Methods and metrics for monitoring of antimicrobial use in animals

Lessons learnt from two peer-reviewed article collections

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Research Topic

Antimicrobial Usage in Companion and Food Animals: Methods, Surveys and Relationships with Antimicrobial Resistance in Animals and Humans

The scope of this article collection is to join researchers interested in AMU monitoring in animals around the world […] in both livestock and companion animals, and use of this information for improving antimicrobial stewardship among antimicrobials end-users (including veterinarians, farmers, and animal owners).

Topic Editors

Miguel Ángel Moreno
Complutense University of Madrid
Madrid, Spain

84 publications

Lucie Collineau
Agence Nationale de Sécurité Sanitaire de l'Alimentation, de l'Environnement et du Travail (ANSES)
Maisons-Alfort, France

26 publications

Carolee Anne Carson
Public Health Agency of Canada (PHAC)
Guelph, Canada

26 publications

Research Topic

Antimicrobial Usage in Companion and Food Animals: Methods, Surveys and Relationships with Antimicrobial Resistance in Animals and Humans

- **Volume I : 2018-2019**
  - **15 articles accepted**

- **Volume II : 2019 – 2020**
  - **13 articles accepted (+1 still under review)**

→ 28 articles accepted so far

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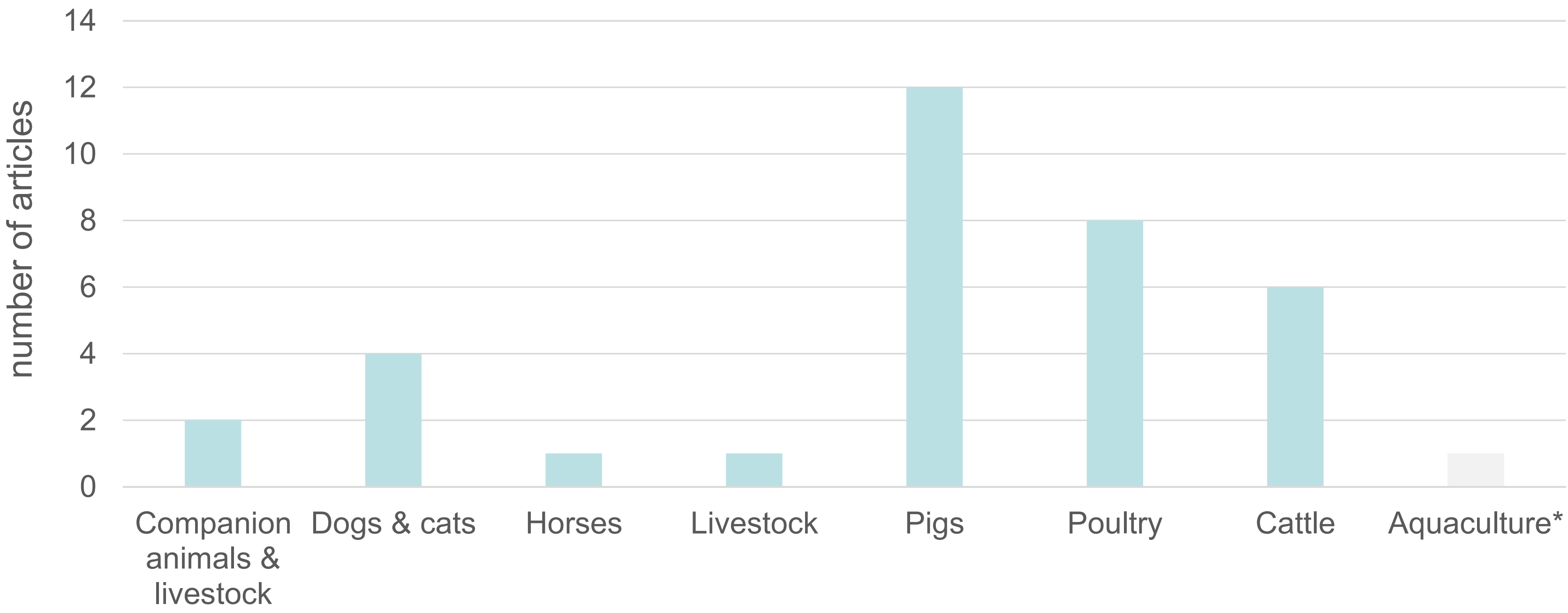
Overview of the articles collection (volumes I + II)

- By type of article

	# of articles
Original research	26
Method paper	2
Review paper	1

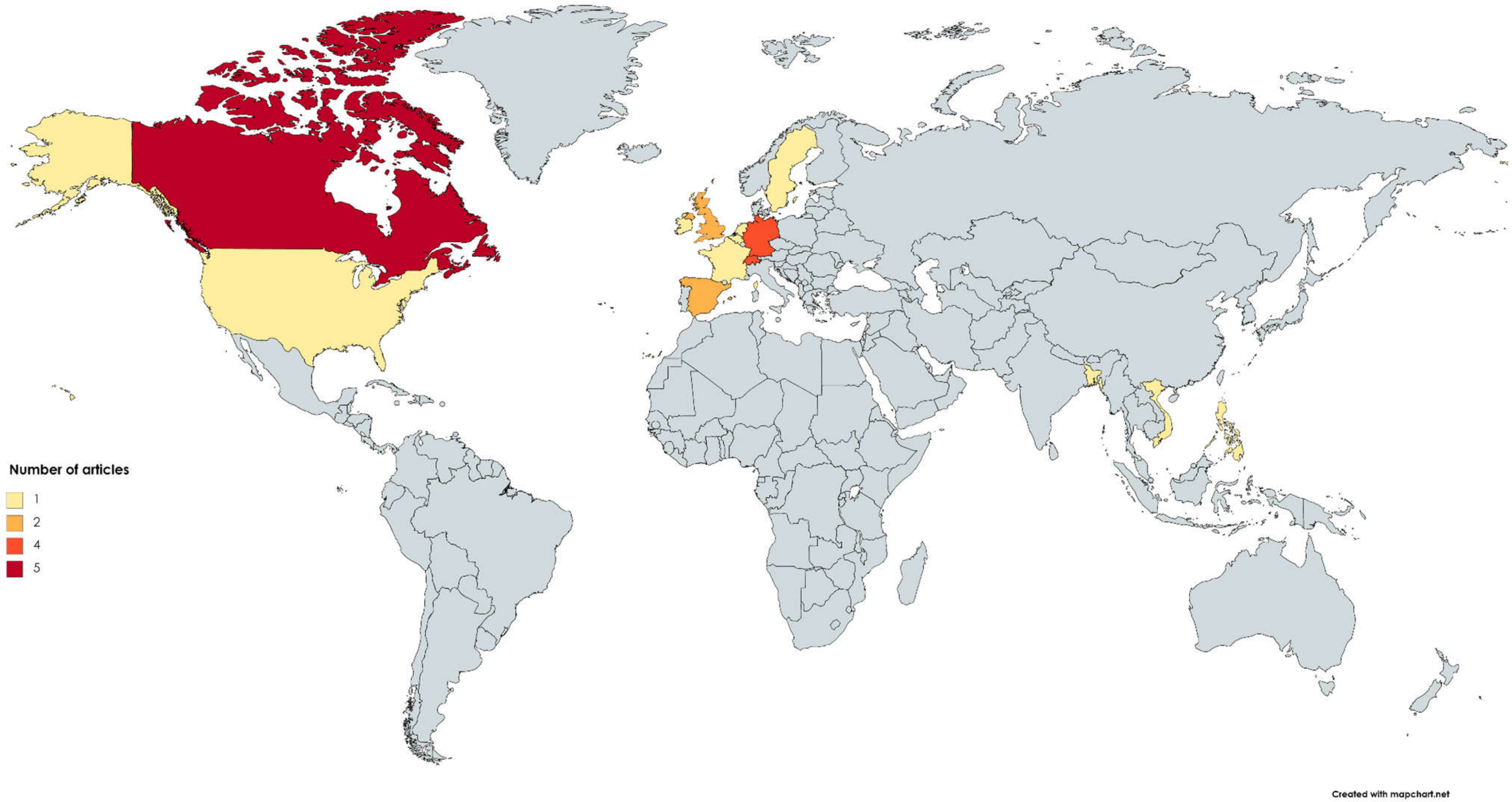
Overview of the articles collection (volumes I + II)

- By animal species



**under review*

Overview of the articles collection (volumes I + II)



Overview of the articles collection (volumes I + II)

- By research questions (as stated in the Research Topic scope)

	# of articles
Compare different metrics to characterize AMU in animals	15
Monitoring trends over time	8
Compare AMU between sectors or users (e.g. benchmarking)	7
Compare AMU between countries	6
Assess the potential for the selection of AMR	1
Common approaches for AMU monitoring in humans and animals	0
Compare national/supra-national vs end-users approaches	0

Lot of room for more integrated & One Health approaches

Overview of the articles collection (volumes I + II)

- By study levels

	# of articles
End-user (farms, veterinarians, vet clinics) data	23
National data	4
Supra-national data	2

A shift from national/sales data to end-user data ('actual' use)

Development of on-farm AMU monitoring systems over time

frontiers in Veterinary Science

REVIEW
published: 21 August 2020
doi: 10.3389/fvets.2020.00540

Check for updates

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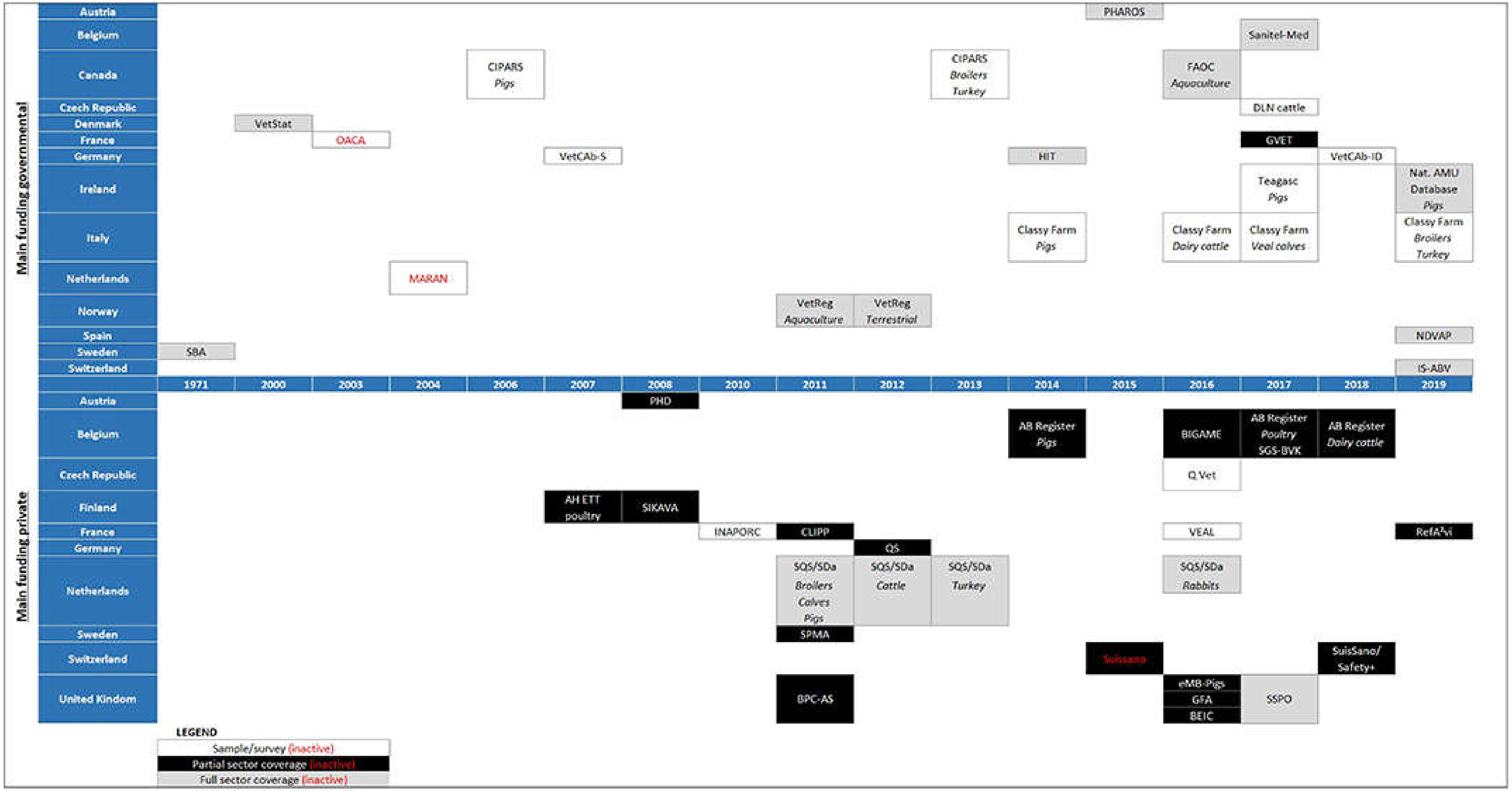
Monitoring of Farm-Level Antimicrobial Use to Guide Stewardship: Overview of Existing Systems and Analysis of Key Components and Processes

Pim Sanders[1†], Wannes Vanderhaeghen[2†], Mette Fertner[3], Klemens Fuchs[4], Walter Obritzhauser[5], Agnes Agunos[6], Carolee Carson[6], Birgitte Borck Høg[7], Vibe Dalhoff Andersen[8], Claire Chauvin[9], Anne Hémonic[10], Annemarie Käsbohrer[5,11], Roswitha Merle[12], Giovanni L. Alborali[13], Federico Scali[13], Katharina D. C. Stärk[14‡], Cedric Muentener[15], Ingeborg van Geijlswijk[1], Fraser Broadfoot[16], Lucie Pokludová[17], Clair L. Firth[5], Luís P. Carmo[18], Edgar Garcia Manzanilla[19,20], Laura Jensen[21], Marie Sjölund[22], Jorge Pinto Ferreira[14‡], Stacey Brown[16], Dick Heederik[1] and Jeroen Dewulf[23]*

Development of on-farm AMU monitoring systems over time



Sanders et al. 2019

anses

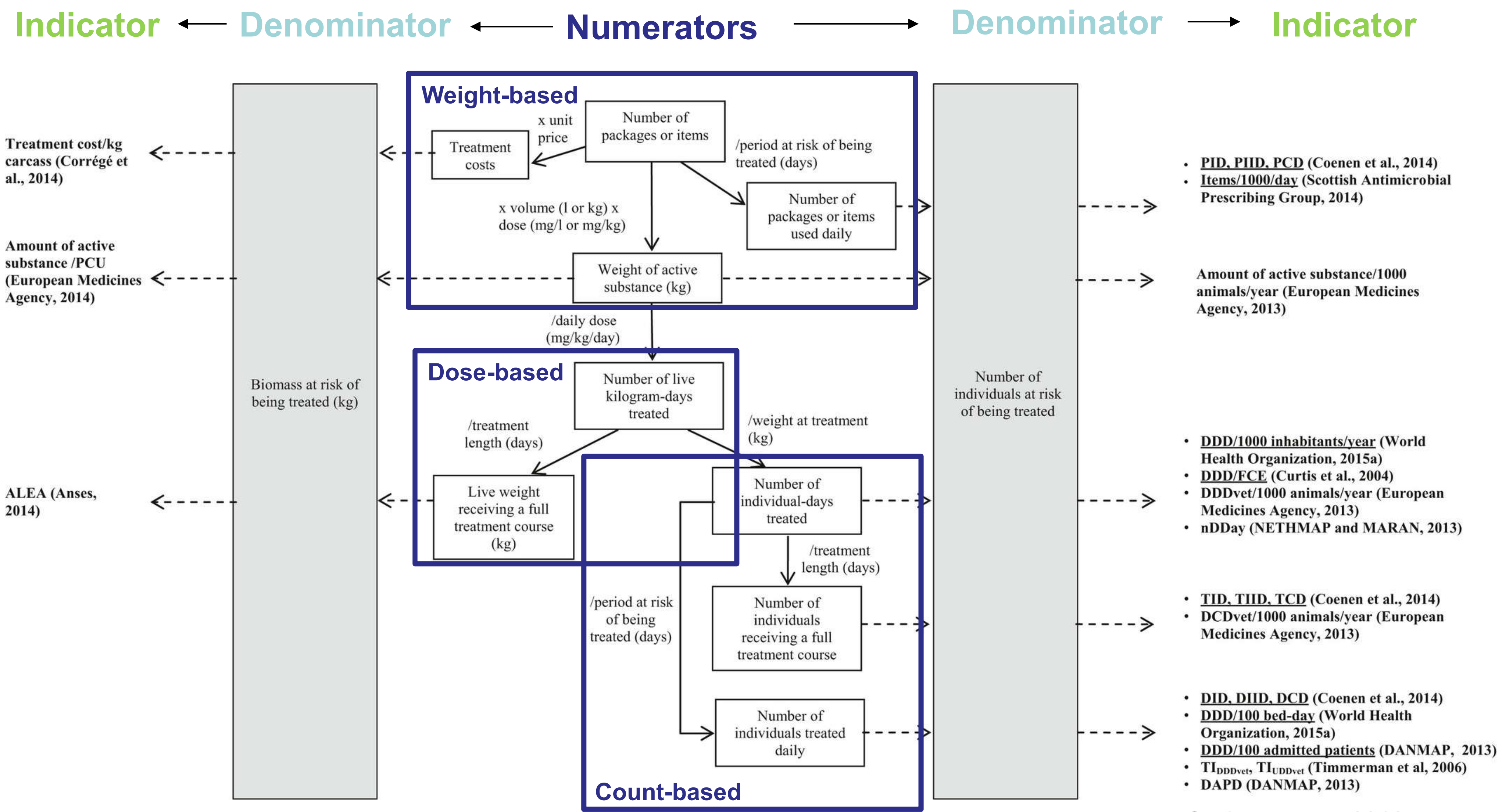
Indicators

- *Quantification is based on 'indicators' of antimicrobial usage, defined as the number of 'technical' units of measurement (i.e. the amount of antimicrobials) consumed and normalized by the population at risk of being treated in a defined period (European Medicines Agency, 2013)*

Numerator

$$Indicator = \frac{amount\ of\ antimicrobials}{population\ at\ risk\ of\ being\ treated}$$

Denominator



Collineau et al. 2016

Overview of indicators used for AMU monitoring at farm level

Country[a]	System(s)	Type[b]	Indicator[c]	Formula of indicator[c,d]
Austria	PHAROS	Dose based	DDDvet/kg/year	mg AB used/DDDvet × n animals at risk × kg standard weight
	PHD	Count based	TH/UTH	n treated herds/n untreated herds
Belgium	All	Dose based	TD_{100}	(mg AB used/$DDDA_{bel}$ × kg animal at risk × n days at risk) × LA – factor × 100
	Sanitel-Med	Dose based*	Contract score	$[(\%\ green\ ACU \div 2) - (\%\ red\ ACU \div 2) + 0,5] \times 100$
Canada	CIPARS	Count based	pp TF|H	n treated flocks | herds/total n flocks | herds
		Dose based	DDDvetCA/PCU	$\left(\frac{\text{Milligrams active ingredient}/DDDvetCA_{mg/kg/day}}{\text{Total animals} \times \text{Standard weight at treatment}}\right)$
			DDDvetCA/1000 AD	$\left(\frac{\text{Milligrams active ingredient}/DDDvetCA_{mg/kg/day}}{\text{Total animals} \times \text{standard weight} \times \text{days at risk}}\right) \times 1,000$
Switzerland	IS ABV	Count based	ATI	n treated animals × n treatment days × n substances/n animals per year
		Dose based	Treatment intensity	(mg AB used/DDD_{vet} or DDD_{CH} × kg animal at risk × n days at risk) x 100
	SuisSano | Safety+	Count based	ATI	n treated animals × n treatment days × n substances/n animals per year "LA Factor" HPCIA Factor
		Dose based	DCDvet/animal/year	(mg AB used/DCD_{vet} × standard weight × n animals at risk per year)
			DCD_{CH}/animal/year	(mg AB used/DCD_{CH} × standard weight × n animals at risk per year)
The Czech Republic	Q VET pigs	Dose based	ADD/100 animal-days	
Germany	HIT	Count based	Treatment frequency	n treated animals × n treatment days × n substances/n animals per day
	QS	Count based	Therapy index	n treated animals × n treatment days /total animal capacity
	VetCAb	Count based	Treatment frequency	n treated animals × n treatment days × n substances/total animal capacity
Denmark	VetStat	Dose based	ADD/100 animal-days	(mg AB used / technical daily dosage (ADD) × kg animal at risk × n days at risk) × 100
Finland	AH ETT poultry	Count based	pp TF	n treated flocks/total n flock

Sanders et al. 2020 (extract)

A clear lack of harmonisation across countries and systems

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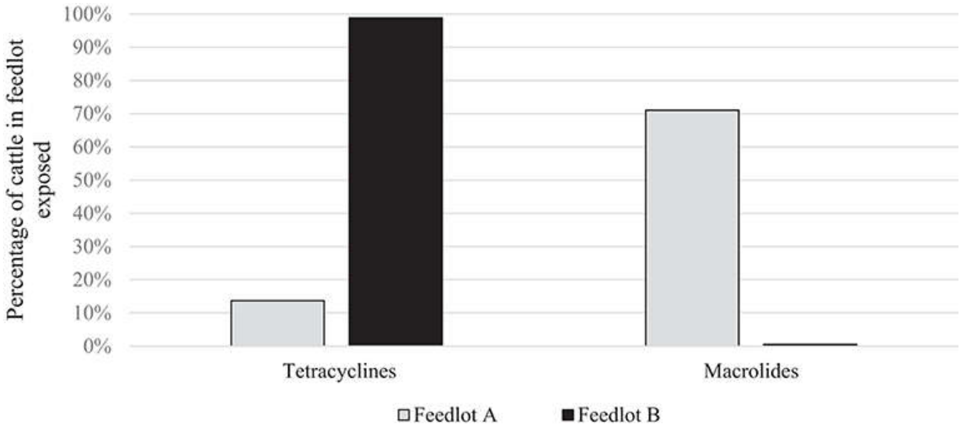
How big is the difference between indicators?

Numerator – comparison of weight-based vs dose-based units

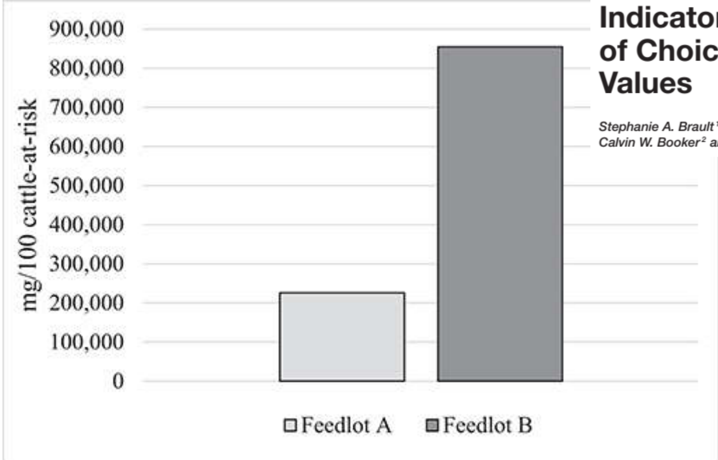
- Weight-based vs dose-based units



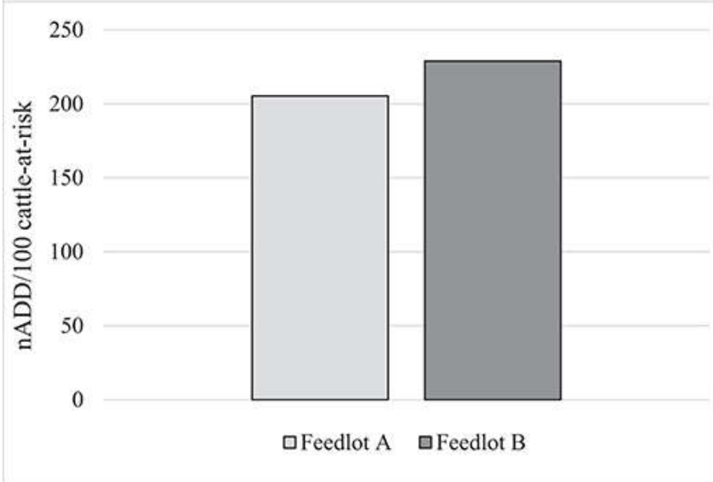
Parenteral antimicrobial drug	ADD_{kg} (mg/kg/day)	Mean weight (kg)	ADD (mg/day)
Macrolides			
Tulathromycin	0.8	375.6	300.5
Tilmicosin	3.3	375.6	1239.5
Tetracyclines			
Oxytetracycline (100 mg/ml)	6.7	375.6	2516.5
Oxytetracycline (200 mg/ml)	10.0	375.6	3756.0
Oxytetracycline (300 mg/ml)	10.0	375.6	3756.0

Calculation of Antimicrobial Use Indicators in Beef Feedlots—Effects of Choice of Metric and Standardized Values

*Stephanie A. Brault[1], Sherry J. Hannon[2], Sheryl P. Gow[3], Simon J. G. Otto[4], Calvin W. Booker[2] and Paul S. Morley[1,5]**



Weight-based

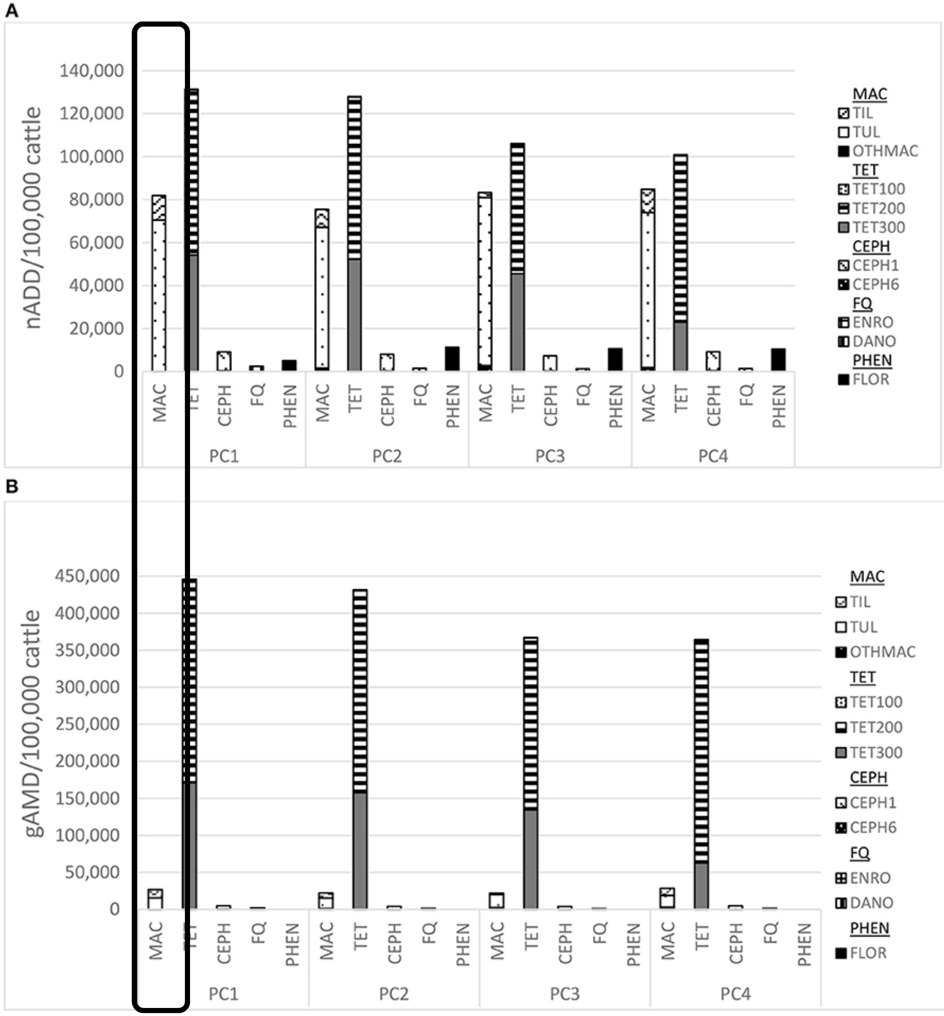


Dose-based

Brault et al. 2019

Numerator – comparison of weight-based vs dose-based units

- Application to real-world data:
  - 36 western Canadian feedlots
  - 4 placement cohorts



Dose-based

Weight-based

Antimicrobial Use on 36 Beef Feedlots in Western Canada: 2008–2012

Stephanie A. Brault[1], Sherry J. Hannon[2], Sheryl P. Gow[3], Brian N. Warr[2], Jessica Withell[2], Jiming Song[2], Christina M. Williams[2], Simon J. G. Otto[4], Calvin W. Booker[2] and Paul S. Morley[1,5]*

Brault et al. 2019

anses

Numerator – comparison of weight-based vs dose-based units

ROUTINE CIPARS AMU ANALYSIS			
	Mean	**Standard error of the mean**	**95% Confidence intervals**
$mg/PCU_{Br}^{(CIPARS)}$	150	4	142–159
nDDDvetCA/1,000 broiler chicken-days at risk $^{(CIPARS)}$	570	13	545–595
$nDDDvetCA/PCU_{Br}^{(CIPARS)}$	20	0.5	19–21
PAIRWISE CORRELATION MATRIX			
	$mg/PCU_{Br}^{(CIPARS)}$	nDDDvetCA/1,000 broiler chicken-days at risk $^{(CIPARS)}$	$nDDDvetCA/PCU_{Br}^{(CIPARS)}$
$mg/PCU_{Br}^{(CIPARS)}$	1		
nDDDvetCA/1,000 broiler chicken-days at risk $^{(CIPARS)}$	**0.7039***	1	
$nDDDvetCA/PCU_{Br}^{(CIPARS)}$	**0.7503***	**0.9667***	1
ALTERNATE AMU ANALYSIS			
	Mean	Standard error of the mean	95% Confidence intervals
$mg/kg_{Br}^{(ALT)}$	73	2	70
nDDDvetCA/1,000 broiler chicken-days at risk $^{(ALT)}$	284	6	271
$nDDDvetCA/kg_{Br}^{(ALT)}$	10	0.2	9
PAIRWISE CORRELATION MATRIX			
	$mg/kg_{Br}^{(ALT)}$	nDDDvetCA/1,000 broiler chicken-days at risk $^{(ALT)}$	$nDDDvetCA/kg_{Br}^{(ALT)}$
$mg/kg_{Br}^{(ALT)}$	1		
nDDDvetCA/1,000 broiler chicken-days at risk $^{(ALT)}$	**0.6878***	1	
$nDDDvetCA/kg_{Br}^{(ALT)}$	**0.7000***	**0.9638***	1

Analysis excluded flocks which were intentionally raised without antibiotics under designated programs for mainstream market such as "Raised without Antibiotics," "Antibiotic-Free," and organic.
CIPARS—Canadian Integrated Program for Antimicrobial Resistance Surveillance.
(CIPARS) Based on routine formula used by CIPARS.
(ALT) kg broiler chicken live pre-slaughter weights, alternate estimation methods.
nDDDvetCA—number of defined daily doses for animals using Canadian standards.
PCU—population correction unit (based on the European Surveillance for Veterinary Antimicrobial Consumption average weight at treatment for broiler chickens at 1 kg).
Br—broilers.
**P < 0.0001, Pearson correlation coefficient.*

Agunos et al. 2020

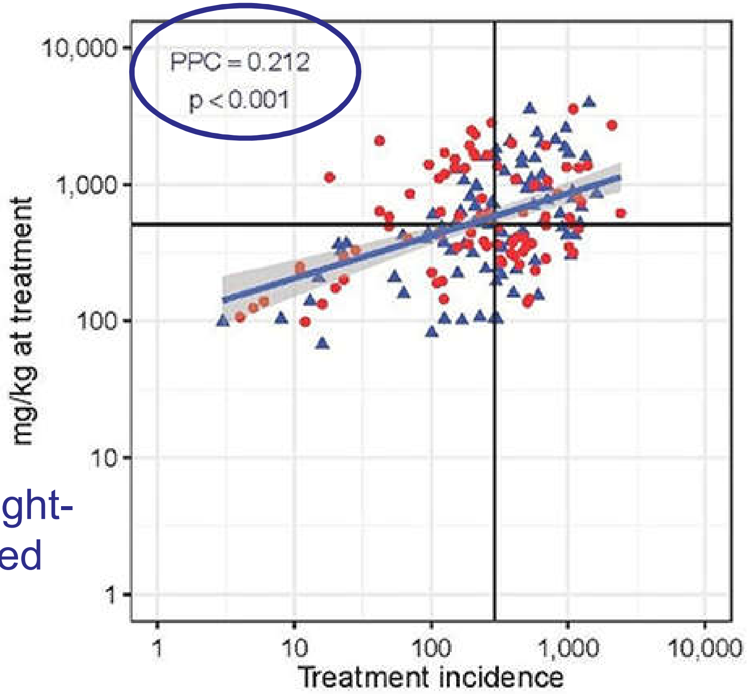
Antimicrobial Use Indices—The Value of Reporting Antimicrobial Use in Multiple Ways Using Data From Canadian Broiler Chicken and Turkey Farms

Agnes Agunos, Sheryl P. Gow, David F. Léger, Anne E. Deckert, Carolee A. Carson, Angelina L. Bosman, Stefanie Kadykalo and Richard J. Reid-Smith*

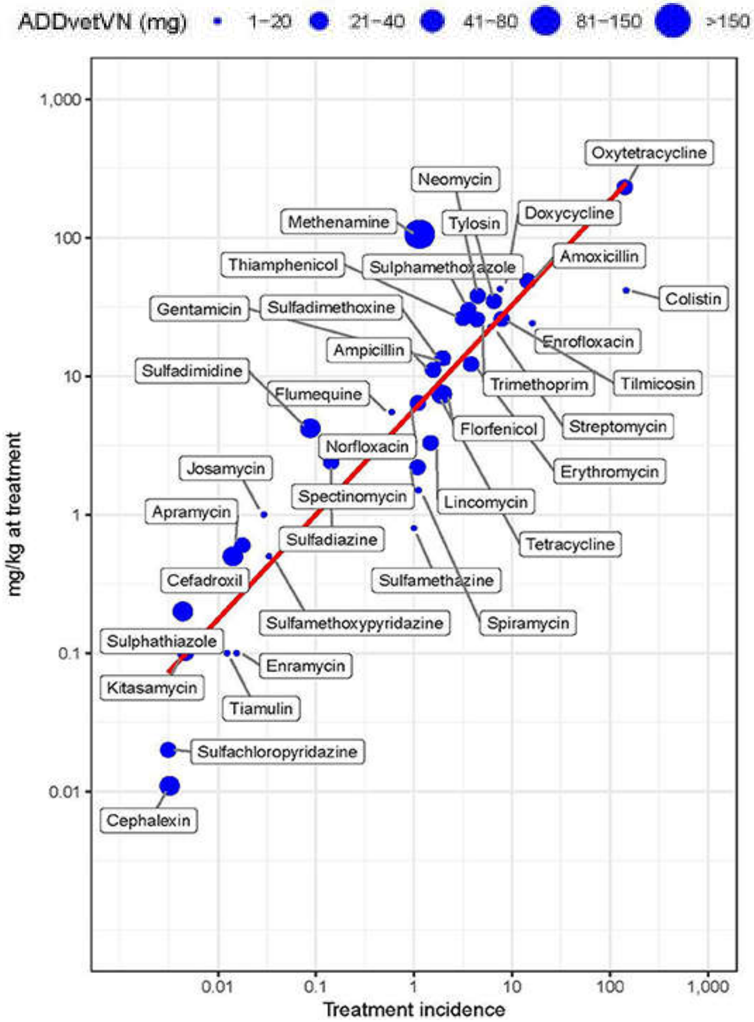
anses

Numerator – comparison of weight-based vs count-based units

Weight-based



Count-based



High-Resolution Monitoring of Antimicrobial Consumption in Vietnamese Small-Scale Chicken Farms Highlights Discrepancies Between Study Metrics

Nguyen Van Cuong[1], Doan Hoang Phu[1,2], Nguyen Thi Bich Van[1], Bao Dinh Truong[1,2], Bach Tuan Kiet[3], Bo Ve Hien[3], Ho Thi Viet Thu[4], Marc Choisy[1,5], Pawin Padungtod[6], Guy Thwaites[1,7] and Juan Carrique-Mas[1,7]*

- Deviation between indicators varies depending on AM active ingredients
- Greatest deviation for those AAIs with very low or very high DDDs

Numerator – Among dose-based units: national vs European DDDs

- Development of DDDs – Canada (pig and poultry)

Species	Route of administration	DDDvetCA:DDDvet Ratio >1.1 *N* (%)	DDDvetCA:DDDvet Ratio <0.9 *N* (%)	DDDvetCA:DDDvet Ratio ≥ 0.9 and ≤1.1 *N* (%)
Poultry	Feed	1 (17)	5 (83)	0 (0)
Poultry	Water	4 (31)	6 (46)	3 (23)
Pigs	Feed	0 (0)	11 (100)	0 (0)
Pigs	Water	5 (29)	7 (41)	5 (29)
Pigs	Injectable	5 (29)	6 (35)	6 (35)
Pigs	Bolus[b]	2 (33)	3 (50)	1 (17)
Poultry and pigs	All routes of administration	17 (24)	38 (54)	15 (21)

DDDvetCAs were considered larger when the ratio of the DDDvetCA/DDDvet was larger than 1.1, smaller when the ratio was <0.9, and equivalent when the ratio was equal to or between 0.9 and 1.1.

[a]European Medicines Agency (12).

[b]Bolus, administered as individual oral treatment.

- DDDvetCAs deviate from DDDvet (especially in feed products)
- DDDvetCAs to be preferred for AMU studies within Canada
- DDDvet to be preferred for comparison between countries

Developing Canadian Defined Daily Doses for Animals: A Metric to Quantify Antimicrobial Use

Angelina L. Bosman[1,2], Daleen Loest[1], Carolee A. Carson[1], Agnes Agunos[1], Lucie Collineau[3] and David F. Léger[1]*

Numerator – Among dose-based units: UDDs vs DDDs

- Used Daily Dose (UDD) vs Defined Daily Dose (DDD)

- Data from the Clinic for Horses (CfH),University of Veterinary Medicine Hannover (TiHo), Germany
- 2017 data: 2,168 horses and 34,432 drug applications
- Comparison between UDD vs RDDCfH (Recommended Daily Dose internally defined by the TiHo Clinic)

Of the 3,831 drug applications where the comparison was possible:

– 94% drug applications were within the range around RDDCfH

Overall, very little deviation between UDDs and DDDs

Antimicrobial Usage in Horses: The Use of Electronic Data, Data Curation, and First Results

Anne Schnepf[1], Astrid Bienert-Zeit[2], Hatice Ertugrul[1], Rolf Wagels[3], Nicole Werner[1], Maria Hartmann[1], Karsten Feige[2] and Lothar Kreienbrock[1]*

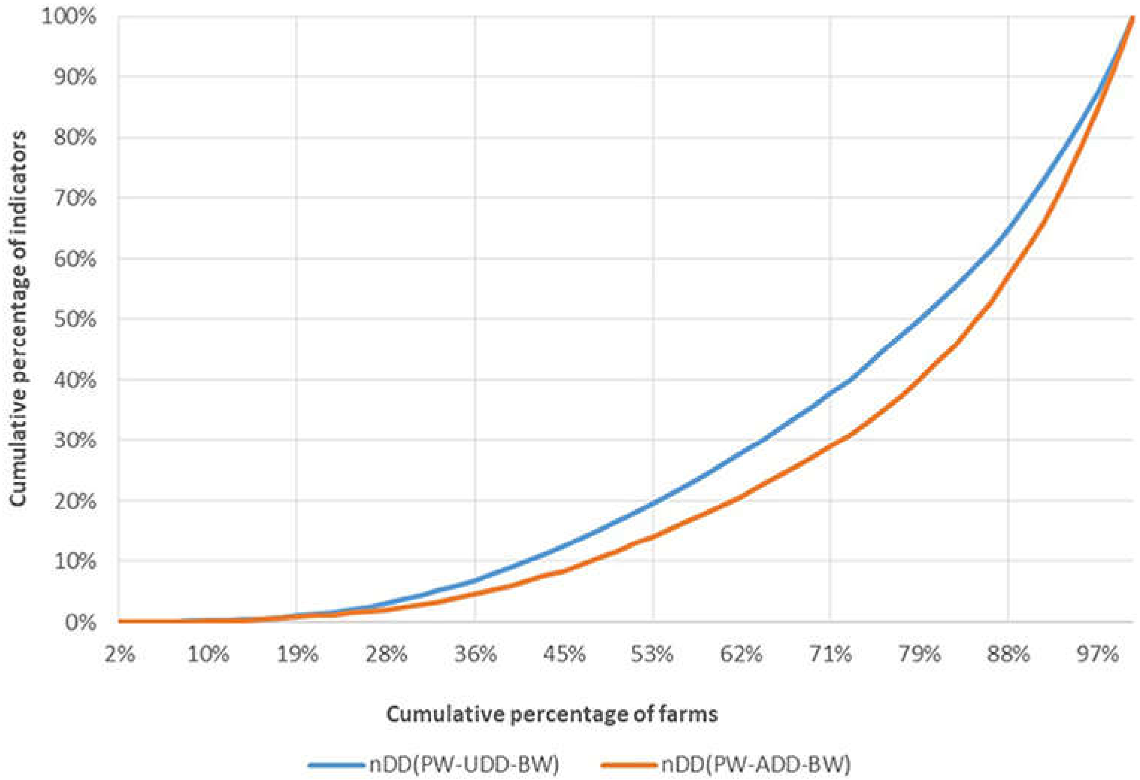
Numerator – Among dose-based units: UDDs vs DDDs

- Used Daily Dose (UDD) vs Defined Daily Dose (DDD)

- n= 70 French pig farms
- Weaning stage
- 2014-2015 data

How Input Parameters and Calculation Rules Influence On-Farm Antimicrobial Use Indicators in Animals

Agnès Waret-Szkuta [1], Victor Coelho [1], Lucie Collineau [2], Anne Hémonic [3], Claire Buy [1], Maxime Treff [1] and Didier Raboisson [1]*



Waret-Szkuta et al. 2019

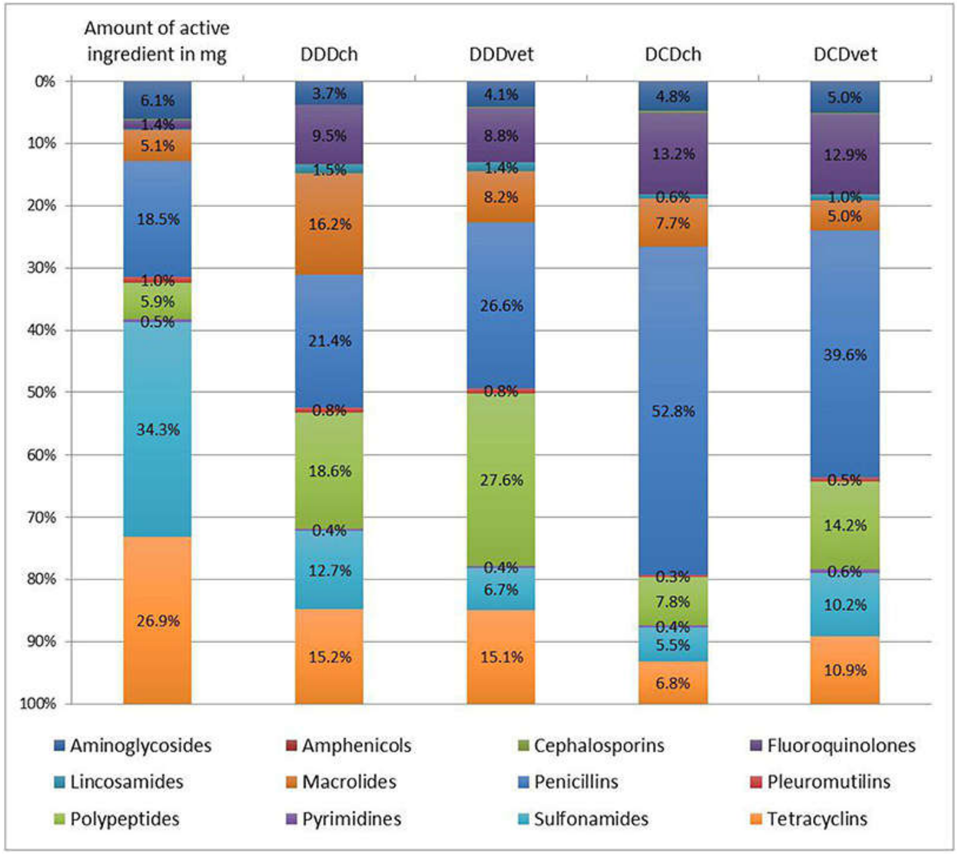
Overall, very little deviation between UDDs and DDDs
The same applied to actual vs theoretical treatment duration

anses

Why does it matter?

To compare between countries

- Comparison of Swiss vs European DDDs and DCDs



Echtermann et al. 2019

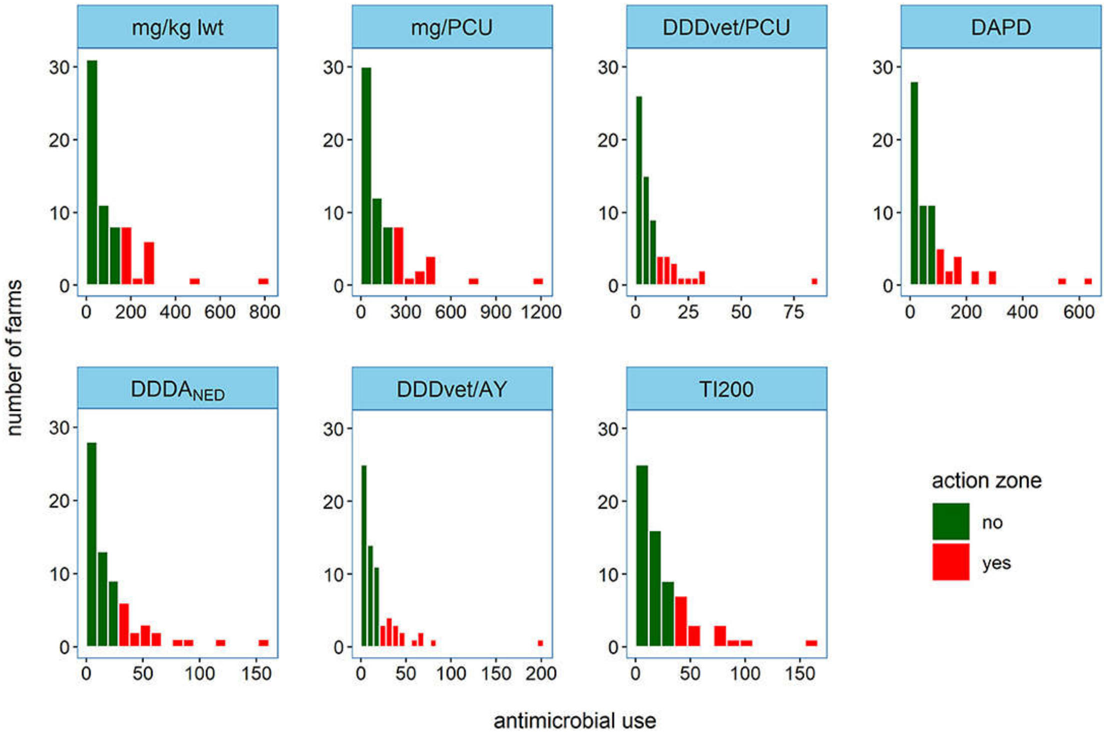
Antimicrobial Drug Consumption on Swiss Pig Farms: A Comparison of Swiss and European Defined Daily and Course Doses in the Field

Thomas Echtermann[1], Cedric Muentener[2], Xaver Sidler[1] and Dolf Kümmerlen[2]*

- Similar AMU results obtained at farm level
- Nevertheless, marked differences could be observed in the assessment of the use of specific antimicrobial classes

For benchmarking purposes

- Dose-based vs Count-based units → Impact on farm benchmarking
- N=67 pig farms, 2016 data



Does the Use of Different Indicators to Benchmark Antimicrobial Use Affect Farm Ranking?

Lorcan O'Neill[1,2], Maria Rodrigues da Costa[1,2], Finola Leonard[2], James Gibbons[3], Julia Adriana Calderón Díaz[1], Gerard McCutcheon[1,4] and Edgar García Manzanilla[1,2]*

	mg/PCU	mg/kg lwt	$DDDA_{NED}$	DAPD	DDDvet/PCU	DDDvet/AY	TI200
mg/PCU	1 n = 0	0.92 n = 1	0.84 n = 2	0.84 n = 2	0.76 n = 3	0.76 n = 3	0.76 n = 3
mg/kg lwt		1 n = 0	0.84 n = 2	0.84 n = 2	0.84 n = 2	0.84 n = 2	0.76 n = 3
$DDDA_{NED}$			1 n = 0	0.84 n = 2	0.76 n = 3	0.76 n = 3	0.76 n = 3
DAPD				1 n = 0	0.84 n = 2	0.92 n = 1	0.92 n = 1
DDDvet/PCU					1 n = 0	0.84 n = 2	0.76 n = 3
DDDvet/AY						1 n = 0	0.92 n = 1
TI200							1 n = 0

Kappa coefficient

#farms with disagreement between both indicators

O'Neill et al. 2020

High users vary between indicators

For benchmarking purposes

- Dose-based vs Count-based units → Impact on farm benchmarking
- N= 893 Swiss pig herds

Animal Treatment Index (=number of treatments per animal per year) vs nDDDch/animal/year

	5% High usage		10% High usage		25% High usage		Correlation
	a	k	a	k	a	k	r
Fattening pigs	98%	0.844	93%	0.671	75%	0.510	0.673
Weaned piglets	97%	0.708	97%	0.846	96%	0.911	0.910
Suckling piglets	96%	0.643	91%	0.528	77%	0.554	0.793
Lactating sows	96%	0.634	96%	0.771	88%	0.77	0.889
Gestating sows	95%	0.539	92%	0.583	77%	0.553	0.657

Kuemmerlen et al. 2020

a: agreement when defining 5, 10, and 25% high usage farms
k *:* Kappa coefficient
r *:* Spearman‘s Rho correlation coefficients

Agreement of Benchmarking High Antimicrobial Usage Farms Based on Either Animal Treatment Index or Number of National Defined Daily Doses

Dolf Kuemmerlen[1], Thomas Echtermann[1], Cedric Muentener[2] and Xaver Sidler[1]*

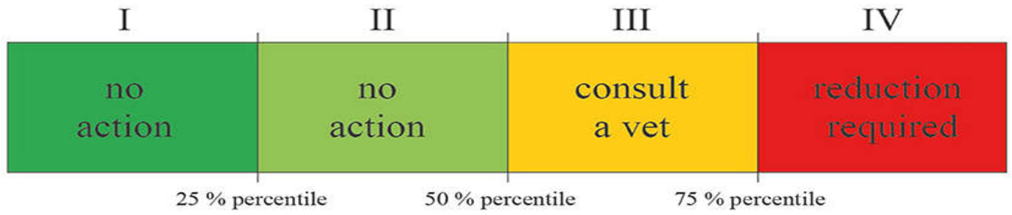
High users vary between indicators.
Deviation between indicators depends on age groups.

For benchmarking purposes

- Used Daily Dose (UDD) vs Defined Daily Dose (DDD)
- Treatment frequency = number of treatment days per given time period and farm
- Benchmarking based on TF_{UDD} vs TF_{DDD}
- Broiler (n=40 holdings), suckling piglets (n=135), and fattening pigs (n=449)

Used Daily Dose vs. Defined Daily Dose—Contrasting Two Different Methods to Measure Antibiotic Consumption at the Farm Level

Svetlana Kasabova[1], Maria Hartmann[1], Nicole Werner[1], Annemarie Käsbohrer[2,3] and Lothar Kreienbrock[1]*



TF_{UDD}	TF_{DDD} I		II		III		IV	
	n	%	*n*	%	*n*	%	*n*	%
I	29	87.9	4	12.1	0	0	0	0
II	4	11.8	20	58.8	9	26.5	1	2.9
III	0	0	9	26.5	16	47.1	9	26.5
IV	0	0	1	2.9	9	26.5	24	70.6

Dark and light green category, no action needed; yellow category, veterinary consulting useful; red category, reduction required.

Kasabova et al. 2020

High users vary between indicators.
Agreement appears lower in the medium range (medium users)

anses

Numerator – Summary of main findings

- Deviation between Weight-based vs Dose-based vs Count-based units
  - Deviation depends on AM active ingredients/classes (and consequently on age groups)
  - This has an impact on benchmarking
- DDDs and DCDs vary between countries and with EMA
  - This has on impact for international comparisons
  - DDDvet and DCDvet to be preferred for international comparison
  - National DDD and DCDs to be preferred for national studies
- Little deviation between UDD and DDD (pig and horses)
- Little deviation between used and theoretical treatment duration (pigs)
- Careful with the selection of numerator units
- You don't have to select only one

Numerator – Possible conversion from one unit to another

- Conversion of sales data to the number of potential treatments
- Calves and pigs in Switzerland - 2011 to 2015

$$\text{Number of ACDs} = \frac{\text{total quantity of active ingredient sold in one year (mg)}}{\text{daily dose } \left(\frac{mg}{kg}\right) \times \text{duration of tratment (days)} \times \text{weight at treatment (kg)}}$$

Extrapolating Antibiotic Sales to Number of Treated Animals: Treatments in Pigs and Calves in Switzerland, 2011–2015

Rosa Stebler[1,2], Luís P. Carmo[3], Dagmar Heim[4], Hanspeter Naegeli[5], Klaus Eichler[1] and Cedric R. Muentener[5]*

Decreases in oral use of macrolides were partly (pigs) or completely (calves) compensated by the application of long acting injectables.

The conversion allowed detection of trends that would not be obvious when only assessing sales data

	2011	2012	2013	2014	2015
PIGS					
Macrolides, premix	0.186	0.199	0.191	0.160	0.145
Macrolides, injections	0.152	0.153	0.171	0.165	0.170
Fluoroquinolones*	0.128	0.115	0.142	0.136	0.126
Cephalosporins*	0.073	0.062	0.064	0.067	0.061
CALVES					
Macrolides, premix	1.183	1.087	0.998	0.891	0.862
Macrolides, injections	0.241	0.239	0.291	0.287	0.303
Fluoroquinolones*	0.156	0.145	0.171	0.165	0.166
Cephalosporins*	0.133	0.123	0.121	0.119	0.112

*Only available as injections.

Stebler et al. 2019

And how about the denominator?

Denominator – comparison of biomass vs number of animals at risk

- Broiler (n= 947) and Turkey flocks (n=427) in Canada
- PCU or Biomass pre-slaughter vs number of animal-days at risk

ROUTINE CIPARS AMU ANALYSIS			
	Mean	**Standard error of the mean**	**95% Confidence intervals**
$mg/PCU_{Br}^{(CIPARS)}$	150	4	142–159
nDDDvetCA/1,000 broiler chicken-days at risk $^{(CIPARS)}$	570	13	545–595
$nDDDvetCA/PCU_{Br}^{(CIPARS)}$	20	0.5	19–21
PAIRWISE CORRELATION MATRIX			
	$mg/PCU_{Br}^{(CIPARS)}$	nDDDvetCA/1,000 broiler chicken-days at risk $^{(CIPARS)}$	$nDDDvetCA/PCU_{Br}^{(CIPARS)}$
$mg/PCU_{Br}^{(CIPARS)}$	1		
nDDDvetCA/1,000 broiler chicken-days at risk $^{(CIPARS)}$	**0.7039***	1	
$nDDDvetCA/PCU_{Br}^{(CIPARS)}$	**0.7503***	**0.9667***	1
ALTERNATE AMU ANALYSIS			
	Mean	Standard error of the mean	95% Confidence intervals
$mg/kg_{Br}^{(ALT)}$	73	2	70
nDDDvetCA/1,000 broiler chicken-days at risk $^{(ALT)}$	284	6	271
$nDDDvetCA/kg_{Br}^{(ALT)}$	10	0.2	9
PAIRWISE CORRELATION MATRIX			
	$mg/kg_{Br}^{(ALT)}$	nDDDvetCA/1,000 broiler chicken-days at risk $^{(ALT)}$	$nDDDvetCA/kg_{Br}^{(ALT)}$
$mg/kg_{Br}^{(ALT)}$	1		
nDDDvetCA/1,000 broiler chicken-days at risk $^{(ALT)}$	**0.6878***	1	
$nDDDvetCA/kg_{Br}^{(ALT)}$	**0.7000***	**0.9638***	1

Analysis excluded flocks which were intentionally raised without antibiotics under designated programs for mainstream market such as "Raised without Antibiotics," "Antibiotic-Free," and organic.
CIPARS—Canadian Integrated Program for Antimicrobial Resistance Surveillance.
(CIPARS)Based on routine formula used by CIPARS.
(ALT)kg broiler chicken live pre-slaughter weights, alternate estimation methods.
nDDDvetCA—number of defined daily doses for animals using Canadian standards.
PCU—population correction unit (based on the European Surveillance for Veterinary Antimicrobial Consumption average weight at treatment for broiler chickens at 1 kg).
Br—broilers.
**P < 0.0001, Pearson correlation coefficient.*

Agunos et al. 2020

Antimicrobial Use Indices—The Value of Reporting Antimicrobial Use in Multiple Ways Using Data From Canadian Broiler Chicken and Turkey Farms

Agnes Agunos, Sheryl P. Gow, David F. Léger, Anne E. Deckert, Carolee A. Carson, Angelina L. Bosman, Stefanie Kadykalo and Richard J. Reid-Smith*

Very high correlation between biomass and number of animal-days at risk

Denominator – within biomass approches: weight at treatment vs at pre-slaughter

- Broiler (n= 947) and Turkey flocks (n=427) in Canada

Antimicrobial Use Indices—The Value of Reporting Antimicrobial Use in Multiple Ways Using Data From Canadian Broiler Chicken and Turkey Farms

Agnes Agunos, Sheryl P. Gow, David F. Léger, Anne E. Deckert, Carolee A. Carson, Angelina L. Bosman, Stefanie Kadykalo and Richard J. Reid-Smith*

	Average weight at treatment (ESVAC)	**Pre-slaughter weight (CIPARS)**
Broilers	1 Kg	2 Kg
Turkeys	6.5 Kg	10 Kg

-50 % AMU

-33 % AMU

Weight at treatment vs pre-slaughter weight:

- Any of those can be used to study trends over time
- Careful when comparing AMU between populations using mg/PCU vs mg/biomass slaughtered

Denominator – within biomass approches: theoretical vs actual weight at treatment

Parenteral antimicrobial drug	ADD_{kg} (mg/kg/day)	Mean weight (kg)	Standard ADD (mg/day)	Antimicrobial used (mg)	nADD (mean weight)	nADD (actual weight)	Variation (%)
Macrolides							
Tulathromycin	0.83	336	280.0	400,310,350	1,429,680	1,869,247	−23.5
Tilmicosin	3.33	336	1,120.0	189,139,740	168,875	214,741	−21.4
Gamithromycin	2.00	336	672.0	15,009,300	22,335	28,274	−21.0
Tildipirosin	1.33	336	448.0	3,578,760	7,988	9,195	−13.1
All macrolides					1,628,878	2,121,457	−23.2
Tetracyclines							
Oxytetracycline (100 mg/ml)	6.70	336	2,251.2	9,386,200	4,169	4,375	−4.7
Oxytetracycline (200 mg/ml)	10.00	336	3,360.0	6,882,331,720	2,048,313	1,899,370	7.8
Oxytetracycline (300 mg/ml)	10.00	336	3,360.0	3,435,537,840	1,022,482	1,169,307	−12.6
All tetracyclines					3,074,964	3,073,052	0.0
Beta-lactams							
Ceftiofur hydrochloride or sodium	1.10	336	369.6	113,460,385	306,982	213,103	44.1
Ceftiofur crystalline free acid	2.20	336	739.2	6,793,000	9,190	7,589	21.1
Procaine penicillin	6.67	336	2,240.0	4,334,700	1,935	1,649	17.4
All beta-lactams					318,107	222,341	43.1
All antimicrobial drugs					5,051,948	5,416,850	−7.3%

Brault et al. 2020

Variation between mean weight and actual weight at treatment varies between antimicrobial classes

Denominator – towards improved comparability between populations

- ‘Improved PCU’ considering animal demographics

Production type	w_k Subregion 2	AMU^*_k in mg/kg Subregion 1	Weighted, expected AMU
Fattening pigs	52.4	80.1	42.0
Dairy cows	31.3	10.0	03.1
Calves	10.3	28.2	02.9
Beef cattle	06.0	11.4	00.7
$\sum$	100.0		48.7

Hommerich et al. 2019

Standardization of Therapeutic Measures in Antibiotic Consumption Monitoring to Compare Different Livestock Populations

Katharina Hommerich, Charlotte Vogel, Svetlana Kasabova, Maria Hartmann and Lothar Kreienbrock*

- Indirect standardization method
- Expected AMU in subregion 2 is extrapolated from AMU in subregion 1 (= standard population)
  - Assuming similar treatment habits in subregions 1 and 2
  - Correcting for animal demographics in subregion 2

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Denominator – Summary of main findings

- High correlation between biomass and number of animals at risk
- Weight at treatment deviate from weight at pre-slaughter
  - Deviation varies between animal species
- Theoretical weight at treatment deviate from actual weight at treatment
  - Deviation varies between antimicrobial classes
- PCU could be improved by taking into account animal demographics

Which applicability to LMIC countries?

Applicability to LMIC countries

- Pilot cross-sectional study in 93 poultry and swine commercial and backyard farms in the Philippines
- Interview and questionnaire-based data collection
- Indicator = % of farms using AAI over the total number of farms
- No AMU quantification was performed

- Still useful to inform about AM practices
  - For example: >30% of pig and poultry farms use enrofloxacin

Antimicrobials Used in Backyard and Commercial Poultry and Swine Farms in the Philippines: A Qualitative Pilot Study

Toni Rose M. Barroga[1,2], Reildrin G. Morales[1,3], Carolyn C. Benigno[4], Samuel Joseph M. Castro[2], Mardi M. Caniban[2], Maria Fe B. Cabullo[2], Agnes Agunos[4†], Katinka de Balogh[4] and Alejandro Dorado-Garcia[5]*

Antimicrobial class	Antimicrobial active ingredient	Poultry farms *n* (%)	Swine farms *n* (%)
Aminoglycosides	Apramycin	0 (0%)	1 (2%)
	Gentamicin	**0 (0%)**	**7 (13%)***
	Neomycin	0 (0%)	1 (2%)
	Streptomycin	2 (5%)	2 (4%)
Cephalosporins	Ceftiofur	0 (0%)	2 (4%)
	Cephalexin	0 (0%)	1 (2%)
Fluoroquinolones	Ciprofloxacin	0 (0%)	1 (2%)
	Danofloxacin	0 (0%)	1 (2%)
	Enrofloxacin	13 (33%)	19 (36%)
	Levofloxacin	1 (3%)	0 (0%)
	Norfloxacin	**10 (25%)**	**3 (6%)***
Lincosamides and aminocyclitols	Lincomycin	0 (0%)	3 (6%)
	Lincomycin-spectinomycin	0 (0%)	1 (2%)
Macrolides	**Erythromycin**	**3 (8%)**	**0 (0%)***
	Kitasamycin	1 (3%)	0 (0%)
	Tilmicosin	2 (5%)	4 (8%)
	Tulathromycin	0 (0%)	1 (2%)
	Tylosin	**3 (8%)**	**14 (25%)***
Penicillins	Amoxicillin	8 (20%)	11 (21%)
	Penicillin	1 (3%)	1 (2%)
Phenicols	Florfenicol	4 (10%)	5 (9%)
	Thiamphenicol	1 (3%)	0 (0%)
Phosphonic acid derivatives	**Fosfomycin**	**4 (10%)**	**(0%) ***
Pleuromutilins	**Tiamulin**	**0 (0%)**	**12 (23%) ***
Polypeptides	Colistin	5 (13%)	6 (11%)
Tetraycyclines	Chlortetracycline	0 (0%)	2 (4%)
	Doxycycline	6 (15%)	11 (21%)
	Oxytetracycline	**4 (10%)**	**16 (30%)***
Trimethoprim and sulfonamides	Trimethoprim-sulfadiazine	5 (13%)	2 (4%)
	Trimethoprim-sulfamethoxazole	2 (5%)	0 (0%)

**Significant differences between poultry and swine farms (P ≤ 0.05), Fisher exact test (represented in bold fonts).*

anses

Applicability to LMIC countries

- A cross-sectional study
- 57 commercial layer and 83 broiler farms in eight sub-districts of the Chattogram district, Bangladesh
- Indicator = % of farms using AAI over the total number of farms
- Interview and questionnaire-based data collection

- No AMU quantification performed.
  - layer farms: ciprofloxacin (37.0% of farms), amoxicillin (33.3%) and tiamulin (31.5%),
  - broiler farms, colistin (56.6%), doxycycline (50.6%) and neomycin (38.6%)
- 85% of farmers used AM prophylactically
- *“It is recommended, that commercial poultry farmers should keep records of antimicrobials used with dosage and duration of administration along with indication of use. This would allow […] to evaluate the appropriate use of antimicrobial agents under an antimicrobial stewardship approach”*

A cross-sectional study of antimicrobial usage on commercial broiler and layer chicken farms in Bangladesh Provisionally accepted The final, formatted version of the article will be published soon. Notify me

Tasneem Imam[1*], Justine Gibson[1], Mohammad Foysal[2], Shetu B. Das[2], Suman D. Gupta[1], Guillaume Fournié[3], Md A. Hoque[2] and Joerg Henning[1]

Applicability to LMIC countries

- Cohort study in the Mekong Delta (Vietnam)
- 203 flocks raised in 102 of small-scale chicken farms

- AMU data collection:
  - Farm log-book to record quantitative AMU data
  - Drug containers

- Denominator data collection:
  - Number of animals at risk: on-farm demographics (mortality, etc)
  - Biomass: animal weight based on weekly weightings of 10 randomly-selected chickens from 11 representative flocks

- Four farm visits per production cycle
  - to review the product containers
  - to verify the collected data
  - Data entry in a web-based application

→ **Indicators: mg/kg at treatment , mg/kg sold, Treatment incidence**

High-Resolution Monitoring of Antimicrobial Consumption in Vietnamese Small-Scale Chicken Farms Highlights Discrepancies Between Study Metrics

Nguyen Van Cuong[1], Doan Hoang Phu[1,2], Nguyen Thi Bich Van[1], Bao Dinh Truong[1,2], Bach Tuan Kiet[3], Bo Ve Hien[3], Ho Thi Viet Thu[4], Marc Choisy[1,5], Pawin Padungtod[6], Guy Thwaites[1,7] and Juan Carrique-Mas[1,7]*

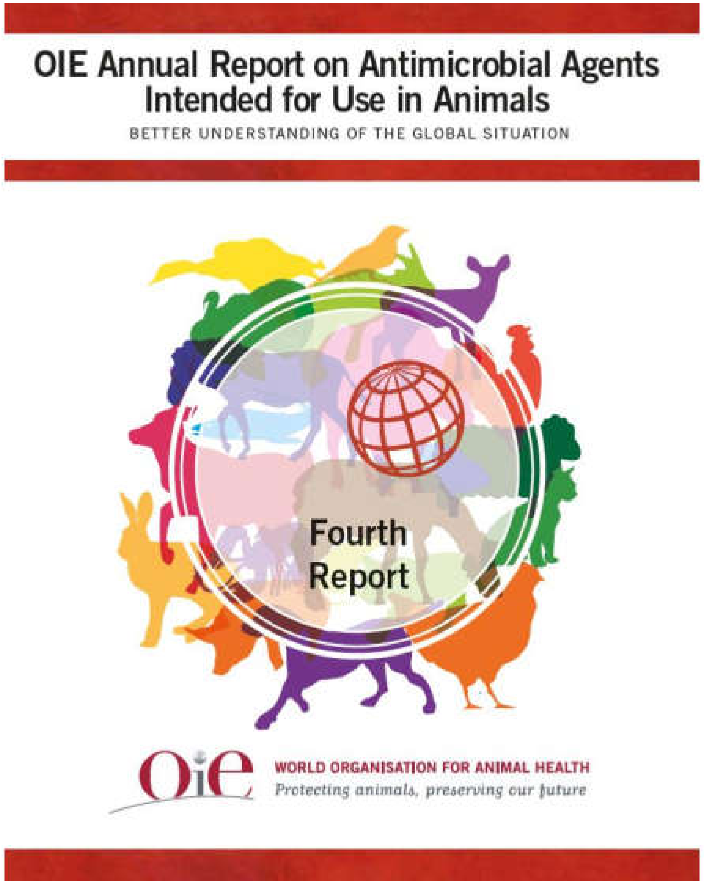
AMU quantification possible via prospective study design

Towards a global AMU monitoring approach – the OIE framework

OIE Annual Report on Antimicrobial Agents Intended for Use in Animals: Methods Used

Delfy Góchez[1], Margot Raicek[1], Jorge Pinto Ferreira[1], Morgan Jeannin[1], Gerard Moulin[2] and Elisabeth Erlacher-Vindel[1]*

[1] *Antimicrobial Resistance and Veterinary Products Department, World Organisation for Animal Health (OIE), Paris, France,*
[2] *Agence nationale de Sécurité Sanitaire, Alimentation, Environnement, Travail (ANSES), Fougères, France*



- Indicator retained by the OIE: $\frac{Antimicrobial\ agents\ reported\ (mg)}{animal\ biomass\ (kg)}$

Towards a global AMU monitoring approach – the OIE framework

- ESVAC approach not applicable at a global level (too detailed) → OIE had to come up with a new approach
- Animal biomass = biomass of animals present during the year of analysis in a specific country (proxy of those likely exposed to the quantities of antimicrobial agents reported)
- Data source: OIE WAHIS, and FAOSTAT (as a complementary dataset)
- Example: swine biomass calculation:

Swine biomass = (*live weight* × *number slaughtered*) + (*census population* × *sow weight* × 0.09)

- Defined by region (e.g. 240 Kg in Asia) → *sow weight*
- *live weight* (*kg*) = *carcass weight* (*kg*) / *conversion coefficient* (*k*)
- (*live weight* × *number slaughtered*): Expected biomass of fattening pigs slaughtered in a country in 1 year
- (*census population* × *sow weight* × 0.09): Expected biomass of pigs retained for breeding purposes
- 0.09: expected percentage of sows in a given swine population (Eurostat)

- Cat and dogs: yet to be included

Other applications of AMU quantifications

AMU quantification & Risk factors for AMU

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 26 July 2019
doi: 10.3389/fvets.2019.00244

Check for updates

Monitoring Antibiotic Usage in German Dairy and Beef Cattle Farms—A Longitudinal Analysis

Katharina Hommerich[1], Inga Ruddat[1], Maria Hartmann[1], Nicole Werner[1], Annemarie Käsbohrer[2,3] and Lothar Kreienbrock[1]*

Effect of time, herd size and region

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 30 October 2020
doi: 10.3389/fvets.2020.568881

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Antibiotic Use in Organic and Non-organic Swedish Dairy Farms: A Comparison of Three Recording Methods

Gabriela Olmos Antillón[1], Karin Sjöström[1], Nils Fall[1], Susanna Sternberg Lewerin[2] and Ulf Emanuelson[1]*

Effect of organic vs non-organic production

ORIGINAL RESEARCH ARTICLE
Front. Vet. Sci. | doi: 10.3389/fvets.2020.566529

Antimicrobial usage among different age categories and herd sizes in Swiss farrow-to-finish farms

Provisionally accepted The final, formatted version of the article will be published soon. Notify me

Thomas Echtermann[1*], Cedric Muentener[2], Xaver Sidler[1] and Dolf Kuemmerlen[1]

[1]Division of Swine Medicine, Department of Farm Animals, University of Zurich, Switzerland
[2]Institute of Veterinary Pharmacology and Toxicology, University of Zurich, Switzerland

Effect of age category and herd size

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 30 October 2020
doi: 10.3389/fvets.2020.558455

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Comparing Farm Biosecurity and Antimicrobial Use in High-Antimicrobial-Consuming Broiler and Pig Farms in the Belgian–Dutch Border Region

Nele Caekebeke[1], Franca J. Jonquiere[2], Moniek Ringenier[1], Tijs J. Tobias[2], Merel Postma[1], Angelique van den Hoogen[2], Manon A. M. Houben[3], Francisca C. Velkers[2], Nathalie Sleeckx[4], J. Arjan Stegeman[2] and Jeroen Dewulf[1] on behalf of the i-4-1-Health Study Group[1]*

OPEN ACCESS

Effect of biosecurity and production practices

AMU quantification to link AMU and AMR

- AMR Index:

$$AMR\ Ix_{Poultry} = \frac{R_{BrY} \times .PCU_{BrY}}{PCU_{PoultryY}} + \frac{R_{TkY} \times .PCU_{TkY}}{PCU_{PoultryY}}$$

Voluntary elimination of preventive C3G use by the Canadian poultry industry (May 2014)

	2013	2014	2015	2016	2017
PRIMARY AMU INDICATOR[a]					
mg/$PCU_{poultry}$, total AMU	94	78	56	107	128
mg/$PCU_{poultry}$, ceftiofur use	0.08	0.01	0.00	0.00	0.00
SECONDARY AMU INDICATOR[a]					
mg/$PCU_{poultry}$, gentamicin and lincomycin-spectinomycin use	0.04	0.06	0.28	0.03	0.07
PRIMARY AMR INDICATOR[a]					
AMR $Ix_{Susceptible\ E.\ coli}$	0.29	0.24	0.24	0.26	0.19
SECONDARY AMR INDICATOR[b]					
AMR $Ix_{CRO-R\ E.\ coli}$	0.19	0.20	0.09	0.07	0.07
AMR $Ix_{\geq 2Multiclass-R\ E.\ coli}$	0.53	0.50	0.60	0.61	0.59
AMR $Ix_{CIP-R\ Campylobacter}$	0.23	0.40	0.35	0.42	0.41
AMR $Ix_{GEN-R\ E.\ coli}$	0.11	0.14	0.24	0.22	0.22

High correlation between ceftiofur use and ceftriaxone resistance

Antimicrobial Use and Antimicrobial Resistance Indicators—Integration of Farm-Level Surveillance Data From Broiler Chickens and Turkeys in British Columbia, Canada

Agnes Agunos, Sheryl P. Gow, David F. Léger, Carolee A. Carson, Anne E. Deckert, Angelina L. Bosman, Daleen Loest, Rebecca J. Irwin and Richard J. Reid-Smith*

anses

AMU quantification and antimicrobial stewardship

frontiers in Veterinary Science
ORIGINAL RESEARCH
published: 02 July 2019
doi: 10.3389/fvets.2019.00218

Check for updates

Pharmaceutical Prescription in Canine Acute Diarrhoea: A Longitudinal Electronic Health Record Analysis of First Opinion Veterinary Practices

David A. Singleton[1], P. J. M. Noble[2], Fernando Sánchez-Vizcaino[3], Susan Dawson[2], Gina L. Pinchbeck[1], Nicola J. Williams[1], Alan D. Radford[1] and Philip H. Jones[1]*

Therapeutical management of canine acute diarrhoea

frontiers in Veterinary Science
ORIGINAL RESEARCH
published: 17 October 2019
doi: 10.3389/fvets.2019.00329

Check for updates

Antimicrobial Use on 36 Beef Feedlots in Western Canada: 2008–2012

Stephanie A. Brault[1], Sherry J. Hannon[2], Sheryl P. Gow[3], Brian N. Warr[2], Jessica Withell[2], Jiming Song[2], Christina M. Williams[2], Simon J. G. Otto[4], Calvin W. Booker[2] and Paul S. Morley[1,5]*

Therapeutical management of bovine respiratory disease (BRD)

frontiers in Veterinary Science
ORIGINAL RESEARCH
published: 13 November 2020
doi: 10.3389/fvets.2020.00545

Check for updates

Quantifying Antimicrobial Exposure in Dogs From a Longitudinal Study

María Méndez[1] and Miguel A. Moreno[1,2]*

ORIGINAL RESEARCH
published: 04 December 2018
doi: 10.3389/fvets.2018.00309

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Antimicrobial Prescriptions for Dogs in the Capital of Spain

Bárbara Gómez-Poveda[1] and Miguel A. Moreno[1,2]*

AM prescription patterns in dogs

frontiers in Veterinary Science
ORIGINAL RESEARCH
published: 28 May 2019
doi: 10.3389/fvets.2019.00158

Check for updates

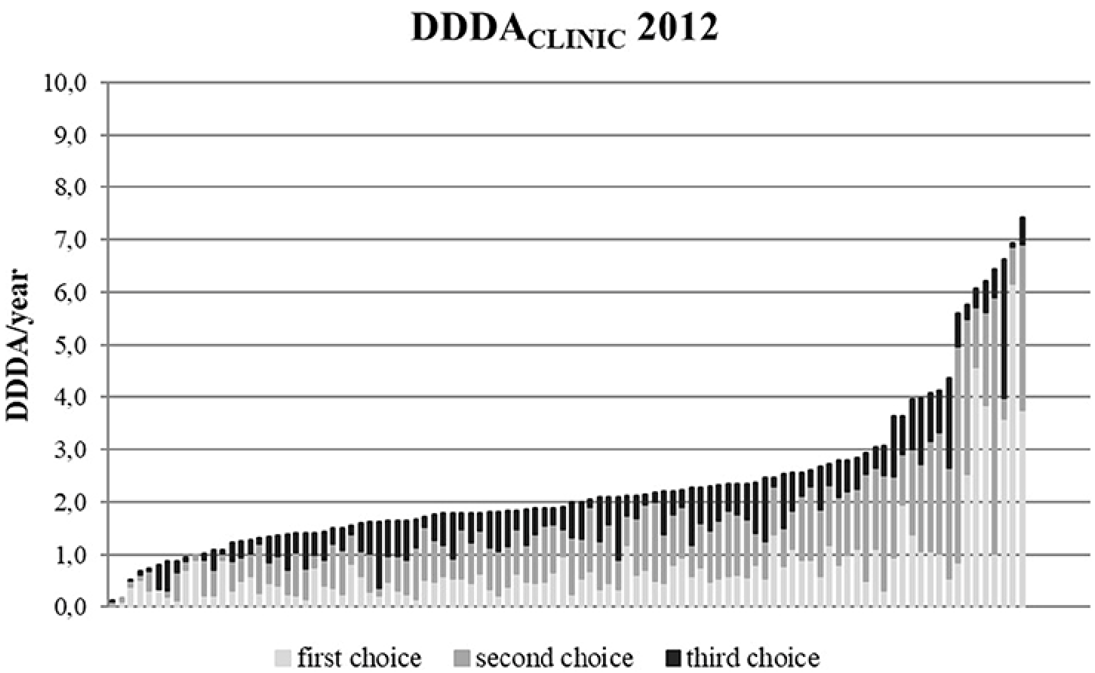
Quantifying Antimicrobial Use in Dutch Companion Animals

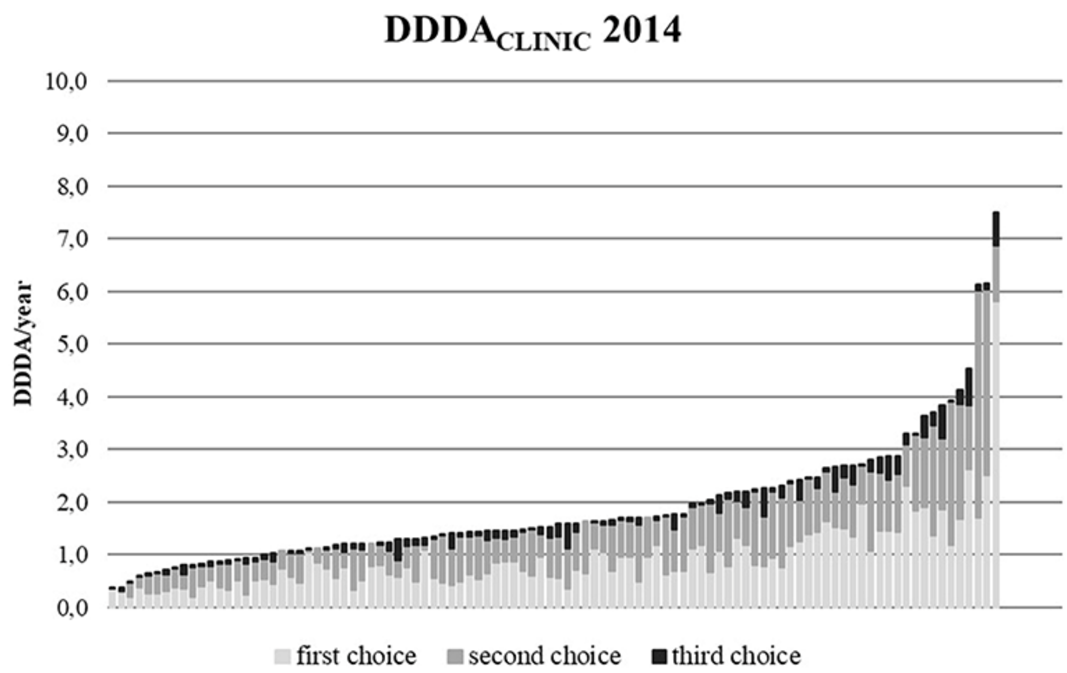
Nonke E. M. Hopman[1], Marloes A. M. van Dijk[1], Els M. Broens[1], Jaap A. Wagenaar[1,2,3], Dick J. J. Heederik[2,4] and Ingeborg M. van Geijlswijk[2,5]*

[1] Department of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, Netherlands, [2] The Netherlands Veterinary Medicines Institute (SDa), Utrecht, Netherlands, [3] Wageningen Bioveterinary Research, Lelystad, Netherlands, [4] Division Environmental Epidemiology, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, Netherlands, [5] Pharmacy Department, Faculty of Veterinary Medicine, Utrecht University, Utrecht, Netherlands

AMU quantification and antimicrobial stewardship

- 100 veterinary clinics providing procurement data over 2012-2014
- Indicator = $DDDA_{CLINIC}$/year = theoretical #days /year an average animal (dog, cat, rabbit) was treated with an AM





Hopman et al. 2019

Third choice: Fq, C3G/C4G (NL policy on veterinary AMU)

Social science approches of AMU quantification

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 02 August 2019
doi: 10.3389/fvets.2019.00257

Check for updates

Exploring Perspectives on Antimicrobial Use in Livestock: A Mixed-Methods Study of UK Pig Farmers

Lucy A. Coyne[1], Sophia M. Latham[1], Susan Dawson[2], Ian J. Donald[3], Richard B. Pearson[4], Rob F. Smith[2], Nicola J. Williams[1] and Gina L. Pinchbeck[1]*

Pig farmers behaviors and attitudes towards AMU

frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 08 September 2020
doi: 10.3389/fvets.2020.00582

Check for updates

Small and Large Animal Veterinarian Perceptions of Antimicrobial Use Metrics for Hospital-Based Stewardship in the United States

Laurel E. Redding[1], Brandi M. Muller[2] and Julia E. Szymczak[2]*

How veterinary clinicians think about AMU metrics

- Two veterinary hospitals in the Eastern US
- Semi-structured interviews with 34 veterinary clinicians (22 small animal and 12 large animal)

- Perceptions and understanding of different AMU metrics, and response to receiving an individualized prescribing report
  - % of visits in which an antimicrobial of highest priority was prescribed
  - number of ADDs per 1,000 patient-days
  - average number of ADDs per patient
  - the average number of antimicrobial classes prescribed per visit
  - rankings of the most frequently prescribed classes

How veterinary clinicians think about AMU metrics

- Respondents interested in seeing how their prescribing compared to that of their peers
- Doubt that the reports accurately captured the complexities of their prescribing decisions
- Metrics associated with ADDs confusing
- Only 38% respondents felt the reports would change how they used antimicrobials

“The ADD doesn’t make a ton of sense to me, like I feel like I need to like really stop and read the sentences and think through them very slowly to actually understand what they’re saying. But again, I am not a statistician.“

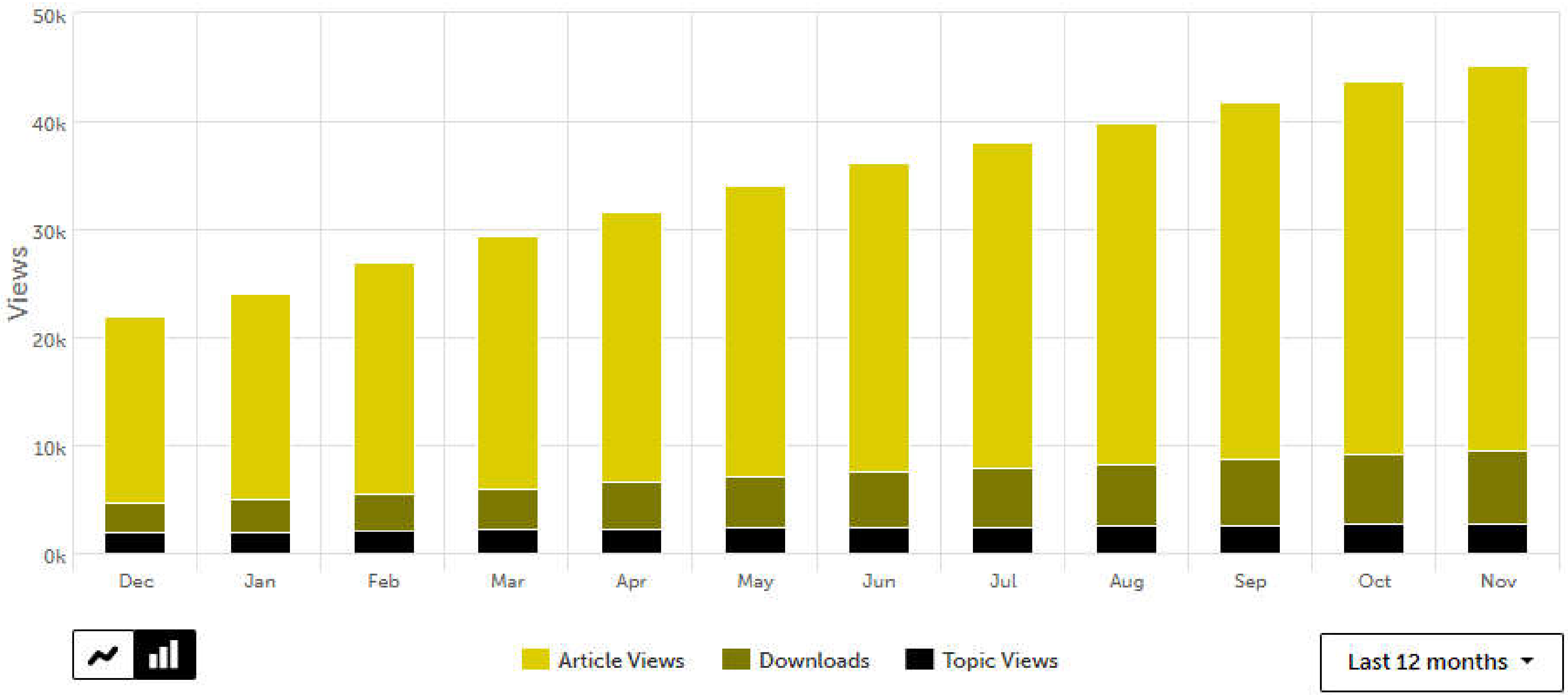
For AMU quantification to foster changes in AM prescription behaviours, and eventually improve antimicrobial stewardship, we need to keep it (relatively) simple

Take home messages

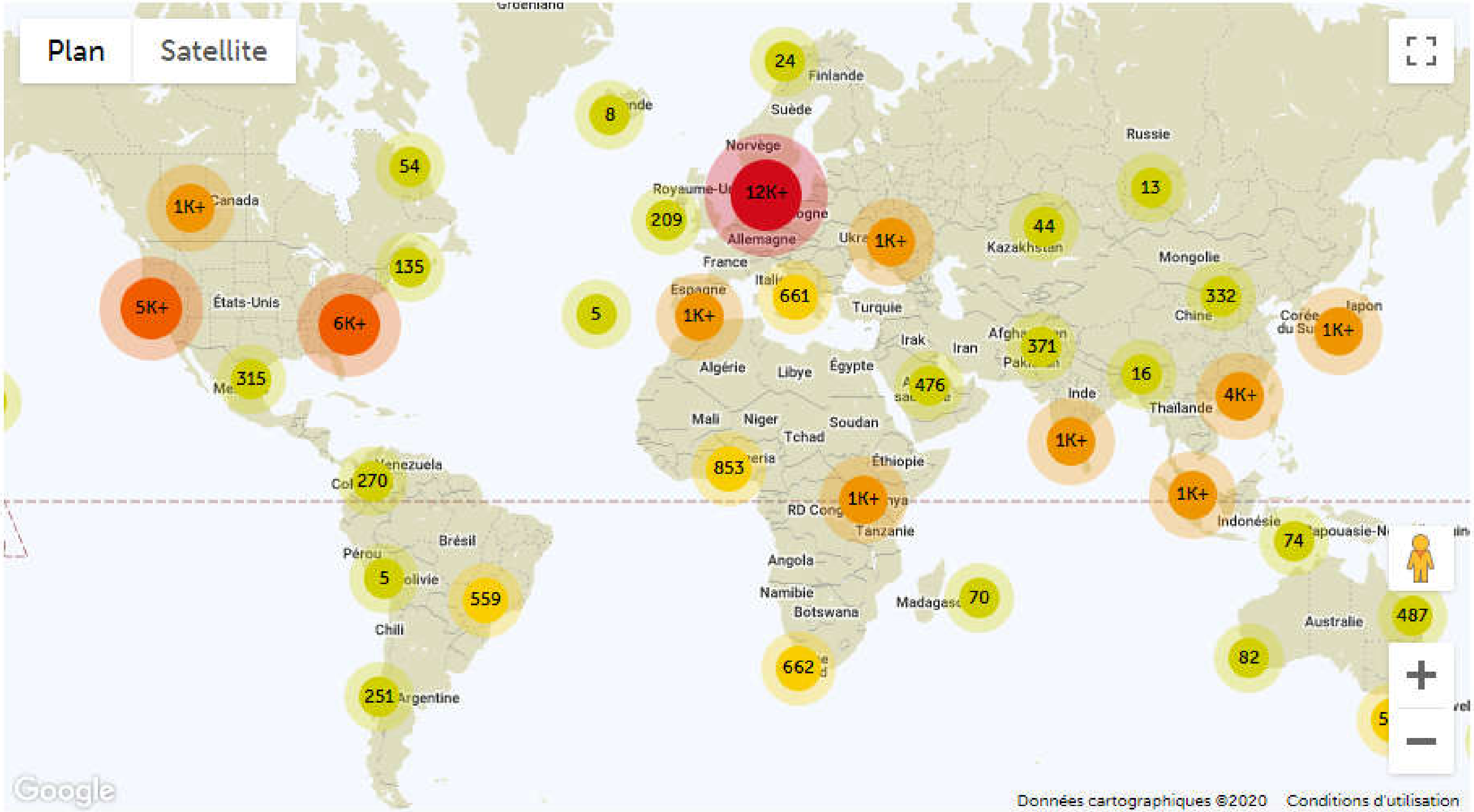
- Moving from national/sales data towards end-user/use data collection
  - The area of Big data (digitalization and centralization of AM prescriptions, farm records, etc)
  - Upcoming implementation of the EU Regulation (EU) 2019/6
- Farm-level AMU monitoring is still not harmonized
- Some aspects of AMU quantification are largely uncovered
  - Some animal species / sectors are under-investigated (fish, horses, companion animals)
  - Need for a One health approach of AMU monitoring; with common metrics in human/animal medicine
  - AMU and AMR monitoring to be further integrated
- AMU studies in LMIC countries
  - AMU quantification is still a challenge ; possible prospectively
  - OIE framework will facilitate AMU quantification in LMIC countries
- AMU quantification in animals is still a very active research area

Research topic volume I - Last 12 months

45,131 total views 35,637 article views 6,780 article downloads 2,714 topic views



Research topic volume I - Last 12 months



Other ongoing initiatives in the US

- *In 2016, FDA awarded funds in the form of cooperative agreements to support pilot projects for the collection of farm-level antimicrobial use data in animal agriculture […]*
- *Information from the first 2 years of the pilot projects is presented in this special issue, along with discussions related to challenges of collecting and reporting antimicrobial use data.*

Other ongoing initiatives in Asia

FAO-USAID Regional Project on AMR in Asia

Short working title: FAO-USAID Regional Project on AMR in Asia

Full project title: Addressing Antimicrobial Usage in Asia's Livestock, Aquaculture and Crop Production Systems (OSRO/RAS/502/USA)

Donor: USA

Focus Countries: Indonesia, Thailand and Viet Nam

Focus Sub-regions: ASEAN and SAARC

Period: 1 October 2015—31 December 2020

Contact person (division): Mary Joy Gordoncillo (RAP, ECTAD)

Objectives: Promote a more prudent use of antimicrobial in the livestock and aquaculture production industries as well as the crop production sector in Asia leading to minimizing the likelihood of antimicrobial resistance (AMR) development and spread.

Output 4: Strengthened capacities in surveillance and heightened implementation of the same in selected countries

- Improvement of tools for AMR surveillance in food and agriculture in the region including the following:
  - Regional Antimicrobial Resistance (AMR) Monitoring and Surveillance Guidelines Series
    - *Volume 1: Monitoring and surveillance of AMR in bacteria from healthy animals intended for consumption*
    - Volume 2: Monitoring and surveillance of AMR in bacterial pathogens from diseased livestock and poultry
    - Volume 3: Monitoring and surveillance of AMR in aquaculture
    - Volume 4: Monitoring and surveillance of AMR in animal environment
    - Volume 5: Monitoring and surveillance of antimicrobial usage at the farm level

Thank you

Research Topic

Antimicrobial Usage in Companion and Food Animals: Methods, Surveys and Relationships with Antimicrobial Resistance in Animals and Humans

- Volume I: https://www.frontiersin.org/research-topics/7641/antimicrobial-usage-in-companion-and-food-animals-methods-surveys-and-relationships-with-antimicrobi
- Volume II: https://www.frontiersin.org/research-topics/12106/antimicrobial-usage-in-companion-and-food-animals-methods-surveys-and-relationships-with-antimicrobi

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