

Determining the incidence of risk factors for the predictors/markers of cardio/coronary vascular disease (CVD), a non-communicable disease in an HIV sero-discordant population who received early or late Anti-retroviral therapy (ART)

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- Globally the burden for Non-communicable diseases (NCDs) is 71% of 41 million annual deaths,
- In Sub-Saharan Africa (SSA) the burden of NCDs is large, growing and projected to overtake infectious diseases as major sources of morbidity and mortality by 2030*,
- HIV is a risk factor for development of cardio/coronary vascular disease (CVD), with a risk similar to smoking,
- Understanding risk factors for predictors/markers of CVD, among populations living with HIV is critical to mitigating it's onset.

*Ref: Guwatudde et al.

- HPTN 052 was a randomized clinical trial of HIV sero-discordant couples with CD4 count 350-550 cells/ml³ , comparing immediate versus delayed initiation of ART,
- This was a multisite study conducted in Brazil (Porto Alegre, Rio de Janeiro); India (Chennai and Pune); Malawi (Blantyre and Lilongwe); Thailand (Chiang Mai); Zimbabwe (Harare); and USA (Boston and Massachusetts),
- Results of the study showed that Early ART initiation:
 - decreased HIV acquisition in negative partners by 96%.
 - favored health outcomes for partners living with HIV,
- DSMB review meeting of the study in April 2011 recommended to stop delayed-ART initiation arm and start everyone on early-ART initiation.

- To determine the **prevalence of predictors of CVD** (hypertension , diabetes, dyslipidaemia, obesity, elevated liver enzymes, or renal disorders) measured as grade 2 or higher across the arms prior to DSMB recommendations.
- To determine the **incidence of predictors of CVD** (hypertension , diabetes, dyslipidaemia, obesity, elevated liver enzymes, or renal disorders) across the arms post the DSMB recommendations.

Objectives

- To compare the incident risk factors for CVD across arms of early and late initiation of ART for the People living with HIV,
- To examine the association of age and sex with risk factors for CVDs,
- To estimate the cumulative incidence of event/predictors of CVD.

Methods/Analysis Plan

Variables of interest were identified using case report forms:

- Hypertension
 - Hypertension, Systolic hypertension, or Blood pressure increased.
- Diabetes
 - Diabetes, Diabetes Mellitus, Hyperglycaemia, Type 2 Diabetes Mellitus, Diabetic Ketoacidosis, Diabetic vascular disorder, Blood glucose increased.
- Dyslipidaemia
 - Dyslipidaemia, Hypercholesterolaemia, Hypertriglyceridemia, Blood triglycerides increased, Low density lipoproteins increased, Blood cholesterol increased.
- Liver disorders
 - Aspartate amino transferase increased, Alanine amino transferase increased, Hepatic enzyme increased, Transaminases Increased.
- Renal disorders
 - Hypercreatinaemia, Blood creatinine increased
- Obesity

- Prevalence: Events with DAIDS toxicity Table Grade ≥ 2 and pre-existing conditions prior to enrollment were quantified from the start of study to the DSMB recommendations.
- Incidence: The following participants were excluded to determine incidence and cumulative incidence post DSMB recommendations.
 - Participants who did not have an ART start date.
 - Participants who terminated prior,
 - Participants who had the conditions prior,
 - Participants who study exit visit was prior.

Methods/Analysis Plan

- Descriptive analysis of the population was done.
- Categorical variables were summarized with percentages of each categories.
- The Chi-square test was performed for independence to look for an association between two categorical variables Arm and adverse events that were grade 2 or higher.
- Frequencies of the grade 2 or higher adverse events were determined by category.
- Cumulative incidence by arm was determined after the DSMB date .

Demographic distribution by arm

Variables	Total	Demographic Table	
		Delayed arm	Immediate arm
Age Group			
18-25	252/1491 (17%)	129/716 (18%)	123/775 (16%)
26-40	951/1491 (64%)	457/716 (64%)	494/775 (64%)
41-65	287/1491 (19%)	130/716 (18%)	157/775 (20%)
66 and above	1/1491 (<1%)	0/716 (0%)	1/775 (<1%)
Sex			
Male	749/1491 (50%)	353/716 (49%)	396/775 (51%)
Female	742/1491 (50%)	363/716 (51%)	379/775 (49%)
Marital Status			
Single	80/1491 (5%)	37/716 (5%)	43/775 (6%)
Married	1164/1491 (78%)	557/716 (78%)	607/775 (78%)
Living with partner but not married	240/1491 (16%)	118/716 (16%)	122/775 (16%)
Separated OR Divorced OR widowed	7/1491 (<1%)	4/716 (1%)	3/775 (<1%)

Prevalence and incidence of risk factors

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Prevalence

Immediate Arm: 46/1491 (3.1%)
Delayed Arm: 42/1491 (2.8%)

2

Incidence

Immediate Arm: 15/1491 (1.0%)
Delayed Arm: 24/1491 (1.6%)

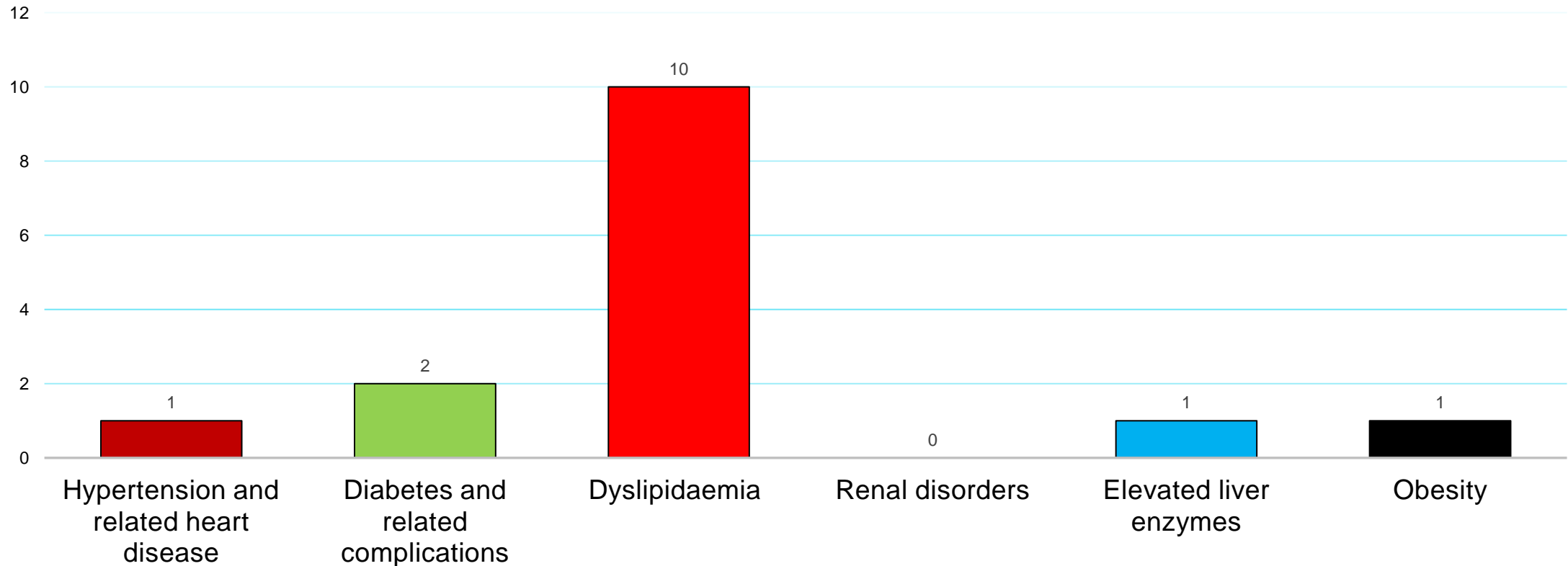
Results : Chi square test of association

	Immediate	Delayed
No adverse event	738 (98.3%)	623 (96.6%)
Adverse event	13 (1.7%)	22 (3.4%)

P= 0.0754 (chi-square test of association)

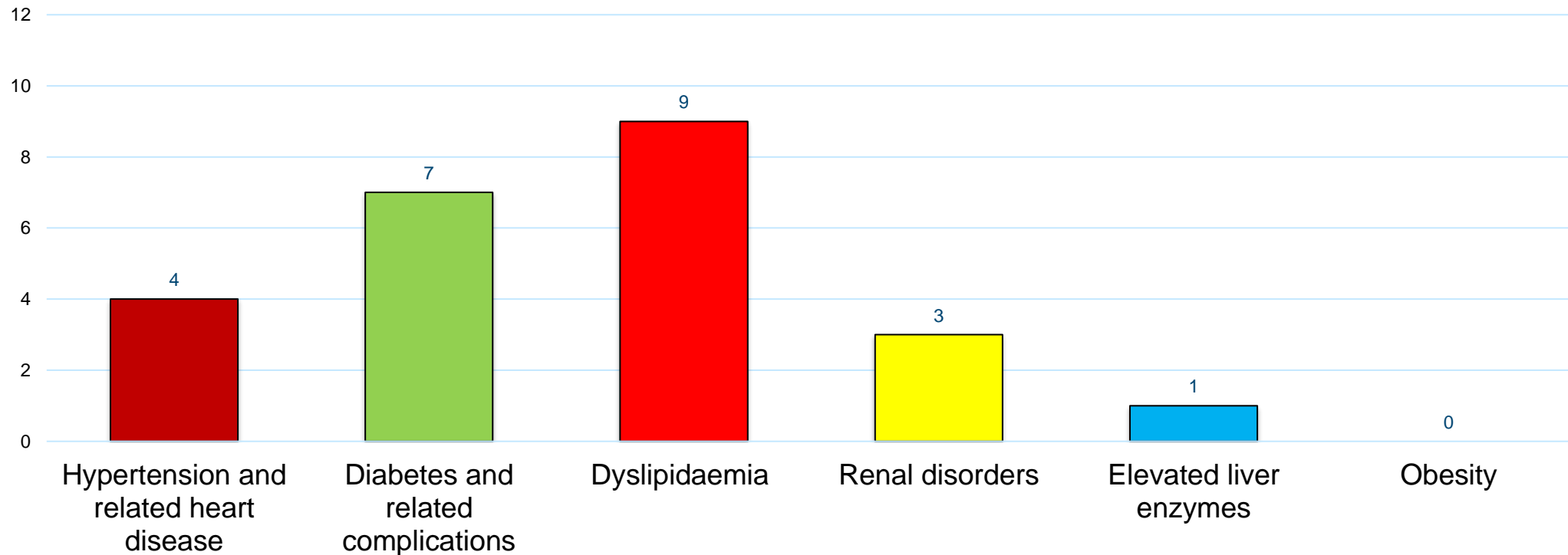
Frequency of adverse events immediate arm

AE Total Incidence (15) Immediate Arm

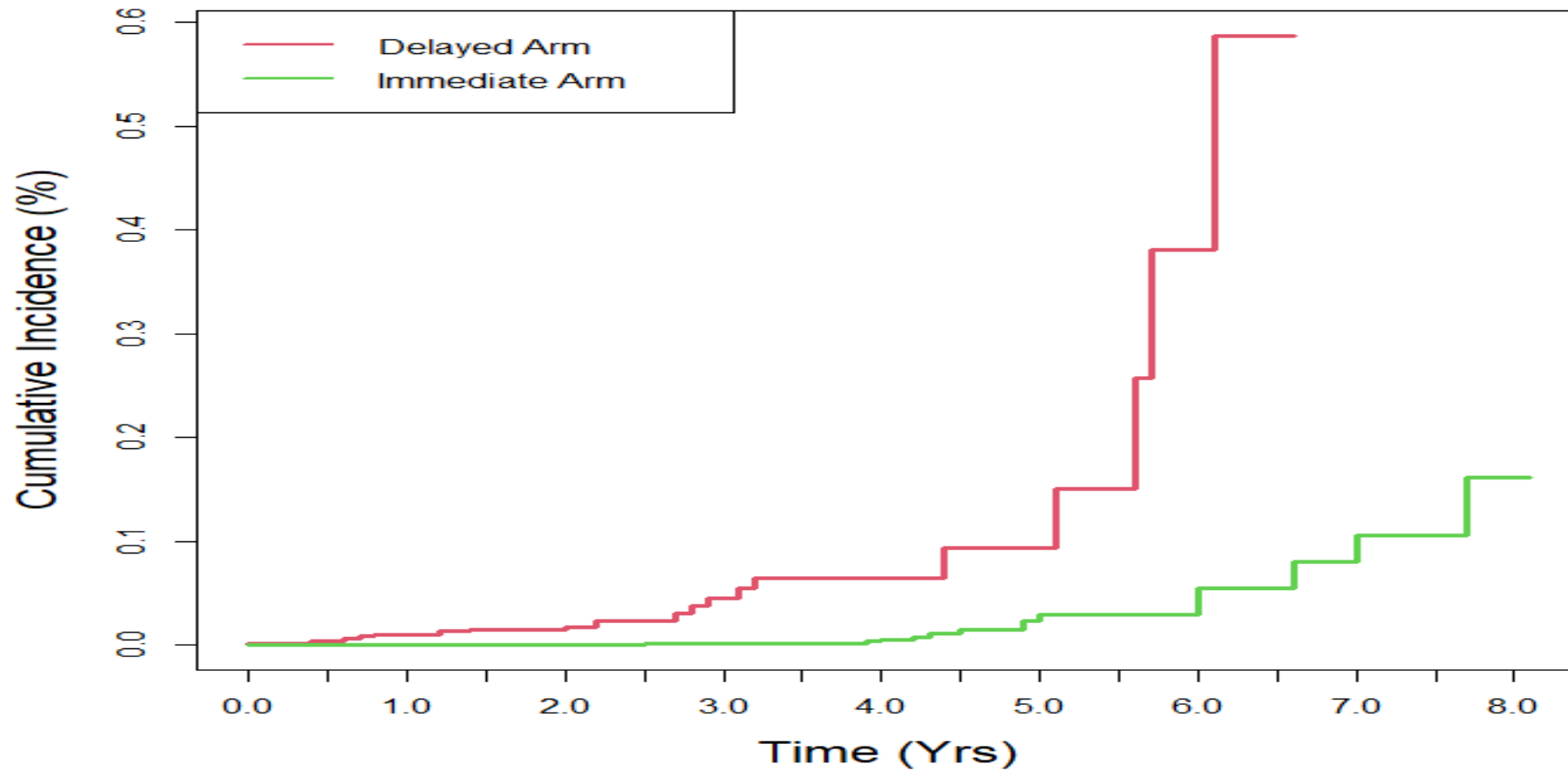


Frequency of adverse events delayed arm

AE Total Incidence (24) Delayed Arm



Cumulative Incidence by arm



Results

Variable	P value	Odds ratio	Lower 95%CI	Upper 95%CI
Delayed ART Therapy versus Immediate ART Therapy.	0.0649	1.926	0.960	3.862
Sex Female versus male	0.0470	0.454	0.208	0.989
Age	0.2167	1.025	0.986	1.066

- Adverse Cardiovascular risks were uncommon overall
- Dyslipidaemia was the most common adverse event
- While adverse events were increased in the delayed arm, this was not statistically significant.
- Females were 55% less likely to get AE complications as compared to the males.

- Early initiation of ART may be beneficial in reducing cumulative risk of people living with HIV developing grade 2 or higher risk factors for CVD.
- The prevalence and incidence of adverse events requiring intervention were low however it is important to screen for these risk factors at HIV diagnosis so that clients can be advised on the benefits of initiating ART.
- PLWH taking ART should thus be offered screening for risk factors for cardiovascular diseases as routine care.
- Recent results from the REPRIEVE study highlight reduced cardiovascular risk in PLWH taking pitavastatin suggest expanded use of statins in routine care.

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