UNAIDS Reference Group on HIV Estimates, Modelling, and Projections: Technical Meeting on HIV Incidence Estimates—Meeting Report

Date: 10th May 2024

Time: 14:00 - 17:00 SAST

Location: Microsoft Teams

Chairs:

- Prof Lloyd Mulenga, Director of Infectious Diseases, Zambian Ministry of Health; Infectious Diseases Division Chief, University Teaching Hospital
- Dr Wilford Kirungi, Principal Medical Epidemiologist, Ugandan Ministry of Health, HIV Strategic Information.

Table of Contents

Executive Summary

Background

The UNAIDS global HIV epidemiological estimates describe the scale and historic trends of HIV epidemics in countries around the world at global, regional, national, and sub-national levels. The estimates are derived using mathematical models fitted to relevant national HIV surveillance data in each country. Methods for estimating HIV incidence are developed with guidance from the UNAIDS Reference Group on Estimates, Modelling, and Projections (Reference Group; http://www.epidem.org).

Accurately understanding HIV incidence and ensuring that model estimates and projections are consistent with data and evidence is critical for planning the national and global HIV response. The October 2020 UNAIDS Reference Group meeting reviewed HIV incidence data against modelled estimates, resulting in changes to assumptions about the sex ratio of HIV incidence and average impact of ART coverage on transmission rate.

Reflecting a continued effort to validate modelled HIV incidence estimates and trends against incidence estimates from research studies, this meeting aims to compare modelled and empirical estimates at the district level where the studies were conducted, and to identify and understand differences in incidence levels.

Meeting Objectives

The primary objectives were to:

1. Assess the consistency of recent HIV incidence estimates derived from mathematical models with those obtained from empirical measurements in terms of levels and trends.
2. Identify and discuss systematic differences in incidence levels and age distribution by study type (population survey, cohort study, prevention trial) and population.
3. Evaluate empirical data for indications of systematic differences or changes over time in the age distribution of new infections compared to modelled estimates.
4. Propose priority areas for research, revisions to assumptions, and methodological developments needed to enhance the models used to estimate national HIV incidence trends.

The meeting was organised into two sessions. The first session involved plenary presentations on empirical HIV incidence data in sub-Saharan Africa and comparison with mathematical modelled estimates. This included presentations on the modelling methods and assumptions used to estimate national HIV incidence trends, incidence data from household surveys, clinical trials, and population cohorts, and a systematic review of empirical HIV incidence data and comparison to matched modelled

estimates. The second session involved plenary discussion to reach consensus recommendations around the meeting objectives.

Conclusions and recommendations

- HIV incidence levels and rates of HIV incidence decline were generally consistent between incidence data measured from general population studies and location / sex / age matched mathematical modelled estimates.
- Clinical trials and observational studies among specific populations measured systematically higher HIV incidence, indicating ability to identify population groups with disproportionately high HIV incidence and continued need for increased HIV prevention.
- Clear messaging about and common understanding of HIV incidence estimates is important. Specific recommendations when communicating about HIV incidence trends include clear messages about:
    - 'Declining' HIV incidence is not the same as HIV incidence being 'low' or controlled.
    - Sustained and in some cases expanded HIV intervention programmes are required to continue current declining trends. Terminology referring to the 'end of AIDS' in 2030 may be counterproductive towards connoting this.
    - Some population groups continue to experience disproportionately and unacceptably high HIV incidence; this heterogeneity and its implications for need for increased and more effective HIV prevention should not be undermined by reporting on overall declining trends.
    - Large HIV incidence declines recorded in Eastern and Southern Africa, the region with the most available data, is not the norm globally. Care should be taken to convey the heterogeneity in incidence trends across global regions and among population groups affected by HIV.
- Population cohort studies that prospectively measured HIV incidence consistently implied a shift in new HIV infections towards older age groups as incidence declines, while national Population HIV Impact Assessment household surveys using cross-sectional recent infection testing algorithms implied a shift towards younger age groups. Mathematical model estimates currently assume no systematic change over time in the age distribution of new infections. This difference merits further investigation and consideration about the implications for model assumptions.
- Continued and improved ability to estimate HIV incidence and populations and locations where new infections continue to occur as overall new infections decrease requires (1) improvements in the quality of routine program data, especially from antenatal clinics and key population programmes, and (2) prioritisation of data collection efforts that can provide the most significant impact on modelling and program design.

Agenda

The objectives of the meeting were addressed through a series of presentations and a discussion among all participants, with the following agenda:

Time (SAST)	Title	Presenters
Chair: **Prof Lloyd Mulenga**		
14.00-14.15	Opening remarks	Mary Mahy Mike Reid
14.15-14.35	Description of data and methods to quantify incidence trends in national HIV estimates	John Stover Drew Voetsch Mary Mahy
14.35-14.55	HIV incidence data from clinical trials	Jirair Ratevosian
14.55-15.15	HIV incidence from population cohort studies	Elphas Okango Victor Ssempijja Daniel Kwaro
15.15-15.35	Updated systematic review of HIV incidence trends in sub-Saharan Africa	Kate Grabowski
15.35-15.40	Stretch break	
15.40-16.00	Triangulation of empirical HIV incidence with modelled estimates	Oliver Stevens
Chair: **Dr Wilford Kirungi**		
16.00-17.00	Discussion	

1. Opening remarks

Mary Mahy, director of Data for Impact in UNAIDS, described UNAIDS' continuous commitment to enhancing the accuracy and precision of HIV estimates. The UNAIDS Reference Group on HIV Estimates, Modelling, and Projections (Reference Group; https://www.epidem.org) convenes regular biannual meetings to integrate review the latest scientific advancements evidence and incorporate findings into these estimates. Mahy highlighted the fundamental purpose of HIV epidemic estimates to empower countries to tailor and strengthen their HIV response strategies effectively. She stressed the importance of clear communication, especially when discrepancies arise between modelled estimates and empirical study findings. Such clarity ensures that health ministers and key policymakers can confidently utilize all relevant data to inform their national strategies and address their specific epidemic challenges.

In closing, Mahy noted the departure of Irum Zaidi from after 20 years of service to the PEPFAR programme, acknowledging her longstanding significant contributions to the UNAIDS Reference Group and innovation in use of data to guide the global HIV response.

Mike Reid, Chief Science Officer for PEPFAR, noted that consensus, objective, and nationally owned HIV estimates are heavily relied upon for PEPFAR planning and

decision making. Reid underscored the critical nature of integrating diverse data sources to refine HIV estimates.

Session chair **Prof Lloyd Mulenga** from the Ministry of Health in Zambia, introduced the session by highlighted the importance of a common language in communicating estimates across different sources and stakeholders, stressing the challenges faced in alignment during programming.

2. Description of Data and Methods to Quantify Incidence Trends in National HIV Estimates

Presenters: John Stover, Avenir Health; **Drew Voetsch,** CDC; **Mary Mahy,** UNAIDS

John Stover described the data and methods used to estimate national HIV incidence trends by sub-Saharan African countries. The model used by countries in the region (except South Africa) is the Estimation and Projection Package (EPP). EPP is an integrated demographic and infectious disease transmission model that estimates HIV incidence over time, primarily from data on HIV prevalence from national household surveys and HIV prevalence trends among pregnant women attending antenatal clinics. EPP also may include cross-sectional HIV incidence measured in household surveys, but not other empirical HIV incidence data (which are typically not nationally representative). The HIV transmission rate over the course of the epidemic is estimated as a flexible smooth function in a Bayesian statistical inference framework. The model accounts for reduction in HIV transmission rate as ART coverage increases. Stover described how EPP has been updated over the years reflecting changing epidemiologic patterns, new evidence about key model assumptions, and changes in treatment eligibility.

Drew Voetsch described HIV incidence measured in Population HIV Impact Assessment (PHIA) surveys. PHIA surveys measured HIV incidence cross-sectionally in a nationally representative sample of adults using a recent infection testing algorithm. Surveys have been conducted in 13 high HIV burden African countries since 2015, with seven countries implementing two surveys around five years apart providing data about incidence trends. Voetsch outlined the survey designs and indicators measured.

Mary Mahy provided a comparison **of HIV incidence estimates from the Spectrum model and from PHIA surveys** in the same year. Spectrum estimates were from the UNAIDS estimates reported in 2023 for all countries. Overall, incidence levels were similar between modelled estimates and survey-measured HIV incidence. In countries with high incidence (above 0.5%), the Spectrum model sometimes had higher incidence estimates than those measured from surveys. In Eswatini and Zambia, which had two surveys, incidence declined similarly between the survey rounds and Spectrum model estimates. However, in the Zimbabwe, incidence did not change between surveys, contrasting with Spectrum results in which incidence was estimated to decline. Survey estimates had wide uncertainty ranges.

3. HIV Incidence Data from Clinical Trials

Presenter: Dr Jirair Ratevosian, Yale University

Overview: The presentation provided an overview of HIV incidence data measured in recent HIV prevention clinical trials globally. Persistently high HIV incidence rates were observed despite available prevention technologies like PrEP. These observations of populations with very high incidence are important to consider when assessing progress towards and strategies to achieve upcoming UNAIDS 2025 and 2030 targets.

Key Findings

HIV incidence measures were summarised from four trials:

1. **ECHO Trial**: In a trial conducted among young women seeking contraception in four countries (eSwatini, Kenya, South Africa, and Zambia), HIV incidence was extremely high, above 3% per annum. There was no significant difference in HIV risk among women using three different contraceptive methods (the primary study outcome).
2. **HVTN 702 (Uhambo)**: This vaccine trial in South Africa recorded an annual incidence rate exceeding 4% among women.
3. **Imbokodo Trial**: This vaccine trial among cisgender women in Malawi, Mozambique, South Africa, Zambia, and Zimbabwe tested vaccine strategies and reported high HIV incidence rates (4.3%).
4. **Mosaico Trial:** This trial among cisgender men and transgender individuals who have sex with men were conducted across multiple countries including the United States and several in Europe and Latin America and found an overall incidence rate of 4.1%.

Ratevosian identified several critical issues based on the data from these trials:

- Across different regions and populations, the trials reported consistently high HIV incidence rates. This trend is particularly concerning in regions like Eastern Europe, Central Asia, and the MENA region, where incidence rates are rising.
- Despite the proven efficacy of PrEP, its impact at the population level has been limited by low uptake and adherence over time. Ratevosian stressed the importance of addressing social and other barriers that limit the full impact of PrEP.
- The trials underscore the impact of social determinants on HIV incidence. Legal barriers and punitive laws, particularly affecting key populations, have been shown to increase HIV prevalence and incidence among men who have sex with men (MSM).
- Data from clinical trials and other incidence data provide additional empirical sources to potentially improve HIV incidence estimates and tailor prevention strategies more effectively.
- Messaging around changes in HIV incidence estimates should be improved, particularly ensuring clarity that while estimates suggest incidence overall has been declining, it remains unacceptably high in many locations and population groups and further HIV prevention efforts are needed to reduce HIV incidence.

Ratevosian called to move away from messaging referring to the 'end of AIDS', ensuring that stakeholders, including policymakers, receive clear, accurate information that can drive effective advocacy and sustained funding for HIV prevention globally.

4. HIV Incidence from Population Cohort Studies

Presenters: Elphas Okango, AHRI HDSS, South Africa; **Victor Ssempijja**, Rakai Community Cohort Study, Uganda; **Daniel Kwaro**, Siaya HDSS, Kenya

Overview: Findings from three population cohort studies, including the Siaya HDSS (Kenya), AHRI HDSS (South Africa), and the Rakai Community Cohort Study (Uganda) were presented, showing consistent declines and persistent sex disparities, as summarised in the table below.

Cohort Study	Focus & Key Data Collected	Summary of HIV Incidence and Prevalence	Sex Differences	Age Shifts and Trends
AHRI HDSS (South Africa)	Routine collection of demographics, socioeconomic data, HIV status, and other health information from adult individuals in all households in the area.	Substantial decline in HIV incidence since 2011. In 2021, HIV prevalence was about 28% for males and 45% for females.	Incidence rates ~2.7x higher in women than in men. Recent data suggests slight decrease in female to male rate ratios.	Increasing proportions of new infections occurring among older age groups.
Siaya HDSS (Kenya)	HIV and demographic surveillance, in a subset of the district. ~32,000 people aged 13+ included in incidence cohort.	Substantial decrease in HIV incidence over time. HIV prevalence is 10%, higher than 4% national prevalence 4%.	Higher incidence rates in women.	A shift towards older age groups in new infections, with fewer new infections among younger individuals.
Rakai Community Cohort Study (Uganda)	Open, population-based study; high HIV burden; focuses on residents aged 14 to 49, recently extended to older adults.	Substantial decline in HIV incidence since 2007-9. High HIV burden with ~15% prevalence among women and 8% among men in 2022.	Incidence in women still higher than in men but with a narrowing gap in recent years (following period of increasing ratio).	Decreased proportion of new infections among age 15-24 years. Increasing proportion from among older age groups.

The three cohorts showed remarkably similar declines in incidence since 2011 and, to different extents, a narrowing of the gender disparity in recent years. The clearest shift in age distribution of new infections to older ages is apparent in the AHRI cohort, but all three cohorts show a decrease in the proportion of new infections that are among 15-25-year-olds over time.

5. Systematic Review of HIV Incidence Trends in Sub-Saharan Africa

Presenter: Kate Grabowski, Johns Hopkins University

Overview: Kate Grabowski presented the findings from a systematic review published in 2021 of empirical HIV incidence data across Sub-Saharan Africa. Results of the review indicated (1) declining incidence in eastern and southern Africa, (2) limited data in central and western Africa, and (3) an increase in the female-to-male HIV incidence ratio.

Methodological Overview

Criteria	Description
Data Type	Prospective serology, retrospective cohorts, cross-sectional studies using lab-based measurements (e.g., LAg-avidity assay).
Geographic Focus	Southern and Eastern Africa, with limited data from Western Africa. Excluded Central Africa due to lack of data.
Population Focus	Individuals aged 15+; focus on general population samples without specific behavioural risks for HIV acquisition.
Inclusion Years	Empirical data published between 2010 and 2019.
Exclusion Criteria	Studies estimating incidence from age-specific seroprevalence curves using mathematical models.
Minimum Sample Size	Studies with at least 50 persons or 50 person-years of follow-up.

Key Findings

1. HIV incidence declined in Eastern and Southern Africa between 2010 and 2019, which aligns with the trends observed in modelled estimates.
2. The incidence rates from the studies are mostly below 1% per 100 person-years in Eastern Africa. Studies in Southern Africa, particularly South Africa, reported substantially higher rates.
3. There is a lack of recent empirical data, with many studies concluding as ART became more widespread around 2010. The lack of recent empirical data post-2020 highlights a critical gap in current HIV incidence understanding.
4. The review observed generally higher HIV incidence rates in women compared to men across the studies. The female to male HIV incidence ratio appears to be increasing between 2010 and 2019 in general population studies.

Challenges and Limitations:

- The systematic review was challenging due to the complexity of identifying relevant studies, as many did not use 'incidence' in their titles or abstracts.
- No risk of bias analysis was conducted due to the nature of the review, which focused on empirical data collection rather than estimating causal effects.
- Most of the reviewed data were collected before significant public health interventions like universal test and treat, reflecting incidence rates before these interventions fully impacted the populations.

There is a need for ongoing monitoring of HIV incidence, especially in key populations and regions with limited data, to effectively measure the impact of public health interventions.

The **ongoing update of the review** aims to incorporate more recent data. This new review has identified substantial data among PrEP-eligible individuals and users, a new risk cohort since the previous review.

6. Triangulation of Empirical HIV Incidence Estimates with Modelled Estimates

Presenter: **Oliver Stevens**, Imperial College London

Overview: Oliver Stevens presented an analysis comparing empirical HIV incidence observations from longitudinal studies and PHIA surveys with modelled incidence estimates.

Objectives Addressed

1) Are mathematical-model derived estimates of HIV incidence consistent with empirical HIV incidence observations?
2) Among empirically measured incidence observations, are there systematic differences in incidence level and age distribution by study type?
3) Do empirical incidence data indicate systematic differences or changes over time in the age distribution of new infections compared to modelled estimates?

Methods and Data Sources

- Empirical HIV incidence data collated from Joshi et al. systematic review and supplemented by newer or more granular data from cohort studies, PHIA surveys, and the Universal Testing and Treatment trials.
- Empirical observations were matched to modelled estimates from Spectrum and Naomi by sub-national area, year, age group, and sex. For studies restricted to sexually active study populations, matched modelled estimates were adjusted for the percentage of the study-eligible age range who were recently sexually active to mirror study inclusion criteria where appropriate.
- Empirical observations were compared against modelled estimates using mixed-effect Poisson regression, adjusting for sex, study type, and study representativeness.

Key Findings

1. Empirical incidence observations were highly correlated with modelled estimates, and there was no evidence that this varied at differing HIV incidence levels nor by sex.
2. Prospective cohorts and control arms of trials showed about 30-40% higher incidence compared to modelled estimates. Estimates from PHIA surveys (designed to be representative of the population) were consistent with Spectrum estimates.
3. Empirical data from cohort studies indicate a sustained decline in the proportion of new infections under age 25, while PHIA survey data implied the opposite trend.
4. Spectrum estimates a younger age pattern of infections than cohort data.

Challenges Highlighted

- The ability of studies to representatively sample the population significantly impacts the alignment between modelled and empirical data.
- Models are calibrated to PHIA surveys, so identifying aligned incidence estimates does not reflect a fully independent assessment.
- Most empirical data were collected before significant public health interventions, like universal test and treat, reflecting pre-intervention incidence rates.

Conclusions and Recommendations

- The close alignment of modelled estimates with empirical observations across diverse settings increases confidence about trends reported in current modelled estimates. However, the noted discrepancies suggest areas for refinement, especially in capturing demographic shifts in the pattern of new infections.
- Further investigations are necessary to understand the persistent discrepancies in incidence levels between different study methodologies and the shifting age distribution of HIV incidence.

7. Discussion

Chair: Dr Wilford Kirungi

Clarifying questions

A participant asked how much the PHIA data contributes to the Spectrum model, to which John Stover described that Spectrum significantly uses PHIA data in model fitting, including estimates of prevalence, incidence, and ART coverage. In addition, PHIA prevalence estimates by age and sex are used to distribute new infections.

Reflections on Presentations

Potential Causes for Varying Age Patterns in PHIAs vs. Cohort Studies

Participants prompted discussion about the different direction of changes in age distribution in PHIA surveys versus cohort studies, postulating that this could be due to differences in study methods or reflecting shifts in behaviour or service uptake among newer generations.

Stevens acknowledged the complexity behind the differing age patterns noted between PHIAs and cohort studies:

- PHIAs capture only more current dynamics affecting younger populations, such as new social or economic challenges, or perhaps changes in risk behaviour and access to or uptake of health services. Cohort studies show a longer time series, with temporal overlaps with PHIAs in recent years.
- The methodological differences between PHIAs and cohort studies could contribute to these discrepancies. PHIA surveys rely on recent infection testing algorithms that use multiple biomarkers (LAg Avidity assay, VL test, ARV metabolite) to distinguish recent from long-term infections and require assumptions about the duration of recent infection and false recent proportion. Cohort studies may be more susceptible to participation biases due to their design of following the same group over time.
- Stevens suggested that triangulating additional data such as ART coverage and viral load suppression (VLS) by age could provide more context to these trends, offering a fuller picture of the factors influencing these age-specific incidence rates.

Subnational Estimates of HIV Incidence

- The uniformity in the decline in HIV incidence across the three population cohort studies that are geographically and demographically diverse was noted. This suggests effective widespread implementation of HIV interventions that are impacting broad regions. However, the similarities in decline rates also prompt a deeper look into local or district-level data to understand the nuances that might not be apparent at the national or provincial level.
- Concerns were expressed about the limitations of current HIV incidence models, which are calibrated at national level, given the heterogeneous nature of the epidemic at smaller scales. A participant questioned the models' ability to identify and incorporate the diverse infection patterns across different regions to effectively guide targeted interventions. In response, Imai-Eaton described the integration of national and subnational data into models such as Spectrum and Naomi, to tackle heterogeneities observed across different regions and provide accurate district-level estimates. However, capturing time-varying trends at the subnational level remains challenging, highlighting the need for improved data sources. He also highlighted the need to consider broader dimensions of heterogeneity, such as socioeconomic factors, particularly as the epidemic increasingly affects marginalized populations.

Data Representativeness and Integration into Models

The integration of various data types—ranging from clinical trial data to routine program data—and the challenges in ensuring these data sources are representative and valid for modelling purposes, were discussed.

- The importance of representativeness in incidence data used in modelling was highlighted, whether derived from surveys, cohort studies, clinical trials, or programs, emphasising the need to clearly define the populations being studied to ensure accurate extrapolation.
- Population surveys (such as PHIA surveys) are integrated into national modelled incidence estimates. However, clinical trials and observational research studies are not formally incorporated into model fitting because they are conducted among study populations with specific characteristics in selected subnational geographic areas. These studies often report higher incidence rates due to the specific populations they study.

Systematic biases in estimates from cohorts and surveys due to non-participation

Concerns were raised regarding lower response rates and uptake of testing and participation among younger age groups and the imprecision this may introduce into the data. Cohort and PHIA survey teams discussed adjustments for refusal that are made using statistical tools. Tanser and others noted that comprehensive sensitivity analyses have been undertaken to assess the potential impact of differential non-response mechanisms, and generally found overall magnitudes of incidence decline to be robust.

Recommendations

Enhancing Data Collection and Model Refinement

A recurring discussion theme for future priorities involved improved and expanded data collection, with participants highlighting the importance of models in identifying and understanding where there's a disconnect between programme data and survey data.

- Improvements in the quality of routine program data, especially from antenatal clinics and key population programmes, were identified as essential for more accurate modelling.
- With potential future constraints on funding and resources, there was a strong push to prioritize data collection efforts that can provide the most significant impact on modelling and program design. This prioritization is crucial for adapting to changing epidemic dynamics and ensuring effective resource allocation.
- There was a call for more granular data to understand geographic locations with high HIV incidence (‘hotspots’) and guide interventions.

- The importance of refining models to better estimate HIV incidence among key populations and children was stressed. Targeted resource allocation is required, especially in the context of tightening global budgets, to effectively close equity gaps. A major ongoing priority for the UNAIDS Reference Group is developing and refining models for these populations. However, returning to the theme of improved and expanded data collection, the accuracy of resulting estimates fundamentally relies on more consistent and regular data collection for these groups.

Use of Testing History Data

The potential to reanalyse PHIA data using testing history data method developed by Fellows *et al*. was suggested, especially to overcome some limitations of current biomarker-based incidence estimates. This approach is valuable for disaggregating data by age, sex, and geography, areas where current methods face limitations. Drew Voetsch noted that this testing history method has aligned well with biomarker estimates in most countries, except for a few outliers like Lesotho, indicating its potential utility in improving the accuracy of HIV surveillance data.

Messaging and Communication

Clear communication is needed when disseminating HIV incidence data and estimates, ensuring that all stakeholders and consumers have a unified understanding of the implications.

- The importance of clear messaging was underscored, particularly distinguishing that while HIV incidence is declining rapidly in many epidemics (especially Eastern and Southern Africa), incidence is not 'low'. Recorded incidence declines are from an extremely high initial incidence level, and sustained and further interventions are required to reach low incidence; for example, among young women.
- There are population groups among whom incidence remains disproportionately and unacceptably high.
- The large incidence declines recorded in Eastern and Southern Africa, the region with the most available data, is not the norm globally. Care should be taken to convey the heterogeneity in incidence trends across global regions and among population groups affected by HIV.

Rapid declines in HIV incidence estimates in some populations and at national level should not be communicated as the 'end of AIDS'.

Meeting materials

Documents relevant to the meeting are available on www.epidem.org, including:

1. A working paper by Stevens et al (not for citation or sharing) titled: "***Comparing empirical HIV incidence observations with modelled incidence estimates in high-burden HIV epidemic settings"*.**

2. A document including speaker bios, agenda, and objectives of this meeting.

3. A folder with presentations.

Relevant open source published papers include:

- **K Joshi et. al.** Declining HIV incidence in sub-Saharan Africa: a systematic review and meta-analysis of empiric data**. J Int AIDS Soc. 2021** Oct;24(10):e25818. doi: 10.1002/jia2.25818.

- **J Stover, R Glaubius**. Methods and Assumptions for Estimating Key HIV Indicators in the UNAIDS Annual Estimates Process. **J Acquir Immune Defic Syndr. 2024** Jan 1;95(1S):e5-e12. doi: 10.1097/QAI.0000000000003316.

- **Eaton et. al.** The Estimation and Projection Package Age-Sex Model and the r-hybrid model: new tools for estimating HIV incidence trends in sub-Saharan Africa. **AIDS. 2019** Dec 15;33 Suppl 3(Suppl 3):S235-S244. doi: 10.1097/QAD.0000000000002437

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