

Drug resistant tuberculosis in the Greater Mekong Subregion: Risk of transmission and the need for operational research

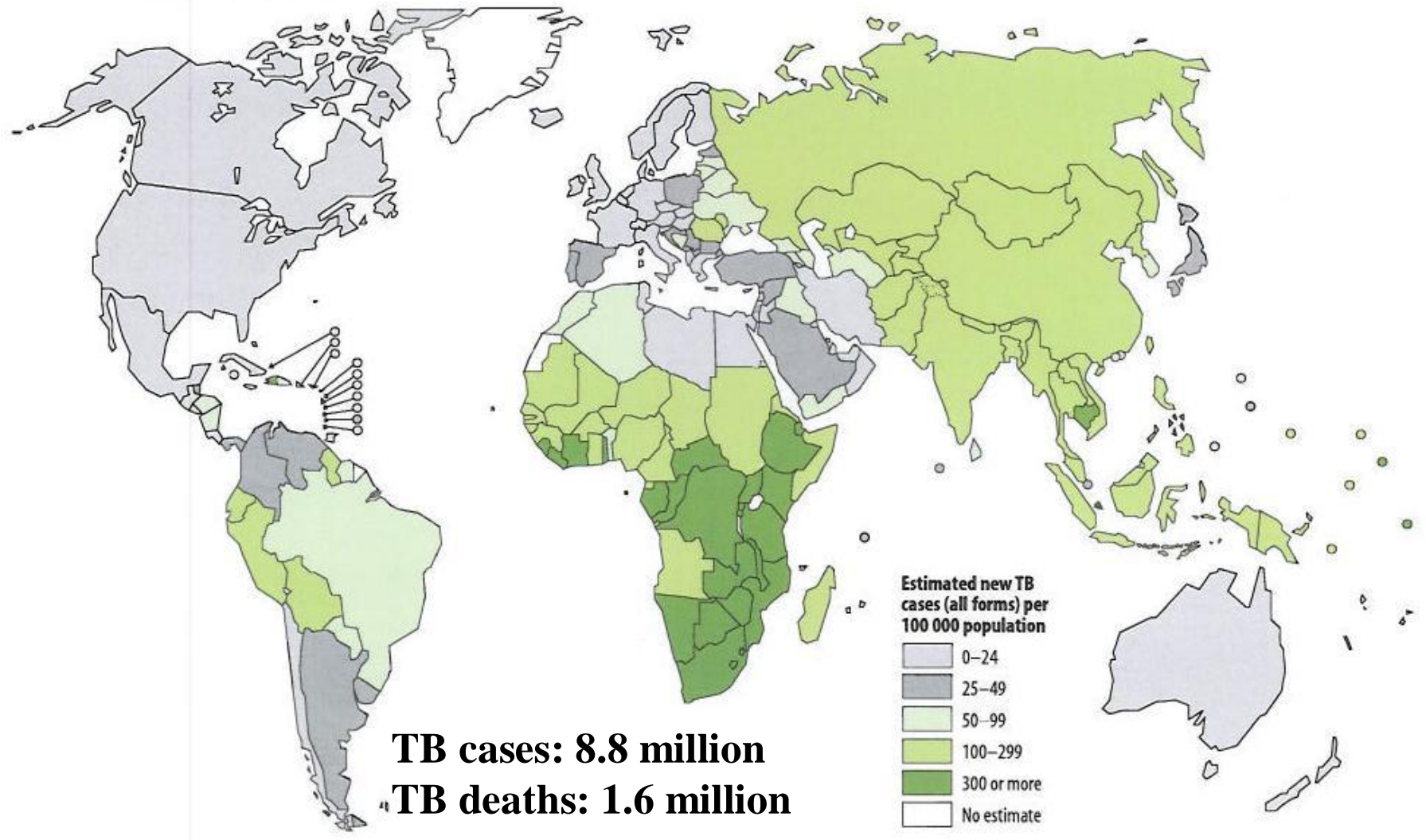
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Global tuberculosis burden

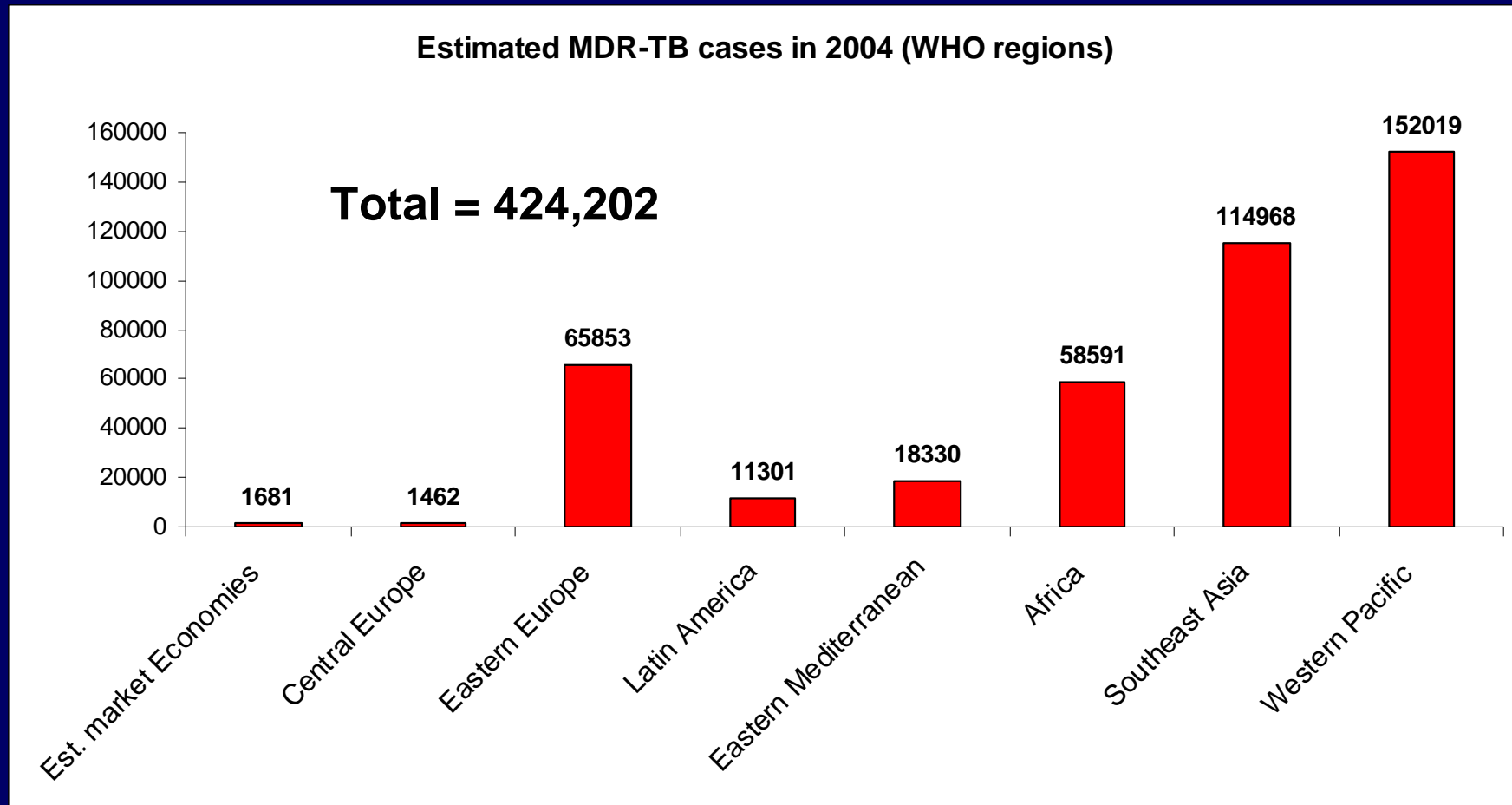
Estimated TB incidence rates, 2005



WHO 2007



Global burden of drug resistant TB



Adapted from Zignol et al JID 2006

Extensively drug resistant TB (XDR-TB)

- MDR-TB plus resistant to a fluoroquinolone and an injectable (Capreomycin/ Kanamycin/ Amikacin)
- Poor surveillance
- High mortality, particularly among HIV positive
- Potential nosocomial transmission
- Estimated at 7% of all MDR-TB cases and increasing, but urgent need to gather more data



MDR-TB treatment

- Revised global Plan calls for 1.6 million MDR-TB cases to be treated by 2015
- Global budget for 2007-2008 estimated at 2 billion USD
- Green Light Committee for access to second-line drugs and technical support
- To date, treatment approved for 24,994 patients in 40 countries
- But, limited experience in scale up of MDR-TB treatment



Cost per patient for MDR-TB treatment (USD)

\$2,381	Peru
\$2,840	Thailand
\$3,355	Philippines
\$15,856	South Korea
\$17,529	Turkey
\$89,594	USA



Transmission of DR-TB strains (molecular epidemiology)

- Association of MDR-TB with clustering of genetically identical strains suggests high transmission, but this varies in different contexts
- Potential to be re-infected or even super-infected with a new strain (nosocomial transmission)
- Beijing strains often associated with drug resistance and may be more virulent
- Beijing strains associated with treatment failure and relapse in Vietnam
- Longer duration of infectiousness (due to poor treatment) results in more people infected



Greater Mekong Subregion

	Lao PDR	Cambodia	Viet Nam
TB incidence (/100,000/year)	155	506	175
Case detection (all new cases)	40%	49%	60%
TB drug resistance	No data available Estimated MDR-TB in 2% of new cases and 15% of previously treated	Survey in 2000/01: no MDR-TB among new cases, 3% among prev. treated Repeat survey in 2006/07 (no data yet)	Survey in 1996: 2.3% MDR-TB among new cases. HCM City, 1998-2000: MDR-TB in 4% new and 25% prev. treated



Research questions

- To determine the level of drug resistant TB circulating in Laos
- Assess associations between HIV infection and TB and particularly drug resistant TB
- Describe the diversity of TB strains in Laos and Cambodia (recent transmission)
- Explore TB strain diversity and associations with drug resistant TB (comparisons across countries)



Hot zones for MDR-TB

- Taking averages for countries or regions potentially masks small zones with extremely high MDR-TB prevalence
- Slow expansion of DOTS leaves segments of the population with poor TB control
- Amplification of resistance to MDR-TB
- Neglect of treatment failures
- Relative 'fitness' of DR-TB strains compared to susceptible (related to strain genotypes)



Conclusions

- Given the costs associated with treating MDR-TB, preventing its emergence is clearly better than dealing with MDR-TB once community transmission is established.
- An understanding of the dynamics of TB transmission and prevailing strain types can only benefit efforts to prevent the emergence of MDR-TB and XDR-TB
- Operational research also aims to build capacity in the region to conduct research and to support improvements in TB programme quality



Collaborations and Capacity

- Burnet Institute, Lao PDR, Australia
- National Tuberculosis Centre, Lao PDR
- National Centre for Tuberculosis and Leprosy Control (CENAT), Cambodia

