
Antimicrobial Use in German Livestock from 2011 to 2020 – Longitudinal Development and Its Reasons

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Health in the Human-Animal-Environment Interface

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Antibiotic MOSS in Germany

Umstrittene Medikamente

14.09.2012, 11:42

Aigner will Einsatz von Antibiotika in Tierhaltung eindämmen

Gefahr im Futter: Erst vor wenigen Tagen wurde deutlich, dass Nutztiere erheblich mehr Antibiotika bekommen als bislang angenommen. Nun legt Verbraucherschutzministerin Aigner ein Gesetz vor, das den Einsatz der Medikamente beschränken soll.

ANZEIGE

ab
17,95
€/Monat⁽⁵²⁾

Surfen schon ab 17,95 €/M
Highspeed Internet und Telefonie ab 17,95 €/Monat. Ab jetzt fast überall verfügbar!

approx 1,700 t active components (in 2011)

German Livestock in 2010

| | # Animals in Mio | Average kg | Biomass t |
|---------|---------------------|---------------|--------------|
| Chicken | 480 | 2 | 960,000 |
| Turkey | 25 | 20 | 500,000 |
| Geese | 0.5 | 5 | 2,500 |
| Ducks | 11 | 3,5 | 38,500 |
| Pigs | 55 | 100 | 5,500,000 |
| Cows | 13 | 500 | 6,500,000 |

Antibiotic MOSS in Germany

- | | |
|--|---------------------|
| ▶ Legal Acts | When does it start? |
| ▶ DIMDI-AMV | ▶ 2011 |
| ▶ Medicinal Products Act, 16. amendment | ▶ 2014 |
| ▶ Agricultural industry | ▶ 2013 |
| ▶ QS | |
| ▶ Scientific monitoring | ▶ 2007 |
| ▶ VetCAb | |
| ▶ Specialised investigations | ▶ 2003 ??? |
| ▶ TBI,... | |

Antibiotic MOSS in Germany

▶ Legal Acts

- ▶ DIMDI-AMV
- ▶ Medicinal Products Act, 16. amendment

▶ Agricultural industry

- ▶ QS

▶ Scientific monitoring

- ▶ VetCAb

▶ Specialised investigations

- ▶ TBI,...

What is reported?

- ▶ Sales data
- ▶ Use data

- ▶ Use data

- ▶ Use data and amounts

- ▶ Treatment course

Antibiotic MOSS in Germany

▶ Legal Acts

- ▶ DIMDI-AMV
- ▶ Medicinal Products Act, 16. amendment

▶ Agricultural industry

- ▶ QS

▶ Scientific monitoring

- ▶ VetCAb

▶ Specialised investigations

- ▶ TBI,...

Who is reporting?

- ▶ Producers, traders
- ▶ farmers
- ▶ farmers
- ▶ Farmers, vets
- ▶ scientists

Antibiotic MOSS in Germany

▶ Legal Acts

- ▶ DIMDI-AMV
- ▶ Medicinal Products Act, 16. amendment

▶ Agricultural industry

- ▶ QS

▶ Scientific monitoring

- ▶ VetCAb

▶ Specialised investigations

- ▶ TBI,...

Completeness

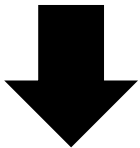
- ▶ all sales; no specification
- ▶ - fattening only
- ▶ - minimum size

- ▶ members only

- ▶ - representative sample
- ▶ - fattening, dairy, ...

- ▶ special investigation

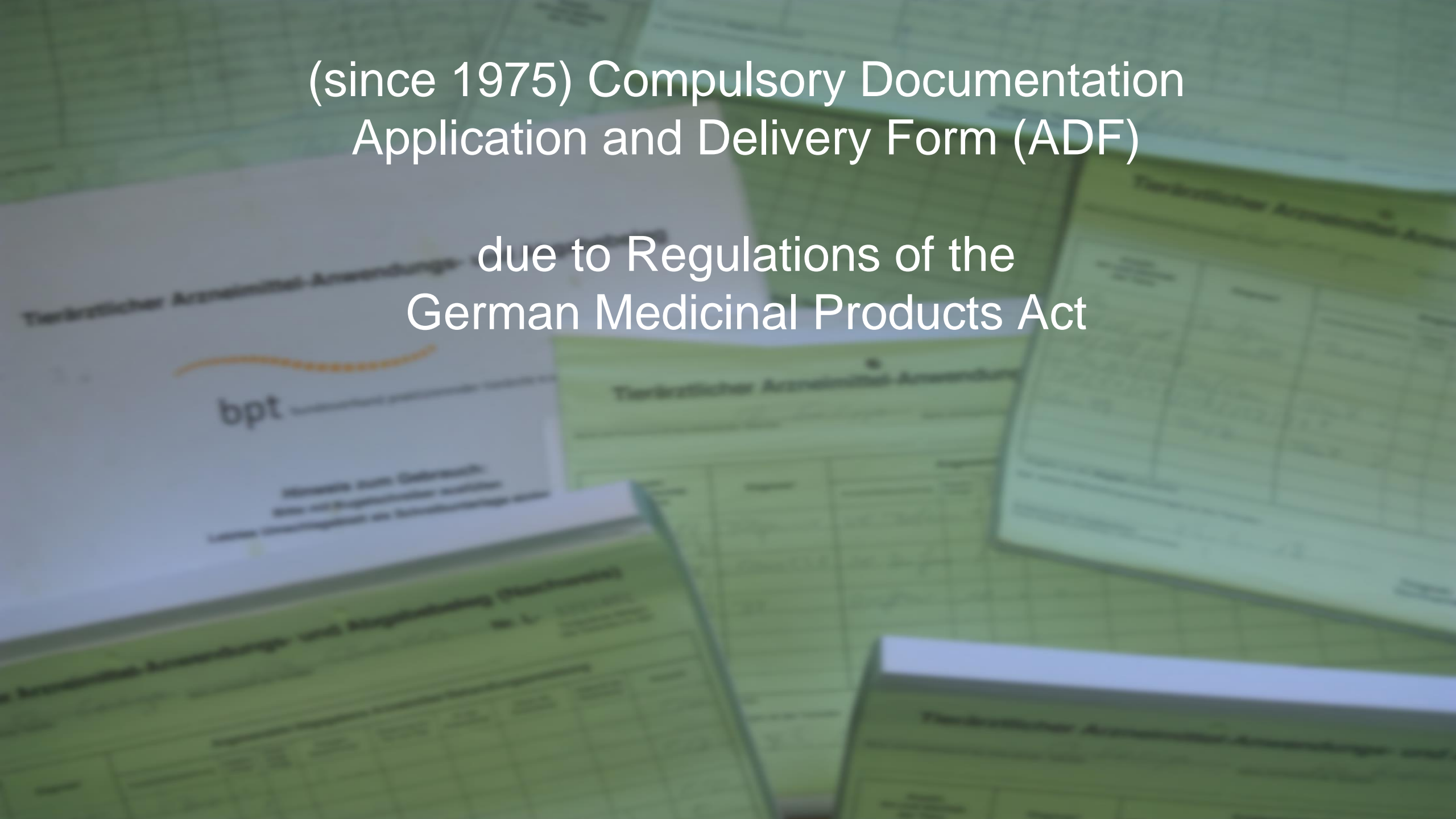
How gets the information from stable to database?



„Application and delivery form“

(since 1975) Compulsory Documentation Application and Delivery Form (ADF)

due to Regulations of the
German Medicinal Products Act



Compulsory Documentation per Farm Application and Delivery Form (ADF)

- ▶ Date of drug delivery / date of treatment
- ▶ Serial document number of the application and delivering form (ADF)
- ▶ Name and address of the veterinarian in charge
- ▶ Name and address of the livestock owner
- ▶ Number, species and identity of the animals treated
- ▶ Diagnosis
- ▶ Name of the medicinal product used
- ▶ Amount of the medicinal product delivered or applied
- ▶ Batch number
- ▶ Treatment duration, dose per animal and day
- ▶ Withdrawal period

Medicinal Products Act, Germany



Bundesanzeiger

Herausgegeben vom
Bundesministerium der Justiz
www.bundesanzeiger.de

Bekanntmachung

Veröffentlicht am Freitag, 22. Februar 2013
BANz AT 22.02.2013 B2
Seite 1 von 2

- ▶ Calculation of animals under study

**Bundesministerium
für Ernährung, Landwirtschaft und Verbraucherschutz**

**Bekanntmachung
des Berechnungsverfahrens
zur Ermittlung der Therapiehäufigkeit eines Tierhaltungsbetriebes
durch die zuständige Behörde**

Vom 21. Februar 2013

Bundesgesetzblatt Jahrgang 2013 Teil I Nr. 62, ausgegeben zu Bonn am 16. Oktober 2013

3813

- ▶ Calculation of treatment frequency, benchmarking and regulation measures

**Sechzehntes Gesetz
zur Änderung des Arzneimittelgesetzes**

Vom 10. Oktober 2013

Measures of Antibiotics Consumption

for details please see e.g.

- ESVAC
- AMCRA
- van Rennings et al., 2013
- Hemme et al., 2017
- Kasabova et al., 2018

Basic Measures



Knowledge centre on antibiotic use and resistance in animals in Belgium

Home

About AMCRA

Vision 2024

Recommendations and legislation

Raising awareness

Analysis of antibiotic use

Contact

E-Formulary

The indicator TD100

Antibiotic use can be expressed in a few different ways. As a basic rule, a good indicator consists of a **numerator**(= the number of 'technical units' used) that is standardised using a **denominator**(= the mass of animals).

Download June, 26th 2022: <https://www.amcra.be/en/analysis-of-antibiotic-use/>

Basic Measures

Formula for calculating the TD₁₀₀:

$$\text{TD}_{100} = \frac{\text{mg antibiotic}}{\text{DDDA}_{\text{bel}} \times \text{kg animals 'at risk'} \times \text{days 'at risk'}} \times \text{LA}_{\text{bel}} \times 100$$

Download June, 26th 2022: <https://www.amcra.be/en/analysis-of-antibiotic-use/>

Compulsory documentation

Application and Delivery Form (ADF)

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Treatment frequency (TF), UDD

▶ $TF = \frac{\# \text{ animals treated} \times \# \text{ treatment days}}{\text{population at risk}}$

▶ $UDD = \frac{\text{amount of active substance}}{\# \text{ animals treated} \times \text{animal weight} \times \# \text{ treatment days}}$

▶ $TF = \frac{\text{amount of active substance}}{\text{population at risk} \times \text{animal weight} \times UDD}$

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▶ $TF_{UDD} = \frac{\text{amount of active substance}}{\text{population at risk} \times \text{animal weight} \times UDD}$

Treatment frequency (TF), UDD / DDD

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▶ $TF_{DDD} = \frac{\text{amount of active substance}}{\text{population at risk} \times \text{standard weight} \times DDD}$

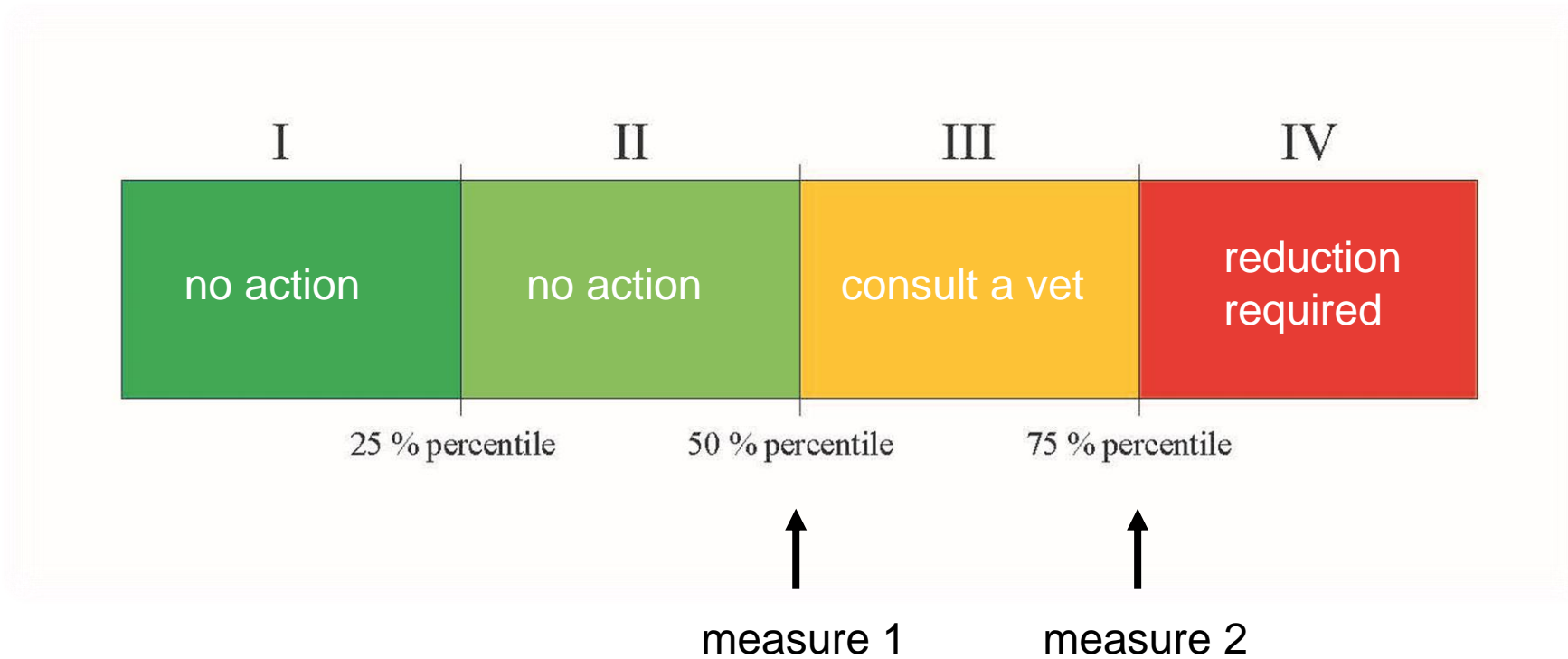
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▶ $TF_{DDD} = \frac{\text{amount of active substance}}{\text{population at risk} \times \text{standard weight} \times DDD} = TI$

Benchmarking areas within the German Medicinal Products Act



16th amendment of the German Medicinal Products Act

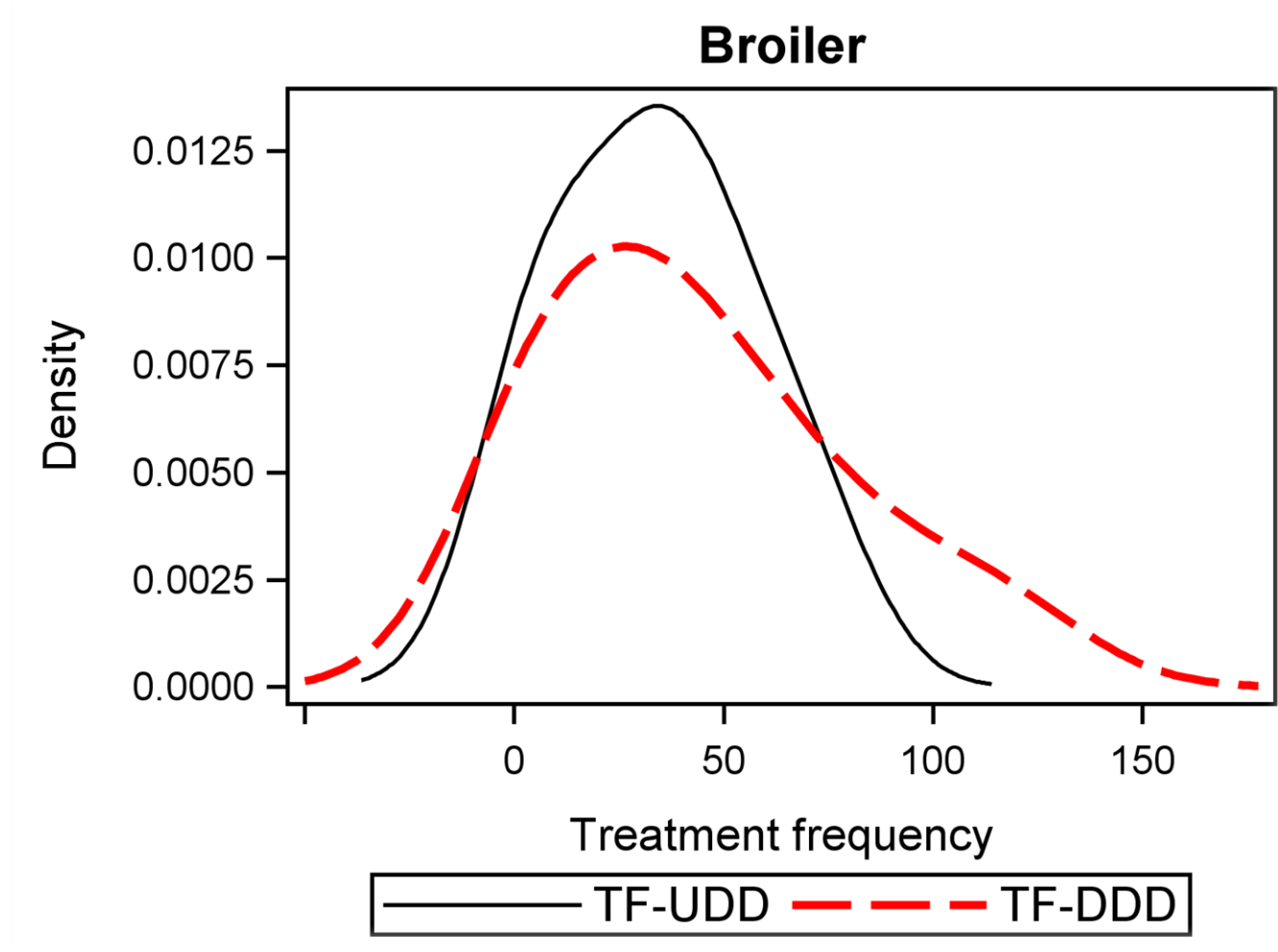
Comparing TF_{UDD} and TF_{DDD}

for details see

Kasabova S, Hartmann M, Werner N, Käsbohrer A, Kreienbrock L.
Used Daily Dose vs. Defined Daily Dose—Contrasting Two
Different Methods to Measure Antibiotic Consumption at the Farm
Level. *Frontiers in Veterinary Science*. 2019;6(116).

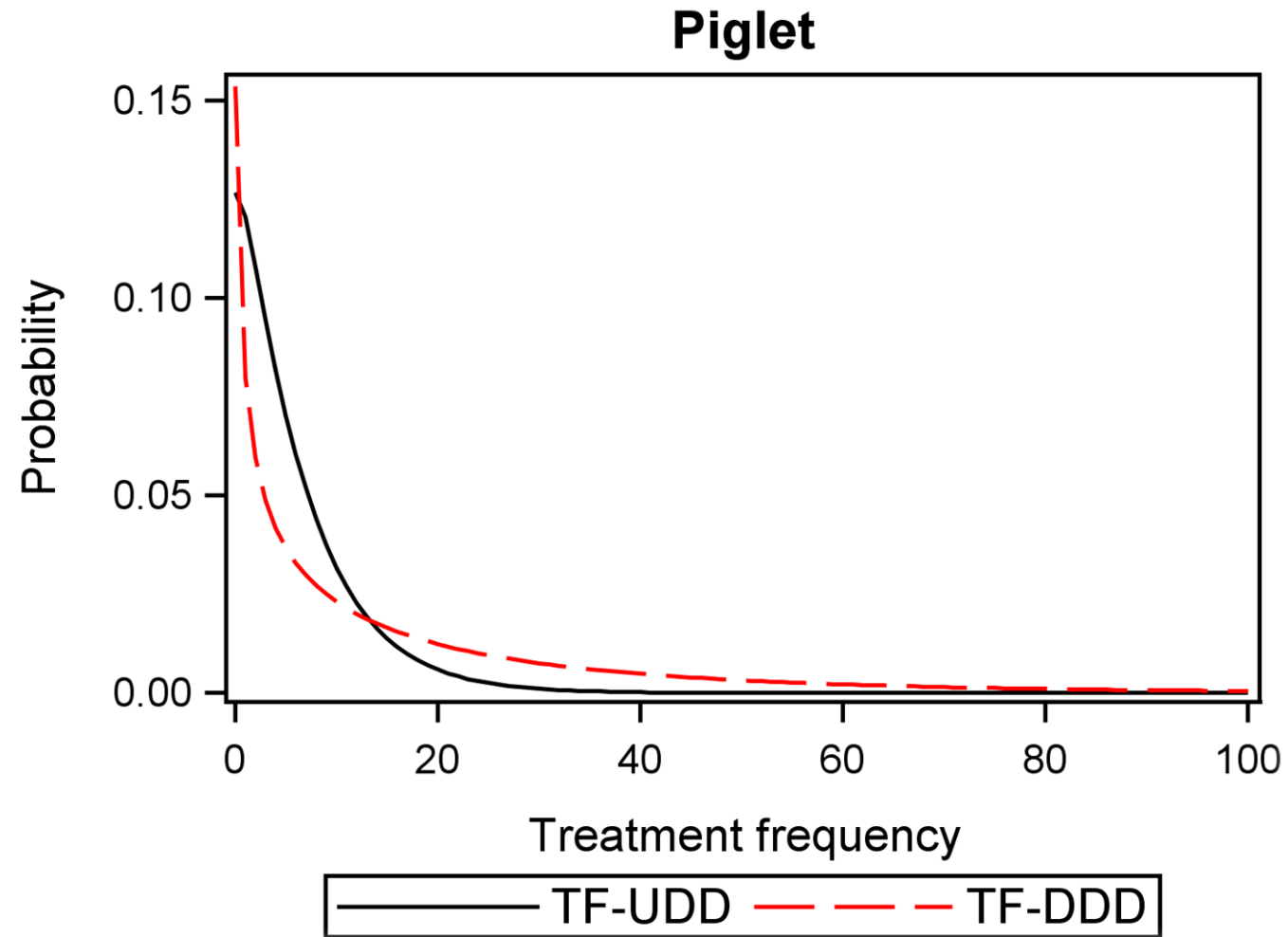


Distribution of the TF_{UDD} and TF_{DDD}



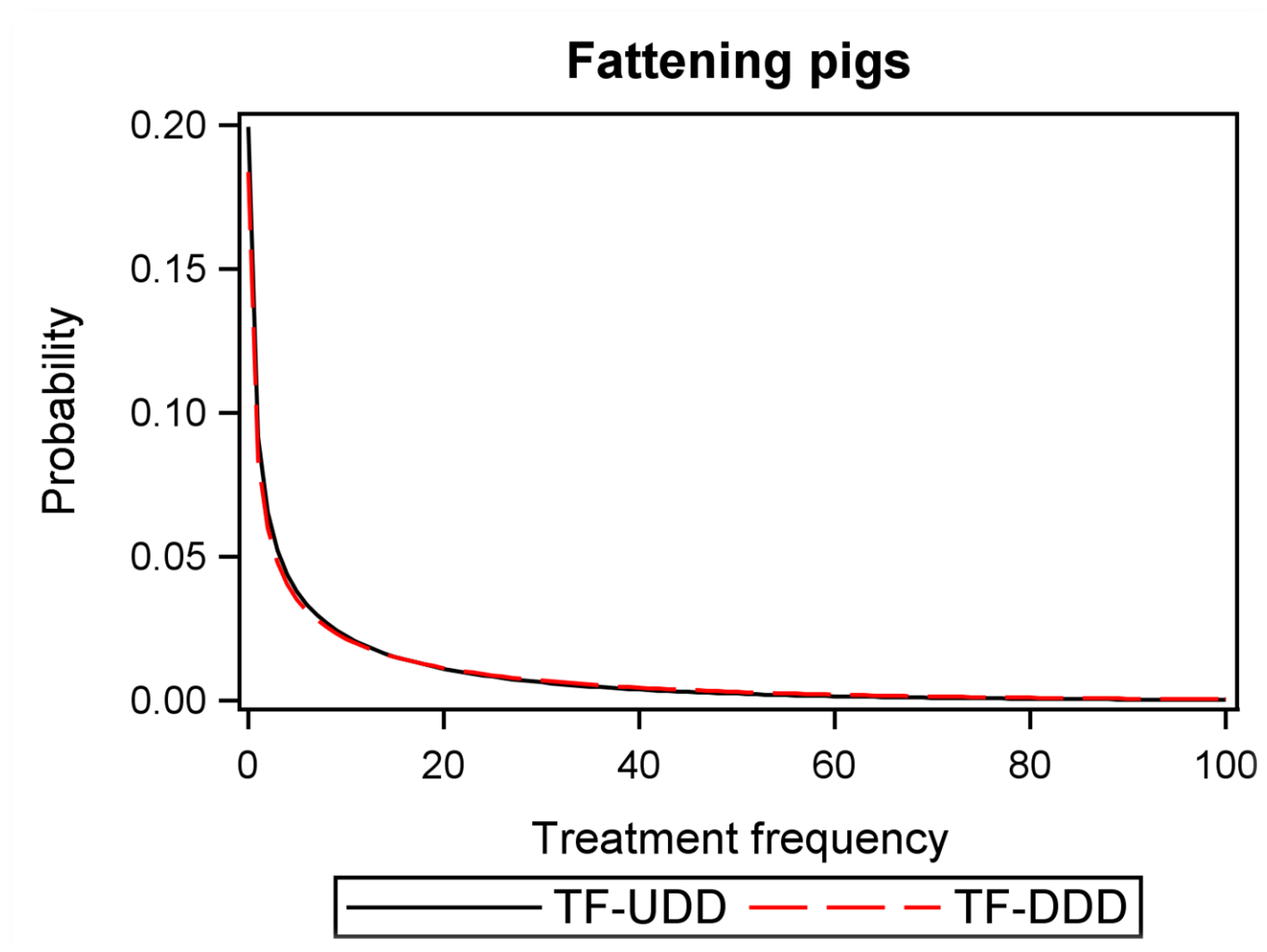


Distribution of the TF_{UDD} and TF_{DDD}







Distribution of the TF_{UDD} and TF_{DDD}



Shift in Statistical Measures

| | n | min | 5% | 50% | 75% | 95% | max | |
|------------|-----|--|---------|------|------|-------|-------|--|
| | |  | Broiler | | | | | |
| TF_{UDD} | 40 | - | 1.0 | 33.9 | 49.2 | 72.7 | 77.6 | |
| TF_{DDD} | 40 | - | 0.3 | 35.2 | 65.8 | 113.3 | 127.7 | |
| | |  | Piglets | | | | | |
| TF_{UDD} | 137 | - | - | 3.5 | 7.5 | 17.4 | 39.3 | |
| TF_{DDD} | 137 | - | - | 6.2 | 15.5 | 92.7 | 187.7 | |



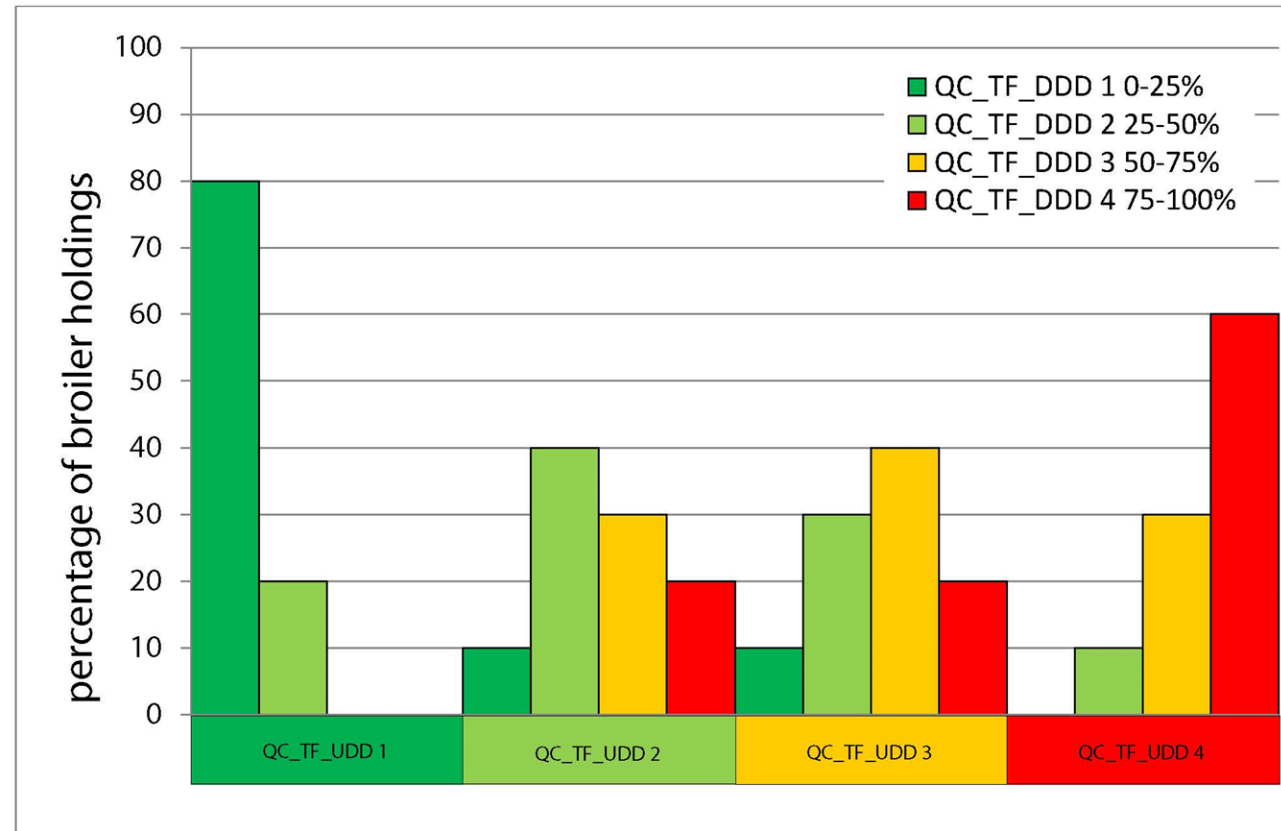
Similarity in the benchmarking due to TF_{UDD} - and TF_{DDD} -distributions for broiler

| TF_{UDD} | TF_{DDD} | | | | | | | |
|------------|------------|------|----|------|-----|------|----|-----|
| | I | | II | | III | | IV | |
| | n | % | n | % | n | % | n | % |
| I | 8 | 20% | 2 | 5% | 0 | 0% | 0 | 0% |
| II | 1 | 2.5% | 4 | 10% | 3 | 7.5% | 2 | 5% |
| III | 1 | 2.5% | 3 | 7.5% | 4 | 10% | 2 | 5% |
| IV | 0 | 0% | 1 | 2.5% | 3 | 7.5% | 6 | 15% |

(overall similarity 55 %)



Amount of Misclassification (UDD as standard)



VetCAb Standard weights

| Production group | from | to | Ø |
|------------------|----------|--------|----------|
| Piglets | 1 kg | 8,8 kg | 4 kg |
| Sow | 110 kg | 290 kg | 200 kg |
| Weaner | 7.5 kg | 30 kg | 15 kg |
| Fattening pigs | 25 kg | 120 kg | 50 kg |
| Broiler | 0.038 kg | 2,3 kg | 0,471 kg |
| Dairy cow | 470 kg | 850 kg | 600 kg |
| Cattle | 80 kg | 800 kg | 300 kg |
| Calve | 28 kg | 250 kg | 150 kg |

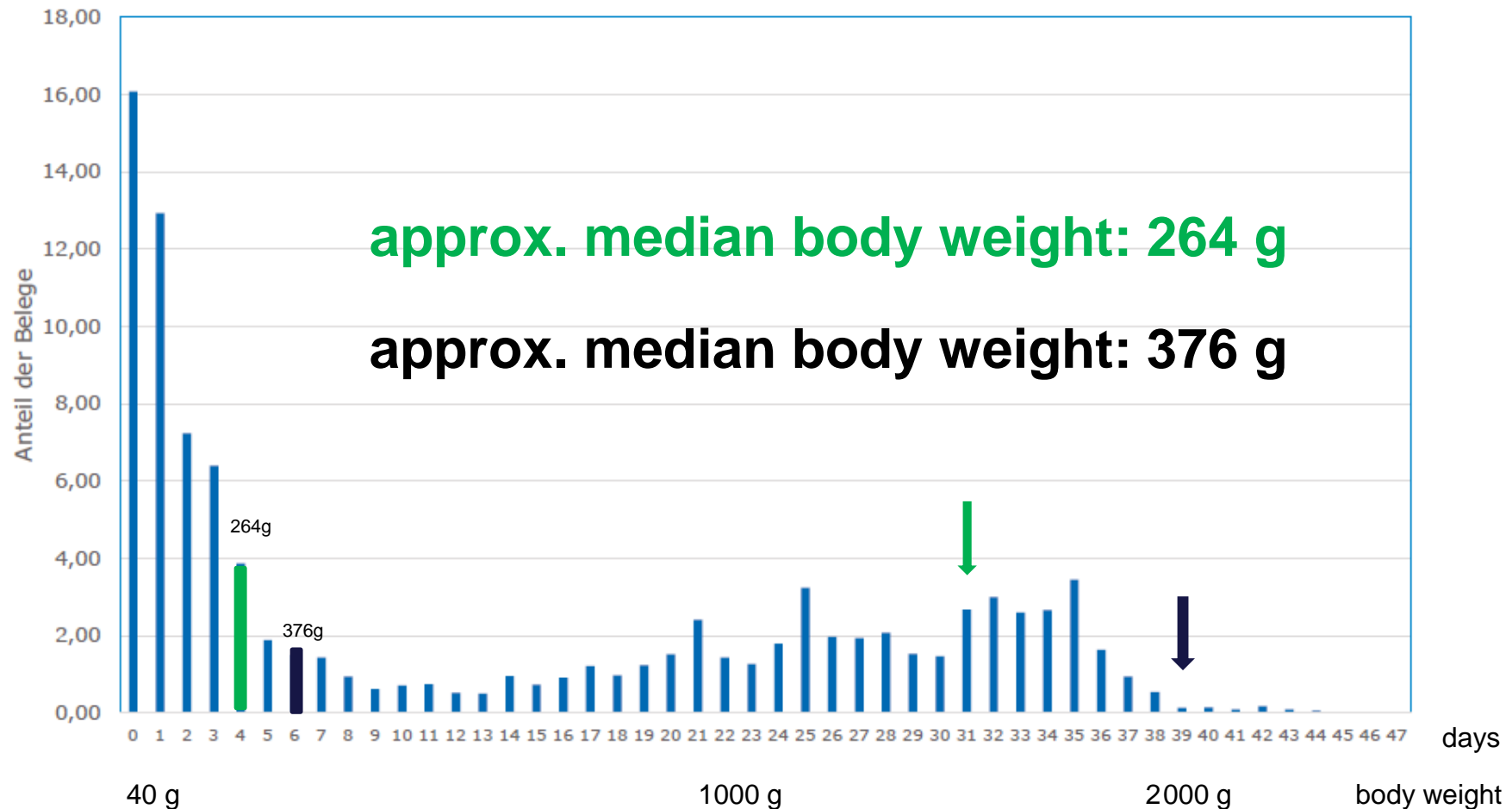
ESVAC Standard Weights

| Species | Weight group/Production type | Ø |
|---------|------------------------------|-------|
| Pigs | Suckling piglets | 4kg |
| | Weaners | 12kg |
| | Sows/boars | 220kg |
| | Finishers | 50kg |
| Cattle | Veal calves | 80kg |
| | Dairy cattle | 500kg |
| | beef cattle | 500kg |
| Poultry | Broilers | 1kg |
| | Turkeys | 6kg |

*Source: Revised ESVAC reflection paper on collecting data on consumption of antimicrobial agents per animal species, on technical units of measurement and indicators for reporting consumption of antimicrobial agents in animals OF
EMA/286416/2012-Rev.1*



The Daily Dosage Uncertainty (in Germany) – an example: treatment weights for broiler ©



If daily weight gain: 56 g (KTBL, 2014)

© QS Qualität und Sicherheit GmbH, Bonn

Estimated Number of Dosage ...

- ▶ ... is prone to several uncertainties like
 - ▶ medical indications
 - ▶ resistance situation
 - ▶ veterinarian's decision
 - ▶ unknown body weights of the animals treated
 - ▶ different UDDs proposed for similar drugs
- ▶ ... follows a statistical distribution
- ▶ ... may be contrasted to DDD from the literature



The Daily Dosage Uncertainty

– an example: Amoxicillin oral for pigs

- ▶ DDD_{Vet}
 - ▶ ESVAC: 17mg/kg BW
 - ▶ VetCAb: 30mg/kg BW

- ▶ Licensed drugs in Germany
 - ▶ Aciphen Kompaktat: 2 x 20mg/kg BW
 - ▶ Centicillin 1000: 2x20mg/kg BW
 - ▶ Amoxicillin Trihydrat: 10mg/kg BW

Conclusion UDD vs DDD

▶ **Treatment Frequency based on UDD**

- ▶ Complex and costly data collection with increased documentation effort
- ▶ Represents the population treated more accurately

▶ **Treatment Frequency based on DDD**

- ▶ data collection effort is substantially lower
- ▶ carries the risk of under- or overestimating the number of animals treated

Sales data for Germany

DIMDI Sales Data

(Deutsches Institut für Medizinische Dokumentation und Information)

| | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|------|-------|-------|-------|-------|------|------|------|------|------|------|
| tons | 1,706 | 1,619 | 1,452 | 1,238 | 805 | 742 | 733 | 722 | 670 | 701 |
| % | 100.0 | 94.9 | 85.1 | 72.6 | 47.2 | 43.5 | 42.3 | 42.3 | 39.3 | 41.1 |

Source: BVL, download: 20. Oktober 2021

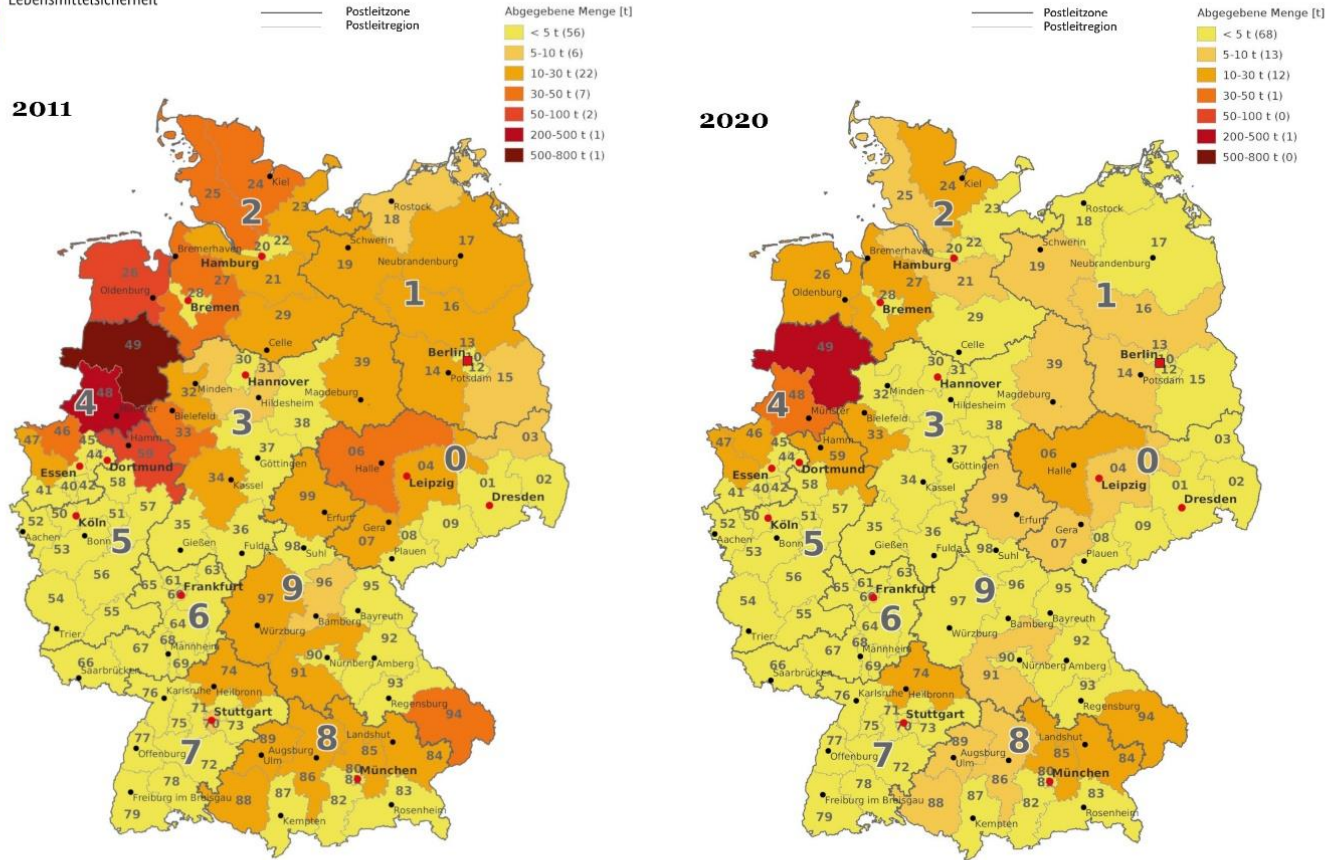
DIMDI Sales Data by Antibiotic Classes

(Deutsches Institut für Medizinische Dokumentation und Information)

| | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
|-----------------------|--------------|--------------|--------------|--------------|------------|------------|------------|
| Tetrazykline | 564 | 566 | 454 | 342 | 221 | 193 | 188 |
| Penicilline | 528 | 501 | 473 | 450 | 299 | 279 | 269 |
| Makrolide | 173 | 145 | 126 | 109 | 52,5 | 54,7 | 54,7 |
| Sulfonamide | 185 | 162 | 152 | 121 | 72,6 | 68,8 | 62,4 |
| Polypeptidantibiotika | 127 | 123 | 125 | 107 | 81,8 | 68,9 | 73,6 |
| Aminoglykoside | 47,1 | 40,5 | 39,4 | 37,8 | 24,7 | 26,1 | 29,3 |
| Folsäureantagonisten | 39,9 | 26,2 | 24,3 | 19,1 | 10,3 | 9,8 | 7,8 |
| Lincosamide | 16,8 | 15,2 | 16,9 | 14,6 | 10,8 | 9,9 | 10,9 |
| Fluorchinolone | 8,2 | 10,4 | 12,1 | 12,3 | 10,6 | 9,3 | 9,9 |
| Pleuromutiline | 14,1 | 18,4 | 15,5 | 13,0 | 11,2 | 9,9 | 13,4 |
| Fenicole | 6,1 | 5,7 | 5,2 | 5,3 | 5,0 | 5,1 | 5,6 |
| Cephalosp., 1. Gen. | 2,0 | 2,1 | 2,1 | 2,1 | 1,9 | 2,0 | 2,0 |
| Cephalosp., 3. Gen. | 2,1 | 2,3 | 2,3 | 2,3 | 2,3 | 2,3 | 2,3 |
| Cephalosp., 4. Gen. | 1,4 | 1,4 | 1,4 | 1,4 | 1,3 | 1,1 | 1,1 |
| Sonstige * | 0,12 | 0,11 | 1,89 | 2,47 | 0,31 | 2,80 | 3,41 |
| Gesamt | 1.706 | 1.619 | 1.452 | 1.238 | 805 | 742 | 733 |

Source: BMG-Evaluation-Report, 2019

Sales Data 2011 vs. 2020 by Region

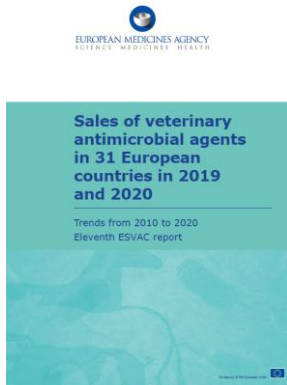
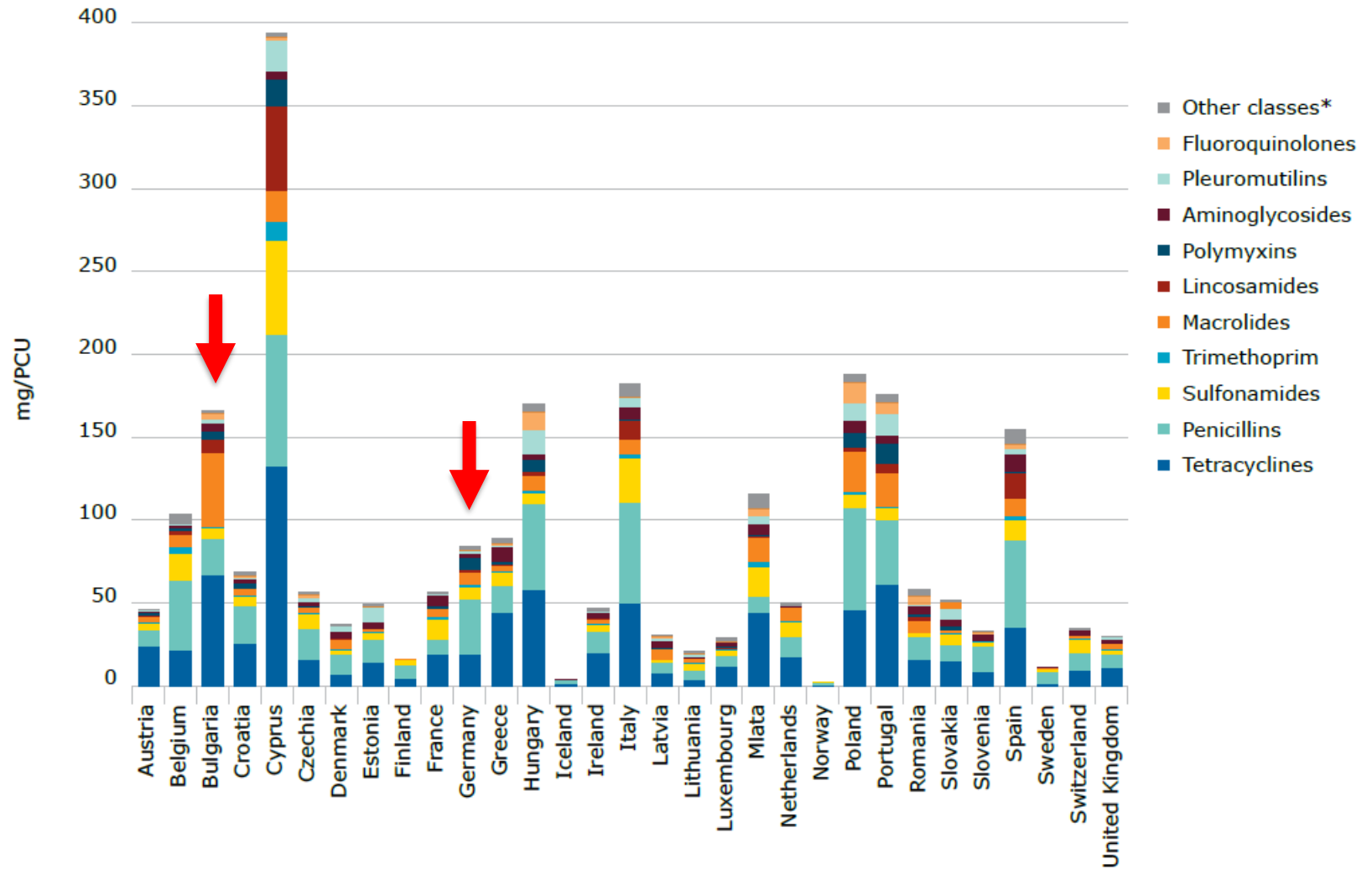


© Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)

Abbildung 1: Antibiotika-Abgabemengen in der Tiermedizin nach Postleitregion in den Jahren 2011 und 2020

https://www.bvl.bund.de/SharedDocs/Pressemitteilungen/_tierarzneimittel/2021/2021_10_12_PI_Abgabemenge_Antibiotika_Tiermedizin.html

AM Sales Data 2020 in Europe

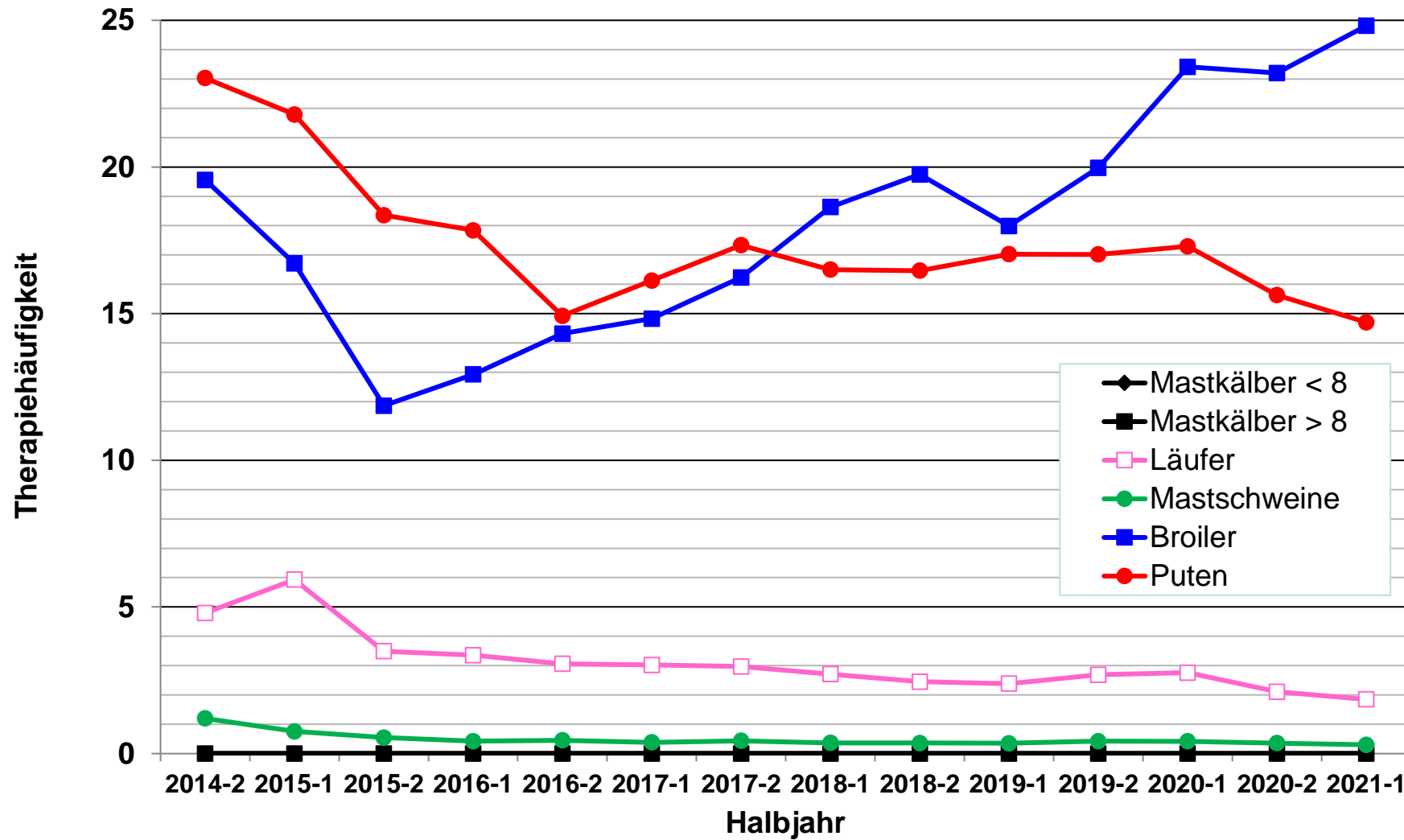


Monitoring data for Germany
due to the German Medicinal Products Act

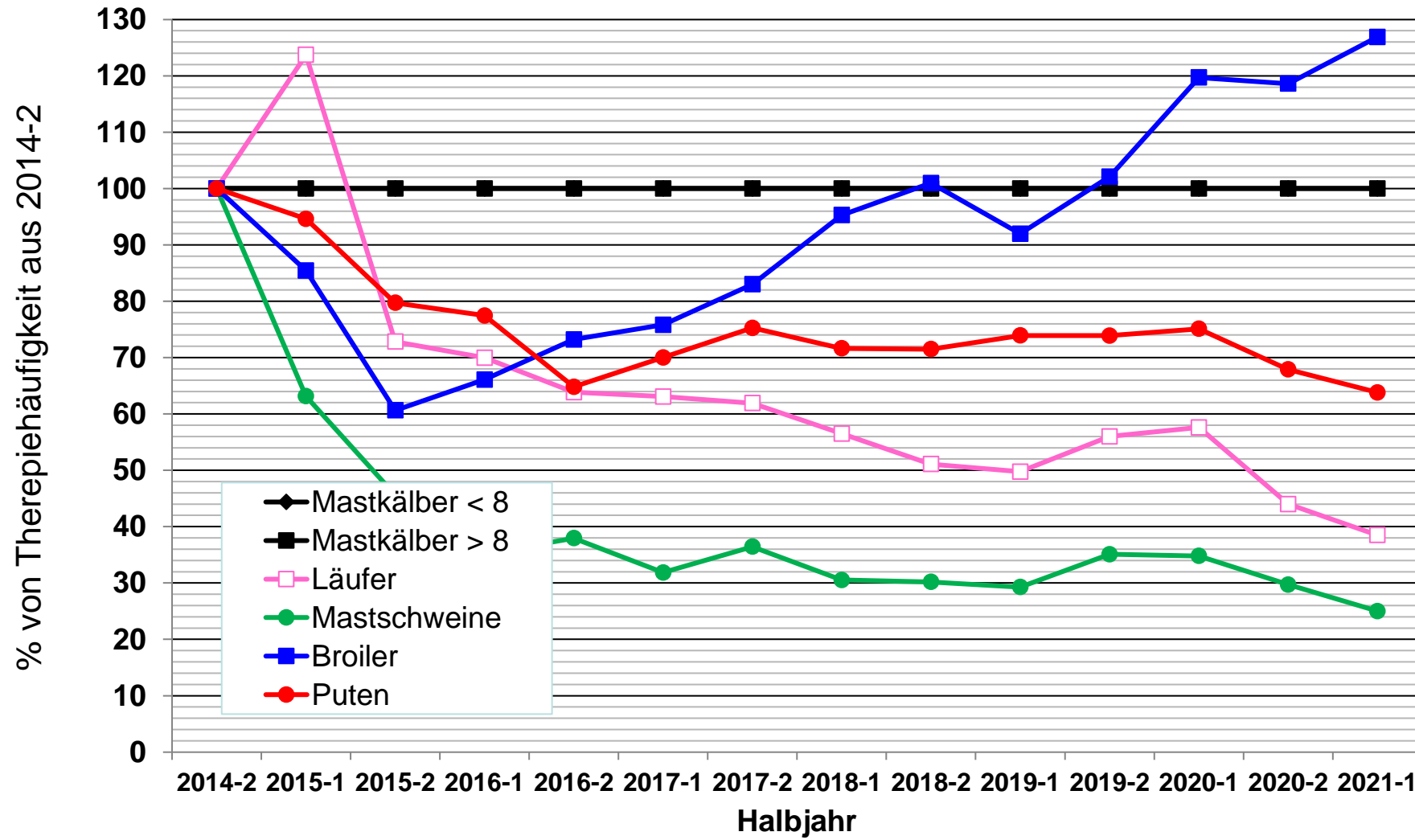
Mandatory Monitoring HI-Tier

- ▶ does only publish the 50%- and the 75%-percentile of the entire distribution of therapy frequencies per animal group
- ▶ is for vet-administrative (i.e. benchmarking) use only
- ▶ does not allow any scientific use (exception: for the 5-year evaluation in 2018/19)

HI-Tier: (absolute) median trends



HI-Tier: (relative) median trends



HI-Tier: Trends by Antibiotic Classes (difference in median treatment frequency)

| Wirkstoffklasse | Mastkälber | Mastrinder | Mastferkel | Mast- schweine | Mast- hühner | Mastputen |
|------------------------|------------|------------|------------|-------------------|-----------------|-----------|
| Aminoglykoside | -0,11 | -0,03 | -0,54 | -0,06 | 0,61 | -0,51 |
| Cephalosporine 3. Gen. | 0,03 | -0,01 | -0,33 | 0,00 | | |
| Cephalosporine 4. Gen. | -0,02 | -0,02 | -0,03 | -0,01 | | |
| Fenicole | -0,03 | -0,04 | -0,02 | -0,01 | | |
| Fluorchinolone | -0,06 | -0,02 | -0,07 | -0,02 | 0,02 | -1,13 |
| Folsäureantagonisten | -1,03 | -0,13 | -1,71 | -1,21 | -1,23 | -1,42 |
| Lincosamide | -0,03 | -0,04 | -0,45 | -0,04 | 0,61 | 0,73 |
| Makrolide | -0,11 | -0,06 | -0,93 | -0,27 | -0,80 | -0,55 |
| Penicilline | -0,13 | -0,03 | -2,69 | -0,51 | -0,87 | -2,27 |
| Pleuromutiline | | | -0,35 | -0,31 | | -0,44 |
| Polypeptidantibiotika | -1,22 | -0,39 | -4,15 | -1,31 | -0,23 | -0,96 |
| Sulfonamide | -1,17 | -0,19 | -1,73 | -1,22 | -1,24 | -0,68 |
| Tetrazykline | -0,97 | -0,11 | -1,86 | -0,99 | -0,53 | -0,76 |

Source: BMG-Evaluation-Report, 2019


VetCAb

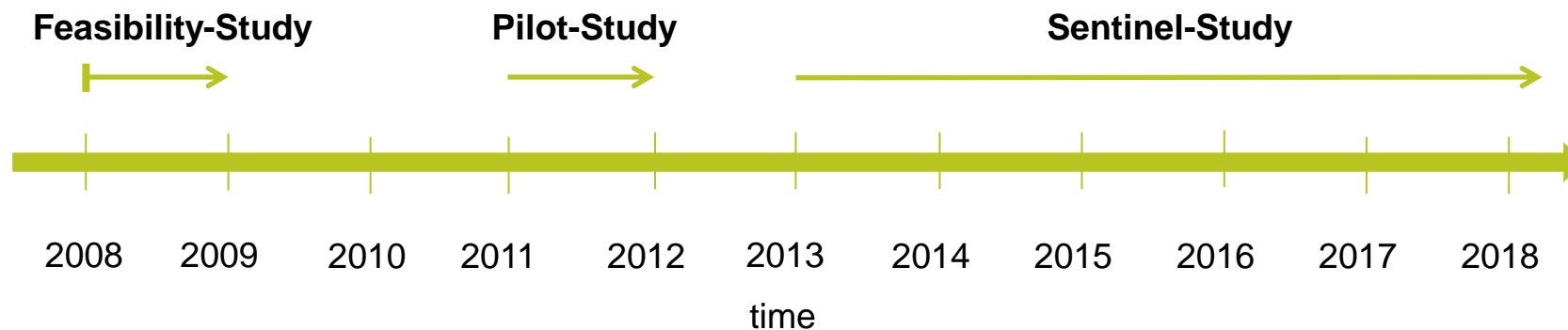


Veterinary Consumption of Antibiotics

- Sentinel Study
in German Food Producing Animals

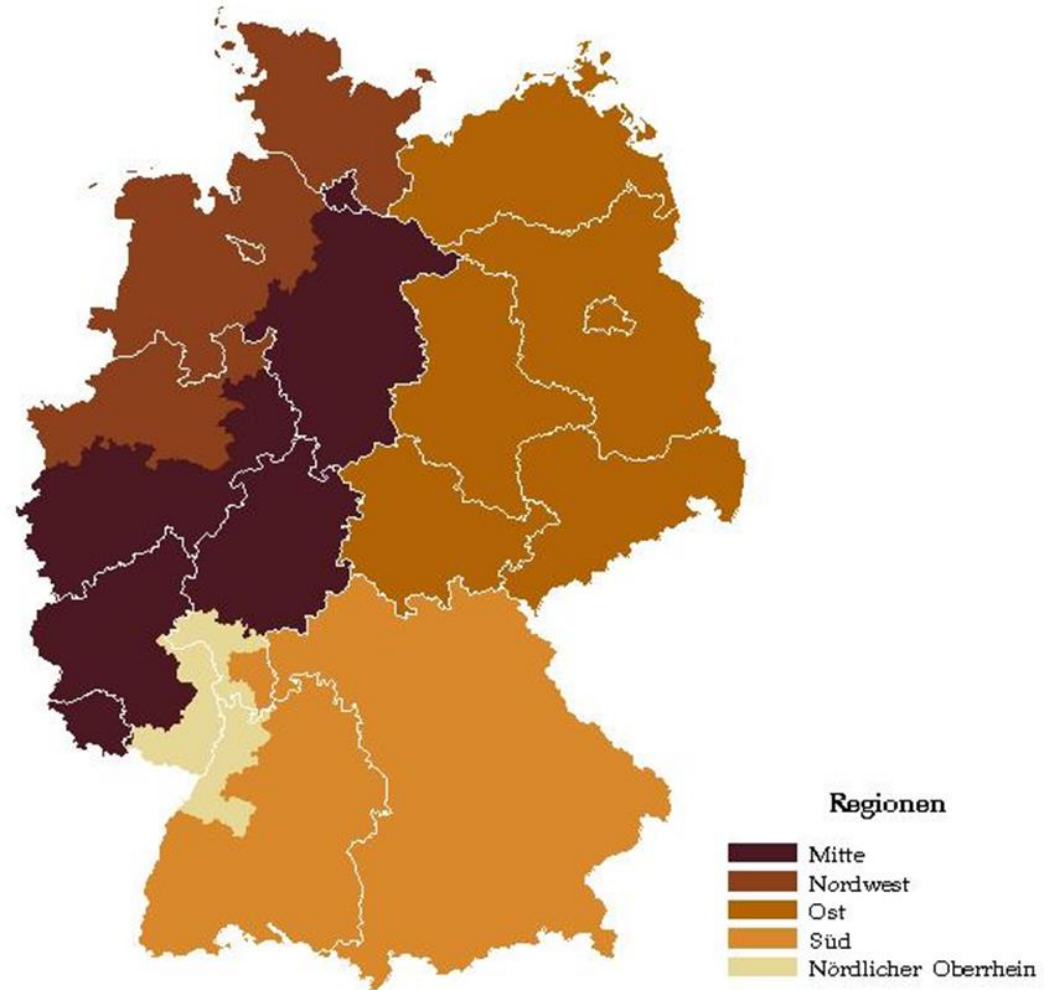
Veterinary Consumption of Antibiotics

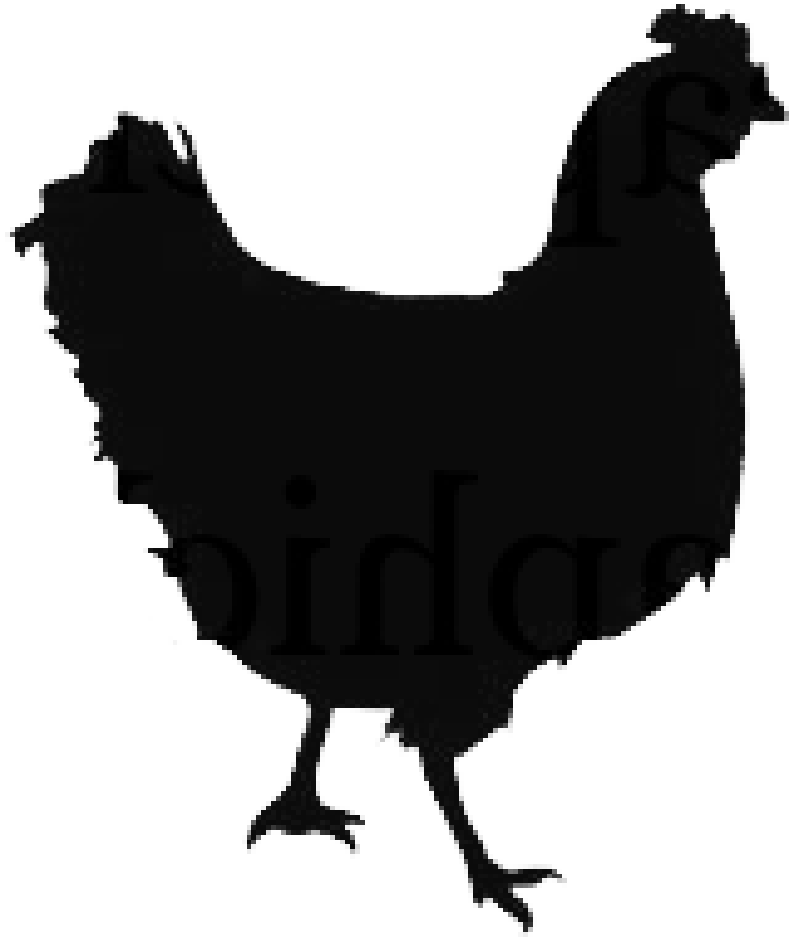
- ▶ **VetCAB**  (Veterinary Consumption of Antibiotics) is a research project, which is carried out to describe the use of antibiotics in farm animals in Germany.
- ▶ The project started as a feasibility study in 2008, and in 2011, a pilot project was carried out in a cross-sectional approach.
- ▶ Since 2013, the VetCAB-Sentinel project is continued as a longitudinal study with ongoing participant recruitment and data collection.



VetCAb – General Objectives

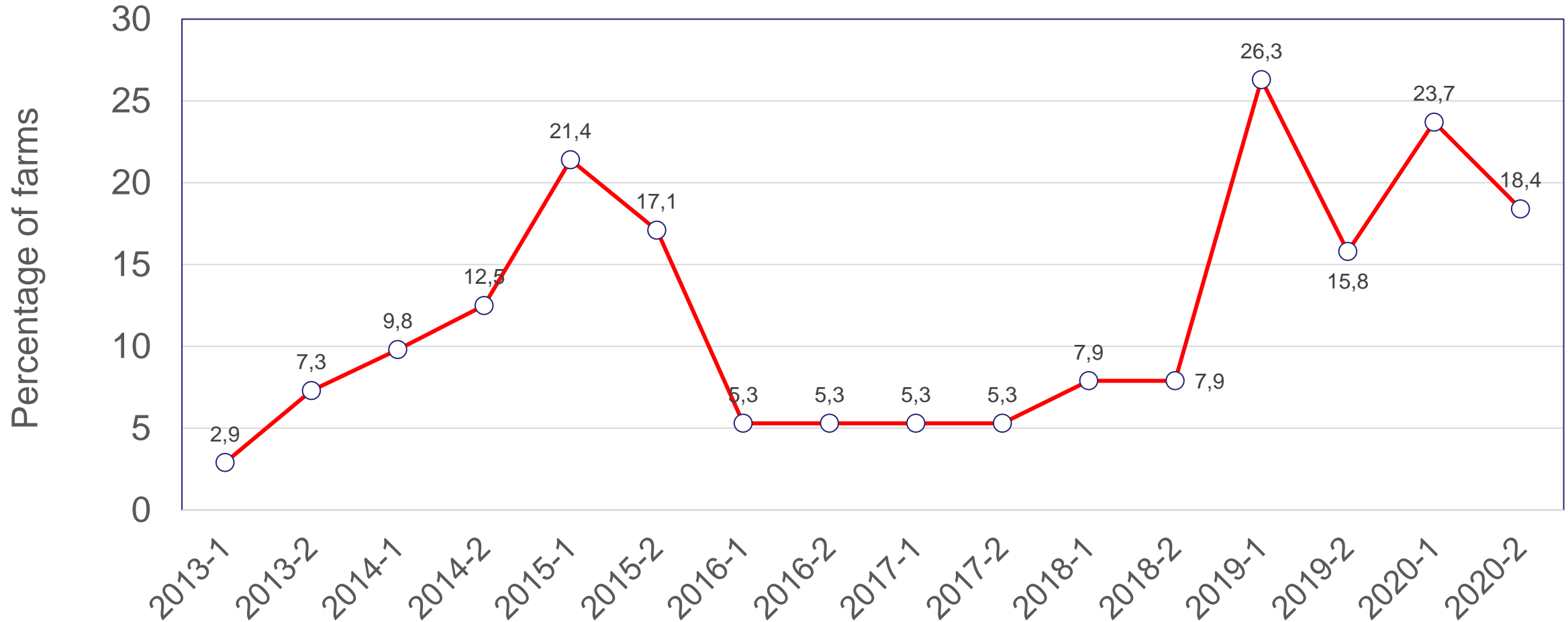
- ▶ Estimation of antibiotics use in Germany
 - ▶ representative
 - ▶ in several regions
- ▶ Antibiotics use in several
 - ▶ Animal species
 - ▶ Age groups





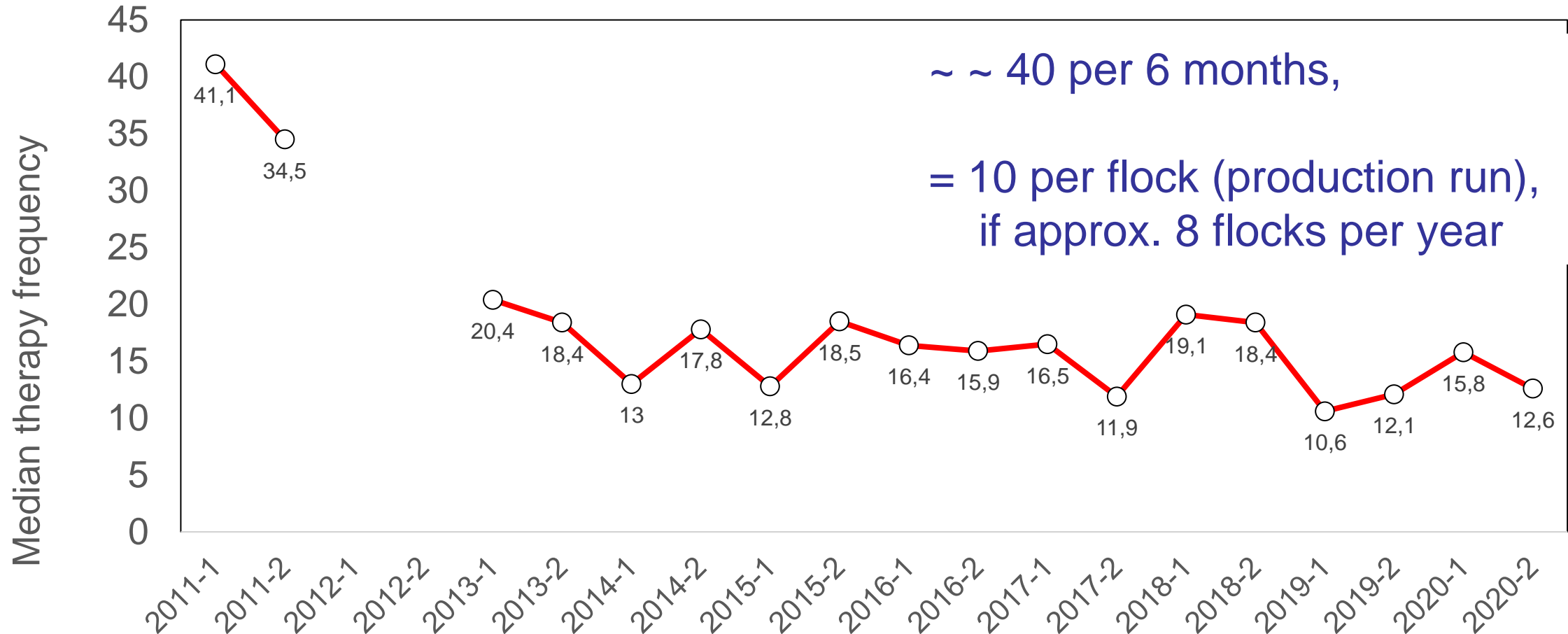


Farms With No Use of Antibiotics



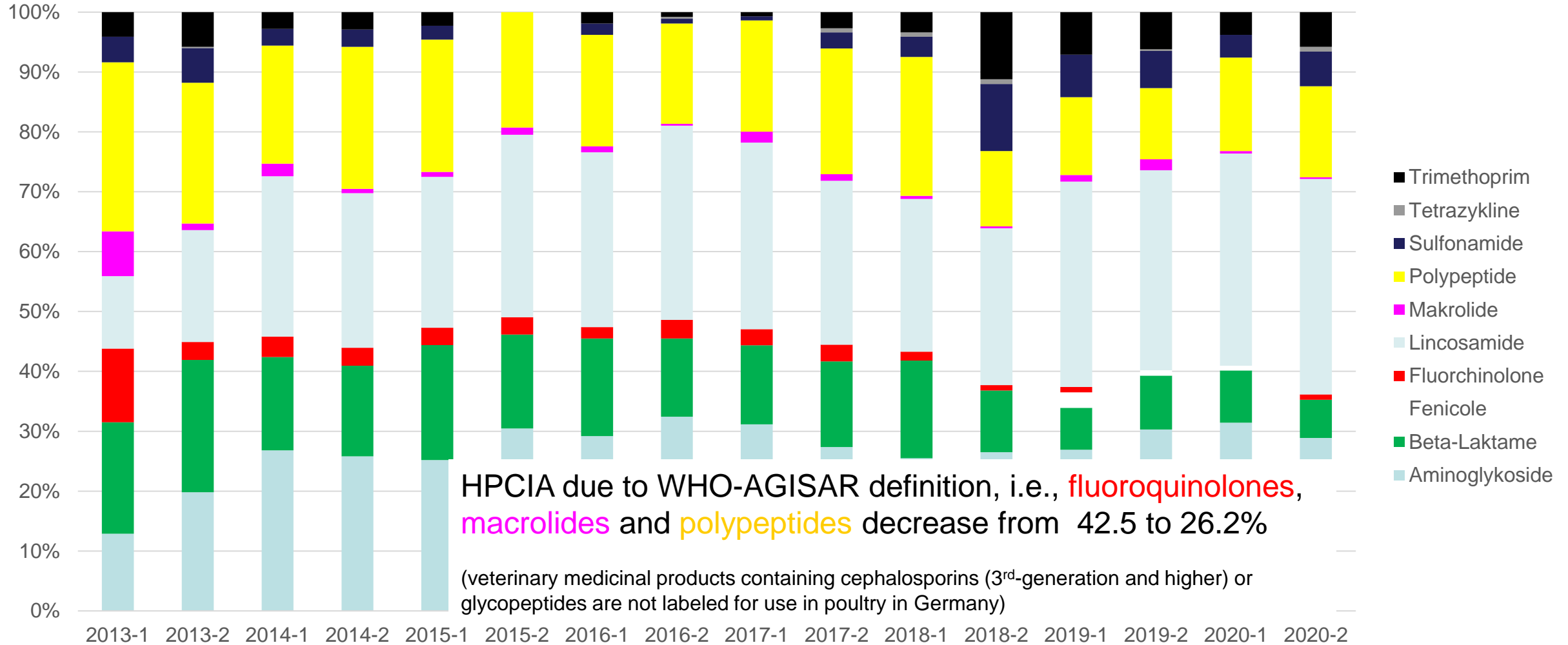


Longitudinal Development of TF Median



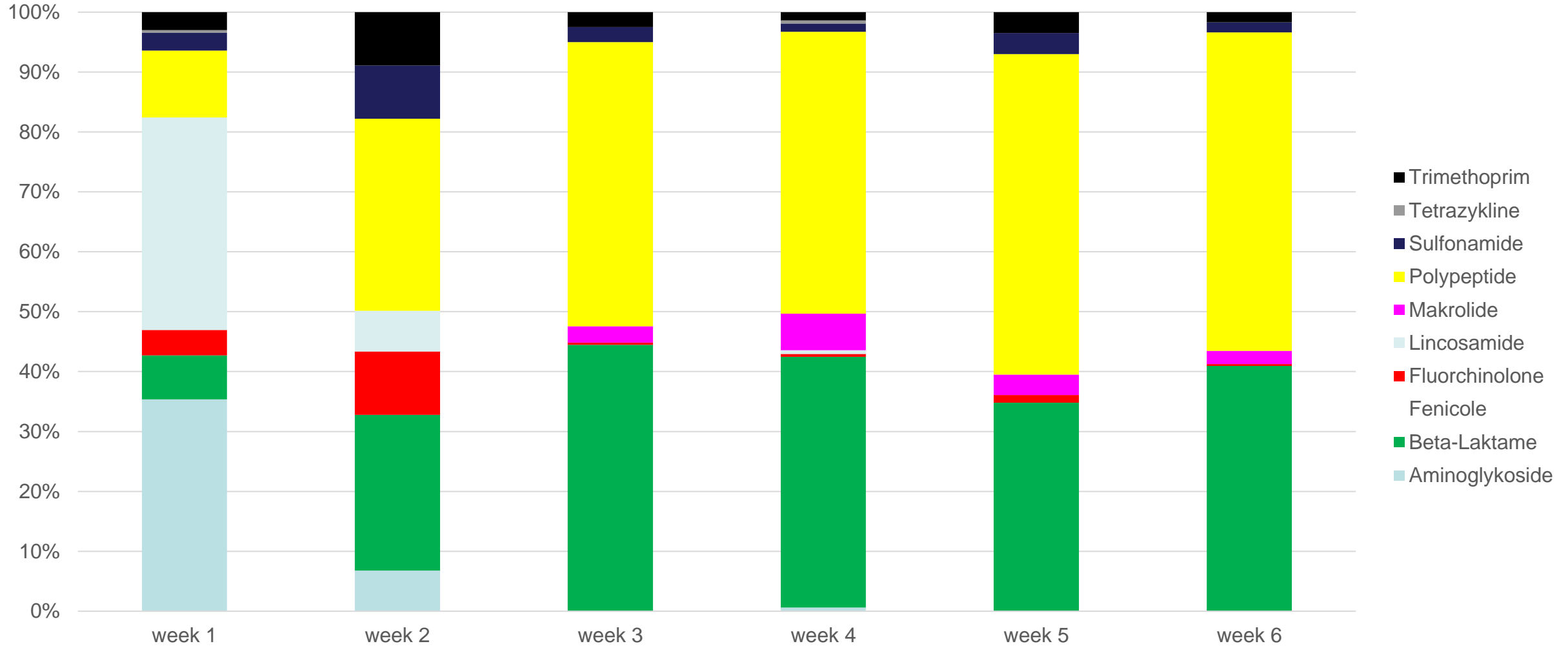


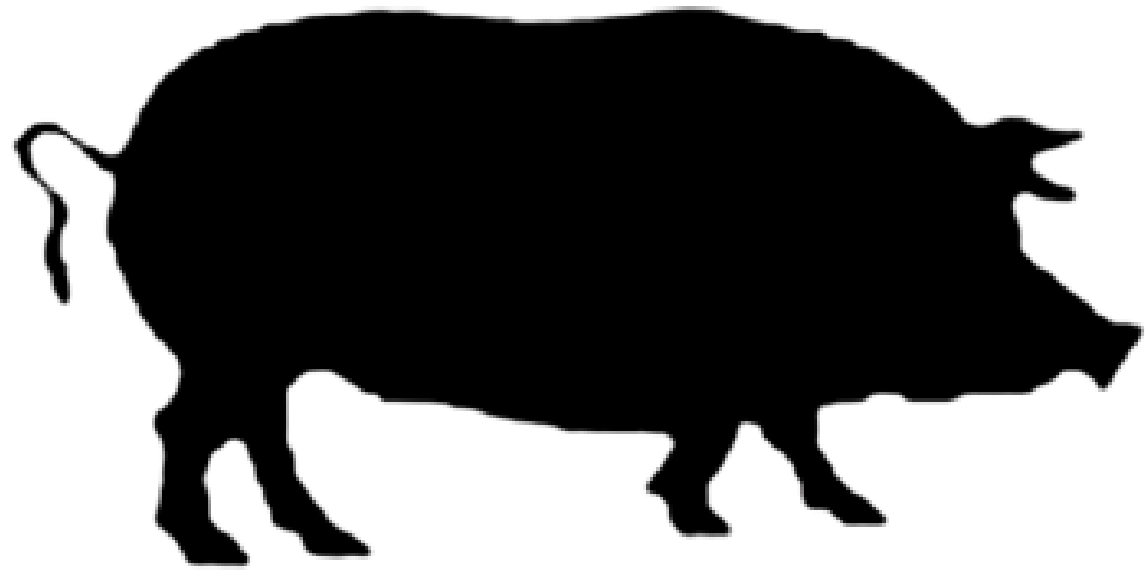
Relative TF in % per active compound and year





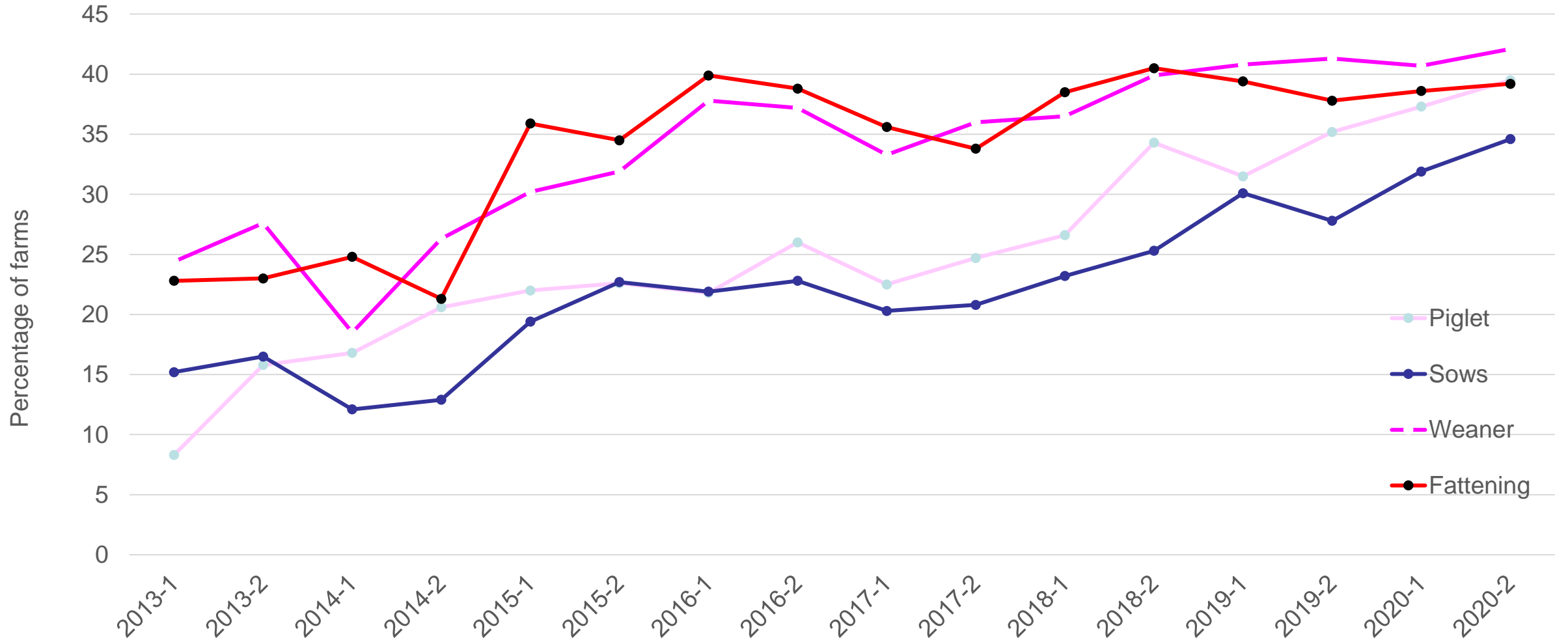
Relative TF in % per active compound and fattening week





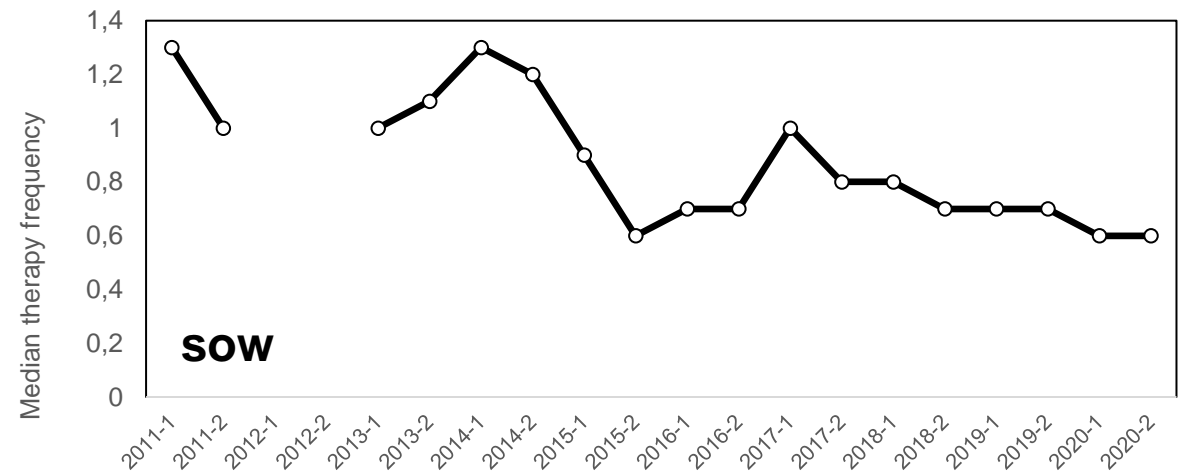
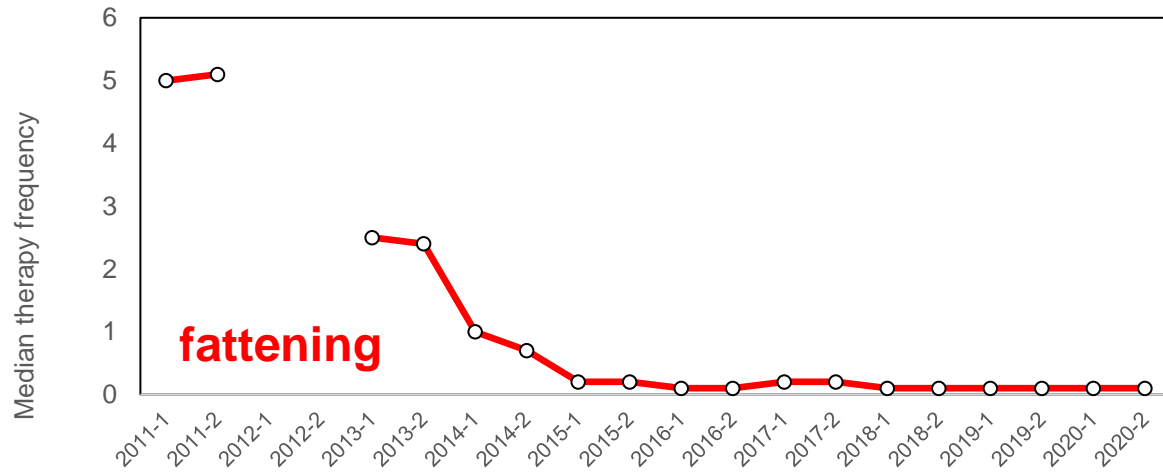
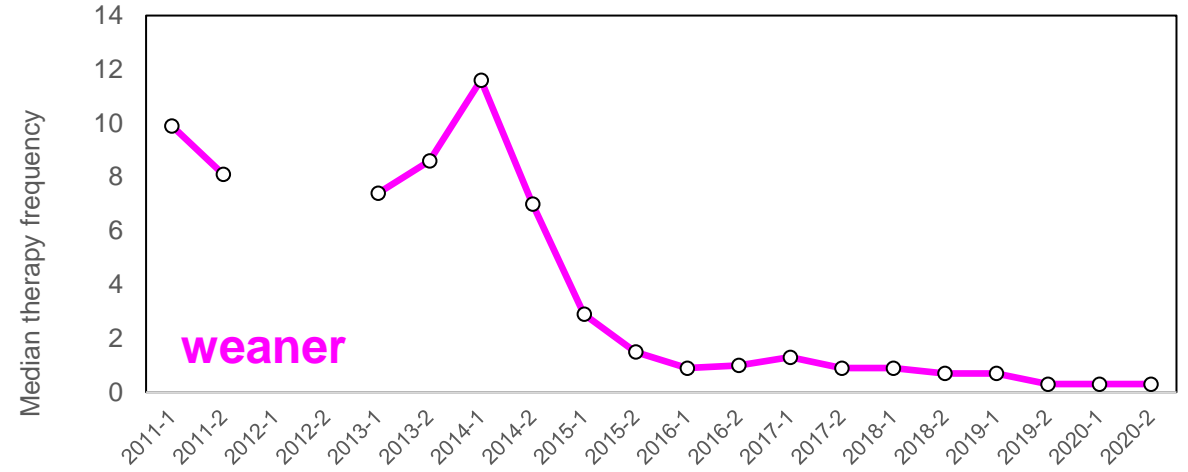
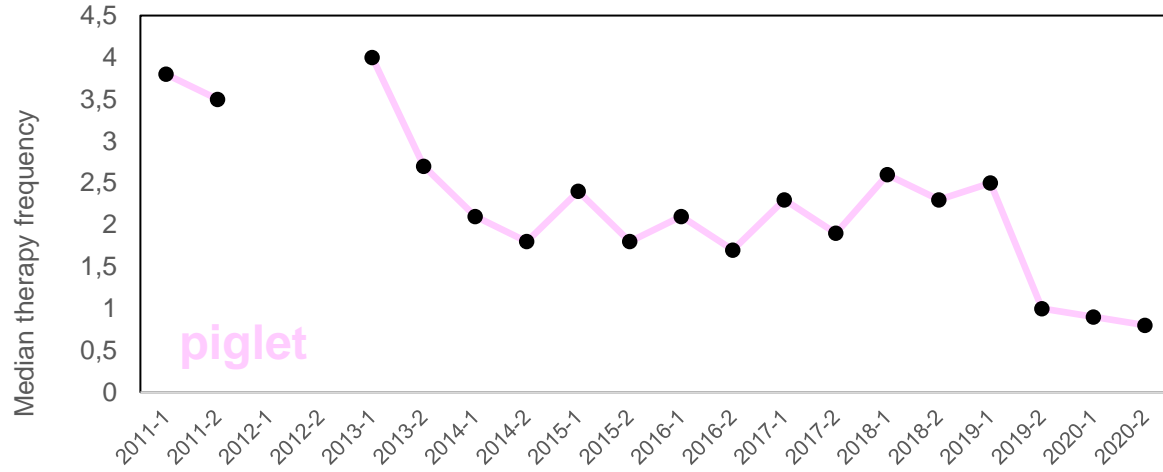


Farms With No Use of Antibiotics

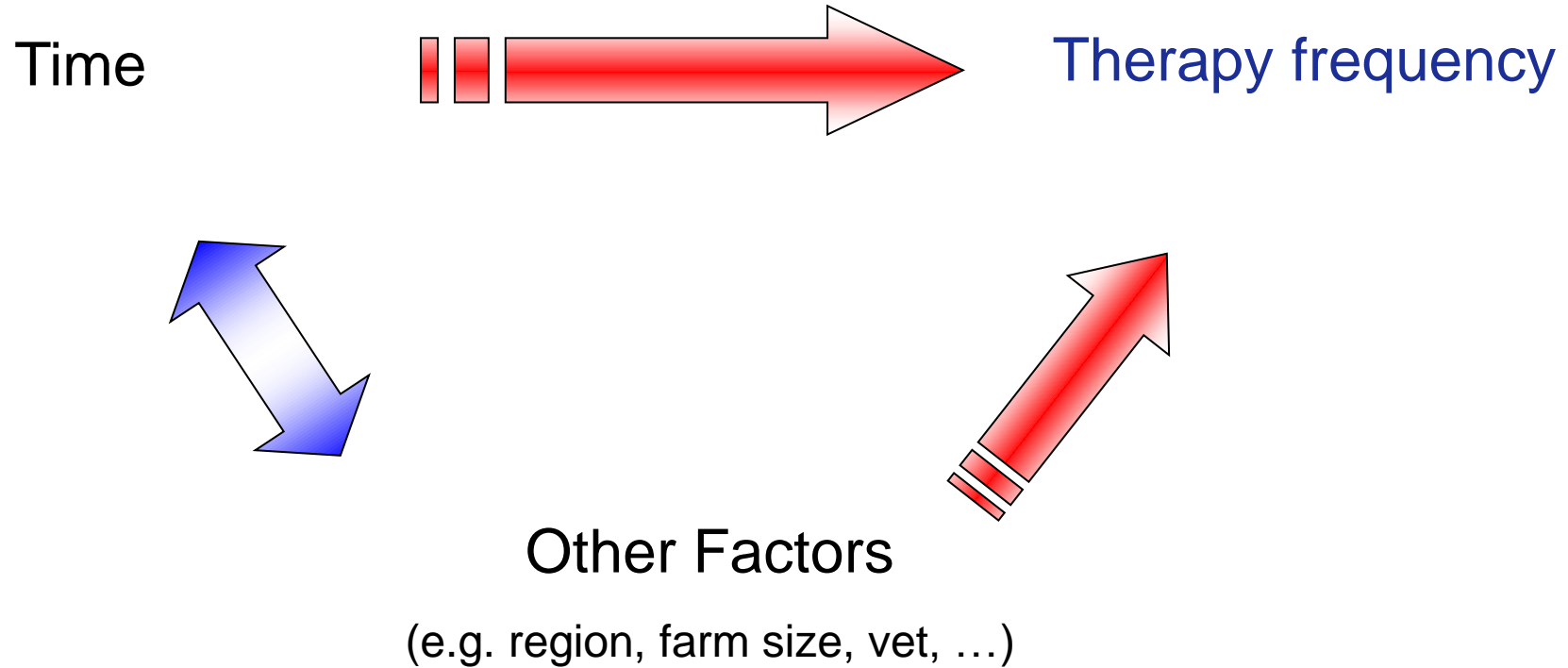




Longitudinal Development of TF Median



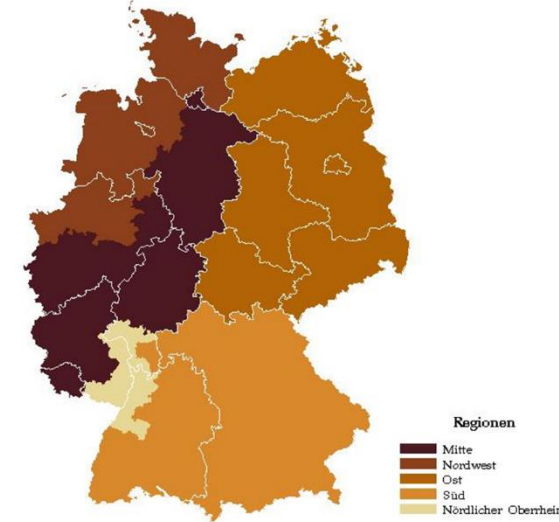
Confounding and Effect Modification



**Multivariable regression modelling
(with interactions)**

Multivariable Models: The Next Step for Prevention

- ▶ Modelling of the treatment frequency using regression models
- ▶ Mixed linear (or logistic) regression of TF with different transformations
 - ▶ Log. Transformation + 0.1
 - ▶ Square root transformation
 - ▶ No-yes AMU
 - ▶ MIXED from SAS, version 9.3 TS Level 1M2
- ▶ 3 to 4-factor analysis of variance, considered factors:
 - ▶ Fixed effects:
 - ▶ Time (Half-year reporting)
 - ▶ Region (4 categories)
 - ▶ Farm size (3 categories)
 - ▶ Farm type
 - ▶ Random effects:
 - ▶ Veterinarian



- lower third
- middle third
- upper third

- Specialists
- Combination
- Changer



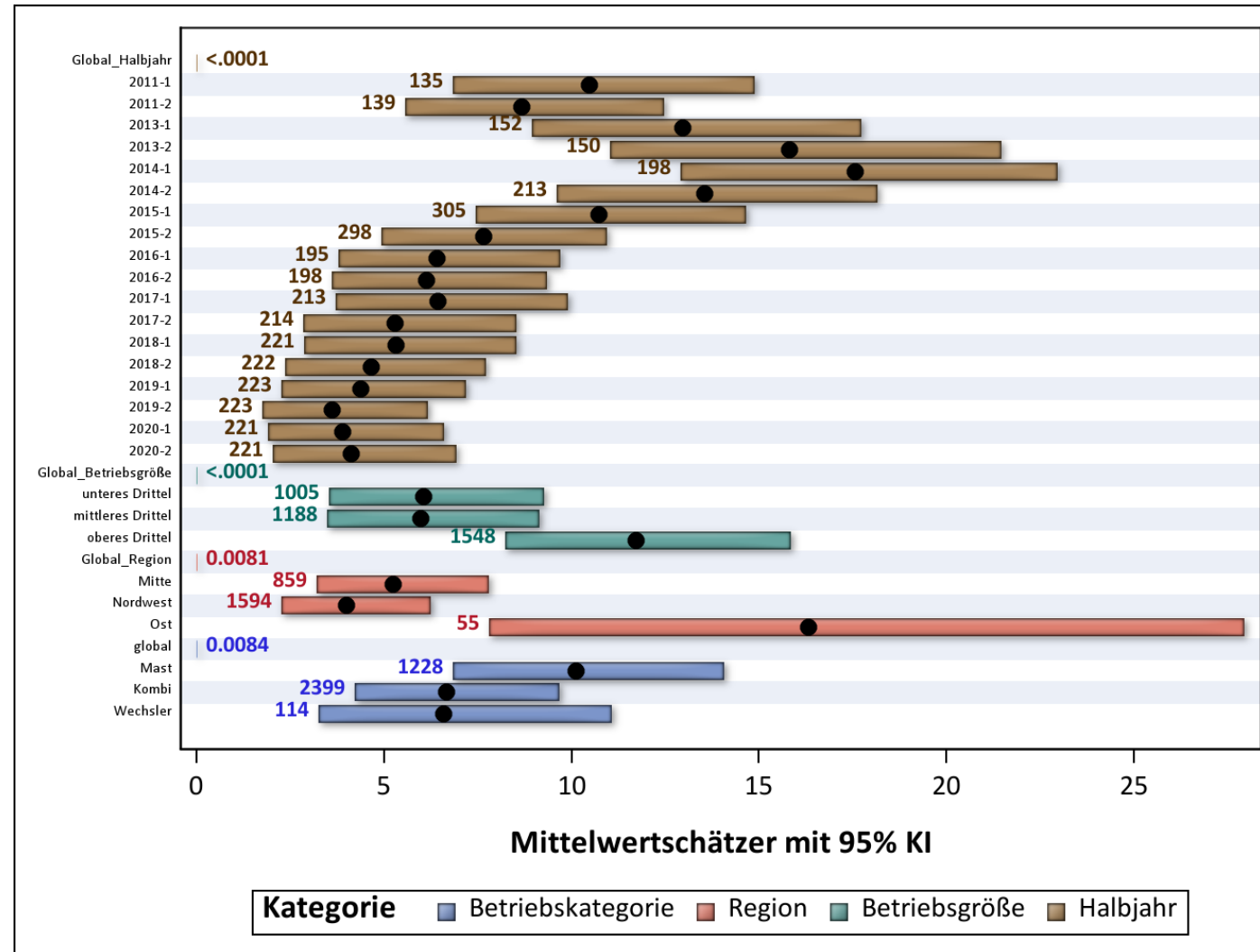
Weaner: Multivariable Models

half-year

farmsize

region

farmtype



Sales Data 2018 by Regions



Source:
https://www.bvl.bund.de/SharedDocs/Bilder/09_Presse/Download_Bilddateien_Presse_Hintergrundinformationen/Grafik_Antibiotika_Abgabemenge2017_Print.jpg;jsessionid=4BD43FF0F1A0DAA52E1AFF9662522F3F.2_cid350?__blob=poster&v=3

© Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL)



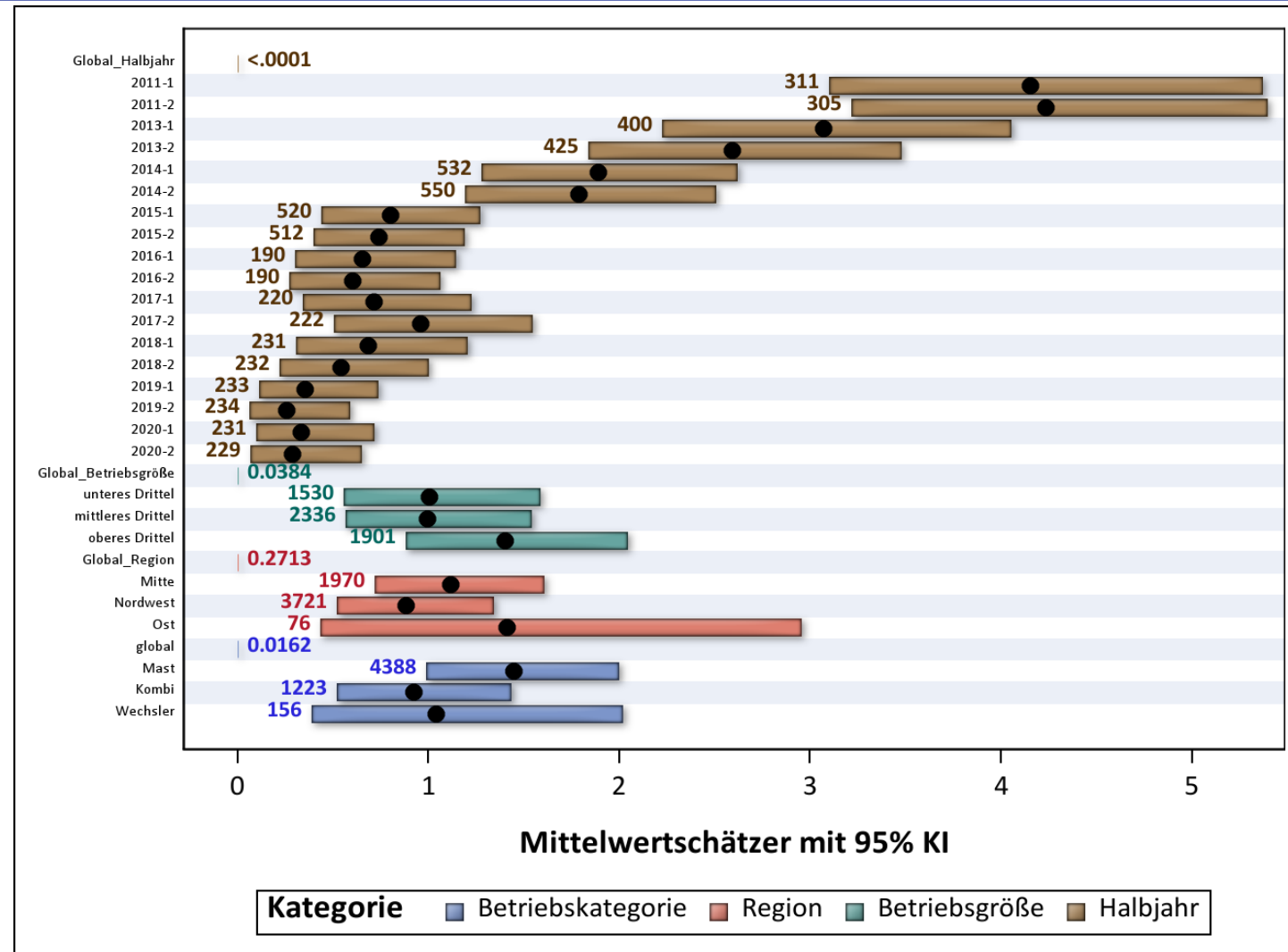
Fattening: Multivariable Models

half-year

farmsize

region

farmtype





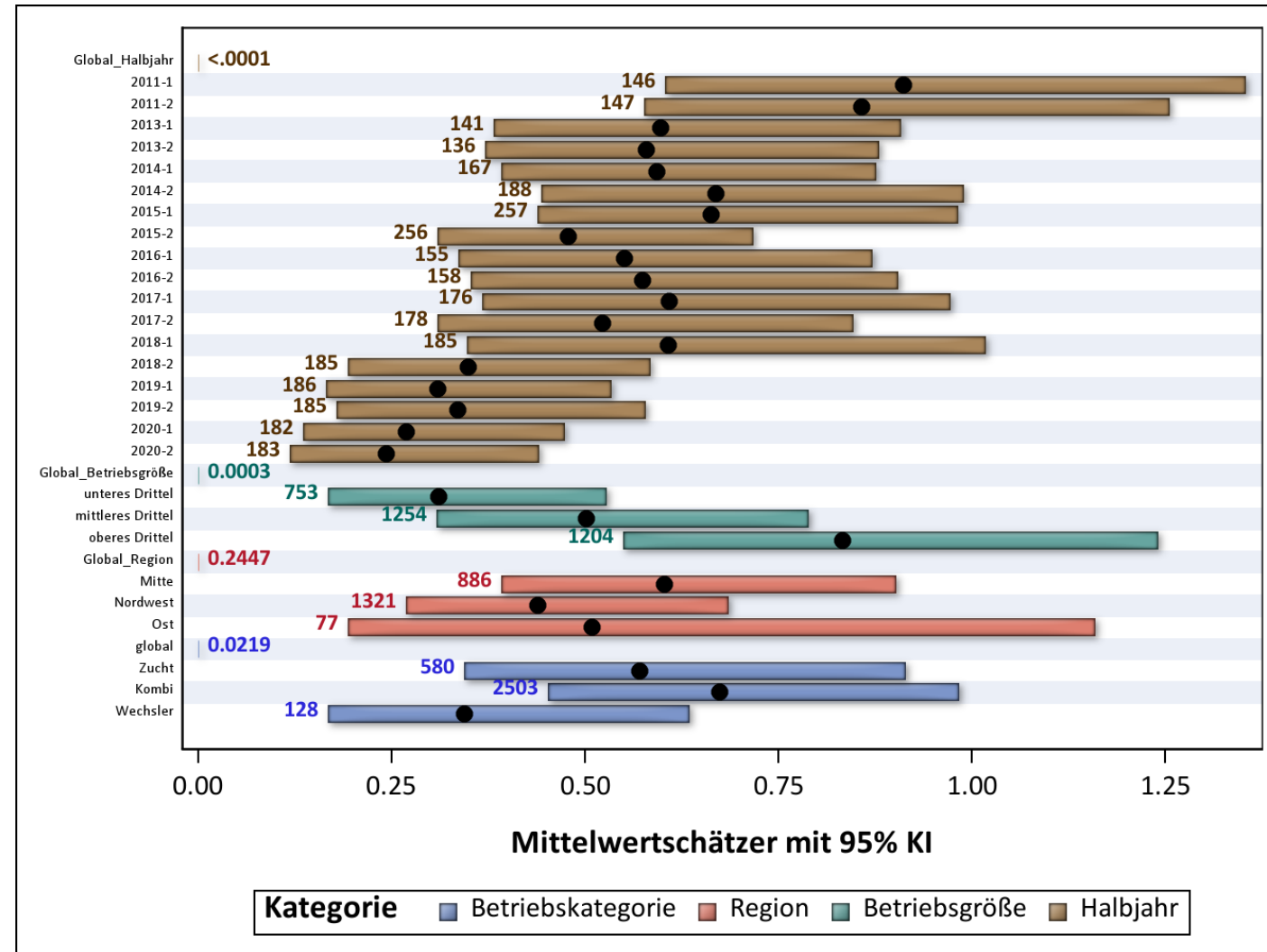
Sow: Multivariable Models

half-year

farmsize

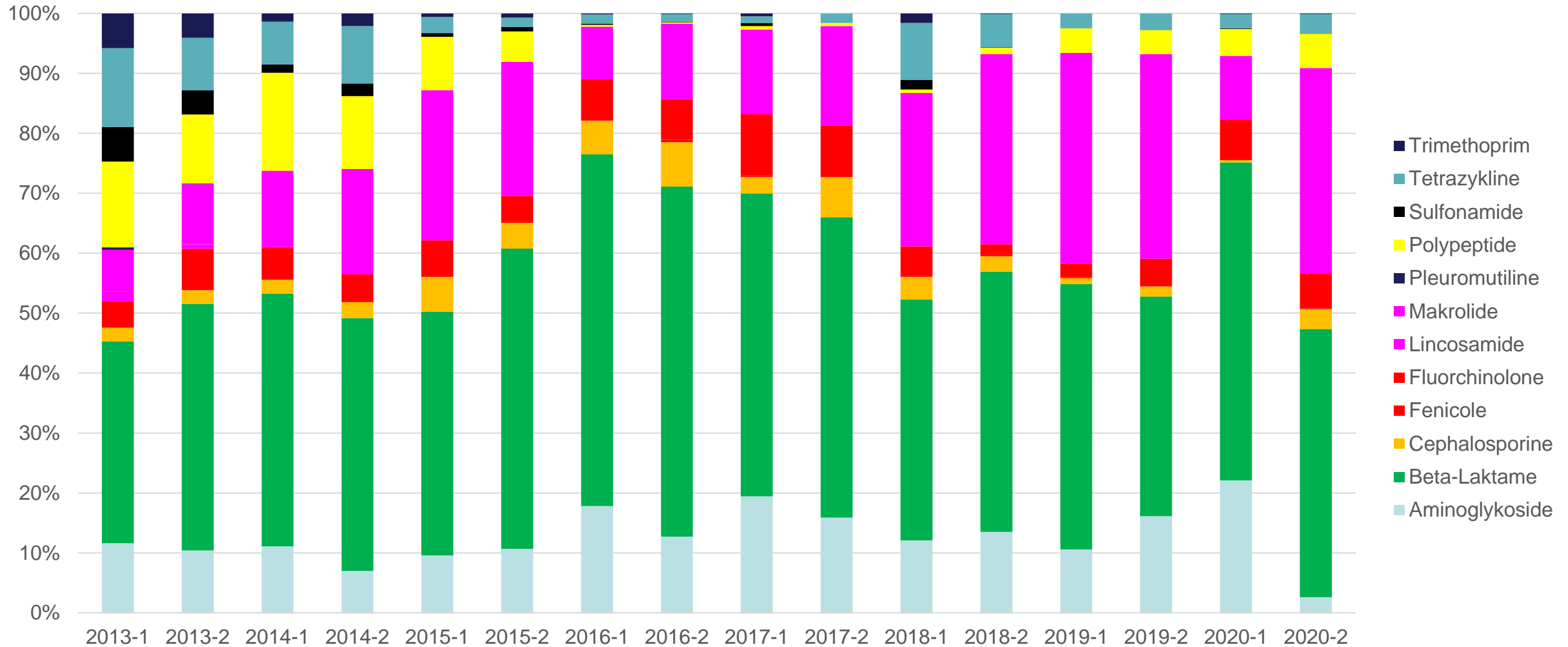
region

farmtype



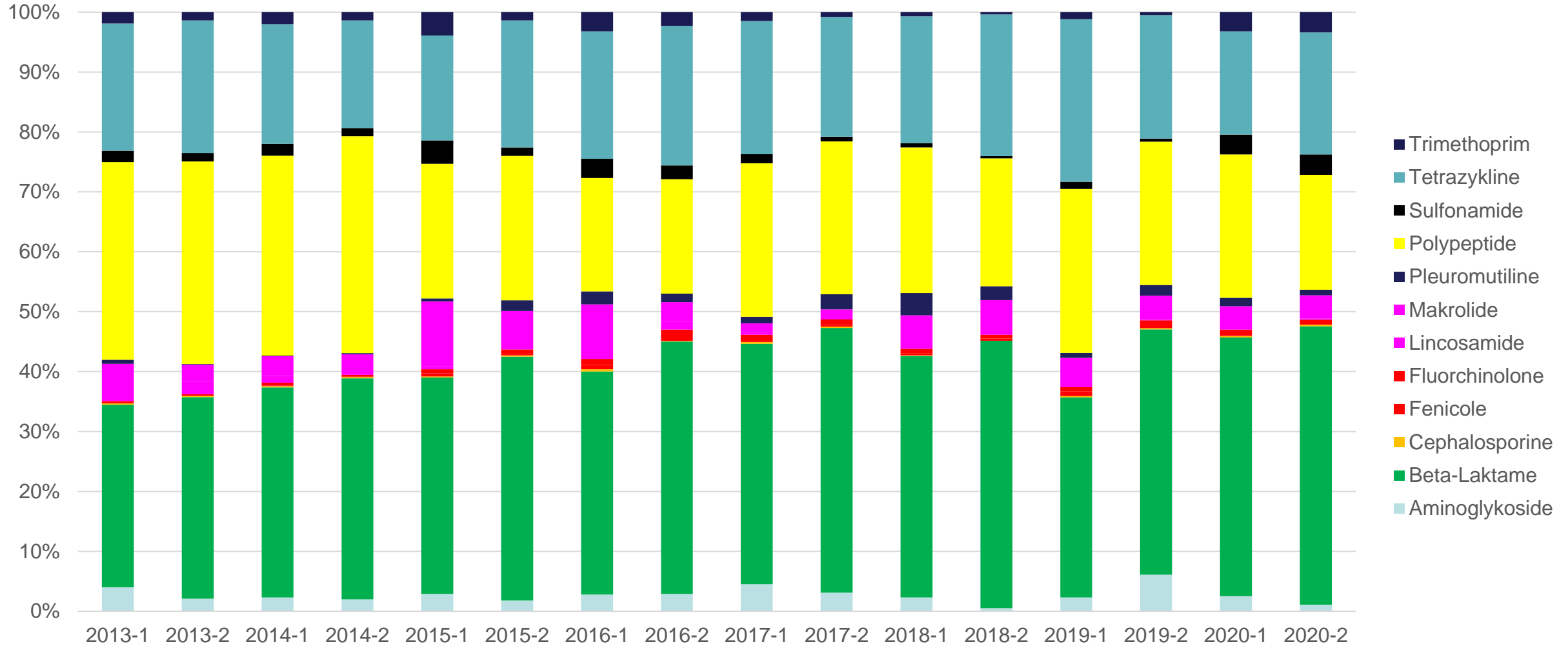


Piglet: Relative TF in % per active compound and year



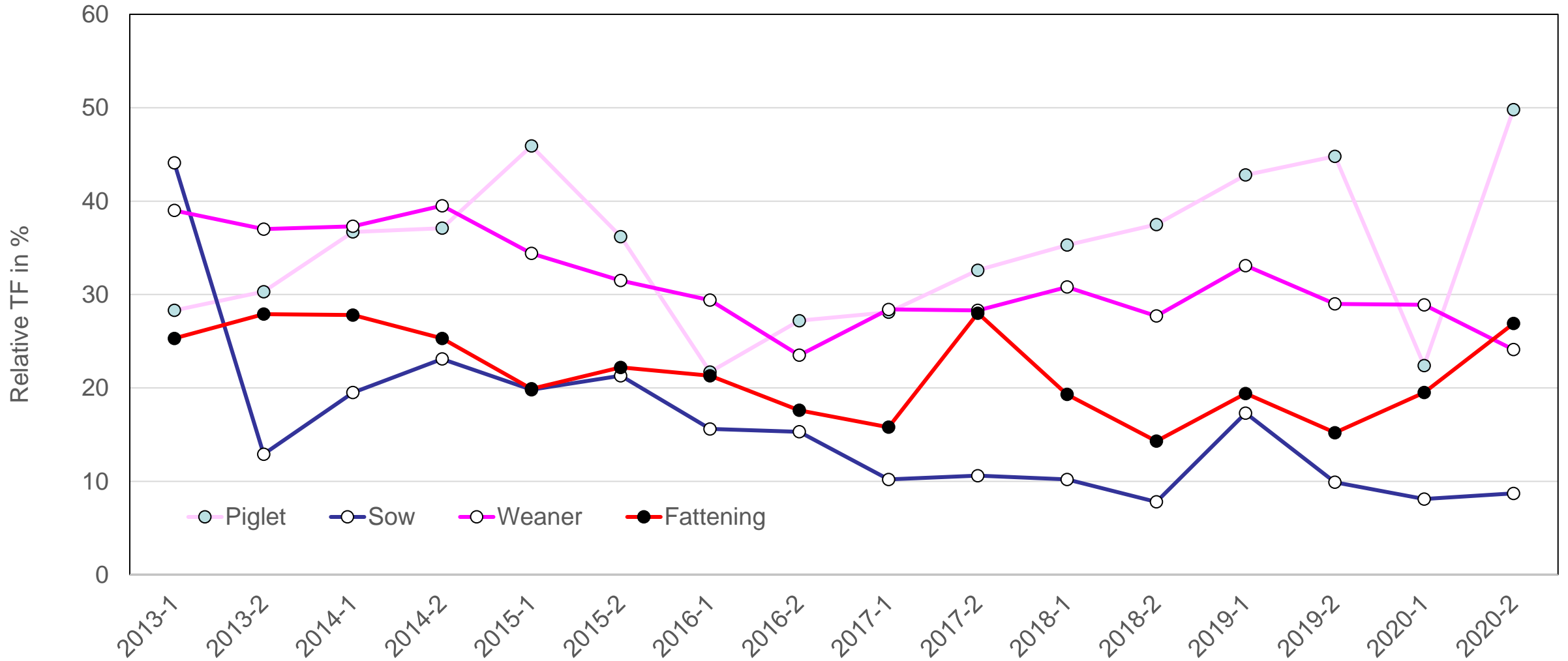


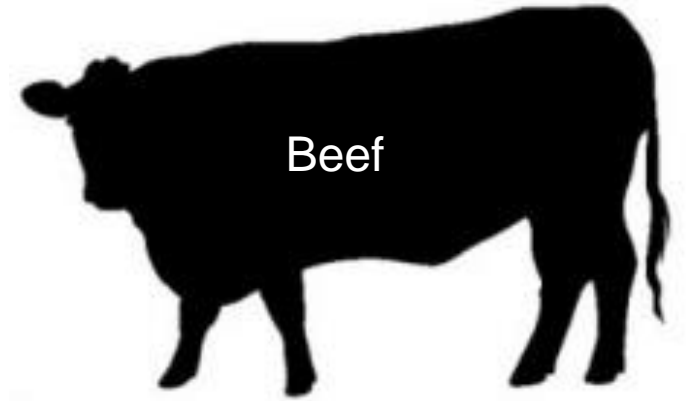
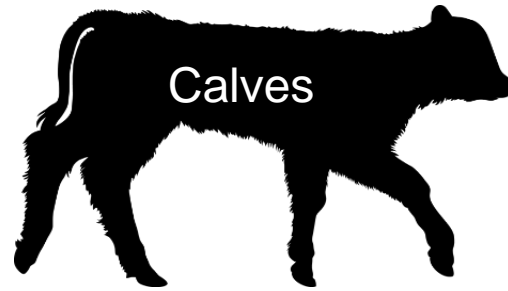
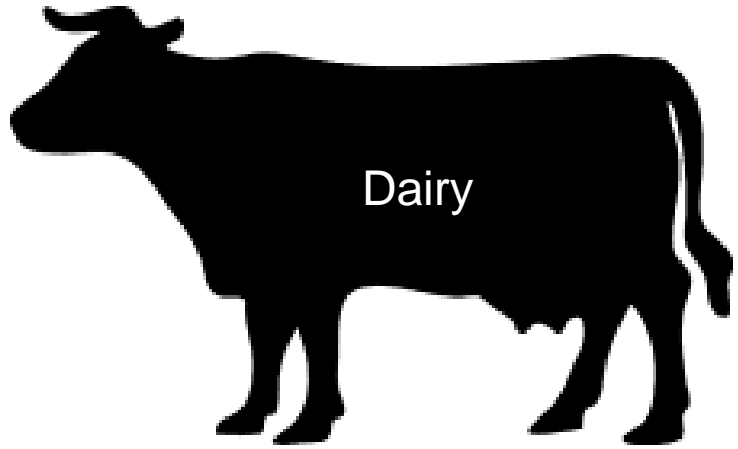
Weaner: Relative TF in % per active compound and year





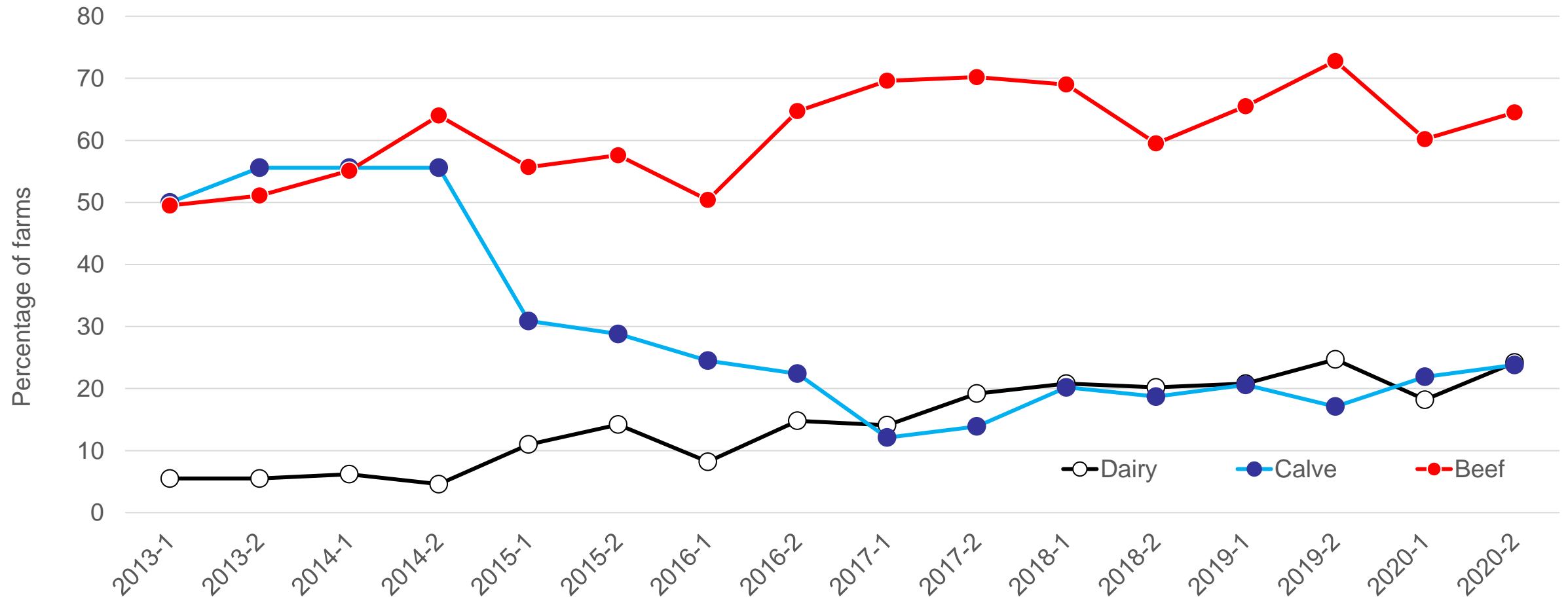
HPCIA-Use in % per year





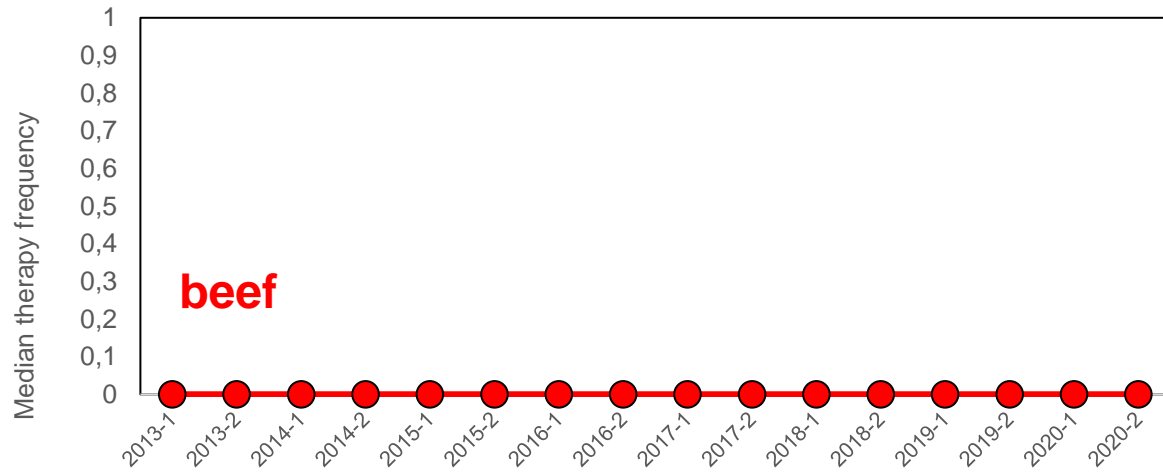
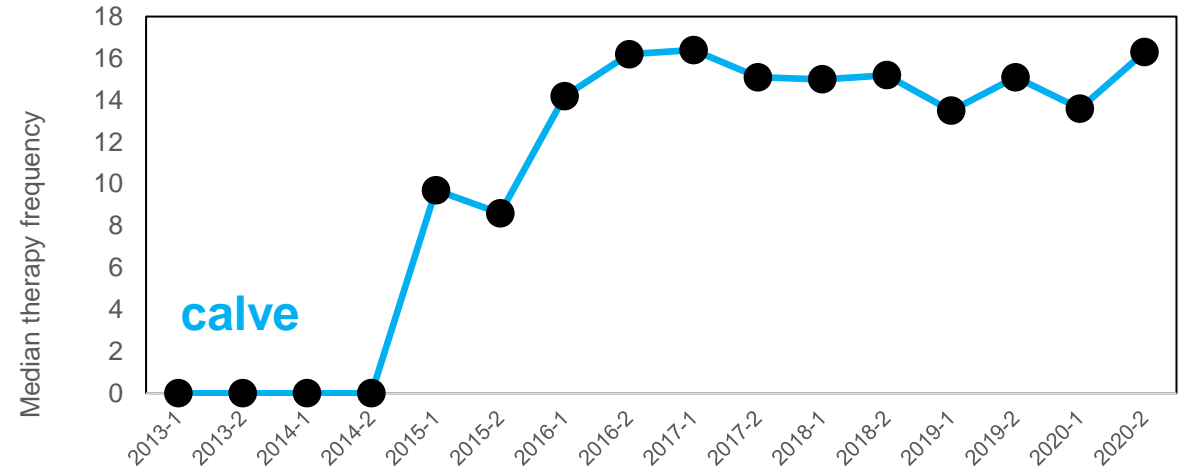
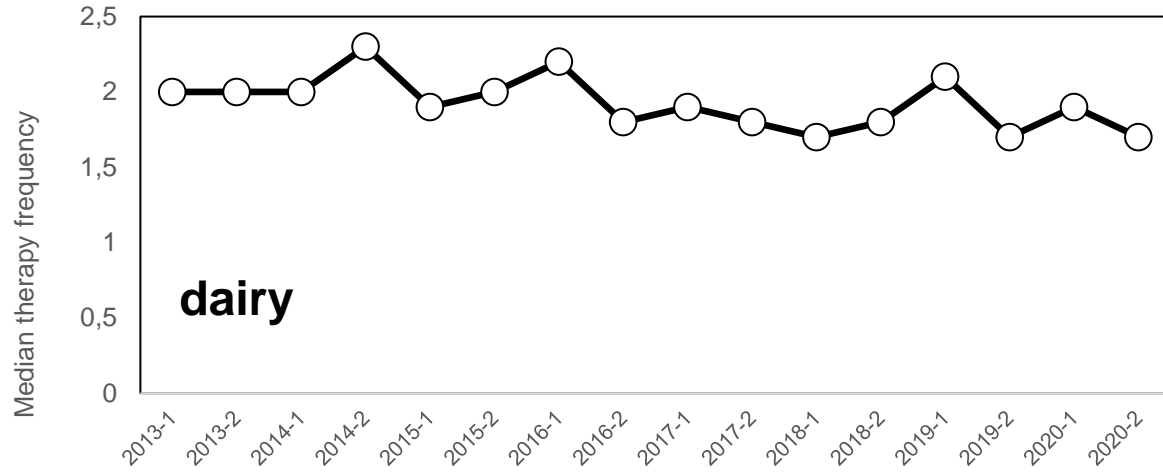


Farms With No Use of Antibiotics



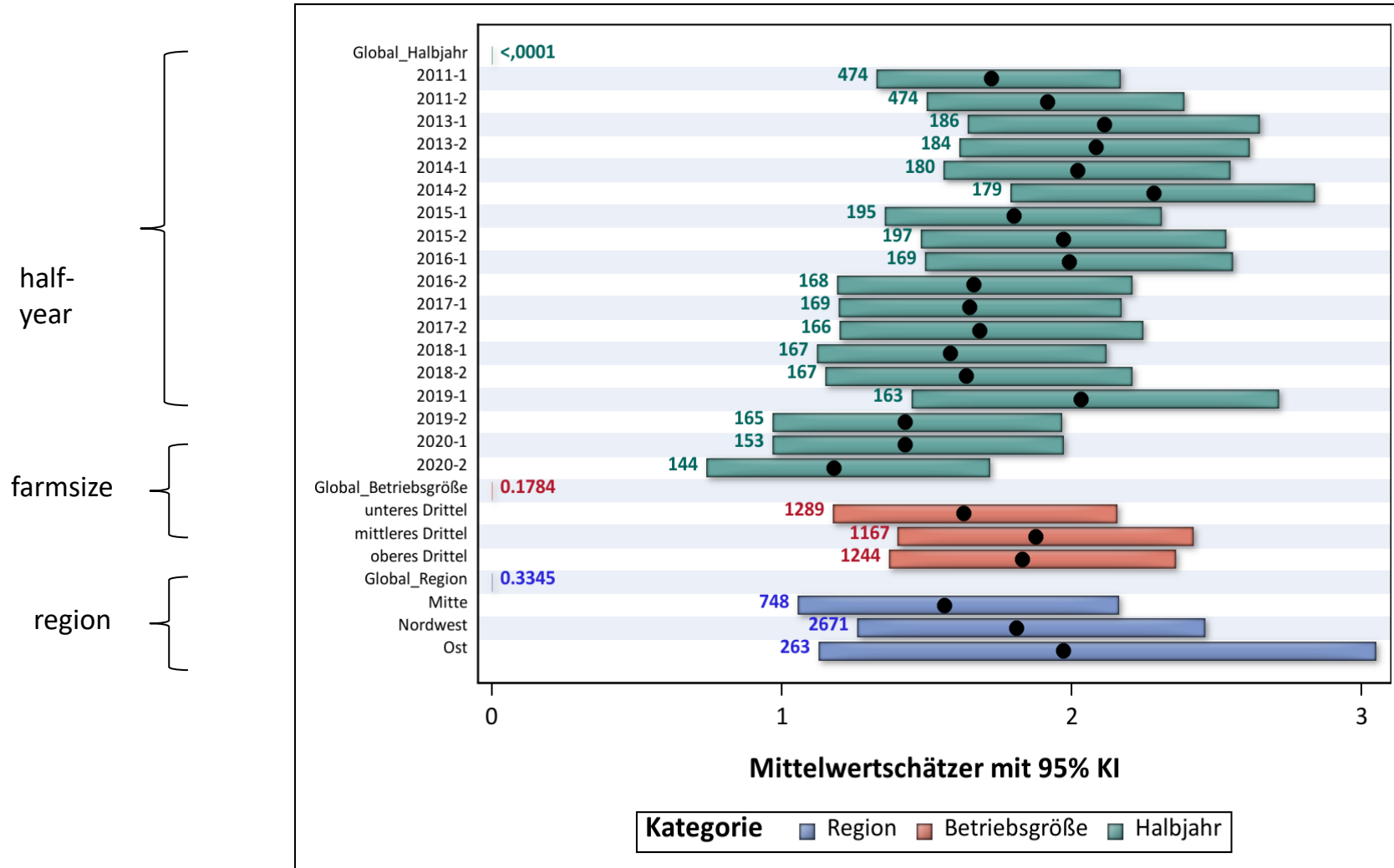


Longitudinal Development of TF Median

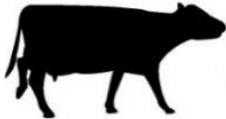






Dairy: Multivariable Models

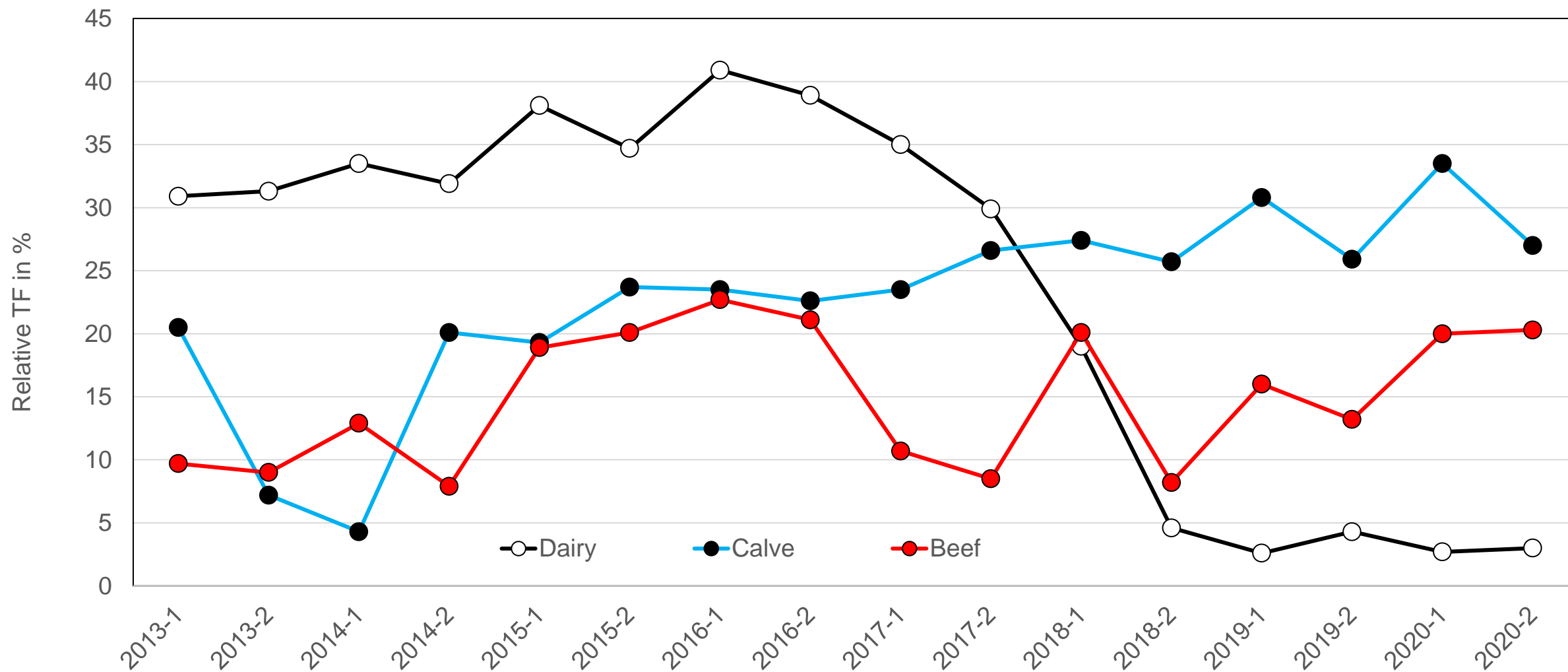


Summary: Impact on the treatment frequency

| Factor | Dairy cow  | Calf  | Beef cattle  |
|-----------------|--|--|---|
| Time | ✓ | ✓ | ✓ |
| Farmsize | | ✓ | ✓ |
| Region | | | |



HPCIA-Use in % per year



Summary and Final Remarks

Summary

Pharmaceutical industry

DIMDI*

Amount sold

Limitations – no animal species
– no animals treated

Farmers and Veterinarians

BVL**

Treatment Frequency

Limitations – fattening only
– no small farms
– no scientific use

Farmers and Veterinarians

VetCAb-S

Treatment Frequency
Antibiotic class
Models

Limitations – cross-sectional data
– panel survival

* German Institute for Medical Documentation and Information

** Federal Office of Consumer Protection and Food Safety

Summary I

- ▶ antibiotics use in Germany is declining
 - ▶ decline differs in different animal species
 - ▶ antibiotics class use in Germany is changing
 - ▶ change in some CIA-classes is less understood

- ▶ Monitoring of antibiotics use in Germany is missing
 - ▶ for small farms
 - ▶ for dairy, laying hens, ducks, geese, ...
 - ▶ for horses, dogs, pets, ...

Summary II

- ▶ antibiotics use systems have to be expanded
 - ▶ to the entire livestock
 - ▶ to an integrated One Health concept
 - ▶ to the observation and linkage to antibiotic resistance
 - ▶ to secondary data use for interested experts

For more information



<https://ibi.tiho-hannover.de/vetcab/>

DAENSCHUTZ IMPRESSUM INTERNER BEREICH



VetAmUR

| | |
|-----------------------------|---|
| Startseite | |
| Informationen zu VetAmUR | ◀ |
| Interesse an der Teilnahme? | |
| Datenschutz in VetAmUR | |
| Begriffserklärungen | ◀ |
| Vorausgegangene Studien | ◀ |

VetAmUR

VetAmUR - das Projekt stellt sich vor

VetAmUR (**V**eterinary **A**ntimicrobial **U**sage and **R**esistance) ist ein wissenschaftliches Projekt zur simultanen Erfassung von Antibiotikaawendung und -resistenz bei Lebensmittel liefernden Tieren in Deutschland. Das Vorhaben wird vom Bundesinstitut für Risikobewertung (BfR) gefördert und vom Institut für Biometrie, Epidemiologie und Informationsverarbeitung der Stiftung Tierärztliche Hochschule Hannover durchgeführt.

Wie bei dem Vorgängerprojekt VetCAb, soll der Antibiotikaeinsatz bei landwirtschaftlichen Nutztieren in Deutschland fortlaufend beschrieben werden, um so eine Datenrundlaae für wissenschaftliche Beurteilunaden

Informationen zur Teilnahme

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Tierärztin Betty Rehberg

**Congratulation to
10 Years of
Excellent Work**



**Thank you for your
attention!**

VetCAb

