Meeting Minutes: UNAIDS Technical Reference Group Meeting on Estimating Cryptococcal Meningitis Deaths among PLHIV

Date: 29 February 2024
Time: 17:30-19:30 SAST
Location: Online
Facilitator: Cari van Schalkwyk
Participants: Listed at the end of this document

Welcome and Introduction

Keith Sabin (UNAIDS) emphasized the need for more detailed, country-specific data on the cause of death among PLHIV. This need is driven by the aim to enable countries to respond effectively to the high proportions of deaths due to cryptococcal meningitis (CM). Sabin emphasized that UNAIDS aims to draw on existing resources and expertise to meet these objectives.

Objectives of the meeting
The purpose of the meeting was to discuss existing methods for estimating CM deaths and to assess their feasibility for implementation in the Spectrum model, with the following objectives:

- Review existing methods for estimating CM burden and deaths among PLHIV.
- Review the availability of CM routine surveillance data in settings with high HIV burden.
- Assess the suitability and feasibility of implementing these methods in the Spectrum model used by country teams to produce national HIV estimates.
- Plan for the coordinated development of improved country-specific estimation methods in collaboration with CM expert groups.

The Global Burden of HIV-associated Cryptococcal Infection 2020: Methodology by Radha Rajasingham, University of Minnesota

Radha Rajasingham discussed the need for estimating CM burden among PLHIV to better quantify resources, measure the impact of new strategies, and guide expanded cryptococcal antigen (CrAg) screening and new meningitis treatments. CrAg is detectable in the blood before people develop full-blown meningitis, and being positive is highly predictive of developing meningitis in an HIV-infected population. Rajasingham presented existing methods to estimate the number of adults with advanced HIV disease using UNAIDS Global AIDS Monitoring (GAM) and Population-Based HIV Impact Assessments (PHIA) data.

Three groups of interest were highlighted to determine the proportion of individuals with CM expected to present to the hospital:

1. Adults who do not know their HIV status.
    - Calculated using Adults living with HIV * (1-%PWH who know their status)
2. New diagnosis of HIV, not yet on ART.
    - Calculated using Adults with known HIV status– Adults on ART
3. On ART, virologic non-suppression.

    - Calculated using Adults on ART * (1-% with suppressed viral loads)

The regional prevalence of cryptococcal infection was estimated through a meta-analysis of studies published between 1989-2021 (no time trend in infection), with results showing the highest burden in Latin America (5.4%) and 3.7% in East and Southern Africa (the region with the most PLHIV).

The number of CrAg+ individuals with CD4 <200 in each of the three groups was calculated by country, using regional estimates for countries with no prevalence studies. Progression to meningitis depended on the presence/absence of a national CrAg screening programme, and whether the individuals are in HIV care or not. The proportions of people with meningitis presenting to medical care, and mortality, varied based on the three defined groups.

Rajasingham showed validation of estimates against data from South Africa, Sierra Leone, Eritrea, and Mali.

Discussion

- In response to a question, Rajasingham clarified that once individuals are on effective ART and are virologically suppressed, their risk of developing CM is close to zero.
- A participant suggested that disaggregating meningitis cases into treated and untreated cases is more appropriate to compare model estimates with NICD estimates for South Africa (which is only a record of treated cases).
- It was suggested that it would be useful to capture information about fluconazole coverage as an input to the model, but tracking its provision specifically for meningitis treatment may be challenging due to its use in treating other diseases.
- The possibility of applying the model over time and capturing time trends was raised, but it was noted that changes in estimates would only reflect changes in the number of people with CD4 counts <200 rather than changes in other factors such as fluconazole coverage, which is currently unknown.
- Discussion regarding the data:
    - Limitations of GAM were highlighted, including incomplete and unvalidated reporting, especially for countries outside of Africa.
    - There is a need for validating the Spectrum model outputs of people with CD4 counts <200 against the sources in Rajasingham's analysis.
    - Overall, it was confirmed that it is possible to replicate Rajasingham's method in Spectrum and additional input editors would need to be added for countries to include their own data where available.
- New GAM indicators have been added in the 2024 estimates round, relating to the CM care cascade: % screened, % diagnosed, % treated.

Next Steps and Recommendations

- Validate Spectrum results for AHD (CD4 <200)
    - PHIA surveys
    - GAM reports
    - Other evidence collated by WHO and CM modelling team.
- Reproduce CM model AIDS deaths results with internal Spectrum model estimates for numbers with CD4 <200.
    - See how results change using internal Spectrum estimates for AHD vs. previously produced modelled results using GAM CD4 <200 and PHIA survey results.

    - Review time trends in CM deaths for plausibility (essentially will reflect modelled changes in % CD4 <200).
    - Review proportion of AIDS deaths attributed to CM vs. total AIDS deaths in Spectrum results.
- Review data reported for new cryptococcal indicators in upcoming GAM reporting round for screening coverage and treatment coverage.
    - Consider whether GAM indicators or other data should be collected as user inputs in Spectrum.
- Share technical details of model with Avenir for consideration about internal calculation and input editor design.

Supporting Documents:

- Presentation slides by Radha Rajasingham, MD.
- Link to publication by Radha Rajasingham, MD.

Meeting Adjourned: 19:15 SAST
Minutes Prepared by: Yuri Munsamy, SACEMA

Meeting Participants

Deepa Jahagirdar	Avenir Health
Guy Mahiane	Avenir Health
John Stover	Avenir Health
Rob Glaubius	Avenir Health
Rowan Martin-Hughes	Burnet
Ray Shiraishi	CDC
Tim Brown	East West Center
Mehran Hosseini	Global Fund
Jeff Imai Eaton	Harvard University
Mathieu Maheu-Giroux	McGill University
Parviez Hosseini	PEPFAR
Cari van Schalkwyk	SACEMA
Yuri Munsamy	SACEMA
Eline Korenromp	UNAIDS
Keith Sabin	UNAIDS
Leigh Johnson	University of Cape Town
Melaku Dessie	USAID
Shona Dalal	WHO
Radha Rajasingham	University of Minnesota
David Boulware	University of Minnesota
Joe Jarvis	LSHTM
Ajay Rangaraj	WHO
Monita Patel	CDC
Danielle Payne	CDC

Pam Groenewald	SA-MRC
Debbie Bradshaw	SA-MRC
Makandwe Nyirenda	SA-MRC