AACTING Meeting 2019 Bern
setting and implementing antimicrobial use use targets: the role of benchmarking

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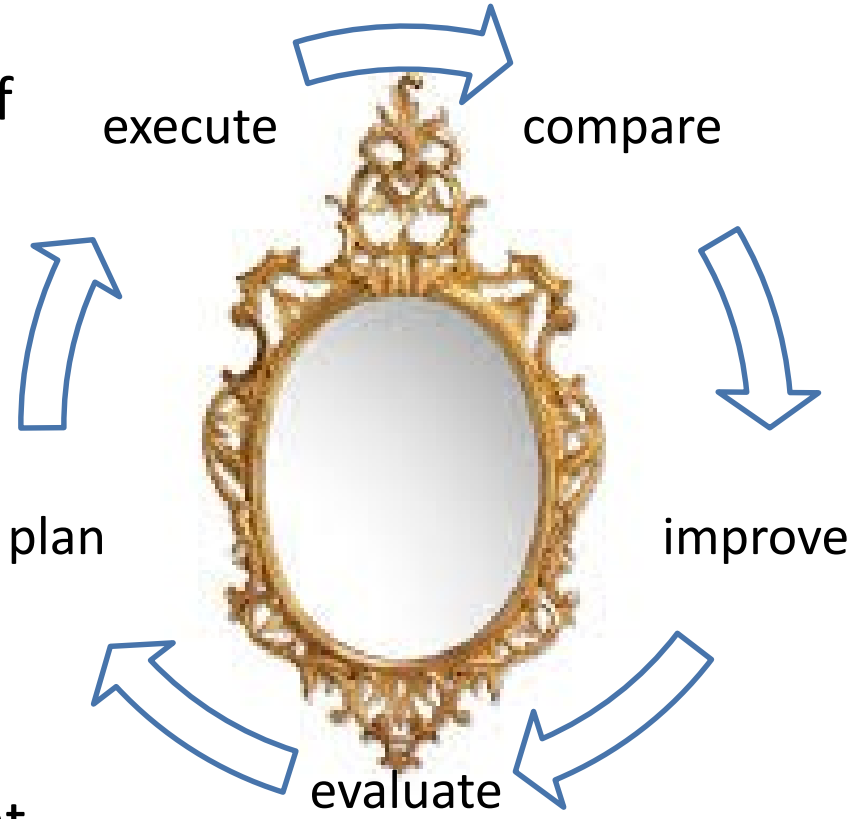
Autoriteit Diergeneesmiddelen

Outline

- The start and early period (2010-2015)
- The critical success factor period (2016-2018)
- Benchmarking veterinarians (2014 and the new approach 2019)
- The rationale for new benchmark values for farms (2016-2018)
- What next?

What is benchmarking?

- **Benchmarking** is the practice of comparing business processes and performance metrics …
- **Benchmarking** is used to measure performance using a specific indicator resulting in a metric of performance that is then compared to others. (Wikipedia 18 06 2019).
- **Benchmarking** can be applied at different levels (country, sector, farm, veterinarian)



Monitoring and benchmarking

- Defined Daily Dose Animal

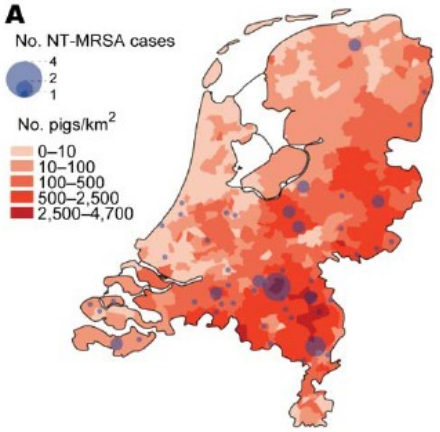
- Species/sector: $DDDA_{NAT(IONAL)}$
  = Σ treated kg days per mass unit in sector$^{\Psi}$ * mass medication/ Σ average kg animal in target category in sector

- Farm: $DDDA_{F(ARM)}$
  = Σ treated kg days per mass unit at farm$^{\Psi}$ * mass medication/ Σ Number of animals in target category at farm* average weight in target category

- Veterinarian: Veterinary Benchmark Indicator /$DDDA_{VET(ERINARIAN)}$
  = weighted average $DDDA_{F(ARM)}$ (weighted by kg animal on a farm)

- $^{\Psi}$ DG Standard SDa, contains information on Dutch registered medicines EAN, REG-NL

A pressing public health agenda … turned veterinary practice in an urgent public health issue



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

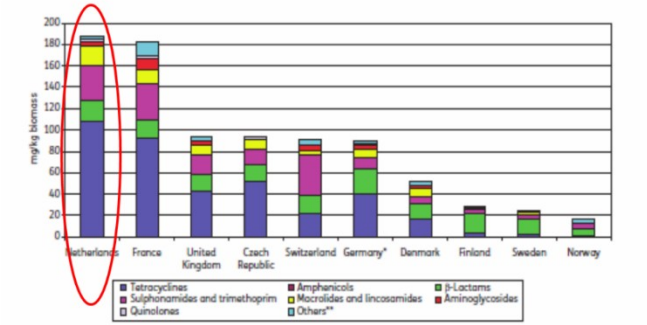
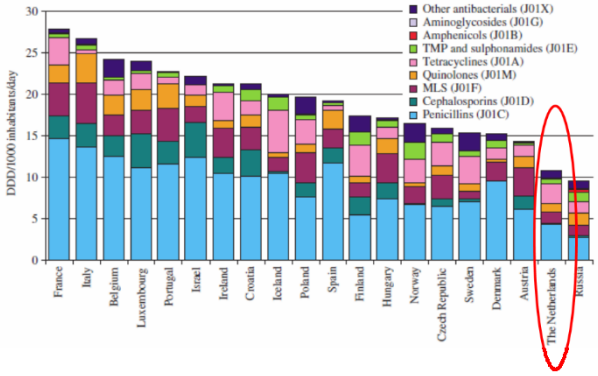


Figure 1. Amounts, in mg, of veterinary antibacterial agents sold in 2007 per kg biomass of pig meat, poultry meat and cattle meat produced plus estimated live weight of dairy cattle. *2005 data. **The substances included vary from country to country.



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

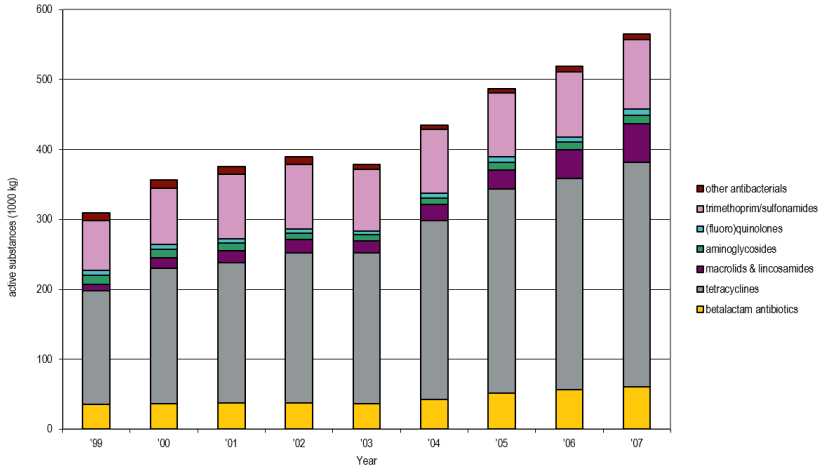
Kari Grave*, Jordi Torren-Edo and David Mackay

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

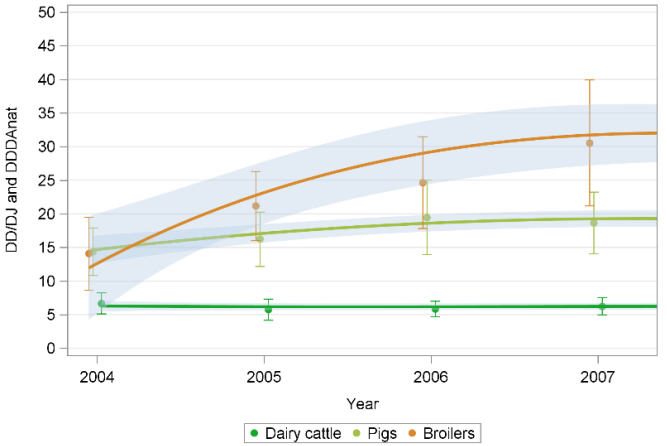
European Surveillance of Antimicrobial Consumption (ESAC): outpatient parenteral antibiotic treatment in Europe

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

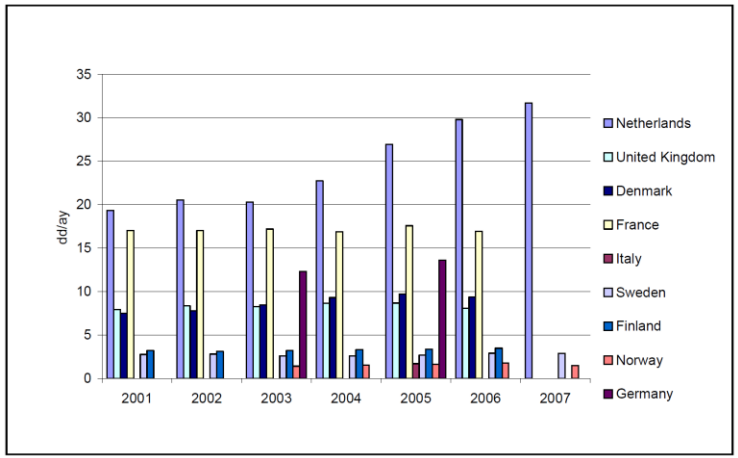
Sales data antimicrobial veterinary medicinal products (1999-2007 in kg in the Netherlands)



MARAN data for samples of farms for three animal species (broilers, pigs, dairy cattle)

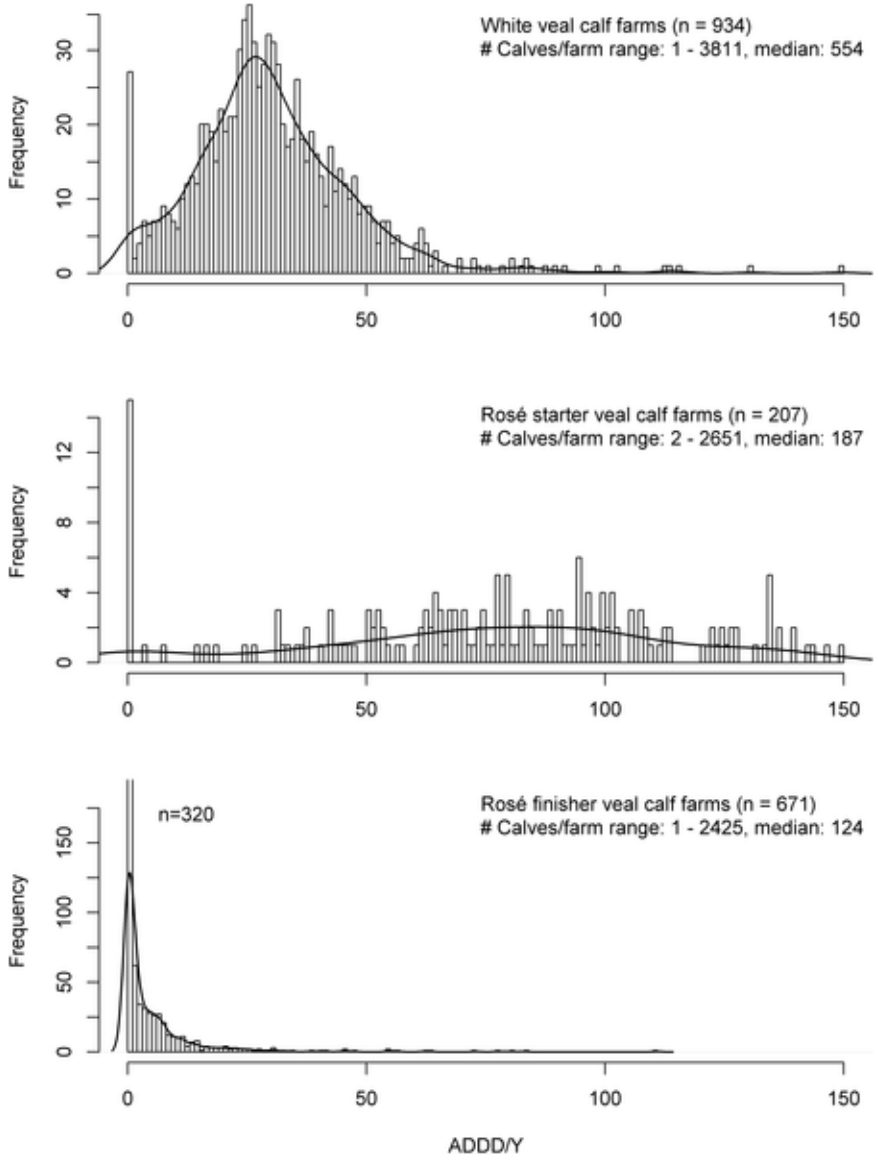


Calculated daily dosages antibiotics from sold/ delivered kg active ingredient per average animal per year in the various countries. MARAN 2007



Increase in usage till 2007

Frequency distributions ADDD/Y 2011 (Bos et al., PLoSOne 2013)



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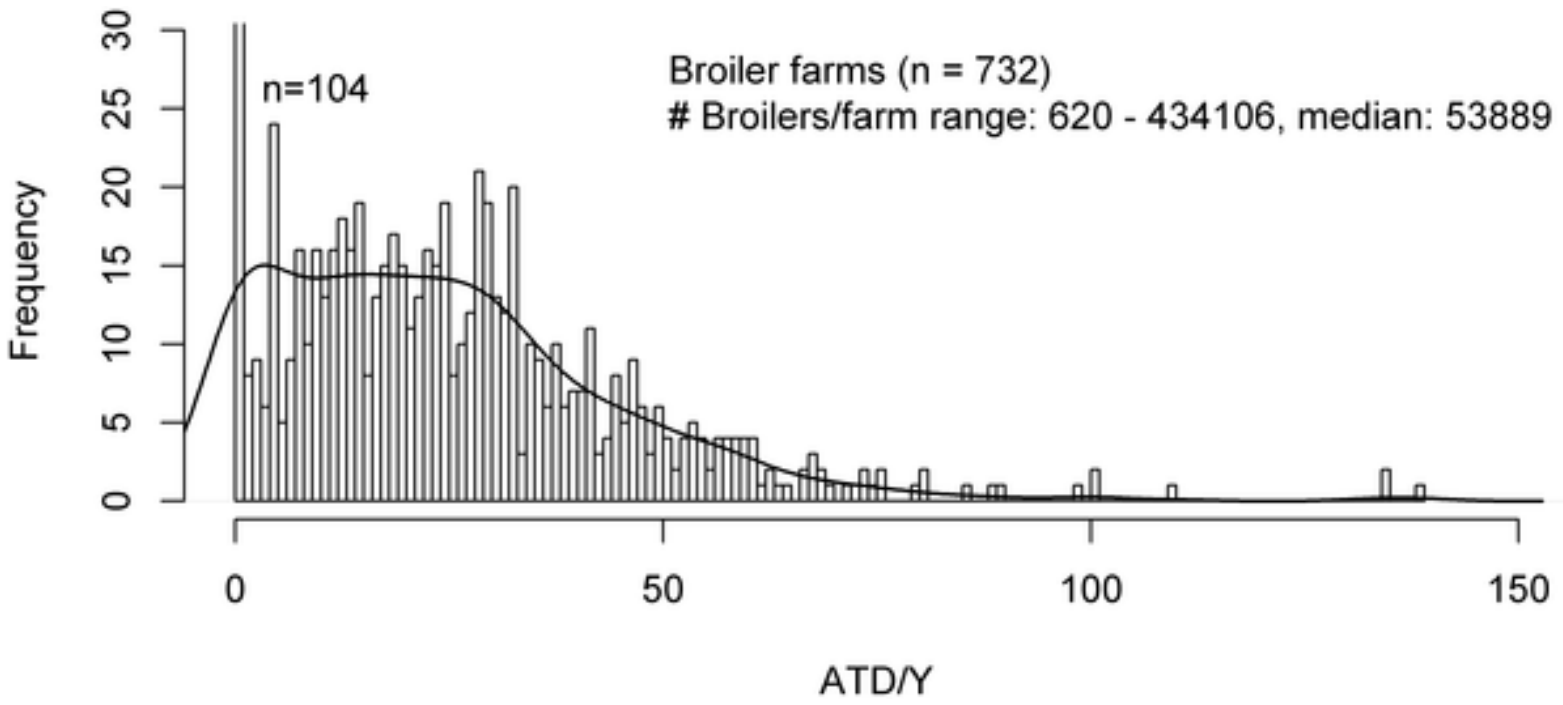
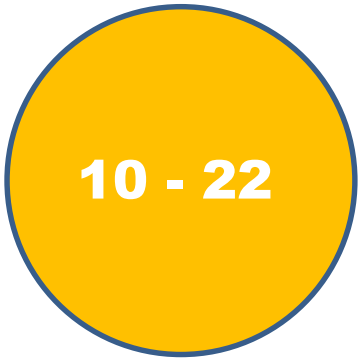


Benchmarking farms ($DDDA_F$)

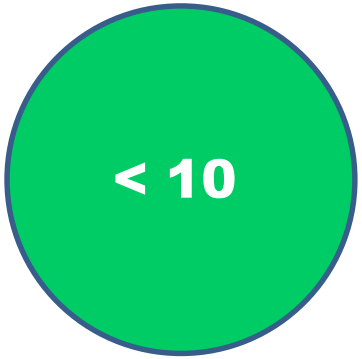
ACTION THRESHOLD

>75 Percentile



SIGNALING THRESHOLD

50 Percentile (median) -75 Percentile



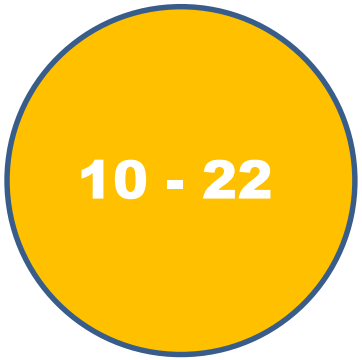
TARGET VALUE

<50 Percentile

Benchmarking farms ($DDDA_F$)

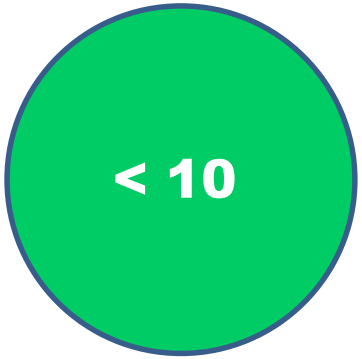
ACTION THRESHOLD

Direct measures required which reduce use of antimicrobials immediately



SIGNALING THRESHOLD

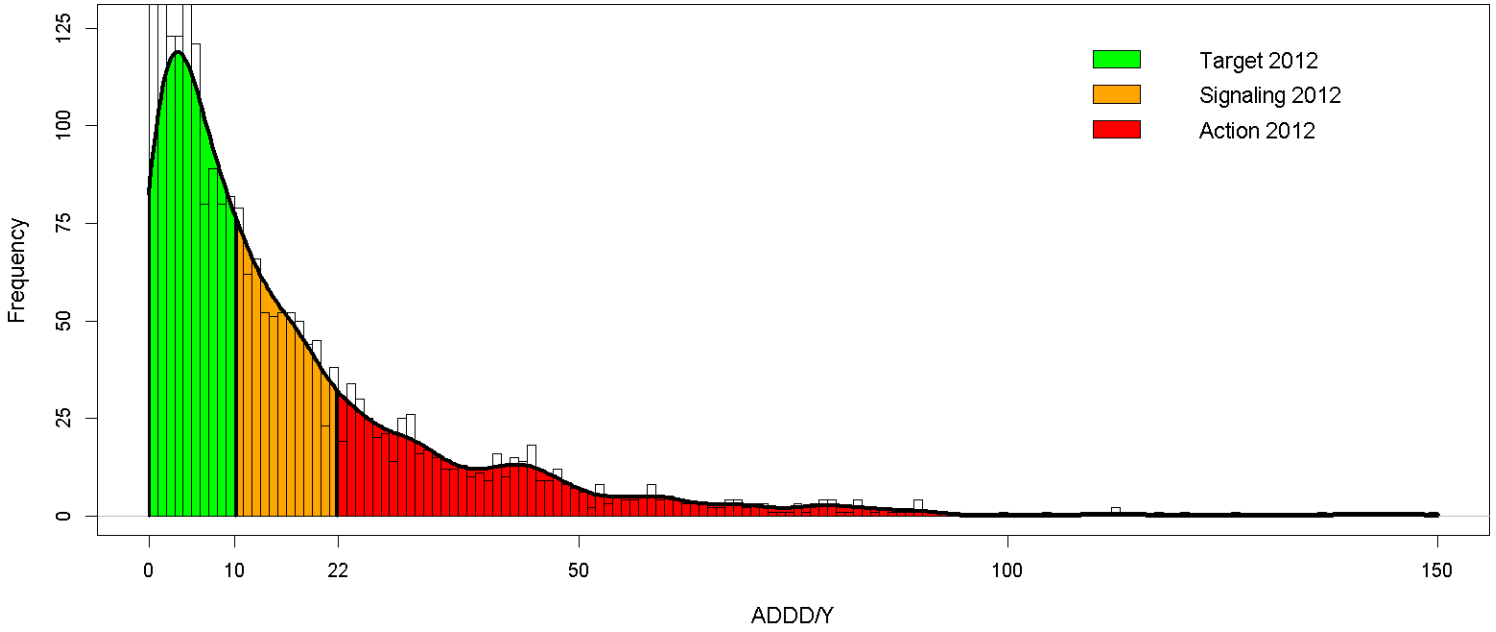
Use of antimicrobials requires attention



TARGET VALUE

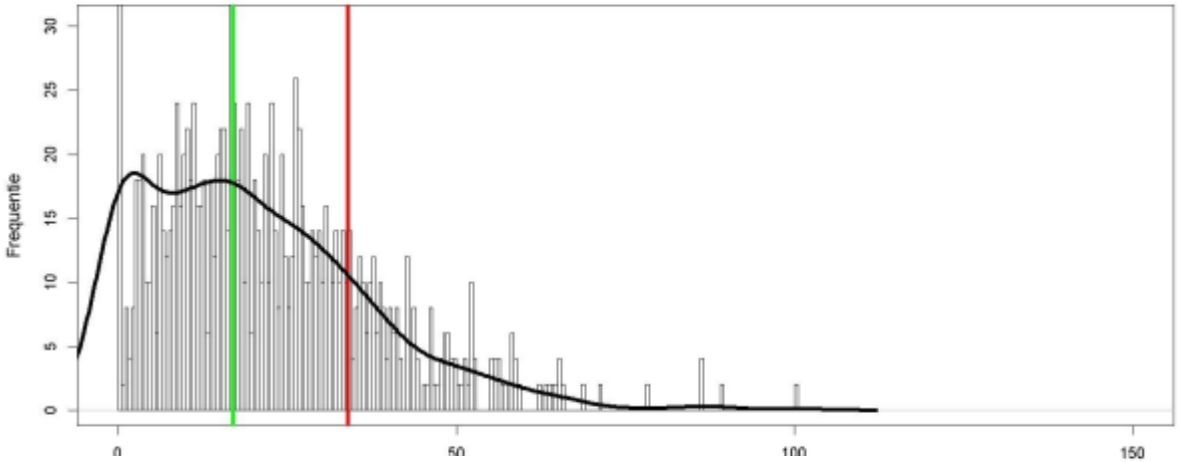
No action required

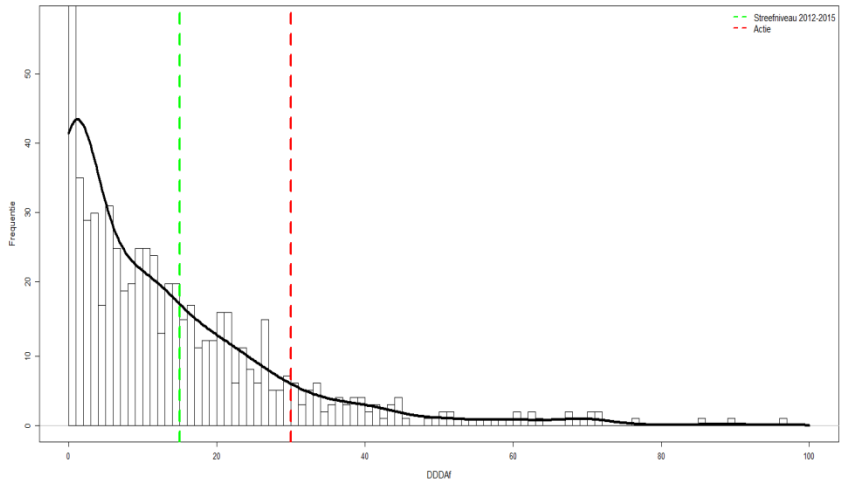
Benchmarking farms ($DDDA_F$)

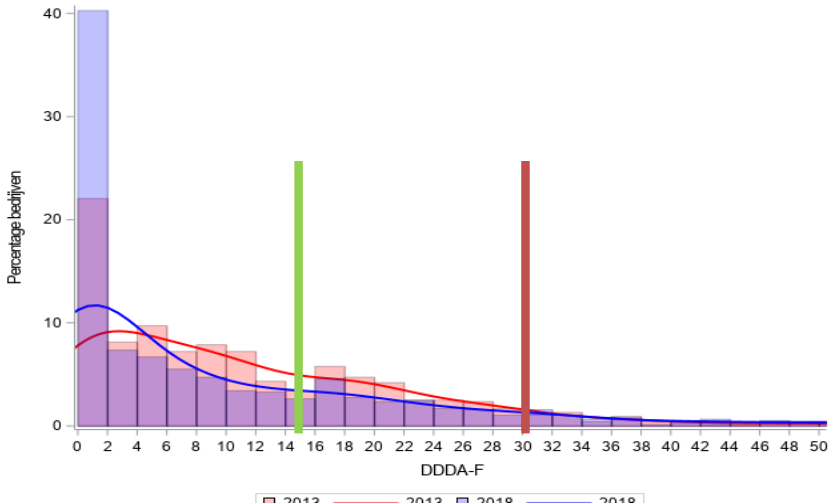


- complete national coverage (>42 000 farms), (relatively) high quality data (through
- sector product quality systems)
- feedback to farmers and veterinarians and follow-up through product quality systems

Benchmarking farms: distributions 2012, 2015, and 2018 (blue) for broilers





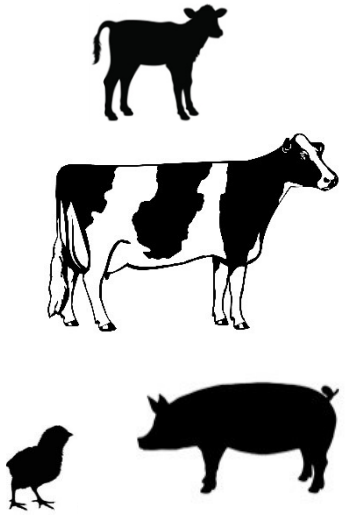


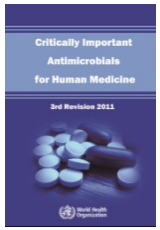
Critical antimicrobials

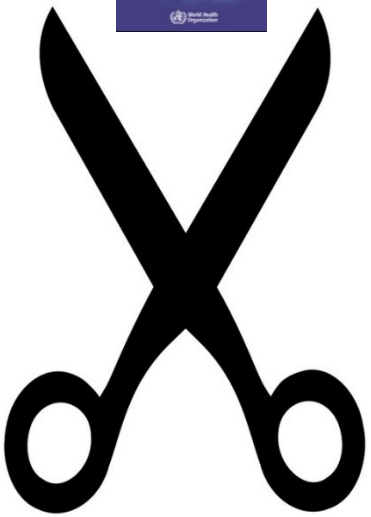
- Netherlands Health Council report:
- Certain antimicrobials should be reserved for humans usage
  - Tigecycline should never be used on veterinary market
  - Discourage veterinary use of carbapenem class antibiotics
  - Find alternatives for the use of colistin in vet medicine

- Resulted in changed formularia for Veterinarians (1st, 2nd, 3rd choice antimicrobials in 2012) and development of guidelines

Benchmarking Critically Important Antimicrobials (2012)

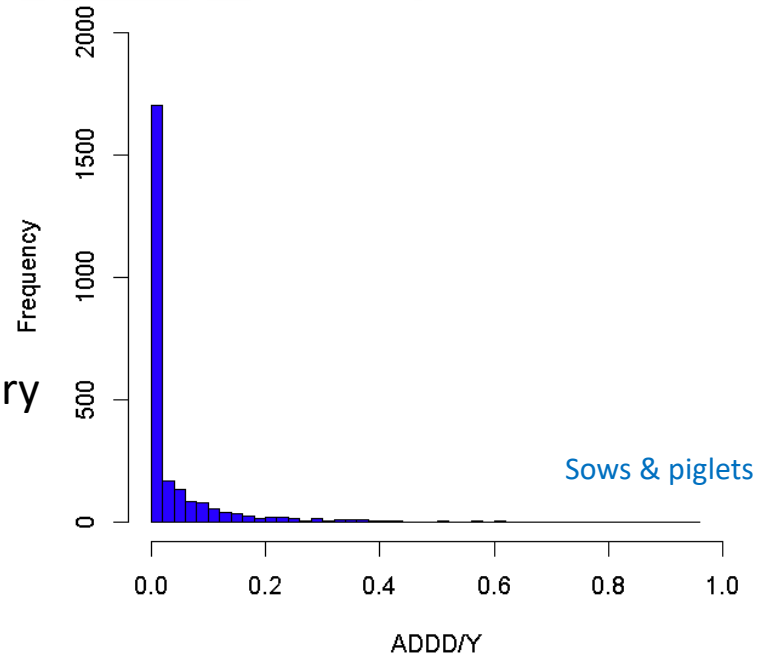




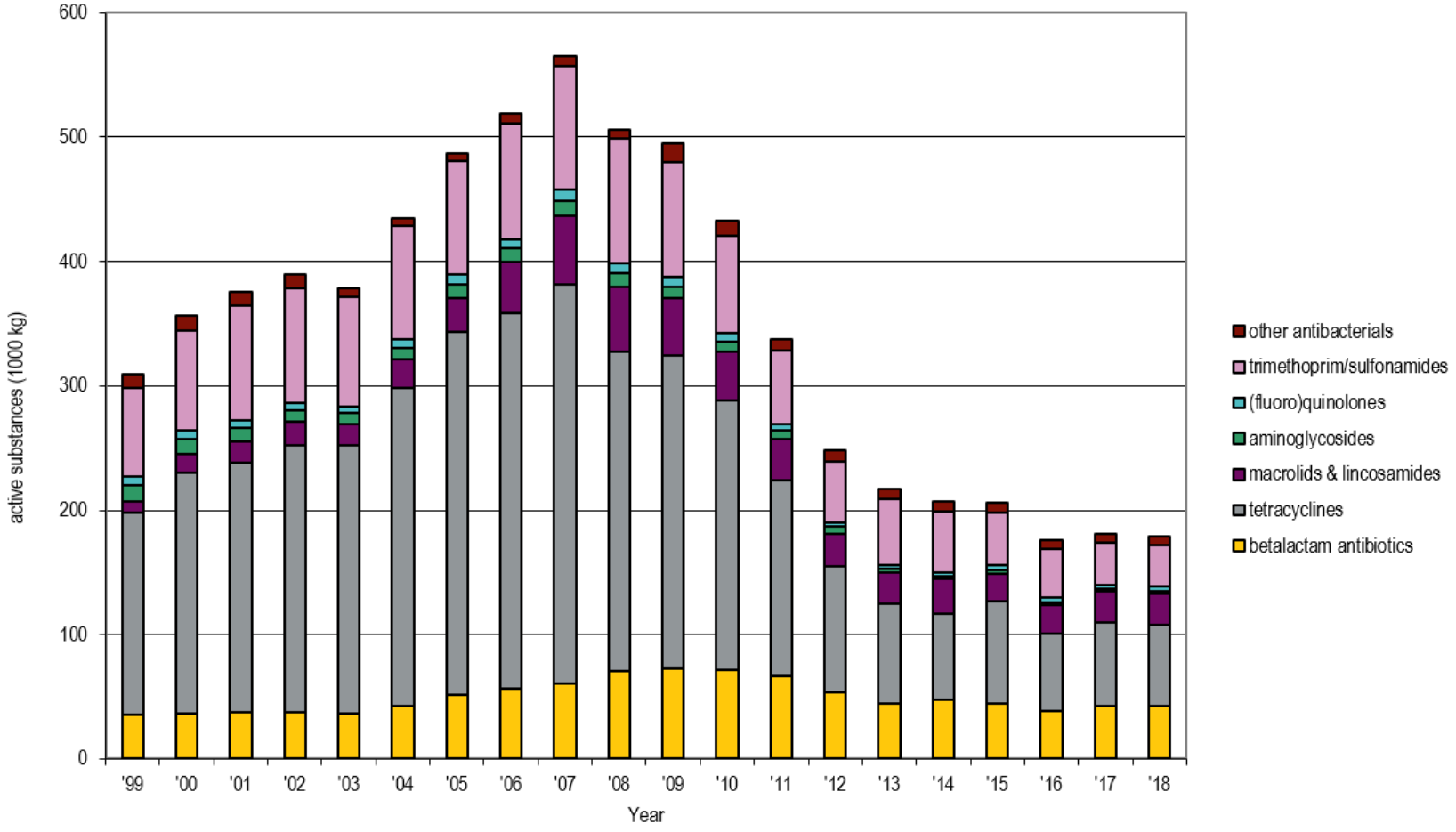


Separated animal and human use for some critical antibiotics:

- Cephalosporins and fluoroquinolones
- Benchmark value in principle 0 for use in veterinary practice
- Followed by ESVAC benchmark for colistin (2016)



Sales data antimicrobial veterinary medicinal products (1999-2018 in kg in the Netherlands)



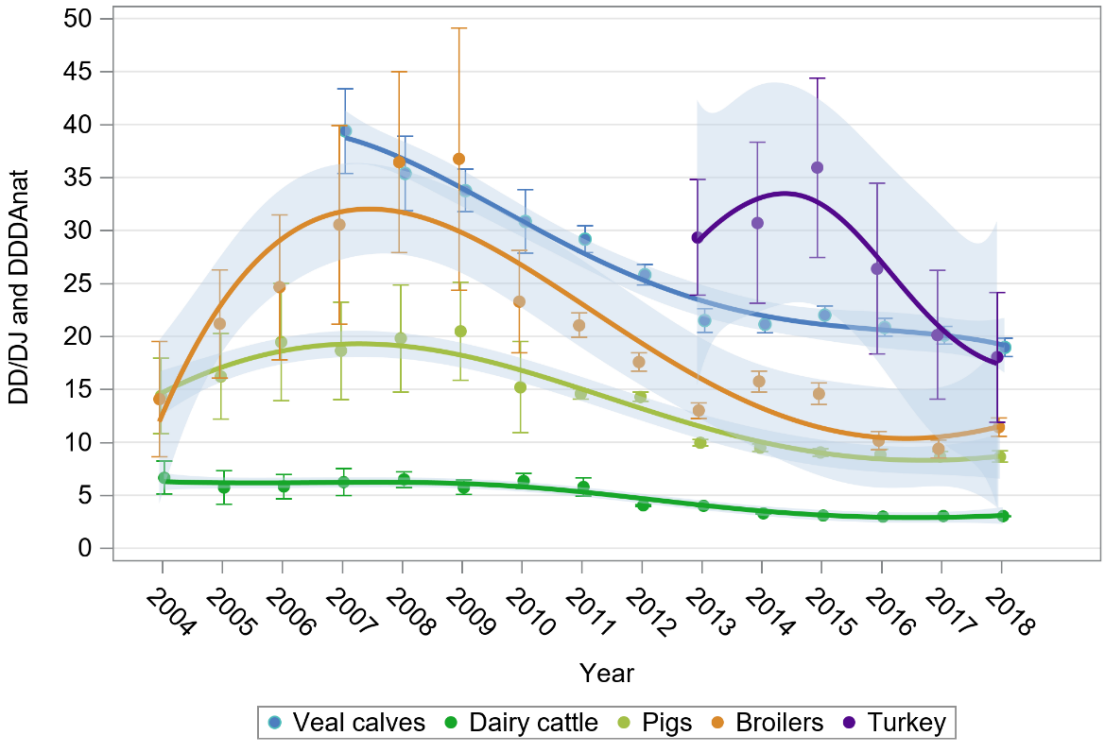
Reduction since 2009 63.8%

Long term trends in antimicrobial usage, combination of LEI WUR (from MARAN) data (sample) and SDa data (complete coverage): $DDDA_{NAT}$ (SDa 2019)

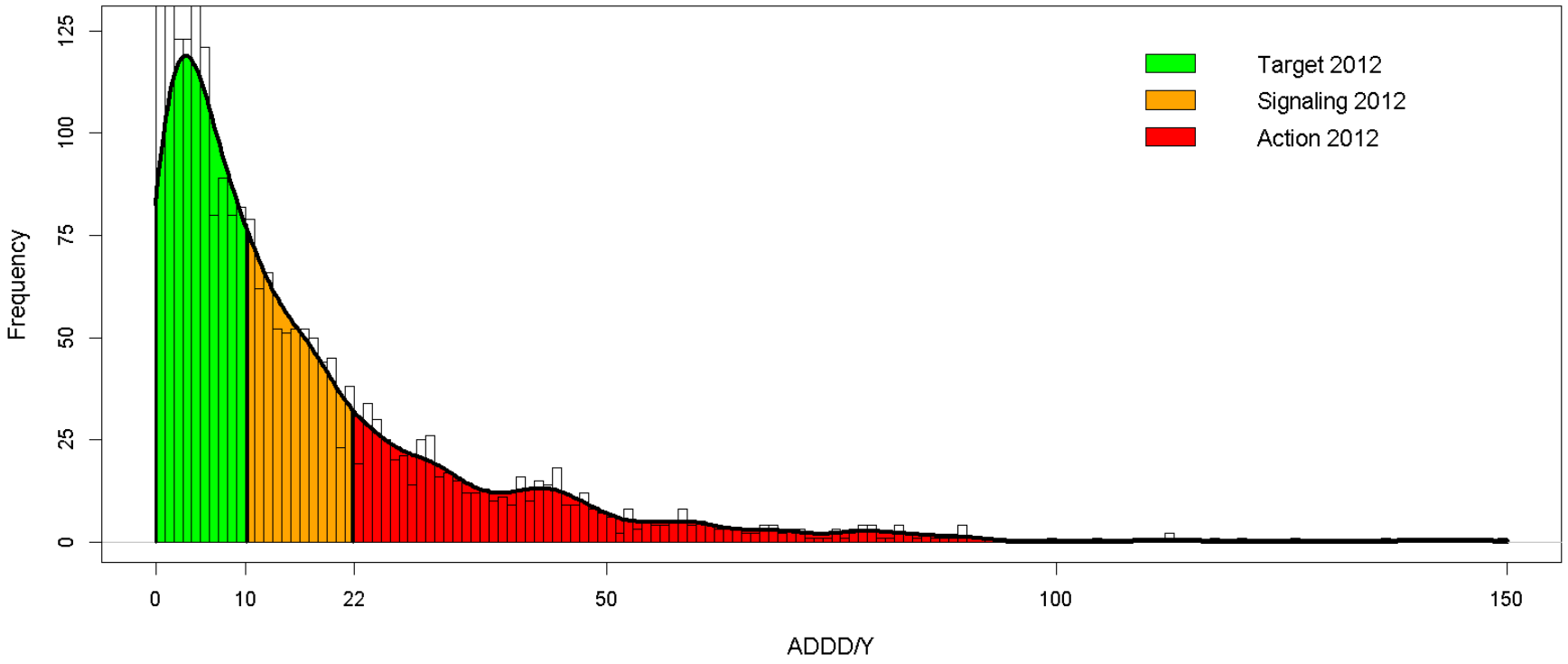
Reduction in AMU since 2009, benchmark year of the government

$DDDA_{NAT}$ since 2009- 2018:

Veal calves	44%
Broilers	68%
Pigs	58%
Dairy cattle	47%
Turkeys	n.a.

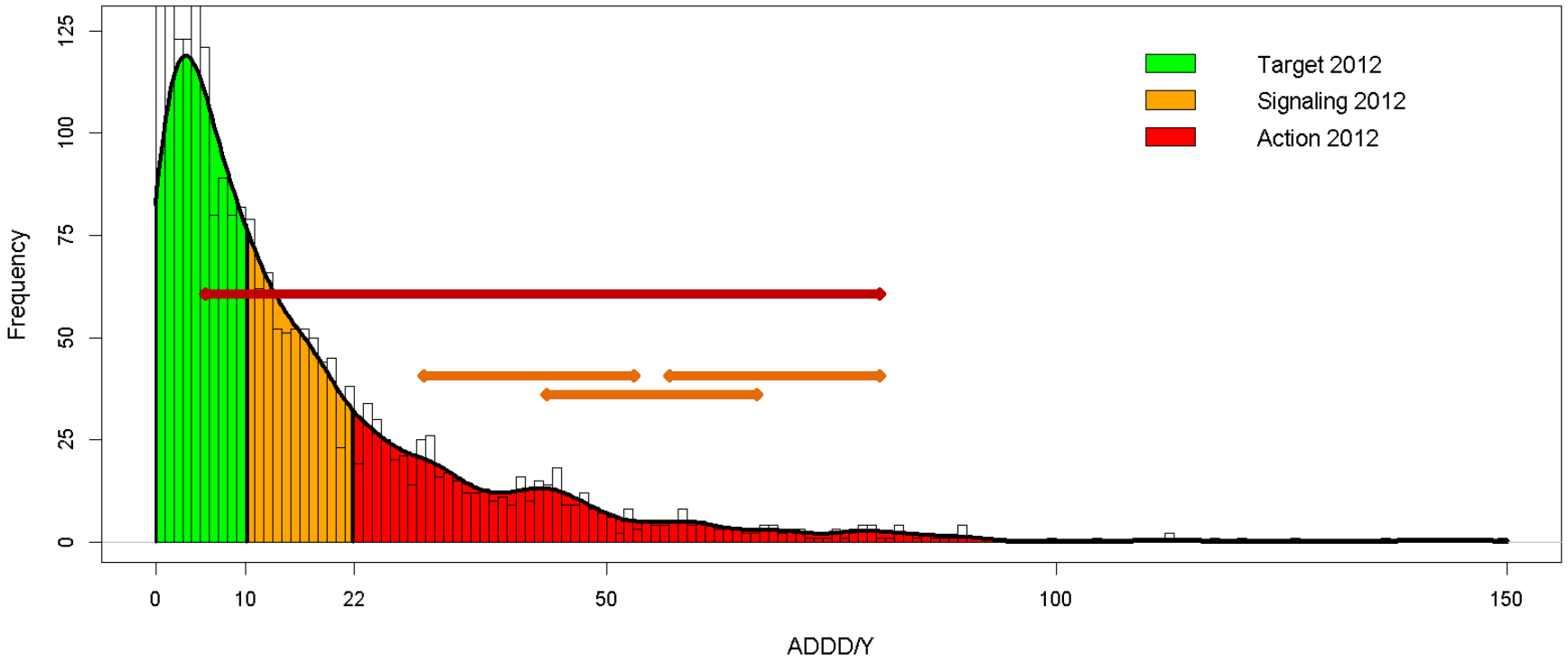


The next phase, more refined data analysis …. and ‘critical succes factor studies’



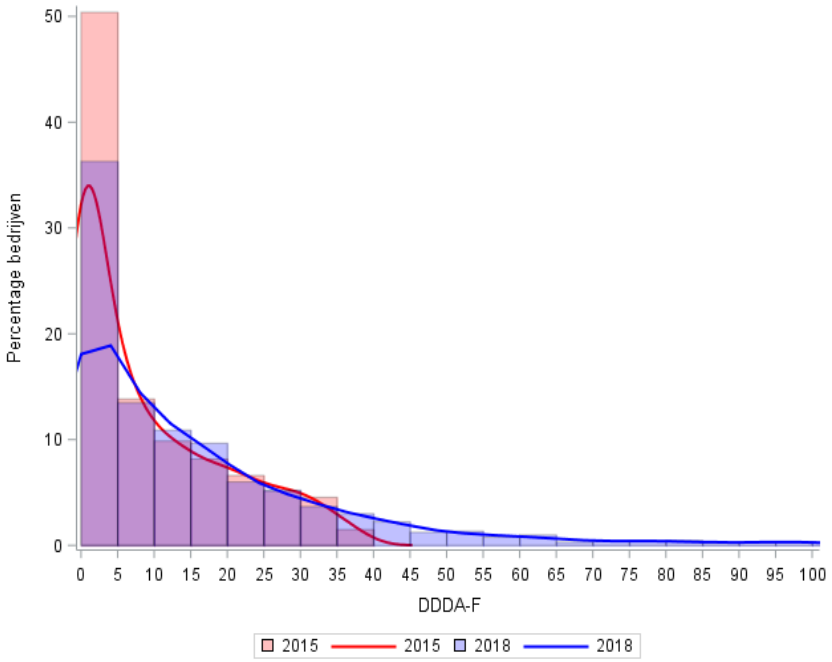
Distributions for most species characterized by (long tails) and more limited skewness than in the early years of benchmarking

How do farms move through these distributions from year to year?

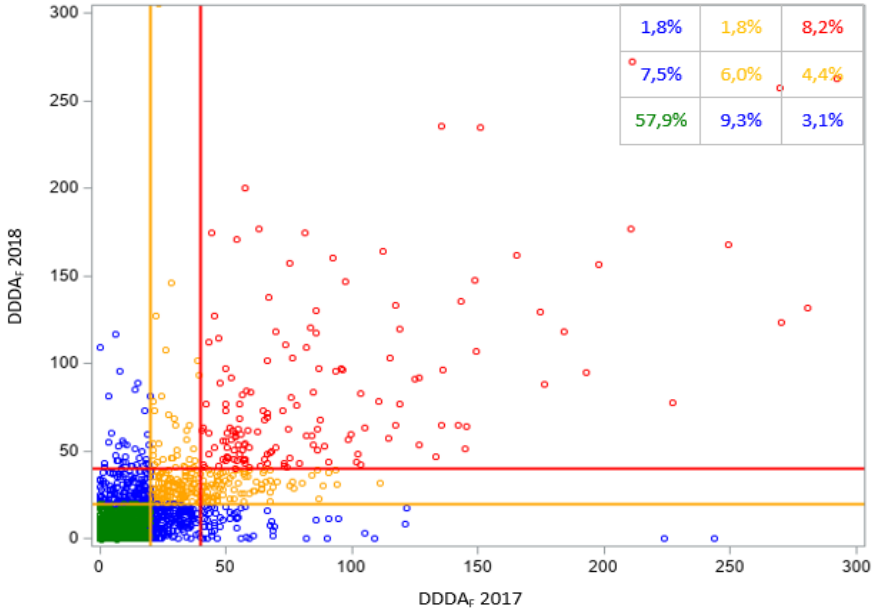


- Between farm variation in AMU relative to within farm variation in AMU over the years
- Is this distribution one distribution or is it built up out of multiple distributions

Weaner pigs



Frequency distributions 2015 and 2018



Correlation between 2017 and 2018 ρ=0.74
Points to structural differences in AMU between farms

Important phases in managing antimicrobials in 2017 and onwards

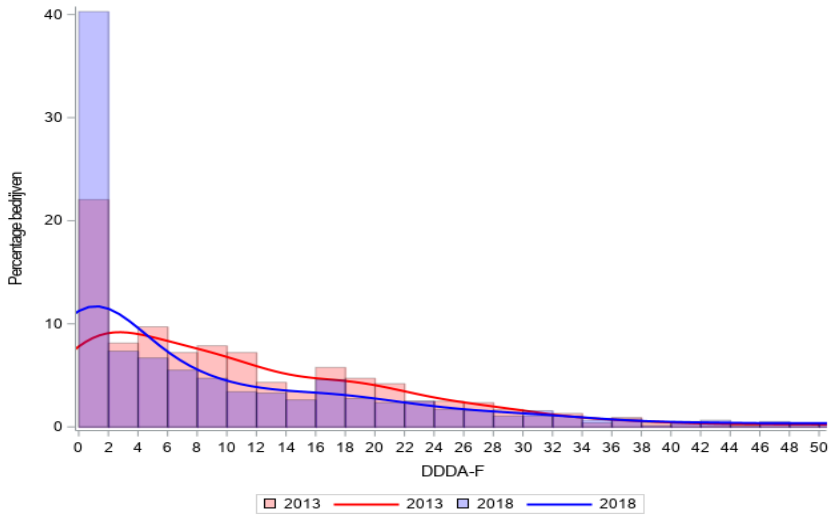
- Initiated a series of commissioned studies subsidized by governments into ***"critical succes factors"*** that should explain why some farms are consistently above target benchmarks

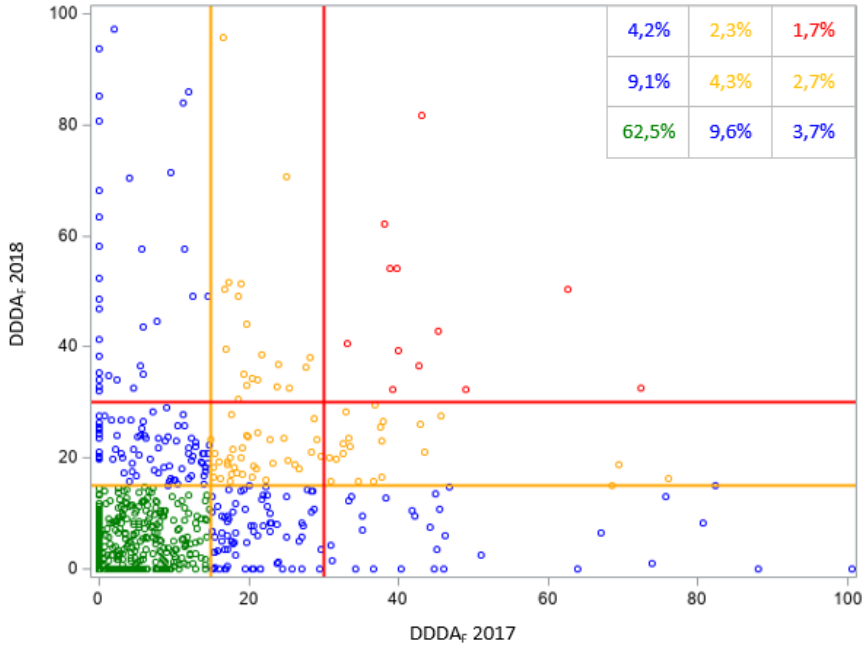
- broiler farms, pig farms, and veal calf farms and veterinarians

- Determinants associated with farm types, biosecurity, management factors, organization of sector, but also attitude, knowledge about antimicrobials, etc. have been identified

- These determinants represent future potential for further AMU reduction > requires implementation and coaching

Broilers





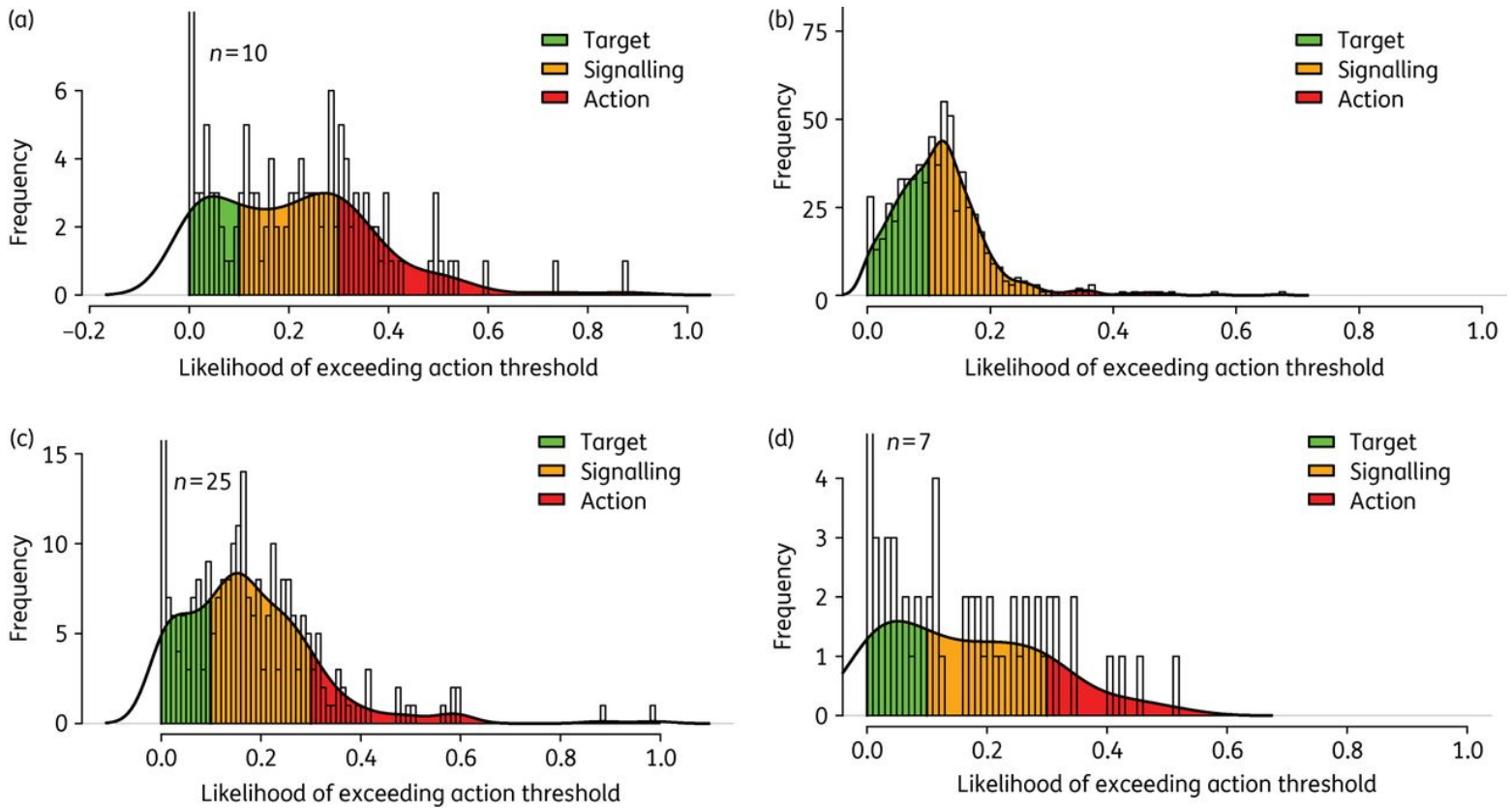
Frequency distributions 2013 and 2018
Change in number of traditional and alternative broiler system farms

Correlation between 2017 and 2018 ρ= 0.19
Points to incidential and time varying differences in AMU between farms

Benchmarking veterinarians

- A VET has a population of farms
- Veterinary Benchmark Indicator (likelihood that a farm of a particular veterinarian is in the action zone)
- VBI of 0.33:
  - a third of the farms of that veterinarian has a AMU in the action zone

Benchmarking veterinarians (Bos et al., JAC 2015)



veal calves (a), cattle (b), pigs (c) and broilers (d)

Depending on the livestock sector 2-30 fold differences exist in prescription pattern

Acceptance has always been an issue; no “professional response”

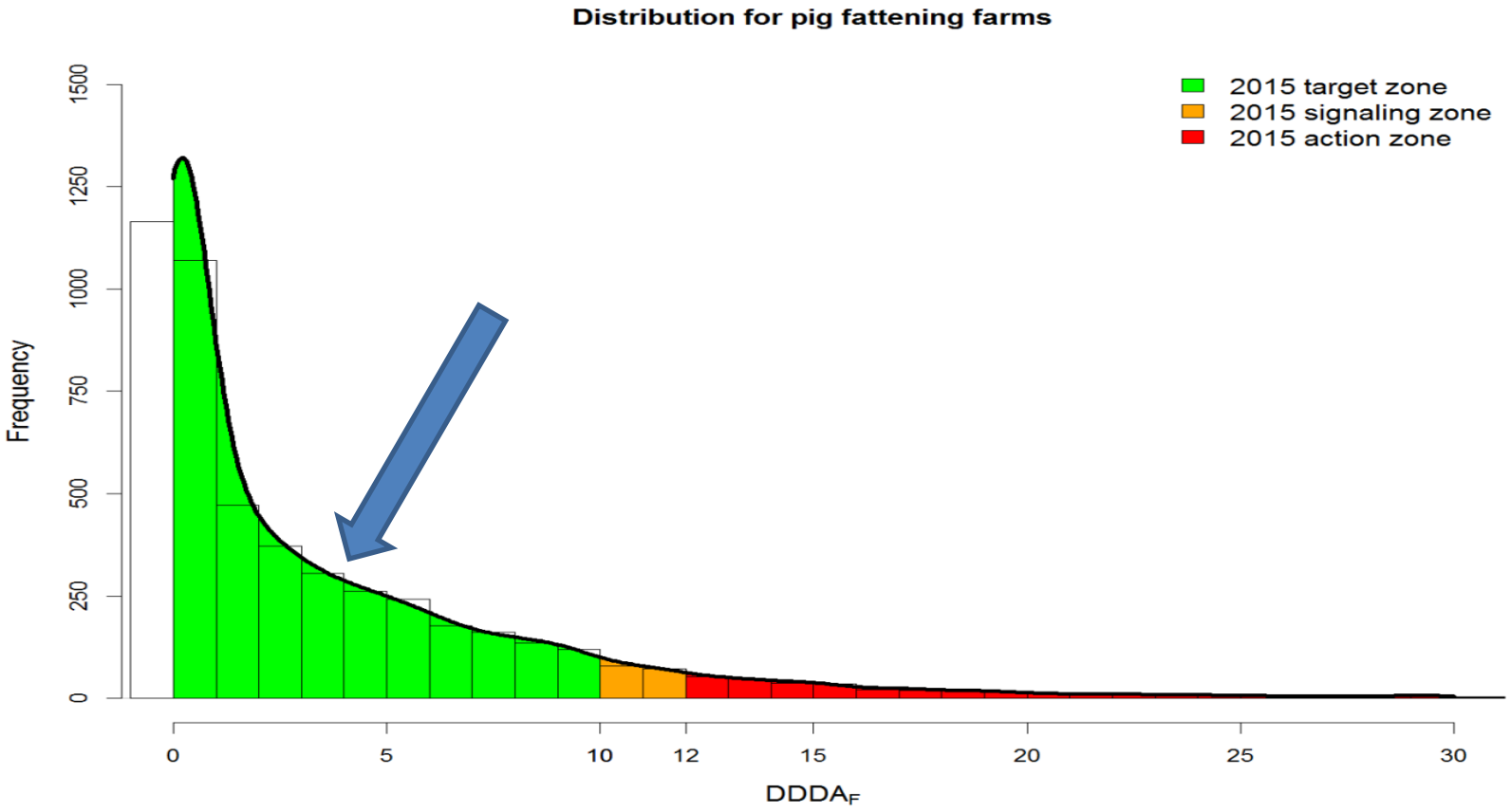
Benchmarking veterinarians

- System reset away from VBI towards $DDDA_{VETERINARIAN}$
- Same benchmark value applies (for farms & veterinarians)
- More transparent and understandable for farmers and veterinarians

Animal species	N of VETs	Mean	Median	P75	P90
Broilers	86	8.5	8.6	12.0	17.1
Turkeys	6	12.6	9.7	25.1	26.0
Pigs	249	5.3	4.5	6.6	10.0
Dairy cattle	732	2.4	2.3	2.6	3.0
Veal calves	134	12.3	10.4	20.3	25.7
Other cattle	720	0.7	0.5	0.9	1.4

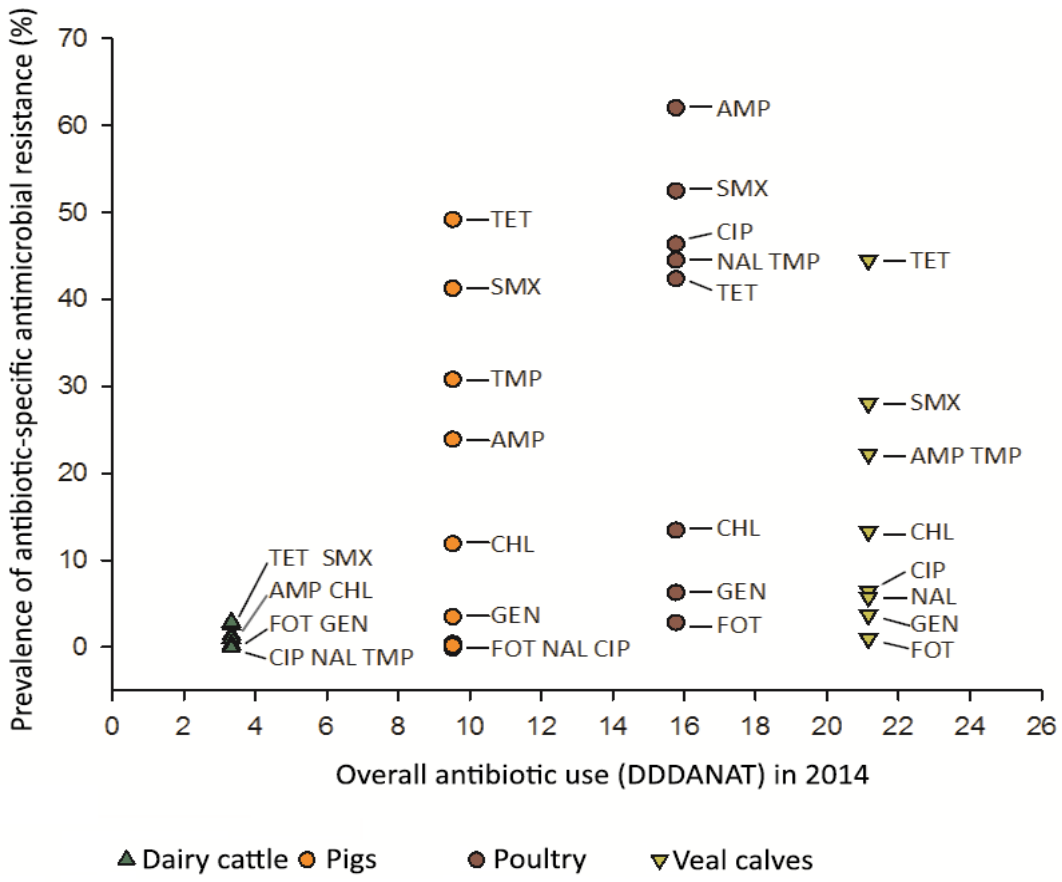
CSF study also indicative of difference at the level of a ‘practice’ in addition to some other determinants

Revising benchmark values 2016-2017: finisher pigs

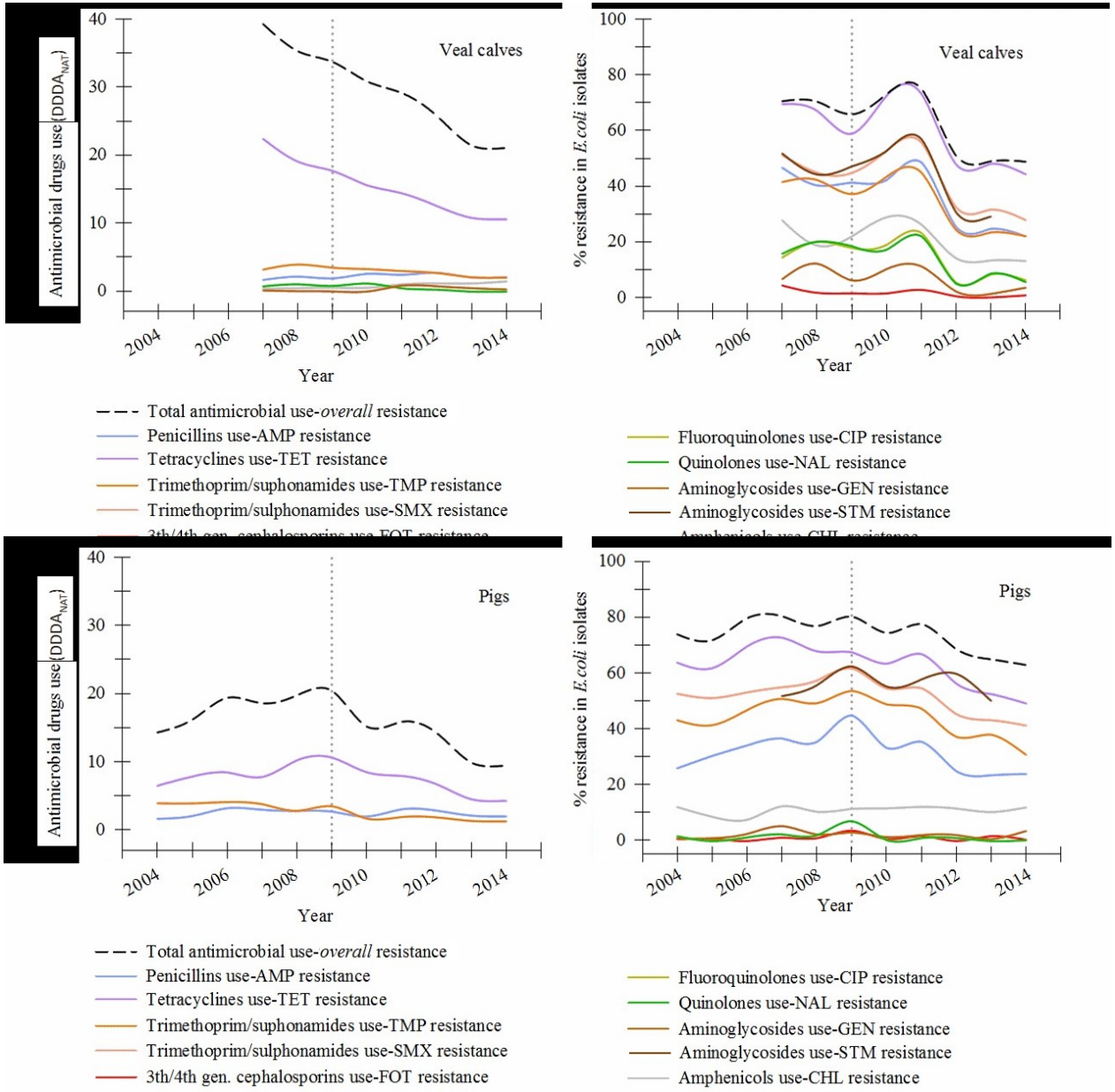


What is the level of desired/controlled use? Can this be defined by the relation between AMU and AMR?

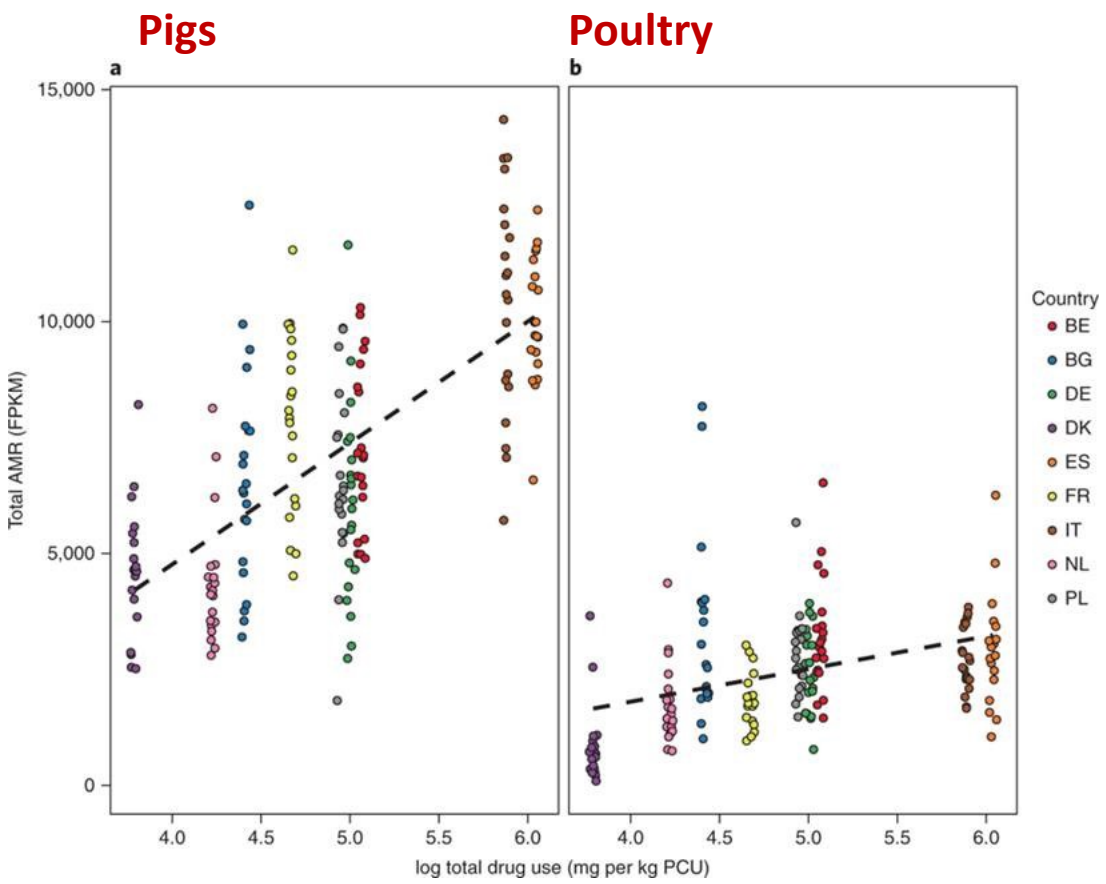
Specific resistance prevalence in resistance monitoring data for 2014 (Dorado-Garcia et al., JAC 2016)



The effect … in resistance monitoring (MARAN 2015)



Revision of the benchmarking approach Munk et al. Nature Microbiol. 2018



- Resistance based benchmarking not possible (2015 report NVMI):
  - Quality of the evidence relatively poor (cross-sectional or ecological studies);
  - Few exposure response relations that can be used for derivation of benchmark values;
  - Many modifying factors

The effect … in resistance monitoring (Dorado-Garcia et al., JAC 2016)

Livestock sector	# of antibiotics to which resistance was detected	Number of isolates	% of the total number of isolates	% of isolates resistant to the antimicrobial concerned									
				AMP	TET	SMX	TMP	CIP	NAL	CHL	FOT	STM	GEN
Broiler farming sector	0	227	12	0	0	0	0	0	0	0	0	0	0
	1	98	5	37	21	8	1	1	0	0	0	29	3
	2	151	8	32	19	18	3	48	49	1	3	24	4
	3	160	8	44	24	38	24	49	49	5	4	62	3
	4	230	12	82	48	67	50	39	39	7	10	53	6
	5	245	13	82	67	87	74	40	41	13	12	76	8
	6	259	13	84	67	95	80	80	80	22	11	72	8
	7	263	14	94	86	98	92	98	98	18	15	90	13
	8	221	11	99	96	100	91	99	100	80	25	99	11
	9	71	4	100	94	100	99	100	100	90	48	100	69
	10	9	0	100	100	100	100	100	100	100	100	100	100
	Total	1,934	100	67	54	66	55	57	57	21	12	62	10

- Resistant strains are often resistant against multiple antimicrobial classes
- Policies to reduce use of specific (critical) antimicrobials as well as total use are important

Revision of the benchmarking approach

- Prudent usage of antibiotics:
  - accurate prior diagnosis/ usage being limited to specific indications / affected animals should receive adequate and timely treatment/ no herd or flock treatment when individual treatment is possible / disease prevention and hygiene in place / optimal contact structures at the sector and farm level.
- Animal husbandry and the production of animal products will always involve administration of antibiotics, as livestock farmers can never fully prevent the introduction of pathogens.

- Refine benchmarking based on 'optimal veterinary practice'
- **Optimal veterinary practice:** regular zero-level use/ limited variation between farms antibiotic use / limited fluctuations over time / Prescription patterns of veterinarians show little variation as well /
- **Provisional benchmark values** in case optimal veterinary practice does not apply,
- Simplified approach (one benchmark value only)

New benchmarkvalues

		Benchmark values valid until end of 2018		Benchmark thresholds valid as of 2019 with specification of type and level	
Species	Bedrijfstype/ leeftijdsgroep	Signaling threshold	Action threshold	Type of benchmark threshold	Action threshold
Veal calves*	White veal farms	23	39	Provisional	23
	Rosé veal starter farms	67	110	Provisional	67
	Rosé veal fatting farms	1	6	Acceptable use	4
	Rosé veal combination farms	12	22	Category will cease to exist	
Pigs	Sows/piglets	10	20	Acceptable use	5
	Weaner pigs	20	40	Provisional	20
	Fattening pigs	10	12	Acceptable use	5
Poultry	Broiler farrms	15	30	Acceptable use	8
	Turkey farms	19	31	Provisional	10¥
Rabbits	Konijnen			Provisional	**
Cattle	Dairy cattle farms	6§		Acceptable use	6
	Rearing farms	2§		Acceptable use	2
	Suckler cow farms	2§		Acceptable use	2
	Beef farms	2§		Acceptable use	2

* Benchmark threshold calculated over 1.5 year

** available data do not allow derivation of a benchmark threshold

¥ calculated using new methodology, using growth curves

§ signaling threshold; action level reached after two subsequent exceedances of signaling threshold

What next?

- Structural changes on the farm or sector level sometimes unavoidable
  - Biosecurity/open/closed
  - Management
  - Breeding (robust species)

- Broader animal health/welfare/infectious disease prevention and innovation agenda (circular farming, climate emissions, environmental health issues)

Conclusions

- Governmental use targets in combination with supporting regulations and subsidies for research were crucial (https://link.springer.com/article/10.1007%2Fs00003-014-0874-z)

- Benchmarking is not just a matter of setting targets, it is a process and involves:
  - Continuous and creative data analysis and reflection on the data to understand the (broader one health and sector specific) context
  - Continous and extensive discussions with stakeholders (livestock farmers and veterinarians) to translate understanding of the context in policy and practical measures

- Benchmarking has been most successful in sectors with individual farmers, less effective in sectors where farms are owned/franchised by large companies/integrations (veal farming)

- Reduction of the tail can lead to considerable AMU reduction. This is a key issue in self regulation; “how to deal with colleagues that stay behind”?

Acknowledgements

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