Impact of initiation of cART according to the WHO recommendations on the survival of HIV-positive patients in Taiwan

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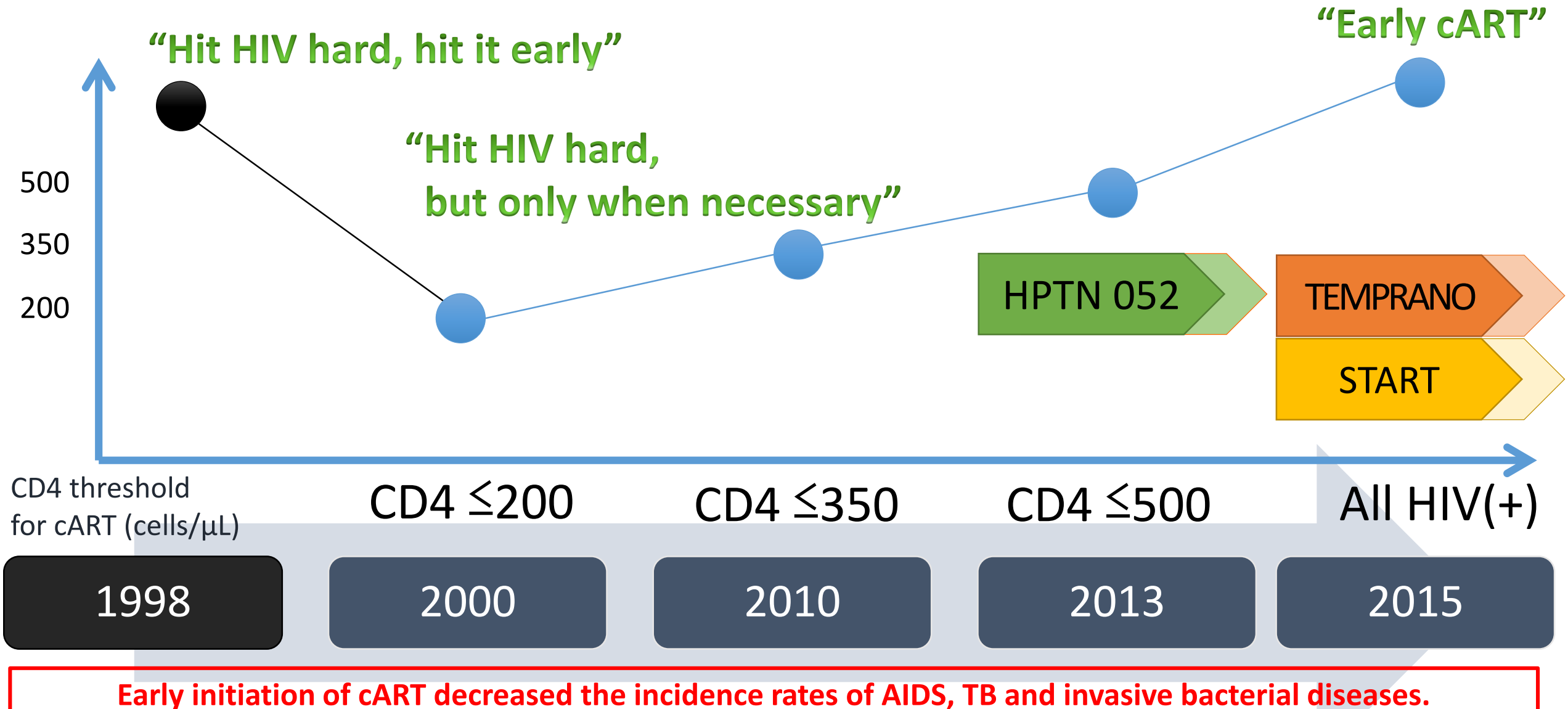
When to Start – WHO Guidelines



Early initiation of cART decreased the incidence rates of AIDS, TB and invasive bacterial diseases.

When to Start – Taiwan Guidelines

cART could be offered even if the patient's CD4 counts higher than the threshold after evaluation and counseling

500
350
200

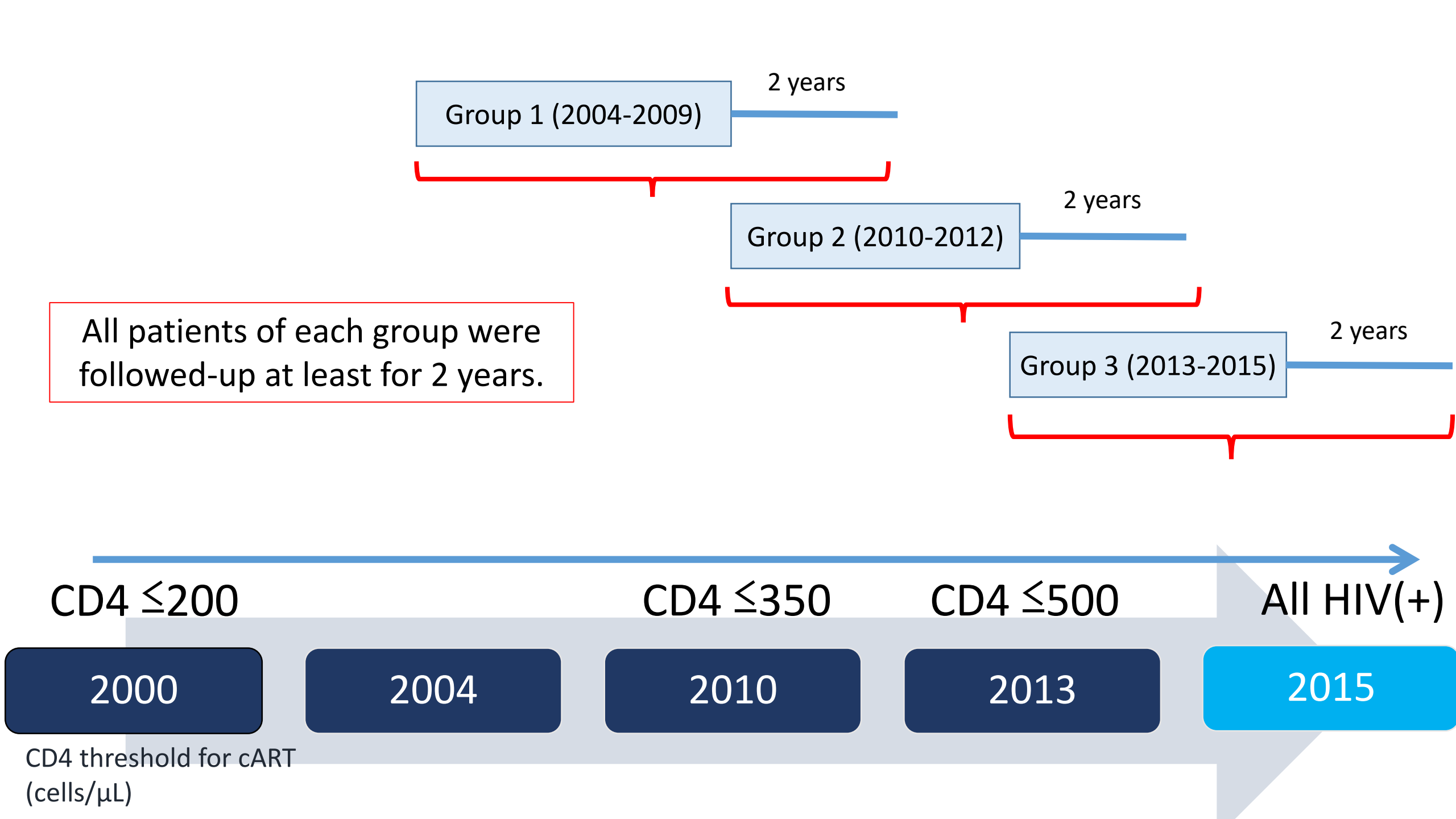
No official guidelines. Most physicians followed DHHS/WHO guidelines.
3 STRs as the first-line regimen June in 2016.

CD4 threshold for cART (cells/μL)

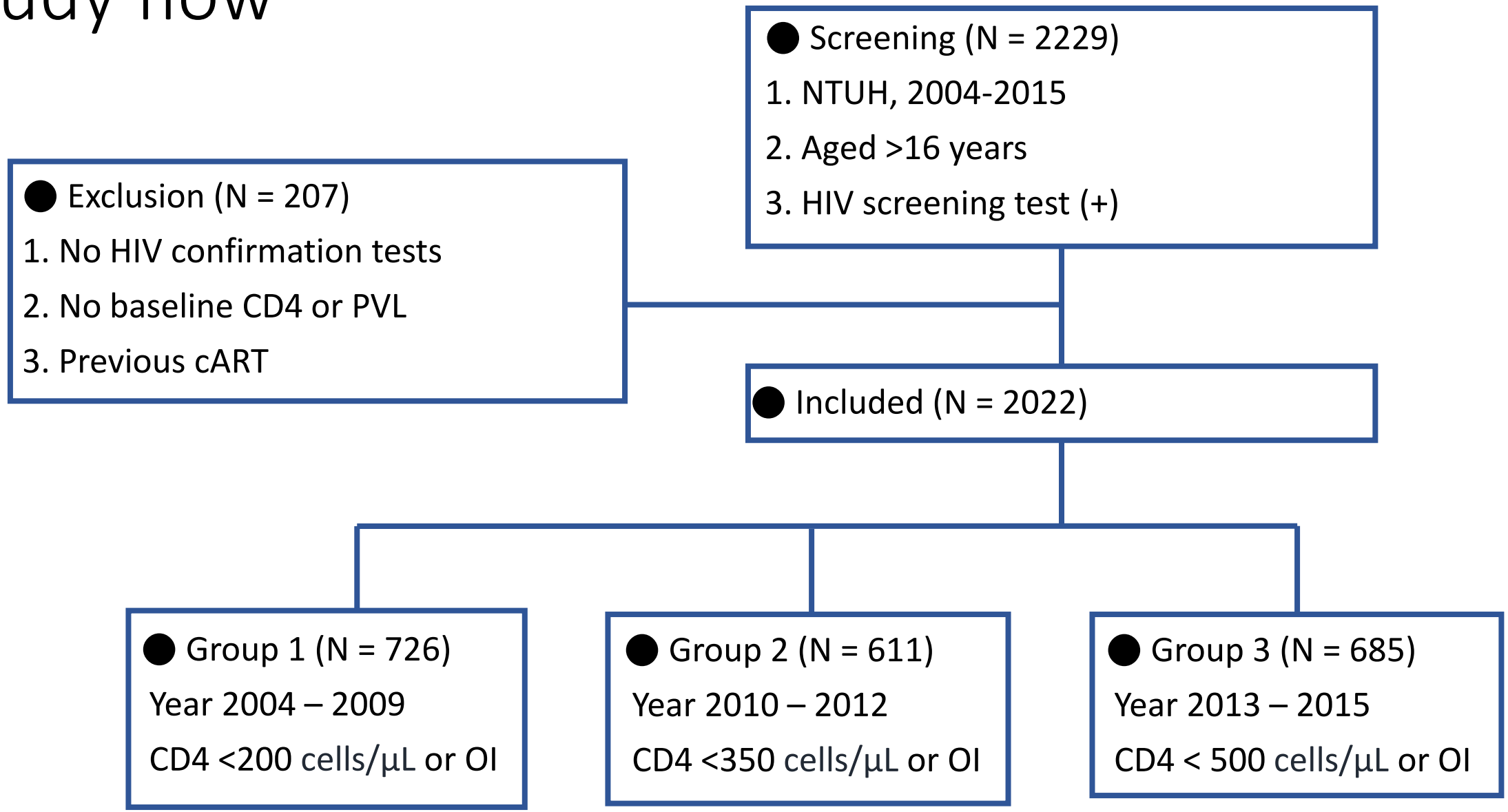
	CD4 ≤200	CD4 ≤350	CD4 ≤500	All HIV(+)
	2008	2010	2013	2015

Methods

- Study design: retrospective cohort study
- Study site: National Taiwan University Hospital
- Study duration: 2004/1/1 – 2015/12/31
- Subjects included: patients with newly diagnosed HIV infection
  - 3 groups were defined according to the year of HIV diagnosis made.
- Data collected:
  - age at diagnosis, gender, risk group of HIV infection, baseline CD4/PVL, clinical manifestations at diagnosis, HBV & HCV coinfection, cART, CD4/PVL upon ART initiation

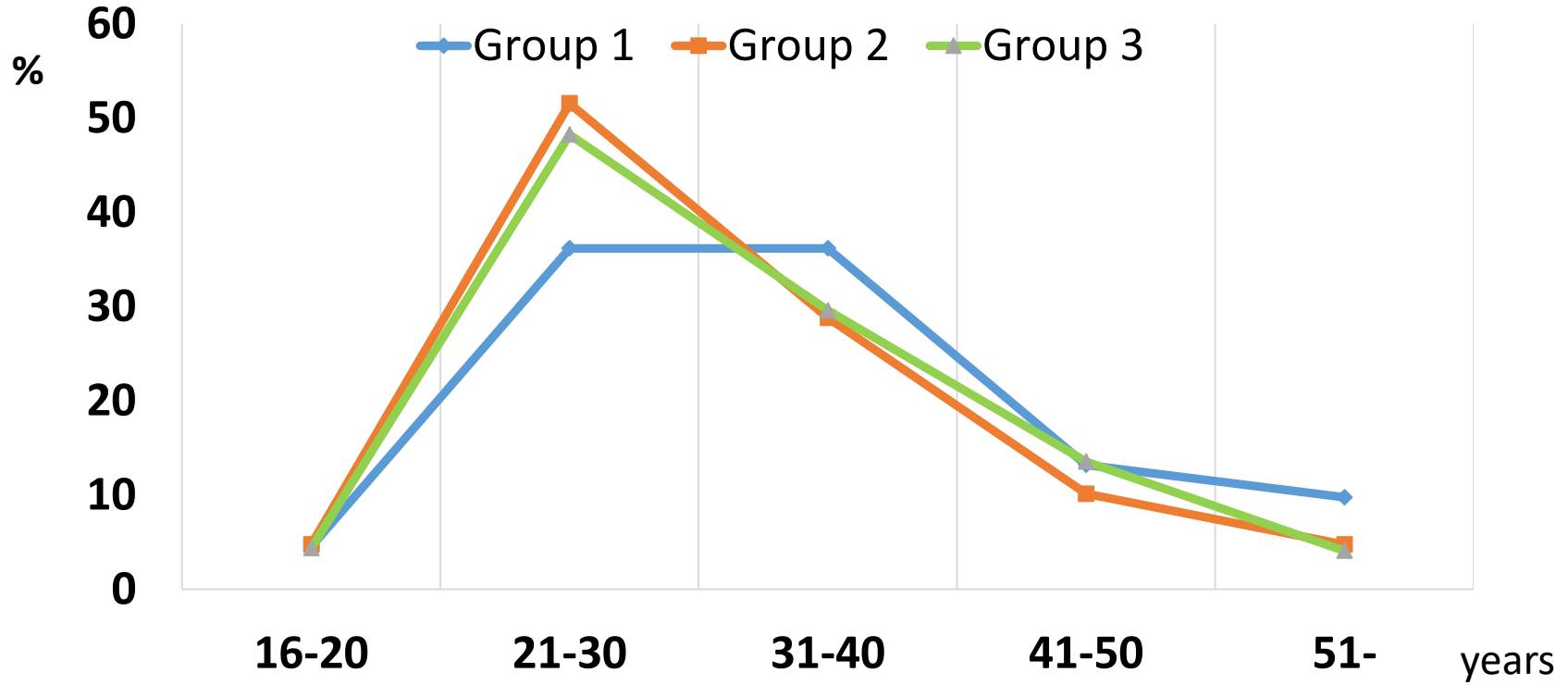

Group 1 (2004-2009)
2 years
Group 2 (2010-2012)
2 years
Group 3 (2013-2015)
2 years
All patients of each group were followed-up at least for 2 years.
CD4 ≤200
CD4 ≤350
CD4 ≤500
All HIV(+)
2000
2004
2010
2013
2015
CD4 threshold for cART (cells/µL)

Study flow


Screening (N = 2229)
1. NTUH, 2004-2015
2. Aged >16 years
3. HIV screening test (+)
Exclusion (N = 207)
1. No HIV confirmation tests
2. No baseline CD4 or PVL
3. Previous cART
Included (N = 2022)
Group 1 (N = 726)
Year 2004 – 2009
CD4 <200 cells/μL or OI
Group 2 (N = 611)
Year 2010 – 2012
CD4 <350 cells/μL or OI
Group 3 (N = 685)
Year 2013 – 2015
CD4 < 500 cells/μL or OI

Baseline Characteristics – Age and Gender

	Total (n=2022)	Group 1 (n=726)	Group 2 (n=611)	Group 3 (n=685)	p	1 VS 2	2 VS 3	1 VS 3
Median age at HIV diagnosis (IQR), years	31 (25-38)	32 (27-40)	29 (25-37)	30 (25-37)	<0.001	< 0.001	0.935	< 0.001



Men, n (%)	1951 (96.5)	682 (93.9)	601 (98.4)	668 (97.5)	<0.001	<0.001	0.288	0.001

Baseline Characteristics - Risk

	Total (n=2022)	Group 1 (n=726)	Group 2 (n=611)	Group 3 (n=685)	p	1 VS 2	2 VS 3	1 VS 3
MSM, n (%)	1700 (84.1)	552 (76.0)	531 (86.9)	617 (90.1)	<0.001	<0.001	0.074	<0.001
Heterosexuals, n (%)	167 (8.3)	101 (13.9)	28 (4.6)	38 (5.5)	<0.001	<0.001	0.430	<0.001
IDUs, n (%)	69 (3.4)	45 (6.2)	12 (2.0)	12 (1.8)	<0.001	<0.001	0.777	<0.001
Others & Unknown, n (%)	94 (4.6)	31 (4.3)	42 (6.9)	21 (3.1)				

*IDU, injecting drug users

Baseline Characteristics – CD4 and PVL

	Total (n=2022)	Group 1 (n=726)	Group 2 (n=611)	Group 3 (n=685)	p	1 VS 2	2 VS 3	1 VS 3
Median CD4 (IQR), cells/µL	262 (80-435)	194 (43-390)	278 (115-438)	310 (134-460)	<0.001	<0.001	0.110	<0.001
CD4<200 cells/µL, n (%)	824 (40.8)	369 (50.8)	225 (36.8)	230 (33.6)	<0.001	<0.001	0.221	<0.001
Median PVL (IQR), log_{10} copies/ml	4.96 (4.40-5.51)	5.10 (4.45-5.66)	4.89 (4.32-5.45)	4.89 (4.40-5.51)	<0.001	<0.001	0.542	<0.001
PVL >5 log_{10} copies/ml, n (%)	967 (47.8)	405 (55.8)	271 (44.4)	291 (42.5)	<0.001	<0.001	0.497	<0.001

Baseline Characteristics – Viral Hepatitis

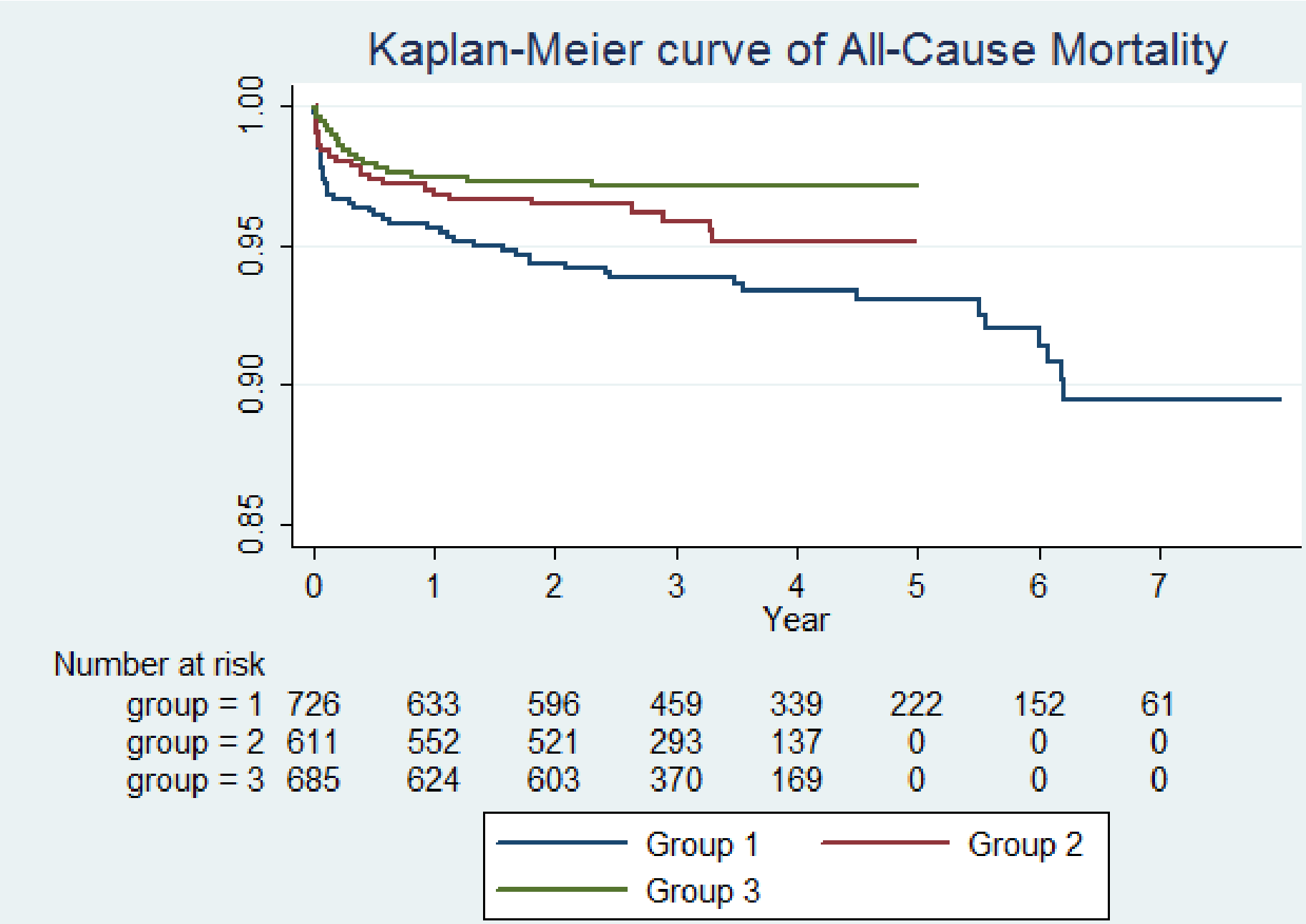
	Total (n=2022)	Group 1 (n=726)	Group 2 (n=611)	Group 3 (n=685)	p	1 VS 2	2 VS 3	1 VS 3
HBsAg (+), n (%)	269 (13.3)	130 (17.9)	82 (13.4)	57 (8.3)	<0.001	0.025	0.003	<0.001
Anti-HCV (+), n (%)	127 (6.3)	70 (9.64)	32 (5.2)	25 (3.7)	<0.001	0.003	0.164	<0.001

Adherence to WHO Guidelines

	Total (n=2022)	Group 1 (n=726)	Group 2 (n=611)	Group 3 (n=685)
With ART use, n (%)	1864 (92.2)	648 (89.3)	558 (91.3)	658 (96.1)

With ART use	Total (n=1864)	Group 1 (n=648)	Group 2 (n=558)	Group 3 (n=658)
Follow WHO guidelines, n (%)	1647 (88.4)	576 (88.9)	488 (87.5)	583 (88.6)
ART earlier than recommended	106 (5.7)	60 (9.3)	24 (4.3)	22 (3.3)
ART deferred	111 (6.0)	12 (1.9)	46 (8.2)	53 (8.1)

- Group 1 – 7 of 12 (58.3%) patients delayed ART due to opportunistic illnesses
- Group 3 – 48 of 53 (90.6%) patients were treated with ART after 2017



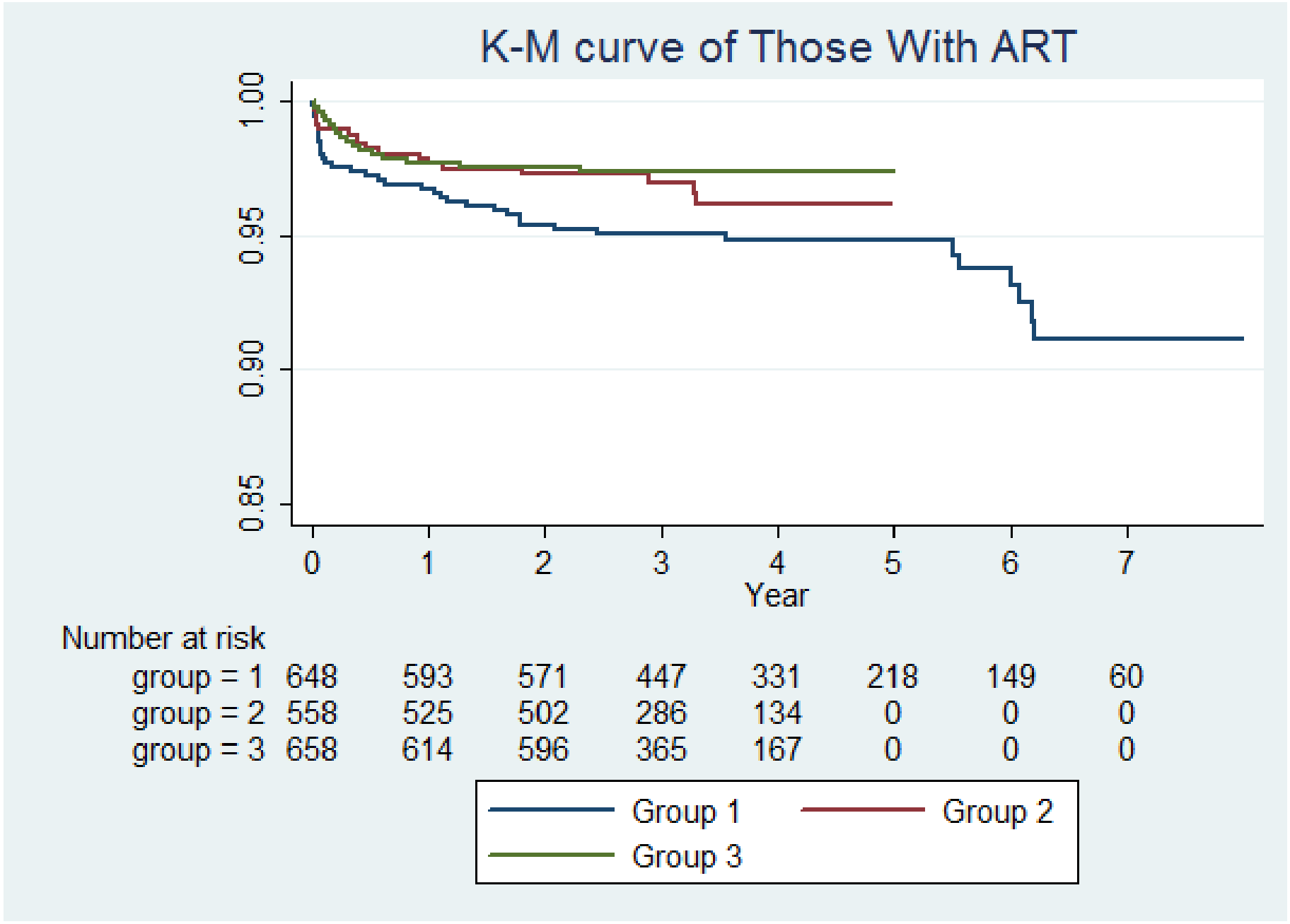
p=0.116

p=0.179

p=0.002

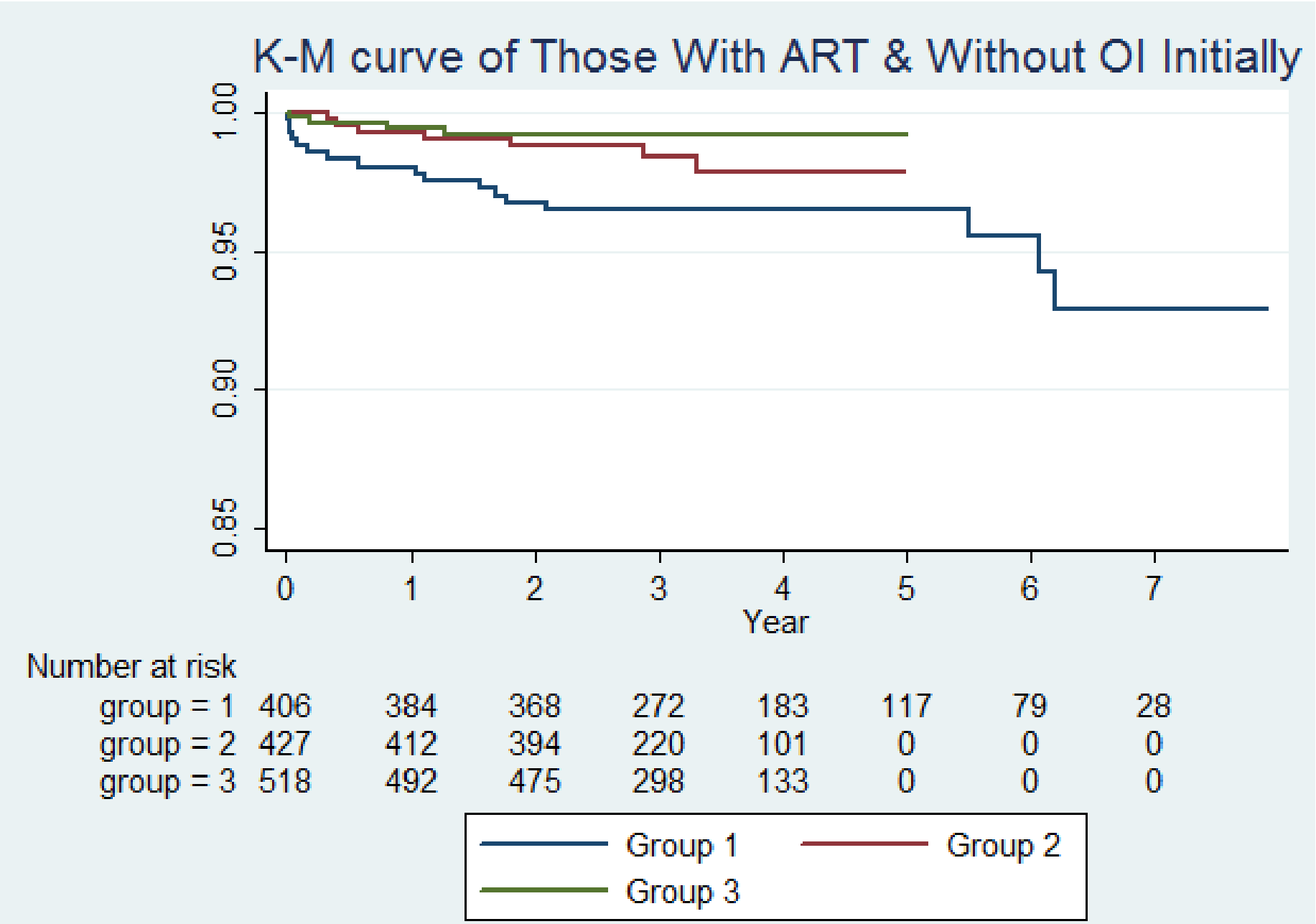
Log rank test

Group 1, 2, and 3
p=0.009



Log Rank test

Group 1,2 and 3
p=0.072



p=0.105

p=0.212

p=0.004

Log Rank test

Group 1,2 and 3
p=0.012

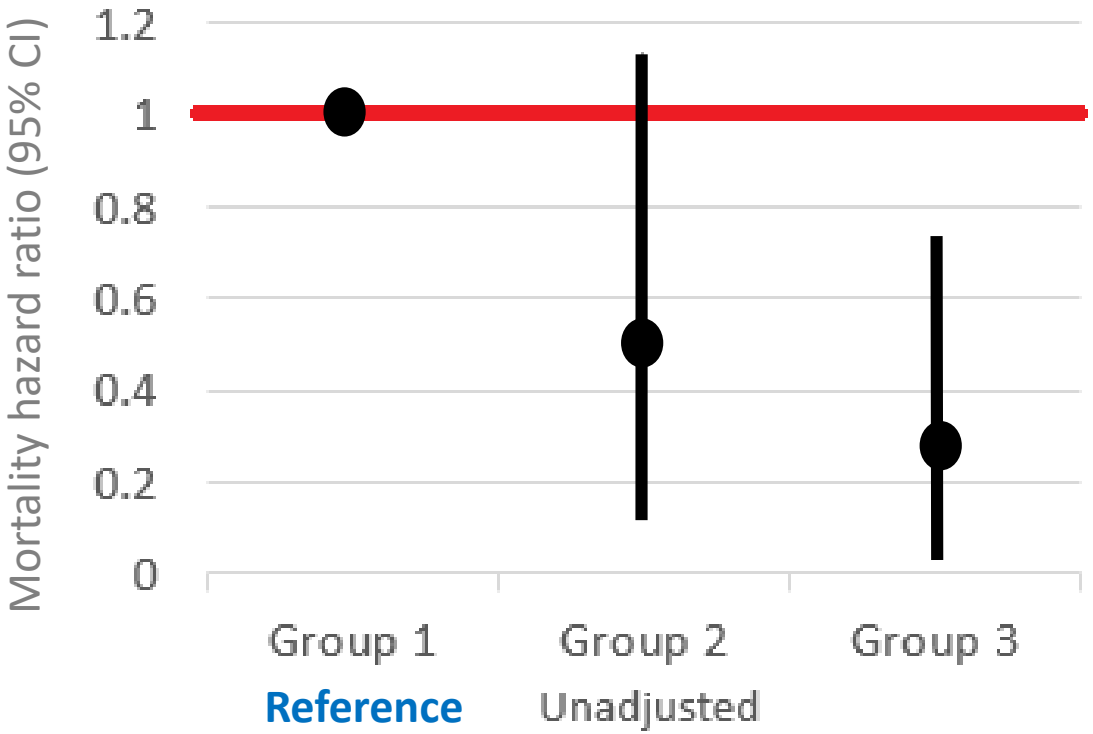
Hazard ratio for all-cause mortality– by study period for those with ART & without OI upon HIV diagnosis

p = 0.111

HR = 0.47 (0.19-1.19)

p = 0.009

HR= 0.23 (0.07-0.67)

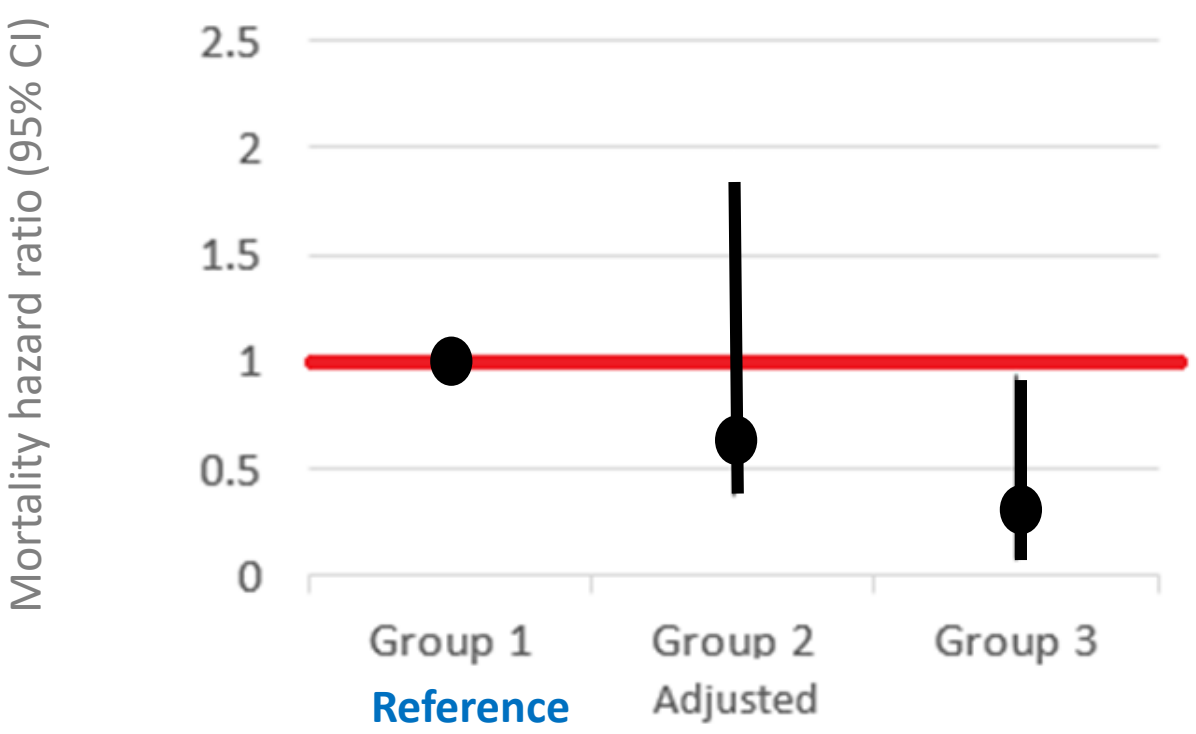


p = 0.419

HR = 0.68 (0.27-1.73)

p = 0.049

HR = 0.32 (0.10-0.99)

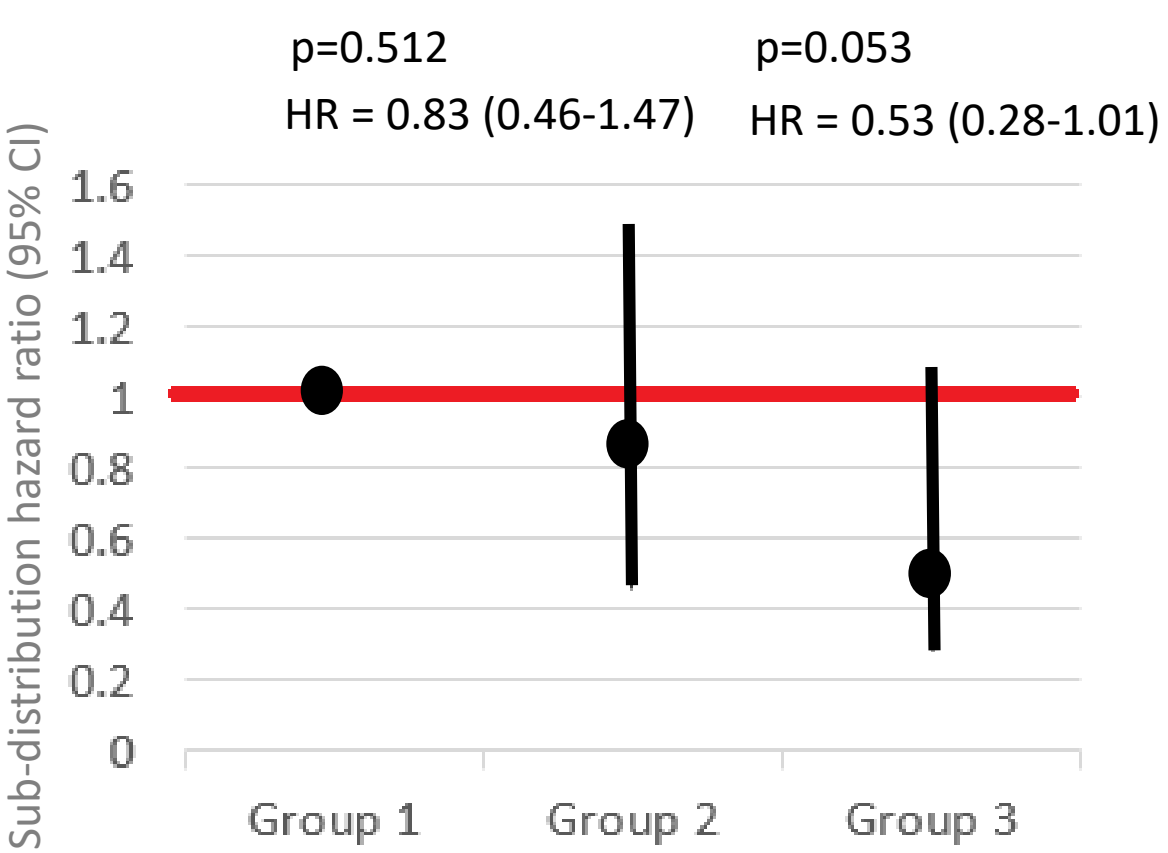


Adjust for age at diagnosis, IVDU, Heterosexual, initial HBV and HCV status, baseline CD4 count

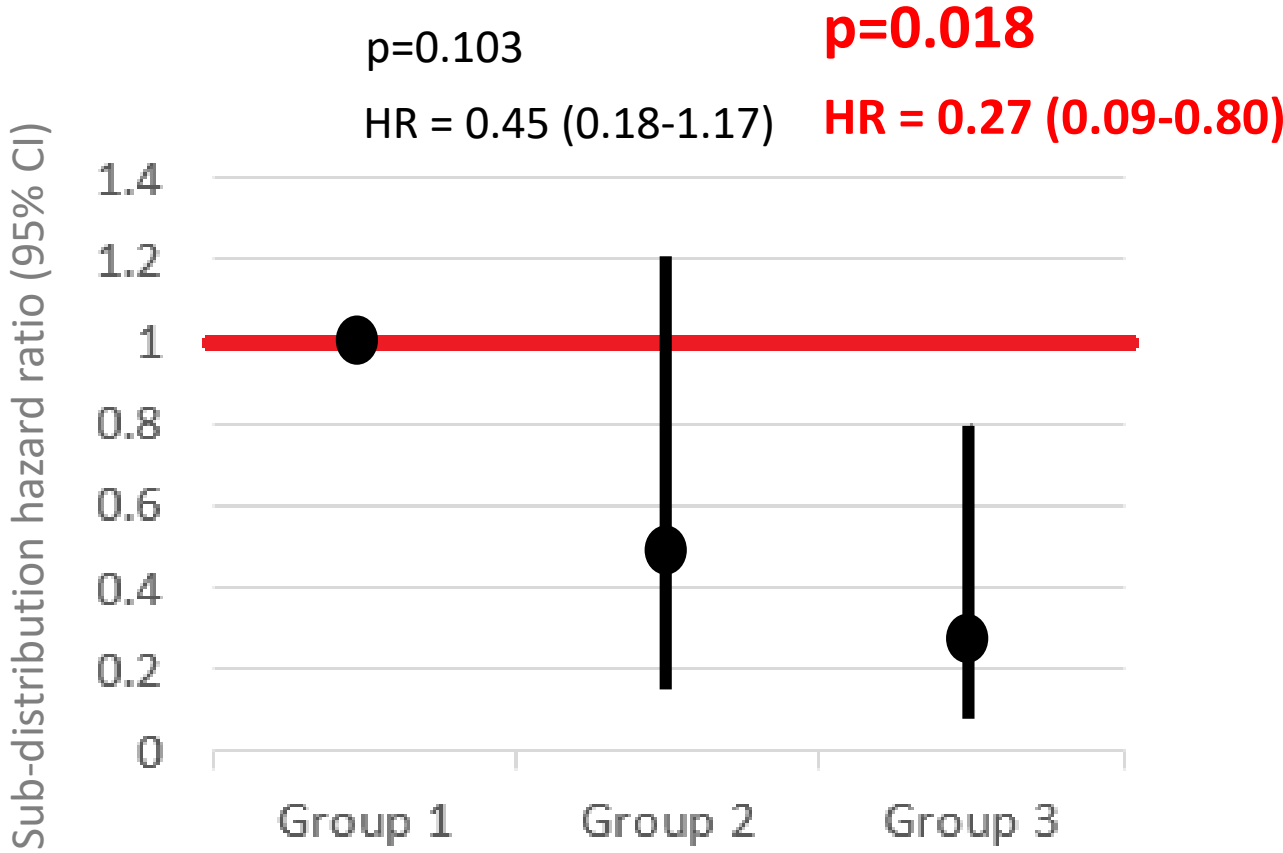
Multivariate Cox Regression

	Univariate analysis			Multivariate analysis		
	HR	p	95% CI	HR	p	95% CI
Age (1 years)	1.08	<0.001	1.06-1.11	**1.08**	**<0.001**	**1.05-1.11**
IVDU	7.43	<0.001	2.89-19.06	**3.65**	**0.044**	**1.03-12.93**
Heterosexual	2.38	0.112	0.82-6.95			
HBV carrier	3.27	0.004	1.48-7.24	**2.25**	**0.049**	**1.01-5.07**
HCV carrier	5.83	<0.001	2.52-13.52	2.24	0.172	0.70-7.16
Baseline CD4 count (cells/mm3)	0.996	0.001	0.993-0.998	**0.997**	**0.009**	**0.994-0.999**

Competing Risk – AIDS-related VS non-AIDS-related death



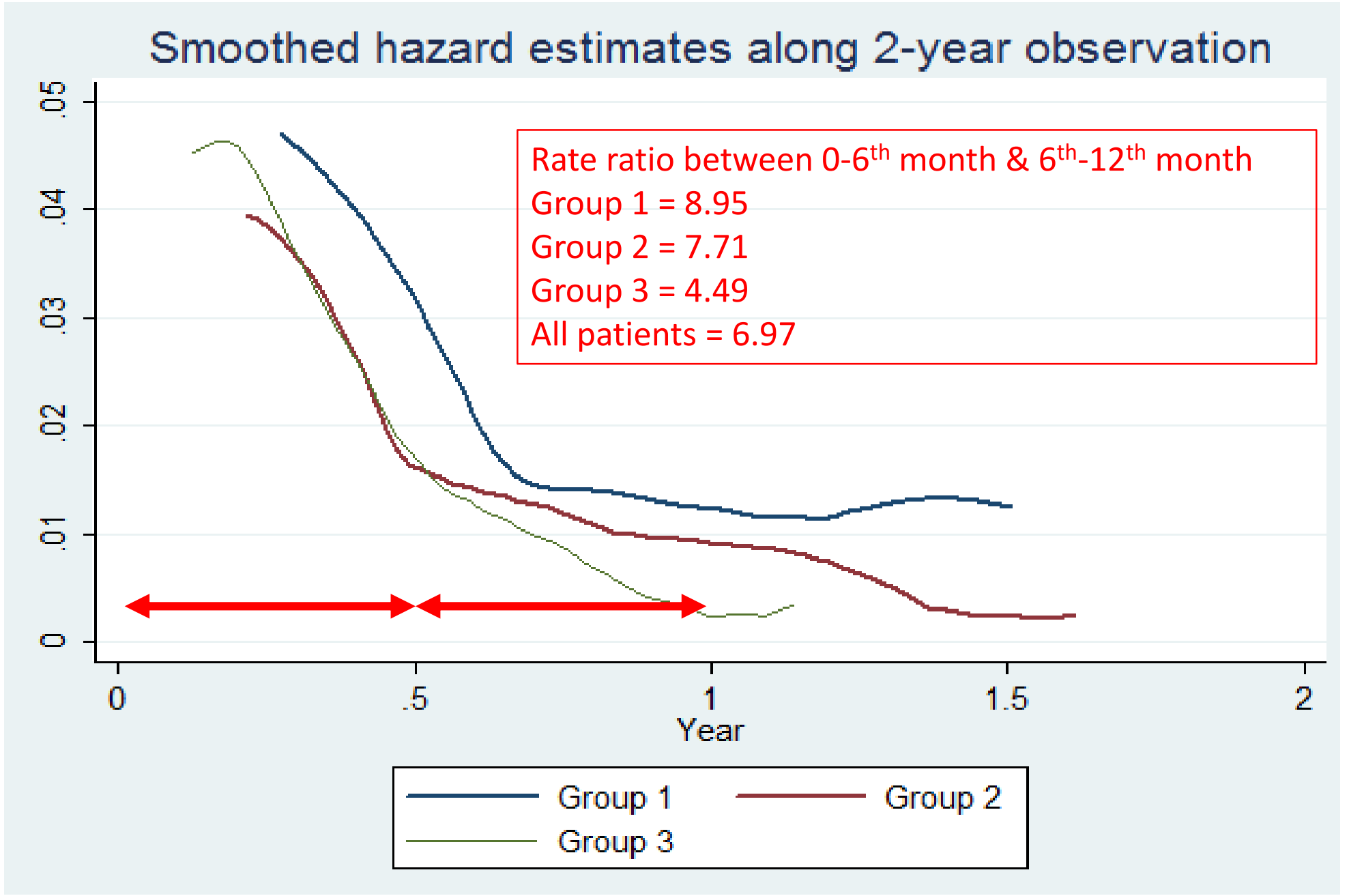
AIDS-related death



Non-AIDS-related death

Interval Between HIV Diagnosis & Death

All death	Total (n=95)	Group 1 (n=51)	Group 2 (n=25)	Group 3 (n=19)
Average duration (days)	517.5	551.1	524.3	406.9
0-30 days, n (%)	32	18 (35.3)	10 (40.0)	4 (21.0)
0-6th month, n (%)	58	28 (54.9)	16 (64.0)	14 (73.7)
6th-12th month, n (%)	8	3 (5.9)	2 (8.0)	3 (15.8)
1st-2nd year, n (%)	12	8 (15.7)	3 (12.0)	1 (5.3)


Smoothed hazard estimates along 2-year observation
1/year
.05
.04
.03
.02
.01
0
Rate ratio between 0-6th month & 6th-12th month
Group 1 = 8.95
Group 2 = 7.71
Group 3 = 4.49
All patients = 6.97
0
.5
1
1.5
2
Year
Group 1
Group 2
Group 3

Summary

- Nearly 90% of the patients were treated with cART by following the then WHO guidelines in our cohort.
- Survival of patients improved along the time periods of cART initiation according to WHO guidelines, especially for those who had no opportunistic illness at diagnosis. Independent factors associated with mortality were age at diagnosis, HBV coinfection, and baseline CD4 count.
- In competing risk regression model, implementing the strategies of cART initiation decreased the mortalities of non-AIDS-related death.
- Mortalities mostly took place within the first 6 months of HIV diagnosis.

Conclusions

- While receiving cART improved survival among HIV-positive patients with no OI as initial presentation, implementing the strategies of early cART initiation recommended by the WHO provided further survival benefit.