Reduction in Antimicrobial Use in Animals – Do We See Effects on Antimicrobial Resistance?

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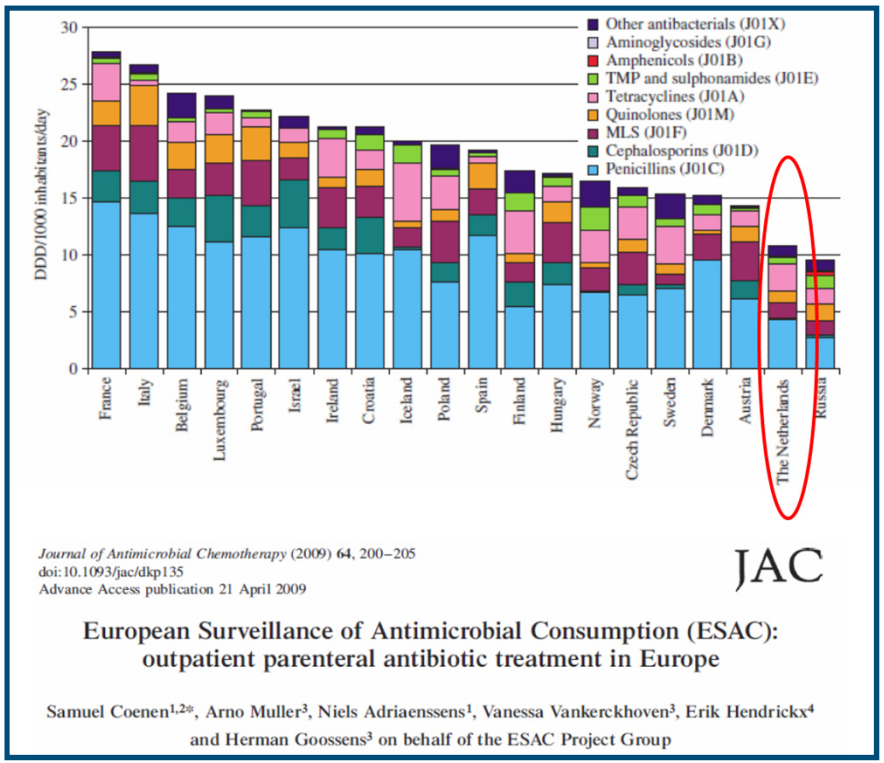
Antibiotic usage in humans and animals in Europe



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 Muller[3], Niels Adriaenssens[1], Vanessa Vankerckhoven[3], Erik Hendrickx[4] and Herman Goossens[3] on behalf of the ESAC Project Group

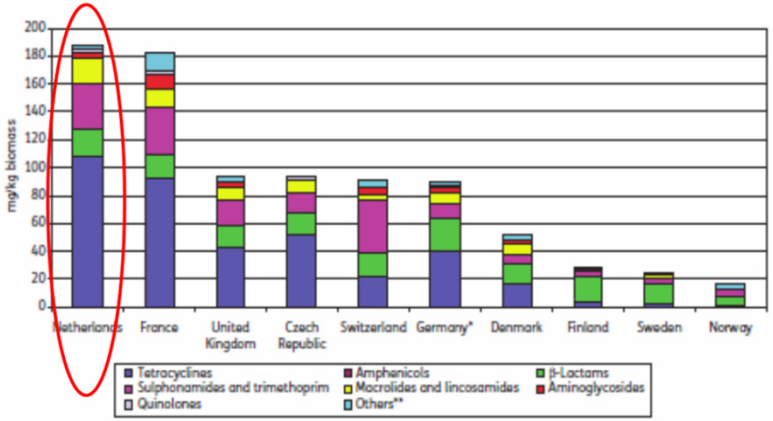


Figure 1. Amounts, in mg, of veterinary antibacterial agents sold in 2007 per kg biomass of pig meat, poultry meat and cattle meat produced plus estimated live weight of dairy cattle. *2005 data. **The substances included vary from country to country.

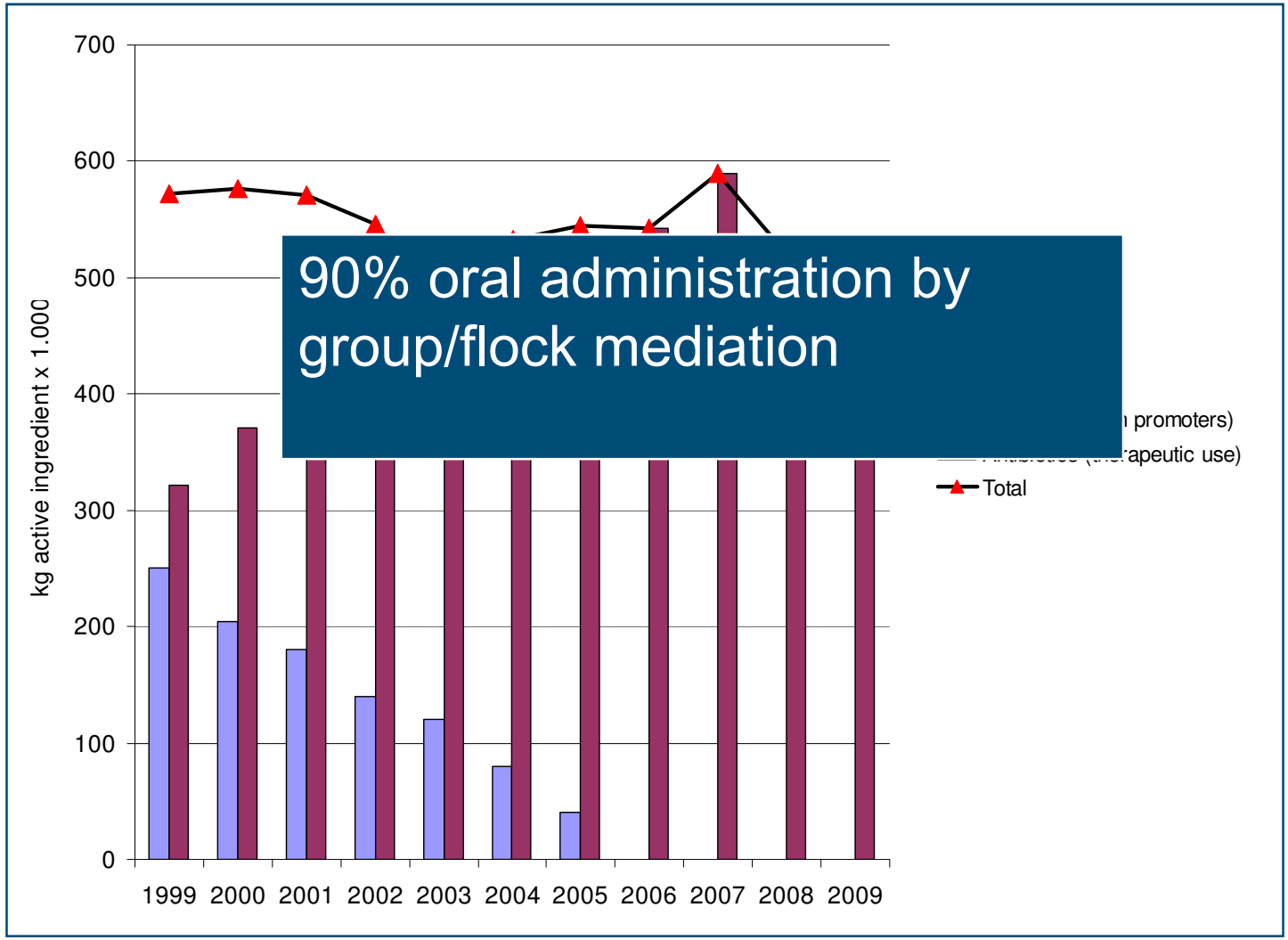
J Antimicrob Chemother 2010; **65**: 2037–2040
doi:10.1093/jac/dkq247 Advance Access publication 29 June 2010

Journal of Antimicrobial Chemotherapy

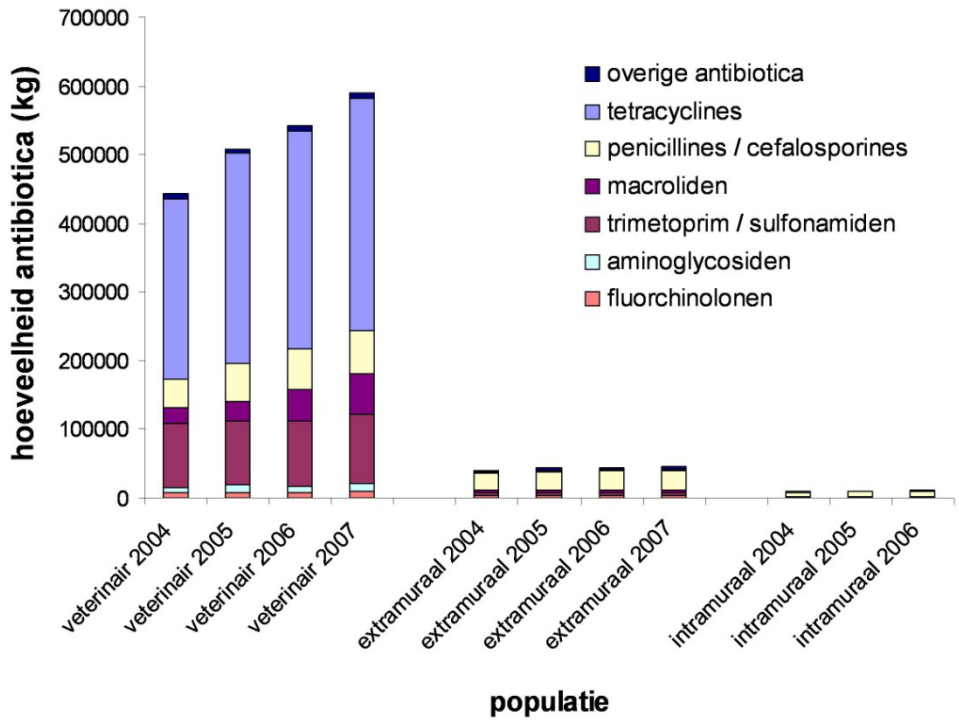
Comparison of the sales of veterinary antibacterial agents between 10 European countries

Kari Grave*, Jordi Torren-Edo and David Mackay

Antibiotic use in animals in NL (Source FIDIN)



Animal versus human use in kg



van Geijlswijk, et al, TvD, 2009

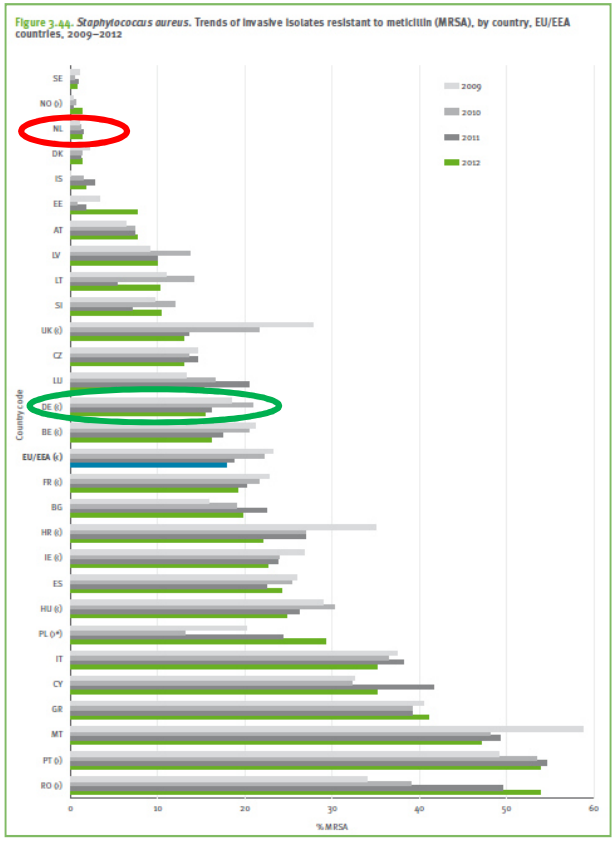
What does this mean

- Dutch food-producing animals are an ideal environment for multidrug resistant organisms
  - Risk??
    - Animal health?
      - Yes, if they cause infections
    - Public health?
      - Yes if:
        - » **Food-borne pathogens**
        - » **Zoonotic organisms**
        - » **Transferable genes**

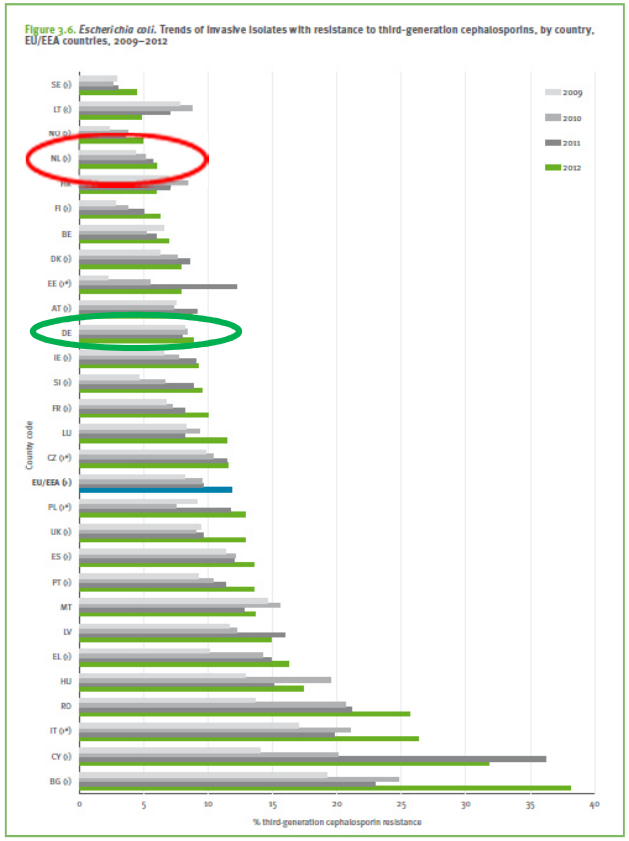
MRSA, ESBLs

EARSS-net 2012 report (ECDC)

MRSA



ESBLs



Live Stock associated MRSA (ST398)

- Many pigs and veal calves carry LA-MRSA in their noses
(poultry, horses, companion animals…)

- Increased risk for carriership of farmers and vets
  - Contact infection, no human to human spread,
  - Food products not considered to be an important source

- Global problem

- In NL, measurable effects in human health care
  - Infections
  - Increased costs

ESBL-Prevalences in the Netherlands

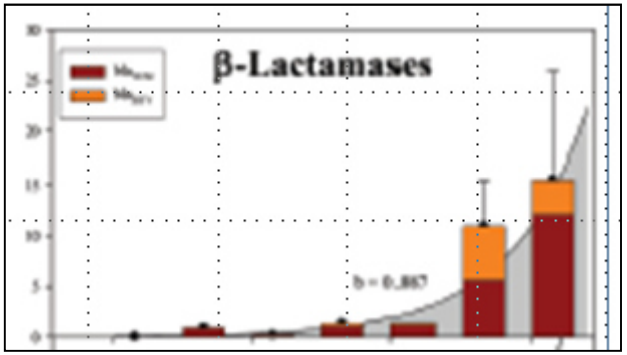
> 50% in (herds) animals

- Broilers (100%)
- Layers
- Veal calves
- Fattening pigs
- Turkeys
- Dogs
- Cattle 41%

Is poultry the source or part of the problem??

Environment

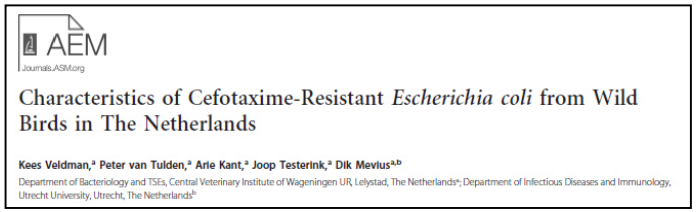
- Soil
- Surface water



Knapp, Dolfing et al. 2009

13% birds (waders)

ESBL-positive


AEM

Journals.ASM.org

Characteristics of Cefotaxime-Resistant *Escherichia coli* from Wild Birds in The Netherlands

Kees Veldman,[a] Peter van Tulden,[a] Arie Kant,[a] Joop Testerink,[a] Dik Mevius[a,b]

Department of Bacteriology and TSEs, Central Veterinary Institute of Wageningen UR, Lelystad, The Netherlands[a]; Department of Infectious Diseases and Immunology, Utrecht University, Utrecht, The Netherlands[b]

“Convenants” (MoA) signed by “all” stakeholders in livestock production in December 3, 2008

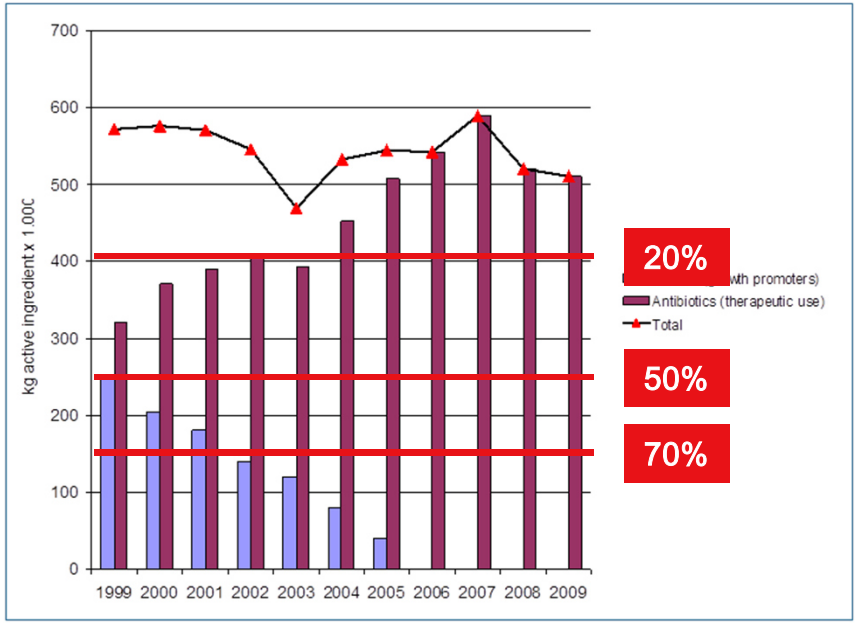
- Control of antimicrobial resistance by
  - One-in-One relation between farmer and vet
    - Better options to control responsible, prudent use of antibiotics
    - Responsibilities for prescription and administration better defined
  - Full transparency in antibiotic use
    - All antibiotic use registered

Reduction targets defined in 2010

- 2010 KNMvD
  - Proposed 20% reduction
- Debate in parliament about ESBLs in poultry
  - Mandatory targets defined (20% in 2011 and 50% in 2013) in addition to the MoA's
  - (70% 2015)

Reduction targets were based on sales data

- 20% reduction indicated a target of 400 tons in 2011
- 50% indicated a target of 250 tons in 2013
- 70% in 2015 (app. 150 tons) was defined as target for livestock production as a whole



FIDIN

Independent control institute essential

Netherlands Veterinary Medicines Authority (SDa)

Spring 2011

- Tasks
  - Define and specify reduction targets by animal species based on DDDA/Y
  - Analyse data
  - Report publically

Table 2. Quantitative benchmark indicators for antibiotics usage (ADDD/Y) in broilers, sows/piglets, fattening pigs, cattle and veal calves for 2013. Green means 'no immediate action required'; orange means 'high usage, requires additional attention'; and red means 'immediate action required'.

	Benchmark Indicators for Individual Farms (AADDD/Y)		
Animal Type	Target Level 2012 - 2015	Signaling Level 2013	Action Level 2013
Cattle			
- Dairy cattle	0 - 3 (4#)	> 3 - 6 (> 4 - 7#)	> 6 (7#)
- Suckler cows	0 - 1	> 1 - 2	> 2
- Beef bulls	0 - 1$	> 1 - 2$	> 2$
- Rearing cattle	0 - 1$	> 1 - 2$	> 2$
Veal calves			
- White veal calves	0 - 23	> 23 - 39	> 39
- Rosé starter	0 - 67	> 67 - 110	> 110
- Rosé fattening	0 - 1	> 1 - 6	> 6
- Rosé combination	0 – 12	> 12 - 22	> 22
Pigs			
- Sows and piglets	0 - 10	> 10 - 22	> 22
- Fattening pigs	0 - 10	> 10 - 13	> 13
Broilers			
- ADDD/Y	0 - 15	> 15 - 30	> 30
- *Treatment days**	*0 - 17**	*> 17 - 34**	*> 34**

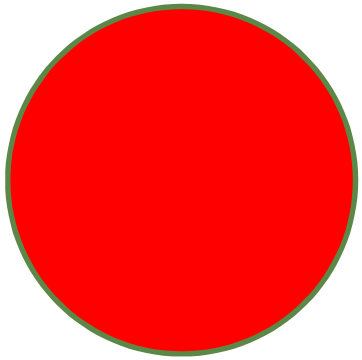
The figure between parentheses is the value determined on the basis of the 'LEI' methodology.

* Expressed as the number of treatment days per year.

$ Indicative values; will be adjusted in the autumn of 2013 or 2014 as necessary.

SDa 2013

BENCHMARKINDICATORS

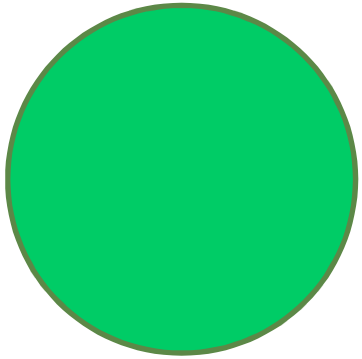


ACTION LEVEL

Direct measures necessary to reduce antibiotic usage

SIGNALING LEVEL

Please be aware



TARGET LEVEL

No direct measures necessary to reduce antibiotic usage

SDa Autoriteit Diergeneesmiddelen

Report of the Health Council Committee

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HOME
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ADVIEZEN
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JONGGR

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

Antibiotica in de veeteelt en resistente bacteriën bij mensen

Status
Gepubliceerd
31 augustus 2011

Download publicaties

Om het probleem van de toenemende resistentie van bacteriën tegen antibiotica te keren, moeten bepaalde soorten antibiotica gereserveerd worden voor menselijk gebruik. Deze middelen zouden uitgesloten moeten worden van gebruik in de veeteelt, om overdracht van resistente bacteriën van dier naar mens tegen te gaan. Dit schrijft de Gezondheidsraad in zijn advies Antibiotica in de veeteelt en resistente bacteriën bij mensen dat de raad vandaag aanbiedt aan de minister van VWS en de staatssecretaris van EL&I.

New targets added

No use in animals of all new antibiotics:
Carbapenems, tigecycline, daptomycin, oxazolidones, mupirocin etc.

Fluoroquinolones and 3rd/4th generation Cephalosporins:
No use in animals unless demonstrated that no alternative treatment options are available

Colistin, beta-lactams, aminoglycosides

All classified as second choice antibiotics

Only allowed unless appropriate diagnostics by vet

Summarizing the reduction targets

- Reduction in sales (20-50-70%)
- Quantitative targets defined by SDa in DDDA/Y
  - Specified by animal species
- Targets aimed at the quality of antibiotic use
  - Zero ADDD/Y for FQ and 3rd/4th gen Cephs
  - Less group treatments
  - No preventive use (EU-regulations implemented)
  - More selective use of dry cow treatments

Measures initiated by the Royal Veterinary Association (KNMvD)

- Re-definition of 1st, 2nd and 3rd choice ABs
- Update formularies
  - Mandatory basis for custom made treatment plan for each farm
  - Health control plan for each farm
  - Implemented in the law (UDD-rule 2013)

Empiric use, allowed to be present on farms

Tabel 1. Omschrijving van de definities voor de keuzevolgorde mogelijkheden voor het voorschrijven van antimicrobiële middelen.

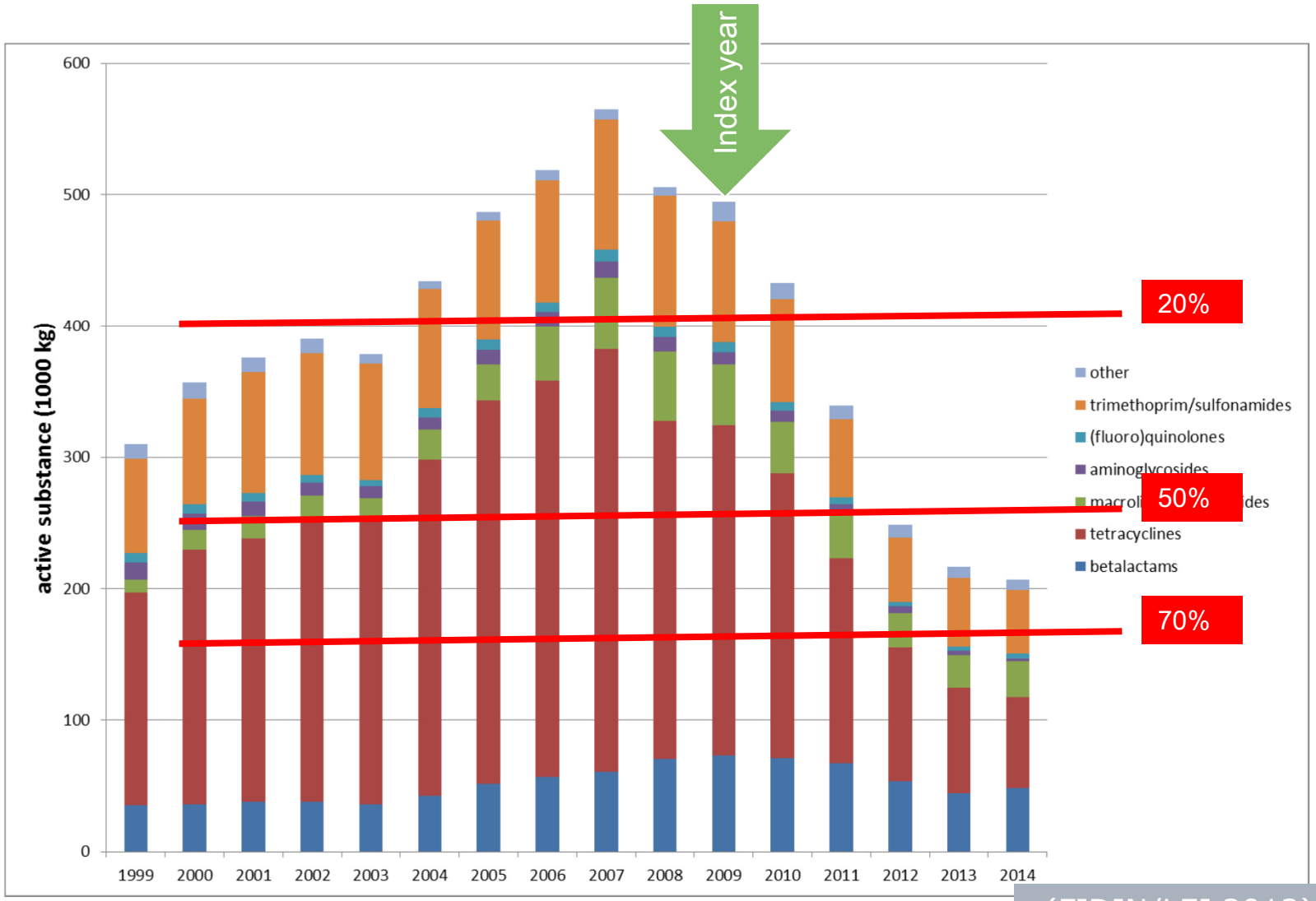
Indeling	Omschrijving
Eerste keuze	Empirische therapie met antimicrobiële middelen die werkzaam zijn tegen de indicatie en geen specifiek negatief resistentie inducerend effect hebben volgens de huidige inzichten. Deze middelen kunnen in een bedrijfsbehandelplan opgenomen worden.
Tweede keuze	**Nee tenzij**, waarbij de noodzaak voor toediening nader wordt onderbouwd. Dat kan o.a. op basis van gevoeligheid van de verwekker, opgebouwde patiënt- of bedrijfshistorie t.a.v. voorkomen van resistentie in dierpathogenen, of klinische noodzaak indien een bacteriologisch onderzoek niet mogelijk is. Deze middelen kunnen slechts bij uitzondering en meestal voor een gelimiteerde periode in een bedrijfsbehandelplan opgenomen worden.
Derde keuze	Dit zijn antimicrobiële middelen die van kritische belang zijn voor de humane gezondheidszorg. **Nee tenzij:** alleen voor individuele dieren als op basis van bacteriologisch onderzoek inclusief ABG is aangetoond dat er geen alternatieven zijn. Indien de gevoeligheidsbepaling niet mogelijk is, dient de dierenarts de keuze te onderbouwen (zie wetgeving en toelichting m.b.t. uitzonderingen op de verplichte gevoeligheidsbepaling). Deze middelen worden niet in een bedrijfsbehandelplan opgenomen, maar slechts in individuele gevallen voorgeschreven.

No unless:

Diagnosis and argumentation by vet (yellow)

No alternatives demonstrated (orange)

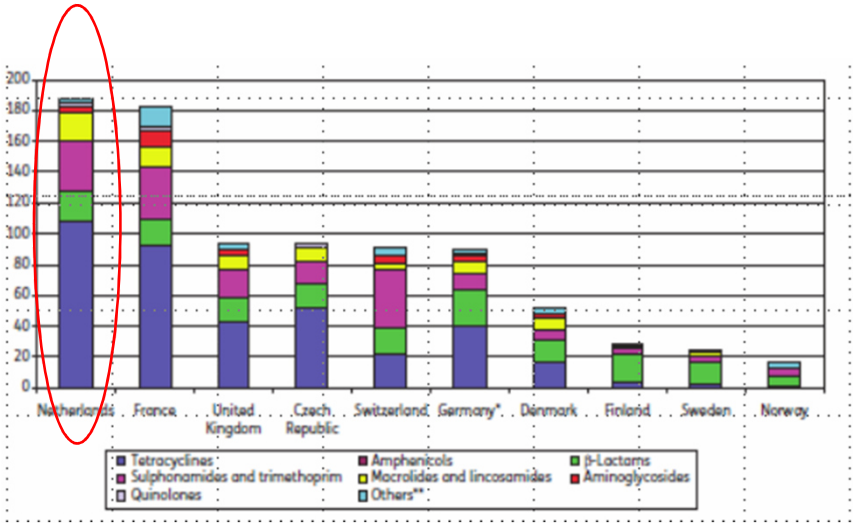
Effect on reduction in sales



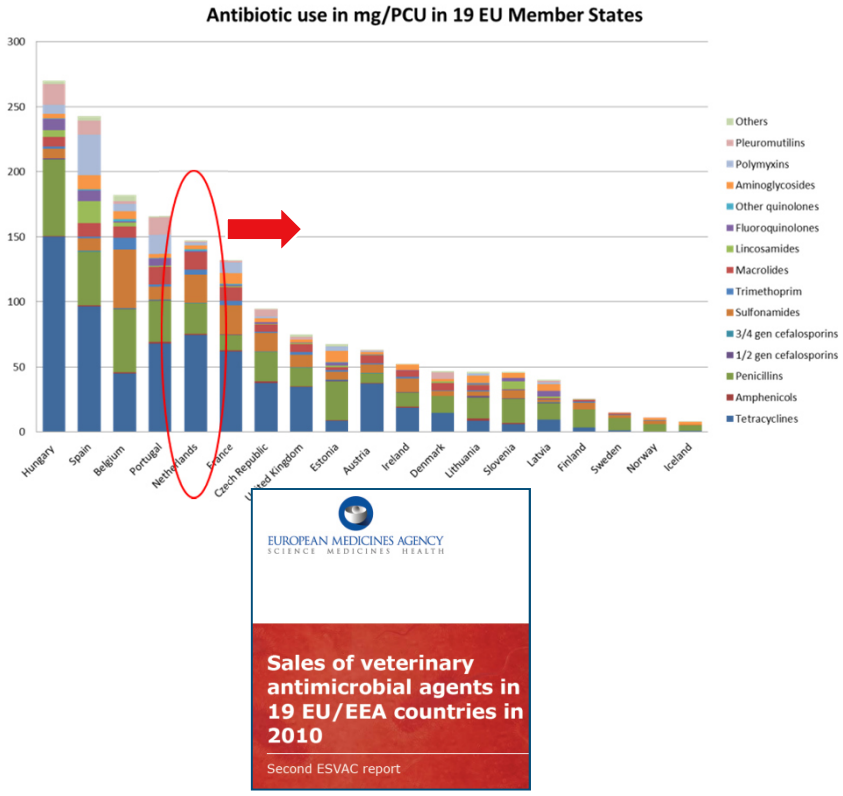
(FIDIN/LEI 2012)
www.maran.wur.nl

Sales of antibiotics for (mg) per kg biomass produced (PCU) in Europe

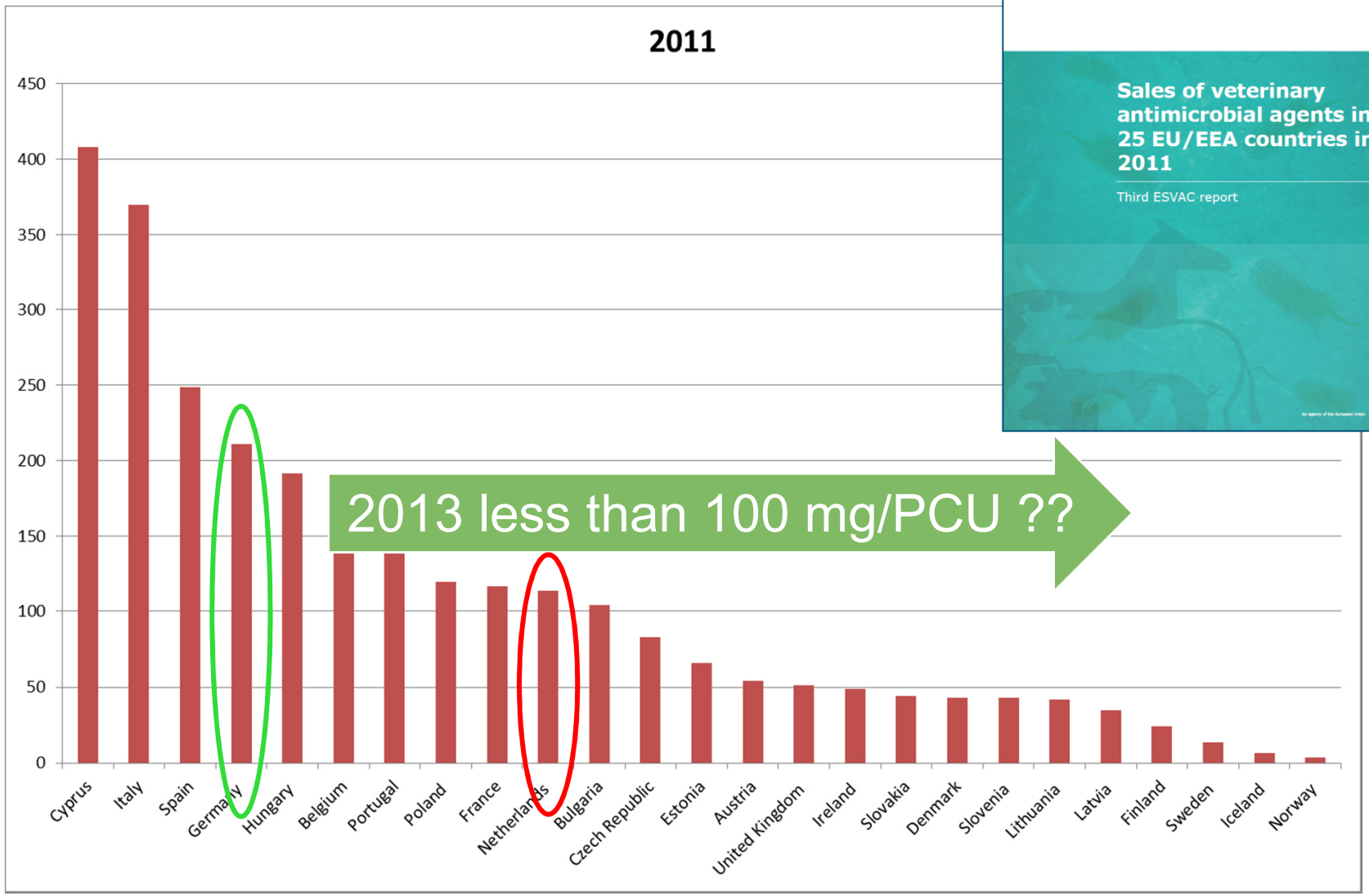
2007



2010



ESVAC 2011


2011
450
400
350
300
250
200
150
100
50
0
Cyprus
Italy
Spain
Germany
Hungary
Belgium
Portugal
Poland
France
Netherlands
Bulgaria
Czech Republic
Estonia
Austria
United Kingdom
Ireland
Slovakia
Denmark
Slovenia
Lithuania
Latvia
Finland
Sweden
Iceland
Norway
2013 less than 100 mg/PCU ??

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
Sales of veterinary antimicrobial agents in 25 EU/EEA countries in 2011
Third ESVAC report

2013 NL = 69 mg/PCU (ESVAC 2013)

Figure 21. Spatial distribution of overall sales of all antimicrobials for food-producing animals, in mg/PCU, for 26 countries, for 2013

Use in DDDA/Y in veal calves

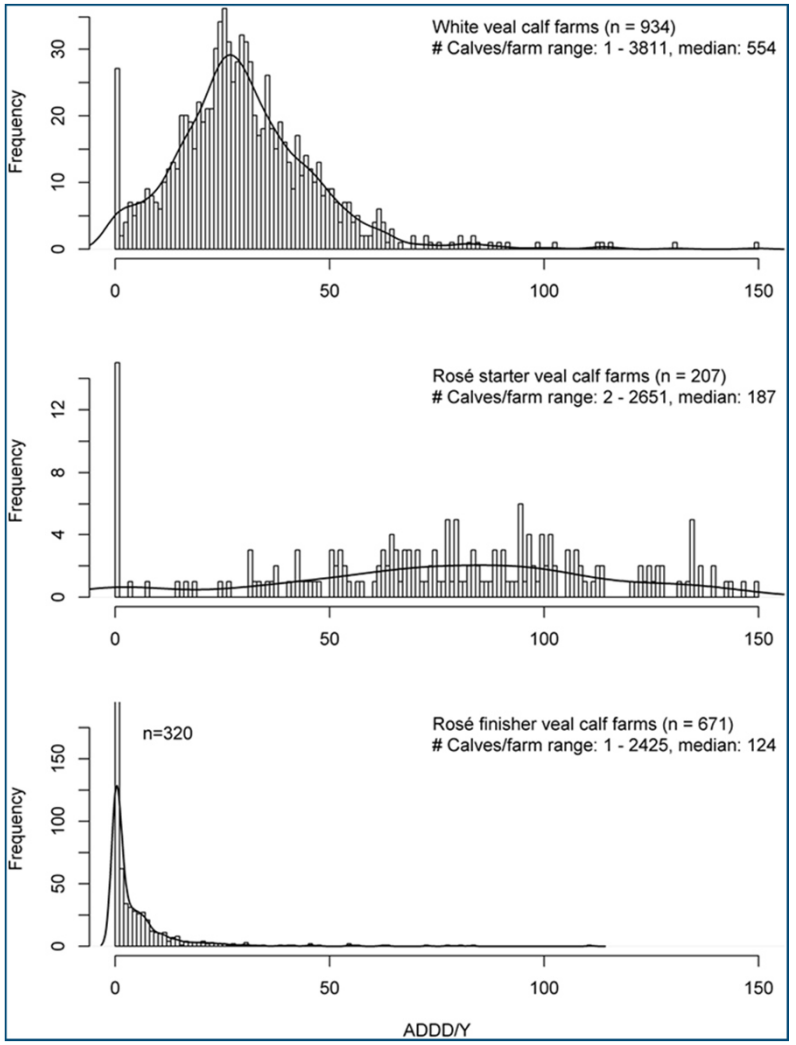
- Use data by livestock sector DDDA/y
  - Translation of sales to usage data

OPEN ACCESS Freely available online

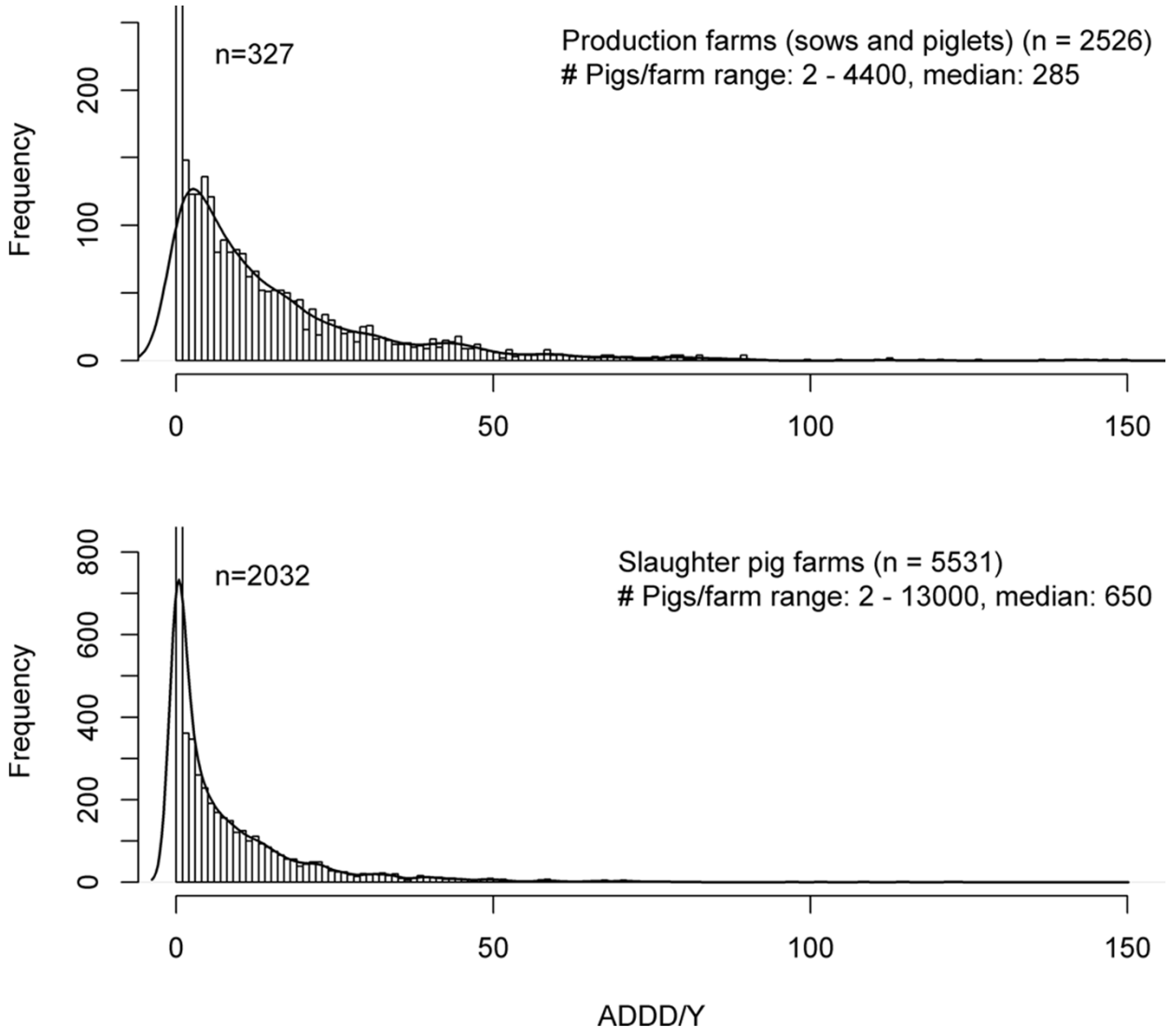
PLOS ONE

Consumption of Antimicrobials in Pigs, Veal Calves, and Broilers in The Netherlands: Quantitative Results of Nationwide Collection of Data in 2011

Marian E. H. Bos[1]*, Femke J. Taverne[2], Ingeborg M. van Geijlswijk[2], Johan W. Mouton[3], Dik J. Mevius[4,5], Dick J. J. Heederik[1], on behalf of the Netherlands Veterinary Medicines Authority (SDa)

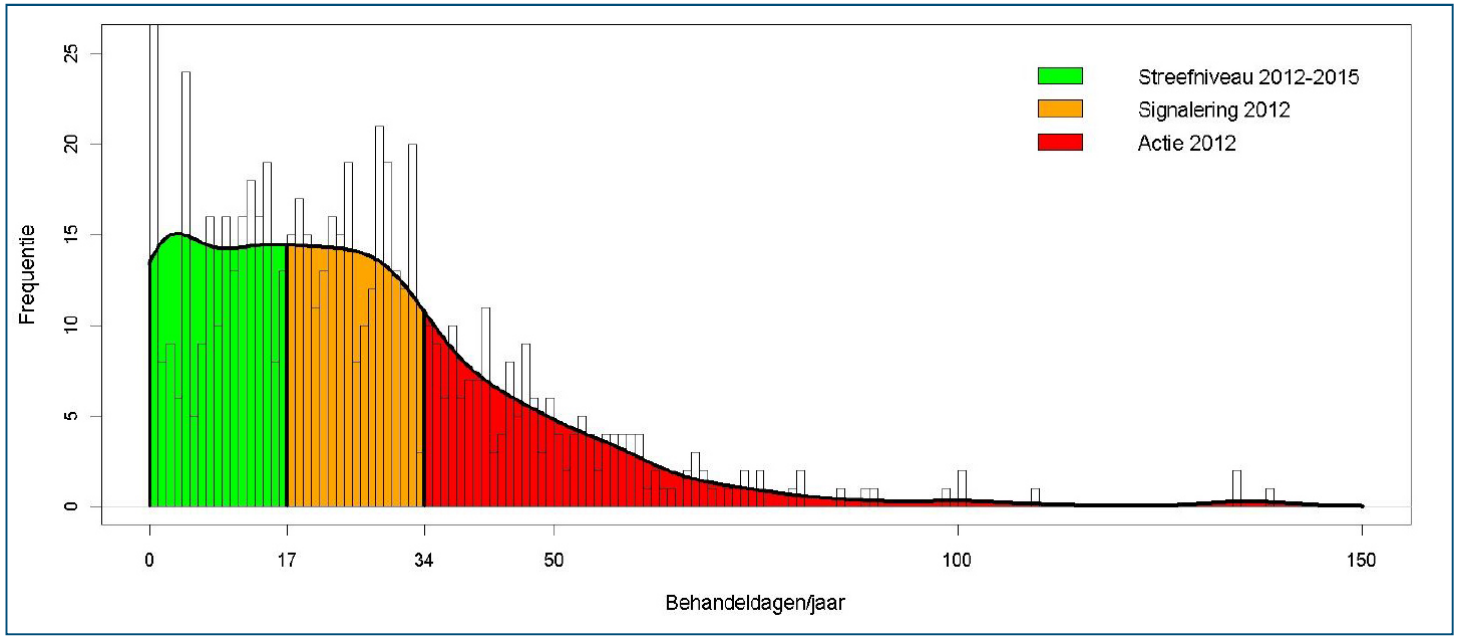


DDDA/Y Pigs

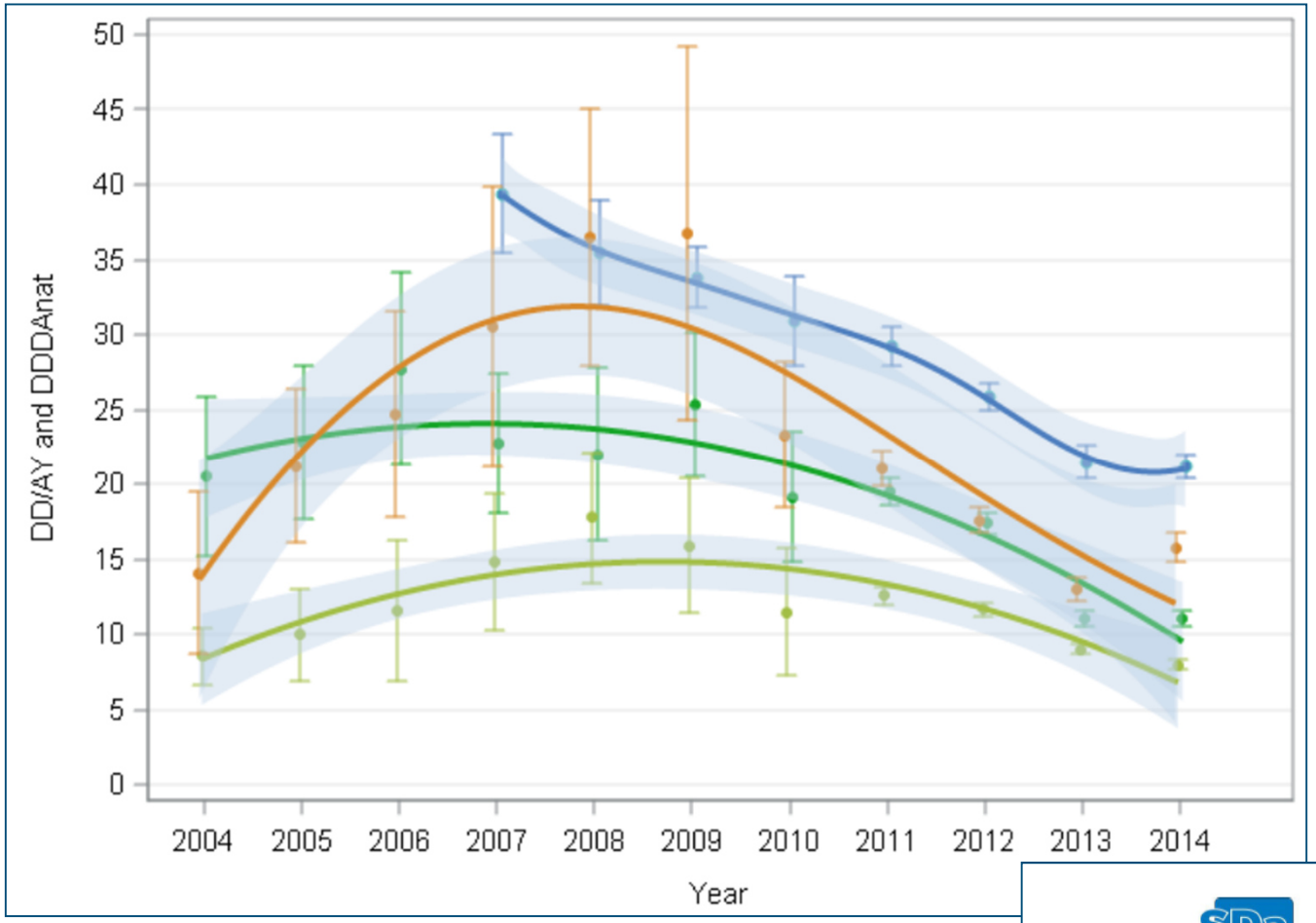

n=327
Production farms (sows and piglets) (n = 2526)
Pigs/farm range: 2 - 4400, median: 285
Frequency
0
100
200
0
50
100
150
n=2032
Slaughter pig farms (n = 5531)
Pigs/farm range: 2 - 13000, median: 650
Frequency
0
200
400
600
800
0
50
100
150
ADDD/Y

Broilers treatment days/Y

2011



Trends in DDDA/Ynat by livestock species

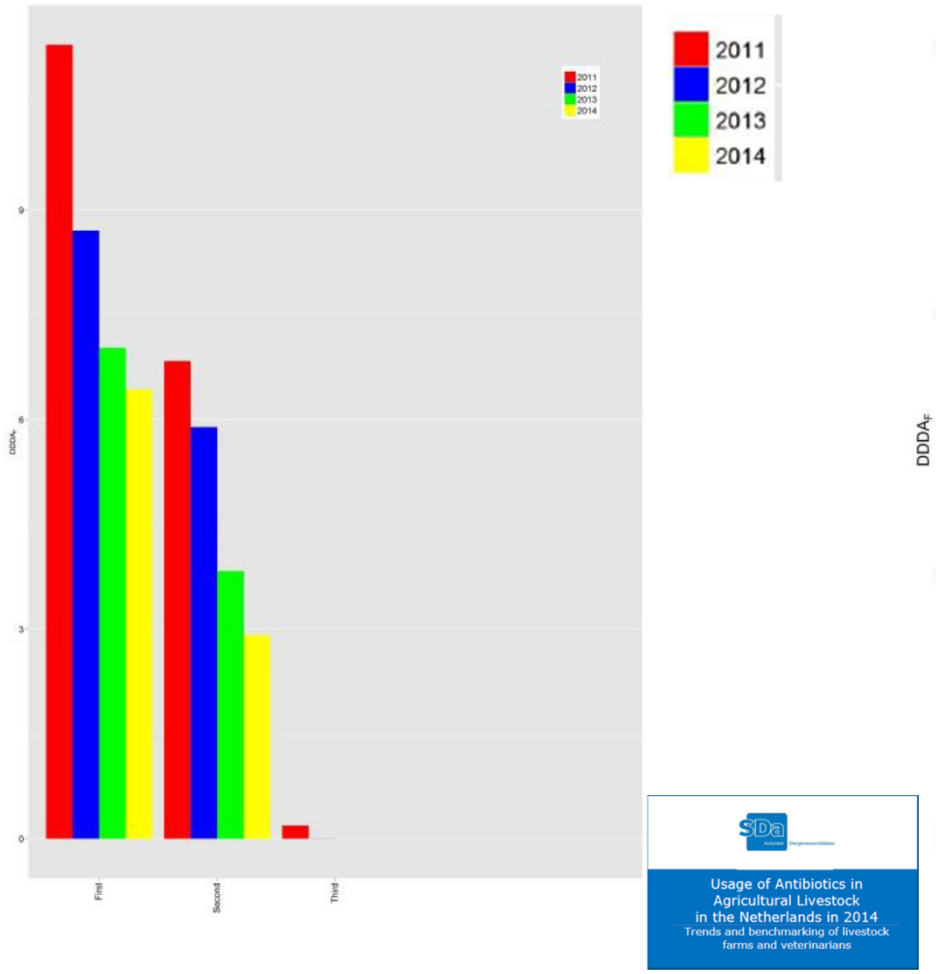


Veal farming sector (blue),
poultry farming sector (orange),
sow/piglet farms (dark green),
pig fattening farms (light green).

Usage of Antibiotics in Agricultural Livestock in the Netherlands in 2014
Trends and benchmarking of livestock farms and veterinarians

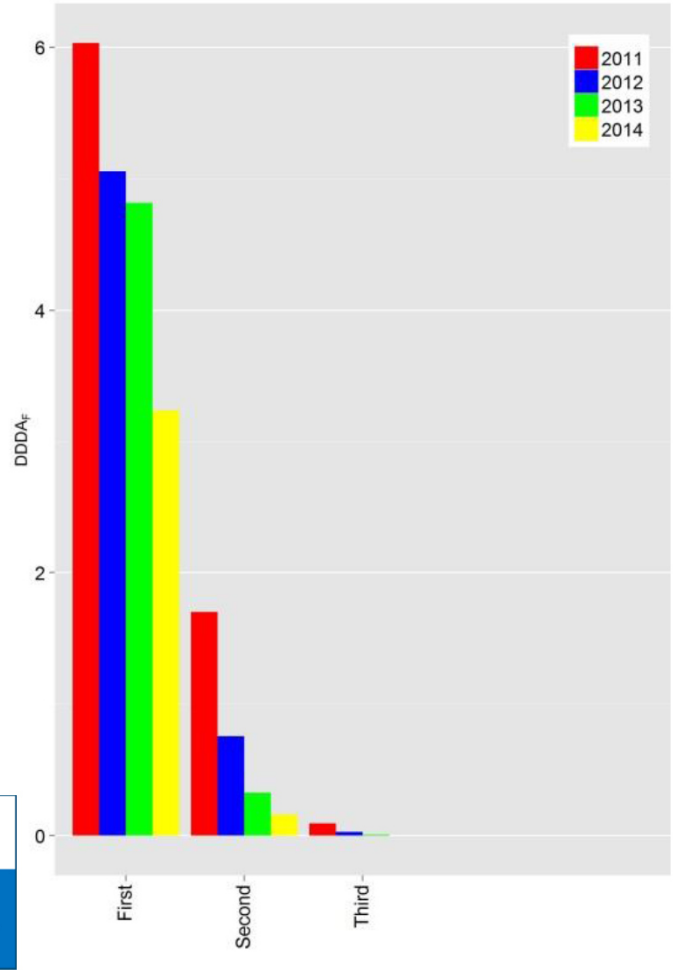
Trends in use of third-choice antibiotics: fluoroquinolones and 3rd/4th generation cephalosporins from 2011 to 2014

Pig production farms

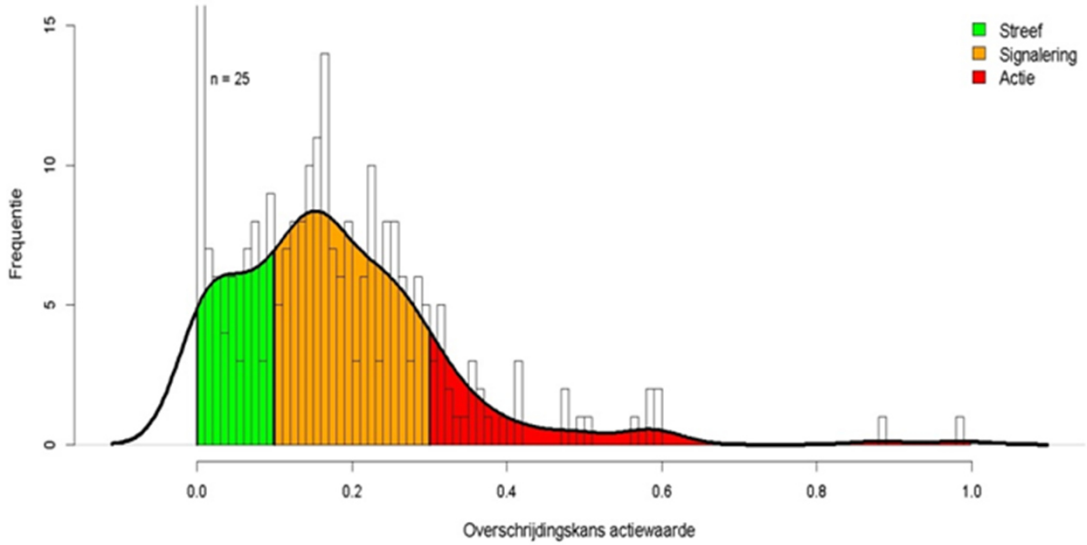


Usage of Antibiotics in Agricultural Livestock in the Netherlands in 2014
Trends and benchmarking of livestock farms and veterinarians

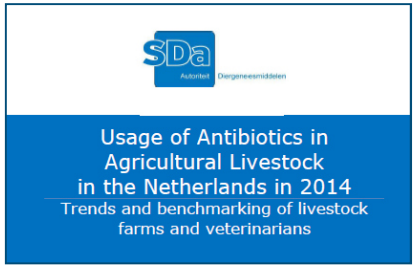
Rosé veal



Bechmarking of veterinarians



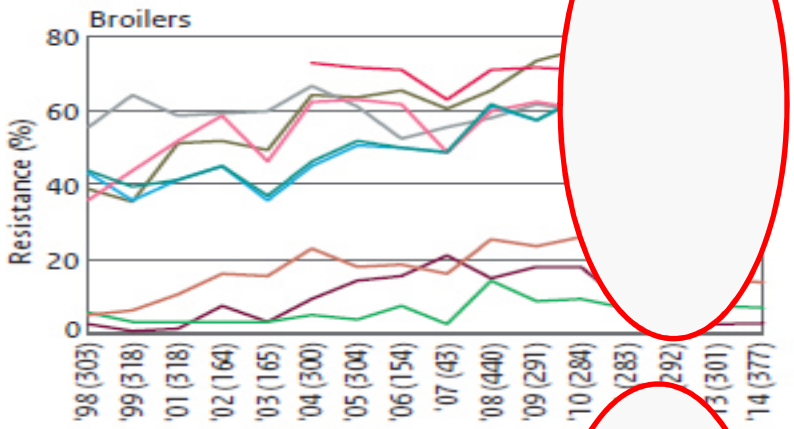
- Based on population of farms it can be identified if vets prescribe systematically more than others
- VBI = veterinary benchmarkindicator

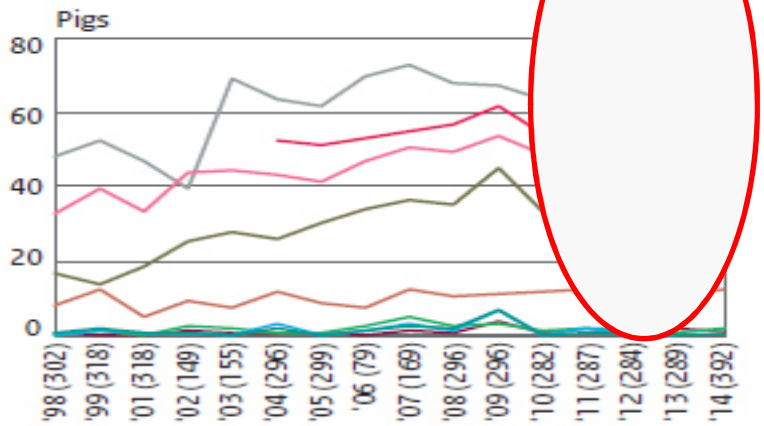


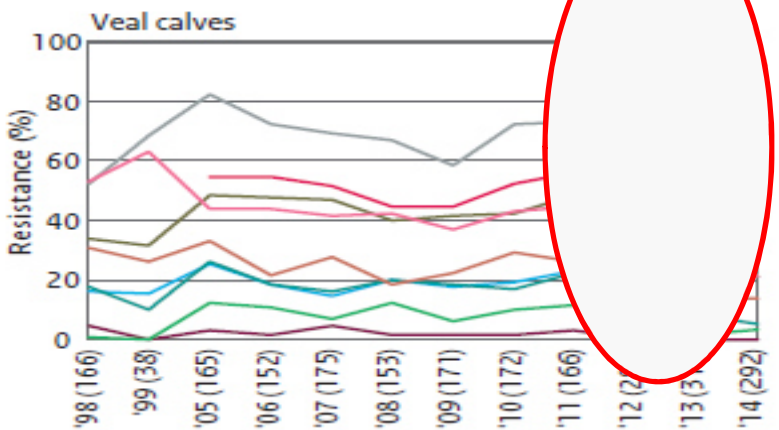
Effect of reductions of antibiotic use in animals on the occurrence of antimicrobial resistance in commensal E. coli

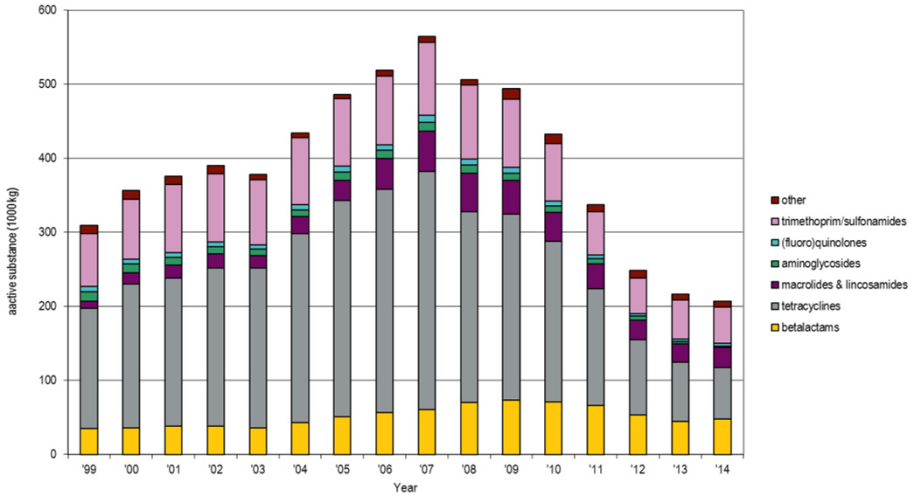
Figure Eco01 Trends in resistance (%) of *E. coli* is[olated] from broilers, slaughter pigs, veal calves and dairy ca[lves in th]e Netherlands from 1998 - 2014.

[Esch]erichia coli









Ampicillin
Tetracycline
Ciprofloxacin
Cefotaxime
Trimethoprim
Nalidixic acid
Gentam
Sulfamethoxazole
Chloramphenicol

Effect of reductions of antibiotic use in animals on the occurrence 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 - 2014.

Escherichia coli

Broilers

Resistance (%)

'98 (303) '99 (318) '01 (318) '02 (164) '03 (165) '04 (300) '05 (304) '06 (154) '07 (43) '08 (440) '09 (291) '10 (284) '11 (283) '12 (292) '13 (301) '14 (377)

Pigs

'98 (302) '99 (318) '01 (318) '02 (149) '03 (155) '04 (296) '05 (299) '06 (79) '07 (169) '08 (296) '09 (296) '10 (282) '11 (287) '12 (284) '13 (289) '14 (392)

Veal calves

Resistance (%)

'98 (166) '99 (38) '05 (165) '06 (152) '07 (175) '08 (153) '09 (171) '10 (172) '11 (166) '12 (266) '13 (317) '14 (292)

aactive substance (1000kg)

Year

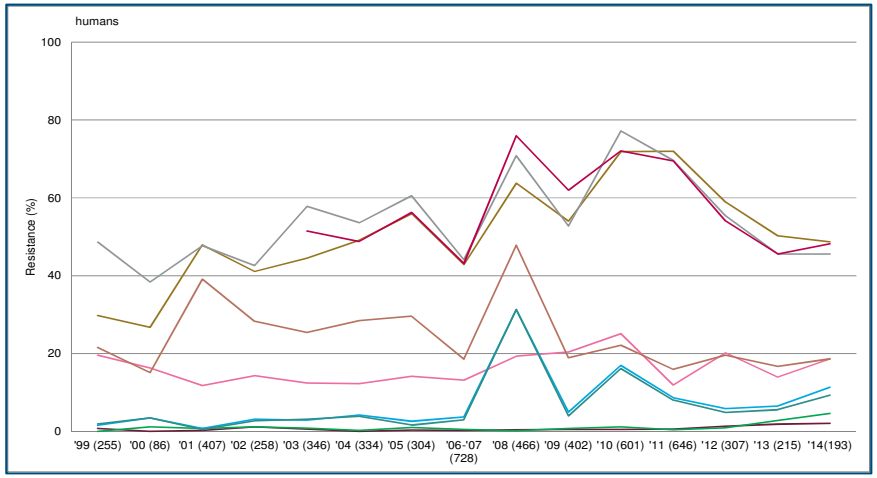
other
trimethoprim/sulfonamides
(fluoro)quinolones
aminoglycosides
macrolides & lincosamides
tetracyclines
betalactams

Ampicillin
Tetracycline
Ciprofloxacin
Cefotaxime
Trimethoprim
Nalidixic acid
Gentam
Sulfamethoxazole
Chloramphenicol

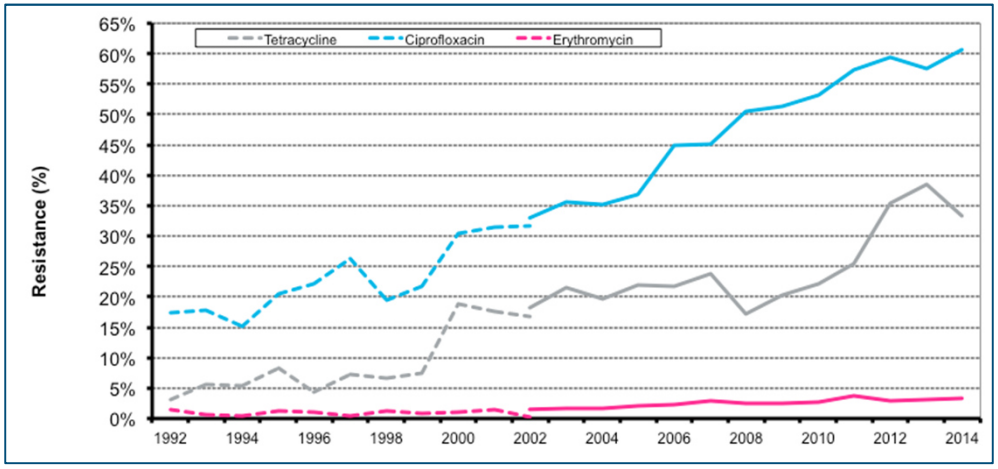
Trends in resistance in *E. coli* isolated from meat

Reduction of resistance in human isolates of FB-pathogens

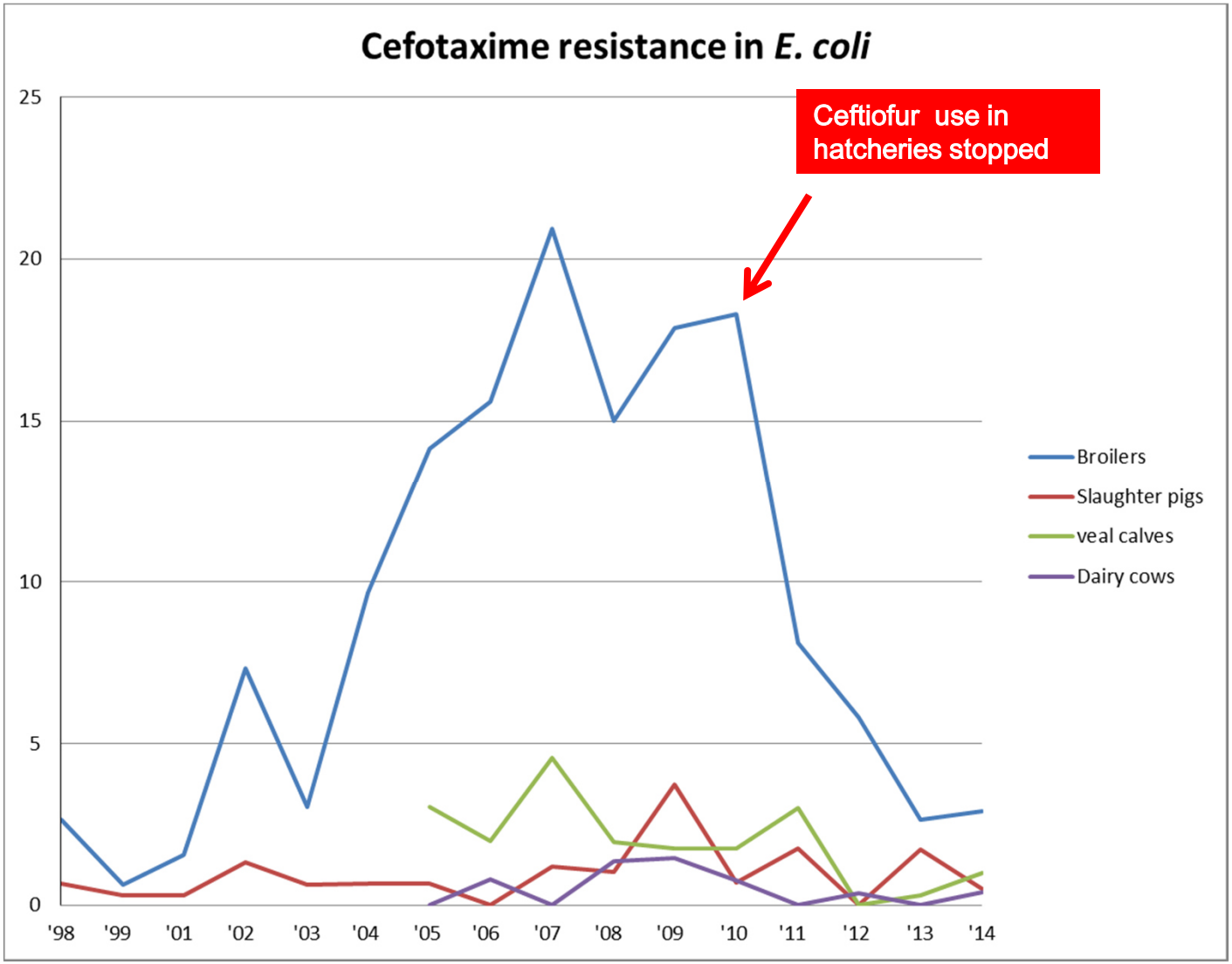
Salmonella Typhimurium



Campylobacter

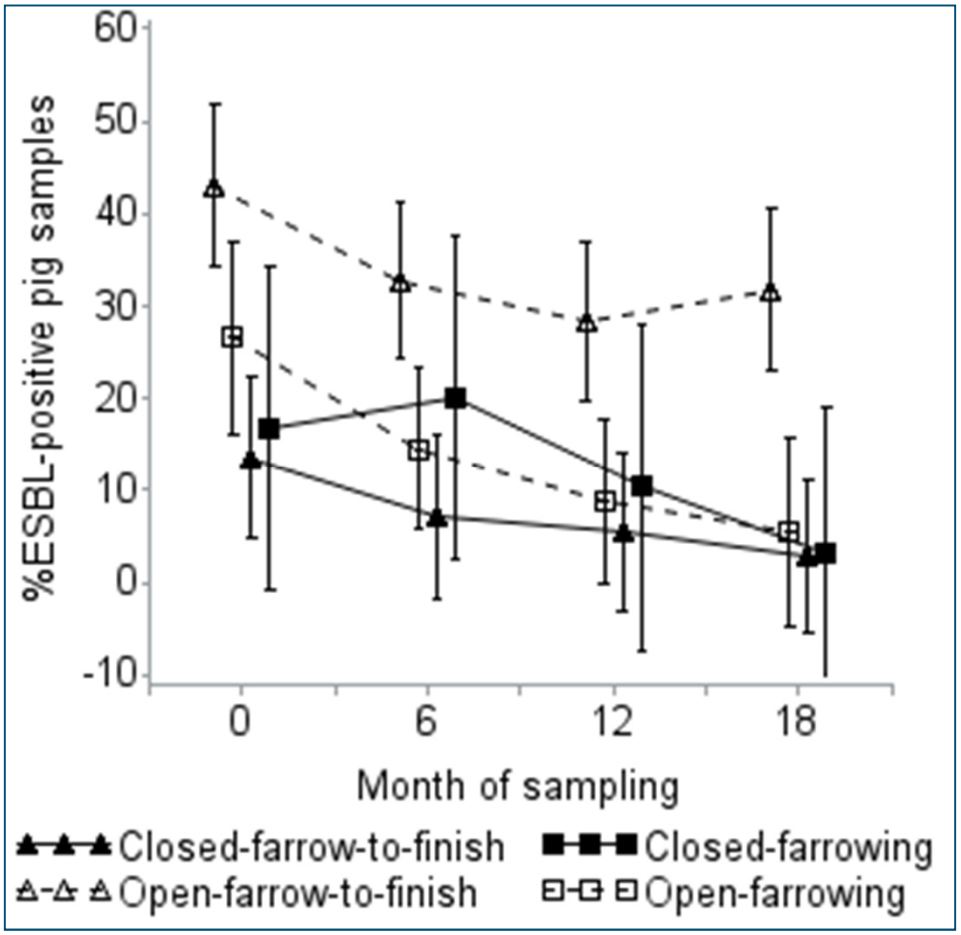


Effect of reduction of 3e-gen cephalosporins



Reduction of ESBLs

- Animals
  - Poultry
    - Faeces 100% - 66%
    - Meat 100% - 67%



W. Dohmen UU-IRAS

Have we realized our reduction-ambitions?

- Yes,
  - Quantity of use
    - in reduction of sales
    - In reduction of prescriptions by vets and usage on farms
  - Quality of use
    - Substantial less use of 3rd choice drugs
    - Less group treatments (pigs, calves)
    - More selective dry cow treatment
  - Surprising fast and substantial effect on the occurrence of resistance in food-animals
    - Limited or no effect in Campylobacter and Salmonella

Critical success factors were

- Clear targets defined by the authorities
- Measures initiated by private animal production sectors icw veterinary association aimed at prudent use and transparency
- Independent control institute (SDa)
  - Benchmarking of farms and vets

Is it sustainable?

- Yes, but it needs an active ongoing policy to more sustainable animal husbandry systems and awareness in all stakeholders involved

Future actions

- Evaluate the implementation of the Health Council Report recommendations in 2016?
  - Policy on 1st, 2nd and 3rd choice drugs and the professional guidelines developed by the KNMvD
  - Reduction targets (quantity, quality)
  - Reduction of AMR (ESBLs, MRSA)
- Evaluate the effect of reduced use on animals health and welfare
- Measures implemented in companion animals