Poster CO139

The Evaluation of Clinical Outcomes from Rapid Start Antiretroviral Therapy in Human Immunodeficiency Virus: A Systematic Review and Meta-Analysis

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Plain Language Summary

- PWH who initiate ART within 7 days of HIV diagnosis have lower mortality than those who begin ART after 7 days

Conclusions

- Our study found that rART was associated with a significant decrease in mortality among PWH compared with nrART
- LTFU was increased in patients who began ART within 7 days, however there is a lack of studies in the United States and a lack of adjusted effects to determine the reason for LTFU
- Clinicians and policy-makers may consider these findings to facilitate rART in patients with HIV infection

Introduction

- The WHO and DHHS HIV guidelines recommend rapid start of anti-retroviral therapy (ART), often defined as initiation of ART within 7 days of HIV diagnosis, with an ideal start time being the same day [1-3]
- The recommendation for rART came as a result of various large randomized controlled trials (RCTs), the DIAMOND [4], RAPID [5], and Same-Day ART vs. Standard of Care [6]
- Results showed rART was associated with improvements in viral suppression. However, mortality was only evaluated in 1 trial and found a 0.51 unadjusted relative risk in same day ART initiation during the 2 year study duration [6]
- The real-world clinical effectiveness of rART is still unclear. A review of observational studies by Ford et al. published in 2018 found that rART increased loss to follow-up (LTFU) [7]
- This study aims to systematically evaluate the clinical benefits of rART initiation in HIV patients from a real-world perspective

Objective

- Synthesize the clinical and outcomes of rapid versus non-rapid ART in real-world setting

Methods

- This study was reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline [8] and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guideline [9]
- The protocol was registered on PROSPERO (CRD42023446629)
- Updated systematic search was performed with PubMed, EMBASE, Web of Science, and ProQuest from January 01, 2017, to January 15, 2023
- This search supplement previous systematic review by Ford et al., and employed a search strategy using terms HIV infection, ART, rapid treatment initiation and their synonyms
- Studies were then screened by titles/abstracts using predefined criteria. Articles meeting inclusion criteria underwent full-text review. Two reviewers independently performed study selection, resolving disagreements through discussion or a third reviewer
- The process of screening was conducted in Covidence

Study Selection Criteria:

- Patients: Patients diagnosed with HIV
- Intervention: rART - refers to the time from HIV diagnosis to ART initiation. The definition of rART for this meta-analysis was ART given within 7 days of HIV diagnosis.
- Comparator: nrART – define as ART given greater than 7 days after HIV diagnosis
- Outcomes: Mortality, LTFU, and viral suppression
- Study Design: Prospective or Retrospective, rapid ART defined as within 7 days of HIV diagnosis
- Given the insufficient number of studies, meta-analyses of viral suppression was not performed
- Quality Assessment: The Risk of Bias in non-randomized studies of interventions (ROBINS-I) was used to assess the quality of studies [10]

Results

Table 1: Summary of Studies Reporting Clinical Effectiveness

Author, Year	Country	Study design	Study period	Patients	Days from HIV Diagnosis to rART Start	LTFU	Viral Suppression	Mortality	Sample size
Ahmed (a), 2021	Ethiopia	Retrospective	2016 – 2018	Adults with HIV	Same Day		x		877
Ahmed (b), 2021	Ethiopia	Retrospective	2016 – 2018	Adults with HIV	Same Day	x			942
Bacon, 2021	US	Retrospective	2013 - 2017	Adults with HIV	Same Day		x		1148
Bantie, 2022	Ethiopia	Retrospective	2016-2020	Adults with HIV	<7	x			507
Chan, 2016	Malawi	Retrospective	2011 - 2012	pregnant women with HIV	Same Day	x			456
Colasanti, 2018	US	Retrospective	2016- 2016	Adults with HIV	<3		x		207
Dah, 2021	Burkina Faso, Cote d'Ivoire, Mali and Togo	Prospective	2015-2019	Adults with HIV (MSM)	<7	x	x		350
Davey, 2020	South Africa	Prospective	2016- 2018	Adults with HIV	Same Day	x	x	x	92609
Gomillia, 2020	US	Retrospective	2016 - 2018	Adults with HIV	<7		x		63
Hoenigl, 2016	US	Retrospective	2010 -2015	Adults with HIV	Same Day		x		86
Huang, 2019	Taiwan	Retrospective	2014- 2018	Adults with HIV	<7	x	x	x	631
Kerschberge (b), 2021	Eswatini	Retrospective	2014 - 2016	Adults with HIV	Same Day	x	x	x	1328
Kimanga, 2022	Kenya	Retrospective	2015 – 2018	Adults with HIV	Same Day	x	x	x	8592
Lebelonyane, 2020	Botswana	Prospective	2013 - 2018	Adults with HIV	Same Day	x	x	x	2517
Lilian, 2020	South Africa	Retrospective	2017- 2018	Adults with HIV	Same Day	x		x	42290
Mgbako, 2022	US	Retrospective	2018 -2019	Adults with HIV	Same Day	x	x		107
Mitiku, 2016	Ethiopia	Retrospective	2013 – 2015	Pregnant women with HIV	Same Day	x			343
Mody, 2021	Zambia	Retrospective	2016 - 2018	Adults with HIV	Same Day	x	x		65673
Monforte , 2019	Italy	Prospective	2016 - 2017	Adults with HIV	<7	x	x		1247
O'Shea, 2022	US	Retrospective	2012 - 2020	Adults with HIV	Same Day		x		116
Pakela, 2020	South Africa	Retrospective	2017 – 2017	Adults with HIV	Same Day		x		826
Patel, 2021	US	Retrospective	2016 - 2020	Youth with HIV	Same Day	x	x		124
Pathela, 2021	US	Retrospective	2016 – 2018	Adults with HIV	Same Day		x		303
Pilcher, 2017	US	Retrospective	2013 - 2014	Adults with HIV	Same Day	x	x		86
Ross, 2022	Sub-Saharan Africa	Prospective	2015 -2019	Adults with HIV	Same Day	x	x	x	29017
Ssebunya, 2017	Uganda	Retrospective	2010 - 2015	Children with HIV	<7		x	x	359
Vogt, 2017	Zimababwe	Retrospective	2004 - 2011	Children with HIV	<7	x		x	1499
Zhao B, 2022	China	Retrospective	2016- 2019	Adults with HIV	<7		x		2494

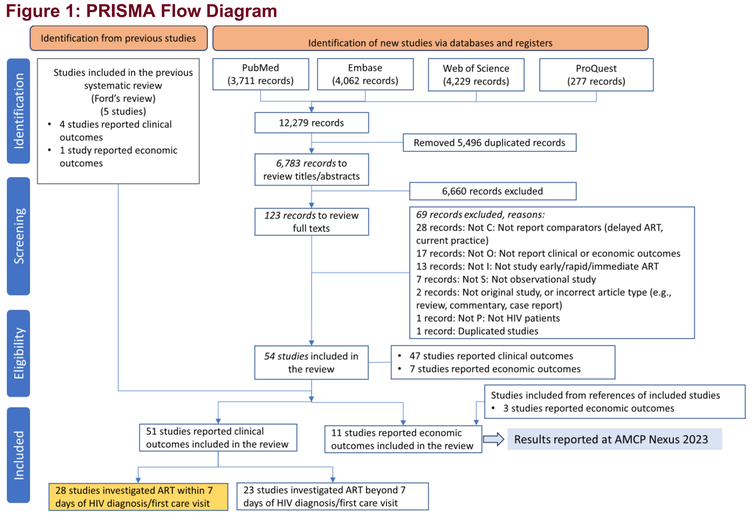
Loss To Follow-Up (LTFU) Results

- **LTFU was increased in patients who initiated ART within 7 days in studies outside the United States**
- Regarding LTFU at 6 and 12 months, the pooled estimates indicated increased LTFU for rART (aRR 1.33 [1.15, 1.55], I2= 34%, p= 0.22 and 1.18 [0.74, 1.89], I2= 87%, p< 0.001), respectively when compared to nrART.
- Sensitivity analysis accounting for all rapid ART definitions provided an estimated aRR (95%CI) 1.25(95%CI , 1.06-, 1.48), with moderate heterogeneity (I2= 70%, P= .02) Regarding LTFU at 6-months
- None of included studies had serious risk of bias. (2- moderate, 1-minimal)
- None of the included studies in meta-analyses of LTFU outcomes were conducted in the US.

Viral Suppression (VS) Results

- O'Shea et al. showed that rapid ART (same day of HIV diagnosis) was associated with higher viral suppression with aHR (95%CI) 2.65 (95%CI, 1.69-4.16)
- Colisanti et al. showed lower viral suppression in rapid ART compared with non-rapid ART; however, the result was not statistically significant, aOR (95%CI) 0.80 (95%CI, 0.40-1.50)
- Given limited studies for these outcomes, meta-analysis was not performed

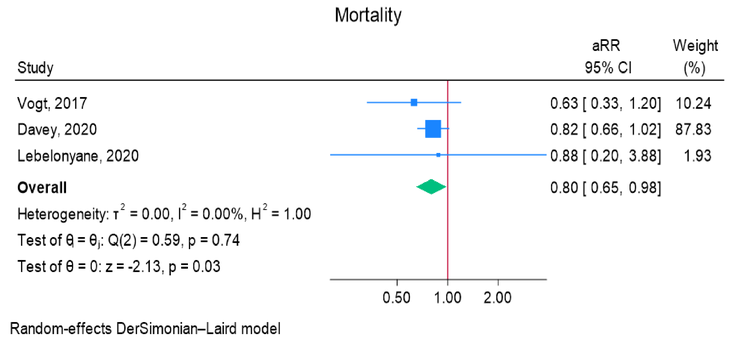
Figure 1: PRISMA Flow Diagram



Literature Review Summary

- A total of **28** studies were included. Seventeen (61%) included data from 2018 or later and 9 (32%) were conducted in the US.
- There were 6 studies reporting viral suppression at <200 copies/mL, of which 1 reported adjusted effects at 6-months and another reported adjusted effects at 12-months
- There were three studies (11%) which reported adjusted effects with LTFU at 6-months, and three studies (11%) reported adjusted effects with LTFU at 12-months

Table 2: Mortality Adjusted-Effects Mortality Analysis



Random-effects DerSimonian–Laird model

Mortality Results

- **There was a decrease in mortality among those who initiated ART within 7 days of HIV diagnosis**
- Three studies (11%) reported adjusted effects and mortality. The pooled adjusted effect for mortality across these 3 studies demonstrated a significant reduction in risk of mortality among patients that received rART compared to nrART (aRR(95%CI) 0.80(0.65, 0.98)). No heterogeneity existed (I2= 0%, p= 0.74)
- A sensitivity analysis considering all definitions of rapid ART showed the effect on mortality continued to show a significant aRR(95%CI) 0.82(95%CI, 0.69-, 0.96), with moderate heterogeneity (I2= 46%, P= .08)
- Bias assessment showed none of the included studies to be at serious risk (2 moderate, 1 low)

References: 1. World Health Organization (WHO). Guidelines 2021; 2. Johns Hopkins University. HIV Clinical Guidelines Program 2022; 3. Department of Health and Human Services (DHHS). Guidelines 2022; 4. Huhn GD, et al. Clin. Infect. Dis. 2019; 5. Coffey S, et al. AIDS. 2019; 6. Koenig SP, et al. PLoS Med. 2017; 7. Ford N, et al. Aids. 2018; 8. Moher D, et al. PLOS Medicine. 2009; 9. Stroup DF, et al. JAMA. 2000; 10. Sterne JAC, et al. BMJ. 2016.

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Abbreviations: ART, antiretroviral therapy; aRR, adjusted risk ratio; LTFU, Loss to follow-up; HIV, human immunodeficiency virus; rART, rapid antiretroviral therapy; nrART, non-rapid antiretroviral therapy; MOOSE, Meta-analysis of Observational Studies in Epidemiology; PRISMA, preferred Reporting Items for Systematic Reviews and Meta-analyses; ROBINS-I, Risk of Bias in non-randomized studies of interventions; RCT, randomized controlled trial; WHO, World Health Organization;