Early mortality after late initiation of antiretroviral therapy (ART)

TREAT Asia HIV Observational Database (TAHOD) of IeDEA Asia-Pacific

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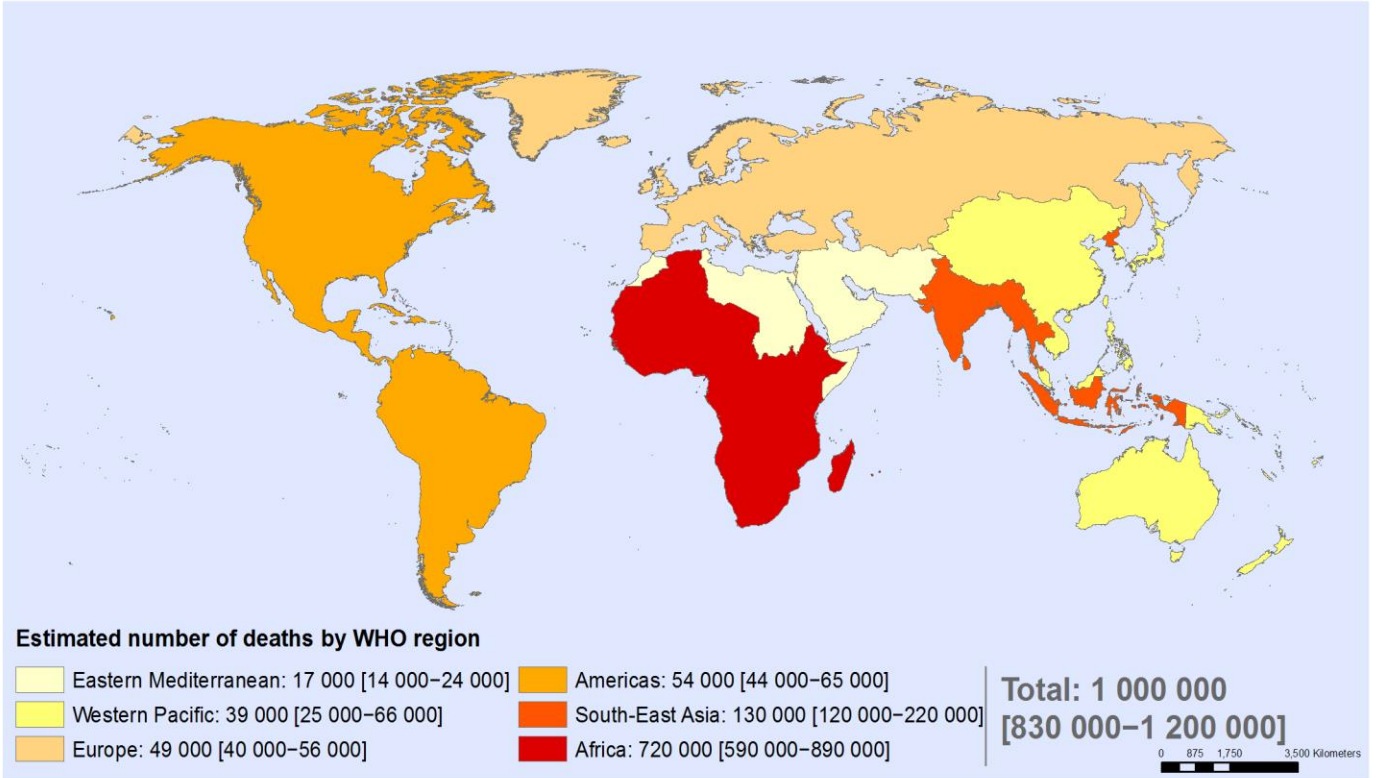
Estimated number of people dying from HIV-related causes, 2016
By WHO region



Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

World Health Organization

Background

- Late initiators of ART despite WHO “Treat All” guidelines

- Primarily in resource-limited settings
  - 20%–25% late initiators
  - 12% died 1-year post-ART initiation

- Asian region: 2nd highest early mortality rates among adult PLHA on ART

Eholie et al. *AIDS Res Ther* 2016;13: 27
Siika et al. *Clin Infect Dis* 2018; 66(suppl_2): S140-S6
IeDEA and ART Cohort Collaborations et al. *J Acquir Immune Defic Syndr* 2014; 65(1):e8-16
Gupta et al. *PLoS One* 2011; 6(12): e28691

Objectives

- To determine the proportion of adults living with HIV who initiated ART late from 2003 - 2018 in the Asian region

- To investigate risk factors associated with early mortality in PLHIV starting ART at low CD4 levels


Japan
1 site
South Korea
1 site
Taiwan
1 site
China
2 sites
Philippines
1 site
India
3 sites
Vietnam
2 sites
Thailand
4 sites
Cambodia
1 site
Malaysia
2 sites
Indonesia
2 sites
Singapore
1 site

Methods

- TAHOD patients who initiated ART between 2003 - 2018
- Late ART initiators: PLHIV who started ART with CD4 <100 cells/µL
- Early mortality: mortality occurring in the first year of ART initiation
- Causes of death: AIDS-related, Immune Reconstitution Inflammatory Syndrome (IRIS)-related, non-AIDS or unknown

Methods

- Fine and Gray's competing risk regression
- Patients in follow-up for more than one year were censored at 12 months
- Follow-up time ended at date of death, date transferred out, or were lost-to follow-up (LTFU) if these events occurred during the analysis time

Patient demographics

	CD4<100 cell/ul at ART initiation	Died within 12 months of ART initiation
	n(%)	n(%)
Total **Median follow up time**	1813 (100) 11.9 months	73 (4) 3.8 months
Age (years) Median (IQR)	35 (29-41)	34 (28-42)
Sex Male Female	 1335 (74) 478 (26)	 58 (79) 15 (21)
HIV Exposure Heterosexual MSM Injecting drug use Other/Unknown	 1208 (67) 268 (15) 186 (10) 151 (8)	 45 (62) 8 (11) 14 (19) 6 (8)

Patient demographics

	CD4<100 cell/ul at ART initiation	Died within 12 months of ART initiation
	n(%)	n(%)
Total **Median follow up time**	1813 (100) 11.9 months	73 (4) 3.8 months
CD4 cell count (cells/ul) at ART initiation Median (IQR)	34 (14-60)	22 (12-41)
Viral Load (copies/mL) at ART initiation Median (IQR)	150000 (70185-440000)	170000 (83984-430000)
World Bank country income Lower Middle Upper Middle High	 779 (43) 800 (44) 234 (13)	 32 (44) 30 (41) 11 (15)

Patient characteristics

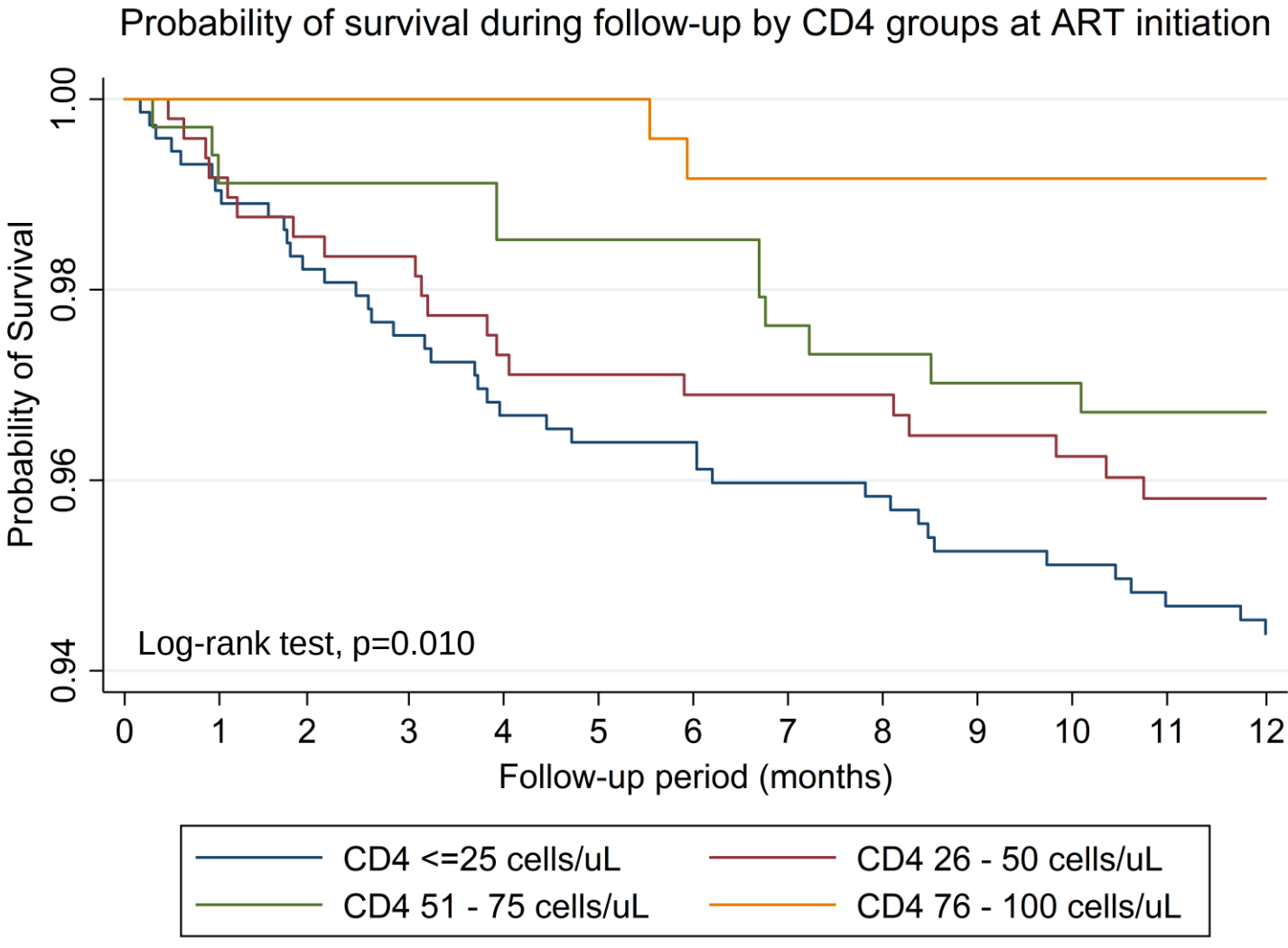
Other covariates included in the analysis:

- Hepatitis co-infections
- BMI
- Haemoglobin
- ALT elevations
- Creatinine
- Tuberculosis (TB)
- *Pneumocystis pneumonia* (PCP)
- AIDS Illness - Other
- Receipt of prophylaxis
- ART Adherence
- Number of ART interruptions

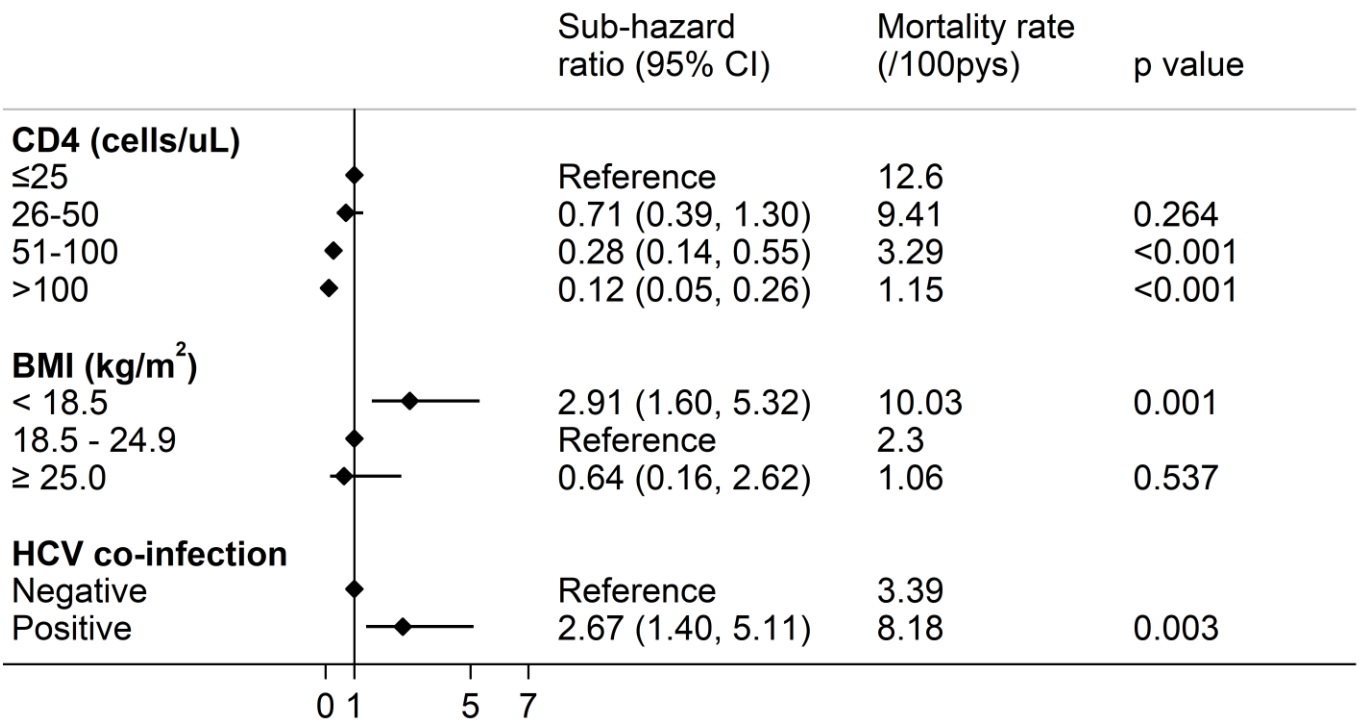
Results

	Year of ART initiation			Total
	2003 - 2007	2008-2012	2013 - 2018	
Number of patients who initiated late (%)	505 (28)	1163 (64)	145 (8)	1813 (100)
Causes of deaths	**Total number of deaths in the first year of ART**			**Total (%)**
AIDS	12	26	0	38 (52)
IRIS	3	7	0	10 (14)
Non-AIDS	3	9	1	13 (18)
Unknown	7	5	0	12 (16)
				73 (100)

Overall 1 year mortality rate: 4.27 per 100 person-years

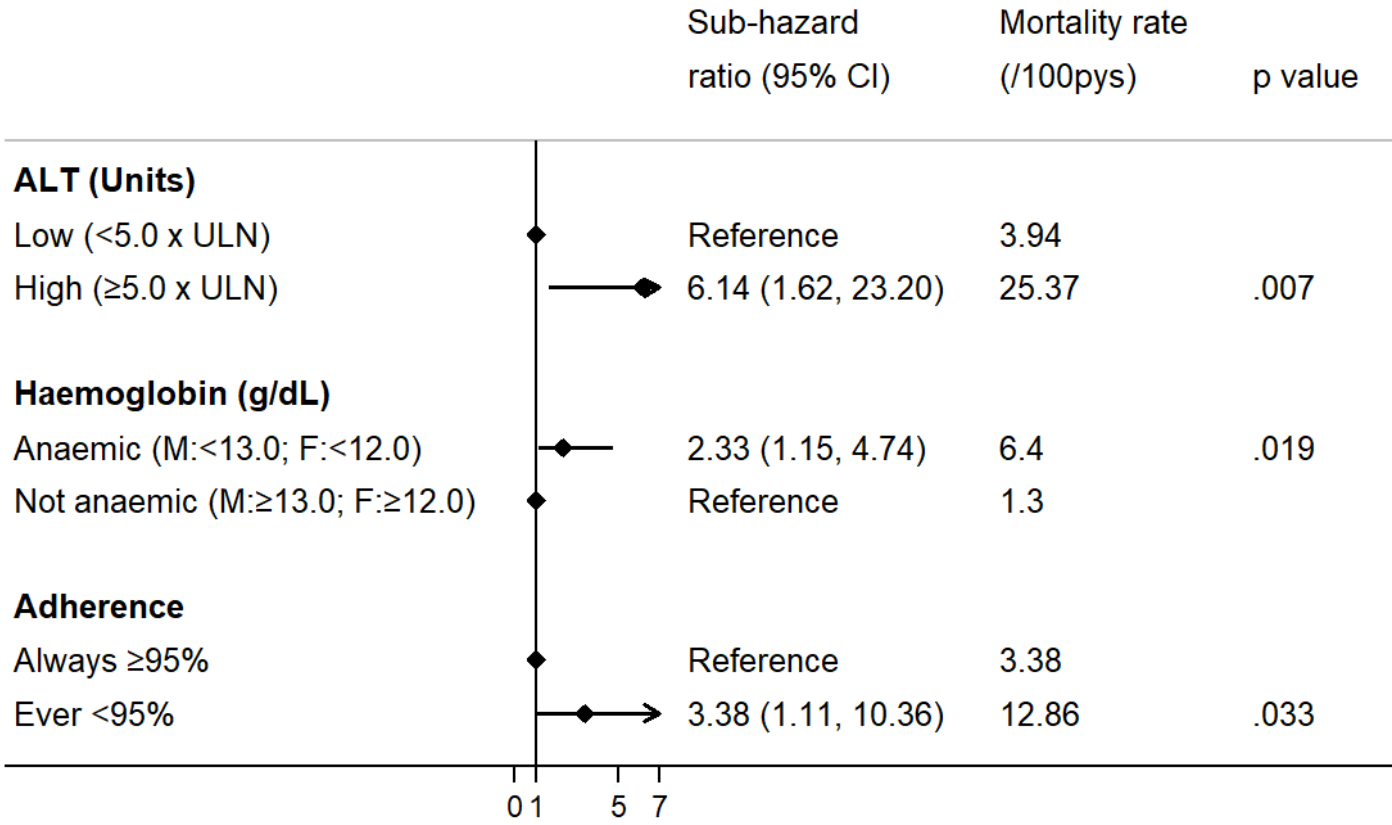

Probability of survival during follow-up by CD4 groups at ART initiation
Probability of Survival
1.00
0.98
0.96
0.94
Log-rank test, p=0.010
0
1
2
3
4
5
6
7
8
9
10
11
12
Follow-up period (months)
CD4 <=25 cells/uL
CD4 26 - 50 cells/uL
CD4 51 - 75 cells/uL
CD4 76 - 100 cells/uL

Forest plot of factors associated with early mortality in patients starting ART with CD4<100 cells/µL



Not reported/not tested categories were included in the multivariate analysis, however, were not graphically displayed.

Forest plot of factors associated with early mortality in patients starting ART with CD4<100 cells/µL



Not reported/not tested categories were included in the multivariate analysis, however, were not graphically displayed.

Summary

- 1-year mortality rate is comparable to the 1-year mortality rate of <5.0 per 100 person years found from clinical trials done in Uganda and Zimbabwe
- Main cause of death in the first year of ART was AIDS-related
- Current CD4 cell counts above 50 cells/μL in the first year of treatment significantly improved survival rates among those who initiated late

Walker et al. *Clin Infect Dis* 2012; 55(12): 1707-18

Limitations

- TAHOD does not link to death registries

- Patient selection process in TAHOD patients may be less representative of the broader clinical population

Conclusions

- Majority of early mortality are due to AIDS-related causes
- Greater effort should be applied to initiating treatment immediately after HIV diagnosis
- Improve ART adherence
- Carefully monitor BMI, HCV co-infection, liver function, and anaemic status

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