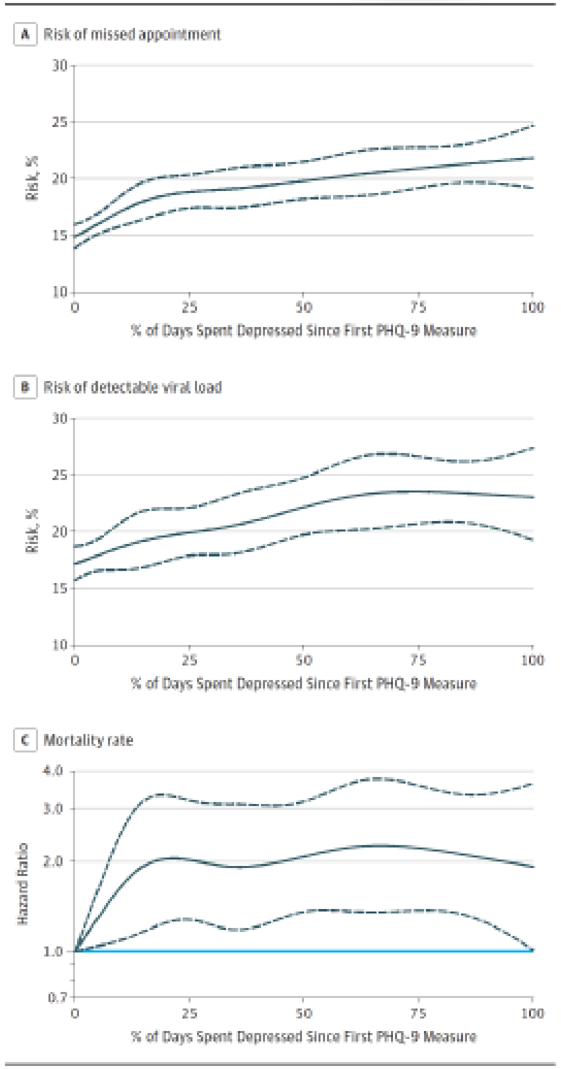
Received or were retained in care**
received medical care for HIV infection once or continuously

Viral suppression***
amount of HIV in the blood was at a very low level.

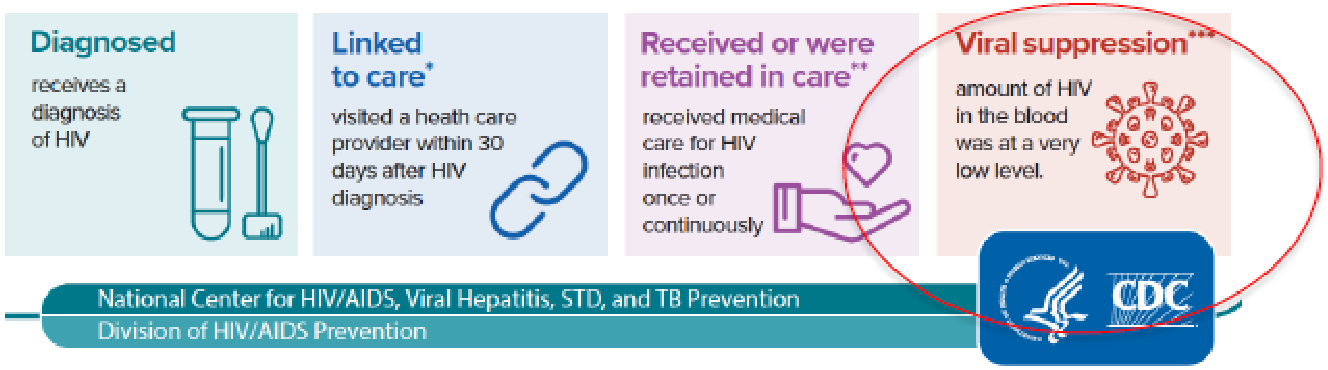
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of HIV/AIDS Prevention

- Observational clinical cohort of 5927 patients (10 767 person-years of follow-up)
- receiving HIV primary care at 6 geographically dispersed US academic medical centers from September 22, 2005, to August 6, 2015.
- 2 or more assessments of depressive severity (PHQ-9)

	Effect Estimate (95% CI)	
Outcome[a]	Per 25% Increase in % of Days With Depression	Comparing Those Always Depressed With Those Never Depressed
All-cause mortality, hazard ratio[b]	1.19 (1.05-1.36)	2.02 (1.20-3.42)
Risk of missing a scheduled appointment, risk ratio[c]	1.08 (1.05-1.11)	1.37 (1.22-1.53)
Risk of having an unsuppressed viral load, risk ratio[c]	1.05 (1.01-1.09)	1.23 (1.06-1.43)



Pence, JAMA Psychiatry 2018



Depression and HIV/AIDS Treatment Nonadherence

Metanalysis on 95 independent samples

- depression was significantly ($P < 0.0001$) associated with nonadherence ($r = 0.19$; 95% CI 0.14 to 0.25).
- Larger effects in studies using interview than in those using self-administered questionnaires.
- When adherence is studied as a continuum significantly stronger effects than dichotomies.
- Effect size was not significantly related to other aspects of adherence or depression measurement, assessment interval (ie, cross-sectional vs. longitudinal), sex, IV drug use, sexual orientation, or study location. Our results suggest that interventions aimed at

reducing depressive symptom severity, even at subclinical levels, should be a behavioral research priority.

Interventions aimed at reducing depressive symptom severity, even at subclinical levels, should be a behavioral research priority.

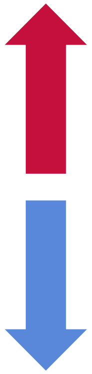
Gonzalez, JAIDS 2011

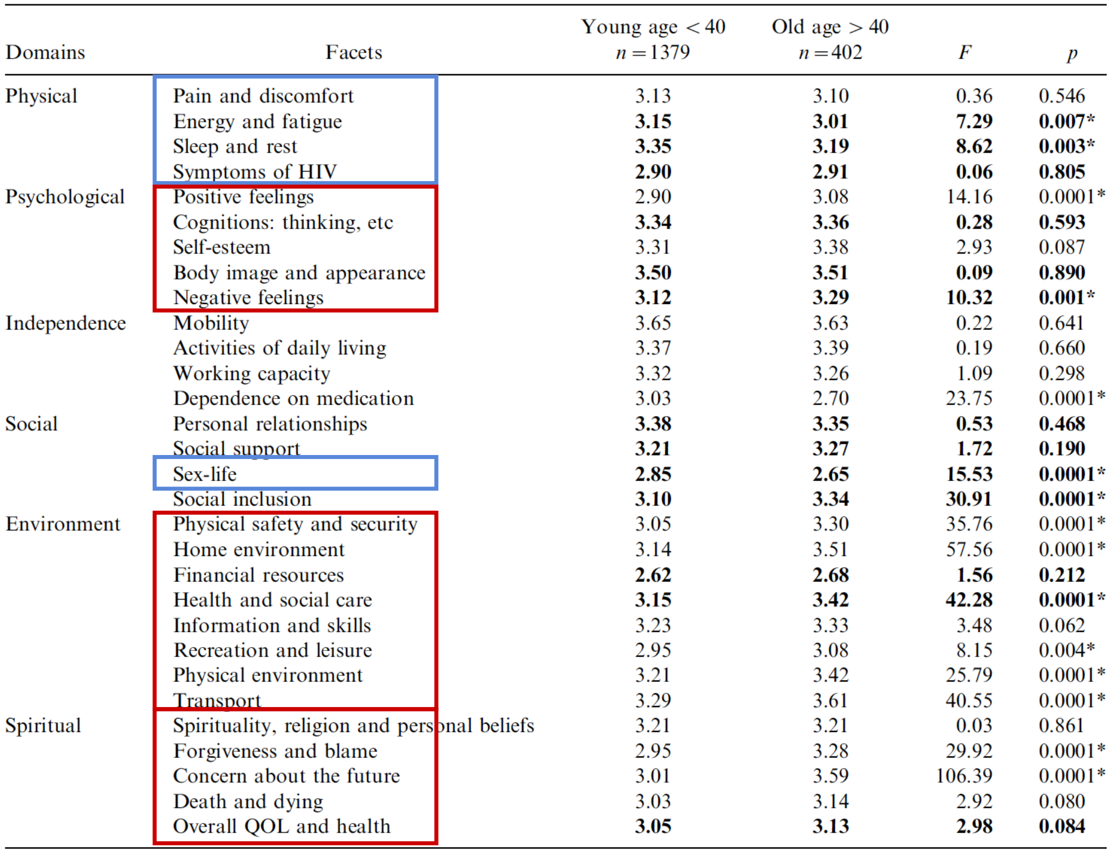
The evaluation of QoL is more complex in OPLWH compared to YPLWH

Combined sample of 2234 HIV-infected adults form 9 “cultures”:

Melbourne, Porto Alegre, Bangalore, New Delhi, Bangkok, Harare, Roma, Dniepropetrovsk, Phnom Penh

Qol was found as poorer for younger people than older [F=9.39, (df=1,2080) p<0.002]



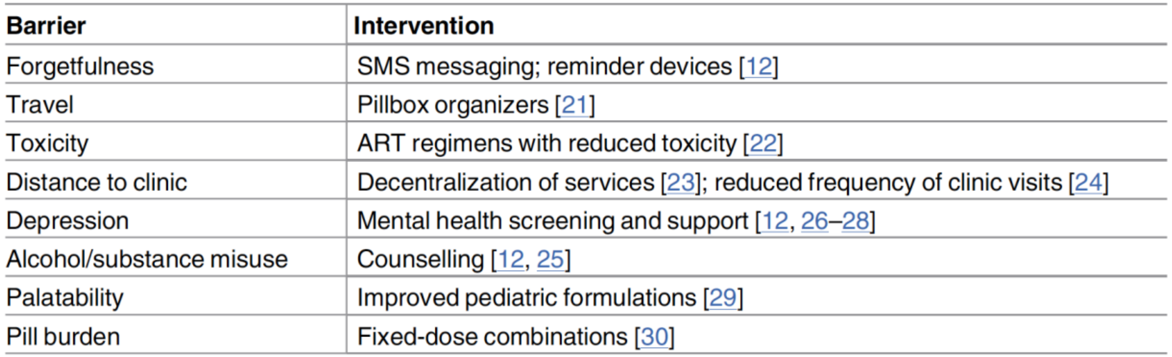


Domains	Facets	Young age < 40 $n = 1379$	Old age > 40 $n = 402$	F	p
Physical	Pain and discomfort	3.13	3.10	0.36	0.546
	Energy and fatigue	**3.15**	**3.01**	**7.29**	**0.007***
	Sleep and rest	**3.35**	**3.19**	**8.62**	**0.003***
	Symptoms of HIV	**2.90**	**2.91**	**0.06**	**0.805**
Psychological	Positive feelings	2.90	3.08	14.16	0.0001*
	Cognitions: thinking, etc	**3.34**	**3.36**	**0.28**	**0.593**
	Self-esteem	3.31	3.38	2.93	0.087
	Body image and appearance	**3.50**	**3.51**	**0.09**	**0.890**
	Negative feelings	**3.12**	**3.29**	**10.32**	**0.001***
Independence	Mobility	3.65	3.63	0.22	0.641
	Activities of daily living	3.37	3.39	0.19	0.660
	Working capacity	3.32	3.26	1.09	0.298
	Dependence on medication	3.03	2.70	23.75	0.0001*
Social	Personal relationships	**3.38**	**3.35**	**0.53**	**0.468**
	Social support	**3.21**	**3.27**	**1.72**	**0.190**
	Sex-life	**2.85**	**2.65**	**15.53**	**0.0001***
	Social inclusion	**3.10**	**3.34**	**30.91**	**0.0001***
Environment	Physical safety and security	3.05	3.30	35.76	0.0001*
	Home environment	3.14	3.51	57.56	0.0001*
	Financial resources	**2.62**	**2.68**	**1.56**	**0.212**
	Health and social care	**3.15**	**3.42**	**42.28**	**0.0001***
	Information and skills	3.23	3.33	3.48	0.062
	Recreation and leisure	2.95	3.08	8.15	0.004*
	Physical environment	3.21	3.42	25.79	0.0001*
	Transport	3.29	3.61	40.55	0.0001*
Spiritual	Spirituality, religion and personal beliefs	3.21	3.21	0.03	0.861
	Forgiveness and blame	2.95	3.28	29.92	0.0001*
	Concern about the future	3.01	3.59	106.39	0.0001*
	Death and dying	3.03	3.14	2.92	0.080
	Overall QOL and health	**3.05**	**3.13**	**2.98**	**0.084**

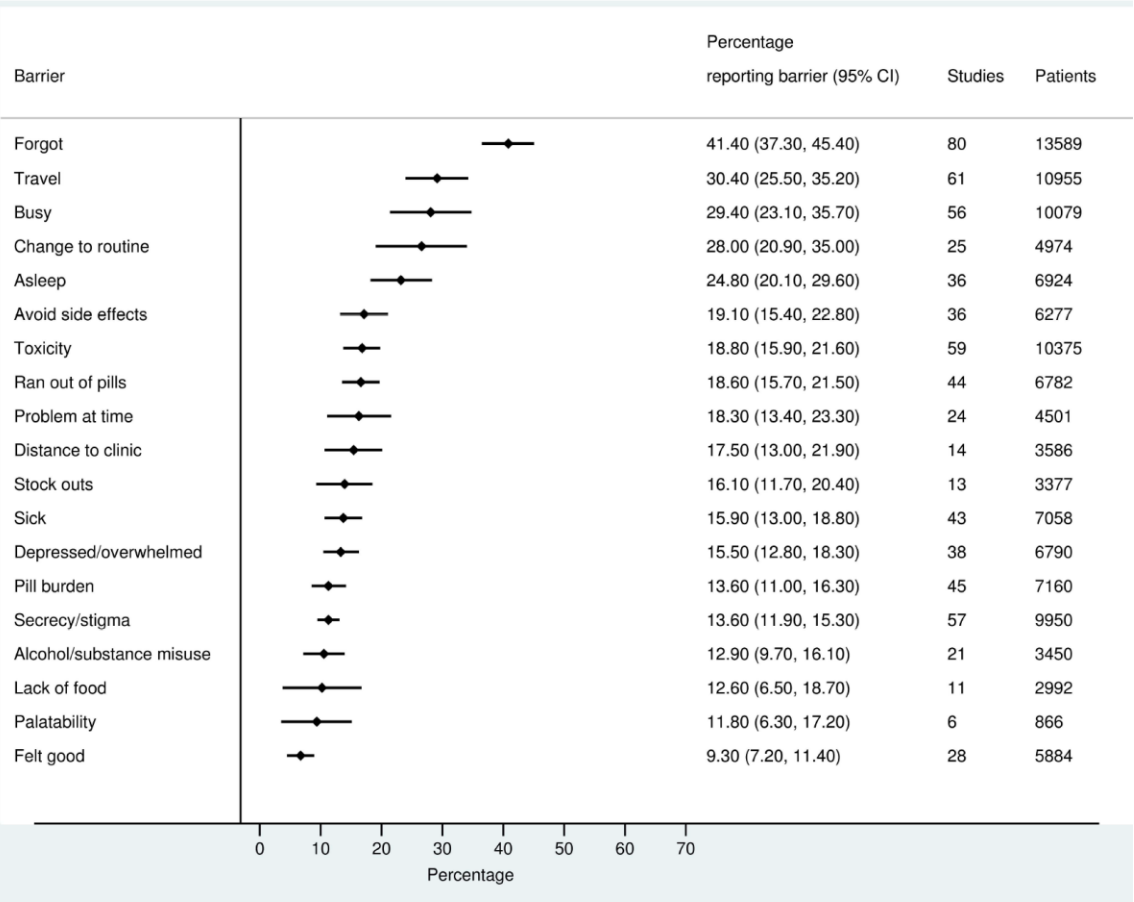
Skevington, AIDS care 2012

Patients reported barriers to treatment adherence in PLWH and need for specific interventions

- (PubMed, Embase, Web of Science, and PsychINFO) from 01 January 1997 to 31 March 2016
- Pooled proportions of reported barriers to adherence per age group (adults, adolescent and children).
- Data from 125 studies that provided information about adherence barriers for 17,061 adults, 1,099 children, and 856 adolescents.



Barrier	Intervention
Forgetfulness	SMS messaging; reminder devices [12]
Travel	Pillbox organizers [21]
Toxicity	ART regimens with reduced toxicity [22]
Distance to clinic	Decentralization of services [23]; reduced frequency of clinic visits [24]
Depression	Mental health screening and support [12, 26–28]
Alcohol/substance misuse	Counselling [12, 25]
Palatability	Improved pediatric formulations [29]
Pill burden	Fixed-dose combinations [30]



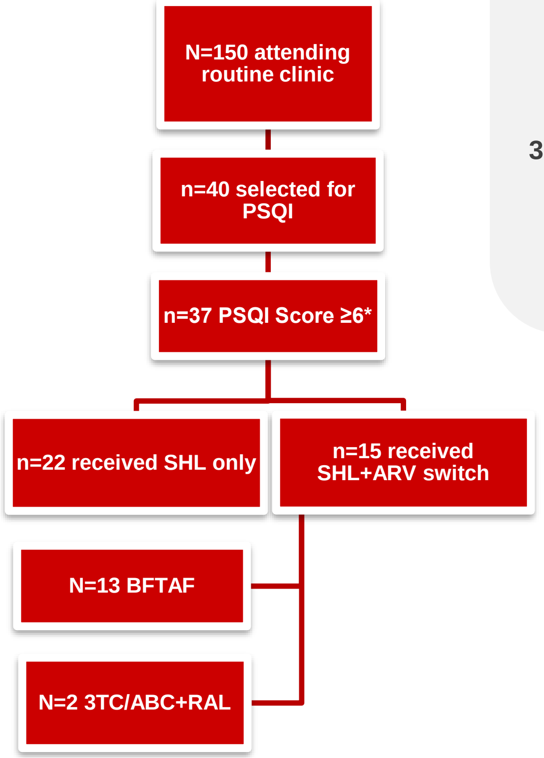
Barrier	Percentage reporting barrier (95% CI)	Studies	Patients
Forgot	41.40 (37.30, 45.40)	80	13589
Travel	30.40 (25.50, 35.20)	61	10955
Busy	29.40 (23.10, 35.70)	56	10079
Change to routine	28.00 (20.90, 35.00)	25	4974
Asleep	24.80 (20.10, 29.60)	36	6924
Avoid side effects	19.10 (15.40, 22.80)	36	6277
Toxicity	18.80 (15.90, 21.60)	59	10375
Ran out of pills	18.60 (15.70, 21.50)	44	6782
Problem at time	18.30 (13.40, 23.30)	24	4501
Distance to clinic	17.50 (13.00, 21.90)	14	3586
Stock outs	16.10 (11.70, 20.40)	13	3377
Sick	15.90 (13.00, 18.80)	43	7058
Depressed/overwhelmed	15.50 (12.80, 18.30)	38	6790
Pill burden	13.60 (11.00, 16.30)	45	7160
Secrecy/stigma	13.60 (11.90, 15.30)	57	9950
Alcohol/substance misuse	12.90 (9.70, 16.10)	21	3450
Lack of food	12.60 (6.50, 18.70)	11	2992
Palatability	11.80 (6.30, 17.20)	6	866
Felt good	9.30 (7.20, 11.40)	28	5884

Shubber, Plos Med 2016

Utility of the Pittsburgh Sleep Quality Index (PSQI) in a Community HIV Clinic

Pilot study to assess use of the PSQI in assessing sleep disturbance in patients before and after clinical intervention with sleep hygiene leaflet (SHL) and ARV switch if indicated

*PSQI score of ≥6 indicative of significant sleep disturbance


N=150 attending routine clinic

n=40 selected for PSQI

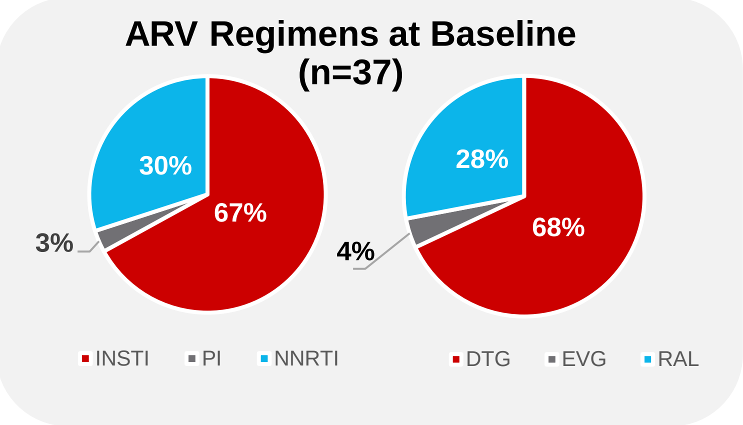
n=37 PSQI Score ≥6*

n=22 received SHL only

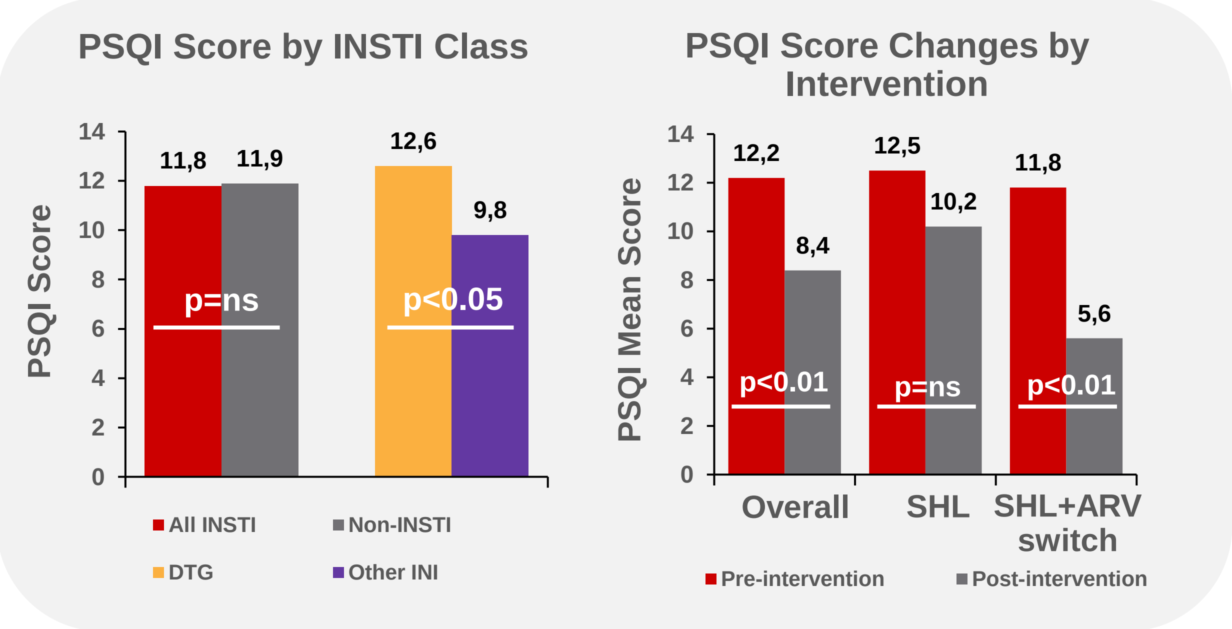
n=15 received SHL+ARV switch

N=13 BFTAF

N=2 3TC/ABC+RAL



- Mean age 40yrs, 84% VL<50cp/mL
- Mental health problems (mean PSQI 13.45) and exposure to antidepressants /antipsychotics (PSQI 14.82), significantly associated with more severe sleep disturbance (p<0.01).



- **DTG was associated with significantly greater sleep disturbance versus other INSTIs (EVG and RAL)**
- **ARV switch (including to B/F/TAF) and provision of sleep hygiene information significantly improved sleep quality within one month of intervention**

Goorney et al. HIV Drug Therapy 2020. Glasgow. P082

ARV, antiretroviral; ns, not significant; VL, viral load

Patient-Reported Outcomes: 12 Months of B/F/TAF in Routine Clinical Practice

Prespecified, descriptive* PRO analysis of a subset of participants from Germany, Canada, France, and the Netherlands who completed PRO questionnaires at both baseline and Month 12

Outcome	PRO tool	TN	TE
Mental Health-related QoL	**SF-36 MCS**	✓	✓
Physical Health-related QoL	**SF-36 PCS**	✓	✓
HIV symptoms – Overall, CNS, GI, Pain, Other	**HIV Symptom Index**	✓	✓
Treatment satisfaction	**HIVTSQs & HIVTSQc**		✓

- The PRO analysis population was comparable to the overall study population in terms of age, gender, and ethnicity

	Overall sample (N=513)		SF-36 (n=221)		HIV-SI (n=250)	
	TN n=84	TE n=429	TN n=38	TE n=183	TN n=43	TE n=207
Age (years), median age (Q1, Q3)	38 (29–48)	49 (40–56)	37 (30, 44)	48 (40, 55)	36 (29, 44)	49 (40, 55)
Age ≥50 years, n (%)	20 (24%)	209 (49%)	8 (21%)	79 (43%)	9 (21%)	96 (46%)
Male, n (%)	76 (91%)	392 (91%)	34 (90%)	170 (93%)	39 (91%)	194 (94%)
White, n (%)	71 (85%)	387 (90%)	33 (87%)	167 (91%)	37 (86%)	188 (91%)

*Statistical testing of differences was not completed for this presentation

CNS, central nervous system; HIVTSQc, HIV Treatment Satisfaction Questionnaire – change; HIVTSQs, HIV Treatment Satisfaction Questionnaire – status; HIV-SI, HIV Symptom Index; HRQoL, health-related quality of life; MCS, mental component score; PCS, physical component score; PROs, patient-reported outcomes; SF-36, 36-item Short Form Health Survey; TE, treatment experienced; TN, treatment naïve

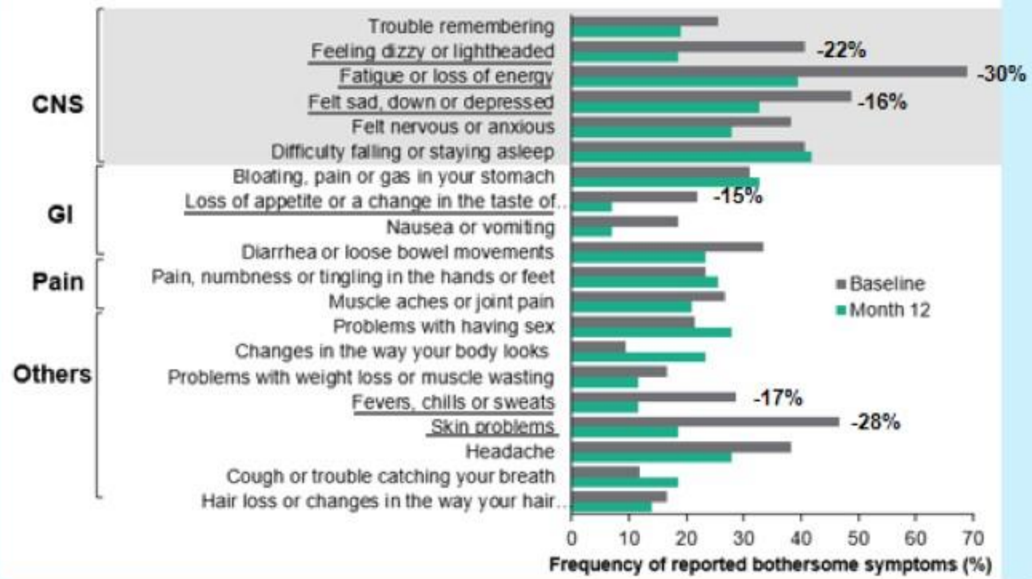
Knechten H, et al. HIV Drug Therapy 2020. Glasgow. P053

Real World Data: BICSTaR Cohort – PRO analysis

Summary of PROs in Treatment-Naïve PLWH*

Treatment-Naive	
Outcome	**PRO tool**
Mental Health-related QoL	*SF-36 MCS*
Physical Health-related QoL	*SF-36 PCS*
• **Numerical improvement in median mental health score (+4.7)[†]** • **Stable physical health score (+0.7)[‡]**	
HIV symptoms	*HIV Symptom Index*
• **Median bothersome symptom count numerically decreased**** • **Three bothersome CNS symptoms had ≥ 15% decrease in prevalence (dizzy, fatigue/loss of energy, depressed)**	

HIV-Symptom Index 'Bothersome' Symptoms[Ω] (n=43)



ΩSymptoms were dichotomised into 'not bothersome' (scores of 0 or 1) or 'bothersome' (scores of 2, 3, and 4). Changes of ≥ 15% from Baseline to Month 12 are underlined

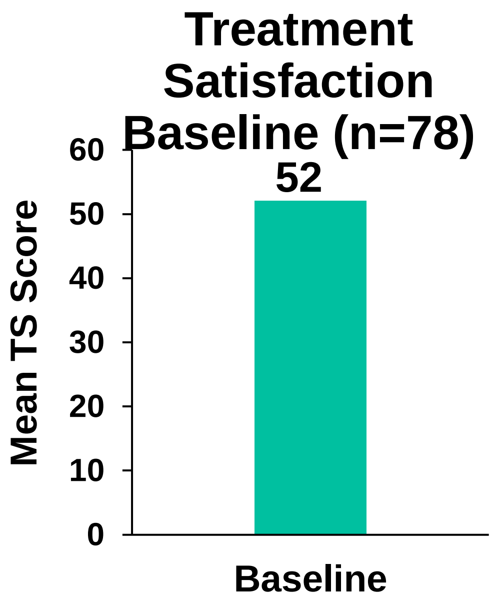
These data support the favourable profile of B/F/TAF after 12 months in a real-world setting using self-reported outcomes from a treatment-naïve population with a high baseline prevalence of comorbidities

CNS, central nervous system; HIVTSQc/s; QoL, quality of life; MCS, mental component score; PCS, physical component score; PROs, patient-reported outcomes; SF-36, 36-item Short Form Health Survey
*Statistical testing of differences was not completed for this presentation
†Median MCS summary score: 44 Baseline and 53 Month 12. ‡ Median MCS summary score: 55 Baseline and 56 Month 12. **Median (IQR) symptom score: 6 (2, 9) Baseline and 3 (2, 7) Month 12.

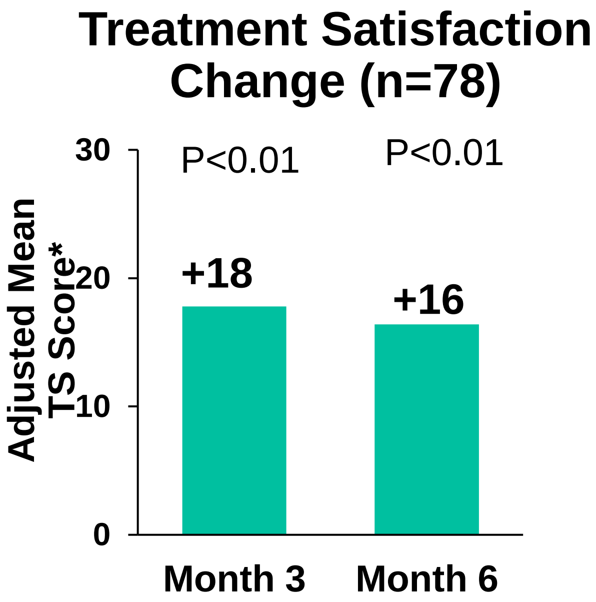
Knechten H, et al. HIV Drug Therapy 2020. Glasgow. P053

Patient Reported Outcomes: Treatment Satisfaction

Treatment Experienced Patients



Range 0 to 60, higher total scores indicate greater satisfaction with treatment



Range -30 to +30, positive total scores indicate improvement in satisfaction with study treatment

Treatment experienced patients had a high level of treatment satisfaction at baseline, but reported a significant improvement at 3 and 6 months after switching to B/F/TAF

*Repeated measures analysis of covariance adjusting for Baseline TS and ‘simplification of ART‘ as the reason for switch to B/F/TAF.

Esser S, et al. EACS 2019. Basel, Switzerland. P2/16


Current HIV Research, 2018, *16*, 425-435

RESEARCH ARTICLE

Real World Patient-reported Outcomes in HIV-infected Adults Switching to EVIPLERA®, Because of a Previous Intolerance to cART. PRO-STR Study

300 with 48-week follow-up, switched to EVIPLERA.
74.7% switched from a NNRTI, 25.3% from a PI/b.
No statistical difference in median CD4+ cell count (baseline: 678.5 cells/mm3; 48-week: 683.0 cells/mm3) neither in virological suppression (≤50 copies/mL) (baseline: 98.3%; 48-week: 95.3%).

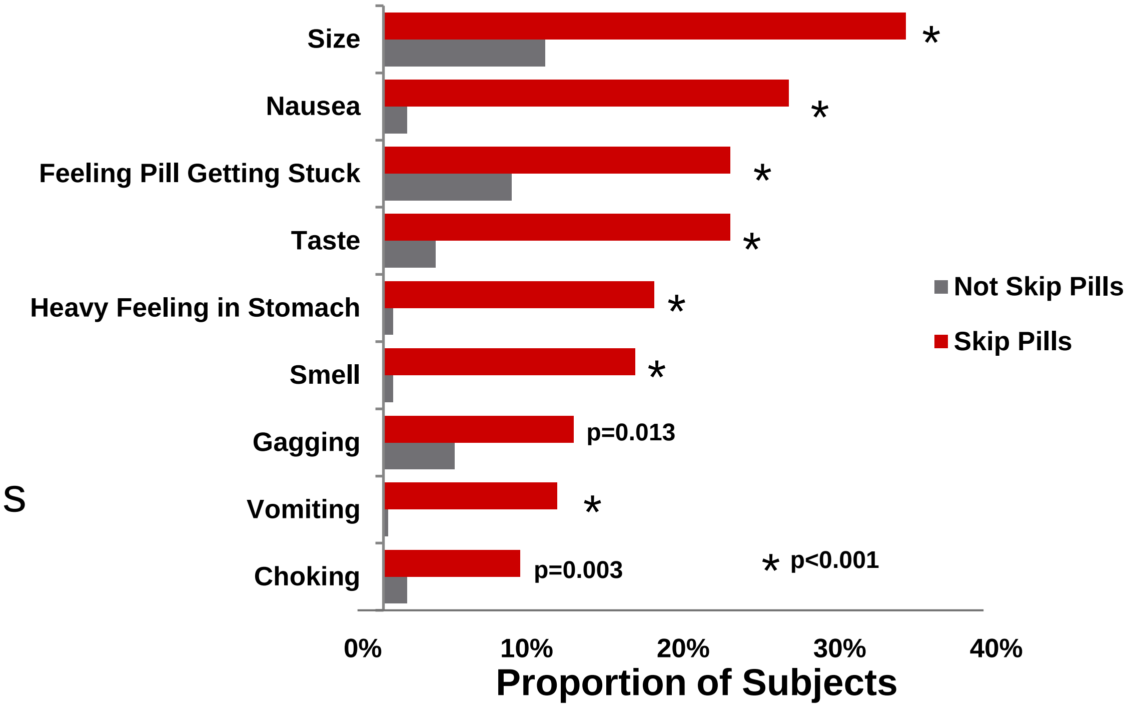
Overall, there was a significant decrease (pvalue≤ 0.05) in number and magnitude of symptoms, while HRQoL, satisfaction and adherence improved significantly.
Most patients prefered EVIPLERA. than previous cART.
According to the type of intolerance, HRQoL was improved, but only significantly in patients with neuropsychiatric and gastrointestinal symptoms.
Adherence improved significantly in patients with metabolic disturbances and satisfaction with EVIPLERA. was higher in the three groups.

Variables Affecting Pill Aversion in Adherent and Non-adherent Patients

Evaluation of pill aversion in adult outpatient HIV population in observational study at a single, large urban tertiary care centre (N=312)

- Anonymous questionnaire during routine clinic visit
- 25% report skipping pills due to pill aversion symptoms
- Associated with patient characteristics, emotions, pill qualities and sensations

Relationship Between Pill Aversion Symptoms and Medication Adherence

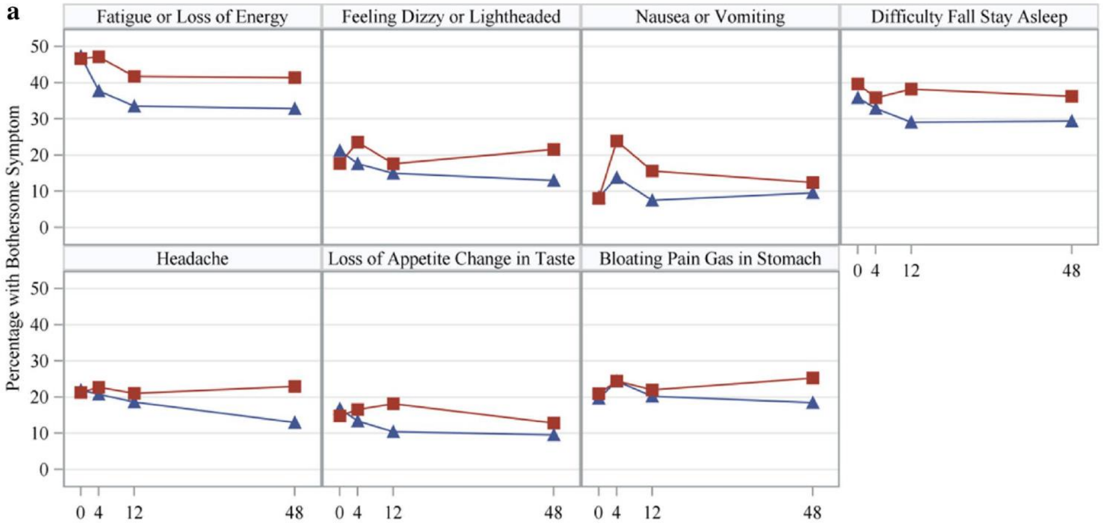


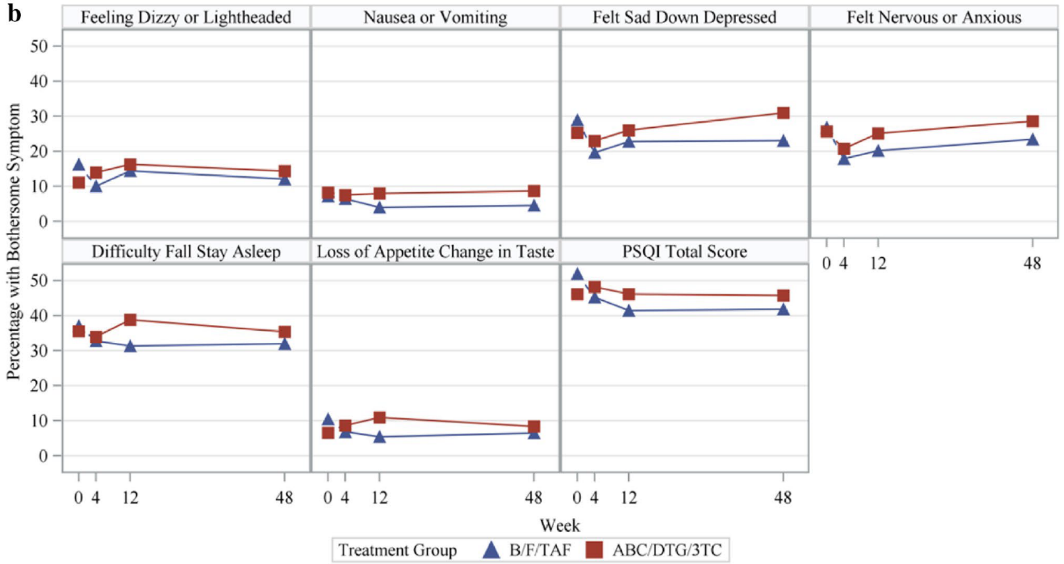
HIV-related pill aversion is a frequent and notable barrier to medication adherence

Dorman R, et al. CROI 2017. Seattle, WA. Poster #469

B/F/TAF was associated with lower prevalence of bothersome symptoms than ABC/DTG/3TC in both treatment naïve and virologically suppressed adults

- A planned secondary of two double-blind, randomised, Phase III studies comparing B/F/TAF with ABC/DTG/3TC: Naïve pts (GS-US-380-1489) and virologically suppressed pts (GS-US-380-1844)
- HIV symptoms distress module (HIV-SI), BL Short Form [SF]-36 Physical Component Summary [PCS], BL SF-36 Mental Component Summary [MCS], Pittsburgh Sleep Quality Index (PSQI) administered at baseline (BL) and weeks 4, 12, and 48

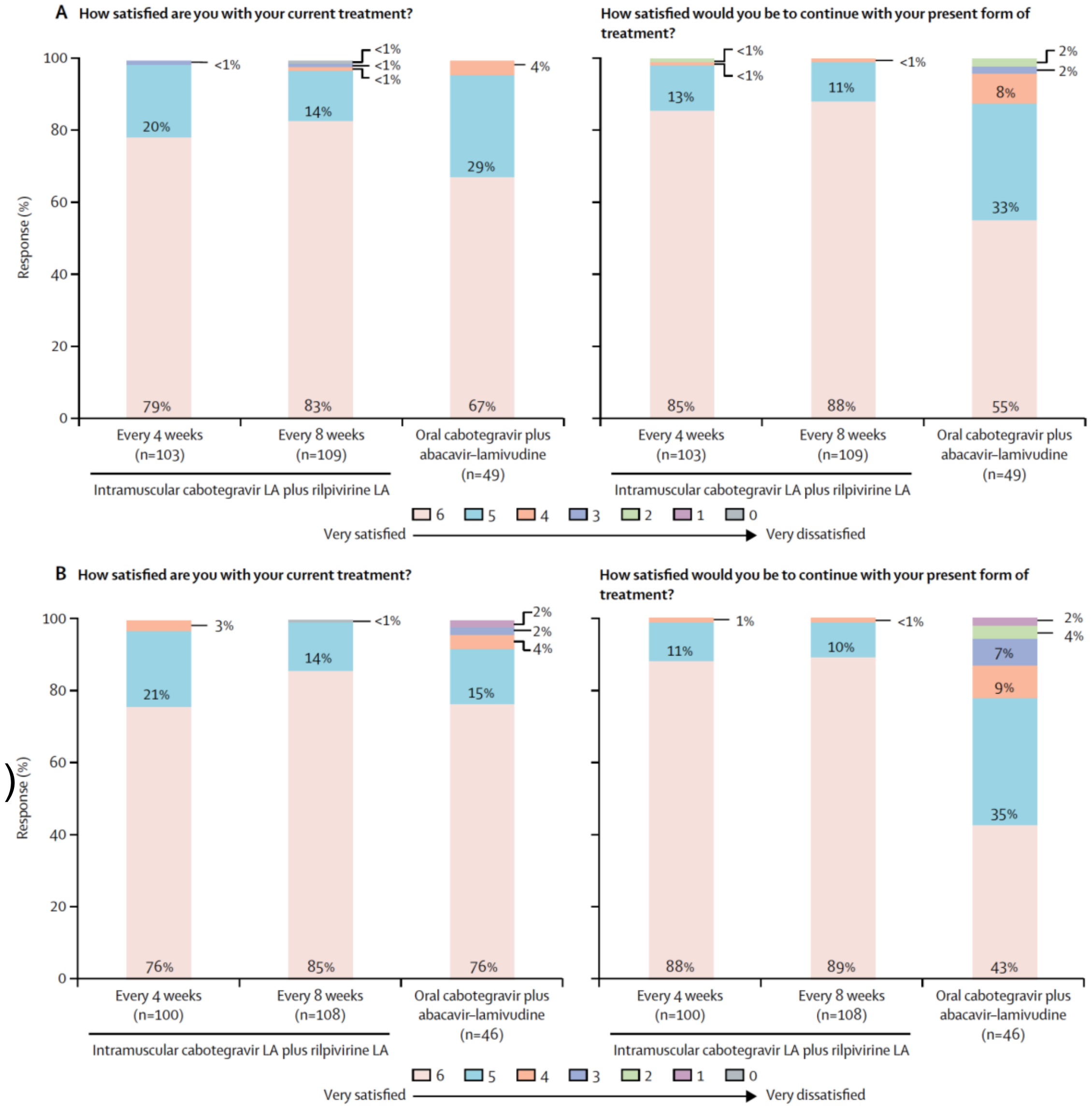




Wohl, Patient Centered Outcome Research 2018

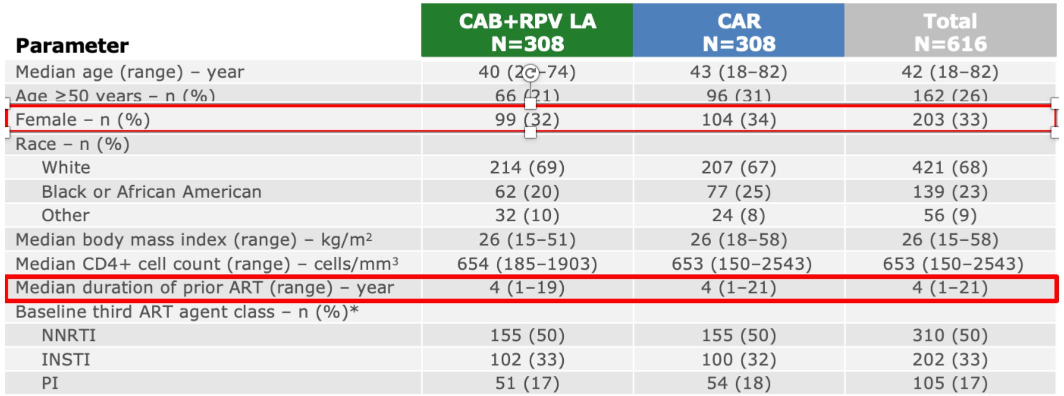
Patients reported outcomes at 48w and 96w in the LATTE-2

- Two-hundred and eighty-six virologically suppressed participants on oral cabotegravir + abacavir/lamivudine once-daily tablets (induction period)
- randomized to cabotegravir LA + rilpivirine LA once every 4 weeks ($n = 115$), once every 8 weeks ($n = 115$), or the continuation of the oral tablet regimen ($n = 56$) during the maintenance period.
- Patient-reported outcome measures included the HIV Medications Questionnaire (HIVMQ) and the HIV Treatment Satisfaction Questionnaire status (HIVTSQ[s]) and change (HIVTSQ[c]) versions at prespecified study visits through Week 96 of the randomized maintenance period.
- participants in the 4-week (median HIVTSQ[s] total score, 63.5; post hoc $P = 0.02$) and 8-week (65.0; post hoc $P < 0.001$) LA injectable groups were significantly more satisfied with treatment than participants in the oral maintenance group (60.0) at Week 96.

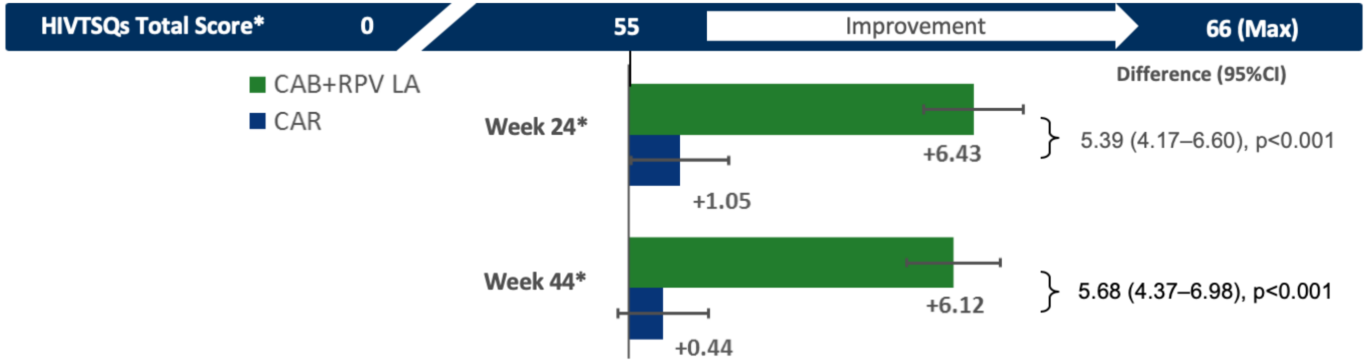


Margolis, Lancet 2017; Murray M, HIV Res Clin Pract 2019

Patient views on long acting HIV treatment: Cabotegravir + rilpivirine as maintenance therapy (ATLAS 48-week results)



Parameter	CAB+RPV LA N=308	CAR N=308	Total N=616
Median age (range) – year	40 (2[illegible]–74)	43 (18–82)	42 (18–82)
Age ≥50 years – n (%)	66 (21)	96 (31)	162 (26)
Female – n (%)	99 (32)	104 (34)	203 (33)
Race – n (%)			
White	214 (69)	207 (67)	421 (68)
Black or African American	62 (20)	77 (25)	139 (23)
Other	32 (10)	24 (8)	56 (9)
Median body mass index (range) – kg/m²	26 (15–51)	26 (18–58)	26 (15–58)
Median CD4+ cell count (range) – cells/mm³	654 (185–1903)	653 (150–2543)	653 (150–2543)
Median duration of prior ART (range) – year	4 (1–19)	4 (1–21)	4 (1–21)
Baseline third ART agent class – n (%)*			
NNRTI	155 (50)	155 (50)	310 (50)
INSTI	102 (33)	100 (32)	202 (33)
PI	51 (17)	54 (18)	105 (17)



- CAB+RPV LA participants demonstrated significantly greater improvement from baseline in treatment satisfaction vs. CAR at Weeks 24 and 44
- While participants in both groups had high baseline scores, the improvements in CAB+RPV LA met the threshold for demonstrating the minimal clinically important difference (MCID)

M. Murray, IAS 2019

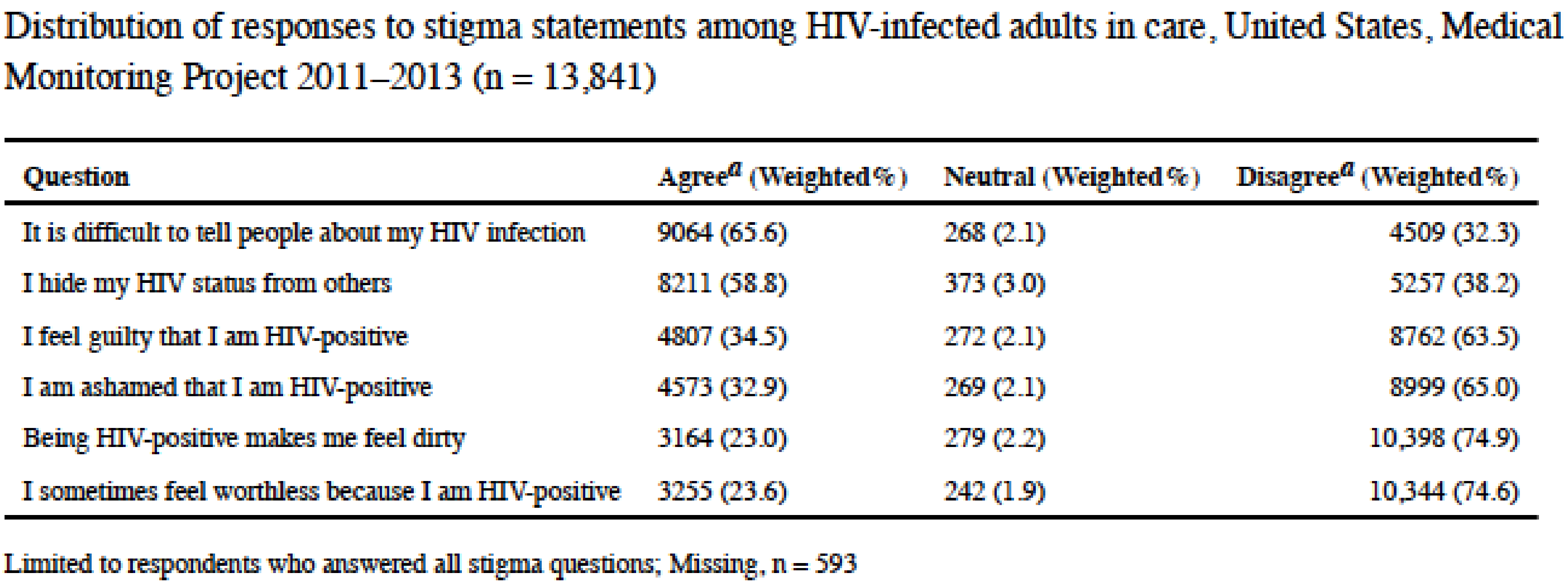
WHAT DOES HIV STIGMA LOOK LIKE?

STIGMA: Socially isolating a member of a community because they are HIV positive.

LET'S STOP HIV
TOGETHER

ACT AGAINST AIDS actagainstaids

Prevalence of Internalized HIV-Related Stigma Among HIV-Infected Adults in Care, United States, 2011–2013



Distribution of responses to stigma statements among HIV-infected adults in care, United States, Medical Monitoring Project 2011–2013 (n = 13,841)

Question	Agree[a] (Weighted %)	Neutral (Weighted %)	Disagree[a] (Weighted %)
It is difficult to tell people about my HIV infection	9064 (65.6)	268 (2.1)	4509 (32.3)
I hide my HIV status from others	8211 (58.8)	373 (3.0)	5257 (38.2)
I feel guilty that I am HIV-positive	4807 (34.5)	272 (2.1)	8762 (63.5)
I am ashamed that I am HIV-positive	4573 (32.9)	269 (2.1)	8999 (65.0)
Being HIV-positive makes me feel dirty	3164 (23.0)	279 (2.2)	10,398 (74.9)
I sometimes feel worthless because I am HIV-positive	3255 (23.6)	242 (1.9)	10,344 (74.6)

Limited to respondents who answered all stigma questions; Missing, n = 593

AIDS Behav. 2017 September ; 21(9): 2600–2608.

PREMs (Patients Reported Experienced Measures)

12° CONGRESSO NAZIONALE
ICAR
Italian Conference on
AIDS and Antiviral Research

Reach out for including all

12-16 ottobre 2020
DIGITAL EDITION

Relationship between General Practitioners and People Living With HIV: what do patients think?

Bruno S.R[1] Poliseno M.[2], Vichi F.[3], Di Biagio A.[4], Genova[4], Pisani L.[5,6],

Saracino A.[2], Santantonio T.[1], Lo Caputo S.[1]

Methods

Multicentre, prospective, observational study, qualitative data collected from 1st December 2019 to 1st February 2020 from the Infectious Diseases Unit of Bari, Foggia, Florence and Genoa are presented.

During the study period, all Italian, adult (≥18 years old) HIV infected patients, assuming cART from more than 6 month and attending the HIV outpatient service of the participating Centers, were offered a self-report, anonymous questionnaire. The participation to the survey was voluntary and was proposed to all patients during the medical visit and/ or the blood check.

Methods

The questionnaire was composed by **15 multiple choice items** in a simple formulation investigating socio-demographic information (sex, school education, town of residence, age, marital status, housing situation) and patient feedbacks about three main topics:

1)**communication of HIV positivity to GPs**

2) **subjective perception of the disease (U=U)**

3)**presence of co-medications and management of Drug-Drug Interactions (DDIs).**

Pearson X^2 test or Fisher's exact test were used, when appropriate, to compare categorical variables (residence, gender, level of education, duration of disease, age, marital status) with the answer given to each topic. Analysis was performed using R v.3.60. A $p<0.05$ was considered statistically significant.

Results

Patients features (%,n)	Total (nr. 672)
Sex	
Males	462 (69%)
Females	210 (31%)
Age	
>50 years	379 (56%)
<50 years	293 (44%)
Education level	
Elementary license or inferior	285 (42%)
High school license or superior	387 (58%)
Geographical position	
Northern Italy*	246 (36%)
Southern Italy**	426 (64%)
Marital status	
Married	241 (35%)
Single	200 (29%)
Living with parents	107 (16%)
Cohabiting	124 (18%)
Time from diagnosis	
<10 years	337 (50%)
>10 years	335 (50%)

Socio-demographic characteristics of 672 PLWHIV participating the survey

*= Northern Italy: Florence, Genoa; ** Southern Italy= Bari, Foggia;

Results: Communication of HIV positivity status to GPs and socio-demographic features

12° CONGRESSO NAZIONALE
Italian Conference on
AIDS and **Antiviral Research**
12-16 ottobre 2020

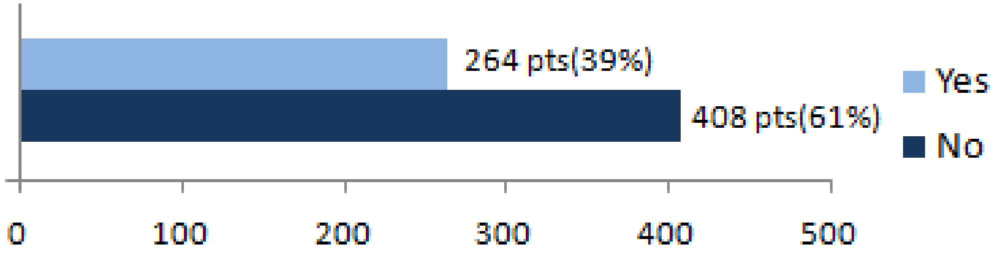
	"Yes"	**"No"**	**p value**
SEX			
Males (N= 462)	341 (74%)	121 (26%)	p= 0.133
Females (N= 210)	167 (79%)	43 (21%)	
AGE			
<50years (N= 293)	182 (62%)	111 (38%)	**p< 0.001**
>50years (N= 379)	326 (86%)	53 (14%)	
EDUCATION LEVEL			
Elementary license or inferior (N= 285)	240 (84%)	45 (16%)	**p< 0.001**
High school license or superior (N= 387)	268 (69%)	119 (31%)	
GEOGRAPHICAL POSITION			
Northern Italy* (N= 246)	212 (86%)	34 (14%)	**p<0.001**
Southern Italy° (N= 426)	296 (70%)	130 (30%)	

	"Yes"	**"No"**	**p value**
MARITAL STATUS			
Married (N=241)	182 (75%)	59 (25%)	p= 0.782
Single (N=200)	153 (76%)	47 (24%)	
Living with parents (N=107)	77 (72%)	30 (28%)	
Cohabiting (N=124)	86 (69%)	28 (31%)	
TIME FROM DIAGNOSIS			
<10years (N=337)	237 (70%)	100 (30%)	**p= 0.001**
>10years (N= 335)	271 (81%)	64 (19%)	

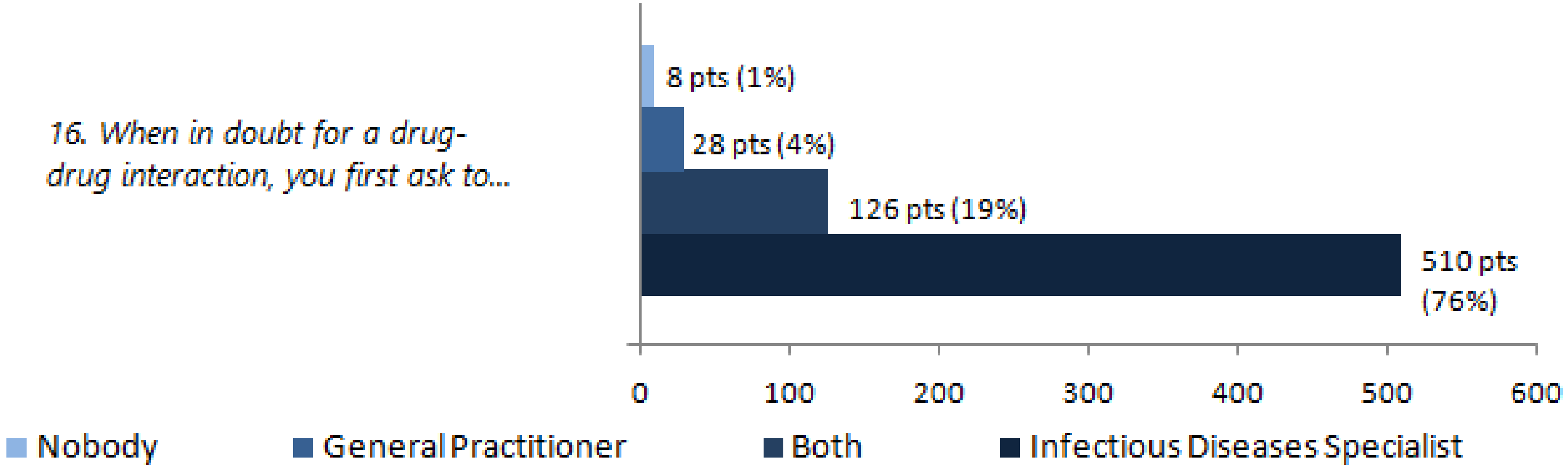
Co-medications and management of DDIs

12° CONGRESSO NAZIONALE
Italian **C**onference on
AIDS and **A**ntiviral **R**esearch
12-16 ottobre 2020

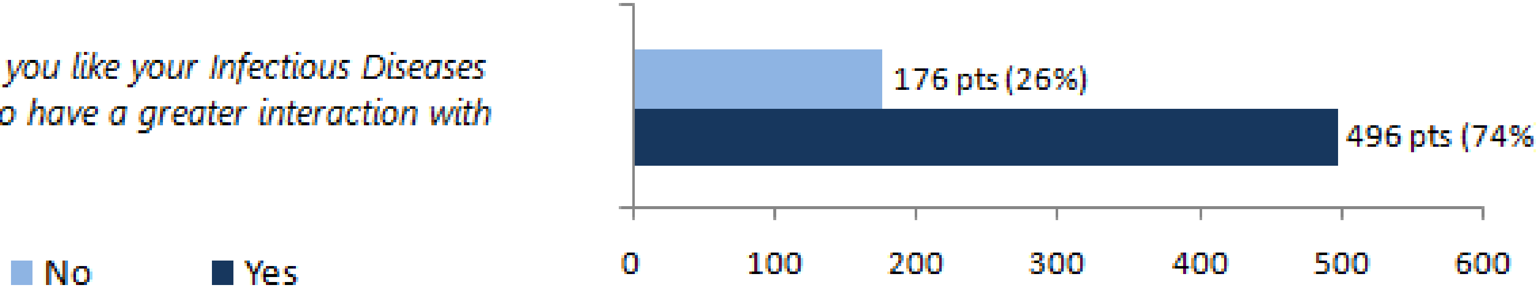
15. Do you take any comedications for other chronic diseases (diabetes, dyslipidemia, hypertension etc)



16. When in doubt for a drug-drug interaction, you first ask to…



17. Would you like your Infectious Diseases Specialist to have a greater interaction with your GP?



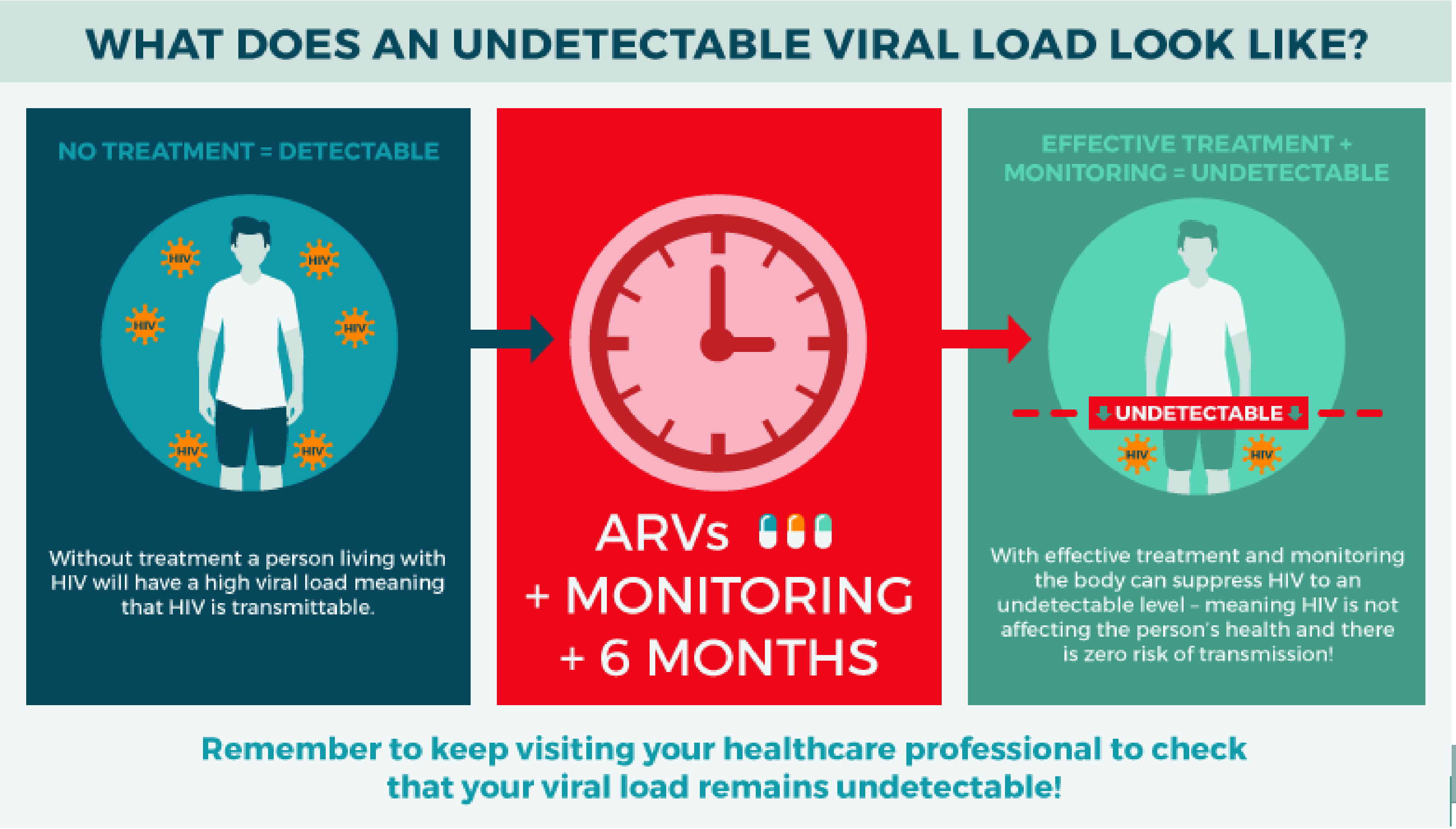
- 39% of the patients received other drugs and
- 76% preferentially consulted the ID Specialist for potential DDIs.
- 74% subjects reported the need of a better communication between the GP and the Infectious Diseases Specialist.

Conclusions

- During the last decade, Italian ID Specialists have taken on almost completely the responsibility of the management of PLWHIV, along with caring for patients suffering from Infectious Diseases other than HIV.
- Fear of social exclusion and privacy violation, along with poor trust in GPs familiarity with cART management, appeared as crucial points that could impair the relationship between GPs and PLWHIV. Greater expenditure should be dedicated in training GPs to make them aware of issues related to HIV infection and other sexually transmitted infections
- The U=U status does not improve the HIV communication status in many patient
- Great help could come from GPs as partners for ID Specialists, but still great work is left to do by these providers to form a solid relationship with their patients.

U=U

UNDETECTABLE = UNTRASMITTABLE



WHAT DOES AN UNDETECTABLE VIRAL LOAD LOOK LIKE?

NO TREATMENT = DETECTABLE

Without treatment a person living with HIV will have a high viral load meaning that HIV is transmittable.

ARVs + MONITORING + 6 MONTHS

EFFECTIVE TREATMENT + MONITORING = UNDETECTABLE

With effective treatment and monitoring the body can suppress HIV to an undetectable level – meaning HIV is not affecting the person's health and there is zero risk of transmission!

Remember to keep visiting your healthcare professional to check that your viral load remains undetectable!

U=U CAMBIA LA VITA?

COSA NE PENSANO I MEDICI

Sergio Lo Caputo
Clinica Malattie Infettive
A.O.U. Ospedali Riuniti Foggia

XXXII Congresso Nazionale

Presidente Prof. Gioacchino Angarano

2 Dicembre 2019 - Sala Murat - Bari

Obiettivo

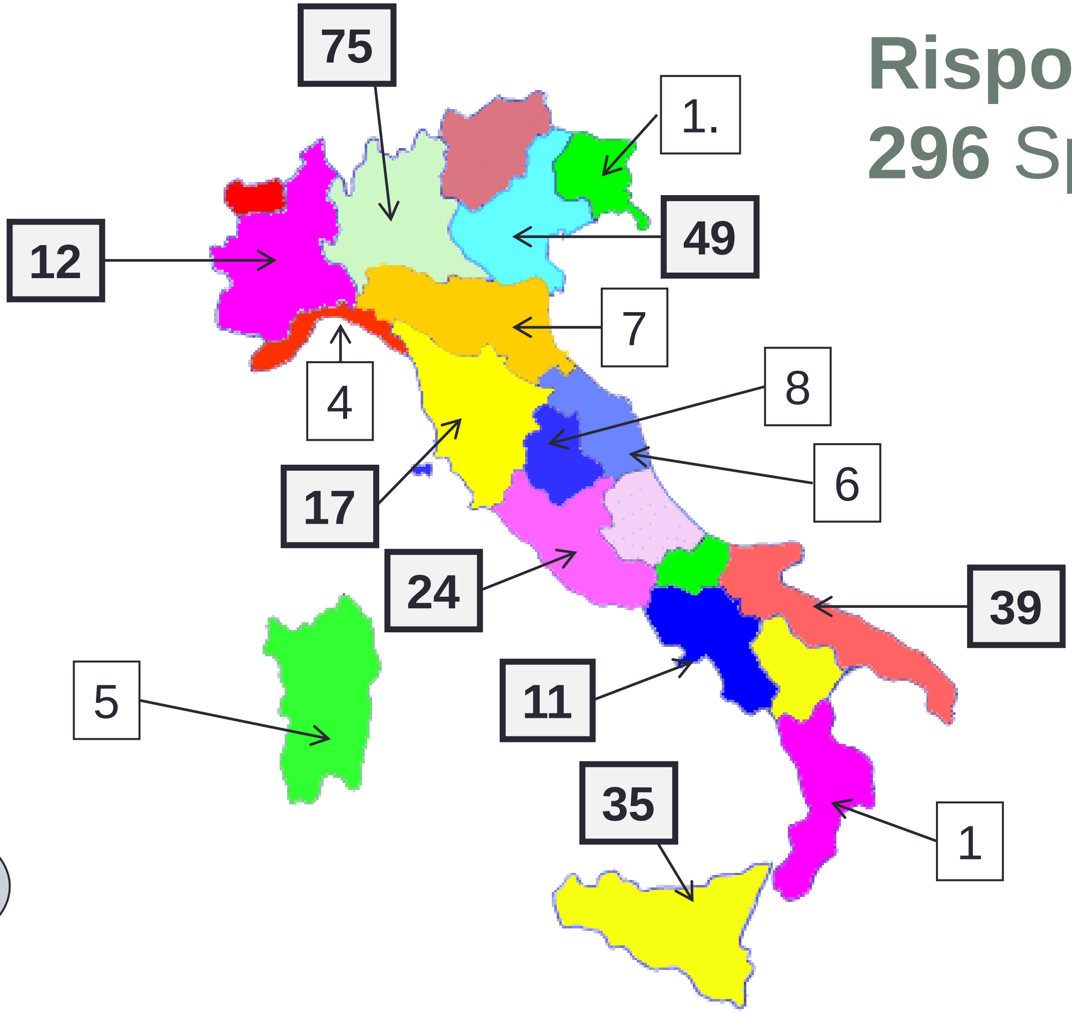
Valutare la percezione degli specialisti in Malattie Infettive circa il rischio di trasmissione di HIV nei pazienti con controllo virologico efficace e le raccomandazioni conseguenti in diversi contesti clinici.

Metodo

- Questionario anonimo rivolto agli specialisti di malattie infettive in attività presso gli ospedali in Italia
- Il questionario comprende **6 domande** che includono **6 scenari clinici** riferiti al potenziale rischio trasmissivo di HIV in pazienti in terapia e virologicamente soppressi
- Le risposte erano predefinite (multi-choice)
- Una sola risposta era valida

Risposte:

296 Specialisti in Mal. Infettive



Stima del numero di Specialisti in MI in attività in Italia: 1000-1200?

D. Ripamonti et al. XVIII SIMIT 2019

U=U message

Solo il 50% degli specialisti ritiene che il rischio trasmissivo sia ZERO

Per **il concepimento,** il 22,3% contempla come opzione la PrEP nel partner HIV negativo e il 7% non è certo dell’assenza di rischio.

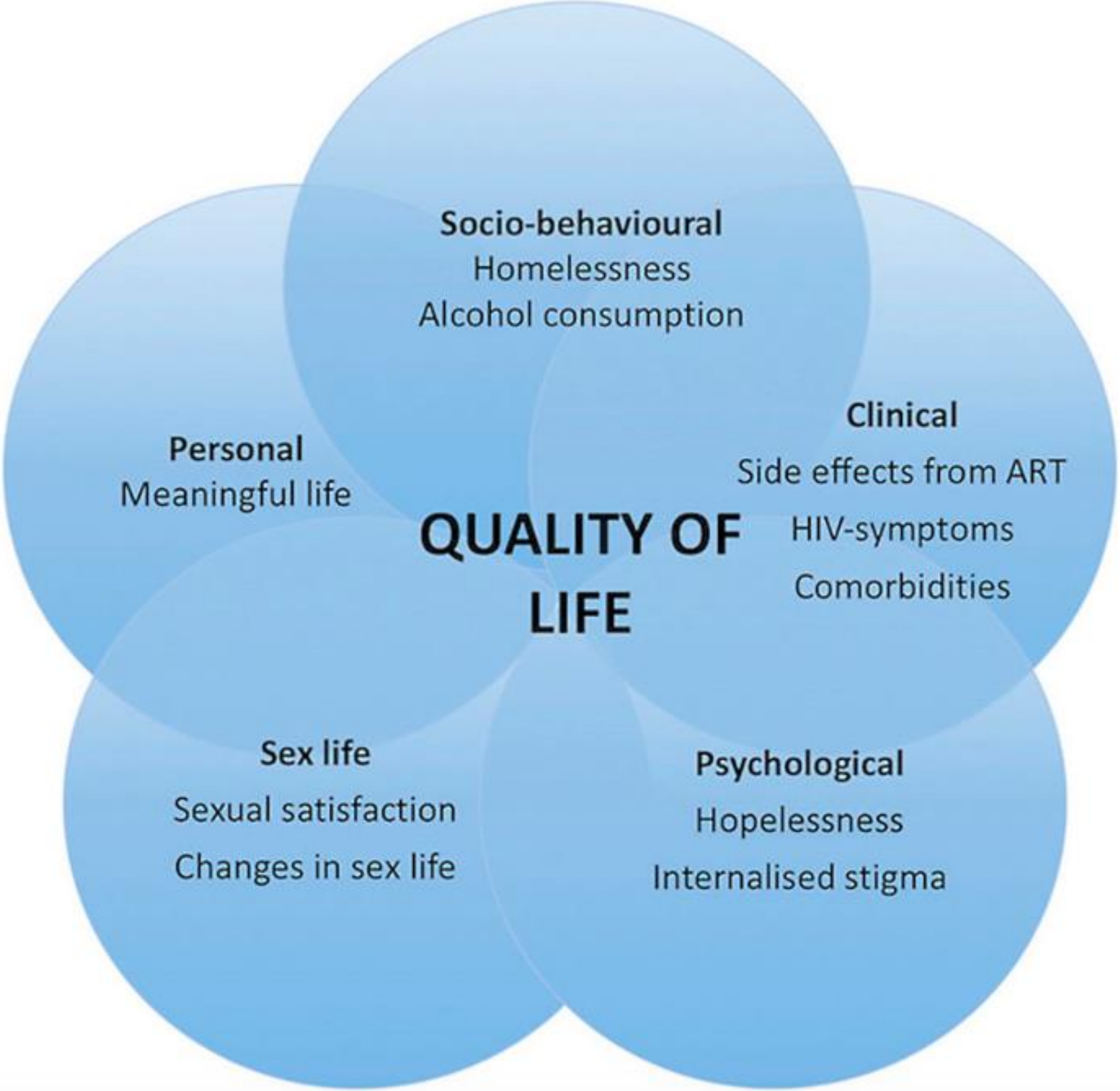
Per **la esposizione sessuale**, il blip viremico < 200 c/ml, seppur dopo 5 anni di soppressione virologica, induce alla raccomandazione di PEP.

Il **pattern di aderenza alla terapia e la storia di controllo virologico** del paziente condizionano l’interpretazione del test virologico e la raccomandazione conseguente.

Paper submitted

PROs

- ✓ Health-related quality of life (HRQOL)
- ✓ Symptoms
- ✓ Function
- ✓ Satisfaction with care or symptoms
- ✓ Adherence to prescribed medications or other therapy
- ✓ Perceived value of treatment



QUALITY OF LIFE

Socio-behavioural
Homelessness
Alcohol consumption

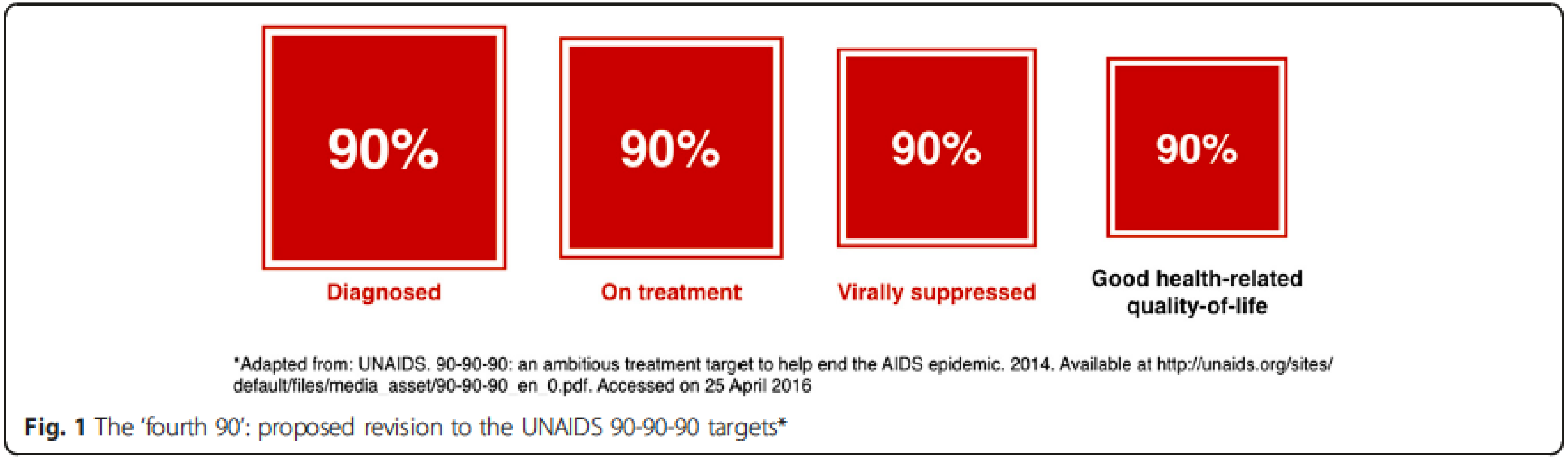
Clinical
Side effects from ART
HIV-symptoms
Comorbidities

Psychological
Hopelessness
Internalised stigma

Sex life
Sexual satisfaction
Changes in sex life

Personal
Meaningful life

Beyond viral suppression of HIV the new quality of life frontier



*Adapted from: UNAIDS. 90-90-90: an ambitious treatment target to help end the AIDS epidemic. 2014. Available at http://unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf. Accessed on 25 April 2016

Fig. 1 The 'fourth 90': proposed revision to the UNAIDS 90-90-90 targets*

Health systems everywhere need to become more integrated and more people-centered to successfully meet the needs of virally suppressed PLHIV. By doing so, these systems can better meet the needs of all of their constituents – regardless of HIV status – in an era when many populations worldwide are living much longer with multiple comorbidities

Lazarus *et al. BMC Medicine* (2016) 14:94