



**KARONGA
PREVENTION
STUDY**

Change In Population TB Incidence Trends After The Roll-Out Of ART in Karonga District, North Malawi: 1986 - 2009

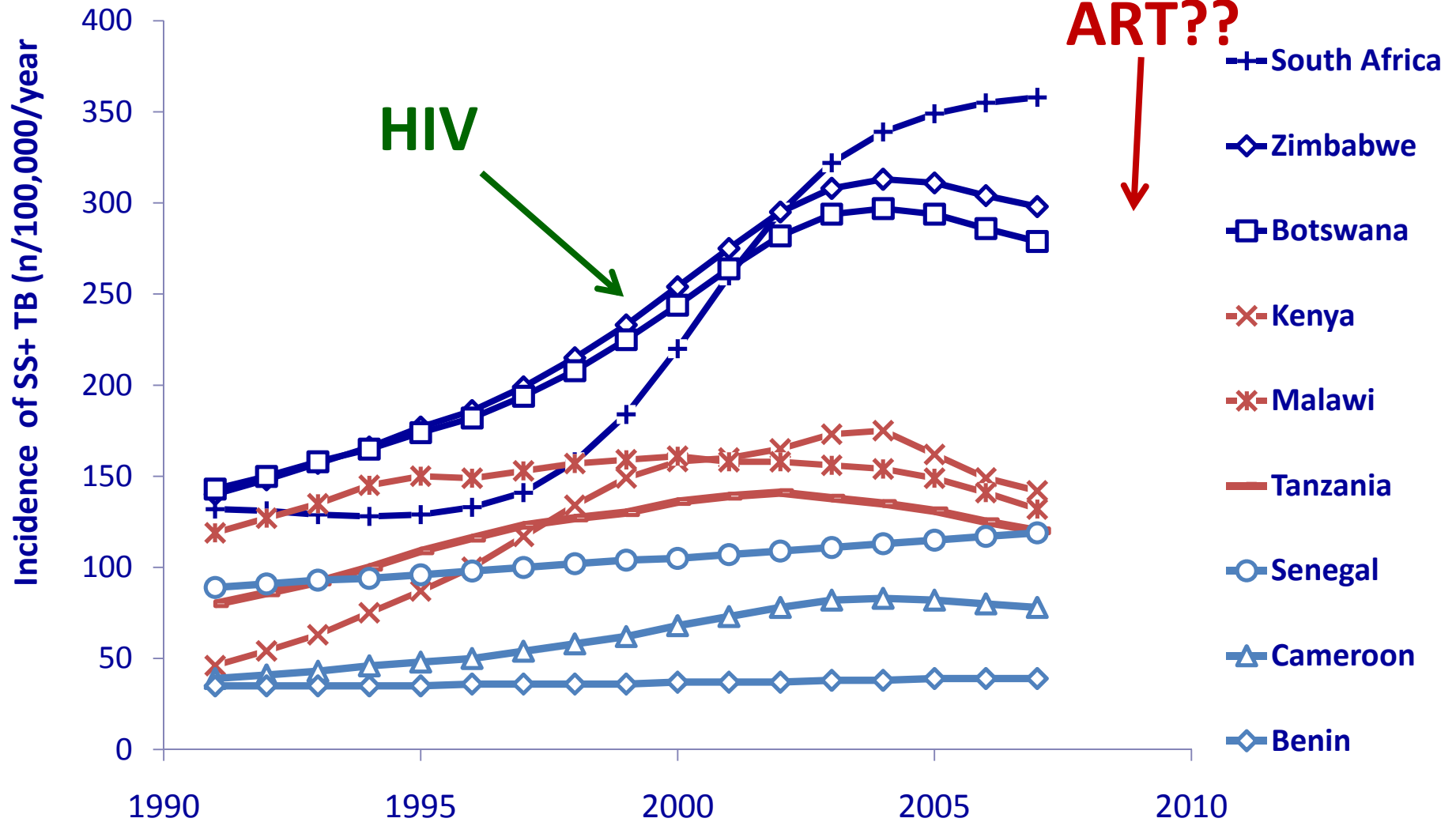
Rein Houben/Sebastian Mboma

Karonga Prevention Study

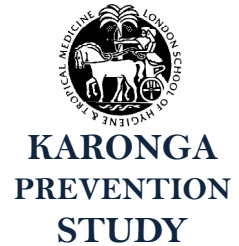
TB incidence over time



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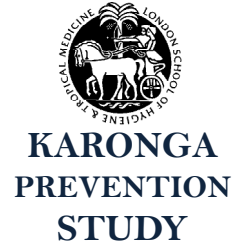


Literature



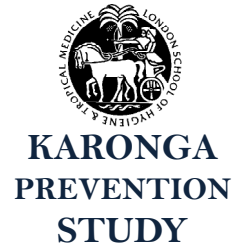
- Williams & Dye (Science – 2003): early start, high coverage and compliance necessary for ART to reduce TB burden in population
- Studies have suggested
 - Relative incidence of TB lower amongst patients receiving ART (in CD4 strata)
 - Late starters (CD4<100) remain at elevated risk of TB
- Limitations
 - Most studies are done in intensely supervised study settings – not representative of rural Africa
 - Few cases of TB
 - No HIV negative or positive comparison group
 - Effect of ART on TB incidence in wider population

Research Questions



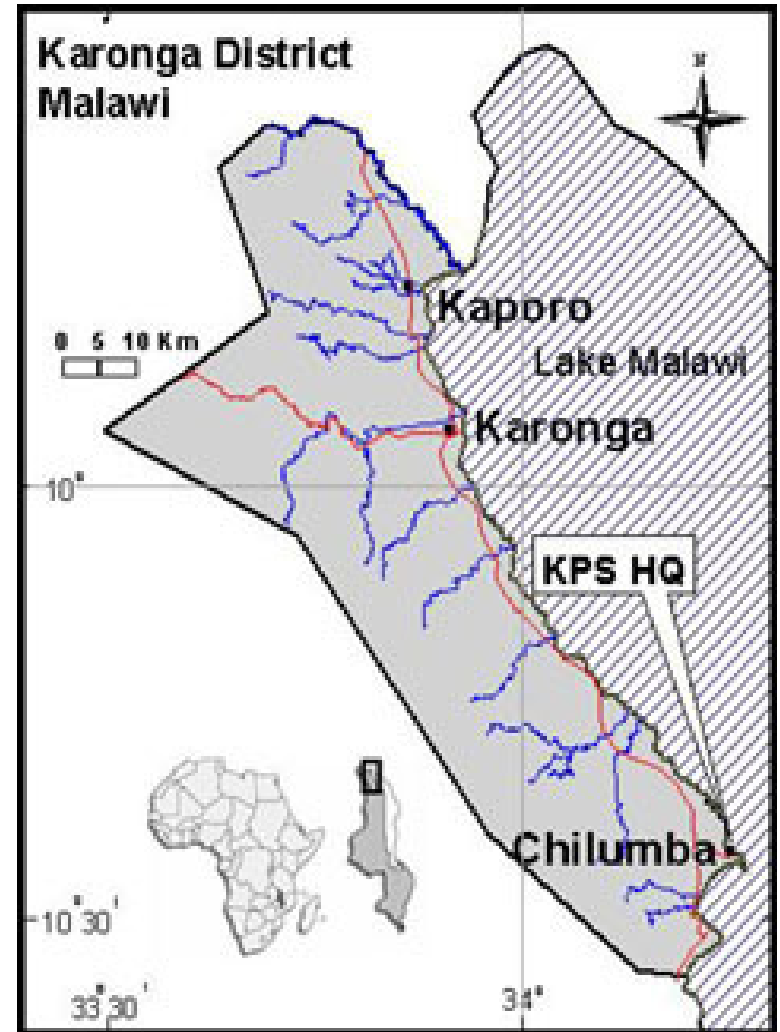
- What is the relative incidence of TB by HIV/ART status?
- What is the effect of the ART roll-out on TB incidence trends in Karonga District?

Karonga Prevention Study



TB epidemiological studies since 1985

- All TB cases
 - Laboratory tests
 - Demographic information
 - HIV status (from 1988)
- ART since July 2005
 - Low level of clinical and laboratory support



Population denominators

Adult population size

- Census in 1988, 1998, 2008

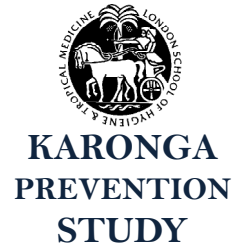
HIV prevalence in population

- Mathematical model based on population data for HIV prevalence White R.G. et al (Epi Inf, 2007)

Uptake of ART in population

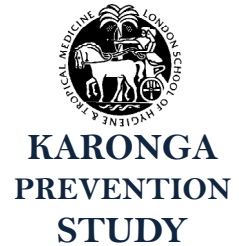
- ART clinic registers
- Person years on ART in Karonga
 - Recently started on ART --> 6 months or less
 - On ART for longer period --> more than 6 months

TB cases



- Main analysis
 - Only new SS+ pulmonary TB cases since Jan 1986 – Aug 2009 (Lab confirmed - at least 1 positive culture or 2 separate smears positive for Mtb)
- Sensitivity analyses on different TB case populations
- HIV and ART status
 - From linked KPS database of previously recorded data
 - Missing HIV and/or ART status were imputed using MICE (Multiple imputation using Chained Equations)

Analysis



- Relative TB incidence (July 2005 – Aug 2009)
 - Rate ratios by HIV status
 - Rate ratios By HIV/ART status
- Incidence trends analysis
 - Piecewise regression to test for change in trend between 1997 – 2005 and 2005 – Aug 2009 periods

Relative incidence (05 – 09)



Period and group	Observed			RR (95% CI)	
	n	py	inc	Crude	Adjusted*
Overall	462	633686	73	n.a.	n.a.
HIV negative	174	567555	31	1	
HIV positive	249	66130	377	12.28 (10.12–14.91)	10.89 (8.87 – 13.36)
HIV+ no ART	124	51602	240	1	1
HIV+ <=6m ART	29	1635	1774	7.38 (4.93 – 11.06)	6.41 (4.25 – 9.67)
HIV+ >6m ART	32	4624	692	2.88 (1.95 – 4.25)	2.46 (1.66 – 3.67)

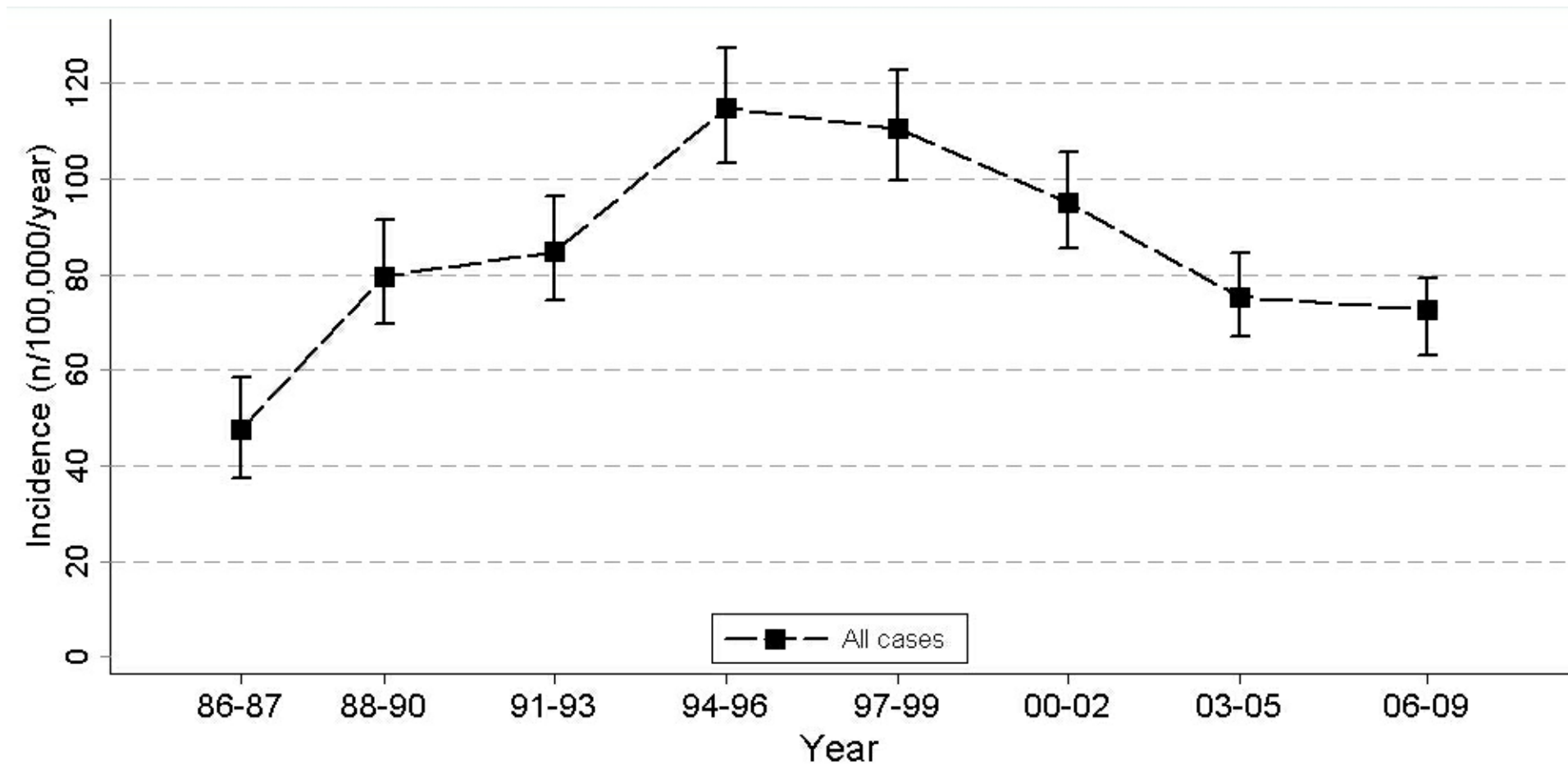
*RR's adjusted for age group (15-24, 25-34, 35-44, 45-54, >=55) and sex

Note: The imputed data show roughly the same results, which suggests that the imputation did not do anything strange or introduce more bias.

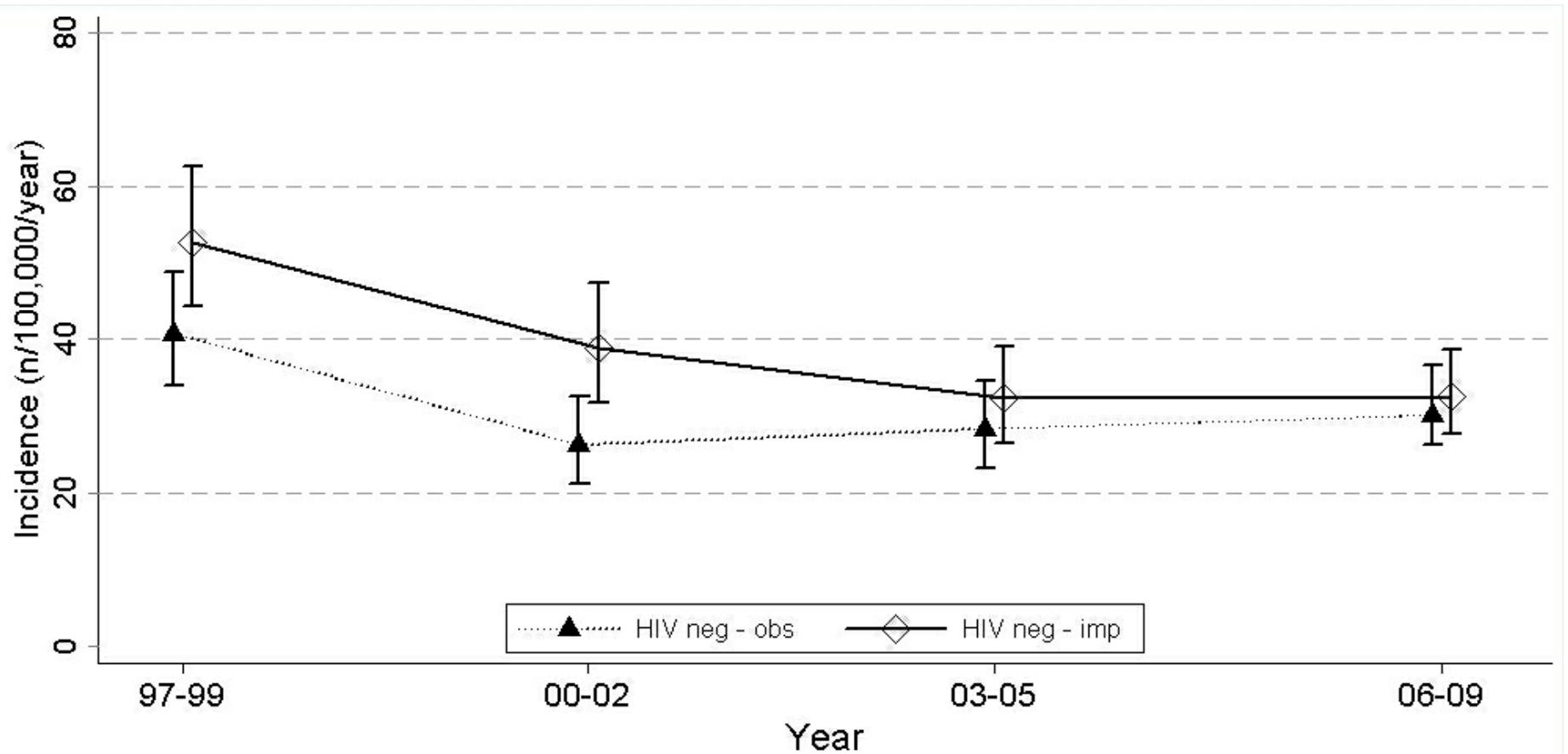
Overall



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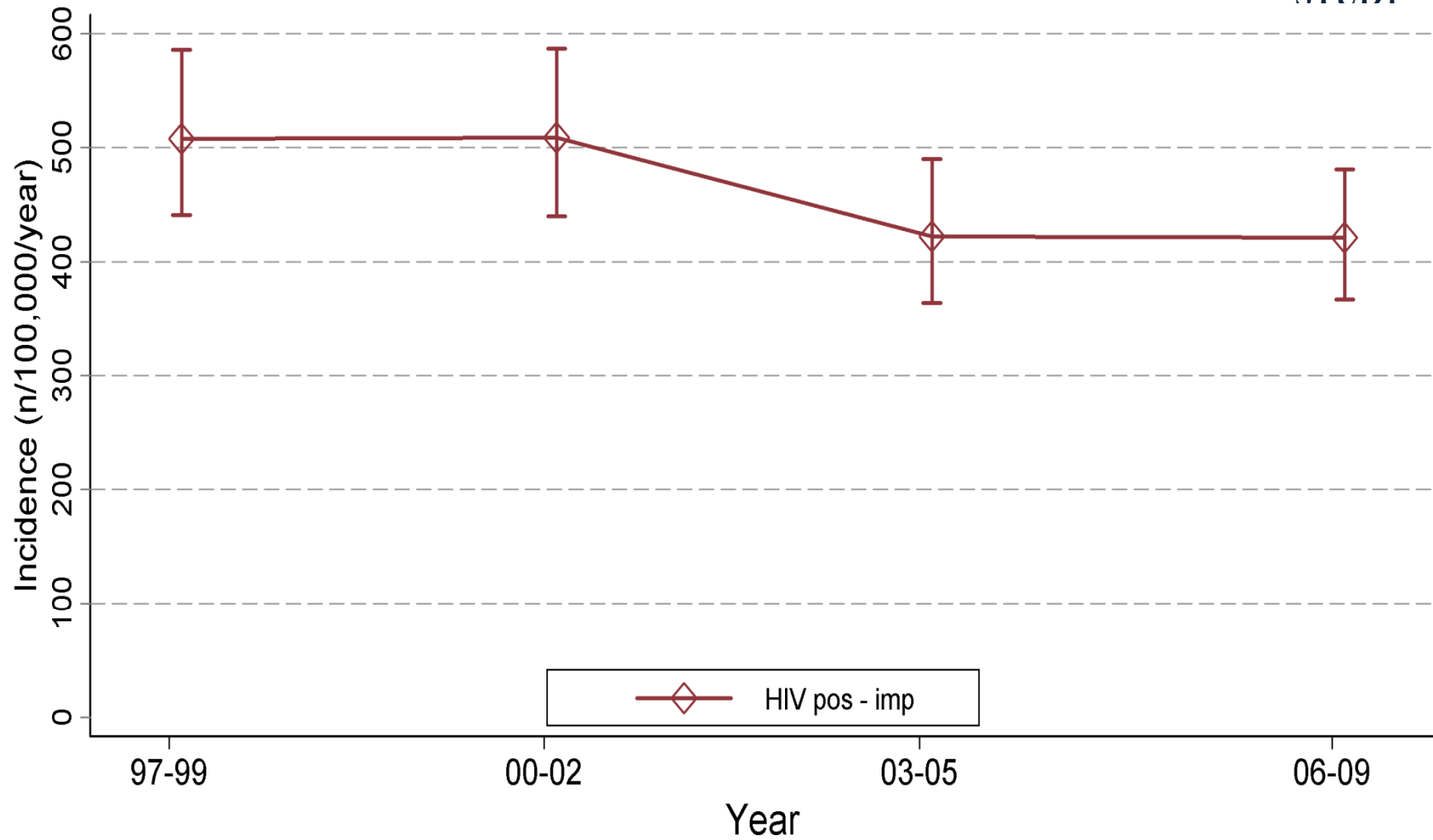
All cases & HIV negative



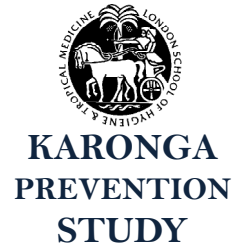
HIV positive



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Change in incidence trend

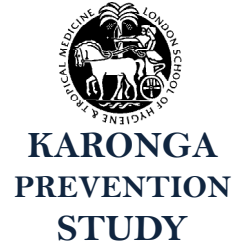


RR express linear annual change in TB incidence, baseline is first year of the period (1997 or 2005). Imputed datasets were used.

Groups	Annual change 1997 – 2005	Annual change 2005 - 2009	P values*
	IRR (95% CI)	IRR (95% CI)	
Overall	0.93 (0.91 – 0.95)	1.01 (0.96 – 1.07)	0.03
HIV negative	0.91 (0.88 – 0.95)	1.09 (0.99 – 1.19)	0.005
HIV positive	0.96 (0.93 – 0.99)	0.99 (0.92 – 1.07)	0.58

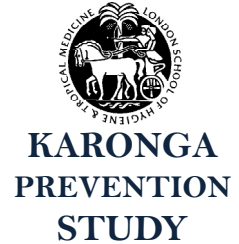
*p-value for change in trend in 2005.

Summary of results



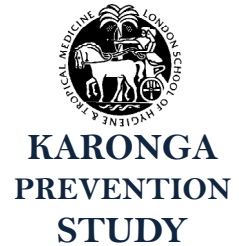
- Relative incidence
 - High incidence early after initiation ART
 - Decreases with time, but still elevated
- Incidence trend
 - Decrease until introduction ART, when it plateaus
- Imputation
 - Does not affect relative incidence estimates
 - Corrects bias in incidence trends

Limitations



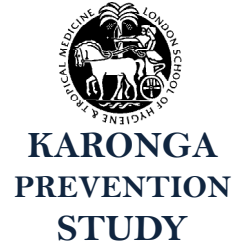
- No CD4 counts
 - Low CD4 at start ART would explain high relative incidences
- Population estimates are always a bit uncertain
- HIV estimates
 - Not include effect ART, but fitted new data reasonably well.

Interpretation



- Well supported DOTS programme controlling TB incidence
 - Area with generalised HIV and moderate TB transmission
- Advent of ART coincided with plateau in TB incidence
 - Affects HIV positive and HIV negative population
 - Very high risk of TB in HIV patients starting ART (too) late
- Incidence trends
 - Extra TB cases following roll-out of ART
 - Direct effect on incidence in HIV positive population
 - Indirect effect in HIV negative population
 - Indirect effect difficult to quantify

Implications/Recommendations



- Start ART earlier
- Further collaboration/Integration of TB and ART programmes
- Intensified case finding in high risk population of patients receiving ART

Acknowledgements

Patients and clinical staff in Malawi

KPS colleagues

Funders

Audience



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wellcome trust

LEPRA



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THANK YOU