Antimicrobial resistance
can affect **anyone**, at any **age**,
in any **country**

#AntimicrobialResistance

World Health
Organization

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DEPARTMENT OF INTERNAL MEDICINE, REPRODUCTION AND POPULATION MEDICINE
VETERINARY EPIDEMIOLOGY

Antibioticumgebruik en resistentie bij dier en mens

Prof. Jeroen Dewulf

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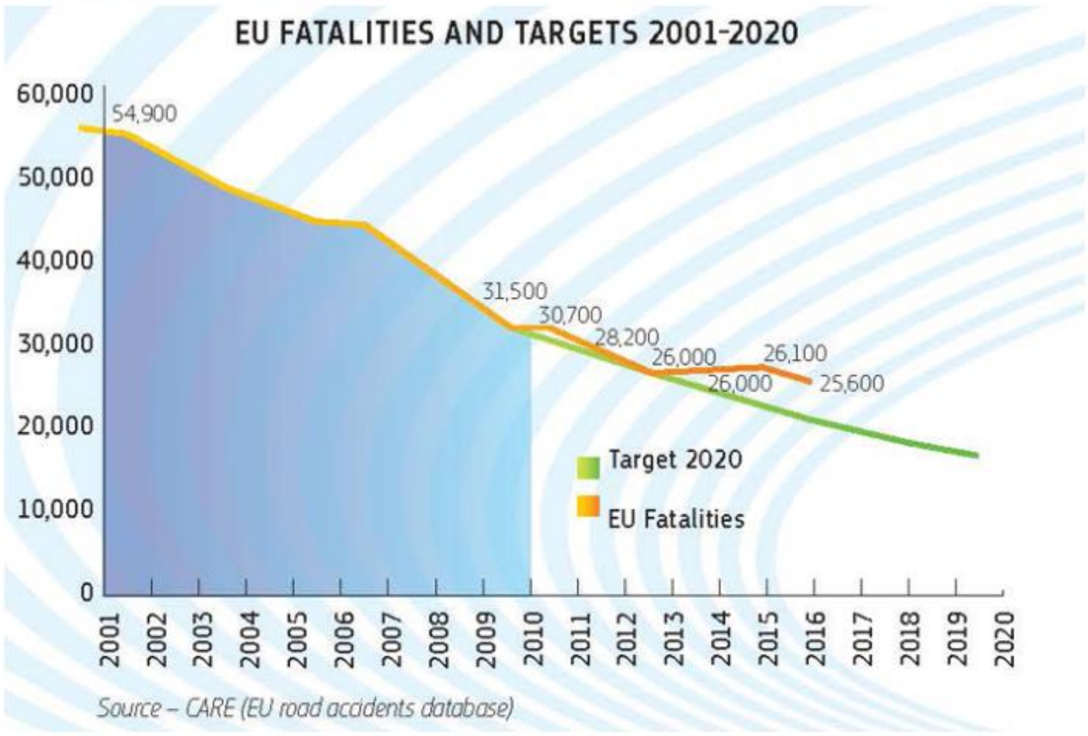
Hoe groot is het probleem?

In het verkeer sterven jaarlijks +/- 25.000 personen in Europa

Hoeveel mensen sterven er jaarlijks door antibioticumresistentie?

1. +/- 13.000
2. +/- 33.000
3. +/- 53.000

Road fatalities in the EU since 2001



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European Centre for Disease Prevention and Control
An agency of the European Union

All topics: A to Z | News & events | Publications & data | Tools | About us

Home > News & events > 33000 people die every year due to infections with antibiotic-resistant bacteria

News & events

33000 people die every year due to infections with antibiotic-resistant bacteria

news story
6 Nov 2018

An ECDC study estimates the burden of five types of infections caused by antibiotic-resistant bacteria of public health concern in the European Union and in the European Economic Area (EU/EEA).

The burden of disease is measured in number of cases, attributable deaths and disability-adjusted life years (DALYs). These estimates are based on data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) from 2015.

Our finding of 170 DALYs per 100 000 population is similar to the combined burden of three major infectious diseases (influenza, tuberculosis, and HIV), which was 183 DALYs per 100 000 population.[17]

Cassini et al., Lancet Infectious Diseases 2018

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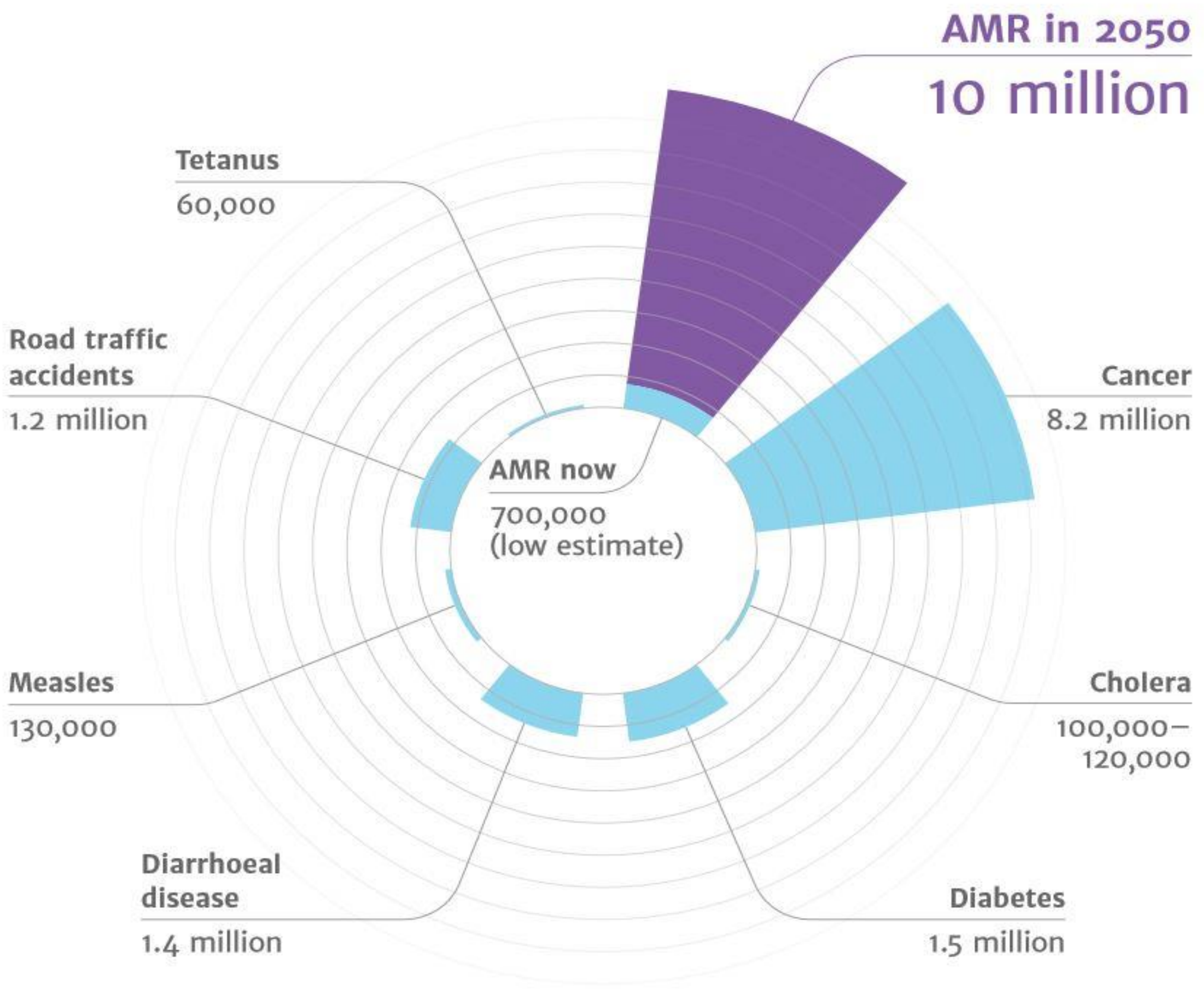

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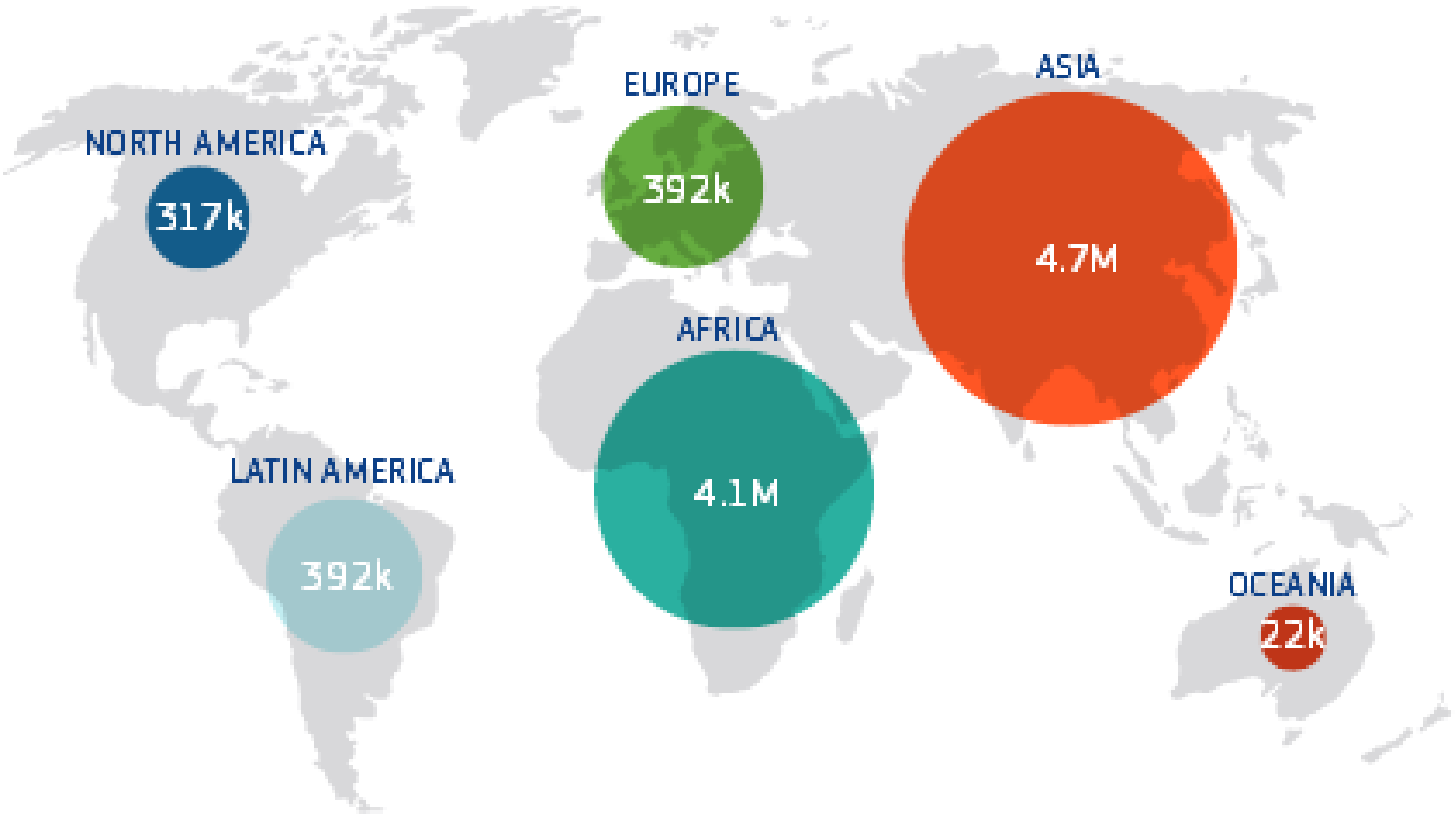
INDIEN WE NIETS DOEN Naar schatting 10 miljoen sterftegevallen tegen 2050 te wijten aan infectie met resistente bacteriën



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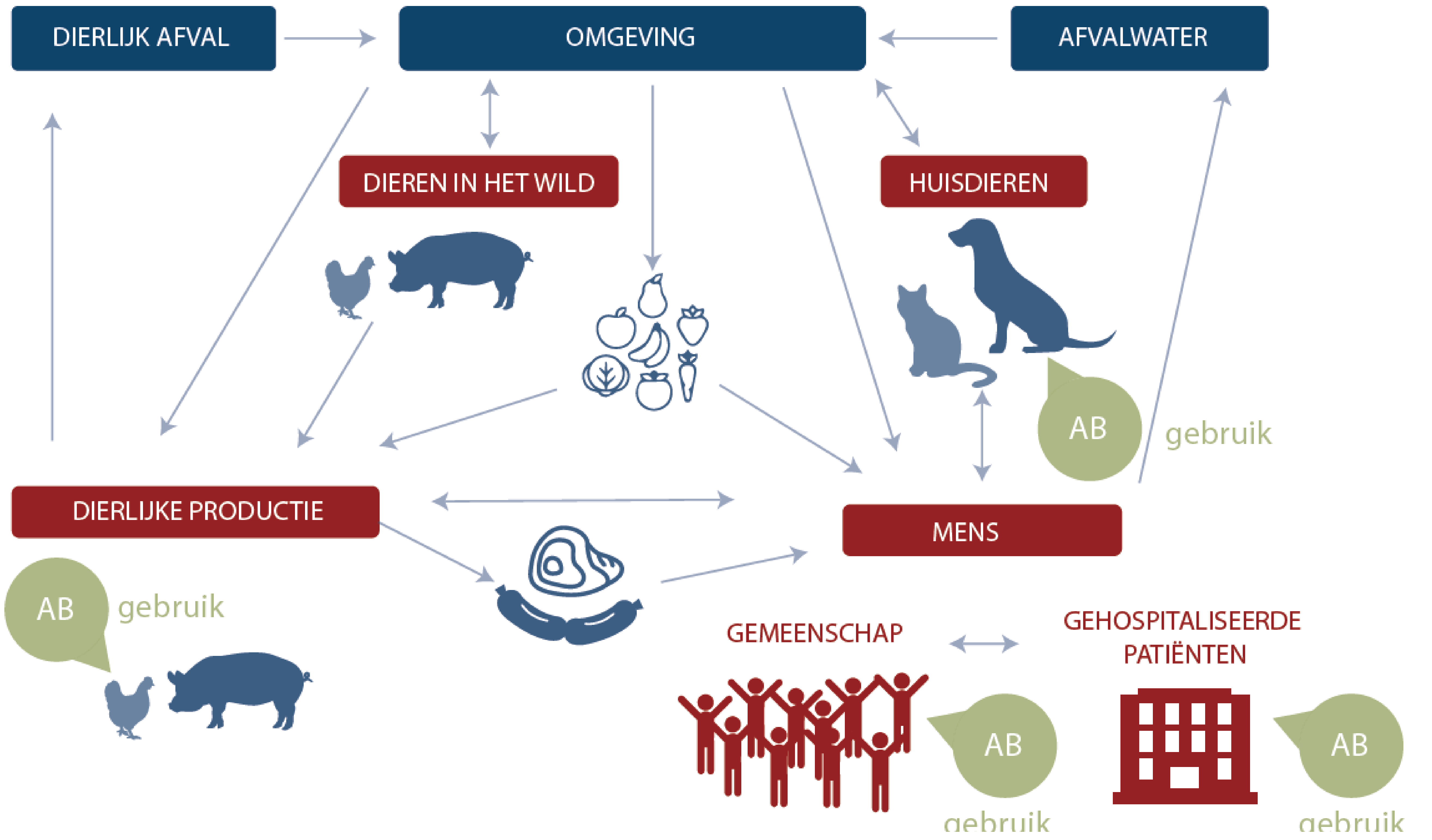
INDIEN WE NIETS DOEN Naar schatting 10 miljoen sterftegevallen tegen 2050 te wijten aan infectie met resistente bacteriën

One World, One health



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Welk % van het ABR bij de mens is een gevolg van AB gebruik bij dieren?

1. <10%
2. 10-25%
3. 25-50%
4. >50%

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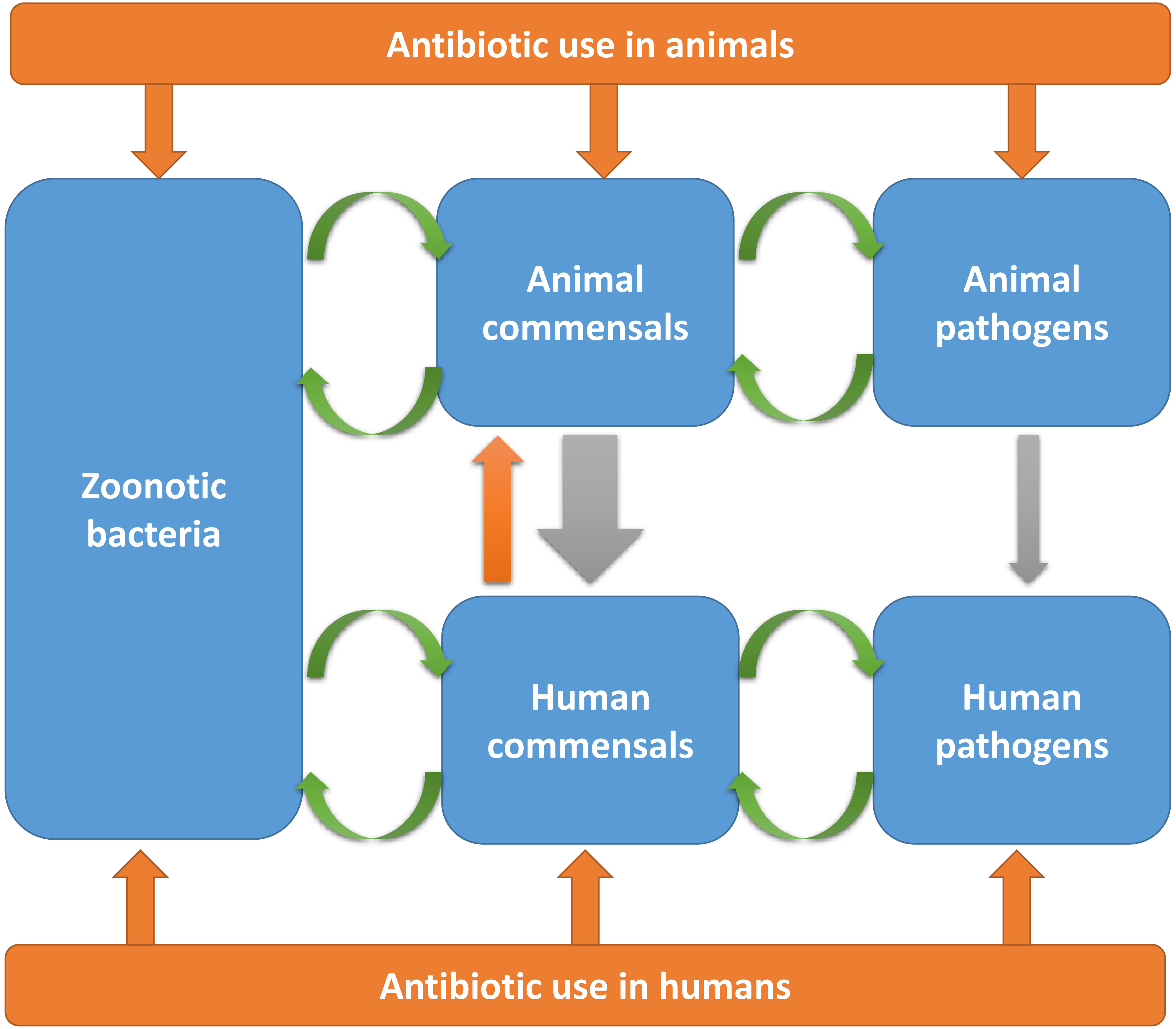

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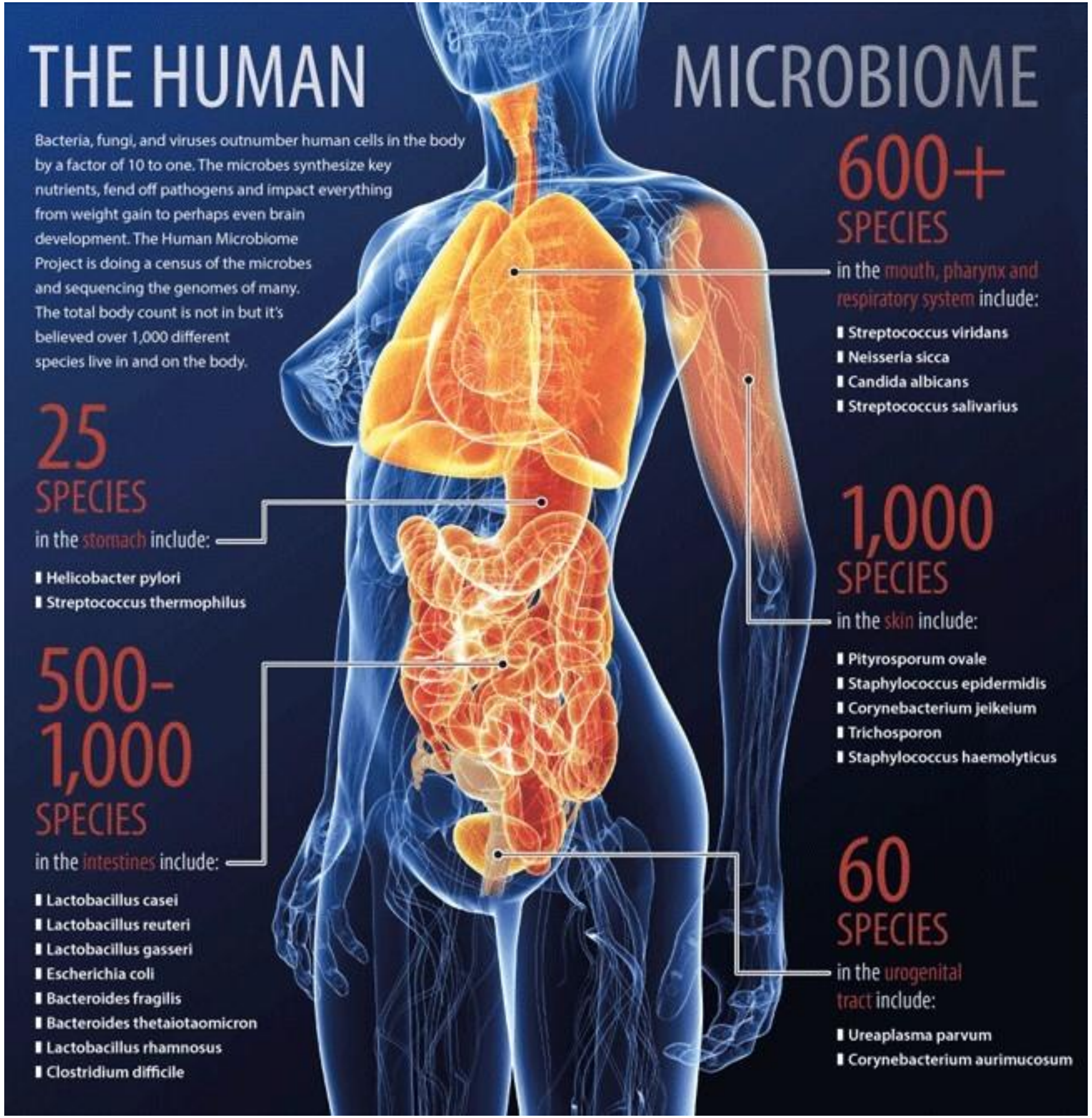

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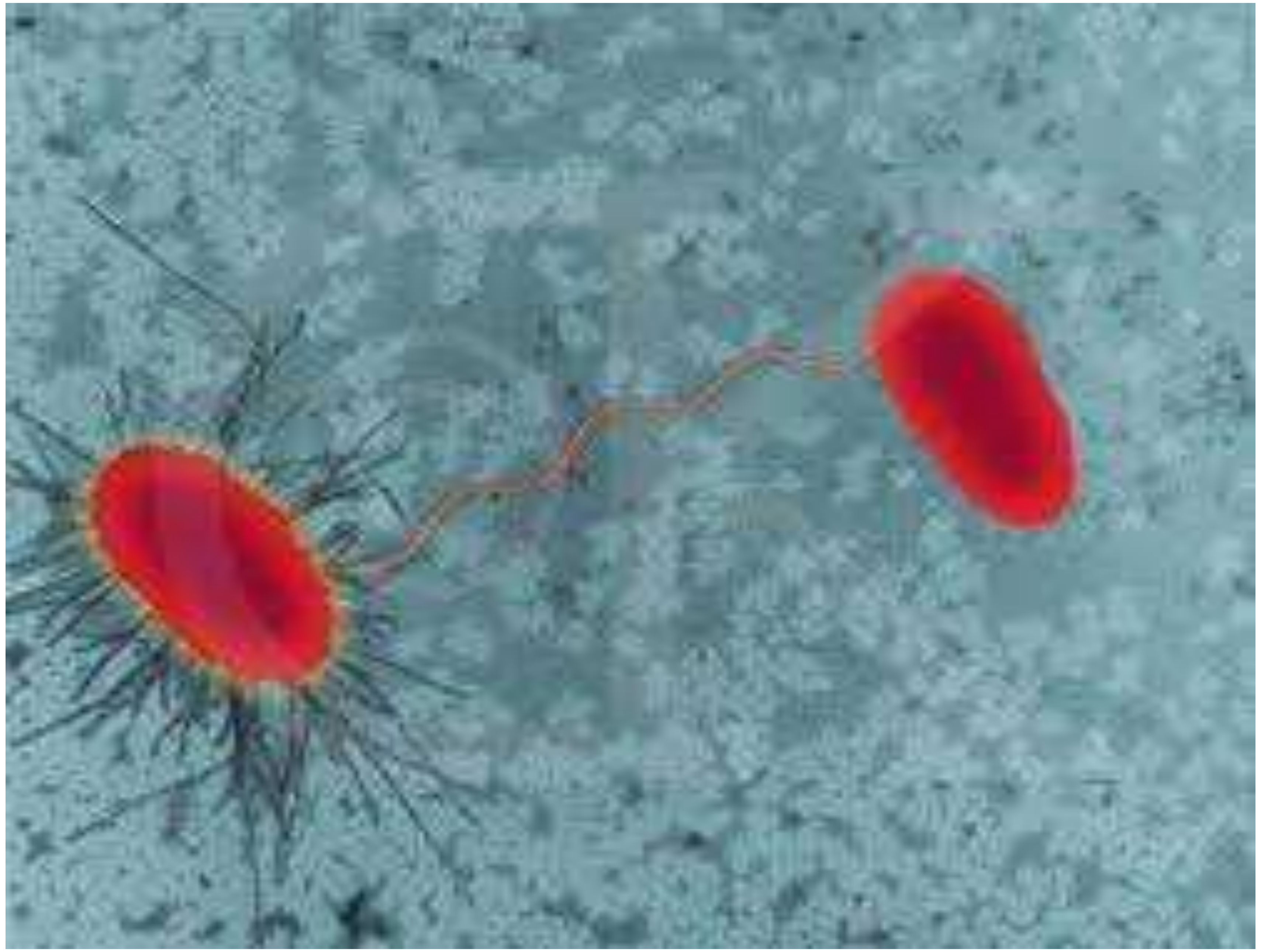
Bacteria have sex.....



With or without antibiotics

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49,7% **47,3%** **21,8%**

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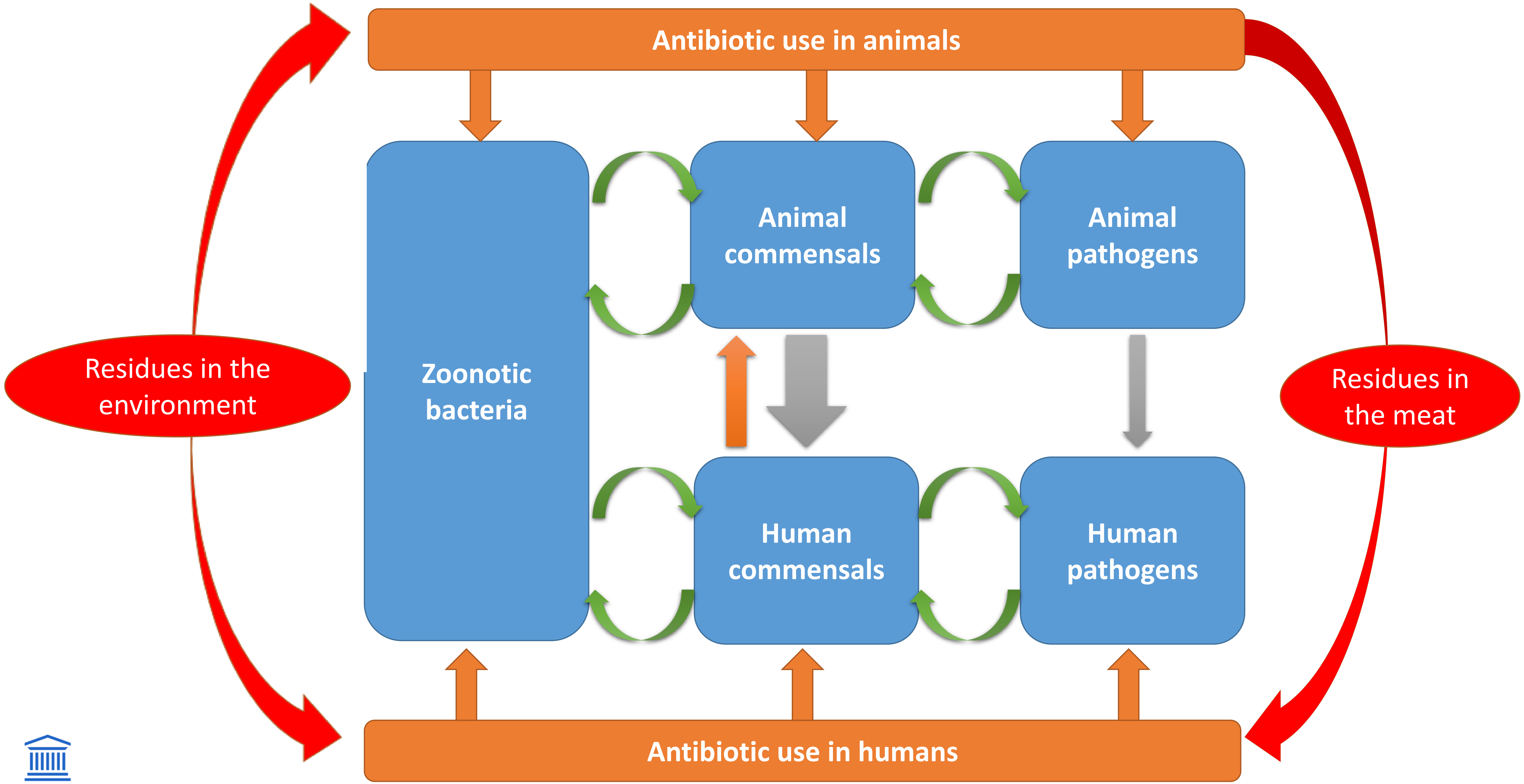
Van Cleven et al., 2018



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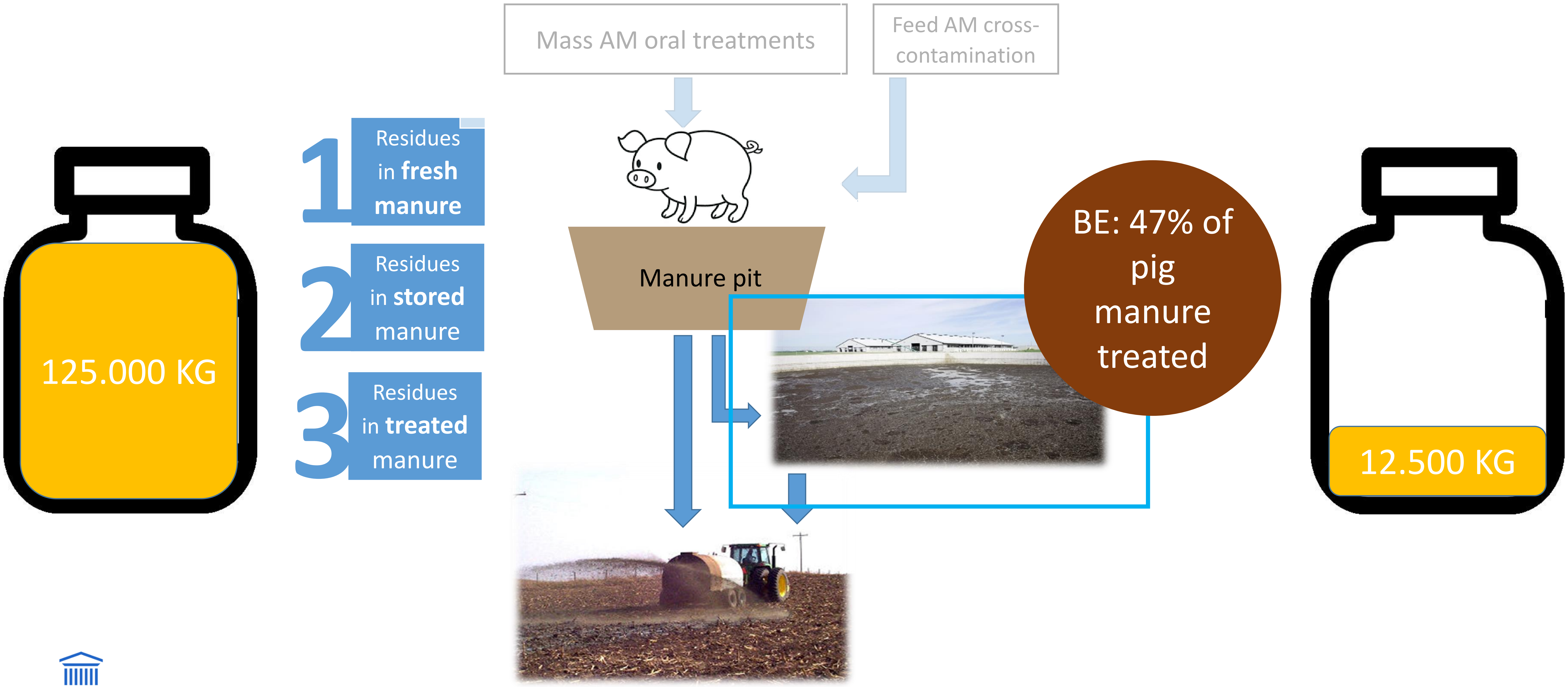

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Filippitzi et al., Chemosphere , 2019

Transmission of antimicrobial resistance from animal-human: Literature data

Do Human Extraintestinal *Escherichia coli* Infections Resistant to Expanded-Spectrum Cephalosporins Originate From Food-Producing Animals? A Systematic Review

Benjamin Lazarus,[1] David L. Paterson,[1] Joanne L. Mollinger,[2] and Benjamin A. Rogers[1,3]

[1]The University of Queensland, UQ Centre for Clinical Research, Royal Brisbane and Women's Hospital, Herston, [2]Biosecurity Sciences Laboratory, Biosecurity Queensland, Department of Agriculture, Fisheries and Forestry, Coopers Plains, Queensland, and [3]Monash Infectious Diseases, Monash Health, Clayton, Victoria, Australia

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To find out whether food-producing animals (FPAs) are a source of extraintestinal expanded-spectrum cephalosporin-resistant *Escherichia coli* (ESCR-EC) infections in humans, Medline, Embase, and the Cochrane Database of Systematic Reviews were systematically reviewed. Thirty-four original, peer-reviewed publications were identified for inclusion. Six molecular epidemiology studies supported the transfer of resistance via whole bacterium transmission (WBT), which was best characterized among poultry in the Netherlands. Thirteen molecular epidemiology studies supported transmission of resistance via mobile genetic elements, which demonstrated greater diversity of geography and host FPA. Seventeen molecular epidemiology studies did not support WBT and two did not support mobile genetic element–mediated transmission. Four observational epidemiology studies were consistent with zoonotic transmission. Overall, there is evidence that a proportion of human extraintestinal ESCR-EC infections originate from FPAs. Poultry, in particular, is probably a source, but the quantitative and geographical extent of the problem is unclear and requires further investigation.

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Food Safety, 2015

Wat houdt het grootste risico in voor de mens (voor overdracht van resistentie van dieren)?

1. Eten van dierlijke producten (vlees, vis, melk, eieren,…)?
2. Direct contact met (huis)dieren
3. Contact met het milieu / omgeving

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Schrauwen *et al. Antimicrobial Resistance and Infection Control* (2017) 6:83
DOI 10.1186/s13756-017-0242-8

Antimicrobial Resistance
and Infection Control

LETTER TO THE EDITOR

Open Access

High prevalence of the *mcr-1* gene in retail chicken meat in the Netherlands in 2015

Eefje J. A. Schrauwen[1,2*], Pepijn Huizinga[1,3], Nick van Spreuwel[1,2], Carlo Verhulst[1], Marjolein F. Q. Kluytmans-van den Bergh[1,4,5] and Jan A. J. W. Kluytmans[1,5,6]

ORIGINAL ARTICLE | EPIDEMIOLOGY

Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains

M. A. Leverstein-van Hall[1,2], C. M. Dierikx[3], J. Cohen Stuart[1], G. M. Voets[1], M. P. van den Munckhof[1], A. van Essen-Zandbergen[3], T. Platteel[1,4], A. C. Fluit[1], N. van de Sande-Bruinsma[2], J. Scharinga[1], M. J. M. Bonten[1,5] and D. J. Mevius[3,6]; on behalf of the national ESBL surveillance group*

1) *Department of Medical Microbiology, University Medical Centre Utrecht, Utrecht,* 2) *Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven,* 3) *Department of Bacteriology and TSEs, Central Veterinary Institute of Wageningen UR, Lelystad,* 4) *SALTRO, Primary Health Care Laboratory, Utrecht,* 5) *Julius Centre for Health Sciences and Primary Care, University Medical Centre, Utrecht and* 6) *Department of Infectious Diseases & Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands*

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Do vegetarians less frequently carry ESBL/pAmpC-producing *Escherichia coli/Klebsiella pneumoniae* compared with non-vegetarians? FREE

Anouk P Meijs, Esther F Gijsbers, Paul D Hengeveld, Christiaan Veenman,
Annika M van Roon, Angela H A M van
Engeline van Duijkeren, Cindy M Dieri

Journal of Antimicrobial Chemotherap
550–558, https://doi.org/10.1093/jac/
Published: 25 November 2019 **Art**

Prevalence of ESBL-E/K carriage was 8.0% in vegetarians (63/785; 95% CI 6.3–10.1), 6.9% in pescatarians (27/392; 95% CI 4.8–9.8) and 3.8% in non-vegetarians (14/365; 95% CI 2.3–6.3). Multivariable analysis showed an OR for ESBL-E/K carriage of 2.2 for vegetarians (95% CI 1.2–4.0) and 1.6 for pescatarians (95% CI 0.8–3.2) compared with non-vegetarians. The predominant MLST was *E. coli* ST131 and the most common ESBL genes were $\textit{bla}_{\text{CTX-M-15}}$, $\textit{bla}_{\text{CTX-M-27}}$, $\textit{bla}_{\text{CTX-M-14}}$ and $\textit{bla}_{\text{CTX-M-1}}$ in all diet groups. Independent risk factors for ESBL-E/K carriage were travel to Africa/Latin America/Asia (OR 4.6; 95% CI 2.8–7.7) in the past 6 months and rarely/never washing hands before food preparation (OR 2.5; 95% CI 1.2–5.0).

Conclusions

Vegetarians and pescatarians did not have a lower risk of ESBL-E/K carriage compared with non-vegetarians, indicating that eating meat is not an important risk factor for ESBL-E/K carriage.

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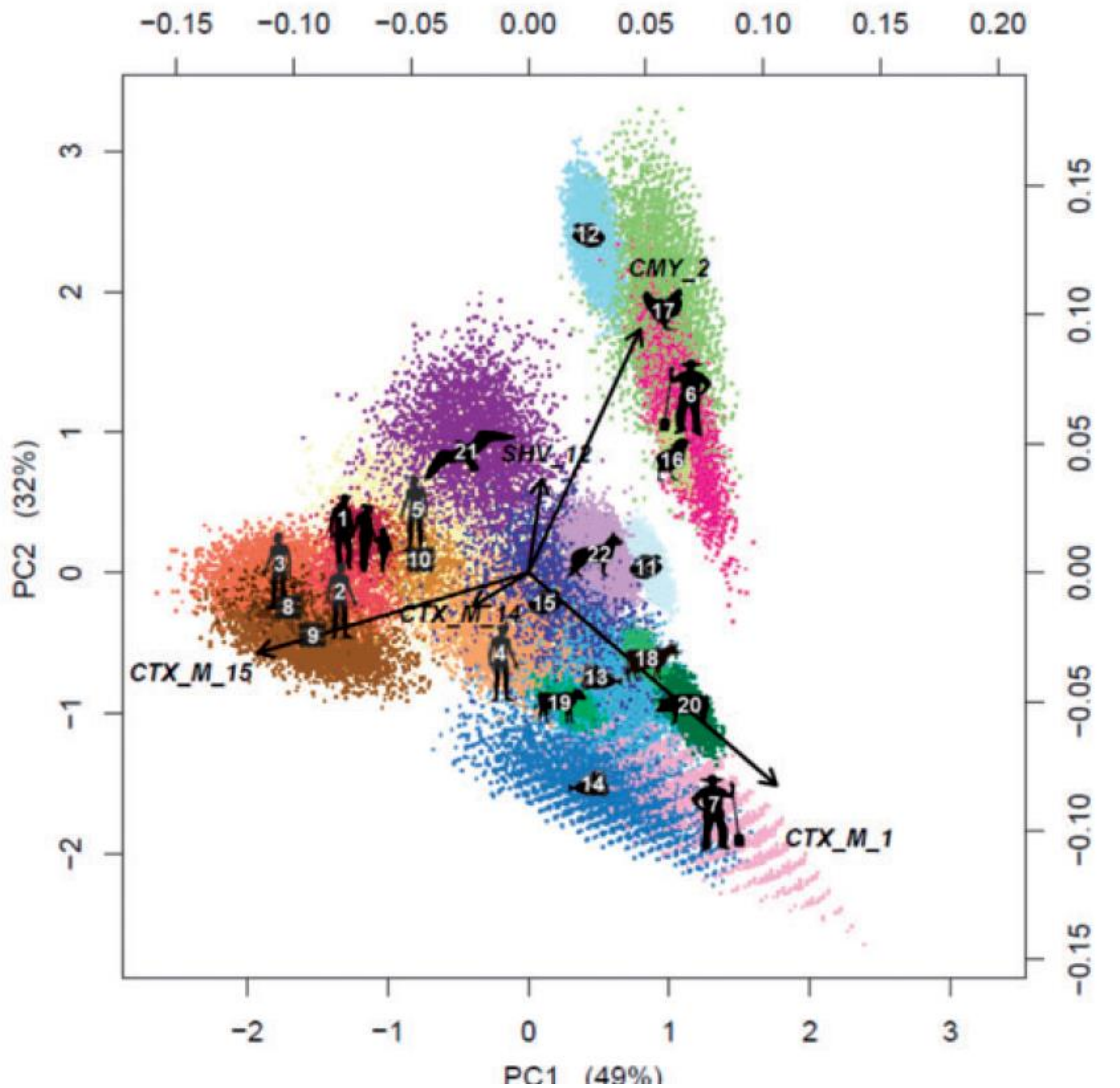
Colour legend for PCA, reservoir numbers in panels, type of reservoir (human [H], environmental [E], food [F] and animal [A])

- 1 H-general population
- 2 H-clinical UTIs
- 3 H-clinical blood
- 4 H-clinical faecal
- 5 H-clinical respiratory, wounds, other
- 6 H-broiler farming community
- 7 H-pig farming community
- 8 E-wastewater
- 9 E-surface water non-recreational
- 10 E-surface water recreational
- 11 F-chicken meat at retail
- 12 F-chicken meat at slaughterhouse
- 13 F-beef at retail
- 14 F-veal calf meat at slaughterhouse
- 15 F-turkey meat at retail
- 16 A-broilers
- 17 A-laying hens
- 18 A-dairy cattle
- 19 A-veal calves
- 20 A-pigs
- 21 A-wild birds
- 22 A-dogs

(c) PCA on ESBL/AmpC gene frequencies
PCs, principal components (% variance explained)



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Alejandro Dorado-Garcıa, 2017, JAC

Waar komt het probleem vandaan?

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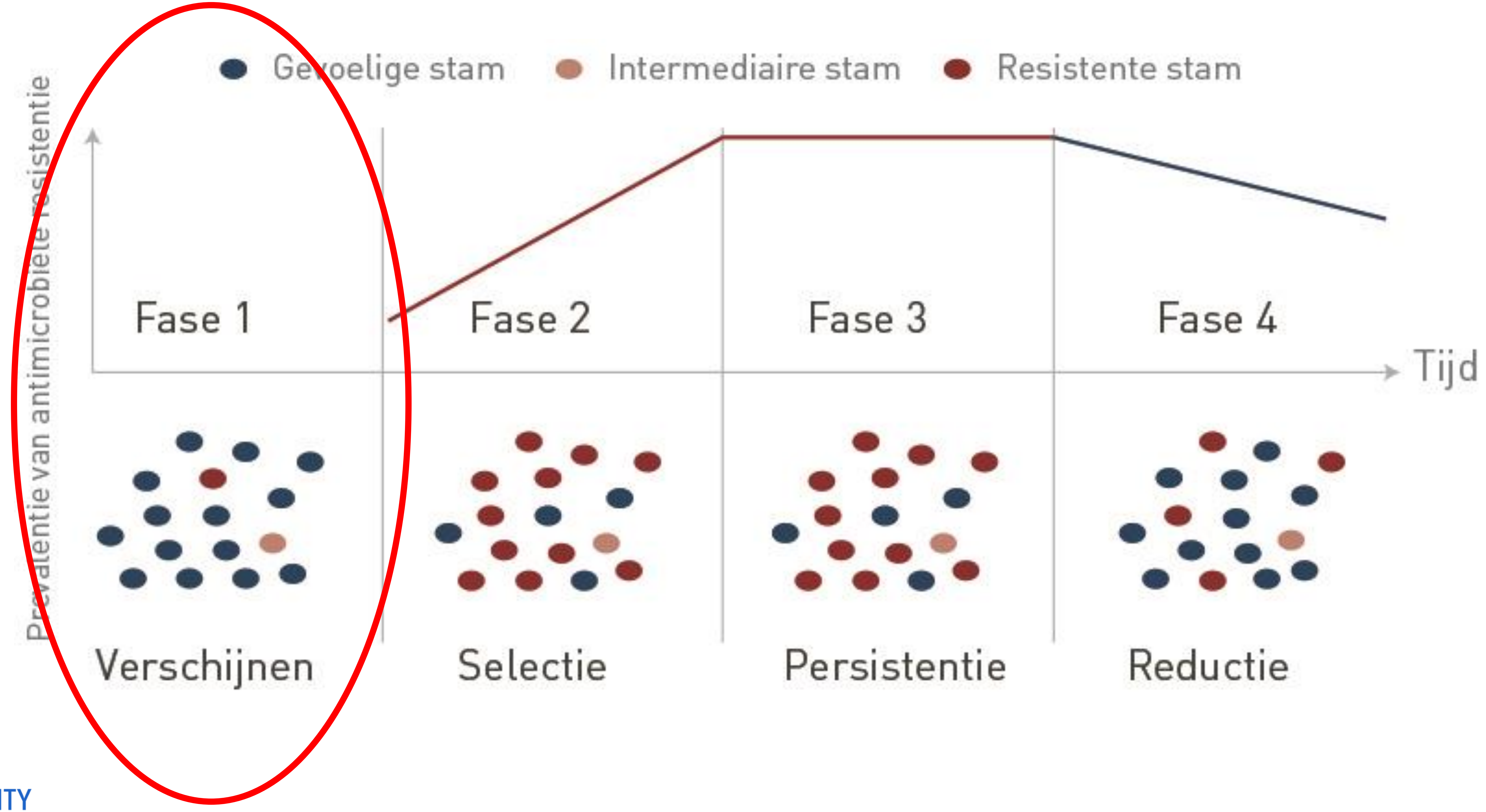
Waar komt het probleem vandaan?



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LETTER

doi:10.1038/nature10388

Antibiotic resistance is ancient

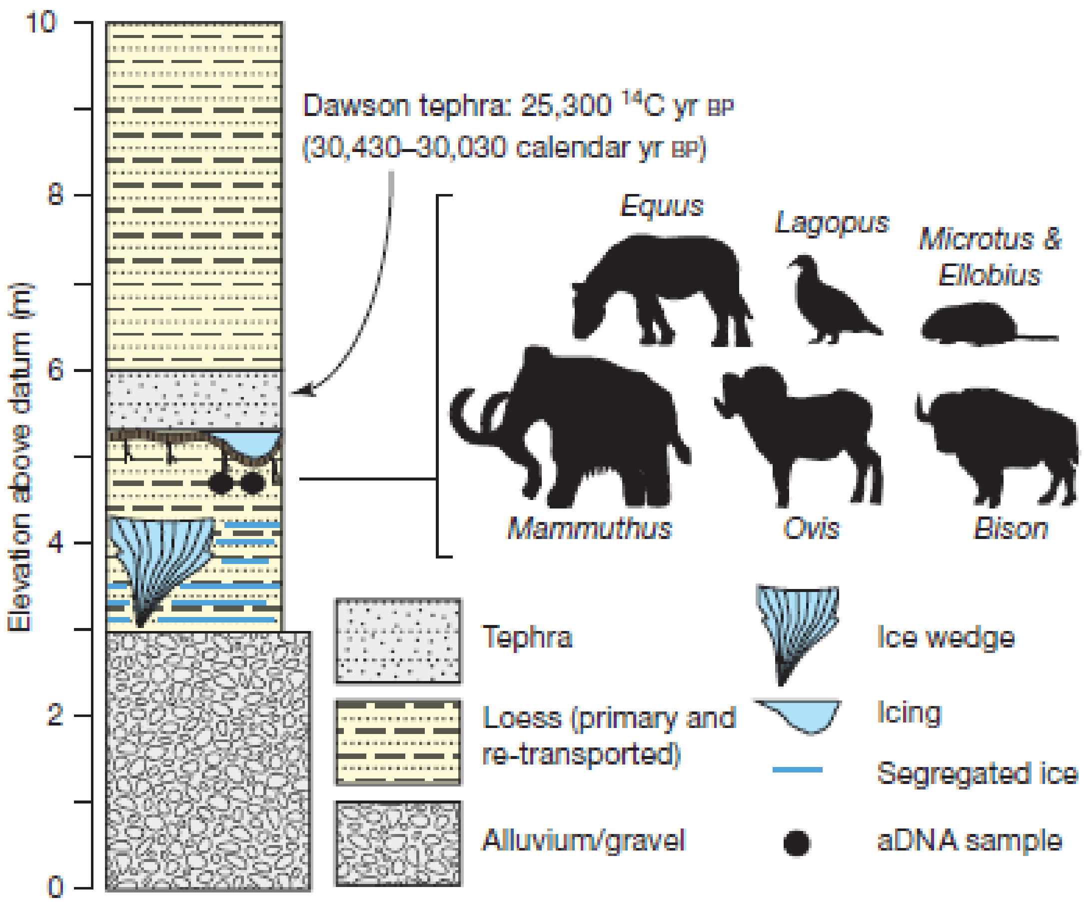
Vanessa M. D'Costa[1,2]*, Christine E. King[3,4]*, Lindsay Kalan[1,2], Mariya Morar[1,2], Wilson W. L. Sung[4], Carsten Schwarz[3], Duane Froese[5], Grant Zazula[6], Fabrice Calmels[5], Regis Debruyne[7], G. Brian Golding[4], Hendrik N. Poinar[1,3,4] & Gerard D. Wright[1,2]

The discovery of antibiotics more than 70 years ago initiated a period of drug innovation and implementation in human and animal health and agriculture. These discoveries were tempered in all cases by the emergence of resistant microbes[1,2]. This history has been interpreted to mean that antibiotic resistance in pathogenic bacteria is a modern phenomenon; this view is reinforced by the fact that collections of microbes that predate the antibiotic era are highly susceptible to antibiotics[3]. Here we report targeted metagenomic analyses of rigorously authenticated ancient DNA from 30,000-year-old Beringian permafrost sediments and the identification of a highly diverse collection of genes encoding resistance to β-lactam, tetracycline and glycopeptide antibiotics. Structure and function studies on the complete vancomycin resistance element VanA confirmed its similarity to modern variants. These results show conclusively that antibiotic resistance is a natural phenomenon that predates the modern selective pressure of clinical antibiotic use.

Recent studies of modern environmental and human commensal microbial genomes have a much larger concentration of antibiotic resistance genes than has been previously recognized[4–6]. In addition, metagenomic studies have revealed diverse homologues of known resistance genes broadly distributed across environmental locales. This widespread dissemination of antibiotic resistance elements is inconsistent with a hypothesis of contemporary emergence and instead suggests a richer natural history of resistance[2]. Indeed, estimates of the origin of natural product antibiotics range from 2 Gyr to 40 Myr ago[7,8], suggesting that resistance should be similarly

with high concentrations of *Escherichia coli* harbouring the *gfp* (green fluorescent protein) gene from *Aequorea victoria* (Supplementary Information).

After fracturing of the samples (Supplementary Fig. 3), total DNA was extracted from a series of five subsamples taken along the radius of each core (Supplementary Information). Quantitative polymerase



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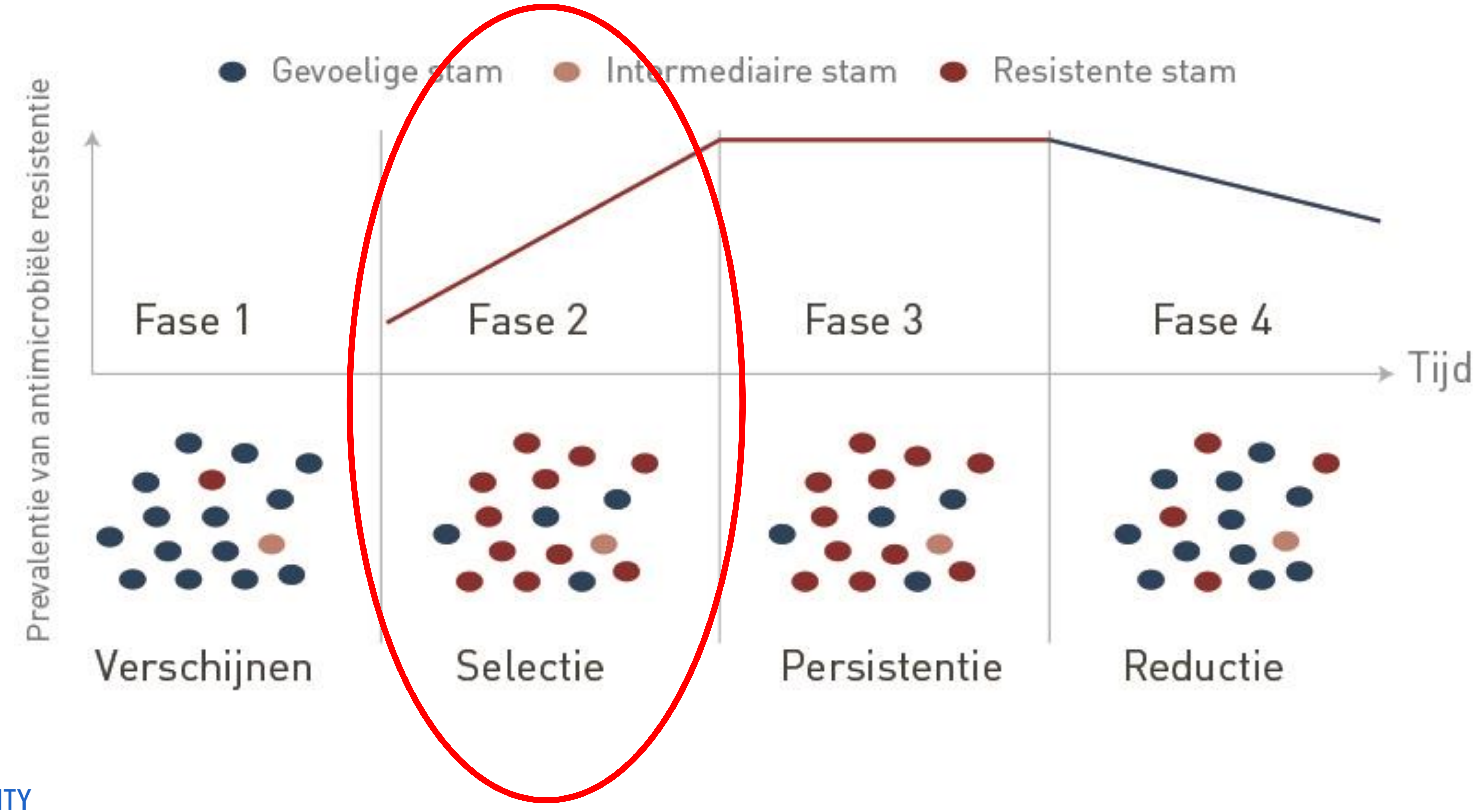
Waar komt het probleem vandaan?



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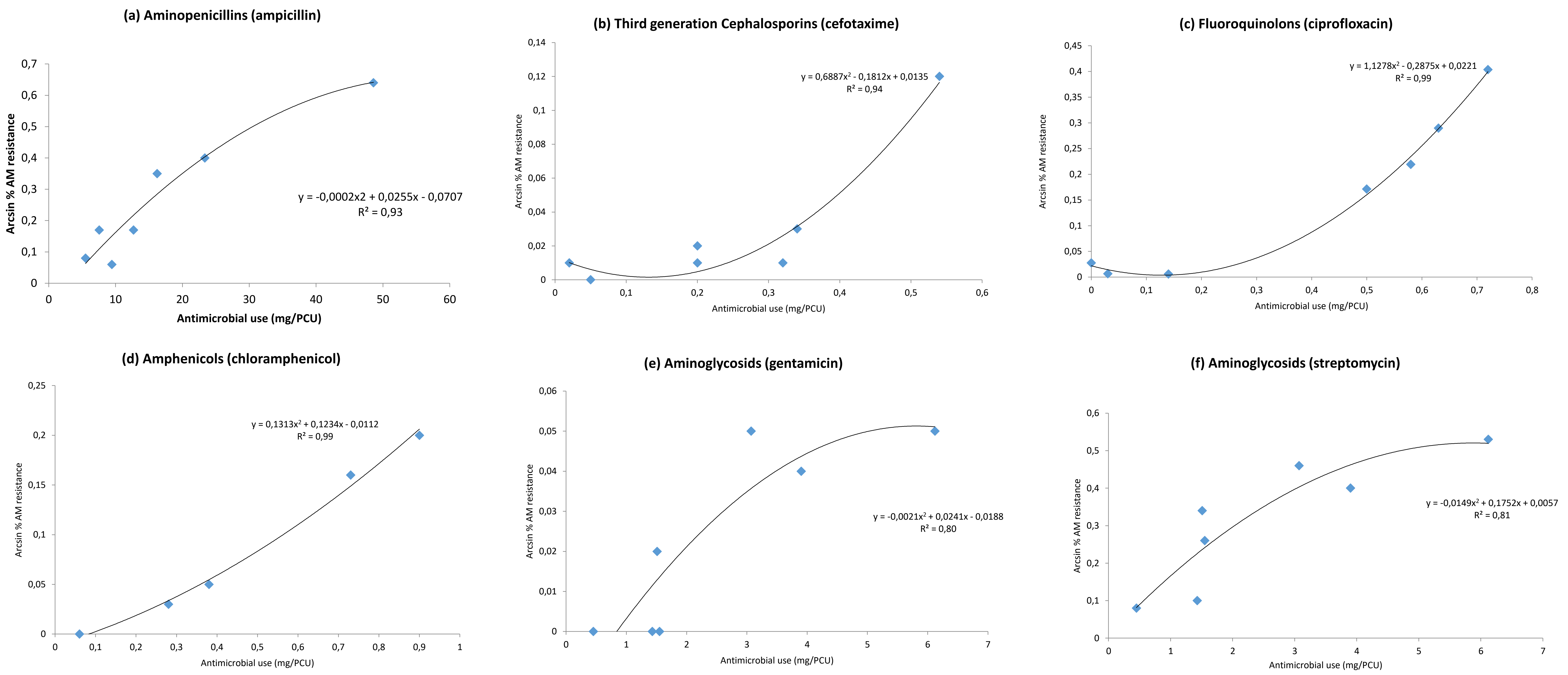

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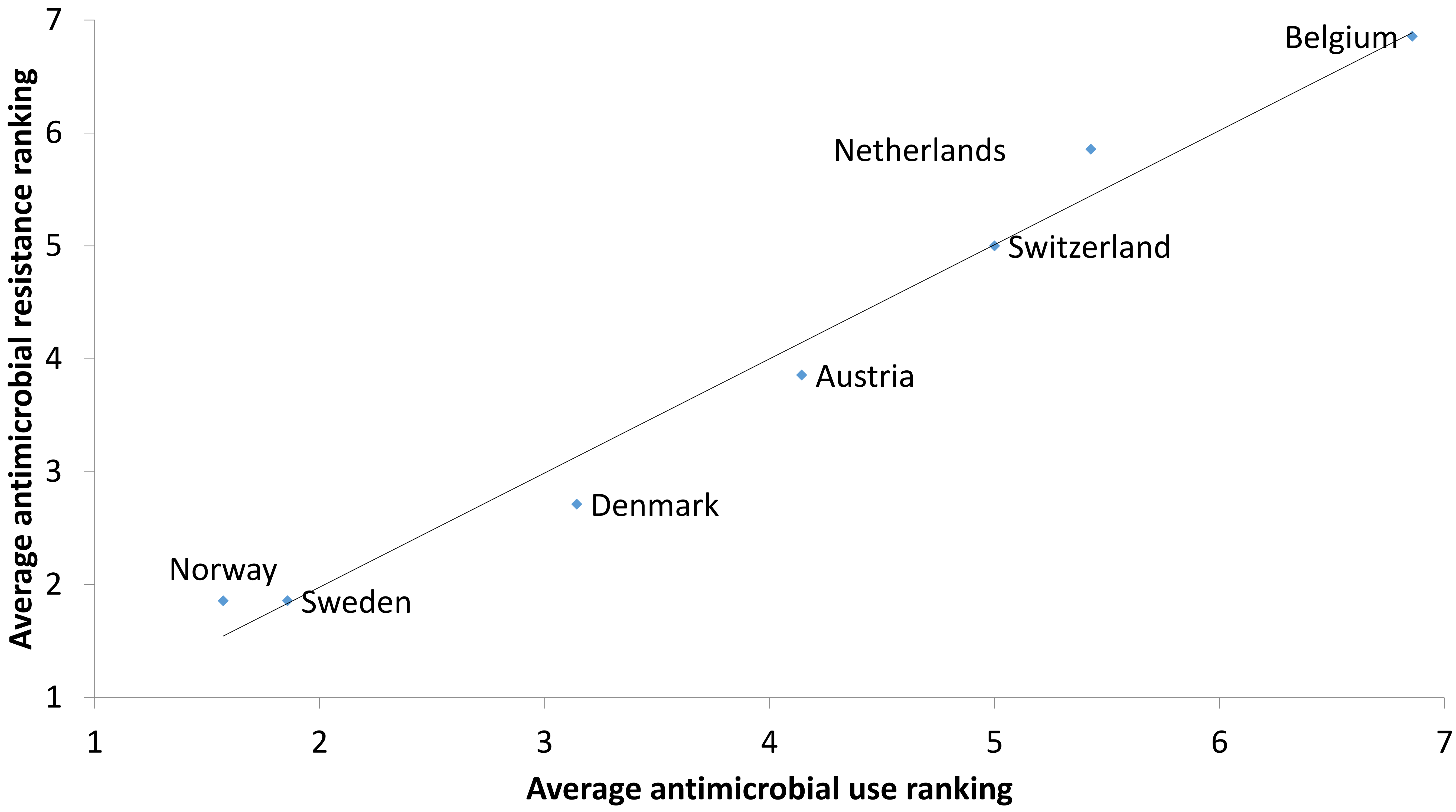
Chantziaras et al., J Antimicrob Chemother, 2014



Chantziaras et al., J Antimicrob Chemother, 2014

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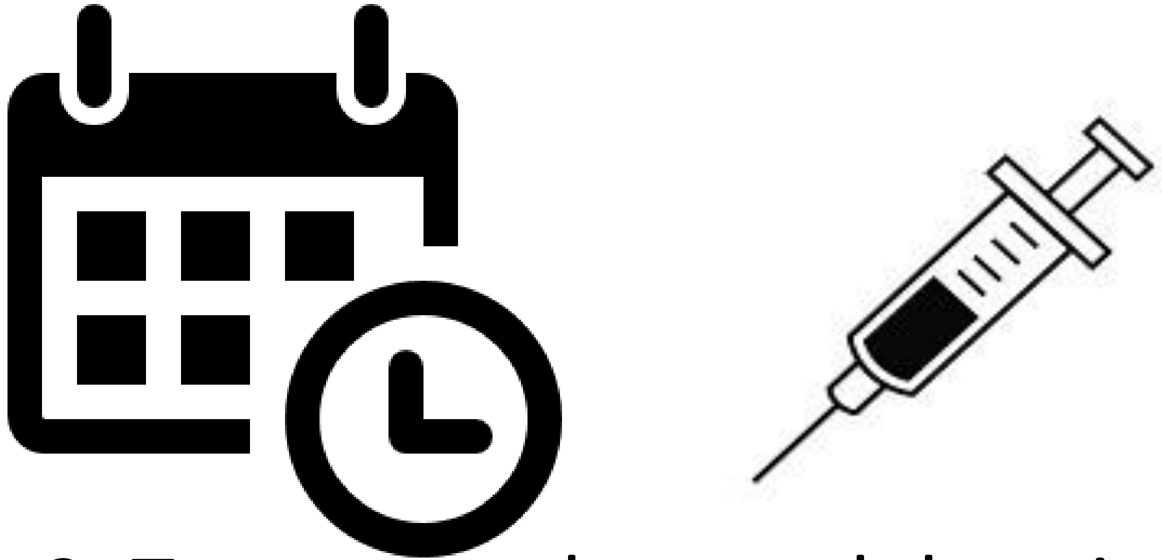
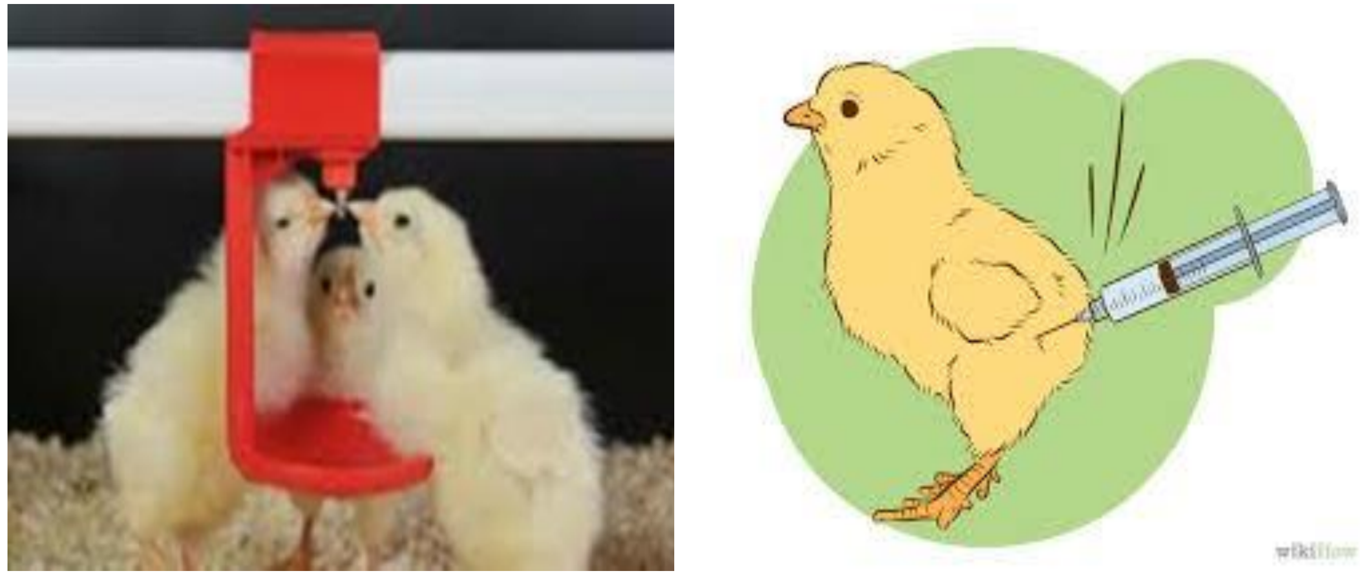
Drivers voor resistentie

1. Total amount of antimicrobial agents



2. Treatment dose and duration

3. Choice of antimicrobials



4. Administration route

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Een gemiddeld varken in België krijgt …% van zijn levensduur (+/- 6 maand) antibioticum

A. +/- 1%
B. +/- 10%
C. +/- 50%

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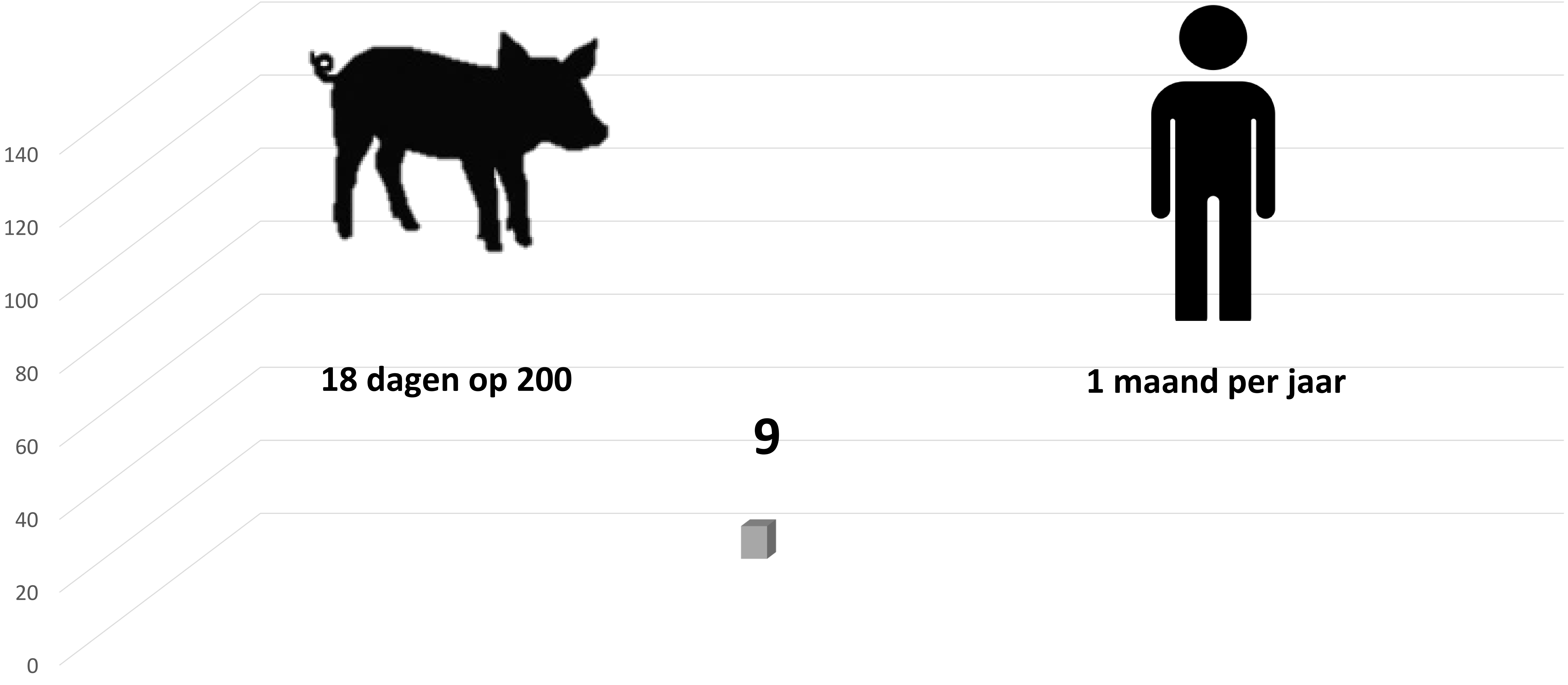
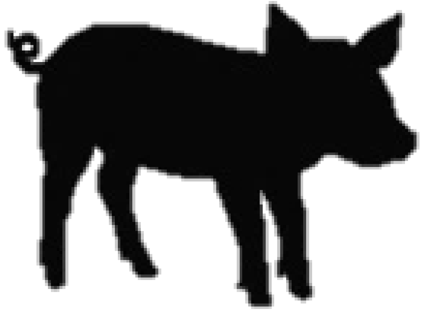
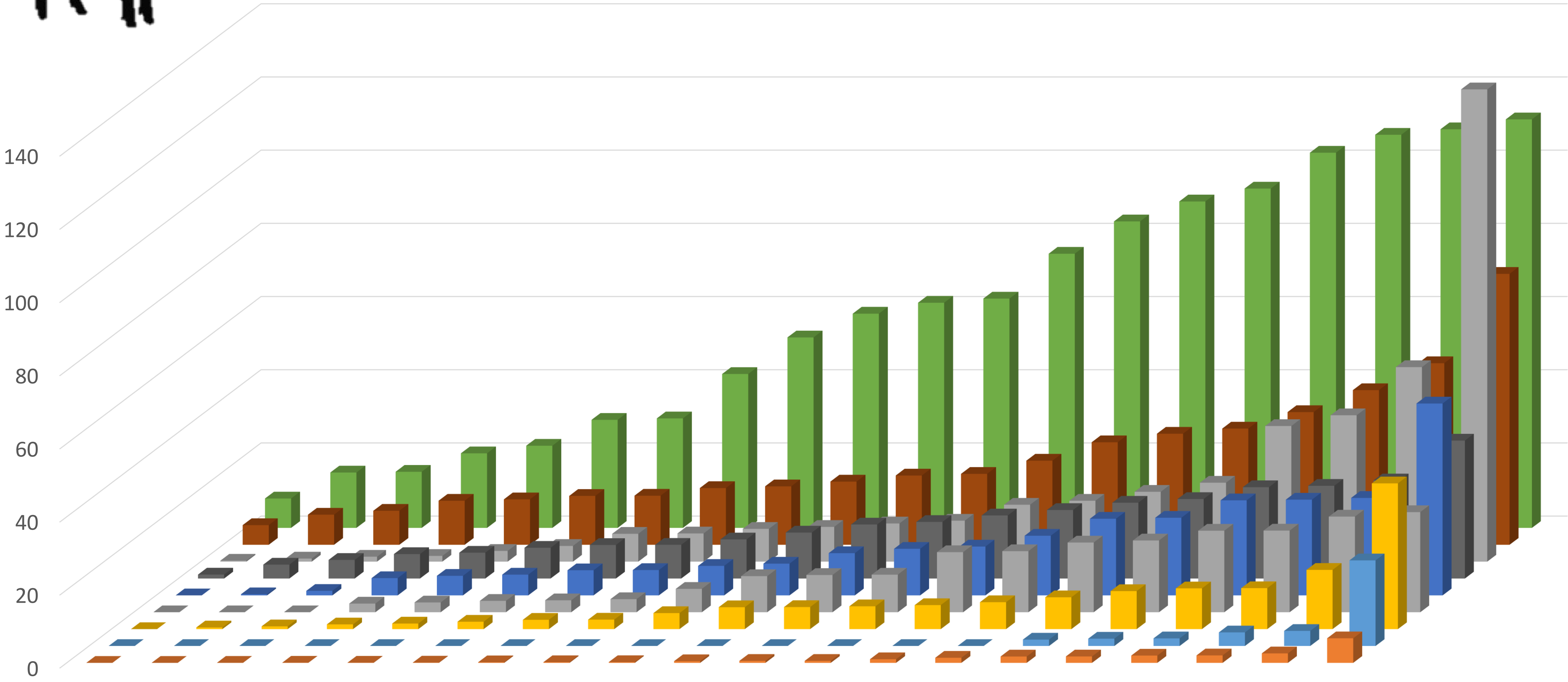
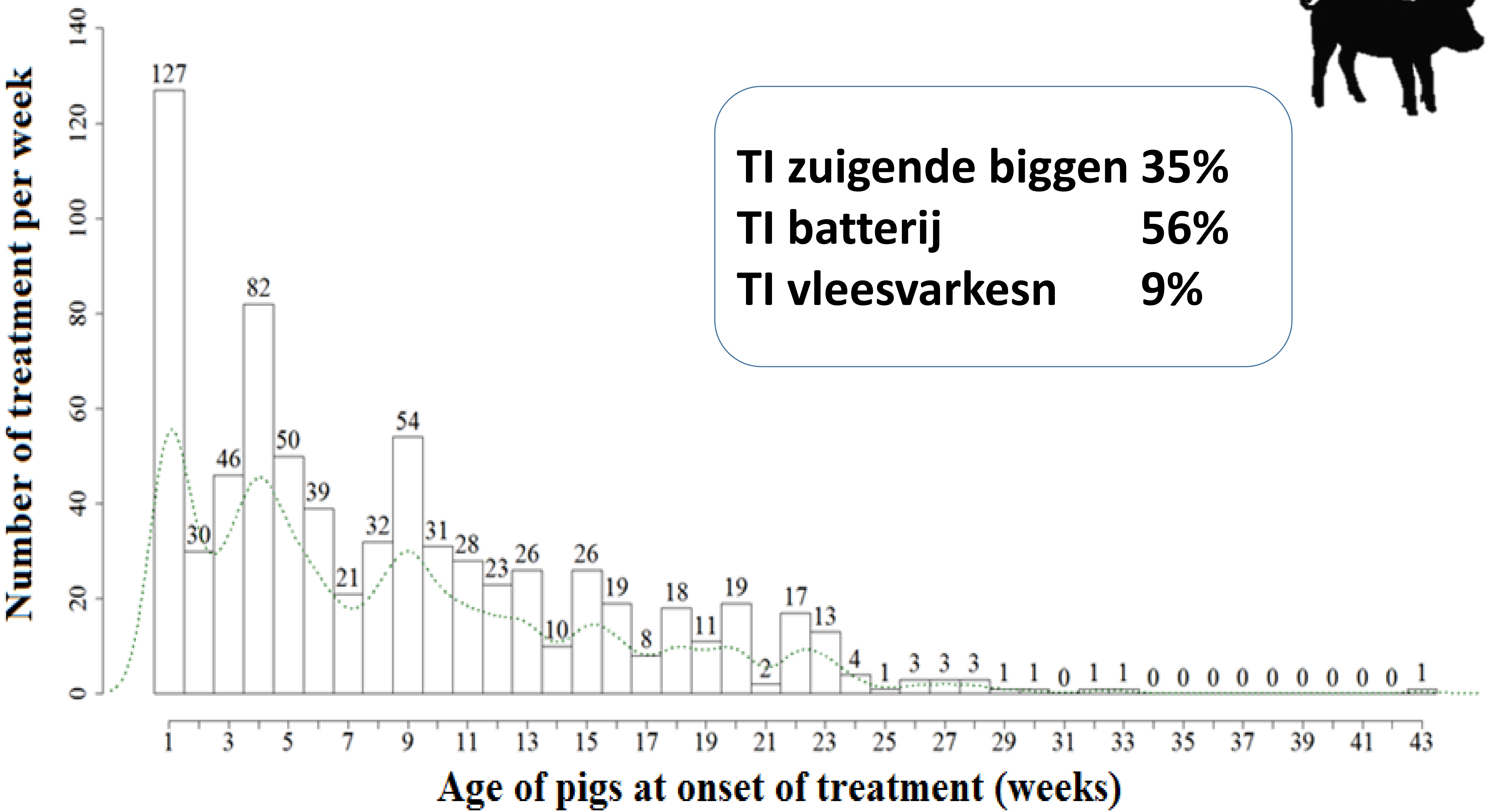


Sarrazin et al., J Antimicrob Chemother, 2019



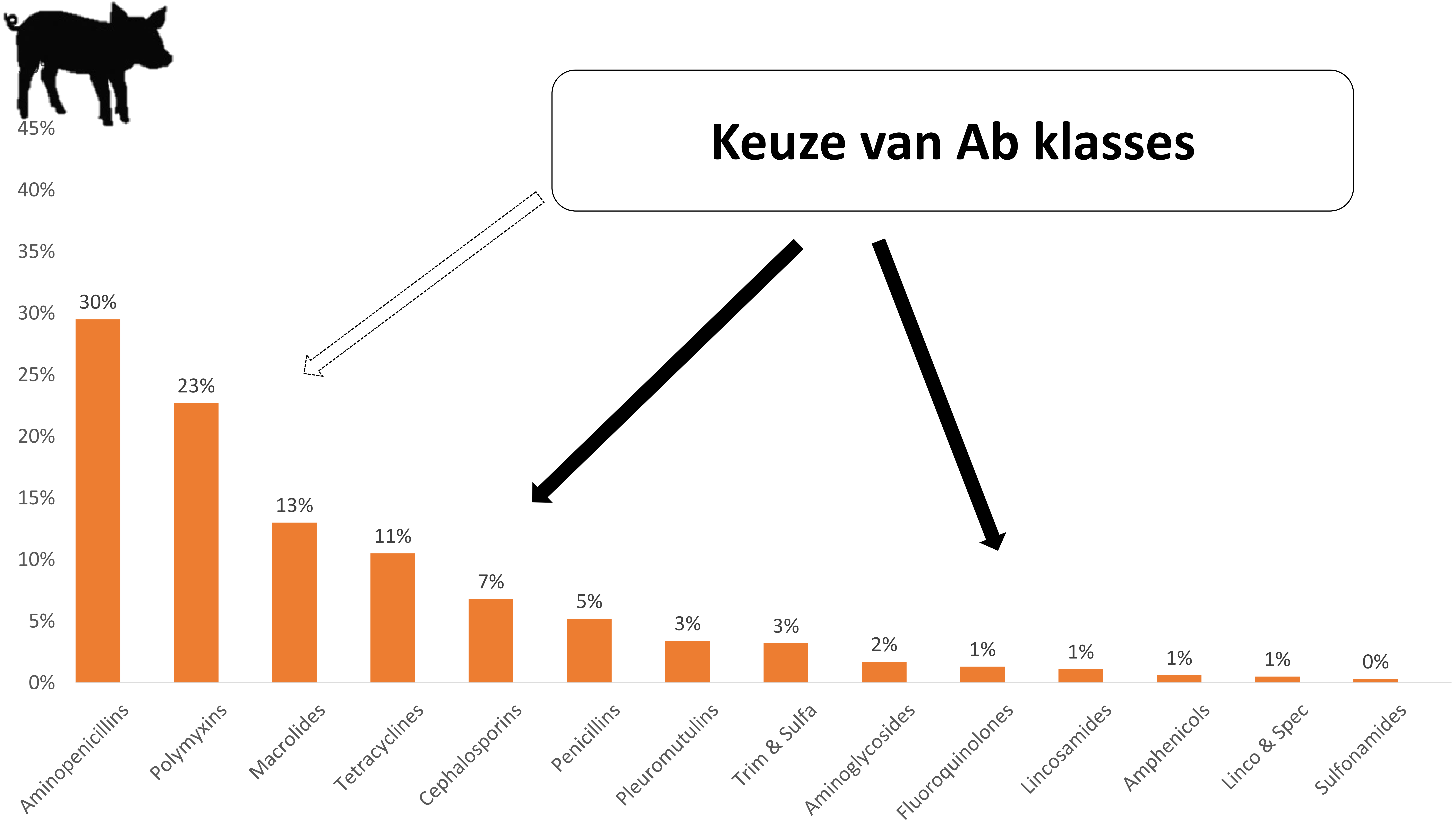


Sarrazin et al., J Antimicrob Chemother, 2019

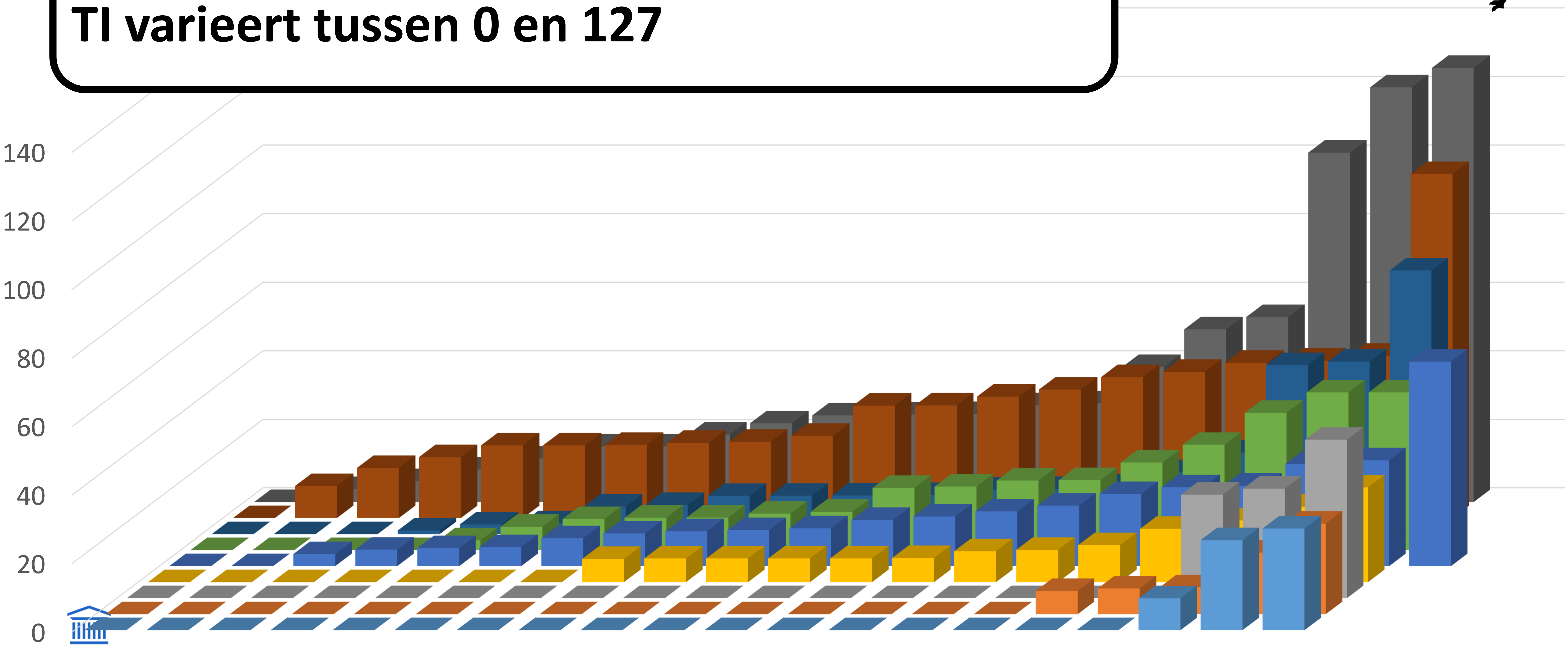


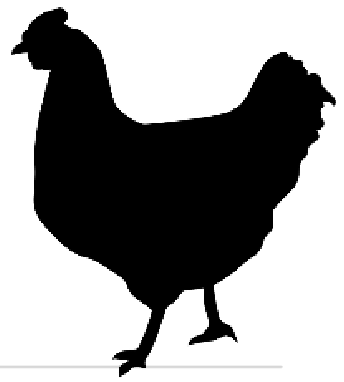
TI zuigende biggen	35%
TI batterij	56%
TI vleesvarkesn	9%

Keuze van Ab klasses



Geen gebruik in 67 rondes (37%)
TI varieert tussen 0 en 127





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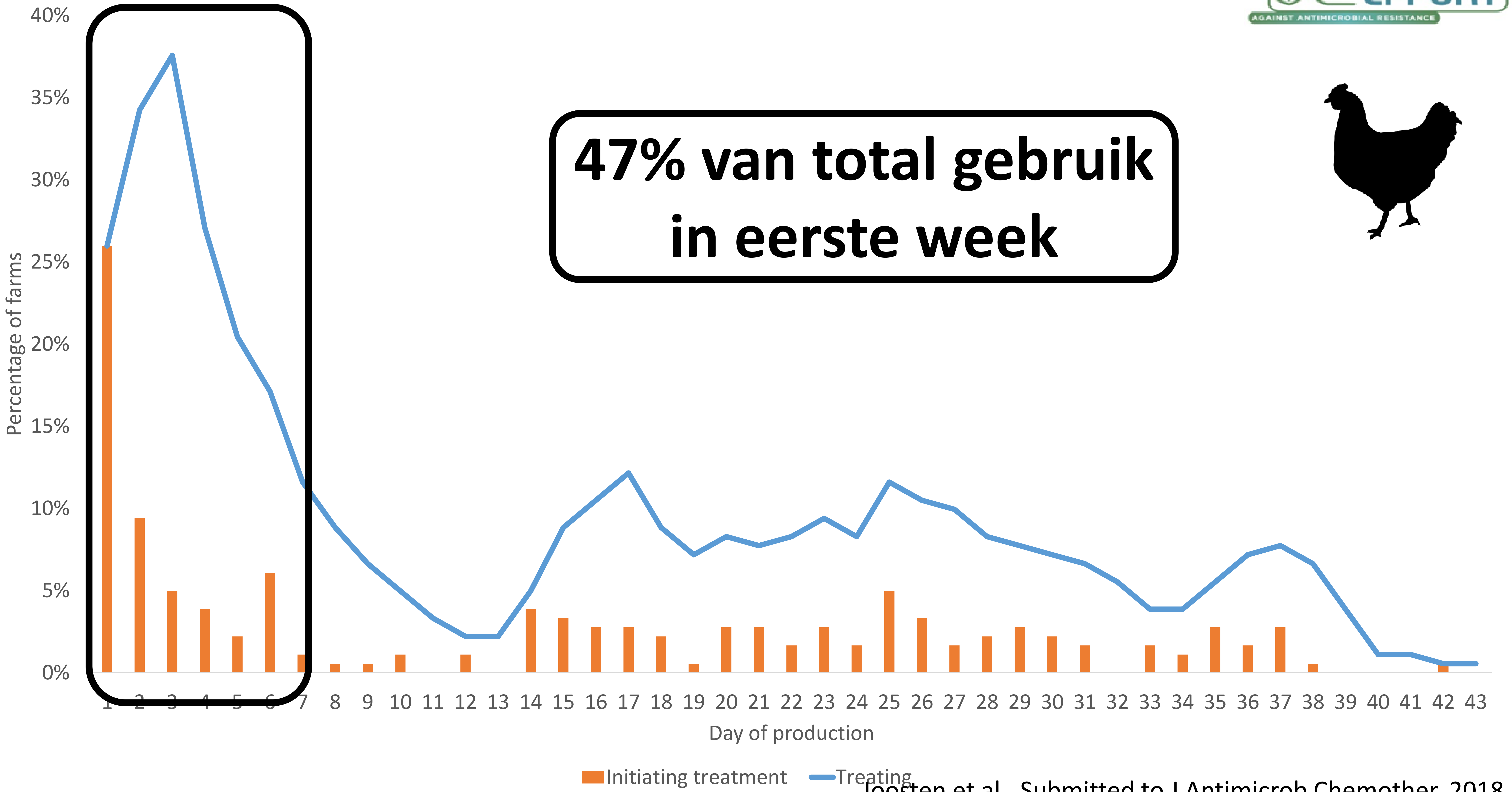
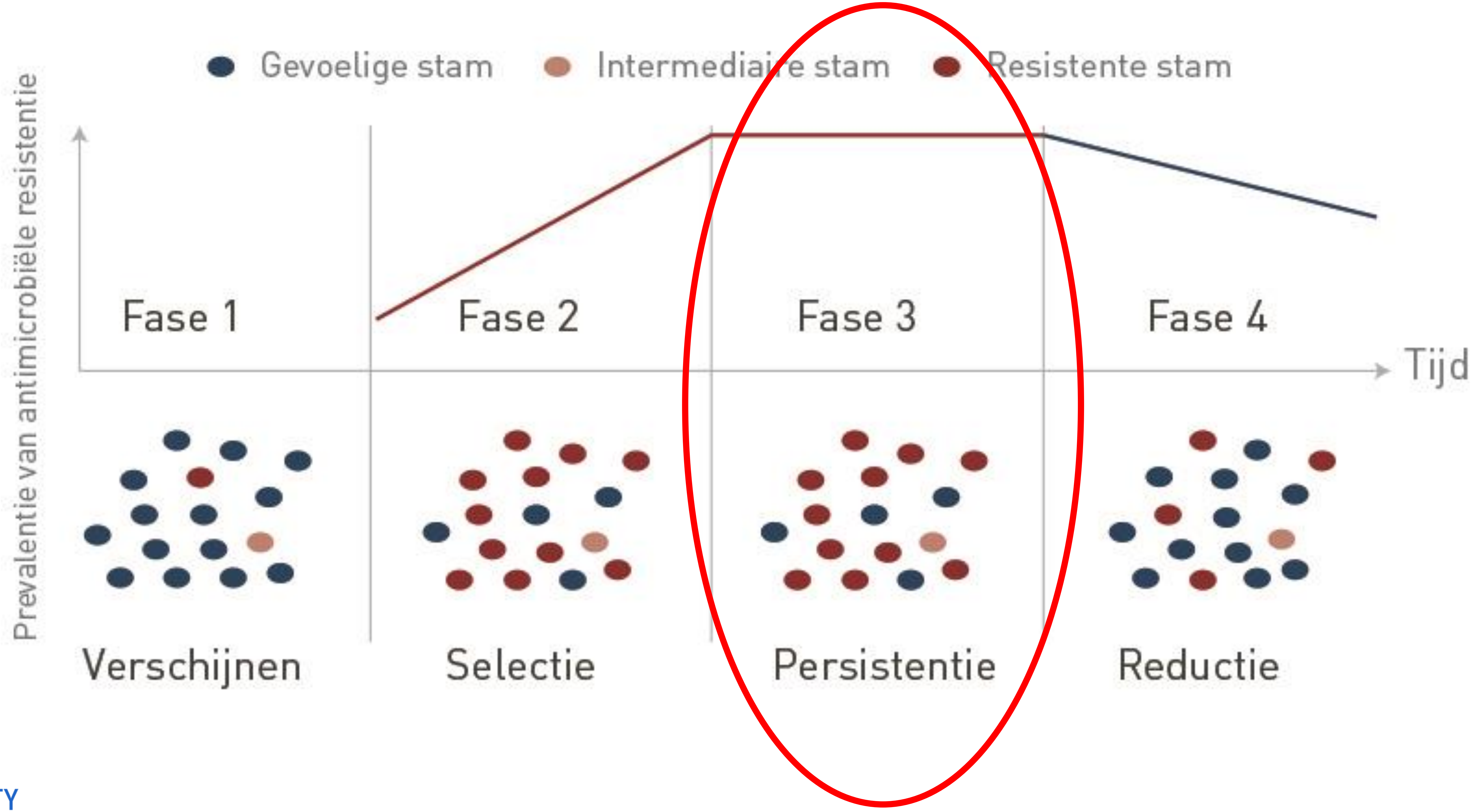
47% van total gebruik in eerste week



Joosten et al., Submitted to J Antimicrob Chemother, 2018

Waar komt het probleem vandaan?



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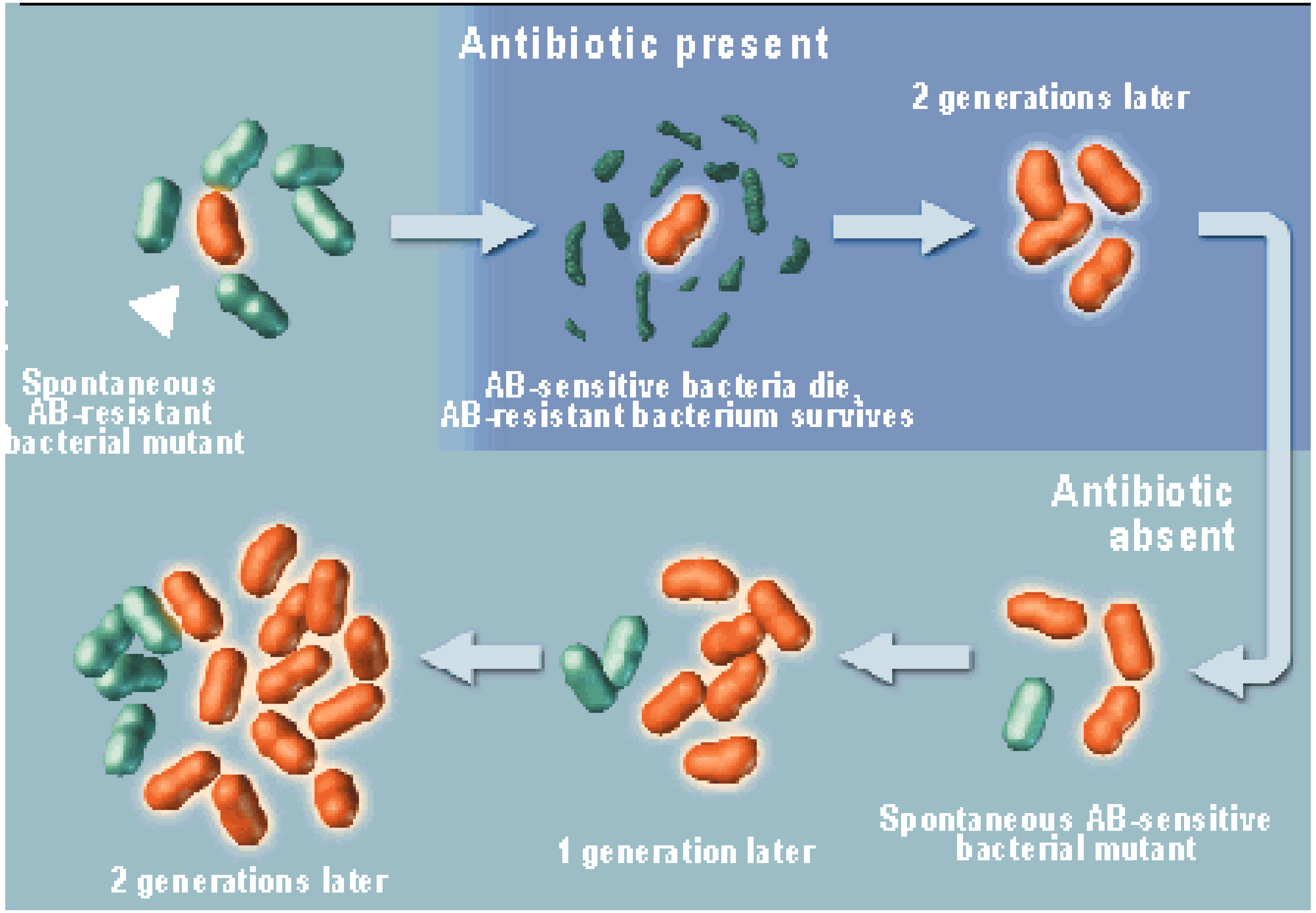
Persistentie van resistentie



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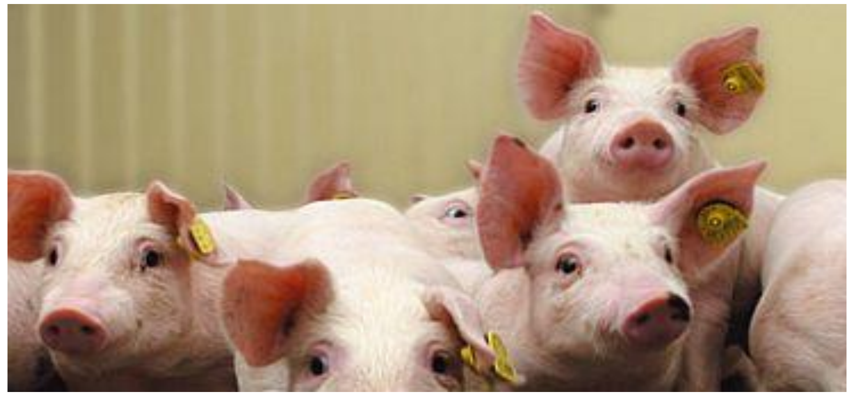
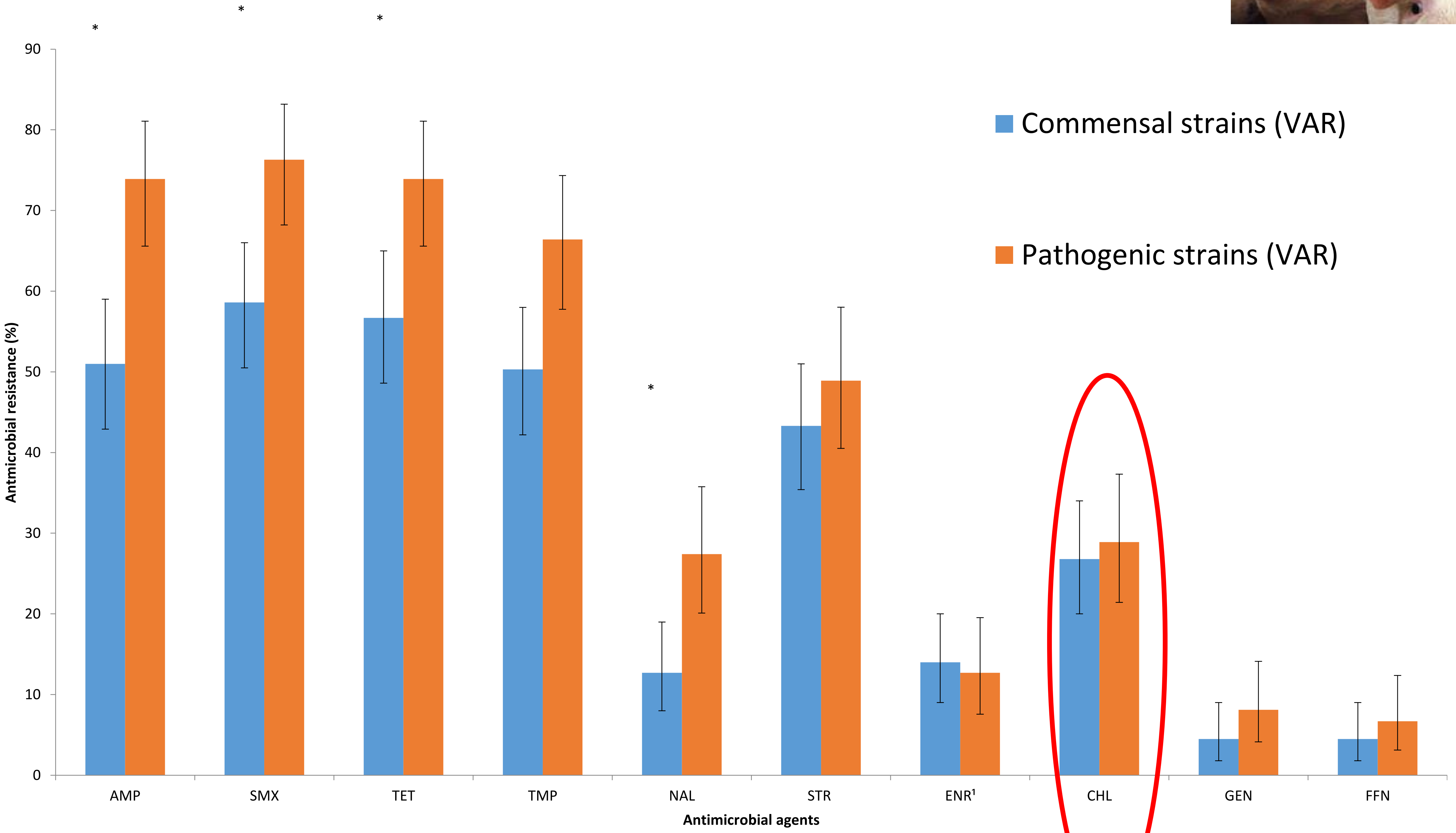
Vleesvarkens: *E. coli*





AMP: ampicillin, SMX: sulfomethoxazole, TET: tetracycline, NAL: nalidixic acid, STR: streptomycin, ENR[1]: enrofloxacin (national monitoring report used ciprofloxacin), CHL: chloramphenicol, GEN: gentamycin, FFN: florfenicol

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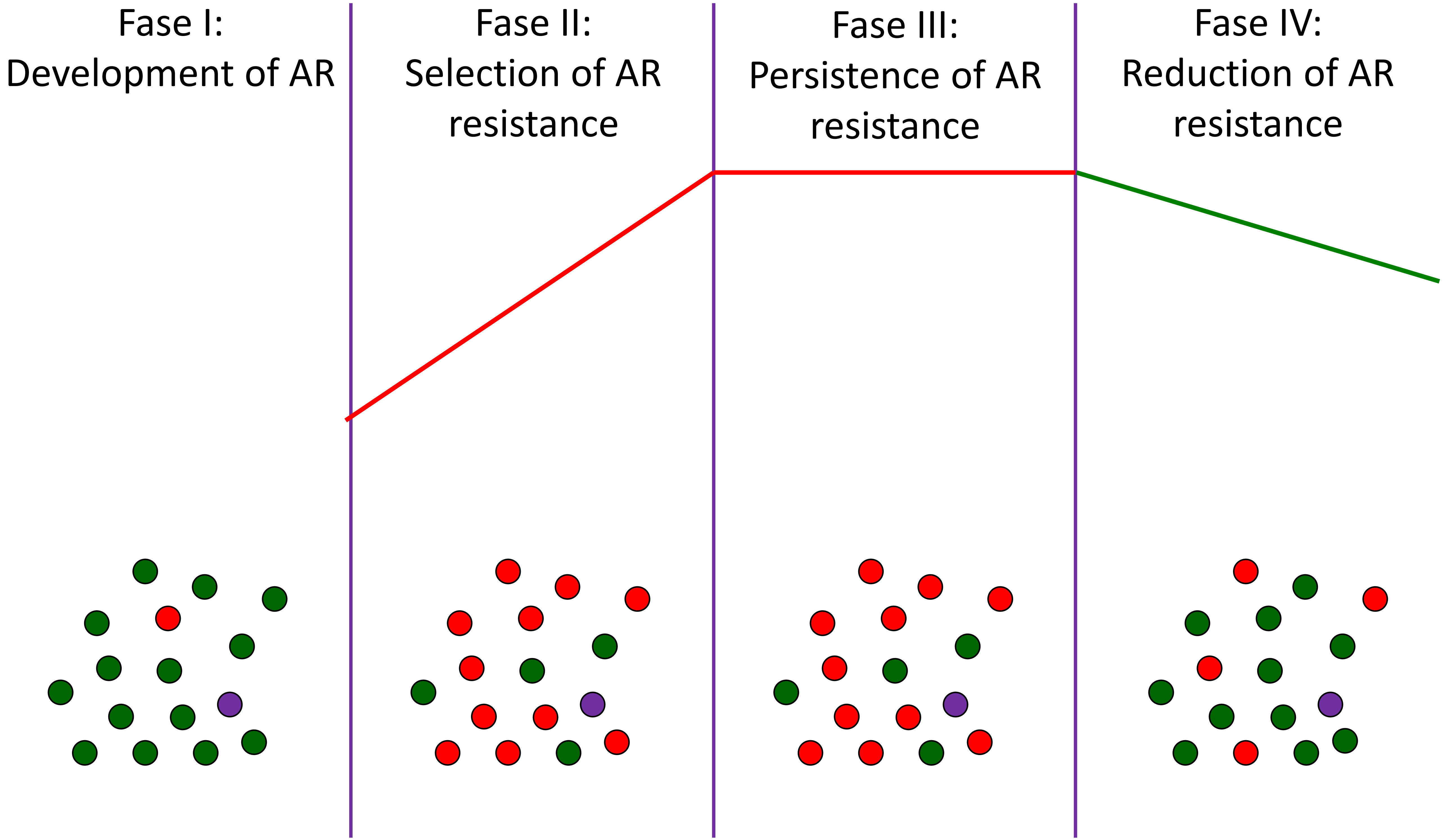
Chantziaras et al., 2014

Epidemiologie van antibioticumresistentie



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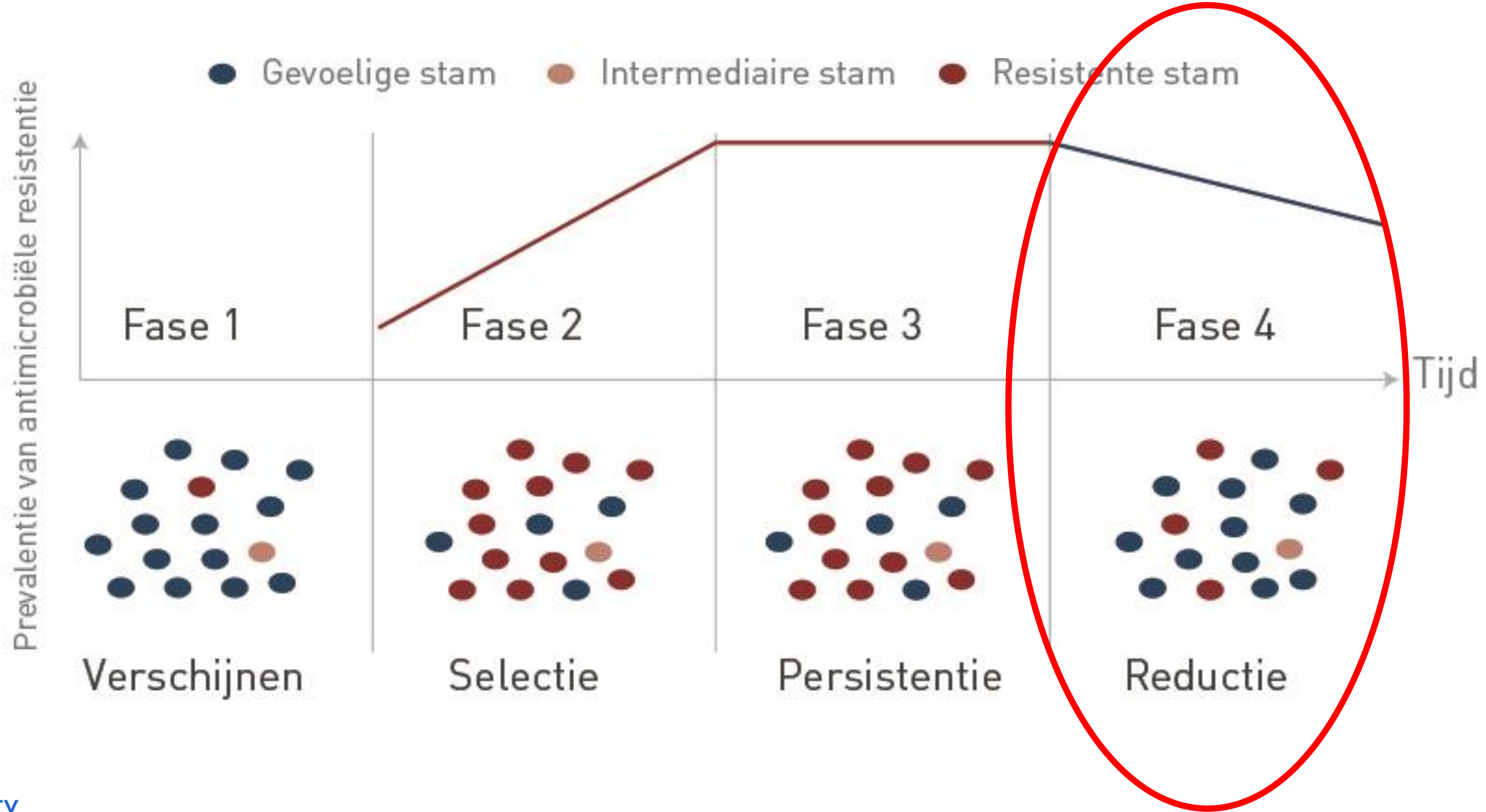
Waar komt het probleem vandaan?



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Minder antibioticum gebruik resulteert in minder resistentie

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Hoe is het antibioticumgebruik bij dieren in België de afgelopen 9 jaar geëvolueerd?

A. Ongeveer met 20% toegenomen
B. Ongeveer gelijk gebleven
C. Ongeveer met 25% afgenomen
D. Ongeveer met 45% afgenomen

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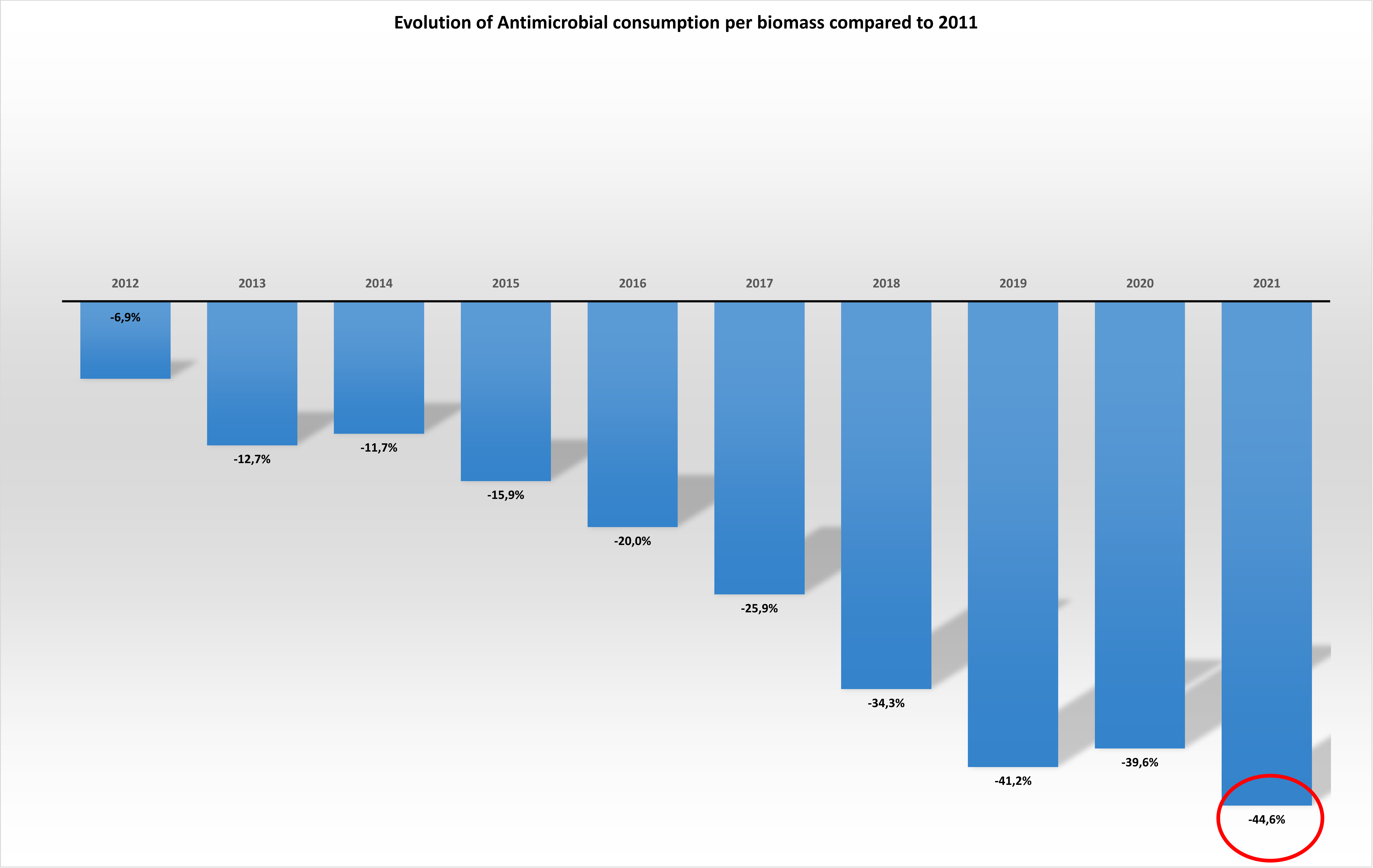
Evolution of Antimicrobial consumption per biomass compared to 2011
2012
2013
2014
2015
2016
2017
2018
2019
2020
2021
-6,9%
-12,7%
-11,7%
-15,9%
-20,0%
-25,9%
-34,3%
-41,2%
-39,6%
-44,6%

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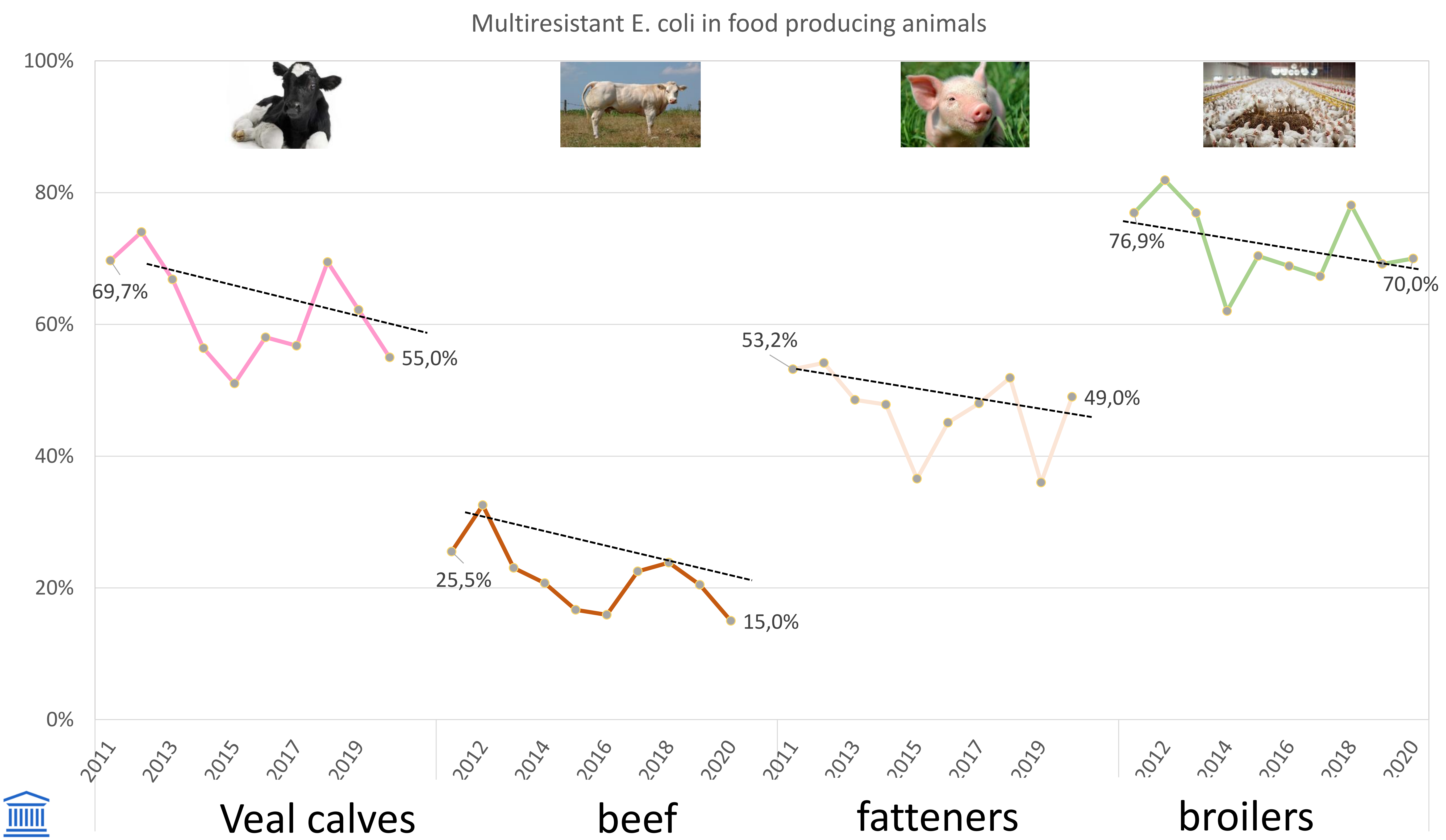

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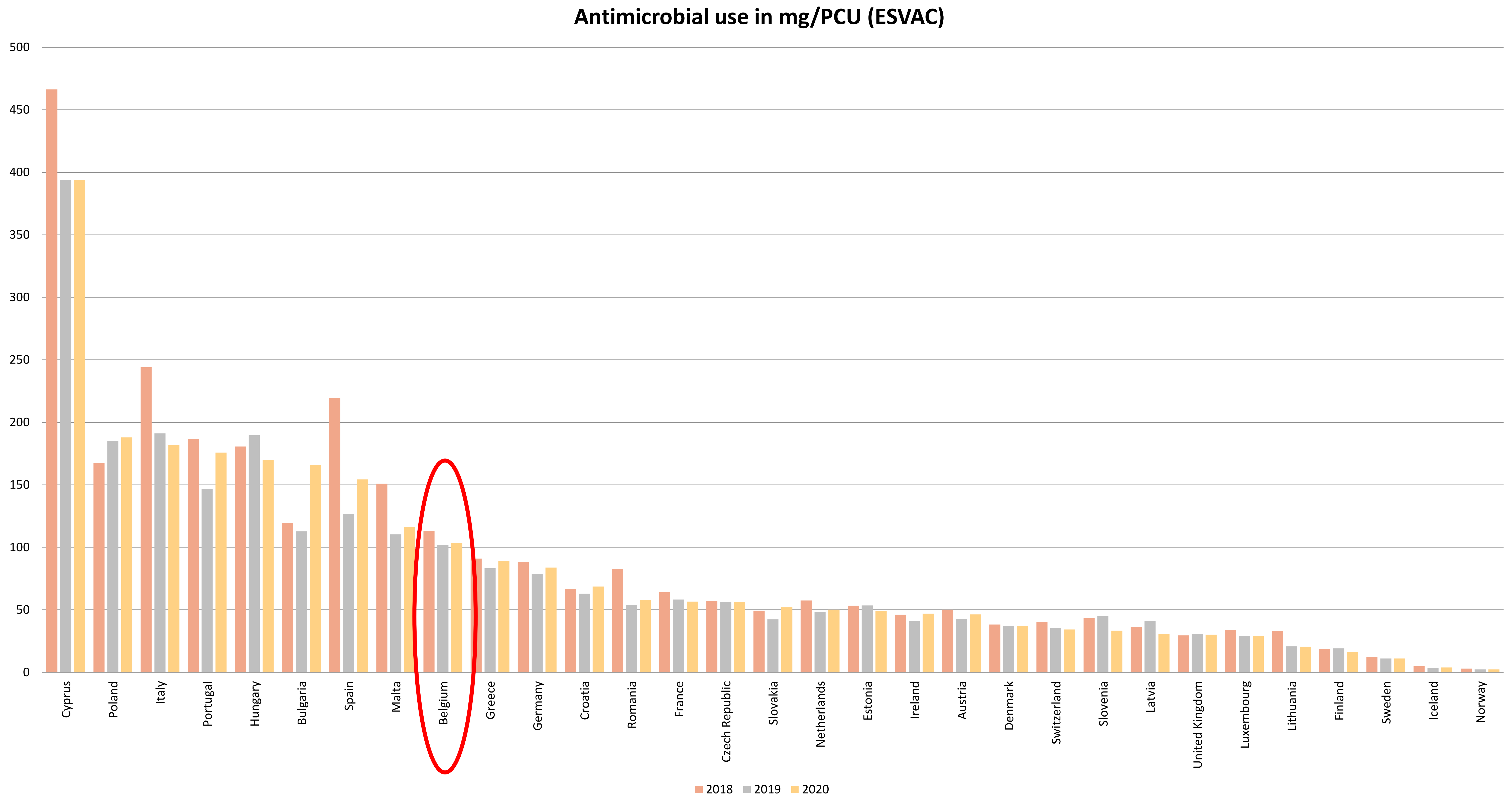
Veterinair gebruik van antibiotic in Europa: ESVAC



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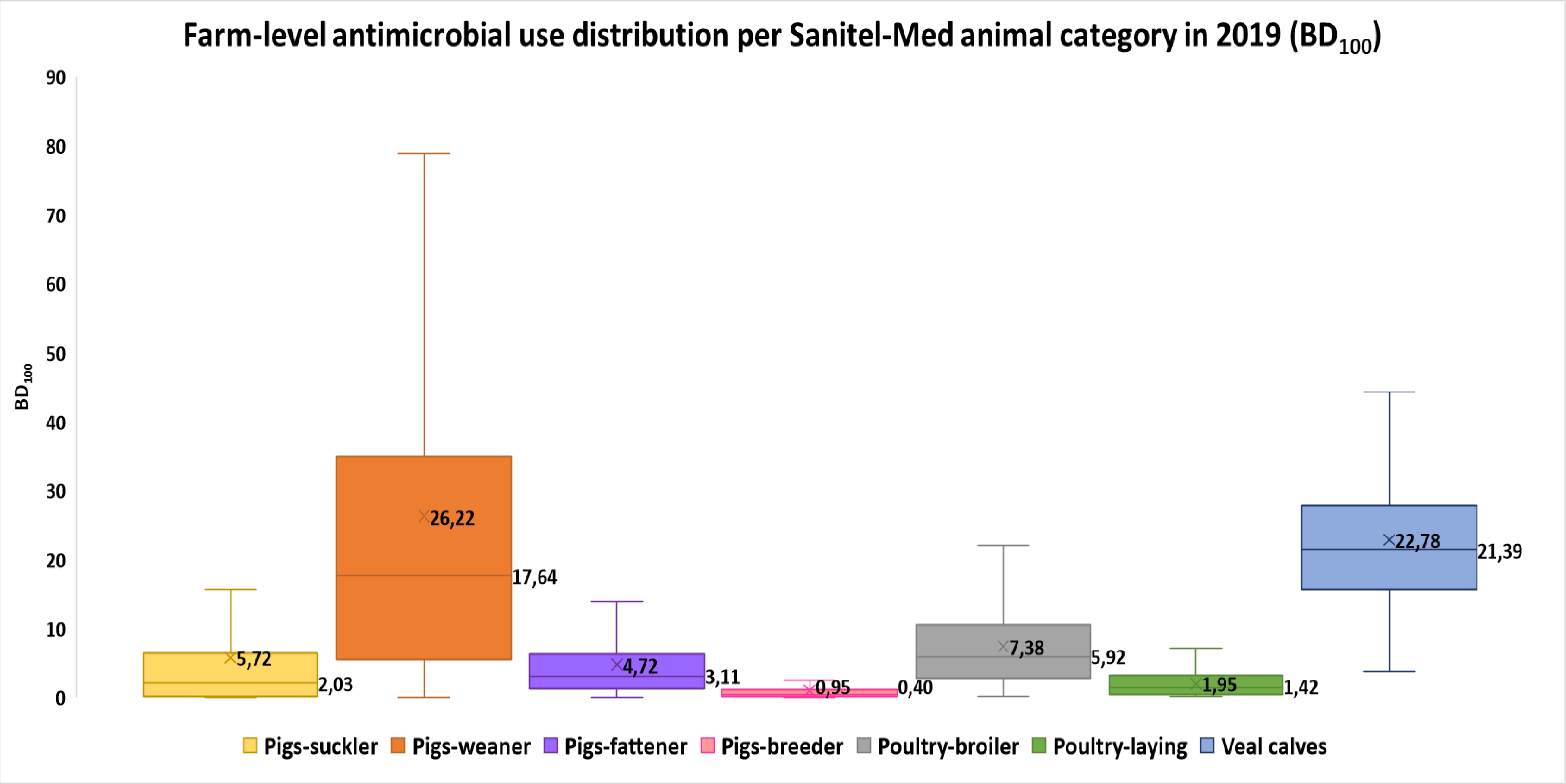
Farm level data collection



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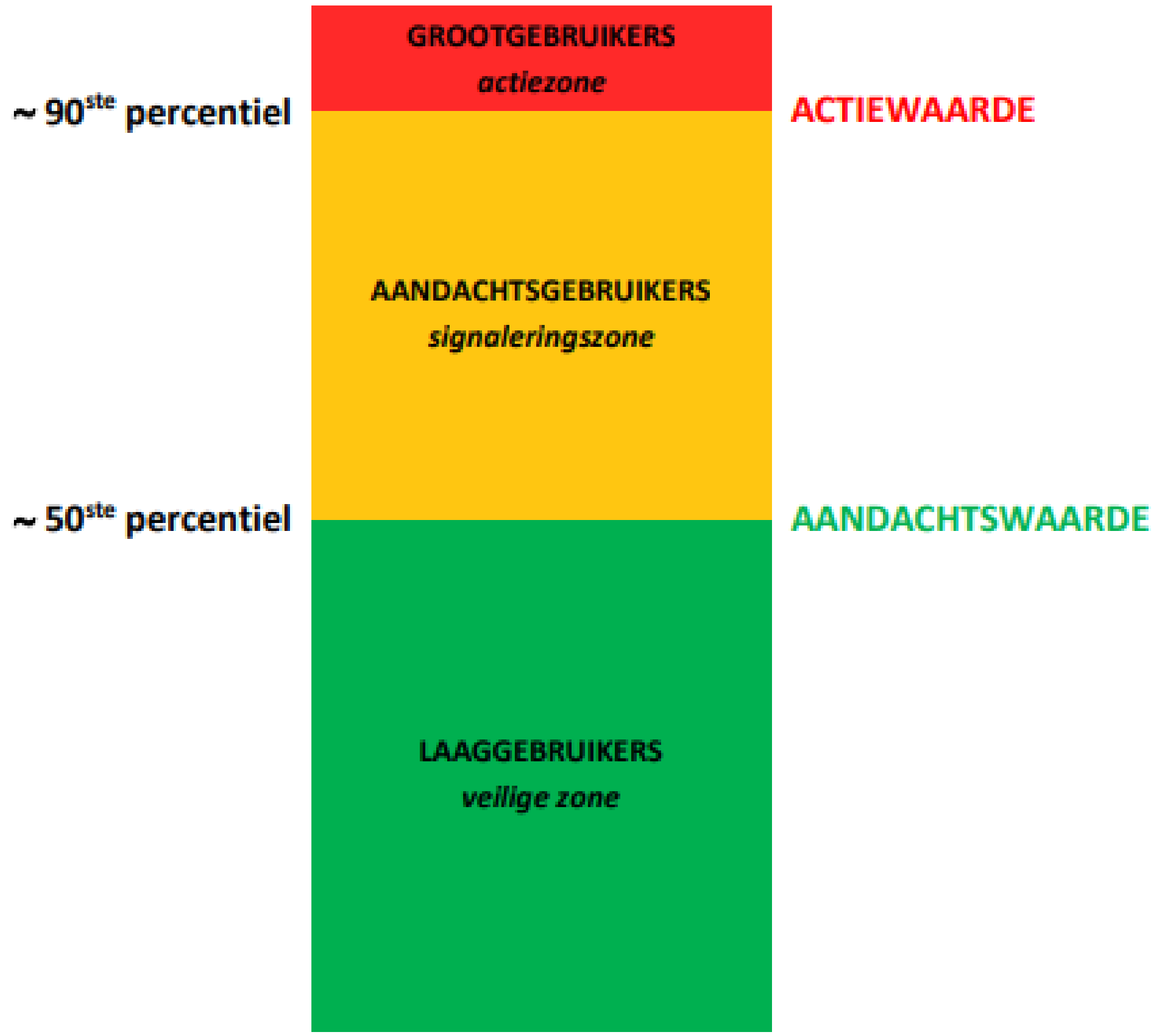
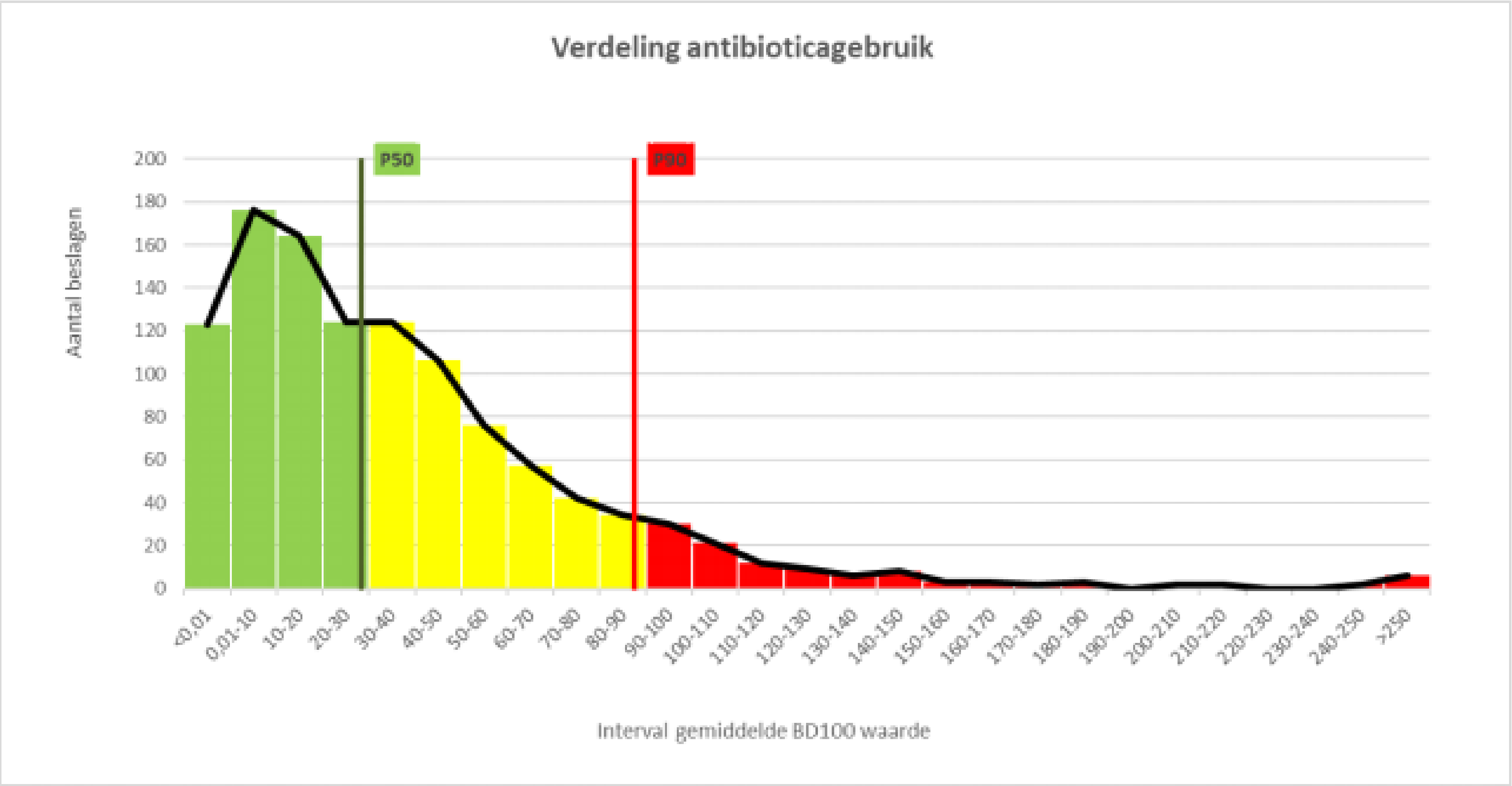
AMCRA
IMPROVE HEALTH, REDUCE RESISTANCE

Data collection and benchmarking, for the benefit of **antimicrobial stewardship**



Figuur 1. Gebruikerscategorieën en grenswaarden voor antibioticagebruik in de veehouderij.



Figuur 2. Voorbeeld van een frequentieverdeling van het antibioticagebruik, met aanduiding van de grenswaarden en gebruikerscategorieën zoals getoond in Figuur 1.

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“An ouince of prevention, is worth a pound of cure”

- Benjamin Franklin -

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Jeroen Dewulf

Full Professor

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