Surveillance issues – Perspectives from working for and with WHO

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What are the seven hills of Ancient Rome?

WHO Structure

- World Health Assembly annual resolutions
- HQ Geneva DG and BOD
- Regional Offices (5) and RD
- Country Officers

WHO Funding/Operation

- Member States untied funds - UN Agency
- Tied funds directly – USAID – politics
- External funding also e.g. Gates, tied
- Operate within a country via its government
- Partnerships with NGOs – but again with government approval to operate

WHO operations - WHA

- 1990s UN AIDS
- 2000 “Millennium Goals”

  TB, HIV, Malaria
- UN ‘Global Fund’

- 2002 SARS/Avian flu

WHO regard for importance of Anti Microbial Resistance

1998 WHA Assembly resolution on AMR

- AMR included in WHO Millennium Goals
- 2001 WHA Assembly resolution on AMR
  - 2002 WHO WPR resolution on AMR
- AMR considerations required for “Global Fund” esp TB
- 2005 WHA renewed resolution on AMR

Working for or with WHO

- Most HQ personnel are epidemiologists
- Little laboratory background
- Need laboratory based input
- Engage expertise by a variety of means: Technical Services Agreement, Agreement for Performance of Work, reference laboratory, Collaborating Centres for …

7 hills

- 1 Quirinal

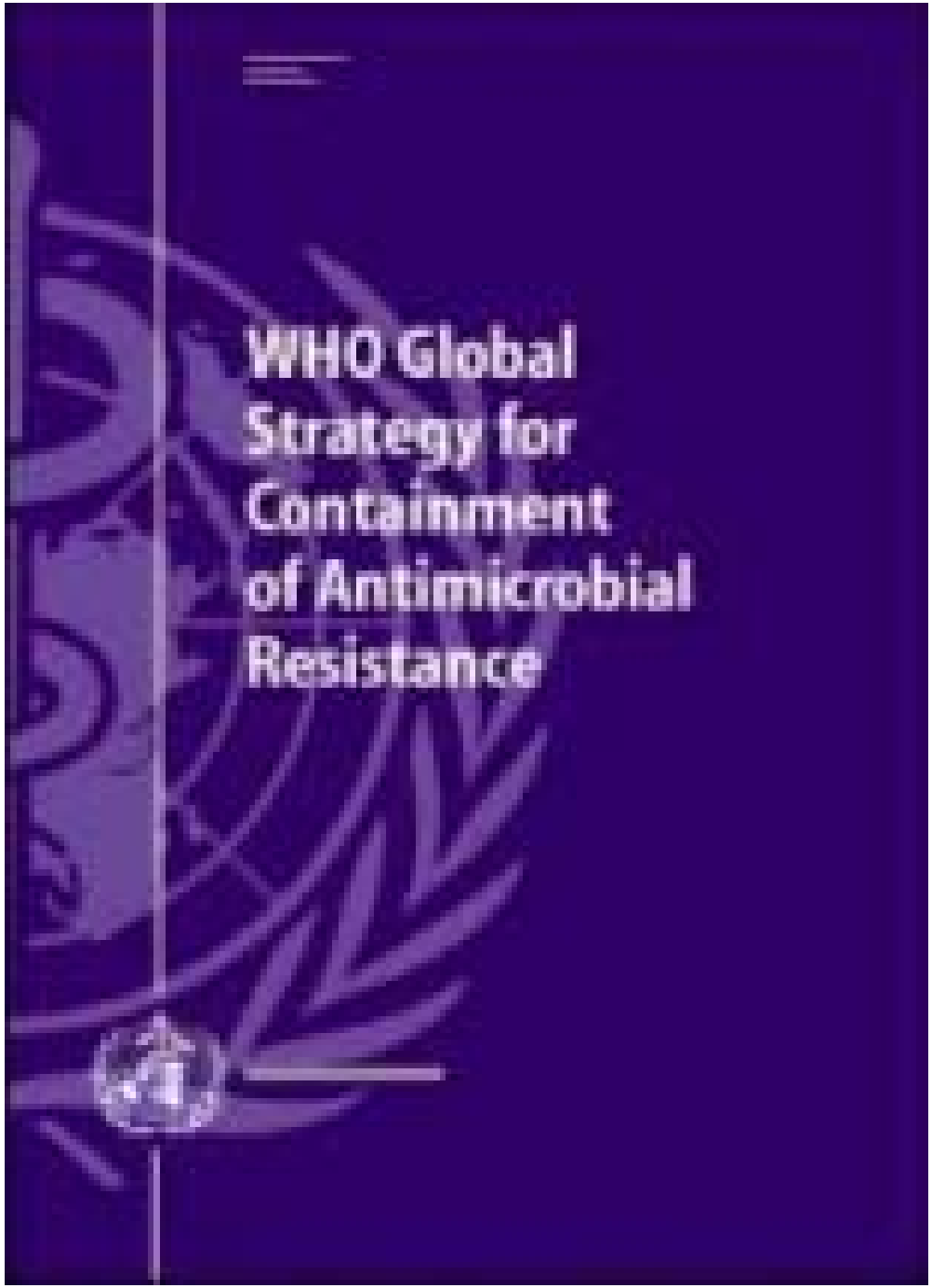
Surveillance for WHO

- Aim is ultimately disease control or a reduction in morbidity and mortality attributable to that disease
  - ANY Surveillance – ASK the question – What is the aim of this surveillance activity?
- Usually for some intervention i.e.
  - *Information for Action*

WHO regard for importance of Anti Microbial Resistance

- WHA and Regional Office resolutions

- 2005: Member states are asked to report back to WHO in 2007 on progress on AMR containment


WHO Global
Strategy for
Containment
of Antimicrobial
Resistance

Global Strategy Document

- “Global” = totality of the approach, not a geographic term
- “Containment” is the outcome = slowing of the rate of AMR increase. Reversal of existing AMR is even harder to achieve.
- GSD launched in Washington on Sept 11 2001

7 hills

- 2 Viminale

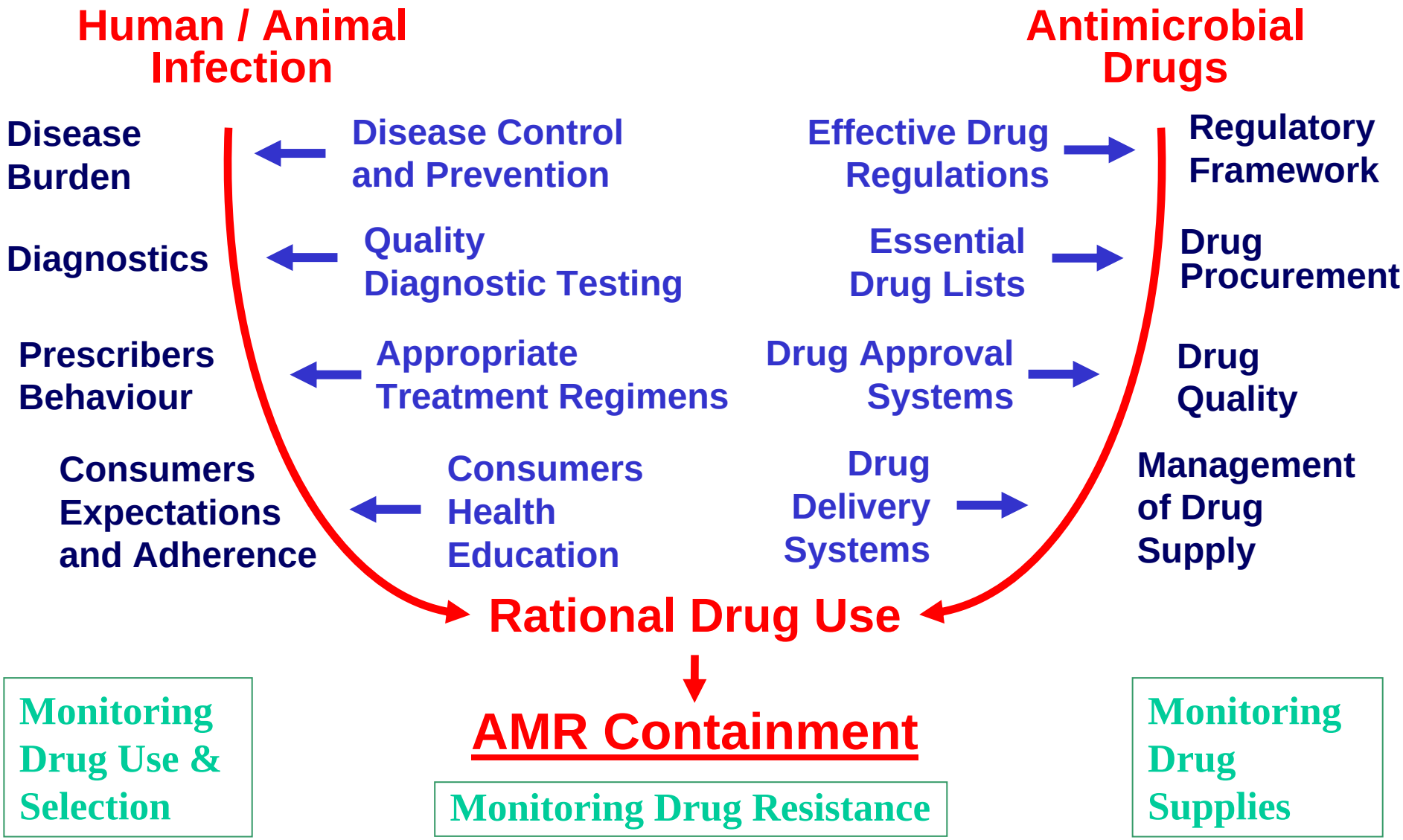
‘Global Strategy’
6 key areas

- reduction in disease burden
- access to appropriate antimicrobials
- improved use of antimicrobials
- *strengthening health systems and surveillance capabilities*
- enforcing regulations and legislation
- encouraging drug and vaccine development

‘Global Strategy’ Interventions

- 67 recommendations for intervention at national level
- 2 ‘fundamental’ and 12 ‘priority’ interventions - evidence and consensus
  - **laboratory strengthening and lab based AMR surveillance is one of the two ‘fundamental’ recommendations**

ARCS: Antimicrobial Resistance Containment and Surveillance



ARCS: Antimicrobial Resistance Containment and Surveillance

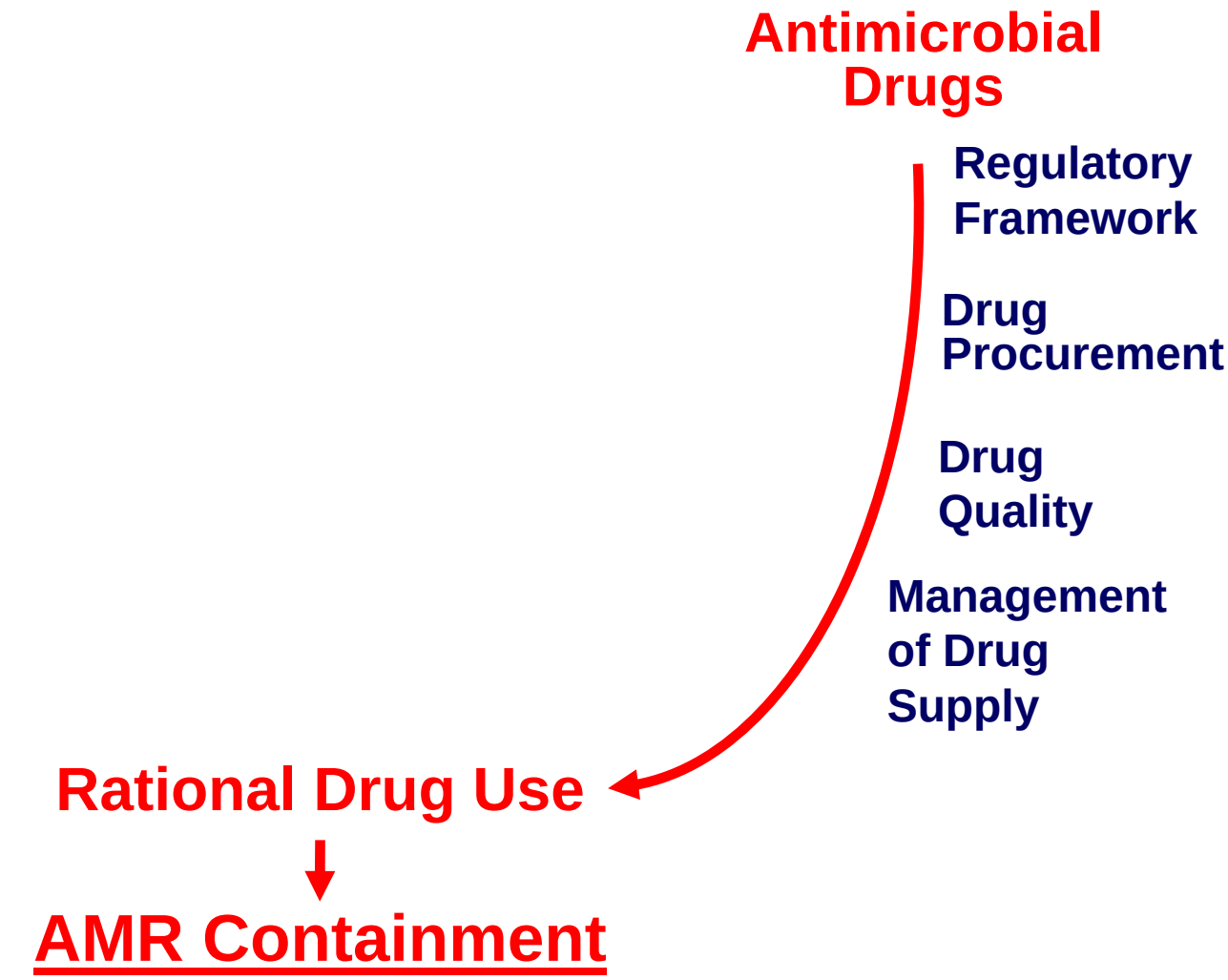
(Simonsen GS et al Bull WHO 2004;82:928)

Rational Drug Use

↓

AMR Containment

ARCS: Antimicrobial Resistance Containment and Surveillance



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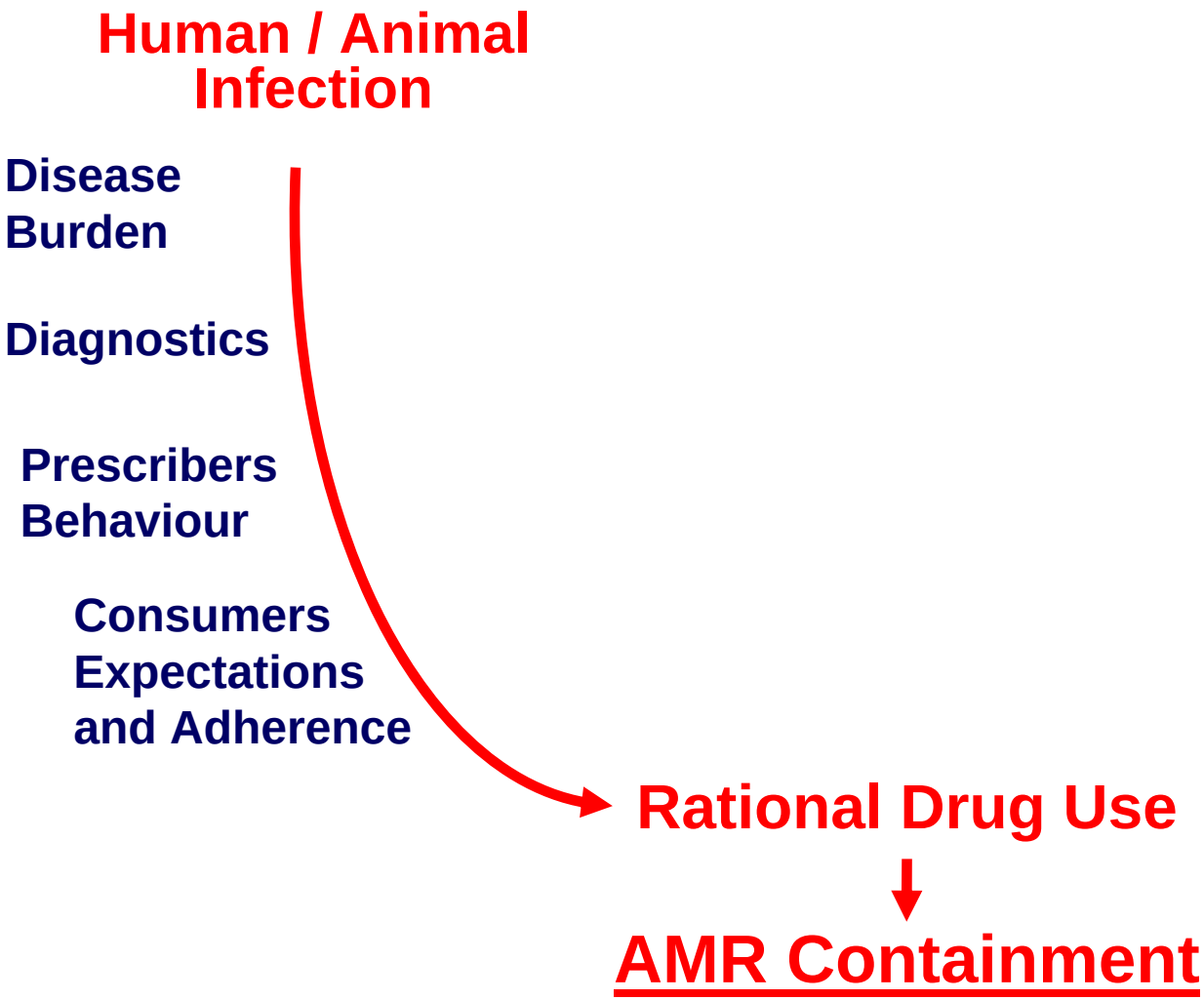

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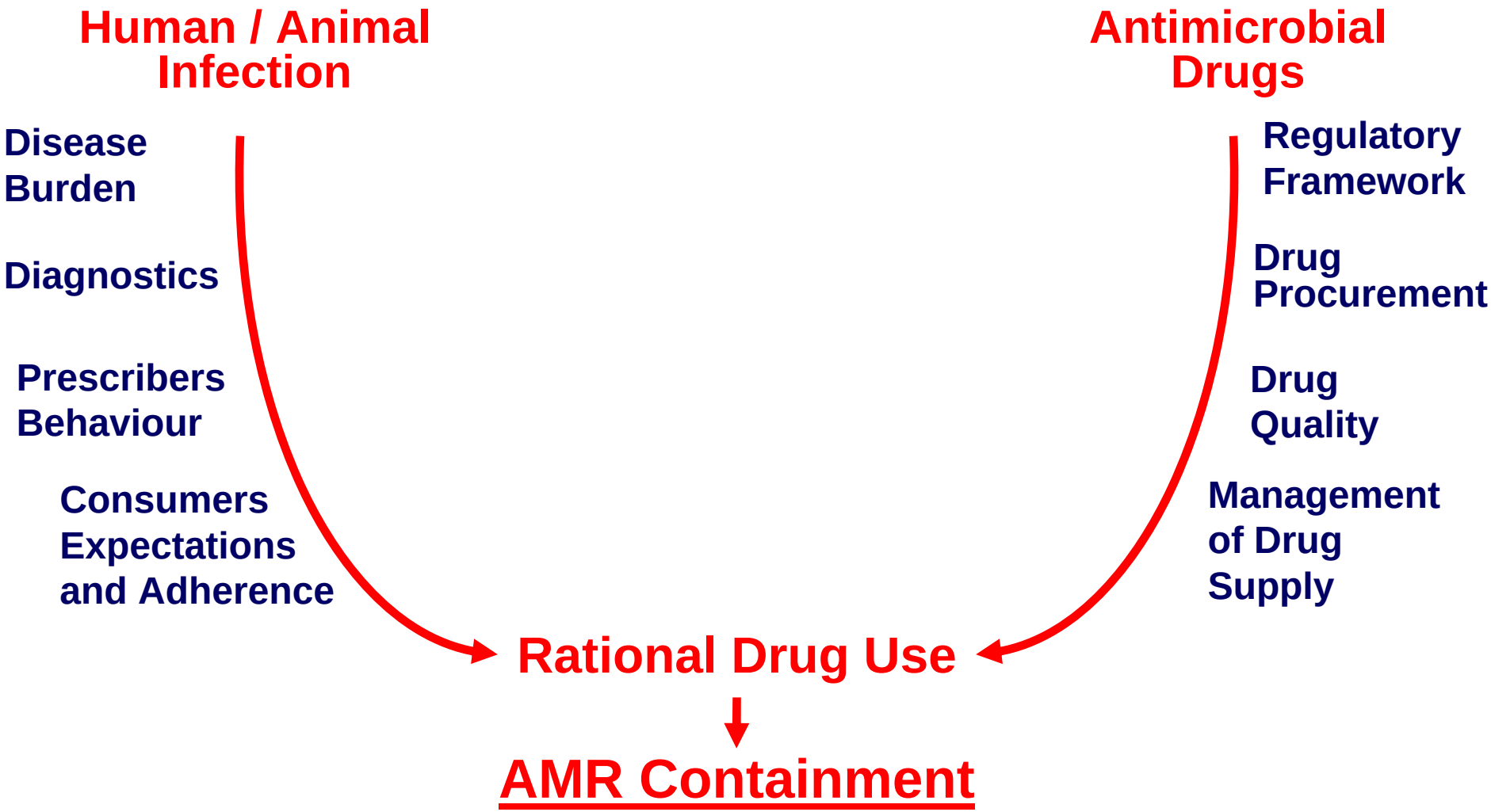

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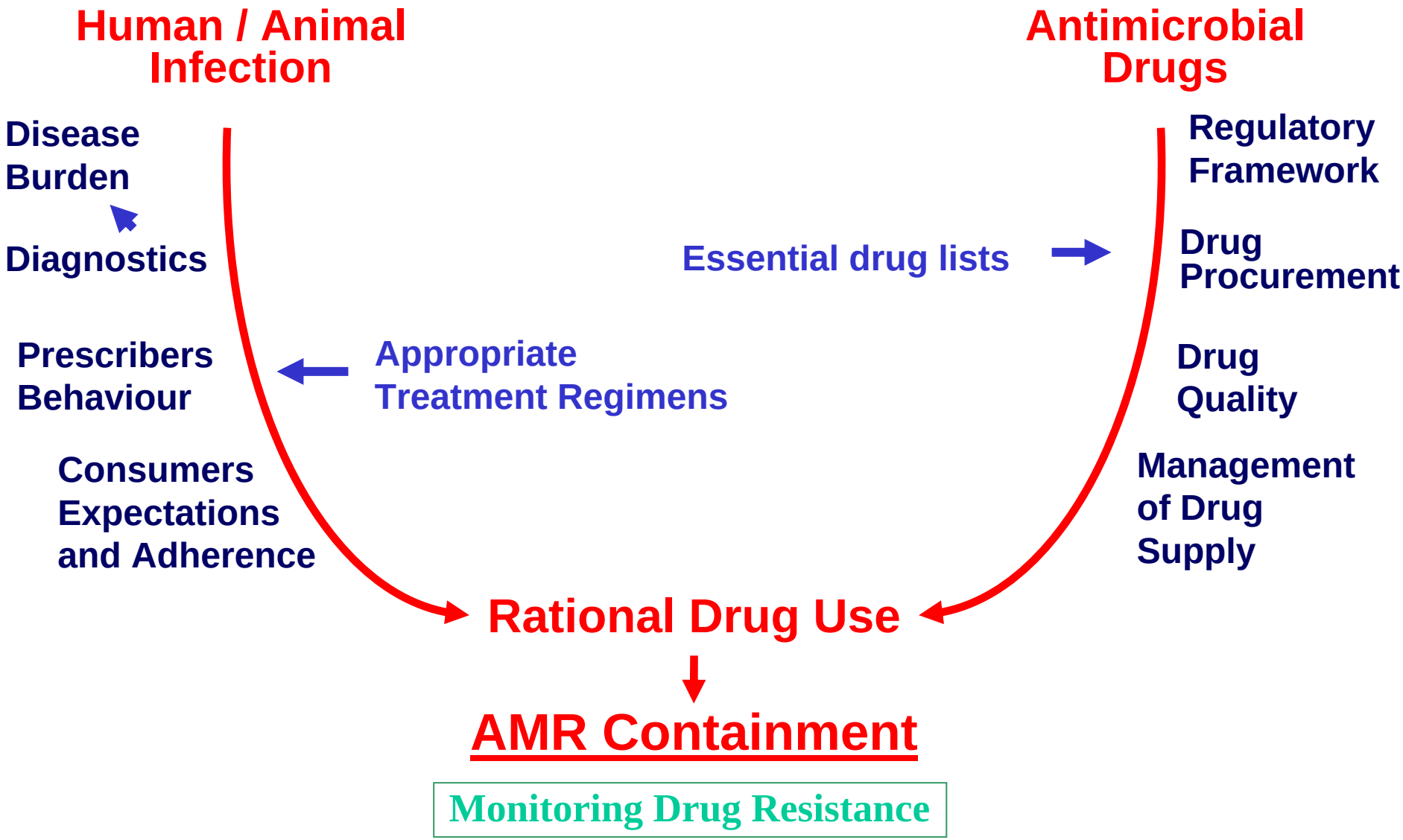


Surveillance standards and AMR

- What information is needed?
- What drugs work- for the individual
- at a population level
- What is a cost/effective approach?
- At what level (%) of AMR should a drug regimen be ceased or modified?
- How does one assess this level?

7 hills

- 3 Aesculine

Control of transmissible disease

- Disease rate **Ro**
- depends on **ß c D**
- **ß** = transmissibility of organism
- **c** = rate of partner, fomite, exchange
- **D** = duration of infectiousness

- For sustained disease control, *all* of the above need to be simultaneously reduced by an integrated approach

Laboratory Contributions to Disease Control Prevention

- Emphasis on
- **ß, D**
- **ß** = transmissibility of organism
- **D** = duration of infectiousness
- For antimicrobials, effective treatment decreases both **ß, D**
- e.g. Rx of HIV provides inoculum reduction decreases ß, but no effect on D

AMR surveillance & standards (WHO)

- BASIC PRINCIPLE - to produce ***valid*** *information for action* - requires
- 1. Epidemiologically valid sources of data
- 2. Proper microbiological standards
- 3. Statistically valid analyses and interpretation
- 4. Dissemination of analysed data which is integrated into programmatic approaches
    - [COMPARABILITY]
- “Stand alone” surveillance - of any kind – is ultimately non-sustainable

"Surveillance Standards for AMR" (WHO)

- Monograph with many useful definitions and advice; describes core activities esp for diseases of Public Health relevance
  - LINKS AMR SURVEILLANCE TO DISEASE SURVEILLANCE
- describes surveillance standards, organism-diseases for surveillance (= where AMR contributes significantly to disease control)

AMR surveillance - applications

- Diseases/organisms of PHI: *AMR is an important factor in disease control*
- TB, malaria, HIV,
- diarrhoeal and respiratory disease, STI, IMD, HAI (limits)
- Bird flu and efficacy and continuing efficacy of antivirals in the face of mass prophylaxis and over use

7 hills

- 4 Caelian

1. Epidemiology: Usual sources of AMR data

- Passively collected diagnostic AST data
- Continuous or periodic surveys of AMR from routine diagnostic data
- Directed surveillance: from (sentinel, total) continuous or periodic surveys; semi-defined sources which may be non-clinical
- Demographic and clinically linked surveys
- Genotypic data - as above (HIV)

(a) Passive, standard testing using diagnostic material: *Pros*

- ‘Better than no data’
- ‘Cheap to obtain’
- ‘Can adjust statistically for source variation’
  ???
- Useful to indicate AMR problems and need for enhanced surveillance
- Sometimes useful for trend data over time
- (careful interpretation needed)

(a) Passive, standard AST testing of diagnostic material:Cons

- *Denominator deficient* and *warm inner glow* surveillance
- Denominators poorly defined, inconsistent within and between institutions, highly variable over time; need complicated statistical manipulation [comparability]
- Routine data is often biased e.g towards resistance, problem cases

(a) Passive, standard AST testing of diagnostic material:Cons

- passively collected data from multiple sources by many means
- Often lacks comparability within and between sources, wider regions
- applicable often only to source from which it is derived i.e. must be disaggregated
- not possible to integrate with disease data

(b) Comprehensive, integrated, continuous, active

- ‘An expensive ideal’ (is it really?)
- can be achieved inexpensively in some situations if integrated with other activity e.g. strain characteristics for vaccines, enhanced disease surveillance, programmatic treatments
- *must* be used in some situations - TB

[c] Sentinel, (periodic or continuous), active, [integrated]

- Intermediate in approach
- more useful than simple passive data
- epidemiologically better defined
- reliable trend data available on occasion
- can be used comparatively and as an alert for the need for enhanced surveillance
- can often be linked to an integrated disease surveillance programme

7 hills

- 5 Palatine

2. Laboratory aspects

- Many successful efforts over the years in terms of improvement, standardisation
- but wide variation remains (virology)
- exclusion/inclusion: single (first) isolates only (treatment naïve, treatment failure only); carriage vs clinical infection; collection protocols vary
- test method: 6 microbiologists provide 12 variations

2. Laboratory aspects

- Quality Control and Quality Assurance - differ; QC often in place, EQAS often not
- International or national reference cultures notably lacking in pooled passive systems
- programme specific EQAS required - needs recognition/acceptance
- ‘satisfaction’ expressed is somewhat misplaced and premature - comparability

3. Data interpretation/analysis/ distribution

- producing, distributing valid and pertinent ‘information for action’ is crucial
- Norwegian experience: ***microbiological*** analysis is the paramount requirement
- surveillance data must be aligned with predefined needs and objectives
- ‘data mining’ [AAC 2002:46:2409-2419] should be replaced by thoughtful ‘farming’

7 hills

- 6 Capitoline

Some bacterial examples: passive, diagnostic AST

- Data mining: TSN, SENTRY, ALEXANDER…
- Often fail on all 3 counts: epidemiologically, methodologically and analytically
- Aggregation of large amounts of poorly defined data amplifies, rather than overcomes, problems

Diseases of Major and Global Importance - WHO

- Global Fund for TB, HIV and Malaria
  - **“Stop TB” – “DOTS”**

DOTS – claimed to cure 94% or more of cases

An example of the ‘fully integrated approach to disease control’

“STOP TB” - DOTS

- **5 elements to DOTS**

- *Government* (political) *commitment*
- *Case detection* (e.g. sputum smear microscopy)
- *Determine Standardized Rx*

  [DOT for 2 month minimum]
- *Reliable drug supply* [potency, continuity]
- *Recording and reporting system for Rx outcomes*

Multi-drug-resistant TB
DOTS-*Plus*

- MDR-TB – isoniazid and rifampicin resistant
- Prolonged [24 mo] Rx needed
- MDR TB > 4% in new TB cases in Eastern Europe, Latin America, Africa and Asia
- Surveillance of AMR in TB required - WHO/IUTLD Global Project on AMR in TB
- Problems of MDR-TB *see* 3rd Global Surveillance Report
- Standards, EQAS, comparability, validity

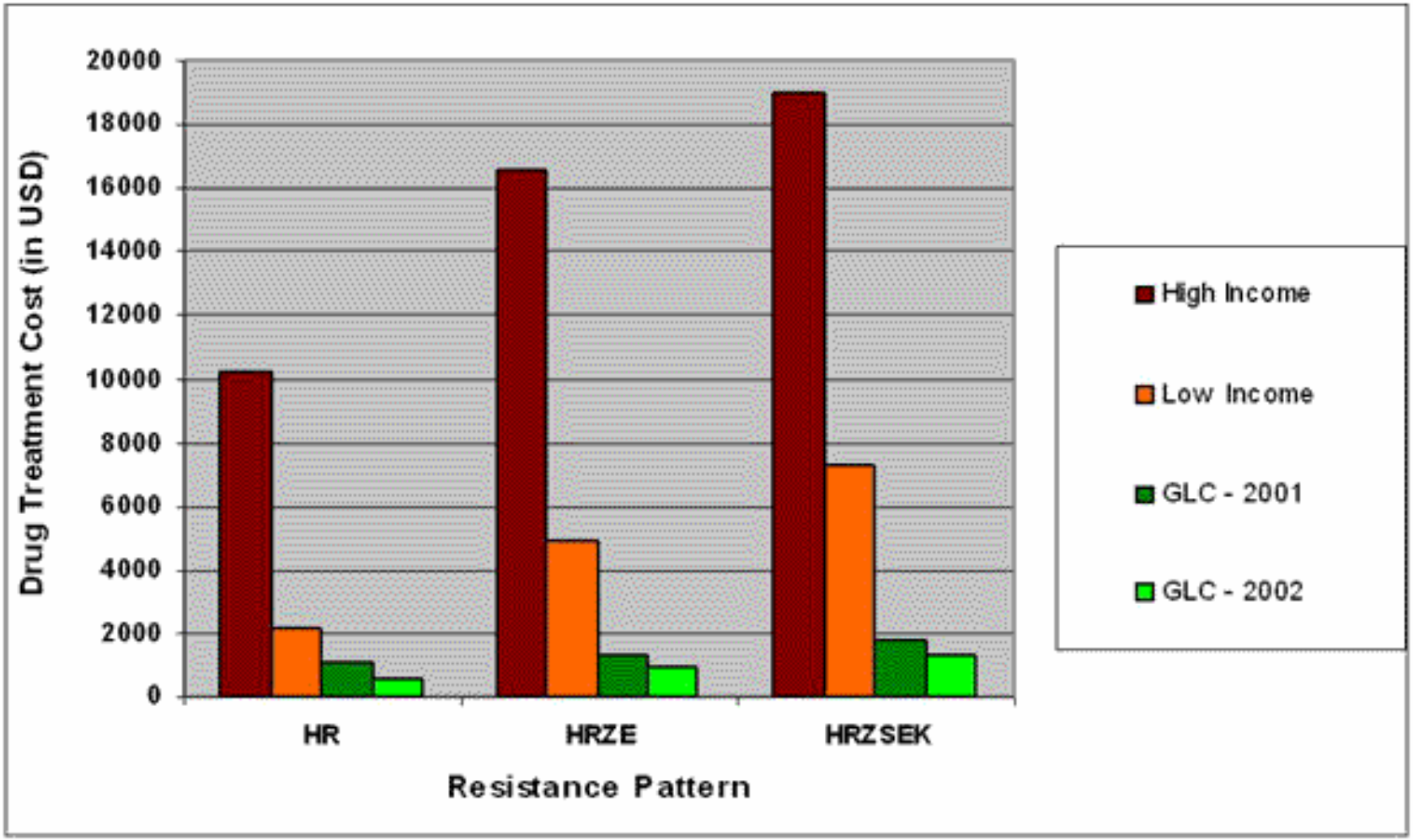
Green Light Committee

- "***provides*** concessionally-priced second-line anti-TB drugs to DOTS-Plus pilot projects meeting requisite standards.
- Currently, prices have been reduced up to 99% compared with the prices in the open market"

Green Light Committee

- DOTS-Plus is being implemented/approved in Bolivia, Costa Rica, Estonia, Haiti, Karakalpakstan (Uzbekistan), Latvia, Malawi, Mexico, Peru, Philippines, parts of the Russian Federation, Honduras, Lebanon and Nepal.

MDR-TB Treatment Regimen Costs



“STOP TB”

- Fully integrated programme
- Focussed on disease control
- Essential Drugs provided so as to maximise outcomes
- Right drugs in the right place
- *MDR TB lab surveillance an essential component of STOP TB*

Monitoring AMR for Public Health Action - TB

- Epidemiologically sound methods
- Microbiologically sound methods
- Active, integrated AMR Data Analysis and reporting
- Action initiated on the basis of established parameters

7 hills

- 7 Aventine

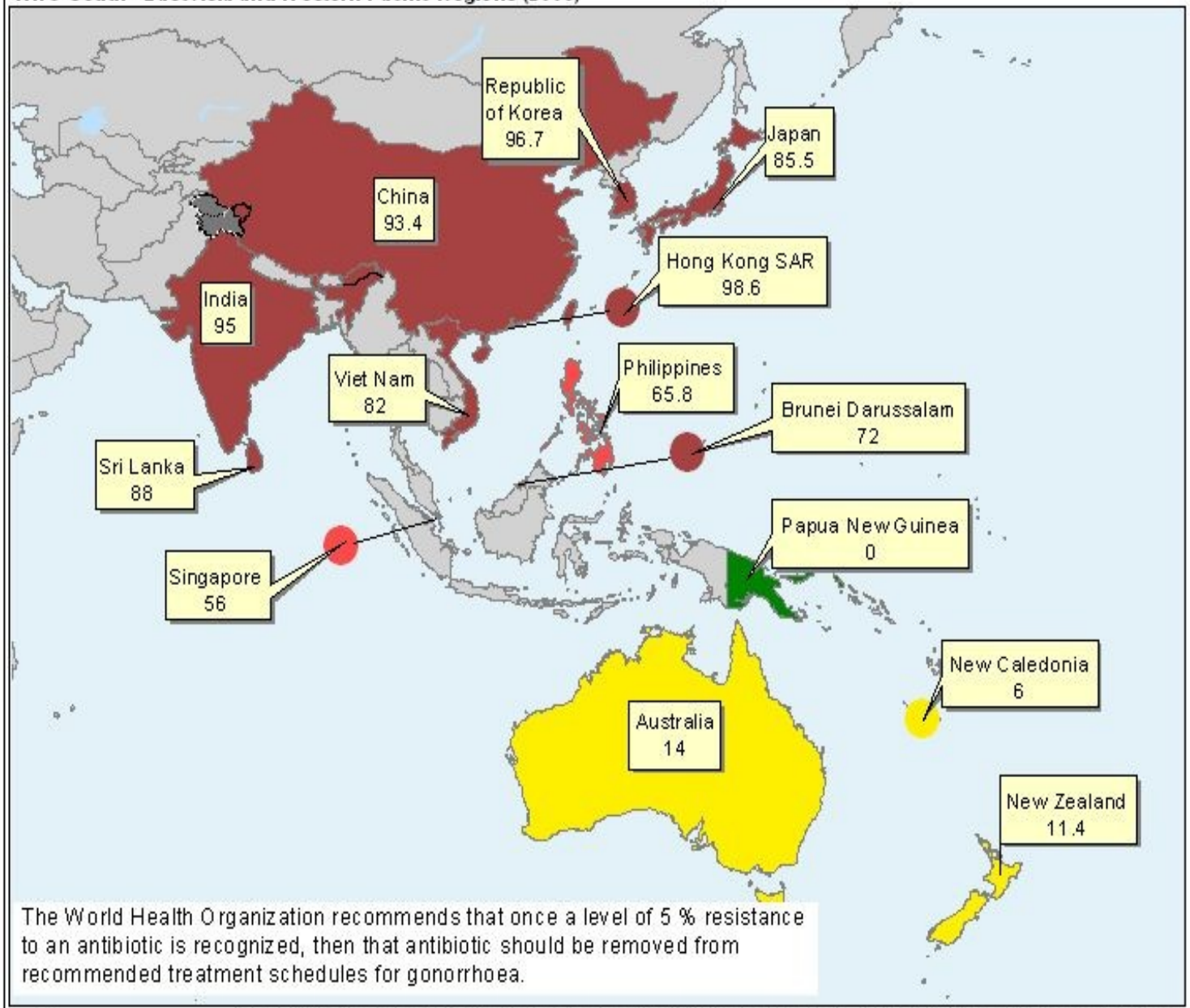
The issues

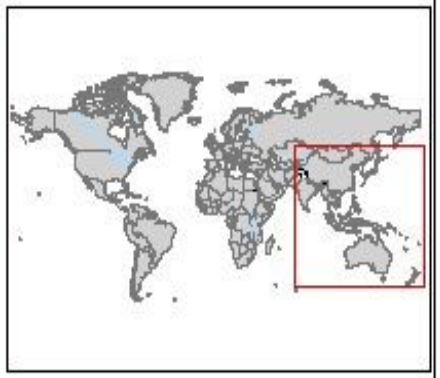
- ‘AMR surveillance’ is a resource with many tools for different applications
- first define objectives, adjust surveillance methods accordingly - choose the right tool
- integrate AMR data with disease control programmes for maximum effect
- COST and cost/benefit

Summary

- AMR surveillance is NOT a stand alone, one size fits all, activity
- specific requirements for multiple purposes
- epi, methods, analysis must ALL be in place
- for most public health purposes, specific AMR activity is best performed as modules integrated with their disease based systems

Quinolone resistance of strains of *Neisseria gonorrhoeae* isolated in countries, areas and territories of the WHO South - East Asia and Western Pacific Regions (2003)





Quinolone (%)

- 0
- 0.1 - 5
- 6 - 15
- 16 - 30
- 31 - 70
- 71 - 100

0 700 1400 Kilometers

The World Health Organization recommends that once a level of 5 % resistance to an antibiotic is recognized, then that antibiotic should be removed from recommended treatment schedules for gonorrhoea.

Data Source: National Ministry of Health / WHO
Map Production:
Public Health Mapping and GIS
Communicable Diseases (CDS)
World Health Organization

World Health Organization