

TB Prevention in PLHIV: Options Other Than Isoniazid

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Approaches to TB Prevention

- Primary Prevention (prevent infection)
 - Reduce exposure
 - Reduce transmission
 - Vaccination
- Secondary Prevention (prevent disease)
 - Chemoprophylaxis (IPT) or ART
- Tertiary Prevention (prevent recurrence)
 - Chemoprophylaxis or ART

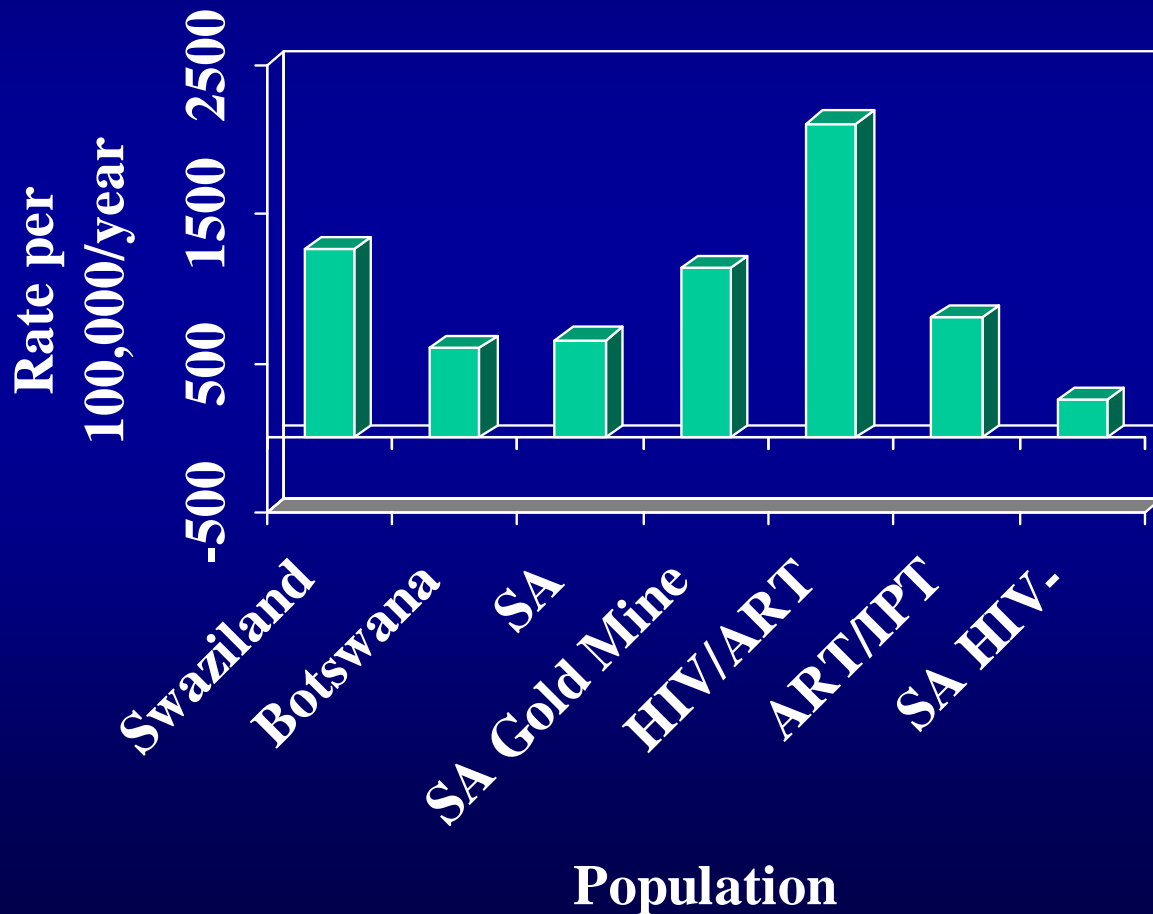
Reasons to Look Beyond IPT

- IPT isn't being used!
 - Toxicity, adherence, resistance and dogma
- IPT isn't enough, even with HAART
- Risk of TB may rise again after completing IPT
- INH resistance

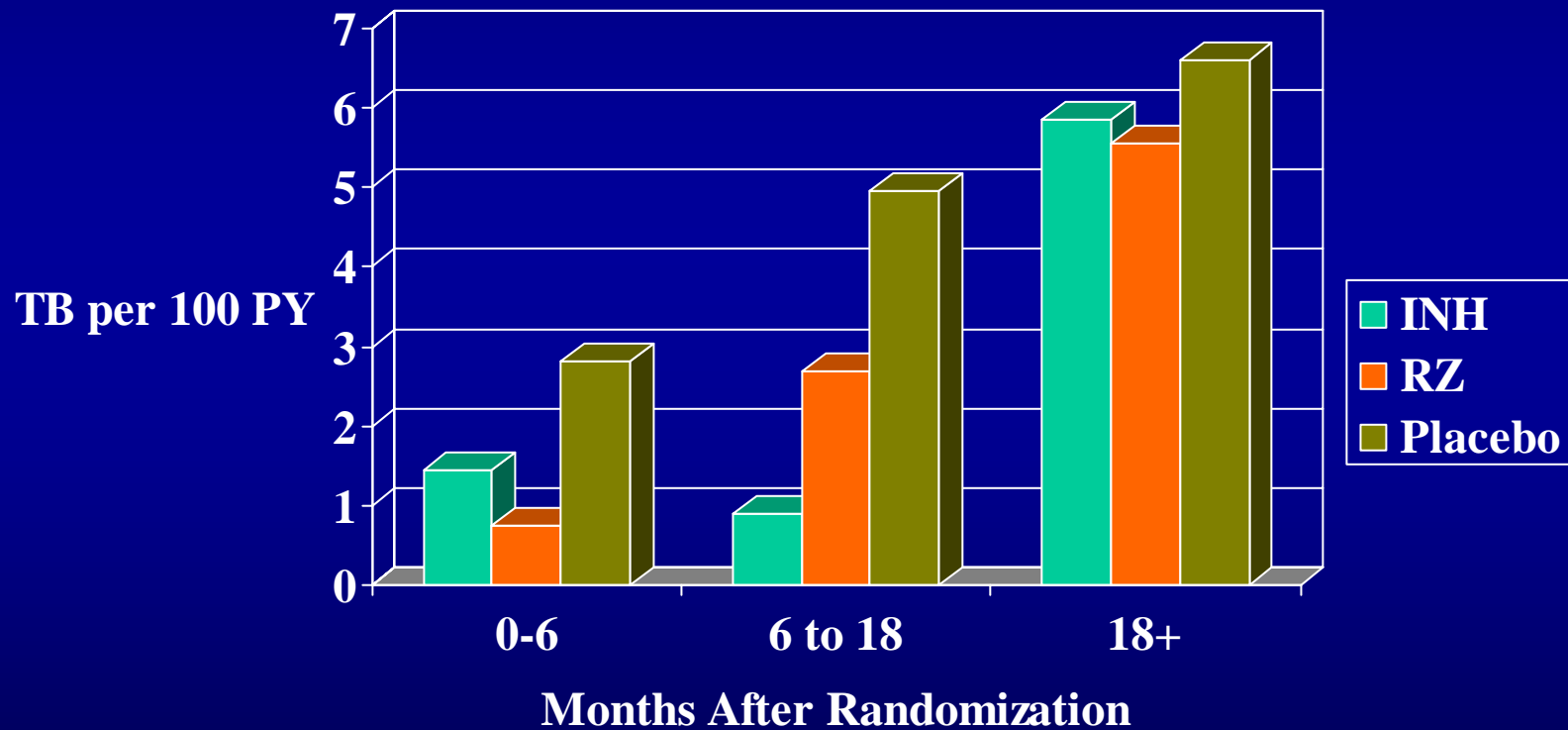
TB Rates in HIV+ Patients With Access to ART and IPT in Rio de Janeiro

Exposure category	Person-Years	TB cases	IR (per 100 PYs)	IRR
Naïve	3,865	155	3.98 (3.38-4.67)	1.0
HAART only	11,627	221	1.91 (1.67-2.18)	0.48 (0.39-0.59)
IPT only	395	5	1.27 (0.41-2.95)	0.32 (0.10-0.76)
Both	1,253	10	0.80 (0.38-1.47)	0.20 (0.09-0.91)
TOTAL	17,142	391	2.28 (2.06-2.52)	

TB Incidence in Selected Populations: African Countries and ART Patients



Durability of Protection Following TB Preventive Therapy



Mwinga et al., AIDS 1998;12:2447

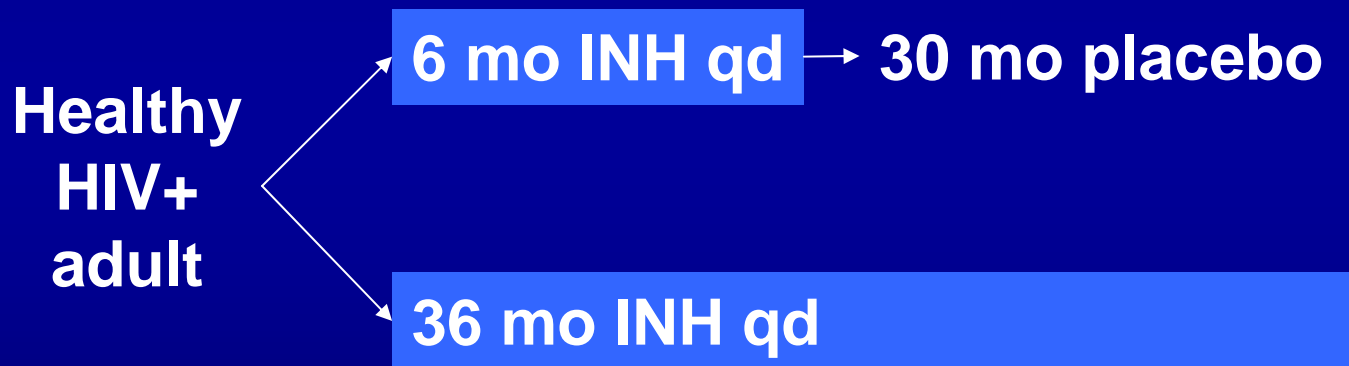
What to use instead of IPT for 6-9 months?

- More INH – continuously or repetitively
- Rifampin \pm INH
- Rifapentine + INH or Moxifloxacin
- PA-824
- Moxifloxacin/PZA
- TMC 207, Otsuka compound, etc.

Botswana IPT Trial Study Design

Randomized Double-Blind Placebo Controlled Trial

2,000 participants- 1,000 per study arm



PHRU/JHU Trial of Novel TB Preventive Regimens for HIV+/PPD+ Adults in Soweto

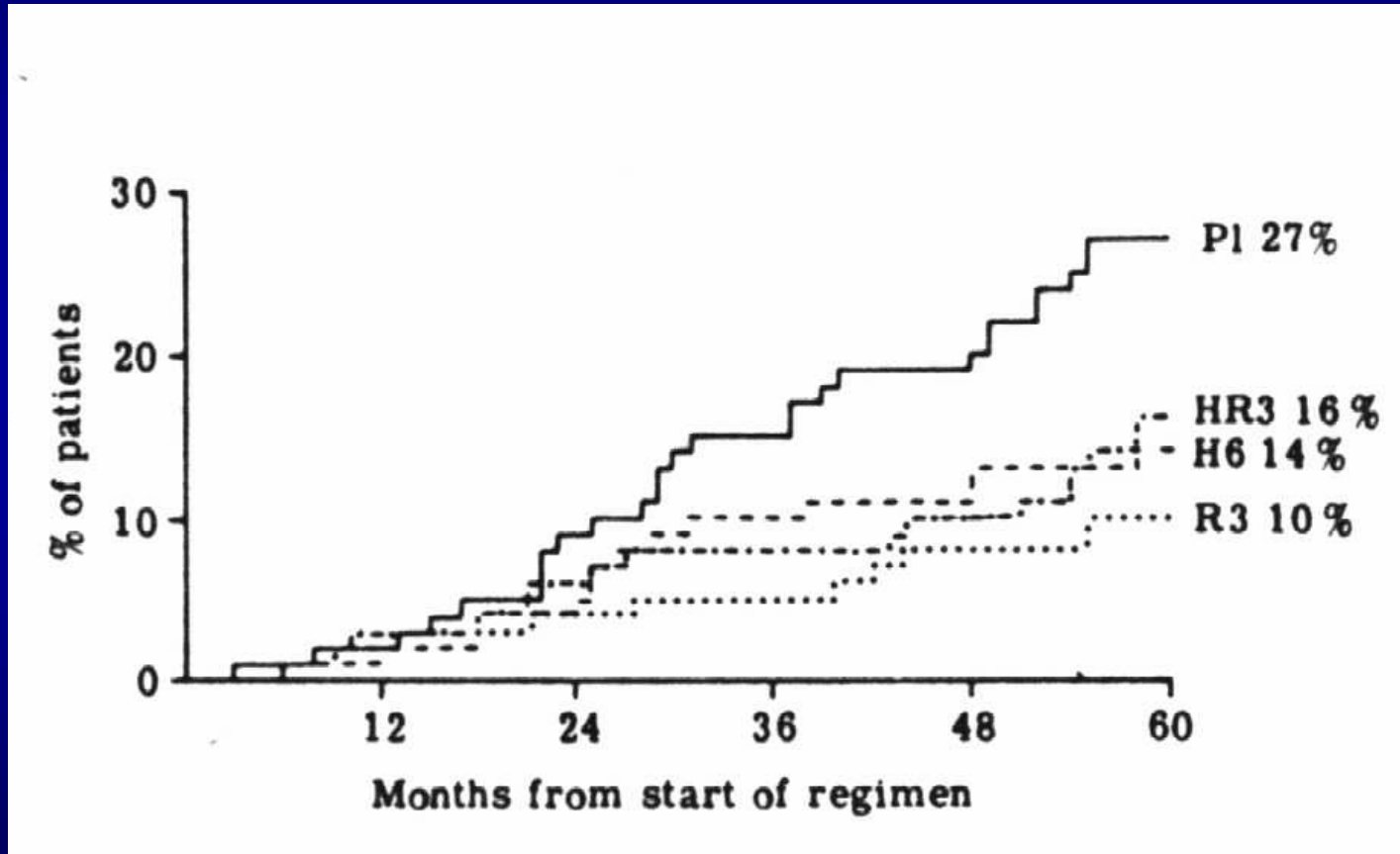
- Patients: HIV+, PPD >5 mm, >18 y.o., CD4 >200
- Regimens
 - Rifapentine/INH weekly x 12 weeks
 - Rifampin/INH twice weekly x 12 weeks
 - INH daily indefinitely (lifelong)
 - INH daily x 6 months (control)
- Median follow up ~ 3.6 years
- Analysis planned for July 2008

Short-Course RIF/INH for Latent TB Infection in HIV+ Patients

<u>Regimen</u>	<u>TB Risk/100 py</u>
INH daily x 6 m	1.1
INH/RIF daily x 3 m	1.3

Whalen et al.

Efficacy of RIF for the Prevention of TB in Patients with Silicosis



Hong Kong Chest Service, et al. Am Rev Respir Dis 1992;145:36-41

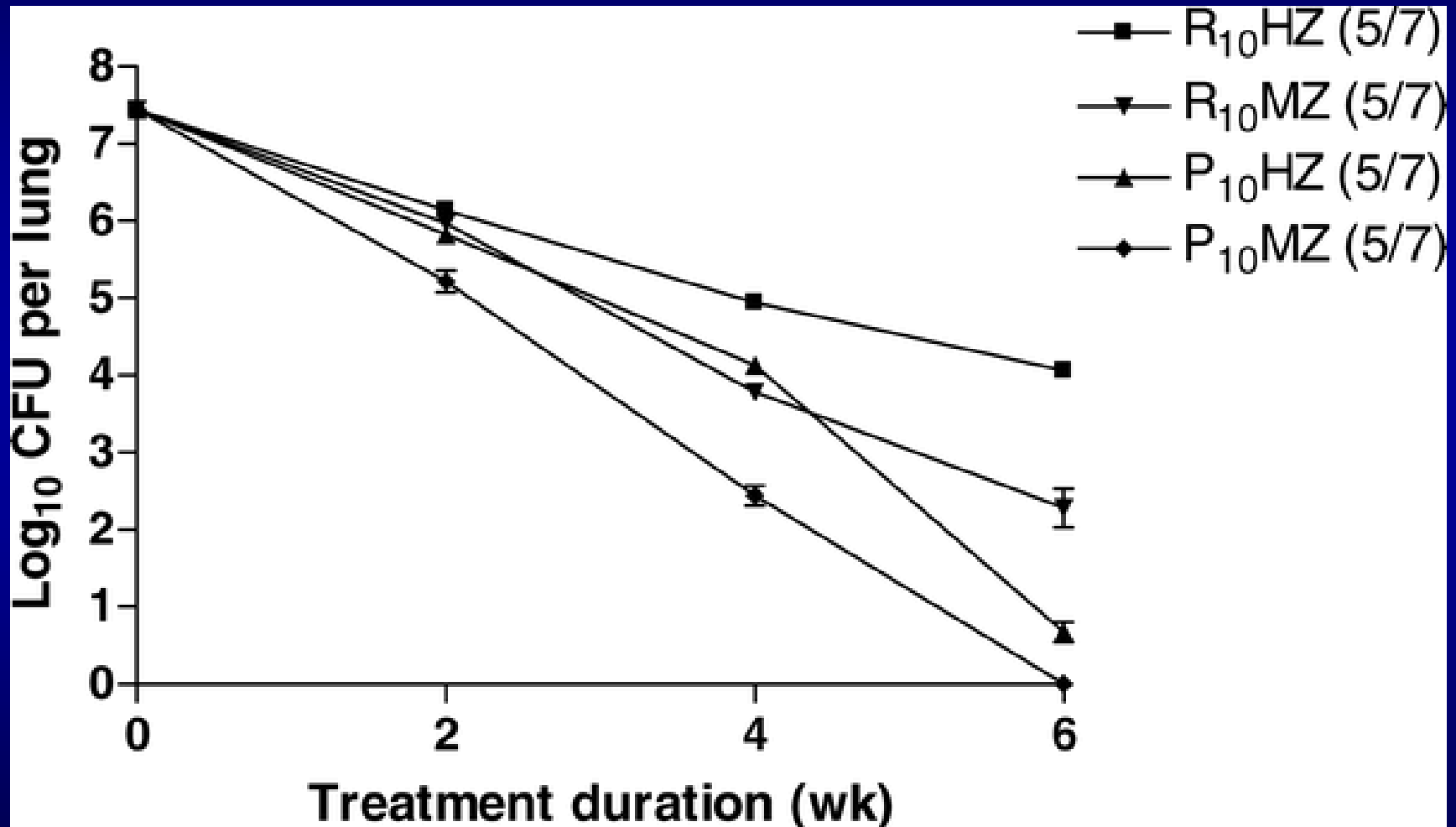
UFRJ/JHU Trial of Weekly Rifapentine/INH in Household Contacts of Pulmonary TB Cases

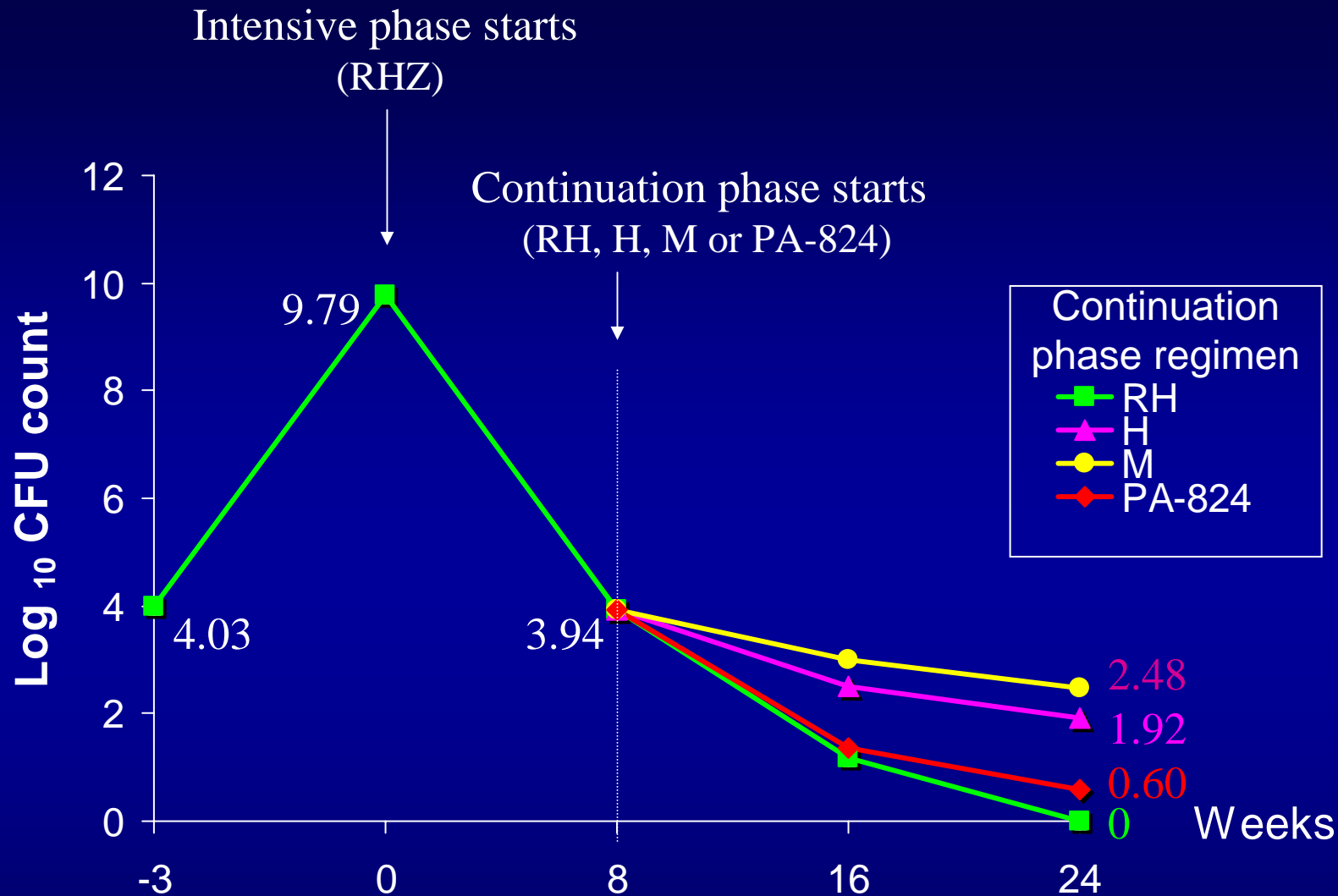
	RPT/INH	RIF/PZA
Number of Patients	206	193
Person-Years of Follow Up	564	522
TB Cases	3 (1.5%)	1 (0.5%)*
TB Rate (Cases/100 Person-Years)	0.5	0.2

*RR 2.8 (95% CI 0.3-26.8), P=0.66

Schechter et al. AJRCCM 2006

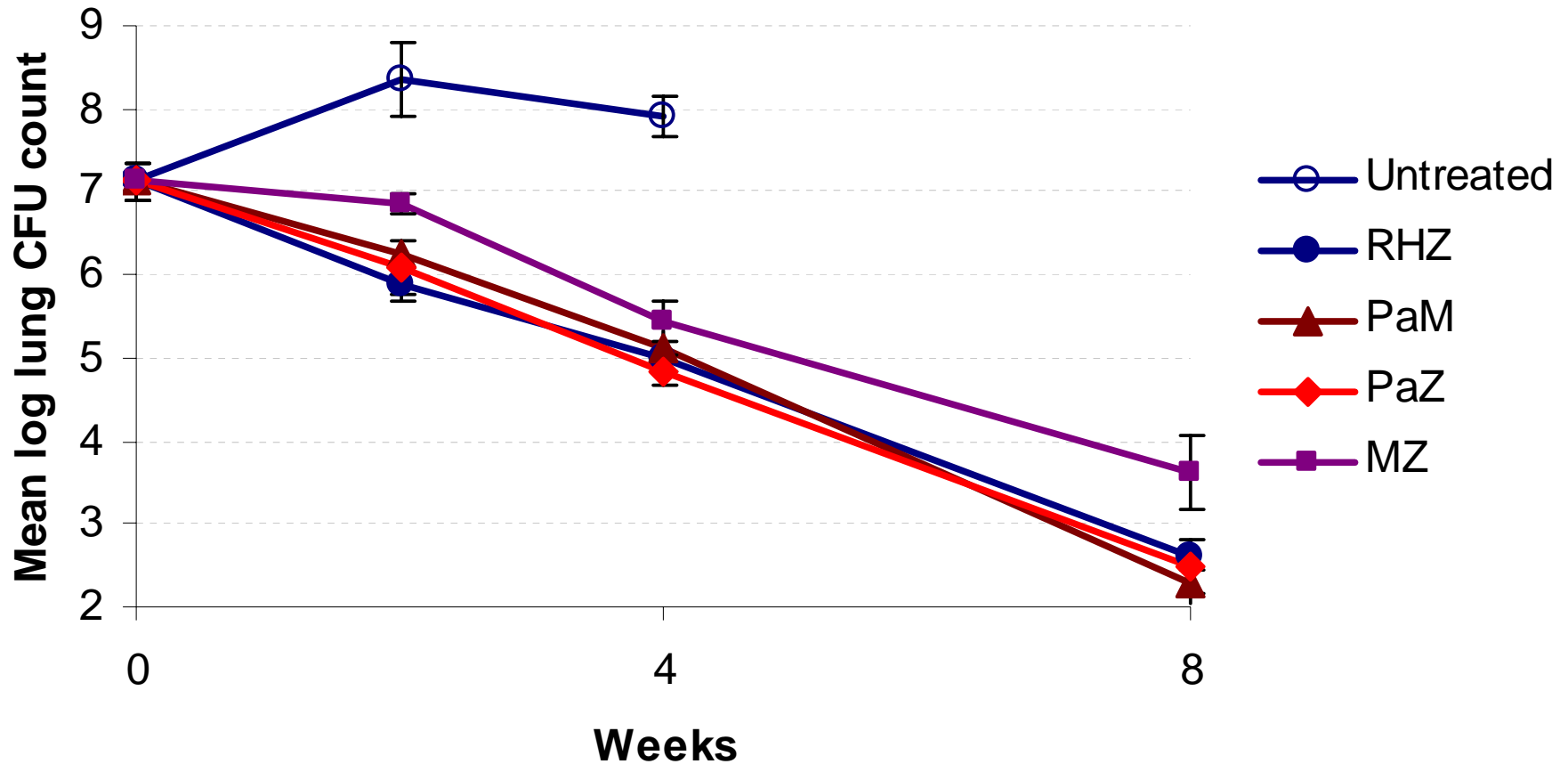
Efficacy of Daily Rifapentine and Moxi in the Mouse Model of *Active TB*





CFU counts in the lungs of mice treated with PA-824 in the continuation phase

PA-824 and Moxi Regimens in Active TB in the Mouse Model



Effect of Secondary Preventive Therapy in HIV+ Patients

Population: HIV+ gold miners with prior TB

Endpoint: TB Incidence

Secondary IPT rate – 5.7 cases/100 PY

No secondary IPT rate – 29.3 cases/100 PY

Relative Risk: 0.19 (0.04-0.42)

Infection Control?



Primary Prevention of TB Infection in Resource-Poor Settings

- Earlier case detection and treatment
- Natural ventilation
- Patient/community education
- Administrative isolation with rapid evaluation for TB and MDR TB
- Personal respiratory protection
- Germicidal *uv* radiation

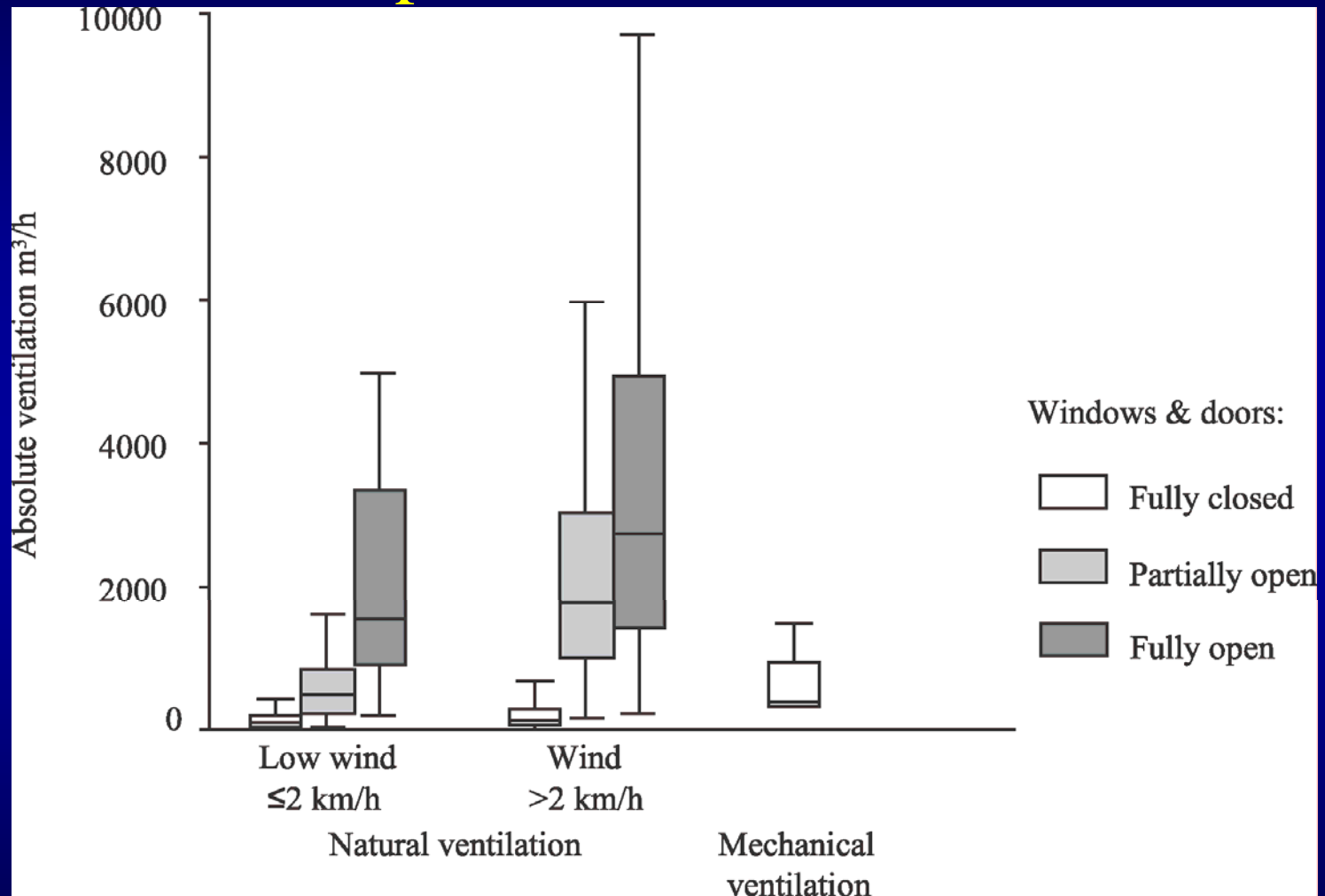
Yield of Contact Investigation as a Tool for Case Detection and Earlier Treatment

- Rio de Janeiro
 - 4% of household contacts of TB cases had active disease
- Zambia/South Africa
 - 6% of households of TB case have second case detected with evaluation

Cavalcante et al., unpublished

ZAMSTAR Study, unpublished

Natural vs. Mechanical Ventilation of Hospital Rooms in Peru



PREVENT DISEASE



CARELESS
SPITTING, COUGHING, SNEEZING,
SPREAD INFLUENZA
and TUBERCULOSIS



RENSSELAER COUNTY TUBERCULOSIS ASSOCIATION, TROY, N. Y.



Church of Scotland Hospital, Tugela Ferry Kwa-Zulu Natal, South Africa



Infection Control, Brazilian Style



Conclusions

- Options other than IPT
 - Rifamycins, new drugs, secondary PT
- Primary prevention
 - Case finding
 - Infection control – simple solutions can be implemented now

TB & HIV

FIND TB

TREAT TB

PREVENT TB