

Synergist effect of antiretroviral therapy adherence and viral load suppression on quality of life of people with HIV/AIDS

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ABSTRACT

Aims: This study investigated the synergistic and independent effects of adherence to antiretroviral therapy (ART) and viral load on quality of life (QoL) among people with HIV/AIDS. **Methods:** This was a cross-sectional study of 129 patients with HIV/AIDS. The WHOQOL-BREF and the Morisky Medication Adherence Scale were used to measure QoL and adherence respectively. Information on viral load and CD4 cell count was obtained from patients' records and verified by a physician. An additive interaction method was used to estimate the synergistic effect of the linear regression. **Findings:** Patients who were adhering to ART and had an undetectable viral load had significantly higher scores on four domains of QoL – environment, physical health, social relationships and psychological – than those who were non-adherent. Moreover, ART adherence and undetectable viral load had a positive synergistic effect on QoL after controlling for covariate variables. **Conclusion:** Participants were more likely to have a good QoL if they had both undetectable viral loads and good ART adherence.

Key words: Adherence ■ Antiretroviral therapy ■ CD4 cell count ■ HIV/AIDS ■ Quality of life ■ Viral load

HIV and AIDS are regarded as global public health threats and pose a considerable challenge to healthcare systems (UNAIDS, 2022); AIDS has gone from being a fatal disease to a chronic condition (Zhou et al, 2020). There are approximately 38.4 million individuals diagnosed with HIV, with 1.5 million new infections occurring in 2021 (UNAIDS, 2022).

In Indonesia, the number of individuals with HIV declined from 640 000 in 2019 (UNAIDS, 2019) to 540 000 in 2022 (UNAIDS, 2022). However, the mortality rate is approximately 4.44% in individuals diagnosed with HIV/AIDS (UNAIDS, 2019). The high prevalence of early mortality in patients with HIV/AIDS means the factors that determine quality of life (QoL) related to disease burden and therefore health need to be better identified (Castro et al, 2019).

QoL assessment has emerged as a critical element of epidemiological and clinical trials related to HIV/AIDS in recent years. Researchers increasingly recognise the importance of QoL on wellbeing, providing good functional capacity in physical health, social relations and psychological QoL domains (Ghiasvand et al, 2019; Vu et al, 2020). Knowing the determinants of QoL and their modifiable factors can be advantageous when drawing up strategies to improve QoL and, ultimately, life satisfaction in HIV/AIDS patients (Ghiasvand et al, 2020).

Notably little research has been undertaken on the determinant factors of QoL in Indonesians diagnosed with HIV/AIDS and the studies that have been done did not investigate adherence to medical treatment and biological markers as determinant factors (Astoro et al, 2007; Lindayani et al, 2018a; Handayani et al, 2019). In addition, evaluations of harmful determinant factors, including non-adherence to therapeutic regimens and poor levels of biological markers that could affect QoL, could be used to help support the personalised healthcare that can gradually improve QoL (Degroote et al, 2014; Castro et al, 2019).

Adherence to antiretroviral therapy (ART) regimens for HIV/AIDS reduces viral proliferation and limits development of HIV infection into AIDS to improve QoL (Dinsa Ayeno et al, 2020). Previous studies have indicated that adherence to ART impacts QoL (Huang et al, 2013; Degroote et al, 2014; Liping et al, 2015; Reis et al, 2020). The World Health

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Organization (WHO) has reported that ART adherence has improved QoL in European region countries (Popping et al, 2021).

However, ART adherence and its impact on QoL in developing countries are still concerns (Oguntibeju, 2012; Dinsa Ayeno et al, 2020). The Indonesian Ministry of Health (2018) has reported that ART is implemented and fully subsidised at primary healthcare centres but only 41% of those diagnosed with HIV/AIDS have received the therapy.

UNAIDS (2019) has reported that ART is implemented and fully subsidised at primary healthcare centres, but only 16.95% of those diagnosed with HIV/AIDS have received it.

Only one cross-sectional research study has suggested that having a good level of adherence to ART was independently significantly associated with QoL in Indonesians with HIV/AIDS; QoL was 11.06-fold greater than in those who were non-adherent. However, QoL was assessed in only a small sample (Suswani et al, 2018). Adherence to ART may have positive effects on all areas of QoL, including in the environment, physical health, social relations and psychological domains, in individuals with HIV/AIDS in Indonesia. Therefore, these associations require clarification.

Scientific data indicate that viral load (VL) and CD4 cell count are biological markers that are related to QoL in people with HIV/AIDS (Rzeszutek and Gruszczynska, 2018). Additionally, undetectable VL was not significantly correlated with total QoL compared with detectable VL, but was correlated with a 1.32-fold higher score in the psychological health QoL domain compared with detectable VL. Moreover, undetectable VL was correlated with the environmental, physical health and social relationships domains of QoL (Cho et al, 2020).

Low scores in physical health, psychological, social relationships and environmental QoL domains are significantly associated with detectable VL (Reis et al, 2020). However, CD4 cell count is not correlated with QoL (Cooper et al, 2017; Reis et al, 2020). Moreover, no study has examined the relationship between VL and CD4 as biological markers affecting Indonesians' QoL. Consequently, the roles of VL and CD4 cell count in QoL among people with HIV/AIDS remain undetermined.

Previous research has found that low or undetected VLs were associated with adherence to ART in HIV/AIDS (Vrijens et al, 2005) and that ART adherence and undetectable VL were independently associated with QoL in people with this condition (Reis et al, 2020).

The authors hypothesised that adherence to ART and an undetectable VL would be significantly synergistic and independently impact QoL. The present study explored the effects of adherence to ART and undetectable VL and CD4 cell count as well as their synergistic effect on QoL, including on the environment, psychological, social relationships and physical health domains, in Indonesians diagnosed with HIV/AIDS.

Methods

Study design and participants

This study had a cross-sectional design and was conducted between 17 December 2020 and 27 February 2021. Participants who attended HIV clinics at two community health centres

and branches of a non-governmental AIDS organisation in Yogyakarta Province, Indonesia, were enrolled.

The inclusion criteria were respondents who: were Indonesian nationals aged ≥ 18 years; had received a diagnosis of HIV/AIDS, verified with medical information and confirmed by a physician; were able to understand spoken and written Bahasa; and agreed to take part in the study and provided signed informed consent. Exclusion criteria included respondents who had psychiatric disorders, were pregnant, were unable to communicate or had disabilities.

Sample size calculation

Sample size calculation requires a medium effect size (f) of 0.15 (Khumsaen et al, 2012), an alpha level of 0.05 and a power value of 0.90. Consequently, the sample size required for the present study needed to be 107. In light of an estimated attrition rate of 20%, the sample size was increased to 129 respondents.

Instruments

The questionnaire survey was conducted by trained nurses. The survey included participants' age, occupation, sex, education level, sexual orientation, marital status and duration of treatment (Astoro et al, 2007; Lindayani et al, 2018a; Handayani et al, 2019).

Assessment of quality of life

The WHOQOL-BREF is a 26-item questionnaire with each item scored on a 1–5 scale. Items are divided into four domains: environment; psychological; physical health; and social relationships (WHO, Division of Mental Health, 1996). The three negatively phrased items are reverse scored.

The WHOQOL-BREF has been widely applied in HIV/AIDS research (Hsiung et al, 2005; Liping et al, 2015; Maleki et al, 2020). It has been translated and validated in the Indonesian population with HIV/AIDS (Martina et al, 2017; Putra et al, 2019). The Cronbach's alpha value for the Bahasa version indicates an excellent index of internal consistency with 0.83, 0.90, 0.79 and 0.89 for the environmental, psychological, social relationships and physical health domains respectively (Martina et al, 2017).

Assessment of adherence to treatment

Adherence to antiretroviral therapy (ART) was evaluated using the Morisky Medication Adherence Scale (MMAS), which consists of eight questions. The score on the MMAS-8 ranges from 0 to 8; lower scores indicate poor or non-adherence. An MMAS-8 score in a range of 0–5 indicates non-adherence and 6–8 indicates adherence (Morisky et al, 2008). A physician validated ART adherence while medicine was being taken, and this was recorded in the patient's medical record and used in the study. The MMAS-8 Indonesian version among patients with HIV has excellent reliability with Cronbach's alpha of 0.89 (Yafi, 2018).

Assessment of biological biomarkers

The most recent VL status was identified using medical records and verified by a physician. Data were interpreted and dichotomised into: VL undetectable or suppressed with < 100

Table 1. Relationships demographic characteristic and determinant factors with quality of life score from the WHOQOL-BREF in participants living with HIV/AIDS (n=129)

Variables	Total participants	Physical health		Psychological		Social relationships		Environmental	
	n (%)	Mean (SD)/r	P	Mean (SD)/r	P value	Mean (SD)/r	P value	Mean (SD)/r	P value
Age (years) ^a	129 (100)	0.14	0.108	0.14	0.116	0.07	0.475	0.03	0.749
Sex ^b			0.802		0.652		0.700		0.381
Male	86 (66.7)	12.74 (3.12)		12.69 (2.96)		13.47 (2.66)		14.17 (2.17)	
Female	43 (33.3)	12.60 (2.90)		12.93 (2.85)		13.65 (2.53)		13.79 (2.41)	
Marital status ^b			0.127		0.178		0.091		0.101
Not married	94 (72.9)	12.95 (3.13)		12.97 (3.00)		13.74 (2.72)		14.24 (2.33)	
Married	35 (27.1)	12.03 (2.71)		12.23 (2.65)		12.94 (2.22)		13.51 (1.95)	
Occupation ^b			0.965		0.484		0.639		0.564
Not working	32 (24.8)	12.72 (3.10)		12.44 (3.11)		13.72 (2.67)		14.25 (2.30)	
Employed	97 (75.2)	12.69 (3.03)		12.88 (2.86)		13.46 (2.60)		13.98 (2.24)	
Education ^b			0.646		0.920		0.905		0.663
ISCED <3	88 (68.2)	12.78 (2.98)		12.78 (3.07)		13.55 (2.68)		13.99 (2.30)	
ISCED ≥3	41 (31.8)	12.51 (3.18)		12.73 (2.59)		13.49 (2.49)		14.17 (2.16)	
Sexual orientation ^b			0.119		0.054		0.075		0.100
Heterosexual	52 (40.3)	13.21 (3.11)		13.37 (2.83)		14.02 (2.49)		14.44 (2.21)	
Non-heterosexual	77 (59.7)	12.35 (2.96)		12.36 (2.92)		13.19 (2.66)		13.78 (2.25)	
Length of ART (years) ^b			0.003		<0.001		0.019		0.015
≥1	64 (49.6)	11.91 (2.53)		11.80 (2.58)		12.98 (2.31)		13.56 (1.89)	
<1	65 (50.4)	13.48 (3.30)		13.72 (2.93)		14.06 (2.79)		14.52 (2.48)	
Viral load			<0.001		<0.001		<0.001		<0.001
Detectable	83 (64.3)	10.89 (1.96)		11.04 (1.75)		12.14 (1.89)		12.72 (1.42)	
Undetectable	46 (35.7)	15.96 (1.53)		15.89 (1.77)		16.02 (1.73)		16.43 (1.29)	
CD4 cell count (cell/mm ³)			<0.001		0.002		0.008		0.002
<200	89 (69.0)	12.01 (2.85)		12.25 (2.83)		13.11 (2.51)		13.62 (2.10)	
≥200	40 (31.0)	14.23 (2.90)		13.93 (2.80)		14.45 (2.62)		15.00 (2.30)	
Adherence to ART			<0.001		<0.001		<0.001		<0.001
Non-adherence	77 (59.7)	10.91 (1.93)		11.04 (1.75)		12.09 (1.84)		12.69 (1.29)	
Adherence	52 (40.3)	15.35 (2.37)		15.33 (2.37)		15.65 (2.08)		16.06 (1.82)	

ART: antiretroviral therapy; ISCED: International Standard Classification of Education; Non-heterosexual: bisexual, homosexual, something else, don't know.

^aPearson's correlation, ^bIndependent t test

viral copies/ml detected); or detectable or unsuppressed with 100–500 viral copies/ml detected (Cho et al, 2020). The categories chosen reflect the CD4 cell count ranges used in a previous study; CD4 cell counts (cell/mm³) were <200 and ≥200 (Lindayani et al, 2018b). CD4 counts were also validated by the physician and medical records.

Ethical considerations

The institutional review board of Sekolah Tinggi Ilmu Kesehatan Ngudia Husada Madura evaluated and approved the study protocol (IRB: 709/KEPK/STIKES-NHM-/EC/IX/2020),

which complied with the Declaration of Helsinki. Each participant gave written informed consent after receiving both verbal and written information about the research.

Statistical analysis

The distribution of demographic data and determinant factors between groups were assessed using frequency (*n*) and percentage. The continuous variables are shown as means with standard deviations (SDs) and were analysed using a t-test, Pearson's correlation or Spearman's rank correlation as appropriate. Multicollinearity was examined using a variance inflation factor

Table 2. Adjusted β coefficients and 95% confidence intervals (CIs) of adherence ART status, VL, CD4 cell counts, and QoL in participants living with HIV/AIDS (n=129)

Variables	Physical health		Psychological		Social relationships		Environmental	
	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)
Adherence to ART								
Non-adherent	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Adherent	4.34 [3.69–5.19]**	2.00 [1.15–2.85]**	4.29 [3.57–5.01]**	1.96 [1.15–2.78]**	3.56 [2.87–4.25]*	1.94 [1.05–2.84]**	3.37 [2.83–3.91]**	1.79 [1.14–2.43]**
Viral load								
Detectable	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Undetectable	5.07 [4.40–5.73]**	3.07 [2.13–4.00]**	4.86 [4.22–5.49]**	3.02 [2.13–3.92]**	3.88 [3.21–4.54]**	2.28 [1.29–3.27]**	3.71 [3.21–4.21]**	2.24 [1.53–2.95]**
CD4 cell counts (cell/mm³)								
<200	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
≥200	1.11 [0.57–1.65]**	0.52 [0.17–0.87]*	0.84 [0.31–1.37]**	0.19 [–0.15, 0.53]	0.67 [0.19–1.15]**	0.14 [–0.24, 0.51]	0.69 [0.28–1.10]**	0.15 [–0.12, 0.42]

Note: Adjusted β coefficients and 95% CI were estimated using multiple linear regression after adjusting for age, occupation, gender, education, sex orientation, marital status, and time of treatment. ART: antiretroviral therapy; CI: confidence interval; QoL: quality of life; VL: viral load

* $P < 0.05$; ** $P < 0.001$

(VIF) of <10 (García et al, 2015). The data had a low impact on multicollinearity; it had a maximum VIF of 2.49.

The adjusted coefficients and 95% confidence intervals (CIs) for QoL were obtained by conducting a multiple linear regression after adjusting for potential confounding variables such as age, occupation, sex, education, sexual orientation, marital status and time of treatment.

In addition, the synergistic interaction effect between ART adherence with undetectable VL on the four QoL domains was verified after forming four dummy variables for the accompanying four (2 x 2) conditions: detectable VL and ART non-adherence (the reference condition or β_{00}); detectable VL and ART adherence (β_{10}); undetectable VL and ART non-adherence (β_{01}); and undetectable VL and ART adherence (β_{11}). The authors computed the additive interaction or synergistic effect utilising the following categories:

- If $\beta_{11} = \beta_{01} + \beta_{10}$, no interaction
- If $\beta_{11} > \beta_{01} + \beta_{10}$, positive interaction
- If $\beta_{11} < \beta_{01} + \beta_{10}$, negative interaction (Knol et al, 2007; Rias et al, 2020).

In the synergistic effect analysis, to calculate the 95% CI, the authors also controlled for the confounding variables of age, occupation, sex, education, sexual orientation, marital status, duration of treatment and CD4 cell counts.

Statistical analyses were performed using SPSS version 25.0 with $P < 0.05$ considered statistically significant.

Results

Table 1 presents the respondents' demographic characteristics. The 129 patients with HIV/AIDS who participated in this

research showed no significant differences regarding age, occupation, sex, education, sexual orientation and marital status in all domains of QoL. The authors did find a significant difference regarding duration of treatment in all domains of QoL, whereby the means (SD) of all domains of QoL were significantly higher in respondents with an undetected VL than those with a detected VL ($P < 0.001$). Moreover, the means (SD) of all domains of QoL were significantly higher ($P < 0.001$) in respondents who adhered to ART (Table 1).

Table 2 presents the adjusted β coefficients and 95% CIs of ART adherence, undetectable VL and CD4 cell counts for QoL. Patients who adhered to ART exhibited significantly higher physical health ($\beta = 2.00$; 95% CI (1.15–2.85)), psychological ($\beta = 1.96$; 95% CI (1.15–2.78)), social relationships ($\beta = 1.94$; 95% CI (1.05–2.84)) and environmental ($\beta = 1.79$; 95% CI (1.14–2.43)) scores than those who did not. Patients with undetectable VL had significantly higher ($\beta = 3.07$; 95% CI (2.13–4.00)), psychological ($\beta = 3.02$; 95% CI (2.13–3.92)), social relationships ($\beta = 2.28$; 95% CI (1.29–3.27)) and environmental ($\beta = 2.24$; 95% CI (1.53–2.95)) scores than those with detectable VL. The authors also found no significant association between CD4 cell count and physiological, social relationships and environment QoL domains after controlling for confounding factors, but there were significant differences regarding the physical health domain (Table 2).

The synergistic effects between ART adherence and the HIV/AIDS-related predictor of VL on QoL are shown in Table 3. The adjusted β coefficients of physical health, physiological, social and environment domains were 5.16 (95% CI (4.48–5.84)), 5.11 (95% CI (4.47–5.75)), 4.29 (95% CI

Table 3. Synergistic effect of ART adherence and viral load for quality of life in participants living with HIV/AIDS (n=129)

Variables	Physical health		Psychological		Social relationships		Environmental	
	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)	Unadjusted coefficients β (95% CI)	Adjusted coefficients β (95% CI)
Both detectable VL and non-adherence to ART	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Both detectable VL and adherence to ART	1.20 (0.19–2.21)*	1.47 (0.50–2.43)*	1.03 (0.72–1.99)*	1.28 (0.36–2.19)*	1.29 (0.25–2.33)*	1.58 (0.56–2.61)*	1.20 (0.45–1.95)*	1.34 (0.60–2.07)**
Both undetectable VL and non-adherence to ART	2.45 (1.07–3.83)**	2.03 (0.64–3.42)*	1.95 (0.64–3.25)*	1.69 (0.38–3.00)*	1.71 (0.29–3.12)*	1.58 (0.11–3.05)*	1.78 (0.76–2.81)**	1.36 (0.31–2.42)*
Both undetectable VL and adherence to ART	5.66 (5.02–6.30)**	5.16 (4.48–5.84)**	5.46 (4.86–6.07)**	5.11 (4.47–5.71)**	4.42 (3.76–5.08)**	4.29 (3.57–5.01)**	4.20 (3.73–4.68)**	4.11 (3.59–4.62)**

Note: Adjusted β coefficients and 95% CI were estimated using multiple linear regression after adjusting for age, occupation, sex, education, sexual orientation, marital status, time of treatment, and CD4 cell counts.

ART: antiretroviral therapy; CI: confidence interval; VL: viral load

* $P < 0.05$; ** $P < 0.001$

(3.57–5.01)) and 4.11 (95% CI (3.59–4.62)) respectively in patients who had undetectable VL and adhered to ART, and were higher than in patients who had both detectable VL and non-adherence to ART. Furthermore, the findings indicate there was a positive synergistic effect of undetectable VL and ART adherence on the physical health (5.16 > 2.03 + 1.47), physiological (5.11 > 1.69 + 1.28), social relationships (4.29 > 1.58 + 1.58) and environment domains (4.11 1.36 + 1.34) (Table 3).

Discussion

This is the first study to explore the relationship between VL and QoL among Indonesians with HIV/AIDS. ART adherence and undetectable VL synergistically increased QoL in environment, social relationships, psychological and physical health domains.

Previous research has shown that ART adherence is correlated with a high QoL score (Dinsa Ayeno et al, 2020; Reis et al, 2020). Our findings indicate adherence to ART was significantly associated with higher scores in all domains of QoL. This result is in line with a previous study (Liping et al, 2015), which found that people who adhered to ART had a higher prediction score in the QoL physical health domain ($\beta = 1.23$; CI (0.35–2.11)). Moreover, ART adherence was the strongest predictor for better scores for social relationships ($\beta = 1.18$; 95% CI (0.26–2.10)) and environment ($\beta = 1.10$; 95% CI (0.30–1.86)) domains but not for the psychological domain (Liping et al, 2015). However, in another study, ART adherence was most strongly correlated with the psychological domain (Reis et al, 2020).

In the present study, the significant relationship between ART adherence and higher physical health, social relations and environmental but not psychological scores might be explained by various reasons, such as the secondary effects of drugs and the therapeutic schema (Parienti et al, 2009).

Another crucial finding in this research was that an undetectable VL was correlated with higher physical health, psychological, social relations and environmental QoL scores, but no significant relationship was identified between CD4 cell and the QoL domains except for the physical health domain after controlling for confounding factors.

In line with these results, a cohort study has reported that a higher CD4 cell count (≥ 200 –499 cell/mm³) was positively predictive in the QoL domain of physical function but there was no significant difference in the psychological component score (Emuren et al, 2020). Moreover, CD4 cell count did not influence psychological, social relations and environmental QoL domains (Reis et al, 2020). Among the HIV/AIDS biological biomarkers, only CD4 cell counts were independently linked with the physical health QoL domain (Emuren et al, 2020).

This is in line with previous research that has indicated a low CD4 cell count is a more strongly prognostic of HIV/AIDS progression than HIV ribonucleic acid level while on highly active ART, so is among the most accurate predictors of elevated physical health (Tarwater et al, 2004; Emuren et al, 2020).

Furthermore, the finding in the present study that undetectable VL is significantly correlated with high scores in the physical health, psychological, social relationships and environmental QoL domains was consistent with previous studies, in which a high or detectable VL was shown to be significantly associated with a low score in all domains of QoL (Reis et al, 2020).

Damage to the hippocampus has been linked not only to a variety of neurological and psychiatric illnesses but also to some physical diseases, which indicates its condition impacts bodily functions and memory (Lu et al, 2018). There were consistent connections between the hippocampal response and CD4 cell

count and VL measurements (Nir et al, 2021). Moreover, the high volume of grey matter in the hippocampus mediates the link between self-esteem and physical health, indicating a critical role in the brain circuitry that links self-esteem to physical health (Lu et al, 2018). Higher VLs are associated with smaller amygdala volumes, which might account for their correlation with the domains of attention, verbal fluency and motor functioning (Nir et al, 2021), social adversity and cognitive performance (Thames et al, 2018). This mechanism might provide new insight into the pathways that affect QoL among patients with HIV/AIDS.

A major finding of the present study concerns the relationship where the combination of an undetectable VL and ART adherence synergistically increases all domains of QoL compared with detectable VL and ART non-adherence. The potential mechanism for this synergistic effect on QoL, including on the physical health, psychological, social relations and environmental domains, might be explained by the relationship between undetectable VL and ART adherence. ART adherence is positively associated with undetectable VL (Vrijens et al, 2005). Additional research has shown that, independently of undetectable VL (Reis et al, 2020), ART adherence (Liping et al, 2015) is linked to better QoL. These earlier results are comparable with our finding that patients with HIV/AIDS with an undetectable VL and ART adherence had a higher QoL score than those who met only one of these parameters.

Self-reported ART non-adherence is associated with higher levels of inflammatory biological markers in VL that are suppressed by ART; and significantly reduces at least one biomarker of immune activation – CD4 cell counts (Castillo-Mancilla et al, 2018; 2019). One reason for the findings of the present study is that ART non-adherence may result in low-level viral replication, with VL undetectable in the majority of clinically accessible assays, but with bursts of inflammation and immunological activation (Castillo-Mancilla et al, 2018; 2019). This study provides additional information, showing that both maintaining ART adherence and avoiding detectable VL are likely to be helpful strategies for optimising QoL.

Limitations

A limitation of this research is that the QoL might have been overestimated because participants were recruited from ART clinics and NGOs. Patients provided with ART therapies generally have a better QoL than those not receiving them.

Therefore, although the authors adjusted for many potential confounding variables, they cannot eliminate the possibility that VL and CD4 cells count are affected by factors other than HIV/AIDS. Instead, they established that ART adherence and undetectable VL have a synergistic effect on boosting QoL in patients with HIV/AIDS and that this is potentially valuable and may help promote programmes for regulating and improving QoL in patients with HIV/AIDS.

Ultimately, a large, cluster-randomised, multi-site investigation would provide more substantial evidence on the individual and combined effects of ART adherence and undetectable VL and other biological markers on QoL, thereby guiding future nursing research and practice.

Conclusion

ART adherence is independently related to a better QoL. Patients with undetectable VL had significantly higher scores in physical health, psychological, social relationships and environmental QoL domains.

Adherence to ART and an undetectable VL have a positive, synergistic effect of promoting QoL, including in the physical, psychological, social relationships and environmental domains, among patients with HIV/AIDS in Indonesia.

In line with these findings, nurse educators and health providers should promote specific strategies, including aiming to increase the proportion of patients whose VL levels are undetectable and encouraging adherence to ART among patients with HIV/AIDS. **BJN**

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- Astoro NW, Djaoui S, Djoerban Z, Prodjosudjadi W. Quality of life of HIV patients and influential factors. *Acta Med Indones*. 2007;39(1):2–7
- Castillo-Mancilla JR, Morrow M, Boum Y et al. Brief report: higher ART adherence is associated with lower systemic inflammation in treatment-naïve Ugandans who achieve virologic suppression. *J Acquir Immune Defic Syndr*. 2018;77(5):507–513. <https://doi.org/10.1097/QAI.0000000000001629>
- Castillo-Mancilla JR, Phillips AN, Neaton JD et al. Incomplete ART adherence is associated with higher inflammation in individuals who achieved virologic suppression in the START study. *J Int AIDS Soc*. 2019;22(6):e25297–e25307. <https://doi.org/10.1002/jia2.25297>
- Castro R, De Boni RB, Luz PM et al. Health-related quality of life assessment among people living with HIV in Rio de Janeiro, Brazil: a cross-sectional study. *Qual Life Res*. 2019;28(4):1035–1045. <https://doi.org/10.1007/s11136-018-2044-8>
- Cho H, Jiang Y, Li X, Deming M. The relationship between self-reported viral load suppression and quality of life among people living with HIV in South Carolina. *AIDS Care*. 2020;32(9):1198–1205. <https://doi.org/10.1080/09540121.2019.1698706>
- Cooper V, Clatworthy J, Harding R, Whetham J; Emerge Consortium. Measuring quality of life among people living with HIV: a systematic review of reviews. *Health Qual Life Outcomes*. 2017;15(1):220. <https://doi.org/10.1186/s12955-017-0778-6>
- Degroote S, Vogelaers D, Vandijck DM. What determines health-related quality of life among people living with HIV: an updated review of the literature. *Arch Public Health*. 2014;72(1):40. <https://doi.org/10.1186/2049-3258-72-40>
- Dinsa Ayeno H, Megersa Atomsa K, Melesie Taye G. Assessment of health-related quality of life and associated factors among HIV/AIDS patients on highly active antiretroviral therapy (HAART) at Ambo General Hospital, West Shewa, Ethiopia. *HIV AIDS (Auckl)*. 2020;12:467–478. <https://doi.org/10.2147/HIV.S259510>

KEY POINTS

- Adherence to antiretroviral therapy (ART) is independently associated with a better quality of life in the physical health, psychological, social relations and environmental quality-of-life domains
- Patients with an undetectable viral load had a significantly higher quality of life in the physical health, psychological, social relations and environmental quality-of-life domains
- Adherence to ART and an undetectable viral load together had a positive synergistic effect on improving all domains of quality of life – physical health, psychological, social relations and environmental – among patients with HIV/AIDS in Indonesia

- Emuren L, Welles S, Macalino G et al. Predictors of health-related quality of life among military HIV-infected individuals. *Qual Life Res.* 2020;29(7): 1855–1869. <https://doi.org/10.1007/s11136-020-02441-5>
- García CB, García J, López Martín MM, Salmerón R. Collinearity: revisiting the variance inflation factor in ridge regression. *J Appl Stat.* 2015;42(3): 648–661. <https://doi.org/10.1080/02664763.2014.980789>
- Ghiasvand H, Waye KM, Noroozi M, Harouni GG, Armoon B, Bayani A. Clinical determinants associated with quality of life for people who live with HIV/AIDS: a meta-analysis. *BMC Health Serv Res.* 2019;19(1):768. <https://doi.org/10.1186/s12913-019-4659-z>
- Ghiasvand H, Higgs P, Noroozi M et al. Social and demographical determinants of quality of life in people who live with HIV/AIDS infection: evidence from a meta-analysis. *Biodemogr Soc Biol.* 2020; 65(1):57–72. <https://doi.org/10.1080/19485565.2019.1587287>
- Handayani S, Ratnasari NY, Husna PH, Marni, Susanto T. Quality of life people living with HIV/AIDS and its characteristic from a VCT centre in Indonesia. *Ethiop J Health Sci.* 2019;29(6):759–766. <https://doi.org/10.4314/ejhs.v29i6.13>
- Hsiung PC, Fang CT, Chang YY, Chen MY, Wang JD. Comparison of WHOQOL-BREF and SF-36 in patients with HIV infection. *Qual Life Res.* 2005;14(1):141–150. <https://doi.org/10.1007/s11136-004-6252-z>
- Huang L, Li L, Zhang Y, Li H, Li X, Wang H. Self-efficacy, medication adherence, and quality of life among people living with HIV in Hunan Province of China: a questionnaire survey. *J Assoc Nurses AIDS Care: JANAC.* 2013;24(2):145–153. <https://doi.org/10.1016/j.jana.2012.04.006>
- Khumsaen N, Aoup-Por W, Thammachak P. Factors influencing quality of life among people living with HIV (PLWH) in Suphanburi Province, Thailand. *J Assoc Nurses AIDS Care.* 2012;23(1):63–72. <https://doi.org/10.1016/j.jana.2011.01.003>
- Knol MJ, van der Tweel I, Grobbee DE, Numans ME, Geerlings MI. Estimating interaction on an additive scale between continuous determinants in a logistic regression model. *Int J Epidemiol.* 2007;36(5):1111–1118. <https://doi.org/10.1093/ije/dym157>
- Lindayani L, Chen YC, Wang JD, Ko NY. Complex problems, care demands, and quality of life among people living with HIV in the antiretroviral era in Indonesia. *J Assoc Nurses AIDS Care.* 2018a;29(2):300–309. <https://doi.org/10.1016/j.jana.2017.10.002>
- Lindayani L, Ibrahim K, Wang JD, Ko NY. Independent and synergistic effects of self- and public stigmas on quality of life of HIV-infected persons. *AIDS Care.* 2018b;30(6):706–713. <https://doi.org/10.1080/09540121.2017.1396282>
- Liping M, Peng X, Haijiang L, Lahong J, Fan L. Quality of life of people living with HIV/AIDS: a cross-sectional study in Zhejiang Province, China. *PLoS One.* 2015;10(8):e0135705–e0135719. <https://doi.org/10.1371/journal.pone.0135705>
- Lu H, Li X, Wang Y, Song Y, Liu J. The hippocampus underlies the association between self-esteem and physical health. *Sci Rep.* 2018;8(1):17141. <https://doi.org/10.1038/s41598-018-34793-x>
- Maleki MR, Derakhshani N, Azami-Aghdash S, Naderi M, Nikoomeanesh M. Quality of life of people with HIV/AIDS in Iran: a systematic review and meta-analysis. *Iran J Public Health.* 2020;49(8):1399–1410. <https://doi.org/10.18502/ijph.v49i8.3861>
- Martina SE, Thongpat S, Nitirat P. Quality of life of HIV-infected women in Medan, North Sumatera, Indonesia. *Int J Sci Basic Appl Res.* 2017;36(5):319–324
- Ministry of Health (Indonesia). Annual health report. 2018. <https://pusdatin.kemkes.go.id/article/view/19042200004/situasi-umum-hiv-aids-dan-tes-hiv.html> (accessed 14 December 2022)
- Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. *J Clin Hypertens.* 2008;10(5):348–354. <https://doi.org/10.1111/j.1751-7176.2008.07572.x>
- Nir TM, Fouche JP, Ananworanich J et al. Association of immunosuppression and viral load with subcortical brain volume in an international sample of people living with HIV. *JAMA Netw Open.* 2021;4(1):e2031190–e2031190. <https://doi.org/10.1001/jamanetworkopen.2020.31190>
- Oguntibeju O. Quality of life of people living with HIV and AIDS and antiretroviral therapy. *HIV/AIDS (Auckl).* 2012;4:117–124. <https://doi.org/10.2147/HIV.S32321>
- Parienti JJ, Bangsberg DR, Verdon R, Gardner EM. Better adherence with once-daily antiretroviral regimens: a meta-analysis. *Clin Infect Dis.* 2009;48(4):484–488. <https://doi.org/10.1086/596482>
- Popping S, Kall M, Nichols BE et al. Quality of life among people living with HIV in England and the Netherlands: a population-based study. *Lancet Reg Health Eur.* 2021;8:100177. <https://doi.org/10.1016/j.lanepe.2021.100177>
- Putra INAM, Waluyo A, Yona S. The relationship between family acceptance and quality of life and self esteem of PLWH MSM in Medan, North Sumatera, Indonesia. *Enferm Clin.* 2019;29:291–294. <https://doi.org/10.1016/j.enfcli.2019.04.036>
- Reis A, Lencastre L, Jonsson C, Guerra MP. Treatment adherence, meaning in life and affects in quality of life of HIV/AIDS patients. *J Happiness Stud.* 2020;21(7):2405–2417. <https://doi.org/10.1007/s10902-019-00182-y>
- Rias YA, Kurniasari MD, Traynor V et al. Synergistic effect of low neutrophil-lymphocyte ratio with physical activity on quality of life in type 2 diabetes mellitus: a community-based study. *Biol Res Nurs.* 2020;22(3):378–387. <https://doi.org/10.1177/1099800420924126>
- Rzeszutek M, Gruszczynska E. Consistency of health-related quality of life among people living with HIV: latent state-trait analysis. *Health Qual Life Outcomes.* 2018;16(1):101. <https://doi.org/10.1186/s12955-018-0929-4>
- Suswani A, Arsin AA, Amiruddin R, Syafar M, Palutturi S. Factors related quality of life among people living with HIV and AIDS in Bulukumba. *Int J Community Med Public Health.* 2018;5(8):3227–3231. <https://doi.org/10.18203/2394-6040.ijcmph20182966>
- Tarwater PM, Gallant JE, Mellors JW et al. Prognostic value of plasma HIV RNA among highly active antiretroviral therapy users. *AIDS.* 2004; 18(18):2419–2423
- Thames AD, Kuhn TP, Mahmood Z et al. Effects of social adversity and HIV on subcortical shape and neurocognitive function. *Brain Imaging Behav.* 2018;12(1):96–108. <https://doi.org/10.1007/s11682-017-9676-0>
- UNAIDS. Snapshot 2019. Indonesia. 2019. <https://www.aidsdatahub.org/sites/default/files/resource/indonesia-country-card-snapshot-nov-2019.pdf> (accessed 18 December 2022)
- UNAIDS. Fact sheet 2022. Global HIV statistics. 2022. https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf (accessed 18 December 2022)
- Vrijens B, Goetghebeur E, de Klerk E, Rode R, Mayer S, Urquhart J. Modelling the association between adherence and viral load in HIV-infected patients. *Stat Med.* 2005;24(17):2719–2731. <https://doi.org/10.1002/sim.2130>
- Vu GT, Tran BX, Hoang CL et al. Global research on quality of life of patients with HIV/AIDS: is it socio-culturally addressed? (GAPRESEARCH). *Int J Environ Res Public Health.* 2020;17(6):2127–2141. <https://doi.org/10.3390/ijerph17062127>
- World Health Organization, Division of Mental Health. WHOQOL-BREF: introduction, administration, scoring and generic version of the assessment: field trial version, December 1996. 1996 <https://apps.who.int/iris/handle/10665/63529> (accessed 14 December 2022)
- Yafi SR. Hubungan Efikasi diri dan Makna Hidup dengan Kepatuhan Pengobatan Antiretroviral Therapy (ART) Pada Lelaki Seks Lelaki Seropositif HIV di Yayasan Teratak Jiwa Hati Sumatera Barat [Relationship between self-efficacy and the meaning of life with adherence to antiretroviral therapy (ART) in HIV-seropositive male sex at the Teratak Jiwa Hati Foundation, West Sumatra] (in Indonesian). MSc thesis submitted to Universitas Andalas, 2018. <http://scholar.unand.ac.id/34988/> (accessed 14 December 2022)
- Zhou G, Li X, Qiao S, Shen Z, Zhou Y. HIV symptom management self-efficacy mediates the relationship of internalized stigma and quality of life among people living with HIV in China. *J Health Psychol.* 2020;25(3):311–321. <https://doi.org/10.1177/1359105317715077>

CPD reflective questions

- What impact might good adherence to antiretroviral therapy (ART) have on the quality of life of patients with HIV/AIDS?
- Why is a good quality of life essential in people with HIV/AIDS?
- Why should adherence to ART and maintaining an undetectable viral load be encouraged among people with HIV/AIDS?