

A major reduction in the use of antimicrobials for livestock in the Netherlands since 2007: critical success factors

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Outline

- The need for action
- Historical facts of antimicrobial use in Dutch husbandry
- A window of opportunity
- Antimicrobial usage 2007-2015
- Surveillance data antimicrobial resistance 1998-2015
- The future



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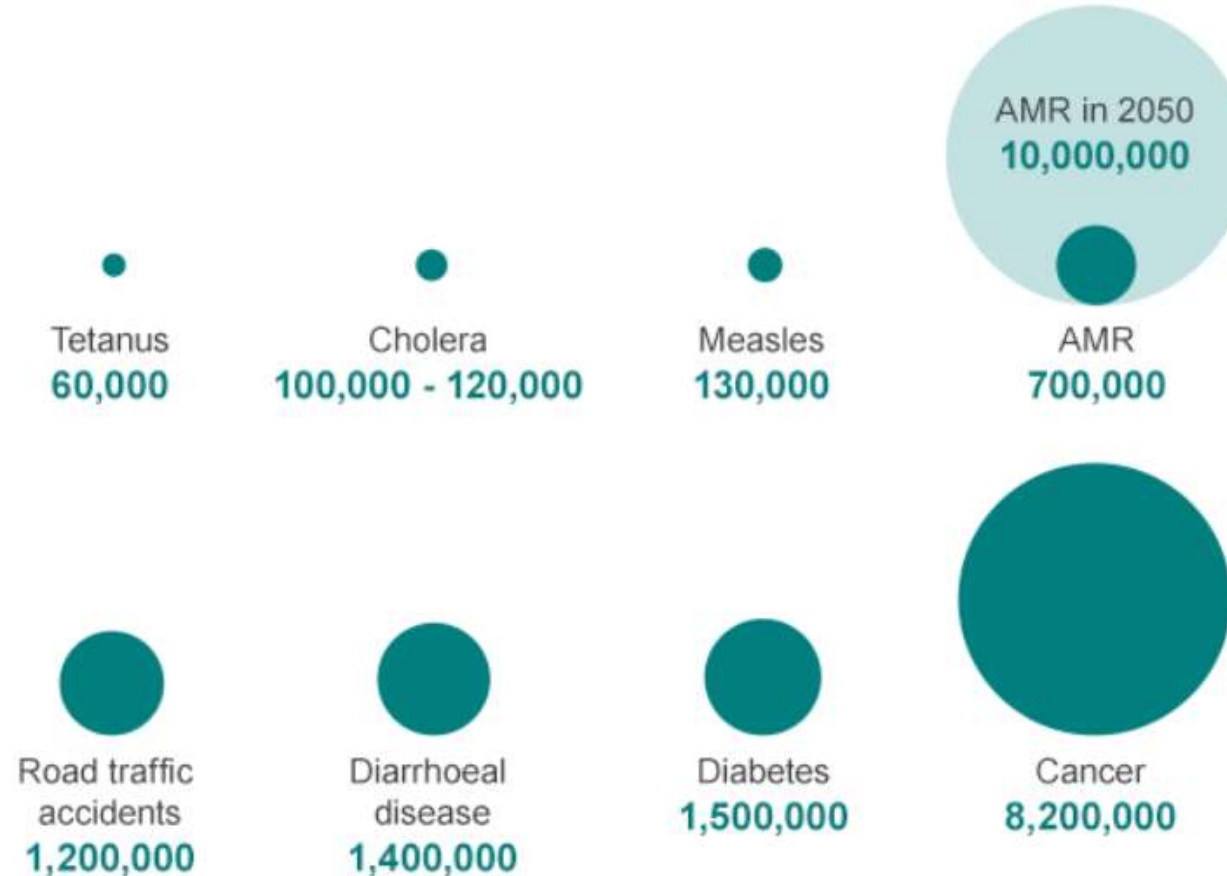
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AMR Review (Jim O'Neill) 2016

Deaths attributable to antimicrobial resistance every year compared to other major causes of death



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Antimicrobials....

The only drugs that have a positive effect for you (or your animals) and a negative effect for the society

Decision to use should not be at the individual level but by prescription only and according to guidelines developed by professionals



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Global level

- WHO, FAO and OIE all adopted in their General Assemblies in 2015 a resolution to contain AMR.
- WHO: Global Action Plan => member states will prepare a National Action Plan with a One Health approach (ready 2017).
- September 21st 2016: resolution adopted in the UN-General Assembly in New York



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Precautionary principle



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The Netherlands

$\times 10^6$

people	17,0
dairy cows	1,6
veal calves	0,9
pigs	13,0
chicken	104,0

2nd in exporting of
agricultural products



Dutch Veterinary Antibiotics Policy

- Published in March 1994
 - Usage and AMR surveillance
 - Guidelines for restricted use of antibiotics for all major animal species (*formularia*)

Tijdschr Diergeneeskd, 1994 Mar 15;119(6):160-83.

[Guidelines for veterinary use of antibiotics: recommendations of a work group. Beleidsgroep Veterinaire Apotheek, Koninklijke Nederlandse Maatschappij voor Diergeneeskunde].

[Article in Dutch]

van den Boogaard AE, Breeuwsma AJ, Julicher CH, Mostert A, Nieuwenhuijs JH, Vaarkamp H, Verhoeff J, Vulto A.

Beleidsgroep Veterinaire Apotheek, Koninklijke Nederlandse Maatschappij voor Diergeneeskunde.



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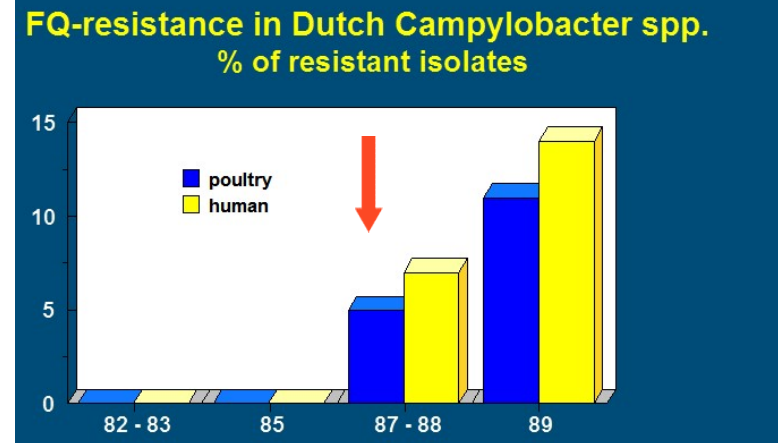
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Dutch Veterinary Antibiotics Policy

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Endtz et al. J. Antimicrobial
Chemotherapy (1991)

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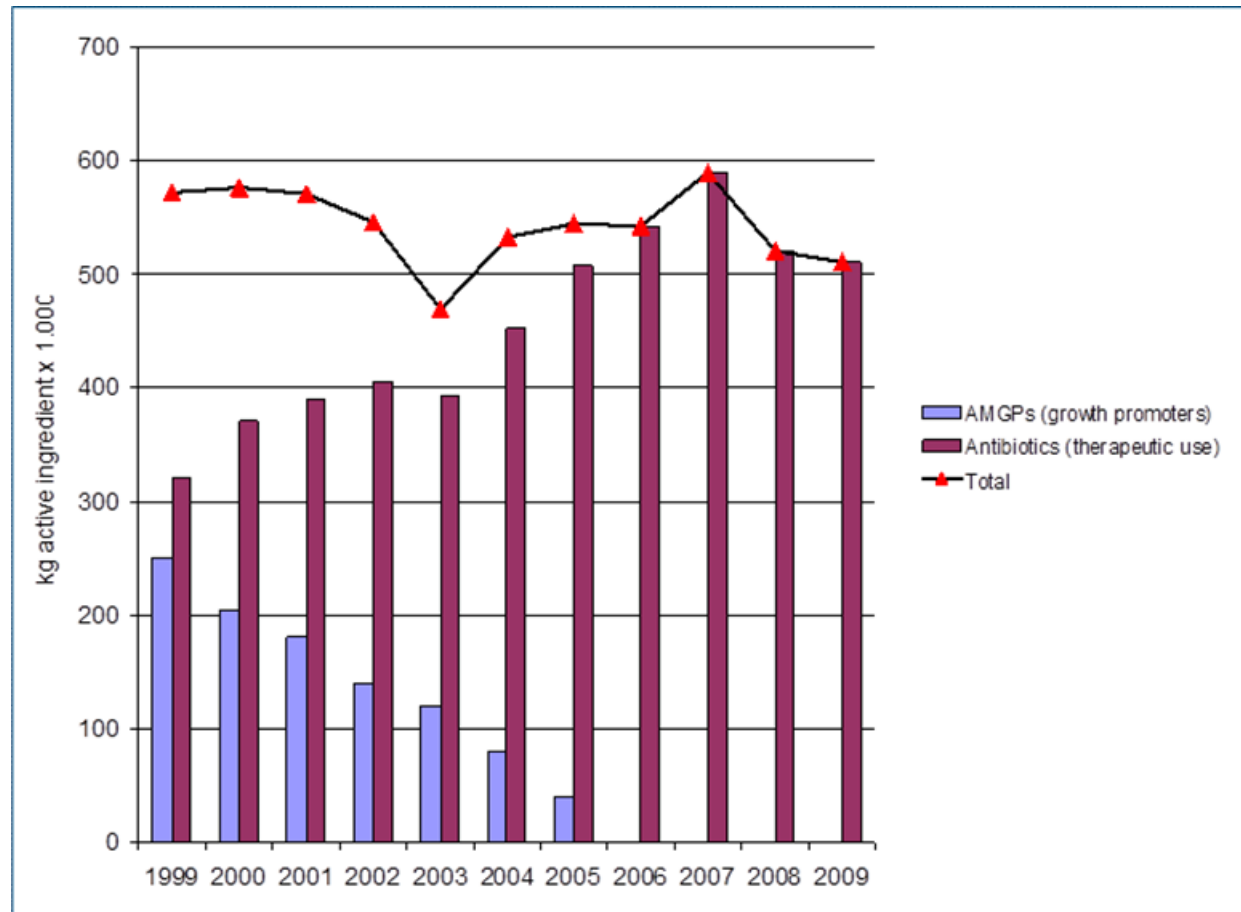
Beleidsgroep Veterinaire Apotheek, Koninklijke Nederlandse Maatschappij voor Diergeneeskunde.



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Effect of the ban of AGPs on Dutch AMU in animals



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Window of opportunity (1): usage

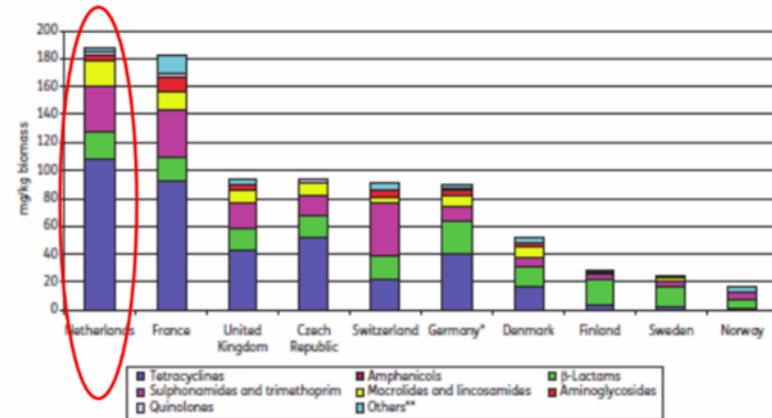
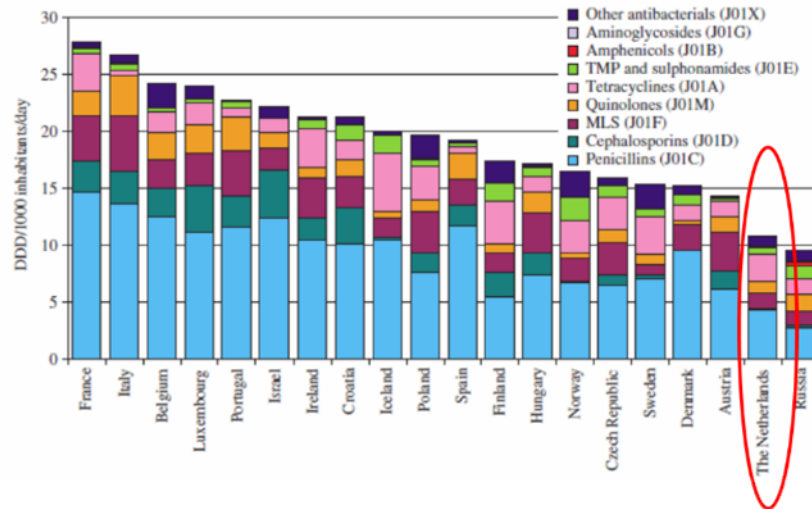


Figure 1. Amounts, in mg, of veterinary antibacterial agents sold in 2007 per kg biomass of pig meat, poultry meat and cattle meat produced plus estimated live weight of dairy cattle. *2005 data. **The substances included vary from country to country.

Journal of Antimicrobial Chemotherapy (2009) 64, 200–205
doi:10.1093/jac/dkp135
Advance Access publication 21 April 2009

JAC

European Surveillance of Antimicrobial Consumption (ESAC): outpatient parenteral antibiotic treatment in Europe

Samuel Coenen^{1,2*}, Arno Muller³, Niels Adriaenssens¹, Vanessa Vankerckhoven³, Erik Hendrickx⁴
and Herman Goossens³ on behalf of the ESAC Project Group

J Antimicrob Chemother 2010; 65: 2037–2040
doi:10.1093/jac/dkq247 Advance Access publication 29 June 2010

Journal of
Antimicrobial
Chemotherapy

Comparison of the sales of veterinary antibacterial agents between 10 European countries

Kari Grove*, Jordi Torren-Edo and David Mackay



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Window of opportunity (2): LA-MRSA (2005)

Prevalence MRSA veal farms: 88%
veal farmers: 33%
family members: 8%

Prevalence MRSA on pig farms: >70%
pig farmers: 49%
family members: 3%

NEWSFOCUS

INFECTIOUS DISEASE

From Pigs to People: The Emergence of a New Superbug

The discovery of a novel strain of MRSA able to jump from livestock to humans has sparked a multicountry effort to see how dangerous it might be

The first infection was puzzling, almost inexplicable. In July 2004, Andreas Voss of Radboud University Nijmegen Medical Center in the Netherlands admitted a 6-month-old girl for surgery to repair a congenital heart defect.

Because an infection with the common bacterium *Staphylococcus aureus* would pose a grave risk following heart surgery, Voss and his colleagues screened the baby girl for the microbe. They found not just *S. aureus* but also a menacing drug-resistant form known as methicillin-resistant *S. aureus* (MRSA). The physicians were flummoxed. Although MRSA has reached epidemic proportions in

or other livestock harbored MRSA, and no MRSA strain had ever been known to jump from livestock to humans. If the Dutch doctors' fears were correct, a novel strain had just gained that ability, opening up a new route for a potentially dangerous superbug to spread among humans. "Initially, we were very much afraid that this would be a major problem that could spread to the entire population," says Jan Khytmans, a microbiologist at VU University Medical Center in Amsterdam



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Window of opportunity (3): ESBLs (2010)



ORIGINAL ARTICLE

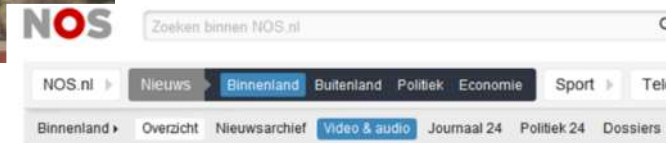
EPIDEMIOLOGY

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

M. A. Leverstein-van Hall^{1,2}, C. M. Dierikx³, J. Cohen Stuart¹, G. M. Voets¹, M. P. van den Munckhof¹, A. van Essen-Zandbergen³, T. Platteeuw^{1,4}, A. C. Fluit¹, N. van de Sande-Bruinsma², J. Scharinga¹, M. J. M. Bonten^{1,5} and D. J. Mevius^{3,6}; on behalf of the national ESBL surveillance group*

Extended-Spectrum β -Lactamase-Producing *Escherichia coli* From Retail Chicken Meat and Humans: Comparison of Strains, Plasmids, Resistance Genes, and Virulence Factors

Jan A. J. W. Kluytmans,^{1,2,3} Ilse T. M. A. Overdeest,^{1,2} Ina Willemsen,¹ Marjolein F. O. Kluytmans-van den Bergh,¹ Kim van der Zwaluw,⁴ Max Heck,⁴ Martine Rijnsburger,³ Christina M. J. E. Vandembroucke-Grauls,³ Paul H. M. Savelkoul,³ Brian D. Johnston,⁵ David Gordon,⁶ and James R. Johnson⁵



Sterfgeval door resistente ESBL-bacterie



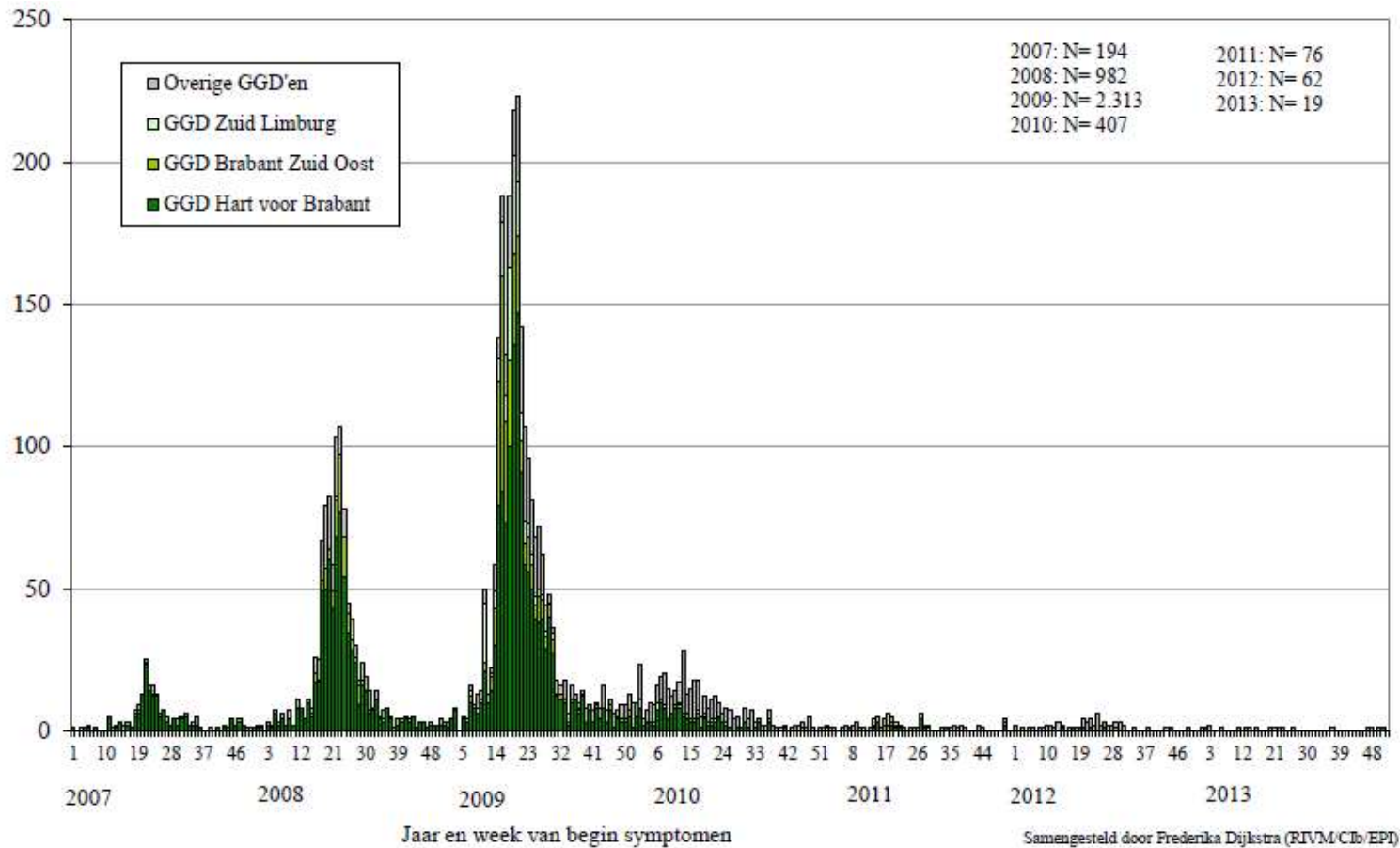
vrijdag 24 september 2010, 15:54 | 2263 keer bekeken | Duur: 01:59

VIDEO Voor het eerst is iemand overleden aan een infectie veroorzaakt door een resistente bacterie die in vrijwel alle kip in Nederland zit. Onderzoekers gaan ervan uit dat de patiënt die resistente ESBL-bacterie heeft opgelopen door het eten van besmette kip. Daarmee lijkt voor het eerst een verband aangetoond.



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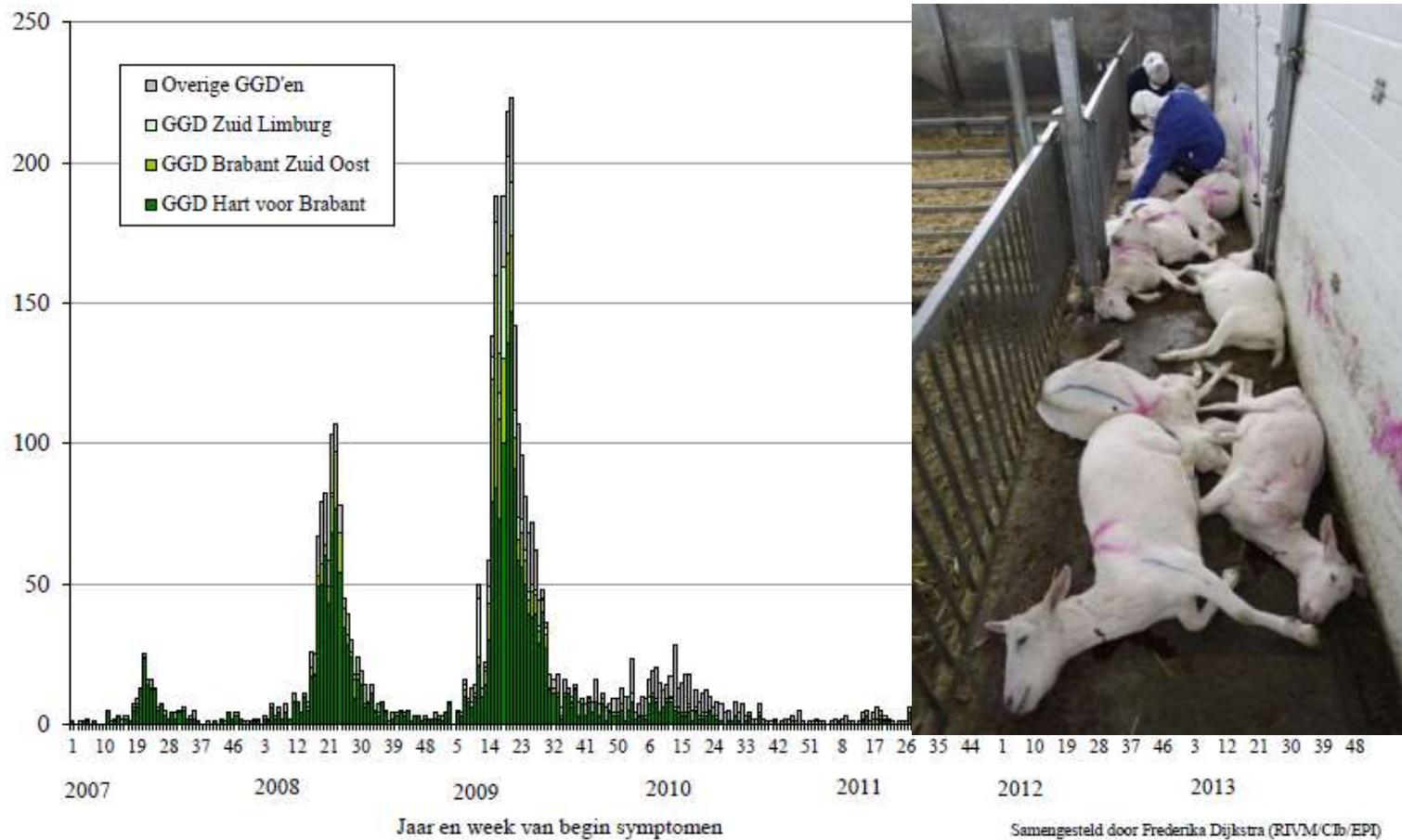
Window of opportunity (4): Q-fever outbreak (2007-2009)



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Window of opportunity (4): Q-fever outbreak (2007-2009)



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Exposure of the general public.....

- Newspapers, television,



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Dutch measures initiated to contain usage and resistance


- 2008: Covenant signed by the animal sectors and KNMvD (Dutch Association for Veterinarians)
 - Mandatory 20% reduction in 2011, 50% in 2013 and 70% in 2015 (reference to 2009 and based on sales data) set by government (April 2010).
 - Establishing an independent Veterinary Medicines Authority (SDa) (early 2010)
 - All antimicrobial use on farms transparent by end of 2011 (requested by government)
 - 1 to 1 relationship between a vet and a farmer (farm health and farm treatment plan)
 - Discussion about prescribing and selling of antimicrobials by veterinarians
-



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Report of the Dutch Health Council



HOME
NIEUWS
ADVIEZEN
OVER ONS
JONGGR

Optimale gezondheidszorg
Preventie
Gezonde voeding
Gezonde leefomgeving
Gezonde arbeidsomstandigheden
Innovatie en kennisinfrastructuur


Health Council of the Netherlands

Antibiotics in food animal production and resistant bacteria in humans

Status
Gepubliceerd
31 augustus 2011

[Download publicaties](#)

- Ban Critically Important Antimicrobials for human use (WHO-list) – cephalosporines, fluoroquinolones
- Redefine 1st, 2nd, 3rd choice antimicrobials
- Reconsider *formularia*
- Only 1st choice antimicrobials on farm (temporary exceptions for 2nd); 3rd choice only after bacteriological analysis and susceptibility testing.



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Implementation of the Health Council recommendations and other new legislation

- Ban on prophylactic use (2011)
- Antimicrobials administered exclusively by veterinarian, unless farmer complies with strict conditions
- Susceptibility testing mandatory for 3rd choice antimicrobials (3rd, 4th gen. cephalosporins and fluoroquinolones)



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Netherlands Veterinary Medicines Authority(SDa)

- Established in 2010
- Independent body to:
 - Define targets for AM-usage in pigs, cattle and poultry
 - Report annual trends
 - Identify frequent or mis-users/prescribers
 - Assess improvement plans for each animal sector
- How the SDa is doing the work:
 - Yearly data from all farms (appr. 42,000) to SDa
 - Data analysis
 - Define and specify benchmarks by animal species

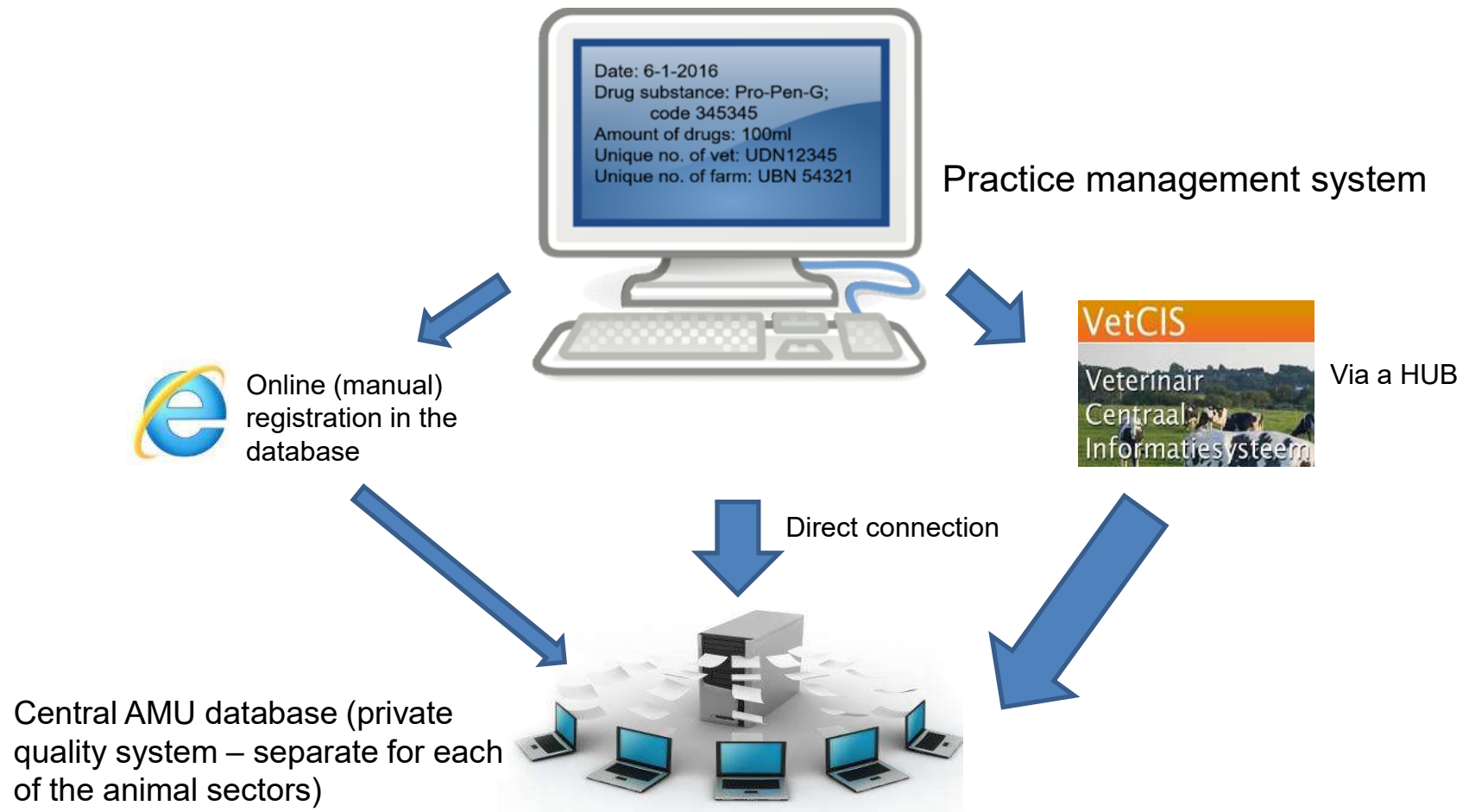
www.autoriteitdiergeneesmiddelen.nl



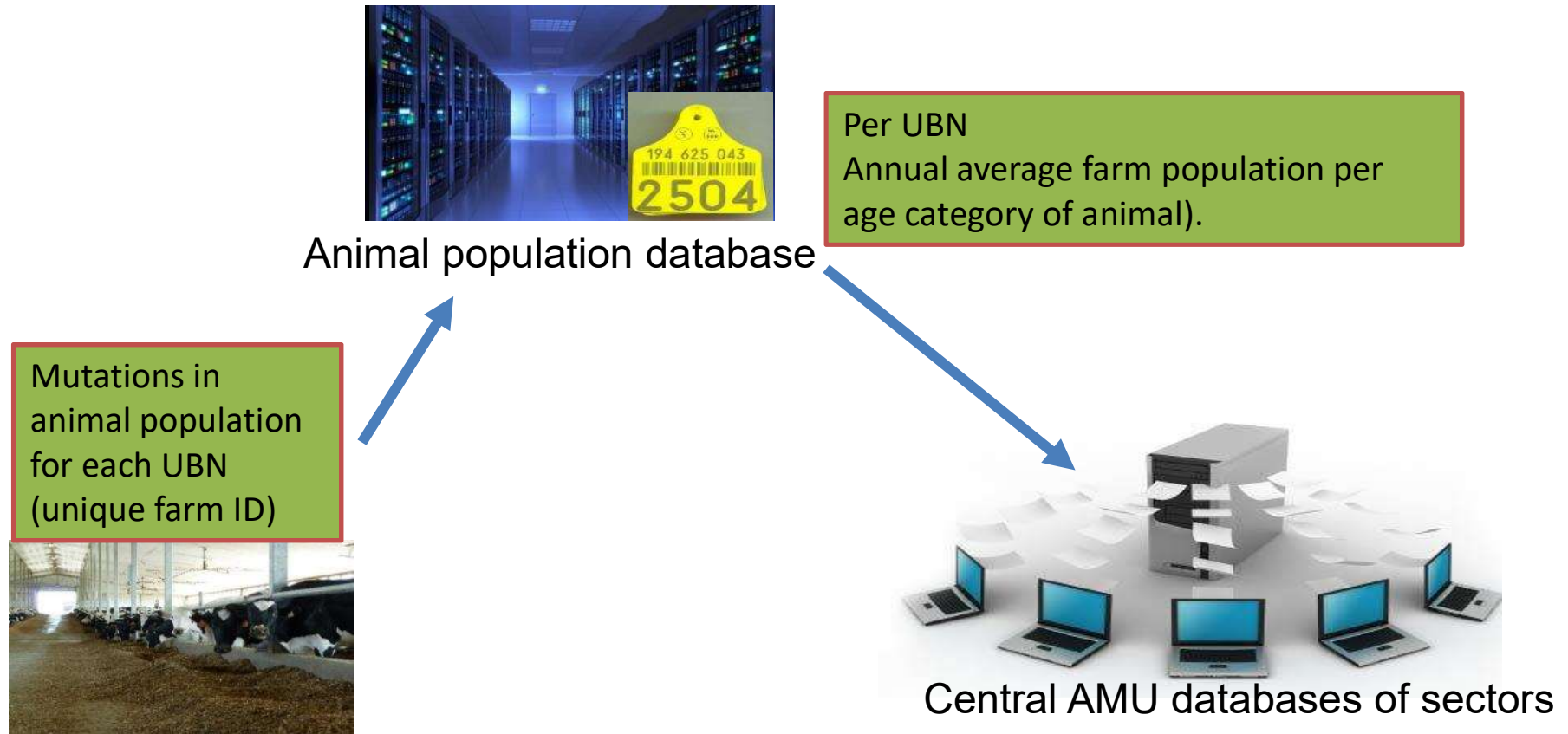
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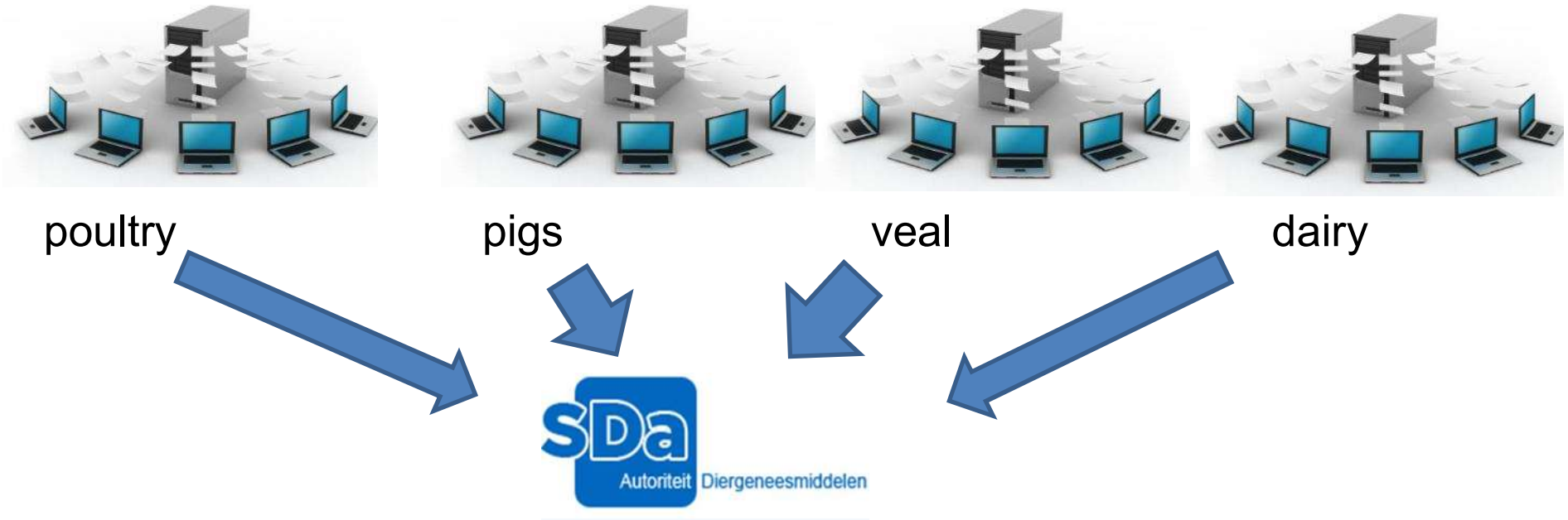
Data processing: AMU numerator (prescription data)



Data processing: AMU denominator (number of animals per farm)



Data processing: data from vet practice to SDa



SDa receives all AM delivery data and # animal data for ~42,000 livestock farms anonymized from four major sectors (>850,000 records) through animal sectors (quality systems)



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Three outcomes of data analysis by SDa

Animal Defined Daily Dose (DDDA) =
treatable weight (kg)/animals at risk (kg)

1. Monitoring trends: **DDDA_{NAT}** per sector
2. Benchmarking: **DDDA_F** at farm level
3. Benchmarking: **DDDA_{VET}** per veterinarian

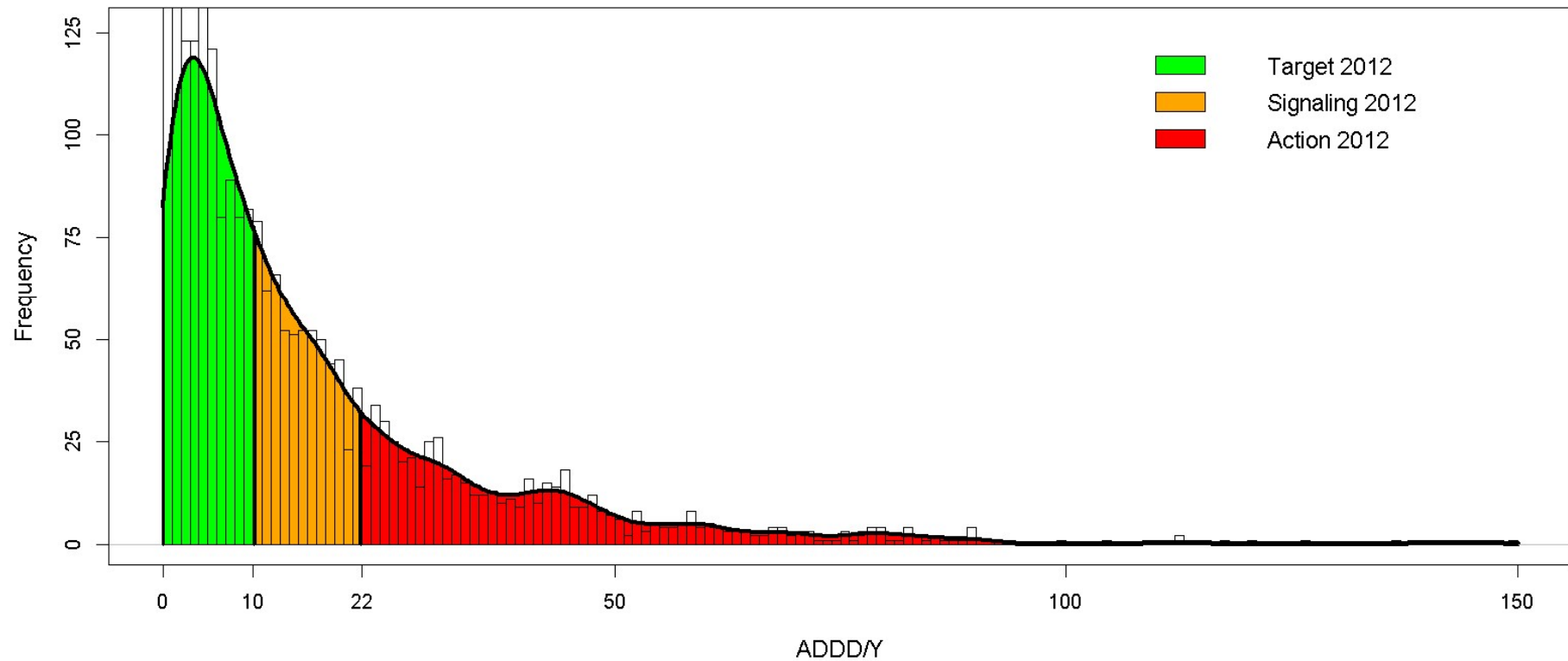


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Benchmarkvalues sows and piglets 2012 (example)



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Sows benchmark values 2012 (example)

**> 13
ADDD/Y**

**Immediate measures required which reduce use
of antimicrobials immediately**

10 - 13

Use of antimicrobials requires additional attention

< 10

No immediate action required

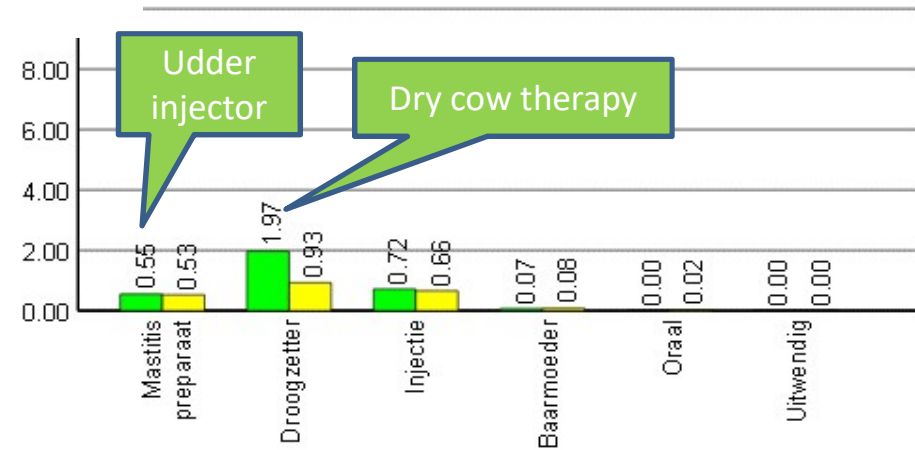
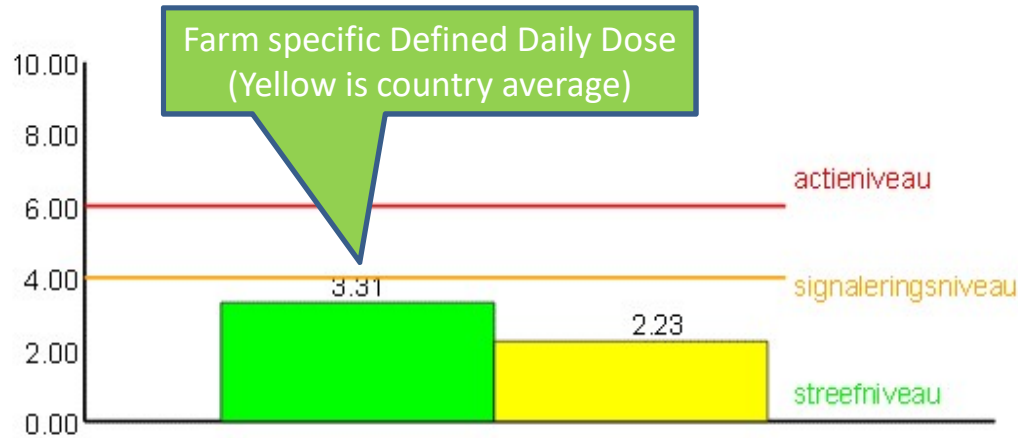


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Quarterly antibiotic use report to the farmer



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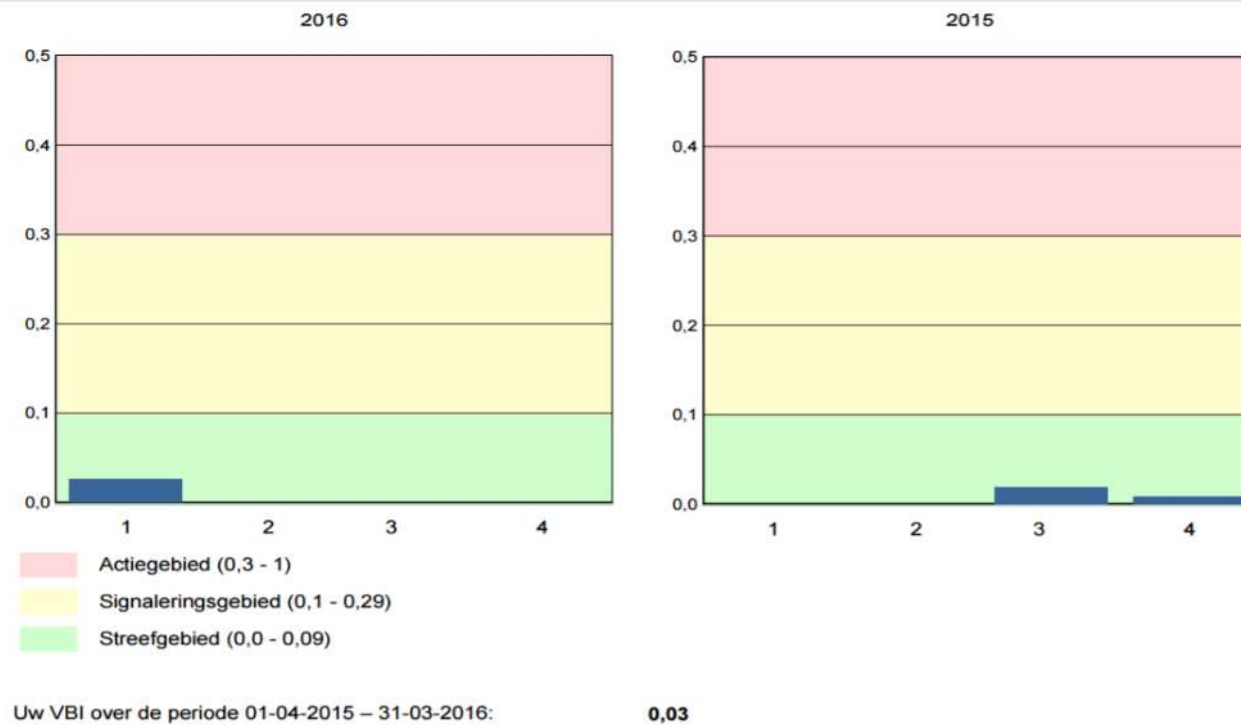
Veterinarians: differences in prescription pattern

- 5-20-fold differences (20 = exceptional)
- Veterinary Benchmark Indicator (VBI)

	I
Action zone	> 0,30
Signaling zone	0,10 – ≤ 0,30
Target zone	< 0,10



Quarterly report of VBI to the individual vet

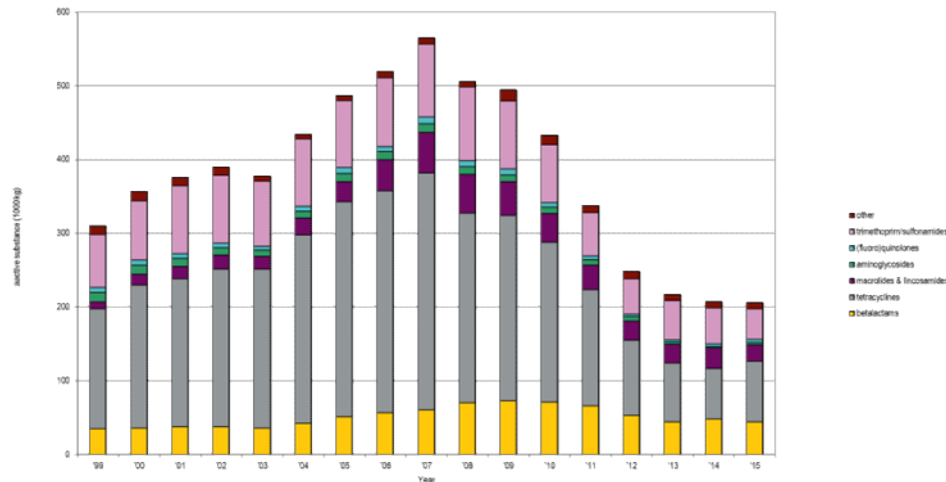


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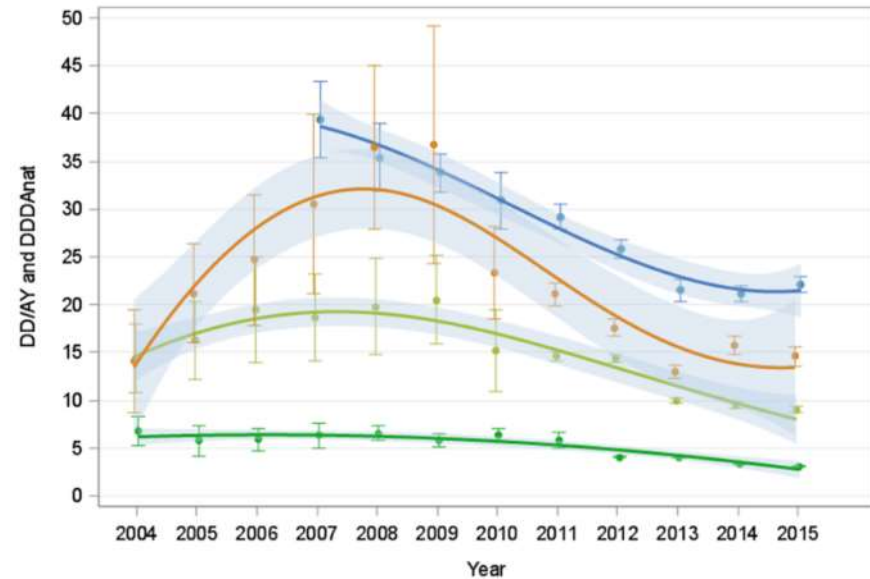
Effect of policy

Sales data of antimicrobials in the Netherlands



- ~ 65% reduction (2007-2015)
- 58.4% reduction in 2015 to reference year 2009
- Fluoroquinolones and 3rd/4th-gen cephalosporines usage reduced to a minimum
- 68% reduction in use of colistin (2011-2015)

DDD/AY for different sectors

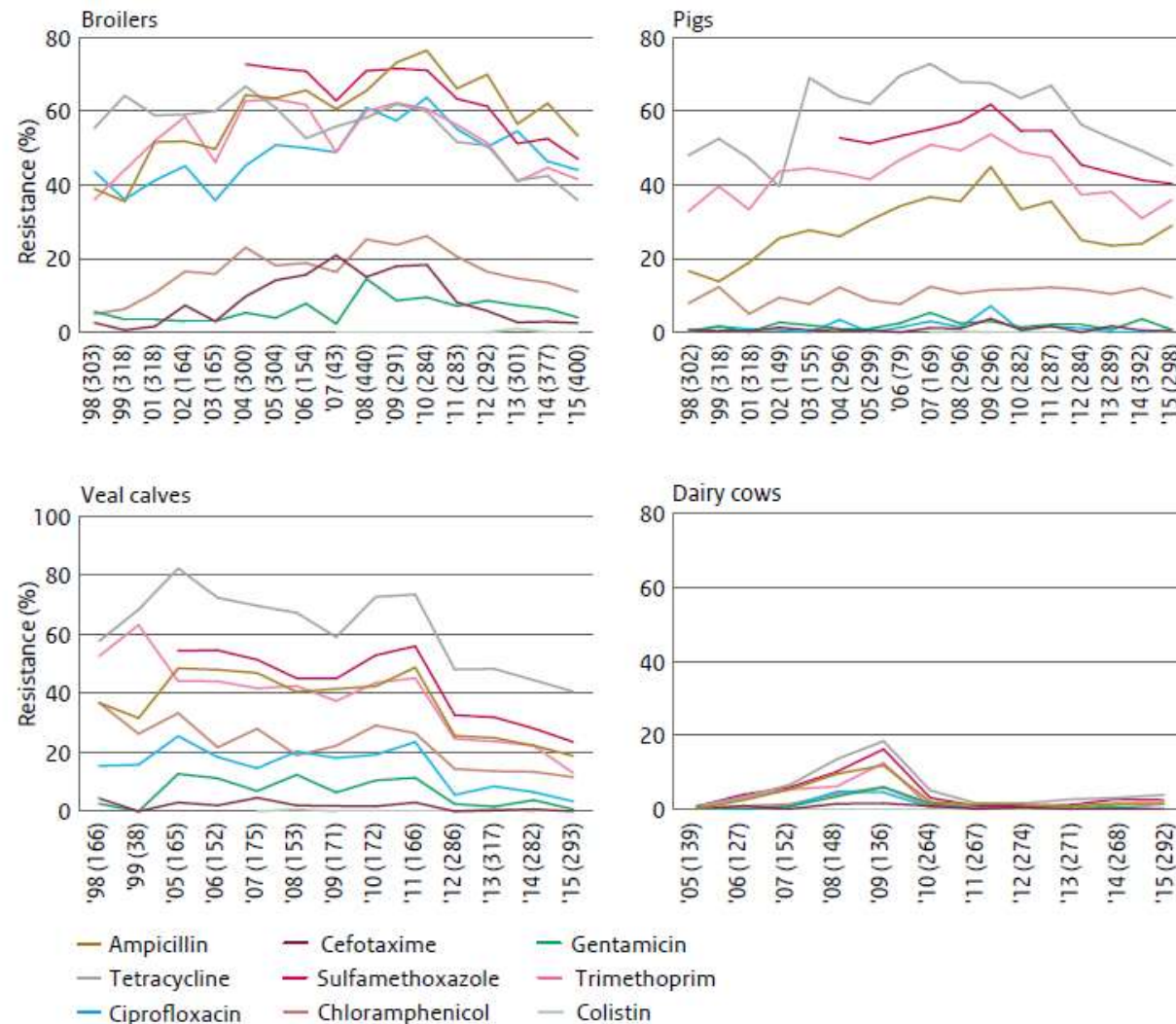


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Surveillance of antimicrobial resistance in commensal *E. coli*

Figure Eco01 Trends in resistance (%) of *E. coli* isolated from broilers, slaughter pigs, veal calves and dairy cattle in the Netherlands from 1998-2015.



Critical success factors

- Public pressure
- All parties involved (stakeholders)
- Clear targets defined by the government
- Measures initiated by well organised private animal production sectors and veterinary association; implementation by private sectors with using their production chain quality systems; enforcement of law by government
- Usage fully transparent: from > 42,000 farms DDDAs available
- Independent institution (SDa) accepted by all parties involved



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Diversity in the world.....

- AMR and AMU
- Residues
- Counterfeit drugs
- Overuse vs. lack of availability of (good quality) drugs
- Over the counter availability: imprudent self medication
- Legislation and enforcement
- Knowledge
- Lack of veterinary services (#vets/#animals)
- Housing conditions, biosecurity, climate



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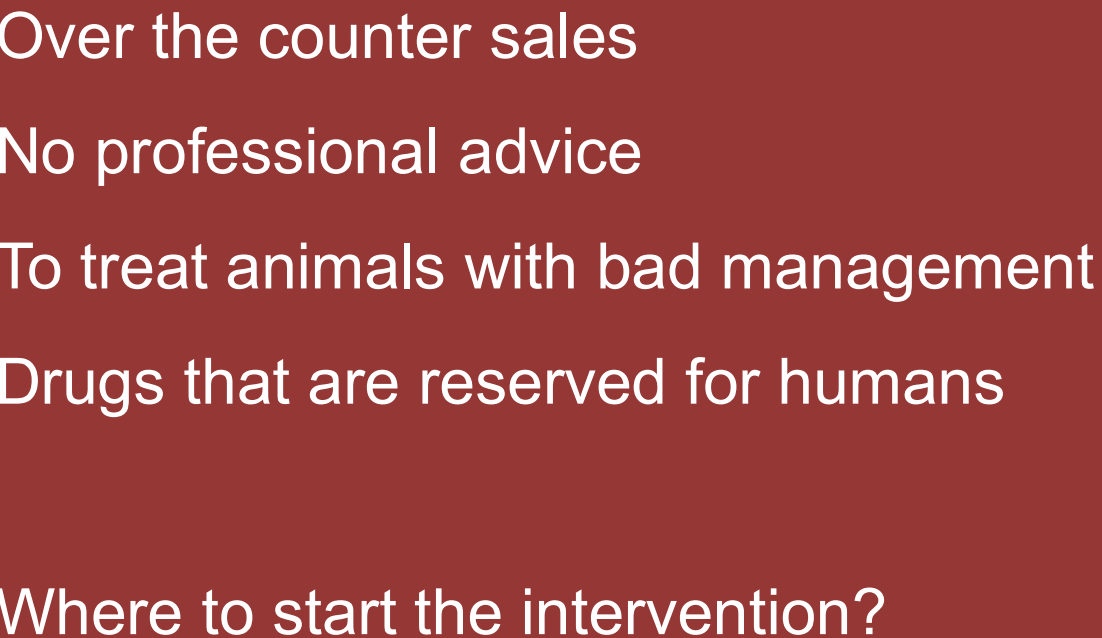
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- 
- Over the counter sales
 - No professional advice
 - To treat animals with bad management
 - Drugs that are reserved for humans
 - Where to start the intervention?



Conclusions and future

- *Window of opportunity* used for action
- Facts => public awareness/pressure => politics => action => facts
- Huge reduction in use followed by reduction in resistance in animals
- Effect in humans?
- Low-hanging fruit has been harvested
- Animal husbandry without antimicrobials is impossible – what is acceptable usage? (welfare, economics)
- Include other sectors (companion animals, rabbits, horses...), focus on the “red” farms
- Preparedness for carbapenem resistance in the food chain



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EFFORT: Ecology from Farm to Fork Of microbial drug Resistance and Transmission (2014-2018)

Objectives

- Understanding the epidemiology of AMR in the food chain
- Understanding the ecology of AMR in the microbial communities
- Understanding the relative contribution of the exposure routes of AMR from animals to humans
- Understanding the economic impact and animal welfare aspects of AMR in the food chain

- Sampling in 9 European countries (pigs and poultry) + smaller sectors in a selection of countries



Output of EFFORT

- AMR: comparison between phenotypic resistance (*E. coli*) and metagenomics (genes)
- Exposure of AMR to humans through food of animal origin
- Relation AMU and farm management – AMR
- Environmental contamination with AMR organisms
- Effect (and feasibility) of interventions on AMR
- Relation AMU and economic and welfare aspects
- Knowledge about successful clones (plasmids)



Role of the Netherlands (EU-presidency 2016)



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"The Triumph of Death" by Flemish painter Pieter Breugel in his mid-16th-century reflects the social upheaval and terror that followed plague.

Image courtesy Museo del Prado, Madrid

