Is antibiotic resistance reversible? Evidence from humans and food animals

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Antibiotic resistance: a problem.

- **Antibiotic resistance = direct consequence of antibiotic use**

- **Consequences of antibiotic-resistant infections:**
  - **Currently: est. 700,000 lives/year globally**
  - **By 2050: est. 10M lives/year globally**

O'Neill, J., S. Davies, and J. Rex, *Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations* 2014.

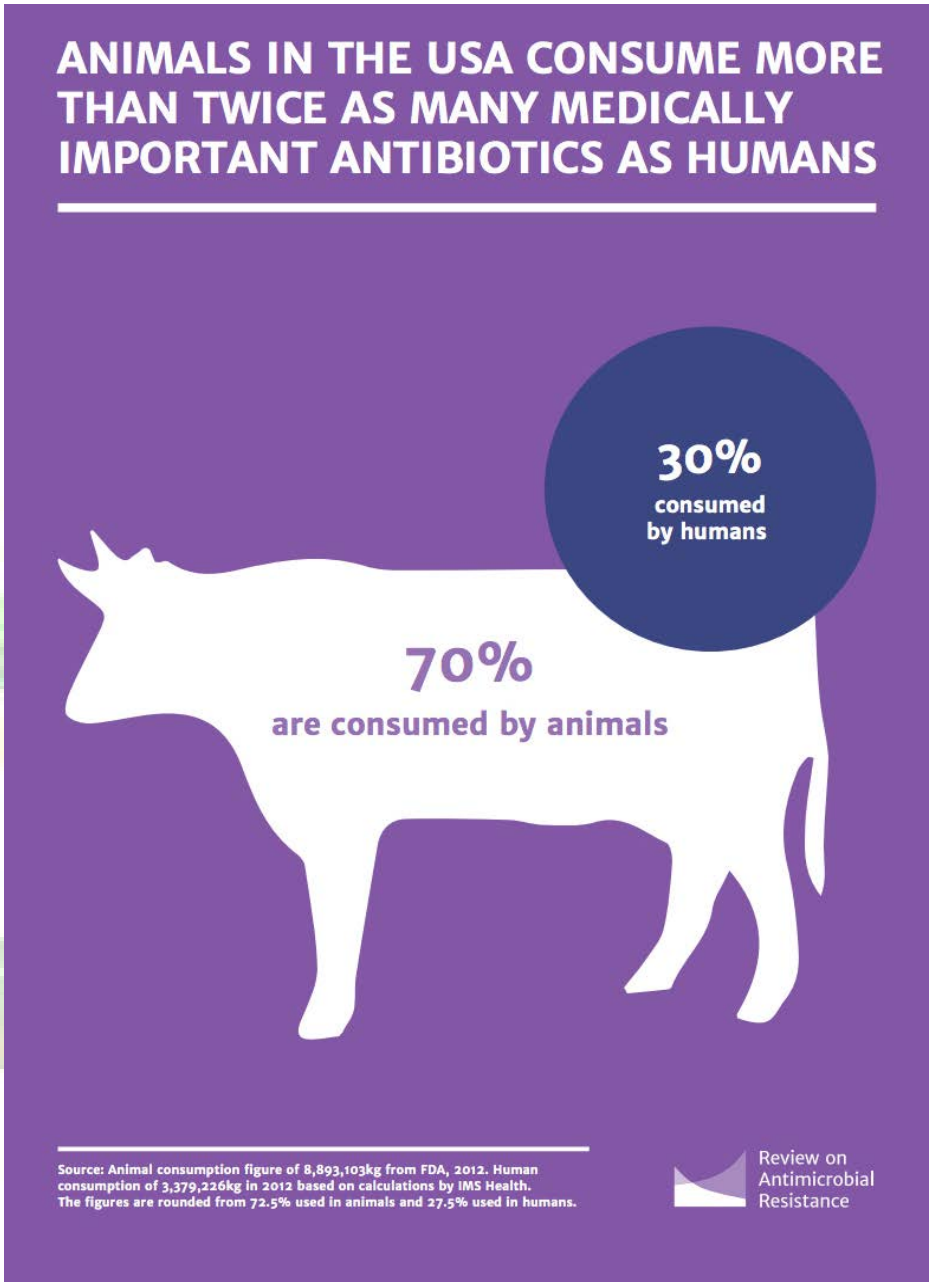
Source of the problem

1) **Pace of discovery of new antibiotics has slowed**

2) **Antibiotic use is rising…**

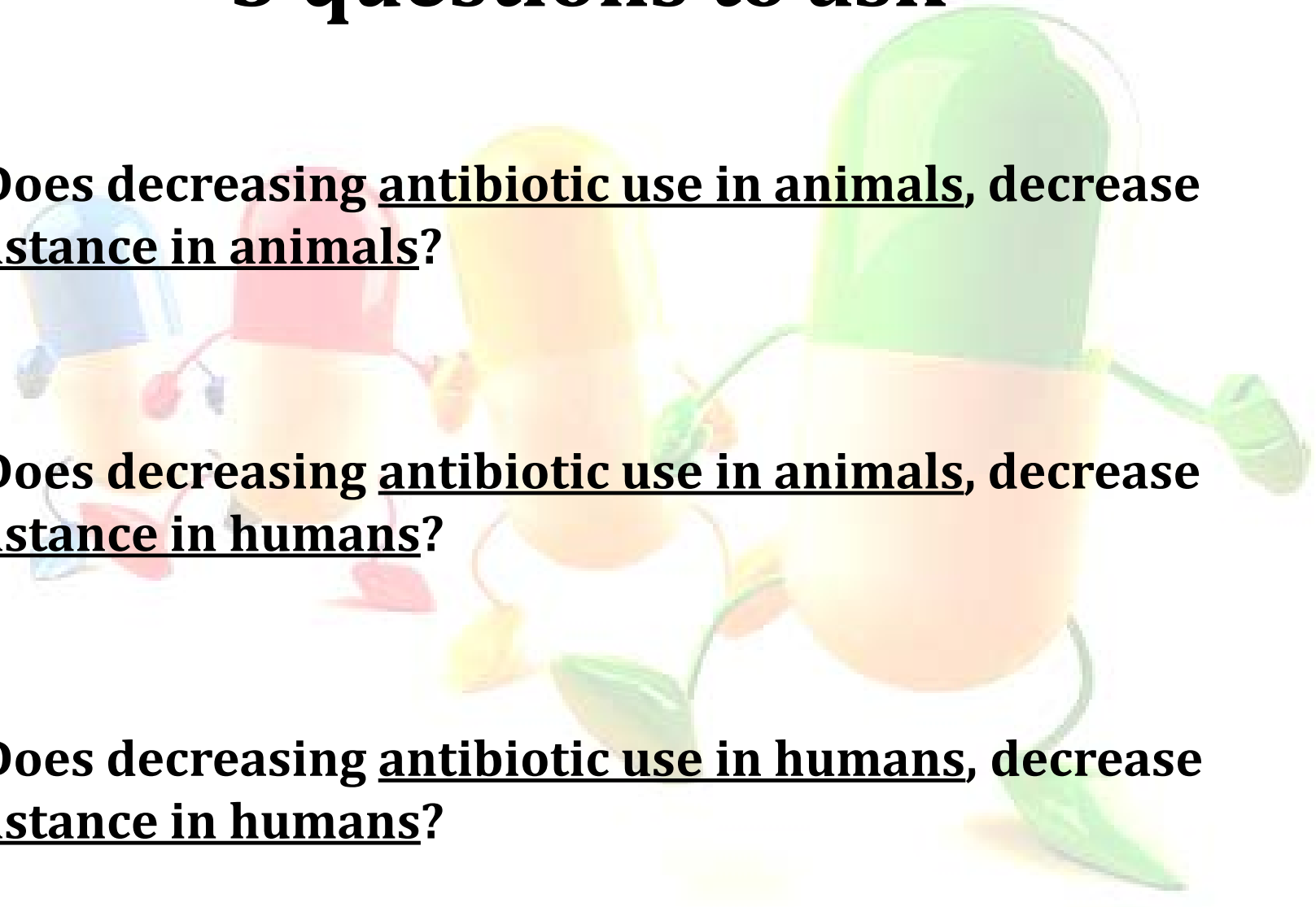
- **In humans**

- **In animals**



Jim O'Neill et al, 2015, Antimicrobials in Agriculture and The environment: Reducing unnecessary Use and waste

3 questions to ask



1) Does decreasing antibiotic use in animals, decrease resistance in animals?

2) Does decreasing antibiotic use in animals, decrease resistance in humans?

3) Does decreasing antibiotic use in humans, decrease resistance in humans?

Questions 1 & 2: WHO systematic review

- **Systematic review of evidence for WHO in 2016**
- **Aim: To underpin the guideline to preserve the long-term effectiveness of antimicrobials critical for human medicine**
- **Focus:**
  - **Does limiting the use of antimicrobials in food animals reduce resistant elements in**
    1) food animals; and
    2) humans

Questions 1 & 2: WHO systematic review

- No date, language restrictions
- Study designs included:
  - Animal question: cohorts, RCTs, reviews
  - Human question: before & after, ITS, cohorts, RCTs, reviews

3 questions to ask

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Question 1: WHO systematic review

- 89 studies included
- Adequate evidence to conclude that limiting ABs in animals reduces resistance in animals
- N.B. considerable heterogeneity: design, species, isolates, environs, ABs, routes of administration, sampling timeframes, methods…
- … precludes estimating the magnitude of effect

3 questions to ask

1) Does decreasing antibiotic use in animals, decrease resistance in animals?

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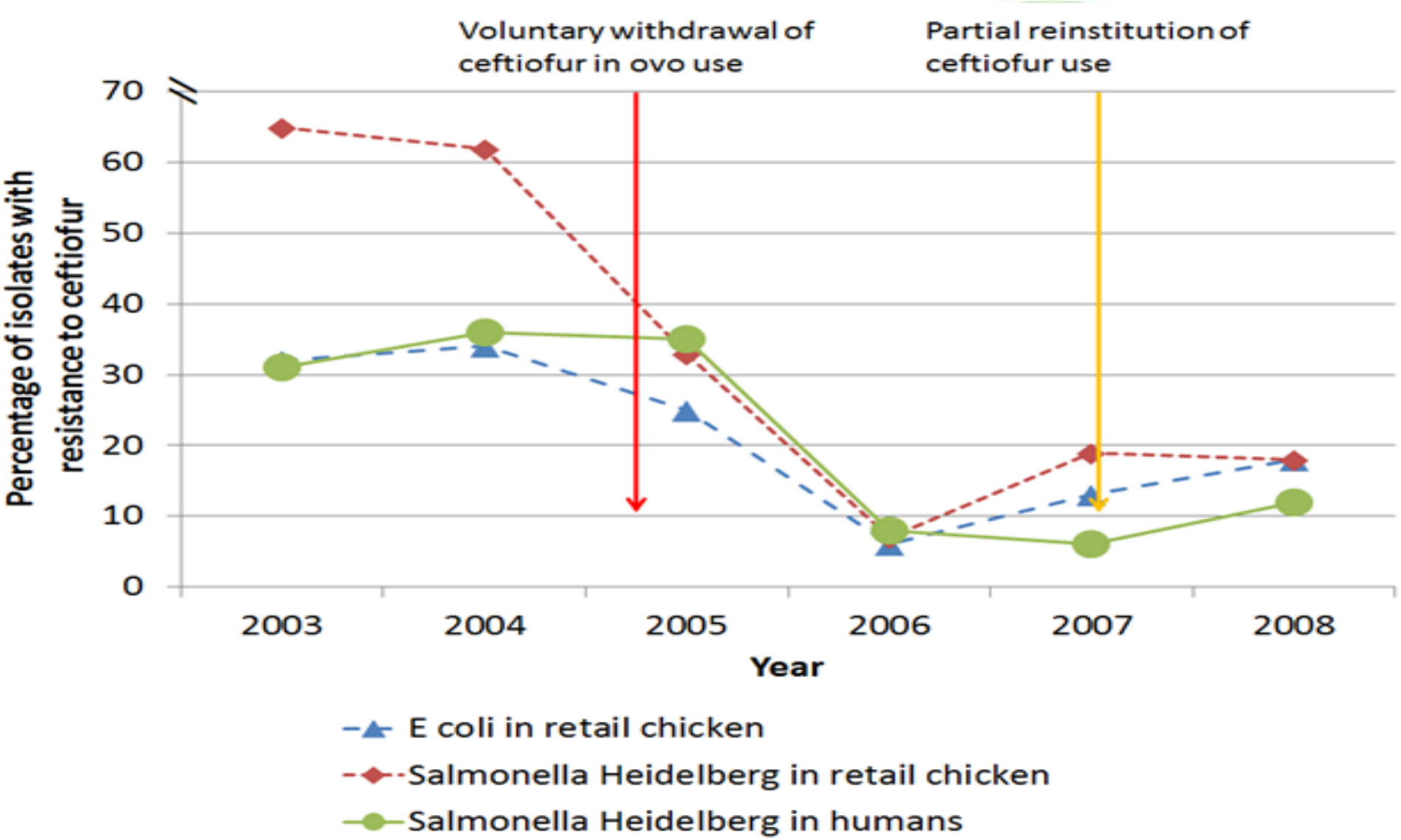
Question 2: WHO systematic review

- **4 studies included**

- **1 study directly answering the question: Dutil 2010**
  - **Interrupted time series**
  - **Quebec, Canada**
  - **Ceftiofur injections into eggs in chicken hatcheries**
    - **Voluntary withdrawal (2005)**
    - **Subsequent partial reintroduction (2007)**

Dutil, et al. 2010, *Ceftiofur Resistance in Salmonella enterica Serovar Heidelberg from Chicken Meat and Humans, Canada*

Question 2: WHO systematic review



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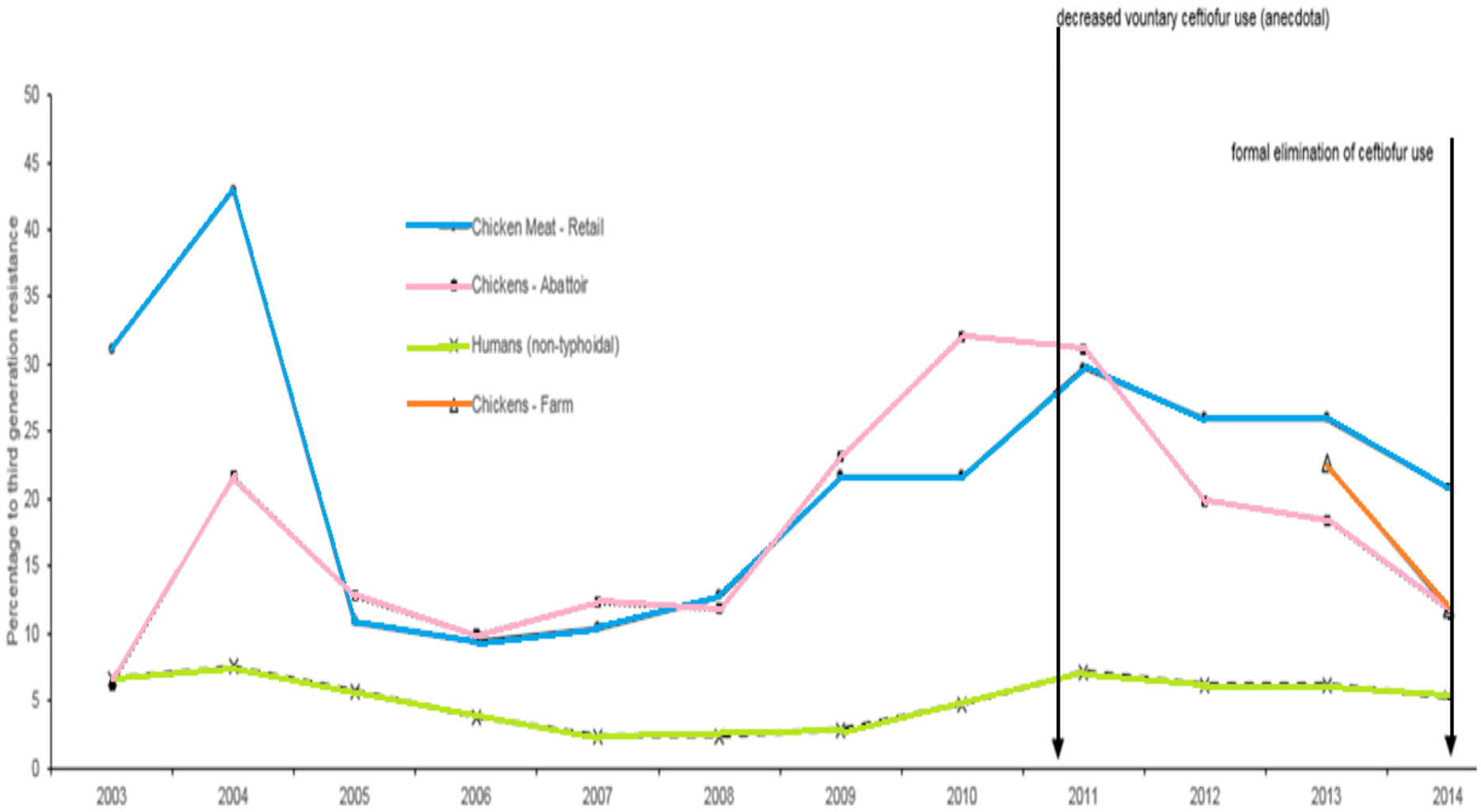
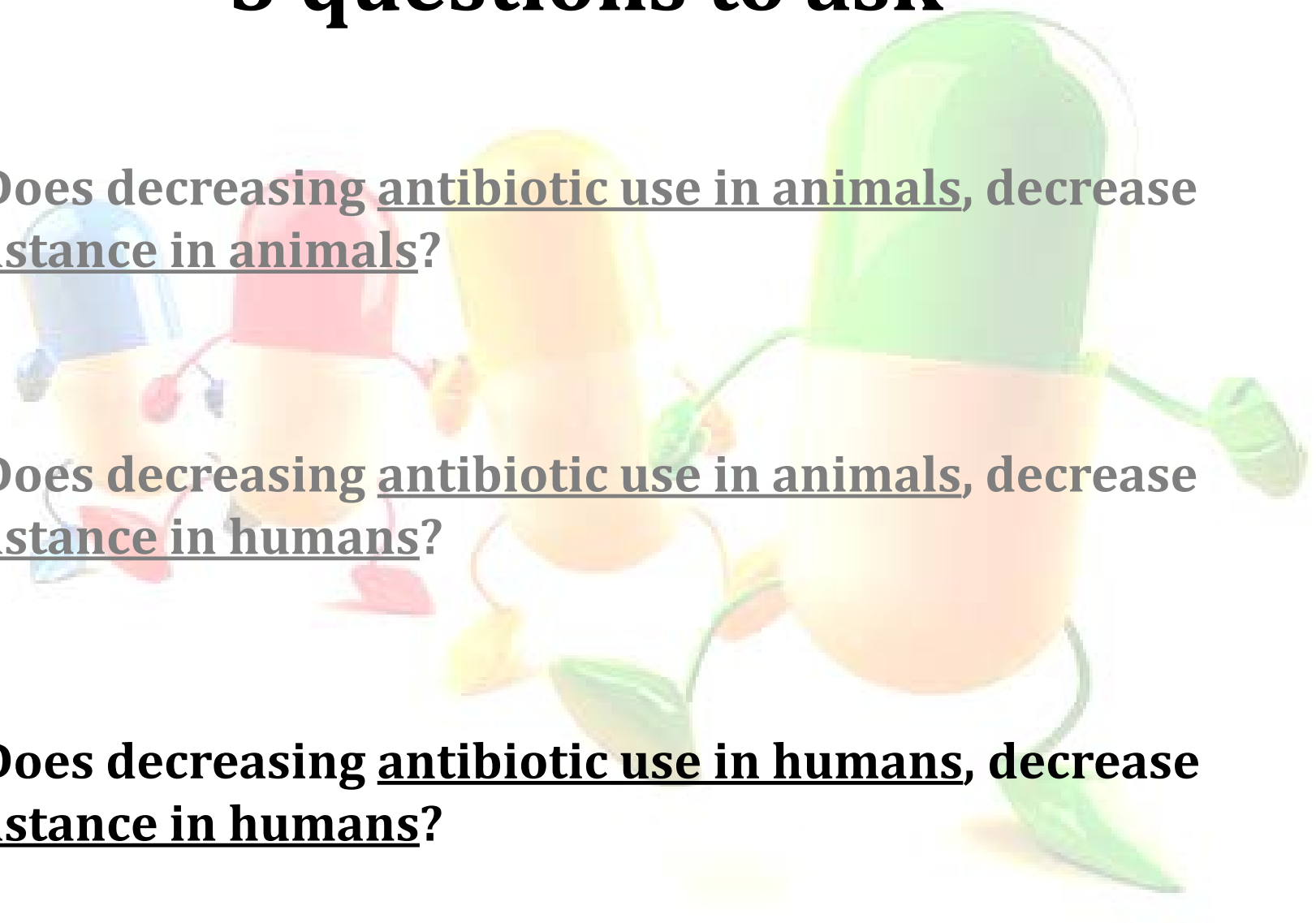


3 questions to ask



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Question 3: Costelloe systematic review

- **Focus: impact of AB prescribing in primary care, on AB resistance in patients**

- **Findings:**
  - **Exposure to antibiotics causes resistance**
  - **The resistance is the greatest right after exposure…**
  - **… but resistance decreases over time**

Costelloe et al, 2010, Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis

Question 3: Costelloe systematic review

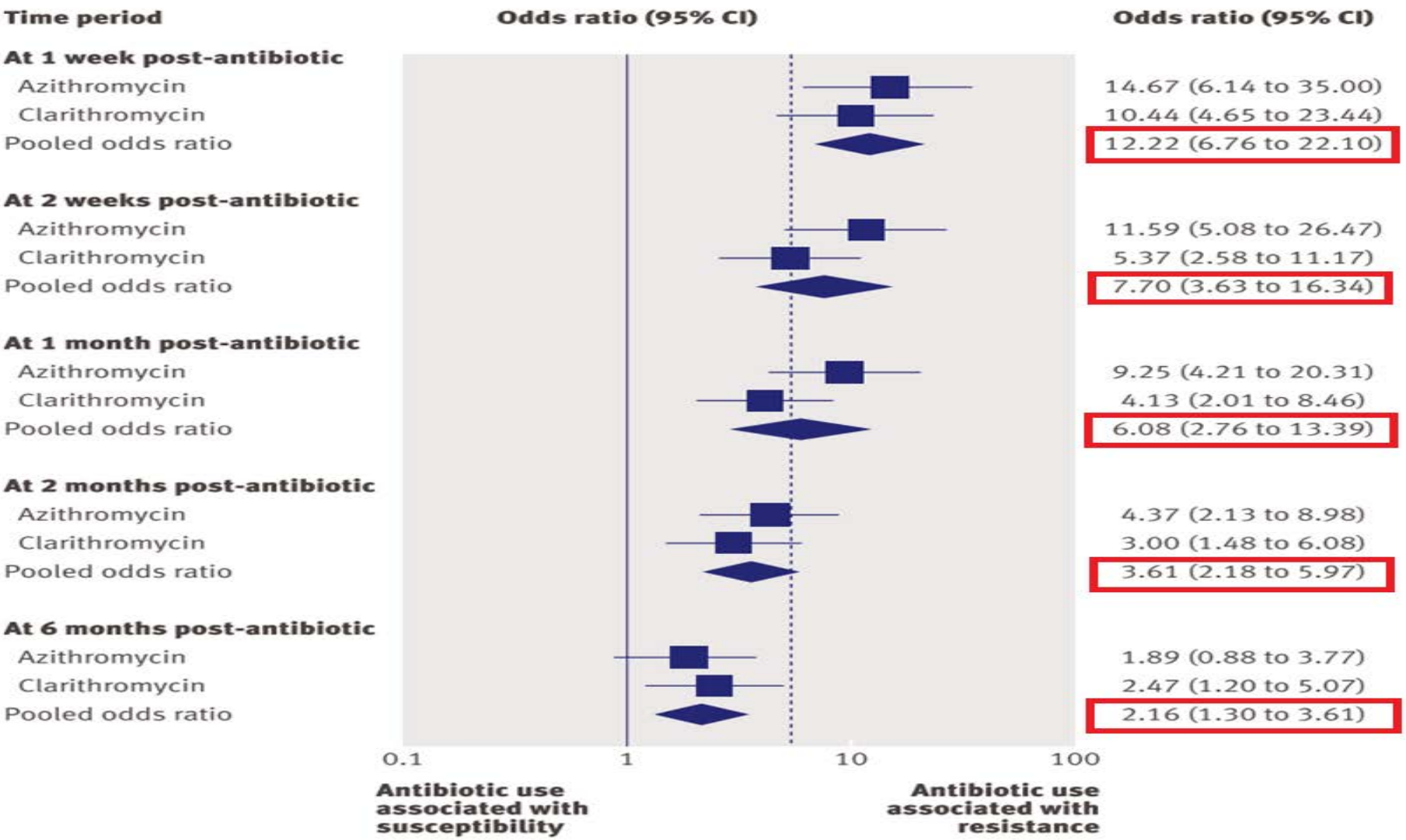

Fig 4 | Forest plot showing individual analytic and pooled ORs (log scale) for resistance in respiratory tract streptococci of healthy volunteers from the Malhotra-Kumar study[35] and previous antibiotic prescribing

Question 3: Costelloe systematic review

- Costelloe review now 7 years old
- Literature searches nearly 8 years old
- Moreover:
  - Cannot replicate the search strategy…
  - … or the results
  - Re-doing it anew

Conclusions: Is antibiotic resistance reversible?

- **Limiting the use of antibiotics in humans and animals decreases resistance**
- **Usefulness of antibiotics can be conserved by reducing their use**
- **Caveats:**
  - **evidence base somewhat limited**
  - **evidence quality is variable**
  - **cannot quantify the effect**
- **Role for surveillance and reporting systems**