Updated Global Mortality Estimates for Children Aged <15 years on Antiretroviral Therapy within IeDEA

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BACKGROUND

The International epidemiology Databases to Evaluate AIDS (IeDEA) consortium's mortality data has informed models used by UNAIDS in estimating the number of children (aged <15 years) living with HIV (CLHIV) globally and annual AIDS-related deaths. Previous mortality estimates used data up to 2017. We updated all-cause mortality among CLHIV on ART and described temporal trends from 2004-2020.

METHODS

We included routinely-collected data from CLHIV on ART during 2004-2020 with recorded CD4 values at ART start, across 59 programs in Africa, the Asia-Pacific and Latin America and the Caribbean.

- We used mixed-effects Poisson regression models to estimate mortality by age, sex, CD4 at ART start, time on ART, region, and calendar period (using linear splines);
- We had separate models for:
  - African and non-African regions,
  - Younger (<5) and older (5-14 years) CLHIV.
- We allowed for distinct covariate effects by ART duration category (<1 year vs. ≥1 year).

Before model fitting, for African regions, we adjusted IeDEA routine data to account for unascertained mortality among those lost to follow-up (LTFU), using data from an IeDEA tracing study of 2013-2017 (n=221) to simulate mortality among those LTFU with a Gompertz survival model.

- In 2020, Children with HIV on ART were surviving longer.
- Our updated data shows continuing declines in mortality since 2017.
- But progress has been slower and less certain among younger children and those on ART for <1 year in Africa.

RESULTS

Among 89,660 CLHIV, we excluded 65% of those aged <5, and 40% of those aged 5-14 years due to lack of CD4 measurements.

Among 43,058 CLHIV included in our analysis (**Table 1**), we observed 3,024 deaths over 171,209 person-years, with a crude recorded mortality rate of 1.8 (95% Confidence Interval [CI]: 1.7-1.8) deaths per 100 person-years.

Mortality declined in more recent calendar years and was highest in those with lower CD4, shorter ART duration, and age <1 year (**Figure**). Mortality rates were similar between sexes.

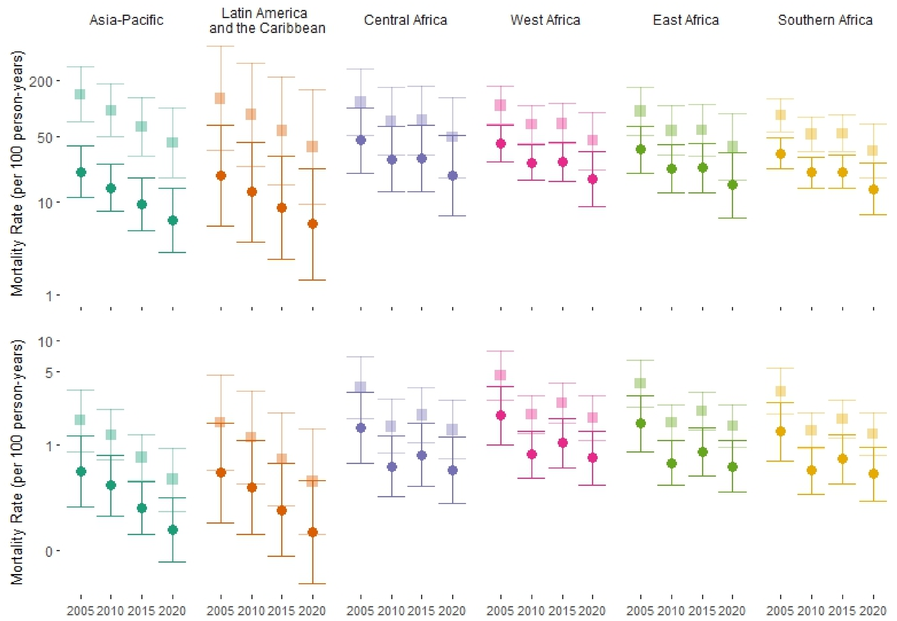
Relative to 2017, mortality rates in 2020 declined for older CLHIV on ART of >1 year; for other age-groups and ART durations, mortality declines varied by region (**Table 2**).

Table 1: Characteristics of CLHIV on ART in 2004-2020 from IeDEA data

		Asia-Pacific N=4,239 (%)	Central Africa N=1,198 (%)	Latin America N=984 (%)	East Africa N=7,311 (%)	Southern Africa N=25,374 (%)	West Africa N=3,952 (%)	Total N=43,058 (%)
Sex	Female	2,027 (47.8)	615 (51.3)	510 (51.8)	3,753 (51.3)	13,318 (52.5)	1,874 (47.4)	22,097 (51.3)
Age at ART start, years	0-4	1,978 (46.7)	340 (28.4)	349 (35.5)	2,020 (27.6)	8,974 (35.4)	1,689 (42.7)	15,350 (35.6)
	5-14	2,261 (53.3)	858 (71.6)	635 (64.5)	5,291 (72.4)	16,400 (64.6)	2,263 (57.3)	27,708 (64.4)
Year of ART Start	2004-2009	2,121 (50.0)	590 (49.2)	534 (54.3)	3,359 (45.9)	10,633 (41.9)	1,490 (37.7)	18,727 (43.5)
	2010-2014	1,379 (32.5)	482 (40.2)	310 (31.5)	3,191 (43.6)	8,947 (35.3)	1,754 (44.4)	16,063 (37.3)
	2015-2020	739 (17.4)	126 (10.5)	140 (14.2)	761 (10.4)	5,794 (22.8)	708 (17.9)	8,268 (19.2)

Figure: Estimated Mortality Rates (and 95% CIs) among male CLHIV on ART over time

Top panel: CLHIV aged 0-1 years, Duration on ART <6 months, CD4% at ART start 0-5% (lighter) and 15-20% (darker shades),
Bottom panel: CLHIV aged 10-15 years, Duration on ART >1 year, CD4 at ART start 0-200 (lighter) and 500-750 (darker shades)



Mortality rates presented on log scale.
Mortality rates shown for selected calendar years.
Categories chosen to demonstrate comparable mortality in higher and lower subgroups

Table 2: Mortality Rate Ratios (95% CI): Mortality rates in 2020 relative to 2017

Duration on ART	Age group	Non-African Regions	African Regions
Within first year on ART	< 5 years	0.79 (0.68-0.92)	0.78 (0.52-1.17)
	5-14 years	0.67 (0.49-0.92)	1.15 (0.81-1.62)
After 1 year on ART	< 5 years	0.73 (0.51-1.04)	1.01 (0.61-1.66)
	5-14 years	0.75 (0.61-0.94)	0.81 (0.68-0.98)

CONCLUSIONS

Since 2017, on-ART mortality among CLHIV continued to decline, particularly for older CLHIV on ART for >1 year and in non-African regions. Declines for younger CLHIV and those on ART for <1 year in African regions were smaller and less certain. Our analysis is limited by declining CD4 measurement. Our updated IeDEA mortality estimates support UNAIDS's continuing efforts to model global pediatric HIV outcomes.

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