

XDR and MDR TB

Urgent Research Priorities



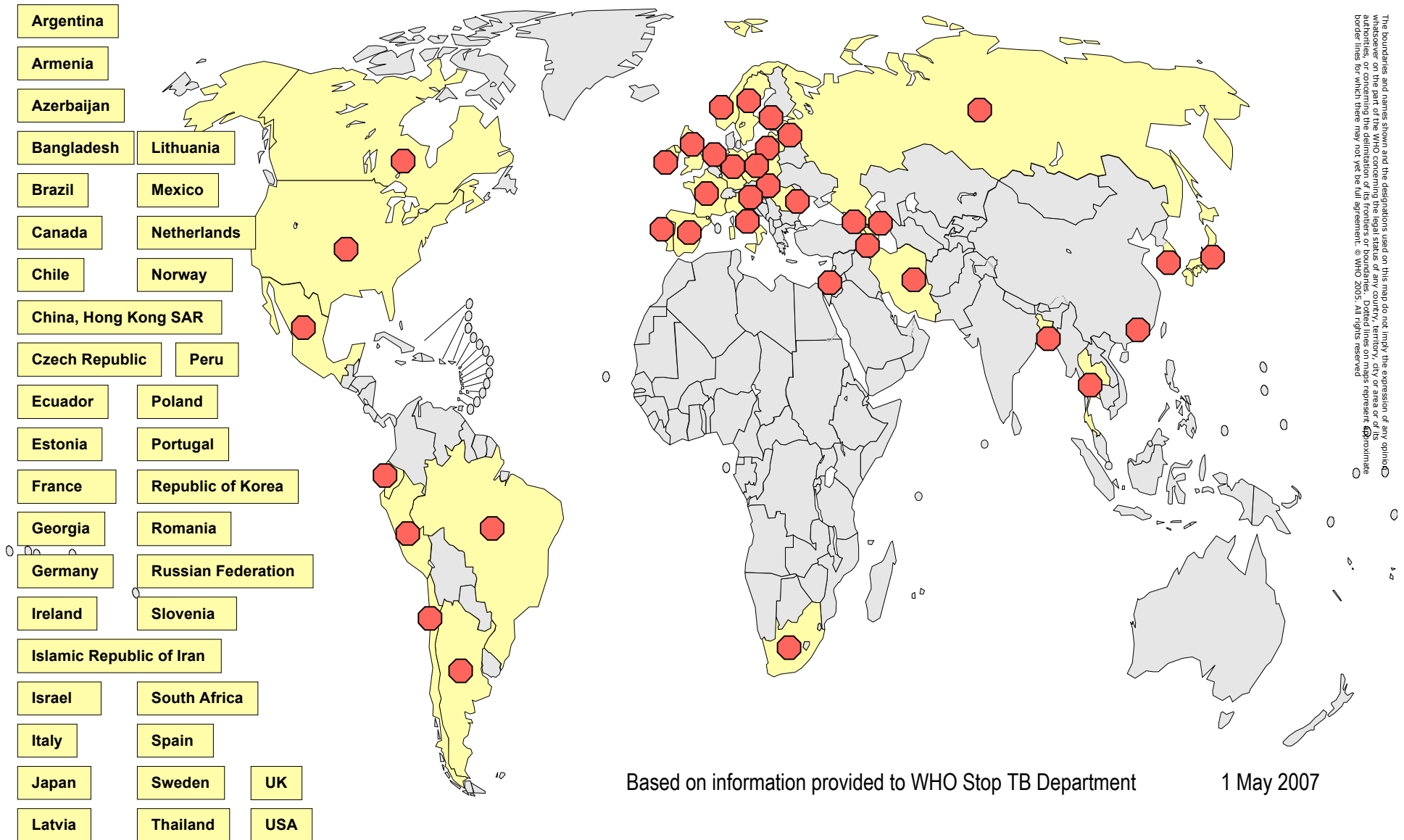
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The Year of MDR XDR TB



- **CDC, WHO report on global XDR TB**
 - XDR TB defined
 - Global distribution
 - Africa, India and Southeast Asia missing
 - HIV not recorded
- **Rural South Africa-Tugela Ferry**
 - Higher rates both of MDR and XDR TB
 - HIV associated
 - Nosocomial transmission
 - Extremely high mortality
- **Global burden estimates**
- **Expert meetings and recommendations**
 - WHO, CDC, NIH, Forum, national and international meetings
- **The ASPE-airborne single patient event**

Countries with XDR-TB Confirmed cases (May 2007)



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion on the part of the WHO concerning the legal status of any country, territory, city or state or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2005. All rights reserved.

Based on information provided to WHO Stop TB Department


1 May 2007

M/XDR TB is a wake up alarm call




- **MDR and XDR TB uncovers past and current deficiencies in TB knowledge, strategies and programs**
- **Illustrates global nature TB drug resistance**
- **For high TB and HIV prevalence areas, threatens success of both StopTB and historic ARV roll out**
- **For high TB and low HIV prevalence areas with high HIV incidence, alerts ominous danger**

MDR XDR TB Research Priorities

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- Broad and complex areas of need
 - Epidemiology
 - Diagnosis
 - Treatment
 - Urgency requires short term and longer term approaches, goals and solutions
 - Operational research essential
 - Resources

Two Case Studies MDR/XDR TB



Tugela Ferry	ASPE
High TB/M/XDR TB and HIV Prevalence	Single case
Diagnostic limitations No microbiologic monitoring	Diagnostic limitations Delayed and discordant results
Standardized treatment	Standardized treatment
TB control program-poor success	?
HIV epidemic	
KZN strain	
Lack of attention to transmission	Puzzling attention to transmission
Absence of treatment options	Limited treatment options
Ethical dilemmas	Ethical dilemmas

Epidemiology



- **Desperate need for epidemiologic characterization and interventions**
 - *Short term*
 - Rapid investigation of “hot spots”
 - Determination of type and site of transmission
 - Acquired vs Primary
 - Nosocomial and community
 - Interruption of transmission
 - *Long term*
 - WHO standardized surveillance procedures
 - Understanding relationship between resistance, virulence, specific strains

Diagnosics



- **Desperate need for modern, rapid M.TB diagnosis and drug susceptibility testing-first and second line, at point of care.**
 - *Short term*
 - case detection (TB and DS) by clinical algorithms and microscopy
 - expansion and availability of existing technologies
 - expansion of SL DST in existing labs
 - rapid mycobacterial culture and DST- MODS
 - testing of available promising rapid tests (rifampin based resistance)
 - expansion of rapid tests to include sentinel SL DST
 - *Longer term*
 - widespread availability of rapid diagnostic technologies and facilities
 - enhanced and respected diagnostic research
 - training and retention of laboratory personnel

Therapeutics



- **Desperate need for new drugs and shorter regimens**
 - *Short term*
 - Speeding drug evaluation and approval process
 - “Salvage therapy”
 - Shorter followup
 - Surrogate markers
 - First and SLD TB and ARV PK and PD interactions
 - Novel treatment delivery strategies for SLD-treatment
 - Community based treatment
 - *Long term*
 - Expanded access
 - Clinical trial results of new therapies
 - Basic research in drug development

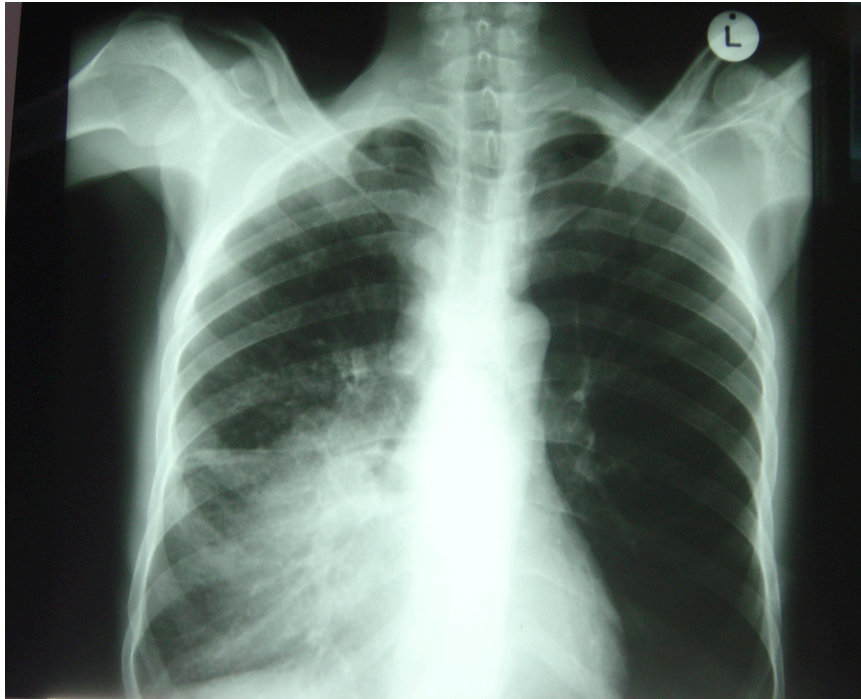
HIV and TB



- **Universal access to antiretroviral therapy**
(decrease susceptible population)
 - *Short term*
 - accelerate ARV roll out
 - start ARVs earlier before TB disease occurs
- **Strengthening TB programs**
 - *Short and long term*
- **Operational research or programmatic collaboration and integration**
 - *Short and long term*

**Urgent need to interrupt
transmission**

Hospital acquired XDR-TB



12 January 2007


Drug susceptible TB



11 April 2007

XDR-TB

Urgent need to interrupt transmission

- 
- Primary nosocomial transmission critical
 - Most sites with no or limited infection control

- ***Short term***

- **focus on developing, implementing and monitoring site appropriate infection control strategies**
 - administrative ,environmental, personal
 - Study effectiveness of strategies individually and in combination

- *Long term*

- Vaccine
- Alleviation of social and economic conditions and health disparities that breed both TB and HIV

Future projections Tugela Ferry

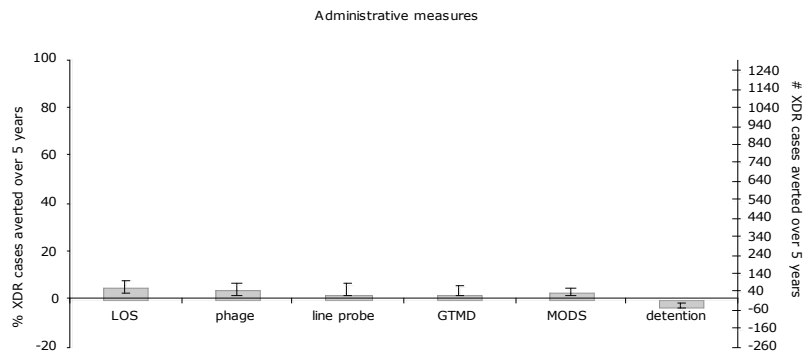
Effect of infection control interventions

(2005-2007)

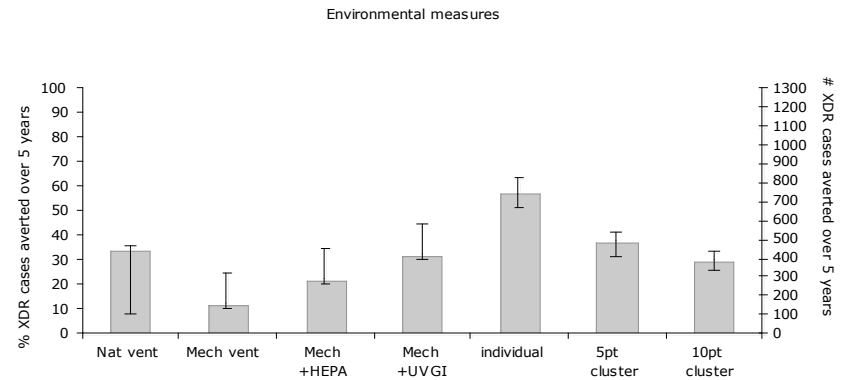
- If no new interventions are introduced, a total of 1,300 cases of XDR tuberculosis predicted
 - Over half nosocomially transmitted.
- Combining available interventions could avert 48% of XDR TB (range 34-50%)
 - mask use, reduced hospitalization time, shift to outpatient therapy, improved ventilation, rapid drug resistance testing, HIV treatment, and reasonable tuberculosis isolation facilities.

XDR TB cases averted over the next five years

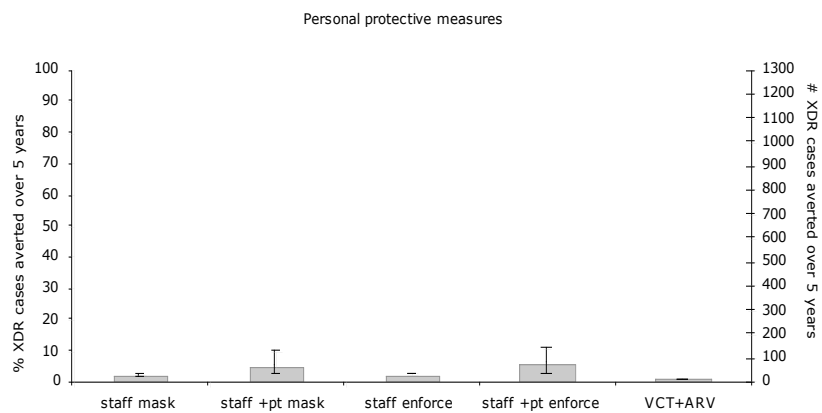
administrative measures.



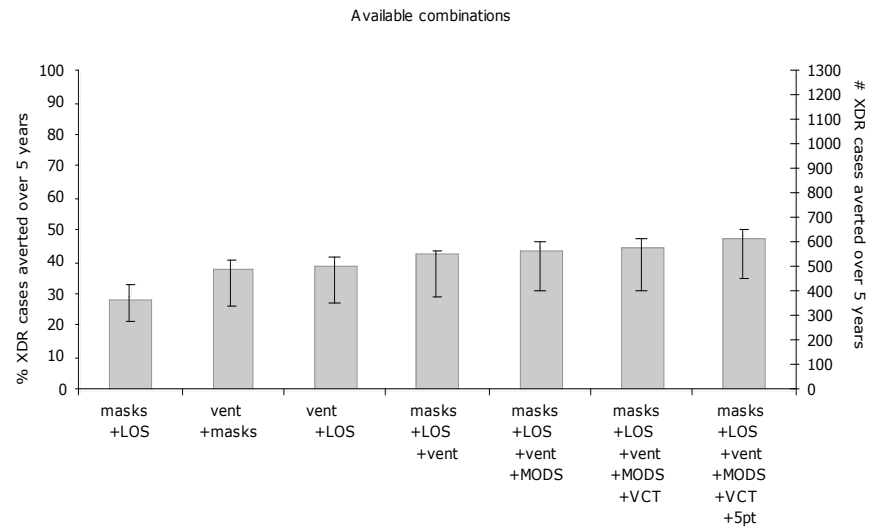
environmental measures



personal protective measures

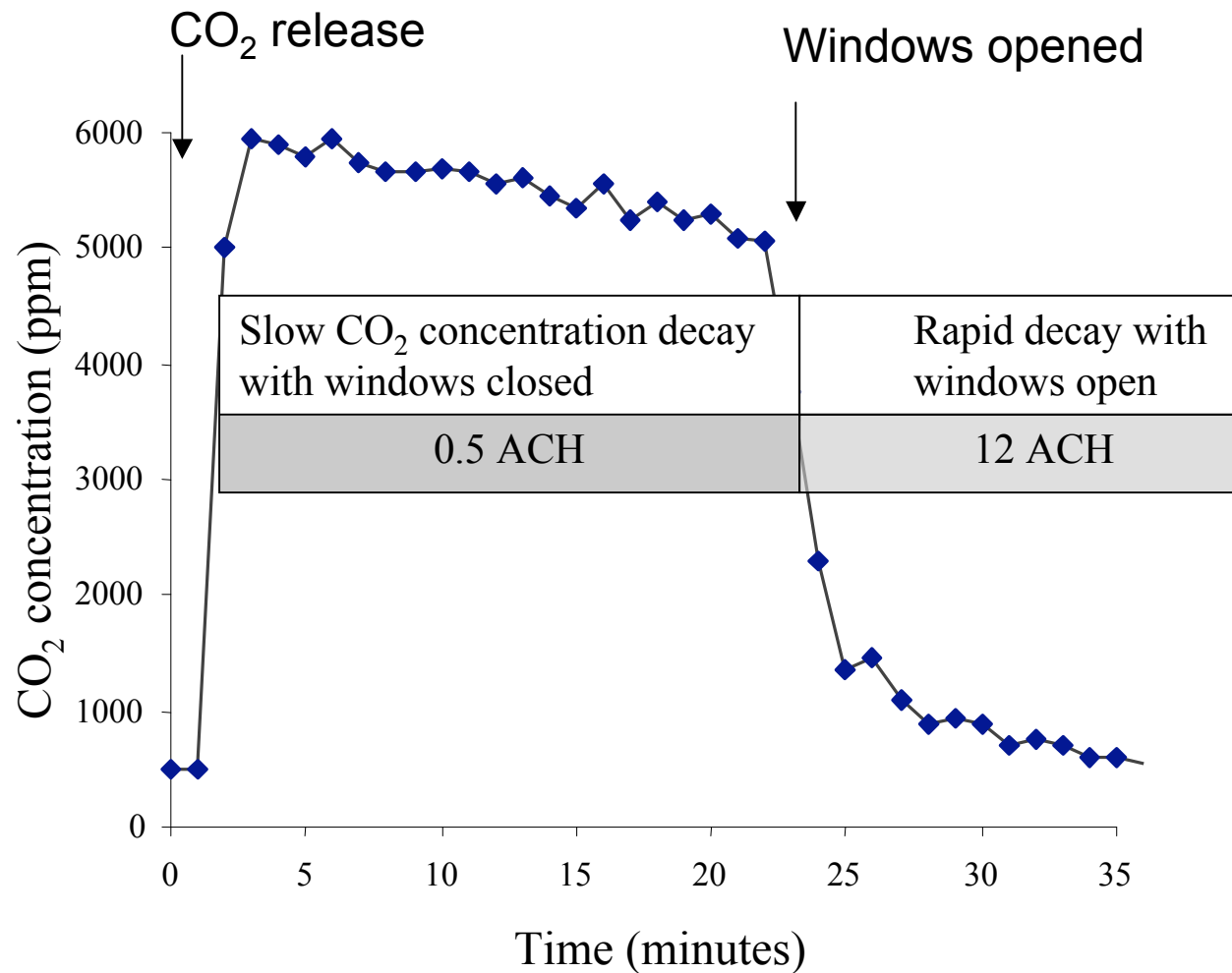


combinations of strategies



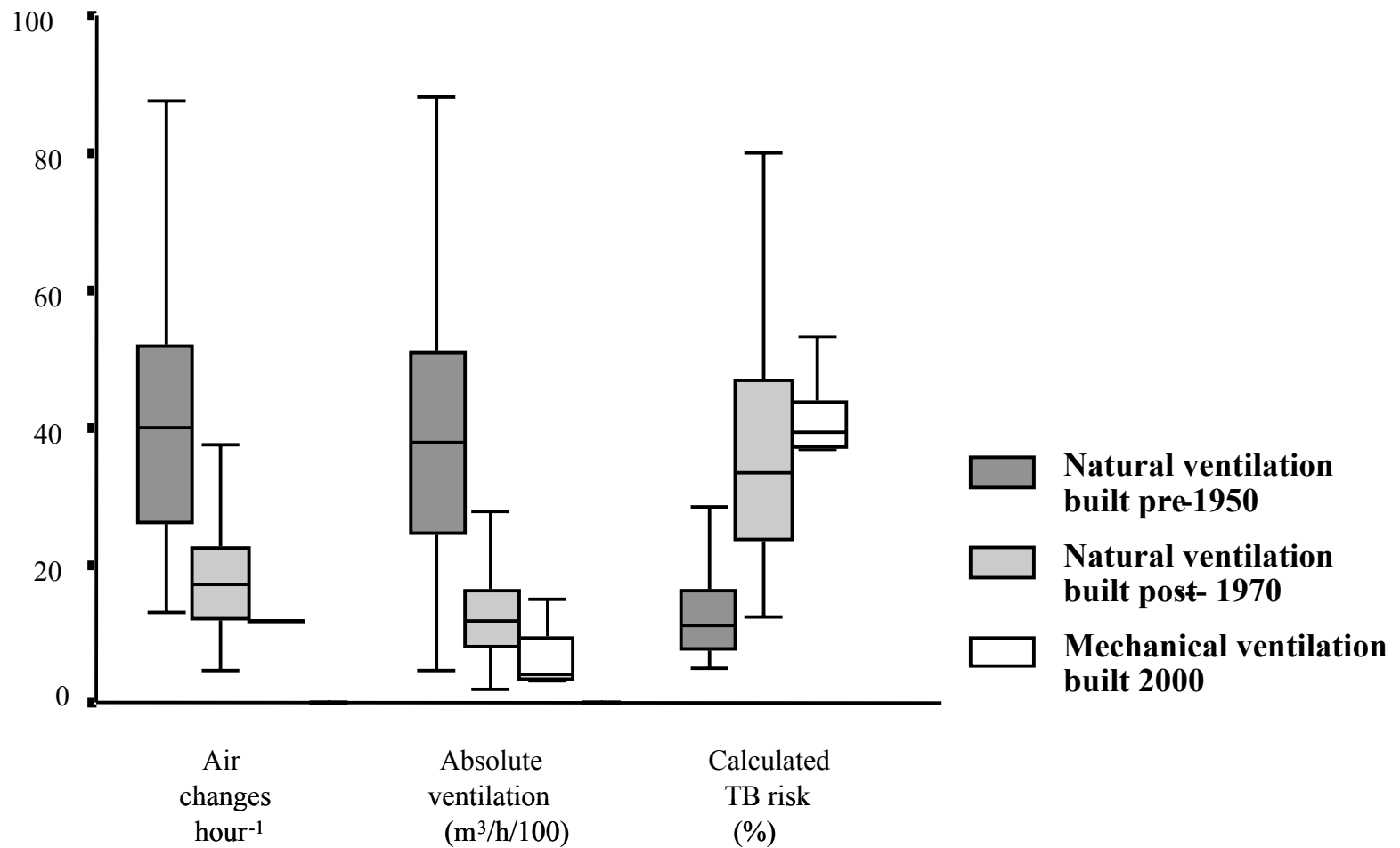
Natural Ventilation for the Prevention of Airborne Contagion

A. Roderick Escombe^{1,2,3*}, Clarissa C. Oeser³, Robert H. Gilman^{3,4}, Marcos Navincopa⁵, Eduardo Ticona⁵, William Pan⁴, Carlos Martínez⁵, Jesus Chacaltana⁶, Richard Rodríguez⁷, David A. J. Moore^{1,2,3}, Jon S. Friedland^{1,2}, Carlton A. Evans^{1,2,3,4}



368 experiments performed over 2 years

Old fashioned vs. modern facilities : ACH, absolute ventilation, risk of TB infection



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