

OPPORTUNISTIC INFECTIONS

Institute of Infectious Diseases, Pune India

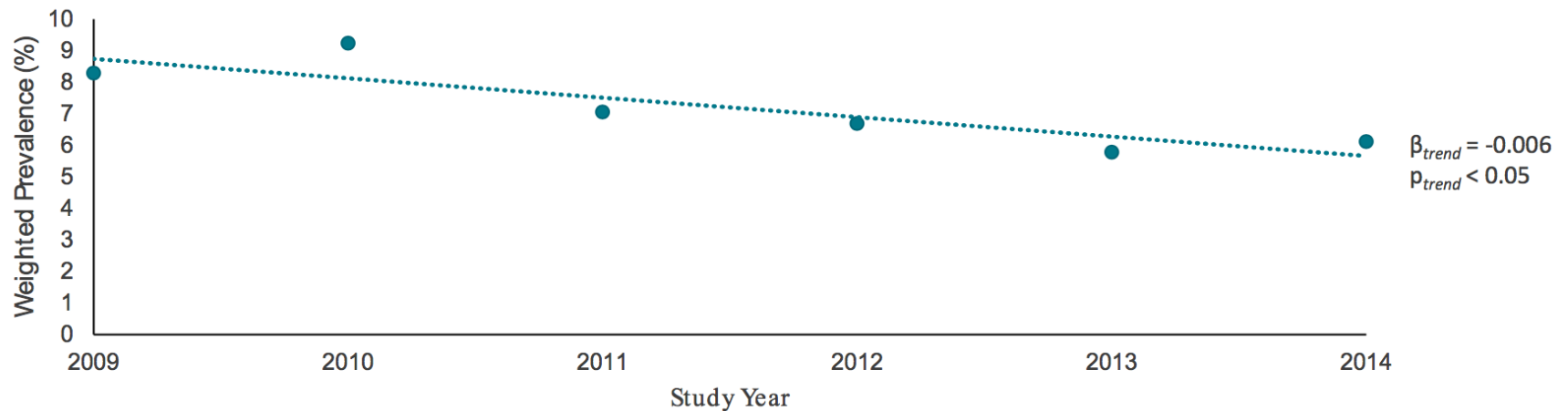
DISCLOSURES

- Nothing to declare

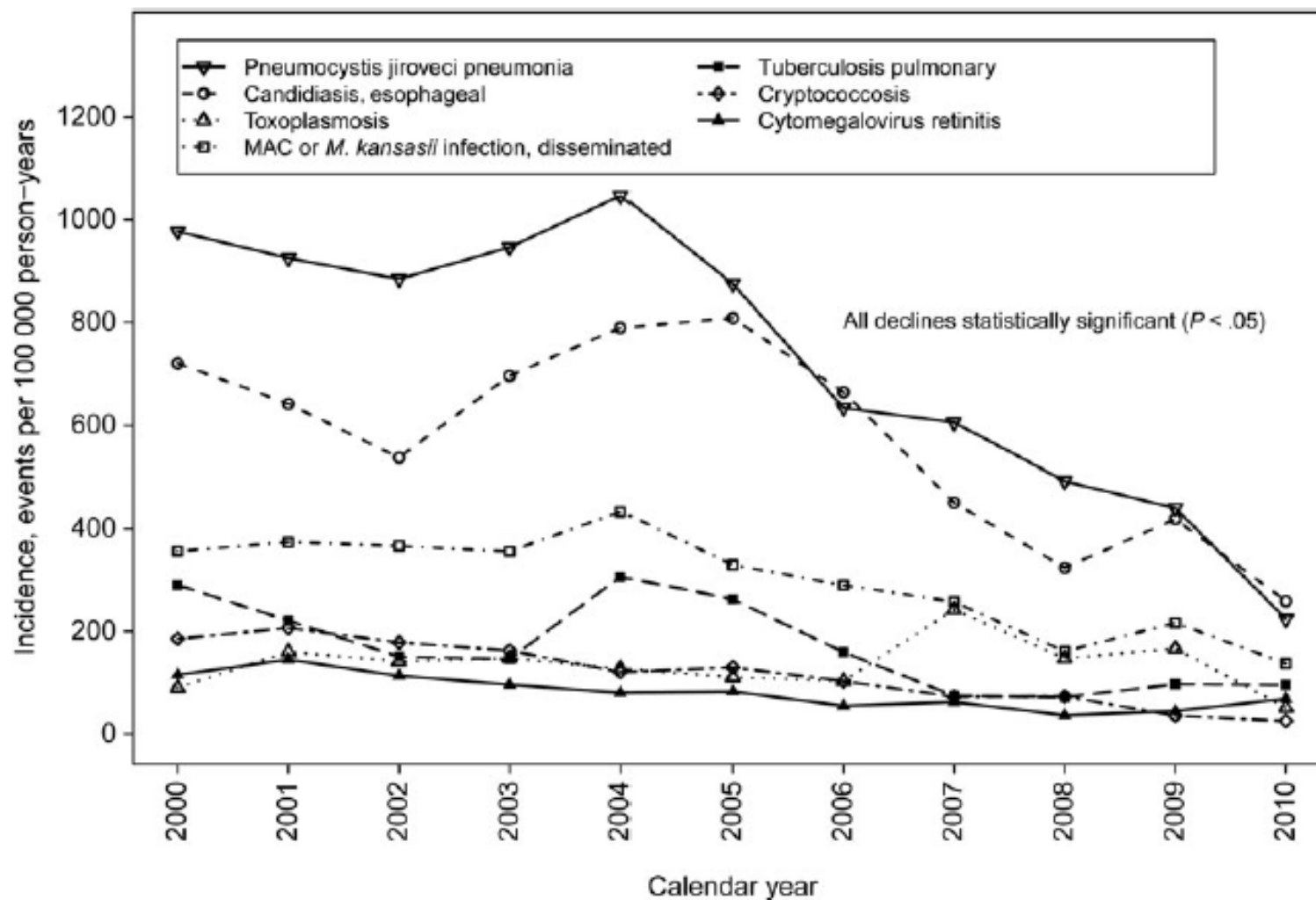
Outline

- The problem
- Bacterial
- Fungal
- Protozoal
- Viral

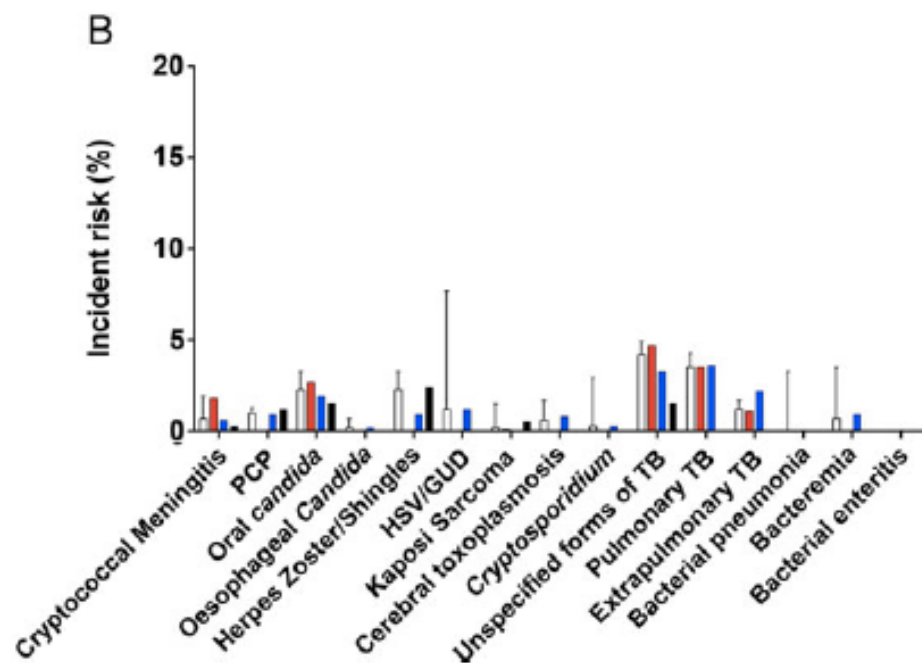
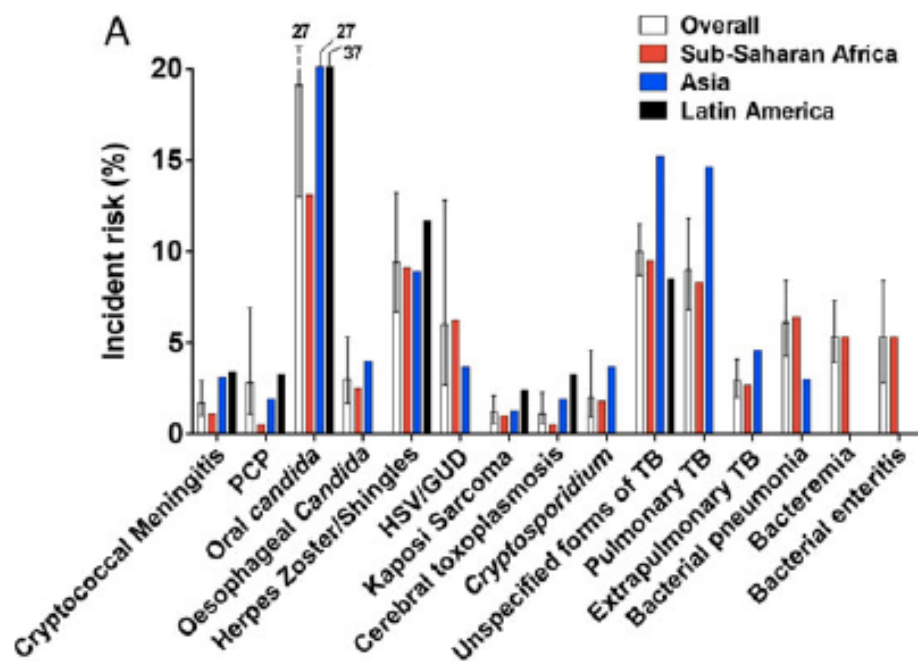
Decline in OI prevalence in HAART era: USA



Declining OI's in NA-ACCORD



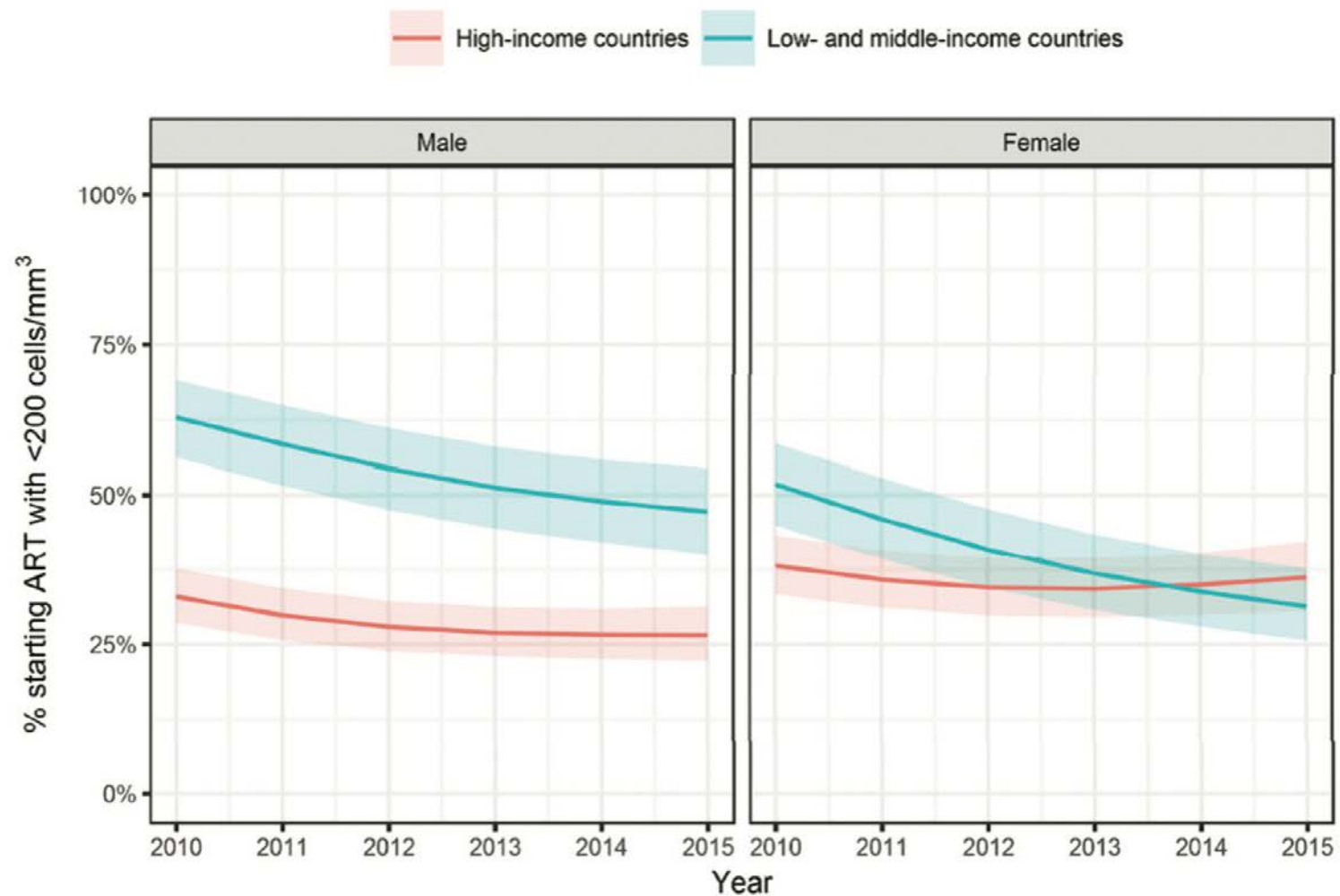
ART: Impact on OI incidence in LMICs



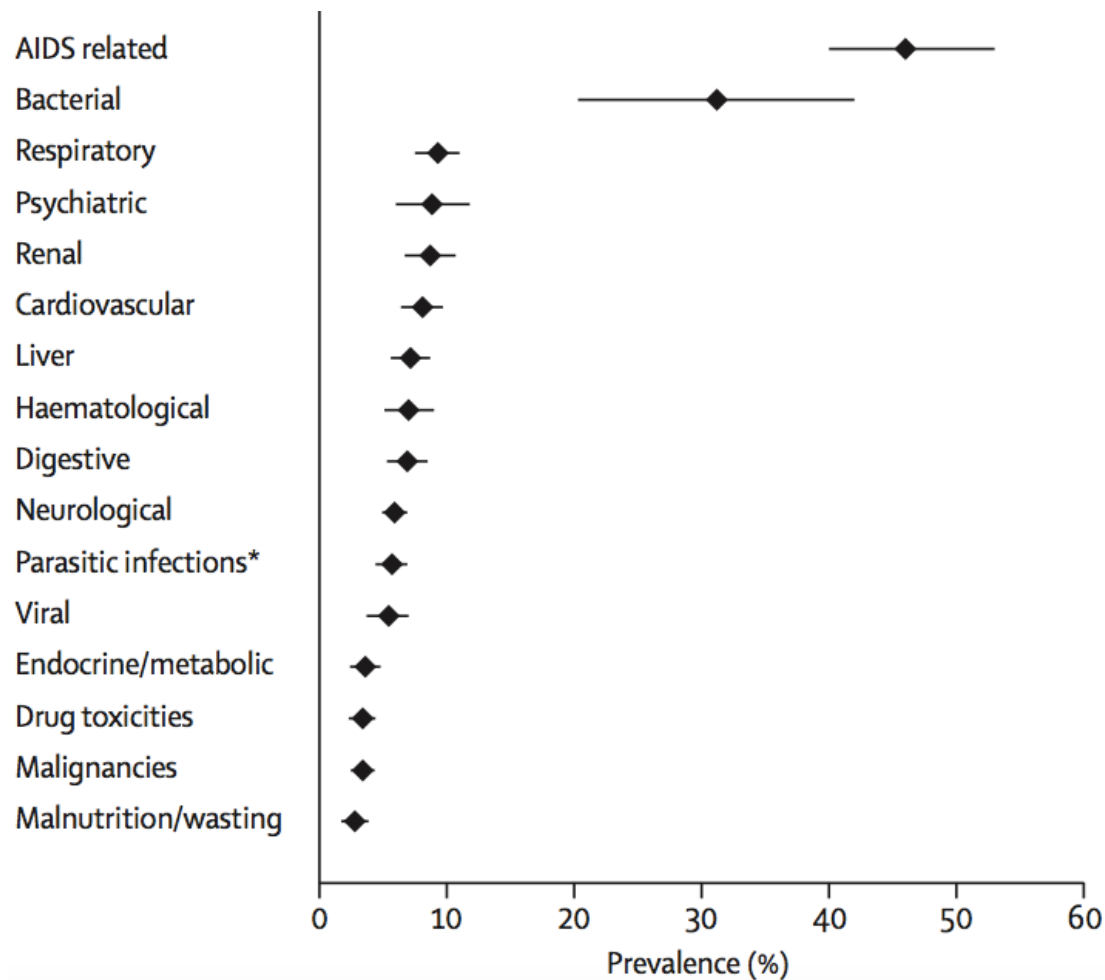
Why do OI's still occur?

- Late HIV diagnosis, missed presentations (*HIV Med.* 2016 Aug 1 (epub), *BMC Infect Dis.* 2012;12:72-72)
- Sub-optimal adherence
 - ARV (*Curr Opin HIV AIDS.* 2015 Jul;10(4):219-25)
 - ART failure
 - Prophylaxis
- Delayed identification of ARV failure
- Immunologic disconnect (*J Int AIDS Soc.* 2014 Mar 3;17:18651)
- Functional immune reconstitution (*Clin Infect Dis* 2009;48:609–11)

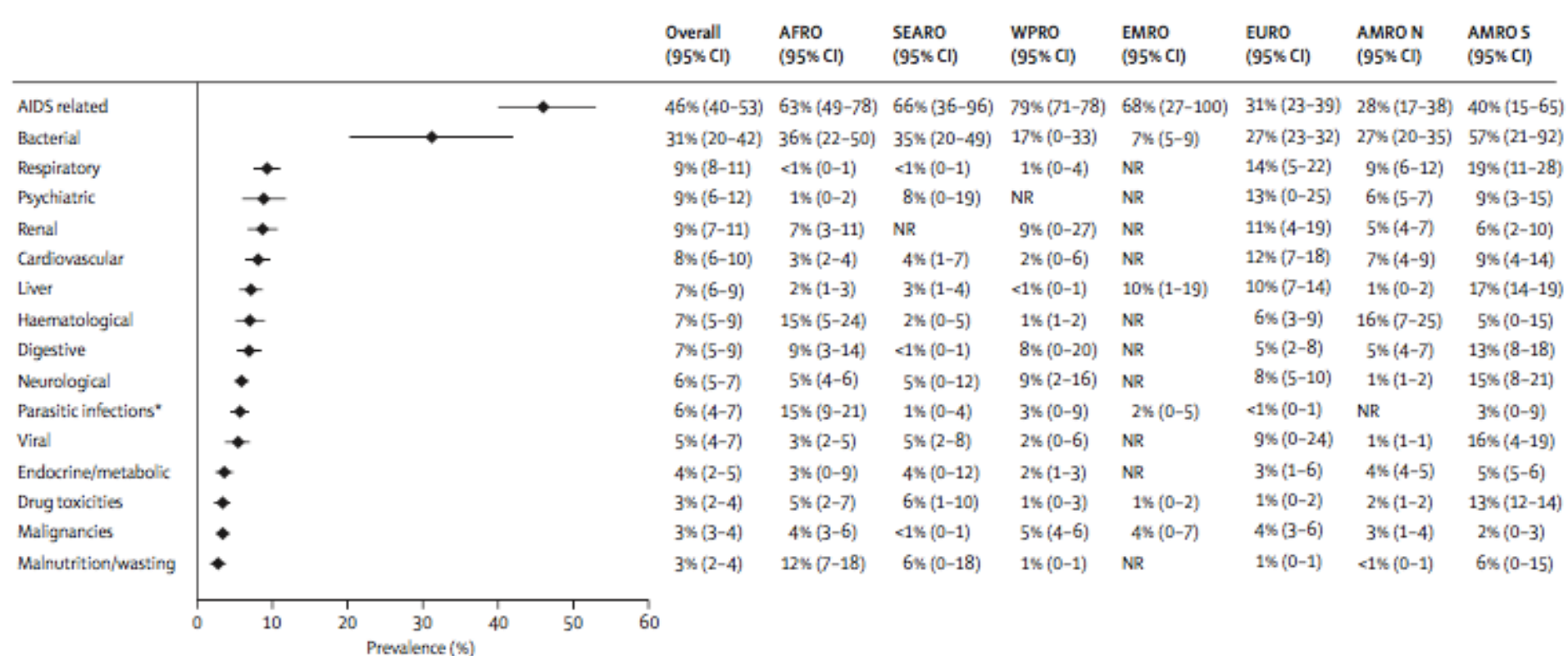
Advanced disease at ART initiation



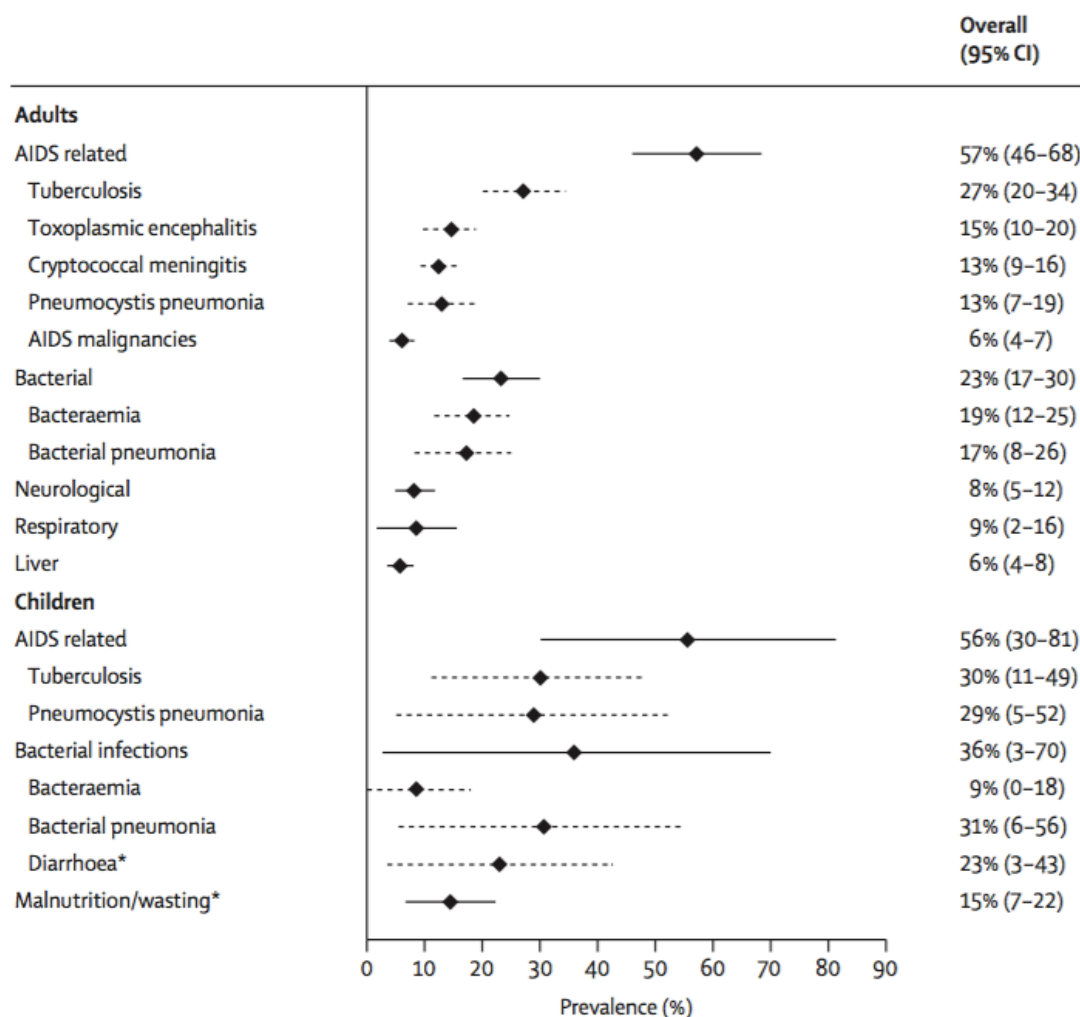
Causes of hospital admissions in adult PLHIV



Causes of hospital admissions in adult PLHIV



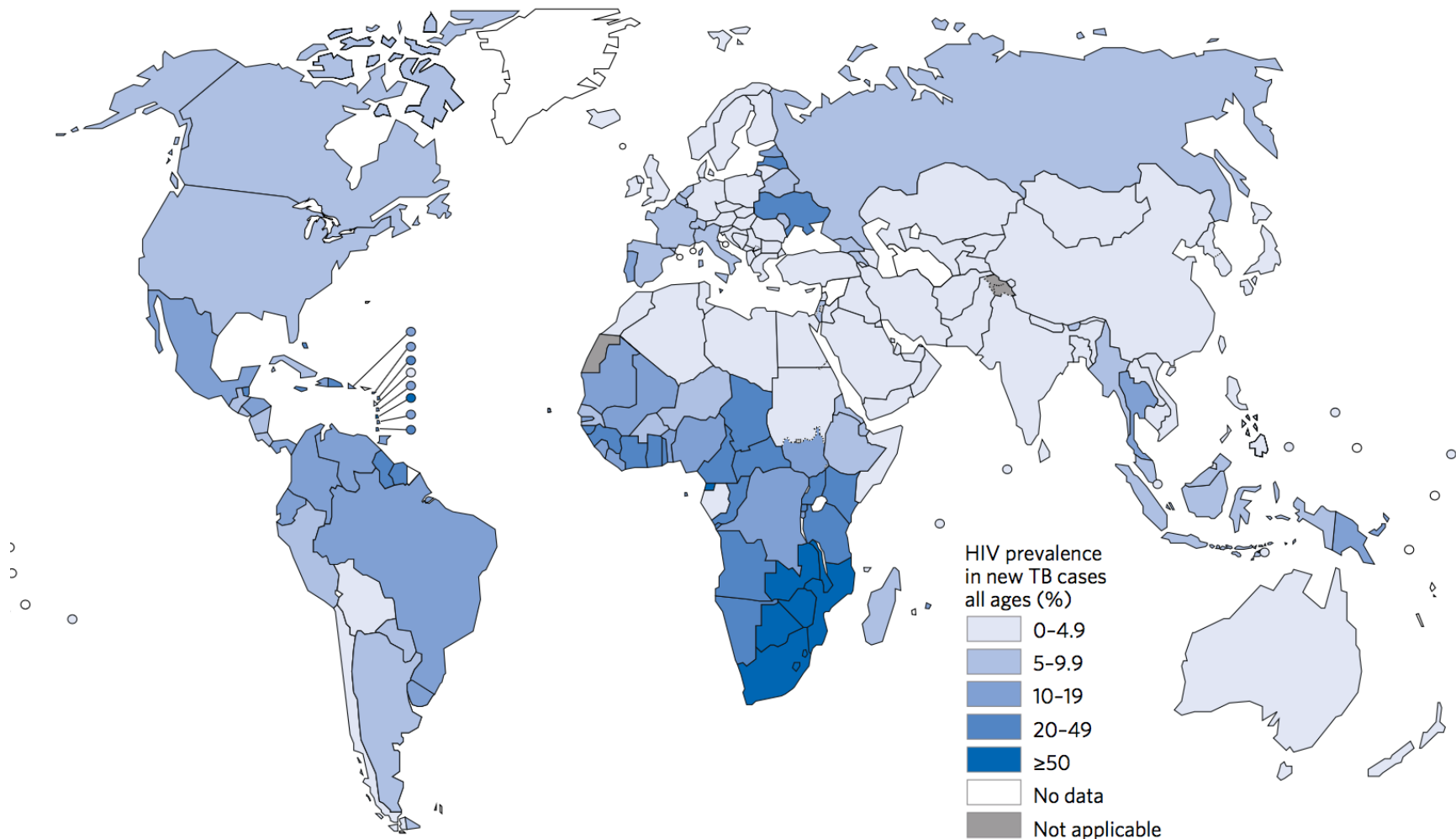
Causes of in-hospital mortality



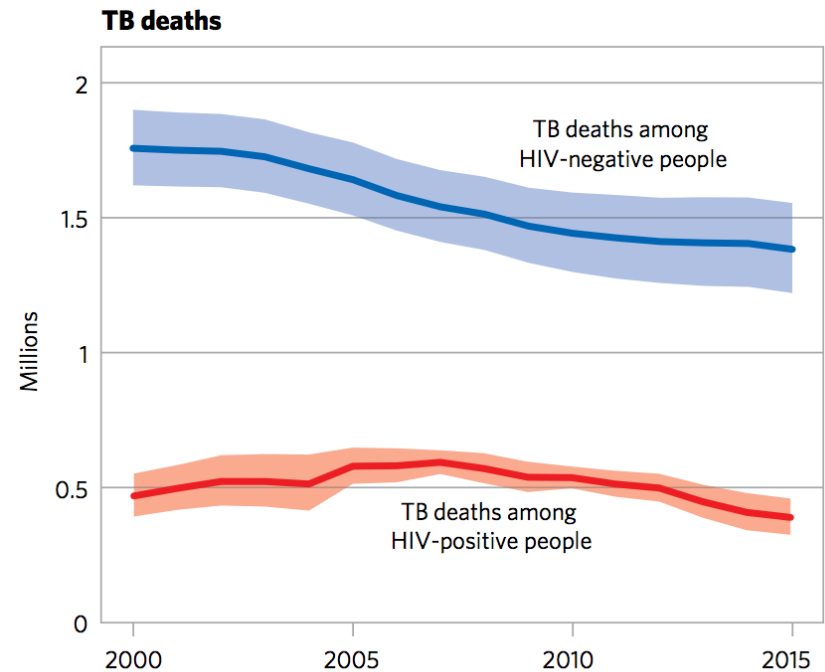
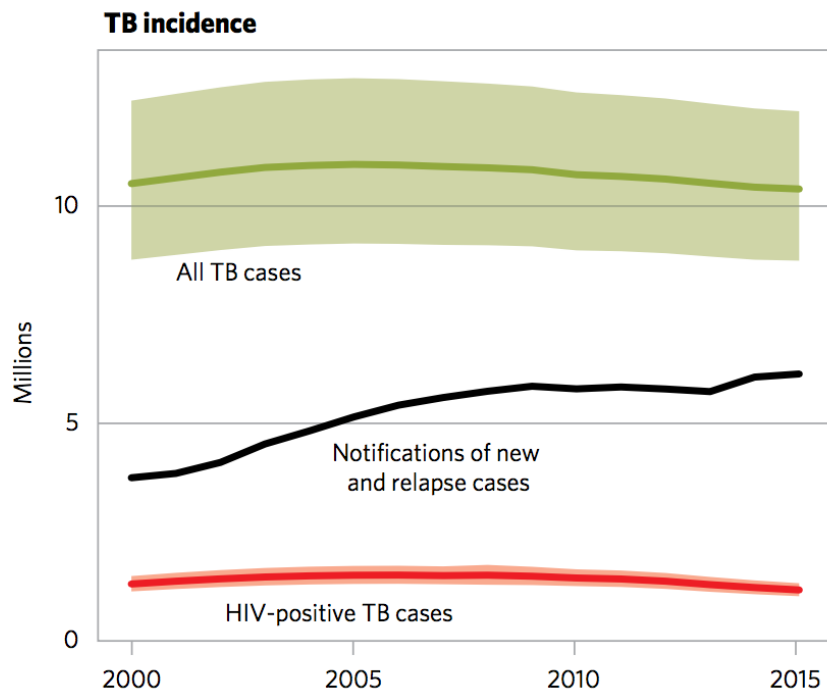
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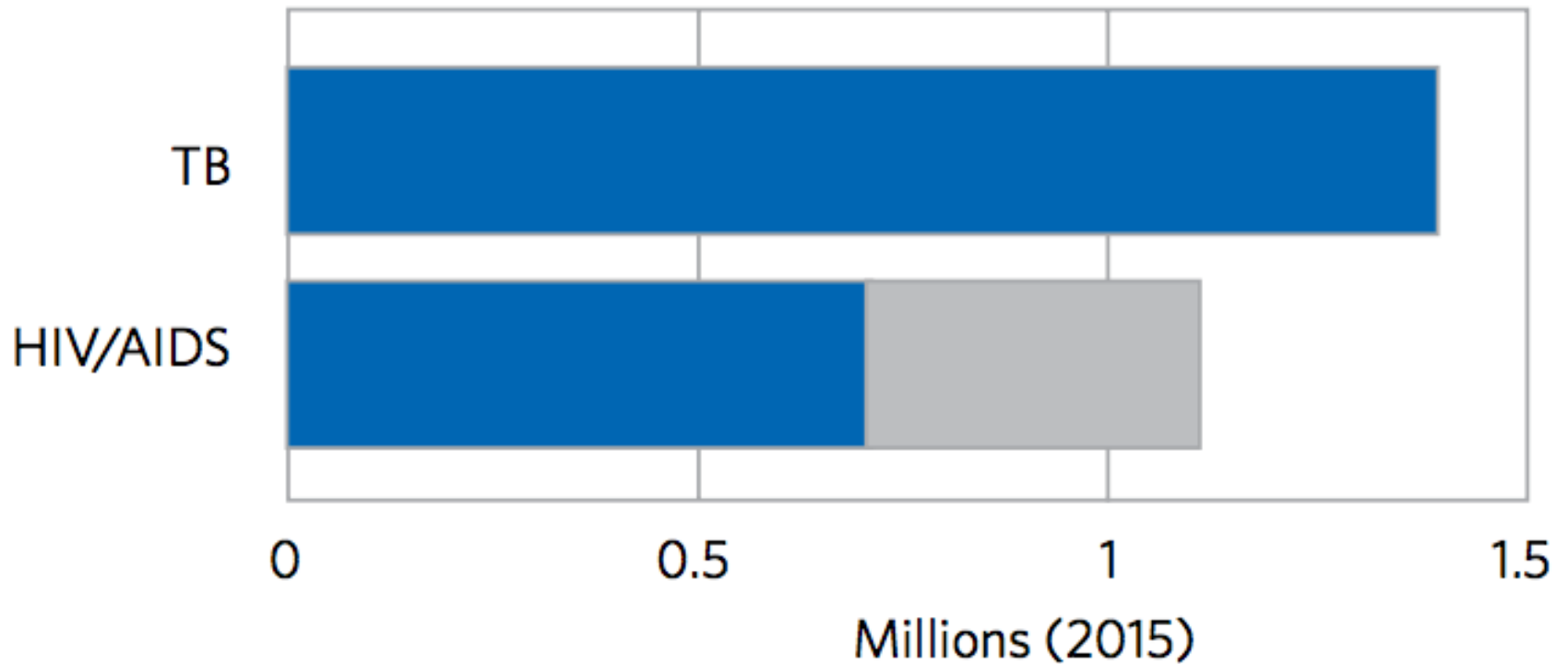
HIV prevalence: New/relapsed TB: 2015



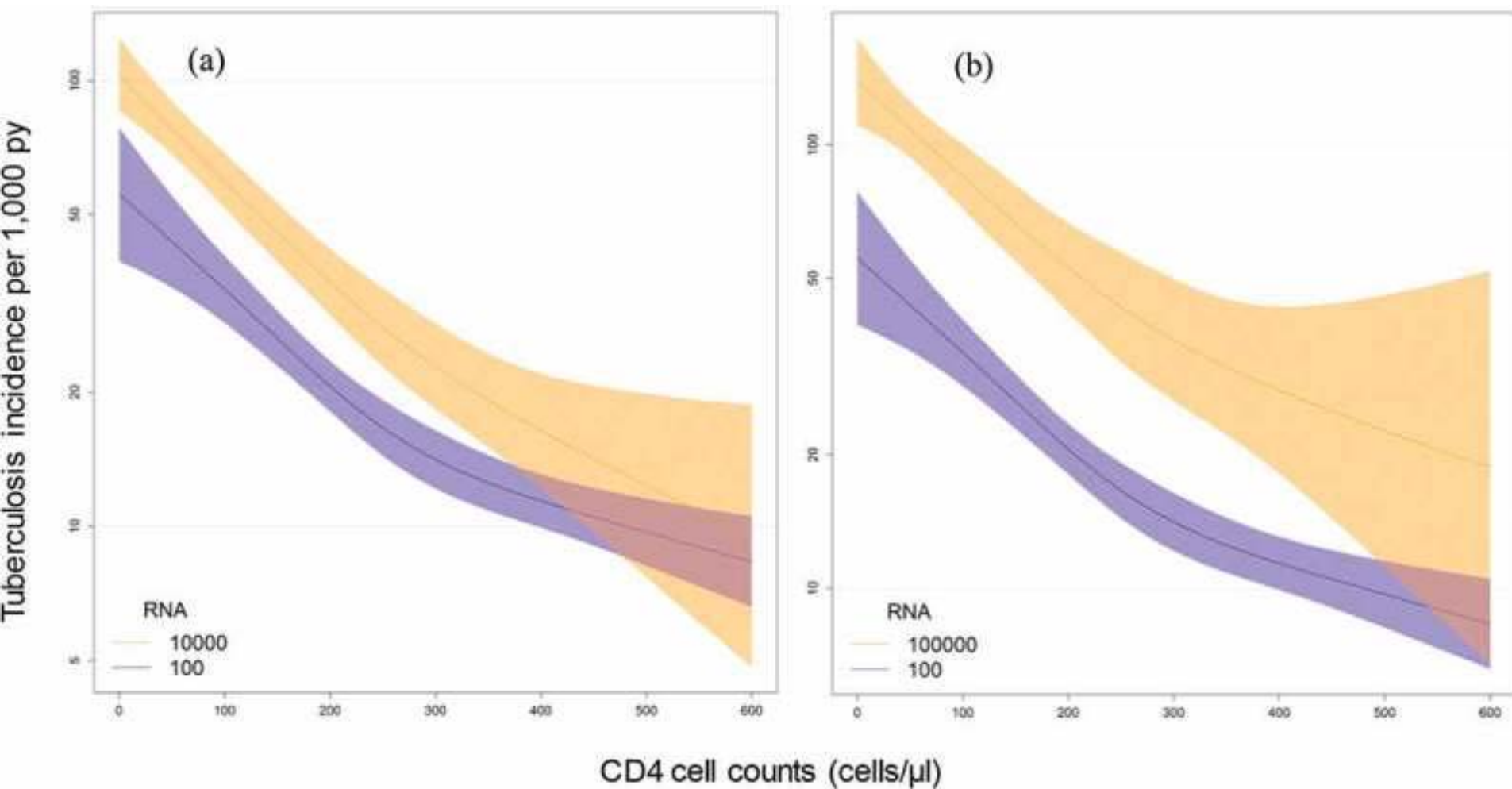
Global TB incidence and deaths



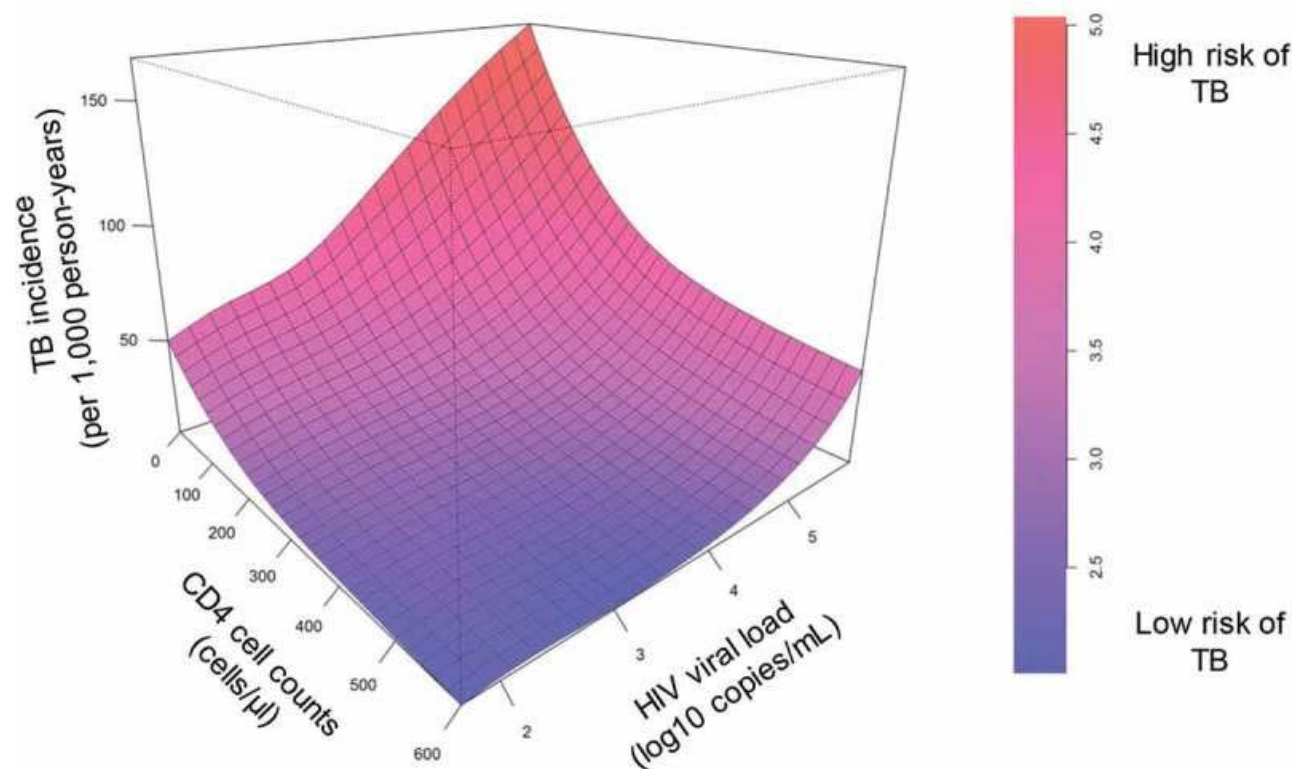
HIV/AIDS and TB deaths in 2015



VL is independent risk factor for TB in SA

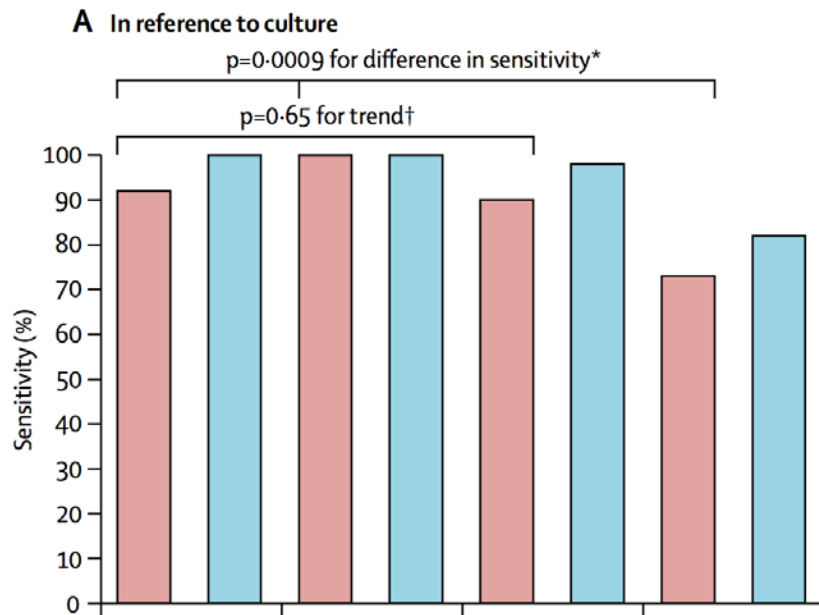


VL independent risk factor for TB in SA

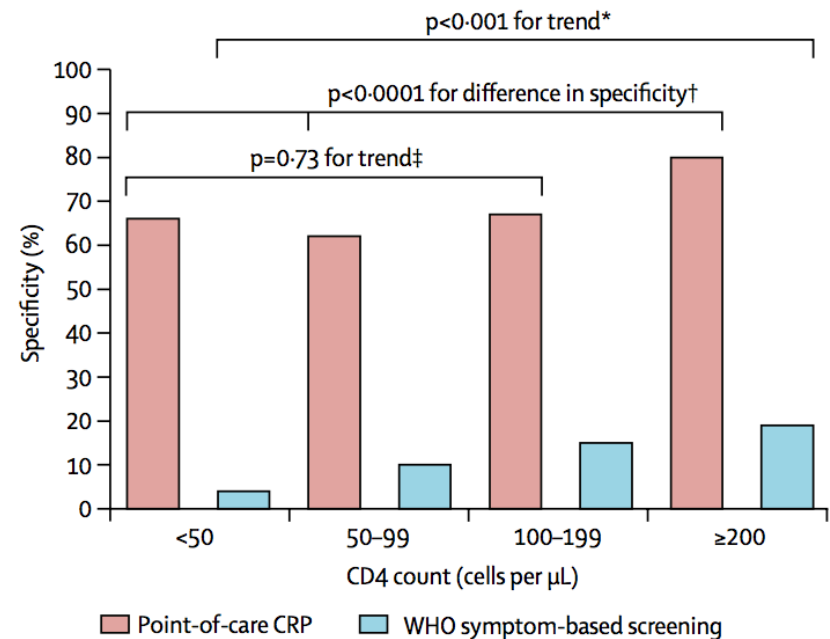


Point of care CRP for TB screening for PLHIV initiating ART

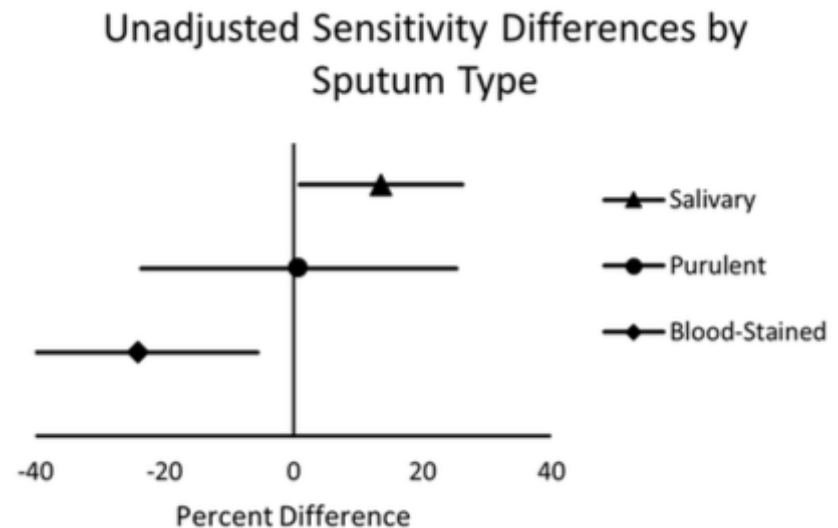
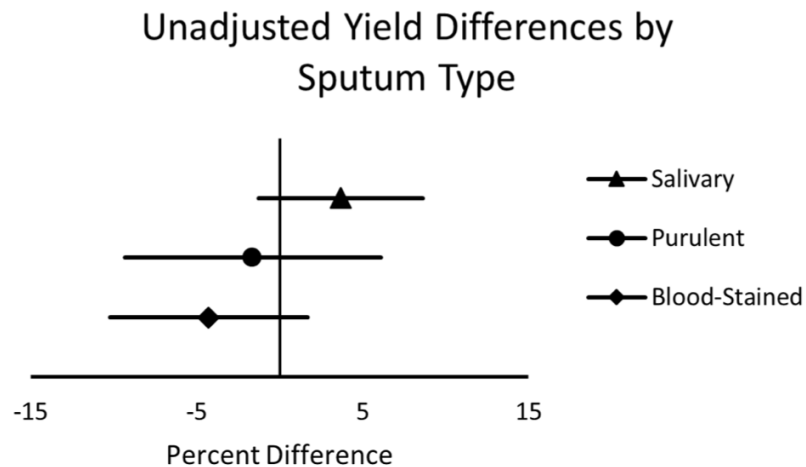
Sensitivity



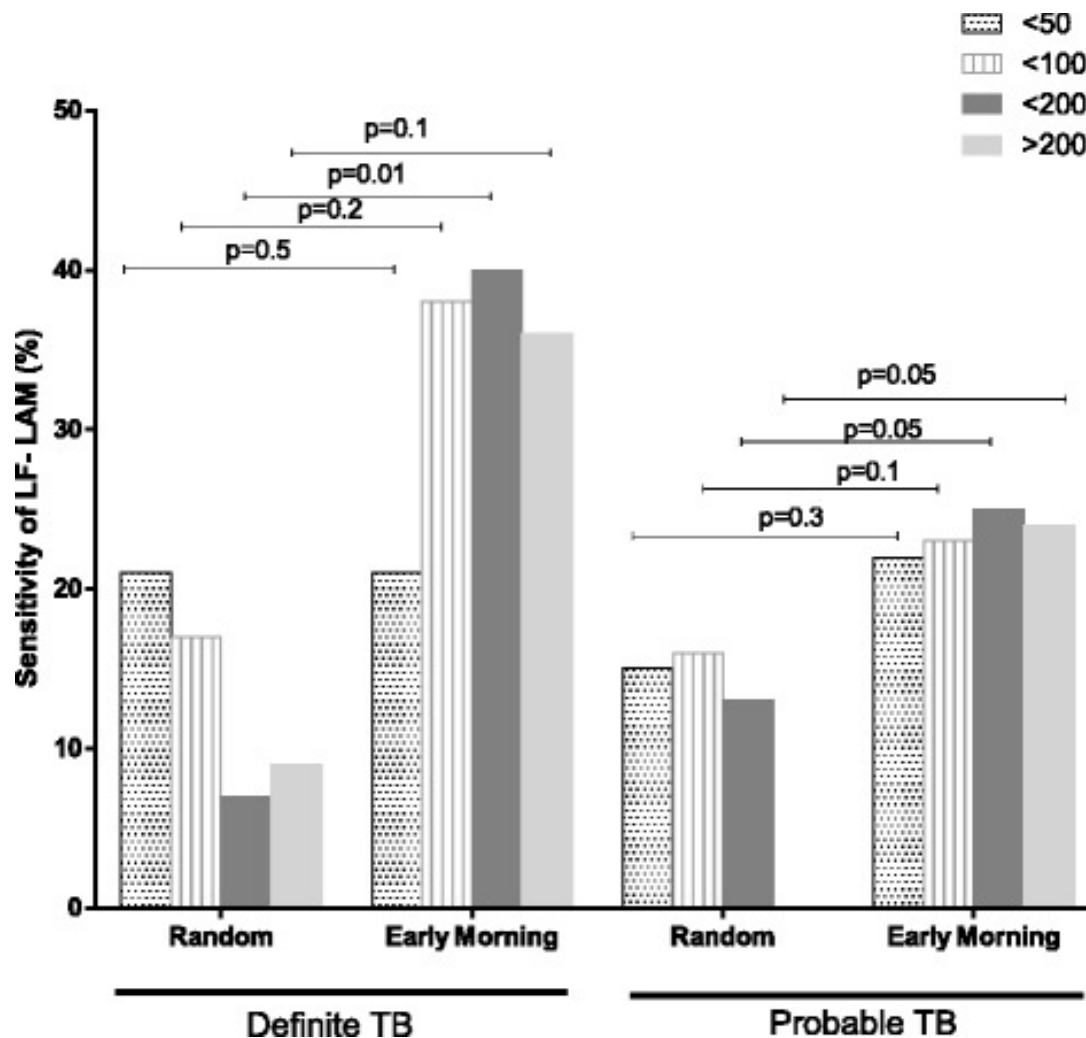
Specificity



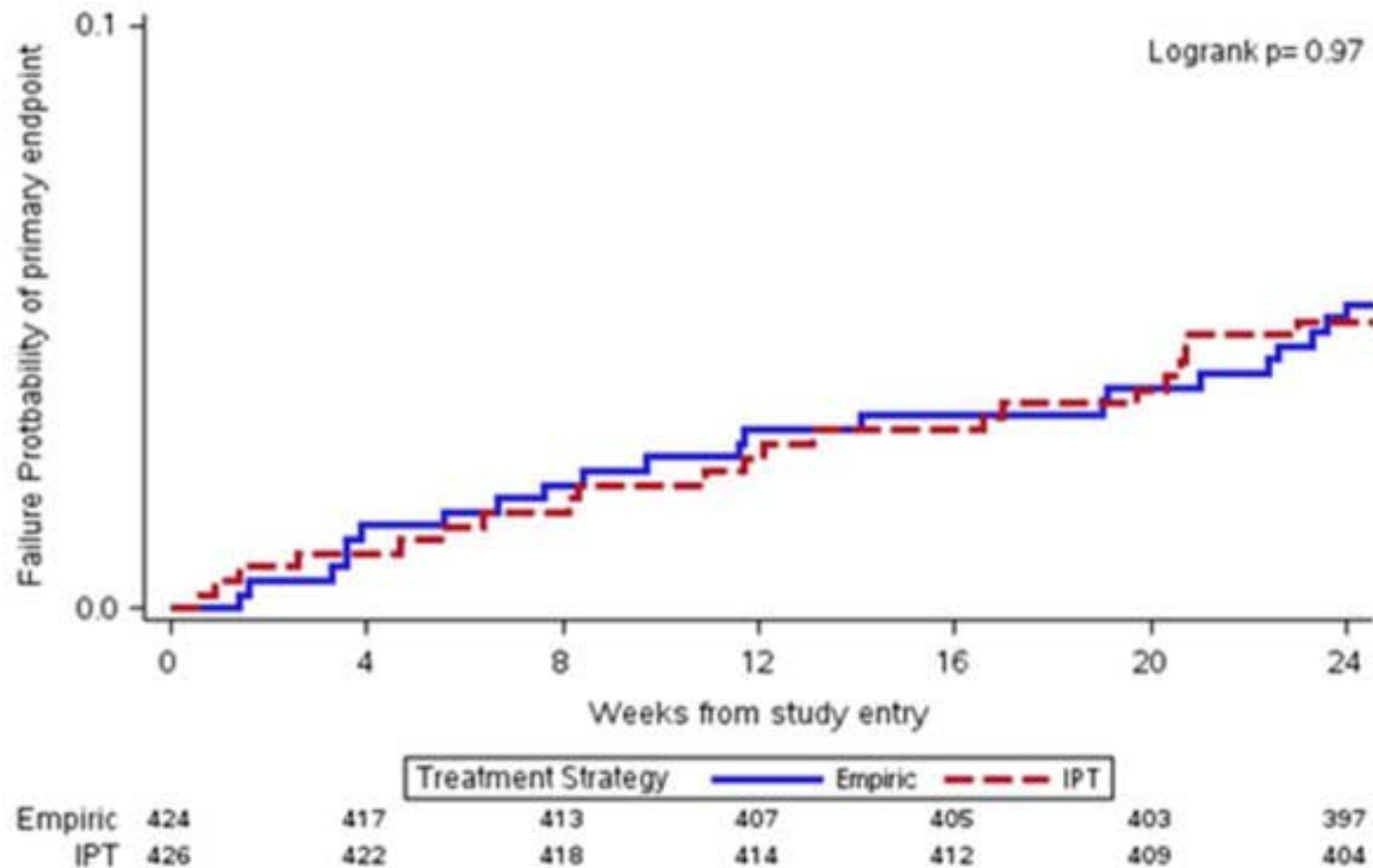
Sputum quality and diagnostic accuracy of Xpert



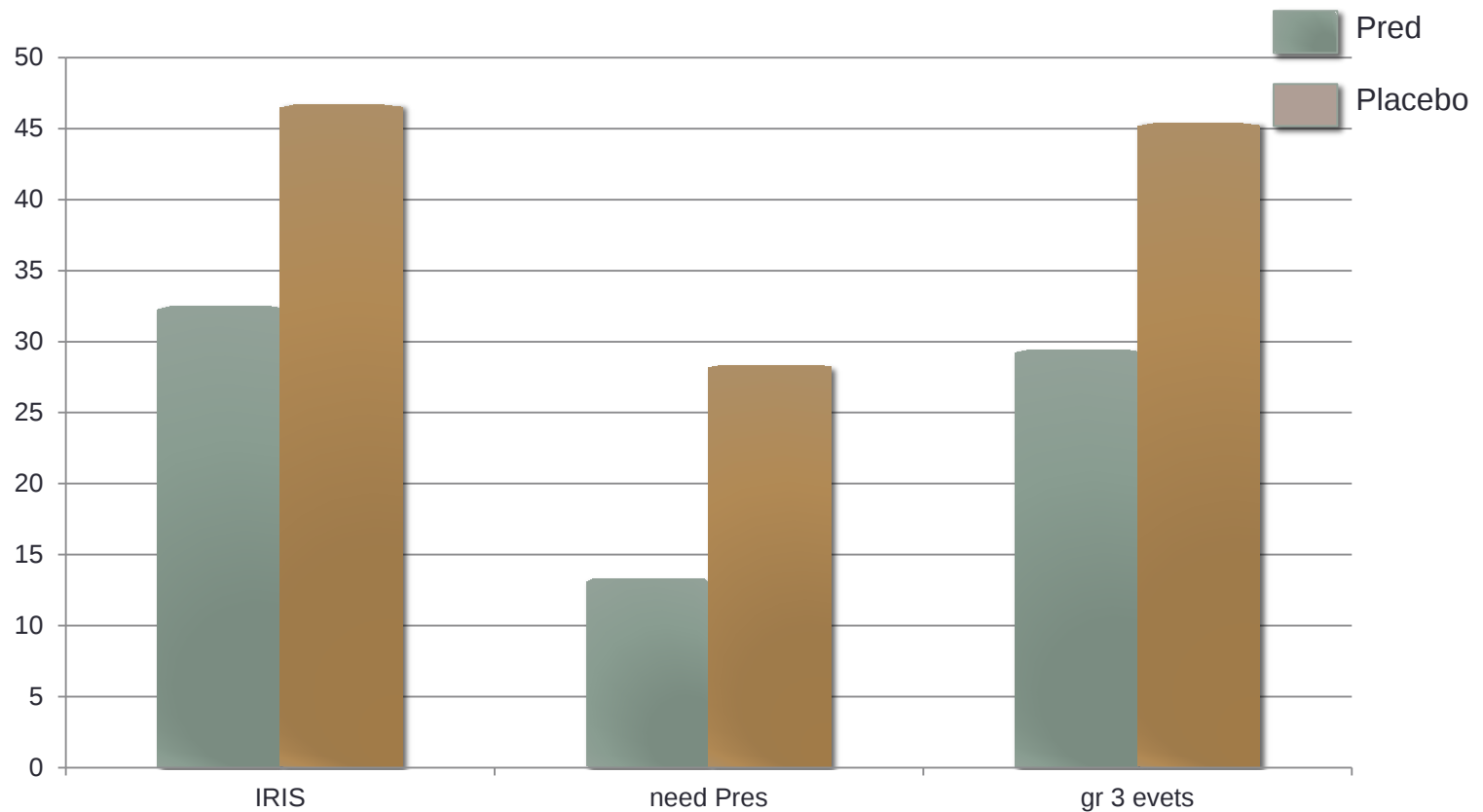
Early morning urinary sample for TB-LAM



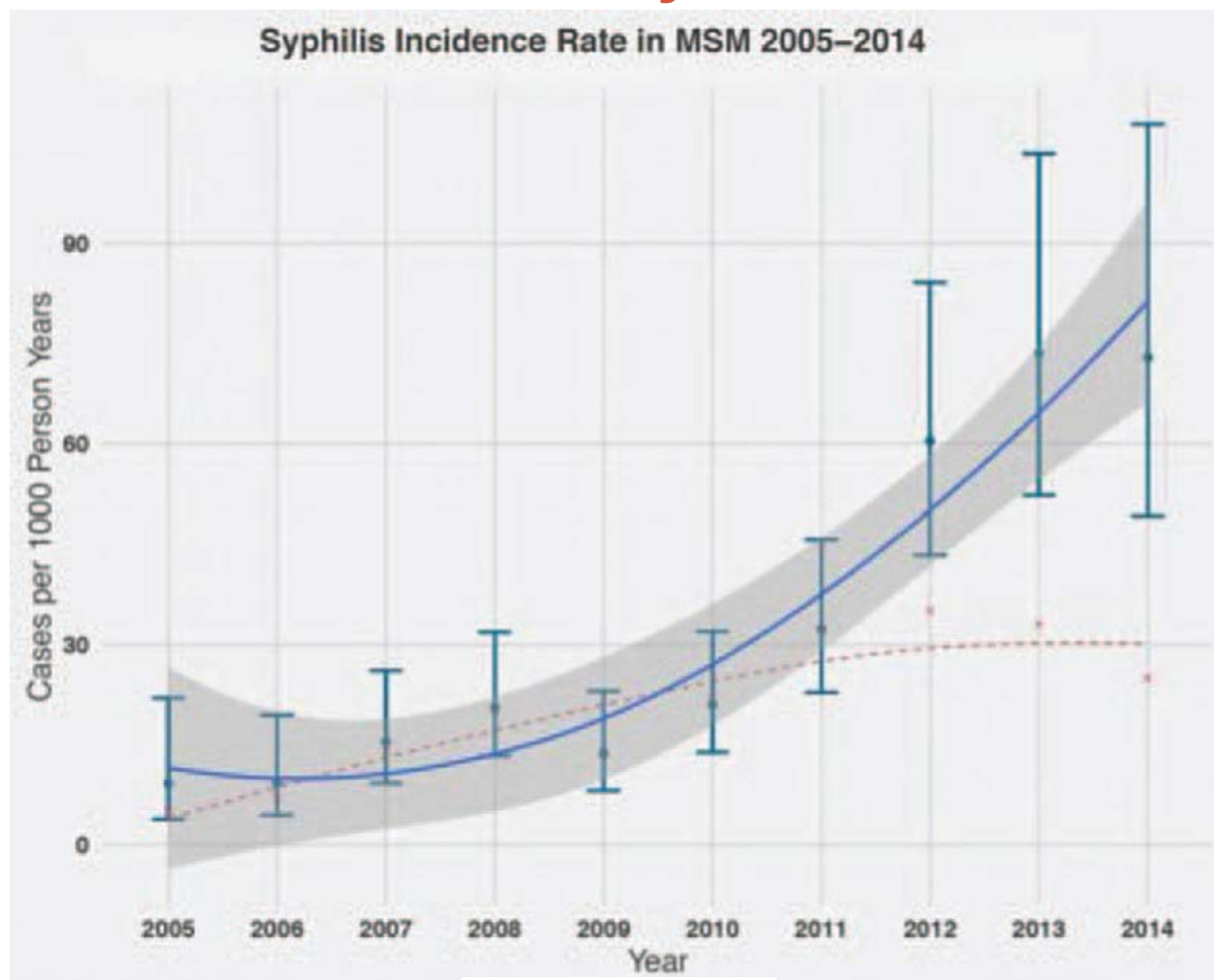
REMEMBER: EMPIRICAL ATT vs IPT with ART



PredART: Prednisolone to prevent paradoxical TB IRIS

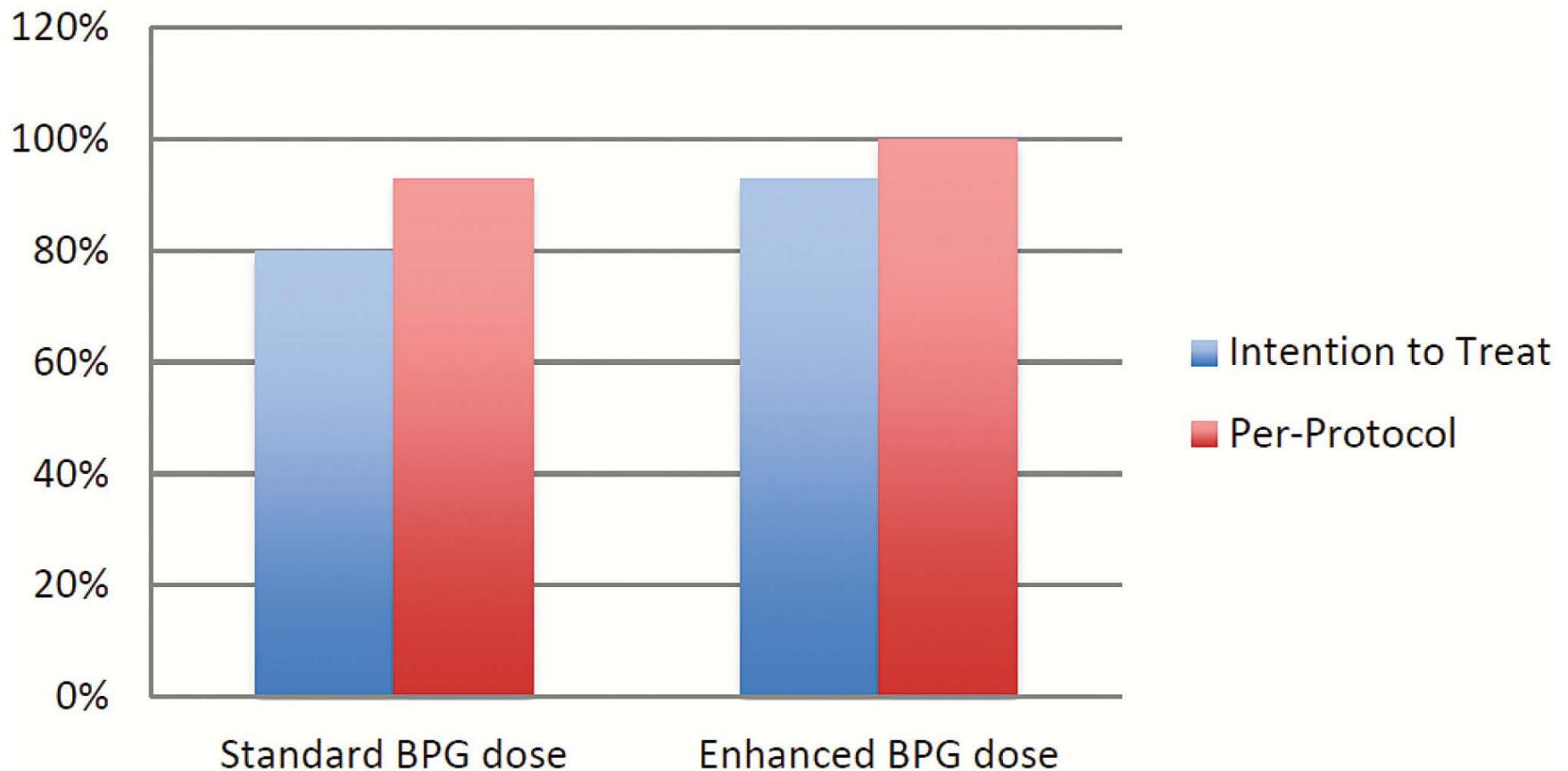


Syphilis incidence amongst HIV + MSM in Swiss HIV cohort study in ART era

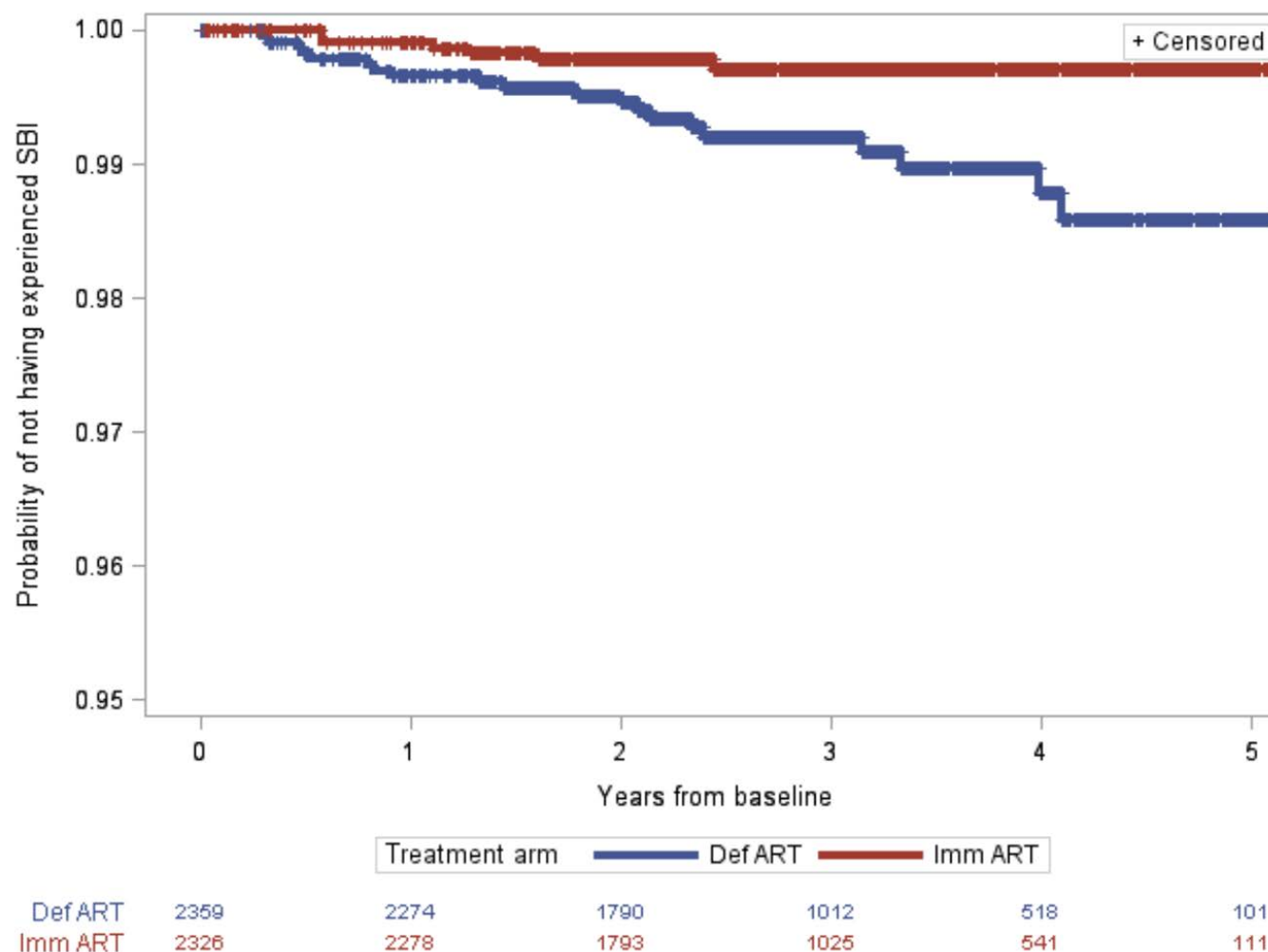


Single dose BPG effective to treat early syphilis amongst PLHIV

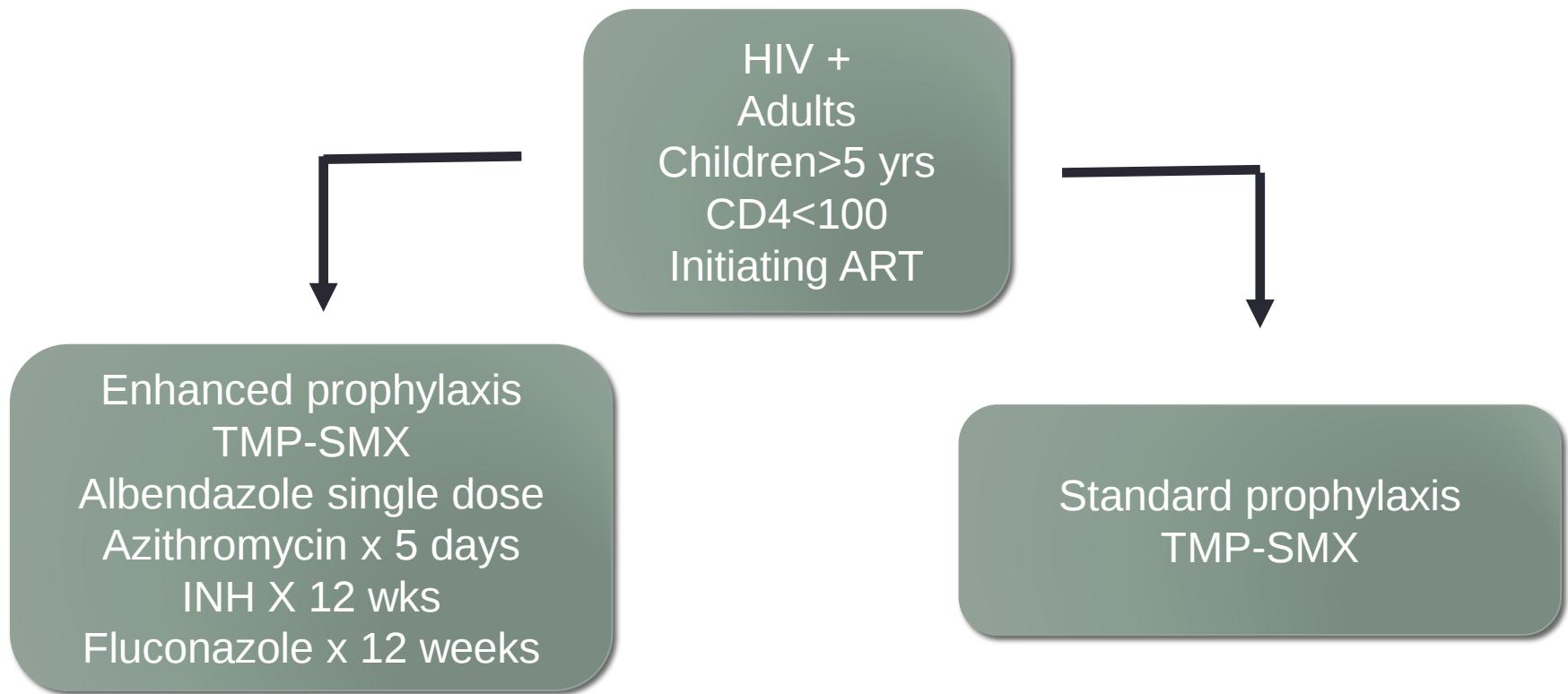
Serological Response



Early ART reduces incidence of severe bacterial infections: START study



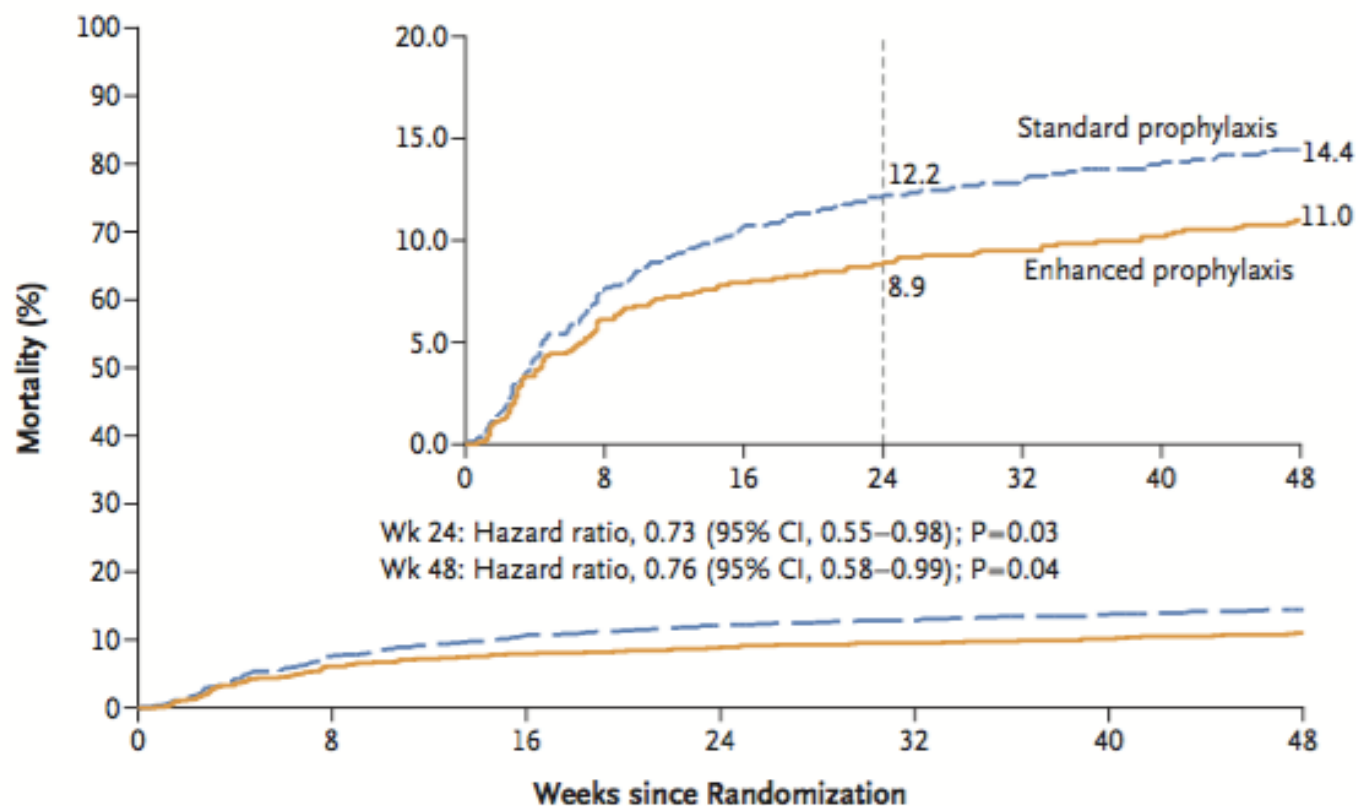
REALITY: Enhanced prophylaxis amongst African PLHIV with CD4<100 at ART initiation



Primary outcome
Death (any cause) up to 24 wks

Overall mortality at 48 weeks

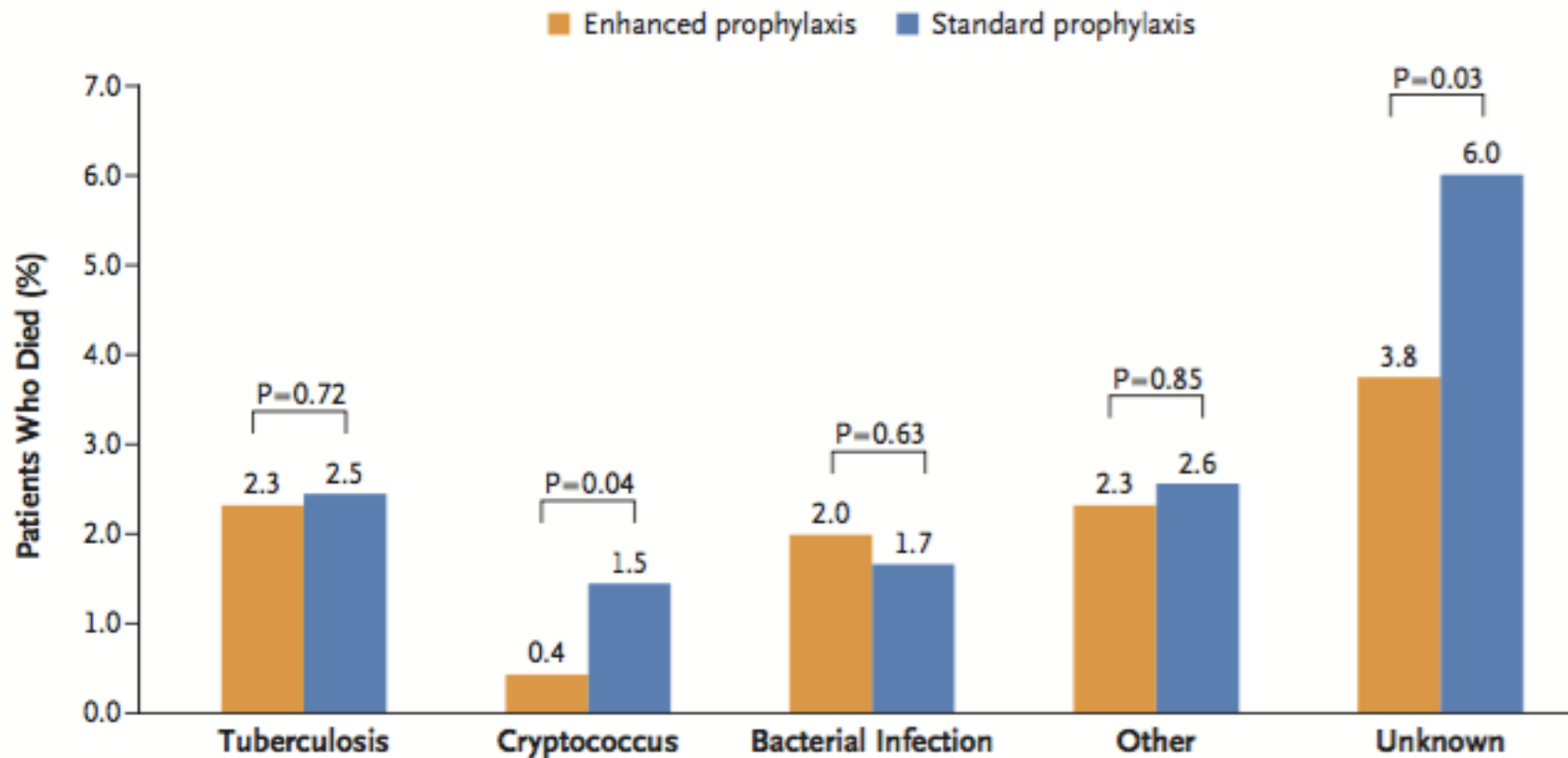
A Overall Mortality



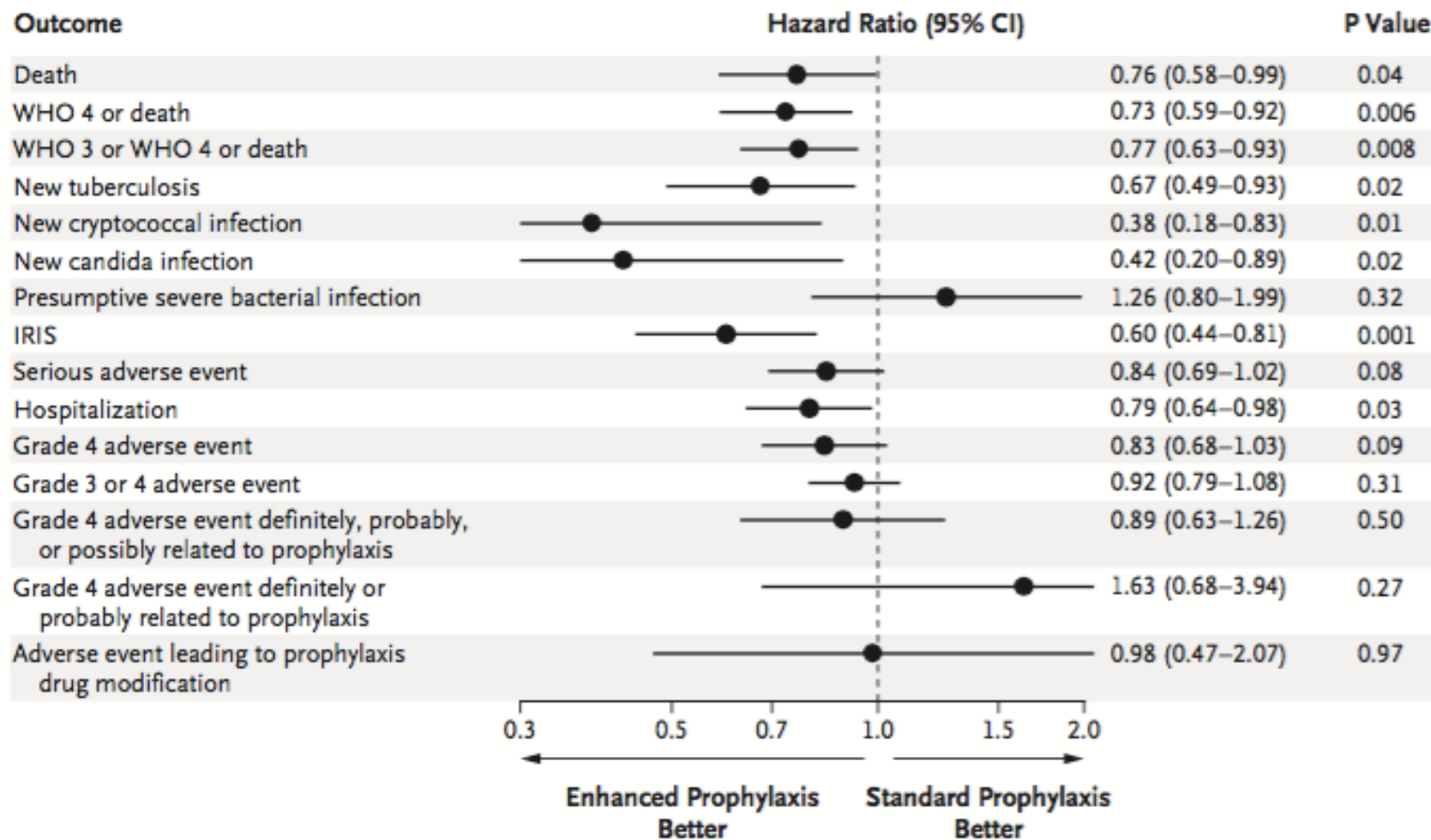
No. at Risk (no. of deaths)

Standard prophylaxis	899 (67)	816 (27)	786 (13)	768 (7)	754 (7)	739 (6)	637
Enhanced prophylaxis	906 (55)	839 (16)	817 (8)	807 (6)	797 (6)	787 (7)	689

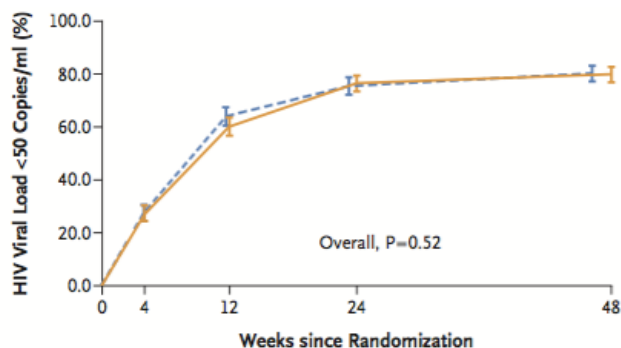
Main causes of death at 48 weeks



Secondary or other outcomes at 48 wks

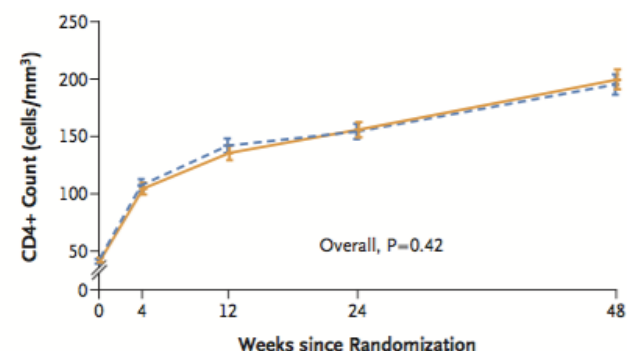


Good virologic and immunologic success



Percentage
Enhanced prophylaxis
Standard prophylaxis
P Value

27.0	60.2	76.6	80.0
27.6	64.1	75.5	80.3
0.79	0.11	0.62	0.88



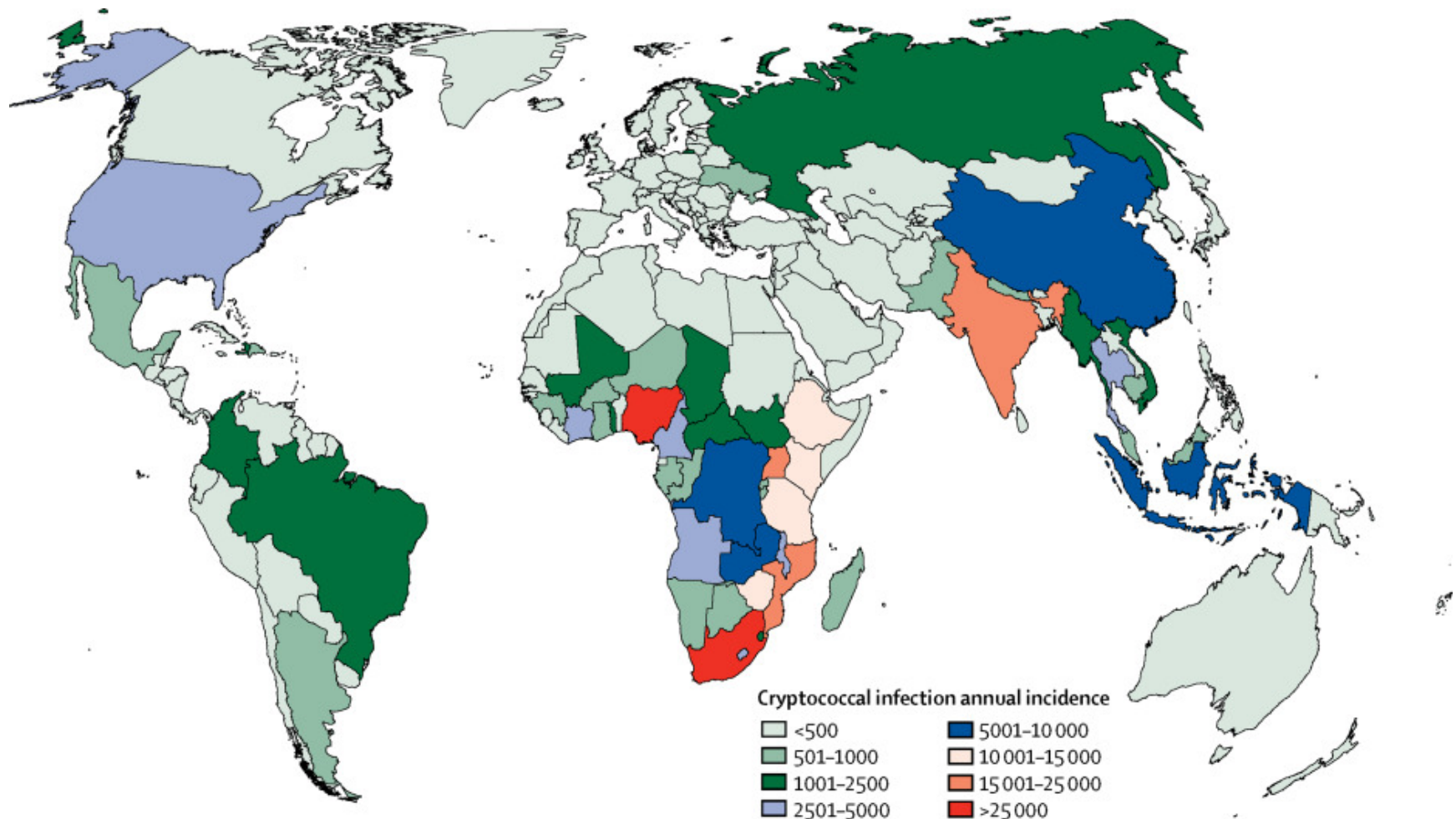
Mean Change from Baseline
Enhanced prophylaxis
Standard prophylaxis
P Value

+62	+92	+113	+156
+66	+100	+112	+152
0.25	0.07	0.85	0.92

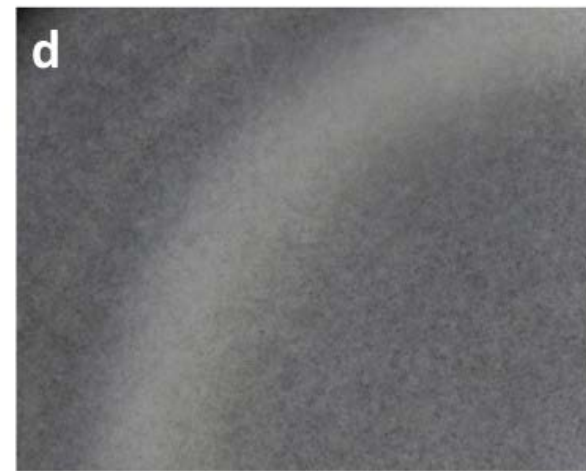
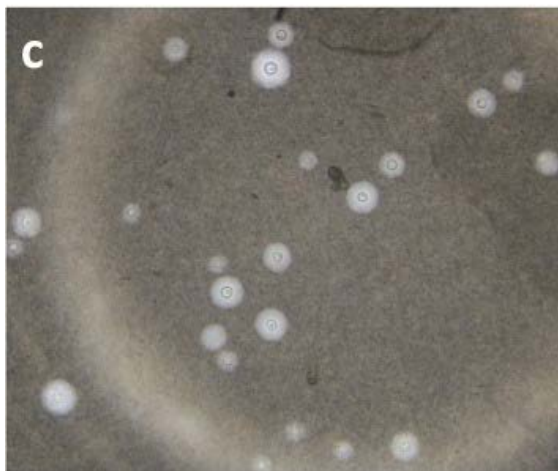
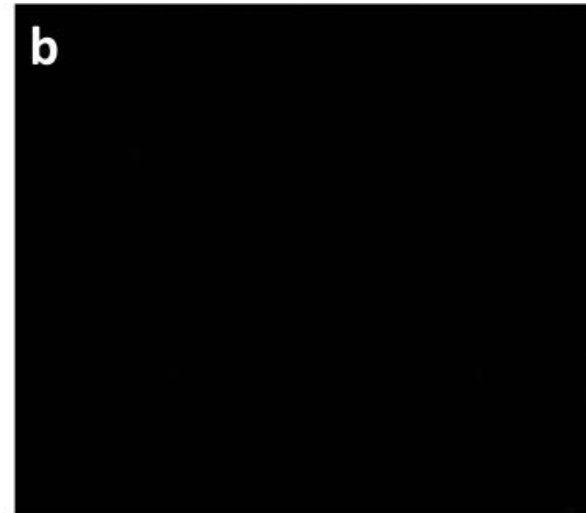
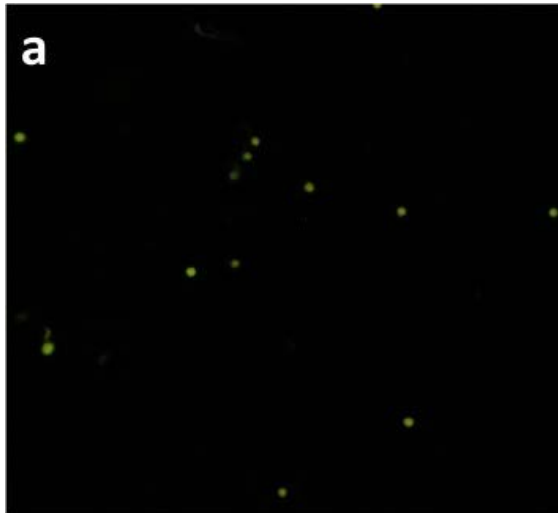
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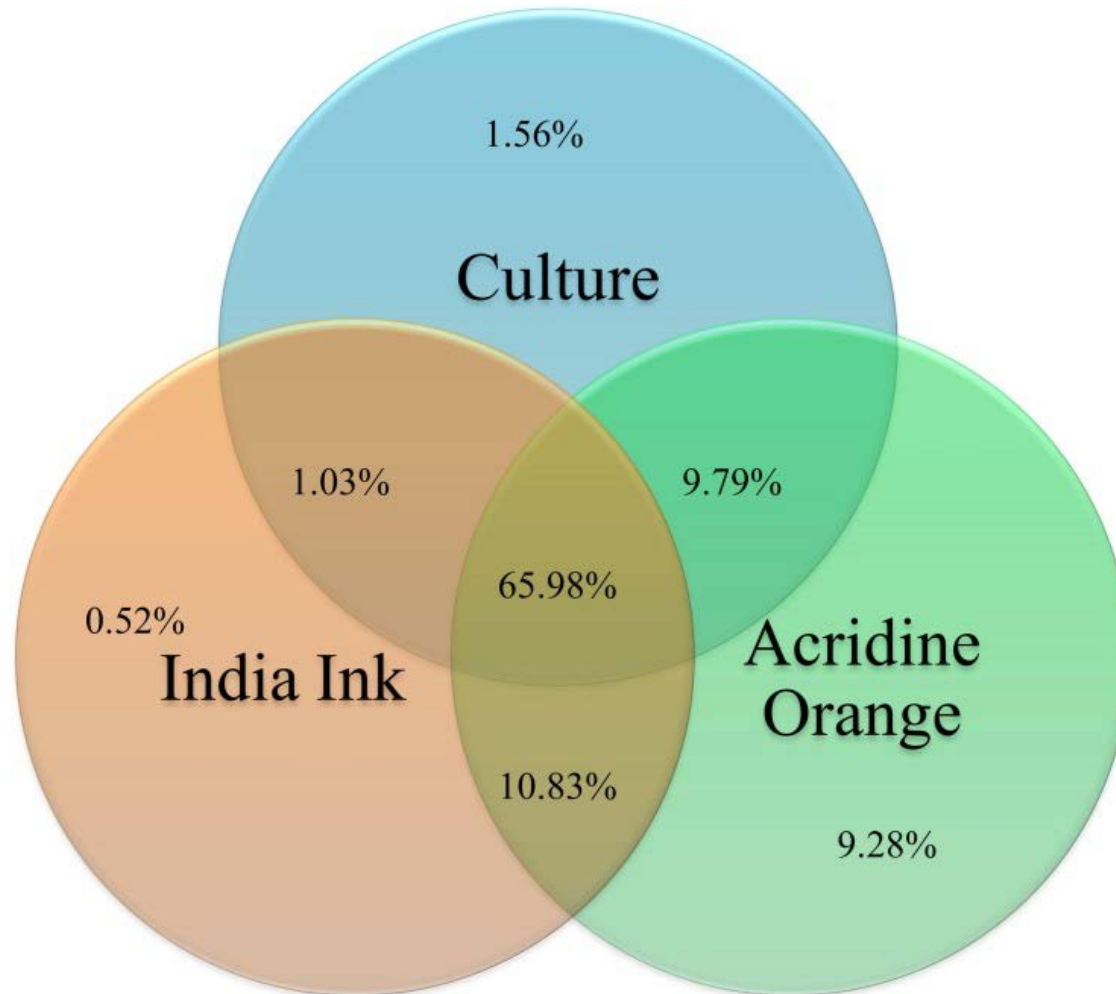
Annual incidence of cryptococcal infection: 2014



Acridine orange vs India Ink for CM



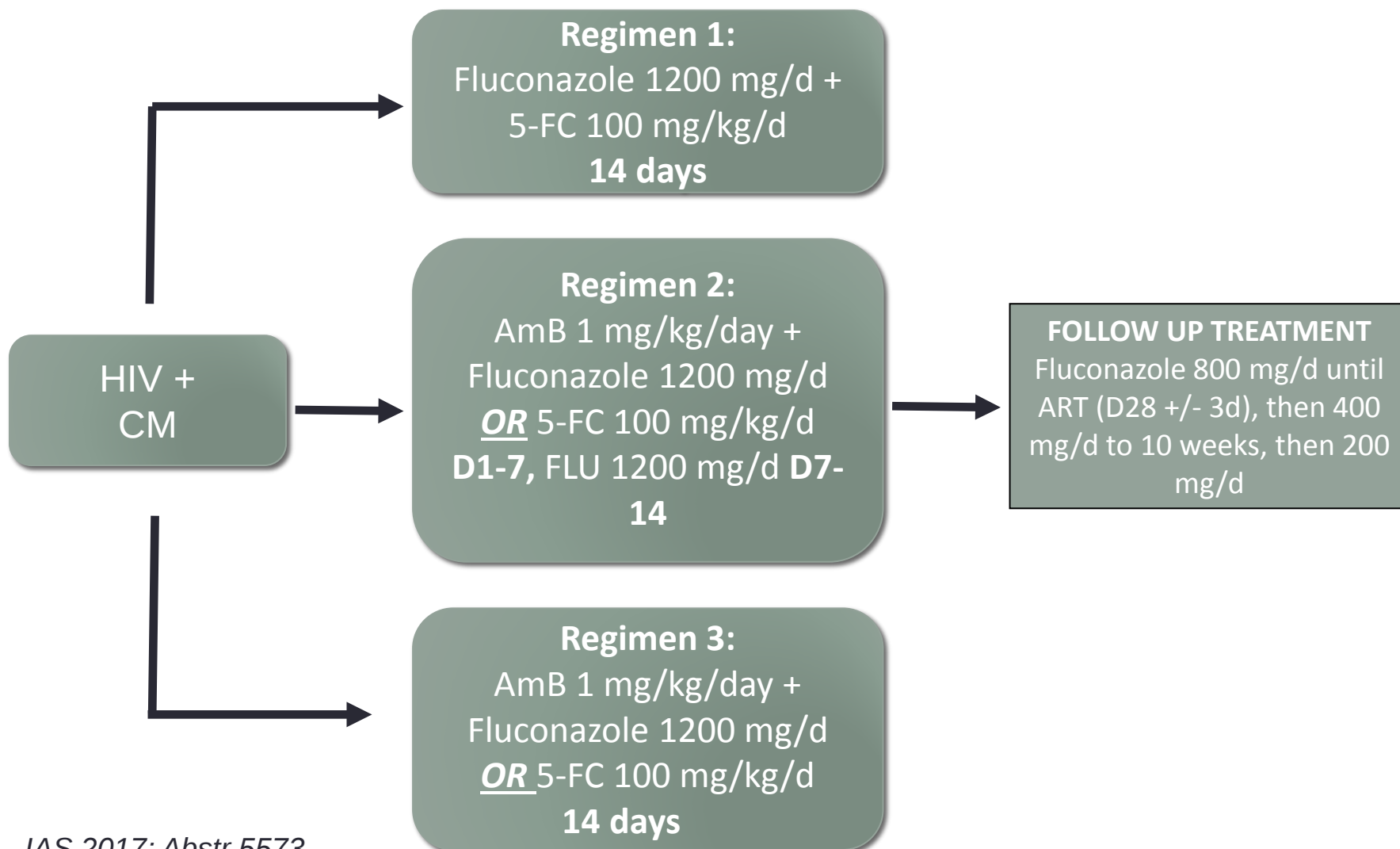
Acridine orange vs India Ink for CM



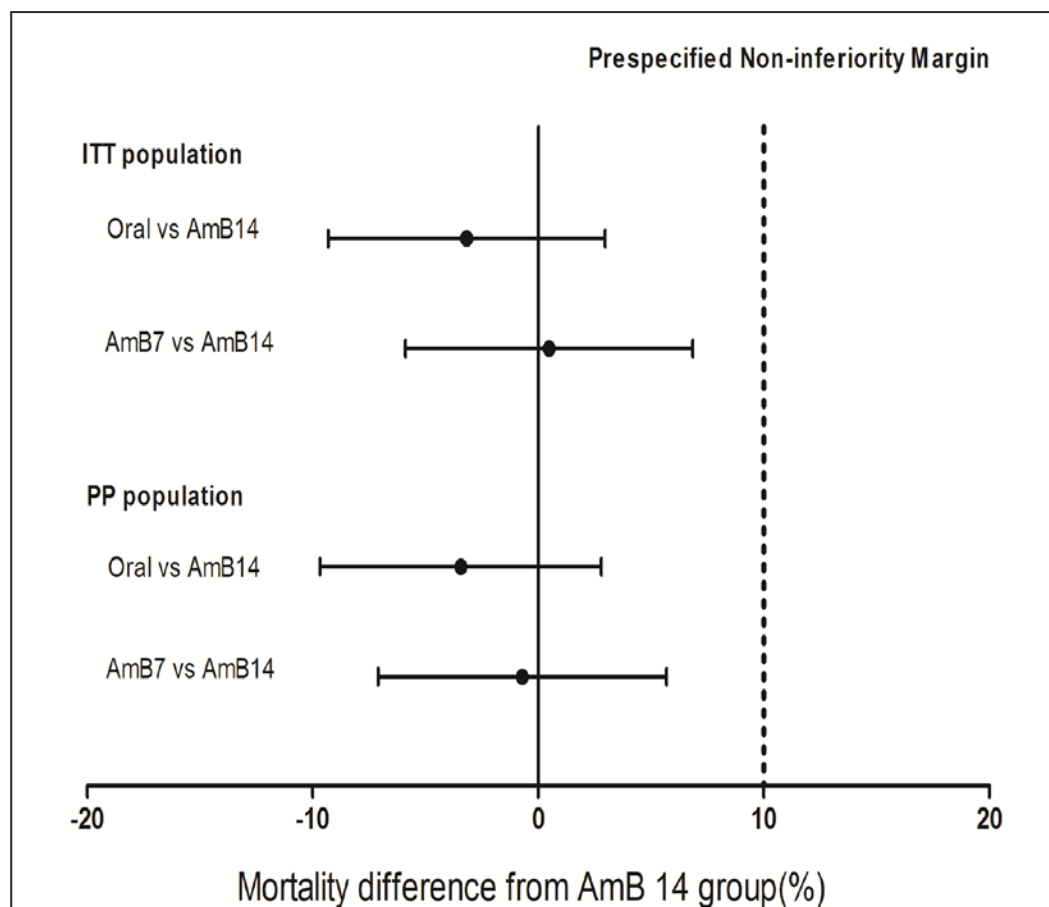
N = 194

ALL SAMPLES CRAG LFA POSITIVE

ACTA: Treatment of CM



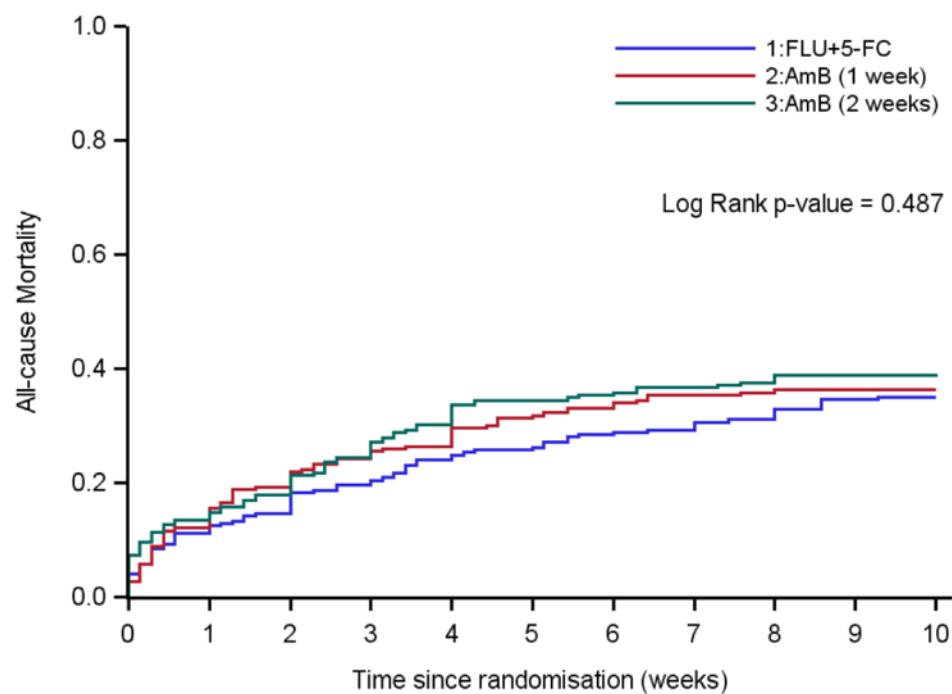
ACTA: Mortality risk difference



Better than 2wk AmB

Worse than 2wk AmB

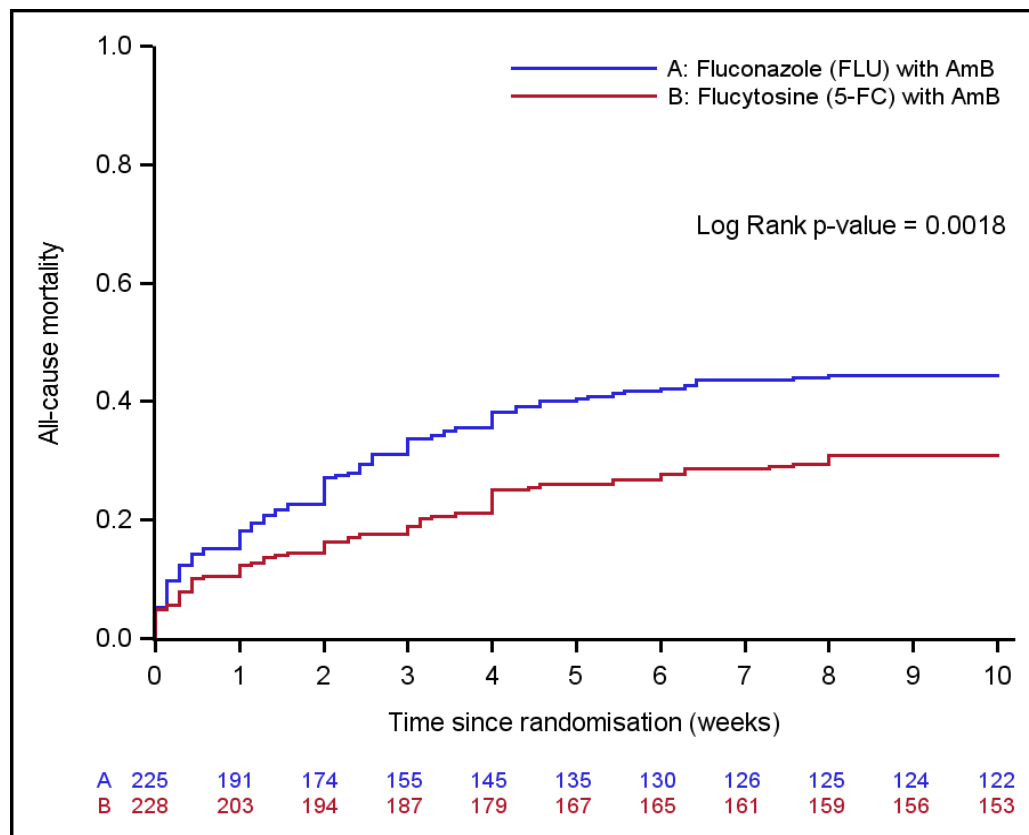
ACTA: Mortality risk difference



1	225	200	192	181	171	167	161	159	155	147	144
2	224	196	180	169	164	152	148	143	142	141	139
3	229	198	188	173	160	150	147	144	142	139	136

Secondary Outcomes	Hazard Ratio (95% CI)			p-value (log-rank test)
	Oral vs 2 weeks AmB	1 week AmB vs 2 weeks AmB		
2 week mortality	0.82 (0.54 to 1.25)	1.01 (0.68 to 1.51)		0.57
10 week mortality	0.83 (0.61 to 1.13)	0.89 (0.66 to 1.21)		0.47

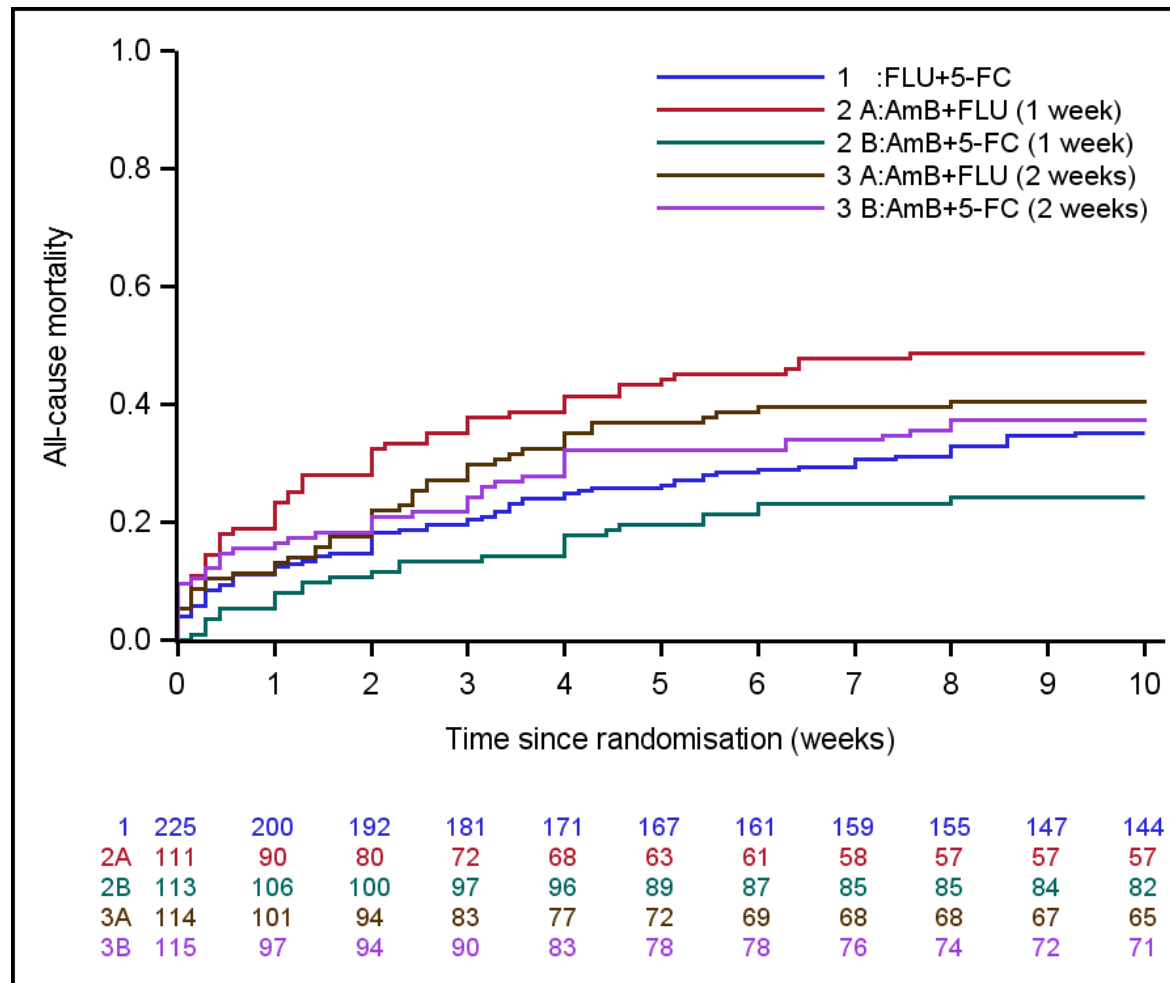
ACTA: FLU vs 5FC



Hazard Ratio (95% CI)		
	AmB+FLU vs AmB vs 5FC	p-value (log-rank test)
10 week mortality	1.62 (1.19 to 2.20)	0.002

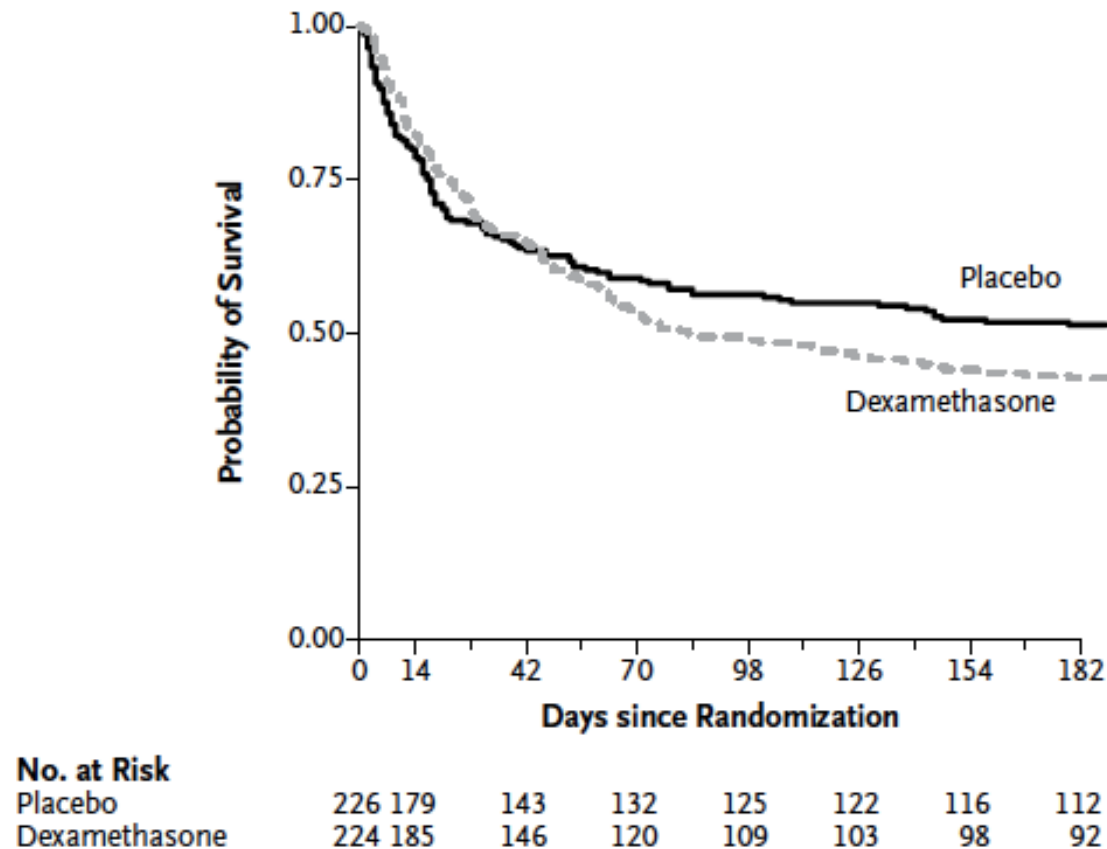
10 week mortality: FLU: **45%** (101/225)
5FC: **31%** (71/228)

ACTA: Cumulative incidence of all cause mortality

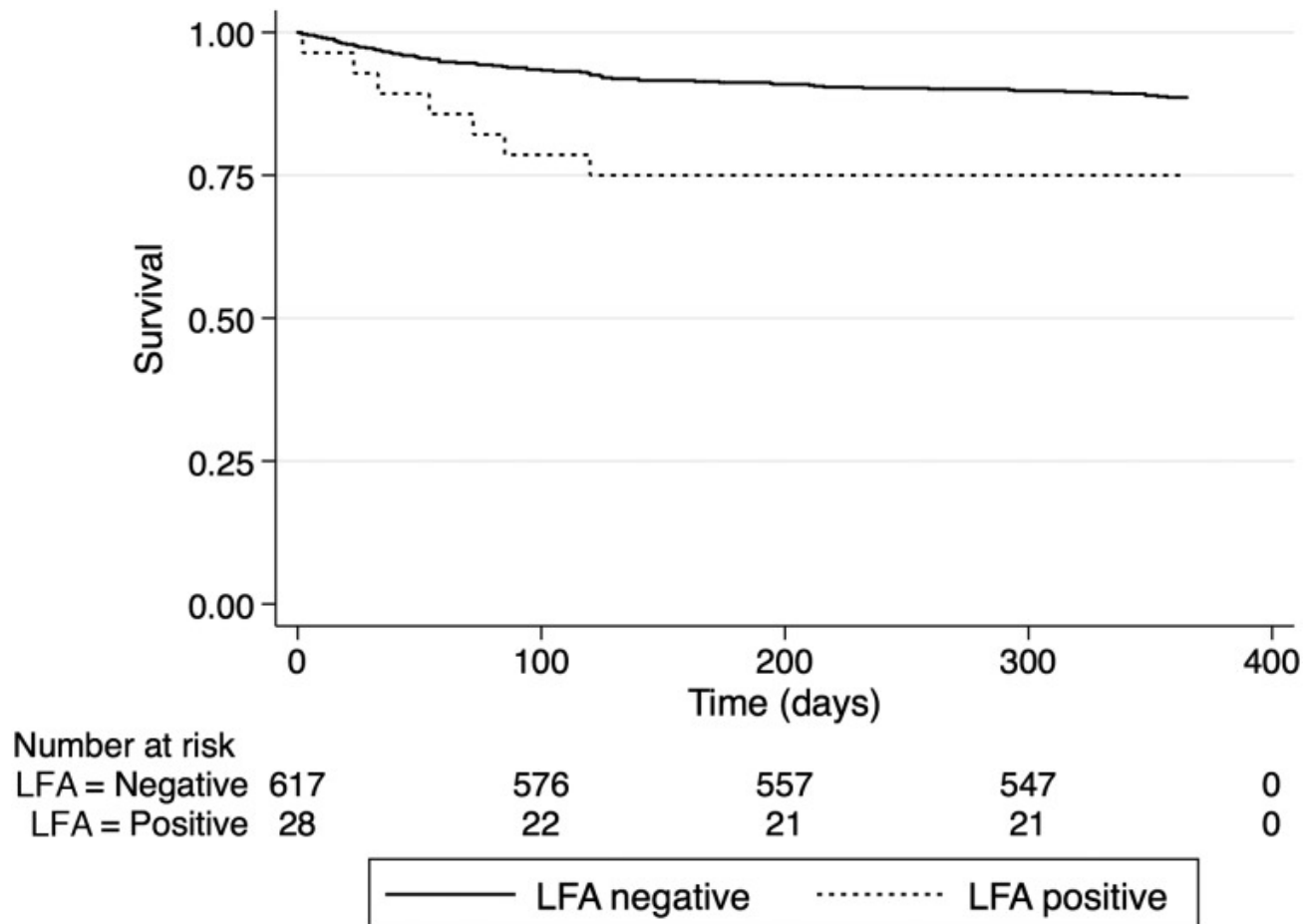


Cryptococcosis: role of steroids

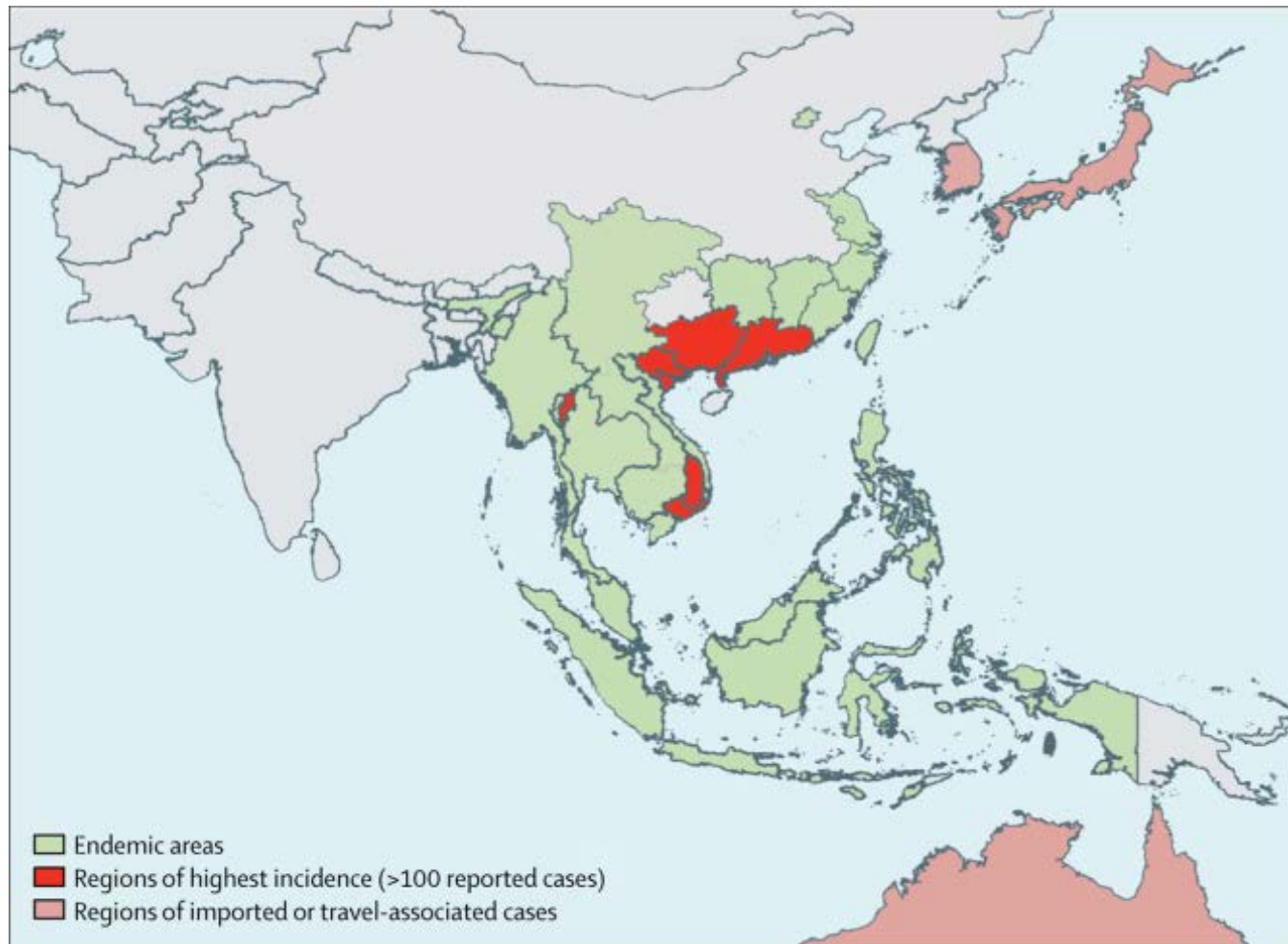
A All Patients



Higher mortality in CrAG +ve in spite of preemptive fluconazole treatment

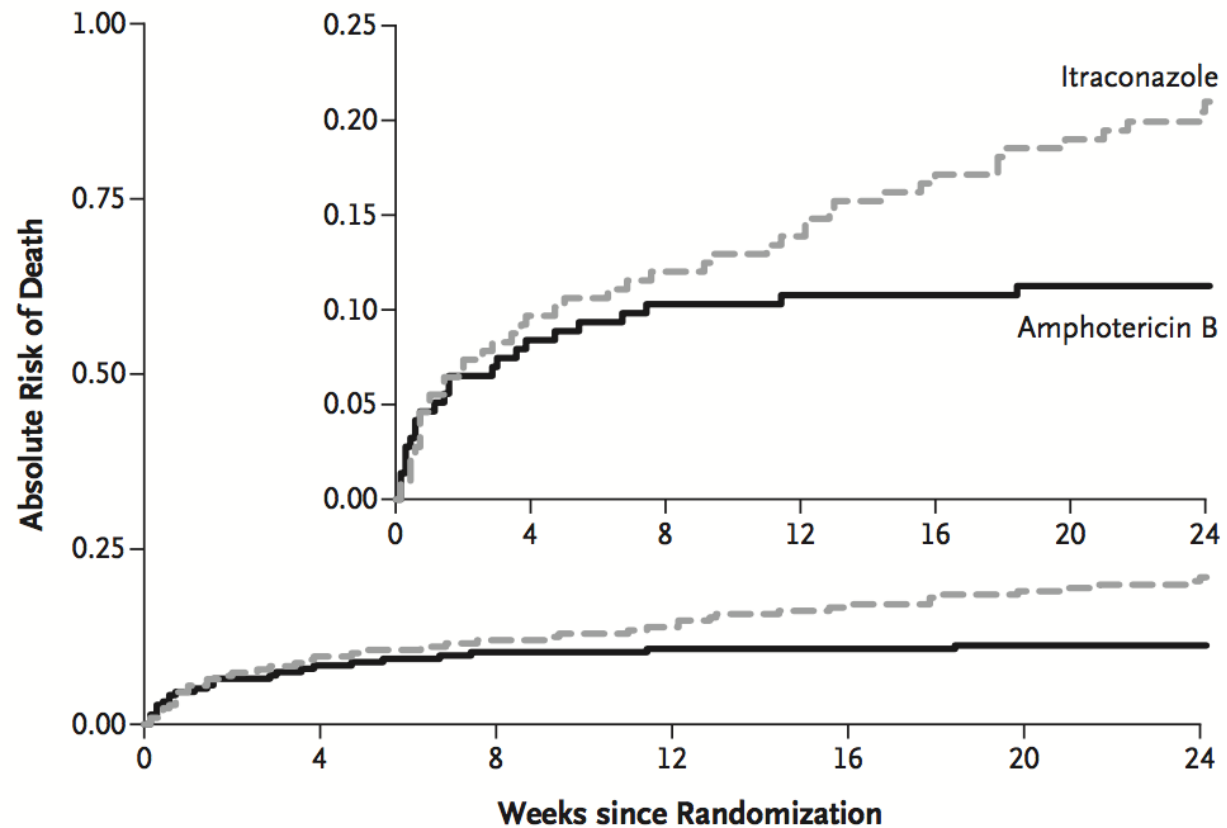


Talaromyces marneffeii



AmpB vs itraconazole for talaromyces

A Cumulative Incidence of Death by Week 24

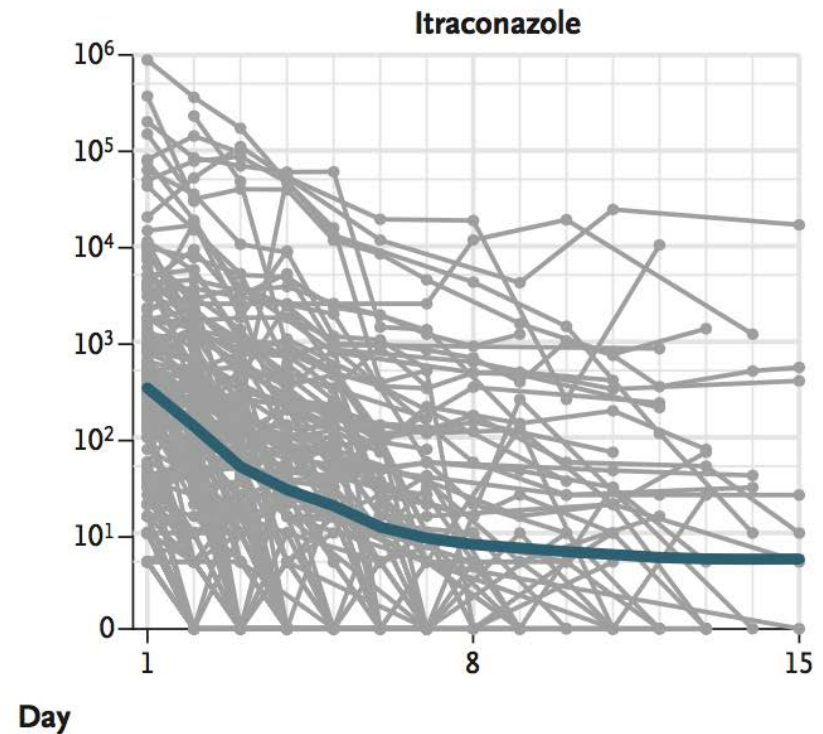
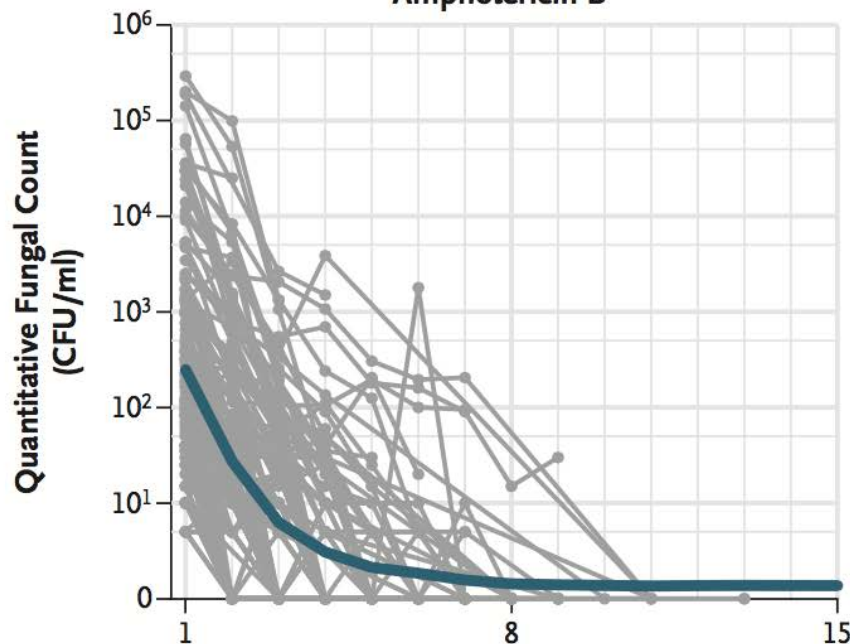


No. at Risk

Amphotericin B	217	194	189	187	187	185	165
Itraconazole	218	194	189	185	179	174	147

AmpB vs itraconazole for talaromyces

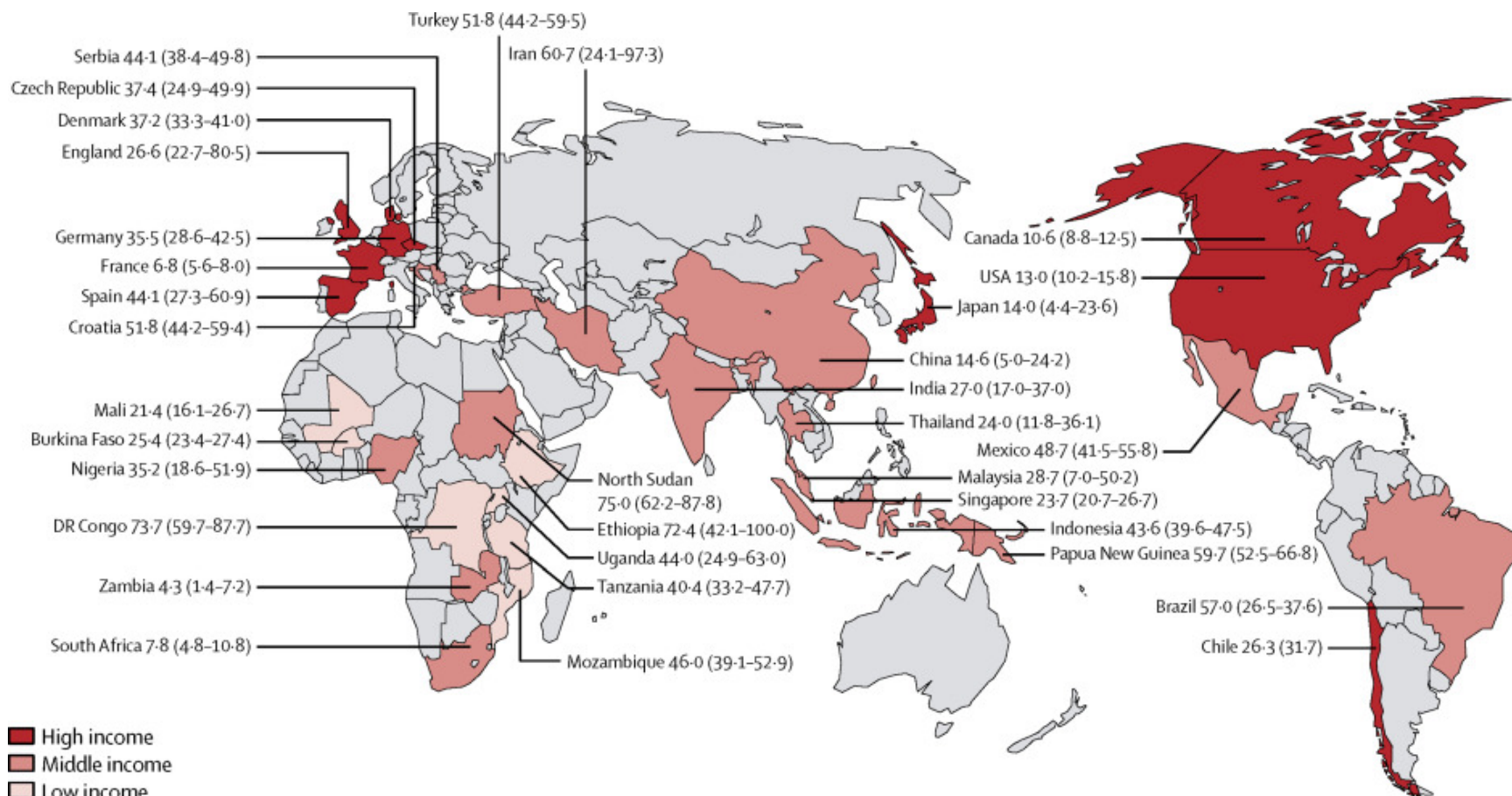
B Fungal Colony-Forming Units in Blood
Amphotericin B



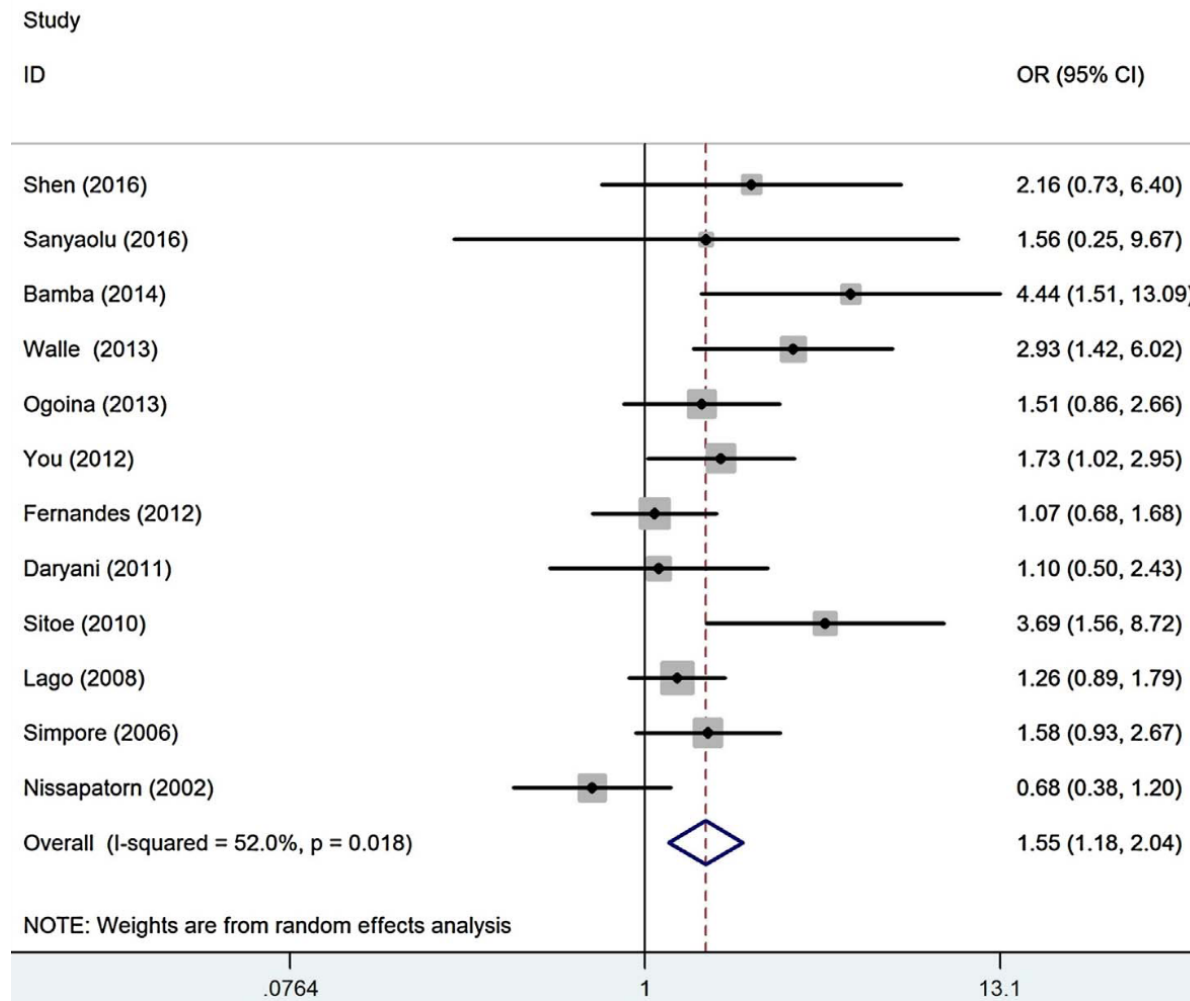
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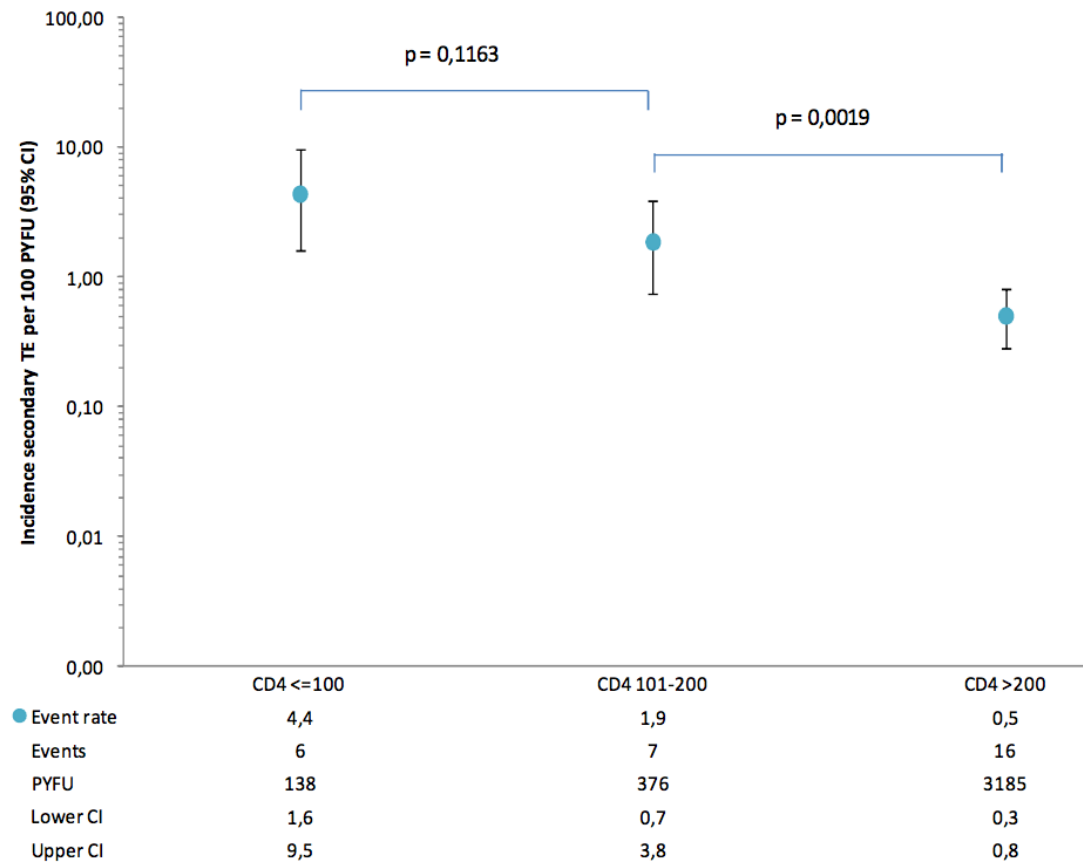
Toxoplasma infection amongst PLHIV



Higher prevalence of Toxo infection amongst PLHIV ns gen population

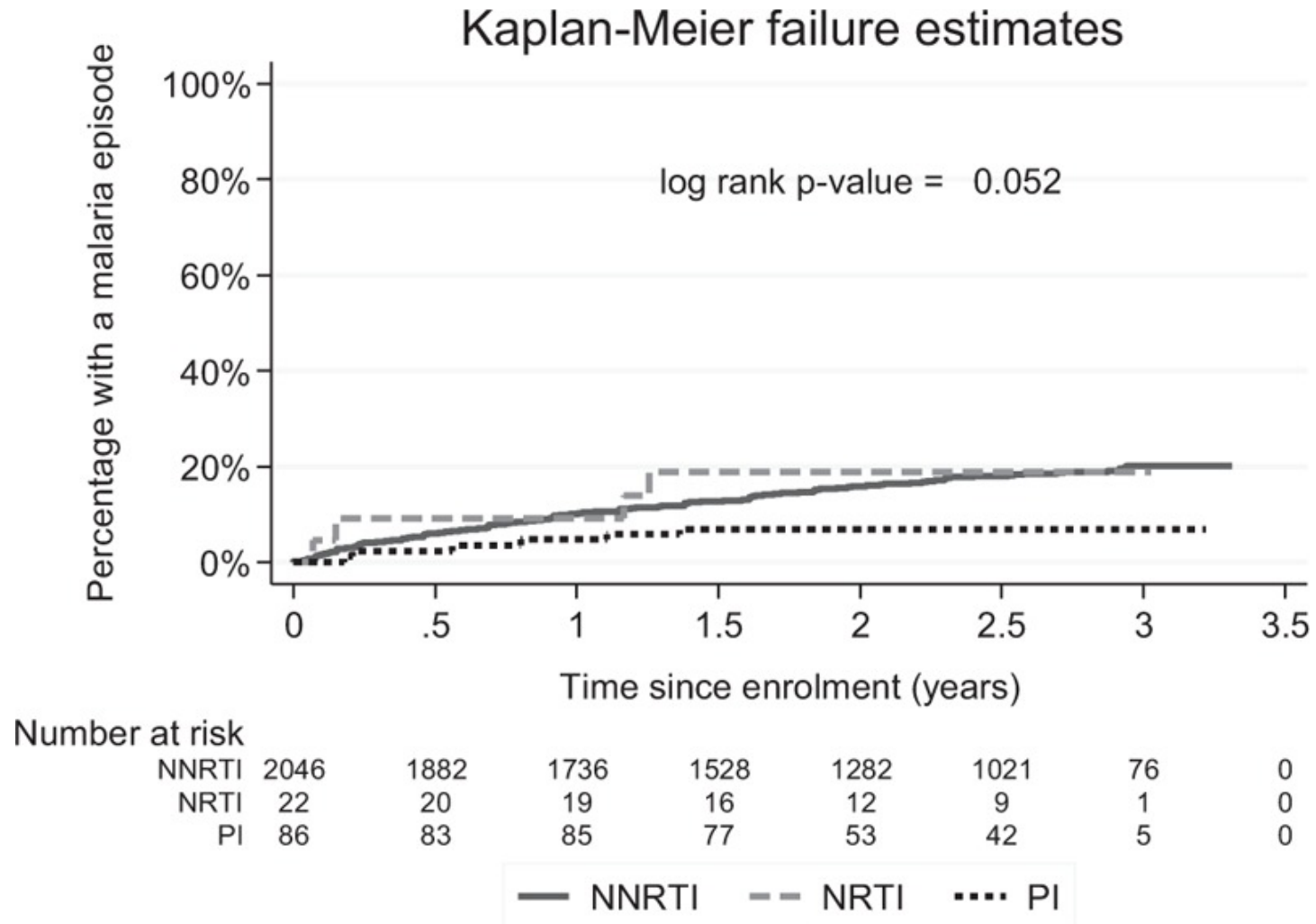


Discontinuing TMP-SMX when CD4 100-200

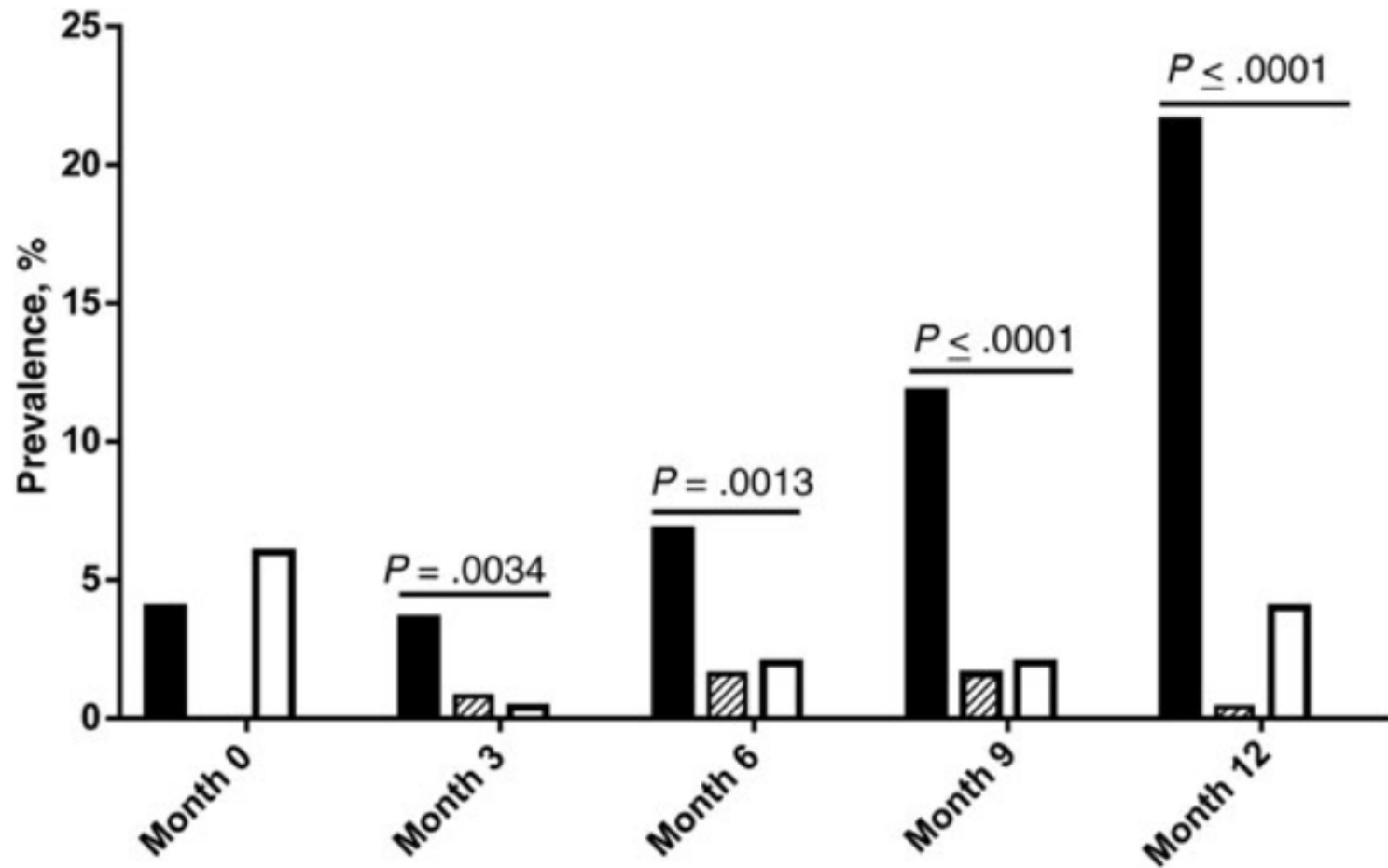


Current CD4

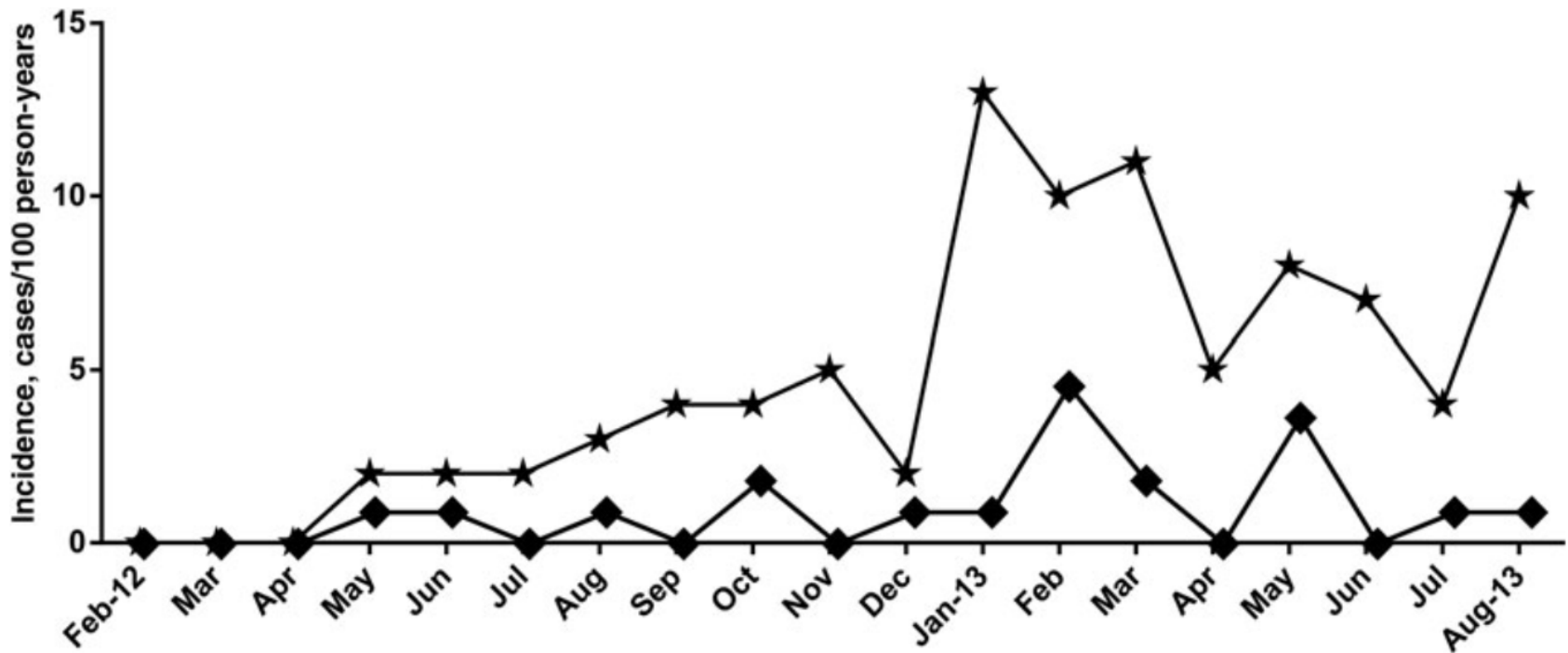
PI based regimens reduce malaria incidence



Stopping TMP-SMX increases malaria amongst PLHIV in kenya



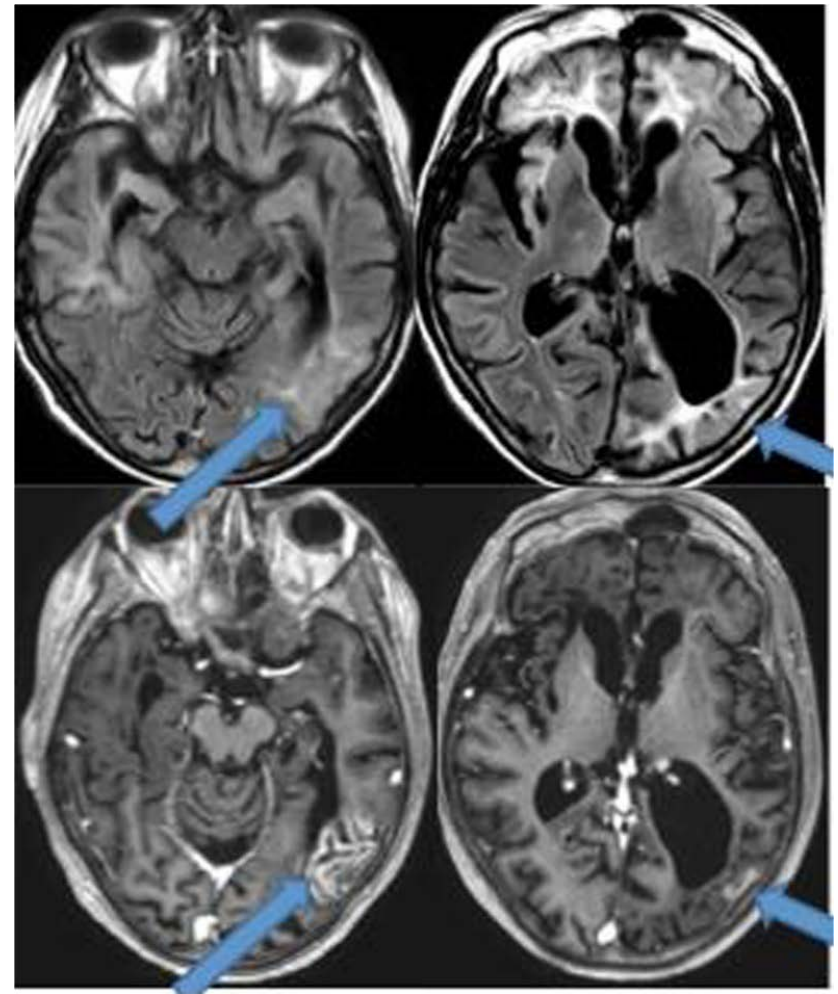
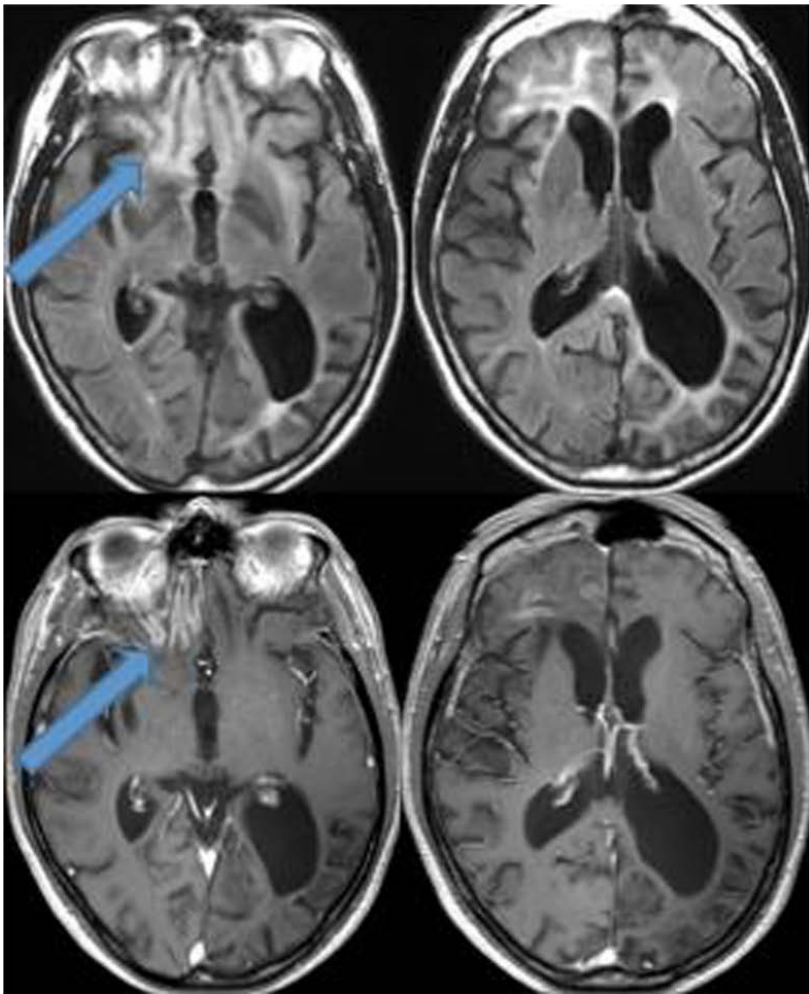
Stopping TMP-SMX increases malaria amongst PLHIV in kenya



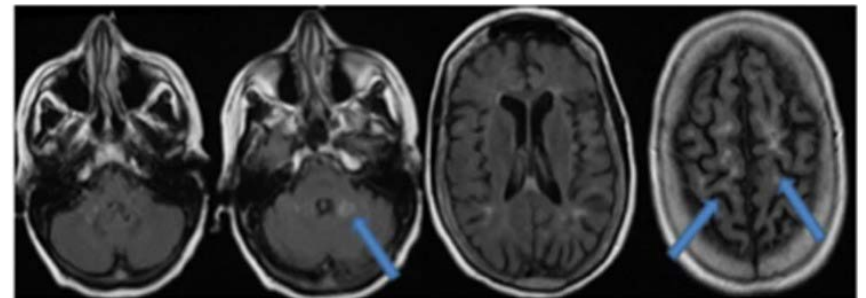
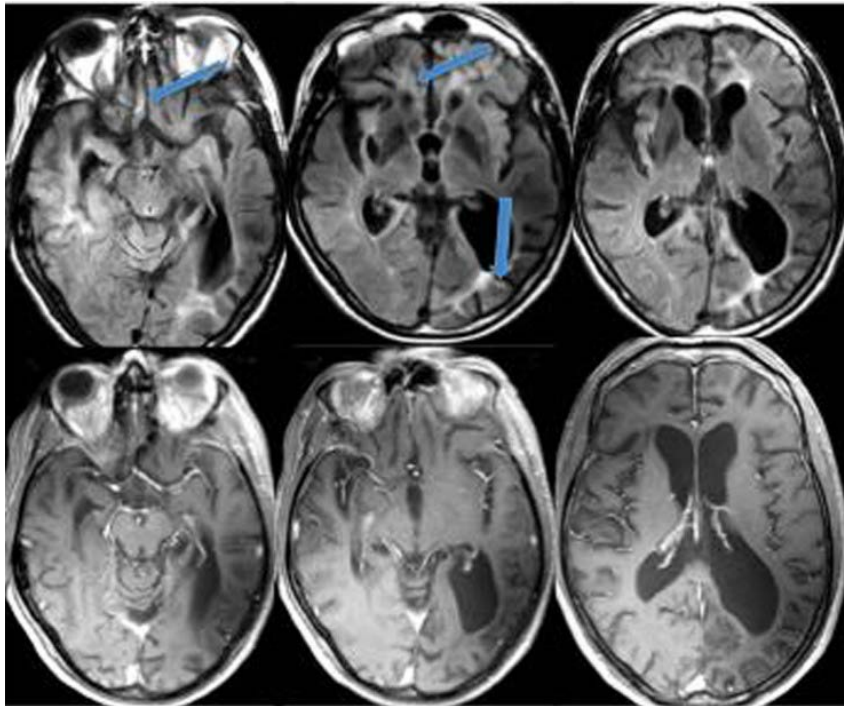
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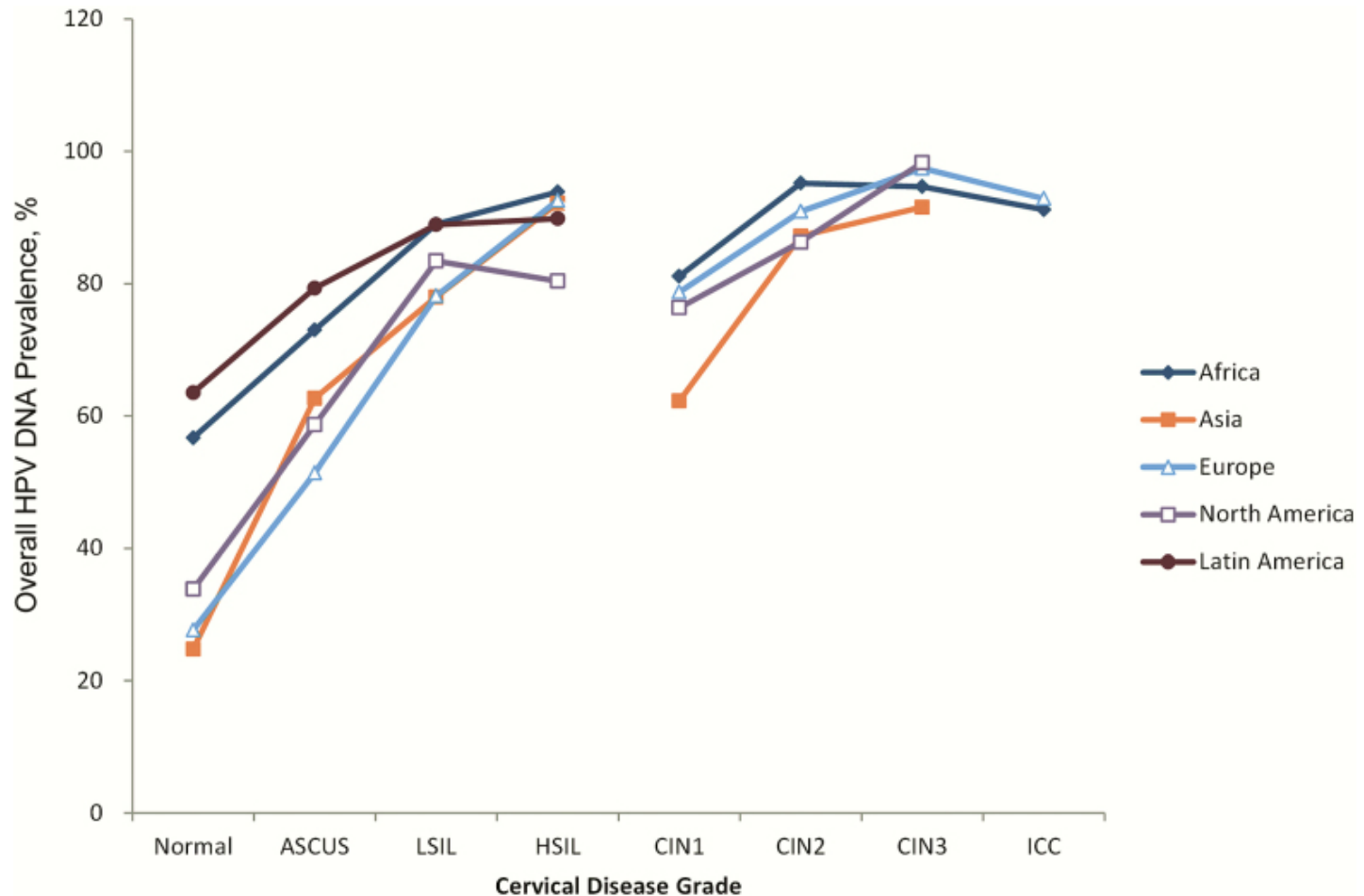
Recurrence of PML despite immune recovery



Recurrence of PML despite immune recovery

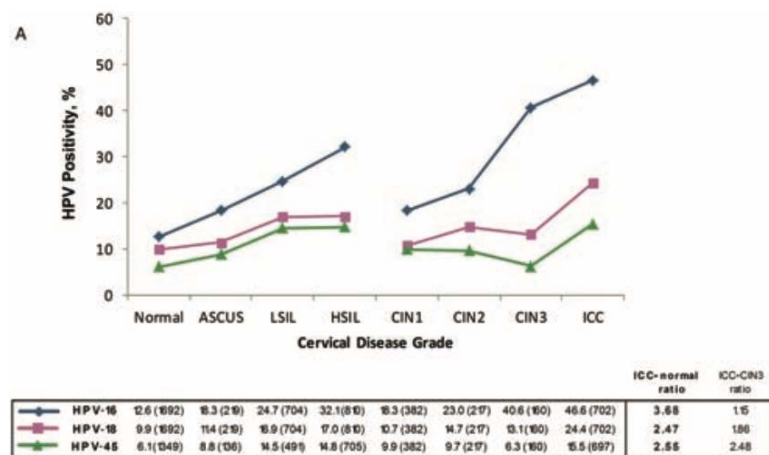


Increasing HPV DNA prevalence with severity of cervical disease amongst WLHIV: Geographic distribution

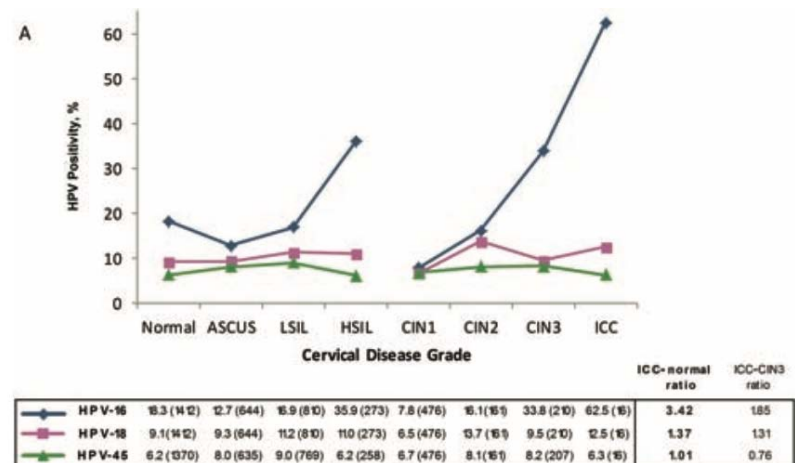


HPV type prevalence: Africa vs NA/Europe

Africa

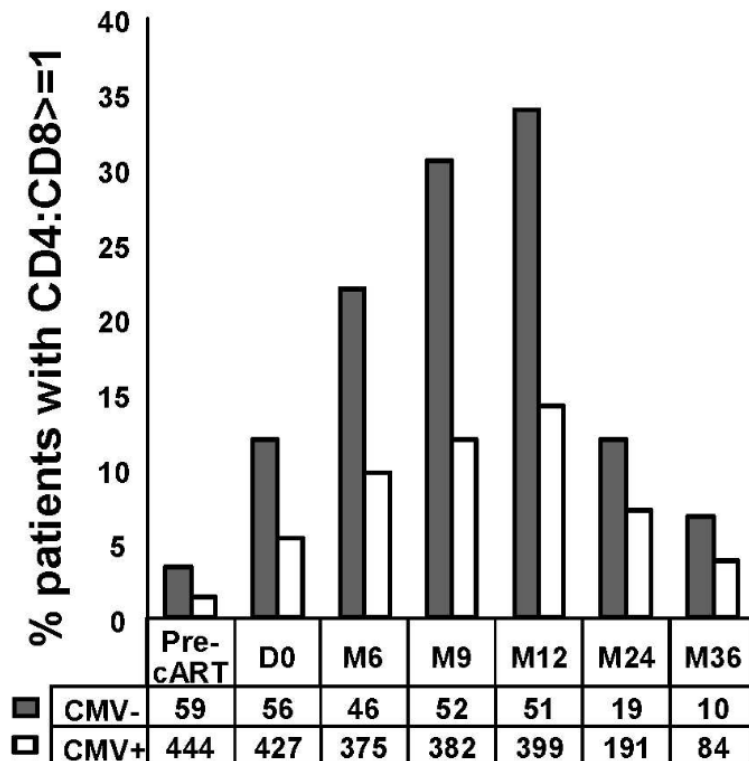


NA/Europe

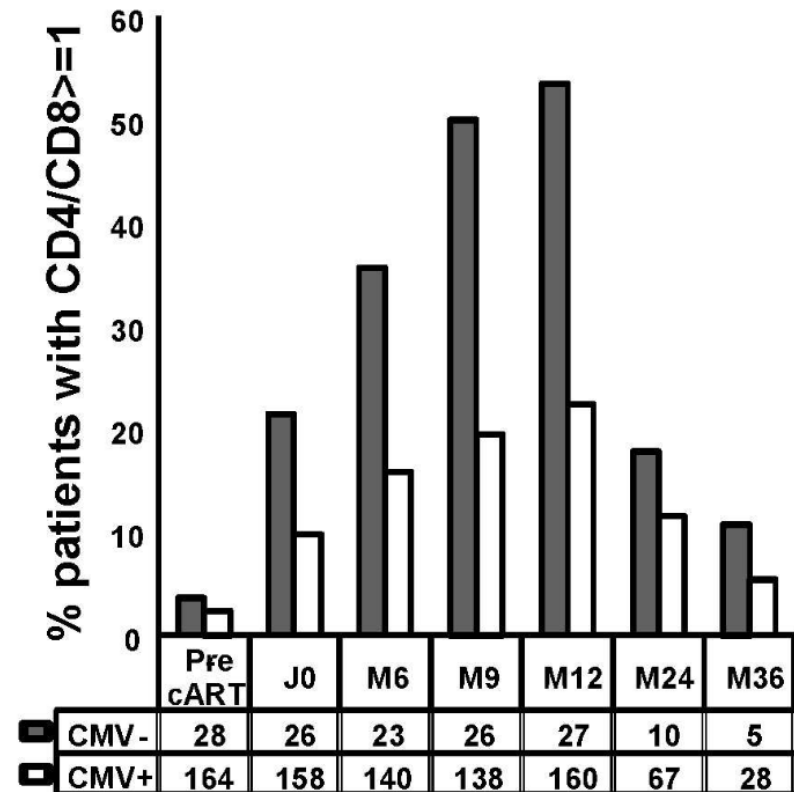


CMV serostatus and normalization of CD4:CD8 ratio on ART

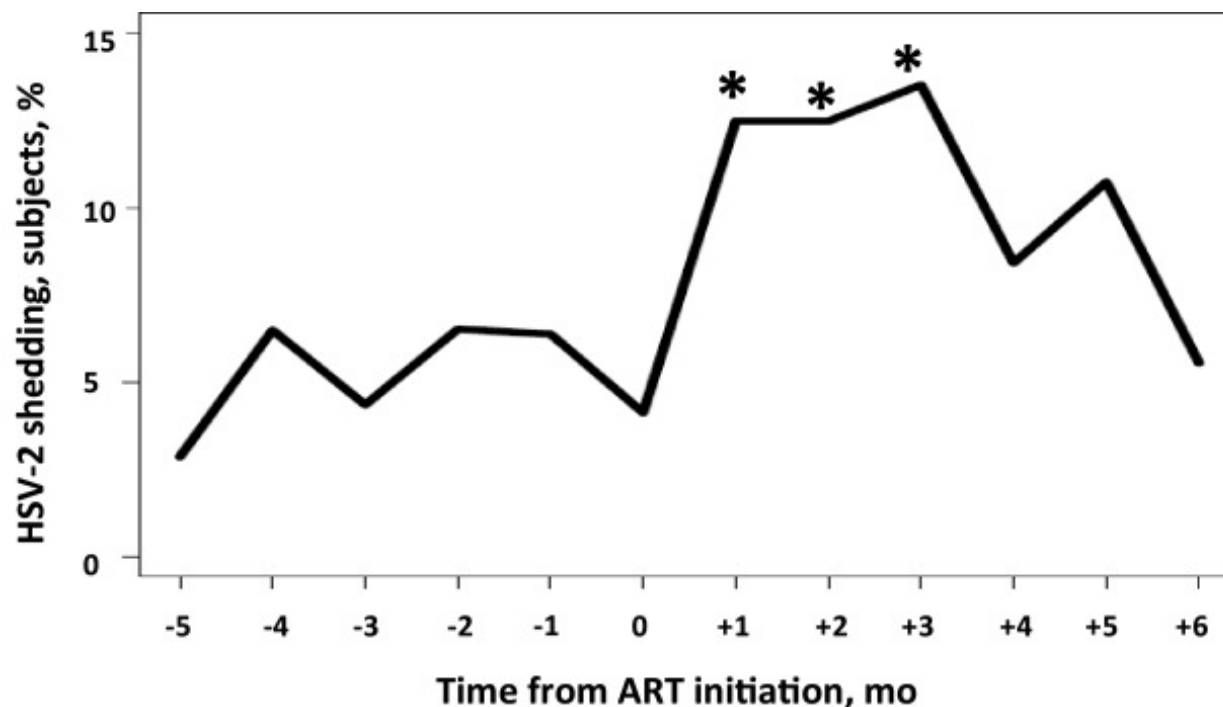
All patients



Amongst CD4>500/mm³



HSV-2 shedding increases in 6 mo's following ART initiation



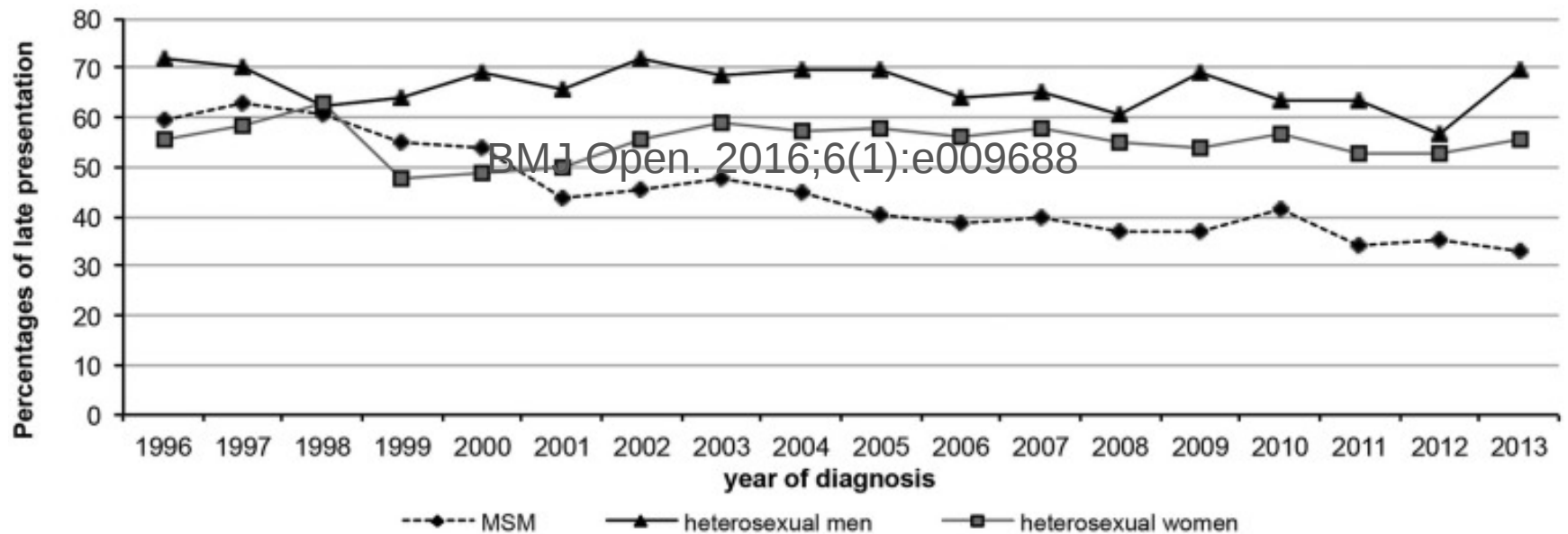
Total	2/70 (2.9)	5/77 (6.5)	4/92 (4.4)	6/92 (6.5)	6/94 (6.4)	4/95 (4.2)	12/95 (12.6)	12/95 (12.6)	13/95 (13.7)	7/94 (7.4)	9/92 (9.8)	5/89 (5.6)
Acyclovir arm	0/29 (0.0)	0/30 (0.0)	0/38 (0.0)	0/36 (0.0)	0/27 (0.0)	0/23 (0.0)	0/22 (0.0)	1/22 (4.5)	2/21 (9.5)	0/18 (0.0)	1/13 (7.7)	0/9 (0.0)
Placebo arm	2/41 (4.9)	5/47 (10.6)	4/54 (7.4)	6/56 (10.7)	6/67 (9.0)	4/72 (5.6)	12/73 (16.4)	11/73 (15.1)	11/74 (14.9)	7/76 (9.2)	8/79 (10.1)	5/80 (6.3)

Summary

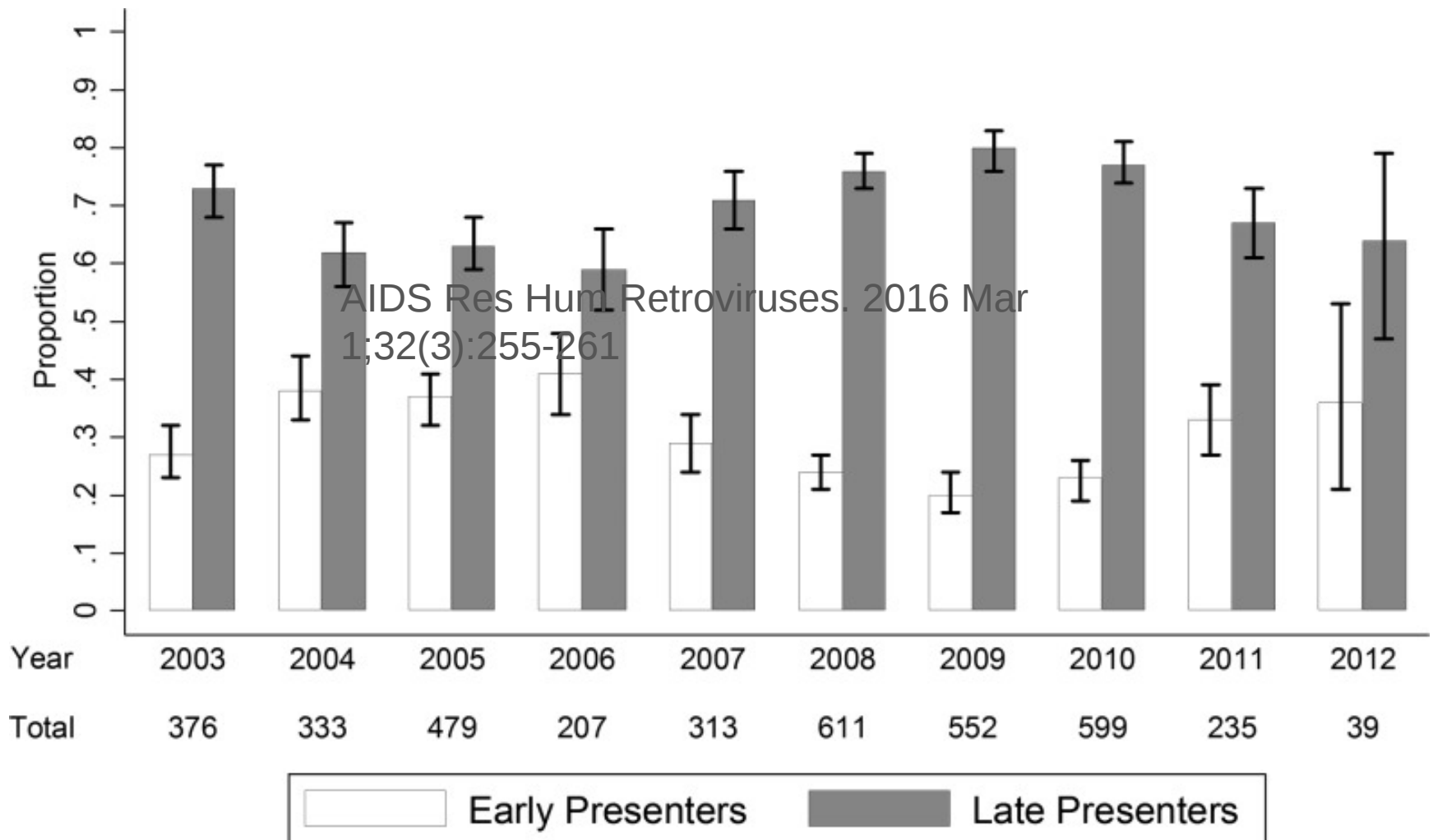
- OI's: Going, Going, but not gone
- Widespread testing for HIV, linkage to care and ART initiation key to reduce burden of OI's
- Preventive strategies e.g. enhanced prophylaxis, vaccination, screening for cancers need to be implemented
- Clinicians must remain knowledgeable about optimal management and prevention of OI's to provide high quality care



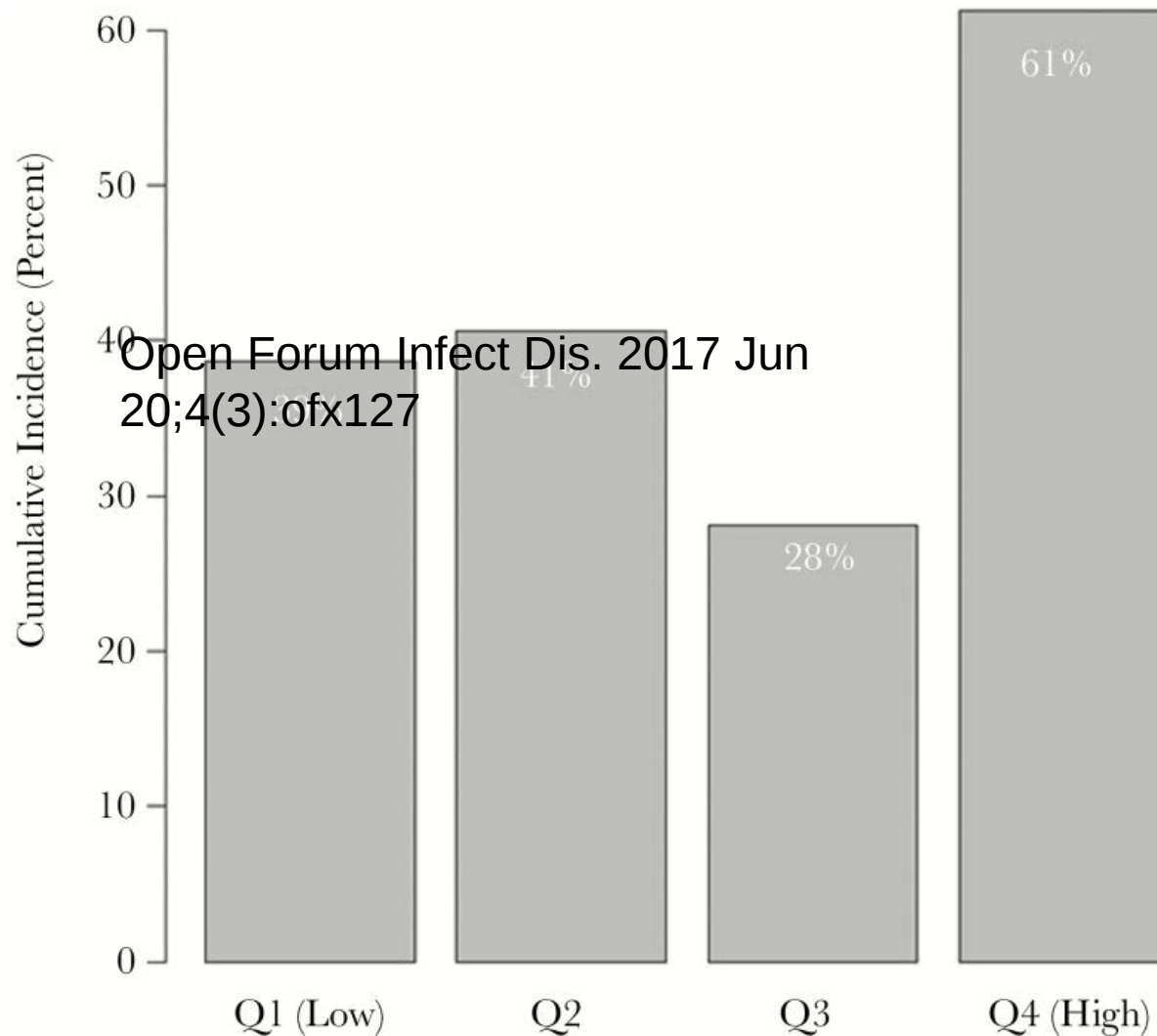
Late presenters in Netherlands



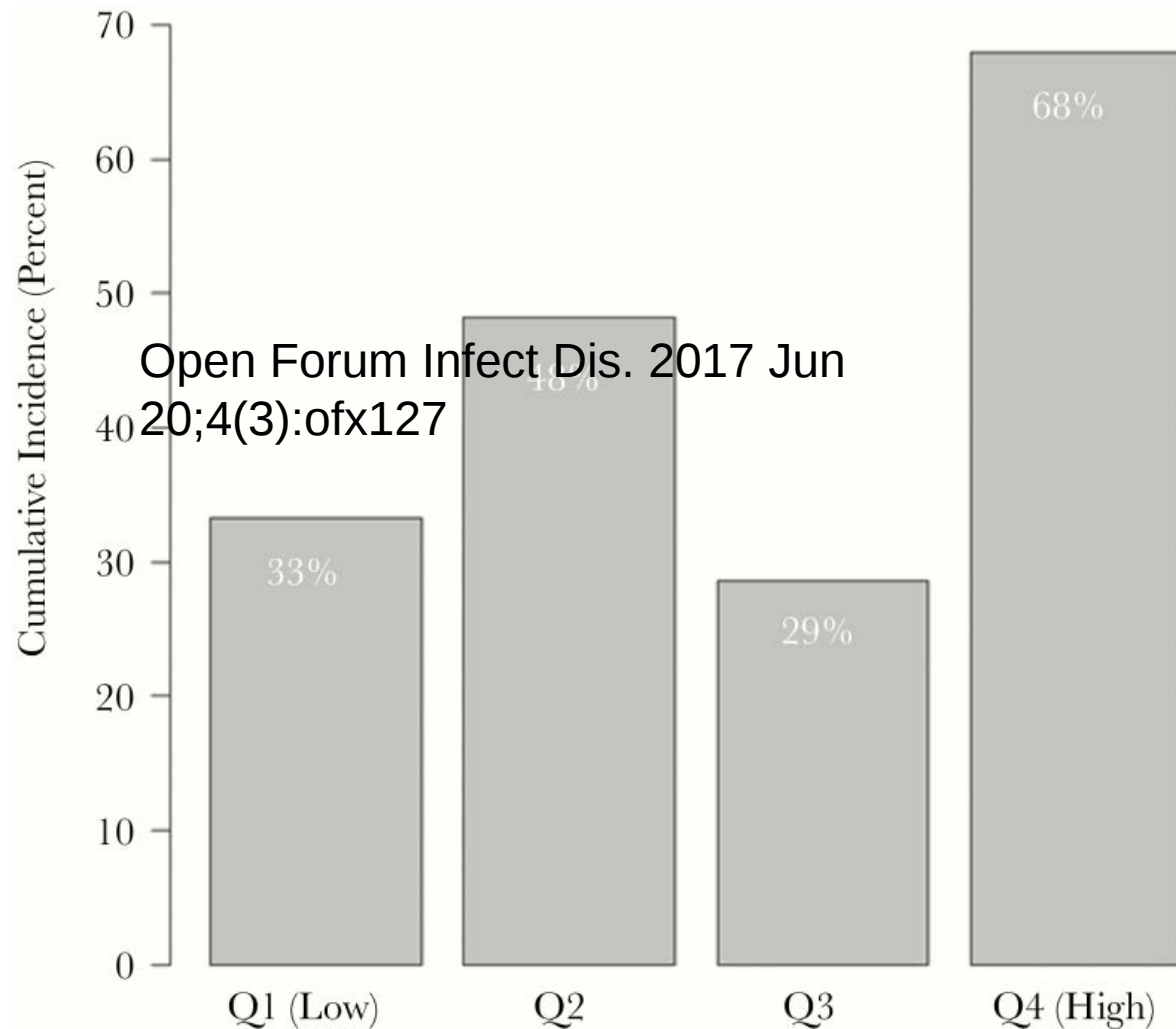
Late presenters in Asia



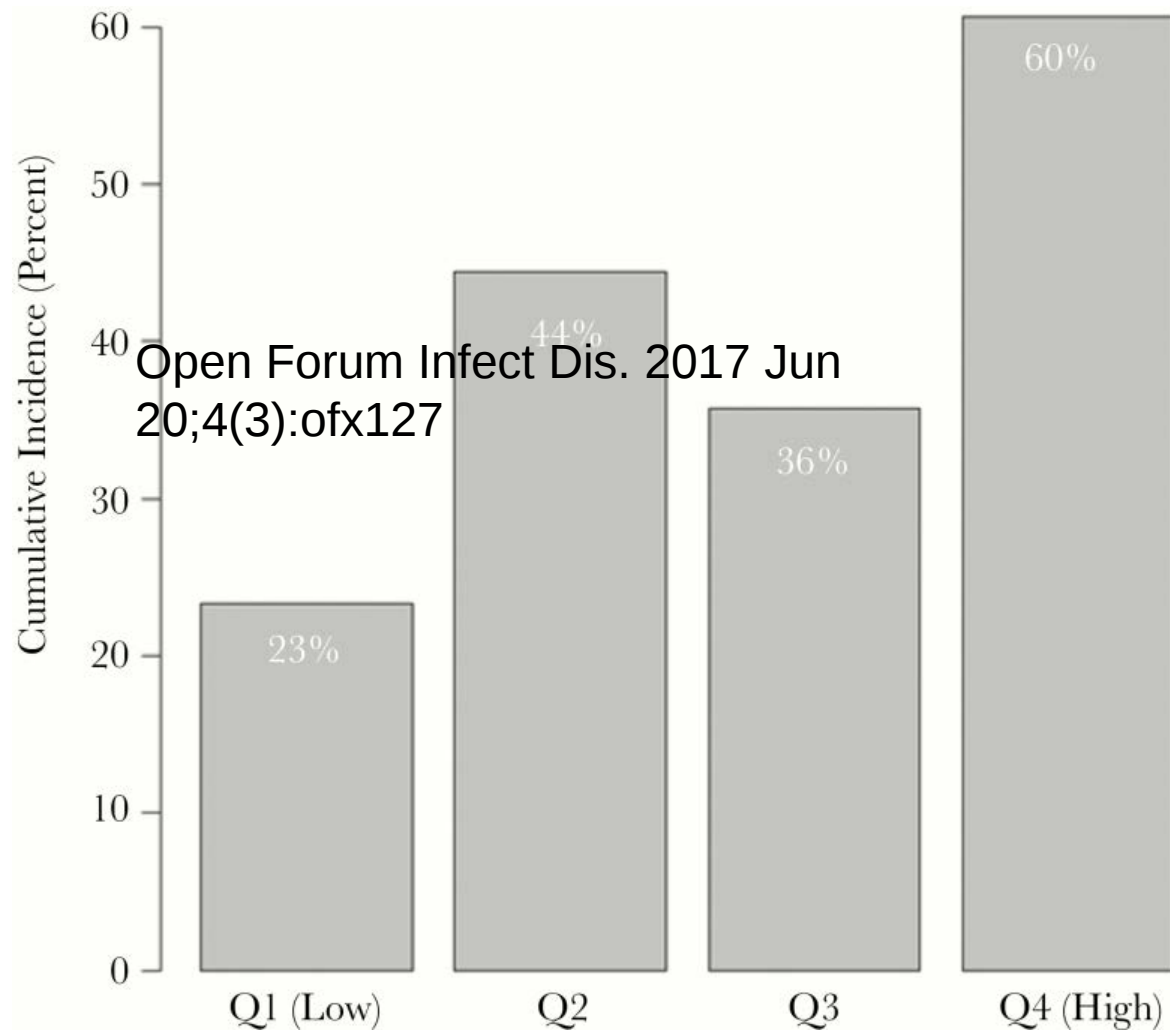
Predicting AKI on AmpB: Urinary NGAL



AKI on AmB: 12 mo mortality by Urinary protein quartiles



AKI on AmpB: AKI by quartiles of Urinary protein



Approach to toxoplasmosis treatment

