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Multicenter, prospective exploratory evaluation of quality of life in people living with HIV

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ABSTRACT:

— ***Objective:*** In the last few years, quality of life (QOL) in people living with HIV (PLWH) gained more attention. Moreover, reaching a good QOL was set up as a main goal for PLWH. Data on QOL of PLWH in Southern Italy are very scarce, as well as data on factors correlated with QOL, we aimed at evaluating QOL in PLWH in our region. We conducted a multicentre, cross-sectional study in a cohort of PLWH in the Calabria region (Southern Italy). This survey-based study was conducted in 7 centers of infectious and tropical disease in Southern Italy.

— ***Patients and methods:*** We interviewed 309 patients, evaluating QOL through WHOQOLHIV-BREF questionnaire. Clinical data were retrieved from medical records.

— ***Results:*** Overall, only 56% of participants reported a good QOL. At the multivariable model, adjusted for a good health self-reported status, statistically significant associations between good QOL and being employed and doing regular physical exercise were found ($p<0.001$ and $p=0.01$, respectively). By contrast, a nega-tive impact of psychiatric disorders, history of fractures, and black ethnicity on good self-reported health status was confirmed ($p=0.04$, <0.001 and $p=0.007$, respectively).

— ***Conclusions:*** This is the first study evaluating QOL in PLWH in Southern Italy. Routinely identifying factors negative-ly associated with good QOL may help clinicians in providing a better quality of care.

— ***Keywords:*** QOL, Heath-related QOL, PLWH, HIV.

— ***Abbreviations:*** cART: Combination antiretroviral treatment; PLWH: people living with HIV; QOL: quality of life; WHOQOLHIV-BREF: World Health Organization Quality of Life for HIV brief version; VL: viral load; ITDUs: Infectious and Tropical Diseases Units; MSM: Men who have Sex with Men; IVDU: Intravenous Drug Use; COPD: Chronic Obstructive Pulmonary Disease.

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INTRODUCTION

Combination antiretroviral treatment (cART) revolutionised epidemiological and clinical characteristics of people living with HIV (PLWH)[1]. CART, started as soon as possible, allows a good immune-virological control, and lets PLWH reach life expectancy comparable with the general population one[1-3].

For this reason, in addition to clinical and virological routine assessments, the evaluation of quality of life (QOL) became a very important outcome[4,5]. Therefore, reaching a good QOL in more than 90% patients who have an undetectable HIV viremia has been set up as a main goal for PLWH[6].

Different studies evaluated QOL in PLWH, and different tools have been implemented for this purpose over time[7]. One of these is the WHOQOLHIV-BREF questionnaire, approved and validated by the World Health Organization (WHO)[7-9]. It is a multiple choice questionnaire based on the evaluation of six domains (physical, psychological, social, environmental, religious and level of autonomy), and specific HIV-related factors. High scores in each domain indicate a better quality of life. Description and meaning of the six domains are reported elsewhere[7,10].

To date, the most important factors which have been associated with QOL are: prescription and type of cART, CD4+ T-cell count, AIDS events, hepatitis coinfections, gender, and age[4,11]. Data regarding QOL of PLWH are quite scarce in the South of Italy. So, our primary objective was to evaluate for the first time in a multicenter and prospective study the general QOL in PLWH in the Calabria region and its possible predictors. As secondary objective, we aimed at evaluating whether the fourth UNAIDS 90 has been reached or not in PLWH with undetectable HIV viral load (VL) in our population[12].

PATIENTS AND METHODS

This study was coordinated by the Infectious and Tropical Diseases Unit of "Mater Domini" teaching hospital in Catanzaro (Italy) and was conducted in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice[13,14]. The local Ethical Committee (Calabria Region) approved the study protocol on 19th July 2018. Written informed consent was obtained from all subjects enrolled.

Participation to the survey was proposed to all PLWH, older than 18 years, attending the Infectious and Tropical Diseases Units (ITDUs) in Calabria (cities of Catanzaro – two centers -, Cosenza, Crotone, Lamezia Terme, Reggio Calabria and Vibo Valentia) for their routine clinical checks from October 1st, 2018 to January 31st, 2019. Patients responded to the questionnaire only once. Patients who were minor, or affected by conditions, which could have impaired understanding and judgments were excluded.

WHOQOLHIV-BREF was used to evaluate QOL. This is a 31-multiple choice questionnaire, which evaluated six aspects having an impact on QOL: physical, psychological, level of independence, social, environmental, and spiritual. The scores for the six domains and in general for quality of life were calculated based on the WHOQOL-HIV BREF score assignment and coding manual[7-9]. Based on the individual assessment of QOL, the participants were divided into two groups: those with a good and poor QOL, respectively. Good QOL was defined for those who reported "good" or "very good" answer in the questionnaire, while poor QOL was defined for those who reported the answer "neither poor nor good", "poor", or "very poor". The same was done for self-reported health status.

Questionnaires with missing answers or not adequately filled out were excluded from the analysis. All narrative comments reported by patients in the questionnaires were recorded.

Data regarding demographics, clinical history, HIV-related characteristics, comorbidities, co-medications (polypharmacy was considered as present if patient were taken 5 or more drugs[15]), risk factors and social life, blood test results were collected. HIV undetectability was defined as HIV RNA lower than 50 copies/ml. We defined multimorbidity as presence of 2 or more chronic non-infectious conditions in the same patient[16]. Social-demographical conditions and habits (i.e., whether patients were employed or not, relational life, physical exercise, smoking, drinking, use of recreational drugs etc.) were investigated through a questionnaire recording social habits that was added to the main questionnaire.

Each participant has been given a unique study identification number and data regarding each patient were transferred onto an Excel® database.

Continuous variables were compared by Student's *t*-test for normally distributed variables and by the Mann-Whitney U test for non-normally distributed variables. Categorical variables were evaluated using the χ^2 or two-tailed Fisher's exact test. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to evaluate the strength of any association that emerged. Values are expressed as median (range) for continuous variables, or as percentages of the group from which they were derived (categorical variables). Two-tailed tests were used to determine statistical significance; a *p*-value of <0.05 was considered to be significant[17]. Clinical and epidemiological characteristics of our cohort, as well as variables related to QOL and with self-reported health status, were presented according to age: PLWH >50 years of age *vs.* PLWH ≤50 years of age; this cut-off was chosen accordingly to the current definition of elderly age for PLWH[18].

Multivariate analysis was used to explore any possible correlation with the main outcome (QOL) and with self-reported health status. For this analysis, we used logistic regression and incorporated variables found to be significant in univariate testing. Possible co-linearity among variables was taken into account.

All statistical analyses were performed using the Intercooled Stata program, version 11, for Windows (Stata Corporation, College Station, TX, USA).

RESULTS

Patient Characteristics

Between October 1st, 2018 and January 31st, 2019, 378 consecutive subjects were offered to participate to the study. Sixty-six subjects refused to participate to the study. Three questionnaires were excluded for incomplete data and/or answers. So, 309 completed questionnaires were evaluable.

Main socio-demographic characteristics and scores reported by participants at QOL questionnaire are described according to age in Table 1.

Patients aged >50 years were more likely to be from Italy than from other countries when compared to those who were younger (96.9% *vs*.77.7%, $p<0.001$); by contrast, a significantly higher rate of patients aged ≤50 years were employed (63.5% *vs*. 41%; $p=0.0001$) and/or alcohol abusers (43.2% *vs*. 31%; $p=0.03$). Furthermore, younger participants were more likely to report good QOL (64.9% *vs*.48.4%, $p=0.004$) and good self-reported health status (70.9% *vs*. 55.9%, $p=0.006$) compared to the older ones. Out of the six analysed domains, statistically significant differences between the two groups (<50 years *vs*.>50 years of age) were found for the physical and spiritual domains. In particular, younger PLWH performed better in the physical domain (mean: 14.7, SD 3.8 *vs*. 14, SD 3.6, $p=0.04$), while elderly ones did better in the spiritual domain (14.1±3.9 *vs*. 15.2±3.7, $p=0.01$).

Table 2 describes HIV-related characteristics and comorbidities among PLWH included in our cohort, according to age. Unprotected sex in men who have sex with men (MSM) was more represented as risk factors for HIV acquisition in the younger patients (23% *vs*.13%, $p=0.02$), while unprotected heterosexual intercourses, IVDU, and blood transfusion were more frequent in the group of older PLWH. Furthermore, older PLWH were more likely to be on cART compared to younger participants (100% *vs*.97.3%, $p=0.04$). As expected, comorbidities, including hepatitis coinfections, were more frequent in the elderly group.

Predictors of Good QOL

At univariate analysis (Table 3), stable employment was significantly associated with good QOL ($p=0.04$), as well as good self-reported health status ($p<0.0001$). Also, age>50 years($p=0.003$), IVDU ($p=0.004$), history of previous fractures ($p=0.0001$) and psychiatric disorders ($p=0.0006$) appeared to have a negative impact on QOL. At multivariable analysis, adjusting for a good self-reported health status for possible co-linearity with good QOL, the following variables resulted being independent predictors of worse QOL: IVDU (OR=0.36, 95%CI 0.16-0.80, $p=0.013$), previous fractures (OR=0.33, 95%CI 0.18-0.61, $p<0.001$), psychiatric disorders (OR=0.53, 95%CI 0.2-0.97, $p=0.043$), and African ethnicity (OR=0.323, 95%CI 0.08-0.66, $p=0.007$). Collinearity was not demonstrated among variables.

Predictors of Good Self-Reported Health Status

Univariate analysis showed that the following factors were positively associated with a good self-reported health status (Table 4): high level of education

Table 1. Main socio-demographic characteristics and scores reported by participants at QOL questionnaire.

Characteristic	Overall N=309 (%)	>50 years N=161(%)	≤50 years N=148 (%)	*p*-value
Gender (Male)	216 (69.9)	117 (72.7)	99 (66.9)	0.27
Country of origin (Italy)	271 (87.7)	156 (96.9)	115 (77.7)	<0.001
Level of education (High)	54 (17.5)	22 (14)	32 (22)	0.07
Employed (Yes)	160 (51.8)	66 (41)	94 (64)	0.0001
Stable partnership (Yes)	125 (40.5)	70 (43)	55 (37)	0.26
Alcohol abuse (Yes)	114 (36.9)	50 (31)	64 (43)	0.03
Active smoking (Yes)	157 (50.8)	90 (56)	67 (45)	0.06
Regular physical exercise (Yes)	100 (32.4)	47 (29)	53 (36)	0.21
Religious (Yes)	229 (74.1)	117 (73)	112 (76)	0.55
High QOL (4-5)	174 (53.6)	78 (48)	96 (65)	0.004
Good self-reported health status	195 (63.1)	90 (56)	105 (71)	0.006
Scores for 6 domains		(Mean ± SD)		*p*-value
Physical	14.35 ± 3.38	13.98 ± 3.62	14.76 ± 3.05	0.04
Psychological	18.84 ± 4.42	18.66 ± 4.57	19.04 ± 4.25	0.45
Level of independence	16.08 ± 3.73	16.07 ± 3.96	16.08 ± 3.47	0.97
Social relationship	14.61 ± 3.92	14.34 ± 3.97	14.91 ± 3.86	0.20
Environment	29.01 ± 6.05	29.26 ± 6.18	28.72 ± 5.91	0.43
Spirituality	14.68 ± 3.88	15.21 ± 3.79	14.11 ± 3.91	0.01

Table 2. HIV-related characteristics and comorbidities.

Characteristic	Overall N=309 (%)	>50 years N=161(%)	≤50 years N=148 (%)	*p*-value	
Risk factors*	MSM	55 (17.8)	21 (13)	34 (23)	0.02
	Heterosexual	257 (83.2)	142 (88)	115 (78)	0.02
	IVDU	78 (25.2)	50 (31)	28 (19)	0.01
	Blood products	10 (3.2)	9 (6)	1 (0.6)	0.01
	Vertical	4 (1.2)	0 (0)	4 (2.7)	0.03
Hepatitis co-infections	Hep B	27 (8.7)	18 (11)	9 (6)	0.11
	Hep C	86 (27.8)	61 (38)	25 (17)	<0.001
	Hep B-C coinfection	9 (2.9)	8 (5)	1 (0.1)	0.02
	Treated HCV	72 (23.3)	51 (31)	21 (15)	<0.001
Late presentation (Yes)		190 (61.5)	103 (67)	87 (60)	0.19
Past AIDS events (Yes)		102 (33)	60 (37)	42 (28)	0.10
Undetectable HIV viral load (Yes)		277 (89.6)	149 (93)	128 (86)	0.08
cART (Yes)	Any therapeutic regimen	305 (98.7)	161 (100)	144 (97)	0.036
	Backbone and PI	62 (20.3)	28 (17)	34 (23)	0.22
	Backbone and NNRTI	56 (18.1)	38 (24)	18 (12)	0.009
	Backbone and INSTI	133 (43)	68 (42)	65 (44)	0.77
	Other	50 (18.6)	25 (16)	25 (17)	0.75
Non infectious comor-bidities (Yes)*	CKD	29 (9.4)	26 (16)	3 (2)	<0.001
	Cirrhosis	8 (2.6)	7 (4)	1 (0,7)	0.04
	COPD	26 (8.4)	18 (11)	8 (5)	0.07
	Diabetes	25 (8.1)	17 (11)	8 (5)	0.09
	Dyslipidaemia	97 (31.4)	61 (38)	36 (24)	0.01
	Ischaemic heart disease	23 (7.4)	16 (9.9)	7 (4.7)	0.08
	Hypertension	92 (29.8)	69 (43)	23 (16)	<0.001
	Malignancies	9 (2.9)	8 (5)	1 (0,7)	0.03
	Obesity	32 (10.3)	17 (11)	15 (10)	0.9
	Osteoporosis	35 (11.3)	31 (19)	4 (3)	<0.001
	Past fractures	78 (25.2)	53 (32.9)	25 (16.9)	0.001
	Neurologic disor-ders	37 (11.9)	26 (16)	11 (7)	0.02
	Psychiatric disor-ders	80 (25.9)	51 (32)	29 (20)	0.02
	Liver Steatosis	67 (21.7)	37 (23)	30 (20)	0.56
Quantitative characteristic			**(Mean ± SD)**		***p*-value**
Years living with HIV	14 ± 10	19 ± 9	9 ± 8	<0.001	
CD4+ cell count at Nadir	294 ± 239	296 ± 246	292 ± 233	0.87	
Current CD4+ cell count	679 ± 362	702 ± 357	655 ± 367	0.26	
Current CD4/CD8 ratio	0.82 ± 0.48	0.84 ± 0.48	0.81 ± 0.49	0.65	
BMI	24.61 ± 4.35	24.67 ± 4.25	24.54 ± 4.47	0.79	
eGFR	96.50 ± 33.99	83.22 ±24.96	110.94 ± 36.61	<0.001	

*Each patient may present more than one.

(p=0.03), stable employment (p=0.01), regular physical exercise (p=0.003) and good QOL (p<0.0001). Factors which were found to be negatively associated with good self-reported health status were: age>50 years (p=0.006), multimorbidity (p=0.04), cirrhosis (p=0.02), chronic obstructive pulmonary disease (COPD) (p=0.007), hypertension (p=0.02), and psychiatric disorders (p=0.0001). At multivariable model, adjusting for a good QOL for possible co-linearity with good self-reported health status, statistically significant associations were confirmed for: being stably employed and doing regular physical exercise (p<0.001 and p=0.01, respectively), as well as the negative impact of psychiatric disorders on good self-reported health status (p=0.04). A statistically significant negative association was also found between black ethnicity and good QOL (p=0.007). Collinearity was not demonstrated among variables.

Narrative Results and "the Third and the Fourth 90's"

As for the social impact of HIV infection, 243/309 (78.6%) of the interviewed PLWH disclosed to be very worried that other people could blame them for being

Table 3. Factors associated with a good QOL.

Qualitative characteristic		QOL 4-5 N=174 (%)	QOL 1-3 N=135 (%)	Odds ratio (IC 95%)	*p*-value
Gender (male)		121 (70)	95 (70)	0.96 (0.57-1.61)	0.87
Country of origin	Italy	153 (88)	118 (87)	1.05 (0.5-2.2)	0.89
	Africa	7 (4.1)	13 (9.6)	0.39 (0.12-1.09)	0.04
	Other Coun-tries	14 (8.1)	4 (2.9)	2.86 (0.86-12.20)	0.05
Risk factors	MSM	37 (21)	18 (13)	1.76 (0.92-3.45)	0.07
	Heterosexual	139 (80)	118 (87)	0.57 (0.29-1.11)	0.08
	IVDU	33 (19)	45 (33)	0.47 (0.27-0.81)	0.004
	Blood prod-ucts	6 (3)	4 (3)	1.17 (0.27-5.75)	0.81
	Other	11 (6)	3 (2)	2.97 (0.76-16.86)	0.09
High level of education (Gradu-ated)		34 (20)	20 (15)	1.39 (0.73-2.7)	0.28
Employed (Yes)		99 (57)	61 (45)	1.6 (0.99-2.58)	0.04
Stable partnership (Yes)		76 (44)	49 (36)	1.37 (0.84-2.2)	0.19
Alcohol abuse (Yes)		61 (35)	53 (39)	0.83 (0.51-1.37)	0.45
Active smoking (Yes)		85 (49)	72 (53)	0.84 (0.52-1.34)	0.43
Regular physical exercise (Yes)		60 (34)	40 (30)	1.25 (0.75-2.1)	0.37
Religious (Yes)		131 (75)	98 (73)	1.15 0.67-1.98)	0.59
Late presentation (Yes)		106 (63)	84 (65)	0.93 (0.56-1.55)	0.79
Being in cART (Yes)		173 (99)	132 (98)	3.93 (0.31-207.55)	0.20
Polypharmacy (Yes)		85 (49)	70 (52)	0.89 (0.55-1.43)	0.60
Multimorbidity (Yes)		93 (53)	82 (61)	0.74 (0.46-1.20)	0.20
Comorbidities (Yes)	CKD	18 (9)	11 (10)	0.95 (0.41-2.32)	0.90
	Cirrhosis	2 (1)	6 (5)	0.19 (0.18-1.07)	0.02
	Diabetes	15 (8)	10 (9)	0.87 (0.35-2.24)	0.74
	Dyslipidaemia	61 (31)	36 (32)	0.99 (0.58-1.68)	0.96
	Ischaemic heart disease	12 (6)	11 (10)	0.61 (0.23-1.59)	0.25
	Hypertension	49 (25)	43 (38)	0.55 (0.33-0.94)	0.02
	Malignancies	6 (3)	3 (3)	1.17 (0.24-7.4)	0.82
	Obesity	20 (10)	12 (10)	0.97 (0.43-2.28)	0.94
	Osteoporosis	19 (10)	16 (14)	0.66 (0.3-1.44)	0.25
	Past fractures	45 (23.1)	33 (28.9)	0.73 (0.42-1.29)	0.25
	Neurologic disorders	23 (12)	14 (12)	0.96 (0.45-2.1)	0.9
	Psychiatric disorders	36 (18)	44 (39)	0.36 (0.2-0.63)	0.0001
	Steatosis	44 (23)	23 (20)	1.15 (0.63-2.14)	0.62
Good QOL		140 (72)	34 (30)	5.98 (3.49-10.29)	<0.001

Quantitative characteristic	QOL 4-5 (Mean ±SD)	QOL 1-3 (Mean ±SD)	*p*-value
Year living with HIV	14 ± 10	15 ± 10	0.35
CD4/CD8 count	0.84 ± 0.47	0.80 ± 0.51	0.42

HIV positive, and that HIV infection was the only thing that was wrong with them. Moreover, 104 out of 309 (33.7%) participants declared to consider themselves as ill just for the presence of HIV infection, even if they were asymptomatic, and had a well-controlled HIV infection.

Regarding the evaluation of the third and fourth 90's[6] in our region, proportion of PLWH who had undetectable HIV VL was 89.6% (277/309). Among these, only 149/277 (54%) reported a good QOL.

DISCUSSION

Our data are the first about QOL amongst PLWH in the Calabria region (Southern Italy).

The most important findings of our study are that regular physical exercise and having employment displayed positive associations with QOL. Therefore, efforts in promotion of regular physical exercise should put in place especially for those who are unemployed. Importantly, African people reported worse QOL. Afri-

Table 4. Factors associated with a good self-reported health status.

Qualitative characteristic		Health 4-5 N=195 (%)	Health 1-3 N=114 (%)	Odds ratio (IC 95%)	*p*-value
Age		90 (46)	71 (62)	0.51 (0.31-.085)	0.006
Gender (male)		137 (70)	79 (69)	1.04 (0.61-1.78)	0.86
Country of origin	Italy	171 (87)	100 (88)	0.99 (0.45-2.1)	0.99
	Africa	13 (6.7)	7 (6.1)	1.09 (0.39-3.33)	0.85
	Other Countries	11 (5.6)	7 (6.1)	0.91 (0.31-2.86)	0.85
Risk factors	MSM	42 (22)	13 (11)	2.13 (1.06-4.55)	0.02
	Heterosexual	155 (79)	102 (89)	0.46 (0.21-0.94	0.02
	IVDU	47 (24)	31 (27)	0.85 (0.49-1.5)	0.55
	Blood products	5 (3)	5 (4)	0.57 (0.13-2.56)	0.39
	Other	5 (2.6)	5 (4.4)	0.57 (0.12-2.55)	0.38
High level of education (graduated)	41 (21)	13 (11)	2.07 (1.02-.42)	0.03	
Employed (Yes)	119 (61)	41 (36)	2.8 (1.78-4.6)	0.01	
Stable partnership (Yes)	80 (41)	45 (39)	1.07 (0.65-1.76)	0.79	
Alcohol abuse (Yes)	70 (36)	44 (39)	0.89 (0.54-1.48)	0.64	
Active smoking (Yes)	102 (52)	55 (48)	1.17 (0.72-1.92)	0.49	
Regular physical exercise (Yes)	75 (38)	25 (22)	2.23 (1.28-3.9)	0.0027	
Religious (Yes)	140 (72)	89 (78)	0.72 (0.38-1.27)	0.22	
Late presentation (Yes)	114 (61)	76 (68)	0.72 (0.42-1.21)	0.19	
Being in cART (Yes)	194 (99)	111 (97)	5.2 (0.41-276)	0.11	
Polypharmacy (Yes)	90 (46)	65 (57)	0.65 (0.39-1.05)	0.07	
Multimorbidity (Yes)	102 (52)	73 (64)	0.62 (0.37-1.02)	0.04	
Comorbidities (Yes)	CKD	18 (9)	11 (10)	0.95 (0.41-2.32)	0.90
	Cirrhosis	2 (1)	6 (5)	0.19 (0.18-1.07)	0.02
	COPD	10 (5)	16 (14)	0.33 (0.13-0.81)	0.007
	Diabetes	15 (8)	10 (9)	0.87 (0.35-2.24)	0.74
	Dyslipidaemia	61 (31)	36 (32)	0.99 (0.58-1.68)	0.96
	Ischaemic heart disease	12 (6)	11 (10)	0.61 (0.23-1.59)	0.25
	Hypertension	49 (25)	43 (38)	0.55 (0.33-0.94)	0.02
	Malignancies	6 (3)	3 (3)	1.17 (0.24-7.4)	0.82
	Obesity	20 (10)	12 (10)	0.97 (0.43-2.28)	0.94
	Osteoporosis	19 (10)	16 (14)	0.66 (0.3-1.44)	0.25
	Past fractures	45 (23.1))	33 (28.9)	0.73 (0.42-1.29)	0.25
	Neurologic disor-ders	23 (12)	14 (12)	0.96 (0.45-2.1)	0.9
	Psychiatric disor-ders	36 (18)	44 (39)	0.36 (0.2-0.63)	0.0001
	Steatosis	44 (23)	23 (20)	1.15 (0.63-2.14)	0.62
Good QOL		140 (72)	34 (30)	5.98 (3.49-10.29)	<0.001

Quantitative characteristic	QOL 4-5 (Mean ±SD)	QOL 1-3 (Mean ±SD)	*p*-value
Year living with HIV	14.6 ± 10.2	14.4 ± 10.24	0.85
CD4/CD8 count	0.86 ± 0.49	0.77 ± 0.48	0.10

can people in our cohort were young (mean age 32 years) and arrived in Italy in the three years before. So, this result could be explained by psychosocial distress and indicates that this population requires much attention[19].

According to literature, elderly PLWH have a better QOL, when compared to younger ones[20]. By contrast, in our study, elderly people reported worse scores of QOL compared to younger ones. This could be due to the lack of a systematic approach to over 50 years old PLWH in our region, to the impact of polypharmacy, or to a long HIV disease history. In particular polypharmacy has been shown to have an important impact in the elderly, for both drug interactions and anticholinergic effects[21].

While older people displayed both worse QOL and worse self-reported health status, comorbidities did appear to influence QOL and self-reported health status differently. In fact, for QOL, only osteoporosis and neurologic disorders appeared to be negatively associat-

ed with it, while for self-reported health status, factors associated were: cirrhosis, COPD, hypertension, psychiatric disorders, and multimorbidity. It is difficult to explain this apparent discordance, however it should be considered that the meaning of the two outcomes (QOL and self-reported health status) is different, which in fact may provide complementary information. Importantly, self-reported health status emerged to be significantly associated to QOL, indicating that all factors identified should be taken as important either for QOL or for self-reported health status.

When the results on QOL were related to the clinical outcomes of ART with the aim of providing estimation of the fourth 90[6] in our region, we found that among those who had undetectable HIV VL, only 149/277 (54%) reported good QOL. This result is important because it highlights the urgency of improving QOL, in terms of patient's perspective and not only in terms of virological control. Indeed, not only QOL is an outcome, but also it should be interpreted as a key parameter to improve virological and clinical results of ART through an improvement of inpatient adherence to treatment[22].

For the reasons discussed above, evaluation of the patient related outcomes measures (PROMs), is becoming the most important objective to consider. Likewise, in the last part of our study, we analysed narrative data from patients' comments. From this perspective, we found that HIV by itself was considered to affect perception of health independently from symptoms. It is conceivable that HIV infection is perceived as a cause of stigma and social isolation, which PLWH suffer from as supported by patients' thoughts. Indeed, a "well-controlled" viro-immunological and clinical status may reduce the impact that HIV can exert on the patients' health[24,25]. Notwithstanding these effects, patients may continue to face frustrating challenges such as the effects of infection on social relationships, negative feelings, depression or anxiety, fear for future, psychosocial discomfort[24].

The stigma around this disease is underpinned by a strong cultural base that cannot be disaggregated from individuals and that sets into motion of a cyclical action leading to the segregation of this vulnerable group, and adverse effects on their QOL[24]. More than 75% of our patients were in fact worried about the fact that someone could know that they have the infection and blame them for this. Moreover, more than 40% of these patients felt sick (in absence of any diseases or symptoms). The lack of information and misconceptions may produce a sense of anxiety and influences people's behaviours and relationships[19]. In order to avoid such concerns, patients should receive a more appropriate and individualized counselling during routine clinical visits or as needed.

Our study presents several limitations such as cross-sectional design, the small number of participants, lack of evaluation of cognitive status and of other specific tools in order to better evaluate QOL and patient reported outcomes. Moreover, results of our study need to be updated.

CONCLUSIONS

Notwithstanding these limitations, we feel that our results are important because they strongly suggest that evaluation of QOL should be routinely performed in order to let clinicians aware of critical issues in patients' life, with the final aim of improving quality of care delivery, health perception by patients and PROMs. Multidimensional services could be useful for this purpose, involving not only HIV specialists[24], but also social workers psychologists, specialist nurses and providers in the territory outside hospitals. Chronic care models should be hypothesized for better care of PLWH[26], especially in the COVID-19 era during which the pandemic may constitute a further obstacle for patients to comply with care at healthcare centers[27].

Ethics approval and consent to participate:
This study was conducted in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice. The local Ethical Committee (Calabria Region) approved the study protocol on 19th Ju-ly 2018. Written informed consent was obtained from all subjects enrolled.

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Competing interests:
All the authors declare to have not any conflict of interest in the publication of this work. This study did not receive any funding from any private or public agencies.
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