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# Mental Health and Antiretroviral Adherence Among Youth Living With HIV in Rwanda

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abstract

**BACKGROUND AND OBJECTIVES:** In Rwanda, significant progress has been made in advancing access to antiretroviral therapy (ART) among youth. As availability of ART increases, adherence is critical for preventing poor clinical outcomes and transmission of HIV. The goals of the study are to (1) describe ART adherence and mental health problems among youth living with HIV aged 10 to 17; and (2) examine the association between these factors among this population in rural Rwanda.

**METHODS:** A cross-sectional analysis was conducted that examined the association of mental health status and ART adherence among youth ( $n = 193$ ). ART adherence, mental health status, and related variables were examined based on caregiver and youth report. Nonadherence was defined as ever missing or refusing a dose of ART within the past month. Multivariate modeling was performed to examine the association between mental health status and ART adherence.

**RESULTS:** Approximately 37% of youth missed or refused ART in the past month. In addition, a high level of depressive symptoms (26%) and attempt to hurt or kill oneself (12%) was observed in this population of youth living with HIV in Rwanda. In multivariate analysis, nonadherence was significantly associated with some mental health outcomes, including conduct problems (odds ratio 2.90, 95% confidence interval 1.55–5.43) and depression (odds ratio 1.02, 95% confidence interval 1.01–1.04), according to caregiver report. A marginally significant association was observed for youth report of depressive symptoms.

**CONCLUSIONS:** The findings suggest that mental health should be considered among the factors related to ART nonadherence in HIV services for youth, particularly for mental health outcomes, such as conduct problems and depression.



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**WHAT'S KNOWN ON THIS SUBJECT:** Previous studies on the relationship between antiretroviral therapy (ART) adherence and mental health in resource-limited settings focus primarily on adults. Findings on this association for children are limited to the United States and similar contexts and have demonstrated mixed results.

**WHAT THIS STUDY ADDS:** Findings from Rwandan youth demonstrate an association between ART adherence and mental health for depression and conduct problems. Integrating mental health and ART services may prevent poor prognosis and transmission of HIV.

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During the past decade, access to antiretroviral therapy (ART) has increased significantly in low- and middle-income countries.<sup>1</sup> Although access to treatment of children also has increased, it has lagged behind adults; children living with HIV are one-third less likely to receive treatment compared with adults.<sup>2</sup> One exception to this trend is Rwanda, which has made significant progress in access to ART for children as well as the overall population; 92% of those eligible have access to care.<sup>3</sup> As access to treatment of children increases, adherence is critical in preventing poor clinical outcomes, drug resistance, and transmission of HIV.

Quality of care also has advanced, with some sites in Rwanda offering directly observed therapy for HIV through daily visits from community health workers (CHWs) specializing in HIV; this program reduced treatment attrition and resulted in a positive change in mean CD4 count.<sup>4</sup> Compared with 4 other countries in sub-Saharan Africa, Rwanda had the lowest rates of loss to follow-up and mortality among children <15 years of age receiving ART.<sup>5</sup> In another study in Rwanda, only 2% of children receiving ART were lost to follow-up over a 2.6-year period.<sup>6</sup> Overall improvement in access to ART and quality of care for children living with HIV is part of a broader range of government policy and program initiatives to improve the health status of children through a decentralized approach that includes CHWs in every village throughout the country.<sup>7</sup>

Adherence to ART among youth involves additional considerations, such as the role of the caregiver (often the parent) in care, the caregiver's HIV status, the youth's degree of autonomy, knowledge of his or her HIV status, as well as developmental stage of the youth.<sup>8-10</sup> For example, adolescents may know how to take their medications and

when they need to take them, but they may not consider the long-term factors related to nonadherence, such as the risk of progression of HIV. A study conducted in Kenya, Mozambique, Tanzania, and Rwanda found that youth ages 15 to 24 were at the highest risk of ART attrition, compared with younger children and older adults.<sup>11</sup> In addition, adherence may be more challenging in resource-limited settings in which families are more likely to be coping with poverty and the child is also at a higher risk of being orphaned by HIV.<sup>12,13</sup> These factors have implications for the mental health status of children and youth living with HIV in low- and middle-income countries.<sup>14</sup>

Findings from the limited literature on mental health and adherence to ART among children and youth living with HIV in the United States vary widely. Although some studies have shown an association,<sup>9,15</sup> others have demonstrated null findings.<sup>16,17</sup> Mixed findings also have been observed in studies among adults in resource-limited settings.<sup>18-20</sup> For example, there was no relationship between nonadherence and depression among participants in a study in rural India.<sup>20</sup> However, among patients receiving ART in Rwanda, depression was associated with a 2.7-fold increase in 2-day treatment interruptions.<sup>21</sup> Similarly, adolescents in Rwanda enrolled in a qualitative study exploring the broader living conditions on ART adherence have described feelings of depression and isolation in relation to nonadherence.<sup>22</sup> However, to our knowledge, there are no published quantitative studies that examine this association among children or youth in resource-limited settings. Given the inconclusive results regarding the association between ART adherence and mental health and the limited data on this relationship among youth in resource-limited settings, the goals of this study were to (1) describe adherence to ART and

mental health problems among youth living with HIV aged 10 to 17 in rural Rwanda; and (2) examine the association between these factors in this population.

## METHODS

### Setting

The study was conducted in collaboration with the Rwandan Ministry of Health (MOH), the Harvard School of Public Health, and Partners In Health/*Inshuti μ Buzima* (PIH/IMB) in Rwanda in the rural districts of Southern Kayonza and Kirehe. Treatment of children and youth living with HIV in this study was a collaborative effort of the MOH and PIH/IMB, including free ART (triple therapy) according to the Rwandan MOH guidelines. Youth >15 years of age were given the same regimen as adults: tenofovir + lamivudine (3TC) + efavirenz (EFV). Nevirapine (NVP) was provided as an alternative if EFV was contraindicated. In addition, abacavir (ABC) was offered instead of tenofovir for first-line therapy. For children ≤15 years of age, first-line therapy included ABC+3TC+EFV or ABC+3TC+NVP if EFV was contraindicated. If children were exposed to single-dose NVP through prevention of mother-to-child transmission of HIV, then kaletra was offered as an alternative. Another first-line regimen for children was zidovudine+3TC+kaletra. For all children and youth, second-line regimens were available in the event of first-line regimen failure.<sup>23</sup> Each patient had a trained CHW that specialized in daily home visits to supervise HIV care; in addition, CHWs, who were members of the same communities as the patients, also served as a vital link between the community and health facilities, promoting access to care.<sup>24</sup> For example, the CHW assisted patients with identifying side effects of ART that may play a role in nonadherence.

The CHW also educated the patient that the provider may be able to change his or her regimen. He or she facilitated access to care and also liaised with those at the clinic to promote adherence.

### Study Design and Population

The design of the parent study from which the data were drawn was a case-control study comparing (1) HIV-positive; (2) HIV-affected (defined as children who are HIV-negative and living with a caregiver who is HIV-positive or had a caregiver who died due to AIDS-related causes); and (3) non-HIV-affected youth ages 10 to 17 on a number of mental health and related psychosocial factors. The study design and methods are described in greater detail in Betancourt et al.<sup>25</sup>

For the parent study, these 3 groups were compared on mental health and related factors to inform policy and programs intended to increase access and/or improve quality of mental health care among youth. For every child, the caregiver who indicated knowing the child best also reported on the child, his or her own mental health, family functioning and parenting, social services provided to the children and family, and socioeconomic status. For the parent study, 683 youth were recruited and interviewed, of which 218 were HIV-positive and accessing care at MOH facilities in collaboration with PIH/IMB in the 2 target districts of the study. Within this group, 193 were receiving ART. This subset of HIV-positive youth on ART forms the sample for the present cross-sectional analysis.

### Measures

Adherence was defined based on responses from the youth and caregiver for items adapted from the Pediatric AIDS Clinical Trial Group (PACTG)<sup>26</sup> and Ivers et al.<sup>27</sup> The first question asked “Within the past month, how often have you refused to

take your ART medications?” and the second asked “Within the past month, how often did you miss a dose of ART medications (including refusals or missed doses for other reasons)?” Nonadherence was defined as either the youth or the caregiver reporting that the youth ever missed or refused a dose of ART medication during the past month.

Mental health status was obtained through self and caregiver report for all measures and focused on a number of dimensions, including depressive symptoms (adapted Center for Epidemiologic Studies Depression Scale for Children,<sup>28</sup> which was validated for use in Rwanda among youth ages 10–17 years),<sup>29</sup> internalizing symptoms (mixed anxiety/depression derived from the Child Behavior Checklist),<sup>30</sup> irritability (Irritability Questionnaire developed by Craig et al),<sup>31</sup> and conduct problems (Youth Conduct Problems Scale-Rwanda).<sup>32</sup> All mental health measures developed outside of Rwanda went through an extensive process of adaptation based on qualitative research and a series of validation exercises.<sup>33,34</sup>

Covariates that were included in the analysis are described in detail by Betancourt et al 2014<sup>25</sup> and were as follows: sex, age, socioeconomic status, depressive symptoms among caregivers (Hopkins Symptom Checklist-25),<sup>35</sup> posttrauma symptoms for caregivers (PTSD Checklist by Weathers et al),<sup>36</sup> parental alcohol use (Alcohol Use Disorder Identification Test),<sup>37</sup> social services access,<sup>38</sup> “good” parenting,<sup>33</sup> family trust/connection (kwizerana),<sup>33</sup> self-esteem (Self-esteem scale by Connor et al),<sup>39</sup> social support (items derived from social support scale developed by Barrera and Ainlay),<sup>40</sup> parental monitoring,<sup>33</sup> hopefulness (Life Satisfaction/Hopefulness scale),<sup>41</sup> prosocial behaviors,<sup>33</sup> harsh punishment (derived from a measure developed by United Nations Children’s Fund),<sup>42</sup> daily hardships,<sup>38</sup>

intimate partner violence (Conflict Tactics Scale),<sup>43</sup> and perceived stigma (HIV Stigma by Association scale).<sup>44</sup> All study questionnaires were administered verbally with trained research assistants.

### Statistical Analysis

Descriptive statistics, including frequencies, means, and SDs, were calculated for sociodemographic characteristics, economic factors, and the level of adherence, as well as degree of psychological symptoms, with the latter analyzed as continuous variables. Bivariate analysis was performed using logistic regression to examine the associations between youth mental health status and ART adherence. To control for confounding variables, multivariate logistic regression was used. Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were also calculated for bivariate and multivariate analysis. For multivariate modeling, the “change-in-estimate” approach was implemented.<sup>45</sup> This strategy compares the parameter estimate (ie, OR) of a given bivariate association with the same association controlling for a confounding variable. If the effect estimate changes by >10%, the confounding factor would be included in the final multivariate model. Sex and age were included as confounding variables, regardless of whether they met the above criteria. Statistical analysis was performed by using Stata, version 12 (Stata Corp, College Station, TX).

### Ethical Review

The Rwandan National Ethics Committee within the Rwandan MOH and the Institutional Review Board at the Harvard School of Public Health approved the study.

### RESULTS

Sociodemographic and economic characteristics are reported in Table

1. The youth were 10 to 17 years old and most were living with  $\geq 1$  of their biological parents (57%). Although nearly all were attending school at the time of the study (93%), the mean for last grade completed was 3, suggesting that the youth were likely to begin schooling at a later age, which can happen within families with limited resources. The interviewed caregivers were on average 47 years old and 80% were women; 53% were a biological parent for the youth and 37% were living with a partner. Nearly two-thirds either had no education or did not complete primary school. Only 65% owned a radio and nearly 74% reported that their family lacked basic necessities (eg, food, housing, medical care) in the past 6 months.

The burden of mental illness was significant in this population of youth living with HIV, based on self-report. For example, among the youth, 51 (26%) achieved a score on the Center for Epidemiologic Studies Depression Scale for Children at or above the cutoff of 30, reflecting a high percentage of the population having symptoms consistent with major depressive disorder. For specific depressive symptoms, ~17% of the youth reported feeling sad or unhappy often during the past week; the same percentage of youth indicated that family members or friends could not help them to feel better. Nearly 14% said they often felt scared or frightened in the past week. More than 16% mentioned that they often felt lonely or isolated and did not have any friends. Approximately 11% had suicidal thoughts in the past week. Nearly 12% deliberately tried to hurt or kill themselves in the past 6 months. Conduct-related problems were also evident in this population, with 15% fighting and >7% stealing sometimes or often in the past 6 months.

For nonadherence to ART, according to youth or caregiver report, 37% either missed or refused

**TABLE 1** Descriptive Characteristics of Youth Living With HIV and Their Caregivers ( $n = 193$ )

Characteristics	<i>n</i> (%) or Median (range)
<b>Child characteristics</b>	
Sex	
Female	96 (50)
Male	97 (50)
Age, y	
10–13	90 (47)
14–17	103 (53)
Head of household's relationship to child	
Mother	55 (29)
Father	55 (29)
Stepmother	1 (0.5)
Stepfather	8 (4)
Grandmother	18 (9)
Grandfather	12 (6)
Aunt	5 (3)
Uncle	8 (4)
Sibling	12 (6)
Other	19 (10)
Currently attending school? ( $n = 191$ ) <sup>a</sup>	
Yes	177 (93)
No	14 (7)
Last grade completed at school ( $n = 176$ )	
Median grade (range)	3 (0–9)
<b>Caregiver characteristics</b>	
Sex	
Female	155 (80)
Male	38 (20)
Median age, y (range)	43 (18–100)
Caregiver's relationship to the child	
Biological parent	102 (53)
Aunt/Uncle	15 (8)
Grandparent	10 (5)
Adoptive parent	7 (4)
Other	59 (31)
Education level	
None	60 (31)
Some primary	60 (31)
Completed primary	43 (22)
Some secondary	21 (11)
Completed secondary	6 (3)
Postsecondary	3 (2)
Current marital status	
Currently living with partner	71 (37)
Have partner but not living with him/her	6 (3)
Previously partnered, but not currently partnered	52 (27)
Single: never partnered	64 (33)
No. people living in home, median (range)	6 (2–17)
No. bedrooms, median (range)	3 (0–9)
Radio ownership	
Yes	126 (65)
No	67 (35)
Family lacked basic necessities in the past 6 months (eg, food, housing, clothing, or medical care) ( $n = 192$ )	
Yes	142 (74)
No	50 (26)

<sup>a</sup> Variables less than  $n = 193$  are due to missing data.

a dose within the past month. However, variation was observed for youth versus caregiver report. The percentage of youth who

self-reported refusing ART was somewhat lower than caregiver report in the past month; caregiver report of missing a dose in the same

time period was approximately half of what the youth indicated, although only the latter was statistically significant. Approximately 84% of caregivers and youth reported that their health workers responded effectively to questions regarding ART side effects.

In bivariate analysis (see Table 2), nonadherence was positively associated with a number of psychological symptom dimensions, including irritability (self-report OR = 1.79, 95% CI 1.06–3.04; caregiver report OR = 1.97, 95% CI 1.22–3.18), and conduct problems (self-report OR = 1.79, 95% CI 1.10–2.90; caregiver report OR = 3.35, 95% CI 2.00–5.61). Self-reported mixed anxiety/depressive symptoms were not associated with adherence (OR = 1.68, 95% CI 0.92–3.07); however, a positive association was observed through caregiver report (OR = 3.57, 95% CI 1.86–6.86). Self-reported depressive symptoms were marginally associated with nonadherence (OR = 1.02, 95% CI 0.99–1.03), whereas caregiver report showed a significant relationship (OR = 1.02, 95% CI 1.01–1.04).

For multivariate analysis, the following relationships between mental health and nonadherence remained associated: conduct problems (as reported by caregiver) (OR = 2.90, 95% CI 1.55–5.43), and depression (as reported by caregiver) (OR = 1.02, 95% CI 1.01–1.04). Self-reported depression remained marginally significant after accounting for confounding variables. The change-in-estimate multivariate modeling strategy demonstrated that none of the potential confounding variables resulted in a change in the OR estimate by more than 10% for depression, reported by the youth and his or her caregiver. Therefore, the final parameter estimate for depression was adjusted only for age and sex (see Table 2).

## DISCUSSION

The results indicated that in the context of an overall strong ART program in Rwanda, adherence to treatment remains an issue for some children and adolescents in rural areas, with youth or caregivers reporting that 37% of children missed or refused a dose in the past month. This may in part be related to the high rate of psychological symptoms among this group of adolescents, reflected by 26% having a level of depressive symptoms comparable with major depression.

The findings demonstrated that after controlling for confounding factors, depression and conduct problems were significantly associated with nonadherence to ART among youth living in rural Rwanda as reported by caregivers. Additionally, self-report of depression was marginally associated. In contrast, mixed anxiety/depression, irritability, and conduct problems (self-report) were not related to ART adherence. Although there was some variation by youth versus caregiver report, the findings suggest that symptoms that may have a greater impact on daily activities, such as depression and conduct problems, may be more important with respect to promoting adherence, as compared with anxiety or irritability.

Similar to the findings from the current study, previous literature has also shown mixed findings in the relationship between mental health and adherence. Among children enrolled in the PACTG, there was a marginal association between depression or anxiety and self-reported nonadherence after controlling for confounding variables (OR = 1.85; 95% CI 0.95–3.61).<sup>46</sup> For women living with HIV in India, severity of depression was associated with nonadherence.<sup>19</sup> In contrast, for youth ages 12–24 enrolled in the Adolescent Trials Network for HIV/AIDS or PACTG in the United States, mental health disorders (eg,

mood disorders, schizophrenia, attention-deficit/hyperactivity disorder) were not associated with ART adherence in logistic regression analyses.<sup>16</sup> Among patients living with HIV and tuberculosis in Peru, depression and nonadherence were related; however, this finding was not sustained after controlling for social support among other variables.<sup>47</sup> This suggests that mental health is an important factor when considering adherence, but that the effect also can be buffered by protective factors.

A number of factors may potentially explain the variation between mental health and nonadherence to ART, including the age of the youth, the definition of adherence, how mental health was measured and which diagnoses/symptom dimensions were assessed, and whether the study controlled for confounding. In addition, the dimension of symptoms (eg, anxiety, conduct problems) may play a role, with some demonstrating an association and others showing no relationship with nonadherence. This is suggested by the present findings, in which we observed an association of depression and conduct problems with nonadherence, whereas no relationship was observed for irritability or mixed anxiety/depression after controlling for confounding. Also important to consider is the potential effect of CHWs who support adherence through daily visits with patients who are HIV-positive in this study. In other studies, CHWs have been shown to support patients with adherence and improve ART outcomes<sup>4,48</sup>; the role of the CHW to encourage adherence may mitigate potentially negative effects of mild to moderate psychological symptoms on ART adherence in this study.

There are a number of limitations in this study. Disclosure of HIV status to the youth, whether they were perinatally infected, how long they have been on ART, and their immunologic status are important

**TABLE 2** Univariate and Multivariate Analysis of the Association of Mental Health Status and Nonadherence to ART Among Youth Ages 10–17 in Rwanda (*n* = 193)

	OR	95% CI	OR	95% CI
<b>Depressive symptoms (self-report)</b>				
Depressive symptoms	1.02	(0.99–1.03)	1.02	(0.99–1.03)
Age	—	—	1.03	(0.90–1.18)
Sex	—	—	0.73	(0.40–1.32)
<b>Depressive symptoms (caregiver report)</b>				
Depressive symptoms	1.02	(1.01–1.04)	1.02	(1.01–1.04)
Age	—	—	1.02	(0.89–1.18)
Sex	—	—	0.74	(0.40–1.35)
<b>Mixed anxiety/depression (self-report)</b>				
Mixed anxiety/depression	1.68	(0.92–3.07)	0.57	(0.20–1.60)
Hopefulness	—	—	0.97	(0.37–2.56)
Daily hardships	—	—	1.09	(0.93–1.26)
HIV-related stigma	—	—	1.29	(1.11–1.48)
Age	—	—	1.08	(0.90–1.29)
Sex	—	—	0.62	(0.30–1.27)
<b>Mixed anxiety/depression (caregiver report)</b>				
Mixed anxiety/depression	3.57	(1.86–6.86)	1.87	(0.83–4.22)
Hopefulness	—	—	0.40	(0.15–1.11)
Daily hardships	—	—	1.01	(0.94–1.09)
Harsh punishment	—	—	2.25	(0.32–15.6)
Self-esteem	—	—	0.91	(0.41–2.02)
Prosocial behavior	—	—	0.69	(0.32–1.49)
Age	—	—	1.04	(0.90–1.22)
Sex	—	—	0.72	(0.38–1.37)
<b>Irritability (self-report)</b>				
Irritability	1.79	(1.06–3.04)	0.91	(0.44–1.88)
Daily hardships	—	—	1.05	(0.92–1.20)
HIV-related stigma	—	—	1.23	(1.09–1.39)
Age	—	—	1.01	(0.87–1.16)
Sex	—	—	0.64	(0.34–1.21)
<b>Irritability (caregiver report)</b>				
Irritability	1.97	(1.22–3.18)	1.07	(0.56–2.05)
Hopefulness	—	—	0.33	(0.12–88)
Daily hardships	—	—	1.02	(0.95–1.10)
Harsh punishment	—	—	2.16	(0.30–15.28)
Caregiver depression	—	—	1.07	(0.56–2.05)
Self-esteem	—	—	0.93	(0.42–2.06)
Prosocial behaviors	—	—	0.62	(0.29–1.32)
Age	—	—	1.06	(0.92–1.23)
Sex	—	—	0.74	(0.39–1.40)
<b>Conduct problems (self-report)</b>				
Conduct problems	1.79	(1.10–2.90)	1.47	(0.87–2.49)
Daily hardships	—	—	1.01	(0.90–1.15)
HIV-related stigma	—	—	1.22	(1.09–1.36)
Age	—	—	1.01	(0.88–1.17)
Sex	—	—	0.66	(0.35–1.24)
<b>Conduct problems (caregiver report)</b>				
Conduct problems	3.35	(2.00–5.61)	2.90	(1.55–5.43)
Hopefulness	—	—	0.27	(0.11–0.67)
Prosocial behaviors	—	—	1.02	(0.48–2.18)
Age	—	—	1.03	(0.90–1.20)
Sex	—	—	0.90	(0.47–1.74)

considerations for ART adherence; however, these were not assessed in the current study. Adherence is also complicated to measure and this study relied on caregiver and self-report which may have underestimated nonadherence rates

and biased results toward the null. Access to viral load status, which is often related to adherence, would have strengthened our approach; however, we did not have access to the clinical data in the participants' files. The relatively small sample size

of the HIV-positive subgroup in this study resulted in wide CIs and may have also contributed to some of the null findings. Finally, generalizability may be limited with respect to age (ie, not including youth <10 years of age) and settings in which there is

access to a CHW that can promote adherence through supervised ART and social support.<sup>4</sup> In contexts without CHW or peer support access, mental health may play a greater role in nonadherence, potentially including irritability and/or anxiety.

## CONCLUSIONS

Although all of the psychological symptom dimensions were not associated with adherence to ART among youth ages 10 to 17 in rural Rwanda, some remained significant or marginally significant after controlling for confounding variables. In particular, depression and conduct problems sustained a relationship with nonadherence to ART. The findings from this study suggest that mental health should be considered

within the context of HIV treatment among youth. Further study on effectiveness of interventions that address mental health problems among youth living with HIV may shed light on strategies that support ART adherence and potentially improve health outcomes in this vulnerable population in resource-limited settings.

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## ABBREVIATIONS

ABC: abacavir  
ART: antiretroviral therapy  
CHW: community health worker  
CI: confidence interval  
EFV: efavirenz  
MOH: Ministry of Health  
NVP: nevirapine  
OR: odds ratio  
PACTG: Pediatric AIDS Clinical Trial Group  
PIH/IMB: Partners In Health/Inshuti Mu Buzima  
3TC: lamivudine

and critical revision of the manuscript for intellectual content; Ms Mushashi contributed to study concept and design, acquisition of the data, drafting of the manuscript, and study supervision; Mr Kim contributed to interpretation of data for analysis and background literature reviews; Dr Kayitshonga contributed to the study concept and design, interpretation of data, and critical revision of manuscript for intellectual content; Dr Binagwaho contributed to the study concept and design, interpretation of data, and critical revision of manuscript for intellectual content; Dr Betancourt conceptualized and designed the study, oversaw acquisition of the data, and contributed to statistical analysis and interpretation of the data, drafting of the manuscript, critical revision of manuscript for intellectual content, obtaining funding, and supervision of the study; and all authors agree to be accountable for all aspects of the work in terms of accuracy and integrity and approved the final version of the manuscript as submitted.

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