Causes of death among infants by HIV status in Zambia, 2020-2021

Wantula Sichembe[1], Annie Mwila[1], Keith Mweebo[1], Priscilla Kapombe[2], Mweene Cheelo[2], Nzali Kancheya[1], Peter Minchella[1], Jonas Z. Hines[1]

[1]U.S. Centers for Disease Control and Prevention, Lusaka, Zambia; [2]Ministry of Health, Lusaka, Zambia

Poster #766

Background

Infant mortality (death of children under the age of 1 year[1]) in Zambia is among the highest in the world, nearly double that of the global average of 28 deaths per 1000 live births[2,3,4].

Some of the notable causes of infant mortality include:
- preterm births and neonatal disorders,
- infectious causes (mostly respiratory and diarrheal diseases) and
- congenital malformations[5].

Infants who acquire HIV from their mothers are at a higher risk of dying compared to those without HIV. This risk of death is worsened in the absence of antiretroviral treatment (ART), with most untreated HIV positive infants dying before their first birthday[6].

We utilized the Zambian Ministry of Health (MOH) routinely collected mortality surveillance data to explore the causes of death and survival time by HIV status among deceased infants in Zambia from 2020 to 2021.

Methods

We analyzed mortality data from the Zambian MOH routine mortality surveillance system.
- Verbal autopsies (VA) are conducted on persons who die in the community or within 48 hours of arrival at health facilities in 27 districts representing ~50% of the population in Zambia[7].
- Information on past medical history and circumstances proximal to death is collected by trained mortality surveillance officers from close relatives or associates using a standardized World Health Organization questionnaire.
- Responses are analyzed by a validated algorithm called InterVA5, that assigns a probable underlying cause of death.
- Only information reported from the respondent is used in the VA and no laboratory or postmortem samples are collected.
- We analyzed causes of death among the deceased infants (defined as children <1 year old) by reported HIV status
- We further analyzed survival time (in days) by HIV status and ART status using R

Results

VAs were conducted for 2,446 infants from 2020 to 2021.
- The median age was 53 days (3-161) and males represented 52% (n=1271).
- Most of the infants died at home (55%) and 51% had received care before their death.
- Sixty-six (2.7%) infants were HIV positive, 1,372 (56.1%) were HIV negative and 1,008 (41.2%) had an unknown HIV status, the vast majority of which were neonates.
- Fifty percent of infants who were HIV positive were on ART (Table 1).
- Among the HIV positive and negative infants, the probable causes of death were mainly indeterminate or infectious causes (Table 2).
- Birth asphyxia, prematurity and neonatal sepsis were the leading probable causes of death among infants with unknown HIV status and these infants with unknown HIV status died younger than those with a known HIV status (median days: 2 vs. 136; p <0.01).
- The survival time for HIV positive infants did not differ from that of HIV negative ones (median days: 136.5 vs 136; p=0.45) (Figure 1).
- Among HIV positive infants, survival time did not differ by ART status (p=0.74) (Figure 2).

Among infant deaths recorded through mortality surveillance in Zambia, infectious diseases and indeterminate causes were the most common causes of death by HIV status

Table 1. Characteristics and circumstances of death among infants undergoing verbal autopsy in Zambia, 2020-2021(N=2,446)

Variable	Overall n (%) (N=2,446)	HIV positive n (%) (N=66)	HIV negative n (%) (N=1,372)	Unknown HIV status n (%) (N=1,008)	p-value*
Sex					
Male	1,271 (52.0)	38 (57.6)	709 (51.7)	524 (52.0)	
Female	1,173 (48.0)	28 (42.4)	663 (48.3)	482 (47.8)	0.64
Missing	2 (0.1)	0 (0)	0 (0)	2 (0.2)	
Median age at death in days (IQR)	53 (3-161)	136 (74-229)	136.5(66-261)	2 (0-9)	<0.01
Age group					
<1 Month	1,012 (41.4)	3 (4.5)	27 (2.0)	982 (97.4)	<0.01
1-3 Months	583 (23.8)	25 (37.9)	548 (39.9)	10 (1.0)	
3-6 Months	416 (17.0)	19 (28.8)	391 (28.5)	6 (0.6)	
6-9 Months	311 (12.7)	15 (22.7)	291 (21.2)	5 (0.5)	
9-12 Months	124 (5.1)	4 (6.1)	115 (8.4)	5 (0.5)	
Province					
Central	84 (3.4)	6 (9.1)	60 (4.4)	18 (1.8)	<0.01
Copperbelt	1,016 (41.5)	17 (25.8)	462 (33.7)	537 (53.3)	
Eastern	14 (0.6)	0 (0)	10 (0.7)	4 (0.4)	
Lusaka	1,191 (48.7)	40 (60.6)	794 (57.9)	357 (35.4)	
Northwestern	10 (0.4)	0 (0)	10 (0.7)	0 (0)	
Southern	122 (5.0)	2 (3.0)	28 (2.0)	92 (9.1)	
Western	9 (0.4)	1 (1.5)	8 (0.6)	0 (0)	
HIV exposure status					
Exposed	217 (8.9)	28 (42.4)	83 (6.0)	106 (10.5)	<0.01†
Unexposed	1,350 (55.2)	4 (6.1)	624 (45.5)	722 (71.6)	
Unknown	879 (35.9)	34 (51.5)	665 (48.5)	180 (17.9)	
ART status					
On ART	33 (1.3)	33 (50.0)	0 (0)	0 (0)	
Not on ART	1,209 (49.4)	15 (22.7)	829 (60.4)	365 (36.2)	
Unknown	1,204 (49.2)	18 (27.3)	543 (39.6)	643 (63.8)	
Respondent relationship to deceased					
Parent	1,554 (63.5)	43 (65.2)	900 (65.6)	611 (60.6)	0.04
Family member	849 (34.7)	23 (34.8)	445 (32.4)	381 (37.8)	
Friend	6 (0.2)	0 (0)	3 (0.2)	3 (0.3)	
Health worker	7 (0.3)	0 (0)	1 (0.1)	6 (0.6)	
Public official	3 (0.1)	0 (0)	2 (0.1)	1 (0.1)	
Another relationship	27 (1.1)	0 (0)	21 (1.5)	6 (0.6)	
Conditions					
Cardiac disease	20 (0.8)	1 (1.5)	18 (1.3)	1 (0.1)	0.54
Asthma	25 (1.0)	3 (4.5)	22 (1.6)	0 (0)	0.14
CKD	4 (0.2)	0 (0)	4 (0.3)	0 (0)	0.88
Liver disease	6 (0.2)	0 (0)	6 (0.4)	0 (0)	0.82
Death year					
2020	904 (37.0%)	25 (37.9)	531 (38.7)	348 (34.5)	0.996
2021	1,542 (63.0)	41 (62.1)	841 (61.3)	660 (65.5)	
Place of death					
Home	1,345 (55.0)	34 (51.5)	915 (66.7)	396 (39.3)	<0.01
Health facility	1,079 (44.1)	30 (45.5)	446 (32.5)	603 (59.8)	
Missing	22 (0.9)	2 (3.0)	11 (0.8)	9 (0.9)	
Died suddenly‡	1,105 (45.2)	21 (31.8)	525 (38.3)	559 (55.5)	<0.01
Received care before death¶	1,248 (51.0)	49 (74.2)	833 (60.7)	366 (36.3)	<0.01

*Calculated using chi-square and ANOVA where applicable
† Analysis excluded HIV positive infants
‡Sudden death defined as dying within 24 hours of being in regular/good health
¶ Indicates person received care for the condition that led to death

Table 2. Top five causes of deaths among infants by HIV status in Zambia, 2020-2021

	HIV status		
Rank	HIV Positive (n = 66) cause (%)	HIV Negative (n = 1372) cause (%)	Unknown HIV status (n = 1008) cause (%)
1	Indeterminate (37.9)	Indeterminate (25.9)	Birth Asphyxia (31.0)
2	Meningitis and Encephalitis (15.2)	Diarrheal diseases (23.8)	Prematurity (28.1)
3	Unspecified infectious diseases(12.1)	Unspecified infectious diseases (17.3)	Neonatal sepsis (11.3)
4	Diarrheal diseases (12.1)	Meningitis and Encephalitis (14.2)	Neonatal Pneumonia (8.2)
5	Cardiac disease (6.1)	Cardiac disease (4.4)	Fresh stillbirth (6.9)

*Cause of death determined by verbal autopsy

Discussion
- Infectious diseases continue to be the leading causes of death among infants.
- The lack of difference in survival time among these deceased infants by HIV status could be because of the high burden of these infectious diseases in this age group[5].
- Indeterminate causes of death were also very high among these infants and could point to critical diagnostic gaps in the health system.
- Infants with unknown HIV status died younger from complications of pregnancy and delivery. Even though not as many infant died within 28 days of life as estimates report[4], this analysis shows that a considerable number still die with 28 days of being born.
- With an insufficient death registry in Zambia, mortality surveillance using VA provides critical information on the causes of death among infants in Zambia as this analysis has shown.

Limitations
- The total number of deceased infants that were eligible for VA during this period could not be established and hence the representativeness of the findings in this paper cannot be ascertained.
- Although the mortality surveillance is done in districts representing approximately 50% of the population in Zambia, the findings cannot necessarily be generalized to the entire country.
- All information was collected from close family members and no specific testing, including HIV testing, is done as part of this surveillance system.

Recommendations
- Improved neonatal care, diagnostics for the indeterminate causes of death and improved management of infectious diseases can improve infants' outcomes.
- Prompt ART initiation using available optimized regimens can also improve the survival of HIV positive infants.
- We also recommend strengthening surveillance by improved death registration through scale-up of civil registration and vital statistics programs throughout Zambia
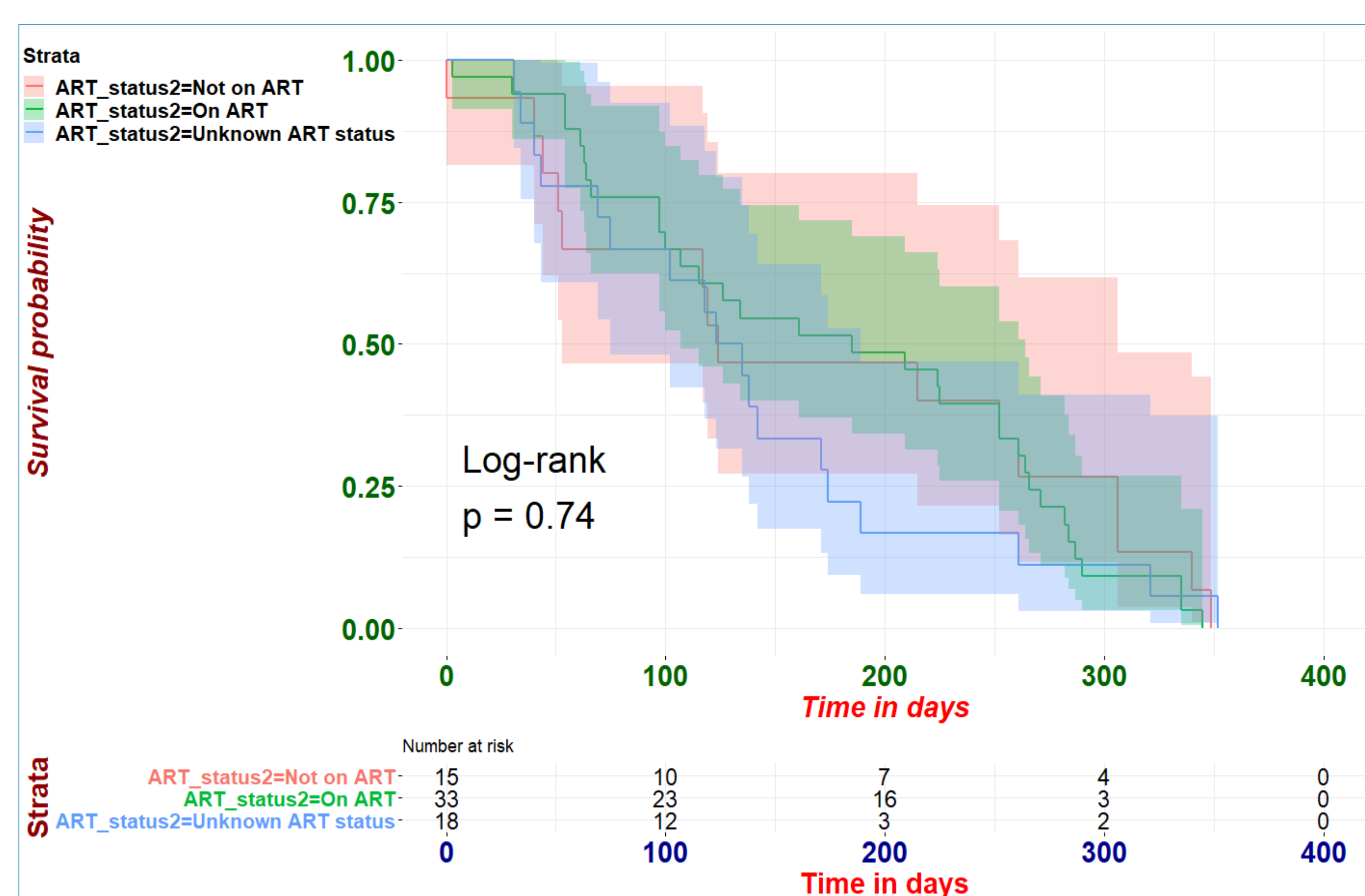
References
1. World Health Organization. The Global Health Observatory: Indicators-Infant mortality rate (between birth and 11 months per 1000 live births) 2023 [Available from: https://www.who.int/data/gho/data/indicators/indicator-details/GHO/infant-mortality-rate-(probability-of-dying-between-birth-and-age-1-per-1000-live-births).
2. Central Statistical Office (Zambia), ICF International, Ministry of Health (Zambia), University Teaching Hospital (Zambia), University of Zambia. Zambia Demographic and Health Survey 2018-2019. Fairfax, United States of America: ICF International; 2020.
3. UN Inter-agency Group for Child Mortality Estimation. Infant Mortality Rate-Total Online Source: Childmortality.org; 2023 [Available from: https://childmortality.org/data/World.
4. Our World in Data. Child deaths by life stage, 1995 to 2017: Zambia Online Source: OurWorldInData.org; 2023 [Available from: https://ourworldindata.org/grapher/child-deaths-by-life-stage?time=1995..2017&country=OWID_WRL~ZMB.
5. Roser M, Ritchie H, Dadonaite B. Child and Infant Mortality OurWorldInData.org OurWorldInData.org 2013 [Available from: https://ourworldindata.org/child-mortality.
6. Becquet R, Marston M, Dabis F, Moulton LH, Gray GE, Coovadia HM, et al. Children Who Acquire HIV Infection Perinatally Are at Higher Risk of Early Death than Those Acquiring Infection through Breastmilk: A Meta-Analysis. PLoS ONE. 2012;7.
7. Kapombe P, Cheelo M, Kamalonga K, Tally L, Stoops E, Mwango C, et al. Most common causes of deaths among persons living with HIV—Zambia, 2020-2021. International AIDS Conference; Montreal, Canada, 2022.

Figure 1. Kaplan-Meier curve on survival time of infants from birth by HIV positive and HIV negative status in Zambia, 2020-2021
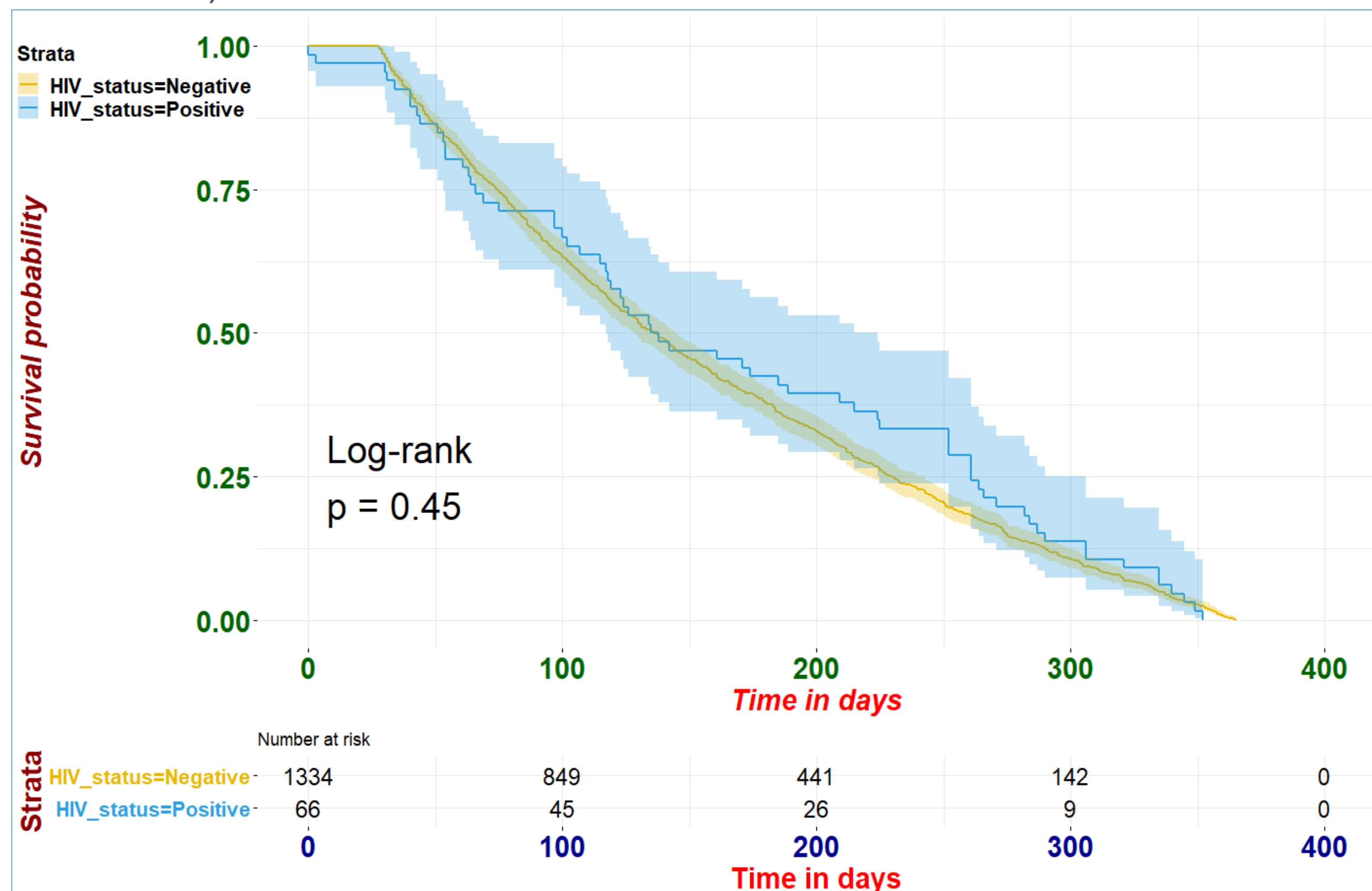
Figure 2. Kaplan-Meier curve of survival time of HIV positive infants by ART status in Zambia, 2020-2021

Presented at IAS 2023, the 12th IAS Conference on HIV Science

IAS 2023 23-26 July