Mortality Under Early Access to Antiretroviral Therapy Versus Eswatini’s National Standard of Care: The MaxART Clustered Randomized Stepped Wedge Trial

Ariel Chao1, Donna Spiegelman1, Shaukat Khan1, Fiona Walsh2, Sikhateau Mazibuko3, Munyaradzi Pasipamire4, Boyang Chai5, Ria Reis6,7, Khudzoe Mlambo5, Wim Delva5,9,10,11,12, Gavin Khumalo3, Mandisa Zwane14, Yvette Fleming5, Emma Mafa4, Anita Hettema1,2, Charlotte Lejeune1, Till Bärnighausen8,15, Velepi Okello18

1Department of Biostatistics, Yale School of Public Health, New Haven, USA. 2Clinton Health Access Initiative (CHAI), Mbabane, Swaziland/Eswatini. 3Clinton Health Access Initiative (CEAI), Boston, USA. 4Eswatini National ART program (SNAP), Ministry of Health, Mbabane, Swaziland. 5Departments of Nutrition, Harvard T.H Chan School of Public Health, Boston, USA. 6Leiden University Medical Center, Leiden University, Leiden, Netherlands. 7Amsterdam Institute for Social Sciences, University of Amsterdam, Amsterdam, Netherlands. 8Children’s Institute, University of Cape Town, Cape Town, South Africa. 9Stellenbosch University, Stellenbosch, South Africa. 10Hasselt University Center for Statistics Diepenbeek, Belgium. 11Gent University, International Centre for Reproductive Health, Gent, Belgium. 12KU Leuven, Rega Institute for Medical Research, Leuven, Belgium. 13Eswatini National Network of People Living with HIV (SWANNEPHA), Mbabane, Eswatini. 14SAF AIDS, Manzini, Eswatini. 15Departments of Global Health and Population, Harvard T.H Chan School of Public Health, Boston, USA. 16Department Office, Ministry of Health, Mbabane, Eswatini.

Competing risks approach used to estimate related and HIV-related mortality rates. Excluded protocol violations (N=80), program (N=23), breastfeeding (N=6), age <18 (N=3), and ART-naive (N=24). HIV-related mortality (HR:0.93, 95% CI: 0.46-1.87, p=0.83)also an important finding that there is no evidence of harm.

Abstract

Introduction

• Current WHO guidelines recommend “treat all” HIV-infected individuals with ART
• MaxART: first Treat All implementation trial in government-managed health system
• Primary findings strongly support scale-up of Treat All – this analysis examines mortality as an additional indicator of its impact

Methods

• Conducted in 14 Eswatini health clinics with clinic-based stepped-wedge design
• All-cause, disease- and HIV-related mortality analyzed using Cox proportional hazard model

Results

• Treat All – no impact on all-cause (HR:1.12, 95% CI: 0.58-2.18, p=0.73), disease-related (HR:1.04, 95% CI: 0.52-2.11, p=0.90), and HIV-related mortality (HR: 0.93, 95% CI: 0.46-1.87, p=0.83)

Conclusion

• No immediate benefit of the Treat All strategy on mortality, nor evidence of harm.

Introduction

• Timing of ART initiation greatly influences survival outcomes among PLHIV1,2,3
• 2016: WHO recommended ART initiation in all adults with HIV, regardless of WHO clinical stage and CD4 count – “treat all” for immediate ART initiation following HIV diagnosis4
• MaxART: to determine the impact of Treat All on care retention and viral suppression versus standard of care (SoC)4
• Secondary analysis examines mortality associated with Treat All compared to later ART-initiation per SoC. Results on longevity will serve as additional indicator of impact.

Methods

• One random pair of clinics transitioned from Eswatini’s SoC for ART initiation to Treat All every 4 months.
• All endpoints analyzed censoring SoC participants at clinic transition.
• Competing risks approach used to estimate disease-related and HIV-related mortality rates.

Results

Table 1: 12-month mortality rates among SoC and Treat All participants, and multivariate-adjusted hazard ratio

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>SoC</th>
<th>Treat All</th>
<th>Hazard Ratio (95% CI)</th>
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<tr>
<td>12-Month Mortality Rate</td>
<td>1.02% (0.40-1.64)</td>
<td>1.00% (0.40-1.59)</td>
<td>0.93 (0.46-1.67)</td>
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Figure 2: Clinic-based step-wedge trial diagram showing number of enrolled participants by clinic pair and steps

Figure 3: Multivariate-adjusted Kaplan-Meier curves by treatment group

Conclusion

• Primary analysis strongly supported scale-up of Treat All to improve retention and viral suppression rates, but mortality analysis inconclusive about impact on longevity among people living with HIV.
• Mortality under Treat All not significantly lower compared to SoC as hypothesized.
• However, since major purpose of Treat All is to decrease infectiousness so there are no new cases, also an important finding that there is no evidence of harm.
• Longer follow-up of participants necessary to establish long-term consequences, particularly mortality, of Treat All.

References