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Advanced HIV disease management and patient outcomes in rural setting - Malawi: a retrospective cohort study

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Abstract

Introduction Advanced HIV disease (AHD) is increasingly becoming a threat to the survival of people living with HIV. Many countries, including Malawi, have adopted and adapted World Health Organization AHD management guidelines to manage the country's HIV cohort better. However, literature regarding adherence to these guidelines and the treatment outcomes remains limited. Therefore, we describe AHD management and patient outcomes at two rural hospitals in Southern Malawi.

Methods We conducted a retrospective cohort study at Neno District and Lisungwi Community Hospitals in Neno District, Malawi. We extracted data from inpatient files, patients' manual charts referred to as "Mastercards" for outpatients attending Integrated Chronic Care Clinic (IC3) and from Electronic Medical Records (EMR) between January 2022 and December 2022. IC3 is a specialized clinic for people with chronic diseases including HIV, AHD and Non-communicable diseases. We used counts and percentages for all categorical variables and median and Interquartile range (IQR) for all continuous variables.

Results During the study period, 343 HIV patients were hospitalized, of which 9.8% ($n=34$) were new HIV infections. Of these, 50.4% ($n=173$) had AHD, and 64.2% ($n=111$) were admitted primarily due to infectious diseases. Tuberculosis (58.6%, $n=65$) was the leading cause of admission. Of 173 hospitalized and classified as AHD, 75% had CD4 ordered, but only 43% ($n=74$) were done. The viral load test was ordered for 34% ($n=59$),) and only 28.8% ($n=17$) were done. TB LAM and CrAg tests were ordered for 64.2% ($n=111$) and 59.5% ($n=103$) of which 69.4% and 72.8% were done, respectively. Among 146 IC3 AHD clients, 46%, 47%, 42% and 40% had CD4, viral load, TB LAM and CrAg tests done, respectively. Overall, 17.9% ($n=31$) of inpatients with AHD died compared to 2.4%($n=4$) among HIV patients without AHD.

Conclusions We found sub-optimal adherence to management guidelines for patients with AHD, with higher deaths reported compared to those without AHD. Therefore, strengthening adherence to AHD management guidelines through quality improvement initiatives and increased availability of diagnostic resources could potentially improve health outcomes for people living with HIV. Further studies should explore patients' perspectives on the quality of AHD clinics.

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Keywords Human immunodeficiency virus, Advanced HIV diseases, Management guidelines, Treatment outcomes, Hospitalization, Integrated chronic care clinic

Introduction

The Joint United Nations Program on HIV/AIDS (UNAIDS) estimated that over 39 million people were living with Human Immunodeficiency Virus (HIV) in 2023, of which 1.3 million were new infections [1]. In the same year, it was estimated that 86% of people living with HIV knew their status, with 76% receiving treatment and 71% virally suppressed [1]. HIV prevalence is region-specific, with eastern and southern Africa having the highest share of the global burden, with over 20 million people as of 2022 and an estimated 260,000 deaths annually [1, 2]. Despite having increased access to antiretroviral therapy (ART) in many Lower and Middle-Income Countries (LMICs), many HIV-infected inpatients continue to present late to care with advanced HIV disease (AHD) [3].

Advanced HIV Disease is a CD4 cell count of less than 200 cells/mm3 or World Health Organization (WHO) clinical stages 3 and 4 in anyone above 5 years [4–6]. All children younger than 5 years are considered to have AHD, given their heightened risk of disease progression and mortality [7]. Ample literature suggests that individuals with AHD are at a greater risk of experiencing severe illnesses and mortality compared to those with a non-advanced form of the disease [8–11]. Being a rural resident, alcohol consumption and not knowing own HIV status in case positive increases the risks of developing AHD [12, 13]. Another study done in Malawi, South Africa and Kenya found that being male and not on ART were more likely to be classified as having AHD [14]. In addition, older people (> 65 years) and those with malnutrition are at more risk of developing AHD compared to the general population [9, 15]. Studies have also found that people with social support and those without comorbidities are less likely to be classified as having AHD [12, 16].

Tuberculosis (TB) remains the most common serious opportunistic infection in people with HIV infection and the leading cause of death among those hospitalized and even worse among those with AHD [17]. In Guinea, TB accounted for 71% of the total deaths among those hospitalized classified as having AHD [18]. Similar findings were reported in Rwanda, where people with advanced HIV disease had higher death rates and higher chances of treatment failure as compared to those without AHD. However, no differences in viral load testing and viral suppression were observed [19]. A systematic review of 29 cohorts indicated that 18.8% of patients with AHD were re-hospitalized after discharge, and 14.1% died post-discharge, with a higher mortality rate in studies from African countries than in the United States of America [17].

In Malawi, a country in southern Africa, estimates from the Joint United Nations Program on HIV/AIDS (UNAIDS) indicated that nearly 1 million people in 2023 were living with HIV, accounting for 8.9% of the country's total population [20]. This makes Malawi among the countries with the highest HIV prevalence rates in Sub-Saharan Africa. In the same year, UNAIDS estimated 11,931(10131-14,581) HIV-related deaths and about 1.4 (1.2–1.6) million AIDS-related illnesses occurred in the country [20]. According to the 2020–2021 Malawi Population-based HIV Impact Assessment Survey (MPHIA), the annual HIV incidence among adults (those aged 15 years and older) in Malawi remains high (0.21%), over 97% of those with known HIV status are on ART, and over 96% of those on ART have suppressed viral load [21]. A survey from three districts by Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) found AHD prevalence to be 40% among people living with HIV in Malawi [22]. Screening for AHD among People Living with HIV (PLWHIV) remains low in most parts of the country due to the limited availability of resources as well as inadequate knowledge among healthcare workers [23].

In 2017, the Malawi HIV guidelines included AHD adapted from WHO guidelines and outlined how advanced HIV disease patients should be managed, including a diagnostic package of CD4 testing, viral load testing, CrAg and TB LAM screening [24, 25]. To improve AHD outcomes, adherence to all treatment protocols—such as cotrimoxazole, TB preventive therapy, treatment for diagnosed Cryptococcal meningitis and TB, viral load testing, and CD4 count testing remains essential and be conducted [24–26]. Understanding adherence to national guidelines for AHD management is essential, as it impacts patient outcomes, yet data on adherence and outcomes remains limited in Malawi [27].

Since 2007, Partners in Health (PIH), an international organization, has accompanied the Ministry of Health in providing access to quality health care in Malawi. In Neno district, the organization supports the Ministry of Health (MoH) for specialized clinics called integrated chronic care clinics (IC3) which include people living with HIV and those with Non-Communicable Diseases [28]. In 2021, the Ministry of Health trained clinicians and nurses and rolled out a designated AHD register and a form for hospitalized AHD patients. IC3 clerks were oriented by the ART coordinator and worked together to ensure that all AHD cases were reported. There is still a paucity of data on the adherence of health workers to

guidelines and how much this influences the outcome of patients. Therefore, we aimed to assess the adherence of healthcare workers to guidelines, management and outcomes of patients with AHD in Neno district, Malawi.

Methods

Study design and settings

We conducted a retrospective cohort chart review study between January 2022 to December 2022 at Neno District Hospital(NDH) and Lisungwi Community Hospital(LCH). Both hospitals are located in Neno, a district in the southern part of Malawi and are the major hospitals serving a population of 153 132 people as of 2023 with a projection of a 4% annual growth rate [29]. The district comprises 13 primary-level health facilities and two secondary-level hospitals, while tertiary-level care is accessed via referral to Queen Elizabeth Central Hospital in Blantyre, approximately four hours away by road. NDH is a 172-bed hospital that handles an average of 4,500 admissions annually, whereas LCH has 120 beds and manages around 4,000 admissions per year [30]. Our study focused on the two secondary-level hospitals, as they provide inpatient care, unlike the 13 health centres, which primarily offer outpatient services. Neno district has one of the highest HIV prevalence in Malawi reported at 11.5% [31]. While the district has several implementing partners, Partners In Health (PIH), support more on HIV to ensure increased access to quality health care for the people of the district. PIH is also helping improve the lives of people with HIV and has even developed special clinics called integrated chronic care clinics (IC3) which include people with HIV so that they can receive quality care and be easily followed up. The majority of the people in Neno, just like many Malawians, live in absolute poverty, spending less than 1 USD per day [32]. Access to electricity remains limited as only about 14.2% of the grid's population is connected [33].

Study population and sample size

We did not calculate a specific sample size but used all patient files available within our study period. We included 343 inpatient files and 146 patient charts referred to as "Master cards" for IC3 clients. These records encompassed patient data from individuals admitted to Neno and Lisungwi hospitals and those attending IC3 clinics for advanced HIV disease (AHD) between January and December 2022.

Data collection

We collected data by extracting information from inpatient files, patient master cards available at the ART clinics, and the OpenMRS electronic medical records system (EMR). Firstly, we accessed the files of all patients admitted between January 2022 and December 2022 at the two hospitals and isolated records with HIV-positive test results. We excluded files for those aged five and below as they were already classified as having AHD, and those not from Neno districts. For IC3 data, we reviewed the patient ART register and extracted clients classified as AHD with their corresponding mastercards who attended clinics in our study period. We matched the IC3 data with inpatient data to ensure that we didn't duplicate patients in our study. From both the mastercards and inpatient files, we collected demographic data including sex and age, admission date, diagnosis, other existing conditions, patient outcome and discharge date. Further data variables including viral load count and CD4 cell count were extracted from EMR. We captured all information from the inpatient files and mastercards into a CommCare application and later exported it to Excel for data analysis.

Data management and analysis

We imported Excel data into Stata 14 for data cleaning and analysis and used descriptive statistics to analyze and summarize the data. We calculated i). the proportion of AHD among the inpatients based on WHO HIV staging and the Malawi HIV treatment guidelines [34], ii) the proportion of AHD cases managed according to national AHD management protocol to access adherence to the protocols. iii) the proportions of inpatients who were discharged alive, died and those who were referred out, and iv) the proportions of those attending outpatient services through IC3 classified as discharged, defaulted, died or transferred out. We had less than 5% of data missing as such we applied multiple imputations by using the median for continuous variables and the most frequent value for categorical variables to deal with the missingness.

Ethical considerations

This study was approved by the National Health Science Research Committee (NHSRC) in Malawi with protocol number 23/04/4063 titled "Evaluation of Clinical Care in PIH-supported sites in Malawi." No consent was obtained from the study participants as we used only the patient charts, including registers, EMR and MasterCard. Authorities at Neno District Hospital and Lisungwi Community Hospital approved the conduct of the study.

Results

During the study period, 343 HIV-positive patients were hospitalized, of which 51.0% ($n = 175$) were admitted to Neno District Hospital (NDH) and the rest to Lisungwi Community Hospital (LCH). Of those at NDH, the majority, 69.1% ($n = 121$), were female and three for every four people (76.0%, $n = 133$) were aged between 15 and 50 years with a median age of 40 years. The situation

was similar in LCH, except for the sex distribution. There was a statistically significant difference in the proportion of males and females with a p-value of 0.002. In the same period, 146 AHD clients attended IC3, where 52.7% ($n=77$) were at LCH and 47.3% ($n=69$) were at NDH. The majority were female ($n=103$, 70.5%) and aged between 15 and 50 years old ($n=105$, 71.9%) (Table 1).

Advanced HIV disease among admitted patients and those newly diagnosed

Of the 343 hospitalized, 9% ($n=32$) were new HIV infections and half (50.4%, $n=173$) were classified as having AHD. Among those new HIV infections, 53% ($n=17$) were classified as having AHD. Infectious diseases were a leading cause of admission, accounting for 64% of the total cases as compared to non-infectious diseases (35.8%) with the difference being statistically significant (p-value 0.003). Of these, TB was the highest contributor (58.6%, $n=65$). The proportion of TB on admission was higher in Lisungwi Community Hospital (76.2%, $n=48$) compared to Neno District Hospital (35.4%, $n=17$) (Table 2).

Cases managed according to the AHD guidelines

Among those hospitalized and classified as AHD ($n=173$), 75% had CD4 ordered, of which 56.9% ($n=74$) were done, while among the 146 clients in IC3, 45.9% ($n=67$) had CD4 results. For viral load, 34% ($n=59$) of inpatients with AHD had the test ordered, and only 28.8% ($n=17$) were done. While among the IC3 clients, 47% ($n=68$) had viral load test results. On TB lam, 64.2% ($n=111$) of the admitted AHD patients had a test ordered, of which 69.3% ($n=77$) were done, and among the IC3 clinic, 42.4% ($n=62$) had results. Lastly, 59.5% ($n=103$) of the patients had CrAg tests ordered, with 72.8% ($n=75$) done, while for IC3 clients, 40.4% ($n=59$) had their results (Table 3).

Preventive therapy distribution, viral load and CD4 follow-up for IC3 clients in AHD clinic

Of the 146 clients attending the IC3 AHD clinic, 82.2% ($n=120$) received CPT in 2022, and 25% ($n=37$) received TpT. Additionally, 25% ($n=37$) of clients received both CPT and TpT during their visits that year. Viral load follow-up was conducted for 64 clients (43.8%) in 2022, with 54.7% ($n=35$) undergoing both an initial viral load test and a follow-up test. Regarding CD4 counts, only 4.1% ($n=6$) of clients had CD4 cell count follow-ups, of which 4 clients completed both initial and follow-up CD4 checks.

AHD patient outcomes at NDH and LCH from January to December 2022

Among the 173 inpatients with AHD, 17.9% ($n=31$) died during admission time, 9.8% ($n=17$) were transferred out, and the majority, 72.2% ($n=125$), were discharged alive. Among those hospitalized without AHD, four people died (2.4%) and the majority (92.4%, $n=157$) were discharged alive (Fig. 1).

Among 146 clients attending the AHD IC3 clinics in 2022, 11(7.5%) clients defaulted, another 11(7.5%) were transferred out, 10(6.9%) did not have the outcome

Table 1 Demographic characteristics of HIV clients hospitalized at NDH and LCH and AHD clients who attended IC3 in 2022

		Hospital			
	Categories	**Neno District Hospital *n*(%)**	**Lisungwi Community Hospital *n*(%)**	**Total**	***P*-value for Chi-Square test**
Inpatients	Number of patients	175 (51.0)	168 (49.0)	343	
	Sex				
	Males	54(30.9)	80(47.0)	134(38.8)	0.002
	Females	121(69.1)	88(53.0)	209(61.2)	
	Age[1]	Median 40(18)	Median 41(17.5)		
	< 15	6(3.4)	2(1.2)	8(2.3)	0.207
	15–50	133(76.00)	133(79.2)	266(77.6)	
	> 50	36(20.6)	33(19.6)	69(20.1)	
Outpatient IC3 clinic	**Number of AHD patients**	**69 (47.3)**	**77 (52.7)**	**146**	
	Sex				
	Males	21(29.0)	22(27.3)	43(29.5)	0.813
	Females	48(71.0)	55(72.7)	103(70.5)	
	Age[1]	Median 27(20)	Median 38(21)		
	< 15	10(17.0)	8(10.4)	18(12.3)	0.190
	15–50	52(75.4)	53(68.8)	105(71.9)	
	> 50	7(7.6)	16(20.8)	23(15.8)	

Median (Inter quartile Range - IQR)

Table 2 Proportion of AHD among admitted patients and among newly diagnosed

Categories	Neno District Hospital *n*(%)	Lisungwi Community Hospital *n*(%)	Total (Percent Among AHD inpatients)	*P*-values
Number of AHD cases	69(39.9)	104(60.1)	173	0.013
Number of new infections	15	17	32	
Number of new infections with AHD	3(4.6)	14(13.5)	17	
Sex				
Males	27(44.9)	55(52.9)	82	0.131
Females	42(55.0)	49(47.1)	91	
Age				
< 15	3(4.4)	2(1.9)	5(2.9)	0.182
15–50	45(65.2)	76(73.1)	121(69.9)	
> 50	21(30.4)	26(25.0)	47(27.2)	
Primary cause of admission among AHD population				
Infectious Diseases	**48(69.6)**	**63(60.6)**	**111(64.2)**	0.081
TB	17(35.4)	48(76.2)	65(58.6)	
Sepsis	9(18.8)	6(9.5)	15(13.5)	
Pneumonia	4(8.3)	5(7.9)	9(8.1)	
Others	18(37.5)	4(3.2)	22(19.8)	
Non-infectious diseases	**21(30.4)**	**41(39.4)**	**62(35.8)**	

Table 3 Tests ordered and tests done among AHD inpatients and AHD IC3 clients

Test Name	Category	Total number of patients	Number of Test Ordered	Number of Tests done
CD4	In patient	173	130(75.1%)	74(56.9%)
	IC3 clients	146	-	67(45.9%)
Viral load	Inpatients	173	59 (34.1%)	17(28.8%)
	IC3 clients	146	-	68(46.6%)
TB Lam	In patient	173	111(64.2%)	77(69.3%)
	IC3 Clients	146	-	62(42.4%)
CrAg	Inpatient	173	103(59.5%)	75(72.8%)
	IC3 clients	146	-	59(40.4%)

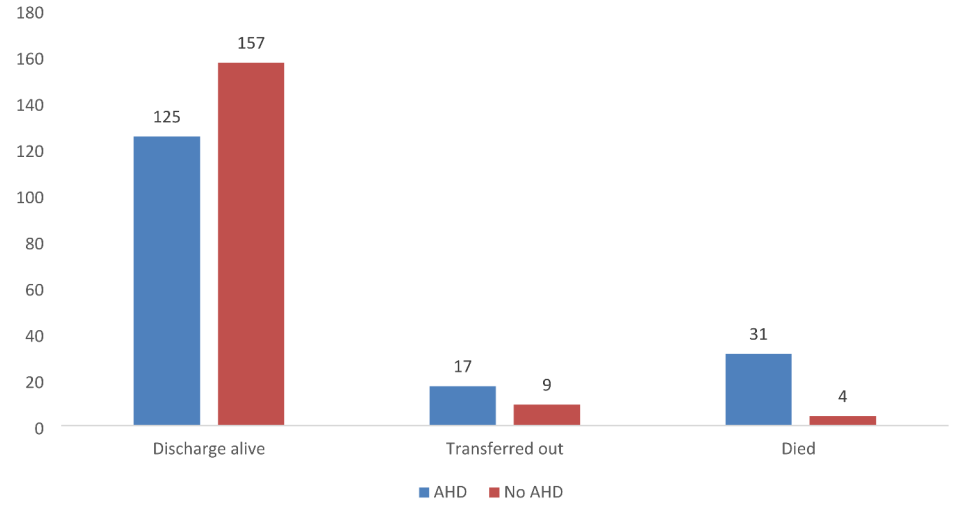

Fig. 1 Patient outcome for AHD and without AHD between January and December 2022

recorded, and 1(0.7%) died in the course of follow-up. Overall, 47.3% ($n=69$) were discharged from the AHD clinic to a normal routine clinic while the rest were still being managed.

Discussion

Our study describes the management and outcomes of patients with AHD at two rural hospitals in Neno district, Malawi. We found that one in ten HIV-admitted patients were new infections and half of those admitted were classified as having AHD. Infectious diseases were the main causes of admissions with TB being the highest contributor. We also found sub-optimal adherence to management guidelines for patients with AHD for both inpatients and IC3 clinic clients. Finally, the outcomes of those with AHD were worse as compared to those without AHD.

We found that half of all HIV patients admitted to two hospitals in 2022 were classified as having AHD, and about one in ten admitted patients were newly diagnosed. Similar findings have been reported at Kamuzu Central Hospital (KCH) in Lilongwe, Malawi where 53% of admitted HIV patients had AHD, and 10.8% of all admitted HIV patients were newly diagnosed [27]. Our two hospitals and KCH are both referral hospitals hence most patients are tested for HIV at the referring health center, resulting in fewer patients arriving without prior testing, except those who go directly to the referral hospitals. Despite having more men than women in IC3 AHD clinic at LCH, this difference wasn't statistically significant. Possible explanations would be time of presenting oneself at the hospital with men reporting late for treatment and low adherence to treatment as compared to women who report early once infected with the disease [2]. The proportion of AHD among admitted HIV patients in our study (50%) was much lower than what was reported in Kenya and the Democratic Republic of Congo (83.7%) and (97.3%) respectively [3]. The differences in proportions may be explained by variations in study sample selection, as our study included all admitted patients, not just those in medical or surgical wards, along with differences in hospital admission criteria, and in the management and follow-up of HIV patients between countries.

Of the infectious diseases recorded, tuberculosis was the highest contributor to admissions among HIV patients in our study. This is not strange, considering that there is enough literature on HIV-TB comorbidity [8, 10, 35–37]. Several other studies have shown the link between HIV and TB; therefore, deliberately, measures have to be put in place to ensure the integration of TB and HIV services, including screening of TB among the HIV cohort at household, community and facility levels. Proactive TB screening through programs such as Community Health Workers [38], Screening for Health and Referrals in the Community (SHARC) and Screening for Health and Referrals in the Facility (SHARF) at the facility [39, 40] could potentially increase early detection of TB among the HIV cohort.

We also observed suboptimal adherence to the recommended guidelines for CD4, viral load, TB LAM, and CrAg testing. Although over half of the individuals had all necessary tests ordered—except for viral load, where only one-third were requested—less than two-thirds of these tests were done. This could be explained by several reasons, including the stock-out of testing materials, knowledge gaps, and limited resources as suggested by a study done at Rumphi District Hospital, Malawi [23]. Our study suggests that one in four patients is not receiving the essential tests for effective management. While our finding differs from a study done in Lilongwe, where up to 97% could access the tests, it is in concordance with many other studies done in rural areas [3, 36, 41, 42]. Further quality improvement projects should be implemented to ensure that tests that are ordered are done and that the results are used to inform decisions.

In our study, the mortality was higher among those hospitalized and classified as an AHD group compared to the non-AHD group. Similar findings have been reported in several other studies done in Kenya, Sierra Leone, Guinea and DRC [9, 10, 12, 13]. The default rate among clients remaining in the AHD clinic was 7.9%, potentially due to strong follow-up systems for HIV patients in Neno, supported by IC3 clinics and community health workers, as demonstrated in previous studies [38, 43, 44]. Future studies should explore the quality of AHD clinic services from the patient perspective and also assess the knowledge, attitude and practice of healthcare workers towards AHD management.

Our study had some limitations. Firstly, as a retrospective study, we found some missing data. However, this was less than 5%, and we used imputation, applying the median for continuous variables and the most frequent value for categorical variables to deal with the missingness. Secondly, the data collection relied on facility records and may not capture all factors, such as individual behaviours and perceptions. Future studies should explore these among healthcare workers managing hospitalized AHD patients and those in AHD clinics. While our study may not be generalizable to urban areas as it was done in one of the remote areas in the country, its results are helpful for similar settings due to common challenges such as stock-out of testing materials. In addition, we did not calculate person-time for the study participants, as this is very important, it should be considered in future studies.

Conclusions

We found that half of the admitted patients had AHD, and TB as a leading cause of admission. We also found sub-optimal adherence to management guidelines for patients with AHD for both inpatients and IC3 clinic clients. Finally, death was higher among those admitted and classified as having AHD compared to those without AHD. We suggest quality improvement projects to ensure adherence towards management guidelines, which would improve treatment outcomes.

Abbreviations/acronyms

AHD	Advance HIV Diseases
ART	Antiretroviral Therapy
EMR	Electronic Medical Records
HIV	Human Immunodeficiency Virus
IC3	Integrated Chronic Care Clinic
IQR	Interquartile range
KCH	Kamuzu Central Hospital
LCH	Lisungwi Community Hospital
LMICs	Lower and Middle-Income Countries
MOH	Ministry of Health
MPHIA	Malawi Population-based HIV Impact Assessment Survey
NDH	Neno District Hospital
NHSRC	National Health Science Research Committee
PLWHIV	People Living with HIV
PIH	Partners in Health
SHARC	Screening for Health and Referrals in the Community
SHARF	Screening for Health and Referrals in the Facility
TB	Tuberculosis
UNAIDS	Joint United Nations Program on HIV/AIDS

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Author contributions

Authors' contributionsGM, MBA and BM conceptualized and designed the study. GM and MBA facilitated data collection. GM analyzed data. GM drafted the manuscript with assistance from MBA. BM, FM, JCDS and LT reviewed the draft manuscript. All authors reviewed the manuscript, provided input, and suggested additions and changes. MBA Provided final edits. All authors read and approved the final manuscript.

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Data availability

Data that supports findings of this study were uploaded to Zenodo and the access code is: 10.5281/zenodo.14502496.

Declarations

Competing interests

The authors declare no competing interests.

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