Used Daily Dose vs. Defined Daily Dose – Advantages and disadvantages of different dosage assumptions for the benchmarking of antimicrobial usage in livestock

Lothar Kreienbrock, Katharina Hommerich,
Maria Hartmann, Karl Rohn, Svetlana Kasabova

Department of Biometry, Epidemiology and Information Processing

WHO-Collaborating Centre for Research and Training for
Health in the Human-Animal-Environment Interface

University of Veterinary Medicine Hannover, Germany

Antibiotics 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

Sales data DIMDI

	2011	2012	2013	2014	2015	2016
t	1,706	1,619	1,452	1,238	805	742
%	100.0	94.9	85.1	72.6	47.2	43.5

Source: BVL, download: September 13th 2017

Scientific MOSS

▶ Veterinary Consumption of Antibiotics
  - Sentinel Study
    in German Food Producing Animals

▶ for Details see Poster:

  ▶ "Monitoring of Antibiotic Usage – Cross Sectional and Longitudinal Data 2011-2015 in a German Livestock Sentinel", Hommerich et al.

Medicinal Products Act, Germany

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Bekanntmachung
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BAnz AT 22.02.2013 B2
Seite 1 von 2

**Bundesministerium
für Ernährung, Landwirtschaft und Verbraucherschutz**

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

Vom 21. Februar 2013

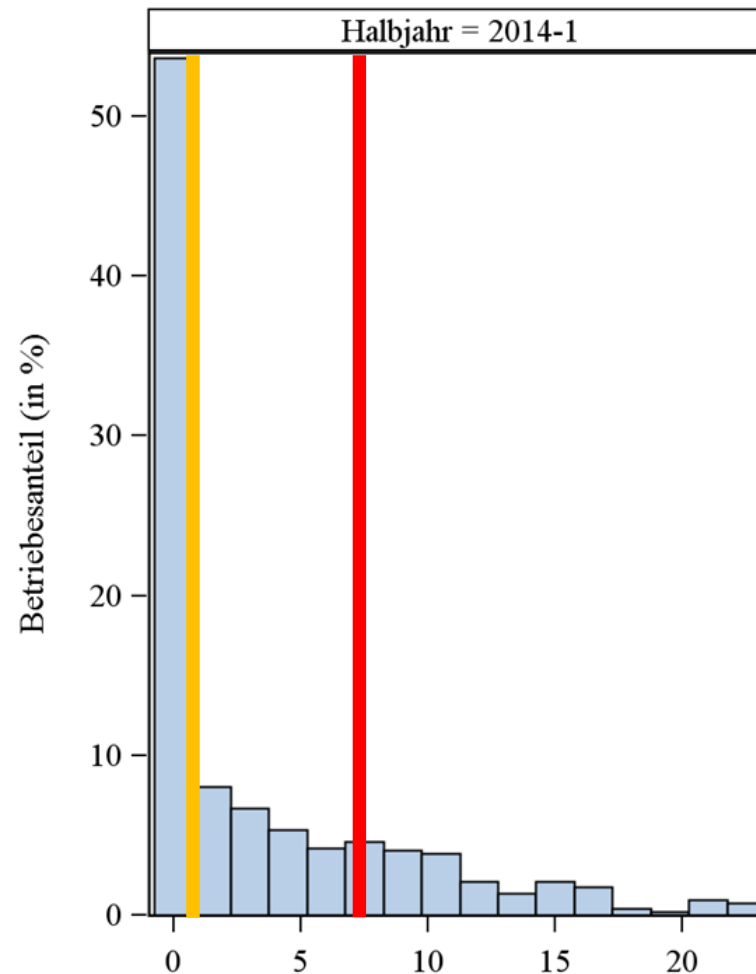Bundesgesetzblatt Jahrgang 2013 Teil I Nr. 62, ausgegeben zu Bonn am 16. Oktober 2013   3813

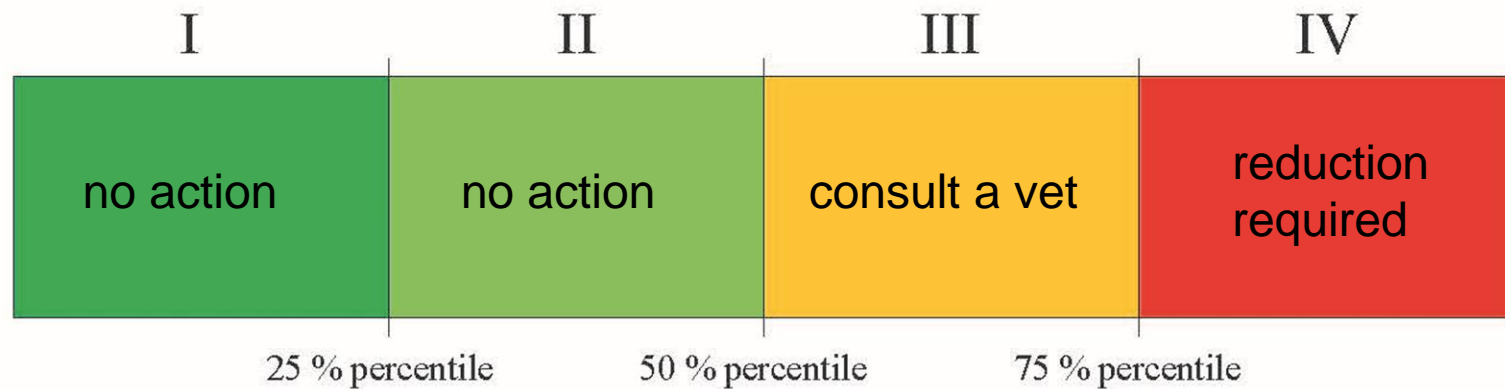**Sechzehntes Gesetz
zur Änderung des Arzneimittelgesetzes**

Vom 10. Oktober 2013

▶ Calculation of animals under study

▶ Calculation of treatment frequency, benchmarking <u>and</u> regulation measures

Distribution of Treatment Frequency

Benchmarking areas
within the German Medicinal Products Act

I	II	III	IV
no action	no action	consult a vet	reduction required

25 % percentile   50 % percentile   75 % percentile

Compulsory documentation
Application and Delivery Form (ADF)

▶ Date of drug delivery / date ot 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

▶ Withdrawel period

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Treatment frequency (TF), UDD

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

▶ $UDD =$

$$\dfrac{\text{amount of active substance}}{\text{\# animals treated} \times \text{animal weight} \times \text{\# treatment days}}$$

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

Treatment frequency (TF), UDD

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

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

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

Treatment frequency (TF), UDD / DDD

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

▶ $\text{UDD} = $

$$\dfrac{\text{amount of active substance}}{\text{\# animals treated} \times \text{animal weight} \times \text{\# treatment days}}$$

▶ $\text{TF}_{\text{DDD}} = \dfrac{\text{amount of active substance}}{\text{population at risk} \times \text{standard weight} \times \text{DDD}}$

Comparing TF_{UDD} and TF_{DDD}

▶ Use data from our VetCAb-Sentinel study

▶ data from 2014 as an example from

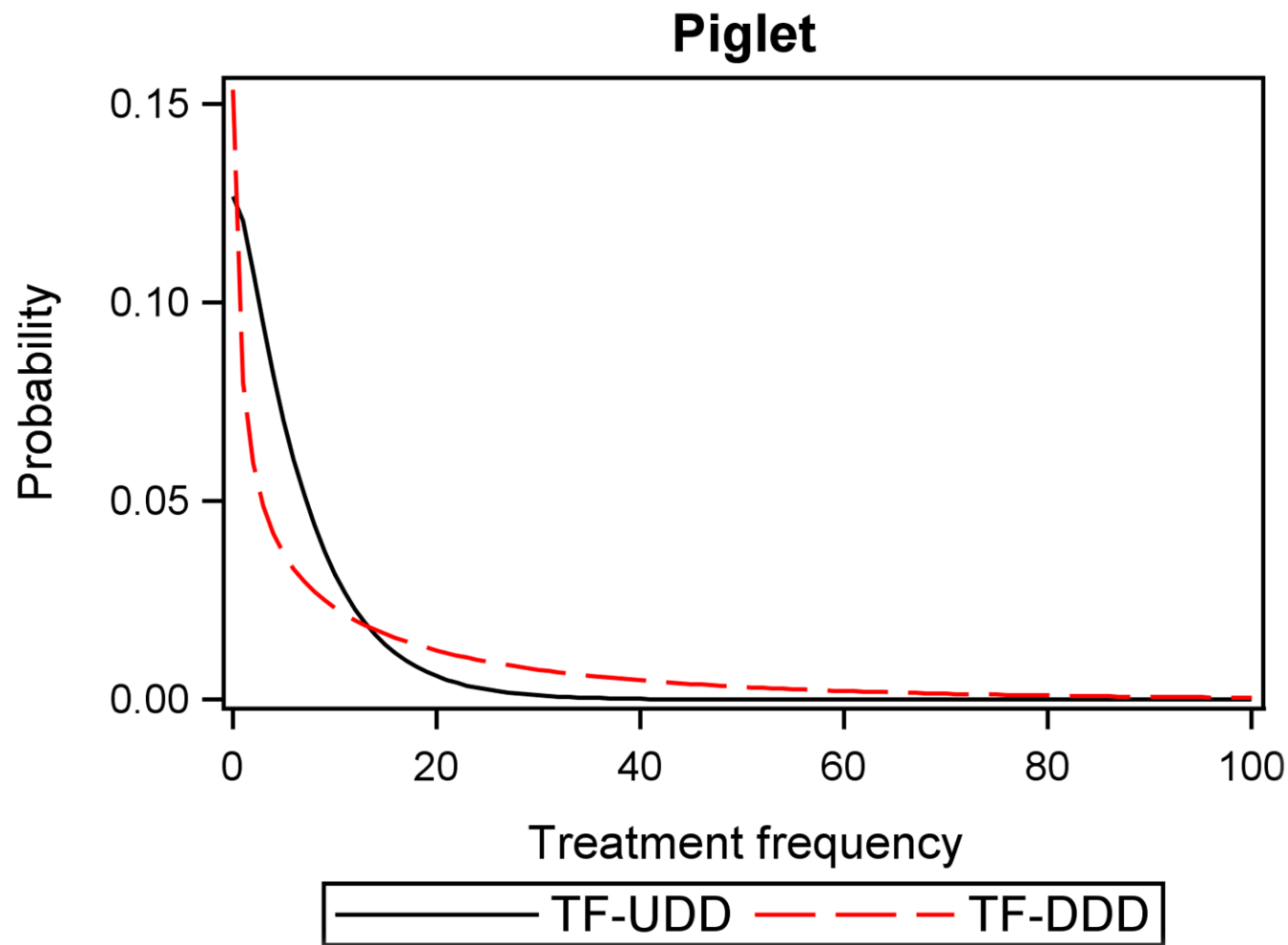 ▶ 40 broiler chicken farms

  ▶ 137 piglet producing farms

Distribution of the TF$_{UDD}$ and TF$_{DDD}$

Broiler

Distribution of the TF$_{UDD}$ and TF$_{DDD}$

Piglet
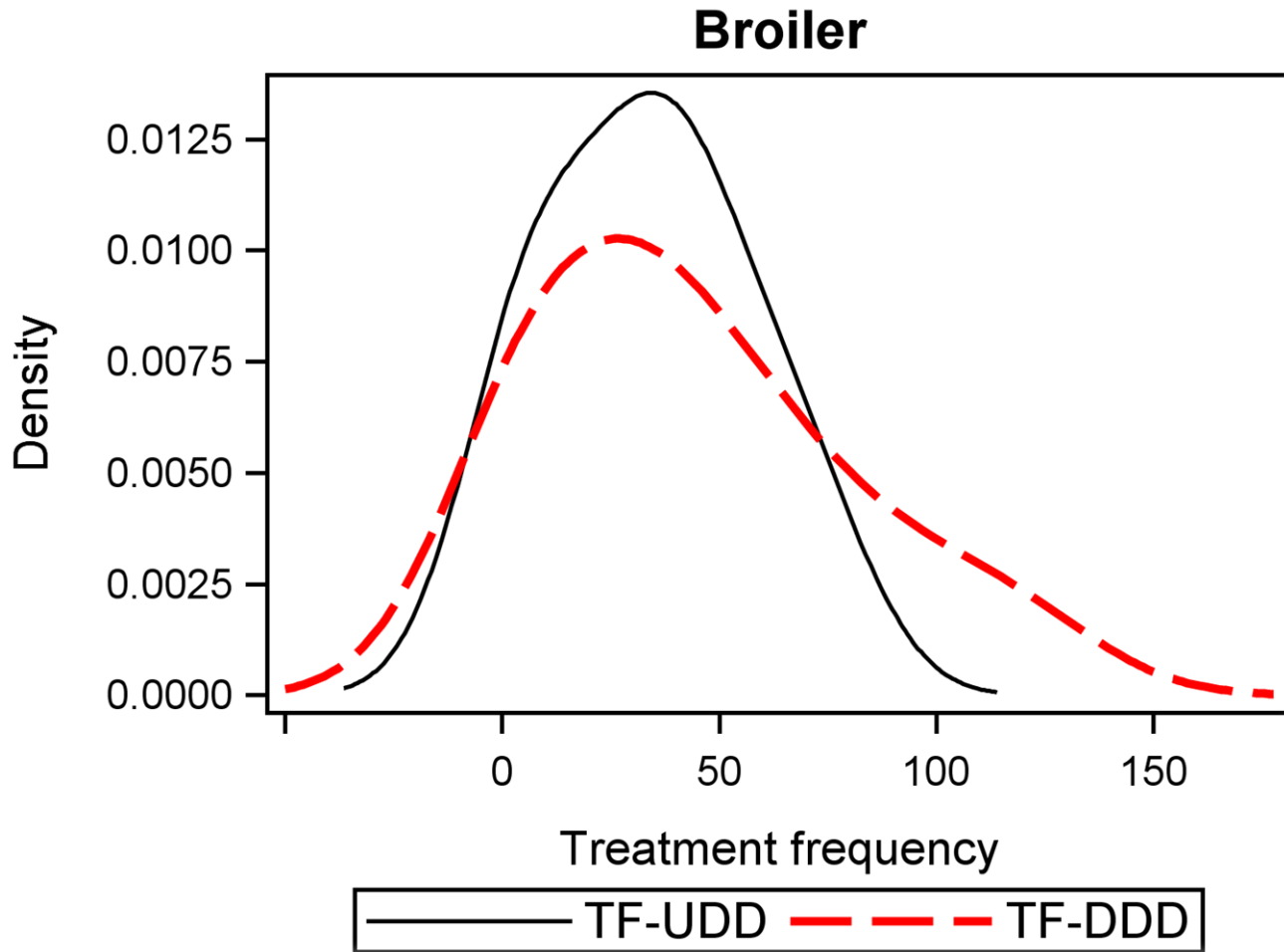
Shift in Statistical Measures

	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)
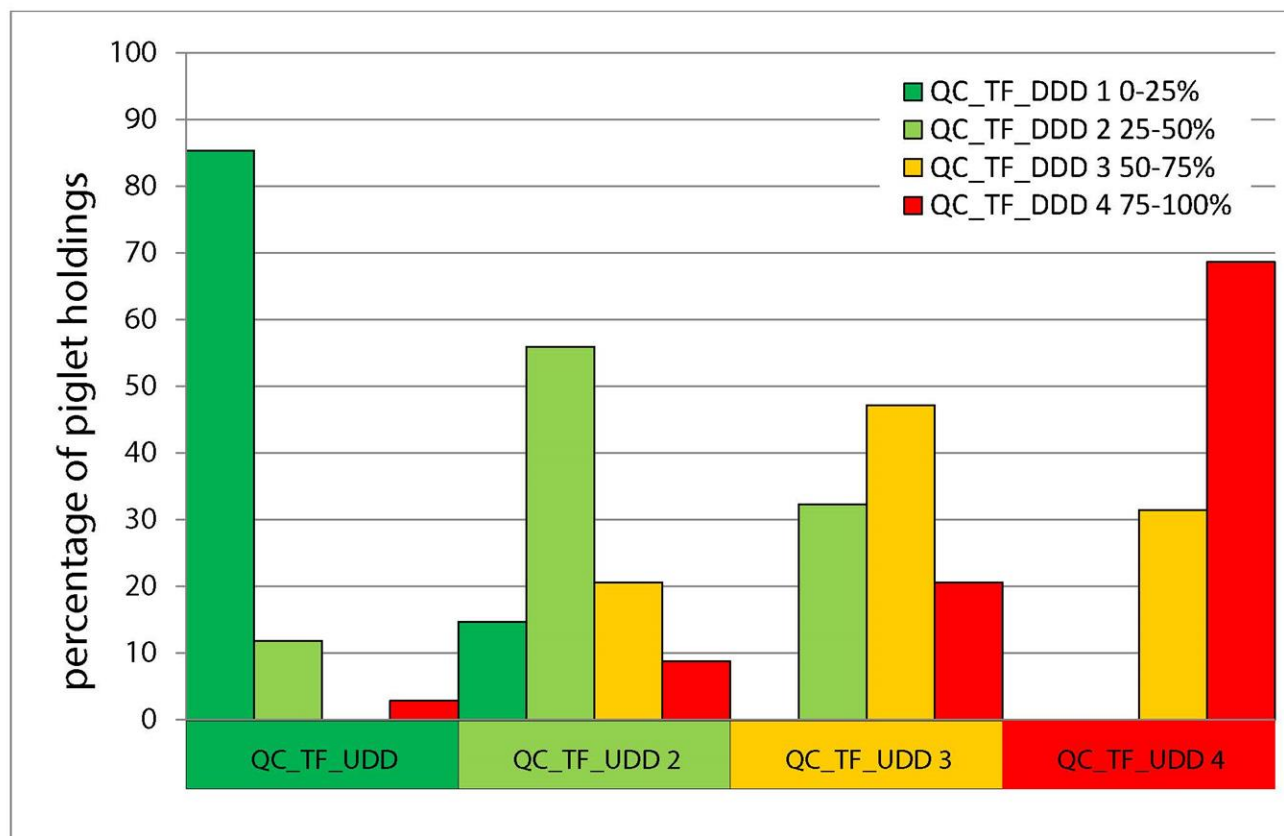
Estimated Number of Dosage …

▶ … 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

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 animals0F
EMA/286416/2012-Rev.1

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

approx. median body weight: 264 g

approx. median body weight: 376 g
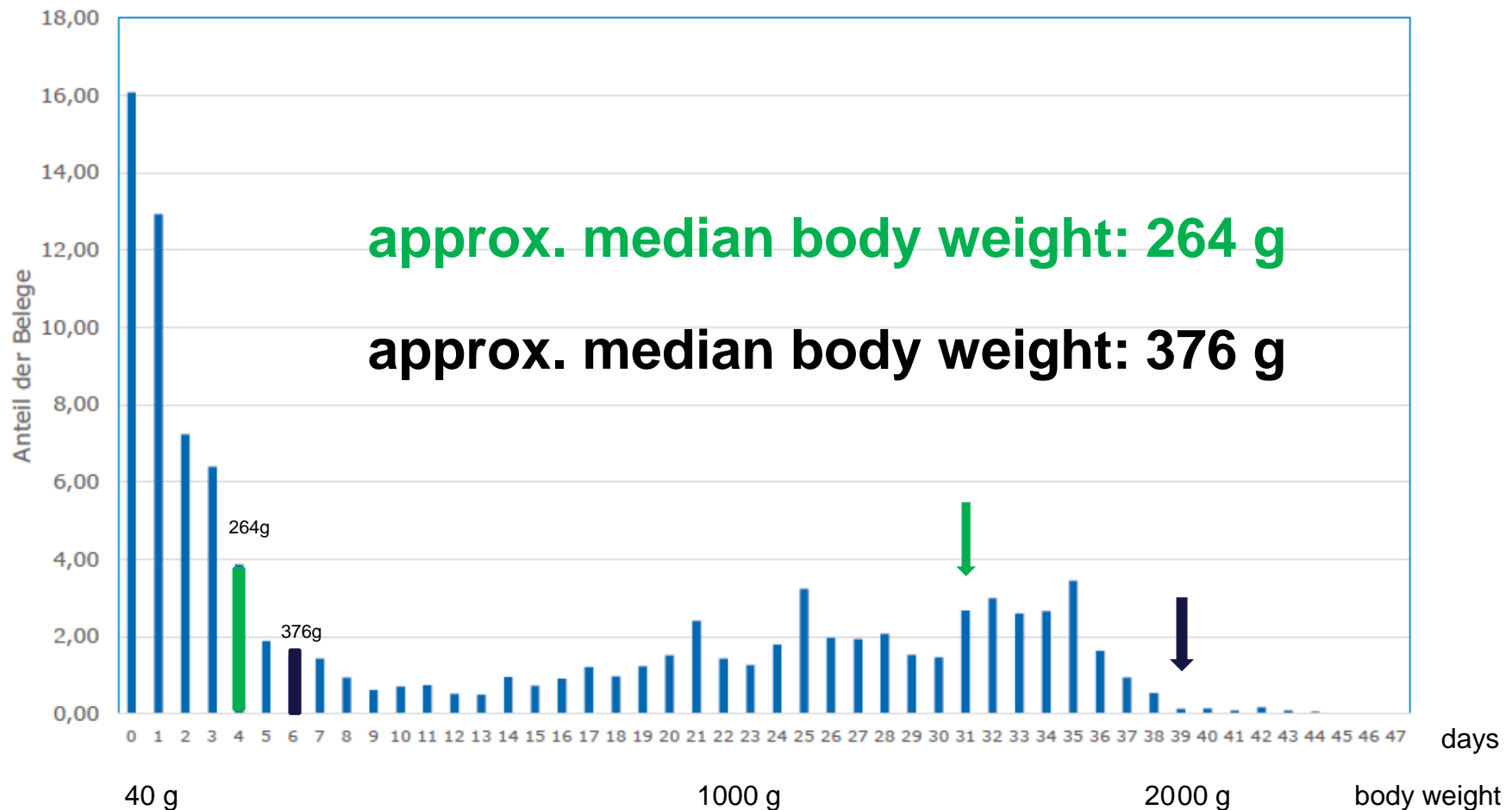
If daily weight gain: 56 g (KTBL, 2014)

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Conclusion
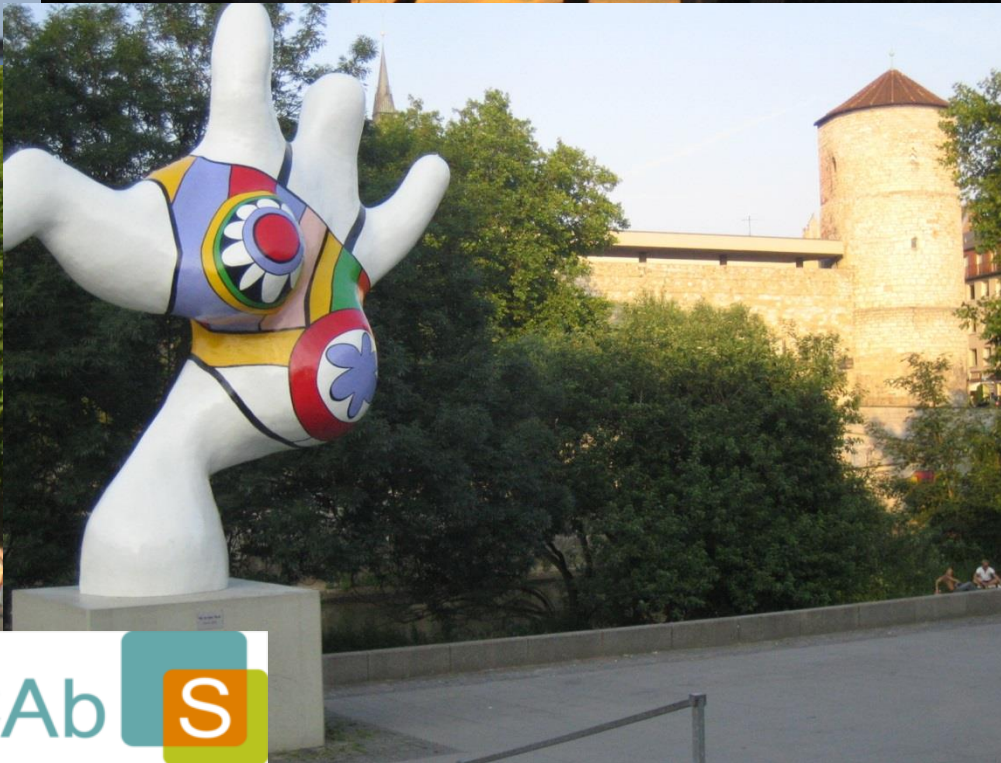
▶ **Treatment Frequency based on UDD**

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

▶ **Treatment Frequency based on DDD**

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

Thank you for your attention!