Depression-mediating pathways from household adversity to antiretroviral therapy non-adherence among children and adolescents living with HIV in Zambia: a structural equation modeling approach

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Abstract

Background: In Zambia, half of children and adolescents living with HIV (CALWH) on antiretroviral therapy (ART) are virologically unsuppressed. Depressive symptoms are associated with ART non-adherence but have received insufficient attention as mediating factors in the relationship between HIV self-management and household-level adversities. We aimed to quantify theorized pathways from indicators of household adversity to ART adherence, partially mediated by depressive symptoms, among CALWH in two Zambian provinces.

Setting: In July-September 2017, we enrolled 544 CALWH aged 5–17 years and their adult caregivers into a year-long prospective cohort study.

Methods: At baseline, CALWH-caregiver dyads completed an interviewer-administered questionnaire, which included validated measures of recent (past 6 months) depressive symptomatology and self-reported past-month ART adherence (never versus sometimes or often missing medication doses). We used structural equation modeling with theta parameterization to identify statistically significant ($p<0.05$) pathways from household adversities (past-month food insecurity, caregiver self-reported health) to depression (modeled latently), ART adherence, and poor physical health in the past 2 weeks.

Results: Most CALWH (mean age: 11 years, 59% female) exhibited depressive symptomatology (81%). In our structural equation model, food insecurity significantly predicted elevated depressive symptomatology ($\beta = 0.128$), which was associated inversely with daily ART adherence ($\beta =$

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−0.249) and positively with poor physical health ($\beta = 0.359$). Neither food insecurity nor poor caregiver health were directly associated with ART non-adherence or poor physical health.

Conclusions: Using structural equation modeling, we found that depressive symptomatology fully mediated the relationship between food insecurity, ART non-adherence, and poor health among CALWH.

Keywords

depression; mental health; HIV treatment; food insecurity; latent variable modeling; sub-Saharan Africa

Introduction

Over 2 million children and adolescents aged 19 years and younger are estimated to be living with HIV.[1] Despite substantial progress in recent years, HIV treatment outcomes among children and adolescents living with HIV (CALWH) remain suboptimal. Only 65% of CALWH <18 years achieve viral suppression after 12 months on antiretroviral therapy (ART),[2] driven in part by treatment adherence challenges. These age groups, therefore, shoulder a substantial burden of AIDS-related morbidity and mortality. In Zambia, one sub-Saharan African country with high adult HIV prevalence (~12%), only about half (54%) of children <15 years on ART have achieved viral suppression.[3] Novel approaches to bolster HIV treatment outcomes in CALWH are urgently needed.

Poor mental health, including depressive symptoms and other manifestations of psychological distress, have entered the scientific discourse as key drivers of ART non-adherence and AIDS-related morbidities among CALWH. Depressive symptoms in children and adolescents have been linked to anticipated and enacted HIV-related stigma—a pervasive challenge to health equity and justice for people living with HIV.[4–6] Although social support (from caregivers, family members, peers, healthcare providers) can foster resilience and mitigate psychological distress,[7,8] support may also insufficiently shield young people from more hazardous consequences of HIV-related stigma, including self-blame and shame, that modulate depressive symptoms.[9,10] Likewise, other sources of adversity accumulating over the life course have been linked to suboptimal HIV treatment outcomes in young people. This includes numerous factors operating at the household level, from food insecurity to caregiver health status.[11–13] Less is known, however, about how depressive symptoms in CALWH can mediate the effects of household adversity on HIV-related and other physical health outcomes.

The consequences of unmet mental health needs in CALWH can be severe. Stigma related to mental health disorders can demotivate care-seeking and even interfere with caregiver recognition of psychological distress in children and adolescents.[14,15] Limited capacities and resources to identify, diagnose, and treat depressive symptoms within health systems also constrain opportunities to deliver mental health care and supportive services.[15] Oft-cited efforts to address psychological distress among CALWH involve family-based interventions (i.e., caregiver strengthening, parent and child communication), frequently facilitated by lay service providers like peers and community health workers.[16] Specialized mental health care

and treatment, however, may be needed for CALWH exhibiting more severe manifestations of psychological distress. The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) has recently acknowledged gaps in addressing the mental health needs of people living with HIV, identifying poor mental health as a bottleneck along the HIV care continuum.[17] Given recent attention towards integrating mental health services into HIV treatment programs,[18] identifying specific pathways to depressive symptoms in CALWH and the impact of these distinct pathways on ART adherence remains a critical priority for HIV treatment programs.

To that end, we used structural equation modeling to test a theoretical model linking sources of household adversity to ART non-adherence and physical health outcomes, partially mediated by depressive symptoms, among CALWH aged 5–17 years in Zambia (Figure 1). Our findings help quantify which pathways most significantly predict depressive symptoms and health-related outcomes in CALWH, identifying intervention priorities for each.

Methods

Setting and Design

We derive data from a baseline assessment of Zambia Family (ZAMFAM), a year-long prospective cohort study of 544 CALWH and caregiver dyads across 8 districts in Central and Eastern Provinces of Zambia. The parent study sought to measure changes in financial, psychosocial, and physical wellbeing, comparing households participating in a PEPFAR-funded community-based, family-centered economic strengthening and psychosocial support intervention (Central Province) to non-participating households (Eastern Province). We report on the multi-component intervention and parent study methods elsewhere.[19]

Briefly, in July-October 2017, we used two-stage, stratified random sampling to identify and recruit households in 4 PEPFAR priority districts in Central Province, where ZAMFAM implementation began in 2015.[19] After randomly sampling 13 wards, households with CALWH aged 5–17 years were arranged sequentially by unique ZAMFAM identification codes and randomly approached for study recruitment until 320 households were pre-consented. We identified 4 districts in Eastern Province with comparable HIV burdens and geographic characteristics (i.e., population size estimates, urbanization) to ZAMFAM-implementing districts in Central Province. Within these matched districts in Eastern Province, we recruited non-intervention CALWH and caregiver dyads using registers maintained by HIV clinics and community-based organizations. All eligible CALWH and their primary caregivers were approached during study recruitment until a sample size threshold of 272 CALWH-caregiver dyads were enrolled.

Participants and Procedures

Study eligibility included: (1) aged 5–17 years (for CALWH) and aged 18 years (for caregivers); (2) English, Bemba, Nyanja, and/or Tonga comprehension; and (3) known HIV serostatus among CALWH aged 10 years. In households with 1 eligible CALWH, we randomly selected 1 CALWH for study inclusion.

Enrolled CALWH and caregiver dyads completed a face-to-face, interviewer-administered structured questionnaire assessing household characteristics, health and wellbeing, and HIV service engagement. After obtaining written parental consent and child assent, we interviewed CALWH aged 10–17 years directly using a structured questionnaire. Caregivers completed interviews on behalf of enrolled CALWH aged <10 years.

Measures

Survey measures covered multiple domains (socio-demographics, household adversity, CALWH health and wellbeing); were collected by self-report or interviewer observation; and were derived from MEASURE Evaluation's Orphans and Vulnerable Children (OVC) Survey Toolkit, which included items and measures of child/adolescent wellbeing that were developed, piloted, and validated during implementation in Zambia and Nigeria.[20]

Measures of household adversity included: caregiver's current self-reported health status (poor or very poor versus fair, good, or very good); household food insecurity, defined as having no food in the home in the past month (at least once versus less than once); caregiver support of corporeal punishment in the home, defined as endorsement (yes versus no) of hitting/beating children as acceptable in the household; death of any household member in the past 12 months (yes versus no); household financial security, measured by caregiver self-report of perceived financial stability relative to neighboring households (less secure versus more or equally secure); and household shelter protection, determined through interviewer observation of the sufficiency of a home's roofing material and walls in providing shelter.

We measured depressive symptoms in CALWH using a 5-item, 3-point ("never", "sometimes", or "always" in the past 6 months) instrument included in MEASURE Evaluation's OVC Survey Toolkit and initially adapted from the Patient Health Questionnaire-9 (PHQ-9), a widely used, validated screening tool for depression in adults and adolescents.[21–23] Items included: (1) little interest or pleasure in activities; (2) feeling down, depressed, or hopeless; (3) trouble falling or staying asleep; (4) sleeping too much or for too long; and (5) feeling irritable or easily annoyed. The scale exhibited modest internal consistency (Cronbach's $\alpha = 0.58$) in the study population.

Other indicators of CALWH health and wellbeing included social support, defined as agreement (yes versus no) with having a person in one's life who provides support across all 4 of the following domains: turning to for suggestions, helping with chores, showing love and affection, and doing enjoyable things with;[20] receiving any psychosocial support services in the past 6 months (yes versus no); and current participation in a support group for CALWH (yes versus no).

We measured ART adherence through CALWH or caregiver self-report of frequency with which CALWH missed medication doses in the past month (never, sometimes, or often), which we collapsed into a dichotomous measure comparing daily (never) to less than daily (sometimes or often) ART use. We also included a measure of CALWH physical health by ascertaining recent prevalence of debilitating illness, defined as CALWH being too sick to participate in daily activities in the past 2 weeks (yes versus no).

Socio-demographics included age, measured in continuous years and dichotomized (5–9 versus 10–17 years); sex (male versus female); residence type, measured at the ward level and classified as urban for localities with 5,000 inhabitants (versus rural);[24] province (Central versus Eastern); current schooling status (enrolled in school versus out-of-school); and household wealth (poorest versus average versus wealthiest), derived from a 30-item index of enumerated household assets collapsed into terciles using principal components analysis.[25]

Analysis

First, we sought to revalidate the depressive symptomatology scale for the study population of CALWH. We began by using principal components analysis to identify the number of domains (or factors) onto which the 5 depressive symptom items clustered. Using parallel analysis, we then plotted eigenvalues and identified the number of domains to extract for exploratory factor analysis (EFA).[26] Next, we implemented EFA using iterative principal factor estimation and a polychoric correlation matrix, which generated loading coefficients and estimates of variance communality for each depressive symptom.[27,28] We inspected coefficients emerging from the EFA model and subsequently excluded items with low factor loading coefficients ($\beta < 0.4$) and high unique item variances ($\delta > 0.6$).[29] We repeated this procedure until a final factor analytic model with adequate factor loadings and item uniqueness emerged. We managed data, calculated descriptive statistics, and performed EFA in Stata/IC 15.1 (StataCorp LLC, College Station, TX).

Next, we used structural equation modeling to identify and quantify theorized pathways from household adversity to poor health and wellbeing among CALWH, partially mediated by depressive symptoms. Our structural equation model, guided by the study's conceptual framework (Figure 1), consisted of two components: a measurement model and a structural model. After obtaining a final EFA model, we used confirmatory factor analysis (CFA) to verify that the depressive symptomatology construct emerging from EFA adequately fit the data. We then fit a path model with all covariates and pathways illustrated in Figure 1, modeling depressive symptoms as a latent (unobserved) construct and all other variables as fixed (observed) measures. We report all coefficients as standardized Y-X beta (β) values with theta parameterization, including corresponding standard errors (SEs) and p-values.[30]

To evaluate the adequacy of the measurement and structural components of the model, we used the following model fit indices and corresponding thresholds: the chi-square goodness-of-fit (χ^2) (p 0.05);[31] the root mean square error of approximation (RMSEA, 0.08);[31] the comparative fit index (CFI, >0.90);[32] the Tucker-Lewis index (TLI, >0.90);[32] and the standardized root mean residual (SRMR, 0.08).[31] Lastly, to examine whether the measurement and structural components of the model varied significantly by socio-demographics (age, sex, residence type, and province), we implemented χ^2 tests of model invariance, comparing calculated log-likelihood differences between constrained and unconstrained measurement and structural models, respectively, for each demographic factor.[33] We conducted CFA and structural equation modeling, including tests of measurement and structural invariance, in MPlus 8.3 (Muthen & Muthen, Los Angeles, CA).

Results

Sample Characteristics

Table 1 presents descriptive characteristics of the study population ($N = 544$). Equal numbers of CALWH-caregiver dyads were recruited from Central ($n = 272$) and Eastern ($n = 272$) Provinces. The mean age of CALWH was 11 years (*std. dev.* 4 years). Over half of CALWH were female (59%), urban residents (66%), and currently out-of-school (66%). Household food insecurity was high, with over half of caregivers reporting having no food at home at least once in the prior month (55%). One-fourth of CALWH's caregivers reported their own current health status as poor or very poor (24%). Caregiver support of corporeal punishment in the home was moderate (19%). Fewer than one-fifth of households had a death in the past 12 months (16%) and lacked basic shelter protection (11%)

Many CALWH exhibited depressive symptomatology, with 81% reporting sometimes or always experiencing at least 1 depressive symptom in the past 6 months. The fraction of CALWH reporting any symptoms of depression was consistent across age groups (5–9 years: 81%, 10–17 years: 82%). The distribution of depressive symptoms (sometimes or always in the past 6 months) was as follows (Figure 2): little interest or pleasure in activities (66%); feeling down, depressed, or hopeless (37%); trouble falling or staying asleep (22%); sleeping too much or for too long (35%); and irritable or easily annoyed (37%).

Despite high prevalence of depressive symptomatology, only one-fourth of CALWH received any psychosocial support services in the past 6 months (26%), and only 13% reported participating in support groups for CALWH. Nearly two-thirds of CALWH, nevertheless, reported social support across 4 domains (65%). One-third of CALWH were too sick for daily activities in the past 2 weeks (32%), and most CALWH reported daily ART adherence to ART in the past month (83%).

Revalidating the Depressive Symptomatology Measure

Results from the parallel analysis supported the extraction of a single factor to represent the depressive symptomatology construct in EFA (Supplemental Digital Content, Figure S1). We excluded 1 depressive symptom ("little interest or pleasure in daily activities") from the unifactorial model due to a low factor loading coefficient ($ß = 0.174$) and high unique item variance ($δ = 0.970$), consistent with findings from the polychoric matrix demonstrating low item correlation ($r < 0.30$) with other depressive symptoms (Supplemental Digital Content, Table S1-S2).

Figure 3 illustrates CFA results for the 4-item, unifactorial depressive symptom construct emerging from EFA. CFA model fit indices suggested the unifactorial construct adequately fit the data (CFI = 0.97, TLI = 0.91, SRMR = 0.03).

Quantifying Theorized Depression-Mediating Pathways to ART Non-Adherence

In the structural equation model partially mediated by depressive symptoms (Figure 4), we identified several significant theorized pathways linking household adversity to poor health vis-à-vis depression. Food insecurity emerged as a significant predictor of elevated

depressive symptomatology ($\beta = 0.128$, SE = 0.052, $p = 0.013$), which was inversely associated with daily ART adherence ($\beta = -0.249$, SE = 0.084, $p = 0.003$). Likewise, elevated depressive symptomatology was significantly associated with debilitating illness ($\beta = 0.359$, SE = 0.059, $p < 0.001$). ART non-adherence, however, was unassociated with debilitating illness ($\beta = 0.017$, SE = 0.096, $p = 0.859$). We also found no statistically significant associations between indicators of household adversity and ART non-adherence. Lastly, poor caregiver health significantly predicted debilitating illness ($\beta = 0.122$, SE = 0.050, $p = 0.016$) but was only marginally associated with depressive symptomatology ($\beta = 0.082$, SE = 0.048, $p = 0.091$).

Model fit statistics indicated the structural equation model fit the data exceptionally well (χ^2 $p = 0.287$, RMSEA = 0.02, CFI = 0.99, TLI = 0.98, SRMR = 0.02). We found no evidence of measurement or structural variance by age, sex, or residence type (Supplemental Digital Content, Table S3).

Discussion

Findings from our cross-sectional study suggest that depressive symptoms fully mediate the impact of household adversity on ART non-adherence on CALWH in Zambia. Using structural equation modeling, we found that indicators of household adversity, specifically food insecurity, were only indirectly associated with ART non-adherence through depressive symptoms. Even in the presence of overlapping socio-structural adversities, CALWH still report high adherence to ART, which could be related to coverage of resilience-fostering psychosocial support interventions (i.e., adherence clubs, family-strengthening interventions) in the study population.[7,34] Over 65% of CALWH reported basic social support across 4 domains, while 26% received formal psychosocial support services. Only in the presence of elevated depressive symptoms did food insecurity predict suboptimal ART adherence and debilitating illness, reaffirming the centrality of psychological distress in the relationship between household adversity, ART non-adherence, and physical health outcomes.

Consistent with studies of CALWH in sub-Saharan Africa, findings from the present study reaffirm the contribution of depressive symptomatology to ART adherence as well as the role of food security in psychosocial wellbeing. A longitudinal study of adolescents living with HIV in South Africa revealed the strong prospective association of depressive symptomatology with subsequent ART non-adherence.[35] Another study of South African adolescents living with HIV found that improved food security and psychological wellbeing were independently associated with ART adherence, but unlike in the present study, depression-mediating pathways from food insecurity to ART adherence were not investigated.[36] Likewise, a recent qualitative study in Tanzania reiterated the impact of food insecurity on adherence to daily ART among adolescents living with HIV,[37] suggesting that efforts bolstering social and financial assets may be key to disrupting social and structural drivers of ART non-adherence. Although food insecurity did not emerge as a statistically significant driver of ART non-adherence, contrary to what other studies have reported, our study findings suggest that addressing food insecurity could improve depressive symptoms, which may also be accompanied by downstream benefits to ART adherence. Randomized

and observational studies have demonstrated the potential for cash transfers to meaningfully rupture pathways from food insecurity and other material asset deprivations to HIV-related outcomes, including improved HIV self-management.[38–40]

In evaluating the psychometric properties of the validated depressive symptom scale used in our study, we found that one symptom ("Little interest or pleasure in activities") was insubstantially correlated with other indicators of depression, resulting in its exclusion from the final EFA model. Among depressive symptoms, this one was endorsed most frequently (66%) by CALWH or their caregiver proxies. While this item was developed to measure anhedonia (or withdrawal from social interactions),[22] the construct validity of this item could be challenged by co-occurring physiological symptoms related to HIV infection and/or treatment. It is unclear, therefore, whether endorsed anhedonia reflect underlying psychological distress or physical manifestations of poor health, whether related to chronic HIV infection or ART side effects.[41–43] Future studies should qualitatively elucidate idioms of psychological distress and manifestations of depressive processes in CALWH.

Nevertheless, an overwhelming fraction of CALWH (>80%) endorsed symptom patterns consistent with depression, suggesting a high need for enhanced therapeutic care and psychosocial support in this population. Beyond food insecurity, other unmeasured factors, including HIV stigma and the absence of meaningful social support, could be driving high burdens of depressive symptomatology in CALWH.[4,9] Given the presence of depressive symptoms in CALWH's experiences with both hunger and ART non-adherence, our findings suggest that enhanced psychological care and psychosocial support, specifically for CALWH in food-insecure households, could address gaps in the HIV care continuum among children and adolescents.

Taken together, our findings have important implications for identifying priority groups among CALWH for psychosocial support, psychological care (e.g., counseling and cognitive-behavioral therapy), and anti-depressive therapies to improve HIV treatment outcomes. However, our findings must be considered with several limitations in mind. First, we captured survey measures through CALWH and/or caregiver self-report, likely inducing social desirability and recall biases. Our measure of self-reported ART adherence was particularly susceptible to response bias, despite the high concordance between self-reported ART use and detectable ART in serum biomarkers reported in other studies.[44] Second, structural equation modeling tests the significance of theorized covariate pathways, but our study's cross-sectional design still precludes assessments of temporal covariate relationships, limiting our inferential scope. Similarly, theorized pathways quantified using structural equation modeling remain plausibly bidirectional, as debilitating illness and ART non-adherence—in addition to being downstream consequences of poor mental health— could also elevate depressive symptomatology. Third, our structural equation model tested pathways theorized *a priori* and did not include an exhaustive list of factors, some of which were unmeasured in the present study (e.g., exposure to violence, times since HIV diagnosis, orphanhood status). These factors have potential to buffer or attenuate statistically significant pathways identified using structural equation modeling, and their exclusion from the final structural model increases the likelihood of residual confounding. Nevertheless, structural equation modeling best practices call for a minimal set of included covariates to

optimize model identifiability.[45] Fourth, our study population reported moderate coverage of psychosocial support and economic-strengthening interventions, potentially diluting the transportability of findings to CALWH in settings with lower service coverage. Fifth, and finally, insights derived from our study of CALWH in Zambia should be cautiously generalized to other populations, including older adolescents and adults.

Our study contributes to bourgeoning evidence that depressive symptoms fully mediate the relationship between sources of household adversity and ART non-adherence in CALWH. Using structural equation modeling, we found that pathways from household adversity, specifically food insecurity were only significantly associated with ART non-adherence through the pathway of elevated depressive symptoms. Our results suggest that in the context of psychosocial support and economic-strengthening service coverage, CALWH report high ART adherence even when confronted with overlapping adversities manifesting at the household level. Prioritizing enhanced, age-appropriate psychosocial support and mental health services for CALWH in food-insecure households, coupled with interventions to address material asset deprivation (i.e., cash transfers), can optimize ART adherence and prevent morbidity associated with HIV infection progression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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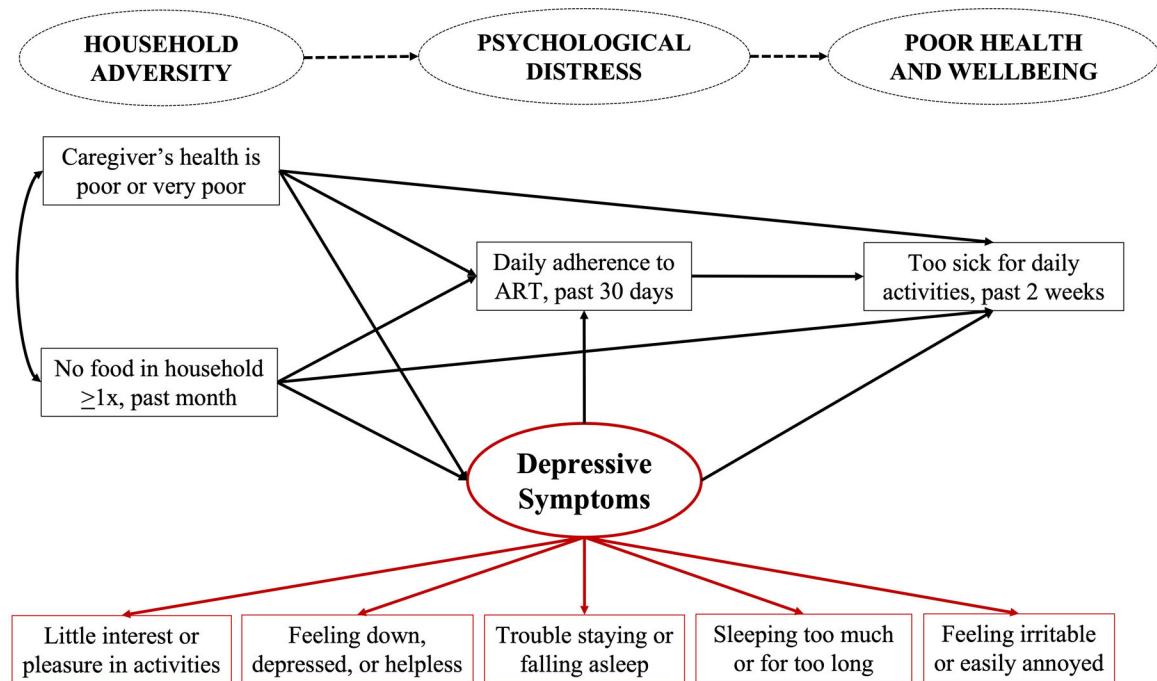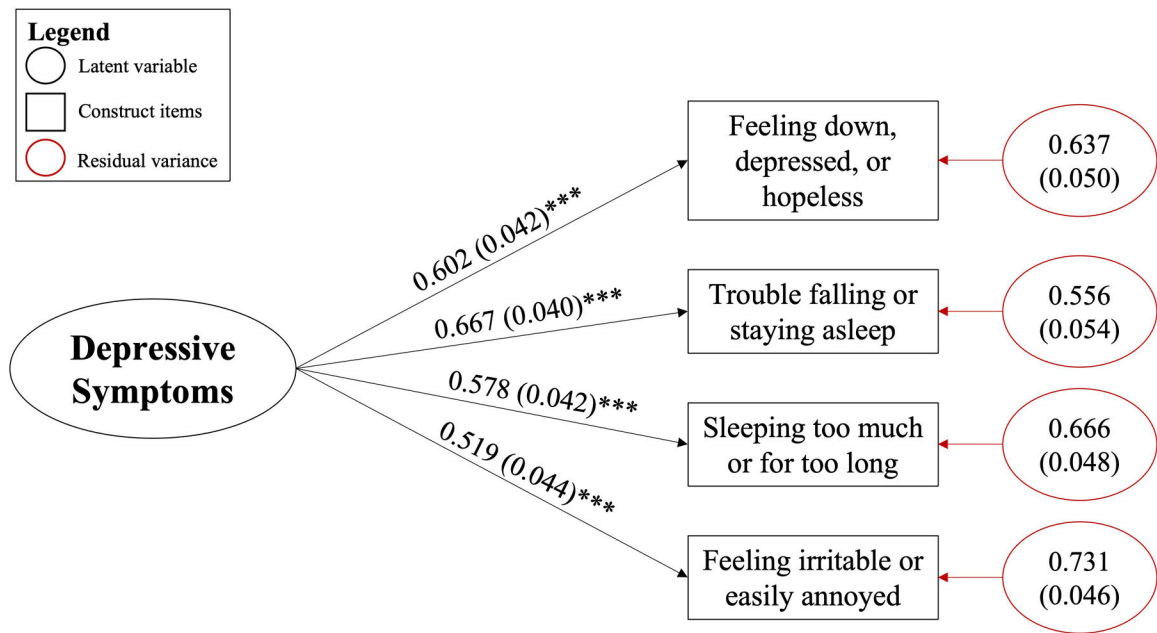
Figure 1.
Theoretical model outlining pathways from household adversity to poor health and wellbeing vis-à-vis mental distress among children and adolescents living with HIV.
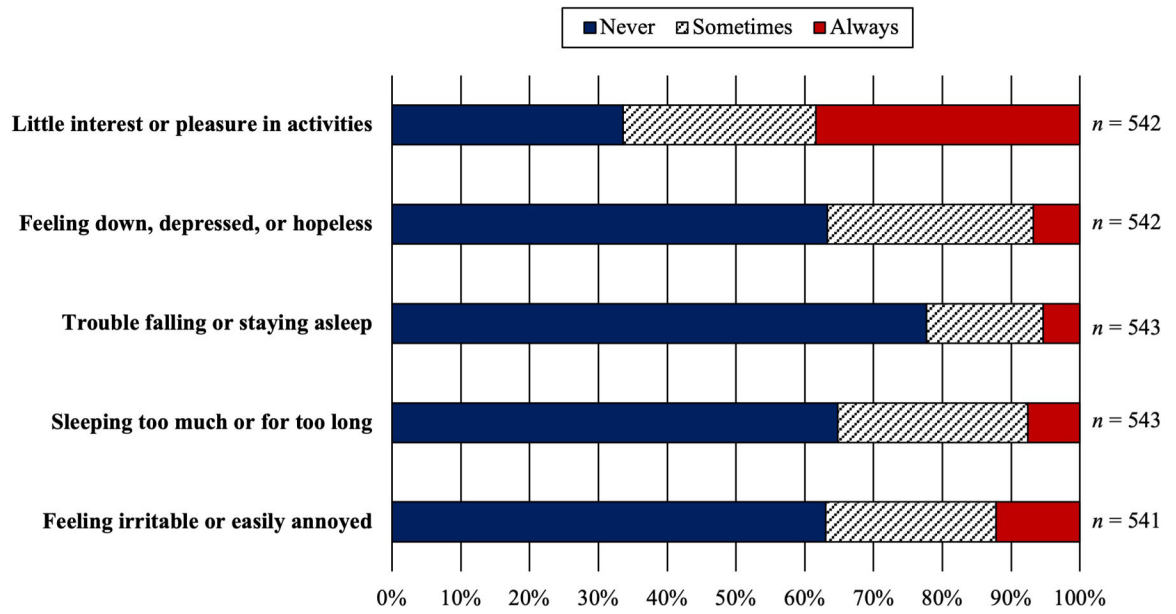
Figure 2.
Depressive symptoms among children and adolescents living with HIV, by symptom frequency in the past 6 months.

Figure 3.

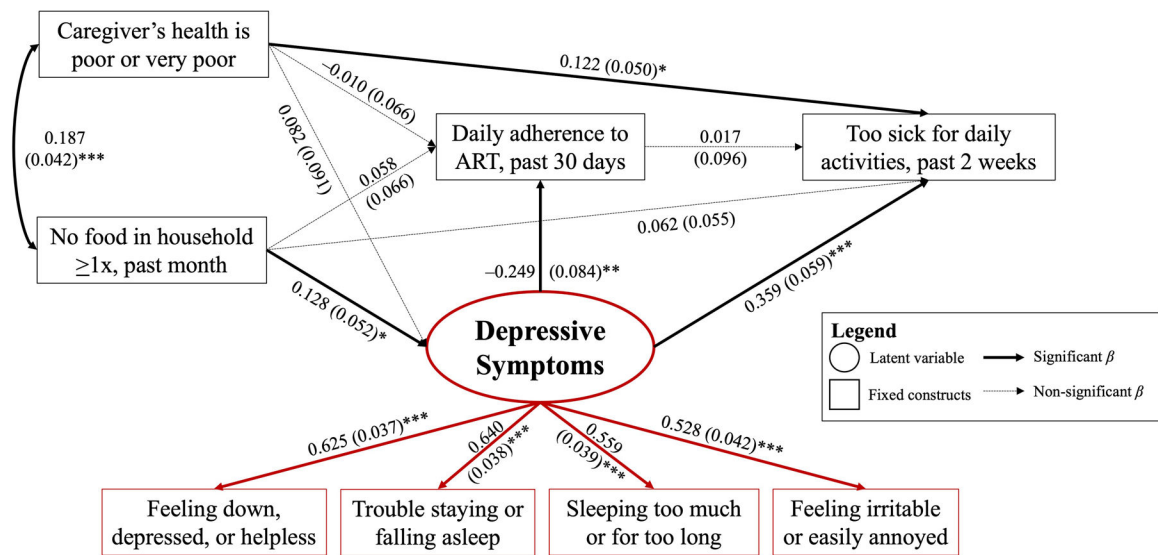Measurement model and fit statistics of the unifactorial depressive symptoms construct among children and adolescents living with HIV ($N = 540$).

Notes: Coefficients reported in measurement model are standardized YX β coefficients (with standard errors).

*** p<0.001. χ^2: chi-square; *RMSEA*: root mean square error of approximation; *CFI*: comparative fit index; *TLI*: Tucker-Lewis index; *SRMR*: standardized root mean residual

Figure 4.

Structural model of pathways from household adversity to HIV medication adherence and sickness vis-à-vis depressive symptoms among children and adolescents living with HIV ($N = 540$).

Notes: Coefficients reported in the structural model are standardized YX β coefficients (with standard errors).

*p<0.05, **p<0.01, *** p<0.001. χ^2: chi-square; *RMSEA*: root mean square error of approximation; *CFI*: comparative fit index; *TLI*: Tucker-Lewis index; *SRMR*: standardized root mean residual.

Table 1.

Descriptive sample characteristics of children and adolescents living with HIV (CALWH) and their caregivers (*N* = 544).

	n	*%*
Socio-Demographics		
Age, in years (*mean, std. dev.*)	10.8	3.6
Age group		
5–9 years	225	41.4
10–17 years	319	58.6
Sex		
Male	226	41.5
Female	318	58.5
Province		
Central	272	50.0
Eastern	272	50.0
Residence type		
Rural	184	33.8
Urban	360	66.2
Current schooling status		
Enrolled in school	187	34.4
Out-of-school	357	65.6
Household wealth		
Poorest	182	33.4
Average	181	33.3
Wealthiest	181	33.3
Household Adversity		
No food in home ≥1x, past month	300	55.2
Caregiver's current health is poor or very poor	131	24.1
Caregiver supports corporeal punishment in home	104	19.1
Death of a household member, past 12 months	85	15.6
Household less financially secure than neighbors	245	45.0
Household lacks basic shelter protection	57	10.5
CALWH Health and Wellbeing		
Current social support across 4 domains	354	65.1
Any depressive symptoms, past 6 months	441	81.1
Received any psychosocial support services, past 6 months	142	26.1
Current participation in a support group for CALWH	72	13.2
Adhered daily to ART, past month	452	83.1
Too sick for daily activities, past 2 weeks	174	32.0