ANTIBIOTIC RESISTANCE

The hidden threat to global health and the missing link to pharmacovigilance

Liselotte Diaz Högberg MPH PhD
Deputy Director, ReAct – Action on Antibiotic Resistance

ISPE mid-year meeting, Stockholm 2009

ReAct Action on Antibiotic Resistance

ReAct is a global multidisciplinary network working towards the goal that current and future generations should have access to effective prevention and treatment of bacterial infections as part of their right to health.

Funded by the Swedish Development Cooperation Agency (Sida) and hosted by Uppsala University

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Action on Antibiotic Resistance

Antibiotics save millions of lives!

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Inadequate Antimicrobial Treatment of Infections -A Risk Factor for Hospital Mortality Among Critically Ill Patients *Kollef et al. Chest, 2000*

Prospective study on 2000 patients in intensive care
(655 patients with infections)

Inadequate antimicrobial therapy

(22,5 % of patients)

Mortality 42%

Adequate antimicrobial therapy

Mortality 17.7%

Kollef et al. Chest, 2000

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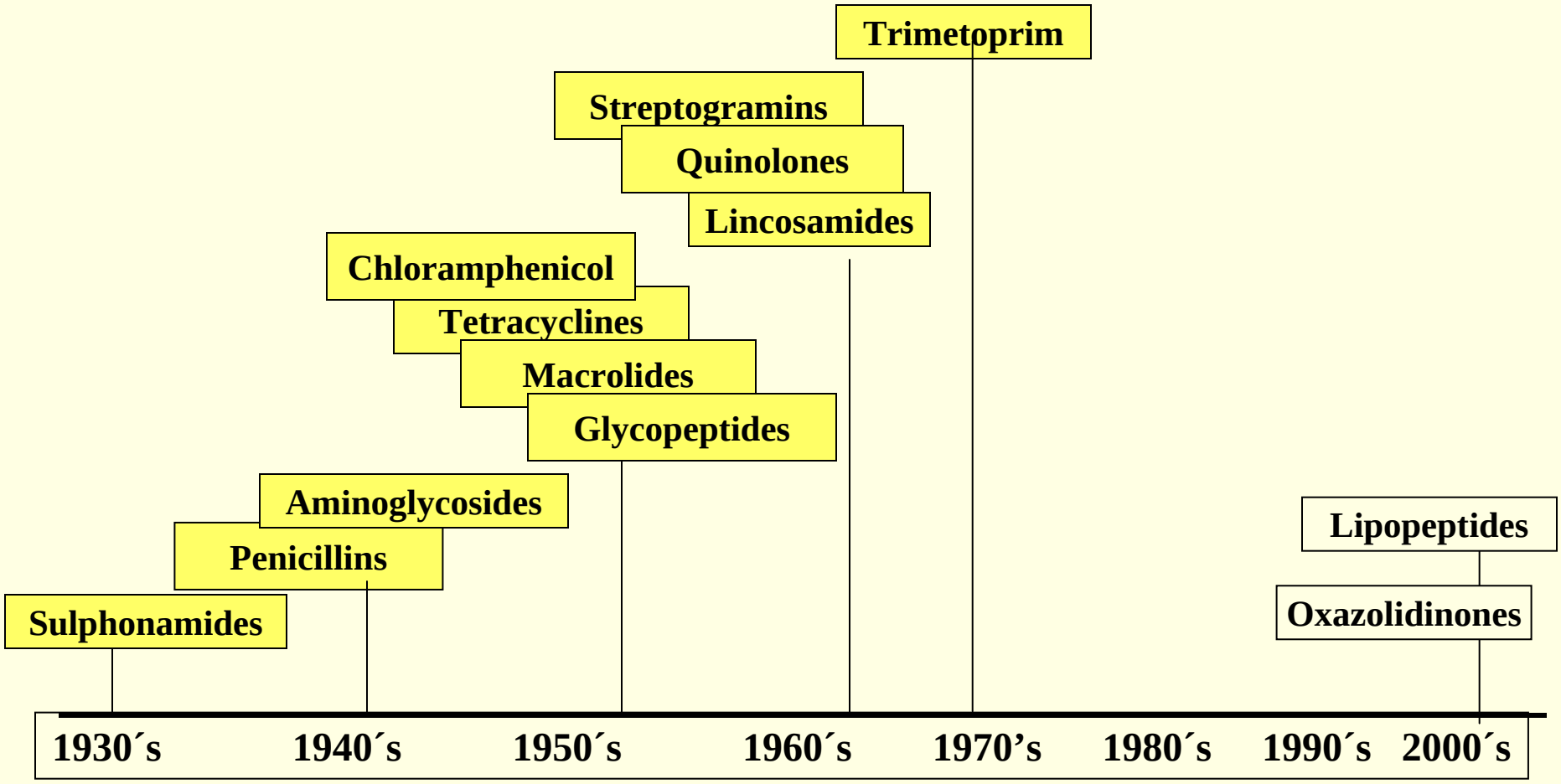
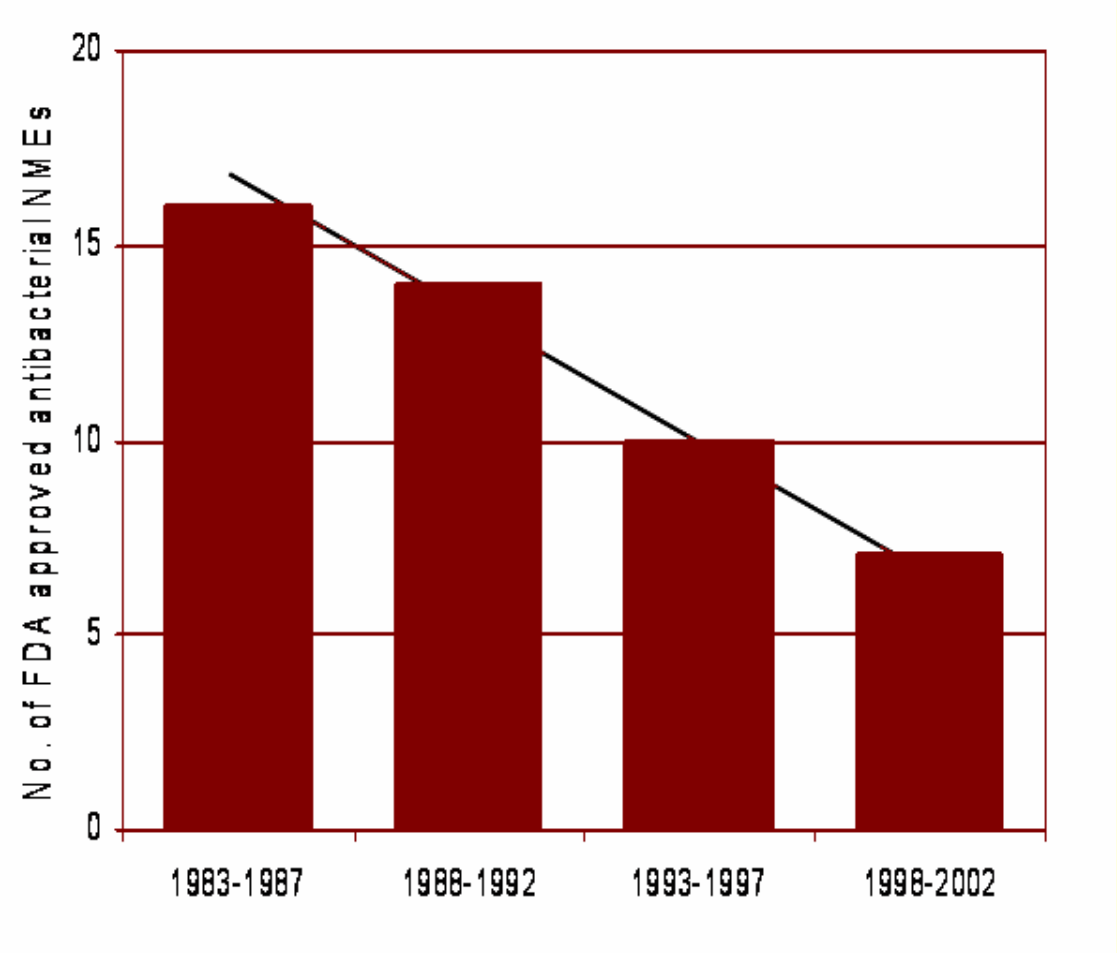
About 70% of the bacteria causing neonatal sepsis in the developing world can not be treated with the antibiotics recommended by WHO….

***Lancet* 2005; 365: 1175–88**

Introduction of New Antibiotic Classes



Antibacterial new molecular entities approved for use in the United States 1983-2002



From Kaplan, Laing et al., Priority medicines for Europe and the world, 2004

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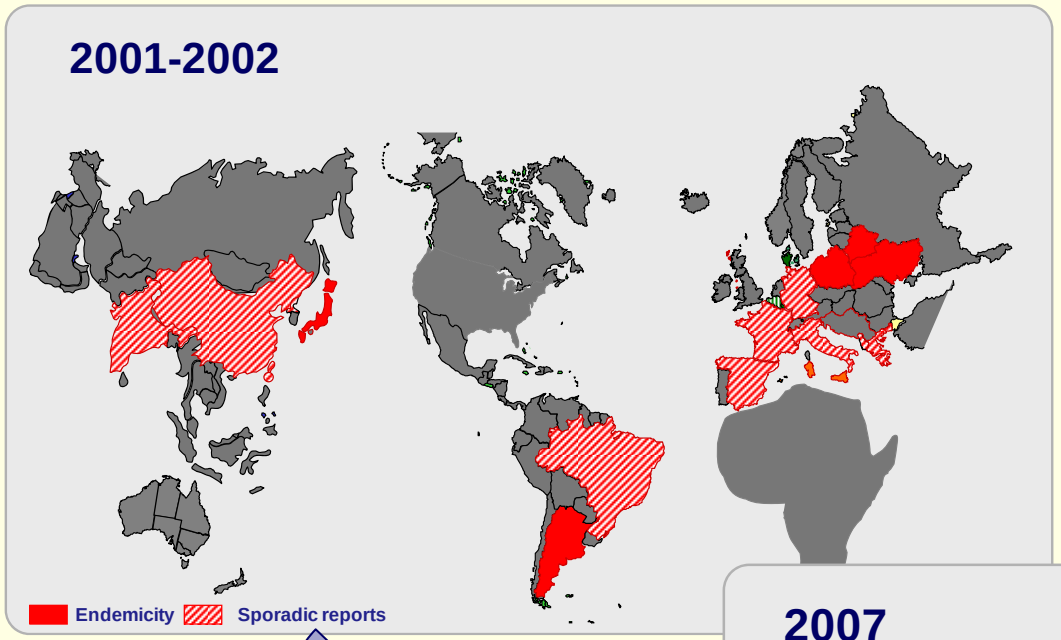
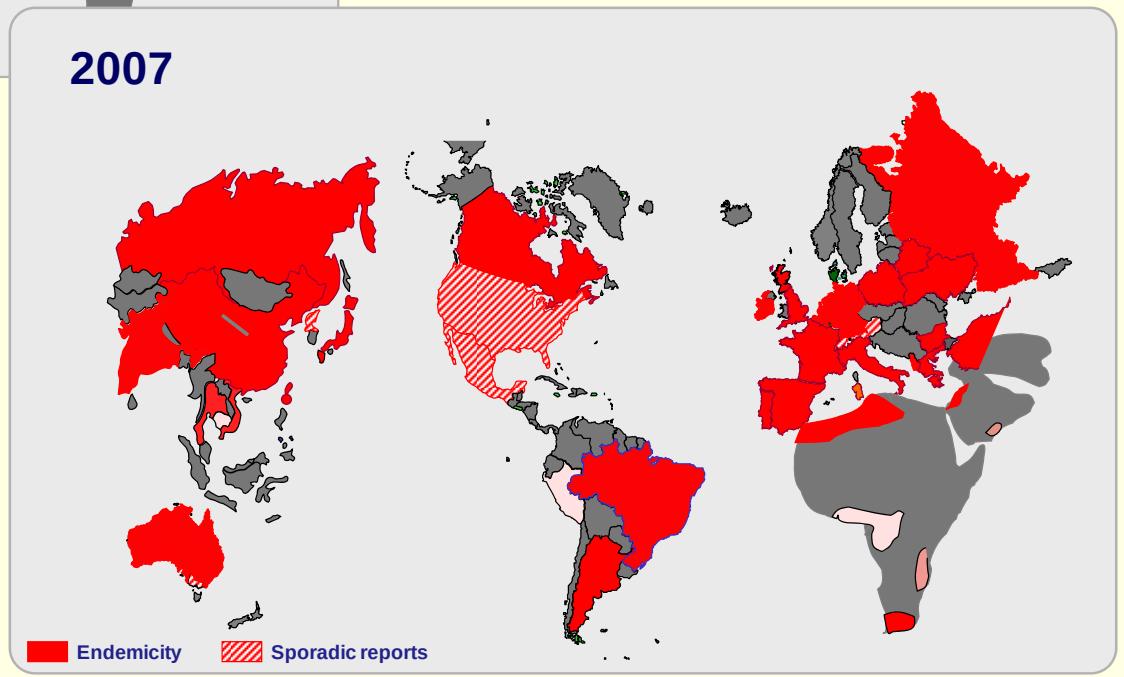
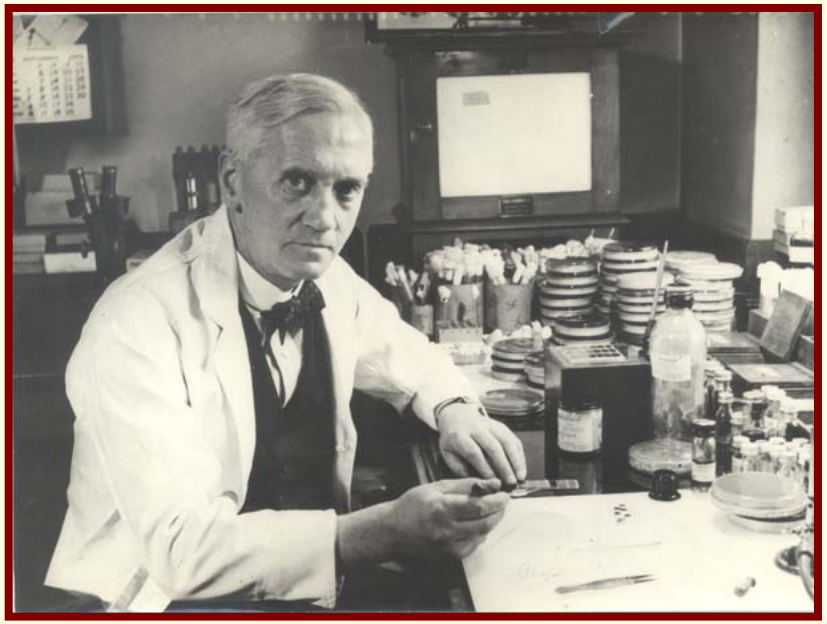
ESBL (CTX-M) producing *Enterobacteriaceae*





If we consider antibiotic resistance as a side effect..

… it is a side effect that is contagious



“It is not difficult to make microbes resistant to penicillin ….

…. The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.”

Alexander Fleming's Nobel Lecture, 1945


RELIEF

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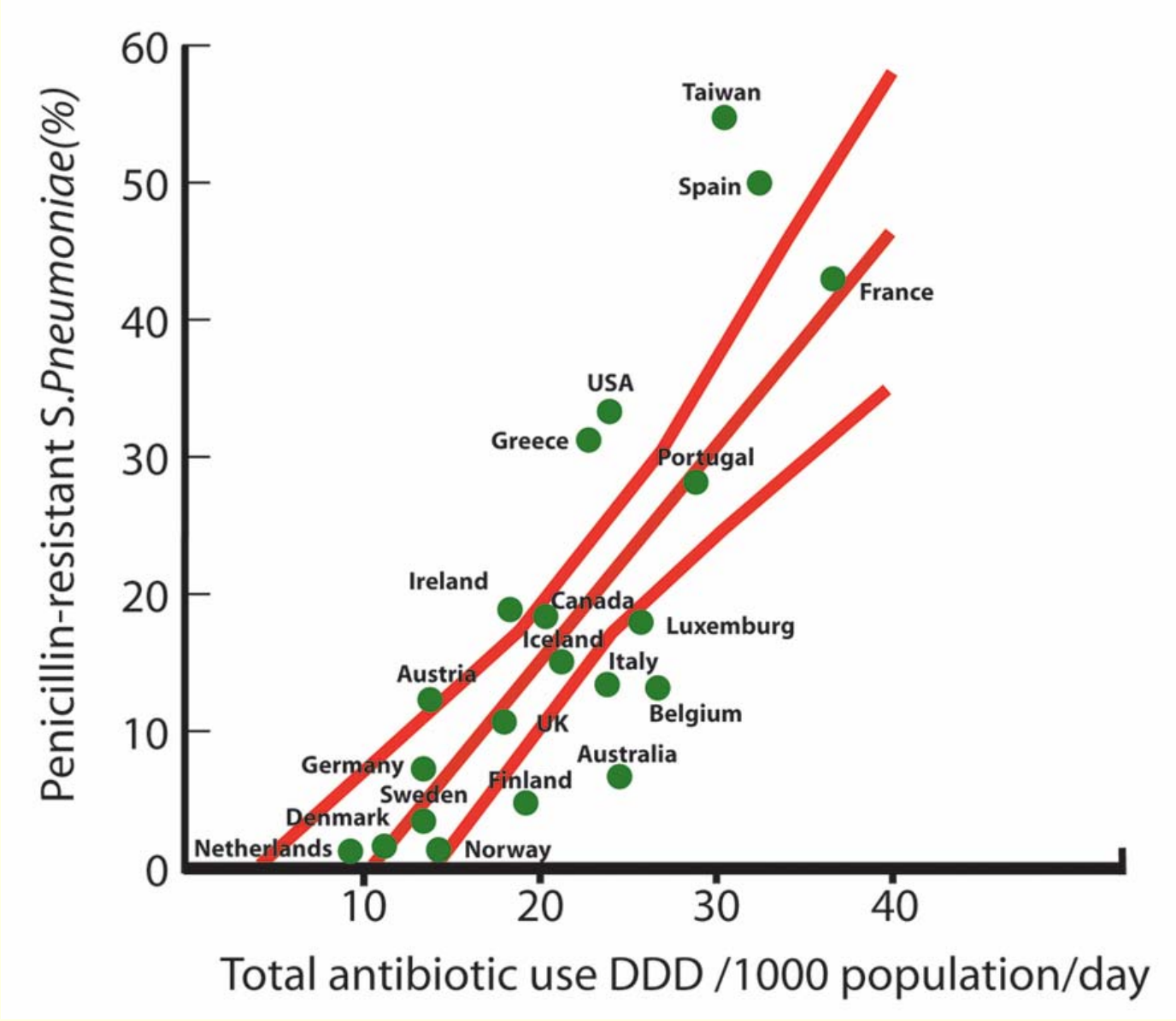

Albright et al. EID 2004;10(3):514-7

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Antibiotic resistance should be regarded as a patient safety issue

- **Higher risk for mortality**
- **Longer treatment periods**
- **Higher risk for complications**
- **Higher costs**
- **Are often preventable**
- **Puts other people at risk**

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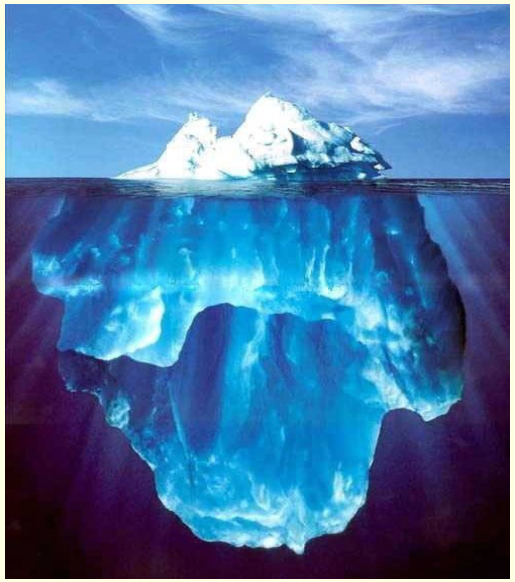
The Global Challenge

Antibiotics are losing their effectiveness at
a pace that was unforeseen just 5 years ago

The drug development pipeline is virtually empty
from antibiotics with a novel mechanism of action

More information is urgently needed



- Lab facilities lacking in many places
- Burden from resistance is needed to inform and motivate policymakers

Measures need to move beyond laboratory reported resistance rates


New innovative methods are needed now!

Can treatment failure due to antibiotic resistance be studied as an adverse drug event?

- Might develop long after drug is on market
- Possible as sentinel tool in population with limited laboratory resources?
- Possible way forward to get more data on consequences of resistance?

Reasons for poor patient response to antibiotic treatment

- Incorrect diagnosis
- Too late
- Counterfeit/poor quality drug
- Inadequate dose
- Patient compliance
- **Resistance**

All of these factors are important when designing an antibiotic resistance control programme!

Which type of signals could be considered?

- Death
- Change of therapy
- Health care utilisation

…..etc

Which type of data sources could be utilised?

- Hospital statistics (mortality, morbidity, pharmacy data)
- Insurance records
- Patients/ health care providers reports

Example 1:

Health care utilisation after antibiotic treatment failure

Wu et al, Clin Ther 2004

- Insurance data, new ab Rx within 4 weeks after first ab Rx
- End points: numbers of hospitalizations and emergency department and office visits within 1 month after the initial ab

- About 10% of patients with respiratory infections who were treated with macrolide antibiotics experienced treatment failure within 4 weeks. Macrolide treatment failure was associated with increased health care utilization

Example 2:

High infection-related neonatal mortality despite access to health-care and antibiotic treatment

Jehan et al. Bull World Health Organ 2009

- An urban population with good access to professional care (1369 live births)
- High 28-day neonatal mortality rate of 47 per 1000 live births Final causes were classified as immaturity-related (26%), birth asphyxia or hypoxia (26%) and infection (23%)
- Almost all (88%) neonates who died received treatment and 75% died in the hospital

Take home message

Antibiotic resistance needs to be measured by its consequences, not only its presence

New tools needs to be developed and other data sources than laboratory records need to be considered

www.reactgroup.org
liselotte.hogberg@medsci.uu.se

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