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A Pharmacovigilance Insights into Adverse Drug Reactions, Antiretroviral Therapy Adherence, and Quality of Life in HIV/AIDS

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ABSTRACT

Antiretroviral therapy (ART) has significantly improved the clinical management of HIV/AIDS; however, its effectiveness may be influenced by adverse drug reactions (ADRs), treatment adherence, and patients' quality of life (QoL). This study aimed to systematically examine the relationships among ADRs, ART adherence, and QoL among people living with HIV/AIDS within an integrated pharmacovigilance framework. A systematic literature review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Literature searches were performed using Google Scholar, Scopus, and ScienceDirect to identify peer-reviewed articles published between 2018 and 2026. Following the screening and eligibility assessment process, 21 articles were included in the qualitative synthesis. The findings indicate that ADRs are associated with lower ART adherence, with one study reporting that the absence of ADRs was associated with higher odds of treatment adherence (adjusted odds ratio [AOR] = 5.33; 95% confidence interval [CI]: 1.95–14.57). Treatment-related discomfort was also identified as a factor contributing to medication non-adherence. Furthermore, ADRs and symptom burden, including pain, fatigue, and neurological symptoms, were associated with poorer functioning and quality of life across physical and psychological domains. ART adherence was generally associated with better QoL, although several studies reported inconsistent or statistically nonsignificant relationships. These variations may reflect differences in patient characteristics, healthcare settings, measurement instruments, clinical conditions, and psychosocial factors, including family support and social stigma. Overall, the evidence suggests that ADRs, ART adherence, and QoL are interrelated dimensions of HIV/AIDS management, although the predominantly observational evidence does not establish causal relationships. Integrating standardized ADR monitoring, patient-centered adverse reaction reporting, adherence assessment, and QoL evaluation into routine HIV care may support more comprehensive and individualized treatment. Further prospective studies and well-controlled interventions are needed to clarify these relationships and evaluate the effectiveness of integrated pharmacovigilance strategies.

Keyword: *Adverse Drug Reaction; Antiretroviral Therapy Adherence; Quality of Life; Pharmacovigilance*

Introduction

Antiretroviral therapy (ART) has substantially reduced morbidity and mortality among people living with HIV/AIDS. However, its long-term effectiveness depends on sustained treatment adherence, which may be compromised by adverse drug reactions (ADRs). A systematic review and meta-analysis in Ethiopia reported a high prevalence of ADRs among patients receiving ART, with factors such as gender, advanced clinical stage, and comorbidities

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associated with their occurrence (Zewdu et al., 2025). Similarly, a retrospective cohort study of children with HIV in Ethiopia identified poor treatment adherence among the factors associated with major ADRs (Tadese et al., 2024). These findings highlight the importance of examining the relationship between ADRs and ART adherence in long-term HIV management.

ADRs may also be associated with poorer quality of life (QoL), while limitations in pharmacovigilance systems may hinder the systematic identification and documentation of their impact on patients. A systematic review of pharmacovigilance systems in developing countries reported limitations in monitoring performance, particularly in process and outcome indicators (Garashi et al., 2022). Consistent with this, a multicenter observational study in Japan of HIV patients newly starting ART showed that treatment adherence was significantly correlated with health-related quality of life, in addition to factors related to patients' clinical decision-making conflicts (Panayi et al., 2024). Collectively, these findings suggest that ADRs, treatment adherence, and QoL are important, interrelated dimensions of HIV care that warrant integrated assessment.

Despite existing evidence on these relationships, previous studies have predominantly examined ADRs, ART adherence, and QoL separately or investigated only selected associations between them. For example, an intervention study involving health information systems in Cyprus and Greece reported improvements in adherence and QoL but did not explicitly incorporate ADRs as a central analytical variable (Sekine et al., 2023). Similarly, a real-world study of HIV patients in the United States examined adherence and QoL without explicitly integrating ADRs into a comprehensive pharmacovigilance framework (Tsega et al., 2024). Consequently, evidence synthesizing all three dimensions within a single pharmacovigilance framework remains limited.

This systematic review addresses this gap by synthesizing evidence on the relationships among ADRs, ART adherence, and QoL in people living with HIV/AIDS within an integrated pharmacovigilance framework. Its novelty lies in bringing these three dimensions together to identify patterns of association and their implications for patient-centered HIV care, rather than treating each relationship independently. Specifically, this study aims to examine (1) the relationship between ADRs and ART adherence, (2) the relationship between ADRs and QoL, (3) the relationship between ART adherence and QoL, and (4) the implications of integrating these dimensions into pharmacovigilance practices. The findings are expected to contribute to the evidence base for HIV pharmacovigilance and inform the development of more comprehensive, proactive, and patient-centered ADR monitoring strategies.

Research Methods

This study employed a systematic literature review (SLR) to examine the relationships among adverse drug reactions (ADRs), antiretroviral therapy (ART) adherence, and quality of life (QoL) among people living with HIV/AIDS. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparent reporting of the literature identification, screening, eligibility assessment, and inclusion processes (Page et al., 2021). A systematic approach was adopted to improve the reproducibility of the search and selection procedures and to minimize potential selection bias (Turnbull et al., 2023).

Literature searches were conducted in Google Scholar, Scopus, and ScienceDirect for articles published between 2018 and 2026. The search strategy combined terms related to the study population, drug reactions, treatment adherence, quality of life, and pharmacovigilance. The principal keywords included "adverse drug reaction," "antiretroviral therapy adherence," "quality of life," "HIV/AIDS," and "pharmacovigilance." Boolean operators were used to combine related terms, with the search strategy adapted to the requirements of each database. The search was conducted using predefined terms and publication limits to identify relevant studies.

Eligibility Criteria and Study Selection

Studies were eligible for inclusion if they (1) involved people living with HIV/AIDS who received ART; (2) investigated at least one relationship involving ADRs, ART adherence, or QoL; (3) reported relevant empirical findings; (4) were published in peer-reviewed journals between 2018 and 2026; and (5) were available in full text in a language accessible to the review team. Studies were excluded if they were duplicates, did not address the research questions, lacked relevant outcome data, had insufficient methodological information for appraisal, or were inaccessible in full text.

The initial search identified 309 records. After 102 duplicate records were removed, 207 records remained for title and abstract screening. Of these, 95 were excluded because they did not meet the relevance criteria, leaving 112 reports for full-text retrieval. Fifty-six reports were excluded at this stage because their full texts were unavailable or they did not meet the preliminary relevance requirements. The remaining 56 full-text articles were assessed for eligibility. Following critical appraisal, 35 articles were excluded: 13 because their variables did not match the research objectives, 13 because of methodological limitations, and 9 for other technical reasons. Ultimately, 21 articles were included in the qualitative synthesis. The selection process was documented using a PRISMA 2020 flow diagram (Figure 1).

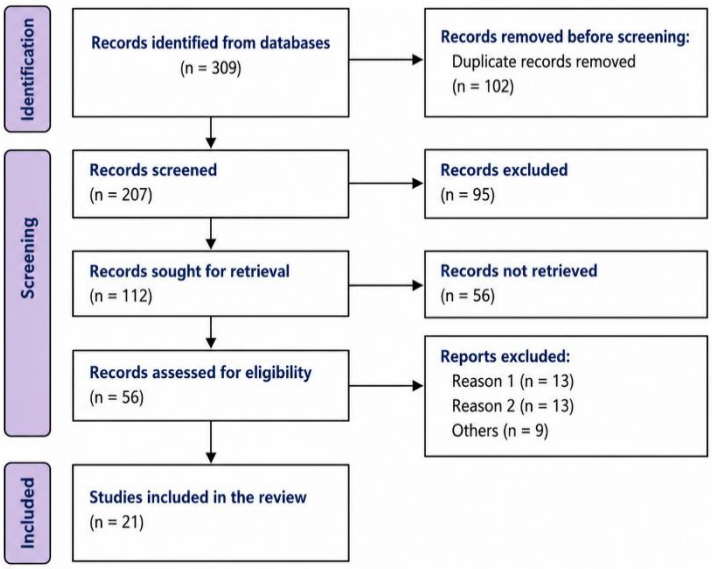


Figure 1. PRISMA Protocol-Based Literature Selection Flowchart

Methodological Quality Assessment and Reviewer Agreement

The methodological quality of the included studies was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Tools, with the appraisal checklist selected according to each study's design. The JBI checklist for analytical cross-sectional studies was used for cross-sectional studies, while the cohort checklist was applied to cohort studies. Appropriate JBI tools were selected for intervention studies and secondary research, where applicable, following verification of their respective designs. The appraisal examined study-specific methodological domains, including participant selection, measurement validity and reliability, identification and management of potential confounding factors, and appropriateness of statistical analysis. The results were used to characterize the methodological strengths and limitations of the evidence and inform the interpretation of the synthesis.

Two reviewers independently screened the records and assessed the full texts against the eligibility criteria. They also independently evaluated methodological quality and extracted relevant study data. Disagreements were resolved through discussion and, when necessary, consultation with a third reviewer.

Data Extraction and Synthesis

Data were extracted using a structured form covering author and publication year, country, study design, participant characteristics, ART regimen where reported, ADR assessment, adherence measurement, QoL instrument, and the principal findings relevant to the research questions. The consistency and suitability of measurement instruments were considered during interpretation, including the use of the WHOQOL-HIV BREF where reported. Evidence concerning ADRs, ART

adherence, and QoL was organized thematically to identify recurring patterns of association, differences across studies, and implications for pharmacovigilance. The findings were synthesized narratively rather than interpreted as proof of causal relationships, taking into account differences in study designs, populations, and measurement approaches.

Result and Discussion

Results

The literature selection process yielded 21 articles that met all inclusion criteria and were suitable as sources for synthesis in this study. These articles originated from various countries with diverse healthcare contexts, covering Sub-Saharan Africa, South Asia, Latin America, and Indonesia, thereby providing a sufficiently broad range of perspectives to address the research questions. In terms of study design, the majority of studies employed a cross-sectional approach, with a small proportion using retrospective cohort studies and pre-post intervention studies. The most commonly used quality-of-life measurement instrument was the WHOQOL-HIV BREF, while the assessment of adverse drug reactions generally utilized the Naranjo scale as well as the Hartwig and Siegel criteria. All articles were categorized into four thematic groups based on the research questions: the relationship between adverse drug reactions (ADRs) and antiretroviral therapy adherence; the relationship between ADRs and quality of life; the relationship between therapy adherence and quality of life; and the integration of these three variables within the pharmacovigilance framework.

Table 1. Synthesis of Systematic Literature Review Results (n = 21)

No	Author (Year)	Country	Study Design	Sample	Main Variables	Key Findings
1	(Abadiga et al., 2020)	Ethiopia	Cross-sectional	305	ADR, ART Adherence	The absence of reported ADRs was associated with higher ART adherence (AOR=5.33; 95% CI: 1.95–14.57)
2	(Adem et al., 2019)	Ethiopia	Cross-sectional	359	ADR (neuropathy), QoL	Didanosine-associated peripheral sensory

						neuropathy significantly reduces QoL
3	(Chukwurah et al., 2020)	United States	Cross-sectional	179	Symptom Burden, Function	Symptom burden (pain, fatigue, depression) predicts a decline in overall function
4	(Desta et al., 2020)	Ethiopia	Cross-sectional	240	HAART adherence, QoL	Low adherence was negatively associated with QoL (AOR=0.40; 95% CI: 0.19–0.86)
5	(Gelaw et al., 2018)	Ethiopia	Cross-sectional	394	ADR Coping strategies, Adherence	Nonadherence as a coping strategy for ADRs was found in 35.5% of patients
6	(Pimentel, 2020)	Brazil	Prospective cohort	Not specified	ADRs, QoL	The number of ADRs was an independent predictor of a Decrease in QoL scores
7	Dash & Rose (2022)	India	Review	174 children	ADRs, Adherence (children)	Grade 1–3 ADRs contribute to nonadherence in the pediatric population
8	(Duru et al., 2019)	Nigeria	Cross-sectional	400	ADRs, Adherence	ADR prevalence 13.7%;

						adherence 85%; ADRs associated with age and sex
9	(Moral et al., 2019)	Peru	Cross-sectional	180	ART adherence, Clinical factors	ART-related discomfort and TB assignificant predictors of nonadherence
10	(Wigatiningtyas, 2026)	Indonesia	Pre- and post-intervention	32	Vitamin D, ADR, QoL	Vitamin D supplementation reduces ADR and improves QoL ($p<0.001$)
11	(Riyani, 2024)	Indonesia	Cross-sectional	133	Stigma, ARV Adherence, QoL	ARV adherence is significantly associated with QoL ($p=0.032$)
12	(Moses et al., 2025)	Uganda	Cross-sectional	312	ADR, Pharmacovigilance	ADR prevalence 76%; low CD4 count and low education level as risk factors
13	(Raziansyah & Pertiwi, 2024)	Indonesia	Cross-sectional	118	Adherence, QoL, Retention	Adherence was significantly associated with QoL ($p=0.005$) And treatment retention ($p=0.003$)
14	(Rahmawati, 2020)	Indonesia	Prospective observational	Varied	ARV adherence, QoL	Moderate-to-low adherence; the relationship between adherence and

						QoL showed p ≥ 0.05
15	(Saputra, 2023)	Indonesia	Cross-sectional	98	IO, ARV Adherence, QoL	ARV adherence is associated with QoL in people living with HIV (p=0.001)
16	(Oumar et al., 2023)	Mali	Cross-sectional	Children aged 1–14 years	ADRs, Adherence (children)	ADRs are more common in non-compliant patients; routine monitoring is necessary
17	(Rantepadang, 2022)	Indonesia	Cross-sectional	38	ARV Adherence, QoL	No significant association between adherence and QoL (p=0.924); other factors are dominant
18	(Sherfa et al., 2021)	Ethiopia	Retrospective cohort	456	ADR, Predictors	ADR incidence 0.53/100 person-months; women and patients with advanced-stage disease ( ) are at higher risk
19	(Zondi & Naidoo, 2022a)	South Africa	Cross-sectional & retrospective	Not specified	ADR Reporting, Pharmacovigilance	72% of patients reported ADRs; patient reports were inconsistent with medical records

20	(Patmawati, 2025)	Indonesia	Cross-sectional	63	Family Support, Adherence, QoL	Adherence was the most dominant factor affecting QoL (p=0.000)
21	(Weldesenbet et al., 2022)	Ethiopia	Retrospective cohort	561	ADRs, Adherence, Time-dependent predictors	Poor adherence predicts earlier ADR (AHR = 8.8; 95% CI: 3.3–23.2)

Based on the overall synthesis table above, it appears that the geographic distribution of the analyzed studies covers Sub-Saharan Africa, South Asia, Latin America, and Southeast Asia particularly Indonesia thereby providing a fairly broad representation of the diversity of epidemiological contexts and health care systems in global HIV/AIDS management. The majority of studies used a cross-sectional design, which allows for data collection from a large population at a single point in time, although this design has limitations in establishing the direction of causality between variables. The most commonly used instrument for measuring quality of life was the WHOQOL-HIV BREF, which covers six main domains: physical, psychological, self-care, social relationships, environment, and spiritual, making it the most comprehensive and internationally standardized measurement tool for people living with HIV/AIDS. ADR assessments in the reviewed studies generally used the Naranjo scale to determine the causal relationship between a drug and the resulting reaction, as well as the Hartwig and Siegel criteria to classify the severity level. The publication range spanning 2018 to 2026 ensures that this synthesis reflects the latest developments in HIV pharmacovigilance, including the shift in antiretroviral regimens from older generations to more modern regimens with better tolerability profiles. Differences in findings across studies identified in this review particularly regarding the relationship between adherence and quality of life indirectly reflect population heterogeneity, variations in the operational definitions of adherence, and differences in the thresholds used to classify patients as adherent or non-adherent, all of which must be critically considered when interpreting the results of this synthesis.

Discussion

1.1 The Relationship Between Adverse Drug Reactions and Adherence to Antiretroviral Therapy in HIV/AIDS Patients

The findings of the reviewed studies suggest that adverse drug reactions (ADRs) are associated with ART adherence. However, the strength and direction of this association should be interpreted in the context of the study designs, measurement approaches, and potential confounding factors. This phenomenon does not stand alone but reflects the complexity of interactions between a drug's pharmacological profile, the patient's immunological status, and the psychosocial factors surrounding the course of their disease. In the cross-sectional study by Abadiga et al. (2020) the absence of ADRs was associated with higher odds of ART adherence (AOR = 5.33; 95% CI: 1.95–14.57). This finding suggests a potentially important relationship between ADR experience and adherence, but the cross-sectional design does not establish that ADRs directly cause non-adherence.

Gelaw et al. (2018) reported that 35.5% of participants used non-adherence as a coping strategy for ART-related adverse effects. This finding indicates that treatment-related discomfort may be an important consideration when assessing adherence behavior. Although treatment interruption can be associated with virological failure and drug resistance, these outcomes should not be assumed to have occurred in the participants unless they were directly assessed in the study.

At the epidemiological level, a hospital-based survey conducted by Duru et al. (2019) of 400 patients in Imo State, Nigeria, found a prevalence of ADRs of 13.7% over the past year, with an overall adherence rate of 85%. The incidence of ADRs in this study was found to be significantly higher among those aged over 50 years (OR=9.28), women (OR=2.55), and rural residents (OR=4.47), indicating that the distribution of ADR risk is uneven within the population and implying the need for more segmented monitoring. Consistent with this, a cross-sectional study by Moral et al. (2019) involving 180 patients in Lambayeque Province, Peru, found that 58.3% of patients were inconsistent in adhering to their therapy, with concomitant tuberculosis, discomfort with the ART regimen, and a history of temporary treatment interruption being the primary risk factors for nonadherence, while having children was a protective factor for adherence.

In the context of the pediatric population, a somewhat different but still relevant pattern was also observed. Dash & Rose, (2022) reported the results of a monitoring study of 174 children undergoing initiation of antiretroviral therapy, in which 78 children (45%) experienced new adverse drug reactions (ADRs) during the observation period; 43.6% were categorized as definite ADRs, 20% as *probable*, and the remainder as possible. Most ADRs were classified as mild (*Grade 1*), and nearly all resolved without requiring a change in medication, although more severe reactions still have the

potential to lead to treatment refusal in this age group. Another study by Zondi & Naidoo, (2022) in children aged 1 to 14 years in Bamako, Mali, showed that nonadherence was found in only 15% of cases, and descriptively, compliant children tended to be younger than noncompliant ones (median 36 versus 72 months), although this difference did not reach statistical significance in the multivariate analysis (p=0.093). Both studies confirm that the approach to managing ADRs in pediatrics requires different and more adaptive monitoring strategies compared to the adult population.

The temporal aspect of the relationship between ADRs and adherence was also examined through a retrospective cohort study of 561 patients in the West Hararghe Zone, Eastern Ethiopia. A study by Dash & Rose, (2022) showed that 90.74% of ADR events first occurred within the first year of therapy initiation, and patients with moderate or poor adherence had an 8.8-fold higher risk (AHR=8.8; 95% CI: 3.3–23.2) and 7.8 times higher, respectively, for experiencing ADRs earlier than patients with good adherence, indicating a bidirectional relationship between adherence and ADRs that forms a negative feedback loop. Sherfa et al. (2021) in a retrospective cohort study of 456 patients in Arba Minch, Southern Ethiopia, found an ADR incidence of 0.53 per 100 person-months, with women (AHR = 2.35) and patients in advanced WHO stages (AHR = 3.0) showing significantly higher risks, while patients receiving care at community health centers actually had a 59% lower risk compared to those in hospitals.

Overall, the reviewed studies indicate an association between ADRs and ART adherence, although the magnitude and direction of the relationship may vary across populations and study designs. Patient-reported discomfort and the use of non-adherence as a coping strategy highlight the importance of ADR assessment in adherence support. Nevertheless, the available evidence does not establish a uniform causal effect across all included studies.

1.2 The Relationship Between Adverse Drug Reaction Incidence and Quality of Life in HIV/AIDS Patients

ADRs are an important clinical factor associated with quality of life among people living with HIV/AIDS receiving ART. However, the extent of this association may differ according to symptom severity, comorbidities, psychological status, and the methods used to assess ADRs and QoL. In the prospective cohort study by Pimentel, (2020), the number of ADRs reported at treatment initiation was associated with subsequent changes in QoL, while anxiety and depressive symptoms were also identified as predictors of later QoL outcomes. These findings provide longitudinal evidence of an association, but they do not necessarily demonstrate that ADRs alone caused the observed changes in QoL.

Peripheral sensory neuropathy, a condition that may be associated with HIV infection and certain antiretroviral regimens, was examined in the study by Adem et al. (2019). Among 359 adult patients with HIV at Gondar University Teaching Hospital, exposure to a didanosine-containing regimen was the strongest reported predictor of peripheral sensory neuropathy (AOR = 4.33), followed by age over 40 years, antituberculosis treatment, and taller stature. Peripheral sensory neuropathy may be associated with pain, tingling, and limitations in daily functioning, which could adversely affect patients' quality of life. However, the extent to which these functional limitations were directly associated with QoL should be interpreted according to the outcomes measured in the original study. These findings align with a study by Chukwurah, (2021) in a study of 179 adults living with HIV in the United States, reported associations between symptom burden, including pain, fatigue, and depressive symptoms, and overall functioning. Social support and the number of comorbidities were also identified as factors associated with symptom burden. Overall, these findings suggest that neurological symptoms, broader symptom burden, and psychosocial factors are relevant to patients' functioning and well-being, although they do not establish that all reported symptoms were caused by ART-related adverse drug reactions.

ADR reporting is another important consideration in pharmacovigilance. Zondi & Naidoo, (2022), in a cross-sectional and retrospective comparative study conducted in the eThekwini Metropolitan Area, South Africa, reported that 72% of patients reported experiencing at least one ADR. The types of reactions reported by patients, including skin rash (11%), differed from those most frequently documented in medical records, namely anaemia (29%) and cardiovascular conditions (23%). This discrepancy suggests that patient-reported experiences and routine clinical documentation may not fully correspond. From a pharmacovigilance perspective, incomplete or inconsistent documentation may limit the comprehensiveness of available safety information. However, the study's findings should not be interpreted as direct evidence that reporting discrepancies caused poorer QoL or delayed the detection of QoL-related outcomes. The report that 36 patients required hospitalization further highlights the clinical relevance of monitoring and documenting suspected ADRs, although the implications for QoL require direct assessment.

Across the reviewed studies, ADRs, neurological symptoms, and broader symptom burden were associated with different aspects of patients' functioning and well-being. These findings suggest that the experience of suspected ADRs may extend beyond physical symptoms and may be relevant to psychological and social functioning. However, the available evidence does not establish that all QoL domains are consistently affected or that the same pattern occurs across all included studies. The hospitalization cases reported by Zondi & Naidoo, (2022) underscore the clinical importance of recognizing and

documenting suspected ADRs. Proactive monitoring and appropriate assessment may help healthcare professionals identify and manage potential safety concerns; nevertheless, the extent to which such measures prevent more serious outcomes or improve QoL requires further evaluation.

Overall, the four studies reviewed suggest that adverse drug reactions (ADRs), peripheral neuropathy, and symptom burden are associated with patients' functioning and quality of life. Physical symptoms, such as pain and neuropathy, as well as psychological symptoms, including anxiety and depression, may be relevant to patients' overall well-being. However, the available evidence does not establish ADRs as causal mediators linking antiretroviral use to QoL, and the strength of these associations may vary according to study design, patient characteristics, and outcome measurement. Furthermore, the discrepancy between patient-reported ADRs and those documented in clinical records, as reported by Zondi & Naidoo, (2022) highlights the importance of strengthening ADR reporting and documentation. Integrating patient-reported experiences with healthcare professionals' assessments may support more comprehensive pharmacovigilance and patient-centered HIV care.

1.3 The Relationship Between Antiretroviral Therapy Adherence and Quality of Life in HIV/AIDS Patients

Consistent adherence to antiretroviral therapy (ART) is an important component of HIV/AIDS management. However, the relationship between adherence and quality of life (QoL) is complex and may vary according to clinical, psychosocial, and healthcare-related factors. A cross-sectional study involving 240 patients at Mizan-Tepi Teaching Hospital in southwestern Ethiopia found that low adherence to highly active antiretroviral therapy (HAART) was independently associated with poorer QoL scores (AOR = 0.40; 95% CI: 0.19–0.86). Good current health status (AOR = 3.38) and family support (AOR = 3.12) were also positively associated with QoL. These findings suggest that adherence, health status, and family support are relevant factors associated with QoL. Nevertheless, because the study used a cross-sectional design, it cannot establish whether low adherence preceded poorer QoL or whether other factors contributed to both outcomes (Desta et al., 2020).

Several studies conducted in Indonesia have also reported associations between ART adherence and QoL, although the findings should not be interpreted as evidence of direct causation. A study involving 118 patients at the VCT Clinic of Ratu Zalecha Regional General Hospital in Martapura found statistically significant associations between treatment adherence and QoL ($p = 0.005$), as well as between adherence and treatment retention ($p = 0.003$). These findings indicate that adherence, QoL, and retention in care were related in the study population; however, the reported associations do not establish that adherence directly

improves QoL or causes better treatment retention (Raziansyah & Pertiwi, 2024). Similarly, a study involving 98 people living with HIV in Jakarta reported statistically significant associations between ART adherence and QoL ($p = 0.001$), opportunistic infections and QoL ($p = 0.030$), and family support and QoL ($p = 0.019$). These findings suggest that clinical and social factors may be jointly associated with QoL. However, the reported results alone do not establish a causal sequence in which non-adherence leads to opportunistic infections and subsequently causes poorer QoL(Saputra et al., 2023).

Riyani (2024), further highlights the potential relevance of psychosocial factors. In a study involving 133 patients at the Pita Aruna Outpatient Clinic of PKJN Dr. H. Marzoeki Mahdi Mental Health Hospital in Bogor, ART adherence ($p = 0.032$) and social stigma ($p = 0.004$) were statistically associated with QoL. Together with employment status, these variables reportedly accounted for 12.2% of the variance in QoL. This finding suggests that QoL may be associated with factors extending beyond medication-taking behavior, including social and economic circumstances. Similarly, a study involving 63 patients at the Sehat Peduli Kasih Foundation in Semarang reported an association between treatment adherence, family support, and QoL ($p = 0.000$ as reported in the original study). Treatment adherence was identified as the strongest variable in the reported analysis compared with family support, marital status, and educational level. The reported confidence interval was 6.670–117.537. These findings support considering psychosocial circumstances alongside adherence when interpreting QoL outcomes; however, the strength and meaning of the reported estimates should be interpreted according to the original statistical model and the measures used.

Nevertheless, not all studies identified a statistically significant association between ART adherence and QoL. Rantepadang (2022), in a study involving 38 patients receiving care at the Airmadidi Community Health Center, reported that 52.6% of participants had low adherence according to the MMAS-8 questionnaire. The Spearman correlation test showed no statistically significant association between adherence and QoL ($p = 0.924$). The authors suggested that social, economic, and health-policy factors may warrant further investigation. Rahmawati (2020), in a prospective observational study conducted at several healthcare facilities in Samarinda, reported moderate-to-low adherence but no statistically significant association between adherence and QoL ($p \geq 0.05$). These findings indicate that the association between adherence and QoL is not consistent across all study populations and settings.

The differences in findings across studies may reflect methodological and clinical heterogeneity. Relevant considerations include sample size, participant characteristics, healthcare settings, treatment duration, ART regimens, comorbidities, psychosocial circumstances, and access to healthcare services. Differences in adherence assessment methods, QoL instruments, outcome definitions, and statistical adjustment for potential confounders may also contribute to the variation in reported associations.

For example, the small sample size in Rantepadang (2022), may have limited the study's statistical power to detect an association, although this possibility cannot be established from the non-significant result alone. Therefore, the findings from individual studies should be interpreted in their methodological context and should not be generalized uncritically to all people living with HIV/AIDS. Several biological and clinical pathways may plausibly explain the relationship between adherence and QoL. Consistent ART use is an important component of achieving viral suppression, while treatment effectiveness and patients' health status may be related to the occurrence of opportunistic infections, functional limitations, and overall well-being. However, these pathways were not necessarily measured or tested directly in every study included in this review and should therefore be considered plausible explanations rather than conclusions established by the entire evidence base. Similarly, family support may be associated with both adherence and QoL, but the extent and direction of these relationships may vary across populations and social contexts.

Overall, the reviewed studies suggest that ART adherence and QoL are related, but the strength and statistical significance of this association vary across settings. Clinical status, family support, stigma, and other contextual factors may also be relevant to patients' QoL. Because most of the available evidence is observational and several studies use cross-sectional designs, causal relationships cannot be established consistently. Future prospective studies with adequate sample sizes, clearly defined outcome measures, and appropriate adjustment for confounding factors are needed to clarify the temporal relationship between adherence and QoL. From a clinical perspective, these findings support an integrated approach to HIV care that addresses medication adherence alongside clinical needs and psychosocial support, rather than focusing exclusively on medication-taking behavior.

1.4 Integrating the Relationship Between ADRs, Treatment Adherence, and Quality of Life from a Pharmacovigilance Perspective

When adverse drug reactions (ADRs), antiretroviral therapy (ART) adherence, and quality of life (QoL) are considered together, the reviewed evidence suggests that these factors are interrelated. Moses et al. (2025) reported that 76% of 312 patients receiving ART experienced ADRs, of which 76.6% were classified as definitely preventable. Significant drug interactions were also associated with a higher likelihood of ADRs. These findings highlight the importance of identifying potential drug-related problems and strengthening ADR monitoring and reporting.

A study conducted by (Weldesenbet et al., 2022) reported an association between adherence status and the timing of ADR occurrence, While Gelaw et al. (2018) found that some patients used non-adherence as a coping strategy for treatment-related discomfort. Together, these findings suggest that ADRs and adherence warrant concurrent assessment. However, the proposed bidirectional relationship should be

interpreted cautiously, as differences in study design and potential confounding factors limit causal conclusions. Although most ADR events in the Weldesenbet et al. (2022) study occurred during the first year of ART, this finding supports attention to early monitoring rather than establishing that all patients face the same level of risk.

Wigatiningtyas (2026), reported reductions in gastrointestinal and neuropsychological ADR measures and improvements in several QoL domains following eight weeks of vitamin D supplementation in a pre–post study of 32 patients. However, without an adequate comparison group, these changes cannot be attributed solely to the intervention. The findings should therefore be considered preliminary evidence requiring further evaluation.

The importance of patient involvement in pharmacovigilance is also supported by Zondi & Naidoo (2022), who identified discrepancies between ADRs reported by patients and those documented in medical records. Such discrepancies suggest that routine documentation may not fully capture patients' experiences. Integrating patient-reported symptoms with healthcare professionals' assessments may therefore improve the completeness of ADR information.

From the perspective of Indonesian patients, a study from Raziansyah & Pertiwi (2024) reported associations between adherence, QoL, and treatment retention, while (Riyani, 2024) identified associations involving adherence, social stigma, and QoL. These findings indicate that clinical and psychosocial factors should both be considered in HIV care.

Overall, the findings of this review suggest that adverse drug reactions (ADRs), antiretroviral therapy adherence, and quality of life (QoL) are interrelated aspects of HIV/AIDS management. However, the strength and direction of these relationships may vary across populations and study designs, and the available evidence does not establish a universal causal relationship among these factors. From a pharmacovigilance perspective, integrating systematic ADR monitoring, patient-centered reporting, adherence assessment, and QoL evaluation may support more comprehensive and individualized HIV care. Early identification and appropriate management of suspected ADRs are important priorities, although their effects on long-term adherence and QoL require further evaluation. Future prospective studies and well-controlled interventions are needed to clarify these relationships and assess the effectiveness of integrated pharmacovigilance strategies.

Conclusion

This systematic review of 21 studies suggests that adverse drug reactions (ADRs), antiretroviral therapy (ART) adherence, and quality of life (QoL) are

interrelated aspects of HIV/AIDS management. The reviewed evidence indicates that ADRs are associated with treatment non-adherence and poorer QoL, while ART adherence is generally associated with better QoL. However, these associations are not consistent across all studies and may vary according to patient characteristics, healthcare settings, study designs, and measurement methods. Although one study reported that patients experiencing ADRs had substantially higher odds of non-adherence (AOR = 5.33; 95% CI: 1.95–14.57), this finding should be interpreted within the context of the individual study and does not establish a causal relationship. Similarly, the available evidence does not conclusively demonstrate that ADRs directly cause QoL deterioration or that adherence alone determines patients' QoL. From a pharmacovigilance perspective, these findings support integrating systematic ADR monitoring, patient-centered reporting, adherence assessment, and QoL evaluation into comprehensive HIV care. Nevertheless, the effectiveness of such integrated strategies requires further evaluation. Future prospective studies and well-controlled interventions are needed to clarify the temporal and potential causal relationships among ADRs, ART adherence, and QoL, while accounting for clinical, sociodemographic, and psychosocial factors.

Recommendations

Healthcare providers should strengthen proactive ADR monitoring, improve patient-centered reporting, and integrate adherence support with clinical and psychosocial care to prevent treatment interruption and improve quality of life among people living with HIV/AIDS.

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