

Prevalence and Incidence of Hypertension and Diabetes Mellitus Among HIV-Infected Individuals Receiving HAART in Chongwe District, Lusaka Province, Zambia

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ABSTRACT

Background: The Zambia National Health Strategic Plan (ZNHSP) 2011–2017 underscores the need for community-level risk factor stratification to bolster insufficient incidence and prevalence data. This study evaluates the prevalence and incidence of hypertension and diabetes mellitus in HIV-infected patients on Highly Active Anti-Retroviral Therapy (HAART) and assesses associations with ARV use.

Methodology: A retrospective cohort analysis was conducted using the SMART CARE database in Chongwe district, involving 2,070 HIV-infected persons on HAART. Statistical analysis included Chi-square, Kruskal-Wallis tests, and logistic regression.

Results: Among participants, 33.8% exhibited hypertension, with an incidence case fatality rate of 85.7 per 1000 person-years (PYFU). Hypertension was notably higher in men (64%) than women (49%) and prevalent in the 18–45 age group (57.2%). The incidence of type II diabetes was 37.4 per 1000 PYFU. Logistic regression highlighted significant predictors for both conditions, including ART combination, age, and smoking status.

Conclusion: High prevalence and incidence rates of hypertension and type II diabetes were observed among HIV-positive individuals on HAART. Certain HAART combinations, particularly two NRTIs plus a PI or INSTI, correlated with increased hypertension risk, while combinations including NNRTI or INSTI were linked to higher diabetes incidence.

Keywords: ARV drug effects, Cardiovascular risk factors, epidemiological trends, Sub-Saharan Africa.

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1. INTRODUCTION

Globally, 37,900,000 people are living with HIV, with a 0.8% adult prevalence. Approximately 770,000 individuals die annually from HIV-related illnesses. Among those aware of their HIV status, 78% are receiving treatment. Most people with HIV, around 68%, live in sub-Saharan Africa. In Zambia, 1,200,000 people are HIV-positive, with an 11.3% adult prevalence and about 17,000 AIDS-related deaths each year [1].

Diabetes mellitus is a significant global health challenge, having more than tripled in adult cases over the past two decades, particularly in low- and middle-income countries

[2], [3]. By 2019, there were 463,000,000 people aged 20 to 79 years living with diabetes, and another 374,000,000 with impaired glucose tolerance. Diabetes and its complications led to an estimated 4,200,000 deaths, mostly in lower-income areas. In Zambia, the estimated diabetes cases were about 222,000 in 2017, with projections indicating an incidence rate of 4%–5% by 2019 [2].

The Global Status Report on Non-Communicable Diseases (NCDs) underscores the severe impact of NCDs on impoverished populations, especially in Sub-Saharan Africa, where poverty aggravates health challenges like diabetes, heart disease, and cancer. The lack of healthcare access, education, and preventive measures



worsens the situation, necessitating urgent health policy interventions [4].

Mental disorders add significantly to the NCD burden in these regions, where social stigma and insufficient mental health services complicate treatment and management [5], [6]. Developing cost-effective strategies for mental health is challenging, like other NCDs [7], [8]. Mental disorders disrupt daily activities and are linked with high rates of substance use, worsening health outcomes [9], [10]. People with mental health issues often suffer from other NCDs, such as obesity, hypertension, and diabetes, which further complicates their health challenges [11].

A 2016 systematic analysis by Mills and colleagues revealed significant global disparities in hypertension prevalence and control across 90 countries. The study found that in 2010, approximately 1,390,000,000 people, or 31.1% of the global population, had hypertension, with a higher prevalence in low- and middle-income countries. The same research indicated less than 20% prevalence in Zambia in 2010, though more recent data from 2019 showed an increase to 25.9% in some regions [12], [13].

In Zambia's Chongwe District, the second largest in Lusaka Province with a population of 182,174, significant numbers of HIV/AIDS and NCD cases were recorded in 2018. The local health information system noted 3899 new hypertension cases and 887 new diabetes cases, highlighting the district's growing healthcare challenges [14].

Since the mid-1990s, widespread antiretroviral (ARV) therapy has significantly reduced HIV morbidity and mortality, transforming it from a fatal disease to a manageable chronic condition [15]. However, HIV and ARVs are associated with an increased risk of chronic comorbidities like Type II diabetes mellitus (T2DM). Studies indicate that T2DM is up to four times more prevalent in those with HIV than in those without, due to both immune response to HIV and metabolic effects of ARVs [16]–[18].

Cardiovascular diseases, bone density reductions, and certain cancers are also seen at higher rates in the HIV-positive population [16]. Managing these comorbid conditions requires integrated healthcare approaches that cover both HIV treatment and other health issues.

Risk factors for T2DM in the general population include age, obesity, smoking, and physical inactivity. For individuals with HIV, additional specific risk factors such as the duration of HIV infection and exposure to certain ARVs increase their susceptibility to diabetes [19], [20].

Nutritional interventions have been shown to be pivotal in managing metabolic risks associated with HIV treatment. Clinical treatment guidelines for people living with HIV (PLHIV) include strategies for both the prevention and management of cardiometabolic risk factors [21]. However, these guidelines predominantly emphasize pharmacological treatments [22].

A significant randomized controlled study demonstrated that dietary strategies could effectively reduce key cardiometabolic risk factors in PLHIV undergoing ARV therapy, impacting hypertension, blood glucose levels, and lipid profiles positively [17], [23], [24].

Despite advancements in ARVs, traditional T2DM risk factors like hypertension and dyslipidemia are escalating

among HIV patients as they age, highlighting the need for early prevention and targeted strategies [25].

Highly Active Antiretroviral Therapy (HAART), involving a combination of three or more antiretroviral drugs, is fundamental in managing HIV. Over 25 medications are available, classified into six distinct classes, providing a robust framework for treatment aimed at maintaining viral suppression and improving patient outcomes [26], [27].

This study examines the prevalence and incidence rates of hypertension and diabetes among HIV-infected individuals on HAART in the Chongwe district. It also explores potential correlations between HAART usage and the emergence of these conditions, aiming to contribute to understanding the metabolic and cardiovascular side effects of long-term HAART. This research will inform clinical practice and policymaking to enhance health outcomes for this vulnerable population.

2. METHOD

2.1. Study Design

This retrospective cohort study utilized data from the SMART CARE electronic database in Chongwe district to assess the incidence rates of hypertension and Type II diabetes mellitus among individuals infected with HIV and undergoing HAART treatment.

2.2. Study Setting

The study was conducted in the Chongwe district using the SMART CARE electronic database, which provided a reliable sampling frame for the ART program.

2.3. Study Population

The study included HIV-positive individuals aged 18 and older who were receiving ART. Participants were selected from six high-volume facilities in Chongwe district, ensuring they had been on ART for at least one year.

2.4. Eligibility Criteria: Inclusion Criteria

Eligibility was determined based on the inclusion of case files in the SMART CARE database, participant age (18 years or older), and a minimum of one year on ART or HAART from January 2006 to April 2021.

2.5. Eligibility Criteria: Exclusion Criteria

Participants were excluded if they were pre-hypertensive or diabetic before starting ART, had chronic conditions (e.g., kidney disease, liver conditions, heart conditions, thyroid disorders), were engaged in polypharmacy, were terminally ill at the start of HAART, or were lost to follow-up, transferred out, or deceased during the study. This was to minimize confounding factors.

2.6. Sample Size and Sampling Techniques

The SMART CARE database contained 50,517 case files from 2006 to 2021. After applying inclusion and exclusion criteria, 8404 individuals were eligible. Stratified random sampling was employed across six high-volume healthcare facilities to ensure a representative sample. The

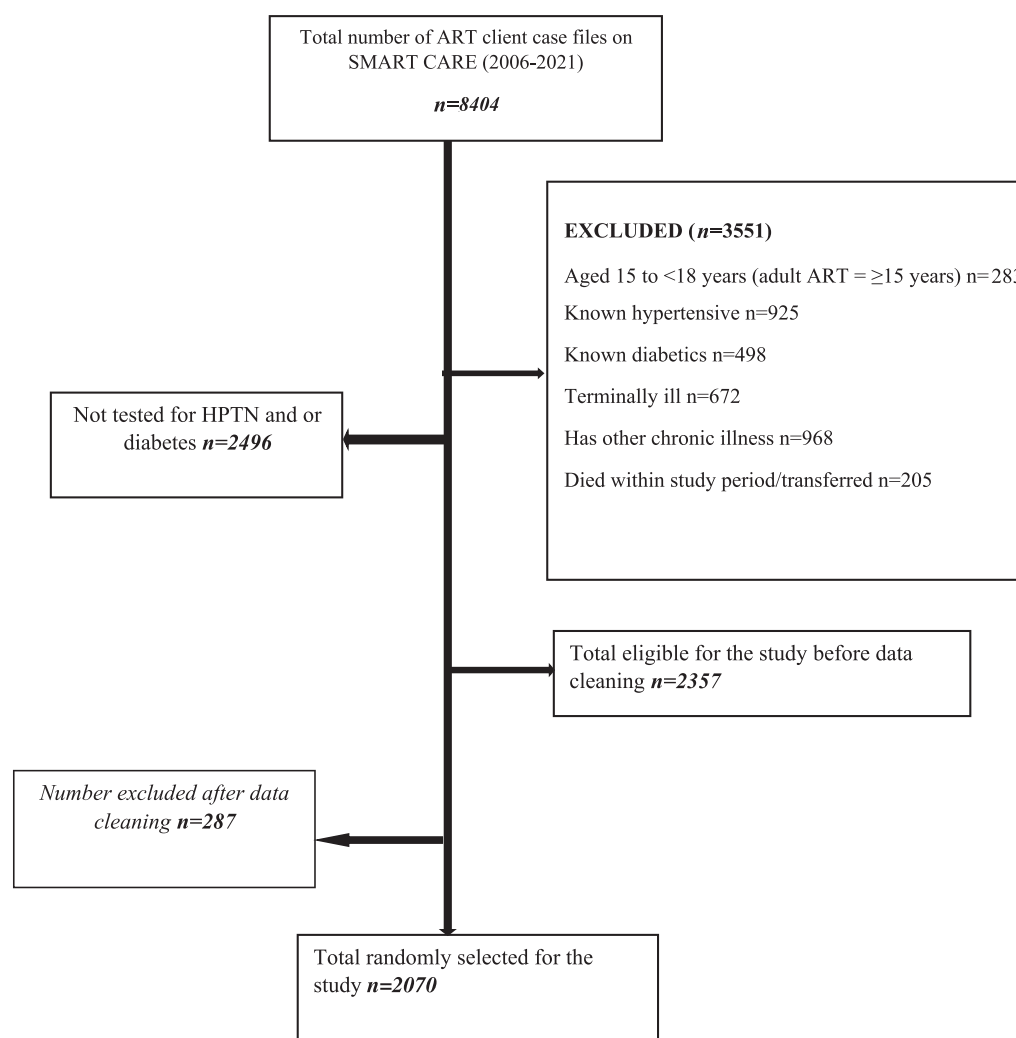


Fig. 1. Flow chart of the screening and selection process for the case files.

sample size for each facility was calculated using Fisher's formula, considering a 36% prevalence of sub-clinical cardiovascular disease, a 95% confidence level, and a 5% margin of error, leading to a final sample size of 2070 [28]. Random sampling was then applied within each stratum to ensure that the sample was proportionally representative of the different sites, as depicted in Fig. 1.

2.7. Data Collection Procedure and Tools

Data were extracted manually from SMART CARE patient files due to system limitations, covering a 15-year period. Information was entered into Excel for cleaning before analysis with SPSS version 20.

2.8. Study Variables: Dependent (Outcome) Variables

Outcome variables included categorized blood pressure readings and blood glucose levels collected 12 months post-ART initiation. Definitions for hypertension and diabetes were based on established medical criteria.

2.9. Study Variables: Independent (Explanatory) Variables

Independent variables included HIV status, ARV use, age (both categorical and continuous), duration on ART,

and body mass index (BMI), categorized from underweight to obese.

2.10. Data Analysis

Descriptive statistics estimated the incidence of hypertension and diabetes. The incidence rate was calculated per total person-years of follow-up [29]. Chi-square and Kruskal-Wallis tests examined associations and differences among categorical and continuous variables, respectively. Logistic regression analyzed determinants of hypertension and diabetes, considering traditional risk factors, and adjusting for confounders.

2.11. Control for Confounders and Extraneous Variables

The study controlled for age, sex, BMI, and duration of ART to mitigate confounder effects, incorporated into regression models to adjust during analysis.

2.12. Ethical Considerations

The study protocol was approved by the University of Zambia Biomedical Research Ethics Committee and the National Health Research Authority. It used secondary data, minimizing participant risk and providing indirect benefits through contributions to national public health strategies.

TABLE I: RESEARCH FACILITY SAMPLE POOL

Facility	n	%
Chongwe District Hospital	354	17.1
Chainda RHC	304	14.7
Chalimbana RHC	265	12.8
Chongwe RHC	364	17.6
Kasisi RHC	425	20.5
Ngwerere RHC	358	17.3
Total	2070	100

3. RESULTS

3.1. Sample Pool Description

The study analyzed 2070 participant records from the SMART CARE electronic database, spanning from 2006 to April 2021. These records represent HIV-positive individuals undergoing HAART in Chongwe district, collected from six primary health facilities. The distribution of participants across these facilities is summarized in Table I, indicating a strategic focus on high-volume sites for robust data representation.

3.2. Socio-Demographic Characteristics

Participants' ages ranged from 18 to 68 years, with a mean age of 40.4 years. The breakdown by gender was nearly equal, with 1,014 males (49.0%) and 1056 females (51.0%). The demographic profile showed 60% were married, 17.7% single, 9.1% divorced, and 5.2% widowed, with 7.9% not disclosing their marital status. Educational backgrounds varied: 46.3% had primary education, 21.8% secondary, 6.5% tertiary, and 25.4% had no formal education. Residency was distributed as 44.6% urban, 33.4% rural, and 22.0% peri urban.

3.3. Clinical Characteristics of the Study Population

The nutritional assessment at HAART initiation indicated that 13.9% were underweight, 60.3% normal weight, 14.8% overweight, and 11.0% obese. Regarding family health history, 18.7% reported hypertension, and 14.2% diabetes, with the majority having no family history of these conditions (81% for hypertension, 85.8% for diabetes). The average duration on HAART was 5.7 years, with varied ART combinations. The most common was EFV + FTC + TDF (Efavirenz + Emtricitabine + Tenofovir) (35.5%), followed by 3TC + DTG + TDF (Lamivudine + Dolutegravir + Tenofovir) (23.2%).

3.4. Prevalence of Hypertension and Type II Diabetes Mellitus in the Study Population

Hypertension prevalence was 33.8%, and Type II diabetes was 14.9%. These conditions were particularly prevalent in patients on certain ART combinations, with some combinations showing a 100% hypertension prevalence. In contrast, the prevalence for diabetes varied significantly among the different regimens.

The highest prevalence of hypertension among different HAART combinations was observed in patients on 3TC (Lamivudine, NRTI) + ABC (Abacavir, NRTI) + LPV/r (Lopinavir, PI), 3TC (Lamivudine, NRTI) + EFV (Efavirenz, NNRTI) + TDF (Tenofovir, NRTI), and DTG

(Dolutegravir, INSTI) + FTC (Emtricitabine, NRTI) + TAF (Tenofovir, NRTI), all recording a 100% prevalence rate with respective participant counts of 86, 19, and 23. The lowest prevalence was found in the regimen combining 3TC (Lamivudine, NRTI) + DTG (Dolutegravir, INSTI) + TDF (Tenofovir, NRTI) at 51.7%.

For Type II diabetes, the highest prevalence was observed in participants on the HAART regimen of EFV (Efavirenz, NNRTI) + FTC (Emtricitabine, NRTI) + TDF (Tenofovir, NRTI) at 31%. The lowest prevalence was recorded in those on 3TC (Lamivudine, NRTI) + EFV (Efavirenz, NNRTI) + TDF (Tenofovir, NRTI) at 5.3%.

3.5. Incidence Rates of Hypertension and Type II Diabetes Mellitus in the Study Population

The incidence rate of hypertension among 2070 case files observed over a fifteen-year period (13,519 person-years of follow-up) was 85.7 cases per 1000 enrolled ART clients annually, according to SMART CARE records from 2006 to 2021. Meanwhile, the incidence rate of T2DM among HIV-infected persons on HAART was 37.4 cases per 1,000 registered ART clients per year.

3.6. Distribution of Different Risk Factors to NCDs

This study investigated the effects of ART combinations on cardiovascular and metabolic health among HIV-positive patients. They found significant variances in systolic and diastolic blood pressures across different ART groups, highlighting a potential influence of medication on cardiovascular health. Notably, both systolic and diastolic pressures showed substantial differences across four main ART combinations, indicating significant impacts ($p < 0.001$ for both).

Contrastingly, the study observed no significant differences in blood sugar levels across ART groups ($p = 0.592$), suggesting that these regimens may not uniformly affect glycemic control. However, analyses of median blood pressures confirmed significant disparities across ART combinations, reinforcing the notion of ART's influence on cardiovascular parameters.

Furthermore, significant differences in the incidence of hypertension and Type II diabetes mellitus were noted among the ART regimens. A Pearson Chi-square test showed considerable variation in hypertension incidence, with 56% of patients developing this condition, particularly among those on specific ART combinations. Diabetes incidence also varied, with the highest observed in patients on the EFV + FTC + TDF combination (31.0%) and the lowest in those on the 3TC + EFV + TDF regimen (5.3%).

These findings highlight the need for personalized approaches in ART management, emphasizing careful consideration of potential adverse effects on cardiovascular and metabolic health.

3.7. Predictors of Hypertension and Type II Diabetes Mellitus Outcomes

Logistic regression analyses to identify the predictors of hypertension and T2DM among HIV-positive patients on HAART were conducted. It was discovered that both conditions are influenced by multiple factors, emphasizing

the complex interplay of genetics, lifestyle, and medication in disease development.

For T2DM, significant predictors included the type of ART, age, and smoking habits. Specifically, patients on the EFV + FTC + TDF + FDC regimen were four times more likely to develop diabetes compared to those on the 3TC + ABC + LPV regimen. Conversely, the risk was lower for those on the 3TC + EFV + TDF regimen. Age also played a role, with those in the 46–55-year age group showing a reduced risk compared to younger adults. Furthermore, smokers had a 26.7% higher risk of developing diabetes.

In terms of hypertension, the analysis revealed that the type of ART regimen, biological sex, family history, and smoking status were significant contributors. Males and smokers had higher odds of developing hypertension, as did individuals with a family history of the condition.

Despite the robust predictive power regarding case classification, the models explained a modest proportion of the outcome variability for both T2DM and hypertension. This suggests that additional unmeasured factors such as dietary patterns, lipid profiles, and individual genetic variances may also significantly impact disease development in this population.

4. DISCUSSION

4.1. Prevalence of Hypertension

The prevalence of hypertension in this study was 33.8% by diagnosis and 56% when assessed by cutoff readings, with men showing a significantly higher prevalence (64%) than women (49%) [$\chi^2 = 49.238$, $df = 1$; $p < 0.001$]. This gender disparity could be attributed to the protective effects of female sex hormones, which influence renal hemodynamics and sodium re-absorption [30]. The prevalence also varied significantly across age groups, with the highest (57.2%) in the 18–45-year bracket [$\chi^2 = 11.194$, $df = 2$; $p = 0.004$], suggesting an association between hypertension and younger adults, similar to findings in Cameroon and Uganda [31]–[33]. Key predictors of hypertension in this cohort included ART regimen, family history, and smoking.

4.2. Prevalence of Type II Diabetes Mellitus

This study reported a Type II diabetes mellitus prevalence of 14.9% by diagnosis and 24.4% by cutoff readings, higher than in similar settings [34], [35]. Factors such as study duration, methodological approaches, and HAART regimen duration likely influenced these disparities, with longer exposure periods possibly increasing diabetes risks [36]. Demographically, no significant gender differences were observed, but age was a determinant, with a peak prevalence of 27.5% in individuals over 55, aligning with observations in a London study [36].

4.3. Incidence Rate of Hypertension

The incidence rate of hypertension among the cohort was 85.7 cases per 1000 person-years, which is lower than rates reported in Cameroon, Uganda, Tanzania, and by a European and Australian study [37]–[40]. Contrarily, a South African survey suggested that ART might reduce

hypertension risk, highlighting the varied effects of ART on hypertension globally [41].

4.4. Incidence Rate of Type II Diabetes Mellitus

The incidence of Type II diabetes mellitus in this study was notably higher at 37.4 cases per 1000 person-years compared to other studies, which reported lower rates [42], [43]. This difference could be attributed to the larger sample size and longer follow-up in this study, as well as differences in ART regimens and cultural practices.

4.5. HAART Combinations Associated with Hypertension

This finding aligns with research by Pangmekheh *et al.*, which associated Tenofovir and Lamivudine use with hypertension, suggesting a role for these NRTIs in its development [15]. Furthermore, a meta-analysis by Fahme and their colleagues indicated that Protease Inhibitors may induce hypertension through inflammatory pathways and increased ROS production [44]. Specifically, Ritonavir-boosted Lopinavir has been linked to activating the adipocyte renin-angiotensin system, contributing to hypertension, and Efavirenz to renal dysfunction and hypertension [45], [46].

However, Byonanebye with their colleagues reported no direct link between PIs and hypertension, though they observed a higher hypertension prevalence with INSTIs, possibly due to weight gain and oxidative stress [40]. Contrasting these findings, other studies, including a cohort in Cameroon and the D.A.D study, found no consistent HAART-hypertension relationship when accounting for confounders [37], [47].

4.6. HAART Combinations Associated with Type II Diabetes Mellitus

Contrary to some studies that found no link between Type II diabetes and specific ART regimens, this research identified significant associations, particularly with regimens combining two NRTIs with an NNRTI or INSTI [48]. This finding is supported by studies linking PI/NRTI treatments to increased diabetes risks, possibly due to mitochondrial toxicity affecting insulin metabolism and lipid profiles [49]–[52]. However, a systematic review highlighted the lack of consistent associations, possibly due to study heterogeneity and methodological limitations [48].

5. CONCLUSION

This study has demonstrated that HIV-positive clients on HAART exhibit a high prevalence and incidence of hypertension and Type II diabetes mellitus. Notably, the male gender is more susceptible to developing hypertension compared to females. Additionally, aging is strongly correlated with an increased risk of developing both hypertension and Type II diabetes mellitus. Specific HAART combinations, particularly those involving two NRTI classes combined with either a PI or an INSTI, were linked to a higher incidence of hypertension. Conversely, regimens combining two NRTIs with an NNRTI or an INSTI, as well as triple therapy involving NRTI, NNRTI, and

INSTI, showed a higher association with Type II diabetes mellitus among treated clients.

5.1. Strengths

The robustness of this study is attributed to its use of routinely collected clinical data from diverse cohorts within a comprehensive national database. This database facilitated multiple readings per case, ensuring that reported prevalences and incidences reflect true diagnoses. The substantial number of case files reviewed significantly enhanced the statistical power of the findings. Moreover, the lengthy study period of 15 years, accounting for 13,519 person-years of follow-up, further bolstered the statistical validity.

5.2. Recommendations

Given the observed high incidence of hypertension among individuals on HAART, it is imperative to consider them for lifestyle modifications, nutritional counseling, and enhanced blood pressure monitoring. Additionally, there is a pressing need for targeted screening and preventive programs, including NCDs and cardiovascular risk assessments, to be integrated into the HAART initiation process for HIV-positive clients, given the not only prevalent hypertension but also the significant incidence of Type II diabetes mellitus observed.

Further research should focus on individual drug comparisons, especially NRTIs, PIs, and particularly INSTIs, as they are becoming the preferred treatment options. These studies should be conducted in larger cohorts within the Zambian context. Moreover, there is a necessity to explore additional factors influencing diabetes outcomes, such as dietary patterns, lipid profiles, and individual variances in pathophysiological changes due to disease progression, which were not examined in this study.

5.3. Study Limitations

This study offers significant insights but also has limitations affecting its validity and generalizability. Using secondary data from the SMART CARE database may introduce biases from data entry errors and gaps, potentially skewing results. The absence of randomization, characteristic of retrospective studies, may lead to selection bias, and the sample may not represent the broader HIV-positive population. Additionally, uncontrolled confounding variables such as genetic factors, socioeconomic status, and lifestyle choices could obscure the true effects of HAART on hypertension and diabetes. The retrospective design limits causal inferences, and changes in health-care protocols over the study's 15-year span may affect data consistency. The manual data handling and variable follow-up times could further compromise data integrity.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

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