A dual analysis of loss to follow-up for perinatally HIV-infected adolescents receiving combination antiretroviral therapy in Asia

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Disclosures

- Gilead

Background

- Adolescents living with perinatally-acquired HIV infection (PHIVA) are an expanding population particularly vulnerable to being lost to follow-up (LTFU).
- PHIVA face additional complexities associated with transition from paediatric to adult HIV services, which poses significant challenges to their care continuum.
- Existing data relating to adolescent LTFU are based on various fixed-time definitions.
- A novel method for estimating scheduled clinic appointments in order to establish a consistent time point from which to assess and measure LTFU has been developed by IeDEA.[1]
  - Permits estimated individualised follow-up schedules and has scope to provide a more precise assessment of LTFU compared to fixed-time definitions.

[1]International Epidemiology Databases to Evaluate AIDS. Haas AD, *et al*. J Int AIDS Soc. 2018;21(2)e25084.

Aims

To analyse LTFU among PHIVA in the TREAT Asia Pediatric HIV Observational Database (TApHOD) using two criteria: (i) 365-day absence of data; and (ii) 90 days late following a estimated next scheduled appointment (IeDEA method) to:

1. Compare cumulative incidence of LTFU

2. Compare factors associated with LTFU

3. Describe characteristics of PHIVA who met one but not both LTFU criteria

Methods

- Study population
  - Regional data from TApHOD.
  - PHIVA (aged 10-19 years) who received combination antiretroviral therapy (cART) 2007-2016.
- LTFU definitions
  - IeDEA LTFU: more than 90 days late for an estimated next scheduled appointment
    - Next scheduled appointment calculated using the interval between a patient's last two clinic visits adjusted for the visit schedule of the clinic and year on antiretroviral therapy.
  - 365-day absence LTFU: more than a 365-day absence of data prior to the date of last data transfer from clinic sites.
- Statistical analyses
  - Descriptive analyses for characteristics of study population.
  - Kaplan-Meier survival analyses for estimating probability of LTFU using each criteria.
  - Competing-risk regression analysis for factors associated with LTFU using each criteria.

Results

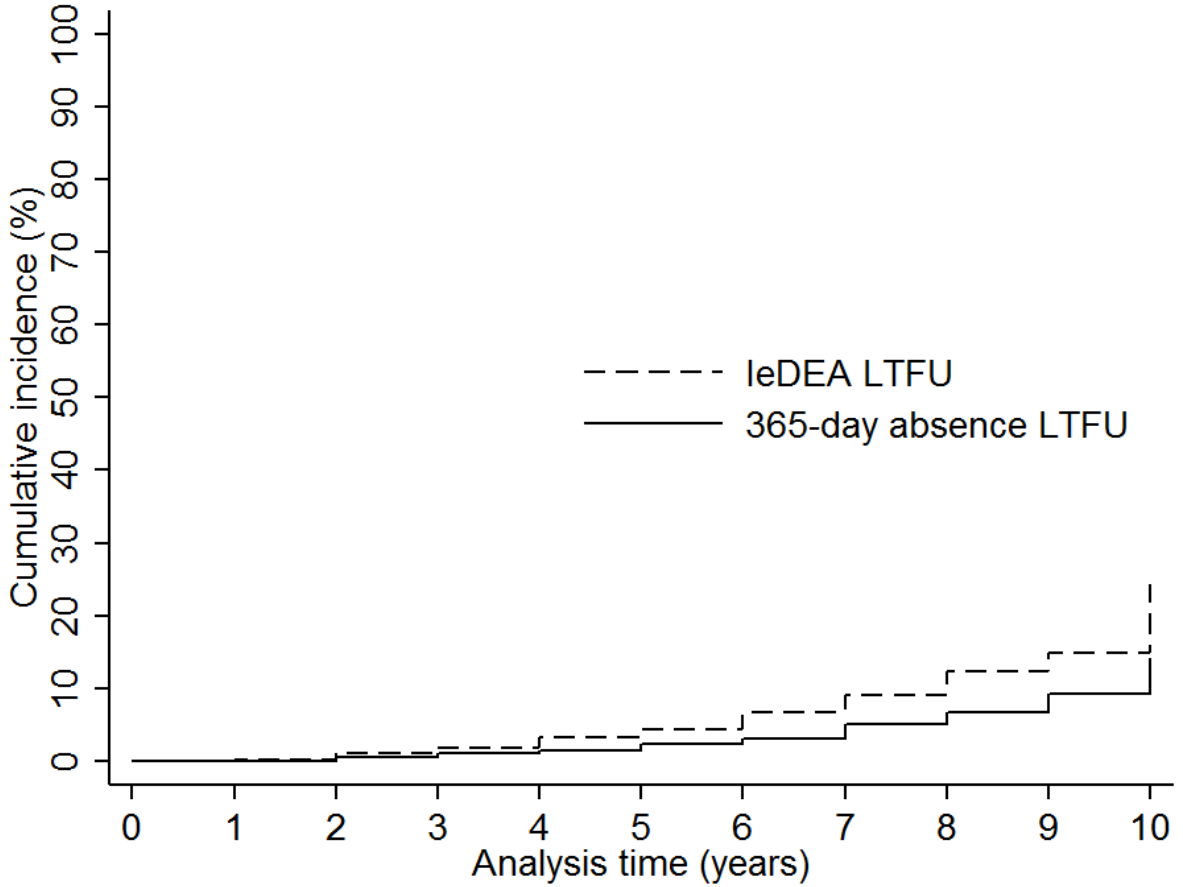
- Total 3,509 PHIVA
  - Median follow-up 5.3 [IQR 3.2, 7.8] years
  - Median age 15.7 [IQR 13.4, 18.2] years at last clinic visit
  - Male = 1,731 (49.3%)
  - Clinic setting: urban = 1,935 (55.1%); semi-urban = 1,360 (38.8%); rural = 214 (6.1%)
- Using IeDEA LTFU criteria
  - 275 (7.8%) PHIVA LTFU at median age 16.1 [IQR 13.8, 17.9] years
  - Male = 145 (52.7%)
  - Clinic setting: urban = 151 (54.9%); semi-urban = 86 (31.3%); rural = 38 (13.8%)
- Using 365-day absence LTFU criteria
  - 149 (4.3%) PHIVA LTFU at median age 15.7 [IQR 13.5, 17.5] years
  - Male = 79 (53%)
  - Clinic setting: urban = 64 (43%); semi-urban = 55 (36.9%); rural = 30 (20.1%)

Results

	Total cohort N=3,509	IeDEA LTFU cohort N=275	365-day absence LTFU cohort N=149
Last CD4 count (cells/µL)			
≥500	1,896 (54.0)	150 (54.6)	65 (43.6)
350-499	394 (11.2)	28 (10.2)	21 (14.1)
200-349	218 (6.2)	24 (8.7)	17 (11.4)
<200	246 (7.0)	22 (8.0)	14 (9.4)
Last HIV viral load (copies/mL)			
Undetectable	1,866 (53.2)	120 (43.6)	48 (32.2)
Detectable <1,000	254 (7.2)	19 (6.9)	7 (4.7)
1,000-9,999	121 (3.5)	15 (5.5)	10 (6.7)
≥10,000	252 (7.2)	29 (10.6)	18 (44.3)

Cumulative incidence of LTFU throughout adolescence for IeDEA and 365-absence LTFU criteria

	IeDEA LTFU	365-day absence LTFU
5-year	4.3%	2.3%
10-year	24.4%	14.1%



Number at risk

IeDEA LTFU	3509	3390	3096	2712	2350	1879	1466	1121	776	504
365-day absence LTFU	3509	3395	3110	2716	2363	1885	1484	1127	786	508

Associated factors with IeDEA LTFU

- Rural clinic setting
  - Rural clinic vs urban clinic — aSHR 1.9 [95%CI 1.2, 3.1]
- Younger age at cART initiation
  - 5-9 years vs <5 years — aSHR 0.4 [95%CI 0.3, 0.6]
  - ≥10 years vs <5 years — aSHR 0.3 [95%CI 0.2, 0.4]
- High HIV viral loads
  - ≥10,000 copies/mL vs undetectable — aSHR 1.9 [95%CI 1.4, 2.7]
- NOT significant on multivariate analysis
  - Age, sex, orphan status, primary caregiver, prior cART regimens, CD4 count, WHO clinical stage.

aSHR = adjusted sub-distribution hazard ratio

Associated factors with 365-day absence LTFU

- Younger age
  - 15-19 years vs 10-14 years — aSHR 0.2 [95%CI 0.1, 0.5]
- Rural clinic setting
  - Rural clinic vs urban clinic — aSHR 3.0 [95%CI 1.6, 5.5]
- Younger age at cART initiation
  - 5-9 years vs <5 years — aSHR 0.5 [95%CI 0.3, 0.8]
  - ≥10 years vs <5 years — aSHR 0.5 [95%CI 0.3, 0.8]
- High HIV viral loads
  - 1,000-9,999 copies/mL vs undetectable — aSHR 2.4 [95%CI 1.3, 4.2]
  - ≥10,000 copies/mL vs undetectable — aSHR 2.3 [95%CI 1.5, 3.8]
- NOT significant on multivariate analysis
  - Sex, orphan status, primary caregiver, CD4 count, WHO clinical stage.

aSHR = adjusted sub-distribution hazard ratio

Discrepant LTFU population

- Met IeDEA but not 365-day absence LTFU criteria (n=134)
  - 88 (65.7%) were aged 15-19 years
  - 8 (6.0%) managed in a rural clinic
  - 81 (60.5%) remained on their first cART regimen
  - 93 (69.6%) had a last HIV viral load as undetectable
  - 106 (79.1%) had a last CD4 count ≥500 cells/μL
  - Median interval between last clinic visit and estimated next scheduled appointment = 84 [IQR 78, 105] days

- Met 365-day absence but not IeDEA LTFU criteria (n=2)
  - Both on cART >10 years, with last HIV viral loads undetectable and last CD4 counts ≥500 cells/μL

Limitations

- Potential for incomplete and inconsistent data reporting.

- Misclassification of LTFU.
  - No tracing to confirm LTFU.
  - No prior tracing studies to provide estimations to account for undocumented mortality and self-transfers.

Conclusions

- Between 14% and 24% of PHIVA in our cohort are estimated to have been LTFU across adolescence.
  - IeDEA criteria provided less conservative LTFU estimates, reflecting shorter time period required to be designated as LTFU.

- Consistent risk factors across both LTFU criteria include earlier age at cART initiation, poor virologic control, and receiving care within rural clinic settings.
  - Identifies impact of treatment fatigue on retention in care, and the need for adolescent-friendly clinics particularly in the context of re-structuring HIV health services.

Conclusions

- Those in the discrepant LTFU population were mainly relatively clinically stable, older adolescents.
  - May reflect changes in practice for stable PHIVA such as less frequent clinic visits or differentiated care models.
  - Undocumented “silent transfers” and LTFU misclassifications cannot be excluded.

- Better tracking of adolescents is required to provide a more definitive understanding of LTFU and establish evidence-based models of care to optimise outcomes.

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