The Prevalence and Determinants of Depression and Anxiety Among Adolescents and Young Adults Living with HIV in the Nampula Province, Mozambique

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Abstract

Adolescents and young adults living with HIV (AYAHIV) in Mozambique represent a uniquely vulnerable demographic, faced with considerable challenges along the HIV care continuum, which are further compounded by their elevated risk of common mental disorders (CMDs). Despite this dual burden, and the purported deleterious treatment outcomes associated with this comorbidity, research in this context remains scarce. We examined the prevalence and determinants of depressive and anxiety disorder symptoms among AYAHIV in Nampula, Mozambique.

This study was informed by cross-sectional data from post-intervention surveys from the CombinADO study, a cluster randomized control trial conducted among 1,715 AYAHIV, aged 10 to 24 years, across 12 clinics in the Nampula Province, Northern Mozambique. 1,358 AYAHIV, aged 15-24 years, were included for analysis. We used logistic mixed effects models to assess factors associated with depressive and anxiety disorder symptoms.

Among Mozambiquan AYAHIV, 21.7% screened positive for depressive symptoms and 21.1% for anxiety symptoms, with higher rates of anxiety symptoms in females (22.33% vs 16.77%, p=0.035) and higher rates of depressive symptoms in those aged 15-19 years (24.63% vs 19.78%, p=0.034). Key risk factors for depressive symptoms included lower family social support (aOR=1.09, 95% CI: 1.01, 1.17) and higher internalized HIV stigma (aOR=1.33, 95% CI: 1.20, 1.48), while protective factors included being a high-school non-completer and below (aOR=0.32, 95% CI: 0.18, 0.57), higher ART adherence (aOR=0.98, 95% CI: 0.96, 1.00), and lower friend social support (aOR=0.87, 95% CI: 0.82, 0.92). For anxiety symptoms, risk factors included female sex (aOR=2.11, 95% CI: 1.34, 3.33), being in a non-cohabitating romantic relationship (aOR=1.73, 95% CI: 1.11, 2.71), and higher internalized HIV stigma (aOR=1.19, 95% CI: 1.08, 1.30). These findings contribute to the emerging body of evidence on the burden of CMDs among AYAHIV in SSA and Mozambique, underscoring the critical need for targeted mental health services in this setting.

Keywords: Adolescents and young adults living with HIV (AYAHIV), mental health, depression, anxiety, determinants, Mozambique.

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List of Abbreviations

ART	Antiretroviral therapy
AYAHIV	Adolescents and young adults living with HIV
CMD	Common mental disorder
cRCT	Cluster randomized control trial
GAD	Generalized anxiety disorder
HIV	Human Immunodeficiency Virus
IQR	Interquartile range
LMIC	Low-to-middle-income countries
PHQ-A	Patient Health Questionnaire Adapted for Adolescents
PID	Participant identifier
SES	Socio-economic status
SSA	Sub-Saharan Africa

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JOURNAL MANUSCRIPT

Introduction

Sub-Saharan Africa (SSA) remains the epicenter of the global HIV epidemic, bearing one of the highest burdens of HIV infections worldwide. Adolescents and young adults, who constitute 23% of the total SSA population, are disproportionately affected, with young women bearing a particularly heavy burden (UNAIDS, 2023; UNICEF, 2023). In 2023, 1.5 million adolescents and young adults aged 10 to 19 years were living with HIV worldwide, approximately 84% of whom reside in SSA, where HIV has emerged as the leading cause of mortality among individuals in this age group (UNAIDS, 2019; UNICEF, 2019; 2024; WHO, 2024). Compared to their adult and pediatric counterparts, adolescents and young adults living with HIV (AYAHIV) encounter more significant challenges along the HIV care continuum, which are further compounded by their elevated risk of common mental disorders (CMDs; Teasdale et al., 2021; Too et al., 2021). The growing comorbidity of HIV and CMDs among adolescents and young adults presents a significant public health challenge, one that remains largely unexplored in SSA, particularly in Mozambique. With an HIV prevalence rate of 13.2%, Mozambique emerges as a critical focal point, home to 1.8 million people living with HIV, 143,000 of whom are adolescents and young adults, who constitute over 30% of the total population (MISAU, 2020; National Institute of Statistics, 2017). While this dual burden of HIV and CMDs is a known challenge, specific data from the Mozambican context is scarce. The few existing local studies on AYAHIV have reported depression prevalence ranging from 7.1% - 11.7% and anxiety prevalence from 10.3% - 12.2% (Di Gennaro et al., 2022; Nguyen et al., 2023). These estimates, while significant, are lower than pooled estimates from other parts of SSA and globally, highlighting a potential evidence gap that this study aims to address (Zhan et al., 2024).

AYAHIV represent a notably vulnerable demographic, forced to navigate the complexities of managing a chronic, stigmatized, and transmittable disease, while simultaneously undergoing the developmental transition from childhood to adulthood (Laurenzi et al., 2020; Vreeman et al., 2017). Notably, in SSA, AYAHIV encounter significant barriers at the health system, interpersonal, and individual levels which hinder their engagement in HIV care, initiation of antiretroviral therapy (ART), uptake of HIV testing, and achievement of viral suppression (Falcao et al., 2021; National Institute of Statistics, 2023; Teasdale et al., 2021). AYAHIV also face various other challenges that impact treatment outcomes, including psychosocial issues, limited social support, and health system barriers such as mistrust of healthcare workers and stigma (Dow et al., 2014; Fair et al., 2018; Gichane et al., 2018; Kim et al., 2017).

These challenges are exacerbated by the overwhelming burden of CMDs, such as depression and anxiety, now recognized as the most widespread non-communicable disease among adolescents

(Askeer et al., 2020). As with HIV, this burden is particularly pronounced in SSA (Jörns-Presentati et al., 2021). Notably, up to 63% of CMDs arise during the critical transition from childhood to adolescence, a period marked by rapid physical and social changes that heighten mental health needs (Solmi et al., 2022; WHO, 2023). This is particularly relevant for AYAHIV, who face heightened mental health needs and a 2-3-fold increased risk of developing CMDs compared to their uninfected peers (Chibanda et al., 2016; Durteste et al., 2019; Lofgren et al., 2020).

The association between HIV and CMDs among AYAHIV is bidirectional. On the one hand, HIV serves as a significant psychosocial stressor that, when combined with ART side effects, persistent stigma, and its effects on the developing brain, increases the risk of CMDs (Ashaba et al., 2019; Kimera et al., 2020). On the other hand, CMDs exacerbate disease progression and unfavorable health outcomes in an already vulnerable AYAHIV population - a connection well documented internationally, but largely unexplored in Mozambique (Mandlate et al., 2023; Mutumba et al., 2016; Kim et al., 2015; Too et al., 2021). Comorbid CMDs have consistently been associated with accelerated disease progression, suboptimal ART adherence, reduced continuity in care and higher risks of substance abuse, sexual risk behaviors and suicidal ideations (Egbe et al., 2017; Kim et al., 2015; Nyongesa et al., 2018). Despite the significant mental health treatment gap and high HIV burden among adolescents in Mozambique, research in this context remains limited. Thus, a comprehensive understanding of the mental health challenges faced by AYAHIV, and the factors associated with this comorbidity, is vital for informing the development of targeted intervention in this context.

Compared to adults and children, AYAHIV in SSA are a particularly vulnerable group, disproportionately faced with the dual burden of HIV and CMDs and their associated challenges along the HIV care continuum during a critical developmental period. Despite their vulnerabilities, AYAHIV rarely feature in research on this topic within the Mozambiquan context, with limited research producing inconsistent findings (Di Gennaro et al., 2022; Nguyen et al., 2023). The existing evidence underscores the urgent need for greater research focus and targeted interventions especially in the context of Mozambique, where gaps in knowledge and mental health services remain significant. As such, this study aimed to measure the prevalence and determinants of depressive and anxiety symptoms among AYAHIV receiving HIV care in Nampula, Mozambique.

Methods

Study design

This study was informed by cross-sectional data from post-intervention surveys from the CombinADO study (NCT04930367), a cluster randomized control trial conducted across 12 clinics in the Nampula Province, Northern Mozambique, from September 2021 to July 2023. The study evaluated the effectiveness of a novel multicomponent intervention, compared to an enhanced standard of care, for improving HIV outcomes among AYAHIV over a 12-month follow-up period. The data for this dissertation were drawn from the 12-month post-intervention survey, which captured both the primary HIV-related outcomes of the trial and the secondary mental health outcomes analyzed here. As the measures of interest for this dissertation were collected only at the post-intervention time-point, the analysis was necessarily restricted to post-intervention data. It was approved by Columbia University Irving Medical Center Institutional Review Board and Comite Nactional de Bioetica para Saude of the Ministry of Health in Mozambique. Further details of the trial are described elsewhere (Mogoba et al., 2021).

Study population

1,715 AYAHIV, aged 10-24 years, actively seeking HIV care in the participating health facilities were enrolled in the parent study. Only those with a confirmed HIV-positive status, who were aware of their status and confirmed their willingness to comply with all study procedures were included. Individuals were excluded if they presented with any acute medical conditions that required immediate medical attention. All eligible participants provided informed consent, or assent and parental informed consent (for those younger than 18), prior to participation (Appendix G). The inclusion and exclusion criteria applied in this dissertation were consistent with those of the parent trial, with the sole modification being a restriction of the age range to 15–24 years, as participants aged 10–14 years were not assessed for depressive and anxiety symptoms in the parent study. As depression and anxiety were the primary outcomes of interest in the present dissertation, only participants aged 15–24 years, who had been assessed for these outcomes in the parent study, were included in the analysis, resulting in a final sample of 1,358 AYAHIV with available mental health data. Informed by previous research conducted in Mozambique, the study's sample size (n=1358) was found to be well-powered to detect effects of a magnitude similar to or smaller than those previously observed in the region (Di Gennaro et al., 2022; Nguyen et al., 2023).

Data collection

This research relied solely on secondary data from the CombinADO study which was collected using a survey questionnaire at 12-months post-intervention implementation. The questionnaire was translated to Portuguese and administered to AYAHIV by trained study staff using electronic tablets in private spaces within the respective health facilities (Mogoba et al., 2021).

Measures

Mental health measures

Patient Health Questionnaire Adapted for Adolescents (PHQ-A). The PHQ-A, a modified version of the PHQ-9, was employed to assess depression symptoms in AYAHIV (Appendix C). The PHQ-9 has demonstrated strong sensitivity and specificity in identifying depression through self-reports in both high- and low-to-middle-income countries (LMIC) (Anum et al., 2019; Makhubela & Khumalo, 2023). The questionnaire comprises nine items, each targeting specific depressive symptoms, which adolescents evaluate based on their experiences over the past two weeks, with anchors *Not at all, Several days, More than half the days*, and *Nearly every day*. Scores range from 0-27, with scores ≥10 indicating prevalence of major depression (Johnson et al., 2002).

Generalized Anxiety Disorder 7 (GAD-7). Anxiety symptoms were measured using the GAD-7 (Appendix C), previously validated for use in adults from LMICs as well as adolescents in both high-income and LMIC settings (Plummer et al., 2016). This seven-item tool prompts participants to rate their experiences of anxiety symptoms over the past two weeks on a four-point scale with anchors *Not at all, Several days, More than half the days*, and *Nearly every day*. Here, scores range from 0 to 21 and a score of ≥10 indicates prevalence of anxiety (Lovero et al., 2022).

Explanatory variables

Potential covariates for this analysis were selected based on their significance in previous literature conducted in SSA (Abebe et al., 2019; Boyes et al., 2019; Cavazos-Rehg et al., 2020; Dow et al., 2016; Ekat et al., 2020; Gadow et al., 2012; Gaitho et al., 2018; Kim et al., 2015; Mellins et al., 2012; Nguyen et al., 2023; Too et al., 2021; West et al., 2019). These included socio-demographic characteristics of AYAHIV, such as self-reported age, sex, level of education, employment history and socio-economic status (SES). We also considered psychosocial factors including social support, ART adherence - assessed via Wilson et al.'s (2016) three-item self-report scale (Appendix C) - and HIV-related stigma, measured using an adapted version of Berger's (2001) 40-item stigma scale (Appendix

C). Clinical characteristics included self-reported health status and viral suppression, assessed using real-time viral load testing and defined as a viral load of less than 50 copies/mL or less than 1000 copies/mL at 12 months post-intervention.

Statistical Analysis

Descriptive and Prevalence Analysis

All statistical analyses were conducted using R Studio (Posit Team, 2024). Descriptive statistics were calculated using median (interquartile range; IQR) and frequency (percent) for continuous and categorical variables, respectively. Simple bivariate analyses (Wilcoxon Rank Sum and Chi Squared tests) were used to compare group differences. Symptoms of anxiety and depression were treated as separate outcome variables.

Analysis of Determinants

To assess all possible determinants of depressive and anxiety symptoms, we fitted separate logistic mixed effects models, accounting for the random effects of each cluster level, i.e., the different clinics.

Univariable Analysis. We first ran univariable analyses to examine the relationship between each pre-specified determinant and our binary outcome variables, symptoms of anxiety and depression (defined as a score of ≥10 on the PHQ-A and GAD-7), separately.

Multivariable Analysis. Multivariable analyses were then run on the determinants with a p-value <0.10 in the univariable analysis for each separate outcome. Age group and sex were included in the multivariable analysis as a priori factors based on extensive evidence from prior literature identifying them as fundamental determinants of CMDs among AYAHIV (Too et al., 2021). Odds ratios and 95% confidence intervals were reported to evaluate the association between each determinant and mental health outcome, using separate models for each measure. A p-value <0.05 was considered statistically significant. The overall fit of each final model was assessed using a goodness-of-fit test, which indicated an adequate fit to the data ($p > 0.05$).

Results

Sociodemographic characteristics

A total of 1,358 participants, aged 15 to 24 years, were included for analysis (*Table 1*); 77% (n=1,048) were female and 23% male (n=310), with males being slightly younger than females (median 19 vs. 21 years, p<0.001). The overall median age was 20 years (IQR 18.0, 22.0), and 60% (n=814) of participants fell within the 20–24-year age range. Only 11% (n=149) of participants were high school completers and above. The majority of younger participants were high school non-completers and below (94% vs. 86%, p<0.001). Additionally, 81% (n=1,102) of participants had never been employed, a higher proportion of whom were females (84% vs. 72%, p<0.001) and younger individuals (90% vs. 75%, p<0.001).

Most participants were classified as either moderate (55%, n=751) or lower SES (24%, n=320), with more females (25% vs. 19%, p<0.001) and those aged 20 to 24 years (28% vs. 17%, p<0.001) in the lower SES category. Conversely, a higher proportion of males (29% vs. 19%, p=0.001) and younger individuals (28% vs. 17%, p=0.001) were categorized as higher SES. Furthermore, 40% (n=547) of participants were married or cohabitating, predominantly females (46% vs. 19%, p<0.001) and older individuals (54% vs. 19%, p<0.001). In contrast, more males (46% vs. 24%, p<0.001) and younger participants (47% vs. 17%, p<0.001) reported not being in a relationship. Social support was slightly higher among males (median 17 vs. 18, p=0.022) and those aged 15-19 years (median 18 vs. 19, p=0.008).

Overall, AYAHIV were highly adherent to ART (median 88; 77.8, 93.3). Notably, females (median 88 vs. 83, p=0.033) and older individuals (median 88 vs. 83, p<0.001) were slightly more adherent than their counterparts. Correspondingly, significantly more females achieved viral suppression at VL<50 copies/mL (62% vs. 54%, p=0.006) and VL<1000 copies/mL (87% vs. 78%, p<0.001), as did older individuals (VL<50 copies/mL: 55% vs. 64%, p=0.001, VL<1000 copies/mL: 81% vs. 88%, p<0.001). In contrast, males (median 37 months vs. 20 months, p<0.001) and younger individuals (median 24 months vs. 21 months, p<0.001) had a significantly longer median ART duration. Similarly, more males (42% vs. 22%, p<0.001) and younger individuals (37% vs. 20%, p<0.001) had been on ART for more than 48 months. Finally, participants were evenly distributed between the intervention groups, although there was a significant difference in the proportion of males and females (p=0.030) and age groups (p<0.001) in each intervention.

Table 1. *Demographic characteristics of AYAHIV in Nampula, Mozambique, by sex and age group*

Characteristic	**Overall,** n=1,358	**Male,** n=310, 23%	**Female,** n=1,048, 77%	**P-value**	**15-19,** n=544, 40%	**20-24,** n=814, 60%	**P-value**
Age [Median (IQR), years]	20 (18.0, 22.0)	19 (17.0, 22.0)	21 (18.0, 22.0)	**<0.001**[1]	18 (16.0, 19.0)	22 (21.0, 23.0)	**<0.001**[1]
Education attainment [n (%)]				0.410[2]			**<0.001**[2]
High School Completers and Above	149 (11)	38 (12)	111 (11)		33 (6)	116 (14)	
High school non-completers and below	1209 (89)	272 (88)	937 (89)		511 (94)	698 (86)	
Ever Employed [n (%)]				**<0.001**[2]			**<0.001**[2]
Never employed	1102 (81)	224 (72)	878 (84)		489 (90)	613 (75)	
Social support[3] [Median (IQR)]							
Overall	18 (15.0, 23.0)	17 (14.0, 22.0)	18 (15.0, 23.0)	**0.022**[1]	18 (14.0, 22.0)	19 (15.0, 23.0)	**0.008**[1]
Family social support	6 (3.0, 8.0)	6 (3.0, 8.0)	6 (4.0, 8.0)	0.657[1]	6 (3.0, 8.0)	6 (4.0, 8.0)	**0.004**[1]
Friend social support	12 (9.0, 16.0)	12 (9.0, 15.0)	12 (10.0, 16.0)	**0.005**[1]	12 (9.0, 15.0)	13 (10.0, 16.0)	0.099[1]
HIV Stigma[4] [Median (IQR)]							
Overall	21 (19.0, 23.0)	21 (19.0, 22.0)	21 (19.0, 23.0)	0.431[1]	21 (19.0, 23.0)	21 (19.0, 23.8)	0.483[1]
Anticipated	7 (5.0, 8.0)	7 (5.0, 8.0)	7 (5.0, 8.0)	0.724[1]	7 (5.0, 8.0)	7 (5.0, 8.0)	0.534[1]
Experienced	5 (5.0, 6.0)	5 (5.0, 6.0)	5 (5.0, 6.0)	0.504[1]	5 (5.0, 6.0)	5 (5.0, 6.0)	0.230[1]
Internalized	8 (7.0, 10.0)	8 (7.0, 9.0)	8 (7.0, 10.0)	0.177[1]	8 (7.0, 10.0)	8 (7.0, 10.0)	0.108[1]
SES Category[5] [n (%)]				**<0.001**[2]			**<0.001**[2]
Lowest	320 (24)	60 (19)	260 (25)		93 (17)	227 (28)	
Moderate	751 (55)	161 (52)	590 (56)		300 (55)	451 (55)	
Highest	287 (21)	89 (29)	198 (19)		151 (28)	136 (17)	
Relationship Status [n (%)]				**<0.001**[2]			**<0.001**[2]
Not in a relationship	397 (29)	143 (46)	254 (24)		256 (47)	141 (17)	
In a relationship but not married/cohabitating	414 (30)	107 (35)	307 (29)		182 (33)	232 (29)	
Married/cohabitating	547 (40)	60 (19)	487 (46)		106 (19)	441 (54)	
Perceived Health Status [n (%)]				0.257[2]			0.762[2]

Characteristic	**Overall,** n=1,358	**Male,** n=310, 23%	**Female,** n=1,048, 77%	**P-value**	**15-19,** n=544, 40%	**20-24,** n=814, 60%	**P-value**
Excellent/very good/good	1000 (74)	236 (76)	764 (73)		403 (74)	597 (73)	
Fair/poor	358 (26)	74 (24)	284 (27)		141 (26)	217 (27)	
Viral Load Results [n (%)]							
Undetectable (VL<50 copies/mL)	819 (60)	166 (54)	653 (62)	**0.006**[2]	300 (55)	519 (64)	**0.001**[2]
Suppressed (VL<1000 copies/mL)	1152 (85)	243 (78)	909 (87)	**<0.001**[2]	439 (81)	713 (88)	**<0.001**[2]
Adherence score[6], *n=1317* [Median (IQR)]	88 (77.8, 93.3)	83 (76.7, 93.3)	88 (77.8, 94.4)	**0.033**[1]	83 (76.7, 88.9)	88 (82.2, 94.4)	**<0.001**[1]
Duration on ART, n=1351[7] [median (IQR), months]	22 (9.2, 51.8)	37 (13.8, 93.4)	20 (8.4, 45.4)	**<0.001**[1]	24 (9.4, 78.5)	21 (9.1, 42.9)	**<0.001**[1]
Categorical months on ART [n (%)]				**<0.001**[2]			**<0.001**[2]
<12 months	420 (31)	67 (22)	353 (34)		165 (30)	255 (31)	
12-24 months	301 (22)	56 (18)	245 (23)		110 (20)	191 (23)	
25-48 months	264 (19)	54 (17)	210 (20)		63 (12)	201 (25)	
>48 months	366 (27)	131 (42)	235 (22)		203 (37)	163 (20)	
Intervention [n (%)]				**0.030**[2]			**<0.001**[2]
CombinADO	678 (50)	138 (45)	540 (52)		228 (42)	450 (55)	
SOC	680 (50)	172 (55)	508 (48)		316 (58)	364 (45)	

Abbreviations: IQR, Interquartile range; SES, socio-economic status; SOC, standard of care; VL, viral load.

[1] Wilcoxon Rank Sum Test

[2] Chi-squared test

[3] Social support score (min=7, max=35 with higher scores indicating less social support); subscales: family (min=3, max=15), friends (min=4, max=20).

[4] Stigma score (min=15, max=40 with higher scores indicating high levels of stigma); factor subscales Anticipated stigma (min=5, max=10); Experienced stigma (min=5, max=15); Internalized stigma (min=5, max=15).

[5] Categories based on SES score (standardized asset score built from combination of presence or absence of electricity, water, toilet in household).

[6] Adherence score (min=17, max=100 with higher scores indicating higher adherence), data collected among those who had taken ART in the last 30 days.

[7] Missing data (n=7), no ART initiation dates.

Prevalence of Common Mental Disorders (CMDs)

Table 2 presents prevalence estimates for positive depression and anxiety screenings amongst AYAHIV, stratified by sex and age group. Overall, 21.7% (n=295) of participants screened positive for depressive symptoms and 21.1% (n=286) screened positive for anxiety symptoms. Notably, significantly more individuals in the younger age group screened positive for depressive symptoms (24.63% vs. 19.78%, p=0.034), while significantly more females screened positive for anxiety symptoms (22.33% vs. 16.77%, p=0.035).

Table 2. *Comparison of depression and anxiety scores by sex and by age group*

Common Mental Disorders	**Overall** n=1358	**Male,** n=310	**Females,** n=1048	**P-value**	**15-19,** n=544	**20-24,** n=814	**P-value**
Depression (PHQ-A)[3]							
Median (IQR)	4 (1, 8)	4 (1, 8)	4 (1, 8)	0.135[1]	5 (1, 9)	4 (1, 8)	**0.048[1]**
Percent screened positive for depressive symptoms [% (n)]	21.72 (295)	19.35 (60)	22.42 (235)	0.250[2]	24.63 (134)	19.78 (161)	**0.034[2]**
Anxiety (GAD-7)[4]							
Median (IQR)	4 (1, 9)	4 (1, 8)	4 (1, 9)	0.360[1]	4 (1, 9)	4 (1, 8)	0.519[1]
Percent screened positive for anxiety symptoms [% (n)]	21.06 (286)	16.77 (52)	22.33 (234)	**0.035[2]**	23.71 (129)	19.29 (157)	0.050[2]

Abbreviations: IQR, Interquartile range; PHQ-A, Patient Health Questionnaire Adolescents; GAD-7, Generalized Anxiety Disorder -7.

[1] Wilcoxon Rank Sum Test

[2] Chi-Squared Test

[3] PHQ-A (min=0, max=27 with higher scores indicating a higher level of depression severity and scores ≥10 indicating major depression).

[4] GAD-7 (min=0, max=21 with higher scores indicating a higher the level of anxiety severity and scores ≥10 indicating generalized anxiety disorder).

Determinants of Common Mental Disorders (CMDs)

Table 3 presents results from univariable and multivariable analyses of key determinants associated with CMDs.

Anxiety (GAD ≥ 10)

In univariable analyses, females (OR=1.88, 95% CI: 1.24, 2.83) and those in a romantic relationship, but not married or cohabitating (OR=1.51, 95% CI: 1.01, 2.26), had increased odds of having anxiety symptoms. Additionally, AYAHIV had 12% higher odds of having anxiety symptoms for every one score increase in anticipated stigma (OR=0.88, 95% CI: 0.78, 0.99) and 22% higher odds for every one score increase in internalized stigma (OR=1.22, 95% CI: 1.12, 1.33).

Multivariate models showed that being female (aOR=2.11, 95% CI: 1.34, 3.33), having a romantic relationship without marriage or cohabitation (aOR=1.73, 95% CI: 1.11, 2.71), and scoring higher for internalized stigma (aOR=1.19, 95% CI: 1.08, 1.30) remained significantly associated with higher odds of having anxiety symptoms.

Depression (PHQ-A ≥ 10)

For depressive symptoms, lower odds were observed among AYAHIV who were high school non-completers and below (OR=0.41, 95% CI: 0.25, 0.66), who perceived their health as excellent, very good or good (OR=0.52, 95% CI: 0.35, 0.77), and who scored higher for friend social support (OR=0.93, 95% CI: 0.89, 0.98) and ART adherence (OR=0.97, 95% CI: 0.95, 0.99). Conversely, achieving viral suppression at VL<1000 copies/mL (OR=1.79, 95% CI: 1.12, 2.88), having a romantic relationship without marriage or cohabitation (OR=1.64, 95%. CI:1.05, 2.57), and scoring higher for anticipated (OR=0.84, 95% CI: 0.74, 0.96), experienced (OR=1.19, 95% CI: 1.06, 1.33) and internalized stigma (OR=1.38, 95% CI: 1.26, 1.51), was linked to increased odds of having depressive symptoms.

In the multivariate models, being a high school non-completer and below (aOR=0.32, 95% CI: 0.18, 0.57) and scoring higher for friend social support (aOR=0.87, 95% CI: 0.82, 0.92) and ART adherence (aOR=0.98, 95% CI: 0.96, 1.00) remained significantly associated with lower odds of having depressive symptoms. Conversely, controlling for other covariates, scoring higher for family social

support (aOR=1.09, 95% CI: 1.01, 1.17) and internalized stigma (aOR=1.33, 95% CI: 1.20, 1.48) was significantly associated with higher odds of having depressive symptoms.

Table 3. *Univariable and multivariable analysis of determinants of depression and anxiety among AYAHIV in Nampula, Mozambique*

Determinants	PHQ-A ≥ 10				GAD-7 ≥ 10			
	Univariable Analysis		Multivariable Analysis		Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	P-value	aOR (95% CI)	P-value	OR (95% CI)	P-value	aOR (95% CI)	P-value
Sex								
Male	Ref		Ref		Ref		Ref	
Female	1.52 (0.97, 2.37)	0.065	1.59 (0.96, 2.66)	0.073	1.88 (1.24, 2.83)	**0.003**	2.11 (1.34, 3.33)	**0.001**
Age	0.99 (0.92, 1.07)	0.846	-	-	0.98 (0.92, 1.04)	0.511	-	-
Age Group								
15-19	Ref		Ref		Ref		Ref	
20-24	1.02 (0.70, 1.49)	0.932	0.88 (0.55, 1.39)	0.574	0.96 (0.69, 1.35)	0.833	0.94 (0.64, 1.39)	0.773
Education Attainment								
High school completers and above	Ref		Ref		Ref			
High school non-completers and below	0.41 (0.25, 0.66)	**<0.001**	0.32 (0.18, 0.57)	**<0.001**	0.78 (0.48, 1.27)	0.323	-	-
Ever Employed								
Employed	Ref				Ref			
Never employed	1.04 (0.66, 1.64)	0.859	-	-	1.10 (0.73, 1.68)	0.641	-	-
Social Support[1]								
Family	1.06 (1.00, 1.13)	0.065	1.09 (1.01, 1.17)	**0.024**	1.00 (0.94, 1.06)	0.951	-	-
Friend	0.93 (0.89, 0.98)	**0.004**	0.87 (0.82, 0.92)	**<0.001**	0.97 (0.93, 1.01)	0.177	-	-
HIV Stigma[2]								
Anticipated	0.84 (0.74, 0.96)	**0.011**	0.92 (0.79, 1.07)	0.296	0.88 (0.78, 0.99)	**0.037**	0.92 (0.81, 1.04)	0.194
Experienced	1.19 (1.06, 1.33)	**0.003**	1.12 (0.99, 1.27)	0.080	1.07 (0.97, 1.18)	0.196	1.01 (0.90, 1.12)	0.893
Internalized	1.38 (1.26, 1.51)	**<0.001**	1.33 (1.20, 1.48)	**<0.001**	1.22 (1.12, 1.33)	**<0.001**	1.19 (1.08, 1.30)	**<0.001**
SES Category[3]								
Highest	Ref		-	-	Ref		-	-
Lowest	1.22 (0.67, 2.23)	0.520	-	-	0.87 (0.50, 1.52)	0.629	-	-
Moderate	0.86 (0.55, 1.35)	0.519	-	-	0.89 (0.60, 1.32)	0.564	-	-
Relationship Status								
Married/cohabitating	Ref		Ref		Ref		Ref	
Not in a relationship	1.09 (0.68, 1.75)	0.726	1.01 (0.56, 1.82)	0.963	1.09 (0.72, 1.65)	0.693	1.46 (0.89, 2.38)	0.131
In a relationship but not married/cohabitating	1.64 (1.05, 2.57)	**0.030**	1.47 (0.87, 2.48)	0.150	1.51 (1.01, 2.26)	**0.045**	1.73 (1.11, 2.71)	**0.016**
Perceived Health Status								
Fair/poor	Ref		Ref		Ref			
Excellent/good/very good	0.52 (0.35, 0.77)	**0.001**	0.69 (0.44, 1.07)	0.097	0.75 (0.52, 1.08)	0.123	-	-

Determinants	PHQ-A ≥ 10				GAD-7 ≥ 10			
	Univariable Analysis		Multivariable Analysis		Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	P-value	aOR (95% CI)	P-value	OR (95% CI)	P-value	aOR (95% CI)	P-value
Viral Load Results								
Undetectable (VL<50	1.39 (0.94, 2.04)	0.096	1.21 (0.71, 2.05)	0.489	1.05 (0.75, 1.49)	0.769	-	-
copies/mL)	1.79 (1.12, 2.88)	**0.016**	1.76 (0.92, 3.37)	0.088	1.44 (0.93, 2.23)	0.104	-	-
Suppressed (VL<1000 copies/mL)								
Adherence score[4]	0.97 (0.95, 0.99)	**<0.001**	0.98 (0.96, 1.00)	**0.027**	0.99 (0.97, 1.00)	0.099	0.99 (0.97, 1.01)	0.257
Duration on ART[5] [months]	1.00 (0.99, 1.00)	0.443	-	-	1.00 (1.00, 1.00)	0.953	-	-
Categorical months on ART								
>48 months	Ref				Ref			
<12 months	1.26 (0.79, 2.03)	0.335	-	-	1.08 (0.70, 1.66)	0.734	-	-
12-24 months	0.93 (0.53, 1.64)	0.800	-	-	1.17 (0.72, 1.89)	0.524	-	-
25-48 months	1.24 (0.72, 2.14)	0.440	-	-	0.98 (0.59, 1.61)	0.926	-	-
Intervention								
SOC	Ref				Ref			
CombinADO	0.85 (0.06, 11.97)	0.904	-	-	0.95 (0.12, 7.34)	0.959	-	-

Note. Only a priori variables (sex and age group), as well as those with p-values <0.10 in the univariable analyses, were included in the multivariable analyses.

Abbreviations: OR, Odds ratio; aOR, Adjusted odds ratio; CI, Confidence interval; PHQ-A, Patient Health Questionnaire Adolescents; GAD-7, Generalized Anxiety Disorder -7; SES, Socio-economic status; VL, Viral load; ART, Anti-retroviral treatment.

Bold values represent $p < 0.05$.

[1] Social support score (min=7, max=35 with higher scores indicating less social support); factor subscales scores: family (min=3, max=15), friends (min=4, max=20).

[2] Stigma score (min=15, max=40 with higher scores indicating high levels of stigma); factor subscales Anticipated stigma (min=5, max=10); Experienced stigma (min=5, max=15); Internalized stigma (min=5, max=15).

[3] Categories based on SES score (standardized asset score built from combination of presence or absence of electricity, water, toilet in household).

[4] Adherence score (min=17, max=100 with higher scores indicating higher adherence), data collected among those who had taken ART in the last 30 days.

[5] Missing data (n=7), no ART initiation dates.

Discussion

To our knowledge, this study represents one of the first known efforts to investigate the prevalence and determinants of CMDs in Mozambiquan AYAHIV. Among AYAHIV engaged in HIV care in Nampula, Mozambique, 21.7% screened positive for symptoms of depression and 21.1% for symptoms of anxiety, with higher rates of anxiety symptoms in females and higher rates of depressive symptoms in those aged 15-19 years. Key risk factors for depressive symptoms included lower family social support and higher internalized HIV stigma, while protective factors included being a high school non-completer and below, having higher ART adherence, and having lower friend social support. For anxiety symptoms, significant risk factors included female sex, being in a non-cohabitating romantic relationship, and higher internalized HIV stigma. These findings contribute to the emerging body of evidence on the burden of CMDs among AYAHIV in SSA and Mozambique, underscoring the critical need for targeted mental health services in this setting.

The prevalence of depressive symptoms in our sample closely resembles the 20.4% reported in Tanzania and 20.7% in Kenya (Mugo et al., 2023; Ramos et al., 2018). Our findings also closely correspond with a recent meta-analysis that reported a pooled global prevalence of 24.6% for major depression in AYAHIV (Zhan et al., 2024). The prevalence of anxiety symptoms in our sample is at the higher end of estimates reported in other SSA regions (2.2%-25%) and surpasses the global pooled estimate of 17.0% (Too et al., 2021; Zhan et al., 2024). Notably, our findings represent the highest recorded estimates for AYAHIV in the Mozambican context to date, exceeding prior estimates for depression (7.1%-11.7%) and anxiety (10.3%-12.2%; Di Gennaro et al., 2022; Nguyen et al., 2023). While the Mozambiquan Ministry of Health has expressed a commitment to transforming its mental health system, the mental health treatment gap persists and there remains a critical lack of research and programs specifically tailored to the adolescent population (Santos et al., 2016). Given the deleterious outcomes associated with untreated CMDs in this young population, these findings advocate for the prioritization of interventions and programs for this vulnerable population in Mozambique, and underscore the critical need for further research to inform the integration of mental health services into routine HIV care for AYAHIV in this context.

We also identified notable age and sex-related disparities in the prevalence of CMDs in our sample. Here, adolescents aged 15–19 years exhibited a higher prevalence of depressive symptoms compared to their older counterparts aged 20–24 years. This finding is incongruent with much of the prevailing evidence, which consistently reports higher rates of depression among older adolescent populations (Abebe et al., 2019; Dow et al., 2016; Getaye et al., 2021). However, as the age range defining “younger” versus “older” adolescents varies considerably across studies - often with younger

adolescents encompassing those aged 10–14 years - our findings are not entirely analogous to previously established trends (Ekat et al., 2020; Gaitho et al., 2018; Zhan et al., 2024). Given our exclusive focus on AYAHIV aged 15-24 years, our younger cohort (15-19 years) appears to align more closely with those deemed “older” in other studies, limiting direct comparisons. This inconsistency in defining age brackets may contribute to the apparent incongruence between our findings and the broader literature and calls for the urgent standardisation of age groups across this emerging field. Moreover, the elevated rates of depressive symptoms in our 15-19 year age group is consistent with global reports, which estimate the peak age of onset for any mental disorder to be 14.5 years old (Solmi et al., 2022). As adolescents aged 15-19 years have developed the cognitive capacity to comprehend the brevity and long-term implications of their diagnoses, coupled with their heightened susceptibility to CMDs, it appears logical that this age group are more inclined to experience elevated psychological stress (Mellins et al., 2012; Too et al., 2021). Ultimately, this finding reveals a critical need for the standardisation of age groups and for further research into the age-related nuances of mental health prevalence among AYAHIV, particularly in regions like Mozambique.

Building on this, our findings also revealed that females exhibited a higher prevalence of anxiety symptoms compared to their male counterparts. This is consistent with evidence from both SSA and global settings, which highlights the elevated rates of internalising mood disorders, such as depression and anxiety, among female AYAHIV (Dessauvagie et al., 2020; Girma et al., 2024; Too et al., 2021). In the context of HIV, females face a disproportionate burden, both in terms of their increased susceptibility to acquiring the virus as well as their markedly higher prevalence of mental health issues (Boakye et al., 2024; Jo¨rns-Presentati et al., 2021, Zhan et al., 2024). This heightened vulnerability is likely driven by a complex interplay of intersecting stressors, including greater exposure to sexual abuse and intimate partner violence. Moreover, the disproportionate stigma and overburdened social roles imposed on women in patriarchal societies, such as those in SSA, exacerbate this vulnerability, with women often bearing the blame for HIV transmission within their families (Boakye et al., 2024; Jo¨rns-Presentati et al., 2020; Nyongesa et al., 2021; Too et al., 2021). However, of note is that our findings stand in contrast to those of Nguyen et al. (2023), the only other study to report on this sex disparity among AYAHIV in Mozambique, which found higher anxiety levels among males compared to females. Coupled with our observation of no sex differences in the prevalence of depressive symptoms, these discrepancies underscore the need for further investigation into this sex disparity in Mozambique so as to guide the development of evidence-based, sex-specific interventions.

Consistent with this, female sex emerged as a significant risk factor for anxiety symptoms across both univariable and multivariable regression analyses. This finding aligns closely with prior research conducted in Mozambique which, using the same measurement instrument, demonstrated an increased odds of anxiety for female AYAHIV compared to males (Di Gennaro et al., 2022). Our findings are also in keeping with evidence from SSA, which consistently indicates that females living with HIV experience significantly higher rates of mental health conditions compared to their male and HIV-negative counterparts (Dessauvagie et al., 2020; Jo¨rns-Presentati et al., 2021; Nyongesa et al., 2021). These findings underscore the persistent sex disparities in mental health outcomes among AYAHIV in SSA and Mozambique, largely attributable to the aforementioned biological, psychological, interpersonal and structural stressors uniquely affecting young women (Boakye et al., 2024; Jo¨rns-Presentati et al., 2021; Nyongesa et al., 2021; Too et al., 2021).

In our sample of AYAHIV, being in a romantic relationship without marriage or cohabitation emerged as a risk factor for anxiety symptoms. While previous research has identified associations between romantic relationships and heightened depressive symptoms among HIV positive and negative adolescents, to our knowledge, this study is the first to establish an association between romantic relationships and anxiety (Kim et al., 2015; Sandberg-Thoma & Kamp Dush, 2013). As AYAHIV are less likely to disclose their statuses to short-term or casual sexual partners, being in a romantic relationship without marriage or cohabitation may heighten anxiety due to fears of stigma, rejection, or unintended disclosure (Gabbidon et al., 2019; Toska et al., 2015). Additionally, navigating intimacy while managing the complexities of living with HIV - such as adherence to treatment, concerns about transmission, and societal judgment - can heighten psychological distress. These relational stressors, coupled with the vulnerability associated with adolescence and young adulthood, may contribute to the observed link between romantic relationships and anxiety in this population.

Internalised stigma (i.e., the extent to which people living with HIV apply negative HIV-related perceptions onto themselves) emerged as a significant risk factor for both depressive and anxiety symptoms in our sample of AYAHIV (Pantelic et al., 2015). To elaborate, higher levels of self-reported internalised stigma were associated with increased odds of screening positive for depressive and anxiety symptoms, independently, and the literature is replete with similar conclusions (Boyes et al., 2019; Dessauvagie et al., 2020; Inman et al., 2024; Masa et al., 2022; Small et al., 2022). In SSA and Mozambique, HIV persists as a deeply stigmatized condition, particularly among adolescents and young adults, and, coupled with its association with CMDs, has been identified as a significant barrier to testing, treatment initiation and ART adherence for AYAHIV (Kimera et al., 2025; Pantelic et al., 2020). These findings call attention to the pervasive impact of internalised HIV stigma on the mental

health outcomes of AYAHIV and underscores the urgent need for more research to inform the development of targeted interventions that address stigma as a critical component of mental health and HIV care strategies.

Unlike stigma, social support is widely regarded as a protective mechanism against CMDs in AYAHIV, and our findings provide partial support for this well-established perspective (Boyes et al., 2019; Gentz et al., 2017, Too et al., 2021; West et al., 2019). Here, lower self-reported family social support (with higher scores indicating less social support) was a risk factor for depressive symptoms. Evidently, social support serves as a protective buffer for individuals facing stressful life events, and simultaneously aids them in managing the distress that accompanies such challenges (Too et al., 2021). A valuable social support network and a strong relationship with ones parents has also been associated with strong ART adherence among AYAHIV (Lowenthal et al. 2014). It therefore follows that higher levels of social support protect against the adversity associated with HIV, and, as such, may act as a buffer against the development of CMDs. However, our finding that lower friend social support levels were associated with a reduced odds of screening positive for depressive symptoms is not in keeping with this understanding and the broader literature. As the protective effects of social support are reduced in the presence of HIV stigma, AYAHIV may be less willing to disclose their HIV status and seek support from members outside of their immediate families (Mak et al., 2007). Thus, the most protective social support may come from caregivers and immediate family members rather than friends, which may account for these unanticipated findings.

Our finding that high school non-completers and below had a lower odds of screening positive for depressive symptoms was similarly unexpected and deviates from existing evidence showing an association between fewer schooling years and an increased likelihood of major depression (Ekat et al., 2020; Gaitho et al., 2018; Kim et al., 2015). As school-related stressors, such as an inability to pay school fees, poor school performance and experiences of HIV-related stigma and bullying, have previously been associated with youth self-reported depression, it is possible that those who have left school may experience reduced exposure to such stressors, thereby mitigating their risk of major depression (Gaitho et al., 2018; Kim et al., 2015). Alternatively, this finding could reflect a form of survivor bias, where AYAHIV who have discontinued schooling may possess other protective factors, such as increased family support or resilience, which offset their risk of depression. Further research is needed to disentangle the complex interplay between educational attainment, school-related stressors, and mental health outcomes among AYAHIV in this context.

CMDs have consistently been associated with poor ART adherence among AYAHIV in SSA and our findings are no exception. Here, higher ART adherence levels were associated with a reduced odds of screening positive for depressive symptoms, a finding that coincides with much of the existing literature (Abebe et al., 2019; Dow et al., 2016; Ekat et al., 2020; Gaitho et al., 2018; Kang et al., 2015; Mutumba et al., 2016). The consistent significant association observed between poor ART adherence and elevated depressive symptoms may be linked to the elevated psychological distress associated with a poor HIV prognosis, one that results from non-optimal adherence (Too et al., 2021). On the other hand, greater ART adherence is likely linked to increased interaction with healthcare services, which involve regular monitoring, social support and engagement with healthcare providers. This increased access to medical and psychological support, may improve overall physical and mental wellbeing, thereby reducing HIV-related distress, resulting in a lower propensity for depressive symptoms. However, such an association remains inconclusive in the Mozambiquan context, where Mandlate et al. (2023) identified a link between non-adherence and only severe mental health problems, and Nguyen et al. (2023) found an association, but only in males. It is also important to note that depression can precede poor ART adherence, highlighting the complexity and bidirectional nature of this relationship and the need for further research in this regard (Too et al., 2021).

Study Limitations and Directions for Future Research

ART adherence and CMDs among AYAHIV vary by mode of infection, with perinatally infected individuals often facing unique challenges that shape both their mental health and adherence to treatment (Abrams et al., 2018; Bucek et al., 2019; Mellins & Malee, 2013; Momplaisir et al., 2015; Nguyen et al., 2020; Petersen et al., 2010; Turner & Honikman, 2016). The inability to distinguish between perinatal and behavioural modes of infection in this study therefore represents a key limitation. Future research should prioritize capturing this differentiation to better understand and address the unique differences stemming from the experiences of perinatally versus behaviourally infected AYAHIV.

Another potential limitation is our use of a self-report measure of adherence, which is largely susceptible to social desirability bias. Despite its prior validation in both the US and South Africa, future research would benefit from incorporating more objective adherence metrics, such as pharmacy refill records or electronic pill monitoring. In addition, the use of screening tools to assess major depression and anxiety in our study limited our ability to confirm a formal diagnoses of these CMDs. To improve diagnostic accuracy in future research, these tools should be used alongside clinical assessments, or alternatively, clinical diagnostic criteria should be relied upon exclusively. An additional limitation is that several exposure variables (e.g., employment status and education

attainment) were dichotomized during the parent trial's data cleaning phase, preventing assessment of alternative categorizations. Future research should explore different variable specifications to capture more nuanced associations with mental health outcomes among AYAHIV.

A further limitation of this study is that it did not specifically analyse the prevalence and determinants of comorbid depression and anxiety. While we established the burden of each condition separately, an analysis of their co-occurrence would offer deeper insights into the compounded mental health challenges faced by a potentially more vulnerable subset of AYAHIV. Investigating the unique factors associated with this comorbidity is a critical and important direction for future research in this population.

Furthermore, given the apparent sex differences in the prevalence and risk of CMDs among AYAHIV, our female-dominant sample presents another notable limitation, and may impact the generalisability of our findings to male AYAHIV. This imbalance also reflects existing sex differences in accessing ART services, a phenomenon previously observed in other contexts (MISAU, 2015). Similarly, our focus on AYAHIV enrolled in HIV care in the Northern province of Nampula limits the generalisability of our findings both to other regions and to AYAHIV not engaged in care. Finally, given the cross-sectional nature of this research, causal relationships could not be delineated. Future research should thus direct attention towards identifying the causal patterns to fully target the key drivers of CMDs among AYAHIV.

Conclusion

The current findings lend themselves to the emerging knowledge base on the burden of CMDs among AYAHIV in Nampula, Mozambique. Our findings clearly demonstrate that CMDs are highly prevalent in this population, with the observed rates of depressive and anxiety symptoms significantly surpassing previous estimates in the country. Female AYAHIV emerged as a particularly vulnerable sub-group, while internalised stigma emerged as a key risk factor for both depressive and anxiety symptoms. Conversely, social support from family members and higher ART adherence were protective against depressive symptoms. These results underscore the urgent need to tailor mental health support to the unique needs and vulnerabilities of AYAHIV, and to incorporate mental health assessments and services into routine care for AYAHIV in Mozambique.

Declaration of Interest Statement

The authors report there are no competing interests to declare.

Author Contributions

PM and the broader CombinADO team conceptualized and designed the study as part of the larger CombinADO project, including the development of study protocols and data collection procedures. The data used in this analysis were collected by the CombinADO team. AB led the data cleaning, statistical analysis, and interpretation of results, and drafted the manuscript. PM and other team members provided critical feedback throughout the analytical and writing process. All authors reviewed and approved the final manuscript.

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Appendices

APPENDIX A: Department and Ethics-Approved Research Protocol

Study Synopsis

Background. The HIV burden amongst adolescents and young adults in Sub-Saharan Africa (SSA) is a major international concern and is alarmingly pertinent in Mozambique. Compared to their adult and paediatric counterparts, adolescents and young adults living with HIV (AYAHIV) contend with more significant challenges and face poorer outcomes along the HIV-care continuum. This distinctly vulnerable demographic faces the additional burden of common mental disorders (CMDs), which frequently co-occur with HIV and have similarly been associated with adverse HIV outcomes among adolescents globally, and in SSA. However, despite the disproportionate HIV and mental health burden faced by adolescents and young adults in Mozambique and SSA, and the purported deleterious outcomes, research in the Mozambiquan context remains scarce. Furthermore, various determinants of CMDs, such as female sex and older age, among AYAHIV have been delineated, however, findings remain inconsistent and scarce in Mozambique. This insufficient research and the inconsistency in its findings provides fertile ground for further exploration into the prevalence and determinants of CMDS among AYAHIV in Mozambique.

Method. The proposed research will utilize secondary data derived from the parent study, CombinADO, a cluster randomized control trial (cRCT) conducted across 12 clinics in the Nampula Province, Northern Mozambique, from September 2021 to July 2023. The main objectives are as follows: (1) To measure the prevalence of depressive and anxiety symptoms among AYAHIV, aged 15-24 years, receiving HIV care at 12 health facilities in Nampula, Mozambique, (2) To investigate the relationship between sex and age on the prevalence of depressive and anxiety symptoms among AYAHIV, aged 15-24 years, receiving HIV care at 12 health facilities in Nampula, Mozambique, and (3) To evaluate other determinants of depressive and anxiety symptoms among AYAHIV, aged 15-24 years, receiving HIV care at 12 health facilities in Nampula, Mozambique. Univariable and multivariable logistic regression analyses will be conducted for depressive and anxiety symptoms separately.

Ethical considerations. The parent study received ethical approval and obtained consent and assent prior to the commencement of the proposed research. The secondary data used in the proposed research will be de-identified, ensuring confidentiality, and will remain password protected and secure. This study has no foreseeable risks or direct benefits.

Literature Review

Introduction

The burgeoning burden of HIV amongst adolescents and young adults has emerged as a major international public health concern. This is notably apparent in Mozambique, where, of the 1.8 million people living with HIV (PLWH), 143 000 are adolescents and young adults aged 10-19 years (MISAU, 2020; National Institute of Statistics, 2017). Compared to their adult and pediatric counterparts, adolescents and young adults living with HIV (AYAHIV) face more significant challenges along the HIV care continuum and, most notably, are at an increased risk of common mental health disorders (CMDs), particularly depression and anxiety (Too et al., 2021). This is largely concerning as comorbid depression and anxiety among PLWH across all age groups has been associated with adverse HIV-related outcomes (Egbe et al., 2017; Nyongesa et al., 2018). The association between comorbid CMDs, herein denoting depressive and anxiety disorders or their associated symptoms, and more severe HIV outcomes has consistently been demonstrated among the older adult population in Mozambique and other Sub-Saharan African (SSA) regions (Mandlate et al., 2023). However, such associations remain under-reported for AYAHIV, with only a handful of studies shedding light on this issue in the region (Di Gennaro et al., 2022; Nguyen et al., 2023). Furthermore, while several determinants of CMDs among older adults living with HIV have been brought to light, findings for AYAHIV remain scarce and inconsistent. Given the paucity of research on the prevalence and determinants of depression and anxiety among AYAHIV in Mozambique, it becomes imperative to explore this association in older cohorts or within the broader international literature, to inform any research conducted in this context.

Search Strategy

The following online databases were searched from their date of inception to August 2024: PubMed, EBSCO (PsychINFO, PsychArticles, ERIC, Cinahl and AfricaWide) and Scopus, with additional searches on Google Scholar as a safeguard. Relevant key search terms and Boolean operators (Table 1) were identified through initial searches of the databases and from prior literature. The search was restricted to English-language articles that offered full-text availability and, given the paucity of research among AYAHIV in Mozambique, included SSA regions as well as an additional search that included international contexts. This strategy ensured a comprehensive collection of relevant literature to support the proposed research. The following inclusion and exclusion criteria were applied during the article selection process:

Inclusion Criteria

Articles focusing on adolescents and young adults (aged 10-24 years) living with HIV (AHAHIV) were included for review. We only included articles investigating the prevalence, determinants or correlates of CMDs among AYAHIV, primarily in SSA, however, international studies were also included where necessary to provide broader context.

Exclusion Criteria

Articles were excluded if they focused exclusively on adult (older than 24 years) or pediatric (younger than 10 years) populations, or on HIV negative individuals, without a relevant AYAHIV comparison group. Finally, articles not published in English, or where the full text was not available in English, were excluded.

Table 4

Table Depicting the Boolean Phrases Used in the Database Search

Key Term	Phrase
Adolescent	adolescent* OR adolescence OR youth* OR "young person*" OR teen* OR teenage*
HIV	HIV OR “Human Immunodeficiency Virus*” OR AYAHIV OR “HIV-positive” OR “HIV infection” OR “Living with HIV”
Mozambique/ Sub-Saharan Africa	Mozambique OR “Nampula Province” OR “Republic of Mozambique” OR “Sub-Saharan Africa” OR “Africa, Southern” OR SSA OR “African Region (WHO)”
Depression/Anxiety	Depression OR “Depressive Symptom*” OR “Depressive Disorder*” OR “Depressive Syndrome*” OR MDD OR “Major Depressive Disorder*” OR Anxiety OR “Anxiety Disorder*” OR “Generalized Anxiety Disorder” OR GAD
Determinants	Determinant* OR “Risk factor*” OR Correlate*

Note. * Denotes any ending in word including, but not limited to, “y”, “s”, “ion”, “ive”, “al”, “ing”, “e”, “ed”, “r”

The Burden of HIV in Sub-Saharan Africa and Mozambique

SSA remains the epicenter of the global HIV epidemic, bearing one of the highest burdens of HIV infections worldwide (UNAIDS, 2023). This burden is disproportionately borne by adolescents and young adults, aged 10 to 24 years, who constitute 23% of the total SSA population (UNICEF, 2023). Moreover, young females in SSA, aged 15 to 24 years, are three times more likely to acquire HIV than their male counterparts and continue to bear a disproportionately heavy burden in the ongoing HIV epidemic (UNAIDS, 2023). In 2023, approximately 1.5 million adolescents and young adults

aged 10 to 19 years were living with HIV worldwide, representing 11% of all new infections recorded that year. Remarkably, around 84% of these AYAHIV reside in SSA, where HIV has emerged as the foremost cause of mortality among those aged 10 to 19 years (UNAIDS, 2019; UNICEF, 2019; 2024; WHO, 2024). Within this context, Mozambique emerges as a critical focal point, bearing the eighth highest HIV prevalence rate worldwide, with adolescents and young adults contributing a notable share of this burden. With an HIV prevalence rate of 13.2%, approximately 1.8 million Mozambicans are living with HIV, 143 000 of which are adolescents and young adults, who constitute over 30% of the total population (MISAU, 2020; National Institute of Statistics, 2017).

AYAHIV represent a notably vulnerable demographic, forced to navigate the challenges of managing a chronic, deeply stigmatized, and transmittable disease, while simultaneously navigating the developmental transition from childhood to early adulthood (Avert, 2020). Among these young individuals, HIV is mostly acquired through vertical transmission (i.e., from their mothers), while a portion are reported to have acquired it horizontally (i.e., through high-risk behaviors; Slogrove & Sohn, 2018). Despite recent gains in the development and dissemination of antiretroviral therapy (ART), AYAHIV in SSA and Mozambique contend with significant barriers at the health system, interpersonal, and individual levels that impede their retention in HIV care, uptake of ART, willingness to test for the disease, and attainment of viral suppression (Falcao et al., 2021; INS, 2023; Teasdale et al., 2021). Furthermore, AYAHIV often encounter additional challenges, such as psychosocial difficulties, inadequate social support, and specific health system related barriers, such as mistrust of healthcare workers and concerns about stigma and discrimination, particularly when accessing sexual and reproductive health services (Dow et al., 2014; Fair et al., 2018; Gichane et al., 2018; Kim et al., 2017). Evidently, compared to their adult and pediatric counterparts, AYAHIV in SSA and Mozambique represent a particularly vulnerable demographic. Confronted with poorer outcomes along the HIV care continuum at a critical, yet complex developmental period, these young individuals warrant increased research interest and informed intervention strategies.

Mental Health Disorders and HIV Among Adolescents and Young Adults Living with HIV

Alongside the burden of HIV is the overwhelming burden of mental health disorders, particularly depression and anxiety, now recognized as the most prevalent non-communicable disease among adolescents (Askeer et al., 2020). As with HIV, this burden appears particularly pronounced in SSA, with recent systematic reviews reporting a 27% and 30% prevalence of depression and anxiety among individuals aged 10–19 years (Jörns-Presentati et al., 2021). As they transition to adulthood, adolescents face rapid physical and social changes, all while navigating their newfound independence and identities. These significant developmental changes can heighten mental health needs, even in

those without a formal diagnosis (WHO, 2023). Given these emerging challenges, it follows that up to 63% of CMDs develop in the period from childhood to adolescence, rendering these individuals particularly vulnerable to the onset and progression of mental health issues (Solmi et al., 2022). However, despite their increased vulnerabilities, adolescents and young adults rarely feature in research on this topic, with only two studies shedding light on the issue in Mozambique (Di Gennaro et al., 2022; Nguyen et al., 2023). Evidently, given their developmental, socio-economic, and health-related vulnerabilities, adolescents in SSA are deeply impacted by mental illness. This impact is notably intensified for those living with HIV (Too et al., 2021).

It is well documented that PLWH from both high and low-income settings have a 2-3 times increased risk of developing CMDs compared to the general population (Chibanda et al., 2016; Durteste et al., 2019; Lofgren et al., 2020). Among AYAHIV, findings from comprehensive global reviews indicate that the prevalence of comorbid depressive and anxiety disorders is as high as 44% and 48.2%, respectively, and, although scarce, research from SSA suggests that the combined prevalence of any psychiatric disorder among AYAHIV is 27% (Dessauvagie et al., 2020; Olashore et al., 2021; Mellins & Malee, 2013; Vreeman et al., 2017). Notably, the association between HIV and CMDs among AYAHIV is bidirectional. On the one hand, HIV serves as a significant psychosocial stressor, and when combined with the side effects of ARTs, the persistent stigma associated with the disease, and its direct or indirect effects on the developing brain, it significantly increases the risk of CMDs in AYAHIV (Ashaba et al., 2019; Kimera et al., 2020). On the other hand, CMDs exacerbate disease progression and unfavorable health outcomes in an already vulnerable AYAHIV population (Mutumba et al., 2016; Kim et al., 2015).

The link between comorbid CMDs and adverse HIV-related outcomes among PLWH, including adolescents, is well described in the international literature (Mandlate et al., 2023; Too et al., 2021). To elaborate, comorbid CMDs have consistently been associated with accelerated disease progression, suboptimal adherence to ART, an increased risk of substance abuse and sexual risk behaviors, suicidal ideations, and reduced continuity in care (Egbe et al., 2017; Kim et al., 2015; Nyongesa et al., 2018). These challenges are particularly pronounced for AYAHIV, who grapple with the compounded burden of both their preexisting vulnerabilities to adverse HIV-related outcomes and the additional strain imposed by CMDs. With their overwhelming burden of HIV, significant mental health treatment gap, and predominantly youthful population, it is surprising that this association, and its purported adverse disease outcomes, has been relatively unexplored among AYAHIV in Mozambique. The two studies that have explored the association in the region have both found an increased prevalence of CMDs among AYAHIV (Di Gennaro et al., 2022; Nguyen et al., 2023). However, Di Gennaro et al. (2022)

identified an increased prevalence of CMDs among females, while Nguyen et al. (2023) found this increase, and its purported association with reduced ART adherence, predominantly in males. It follows that sex may be a notable determinant of CMDs among AYAHIV. However, this insufficient research and the inconsistency in its findings provide fertile ground for further exploration into the prevalence and determinants of CMDs among AYAHIV in Mozambique.

Determinants of Common Mental Disorders among Adolescents and Young Adults Living with HIV

While existing literature has identified multiple correlates of CMDs in PLWH, findings are notably scarce and somewhat inconsistent for AYAHIV in Mozambique. International findings predominantly highlight female sex and older age as significant demographic correlates of CMDS among AYAHIV (Gadow et al., 2012; Kim et al., 2015; Mellins et al., 2012). While most research conducted in SSA mirrors these international findings, one study in Uganda found younger age and male sex to be significant correlates of depression, while some studies report no differences by sex (Abebe et al., 2019; Boyes et al., 2019; Cavazos-Rehg et al., 2020; Dow et al., 2016; Ekat et al., 2020; Gaitho et al., 2018; Kim et al., 2015). As females are commonly exposed to additional risk factors, such as sexual abuse, stigma and intimate partner violence, and are generally considered more at risk for mood disorders, it seems logical that these individuals face a heightened risk of CMDs (Nyongesa et al., 2021; Too et al., 2021).

Moreover, significant research attention has been devoted to the association between comorbid CMDs among AYAHIV and ART adherence, with the general consensus that comorbid CMDs are significantly associated with poor ART adherence (Nguyen et al., 2023; Too et al., 2021). In addition, recent reviews have highlighted fewer schooling years, HIV-related stigma, being in a romantic relationship, being unemployed and being of a lower socio-economic status (SES) as significant correlates of CMDs among AYAHIV in SSA (Too et al., 2021). On the other hand, higher social support and health-related quality of life are the most commonly cited protective indicators against CMDs among AYAHIV (Boyes et al., 2019; Cavazos-Rehg et al., 2020; West et al., 2019; Too et al., 2021). However, to date, there has been a notable absence of research exploring these correlates among AYAHIV in Mozambique.

Conclusion

Through an exploration of the current literature, adolescents in SSA emerge as a particularly vulnerable demographic, disproportionately faced with the dual burden of HIV and CMDs and their associated challenges along the HIV care continuum. Furthermore, female sex and older age appear to

be the most notable correlates of comorbid CMDs among AYAHIV, however, research in the Mozambiquan context remains scarce and inconsistent, as are the intervention strategies and mental health treatment services for this vulnerable demographic.

Rationale

The HIV burden among adolescents and young adults in SSA is undoubtedly a major international concern and is alarmingly pertinent in Mozambique. Compared to their adult and paediatric counterparts, AYAHIV contend with more significant challenges and face poorer outcomes along the HIV-care continuum. In Mozambique, and in various other countries, HIV among adolescents and young adults has consistently been associated with adverse disease outcomes, including lower ART initiation, viral suppression, retention to care, and medication adherence compared to other age groups (Avert, 2020; Teasdale et al., 2021). Furthermore, this already vulnerable population faces an additional mental health burden, which frequently co-occurs with HIV among adolescents globally, and in SSA (Mellins & Malee, 2013; Vreeman et al., 2017). Importantly, this comorbidity has similarly been associated with adverse HIV outcomes, such as accelerated disease progression, suboptimal adherence to ART, and reduced continuity in care (Egbe et al., 2017; Nyongesa et al., 2018). However, despite the disproportionate HIV and CMD burden faced by adolescents and young adults in Mozambique and SSA and the purported deleterious disease outcomes associated with comorbid CMDs among AYAHIV, research in this context remains scarce.

Furthermore, while various determinants of CMDs among AYAHIV have been delineated, findings remain largely inconsistent and scarce in the Mozambiquan context (Di Gennaro et al., 2022; Nguyen et al., 2023). As female sex and older age remain the most notable correlates of CMDs among AYAHIV internationally and in other SSA regions, it follows that the same trends be observed in Mozambique (Too et al., 2021). A deeper understanding of the factors influencing the mental health of AYAHIV is vital for the developmental of effective, evidence-based interventions in the region. Clearly AYAHIV in Mozambique represent a particularly vulnerable demographic and, in light of the limited intervention strategies and significant mental health treatment gap in the region, these young individuals warrant urgent research interest and informed intervention strategies. As such, this research aims to assess the prevalence and determinants of depression and anxiety among AYAHIV receiving HIV care in Nampula, Mozambique.

Background of the Proposed Dissertation

The proposed research will employ secondary data derived from the parent study, CombinADO, a cluster randomized control trial (cRCT) conducted across 12 clinics in the Nampula Province,

Northern Mozambique, from September 2021 to July 2023. Developed in collaboration with the PATC3H program, CombinADO was initiated in response to the National Institute of Child Health and Development's (NICHD) call for research on effective public health interventions for HIV-affected youth in resource-limited settings (Mogoba et al., 2021). The study sought to evaluate the efficacy, uptake, feasibility, and acceptability of a novel multicomponent intervention, compared to an enhanced standard of care (eSOC), on various HIV care and treatment outcomes among AYAHIV, aged 10-24 years, in Nampula, Mozambique (Mogoba et al., 2021). Following its successful conduct and implementation, the CombinADO study administered 12-month post-implementation surveys, encompassing a variety of individual and clinical outcomes, the data from which will inform the proposed cross-sectional research.

Research Question, Aims and Objectives

Research Question

What are the prevalence and determinants of depressive and anxiety symptoms among AYAHIV, aged 15-24 years, receiving HIV care at 12 health facilities in Nampula, Mozambique?

Study Aim

To assess the prevalence and determinants of depressive and anxiety symptoms among AYAHIV receiving HIV care at 12 health facilities in Nampula, Mozambique.

Objectives

Objective 1

To measure the prevalence of depressive and anxiety symptoms among AYAHIV, aged 15-24 years, receiving HIV care at 12 health facilities in Nampula, Mozambique.

Objective 2

To investigate the relationship between sex and age on the prevalence of depressive and anxiety symptoms among AYAHIV, aged 15-24 years, receiving HIV care at 12 health facilities in Nampula, Mozambique.

> *Hypothesis 1*: Females will have a higher prevalence of depressive and anxiety symptoms compared to males.
>
> *Hypothesis 2*: Older AYAHIV (aged 20-24 years) will have a higher prevalence of depressive and anxiety symptoms compared to younger AYAHIV (aged 15-19 years).

Objective 3

To evaluate other determinants of depressive and anxiety symptoms among AYAHIV, aged 15-24 years, receiving HIV care at 12 health facilities in Nampula, Mozambique.

Methods

Study Design

Informed by secondary cross-sectional data collected in the CombinADO trial, this study will analyze the prevalence and determinants of depressive and anxiety symptoms among AYAHIV in the Nampula province, Mozambique. The data will be derived from post-implementation surveys administered to AYAHIV in the primary study, CombinADO.

Study Setting

The CombinADO study was conducted at 12 sites across the Nampula Province, a low-resource setting in Northern Mozambique. In this region, the HIV prevalence among individuals aged 15–24 years is estimated at 4.1%, with only 16% of the clinics providing youth-friendly services (MISAU, 2021). Clinics were selected based on their proximity (within a 4-hour drive from Nampula city), patient load (at least 220 AYAHIV aged 10–24 currently on ART), and their implementation of a one-stop-shop adolescent-friendly service model. Out of 15 eligible clinics, 12 were randomly chosen for participation (Mogoba et al., 2021).

Study Population

All AYAHIV, aged 10-24 years, actively seeking HIV care in the participating health facilities were enrolled in the parent study, along with their caregivers and various key informants. In total, the CombinADO study comprised 1,715 AYAHIV. However, those aged 10-14 years received a refined questionnaire, which was limited in its mental health screenings. As the proposed research is a secondary analysis of various mental health outcomes of the participants in the CombinADO study, we opted to include only the 1,358 AYAHIV aged 15-24 years old. All eligible participants provided informed consent, or assent and parental informed consent (for those younger than 18), prior to participation. The following inclusion and exclusion criteria, as outlined in the parent study, will be upheld in the proposed research:

Inclusion criteria

Eligible study participants included adolescents and young adults with a confirmed HIV positive status, aged 15-24 years. Participants were only eligible if they were aware of their HIV-positive statuses and confirmed their willingness to comply with all study procedures.

Exclusion criteria

Individuals were excluded if they presented with any acute medical conditions that required immediate medical attention.

Data Collection

The proposed research will depend solely on secondary data collected on behalf of the parent study, CombinADO, and, as such, no new data will be collected. The data used in this study was collected using a survey questionnaire at 12-months post-intervention implementation, which was translated to Portuguese and administered by study staff on electronic tablets to AYAHIV in private spaces in the respective health facilities (Mogoba et al., 2021).

Measures

Mental Health Measures

Patient Health Questionnaire Adapted for Adolescents (PHQ-A). The PHQ-A, a modified version of the PHQ-9, was employed to assess depression symptoms in AYAHIV (Appendix C). The questionnaire comprises nine items, each targeting specific depressive symptoms, which adolescents evaluate based on their experiences over the past two weeks. Scores range from 0-27, with scores ≥10 indicating major depression (Johnson et al., 2002).

Generalized Anxiety Disorder 7 (GAD-7). Anxiety symptoms were measured using the GAD-7, a seven-item tool that similarly prompts participants to rate their experiences of anxiety symptoms over the past two weeks on a four-point scale with anchors *Not at all, Several days, More than half the days*, and *Nearly every day* (Appendix C). Here, scores range from 0 to 21 and a score of ≥10 indicates generalized anxiety disorder (GAD; Lovero et al., 2022).

The PHQ-9 has demonstrated strong sensitivity and specificity in identifying depression through self-reports in both high- and low-to-middle-income countries (LMIC; Anum et al., 2019; Makhubela & Khumalo, 2023). Similarly, the GAD-7 has been validated for use in adults from LMICs as well as adolescents in both high-income and LMIC settings (Plummer et al., 2016). Both measures have demonstrated adequate reliability and validity among adolescents in Mozambiquan and SSA contexts and are thereby suited to this research (Di Gennaro et al., 2022; Lovero et al., 2022).

Explanatory Variables

Individual-level characteristics, such as self-reported age, sex, level of education and employment history were obtained via a brief questionnaire (Appendix C). Informed by recent research, these variables will be considered potential determinants of depressive and anxiety symptoms among AYAHIV.

ART Adherence. ART adherence was measured using a three-item self-report scale developed by Wilson et al. (2016; Appendix C). This tool, developed through cognitive interviewing and validated in the United States and South Africa, measures ART adherence over the past 30 days based

on three indicators: (1) the number of missed doses, (2) self-reported adherence quality, and (3) adherence to the prescribed medication regimen. Self-reported adherence over the past 30 days was determined by recoding each item with equal weight and aggregating the three items to produce a score ranging from 0 to 100%, with 0 representing poor adherence and 100 perfect adherence (Wilson et al., 2014, 2016).

Socio-Economic Status (SES). An asset index form captured information regarding individual or family access to various household items as a proxy indicator of SES (Appendix C). SES categories (*low, moderate, high*) were then built by combining scores related to the presence or absence of items such as electricity, water, and a toilet in the household.

Social Support. Social support was assessed using a measure specifically developed for the CombinADO study, which included a series of statements regarding the participants' perceptions of support from family and friends (Appendix C). Participants were asked to rate how true each statement was for them on a 5-point Likert scale, with indicators: *Not at all true, Rarely true, Sometimes true, Often true*, and *True nearly all the time*. The overall social support score ranged from 7 to 35, with higher scores indicating less social support. The measure included two factor subscales: family support with scores ranging from 3 to 15, and friend support with scores ranging from 4 to 20.

HIV-Related Stigma. An adapted version of Berger's (2001) 40-item stigma scale was employed as a measure of self-report HIV stigma among AYAHIV (Appendix C). Here, responses were evaluated across three dimensions: Anticipated stigma, Experienced stigma, and Internalized stigma. Participants indicated their agreement with statements about their treatment and feelings regarding their HIV-positive status with indicators *Agree* or *Disagree* for the anticipated domain, and indicators *Never, Sometimes* and *Most of the time* for the experienced and internalized stigma domains. Overall scores ranged from 15 to 40, with higher scores indicating higher levels of self-reported stigma. This scale is well validated globally, and the shortened version has similarly demonstrated adequate psychometric properties among adolescents in other LMICs (Wanjala et al., 2021a; 2021b).

Perceived Health Status. Perceived health status was assessed with a single question asking participants to rate their general health on a scale with indicators: *Excellent, Very good, Good, Fair* and *Poor.* For the presentation of results, we will combine indicators to create a binary outcome for perceived health. This item captures the participants' self-assessment of their overall health, providing a subjective measure of health status.

Viral Suppression. Viral load was assessed using real-time viral load testing twelve months following intervention implementation. Viral suppression was regarded as a viral load of less than 50 copies/mL or less than 1000 copies/mL at 12 months.

Data Management

In the primary study, all digital data collection tools were encrypted and password protected. Daily data was collected from staff and stored in locked filing cabinets at study sites and, during data collection, datasets were stored on SurveyCTO and accessed via password-protected computers. All hardcopy documents were securely stored in a locked cabinet within a secure office. Participants were identified only by a unique participant identifier (PID) and no personal identifying information was recorded on the data sources. Documents containing personal identifying information were stored separately and accessible only to designated research staff. All records remain securely maintained following the study's completion. The proposed analysis will utilize de-identified electronic data, which will remain password protected.

Statistical Analysis

All statistical analyses will be conducted in R Studio (2024). The data to be used in the proposed research have already undergone thorough cleaning and validation. Depressive and anxiety symptoms will be treated as separate outcome variables. Descriptive statistics, calculated for the overall sample and by sex and age group, will be presented with frequencies (percent) or with medians (interquartile range; IQR) for continuous and categorical variables, respectively. Simple bivariate analyses, such as Wilcoxon Rank Sum and Chi Squared tests will be used to compare group differences. To satisfy our first and second objectives, we will calculate the median (IQR) depression and anxiety scores for the overall sample and by sex and age, as well as the percentage of AYAHIV who met the screening threshold for clinically significant symptoms of depression and/or anxiety, according to the pre-specified cut-off values.

To address our third objective, we will begin by running a null model (i.e., a model with no explanatory variables), and computing the intraclass correlation (ICC) to determine whether there is within cluster variability that would benefit from a random effect. Informed by this, we will either conduct simple logistic regression analyses, or mixed effects logistic regression analyses, accounting for the random effects of each cluster level, i.e., the clinics. For any correlated variables that measure the same or similar determinants, we will select the most clinically meaningful variable for further analysis. We will first run univariable analyses to examine the relationship between each pre-specified determinant and our binary outcome variables, anxiety and depression, separately. We will also identify any interactions that warrant inclusion in the model. Multivariable logistic regression analyses will then be run on the determinants with a p-value <0.10 in the univariable analysis for each separate binary outcome variable. Age group and sex will be included in the multivariable analysis as

a priori factors regardless of statistical significance. The overall fit of the final model will be determined using a goodness of fit test, where a p-value >0.05 will indicate a good model fit.

Ethical Considerations

The parent study, CombinADO, was approved by the Columbia University of Irving Medical Center Institutional Review Board (CUIMC IRB# AAAT5971; Appendix D) and the Comite Nacional De Bioética Para a Saúde de Moçambique (467/CNBS/21; Appendix E). The proposed research will seek ethical approval from the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee (UCT-HREC) before commencing.

Informed consent, or assent and parental informed consent (for those younger than 18), was obtained from all AYAHIV prior to their participation in the parent study (Appendix G). The proposed sub-study will exclusively utilize existing data collected from the CombinADO study. As a result, there will be no direct interaction with participants, and no further consent is required. In addition to the data sharing and usage agreement established by the parent study (Appendix F), this analysis will uphold ethical considerations by ensuring the secure handling of sensitive data, protecting the privacy of participants, and maintaining the highest standards of research conduct. All study-related information, including participant data, will be treated with utmost confidentiality. The data utilized in the proposed research has already been de-identified and remains secure, and password protected, only accessible to the research team. Furthermore, the clinical site evaluations conducted throughout the implementation period were designed to uphold the ethical integrity of the research, ensuring that the rights and well-being of the study population were fully respected, and that the data were accurate and verifiable (Mogoba et al., 2021). Finally, while this study has no foreseeable risks, indirect benefits include an enriched understanding of the burden and determinants of CMDs among AYAHIV in Nampula, Mozambique, which has the potential to inform future intervention in this context.

Timeline

Events	**Jun 2024**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**	**Jan 2025**	**Feb**
Protocol completion and submission									
Data analysis									
Results and discussion									
Manuscript completion									
Final dissertation submission									

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APPENDIX B: HREC Ethics Approval Letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

18 February 2025

HREC REF: 823/2024

Ms Phepo Mogoba
Division of Epidemiology & Biostatistics
FHS
Email: Phepo.mogoba@uct.ac.za
Student: blcash003@myuct.ac.za

Dear Ms Mogoba

PROJECT TITLE: THE PREVALENCE AND DETERMINANTS OF DEPRESSION AND ANXIETY AMONG ADOLESCENTS AND YOUNG ADULTS LIVING WITH HIV IN THE NAMPULA PROVINCE, MOZAMBIQUE-SUB-STUDY LINKED TO 557/2019 (MASTER'S DEGREE OF PUBLIC HEALTH - MS. ASHLEE BLACHER)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

Thank you for your response letter dated 19 December 2024, addressing the issues raised by the Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study, subject to Mozambique approval.

Approval is granted for one year until the 28 February 2026.

Please submit a progress form, using the standardised Annual Report Form (FHS016) or FHS017 if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Ms Ashlee Blacher will also be involved in this study.

Please quote HREC REF 823/2024 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR MARC BLOS
CHAIRPERSON, FACULTY SP HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP),

National Health Research Ethics Council (2024) South African Ethics in Health Research Guidelines: Principles, Processes and Structures, 3rd ed. Department of Health of South Africa. South African Good Clinical Practice Guidelines (SA GCP 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2024) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

APPENDIX C: Parent Study Data Capture Instrument

Patient Health Questionnaire Adapted for Adolescents (PHQ-A)

How often have you been bothered by each of the following symptoms during the past two weeks?						
			Not at all	**Several Days**	**More than half the days**	**Nearly every day**
a.		Feeling down, depressed, irritable, or hopeless?				
b.		Little interest or pleasure in doing things?				
c.		Trouble falling asleep, staying asleep, or sleeping too much?				
d.		Poor appetite, weight loss, or overeating?				
e.		Feeling tired, or having little energy?				
f.		Feeling bad about yourself- or feeling that you are a failure, or that you have let yourself or your family down?				
g.		Trouble concentrating on things like school, work, reading, or watching tv?				
h.		Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you were moving around a lot more than usual?				
i.		Thoughts that you would be better off dead, or of hurting yourself in some way?				

Generalized Anxiety Disorder 7 (GAD-7)

Over the last 2 weeks, how often have you been bothered by the following problems?						
			Not at all	**Several Days**	**More than half the days**	**Nearly every day**
a.		Feeling nervous or anxious	0	1	2	3
b.		Not being able to stop or control worrying	0	1	2	3
c.		Worrying too much about different things	0	1	2	3
d.		Trouble relaxing	0	1	2	3
e.		Being so restless it's hard to keep still	0	1	2	3
f.		Becoming easily annoyed or irritable	0	1	2	3
g.		Feeling afraid as if something awful might happen	0	1	2	3

Explanatory Variables

Q Code	QUESTION	ANSWER
AGE	How old are you?	Age (years): _____
GEND	What is your gender?	1. Male 2. Female 3. Other (specify): _____
EDU1	What level of school do you currently go to?	1. Primary- first grade- SKIP to EMPL1 2. Secondary- first grade- SKIP to EMPL1 3. Technical or vocational school- SKIP to EMPL1 4. University, college or another tertiary institution- SKIP to EMPL1 5. I am not in school
EDU2	What is the highest level of school that you have completed?	1. Never been to school 2. Incomplete primary education 3. Complete primary education 4. Incomplete secondary education 5. Complete secondary education 6. Tertiary education (university) 7. Ensino tecnico basico 8. Ensino tecnico medio 9. Other (specify): _____
EMPL1	Are you currently employed or have you ever been employed?	1. Currently employed 2. Not employed now but was employed during the last year 3. Not employed now but was employed prior to last year 4. Never employed

ART Adherence Measure

ADH1	In the last 30 days, on how many days did you miss at least one dose of any of your ARVs? *Please write the number of days.*	# of days: _____ (0-30)
ADH2	In the last 30 days, how good a job did you do at taking your ARVs in the way you were supposed to?	1. Very poor 2. Poor 3. Fair 4. Good 5. Very good 6. Excellent
ADH3	In the last 30 days, how often did you take your ARVs in the way you were supposed to?	1. Never 2. Rarely 3. Sometimes 4. Usually 5. Almost always 6. Always

Socio-Economic Status Measure

Does your house have the following?		
SES1	A toilet inside	1. Yes 2. No
SES2	Running water inside	1. Yes 2. No
SES3	Electricity inside	1. Yes 2. No

Social Support Measure

Please indicate how true the following statements are to you regarding your family and friends.						
		Not at all true	**Rarely True**	**Sometimes True**	**Often True**	**True nearly all the time**
SOC1	My family is a source of strength and support to me.	5	4	3	2	1
SOC2	People in my family look out for each other.	5	4	3	2	1
SOC3	I feel loved.	5	4	3	2	1
The following statements refer to feelings and experiences that most people have at one time or another in their relationships with friends. Please answer the following questions:						
SOC4	I rely on my friends for emotional support.	5	4	3	2	1
SOC5	There is a friend I could go to if I were just feeling down, without feeling funny about it later.	5	4	3	2	1
SOC6	I have a deep sharing relationship with a number of friends.	5	4	3	2	1
SOC7	My friends come to me for emotional support	5	4	3	2	1

HIV Stigma Measure

Now I am going to read a list of sentences. Please tell me whether you agree or disagree with these statements.			
Anticipated stigma			
	Event	**Agree**	**Disagree**
STIG1	Most people with HIV are rejected when others learn that they have HIV.		
STIG2	Most people believe that a person who has HIV is dirty.		
STIG3	Most people are uncomfortable around someone with HIV.		
STIG4	Telling someone I have HIV is risky.		
STIG5	It's easier to avoid new friendships than worry about telling someone that I have HIV.		

I will continue to read some sentences. Could you now say how much these things have been true for you in the past?				
Experienced stigma				
		Never	**Sometimes**	**Most of the time**
STIG6	People have reacted badly when they find out that I have HIV.			
STIG7	I have lost friends/partners by telling them I have HIV.			
STIG8	I have been teased because of my HIV status.			
STIG9	Some people avoid touching me once they know I have HIV.			
STIG10	Telling others that I have HIV has been a mistake.			

Internalized stigma				
		Never	**Sometimes**	**Most of the time**
STIG11	Sometimes I feel I am not as good as the other adolescents my age because I have HIV.			
STIG12	Sometimes I feel I am a bad person because I have HIV.			
STIG13	Sometimes I feel ashamed I have HIV.			
STIG14	Sometimes I feel it is my fault I have HIV.			
STIG15	I work hard to keep my HIV a secret.			

APPENDIX D: Parent Study Ethical Approval by the Columbia University of Irving Medical Center Institutional Review Board

COLUMBIA|RESEARCH
Human Research Protection Office
Institutional Review Boards

April 16, 2021

Elaine Abrams
823100X - ICP ICAP

Protocol Number: IRB-AAAT5971
Title: CombinADO
Grant #: 4UH3HD096926-03
Approval Date: 04/14/2021 Expiration Date: 04/13/2022
Event Identifier: New Protocol (Y01M00)

The above-referenced event was reviewed and approved by Columbia University IRB 2.

Level of review and outcome: Convened IRB review IRB Meeting Date: 04/14/2021

To view a list of documents that were included in this approval (if applicable) and all other currently approved documents for this study, please refer to the Print Menu for this Event in Rascal. It is important to confirm the status of each document, e.g., active, stamped, etc. Only stamped, active documents can be used with research participants.

Consent Requirements:
Informed consent with written documentation will be obtained from the research participant or appropriate representative

Please Note:
- This research study meets pediatric criteria described in 45 CFR 46.404 under Subpart D, for research not involving greater than minimal risk.
- Permission from at least one parent must be obtained.
- Assent requirement: Assent from all children is required.
- Subjects are 10-17 and written assent will be obtained, unless they are considered an emancipated minor, in which case consent will be obtained for that individual without parental consent.

Protocol:
- Impact of COVID-19: For current information regarding the ramp up of human subjects research activities, please consult the frequently asked questions available at: https://research.columbia.edu/COVID-19_Research/Ramp-up/HS. Any questions regarding ramp up, as it pertains to human subjects research should be directed to irboffice@columbia.edu.
Documents:

- Submit approval from the in-country ethics board prior to the start of research activities.

- Please review the CU IRB Policy on Research with Non-English speaking subjects found at http://www.columbia.edu/cu/irb/policies/documents/Nonenglish_Speaking.doc. The IRB requires translations of any

154 Haven Avenue, 1st Floor New York, NY 10032 212-305-5883 Tel 212-305-1316 Fax
615 West 131st Street, 3rd Floor New York, NY 10027 212-851-7040 Tel 212-851-7044 Fax

materials (e.g., recruitment materials, consent forms, information sheets, etc.) that will be used with subjects. Translations should be submitted as a modification after the English versions are approved. When submitting translations of approved documents, confirm through an attestation that an "Acceptable Translator" was used, as described in the policy, and confirm that all translations are based on an actively approved English version of the document and that the translations are consistent in content, style, and level of readability with the IRB-approved document.

Electronically signed by: Elizaire-Williams, Myriam

IRB-AAAT5971 Protocol (Y01M00)

Researcher Responsibilities:

Any proposed changes in the protocol must be immediately submitted to the IRB for review and approval prior to implementation, unless such a change is necessary to avoid immediate harm to the participants.

Any unanticipated problems that involve risks to subjects must be reported to the IRB in accordance with the Unanticipated Problems: Reporting to the IRB of Unanticipated Problems Involving Risks policy. All submissions for modifications and unanticipated problems must be submitted through Rascal.

Renewal applications should be submitted 60 days before the expiration date of this study through Rascal. Failure to obtain renewal of your study prior to the expiration date will require discontinuance of all research activities for this study, including enrollment of new subjects.

You must file a Closure Report in Rascal when your study has been completed.

APPENDIX E: Parent Study Ethical Approval by the Comite Nacional De Bioética Para a Saúde

REPÚBLICA DE MOÇAMBIQUE
MINISTÉRIO DA SAÚDE
COMITÉ NACIONAL DE BIOÉTICA PARA A SAÚDE
IRB00002657

Exma. Senhora
Dra. Eliane Abrams
ICAP

Ref:467/CNBS/21 **Data 05 de Agosto de 2021**

Assunto: Aprovação do Comité Nacional de Bioética para Saúde (CNBS) referente ao Protocolo de estudo intitulado: "***CombinADO: a cluster-randomized controlled trial to compare the efficacy, uptake, feasibility and acceptability of the CombinADO strategy versus optimized standard of care on viral suppression, ART adherence and retention in HIV care among adolescents and young adults living with HIV ages 10-24yrs in Nampula Province*** "

O Comité Nacional de Bioética para Saúde (CNBS) analisou as correcções efectuadas no Protocolo intitulado: "***CombinADO: a cluster-randomized controlled trial to compare the efficacy, uptake, feasibility and acceptability of the CombinADO strategy versus optimized standard of care on viral suppression, ART adherence and retention in HIV care among adolescents and young adults living with HIV ages 10-24yrs in Nampula Province*** ", registado no CNBS com o número 128/CNBS/2020, conforme os requisitos da Conferência Internacional de Harmonização e Boas Práticas clínicas (ICH&GCP), igualmente cumprindo com a norma E6 do ICH que descreve as responsabilidades e expectativas de todos os participantes na realização de ensaios clínicos incluindo investigadores, monitores e patrocinadores.

Não havendo nenhum inconveniente de ordem ética que impeça a realização do estudo, o CNBS dá a sua devida aprovação aos seguintes documentos:

- Protocolo, versão 1.3 de 02 de Agosto de 2021;
- Consentimentos Informados Inquérito AJVHIV, versão 1.2 de 02 de Agosto de 2021;
- Consentimento para entrevista de saída AJVHIV, versão 1.3 de 02 de Agosto de 2021;
- Consentimento Informado para Profissionais de Saúde de para informantes chaves, versão 1.3 de 02 de Agosto de 2021;
- Permissão para cuidadores para entrevista de saída com AJVHIV (10-17 anos), versão 1.3 de 02 de Agosto de 2021;

Endereço:
Ministério da Saúde - 2º andar dto
Av. Eduardo Mondlane / Salvador Allende
Maputo - Moçambique

C.Postal: 264
Telefone: +258 82 406 6350
E-mail: cnbsmocambique@gmail.com

- Consentimento Informado para Profissionais de Saúde – Custo eficácia, versão 1.1 de 02 de Agosto de 2021;
- Folha de informação 10-11 anos – inquérito e entrevista dc saída, versão 1.0 de 11 de Agosto de 2021;
- Permissão para cuidadores para o inquérito com AJVHIV (10-17 anos), 1.2 de 02 de Agosto de 2021;
- Acordo de Transferência de dados, de 02 de Agosto de 2021.

1. A presente aprovação não substitui a autorização administrativa.
2. Não houve declaração de conflitos de interesse por nenhum dos membros do CNBS.
3. A aprovação terá a validade de um ano, terminando esta 05 de Agosto de 2022. Os investigadores deverão submeter o pedido de renovação da aprovação um mês antes de terminar o prazo.
4. Recomenda-se aos investigadores que mantenham o CNBS informado do decurso do estudo.
5. A lista actualizada dos membros do CNBS encontra-se disponível

Sem mais do momento, queiram aceitar as nossas cordiais saudações.

O Presidente

Dr. João Fernando Lima Schwalbach

APPENDIX F: Parent Study Data Sharing and Usage Agreement

Data-Sharing and Usage agreement

Pheposadi Lekubu Mogoba and CombinADO Study

This agreement establishes terms and conditions under which Pheposadi Mogoba (**the Recipient**) can acquire and use data received from the CombinADO Study (**the Provider**) for the proposed PhD project.

1. Confidentiality of data
    a. The Recipient will not release any information or present results from the data analysis in any manner that would reveal the identity of individual participants in the study.
    b. The Recipient will not release data to a third party without prior approval from the Provider.
    c. The Recipient will not share, publish, or release any findings or conclusions derived from the analysis of data obtained from the Provider without prior approval.
    d. All electronic records will be kept in password-protected files stored on encrypted endpoint (laptop, desktop, etc). All electronic communications of the study data will be through password-protected, encrypted files.
2. Period of agreement
    a. The Recipient will use the data for a PhD project at the University of Cape Town intended to be completed by end of December 2024, the period after which the current agreement will be terminated.
    b. Publications or presentations of the results from the PhD project could take place in both local and international platforms with prior approval from the Provider.
3. Data use and ownership
    a. All data transferred to the Recipient from the Provider shall remain the property of the Provider and shall be returned to the Provider upon the termination of the Agreement.
    b. All data shall be used solely in strict accordance with objectives outlined by the Recipient in the proposed PhD protocol.
    c. The Provider will be cited as the source of data for all data received from the Provider and used by the Recipient in the PhD project, including in publications and presentations.

Signed by **the Recipient**

Signature:

Name (please print): Pheposadi Lekubu Mogoba Date of signing: 2022/02/17

Signed for and on behalf of **the Provider:**

Signature:

Name (please print): Allison Buba Date of signing: 24/02/2022

Deputy Director for Research. CombinADO study

Data-Sharing and Usage agreement

Ashlee Blacher and CombinADO Study

This agreement establishes terms and conditions under which Ashlee Blacher (**the Recipient**) can acquire and use data received from the CombinADO Study (**the Provider**) for the proposed MPH project.

1. Confidentiality of data
    a. The Recipient will not release any information or present results from the data analysis in any manner that would reveal the identity of individual participants in the study.
    b. The Recipient will not release data to a third party without prior approval from the Provider.
    c. The Recipient will not share, publish, or release any findings or conclusions derived from the analysis of data obtained from the Provider without prior approval.
    d. All electronic records will be kept in password-protected files stored on encrypted endpoint (laptop, desktop, etc). All electronic communications of the study data will be through password-protected, encrypted files.
2. Period of agreement
    a. The Recipient will use the data for an MPH project at the University of Cape Town intended to be completed by end of February 2025, the period after which the current agreement will be terminated.
    b. Publications or presentations of the results from the MPH project could take place in both local and international platforms with prior approval from the Provider.
3. Data use and ownership
    a. All data transferred to the Recipient from the Provider shall remain the property of the Provider and shall be returned to the Provider upon the termination of the Agreement.
    b. All data shall be used solely in strict accordance with objectives outlined by the Recipient in the proposed MPH protocol.
    c. The Provider will be cited as the source of data for all data received from the Provider and used by the Recipient in the MPH project, including in publications and presentations.

Signed by **the Recipient**:

Signature: fler.

Name (please print): Ashlee Blacher Date of signing: 29/11/2024

Signed for and on behalf of **the Provider:**

Signature:

Name (please print): Allison Buba Date of signing: 29/11/2024

APPENDIX G: Parent Study Consent and Assent Forms

Assent for Survey, AYLHIV ages 12-17years
Version 1.2, 02August2021

TITLE OF RESEARCH: **Combinado: a cluster-randomized controlled trial to compare the efficacy, uptake, feasibility and acceptability of the CombinADO strategy versus optimized standard of care on viral suppression, ART adherence and retention in HIV care among adolescents and young adults living with HIV ages 10-24yrs in Nampula Province**

Hello. My name is_____. I am from ICAP at Columbia University.

We are doing a research study to learn more about HIV and health services for young people, like you, in Mozambique. The information that we learn will help us to find better ways to help adolescents stay in HIV care and to take their HIV medicines (ART) every day.

We have talked to your parents/guardian and they said it was okay to invite you to take part in this study. This study wants to collect information about people that we use to help us learn new things.

WHY ARE WE DOING THIS STUDY
We are asking approximately 2400 adolescents and young people living with HIV who use HIV health services in various health facilities in Nampula province to take part. We are inviting you because you are a part of this group.

We are doing this study to learn more about adolescents living with HIV in Nampula. We want to find better ways to help HIV-positive adolescents to take their HIV treatment (ART) every day and to have a better health.

This form talks about our survey and the choice that you have to take part in it. This form might have some words that you may not have heard before. Please ask us to explain anything that you do not understand. We want you to ask us any questions that you have at any time.

WHERE WILL THIS STUDY BE CARRIED OUT?
We will conduct this survey in 12 health facilities: CS of 25 Septembro, CS of Muhala Expansão, CS 1 de Maio, CS de Namicopo, CS Anexo Psiquiatrico, HG Marrere, CS Alua, CS Namialo, CS Nacala Porto, CS Angoche, CS Nametil e CS Malema.

WHAT WOULD HAPPEN IF I AGREE TO PARTICIPATE IN THE STUDY?
If you and your parent/guardian decide to join the study, here is what would happen:

- If you agree to take part, we will ask you questions about many topics: we will ask questions about you, your family and where you live, your health, your relationships, your feelings and moods, use of and satisfaction with health services, knowledge about HIV and ART, taking your HIV medicines and some personal questions about your life including questions about sex, drinking and drug use and violence.
- The interview will take place in private and we will use a tablet computer to record your answers. We will not tell your parent/guardian about any of your answers.
- The interview will take about 60-120 minutes.
- We will also be be asking you for a blood sample to test your viral load and the amount of ARVs in your blood. If you agree, a trained nurse will collect approximately 10mls (two teaspoons) of your blood from a vein in your arm. We will share the results of the viral load test with the nurse so that they can be used for your health care. Blood collected during this visit will only be used for the type of testing mentioned above. Blood collected during your visit will not be used for any other testing or purposes outside of this study.
- We will also be looking at and taking information from your clinic records. From these records, we are interested in learning about medical care that you have received.

COULD BAD THINGS HAPPEN IF I TAKE THE SURVEY?

Assent for Survey, AYLHIV ages 12-17years
Version 1.2, 02August2021

You may feel uncomfortable answering some of the questions we will ask. You can refuse to answer any question or stop the survey at any time. We will do everything we can to keep your information private. Also you may feel physical discomfort during the collection of blood. You might have a slight bruising or tenderness. To minimize this, your blood sample will be collect by a nurse who had training in blood collection.

COULD THE STUDY HELP ME?

You will help figure out ways to help children and learn more about how children living with HIV feel about their lives and the health services they use in Mozambique.

WHAT ABOUT CONFIDENTIALITY?

We will not tell other people that you are in this survey and will not share information about you to anyone who does not work in the survey study. Any information about you will have a number on it instead of your name.

The following individuals and/or agencies will be able to look at your research records:

- Study staff and study monitors
- Staff members from groups (ex. Office of Human Research Protections) that protect your rights to ensure that we are protecting your rights
- National Institutes of Health (NIH), the study sponsor

This research is also covered by a Certificate of Confidentiality from the NIH and by the local norms to guarantee the confidentiality of study participants. The researchers with this Certificate may not tell anyone any information that may identify you in any legal setting unless you have given them permission. Study information protected by this Certificate cannot be told to anyone who is not involved in this research except if: 1) there is a US law that requires this; 2) if you have allowed the information to be shared; or 3) if it is used for other research, that is allowed by federal rules protecting individuals involved in research.

Even with these procedures and certificate in place if the study staff learns that you are thinking of hurting yourself or someone else or if someone is hurting you or putting you in danger, study staff will tell your doctor or nurse who will get you any help you may need.

Use of information in future studies

To learn new things, sometimes researchers share information they get from people who are in studies. The information that you give us during this survey is private and will be kept in a safe place. In the future there might be a chance to combine the information you give us with information from other studies also related to adolescent health and HIV. When researchers combine this information, they can learn even more about health problems.

If you agree to be in this study, the information you tell us will be kept by researchers so that it may be used in the future. The information that we keep will not have anything in it that can identify you like your name or birthday. It will be combined with information we get from other people like you in the study. Any researcher who wants to use the data from CombinADO that was already collected must submit a formal data use request which is reviewed and approved by the study principal investigator and the local ethics committee in Mozambique. If a researcher is allowed, they may be able to see and use your information, along with that from many other people like you. They will not be able to tell that the information is coming from you specifically. They will only know that it is information from someone in this study.

You may stop taking part in this study and not allow your information to be used in the future. If you want, you may ask to have the information you give us destroyed. However, it may not be possible to do this once the information has been shared with other researchers

ARE THERE ANY COSTS?

Assent for Survey, AYLHIV ages 12-17years
Version 1.2, 02August2021

There is no cost for being in this study, but we will ask you for your time and that you make yourself available at the health facility.

WILL I BE GIVEN ANYTHING FOR TAKING PART?

You will get 500Mt ($7USD) for your time and transportation to take part in this study.

CAN I LEAVE THE STUDY?

You may stop taking part in the survey at any time. You can refuse to answer any question.This will not affect your healthcare in any way.

QUESTIONS/POINTS OF CONTACT

If you have questions about the study or any problems with the study, you may contact Joana Falcão, ICAP-Mozambique, +258 21315170.

A description of this study will also be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results once they are available. You can search this website at any time.

If you have any questions about your rights as a participant in this study, please contact the Mozambique Ethics and Scientific Review Committee at +258 21 43 08 14/ 42 71 31, the Columbia University Institutional Review Board at +1 212-305-5883 or visit the website at http://www.cumc.columbia.edu/dept/irb/info.html. An IRB is a committee organized to protect the rights and welfare of people involved in research.

Assent for Survey, AYLHIV ages 12-17years
Version 1.2, 02August2021
PERMISSION STATEMENT
If you want to be asked questions after we talk, please write your name below. We will write our name too. This shows we talked about the survey and that you want to take part.

1. Do you agree to do the survey? 'YES' means that you agree to do the survey. 'NO' means that you will NOT do the survey.

   _____Yes _____No

2. Do you agree to let us look at your clinic records? 'YES' means that you will let us look at your records. 'NO' means that you will NOT let us look at your clinic records.

   _____Yes _____No

3. Do you agree to allow us to take one blood sample to measure your viral load. 'YES' means that you agree to allow us to take one blood sample from you. 'NO' means that you will NOT allow us take a blood sample.

   _____Yes _____No

4. Do you agree to allow your information to be used for future research? 'YES' means that you agree to allow your information to be used in the future. 'NO' means that you will NOT allow your information to be used in the future.

   _____Yes _____No

5. Do you agree to allow us to contact you for future follow-up studies after completion of the study? 'YES' means that you agree to allow us to contact you in the future. 'NO' means that you will NOT allow us to contact you in the future.

   _____Yes _____No

Participant signature or mark_____ Date: ___/___/___

Printed name of participant_____

Participant ID number _____

Signature of person obtaining permission_____ Date: ___/___/___

Printed name of person obtaining permission_____

Study staff ID number _____

[For illiterate participants]*
Signature of witness_____ Date: ___/___/___

Printed name of witness_____
* Witness is only required if participant is illiterate

Consent for Survey, AYLHIV ages 18 and older
Version 1.2, 02August2021

TITLE OF RESEARCH: **Combinado: a cluster-randomized controlled trial to compare the efficacy, uptake, feasibility and acceptability of the CombinADO strategy versus optimized standard of care on viral suppression, ART adherence and retention in HIV care among adolescents and young adults living with HIV ages 10-24yrs in Nampula Province**

WHAT IS THE PURPOSE OF THIS STUDY?
Hello. My name is_____. I am from ICAP at Columbia University.

We are doing a research study to learn more about HIV and health services for young people, like you, in Mozambique. The information that we learn will help us to find better ways to help adolescents stay in HIV care and to take their HIV medicines (ART) every day.

This form might have some words in it that are not familiar to you. Please ask us to explain anything that you do not understand.

WHY ARE YOU BEING INVITING TO TAKE PART?
We are asking approximately 2400 adolescents and young people living with HIV who use HIV health services in various health facilities in Nampula province to take part. We are inviting you because you are a part of this group. These participants will be chosen based on their age, gender, and willingness to take part in the study procedures.

WHERE WILL THIS STUDY BE CARRIED OUT?
We will conduct this survey in 12 health facilities: CS of 25 Septembro, CS of Muhala Expansão, CS 1 de Maio, CS de Namicopo, CS Anexo Psiquiatrico, HG Marrere, CS Alua, CS Namialo, CS Nacala Porto, CS Angoche, CS Nametil e CS Malema.

WHAT DO I HAVE TO DO IF I AGREE TO TAKE PART?
If you agree to take part, we will ask you questions about many topics: we will ask questions about you, your family and where you live, your health, your relationships, your feelings and moods, use of and satisfaction with health services, knowledge about HIV and ART, taking your HIV medicines and some personal questions about your life including questions about sex, drinking and drug use and violence.

The survey will take about 120 minutes and your answers will be recorded on a tablet computer. We will ask you to answer these question without having others present. We will not share your answers with your family or your health care providers.

We will also be looking at and taking information from your clinic records. From these records, we are interested in learning about the HIV care you have received.

Blood samples
As part of this study, we will also be asking you for a blood sample to test your viral load and the amount of ARVs in your blood. If you agree, a trained nurse will collect approximately 10mls (two teaspoons) of your blood from a vein in your arm. We wil share the results of the viral load test with the nurse so that they can be used for your HIV care. Blood collected during this visit will only be used for the type of testing mentioned above. Blood collected during your visit will not be used for any other testing or purposes outside of this study.

WHAT ARE THE POTENTIAL RISKS?

Participant Initials: _____

The risks of taking part in the survey are small:

- Some of the questions during the interview may make you uncomfortable because we will ask you about sensitive topics. However, you do not have to answer any questions that you do not want to and we will do everything we can to keep your information private.
- Even though we can not promise complete privacy (confidentiality) we have procedures to protect your confidentiality that are described further bellow.
- Also, there is a small risk of physical discomfort during the collection of blood specimens. You might have a slight bruising or tenderness. To minimize this, your blood sample will be collect by a nurse who had training in blood collection.

WHAT ARE THE POTENTIAL BENEFITS?

You may not receive any personal benefit from taking part in this study. The information gained in this study will help us to develop future HIV-related programs for other young people living with HIV.

WHAT ABOUT CONFIDENTIALITY?

This study has been approved by the Mozambique Ethics and Scientific Review Committee and the Columbia University Medical Center Institutional Review Board (CUMC IRB).

We will do everything we can to keep your participation in the survey and your answers private. We will not tell your family about any of your responses. Any information about you will have a number on it instead of your name.

The following individuals and/or agencies will be able to look at your research records:

- Study staff and study monitors
- Staff members from groups (ex. Office of Human Research Protections) that protect your rights to make sure that we are protecting your rights
- National Institutes of Health (NIH), the study sponsor

This research is also covered by a Certificate of Confidentiality from the NIH and by the local norms to guarantee the confidentiality of study participants. The researchers with this Certificate may not tell anyone any information that may identify you in any legal setting unless you have given them permission. Study information protected by this Certificate cannot be told to anyone who is not involved in this research except if: 1) there is a US law that requires this; 2) if you have allowed the information to be shared; or 3) if it is used for other research, that is allowed by federal rules protecting individuals involved in research.

Even with these procedures and certificate in place if the study staff learns that you are thinking of hurting yourself or someone else or if someone is hurting you or putting you in danger, study staff will tell your doctor or nurse who will get you any help you may need.

Use of information in future studies

To learn new things, sometimes researchers share information they get from people enrolled in studies. In the future there might be a chance to combine the information you give us with information from other studies also related to adolescent health and HIV. When researchers combine this information, they can learn even more about health problems.

If you agree your health information will be kept by researchers so that it may be used in the future. The information that we keep will not have anything in it that can identify you like names or birthdays. Any researcher who wants to use

Participant Initials: _____

the data from CombinADO that was already collected must submit a formal data use request which is reviewed and approved by the study principal investigator and the local ethics committee in Mozambique. If a researcher is allowed, they may be able to see and use your information, along with that from many other people like you. They will not be able to tell that the information is coming from you specifically. They will only know that it is information from someone enrolled in this study.

We do not expect any direct benefits for you from any future use of the your information. You may stop taking part in this study and withdraw permission for your information to be used in the future. However, it may not be possible to delete your information once they have been shared with other researchers.

ARE THERE ANY COSTS?

There is no cost for being in this study, but we will ask you for your time and that you make yourself available at the health facility.

WILL I BE GIVEN ANYTHING FOR TAKING PART?

You will get 500Mt ($7USD) for your time and transportation to take part in this study.

CAN I LEAVE THE STUDY?

You may stop taking part in the survey at any time. You can refuse to answer any question.This will not affect your healthcare in any way.

QUESTIONS/POINTS OF CONTACT

If you have questions about the study or any problems with the study, you may contact Joana Falcão, ICAP-Mozambique, +258 21315170.

A description of this study will also be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results once they are available. You can search this website at any time.

If you have any questions about your rights as a participant in this study, please contact the Mozambique Ethics and Scientific Review Committee at +258 21 43 08 14/ 42 71 31, the Columbia University Institutional Review Board at +1 212-305-5883 or visit the website at http://www.cumc.columbia.edu/dept/irb/info.html. An IRB is a committee organized to protect the rights and welfare of people involved in research.

Participant Initials: _____

Consent for Survey, AYLHIV ages 18 and older
Version 1.2, 02August2021
PERMISSION STATEMENT

Any questions that I had were answered satisfactorily. I have been offered a copy of this consent form.

1. Do you agree to do the survey? 'YES' means that you agree to do the survey. 'NO' means that you will NOT do the survey.

   _____Yes _____No

2. Do you agree to let us look at your clinic records? 'YES' means that you will let us look at your records. 'NO' means that you will NOT let us look at your clinic records.

   _____Yes _____No

3. Do you agree to allow us to take a blood sample? 'YES' means that you agree to allow us to take one blood sample from you. 'NO' means that you will NOT allow us take a blood sample.

   _____Yes _____No

4. Do you agree to allow your information to be used for future research? 'YES' means that you agree to allow your information to be used in the future. 'NO' means that you will NOT allow your information to be used in the future.

   _____Yes _____No

5. Do you agree to allow us to contact you for future follow-up studies after completion of the study? 'YES' means that you agree to allow us to contact you in the future. 'NO' means that you will NOT allow us to contact you in the future.

   _____Yes _____No

Participant signature or mark_____ Date: ___/___/___

Printed name of participant_____

Participant ID number _____

Signature of person obtaining permission_____ Date: ___/___/___

Printed name of person obtaining permission_____

Study staff ID number _____

[For illiterate participants]*
Signature of witness_____ Date: ___/___/___

Printed name of witness_____
* Witness is only required if participant is illiterate

Participant Initials: _____

APPENDIX H: Instructions for Authors for the Targeted Journal (AIDS Care)

Preparing Your Paper

Structure

Your paper should be compiled in the following order: title page; abstract; keywords; main text introduction, materials and methods, results, discussion; acknowledgments; declaration of interest statement; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figures; figure captions (as a list).

Word Limits

Please include a word count for your paper.

The maximum word count for the journal is 7000 words, excluding tables, figures, references, and endnotes.

Format-Free Submission

Authors may submit their paper in any scholarly format or layout. Manuscripts may be supplied as single or multiple files. These can be Word, rich text format (rtf), open document format (odt), PDF, or LaTeX files. Figures and tables can be placed within the text or submitted as separate documents. Figures should be of sufficient resolution to enable refereeing.

- There are no strict formatting requirements, but all manuscripts must contain the essential elements needed to evaluate a manuscript: abstract, author affiliation, figures, tables, funder information, references. Further details may be requested upon acceptance.
- References can be in any style or format, so long as a consistent scholarly citation format is applied. For manuscripts submitted in LaTeX format a .bib reference file must be included. Author name(s), journal or book title, article or chapter title, year of publication, volume and issue (where appropriate) and page numbers are essential. All bibliographic entries must contain a corresponding in-text citation. The addition of DOI (Digital Object Identifier) numbers is recommended but not essential.
- The journal reference style will be applied to the paper post-acceptance by Taylor & Francis.
- Spelling can be US or UK English so long as usage is consistent.

Note that, regardless of the file format of the original submission, an editable version of the article must be supplied at the revision stage.

Checklist: What to Include

1. **Author details.** Please ensure all listed authors meet the Taylor & Francis authorship criteria. All authors of a manuscript should include their full name and affiliation on the cover page of the manuscript. Where available, please also include ORCiDs and social media handles (Facebook, Twitter or LinkedIn). One author will need to be identified as the corresponding author, with their email address normally displayed in the article PDF (depending on the journal) and the online article. Authors' affiliations are the affiliations where the research was conducted. If any of the named co-authors moves affiliation during the peer-review process, the new affiliation can be given as a footnote. Please note that no changes to affiliation can be made after your paper is accepted. Read more on authorship.
2. **CRediT Roles.** From February 2025, this journal collects CRediT roles as part of the submission process and includes them on published articles when supplied by the authors. You may be required to provide CRediT roles (contributor details) for yourself and your co-authors. For more information about CRediT visit Author Services.
3. Should contain an unstructured abstract of 200 words.
4. **Graphical abstract** (optional). This is an image to give readers a clear idea of the content of your article. It should be a maximum width of 525 pixels. If your image is narrower than 525 pixels, please place it on a white background 525 pixels wide to ensure the dimensions are maintained. Save the graphical abstract as a .jpg, .png, or .tiff. Please do not embed it in the manuscript file but save it as a separate file, labelled GraphicalAbstract1.
5. You can opt to include a **video abstract** with your article. Find out how these can help your work reach a wider audience, and what to think about when filming.

6. Between 3 and 6 **keywords**. Read making your article more discoverable, including information on choosing a title and search engine optimization. This journal is using a set of Sustainable Development Goals (SDGs) keywords to tag papers related to the SDGs and highlight them for readers. Please check the details at the link provided for more information on how to participate in this initiative and remember to include the keywords within your manuscript file.
7. **Funding details.** Please supply all details required by your funding and grant-awarding bodies as follows:
   For single agency grants
   This work was supported by the [Funding Agency] under Grant [number xxxx].
   For multiple agency grants
   This work was supported by the [Funding Agency #1] under Grant [number xxxx]; [Funding Agency #2] under Grant [number xxxx]; and [Funding Agency #3] under Grant [number xxxx].
8. **Disclosure statement.** This is to acknowledge any financial or non-financial interest that has arisen from the direct applications of your research. If there are no relevant competing interests to declare please state this within the article, for example: *The authors report there are no competing interests to declare.* Further guidance on what is a conflict of interest and how to disclose it.
9. **Data availability statement.** If there is a data set associated with the paper, please provide information about where the data supporting the results or analyses presented in the paper can be found. Where applicable, this should include the hyperlink, DOI or other persistent identifier associated with the data set(s). Templates are also available to support authors.

10. **Data deposition.** If you choose to share or make the data underlying the study open, please deposit your data in a recognized data repository prior to or at the time of submission. You will be asked to provide the DOI, pre-reserved DOI, or other persistent identifier for the data set.
11. **Supplemental online material.** Supplemental material can be a video, dataset, fileset, sound file or anything which supports (and is pertinent to) your paper. We publish supplemental material online via Figshare. Find out more about supplemental material and how to submit it with your article.
12. **Figures.** Figures should be high quality (1200 dpi for line art, 600 dpi for grayscale and 300 dpi for colour, at the correct size). Figures should be supplied in one of our preferred file formats: EPS, PS, JPEG, TIFF, or Microsoft Word (DOC or DOCX) files are acceptable for figures that have been drawn in Word. For information relating to other file types, please consult our Submission of electronic artwork document.
13. **Tables.** Tables should present new information rather than duplicating what is in the text. Readers should be able to interpret the table without reference to the text. Please supply editable files.
14. **Equations.** If you are submitting your manuscript as a Word document, please ensure that equations are editable. More information about mathematical symbols and equations.
15. **Units.** Please use SI units (non-italicized).

Method Article Type

- Should be written with the following elements in the following order: title page; abstract; keywords; main text introduction, materials and methods, results, discussion; acknowledgments; declaration of interest statement; author contributions statement; references; appendices (as appropriate); table(s) with caption(s) (on individual pages); figures; figure captions (as a list).
- The abstract structure should be as follows: Introduction, Methods, Results, Discussion.
- Should contain between 3 and 6 keywords. Read making your article more discoverable, including information on choosing a title and search engine optimization. This journal is using a set of Sustainable Development Goals (SDGs) keywords to tag papers related to the SDGs and highlight them for readers.
- Should be at between 2500 and 4000 words in length.
- Author Contributions Statement: Please provide an author contributions statement at the end of your article, before the references, that outlines which author(s) were involved in the conception and design, or analysis and interpretation of the data; the drafting of the paper, revising it critically for intellectual content; and the final approval of the version to be published; and that all authors agree to be accountable for all aspects of the work.
- Further information about this article type: Methods articles are a medium length, peer-reviewed article type that describes an advancement or development of current methods and research procedures. These should include adequate and appropriate validation to be considered. Any datasets associated with the paper must publish all experimental controls and make full datasets available where possible. If there are concerns about identifying factors in datasets, these should be discussed with the Editor-in-Chief prior to submission.
- Please note, that authors submitting protocol and methodology articles have the option to share their methods on protocols.io. Please note, this is not required for submission but is encouraged.