.
What can human medicine do to control antibiotic resistance?

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# Gonorrhea is not a serious disease, but…

Antimicrobial Chemotherapy

The ticking time bomb: escalating antibiotic resistance in *Neisseria gonorrhoeae* is a public health disaster in waiting

David M. Whiley[1,2]*, Namraj Goire[1,2], Monica M. Lahra[3], Basil Donovan[4,5], Athena E. Limnios[3], Michael D. Nissen[1,2,6] and Theo P. Sloots[1,2,6]
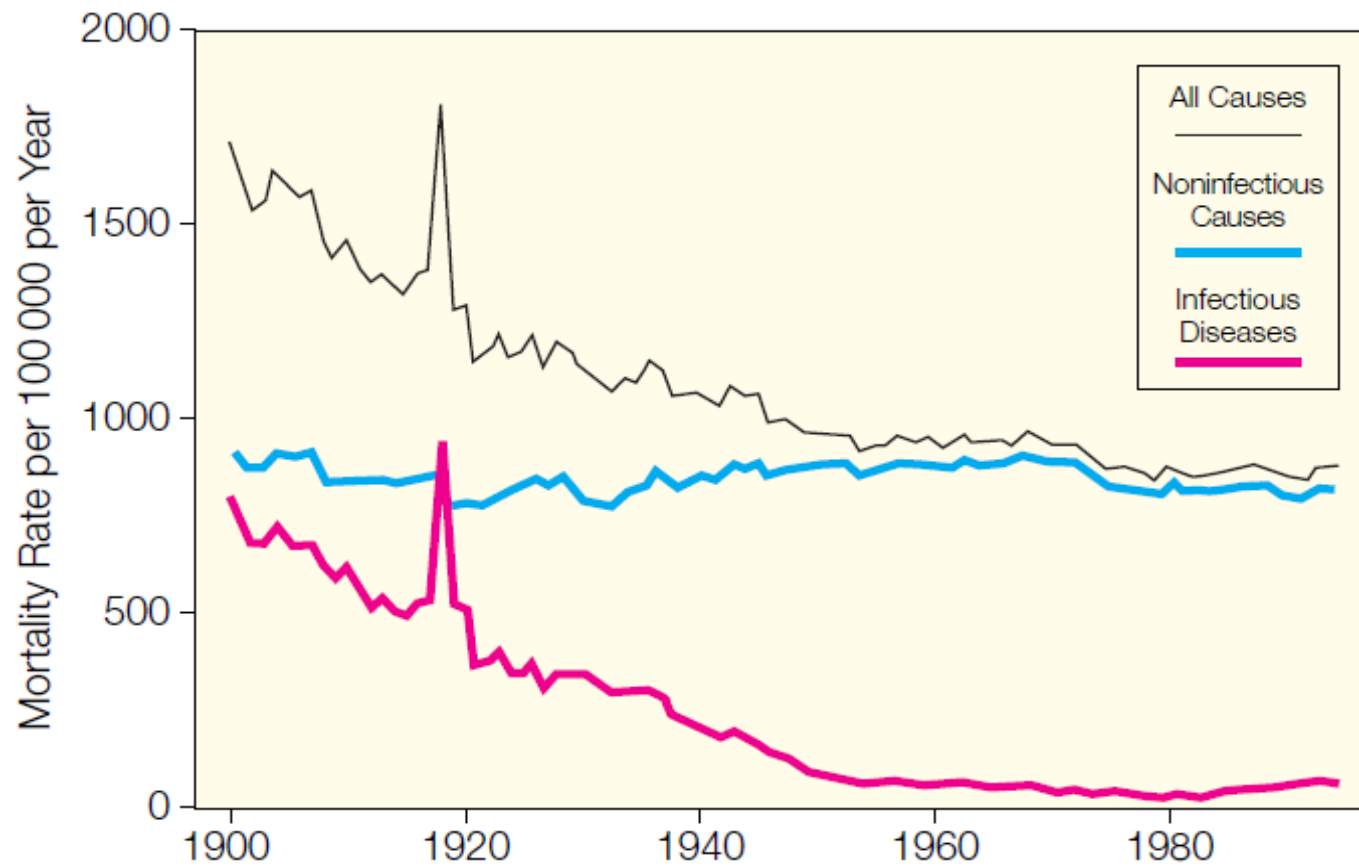
Antibiotics & resistance

- Antibiotics kill bacteria (not virus)

- Antibiotic resistance (AMR) means that antibiotics can not kill the bacteria

- Accoring to WHO AMR is one of the greatest threats to public health
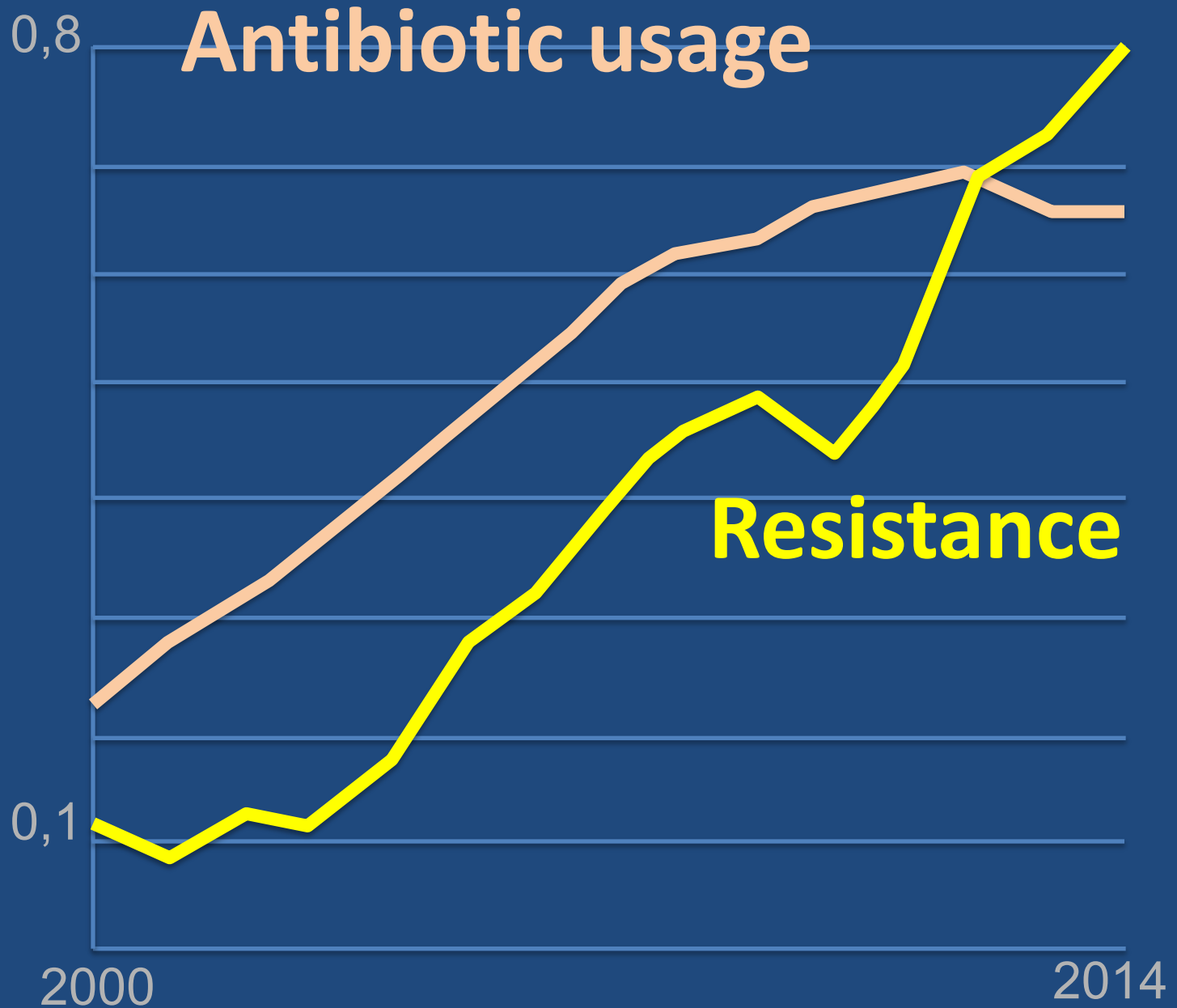
Mortality rate USA 1900-2000. Armstrong, JAMA 1999;281:61-6

Figure 2. Crude Mortality Rates for All Causes, Noninfectious Causes, and Infectious Diseases

1586 tilfeller av pneumokokk-pneumoni 1929-35 i Boston (Tilghman RC, Finland M. Arch Intern Med, 1937)
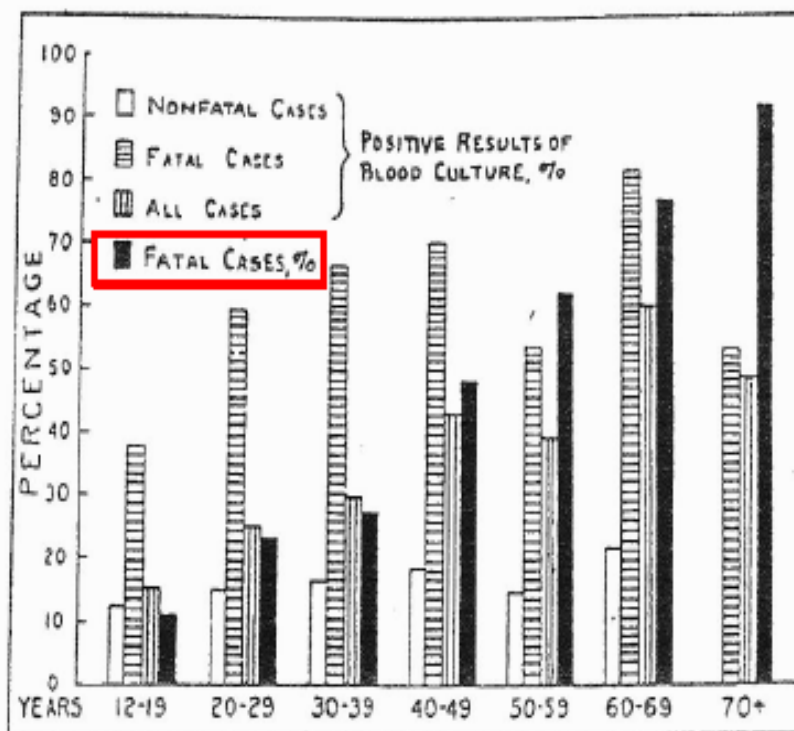
Chart 1.—Comparison of the incidence of bacteremia and the mortality for various age groups.

We are already in the post-antibiotic era in Europe

Figure 3.11. *Klebsiella pneumoniae.* Percentage (%) of invasive isolates with resistance to carbapenems, EU/EEA countries, 2016

Legend:
- < 1%
- 1% to < 5%
- 5% to < 10%
- 10% to < 25%
- 25% to < 50%
- ≥ 50%
- No data reported or fewer than 10 isolates
- Not included

Non-visible countries
- Liechtenstein
- Luxembourg
- Malta
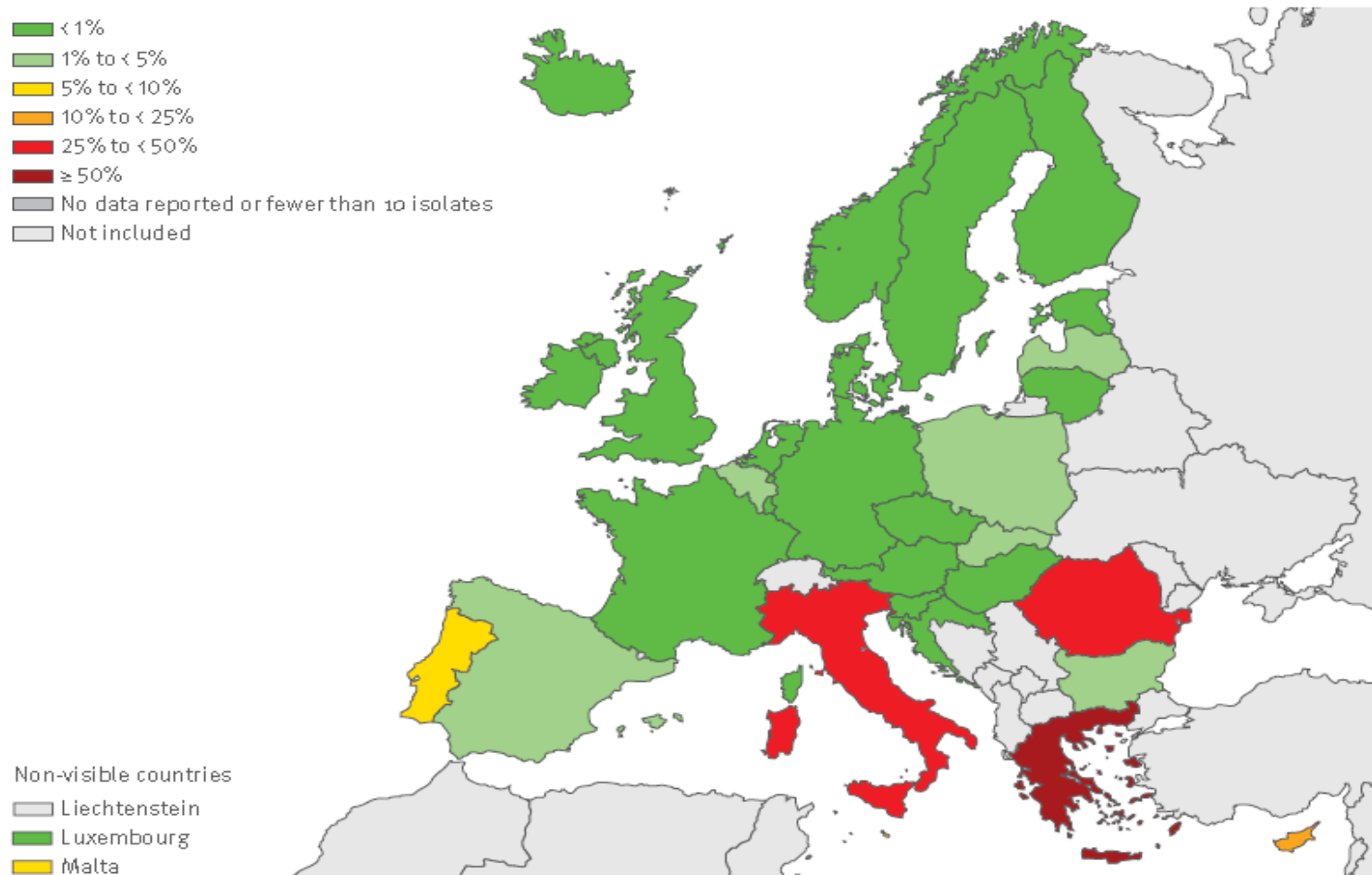
Antibiotics in agriculture

- Animals: 70% «growth promotors»
  - frequent use
  - low dosages
  - low hygiene
  - crowding
- 43 mill AB doses/day
- Illegal use widespread

Dear president Trump

What happens when we give antibiotics?

- We can kill the patogenic bacteriae

- But, simultaneously we select resistant bacteria from the normal bacterial flora

MRSA

CAMRSA

Antibiotic degrading enzyme

Efflux pump

Plasmid

Antibiotic

Antibiotic

Antibiotic altering enzyme
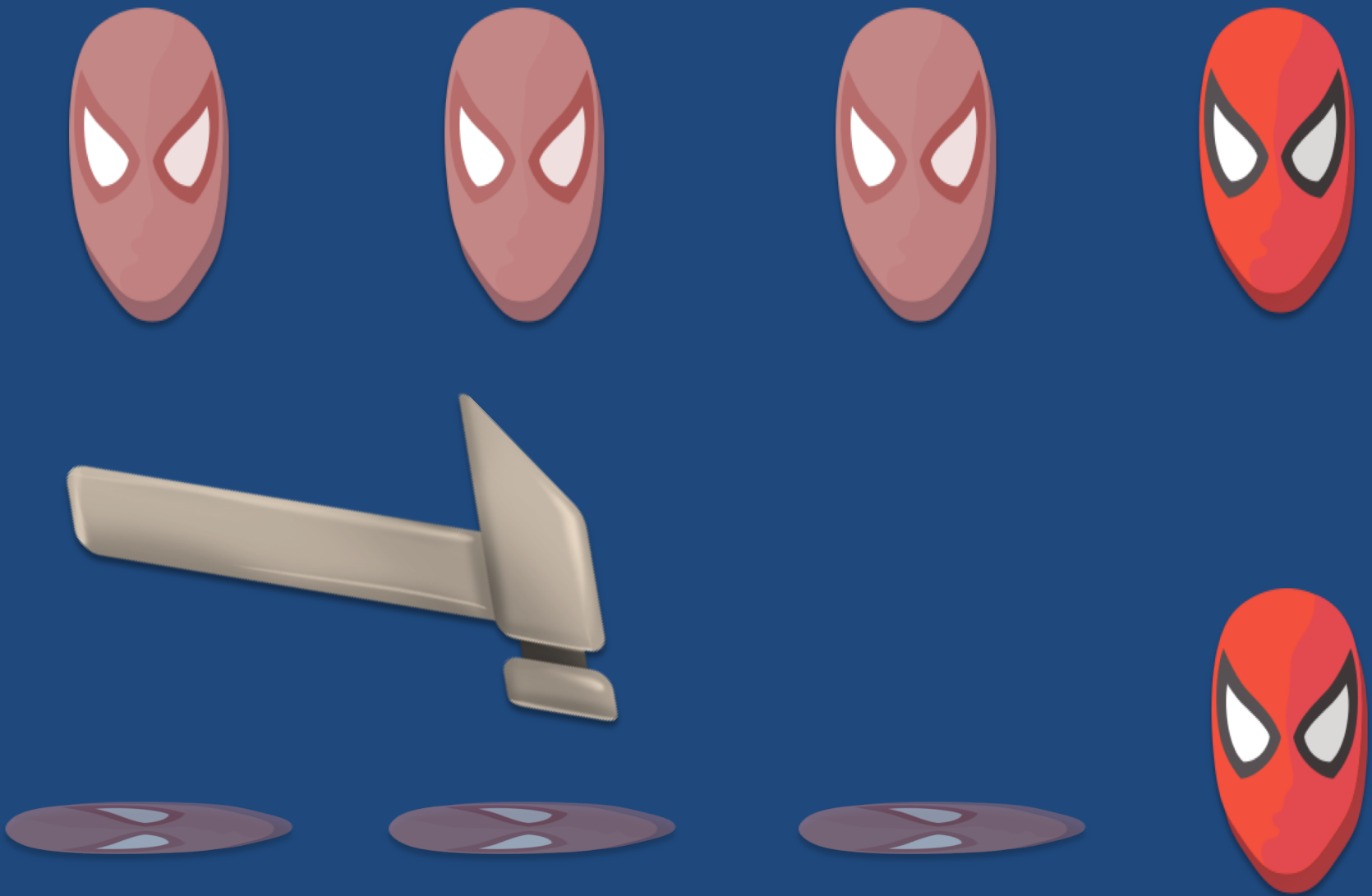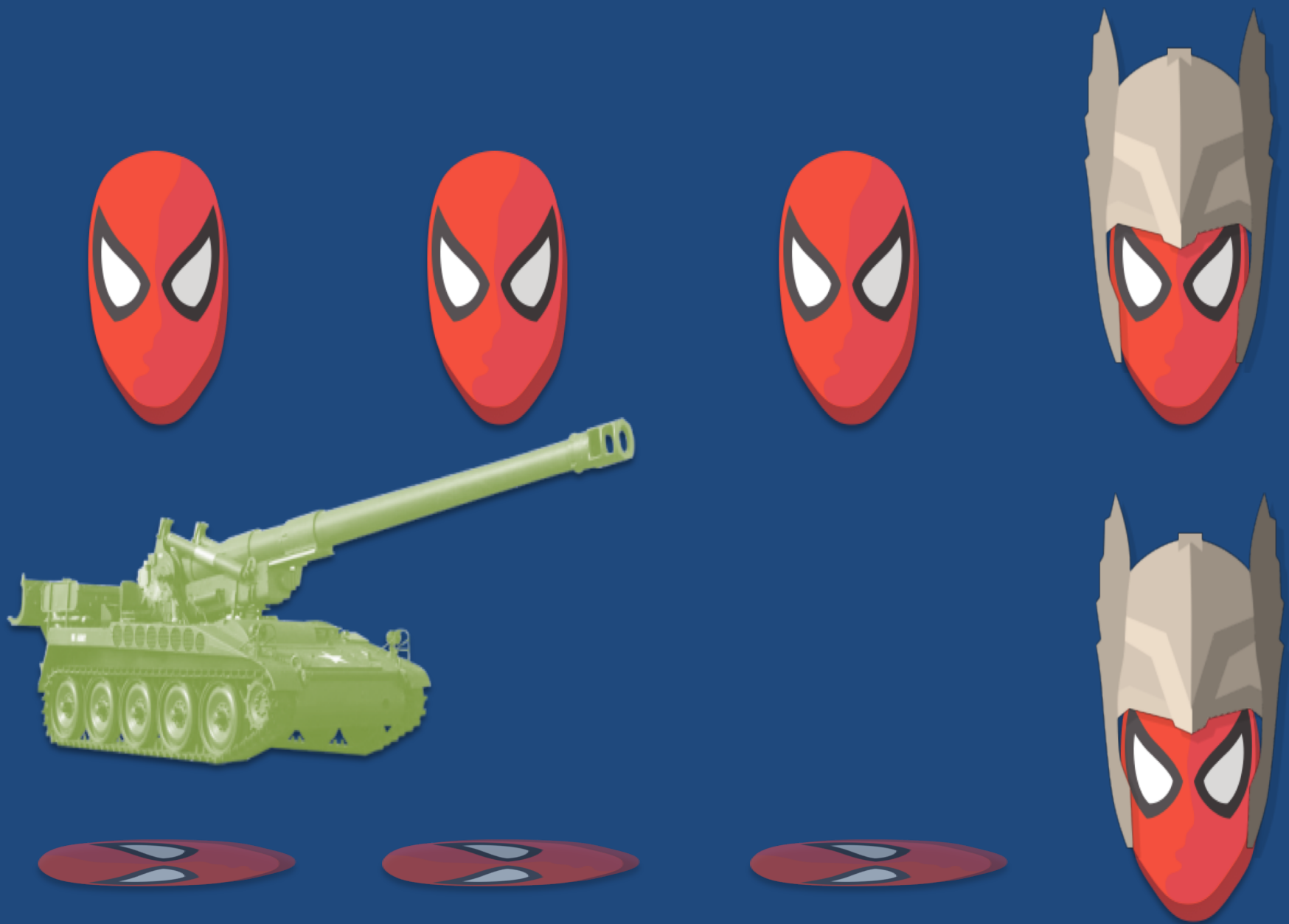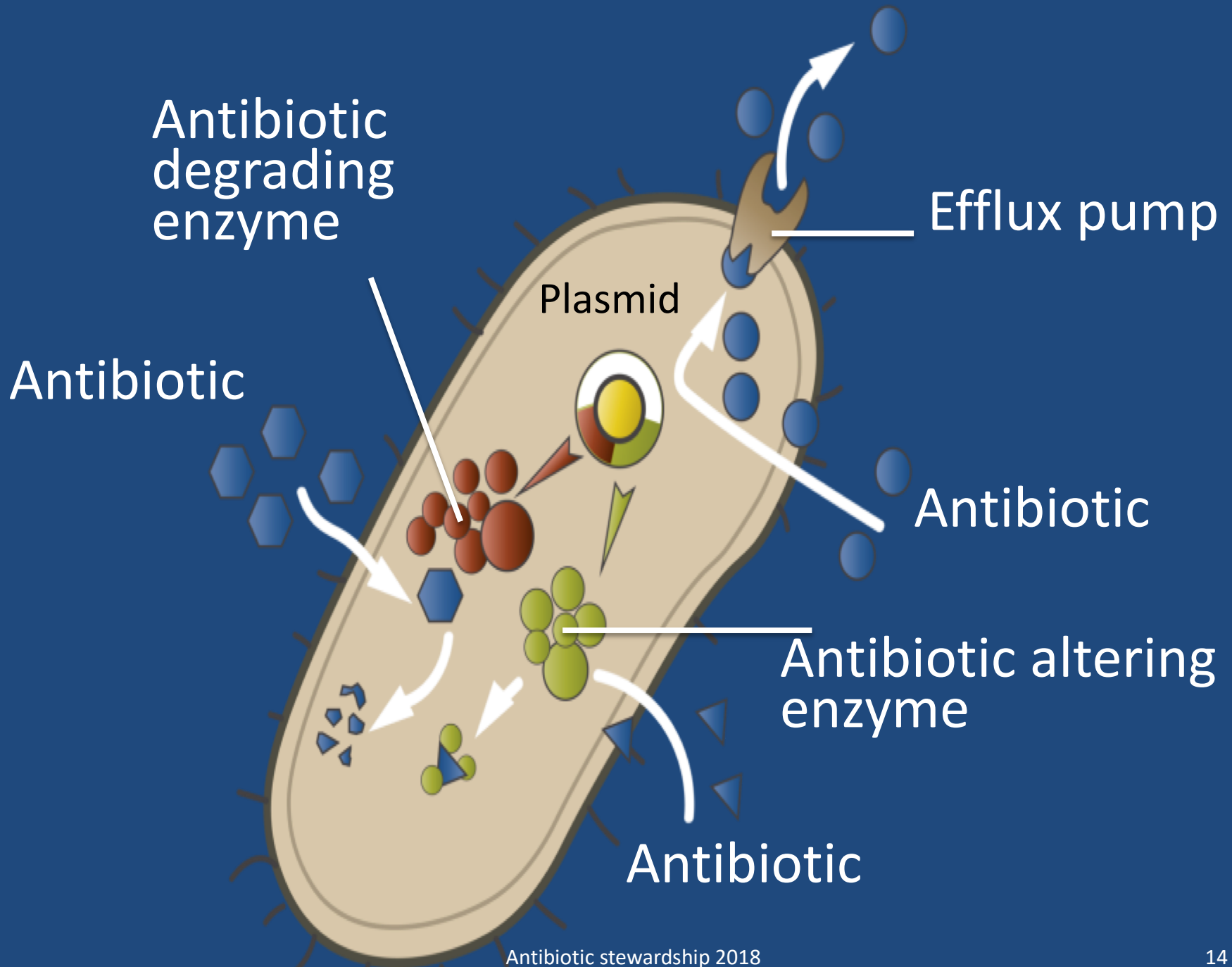
Antibiotic

No new antibiotics the last decades
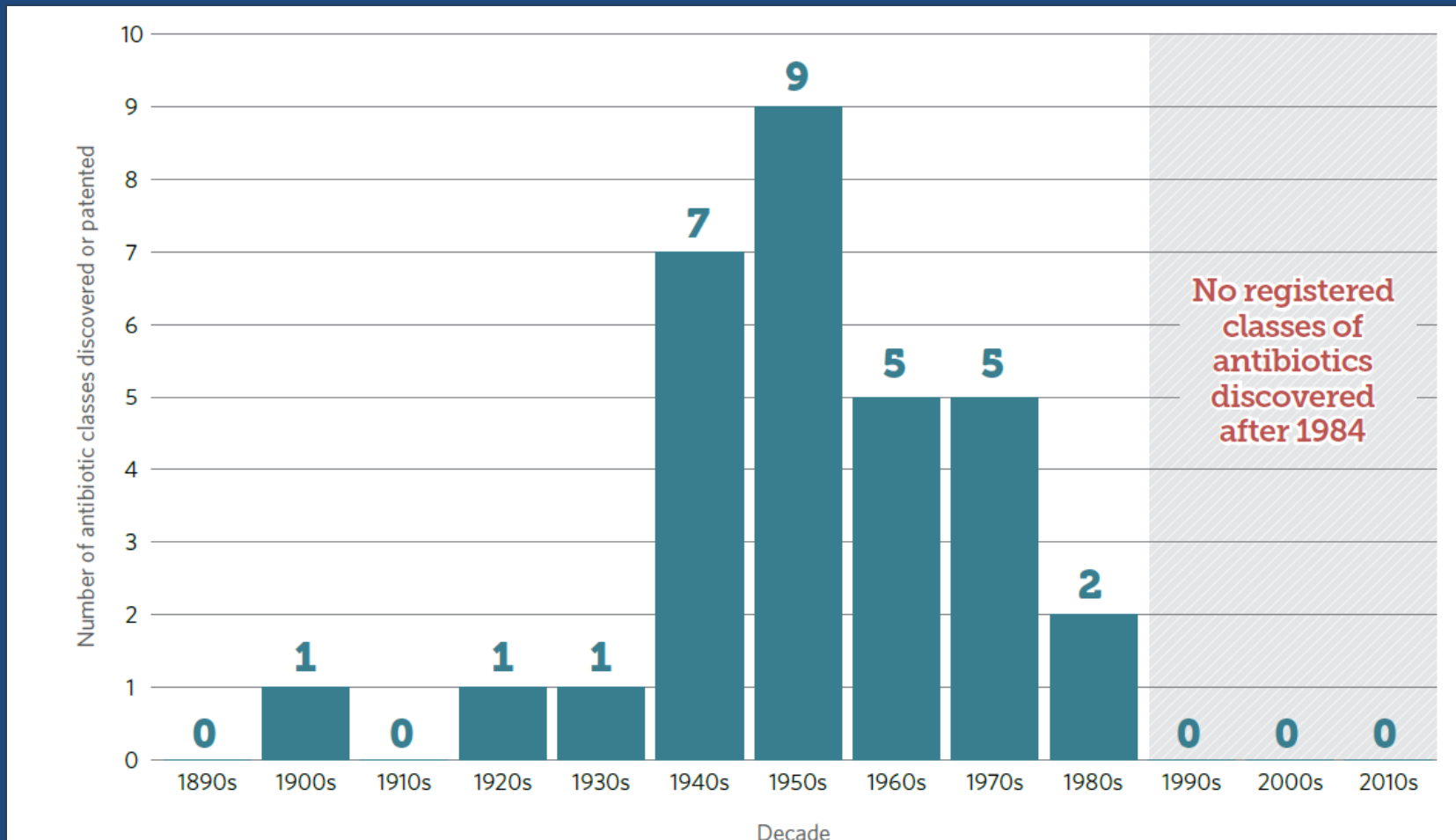
Deaths attributable to AMR every year compared to other major causes of death

AMR in 2050: 10 million
Cancer: 8.2 million
Tetanus: 60,000
Road traffic accidents: 1.2 million
AMR now: 700,000 (low estimate)
Cholera: 100,000–120,000
Measles: 130,000
Diabetes: 1.5 million
Diarrhoeal disease: 1.4 million
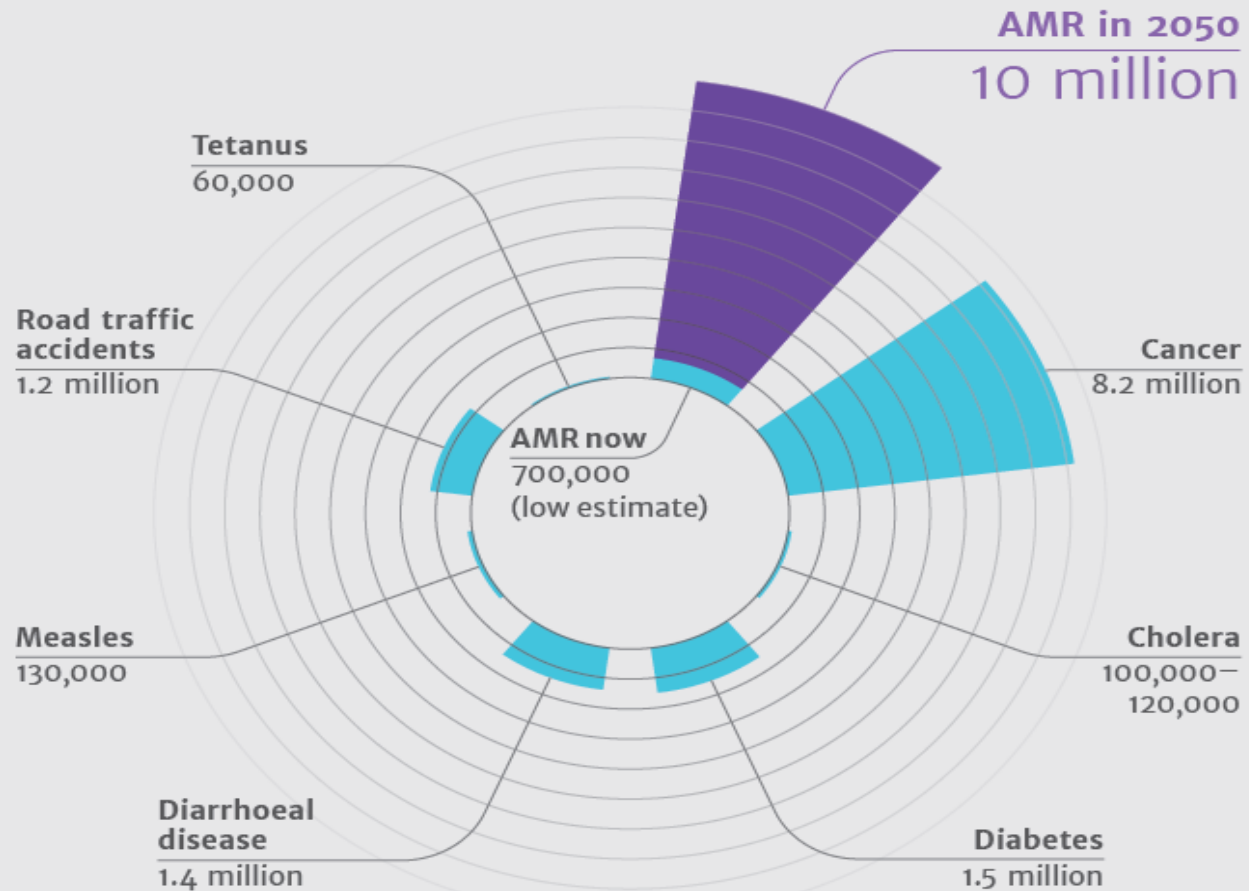
Is there ligth in the tunnel?

We can reduce antimicrobial resistance

- Reduce AB use

- Right drug, dose, and duration

- Making more accurate and rapid diagnoses

- Prohibit AB as growth promotors in husbandry

- Vaccinate

Antibiotic stewardship programs leads to reduction of

- Anibiotic use
- Antibiotic resistance
- Hospital stay
- Antibiotic associated diahorrea
  - Clostridium difficile
- Reduced **costs**

Core elements in antibiotic stewardshiop programs

- Easily available antibiotic guidelines
  – App

- Increase **compliance to guidelines**

- **Shortening** of duration of therapy

- Decrease use of broad-spectrum antibiotics

To avoid resistance you must finish the antibiotic course

- No, it is a myth

- It is an evidence free area

- The longer treatment, the more resistance

Duration of treatment (days) in hospitals
Gap between new knowledge and practice

	Guidelines	New evidence
Pneumonia	**7-14**	**3-5**
Ventilator associated Penumoniae (VAP)	**10-14**	**7-8**
Pyelonephritis (Renal infection)	**10-14**	**7**
Peritonitis (Severe abdominal inf.)	**7-10**	**4**
Exacerbation of chronic bronchitis	**7-10**	**<5**
Gram-neg. sepsis	**10-14**	**8**

Human medicine can decrease resistance and prolong life of current antibiotics

- Political/administrative **leadership** commitment
  - National and global action plans (one health approach)

- Sustainable interventions
  - Digital support systems
  - Physicians must be forced to comply

- More rapid and presice diagnostic tools

Improved use of antibiotics in a paediatric dept.
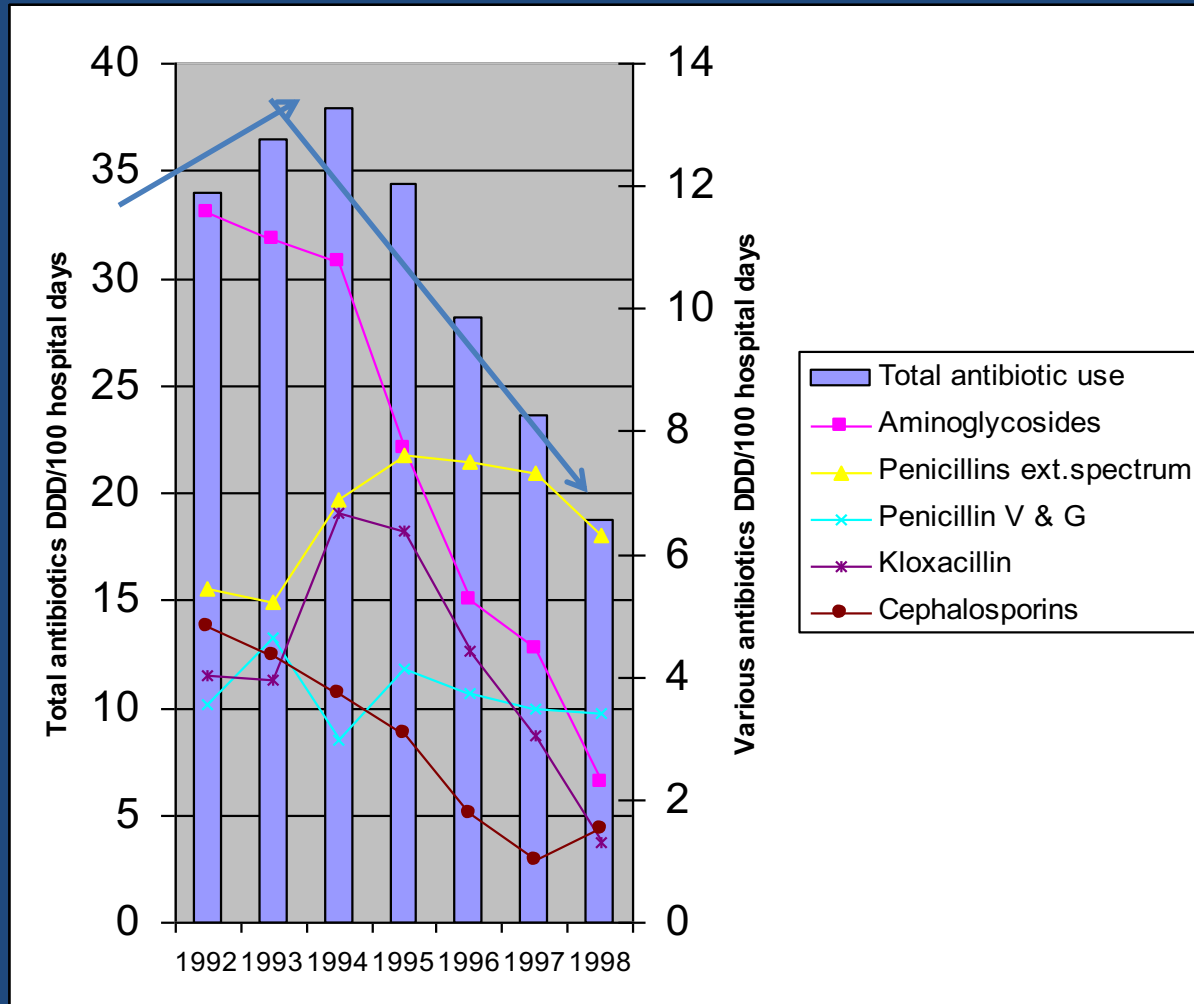
Effects of interventions are not sustainable

Antibiotic use in respiratory tract infections
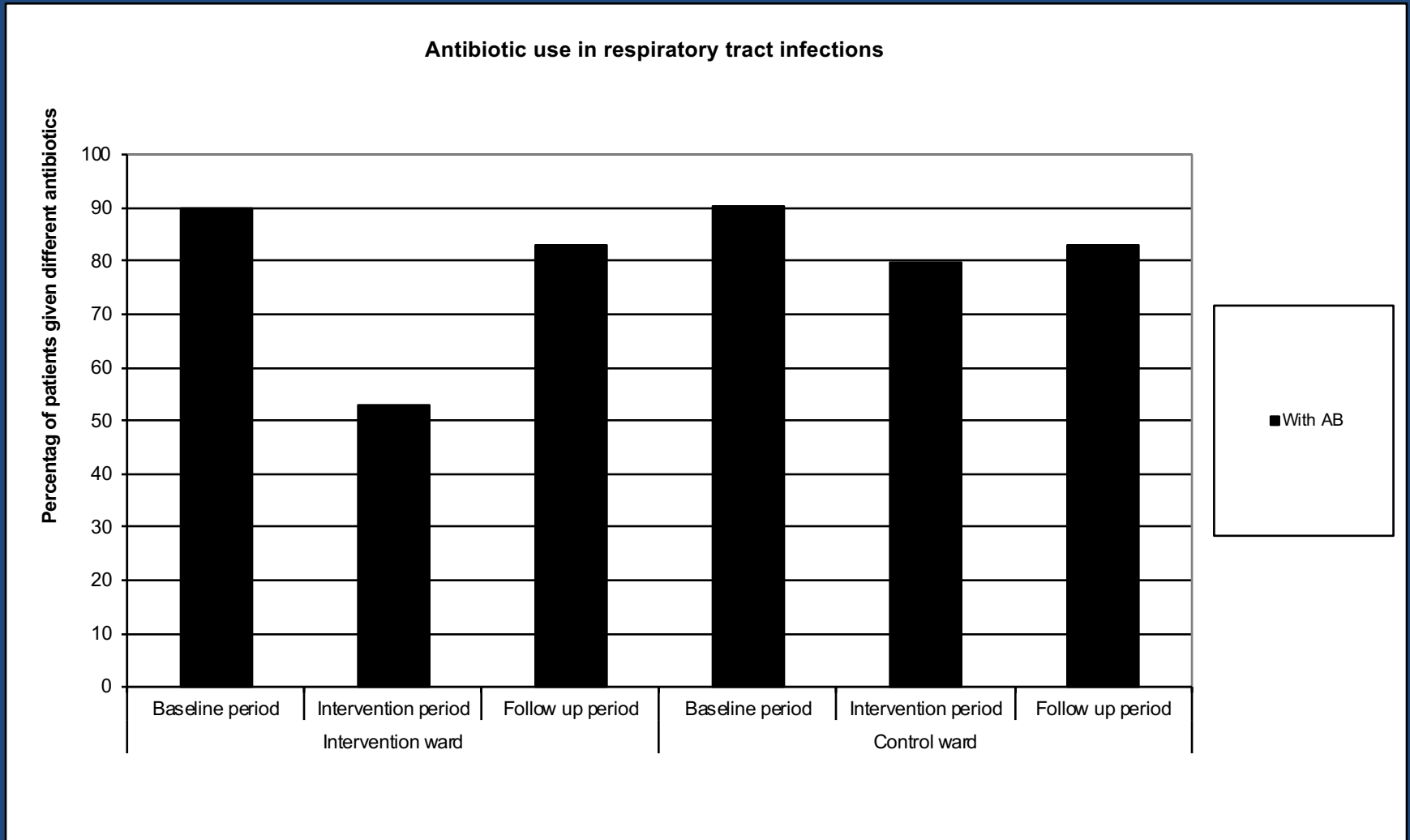
Norwegian action plan: 30 % reduction in AB use 2012-2020
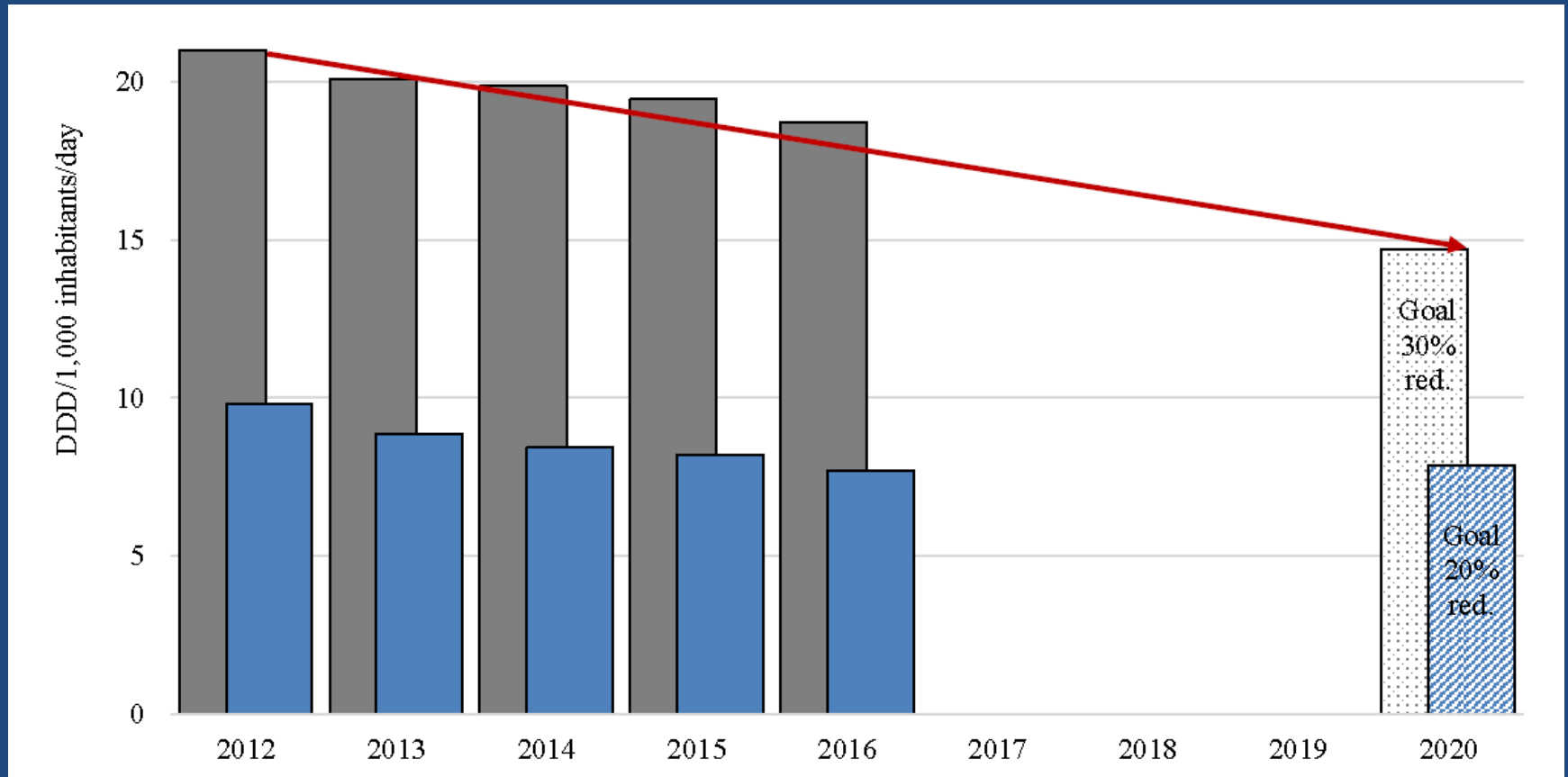
Variation in antibiotic use.
Respiratory tract infections Norway
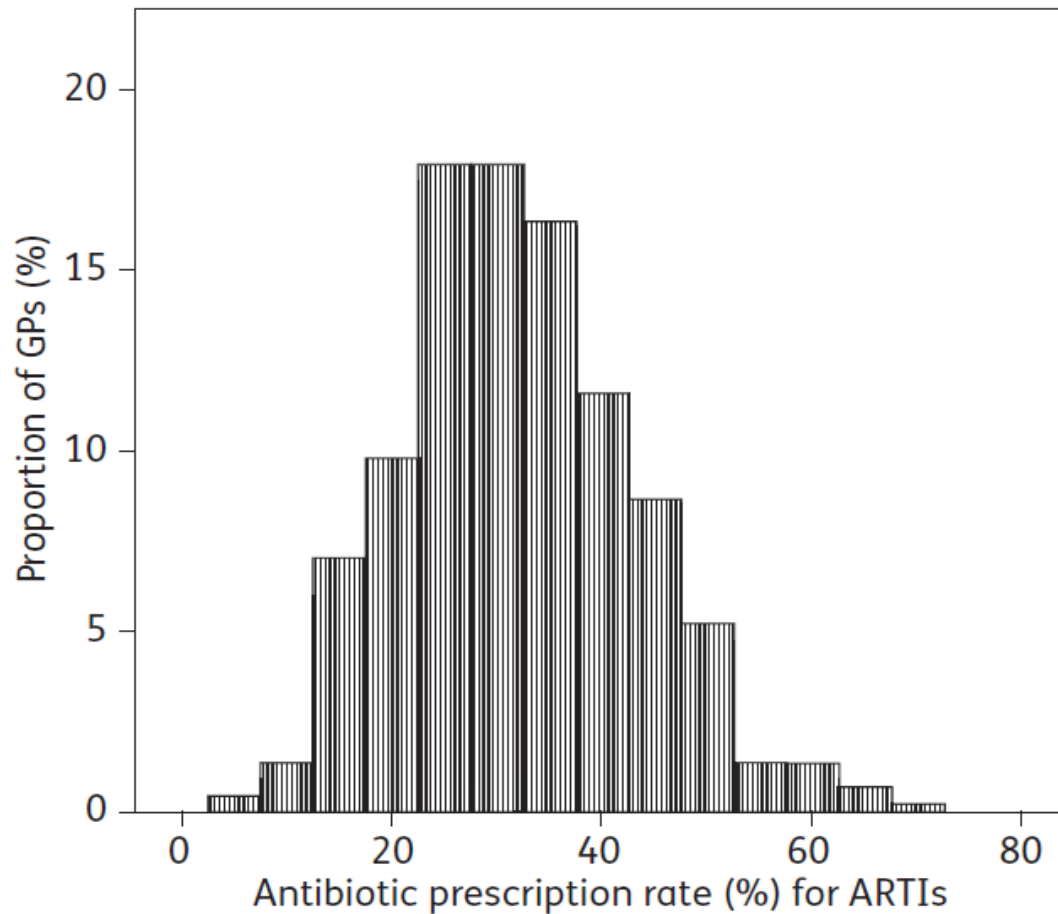
Figure 2. Distribution of 440 GPs' antibiotic prescription rates for ARTIs.

Take home message

- Rational antibiotic use lead to reduction of antimicrobial AMR and costs

- Profylactic AB use in animals must be prohibited

- Vaccination can reduce AMR

- It is a myth that finishing the antibiotic course prevent antibiotc resistance!

Thank you

|

Which intervention works?

- Education?
  - physcians, general population, school children
- Restrictions
- Academic detailing
- Audit and feed-back
- Digital systems with descison support
  - automatic stoporder

Revison of antibiotics after 48-72 h.

- > 85 % of bacteriological samples available

- Allows narrowing (de-escalation) of broad-spectrum therapy

- Leads to less resistance

Rational antibiotic use is

- Giving effective antibiotics with the most limited impact on the normal bacterial flora.

    – Choice of antibiotics

    – Dosage

    – Duration

MDR GNB		Events/patient-days			Incidence ratio (95% CI)
		Before	After		
Apisarnthanarak et al[18]	MDR *Pseudomonas aeruginosa*	13/2889	1/1324		0·08 (0·00–1·41)
Marra et al[31]	Imipenem-resistant *Acinetobacter baumannii*	23/8421	2/8066		0·09 (0·02–0·39)
Apisarnthanarak et al[18]	XDR *A baumannii*	33/2889	2/1324		0·13 (0·03–0·55)
Takesue et al[32]	Metallo-β-lactamase GNB	27/698794	6/635794		0·24 (0·10–0·59)
Cook and Gooch[37]	Carbapenem-resistant *P aeruginosa*	44/220474	13/261318		0·25 (0·13–0·46)
Peto et al[42]	MDR *P aeruginosa*	2/4280	1/4217		0·25 (0·01–5·63)
Takesue et al[32]	MDR GNB	39/698794	10/635794		0·28 (0·14–0·56)
Arda et al[36]	Meropenem-resistant *Acinetobacter* spp	28/285606	10/308852		0·33 (0·16–0·68)
Leverstein-van Hall et al[45]	MDR Enterobacteriaceae	9/19142	4/23583		0·36 (0·11–1·17)
Yeo et al[23]	Carbapenem-resistant *P aeruginosa*	17/20469	8/21798		0·44 (0·19–1·02)
Arda et al[36]	Meropenem-resistant *P aeruginosa*	8/285606	4/308852		0·46 (0·14–1·54)
Marra et al[31]	Imipenem-resistant *Klebsiella pneumoniae*	6/8421	3/8066		0·52 (0·13–2·09)
Marra et al[31]	Imipenem-resistant *P aeruginosa*	15/8421	8/8066		0·56 (0·24–1·31)
Arda et al[36]	Meropenem-resistant *A baumannii*	45/285606	29/308852		0·60 (0·37–0·95)
Meyer et al[34]	Imipenem-resistant *P aeruginosa*	34/13502	33/21420		0·61 (0·38–0·99)
Yeo et al[23]	Carbapenem-resistant *A baumannii*	10/20469	9/21798		0·85 (0·34–2·08)
Zou et al[20]	Meropenem-resistant *P aeruginosa*	185/834560	172/883500		0·88 (0·71–1·08)
Niwa et al[25]	Imipenem-resistant *P aeruginosa*	11/128146	15/113873		1·53 (0·70–3·34)
Aubert et al[43]	Imipenem-resistant *P aeruginosa*	49/5100	44/2548		1·80 (1·20–2·70)
Overall					**0·49 (0·35–0·68)**
I^2=76·2%, p=0·000					

Antibiotic stewardship programme effective ← | → Antibiotic stewardship programme not effective
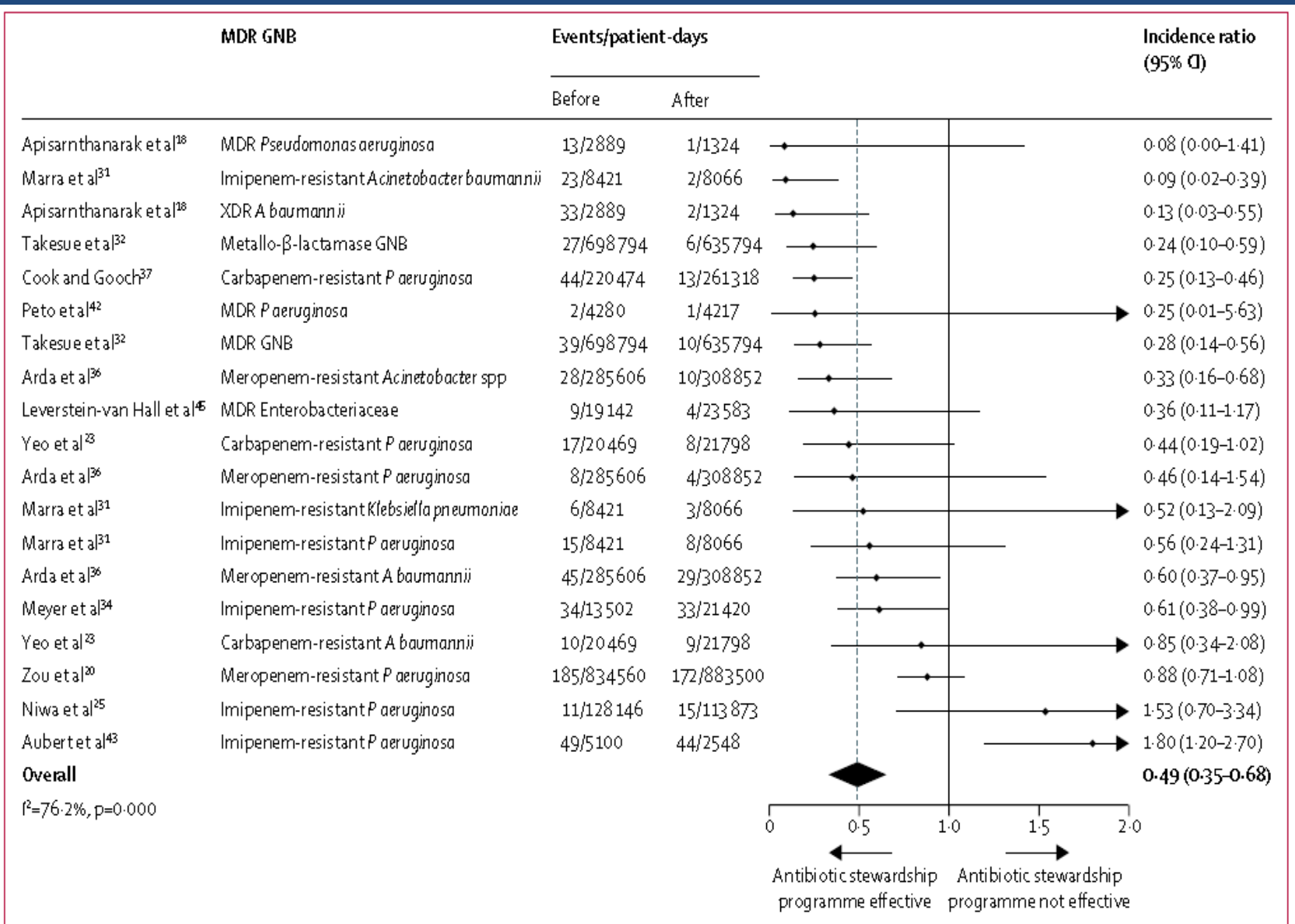
Figure 2: Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of MDR GNB

GNB=Gram-negative bacteria. MDR=multidrug-resistant. XDR=extensively drug-resistant.