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Disclosure of HIV status and associated clinical outcomes of children and adolescents living with HIV in Asia

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Abstract

Disclosure of HIV status is an important part of pediatric care. We studied disclosure and clinical outcomes in a multi-country Asian cohort of children and adolescents with HIV. Those 6–19 years of age who initiated combination antiretroviral therapy (cART) between 2008 and 2018, and who had at least one follow-up clinic visit were included. Data up to December 2019 were analyzed. Cox and competing risk regression analyses were used to assess the effect of disclosure on disease progression (WHO clinical stage 3 or 4), loss to follow-up (LTFU; >12 months), and death. Of 1913 children and adolescents (48% female; median [IQR] age 11.5 [9.2–14.7] years at last clinic visit), 795 (42%) were disclosed to about their HIV status at a median age of 12.9 years (IQR: 11.8–14.1). During follow-up, 207 (11%) experienced disease progression, 75 (3.9%) were LTFU, and 59 (3.1%) died. There were lower hazards of disease progression (adjusted hazard ratio [aHR] 0.43 [0.28–0.66]) and death (aHR 0.36 [0.17–0.79]) for those disclosed to compared with those who were not. Disclosure and its appropriate implementation should be promoted in pediatric HIV clinics in resource-limited settings.

Keywords

HIV; disclosure; children; adolescents; Asia

INTRODUCTION

UNAIDS reported 1.7 million children aged 0–14 years were living with HIV in 2021 (UNAIDS, 2022). Increased access to antiretroviral therapy (ART) have resulted in substantial reductions in AIDS-related morbidity and mortality among children and adolescents (Hayfron-Benjamin et al., 2018). For children with perinatally acquired HIV, disclosure to them of their HIV diagnosis is a major challenge for families and health care practitioners. Previous studies have shown that children and youth living with HIV can benefit both physically and psychologically from being told about their HIV status, and that delayed disclosure or non-disclosure can result in sub-optimal adherence and consequently risks treatment failure (Vreeman et al., 2010; Montalto et al., 2017; Bulali et al., 2018; Ramos et al., 2018). Some studies have reported negative health outcomes of disclosure, such as emotional difficulties and internalized stigma, while others found no physical and mental health differences between those who were aware of their diagnosis and those who were not (Odiachi, 2017; Wiener et al., 2007).

In 2011, the World Health Organization (WHO) released guidelines on HIV disclosure in children, recommending disclosure when a child is 6–12 years (Krauss et al., 2011). The American Academy of Pediatrics (AAP) have also recommended that disclosure takes place prior to adolescence (Committee on Pediatric AIDS, 1999). However, despite these

recommendations and the evidence on the importance of disclosure, many children living with HIV are unaware of their HIV status. In a systematic review on disclosure in resource-limited settings, the proportion of disclosed children in studies that reported prevalence data ranged widely from 0 to 69% (Vreeman et al., 2013). Younger age, perceived inability to understand the meaning of HIV infection, concerns over psychological harm, lack of social support, and lack of skills around how to disclose were the most common reasons mentioned by parents or caregivers for not disclosing to children in different studies (Arrivé et al., 2012; Vreeman et al., 2013; Odiachi, 2017; Shallo and Tassew, 2020).

Previously reported prevalence of HIV disclosure to children was 70% in Thailand (Sirikum et al., 2014) and 41% in India (Bhattacharya et al., 2011). In Thailand, caregivers were fearful of disclosure because of the perceived risks of stigma, discrimination and bullying (Siripong, A. et al., 2007) and possible emotional and behavioral consequences (Boon-yasidhi et al., 2016). Efforts to preserve family harmony and avoid stigma may have increased resistance to HIV disclosure (Jantarapakde et al., 2019).

The prevalence of disclosure and its impact on clinical response to ART are not well studied in Asia. In this study, we aimed to (1) describe the frequency of disclosure in children and adolescents living with HIV in an Asian regional cohort, and (2) assess the effect of disclosed HIV status on ART clinical outcomes, including disease progression, loss to follow-up (LTFU), and death.

METHODS

The TREAT Asia Pediatric HIV Observational Database (TApHOD) of the International epidemiology Databases to Evaluate AIDS (IeDEA) Asia-Pacific is a prospective cohort study conducted in 17 pediatric clinics across six countries: Cambodia (n=1), India (n=2), Indonesia (n=2), Malaysia (n=4), Thailand (n=5), and Vietnam (n=3). These sites are predominantly public or university-based pediatric HIV referral clinics, located in urban or semi-rural areas. For this study, we included patients 6–19 years of age who initiated combination ART (cART; defined as ≥3 antiretrovirals) between January 2008 through December 2018. Children were required to have initiated cART at least 12 months before the site-specific database closure date and have at least one clinic visit during follow-up between ages 6 to 19. We used all available follow-up data up to December 2019.

Ethics review

Ethics approval was obtained through the human research ethics committees at all participating sites, the data management and analysis center at the Kirby Institute (UNSW Sydney), and the coordinating center at TREAT Asia/amfAR (The Foundation for AIDS Research). Consent by parents or legal guardians and assent of the children and adolescents under care were not routinely obtained unless required by the local ethics committee (i.e., in some sites in India, Malaysia, and Thailand).

Definitions

Disclosure was defined as making the child or adolescent aware that they are living with HIV. Disease progression was defined as the first occurrence of a WHO clinical stage 3 or

4 during follow-up. Second-line ART was defined as the second triple-drug regimen with a change in drug class [e.g., nonnucleoside reverse transcriptase inhibitor (NNRTI) to protease inhibitor (PI)], excluding those exposed to mono/dual nucleoside reverse transcriptase inhibitor therapy and known to have been switched without failure of first-line therapy. Patients were considered LTFU when there was no contact with the clinic for >12 months before the site database closure date, with their follow-up period ending one year after their last clinic contact before their 20th birthday.

For laboratory and clinical measurements at cART initiation, we used the single closest value reported during a window period of six months prior to and one week after start. We extended the window period up to three months after cART initiation for weight and height measurements. Weight and height measurements were converted to age- and sex-adjusted z-scores. For characteristics at disclosure and at last clinic visit, the closest value during a window period of six months prior to each time point was used. Weight-for-age z-scores (WAZ) and height-for-age z-scores (HAZ) were calculated using WHO 1977 Standards and WHO 2007 Child Growth Standards, respectively (World Health Organization, 2007, 2019).

Data management and statistical analysis

Detailed methods for cohort data management have previously been reported (Kariminia et al., 2011). Briefly, routinely collected clinical and program data were anonymized and then transferred to the Kirby Institute (UNSW, Sydney, Australia) for management and analysis on a biannual basis. Data were harmonized according to a common data exchange standard. Descriptive analyses were used to report demographic, immunological, and clinical characteristics of the study population at cART initiation by disclosure status. Incidence rates of disease progression, LTFU, and mortality were determined by dividing the number of events by person-years of observation. The beginning of follow-up (baseline) was from the date of cART initiation, or on the date of their 6th birthday for those who initiated cART before age 6. The end point was defined as the date of last contact before the site-specific database closure, first occurrence of WHO clinical stage 3 or 4, turning 19.9 years of age, LTFU, or death.

We used Cox regression analysis to assess predictors of first occurrence of WHO clinical stage 3 or 4 and mortality and competing risk regression based on Fine and Gray's proportional sub-hazards model to identify predictors of LTFU (death as competing event) (Fine & Gray, 1999). Sex and calendar year at cART initiation were included as fixed variables. Age, CD4 cell count, WAZ, AIDS diagnosis, second-line cART, and disclosure status were included as time-updated variables. AIDS was only considered as a covariate for analysis when the outcome was LTFU or mortality. HAZ was not included as a co-variate because the proportion of missing data made it an unreliable measurement. For CD4 and WAZ, values were carried forward for one year if no subsequent measurements were recorded. We did not use multiple imputation to replace other missing data due to the relatively small numbers of covariates available. In the regression analyses, missing data were included as a separate category. We considered clinic as a random effect in the model. Covariates with a p-value of <0.20 in univariate analysis were included in a multivariate model. We selected the final model using a stepwise method and retained covariates with

p-values of <0.05. The adjusted hazard ratios (aHR) and adjusted subdistribution hazard ratios (asHR) were reported with their 95% confidence intervals (95% CI). We tested the proportional hazard assumption using the estat phtest in Stata and no violation was observed. Sensitivity analyses were conducted by excluding patients without data on CD4 or WAZ. Data management and statistical analyses were performed using Stata version 14.2 (StataCorp LP, College Station, TX, US).

RESULTS

As of December 2018, there were 7213 children and adolescents of all ages who had ever received care within the cohort. Of these, 1913 from 15 clinics met the inclusion criteria and were included in the analysis (48% female; median [interquartile range {IQR}] age, 11.5 [9.2–14.7] years at last clinic visit). These clinics were located in five countries: Vietnam (n=1156, 60%; 3 sites), Thailand (n=400, 21%; 5 sites), Indonesia (n=180, 9.4%; 2 sites), Malaysia (n=126, 6.6%; 4 sites), and India (n=51, 2.7%; 1 site). Seventy-nine percent of these sites were located in an urban setting. The median age at cART initiation was 5.8 years (IQR: 3.0–9.2); 52% initiated treatment before age 6 (Table 1). Of children and adolescents with known status, 74% were under the care of one or both parents. At cART initiation, for those with available data, the median CD4 count was 252 cells/mm^3 (IQR: 50–621); 45% had CD4 <200 cells/mm^3. HIV viral load was available in 411 (21%) children, who had a median $\log_{10}$ viral load of 5.2 copies/mL (IQR: 4.7–5.8). Thirty-three percent were severely underweight (WAZ <−3) and 26% were severely stunted (HAZ <−3) at cART initiation. Thirty-nine percent had experienced AIDS.

Of 1913 children and adolescents in the analysis, 795 (42%) had been informed of their HIV status. The proportion of children and adolescents who had been disclosed to was 35% in lower middle-income countries (India, Indonesia, Vietnam) and 59% in upper middle-income countries (Malaysia, Thailand). The median age at disclosure was 12.9 years (IQR: 11.8–14.1). At cART start, compared with children who remained unaware of their HIV status, those who were disclosed to were older (median age: 8.8 vs. 3.9 years), had a higher proportion with CD4 <200 cells/mm^3 (52% vs. 40%), and had a lower proportion who were under the care of biological parents (66% vs. 78%) (Table 1). At disclosure, 6.8% of children and adolescents had previously experienced WHO clinical stage 3 and 4 compared with 3.6% at last visit for those who remained unaware of their HIV status (Table 2). At last clinic visit, the median (IQR) age was 15.8 (IQR: 13.2–16.9) years for those who were disclosed to and 10.3 (IQR: 8.5–11.8) for those who were not. Of 815 adolescents aged >12 years at the last visit, 688 (84%) were reported to have been disclosed to that they were living with HIV (Figure 1).

There were 207 (11%) patients who experienced disease progression to WHO clinical stage 3 or 4 over a median follow-up period of 4.6 years (IQR: 2.4–6.7). Of these, 16% had pulmonary tuberculosis, 12% had severe recurrent bacterial pneumonia, and 6% had persistent oral candidiasis. Over a median follow-up period of 4.7 years (IQR: 2.3–4.6), 75 (3.9%) were LTFU and 59 (3.1%) died. The median age at death was 9.4 years (IQR: 7.3–12.7). Overall, compared to those who were not disclosed to, those who were disclosed to had a similar proportion of LTFU (3.9% vs. 3.9%), but lower proportion of death (0.9%

vs. 4.7%). At five years of follow-up, the probability of being retained in care was higher for those who were disclosed to (98% vs. 89%, Log rank p <0.001) (Figure 2).

Predictors associated with disease progression, LTFU, and death

In the survival analysis, disclosure was protective against disease progression (aHR 0.43, 95% CI: 0.28–0.66) (Table 3). The hazard was lowest among children with CD4 ≥500 cells/mm^3 (aHR 0.11, 95% CI: 0.06–0.18 vs. those with <200 cells/mm^3) and among those with WAZ ≥−2 (aHR 0.27, 95% CI: 0.21–0.35 vs. WAZ <−3). The hazard of being LTFU was lower for those with higher CD4 during follow-up (lowest asHR for ≥500 cells/mm^3 0.30, 95% CI: 0.18–0.49 vs. those with less than 200 cells/mm^3). LTFU was not significantly associated with disclosure (asHR 0.61, 95% CI: 0.28–1.34). With death as a competing event, the hazard of LTFU was significantly increased among those aged 15 to 19 (asHR 2.48, 95% CI: 1.03–5.94 vs. those less than 10 years old) and later start of cART (2013 to 2018) (asHR 4.28, 95% CI: 2.66–6.90 vs. started earlier [2008 to 2009]) (Table 3). The hazard of death was lower for those who were disclosed to (aHR 0.36, 95% CI: 0.17–0.79) (Table 3). The hazard of death was also lowest among patients with CD4 count ≥500 cells/mm^3 (lowest aHR 0.01, 95% CI: 0.01–0.04 vs. CD4 count <200 cells/mm^3), and with WAZ ≥−3 to <−2 (aHR 0.20, 95% CI: 0.11–0.37 vs. WAZ <−3). The risk of death was highest for those who experienced an AIDS diagnosis during follow-up (aHR 2.26, 95% CI: 1.17–4.37).

In the complete case analyses for death and lost to follow-up, we excluded 122 (6.4%) patients without data on CD4 or WAZ. These analyses changed the aHR for different covariates only digitally. In the complete case analysis of disease progression in which we excluded 151 (7.9%) patients without data on CD4 or WAZ, the aHR for the covariate disclosure increased from 0.43 (95% CI: 0.28–0.66) to 0.57 (95% CI: 0.41–1.07).

DISCUSSION

In this study of children and adolescents receiving care at pediatric HIV clinics in Asia, 42% knew that they were living with HIV at a median age of disclosure of 12.9 years with the earliest age at 8.0 years. The risk of disease progression and death was observed to be lower in children and adolescents who had been disclosed to. The prevalence of disclosure in our cohort was consistent with those of studies in India (Bhattacharya et al., 2011), Ethiopia (Abegaz et al., 2019), and South Africa (Madiba, 2012), but it was low compared with the 70% reported in a study in Thailand, which included a larger number of older children (median age of 14.8 years) (Sirikum et al., 2014). The reported proportion of children who have been told about their HIV status was within the wide range reported in a systematic review participated by low- and middle-income countries in Africa and Asia (0% to 69% among children with mean age 8.1 to 13.5) (Vreeman et al., 2013). Similarly, a review of studies in North America and Europe (Pinzon-Iregui et al., 2013) indicated that the proportion of children and adolescents who had knowledge of their HIV status varied widely from 18% to 75%. HIV disclosure may be more challenging in some contexts due to the stigma against people living with HIV and local traditions and norms that discourage discussing sexual health issues. For example, in a global investigation of perceptions of

HIV-related stigma among individuals living with HIV (Nachega et al., 2012), the proportion of respondents who expressed strong concerns about others knowing their HIV status was highest in the Asia-Pacific (43%) and lowest in Africa (16%).

In our study, 16% of adolescents older than 12 reported being unaware of their HIV-positive status. This may be an overestimate because as observed in a study conducted in the United Kingdom (Dorrell & Katz, 2013), adolescents living with HIV may remain silent about their status due to the stigma attached to the infection. In the majority of studies included in a review addressing disclosure among children and adolescents, parents and health workers advised that discussion regarding HIV should be started at age 10 and completed by the mid-teens (Sahay, 2013). Delayed or avoidance of HIV disclosure at a time of increased experimentation with sexual activity and substance use may restrict the use of appropriate measures to prevent onward HIV transmission.

Disclosed children and adolescents in our cohort were less likely to die during the follow-up period than non-disclosed children. A study in Romania (Ferris et al., 2007) among children and adolescents aged 5–17 years and in Kenya (Ngeno et al., 2019) among adolescents aged 10–14 years, also reported that those who were aware of their HIV status had less than half the risk of death compared with those who remained unaware. The authors attributed the survival benefit to improved treatment adherence, although previous studies assessing the association between disclosure and adherence reported mixed results (Arage et al., 2014; Cluver et al., 2015).

Children and adolescents in our study who were disclosed to also appeared less likely to experience subsequent clinical disease progression over the follow-up period. Similarly, the Romanian study (Ferris et al., 2007) described that HIV disclosure was associated with delayed disease progression, characterized by an endpoint of CD4 decline. However, another Kenyan study (Vreeman et al., 2014) did not find an association between disclosure status and clinical indicators like CD4 count and WHO disease stage. Although we did not find an association between HIV disclosure and LTFU, a multicenter study conducted in West Africa (Vreeman et al., 2013) showed that HIV disclosure was associated with better retention in care among younger adolescents (median age 10.4 years). However, as data relating to LTFU are complicated by the different definitions of LTFU used, direct comparisons may be less reliable.

There are a number of limitations to this study. The main challenge was the observational nature of the study and the risk of incomplete and inconsistent data reporting, including with regards to variability in diagnosing and reporting WHO clinical staging. As disclosure reporting was passive, it may have been under or overreported, depending on the interpretation of the definition of disclosure by local clinical staff. There also was potential misclassification of death as LTFU because of the risk of unascertained mortality. In addition, survival bias may have been present in the analysis because we excluded those who died before age six. Although we adjusted our model for a large number of potential confounding variables, our study lacks information on factors such as psychological functioning (e.g., childhood trauma, social support, stressful life events) and treatment adherence prior to or during follow-up. This may have affected our outcomes

and our observed associations may be subject to residual confounding. Research gaps not addressed through our study include examining whether disease progression triggers or is a consequence of disclosure, and the extent to which delays in disclosure negatively impact treatment adherence and retention in care.

CONCLUSIONS

In our Asia regional cohort, most of the children and adolescents with HIV were disclosed to about their HIV status as older adolescents. They experienced reduced mortality and decreased risk of experiencing WHO clinical stage 3 and 4 after disclosure compared to those who had not been disclosed to. The importance of disclosure and global recommendations for how and when this can be done need to be emphasized in local clinical practice guidelines in order to encourage pediatric HIV providers to work with caregivers to start this process at younger ages. Our findings support the need to review reasons for delayed disclosure, and to develop interventions to ensure that adolescents are informed about their HIV status as part of long-term HIV care management in Asia.

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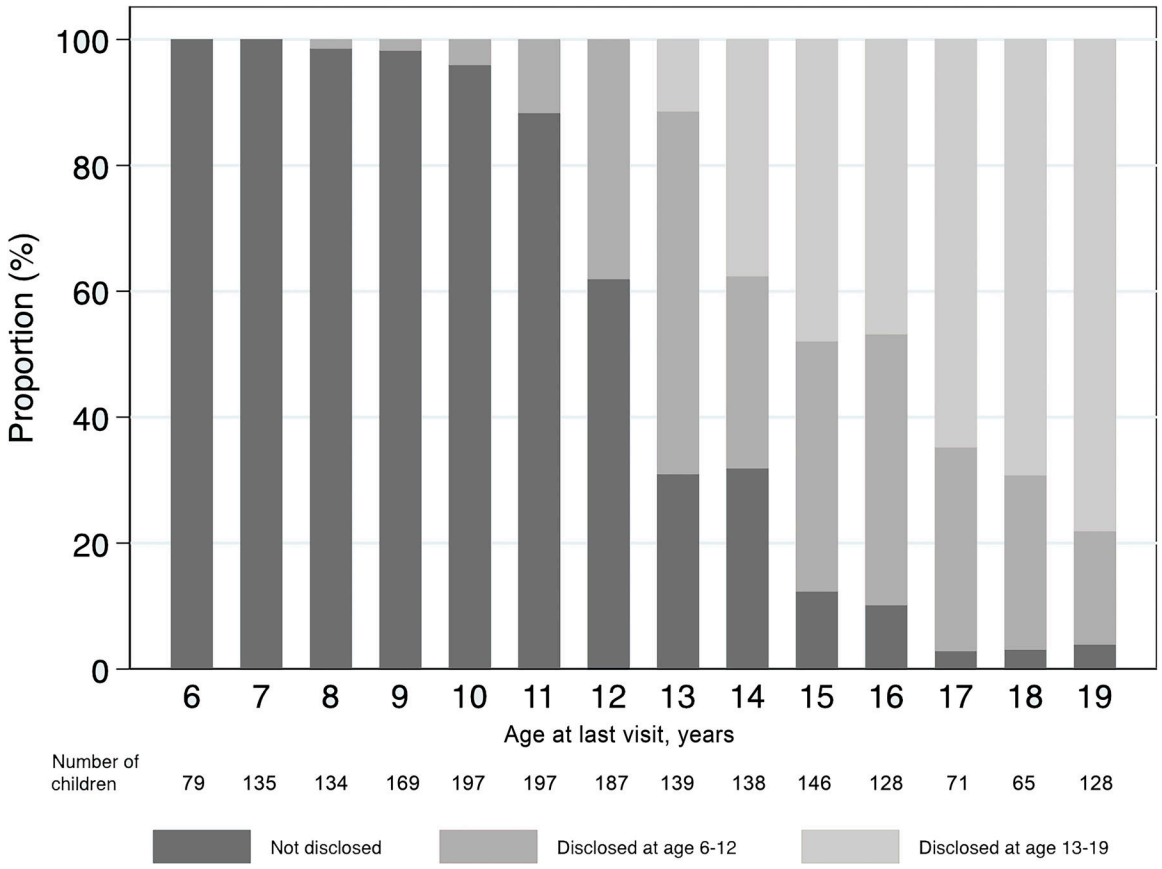

Figure 1.

HIV disclosure status at the last clinic visit in children and adolescents 6–19 years of age after cART initiation in the IeDEA Asia-Pacific cohort (n = 1913).

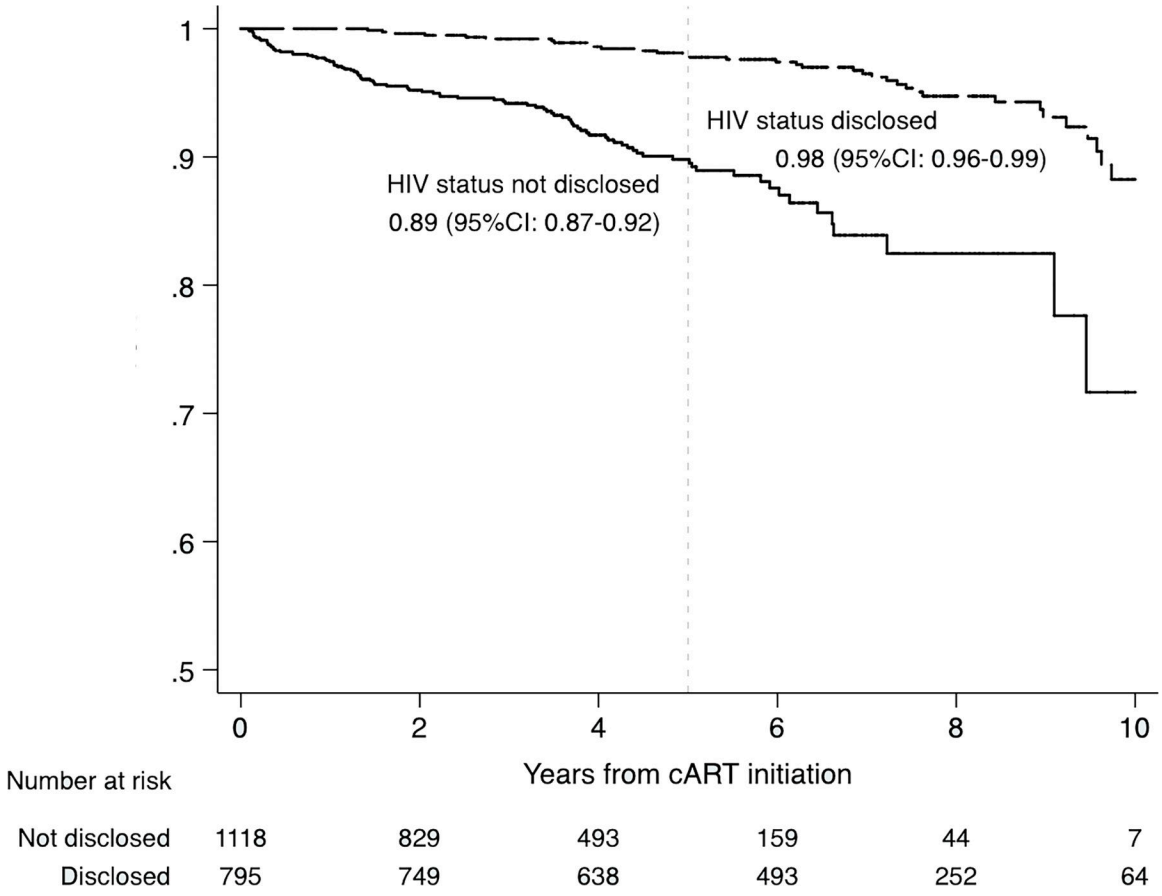

Figure 2.

Probability of retention in HIV care by disclosure status in children and adolescents 6–19 years of age after cART initiation in the IeDEA Asia-Pacific cohort (n = 1913).

Table 1.

Characteristics of children and adolescents at cART initiation by subsequent HIV disclosure status in the IeDEA Asia-Pacific cohort (n=1913)

	All (N=1913)	HIV disclosure between age 6–12 y (n=406)	HIV disclosure between age 13–19 y (n=389)	Not disclosed to (n=1118)
Female sex	913 (48)	224 (55)	180 (46)	509 (46)
Age (years)				
≤5	986 (52)	144 (35)	55 (14)	787 (70)
5–9	541 (28)	169 (42)	114 (29)	258 (23)
10–14	322 (17)	90 (22)	159 (41)	73 (6.5)
≥15	64 (3.4)	3 (0.7)	61 (16)	0 (0.0)
Median (IQR)	5.8 (3.0–9.2)	7.6 (4.7–9.7)	10.9 (7.5–13.9)	3.9 (1.7–6.4)
Facility setting				
Urban	1512 (79)	338 (83)	281 (72)	893 (80)
Mostly urban	219 (12)	49 (12)	77 (20)	93 (8.3)
Mostly rural	182 (9.5)	19 (4.7)	31 (8.0)	132 (12)
Facility level				
Healthcare center	523 (27)	90 (22)	114 (29)	319 (29)
University	1390 (73)	316 (78)	275 (71)	799 (71)
Primary care giver				
Available data, n (%)	1497 (78)	286 (70)	288 (74)	923 (83)
One/both parents	1101 (74)	194 (68)	186 (65)	721 (78)
Family/non-family members Grand parents	334 (22)	85 (30)	84 (29)	165 (18)
Foster care	62 (4.1)	7 (2.4)	18 (6.3)	37 (4.0)
cART before age 6	996 (52)	144 (35)	56 (14)	796 (71)
cART initiation year				
2008–2009	541 (28)	139 (34)	125 (32)	277 (25)
2010–2012	769 (40)	163 (40)	144 (37)	462 (41)
2013–2018	603 (32)	104 (26)	120 (31)	379 (34)
Type of therapy				
cART-NNRTI	1735 (91)	381 (94)	353 (91)	1001 (90)
cART-PI	129 (6.7)	20 (4.9)	24 (6.2)	85 (7.6)
cART-II	15 (0.8)	2 (0.5)	12 (3.1)	1 (0.1)
cART-other	34 (1.8)	3 (0.7)	-	31 (2.8)
Weight-for-age z-score				
Available data, n (%)	1669 (87)	339 (83)	321 (83)	1009 (90)
<−3	556 (33)	97 (29)	100 (31)	359 (36)
−3 ≤ to <−2	317 (19)	66 (19)	60 (19)	191 (19)
≥−2	796 (48)	176 (52)	161 (50)	459 (45)
Median (IQR)	−2.1 (−3.5, −1.0)	−1.9 (−3.2, −1.0)	−2.0 (−3.5, −1.0)	−2.2 (−3.7, −1.0)

	All (N=1913)	HIV disclosure between age 6–12 y (n=406)	HIV disclosure between age 13–19 y (n=389)	Not disclosed to (n=1118)
Height-for-age z-score				
Available data, n (%)	1563 (82)	327 (81)	318 (82)	918 (82)
<−3	406 (26)	73 (22)	58 (18)	275 (30)
−3 ≤ to <−2	419 (27)	90 (28)	96 (30)	233 (25)
≥−2	738 (47)	164 (50)	164 (52)	410 (45)
Median (IQR)	−2.1 (−3.1, −1.1)	−2.0 (−2.8, −1.1)	−2.0 (−2.8, −1.0)	−2.2 (−3.2, −1.2)
WHO clinical stage				
Stages 1 and 2	1168 (61)	263 (65)	248 (64)	657 (59)
Stages 3 and 4	745 (39)	143 (35)	141 (36)	461 (41)
CD4 count (cells/mm^3)				
Available data, n (%)	1598 (84)	334 (82)	324 (83)	940 (84)
<200	721 (45)	165 (49)	180 (56)	376 (40)
200–499	381 (24)	103 (31)	91 (28)	187 (20)
≥500	496 (31)	66 (20)	53 (16)	377 (40)
Median (IQR)	252 (50–621)	204 (43–417)	149 (23–365)	336 (69–812)
CD4 percentage				
Available data, n (%)	1489 (78)	300 (74)	310 (80)	879 (79)
<10	697 (47)	150 (50)	174 (56)	373 (42)
10–24	603 (40)	132 (44)	113 (36)	358 (41)
≥25	189 (13)	18 (6.0)	23 (7.4)	148 (17)
Median (IQR)	11.0 (3.0–19.1)	9.9 (2.6–17.1)	8.4 (2.0–15.0)	12.8 (3.7–21.4)
HIV viral load (copies/mL)				
Available data, n (%)	411 (21)	97 (24)	112 (29)	202 (18)
Median $\log_{10}$ (IQR)	5.2 (4.7–5.8)	5.1 (4.6–5.6)	5.0 (4.5–5.4)	5.5 (5.0–6.1)
WHO stages 3 and 4	207 (11)	57 (14)	55 (14%)	95 (8%)

IQR: interquartile range; cART: combination antiretroviral therapy; NNRTI: non-nucleoside reverse transcriptase inhibitor; PI: protease inhibitor; INSTI: integrase strand transfer inhibitor

Table 2.

Characteristics at disclosure or at last clinical contact among children and adolescents living with HIV in the IeDEA Asia-Pacific cohort

	Disclosed to (n=795)	Not disclosed to (n=1118)	P value
Age years, Median (IQR)	12.9 (11.8–14.1)	10.3 (8.5–11.8)	<0.001
6–9	73 (9.2)	512 (46)	
10–14	606 (76)	566 (51)	
15–19	116 (15)	40 (3.6)	
CD4 count (cells/mm^3)			
Overall, median	579 (348–850)	726 (424–1045)	<0.001
Available data	502 (63)	393 (35)	
6–9 years, median	649 (287–965)	749 (308–1102)	
Available data	52 (71)	197 (38)	
10–14 years, median	596 (363–868)	725 (497–990)	
Available data	382 (68)	181 (32)	
15–19 years, median	491 (264 −651)	576 (342–881)	
Available data	68 (59)	15 (38)	
HIV viral load (copies/mL)			
Overall median	1.6 (1.3–3.0)	1.3 (1.2–1.6)	<0.001
Available data	360 (45)	412 (37)	
6–9 years, median	1.7 (1.6–3.0)	1.3 (1.3–1.6)	
Available data	31 (42)	179 (35)	
10–14 years, median	1.5 (1.3–2.6)	1.3 (1.3–1.6)	
Available data	281 (46)	221 (39)	
15–19 years, median	3.4 (1.4–4.7)	1.5 (1.3–1.6)	
Available data	48 (41)	12 (30)	
WHO clinical stages 3 and 4			
Overall	54 (6.8)	40 (3.6)	0.001
6–9 years	7 (9.6)	27 (5.3)	
10–14 years	39 (6.4)	12 (2.1)	
15–19 years	8 (6.9)	1 (2.5)	

Note: Wilcoxon test was used to compare continuous data and Pearson chi-square or Fisher's exact test, as appropriate, to compare categorical data.
IQR: interquartile range

Table 3.

Predictors associated with disease progression, LTFU, and mortality in children and adolescents 6–19 years of age after ART initiation in the IeDEA Asia-Pacific cohort (n=1913)

	Disease progression			LTFU			Mortality		
Characteristics	**WHO clinical stage 3 and 4 (n=207)**	**aHR (95% CI)**	**p-value**	**LTFU (n=75)**	**asHR (95% CI)**	**p-value**	**Deaths (n=59)**	**aHR (95% CI)**	**p-value**
Sex									
Male	*108*	*1.00*		*41*	*1.00*		*33*	*1.00*	
Female	*99*	*1.04 (0.75–1.44)*	*0.820*	*34*	*0.87 (0.45–1.67)*	*0.681*	*26*	*0.96 (0.59–1.55)*	*0.870*
Current age, years [a]			*0.231*			0.028			*0.162*
6–9	*126*	*1.00*		19	1.00		*33*	*1.00*	
10–14	*74*	*0.92 (0.62–1.36)*	*0.679*	26	0.87 (0.51–1.50)	0.627	*19*	*0.55 (0.23–1.27)*	*0.162*
15–19	*7*	*0.43 (0.16–1.14)*	*0.091*	30	2.48 (1.03–5.94)	0.042	*7*	*0.79 (0.23–2.76)*	*0.712*
HIV disclosed [a]									
No	186	1.00		44	1.00		52	1.00	
Yes	21	0.43 (0.28–0.66)	<0.001	31	0.61 (0.28–1.34)	0.219	7	0.36 (0.17–0.79)	0.011
Year of first cART			*0.420*			<0.001			*0.100*
2008–2009	*73*	*1.00*		22	1.00		*27*	*1.00*	
2010–2012	*80*	*0.85 (0.60–1.21)*	*0.369*	29	1.80 (0.87–3.71)	0.113	*20*	*0.69 (0.44–1.07)*	*0.099*
2013–2018	*54*	*0.81 (0.57–1.16)*	*0.247*	24	4.28 (2.66–6.90)	<0.001	*12*	*0.54 (0.20–1.46)*	*0.227*
Currently on second-line cART [a]									
No	*180*	*1.00*		*57*	*1.00*		*50*	*1.00*	
Yes	*27*	*1.23 (0.73–2.0)*	*0.440*	*18*	*1.29 (0.64–2.62)*	*0.479*	*9*	*0.75 (0.36–1.57)*	*0.442*
Current weight-for-age z-score [a]			<0.001			*0.615*			<0.001
<−3	90	1.00		*16*	*1.00*		38	1.00	
−3 ≤ to <−2	37	0.42 (0.31–0.55)	<0.001	*14*	*0.84 (0.43–1.62)*	*0.597*	6	0.20 (0.11–0.37)	<0.001
≥−2	64	0.27 (0.21–0.35)	<0.001	*41*	*0.80 (0.54–1.20)*	*0.289*	15	0.28 (0.14–0.57)	<0.001

	Disease progression			LTFU			Mortality		
Characteristics	**WHO clinical stage 3 and 4 (n=207)**	**aHR (95% CI)**	**p-value**	**LTFU (n=75)**	**asHR (95% CI)**	**p-value**	**Deaths (n=59)**	**aHR (95% CI)**	**p-value**
Missing	16	-		4	-		0		
Ever diagnosed with AIDS [a, b]									
No	-	-		*28*	*1.00*		10	1.00	
Yes	-	-		*47*	*1.36 (0.68–2.70)*	*0.384*	49	2.26 (1.17–4.37)	0.015
Current CD4 cell count (cells/mm^3) [a]			<0.001			<0.001			<0.001
<200	98	1.00		14	1.00		45	1.00	
200–499	28	0.19 (0.13–0.26)	<0.001	16	0.49 (0.26–0.92)	0.027	9	0.12 (0.06–0.24)	<0.001
≥500	60	0.11 (0.06–0.18)	<0.001	40	0.30 (0.18–0.49)	<0.001	4	0.01 (0.01–0.04)	<0.001
Missing	21	-		5	-		1		

aHR: adjusted hazard ratio; asHR: adjusted subdistribution hazard ratio; 95% CI: 95% confidence interval; cART: combination antiretroviral therapy

Disclosure was our variable of interest and was retained in the final models regardless of its statistical significance. Covariates in italics were not included in the final model. Their aHR were presented individually in the multivariate model adjusted for significant predictors.

[a] Age, HIV disclosure, on second line cART, weight-for-age z-score, AIDS diagnosis, CD4 count are considered time-dependent variables where each patient can contribute to more than one category.

[b] AIDS was only considered as a covariate when the outcome was loss to follow-up or death