



# Eero Tala Lecture: Tuberculosis: A global vision

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Filha ry 100 vuotta 1907-2007  
Tieteellinen Symposium  
Helsinki, 23 August 2007

# Dedication

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- ❖ This presentation is dedicated to a valued and greatly admired colleague and friend, Prof Eero Tala. He was one of the kindest and finest humans I have known.



# Tuberculosis:

*The views of an expert.....*

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- ❖ ...The smallest drops expelled into the air by the patient when he coughs, clears his throat, and even speaks, contain bacilli (that) can cause infection.....
- ❖ ..(The disease) becomes more frequent.....the more there is lack of light and air and the more closely the sick are crowded together ...
- ❖ ...particularly high if healthy people sleep with the sick in the same rooms, and especially in the same bed.....



# Essentials of public health..

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- ❖ ...(Due to) the dangers arising from the spread (of this disease)...prophylactic measures should be taken....
- ❖ ..amidst the variety of means...what measures ...best satisfy scientific requirements...in the fight against contagious disease?
- ❖ The starting-point is the obligation to report...it should be introduced everywhere. It can.....be restricted to those cases which constitute a danger to their acquaintances ..... (smear positive) tuberculosis...



# Managing cases.....

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- ❖ .....we must ensure that (doctors) can judge the cases with respect to the presence of (smear positive) tuberculosis. This can only happen with the establishment of centres where the patient's sputum is examined, without cost.....
- ❖ The reason for the small number of real cures ..... evidently lies in the fact that the treatment (must be prolonged).....



# Elements of disease control.....

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- ❖ ....improvement in housing conditions and knowledge...have played their part in bringing about the decline in tuberculosis...
- ❖ ...institutions (that) provide the poor.....with a true welfare service (are) one of the most powerful weapons which we can use against tuberculosis.....
- ❖ We should not close our eyes to the fact that the fight against tuberculosis needs considerable financial resources. Basically it is only a question of money.....



# The international expert:

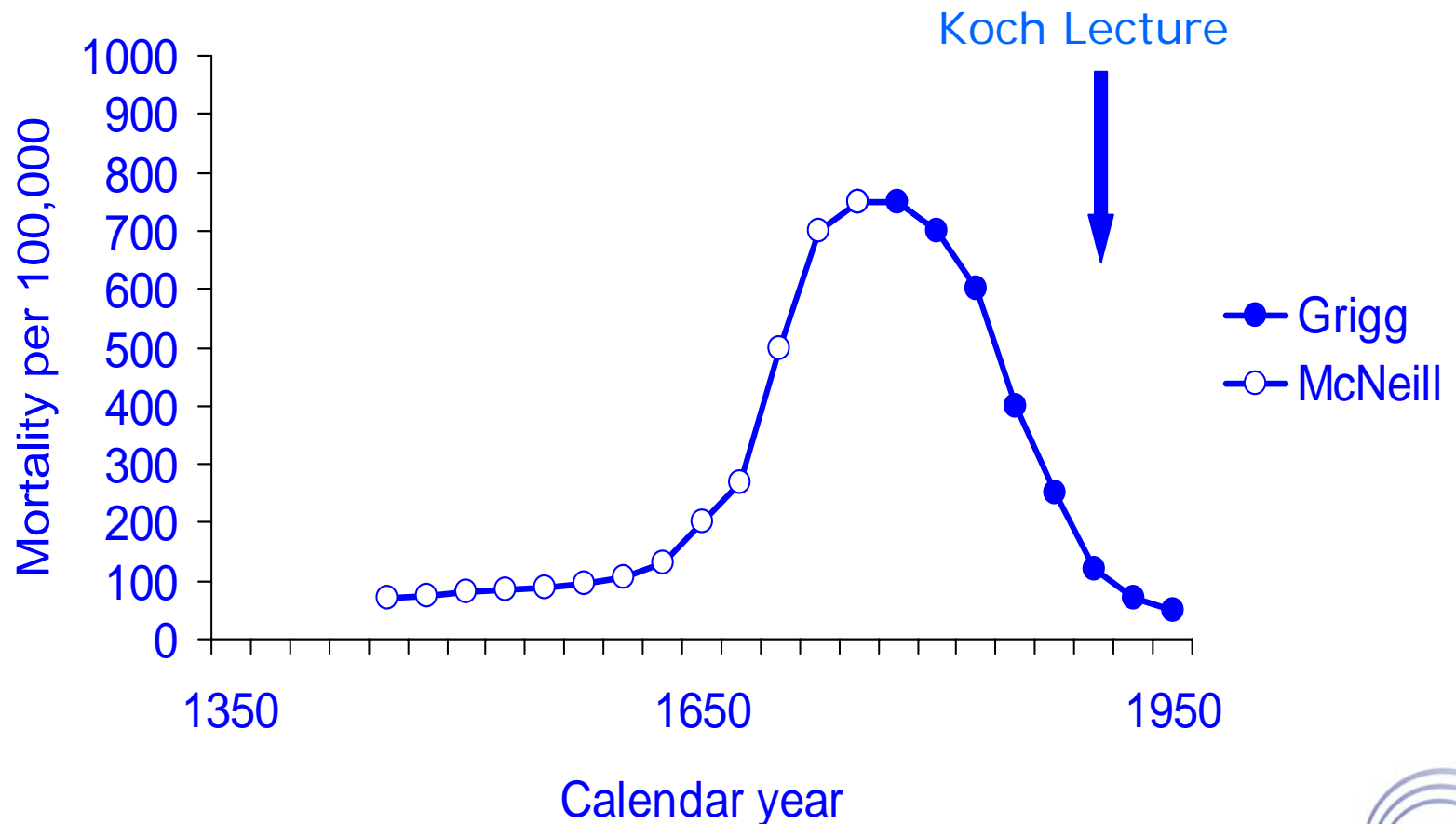
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Robert Koch:

❖ The Nobel lecture of 1905.

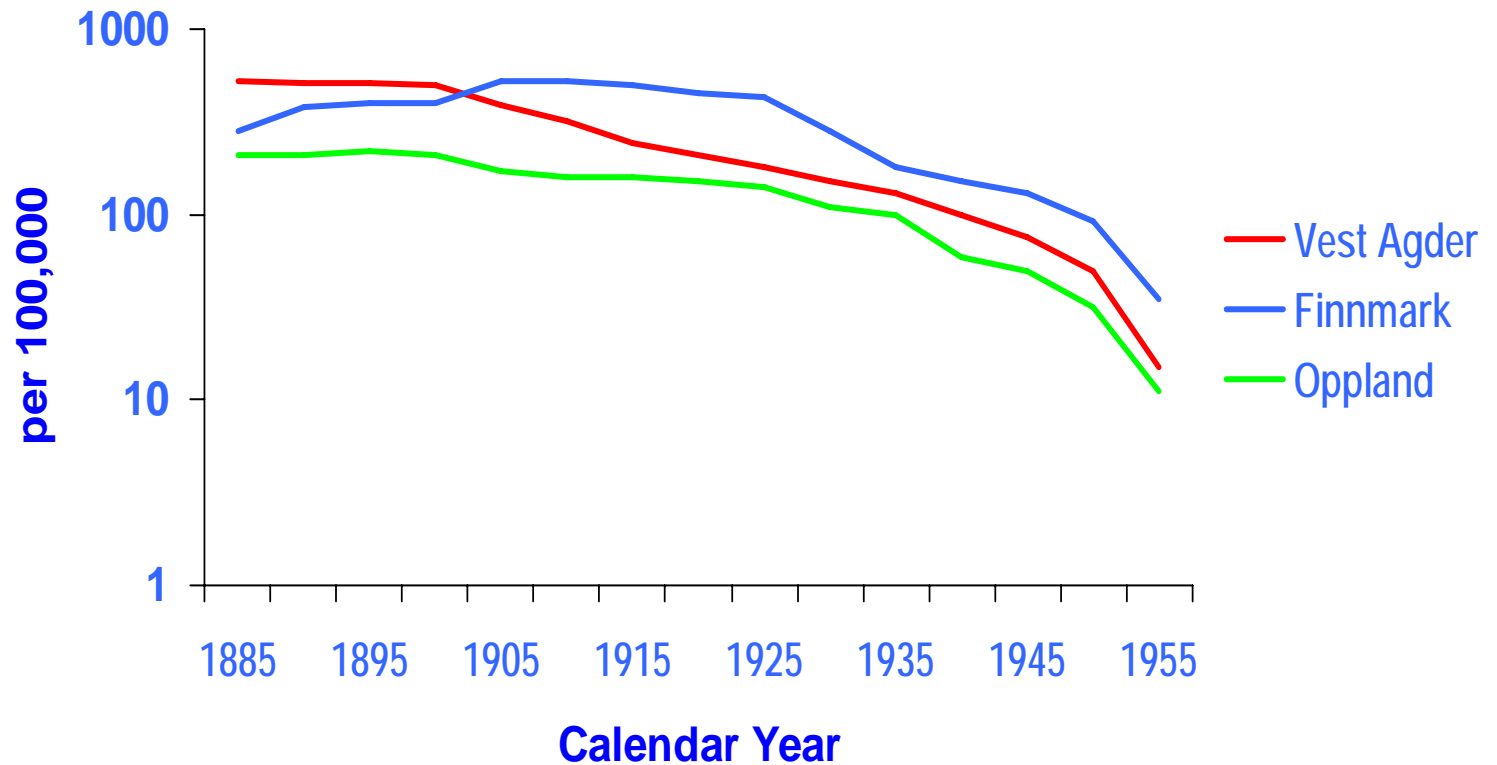


# Hypothetical course of the tuberculosis epidemic in Europe



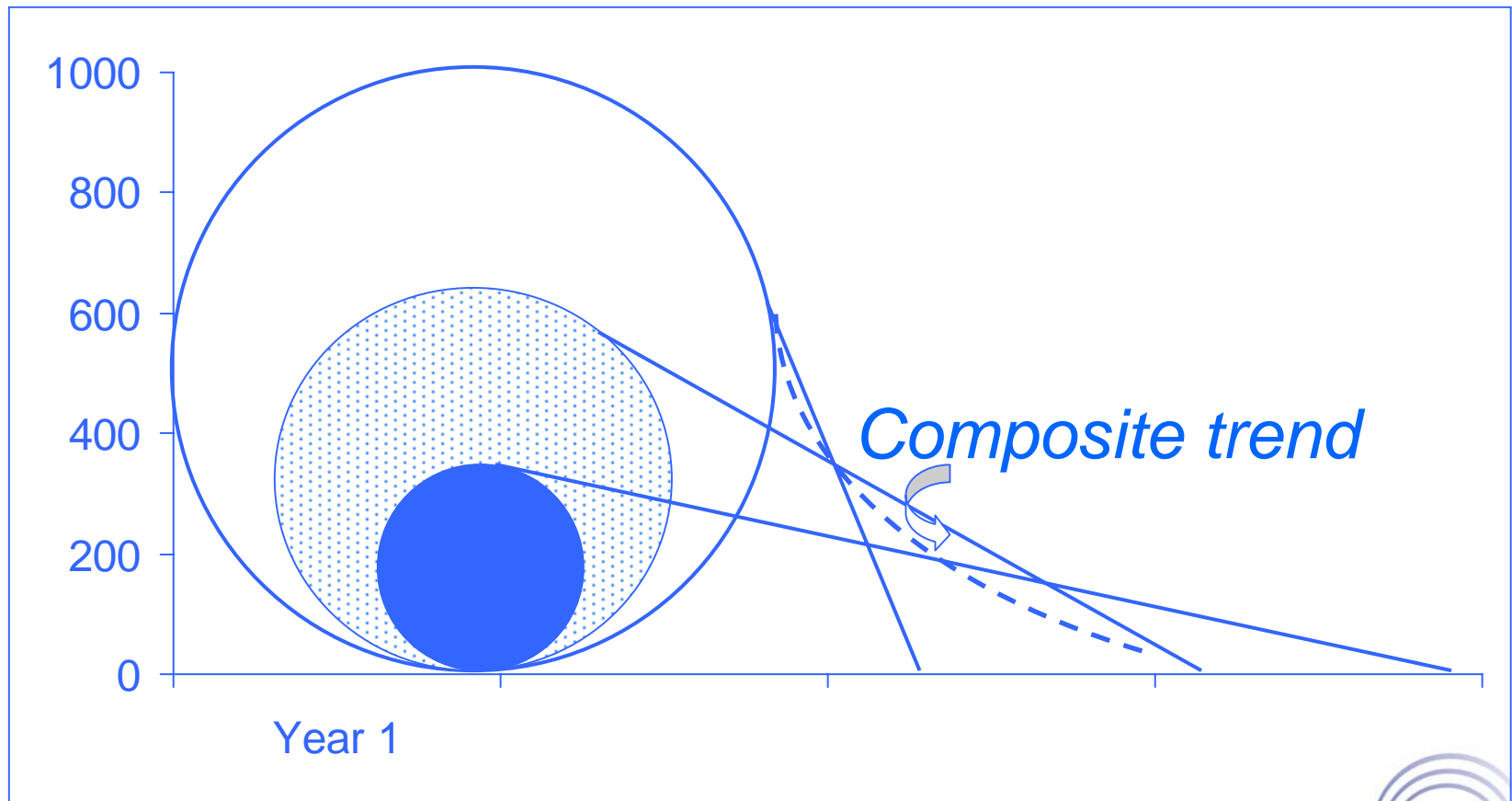
# Natural course of TB

*Trend in mortality, certain counties in Norway*



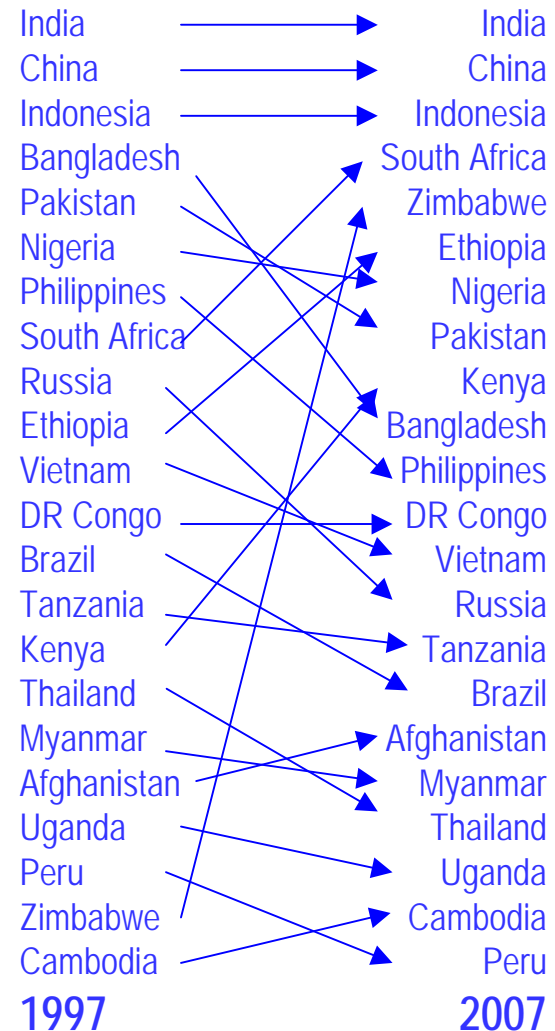
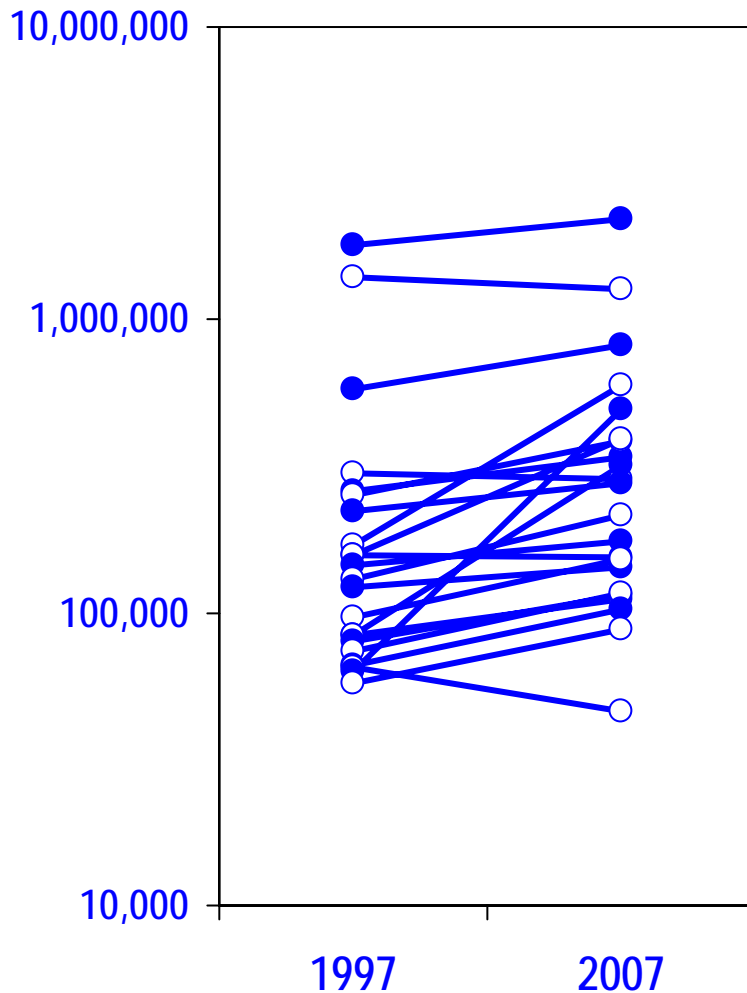
# Trend in tuberculosis

*Theoretical course in a community*



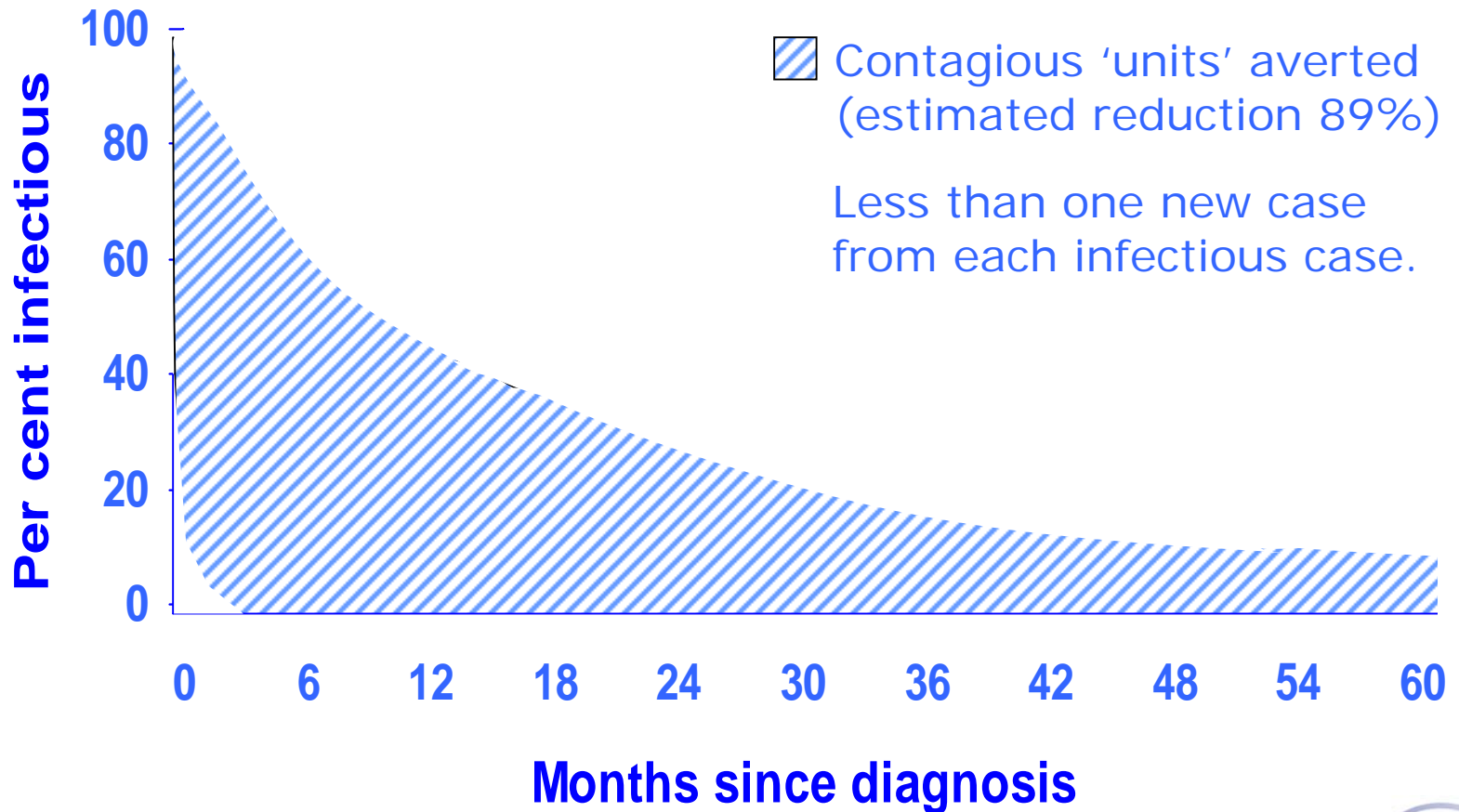
# Measuring TB:

## *Level and trend in high-burden countries*



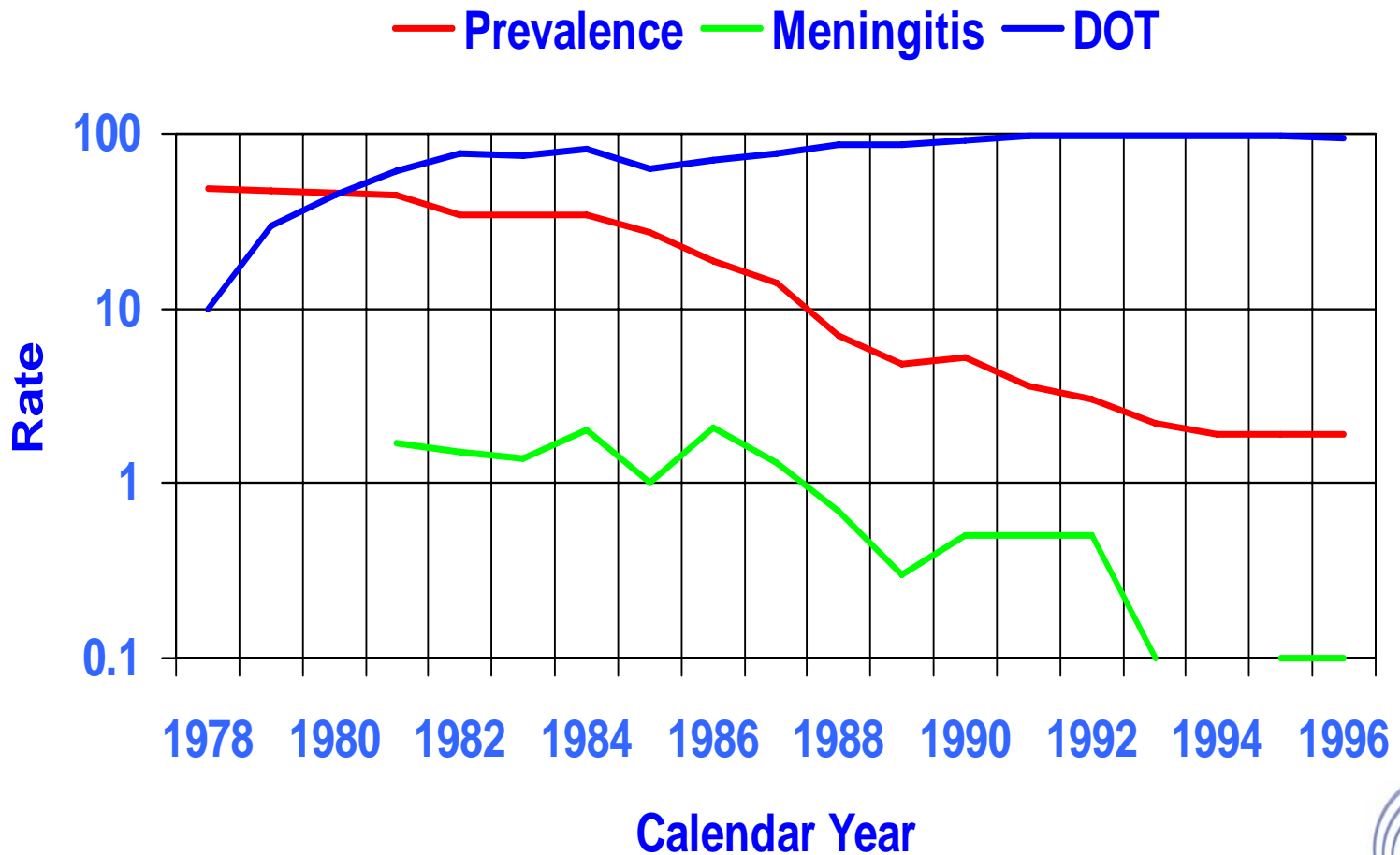
# Current strategy for controlling TB

*'Infectiousness' prevented by treatment*



# Feasibility of controlling TB

## *Trend in TB, Beijing 1978-1996*



# Koch's 'prophylaxis'

## *Lack of Progress*

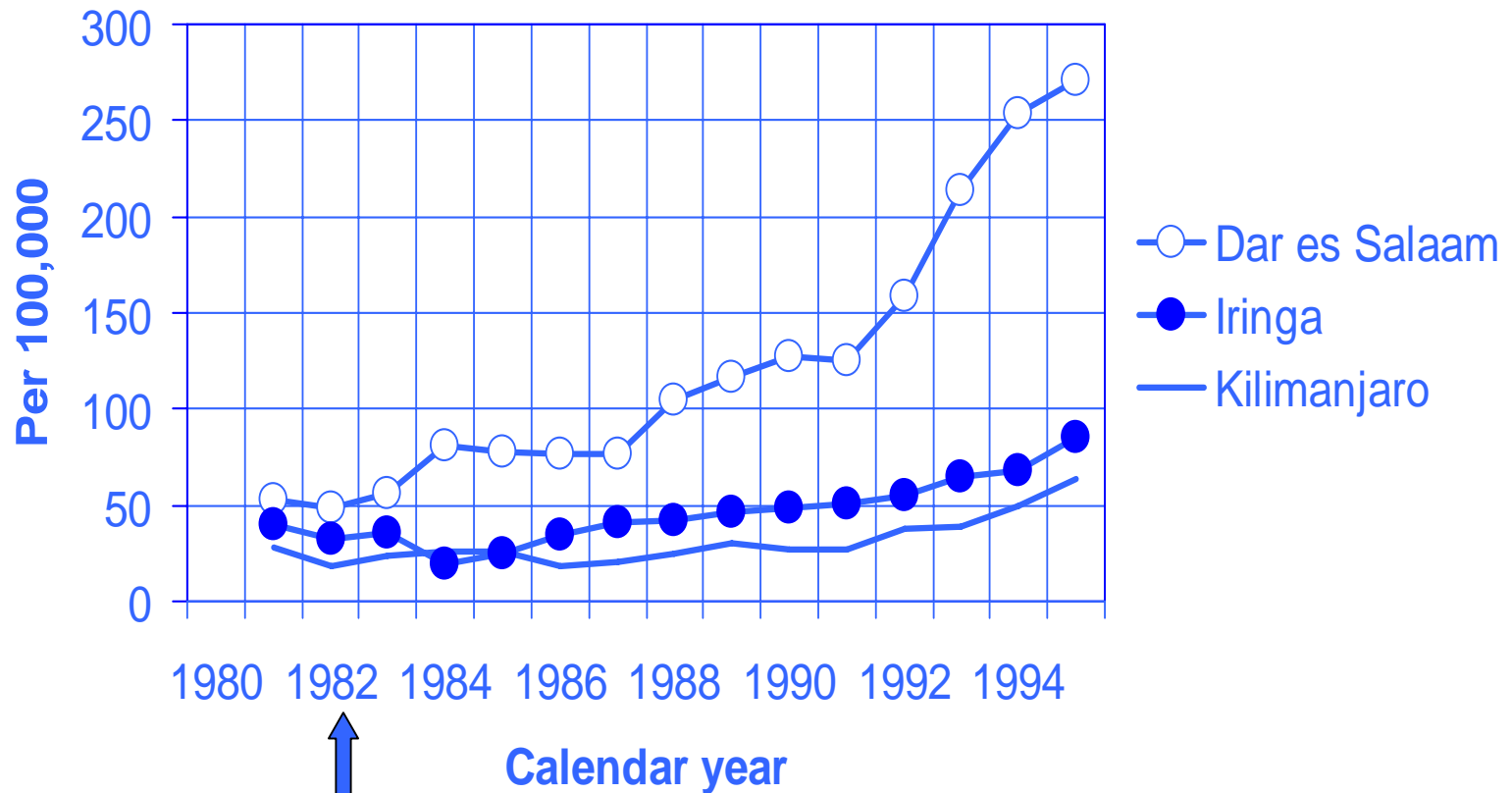
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- ❖ HIV has caused a spiral increase in TB;
- ❖ Treatment still takes too long and drug resistance is prolonging it;
- ❖ In spite of drugs being free-of-charge, costs to patients, families and communities are still high;
- ❖ Economic conditions are worsening.



# HIV rapidly fuels tuberculosis

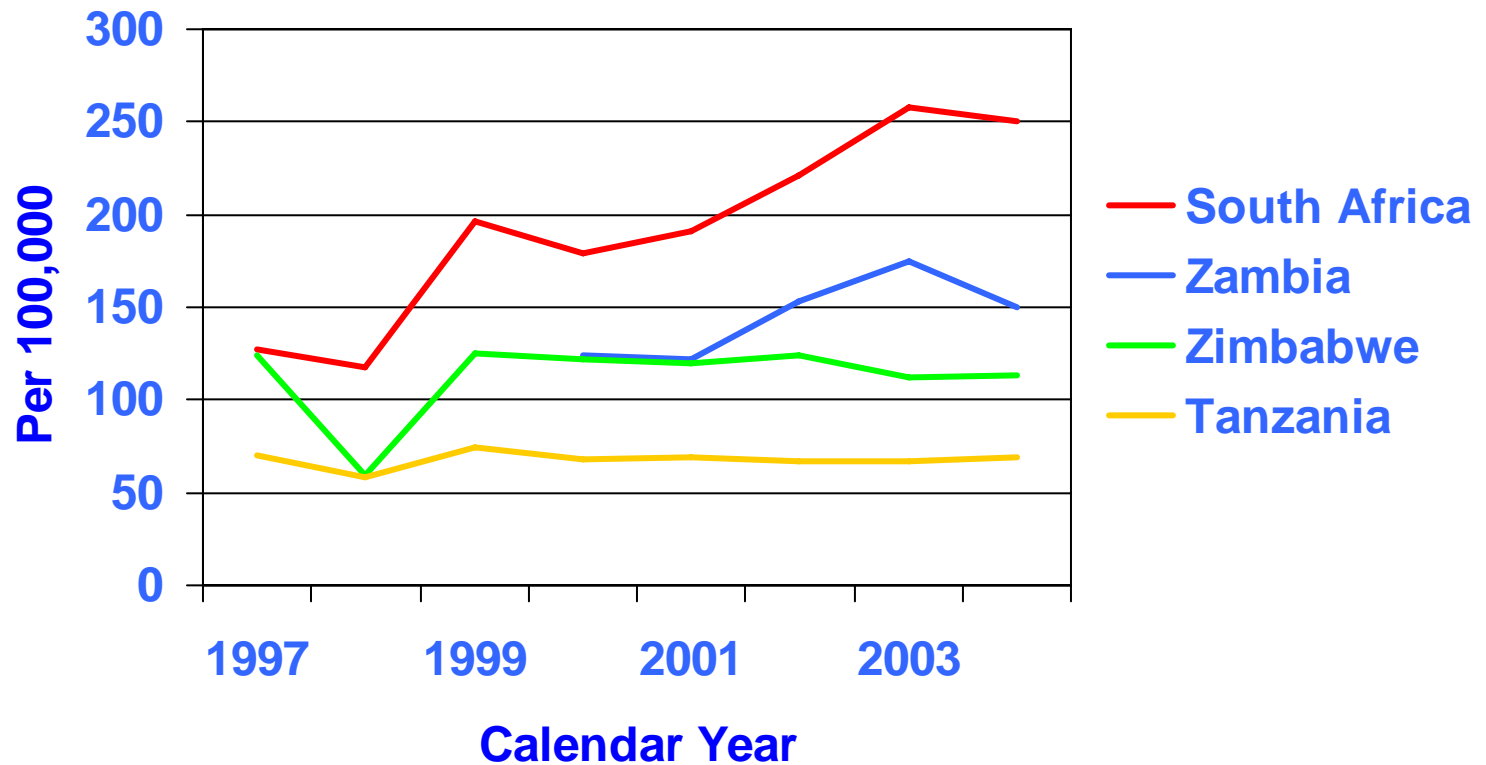
*Tanzania, by region*



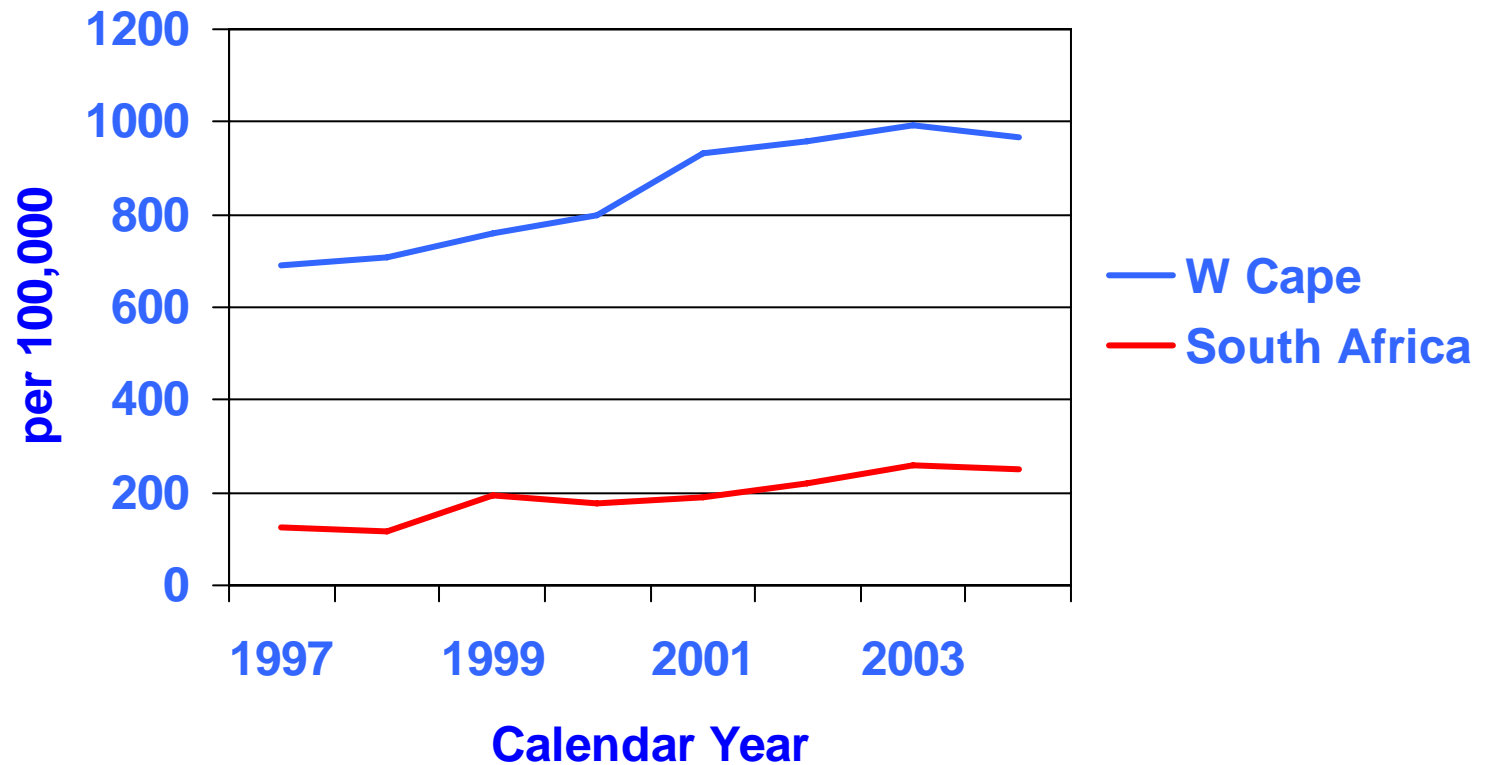
*First case of AIDS*



# Recent trends in tuberculosis – *Is this due to HIV?*



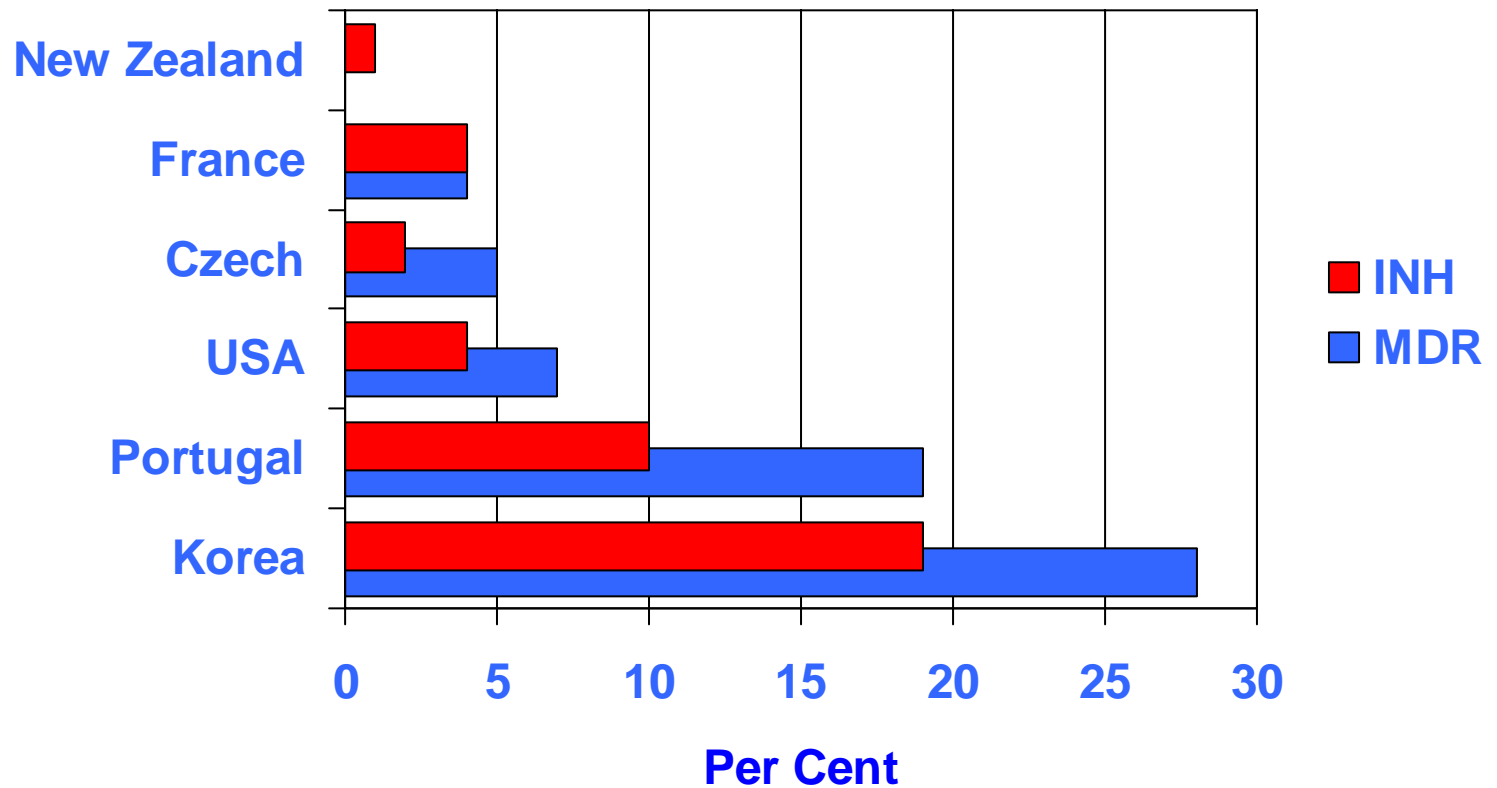
# Epidemic tuberculosis – *This is not due to HIV*



Source: WHO annual reports and W Cape Statistics



# Disease Resistant to Treatment



# MDR-TB 1995-2002

(90 countries)

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## None

- ❖ Andorra
- ❖ Iceland
- ❖ Kenya
- ❖ Luxembourg
- ❖ Malta
- ❖ New Caledonia
- ❖ Scotland
- ❖ Slovenia

## 1 in 10 or 20

- ❖ China
- ❖ Dominican Republic
- ❖ Egypt
- ❖ Mexico
- ❖ Ecuador
- ❖ Iran
- ❖ RD Congo
- ❖ Ivory Coast

## >1 in 10

- ❖ Estonia
- ❖ Israel
- ❖ Kazakhstan
- ❖ Latvia
- ❖ Lithuania
- ❖ Russia
- ❖ Turkmenistan
- ❖ Uzbekistan



# Extensively Drug Resistant TB (And then, Totally Drug Resistant TB)

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- ❖ Resistant to all powerful drugs available;
- ❖ Virtually untreatable;
- ❖ Now appearing in high-burden countries;
- ❖ Natural progression when resistance is established;
- ❖ Contagious to others.



# Treating drug resistant TB

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- ❖ More medications are needed;
- ❖ They are over 100 times more costly;
- ❖ They are more toxic;
- ❖ Treatment duration is tripled.



# Poverty and Economic Disparity

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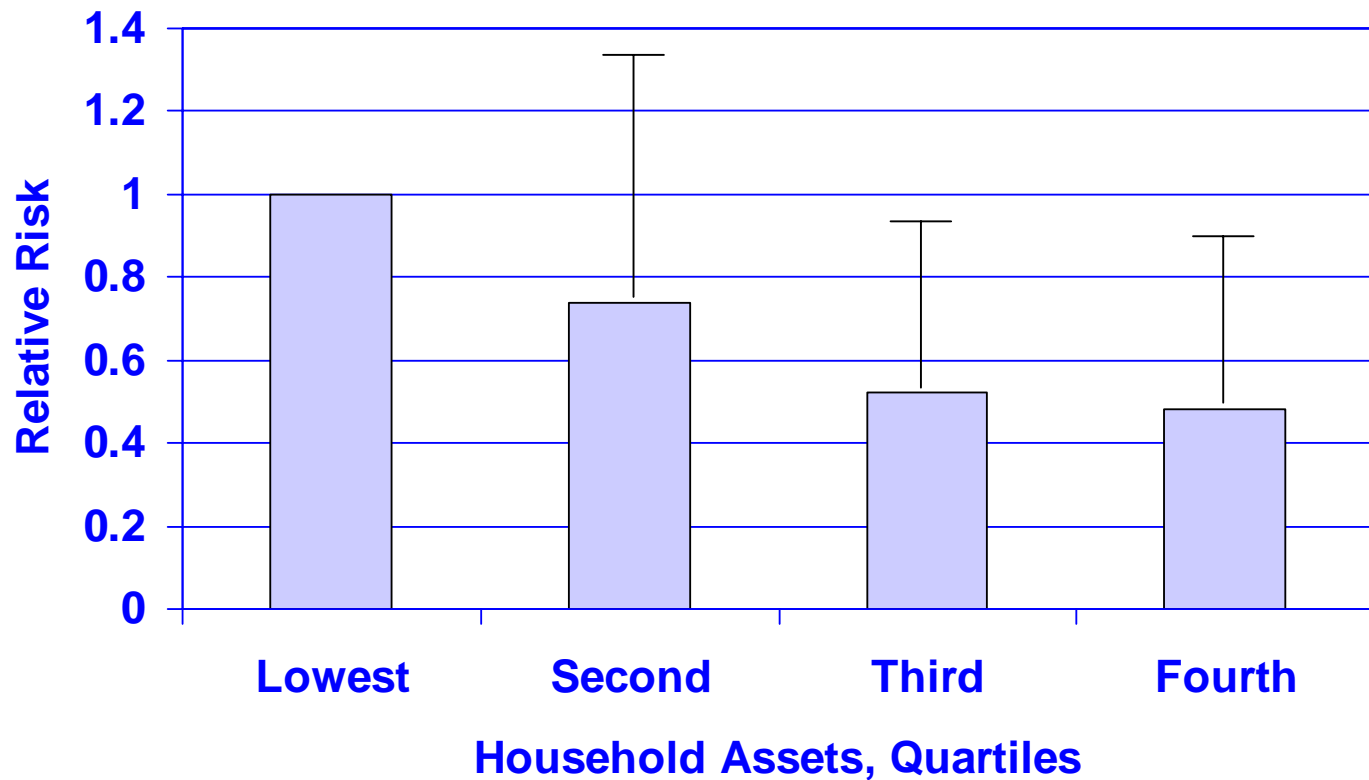
- ❖ Between 1993 and 2002, the number of countries with an absolute Gross National Income less than US\$ 1,000 increased by 50%;
- ❖ Disparity between rich and poor increasing even in wealthy countries.



# The other side of TB:

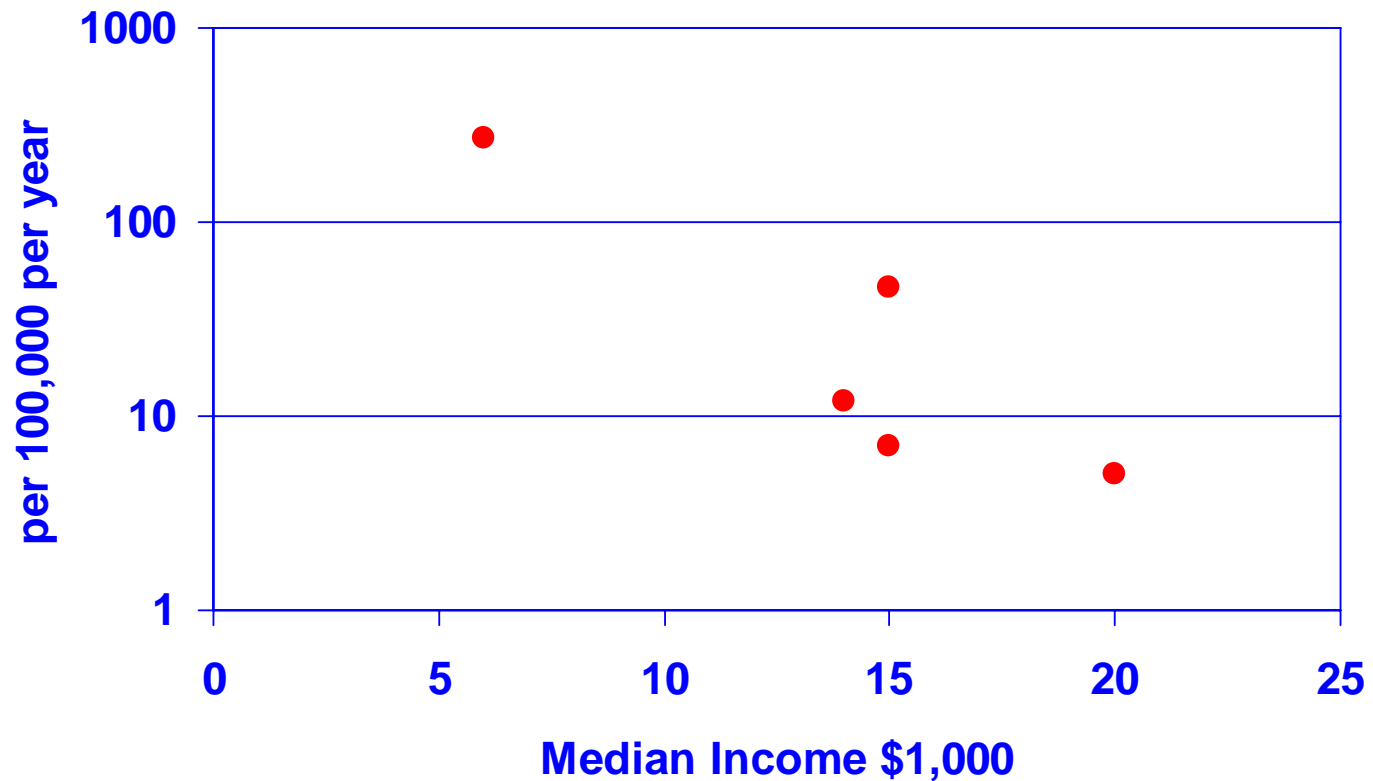
## *Poverty and TB in a developing country*

### TB and Economic Level, Henan China 2002-3

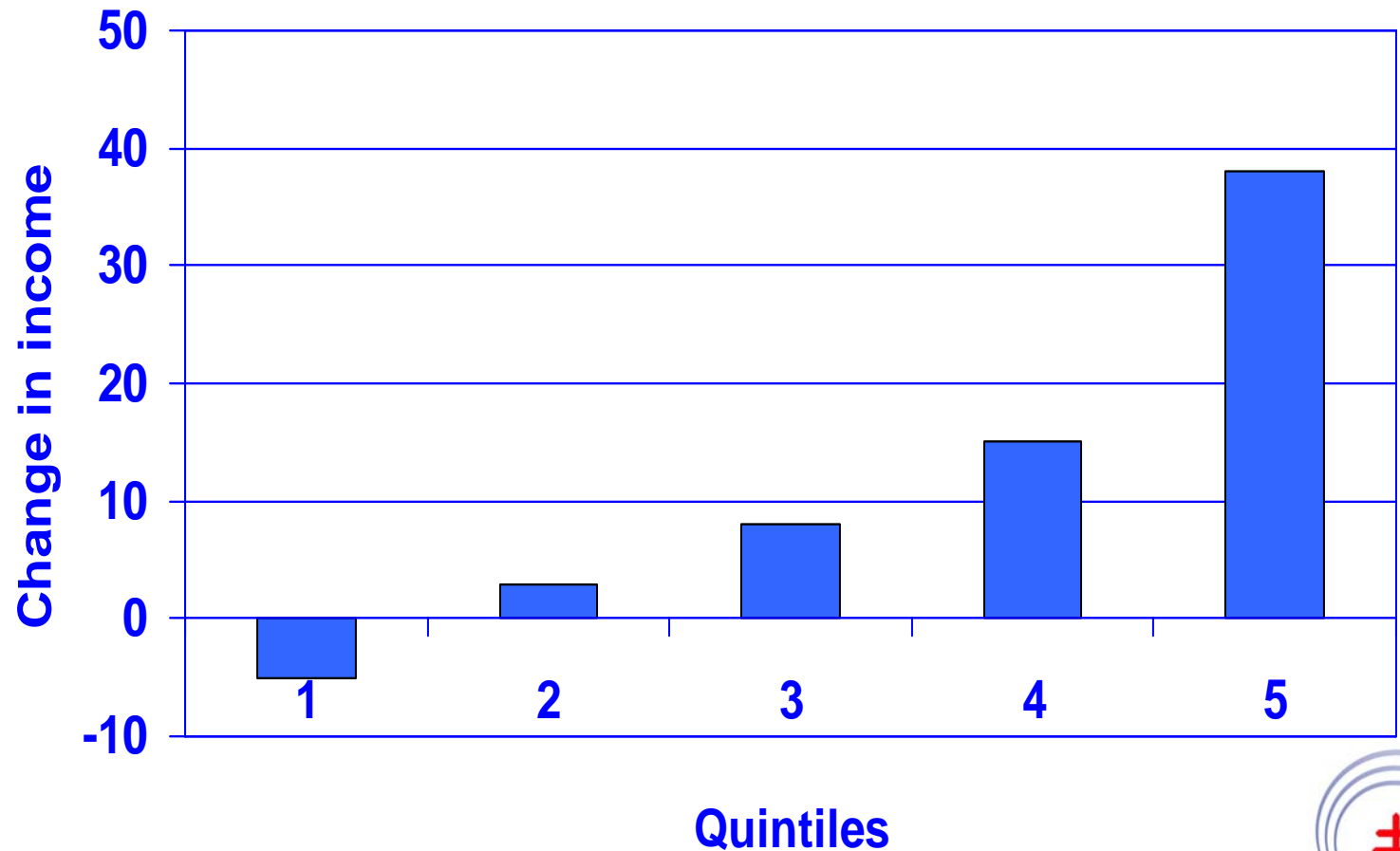


# Not poverty but disparity: *Economic disparity and TB in a rich country*

## TB and Economic Level of Census Tracts, Vancouver 1981



# Trend in income in US 1979-98 by quintile distribution



# Economic Burden of TB

*To patients and their families*

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- ❖ Over 600 consecutive patients in Nepal;
- ❖ Patients lost a mean of 45 work days prior to diagnosis;
- ❖ Costs of the disease were equivalent to 88% of mean monthly income;
- ❖ One-third of this loss was due to medical expenses even though treatment is 'free-of-charge';
- ❖ Many patients lose land or economic livelihood due to these costs.

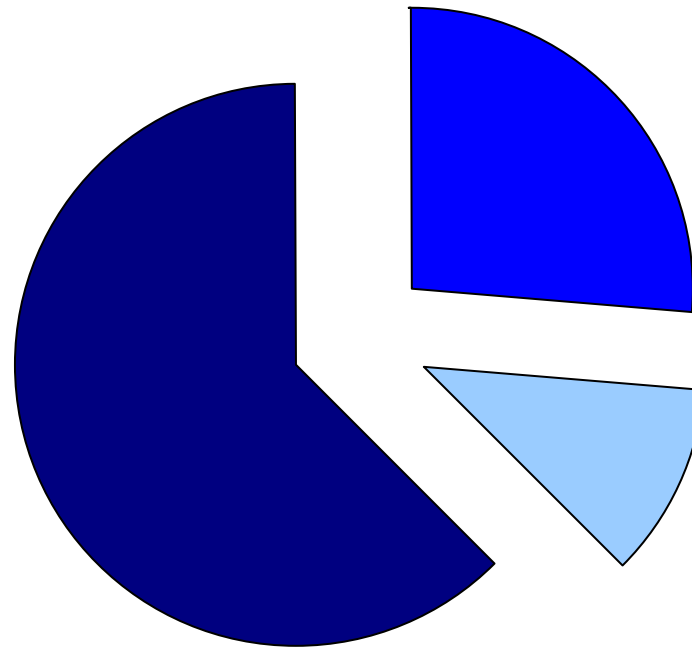


# Cost of TB care

*Henan, China 2002-3*

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- Medical
- Non medical direct
- Indirect



Median Annual Income: Y 3,007

Cost of TB Care: Y 7,367



# Limitation of current tools

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- ❖ Current vaccine is widely applied but with limited epidemiologic impact;
- ❖ Currently available medications are few (5) and old (from 1948-65);
- ❖ Resistance to these medications is rapidly rising.



# (Lack of) promise of new tools

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New medications and vaccines are still a long way off

## ❖ New Drugs

- ✓ Next 'new' regimen in 2015
- ✓ Additional new drugs being 'destroyed'

## ❖ New Vaccines

- ✓ Next 'new' vaccine in 2011



# Koch's 'prophylaxis'

## *Signs of progress*

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- ❖ Registration takes place almost everywhere;
- ❖ Focus on smear positive cases;
- ❖ Diagnostic network extensive;
- ❖ Financial resources are being mobilized;
- ❖ Scientific research has recommenced after a long lapse.



# Achievements in Global TB Control

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- ❖ Case detection was 53% of estimated existing cases in 2004, rapidly increasing toward 70% target;
- ❖ Treatment success was 83% in 2003, near to 85% target;
- ❖ 3 of 7 WHO regions (2 in Asia and the Americas) will reach targets;
- ❖ Seven of the 22 High Burden Countries reached 2005 targets.



# Mobilization of Finances for TB

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- ❖ Cost of TB services in 74 reporting countries in 2006 was US\$ 2 billion;
- ❖ Funding 'gap' for 2006 was US\$ 180 million (9% of total);
- ❖ Global Fund has approved US\$ 7.1 billion, contracted \$ 5.4 billion and disbursed \$3.4 billion;
- ❖ \$2.2 billion (31%) was for TB control.



# Future Scientific Progress

## Key Questions

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*Not 'why?', but 'why not?'*

Why do so few become infected given exposure?

Why do so few develop disease given infection?



# Key Risk Factors and Modifiers

## From Infection to Disease

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### *Risk Factors*

- \* Size of bacterial population
- \* Latency / Reactivation

### *Modifiers*

- \* Cell-mediated immunity
- \* Nutrition/Morphology
- \* Time since infection
- \* Age of patient



# Determinants of Bacterial Concentration

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## *Risk Factors*

- \* Access to environment
- \* Concentration at source
- \* Expulsion from source

## *Modifiers*

- \* Ventilation
- \* Ultra violet light
- \* Size of space unit



# Determinants of Duration of Exposure

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## *Risk Factors*

- \* Time to diagnosis
- \* Time to treatment
- \* Duration of treatment

## *Modifiers*

- \* Susceptibility to drugs
- \* Quality of treatment
- \* Proximity to source



# “Force of Infection”

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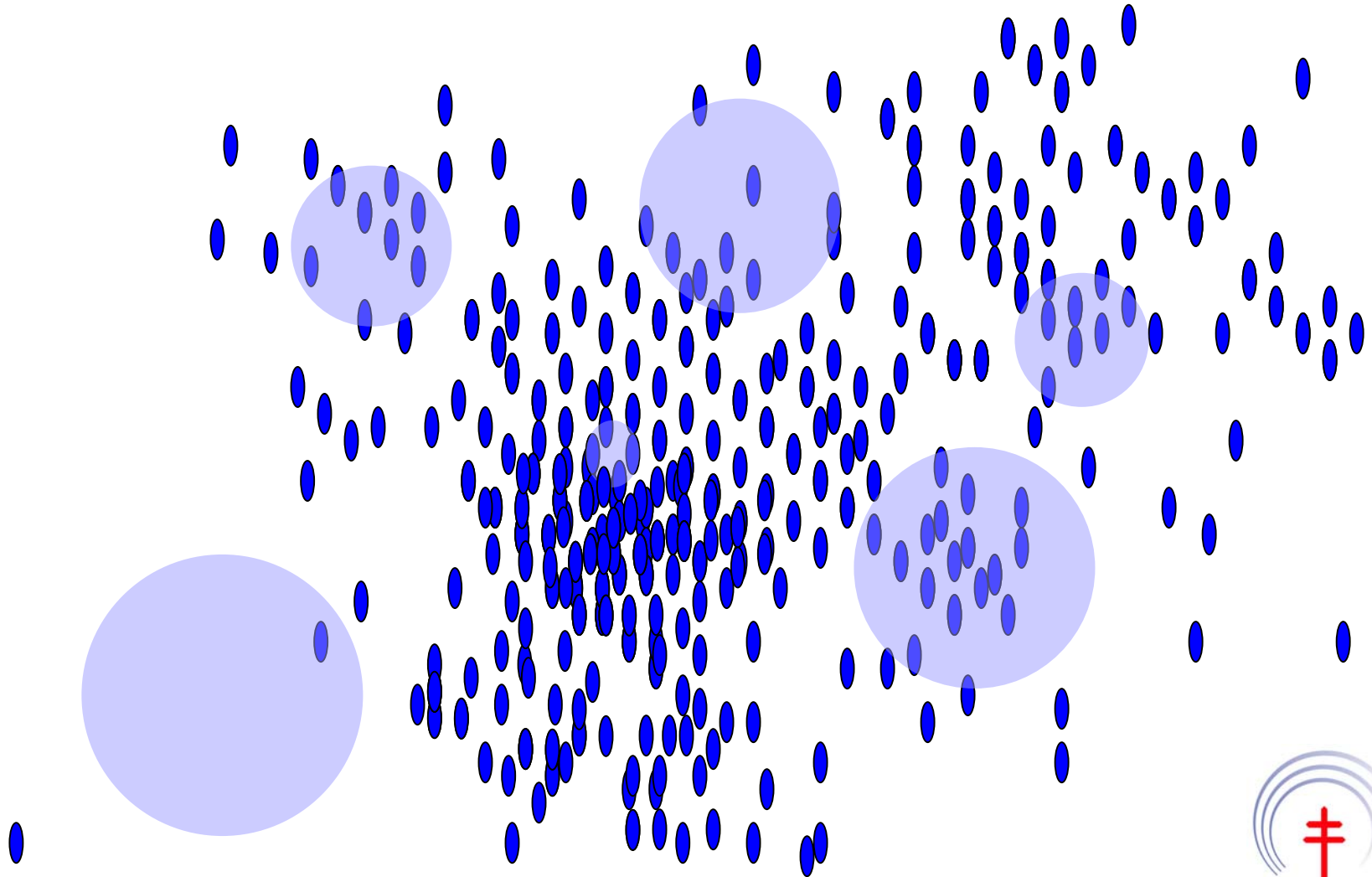
The probability of becoming infected is largely determined by the following exposure factors:

***Concentration x time x number***



# “Force of Infection”

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# What Determines Latency? What Predicts Reactivation?

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- \* Bacterial population size?
- \* Microenvironmental conditions?
- \* Biological / genetic characteristics?



# Global Tuberculosis: Problems and Prospects

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## Problems:

- ❖ Economic disparity widening;
- ❖ Tools (especially treatment) rapidly becoming ineffective;
- ❖ Crucial need is for a breakthrough in vaccine development.

## Prospects:

- ❖ Global awareness / commitment at an all-time high;
- ❖ Services reach more patients today than ever before;
- ❖ Scientific research revitalized.

