

Does Indoor Residual Spraying Provide Added Protection to That Provided By Insecticide Treated Nets in Preventing Malaria?

Results of an Incidence Cohort

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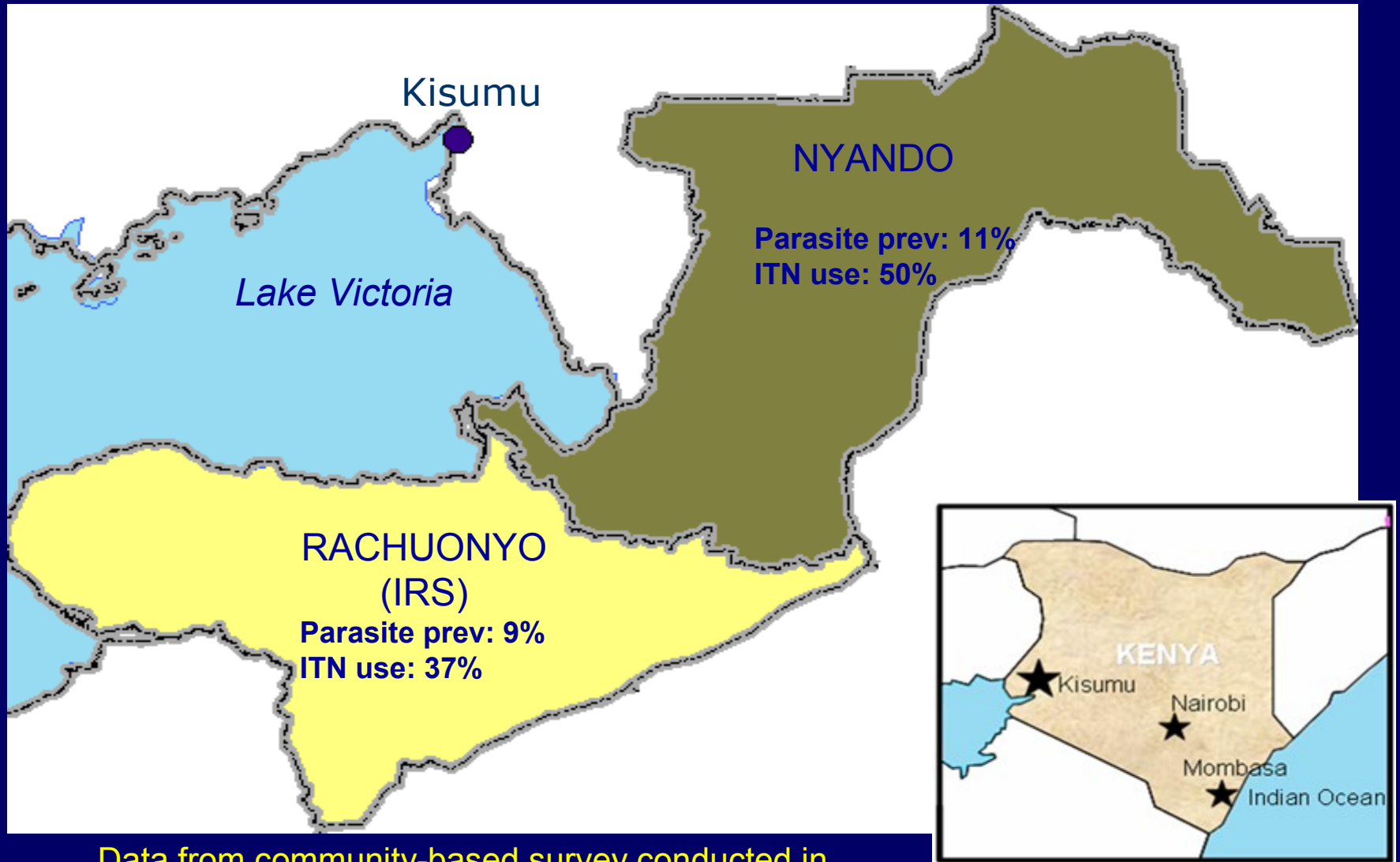
IRS in an Area of Perennial Malaria Transmission

- In August 2008 the Kenya Division of Malaria Control (DOMC) conducted an IRS campaign
 - Area of perennial malaria transmission in western Kenya
 - Using longer lasting insecticide
 - Lambda-cyhalothrin capsule suspension (*Icon CS™*)
 - Reportedly effective 3-6 months (WHOPES)
- Second annual campaign conducted In April 2009
 - Alphacypermethrin (*Fendona™*)
 - Reportedly effective 4-6 months (WHOPES)
- DOMC targeted every home in the selected district for IRS

Objectives

- Following the DOMC's IRS campaign, to measure, through a prospective cohort study
 - the effectiveness of IRS plus ITNs compared to ITNs alone in reducing malaria incidence in an area of perennial malaria transmission
 - One district where DOMC recently applied IRS for the first time (Rachuonyo)
 - Adjacent district with similar malaria transmission levels where DOMC did not apply IRS (Nyando)

Rachuonyo (IRS) and Nyando (no-IRS) Districts, Nyanza Province, western Kenya



Data from community-based survey conducted in April 2009, prior to IRS campaign

Methods

- Incidence cohort from Nov 2008 – Nov 2009
- Randomly selected approximately 80 compounds within 1 km of 6 selected health facilities (~480 compounds total)
 - 3 health facilities in IRS district, 3 in non-IRS district
 - All compound members within selected compounds eligible if:
 - Over 6 months of age
 - Not pregnant
- ITN provided for every sleeping space in included compounds
 - Rachuonyo = “ITN+IRS” cohort
 - Nyando = “ITN, no-IRS” cohort

Enrollment

- Consented/assented participants
 - Interviewed
 - Urine pregnancy test for women of child bearing age
 - Blood sample for blood smear
 - Treated with artemether-lumefantrine (AL) to clear patent/sub-patent parasitemia
 - Provided ITN for every sleeping space

Follow-up

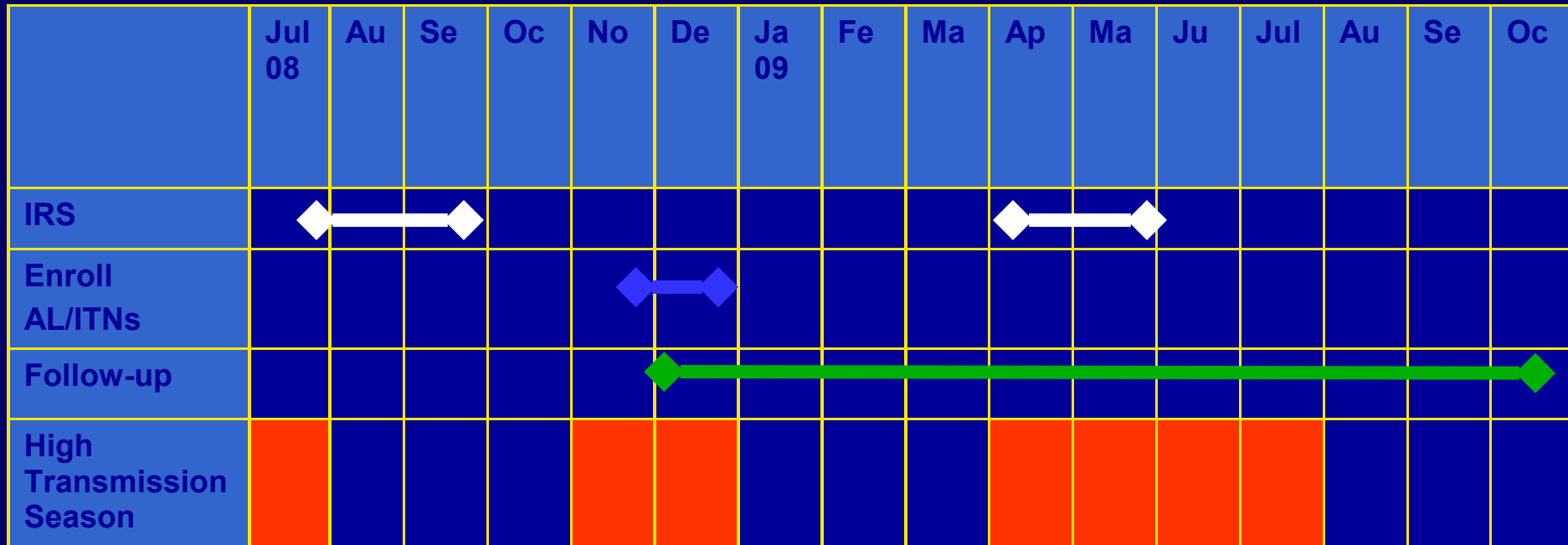
- Participants followed for 9 months or until first malaria parasitemia
- Monthly home visits
 - Questionnaire
 - Blood smear
- Any sick visit with history of fever or suspected malaria:
 - Rapid diagnostic test (RDT) for malaria for treatment
 - Blood smear for end point analysis
 - RDT or blood smear positive treated

Statistical Analysis

- Calculating malaria parasitemia incidence rates
 - Expected duration of minimum inhibitory concentration (MIC) for AL=10.5 days¹
 - Not “at risk” for new malaria infection 10.5 days after AL presumptive treatment at enrollment
 - Began measuring incidence rates 10.5 days after enrollment
 - Decreased time “at risk” by 10.5 days if AL given when BS negative
- Poisson regression model
- GEE to account for correlation within compound
 - In adjusted analysis, controlled for
 - housing type, baseline parasitemia
 - seasonality, ITN use as time varying variables

1. Ezzet, Antimicrobial Agents and Chemo. Vol 44, 2000

Program and Study Timeline



Cohort Baseline Characteristics, By District, November 2008

	ITN+IRS n=921	ITN, no-IRS n=886
Median age (range)	12 (0.5-105)	12 (0.6-91)
Household head completed 1 ^o education	21%	32%*
Housing: Traditional	10%	3%
Semi-permanent	64%	84%*
Permanent	26%	12%*
Open Eaves	90%	94%
IRS in prior year	74%	6%*
Slept under ITN prior night	28%	21%*
Fever prior 2 weeks	49%	33%*

* $p < 0.05$. No significant difference in gender, repellent use, ITN use by age groups, fever prior 2 weeks in children < 5 , antimalarial or ACT use prior 2 weeks

Cohort Baseline Blood Smear Results,

By District, November 2008

	ITN+IRS n=921	ITN, no-IRS n=886
<i>P. falciparum</i> prevalence		
6 mths - 4yr	8%	6%
5-14 yr	12%	9%
≥ 15 yr	2%	2%
Geometric mean parasite density	1008/uL	800/uL

No significant difference in these parameters

Follow-up

	ITN+IRS N = 921	ITN, no-IRS N=866
Completed 9 month follow-up	792 (87%) 7 died, 1 migration, 10 refusal	753 (86%) 3 died, 15 refusal
Parasite period prevalence	13%	29%*
Geometric mean parasite density (parasites/uL)	1770	4292*
ITN use at 9 month visit	72%	98%*

* $P < 0.05$

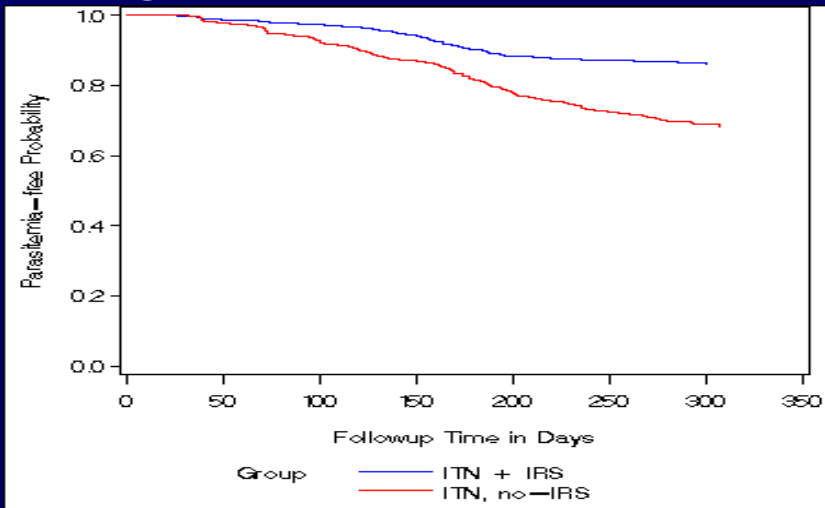
Unadjusted and Adjusted Malaria Parasitemia Incidence, ITN+IRS vs. ITN, no-IRS, by Age Group

	ITN+IRS			ITN, no-IRS			Rate ratio (95% CI)	Adjusted Rate ratio* (95% CI)	Adjusted PE* % (95% CI)
	Events	Person -yr at risk	Rate per 100 person- yr	Events	Person -yr at risk	Rate per 100 person- yr			
Over all	114	627	18	251	570	44	0.41 (0.31,0.56)	0.39 (0.29,0.53)	61 (0.47,0.71)
6 mth – 4 yr	21	146	14	57	133	43	0.34 (0.20,0.56)	0.30 (0.18,0.53)	70 (0.47,0.82)
5-14 yr	70	220	32	137	186	74	0.43 (0.30,0.62)	0.41 (0.28,0.60)	59 (0.40,0.72)
≥15 yr	23	261	9	57	251	23	0.39 (0.23,0.65)	0.43 (0.25,0.73)	57 (0.27,0.75)

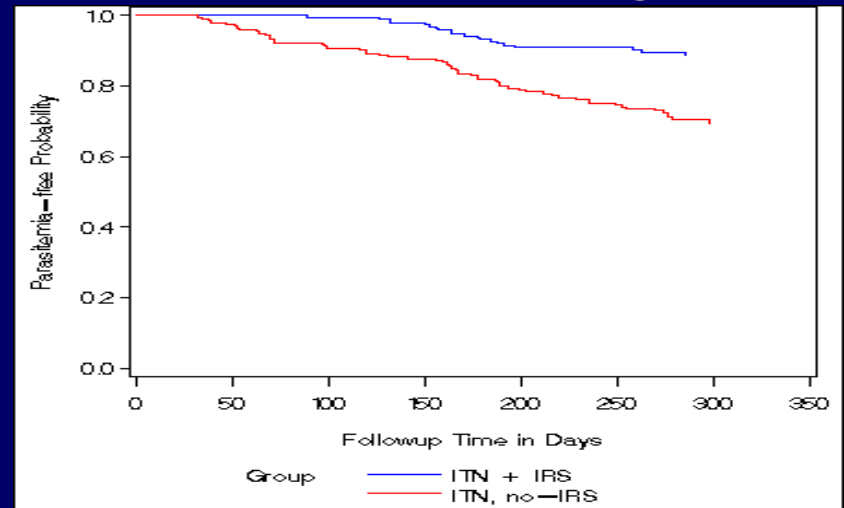
*Adjusted for baseline parasitemia, housing type, and seasonality and ITN use as time varying variables. Interaction between district and ITN use.

Time to First Malaria Parasitemia, ITN+IRS vs. IRS, no-ITN cohorts, Nyanza Province, western Kenya

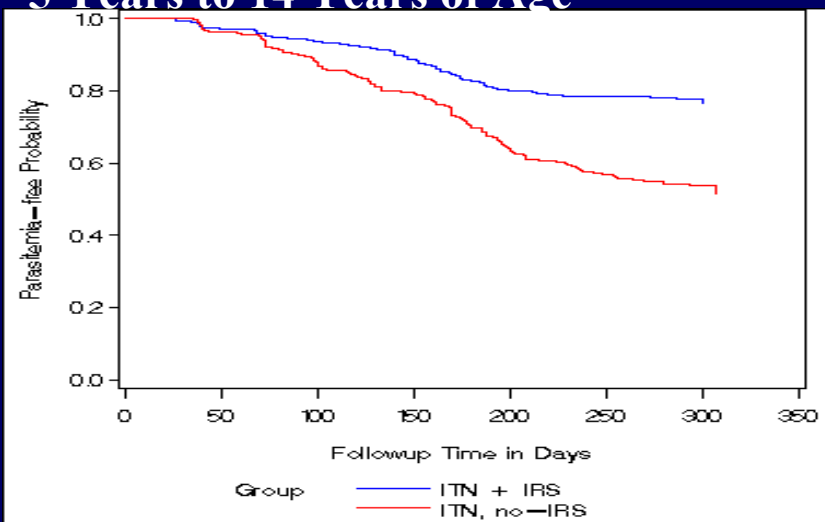
All Ages



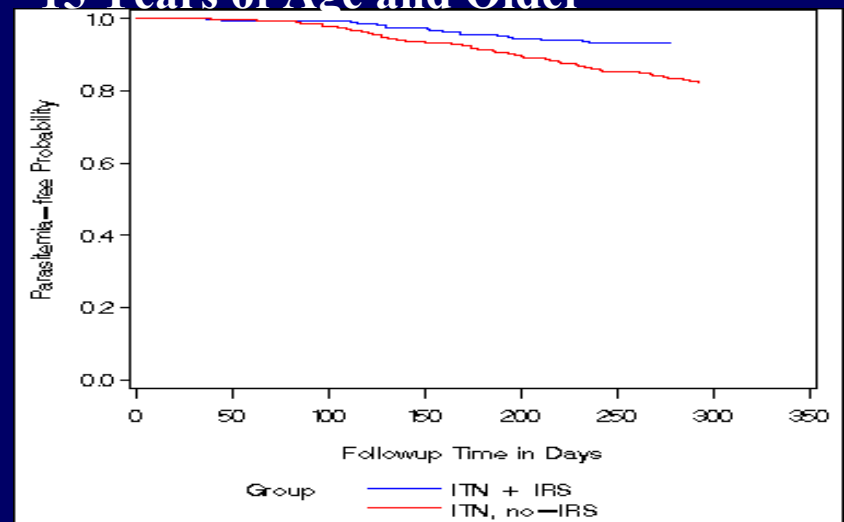
6 Months to Four Years of Age



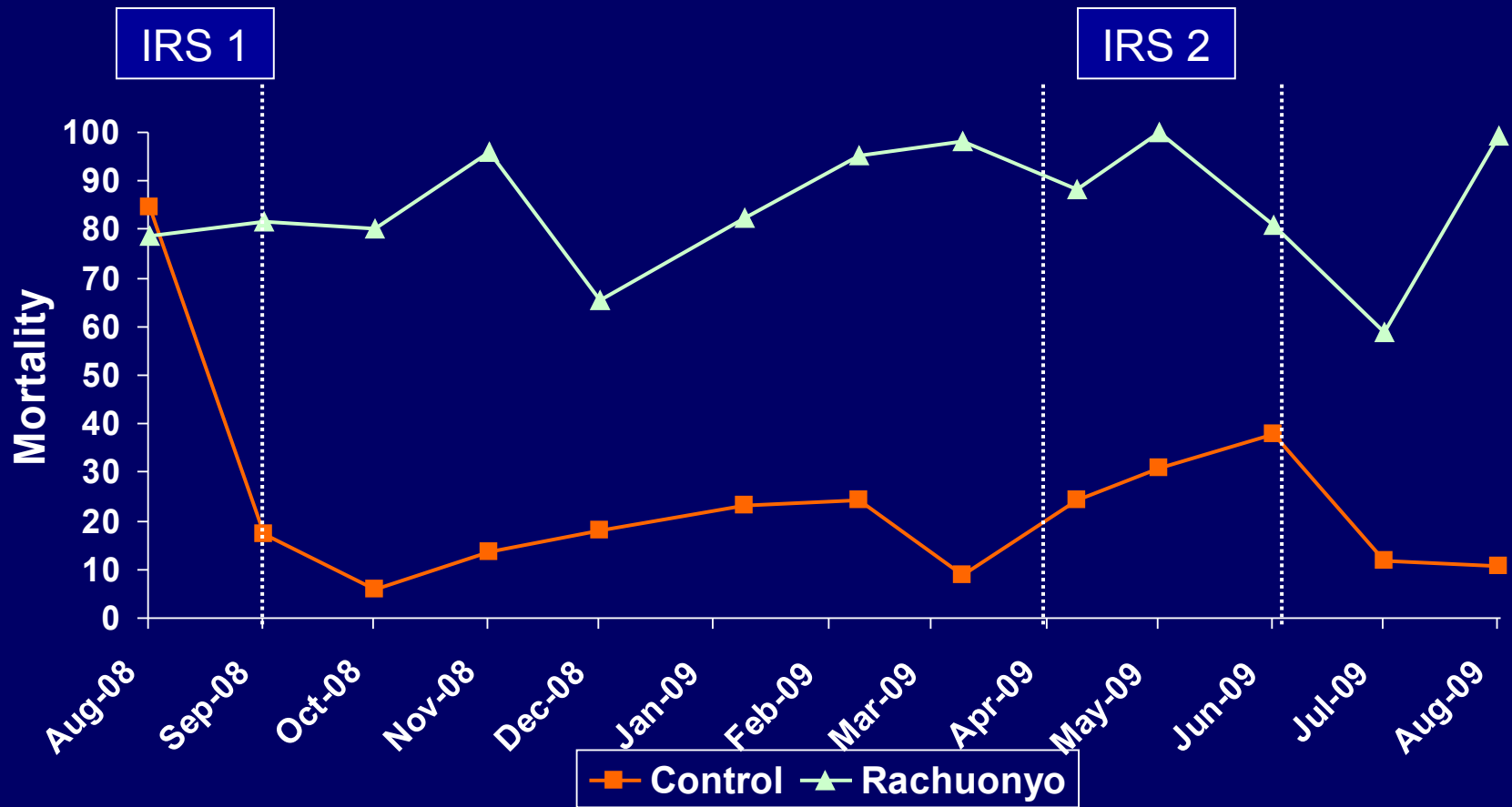
5 Years to 14 Years of Age



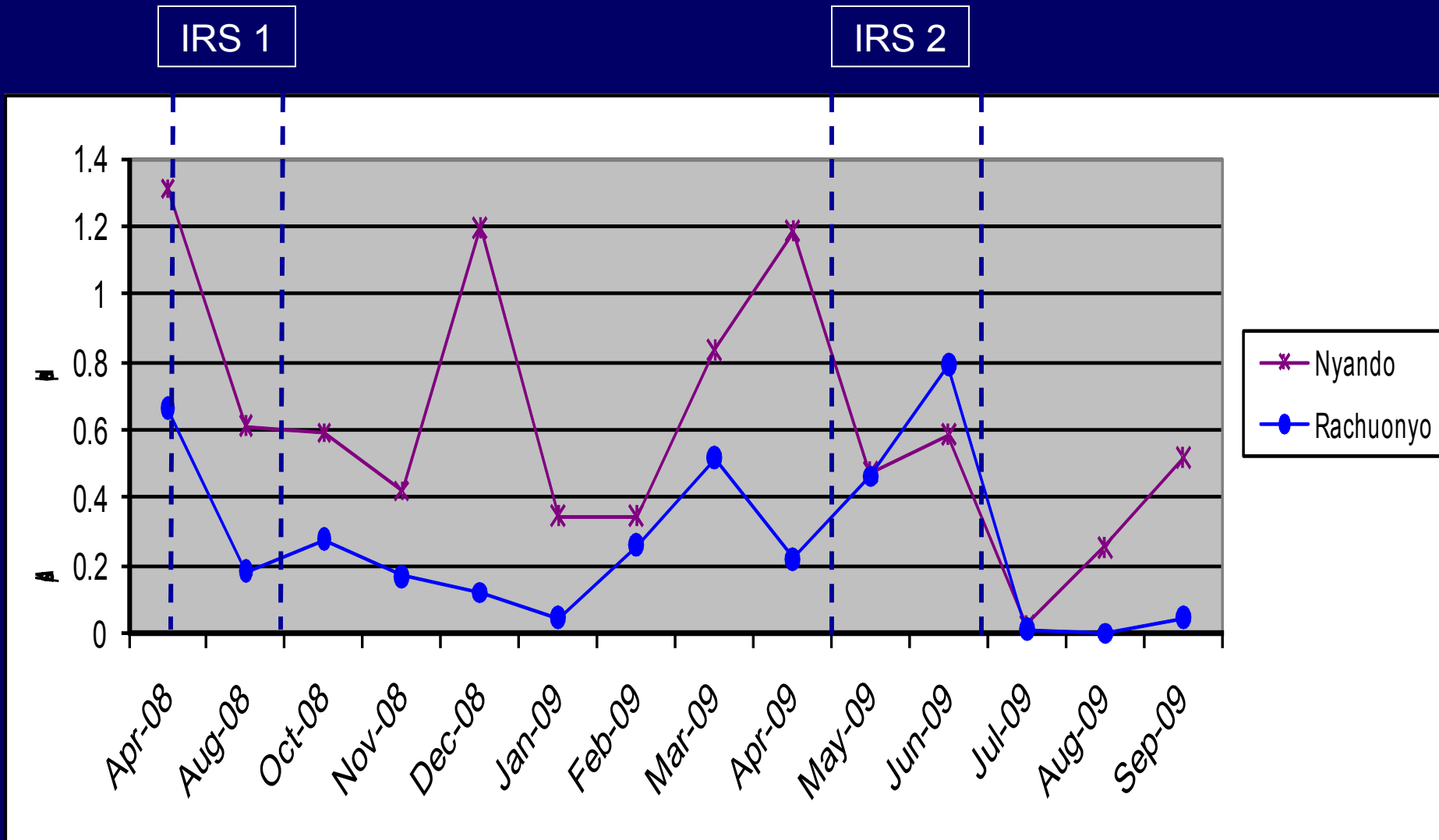
15 Years of Age and Older



Wall Bioassays to Measure Anopheline Mosquito Mortality following IRS in Rachuonyo District (ITN+IRS), Kenya



Number of *Anopheles* per House Before and After IRS, Rachuonyo (ITN+IRS) and Nyando Districts (ITN, no-IRS), Kenya



Limitations

- Not blinded or randomized trial
- No IRS-only arm
- Differences in two districts at baseline
 - Tried to control for these
- Relatively short follow-up period
 - Insecticide resistance may develop with time

Summary

- In this non-randomized study, the combination of IRS and ITNs reduced malaria incidence in area of perennial transmission
 - Combination provided a greater benefit than ITNs alone
 - Reduction in malaria incidence by 61% overall – all in household are protected
 - Reduction in parasite density
 - Beneficial effect despite only 74% of households in the IRS+ITN cohort receiving IRS
 - PMI aims for 85% IRS coverage
- Reduction in ITN use observed in IRS+ITN cohort
 - Need to reinforce importance of ITN use

Discussion

- It may be that this area of East Africa is particularly suited to benefit from combination
 - Two primary vectors are *A. gambiae* ss and *A. Arabienses*
 - Anthrophilic mosquito population driven down by ITNs
 - Zoophilic population became primary vector with high ITN coverage, but may be driven down by IRS due to indoor resting behavior
 - If true, is assumption that we can reduce mosquito populations with IRS, then increase ITN coverage to maintain control valid?

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Time to First Malaria Parasitemia, 6 Months to 4 Years of Age

