CIPARS Farm Surveillance Component: Dairy Cattle

Presented by:
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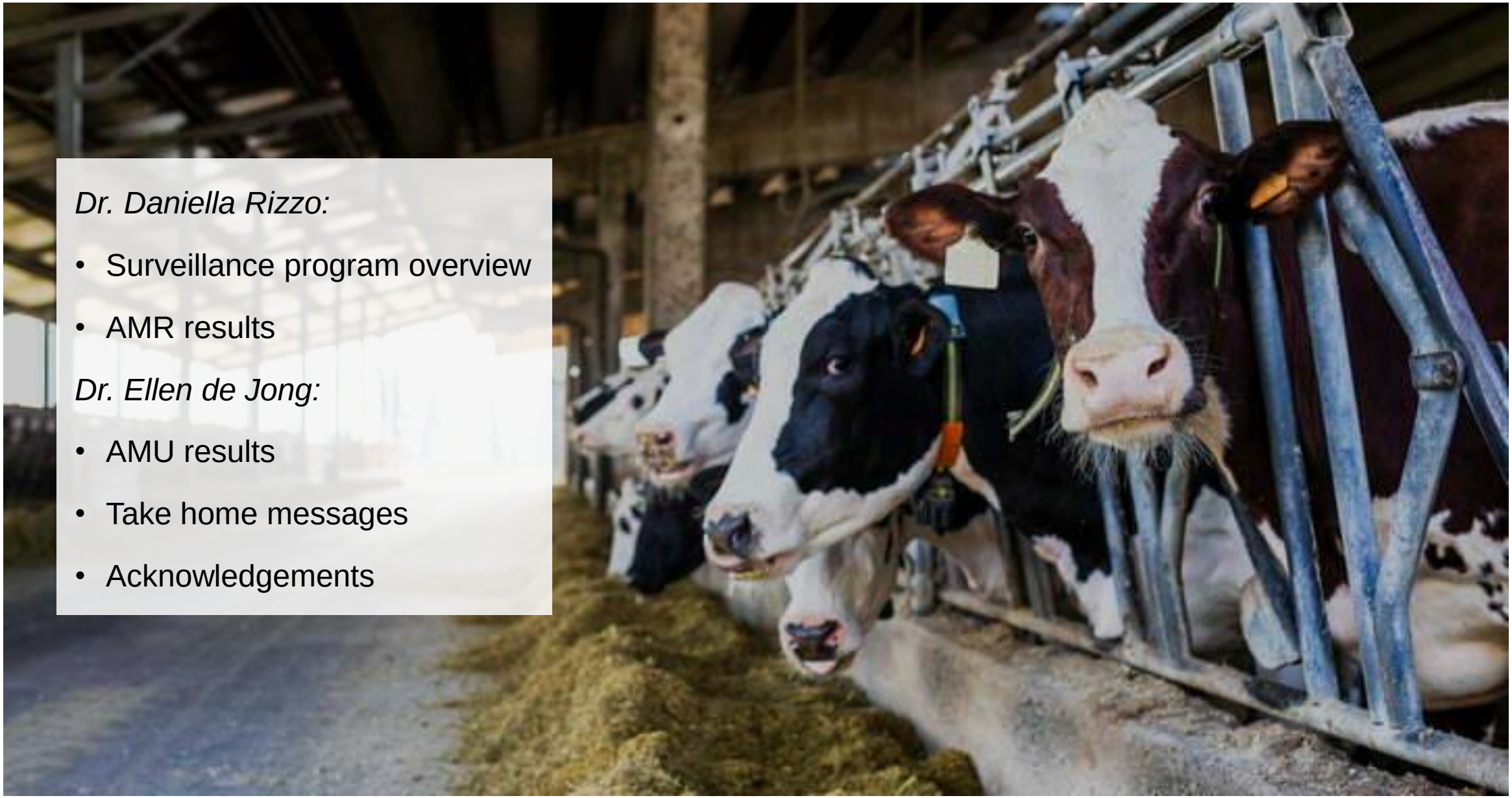
World Antimicrobial Resistance Awareness Week
November 19, 2024

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

Agenda



Dr. Daniella Rizzo:

- Surveillance program overview
- AMR results

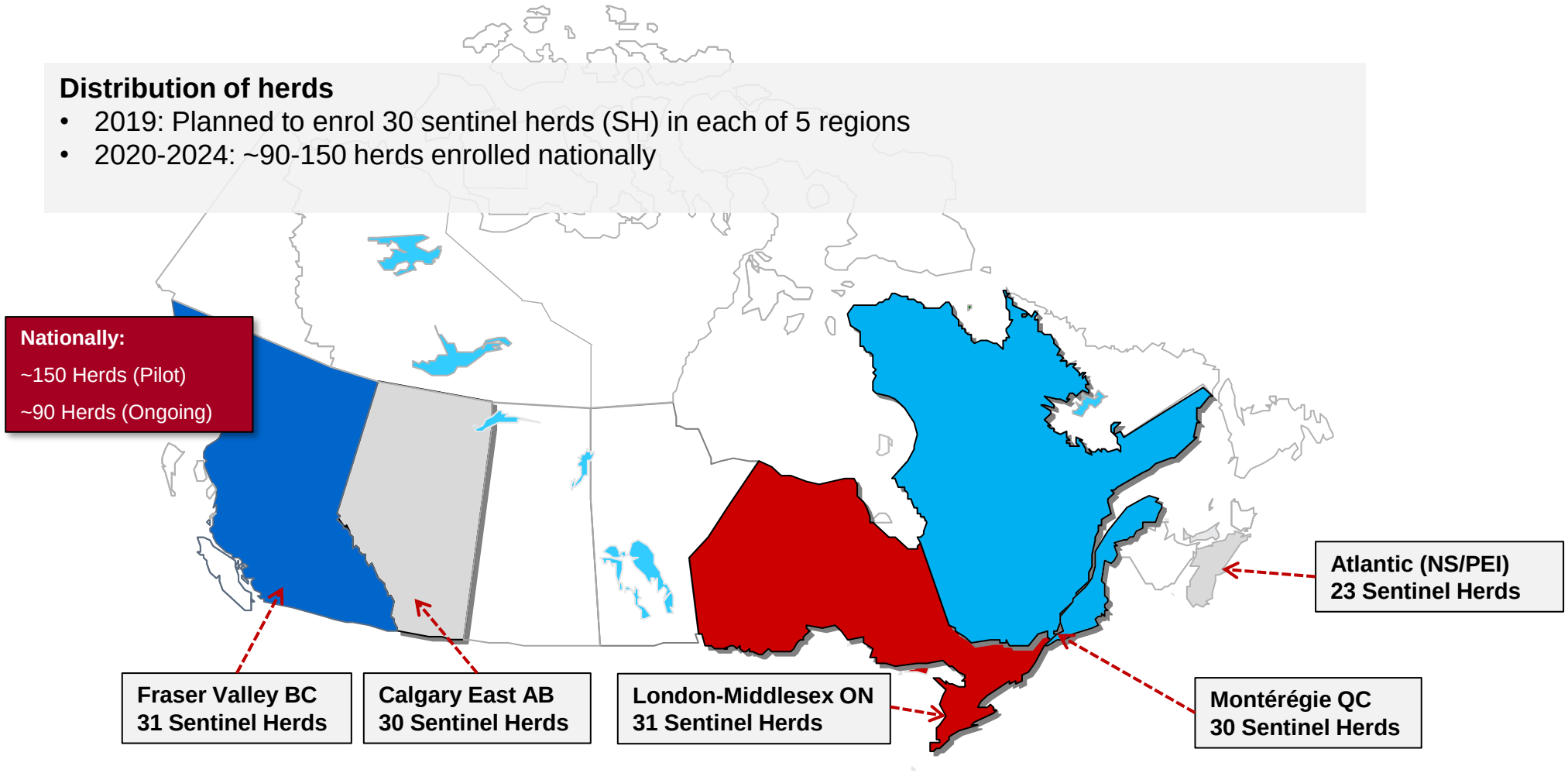
Dr. Ellen de Jong:

- AMU results
- Take home messages
- Acknowledgements

CaDNetASR

Distribution of herds

- 2019: Planned to enrol 30 sentinel herds (SH) in each of 5 regions
- 2020-2024: ~90-150 herds enrolled nationally



Component design: https://doi.org/10.3389/fvets.2021.799622

CaDNetASR Herd Demographics, 2023

Similar to the national average

- Overall median (97) and mean (130) is close to the national average of 99 milking cows per farm[1]

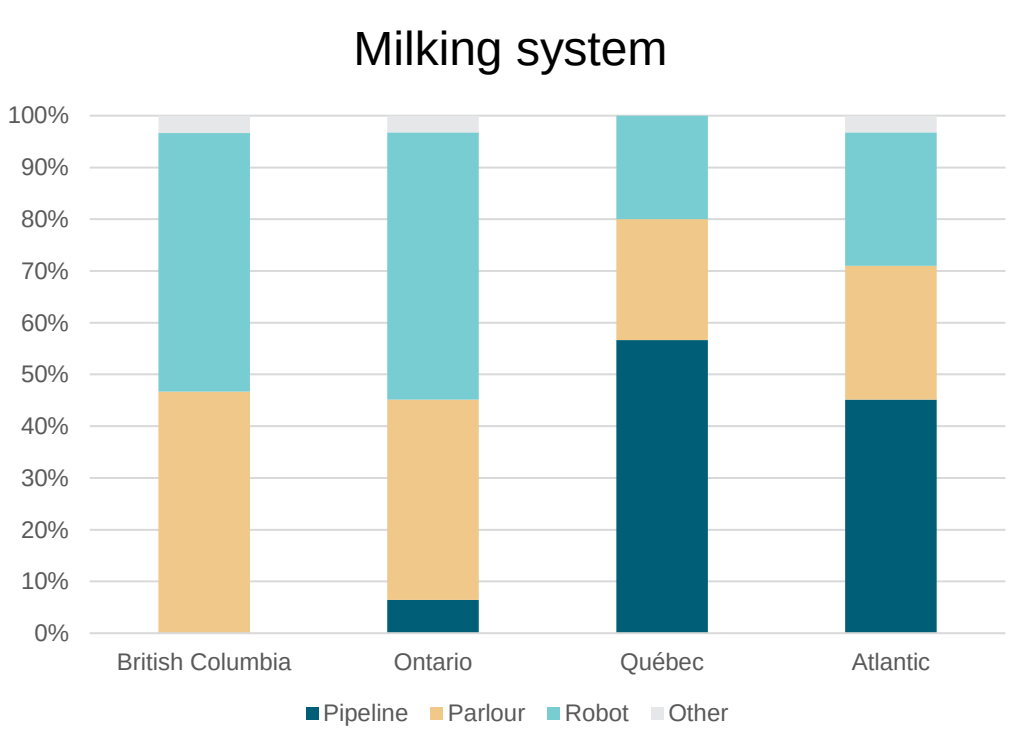
	British Columbia (n = 30)	Ontario (n = 31)	Québec (n = 30)	Nova Scotia/PEI (n = 31)	Overall (n = 122)
Lactating Cows	156 (52 - 338)	112 (49 - 470)	79 (45 - 310)	77 (39 - 321)	97 (39 - 470)
Dry Cows	20 (7 - 53)	16 (5 - 78)	10 (3 - 45)	14 (6 - 80)	15 (3 - 80)
Heifers	128 (0 - 370)	105 (30 - 374)	58 (18 - 160)	71 (20 - 300)	80 (0 - 374)
Calves	22 (1 - 52)	13 (3 - 71)	7 (1 - 20)	7 (0 - 40)	9 (0 - 71)

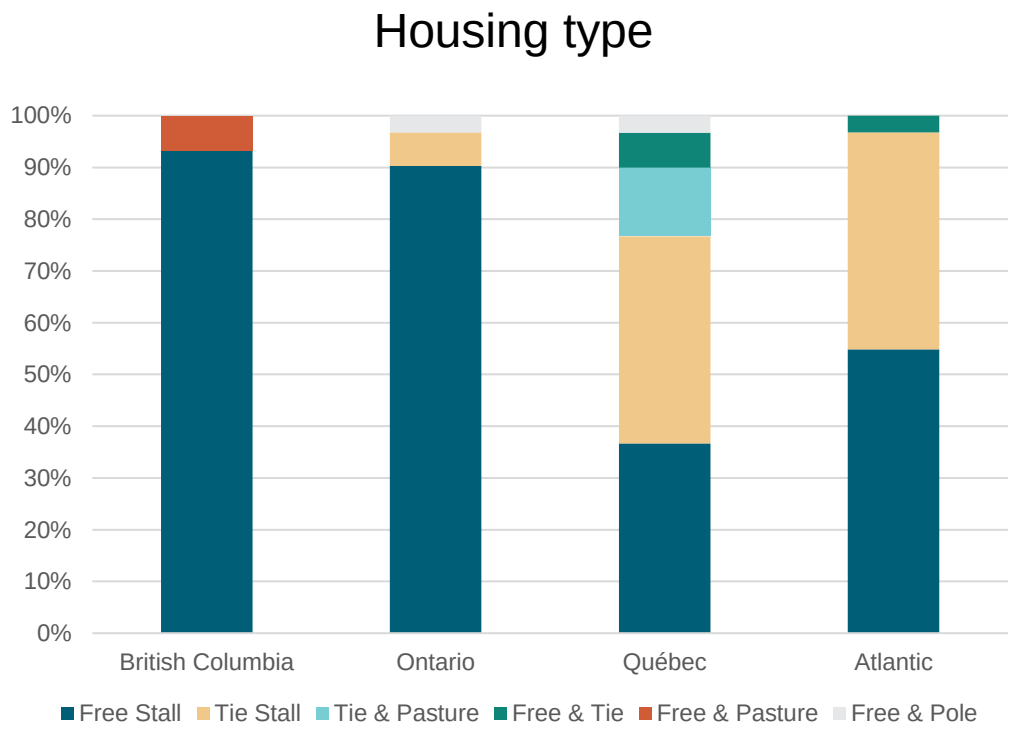
Median (Min – Max)

1: https://dairyfarmersofcanada.ca/en/canadian-goodness/ask-dairy-experts/how-big-average-dairy-farm-canada

CaDNetASR Milking System & Housing Type, 2023

Predominant milking system shifted from parlour to robotic





Farm-Level Antimicrobial Resistance Results

Relevance of antimicrobial panel

Category	Antimicrobial in panel	Relevant products used on dairy farms
I	Cefriaxone/Ceftiofur	Excenel, Excede, Spectramast (LC and DC), Eficur, Cevaxel
	Ciprofloxacin	A180, Baytril, Forcyl
	Colistin	Special Formula
	Amoxicillin-clavulanic acid	-
	Meropenem	-
II	Ampicillin/penicillin/penicillin-novobiocin	Depocillin, Novodry, Polyflex, Procaine, Procillin, Duplocillin
	Azithromycin/Erythromycin	Draxxin, Micotil, Tylan, Zactran, Zuprevo
	Gentamicin	Cocci scour bolus, Calf scour bolus, Neo sulfalyte
	Cefoxitin/Cephalothin	Metricure, Cefa-Lak, Cefa-Dri
	Trimethoprim-sulfamethoxazole	Borgal, Trimidox, Norovet, Super Booster
	Oxacillin	Dry Clox
	Pirlamycin	Pirsue
	Nalidixic acid	-
	Streptomycin	-
III	Tetracycline	Cyclospray, Tetra-250, Onycin, Oxymycin, Oxyvet, Bio-mycin, Kelamycin, Liquamycin
	Chloramphenicol/Florfenicol	Nuflor, Resflor, Florkem
	Sulfisoxazole/Sulphadimethoxine	After calf bolus, Calfspan, Sustain bolus

Categorization system developed by Health Canada's Veterinary Drugs Directorate

2023 Dairy Recovery Summary – Fecal Samples

Pathogen recovery levels are stable

	Escherichia coli		*Salmonella*		*Campylobacter*	
Fecal samples	%	n pos/total	%	n pos/total	%	n pos/total
Calf	100.00%	119/119	1.68%	2/119	24.37%	29/119
Cow	100.00%	122/122	0.82%	1/122	81.15%	99/122
Heifer	95.90%	117/122	3.28%	4/122	77.05%	94/122
All fecal samples combined	98.62%	358/363	1.93%	7/363	61.16%	222/363
Manure Pit	94.26%	115/122	7.38%	9/122	50.00%	61/122
All samples combined	97.53%	473/485	3.30%	16/485	58.35%	283/485

- Samples collected in ON, BC, QC, Atlantic (NS/PEI)
- No samples collected in AB

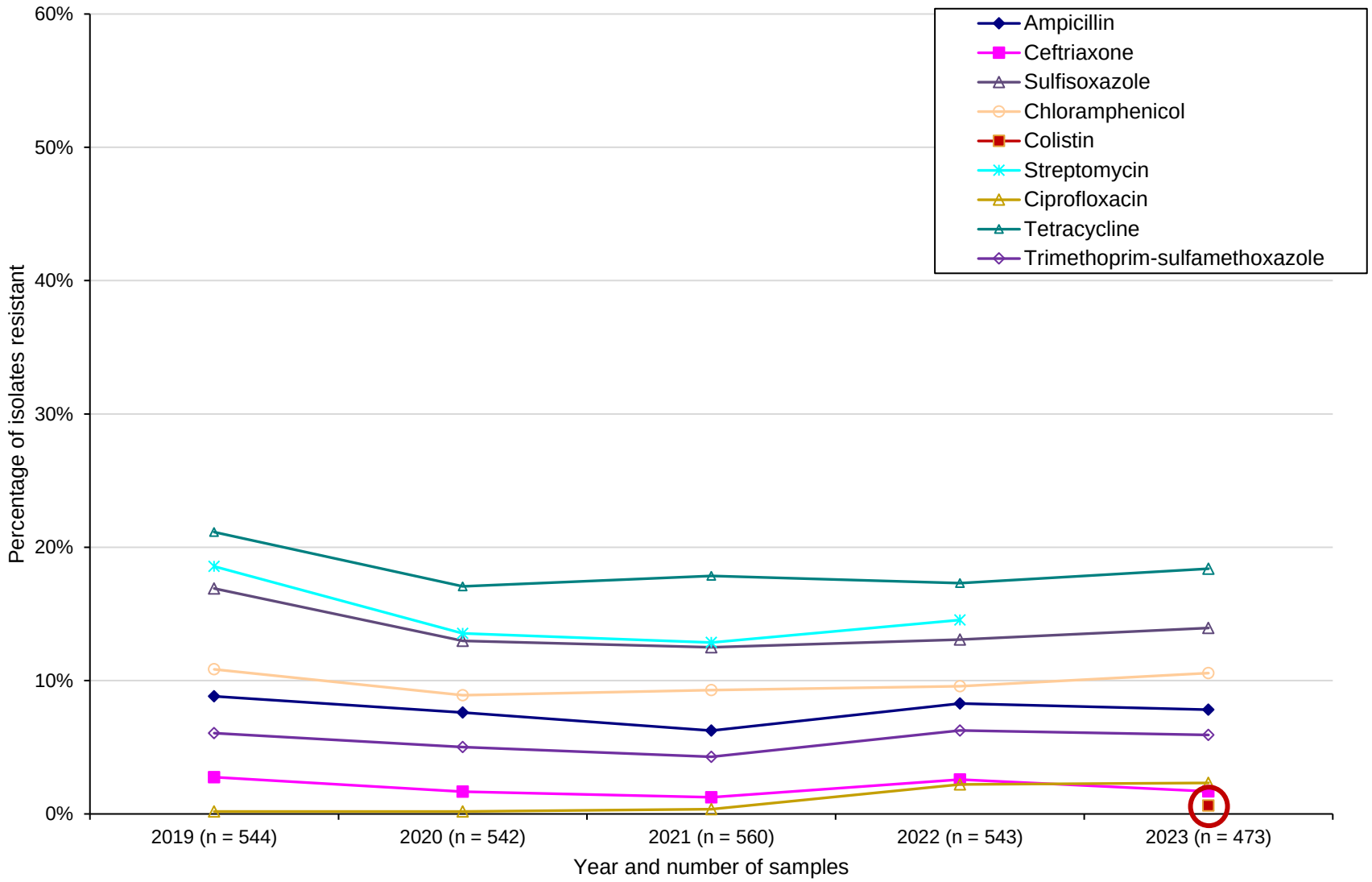
2023 Dairy Recovery Summary – Bulk Tank Milk

Recovered bacteria include intramammary species of interest, both potential pathogens and contaminants

- In the 2023 surveillance year, bacterial pathogens were recovered in 121 bulk tank milk samples
- Pathogens included:
  - *E. coli*
  - *Aerococcus viridans*
  - *Enterococcus* spp.
  - *Klebsiella* spp.
  - *Lactococcus* spp.
  - *Staphylococcus* spp.
  - *Streptococcus* spp.
- In 2022, new procedures were implemented for sample storage (glycerol), which have improved bacterial recovery in bulk tank milk samples

Temporal trends in national *E. coli* resistance

E. coli resistance remains low with stable trends



**Isolates represented in these graphs include composite manure samples taken from pre-weaned calves, post-weaned heifers, lactating dairy cattle, and the manure pit.*

Note: In 2023 there was a panel change, streptomycin is no longer tested, and colistin was added

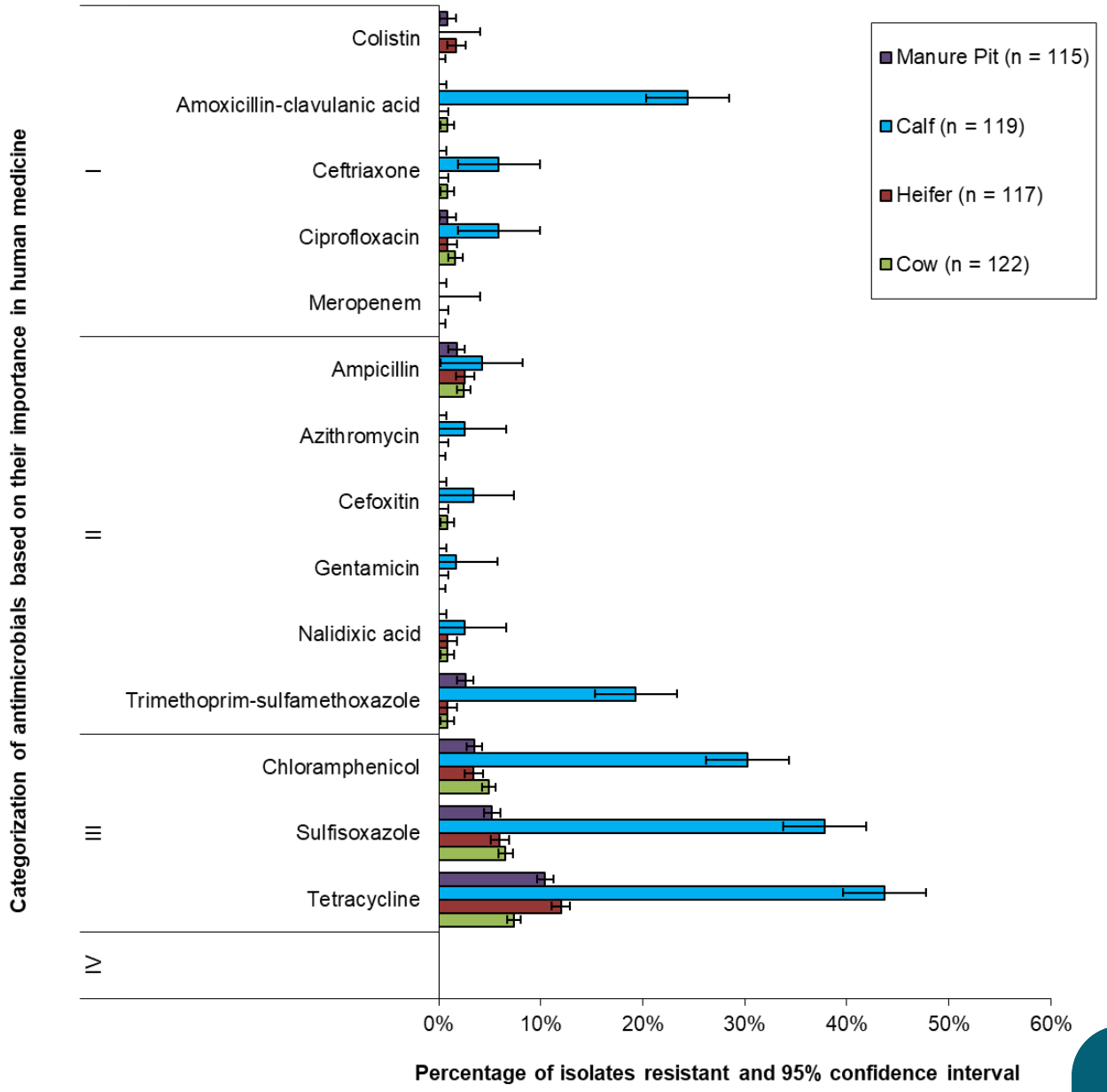
2023 National *E. coli* Resistance by Sample Type

Resistance is most prevalent among isolates from calves

- Category III antimicrobials had the greatest resistance for all sample types
- This is consistent with what has been reported over the past 5 years

Number of antimicrobial classes where >5% of isolates showed resistance

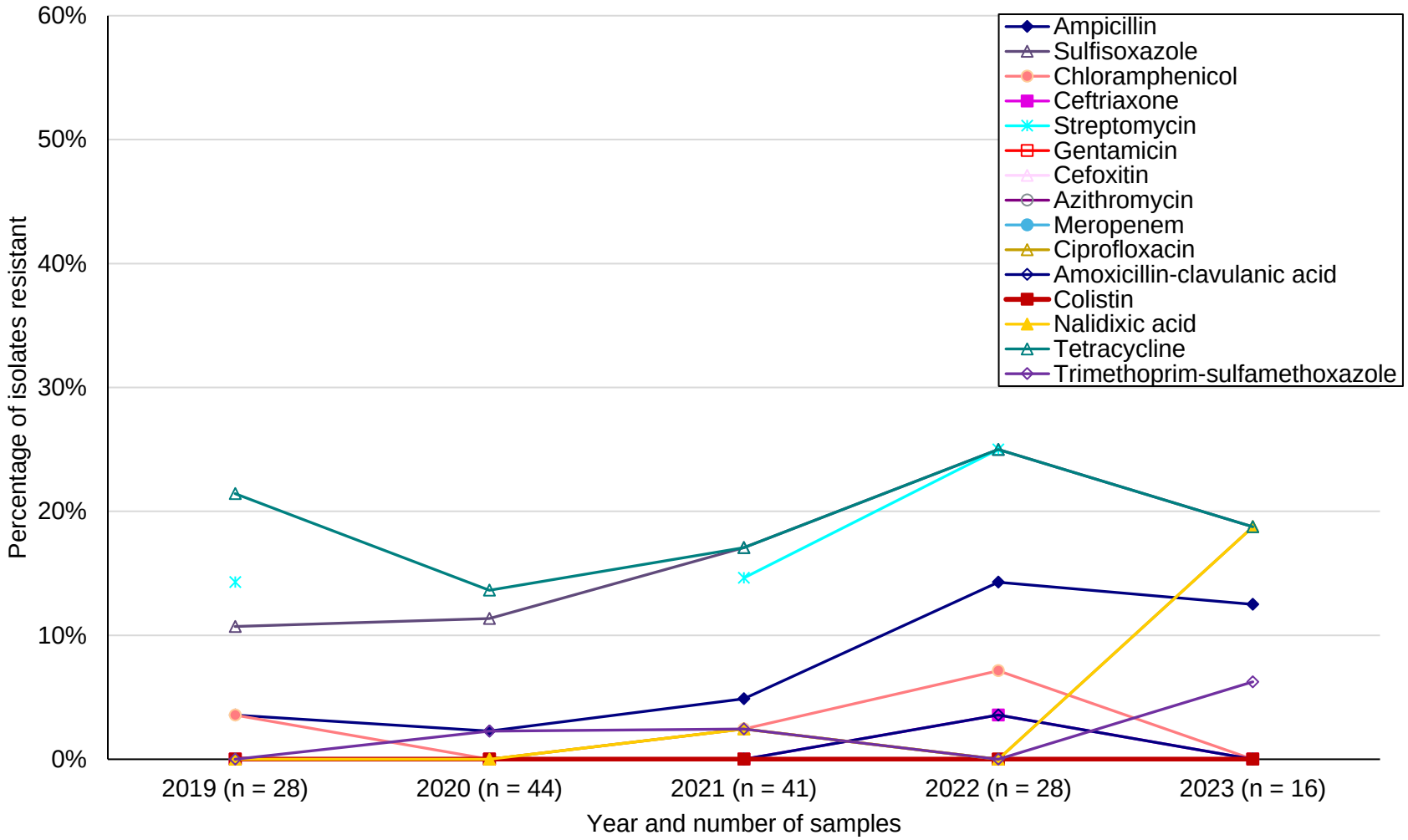
	2019	2020	2021	2022	2023
Manure pit	3	0	2	1	2
Calf	5	5	5	6	5
Heifer	5	3	2	2	2
Cow	0	2	1	1	2



Temporal trends in national *Salmonella* resistance

Monitoring increase in nalidixic acid and ciprofloxacin resistance*

- Much lower *Salmonella* recovery in 2023 compared to previous years
- *Low isolate numbers make trend interpretation difficult
- Nalidixic acid and ciprofloxacin resistance came from 3 *S. Enteritidis* isolates



**Isolates represented in these graphs include composite manure samples taken from pre-weaned calves, post-weaned heifers, lactating dairy cattle, and the manure pit.*

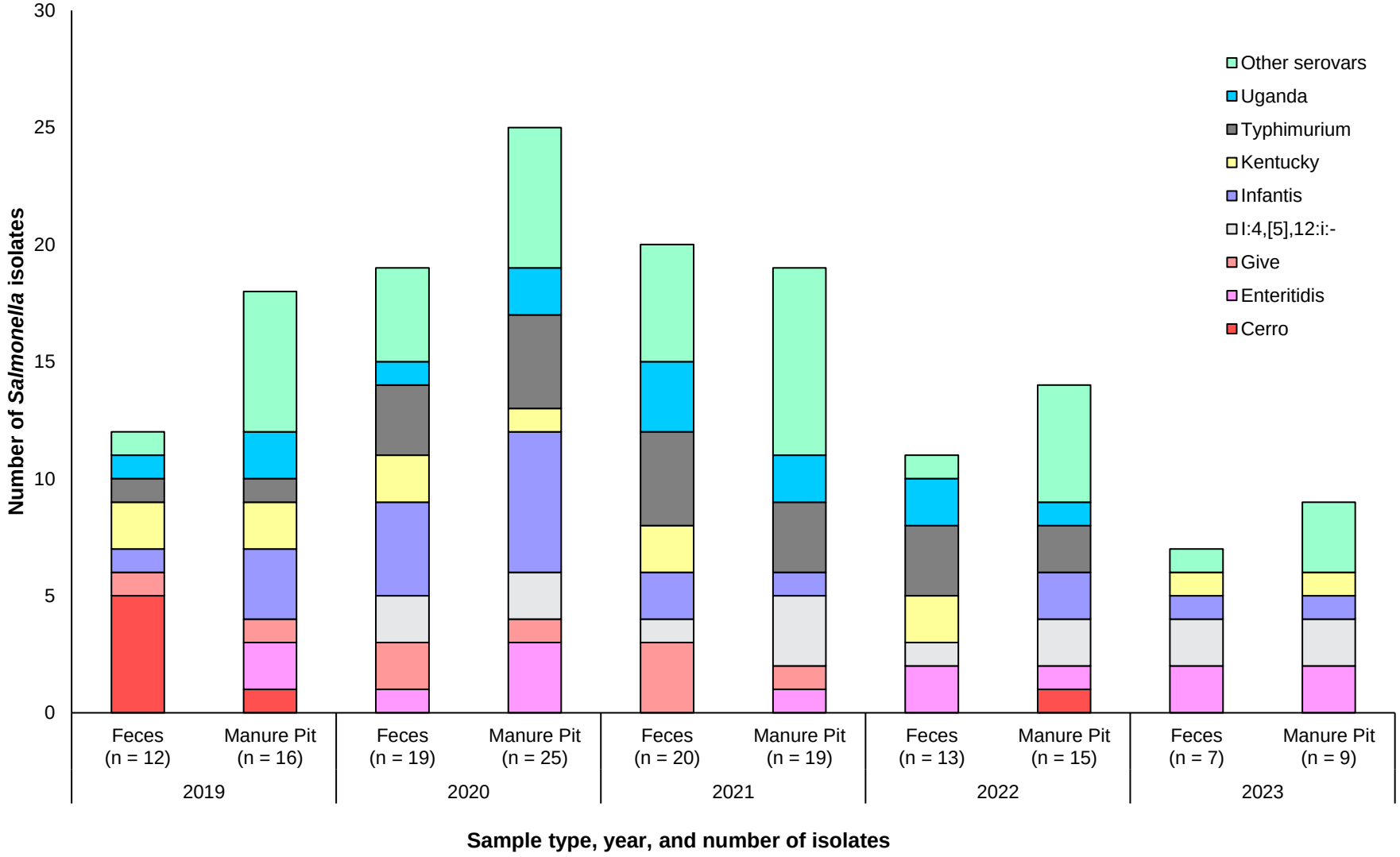
Note: Change to CMV5 panel in 2020 (due to samples being tested in different lab). In 2023: Streptomycin was no longer tested, and Colistin added

Temporal trends in national *Salmonella* serovar distribution

Fecal vs. manure pit sample types

Consistent recovery of *Salmonella* Infantis, Enteritidis and Typhimurium

- *Salmonella* Dublin has not been recovered over the 5 years
- Low recovery in 2023

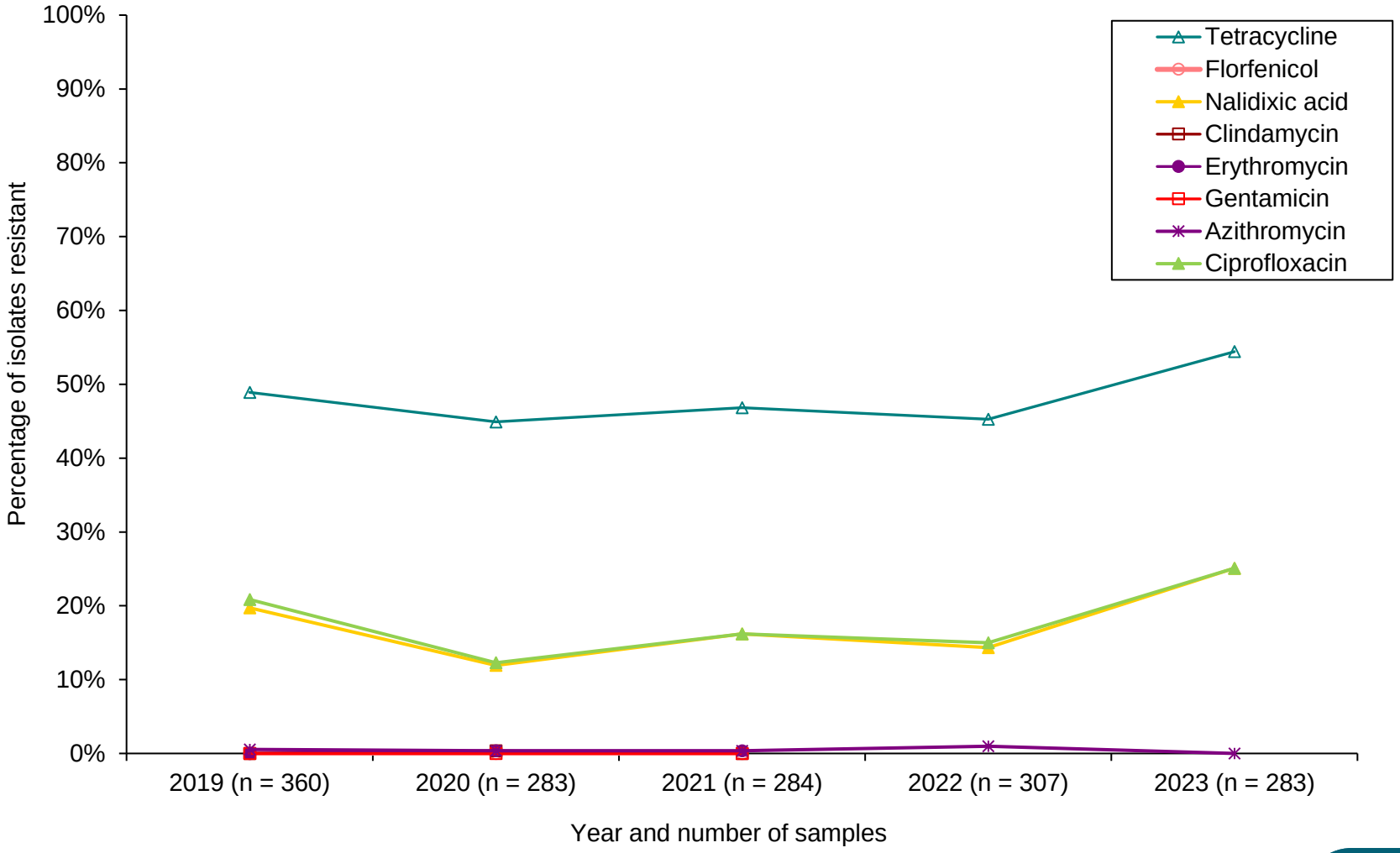


*Feces category includes composite manure samples from lactating cows, heifers and calves, combined.

Temporal trends in national *Campylobacter* resistance

Emergence ciprofloxacin resistance

- Emerging ciprofloxacin resistance (4 *C. coli* and 67 *C. jejuni* isolates)
- 98% of isolates were *C. jejuni*
- Meropenem resistance was tested separately using an E-test in 2023



**Isolates represented in these graphs include composite manure samples taken from pre-weaned calves, post-weaned heifers, lactating dairy cattle, and the manure pit.*

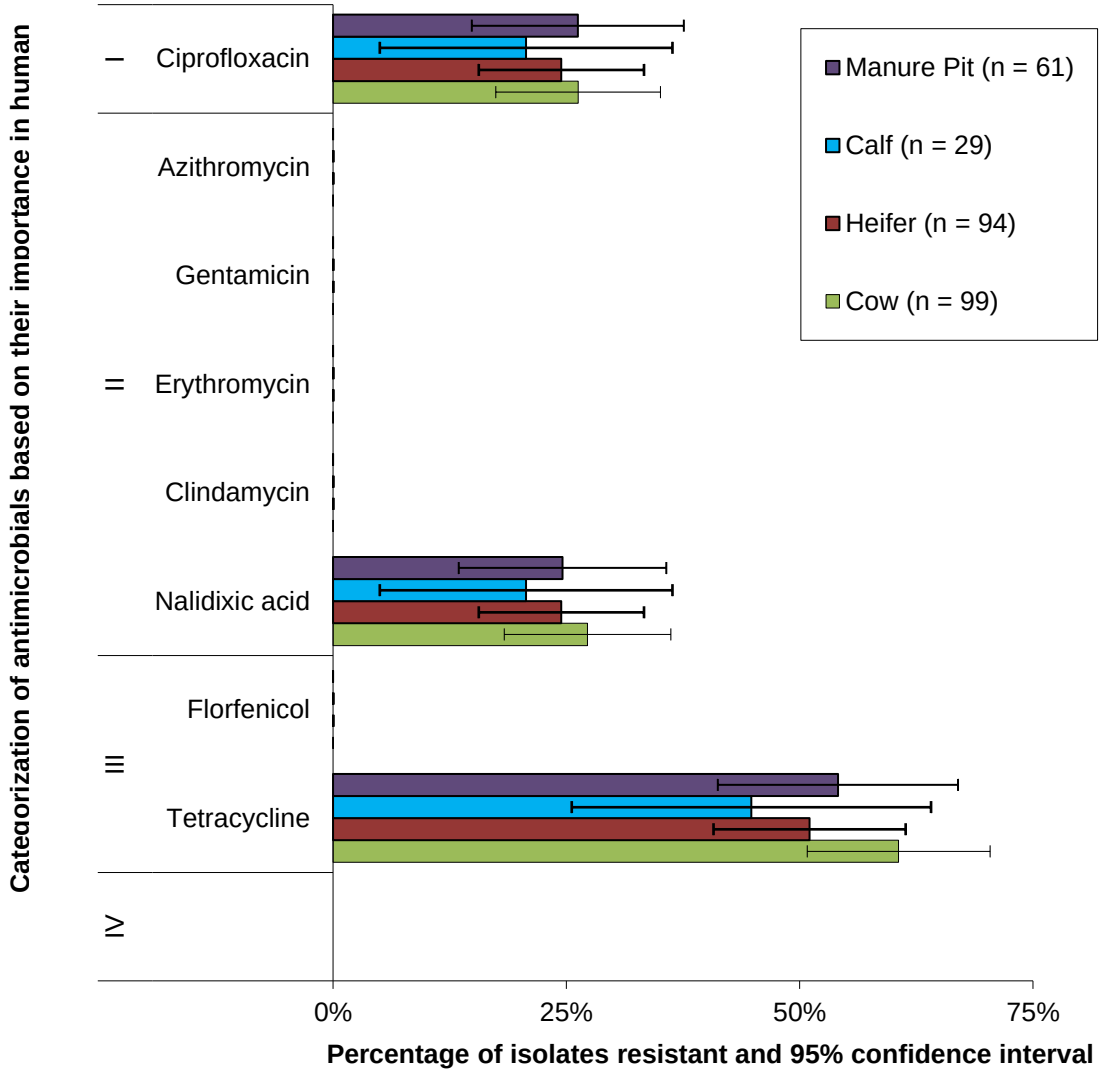
2023 National *Campylobacter* resistance by sample type

Resistance levels are similar across all sample types

- All sample types are contributing to the ciprofloxacin, nalidixic acid and tetracycline resistance increase
- Resistance trends are stable across all years

Number of antimicrobial classes where >5% of isolates showed resistance

	2019	2020	2021	2022	2023
Manure pit	2	2	2	3	2
Calf	2	2	2	2	2
Heifer	2	2	2	2	2
Cow	2	2	2	2	2



Bulk Tank Milk: AMR Data Interpretation

Limited breakpoint availability complicates interpretation

- AMR testing has been focused on *E. coli*, *Klebsiella* spp., *Staphylococcus* spp., and *Streptococcus* spp.
  - Other isolates may be tested for AMR in the future
- We are currently working to collect breakpoints for analysis
- Not all pathogens have available breakpoints – hence data is limited
- Available breakpoints were obtained from CLSI and EUCAST; prioritizing:
  1. Human breakpoints where available;
  2. Cattle mastitis breakpoints where available
- Scoping review protocol: https://atrium.lib.uoguelph.ca/items/a8c9abb5-8cdb-4687-afd2-954b7a569728

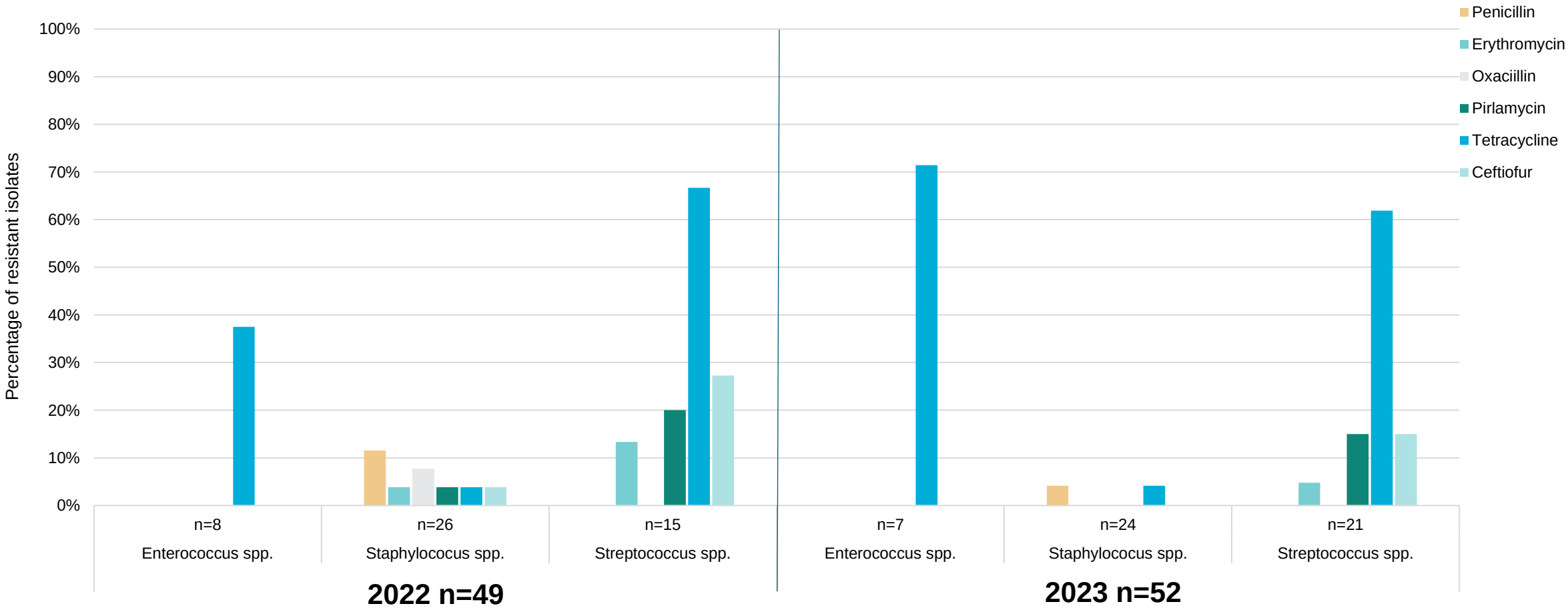
AMR in G+ Pathogens from Bulk Tank Milk Samples

High AMR in *Strep. dysgalactiae* and *Strep. uberis* in 2022 & 2023

	2022 (n = 49)								2023 (n = 52)							
	Enterococcus faecalis	Enterococcus faecium	Staphylococcus aureus	Streptococcus canis	Streptococcus dysgalactiae	Streptococcus parauberis	Streptococcus suis	Streptococcus uberis	Enterococcus faecalis	Enterococcus faecium	Staphylococcus aureus	Streptococcus canis	Streptococcus dysgalactiae	Streptococcus parauberis	Streptococcus suis	Streptococcus uberis
	n=6	n=2	n=26	n=1	n=6	n=2	n=1	n=5	n=3	n=4	n=24	n=0	n=10	n=0	n=1	n=10
Ampicillin	0%	0%		0%	0%	0%			0%	0%			0%			
Penicillin	0%	0%	12%						0%	0%	0%					
Erythromycin	0%	0%	4%	0%	20%	0%	100%	0%	0%	0%	0%		0%		100%	10%
Oxaciillin			8%								0%					
Pirlamycin			4%		17%			25%			0%		0%			30%
Penicillin-novobiocin																
Tetracycline	50%	0%	4%	0%	83%	100%	0%	60%	100%	50%	4%		70%		100%	50%
Cephalothin																
Ceftiofur			4%		17%			40%			0%		10%			20%
Sulphadimethoxine																

Comparing AMR in BTM pathogens, 2022-2023

Tetracycline resistance commonly observed across species



*Note that breakpoints were not always available for every *Streptococcus* spp.; hence different denominators were used for Streptococcus, based on the antimicrobial.
**Also note that there were two fewer *Streptococcus* spp. (*S. canis* and *S. parauberis*) in the 2023 data, compared to 2022.

Low recovery of Gram-negative pathogens

- **2023:** 15 isolates (12 *E.coli*; 1 *K.oxytoca*, 1 *K.pneumoniae*, 1 *K.variicola*)
  - one *E.coli* isolate from Prince Edward Island was resistant to TET
  - one *K.oxytoca* isolate from Nova Scotia was resistant to AMP
- **2022:** 8 isolates (7 *E.coli*, 1 *K.oxytoca*)
  - one *E.coli* isolate from Ontario was resistant to AMP, TET, AMC, SSS, SXT, STR
  - two *E.coli* isolates were resistant to CIP and NAL (one from Ontario and one from Québec);
    - The Québec isolate was also resistant to CRO and SSS

Farm-Level Antimicrobial Use Results

CaDNetASR veterinary dispensing data

- ~150 herds participate in the CaDNetASR program each year
- Veterinary dispensing data was obtained for ~75% of herds
- 2019-2022 data will be presented, 2023 data is pending
- **Two indicators will be presented:**
  - Defined daily doses (DDD) per 1,000 cow-days at risk
  - Milligrams per population correction unit (mg/PCU)

Example

Herd A: In 2020, used 60 bottles of a ceftiofur product on 200 lactating cows.

AMU indicator 1: mg/PCU (population correction)

- For each product, mg active ingredient is defined (for this example product: 4000 mg ceftiofur per bottle)
- Corrected for average weight at treatment (650 kg per lactating cow)

$$\frac{\sum total\ annual\ mg\ dispensed}{\sum population\ corrected\ unit} = \frac{60\ bottles\ \times 4000\ mg\ = 240{,}000\ mg}{200\ cows\ \times 650\ kg = 130{,}000\ PCU} = 1.8\ mg/PCU$$

AMU indicator 2: defined daily doses

- Each product has been assigned a 'DDD' (for this example product: 650 mg per cow per day)
- Corrected for number of animals at risk (200 cows across the whole year)

$$\frac{\sum total\ annual\ DDD}{\sum(herd\ size \times 365)} = \frac{240{,}000\ mg\ /\ 650\ mg = 370\ doses}{200\ cows\ \times 365 = 73{,}000\ cow\ days\ at\ risk} \times 1{,}000\ = 5.1\ DDD\ /\ 1{,}000\ cow\ days\ at\ risk$$

Antimicrobials used on dairy farms

Category 1
Very high importance

Cephalosporins (3rd and 4th gen)

Excenel
Excede 200
Eficur
Ceftiocyl
Cevaxel
Spectramast (LC and DC)

Fluoroquinolones

A180
Baytril
Baytril oral
Forcyl

Polymixins

Special Formula

Category 2
High importance

Aminoglycosides

Cocci scour bolus
Calf scour bolus
Neo sulfalyte
Gentocin

Cephalosporins (1st and 2nd gen)

Metricure
Cefa-Lak
Cefa-Dri
ToDay

Macrolides

Draxxin
Micotil
Tylan
Zactran
Zuprevo

Lincosamides

Pirsue
LS100

Trimethroprim-Sulfamethoxazole

Borgal
Trimidox
Norovet TMPS
Super booster

Penicilins

Depocillin
Dupcillin
Dry Clox
Novodry
Polyflex
Procaine
Procillin

Category 3
Medium importance

Phenicols

Florkem
Nuflor
Resflor

Sulfonamides

After calf bolus
Calfspan
Sustain bolus

Tetracyclines

Bio-mycin
Cyclospray
Kelamycin
Liquamycin
Tetra-250
Onycin
Oxymycin (LA and LP)
Oxyvet (100 and 200)

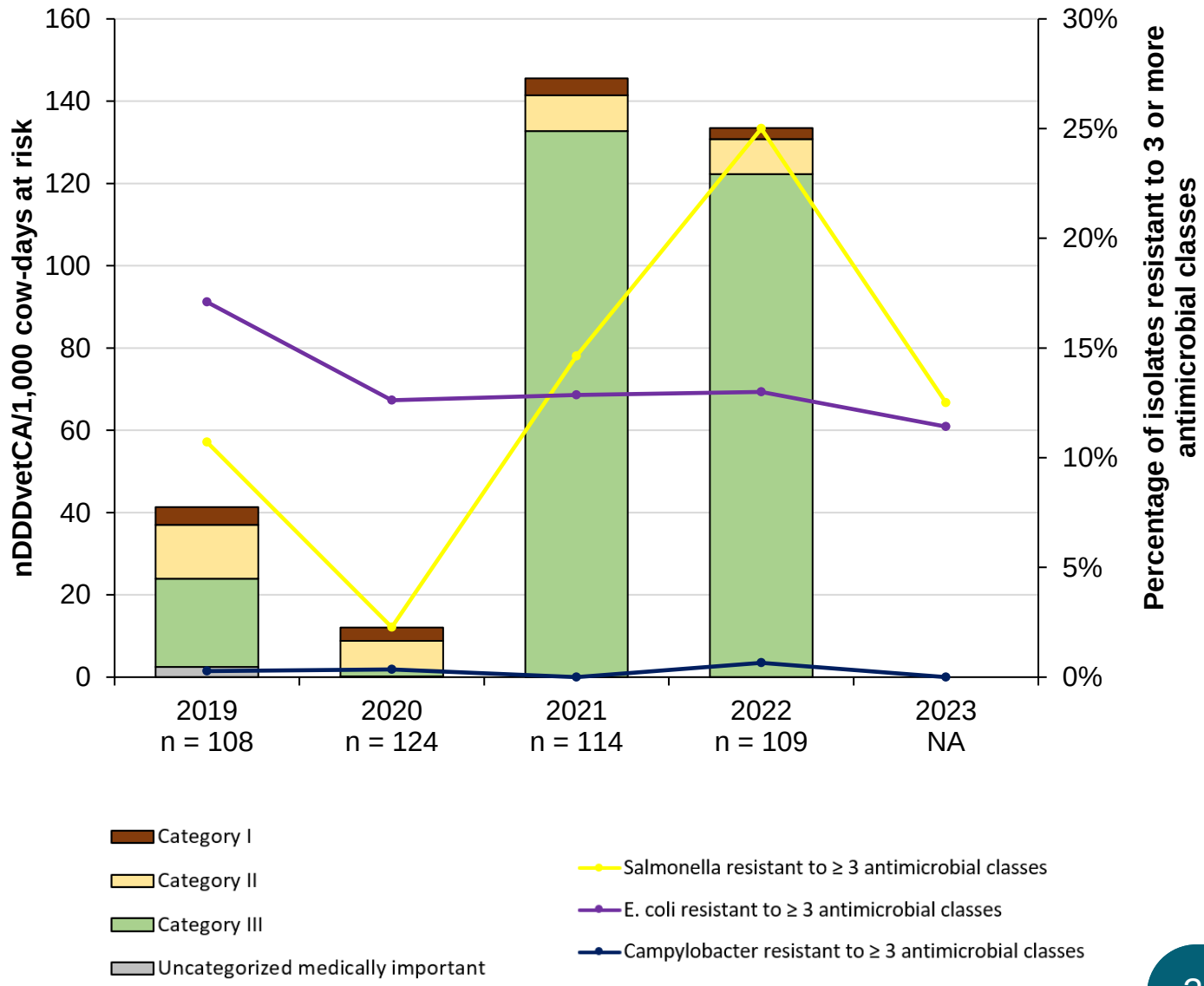
Trimethoprim

Categorization system developed by Health Canada's Veterinary Drugs Directorate

Integrated findings AMU and multiclass AMR

AMU increase due to increased reporting oral tetracyclines in feed and water

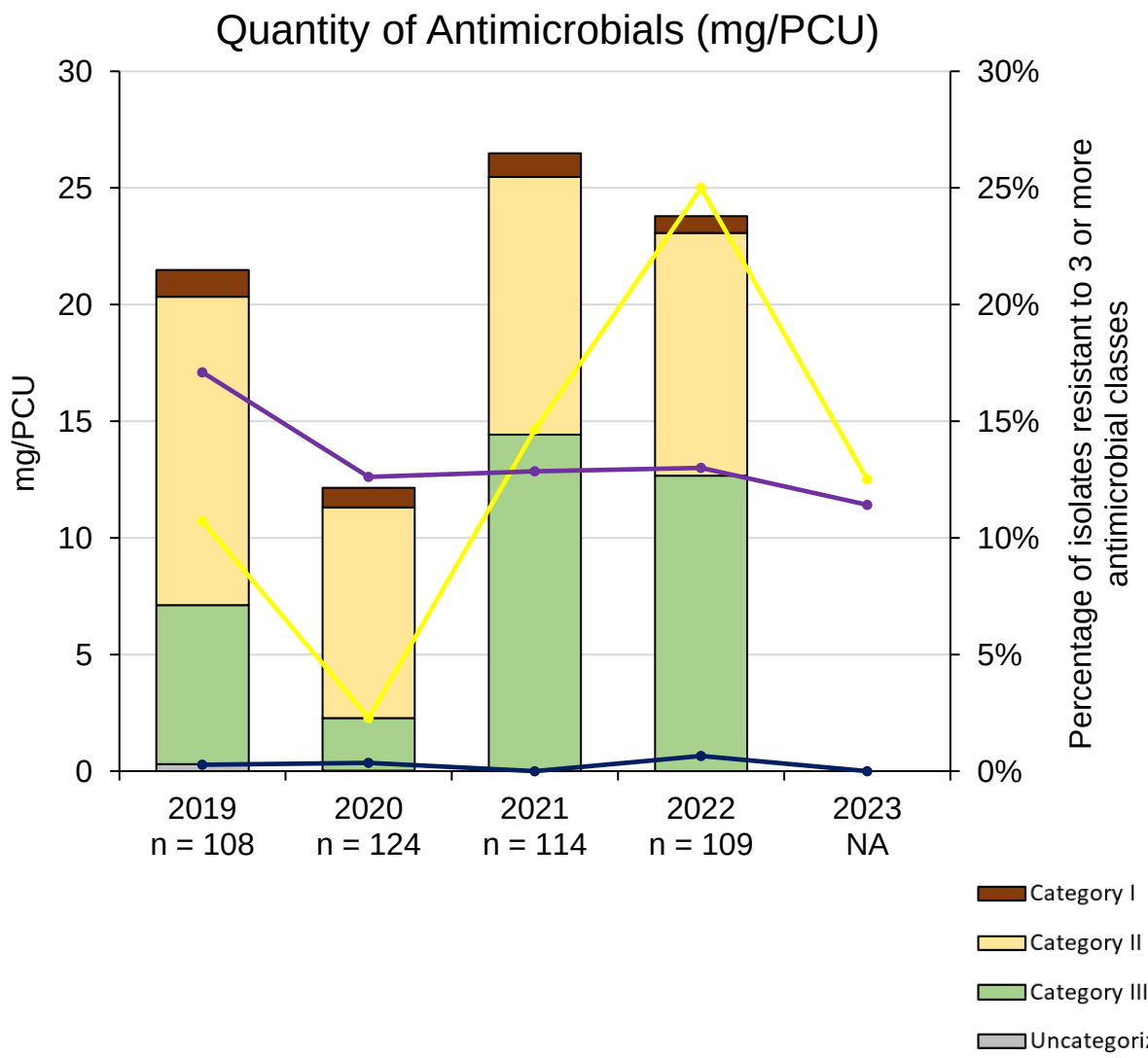
- AMU includes all production classes (calves, heifers, lactating cows, dry cows)
- Multiclass resistance covers fecal samples (not bulk tank milk)

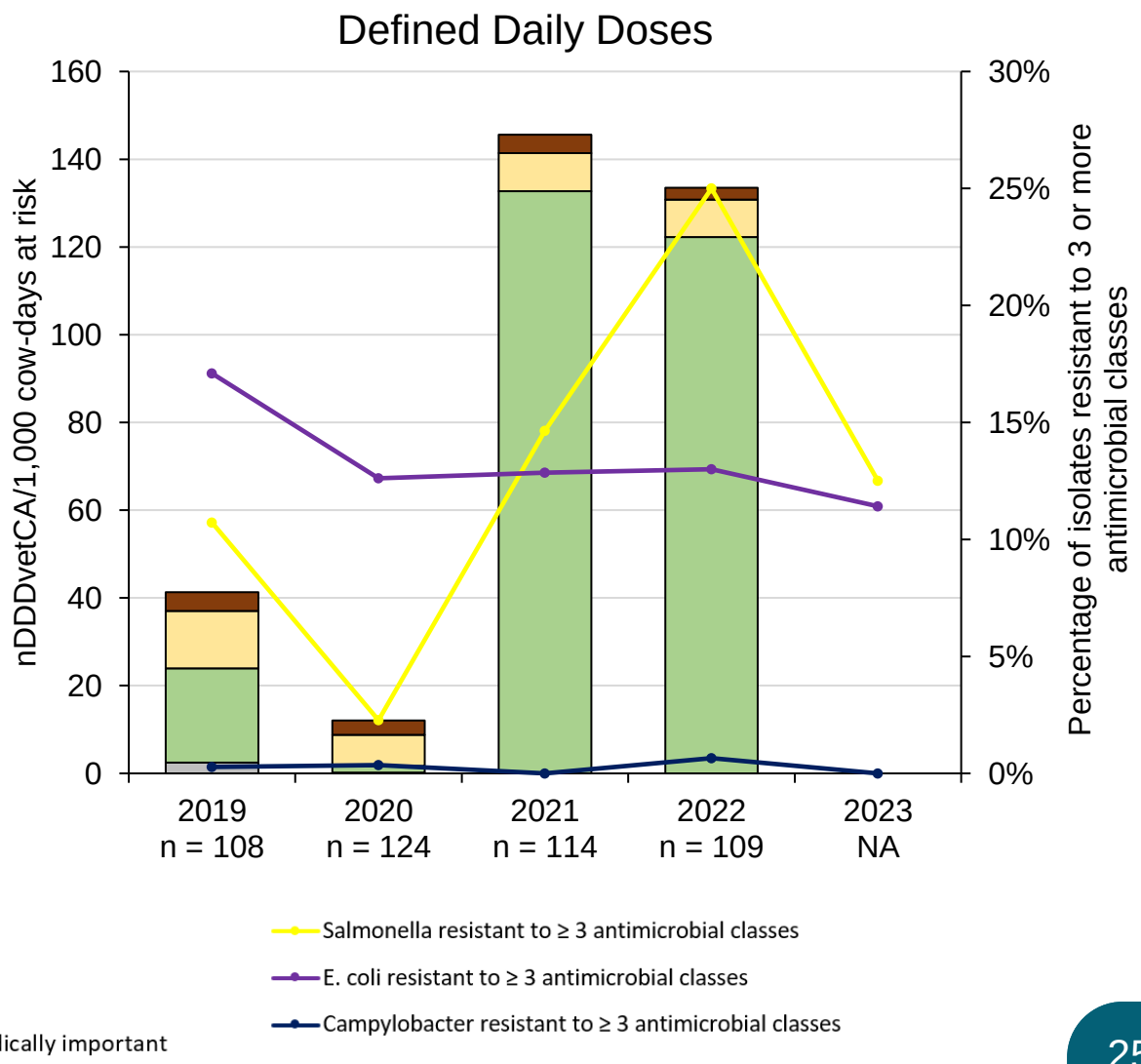


Source: 2019 – 2022 CaDNetASR veterinary dispensing data

Comparing AMU indicators

AMU impacted by indicator used



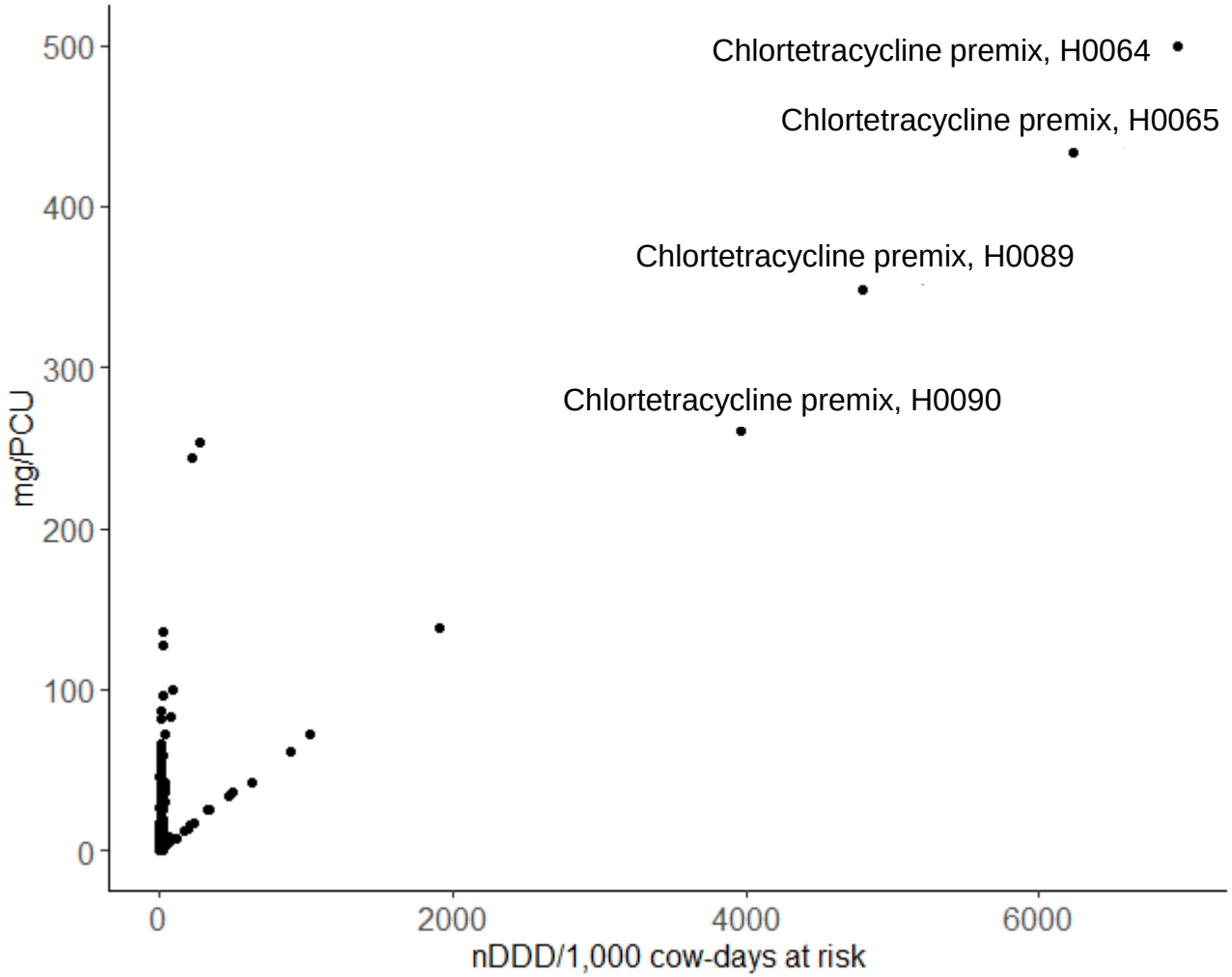


Source: 2019 – 2022 CaDNetASR veterinary dispensing data

Comparing AMU indicators

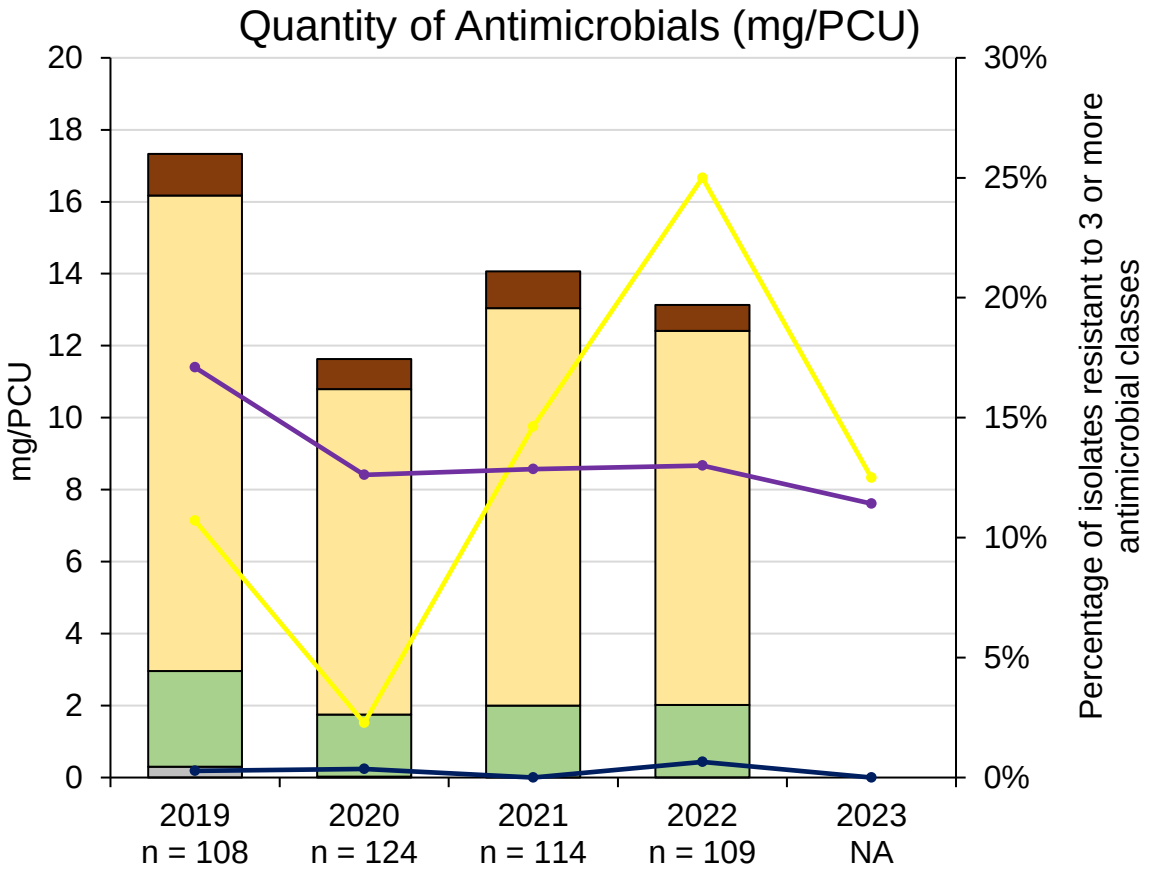
Category 3 oral tetracyclines impact the differences between the AMU indicators

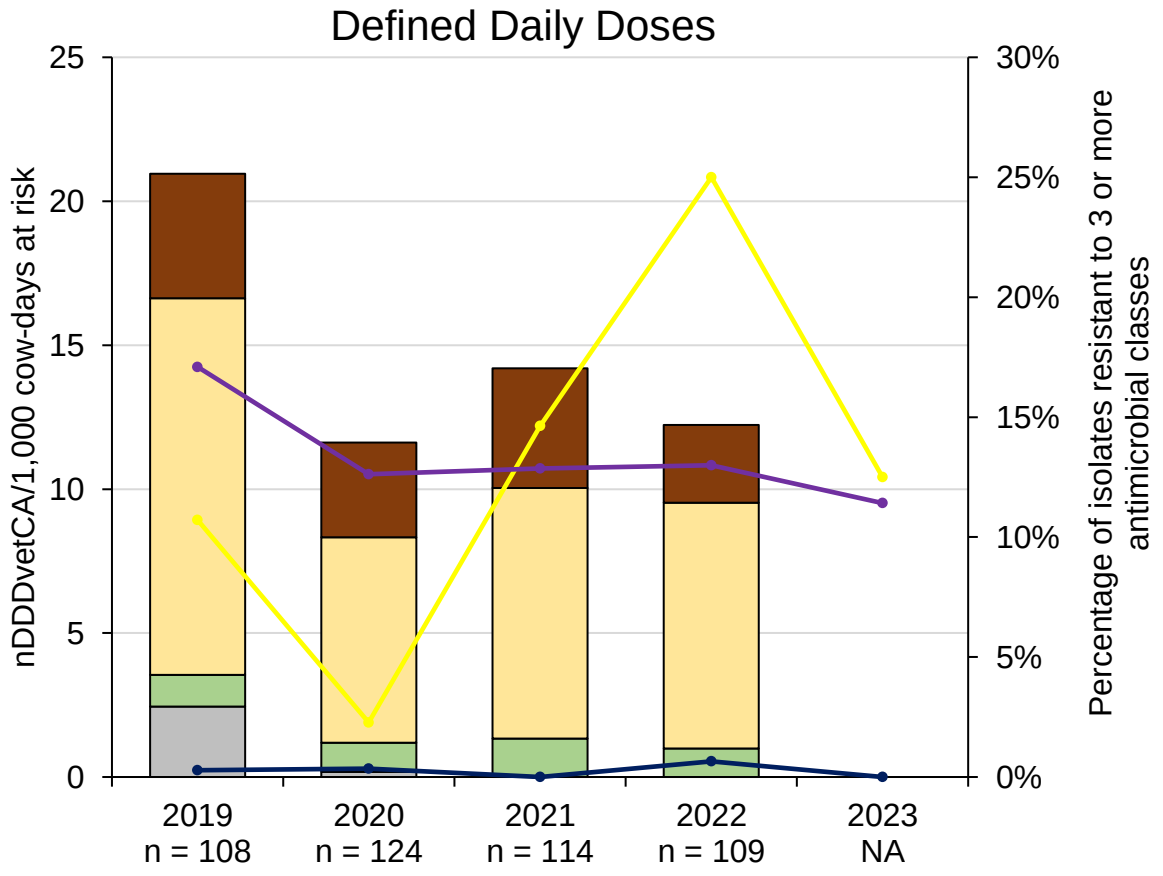
- Chlortetracycline premix products
- Low DDD (90 mg per animal per day)
- Typically administered to groups of animals
- Purchased and used in large quantities
- Few herds responsible for increase in total Category III use



Source: 2019 – 2022 CaDNetASR veterinary dispensing data

Comparing AMU indicators– removing oral tetracycline



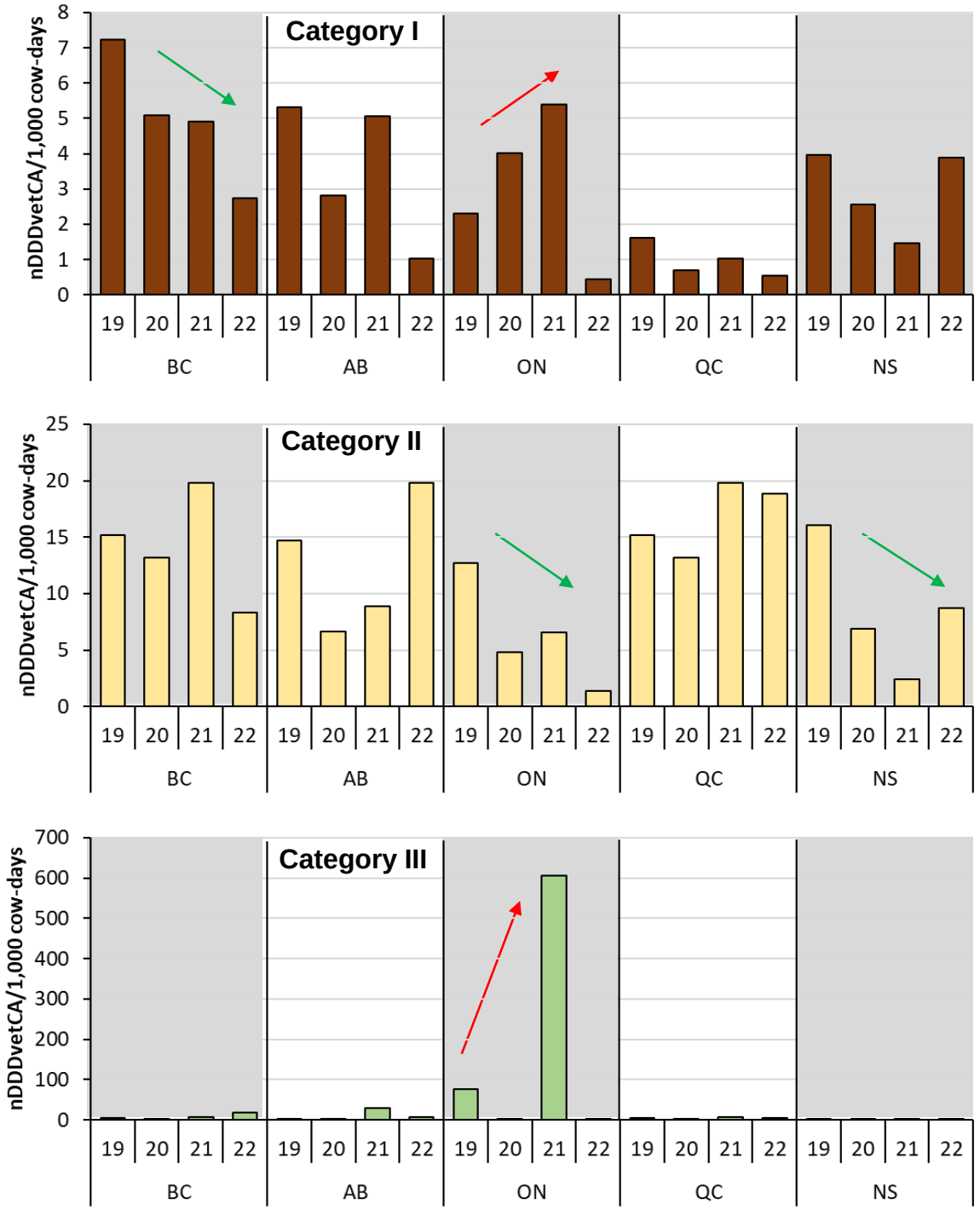


Source: 2019 – 2022 CaDNetASR veterinary dispensing data

AMU per province

Proportion of farms using Category I decreased

- Includes all production classes (calves, heifers, lactating cows, dry cows)
- Proportion of farms using Category I antimicrobials has decreased between 2019 (94%) and 2022 (85%)
- Proportion of farms using Category II antimicrobials has remained stable between 2019 (99%) and 2022 (98%)
- Despite the under reporting prior to 2021, proportion of farms using Category III antimicrobials has decreased between 2019 (84%) and 2022 (77%)



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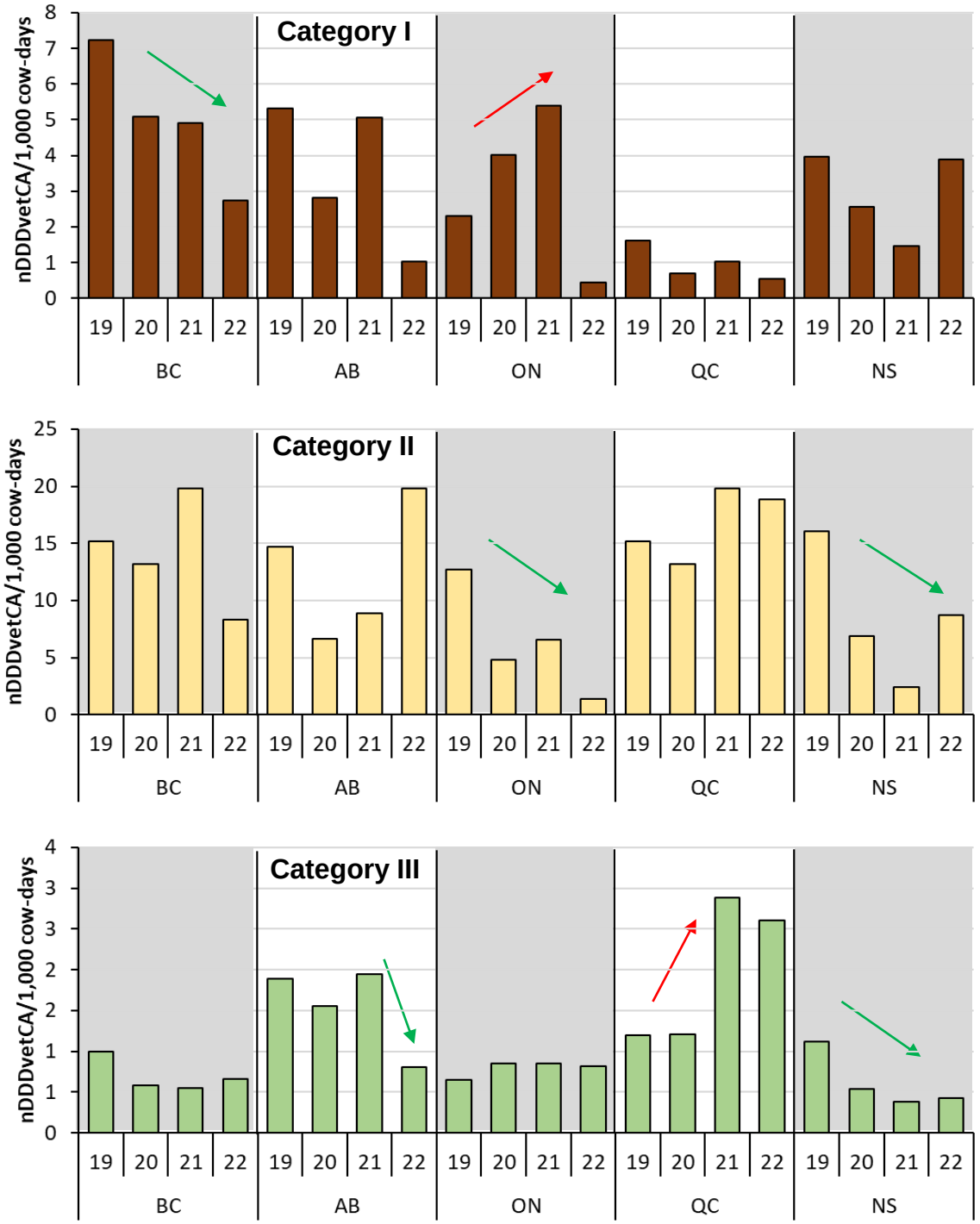
Without oral tetracycline



Source: 2019 – 2022 CaDNetASR veterinary dispensing data

AMU per antimicrobial class

Reduction in cephalosporins and penicillins 2019-2022

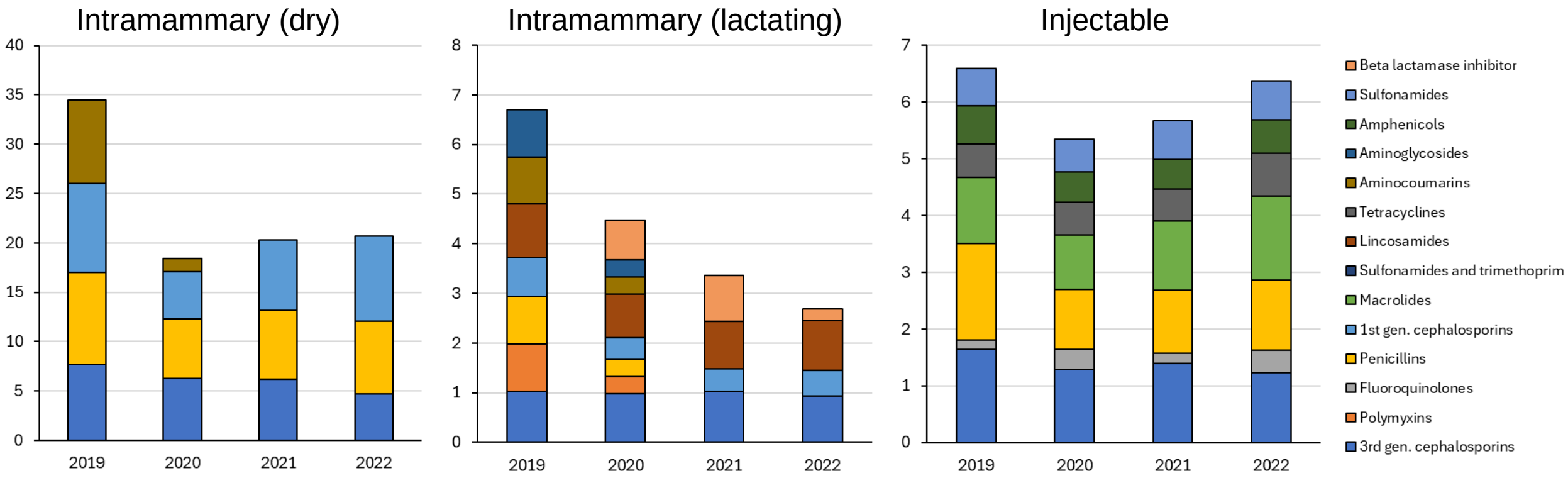
DDDvetCA/1,000 cow-days at risk

		2019	2020	2021	2022	% change (2019 - 2022)
Category I	3rd gen. cephalosporins	3.82	3.16	4.12	2.67	-30%
	Polymyxin B	0.47	0.08	0.00	0.00	-100%
	Fluoroquinolones	0.03	0.05	0.02	0.03	5%
Category II	Penicillins	6.47	3.93	3.92	3.64	-44%
	1st gen. cephalosporins	3.73	1.90	2.82	3.38	-9%
	Macrolides	0.56	0.44	0.61	0.58	3%
	Sulfonamides and trimethoprim	0.53	0.45	0.54	0.54	3%
Category III	Lincosamides	0.24	0.24	0.17	0.20	-16%
	Tetracyclines	20.71	0.91	132.0	121.5	487%
	Aminocoumarins	2.45	0.18	0.00	0.00	-100%
	Aminoglycosides	1.56	0.19	0.64	0.20	-87%
	Amphenicols	0.46	0.39	0.36	0.40	-13%
	Sulfonamides	0.32	0.18	0.35	0.35	10%
	Beta lactamase inhibitor	0.00	0.00	0.02	0.00	N/A

Source: 2019 – 2022 CaDNetASR veterinary dispensing data

AMU per antimicrobial class, stratified by route of administration

Less antibiotic products available for intramammary treatments dry and lactating cows



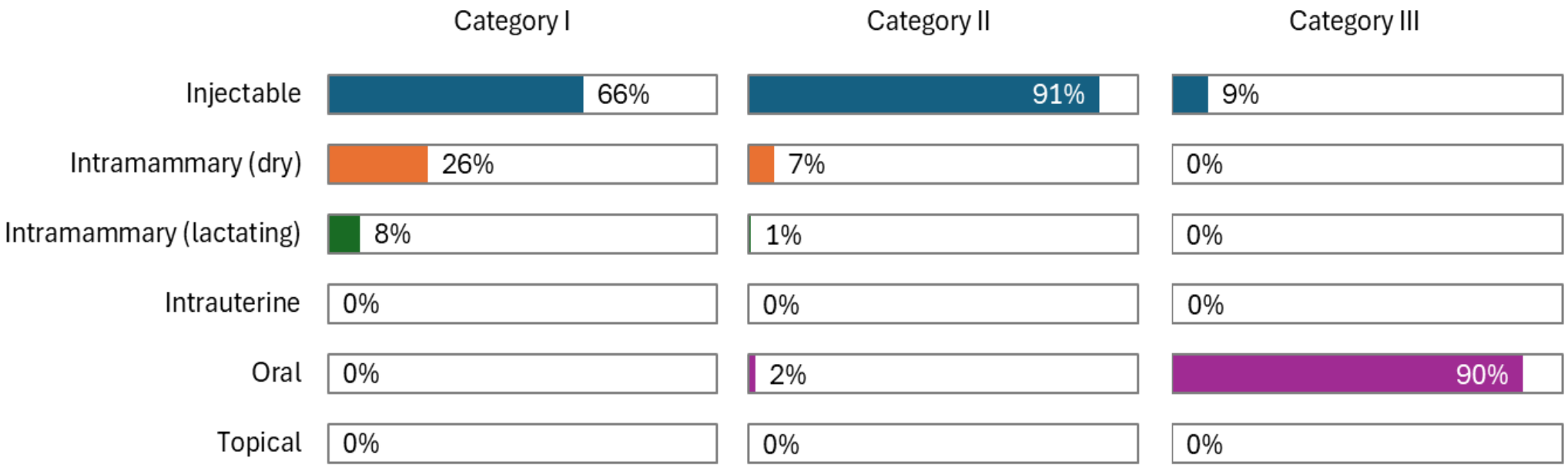
DDDvetCA/1,000 cow-days at risk

Source: 2019 – 2022 CaDNetASR veterinary dispensing data

Administration routes & category of importance

Most Category I and II products are injectables

Percentage of total kg active ingredients sold

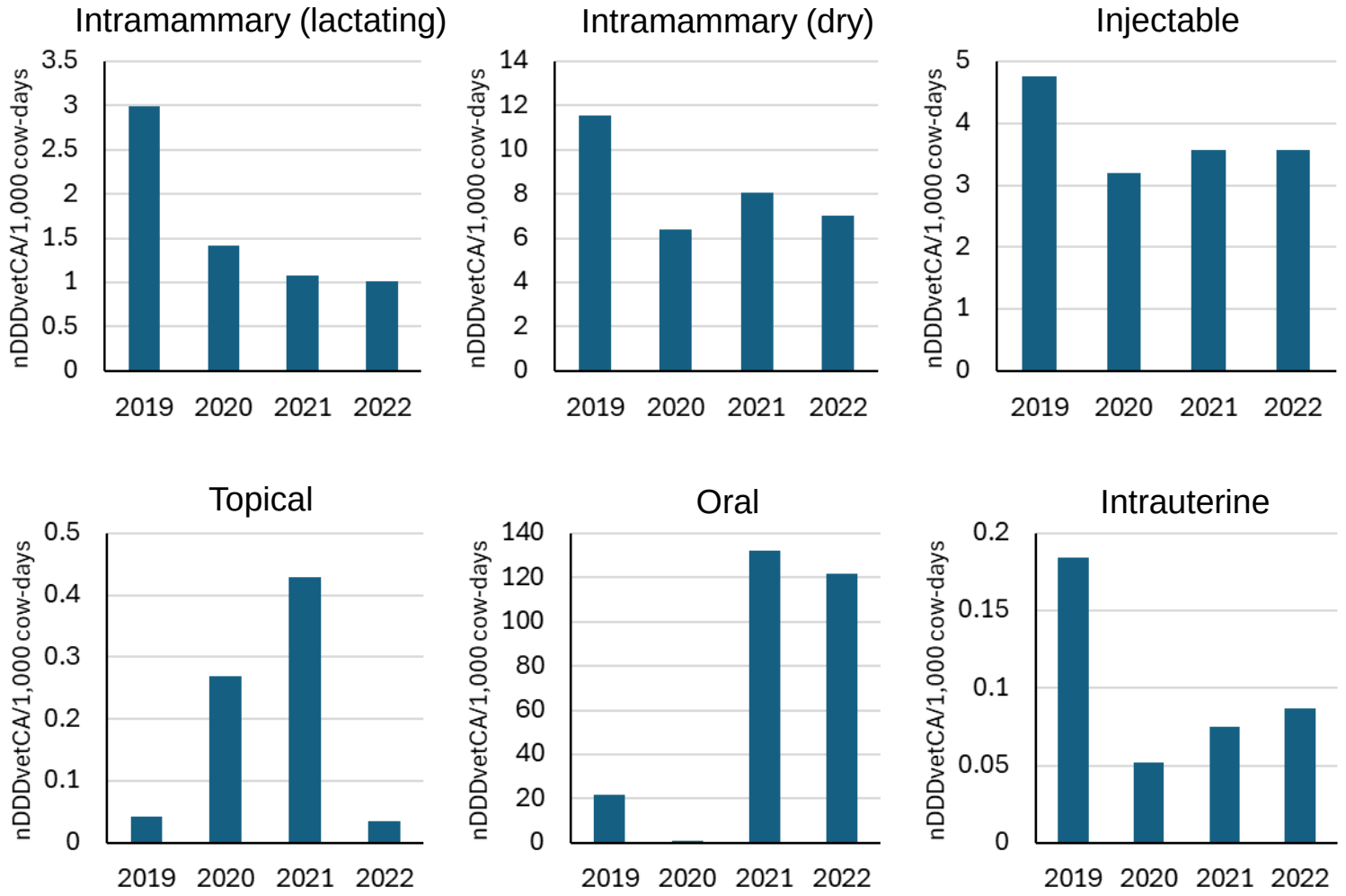


Source: 2022 CaDNetASR veterinary dispensing data

AMU per administration route

Reduction in intramammary and injectable use

- Includes all production classes (calves, heifers, lactating cows, dry cows)
- Oral and topical products are almost exclusively Category III

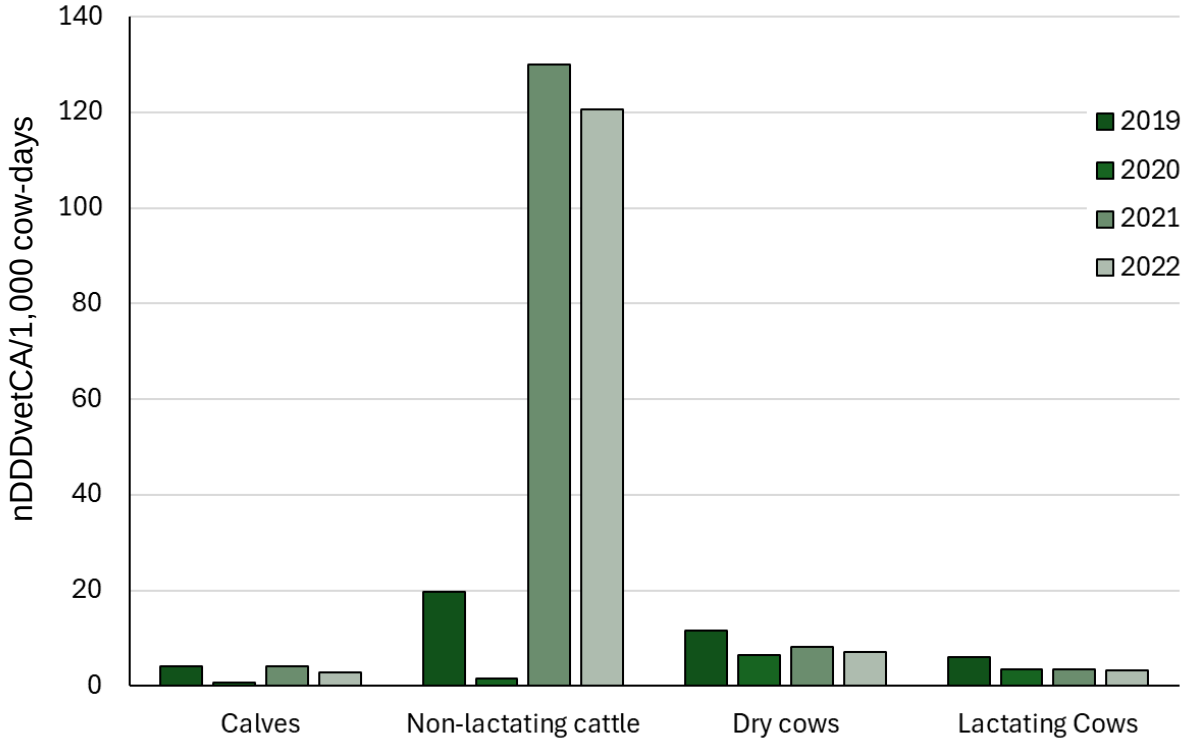


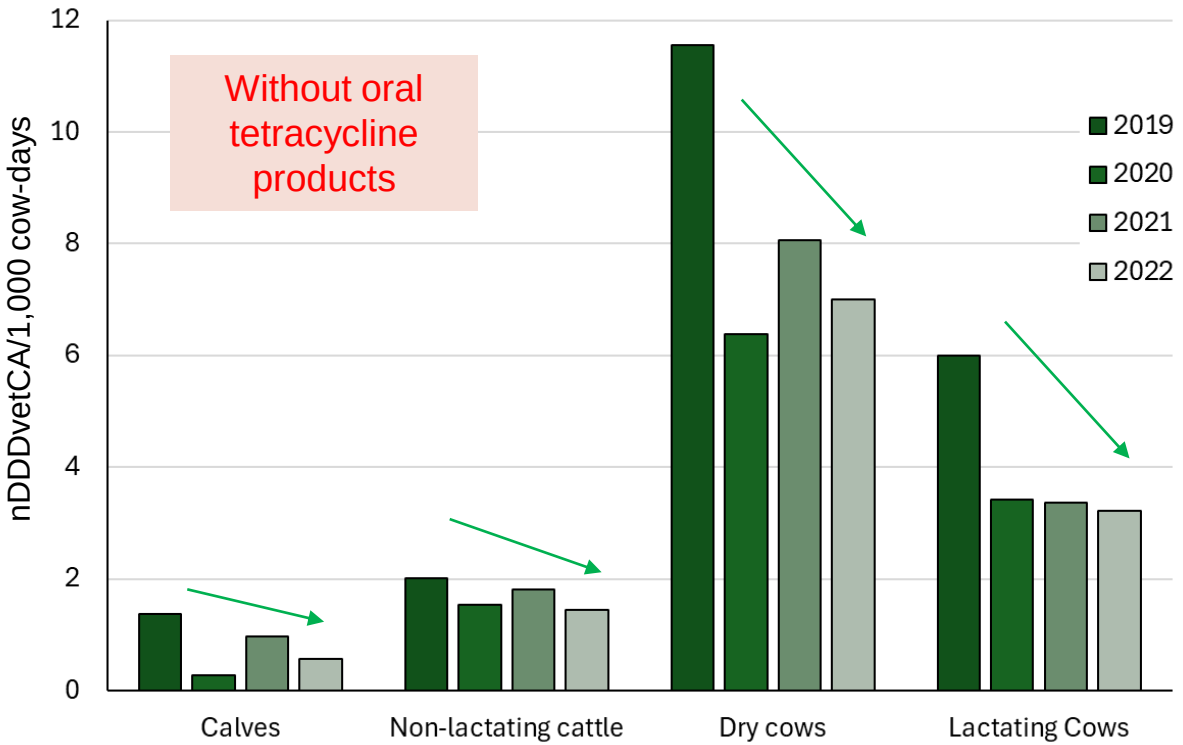
Source: 2019 – 2022 CaDNetASR veterinary dispensing data

AMU per production class

Decrease across classes when excluding oral tetracycline

- Majority of use is attributed to dry cow therapy
- Non-lactating cattle includes products with designation ‘not for use in dairy/lactating cows’ which are frequently used in calves and heifers





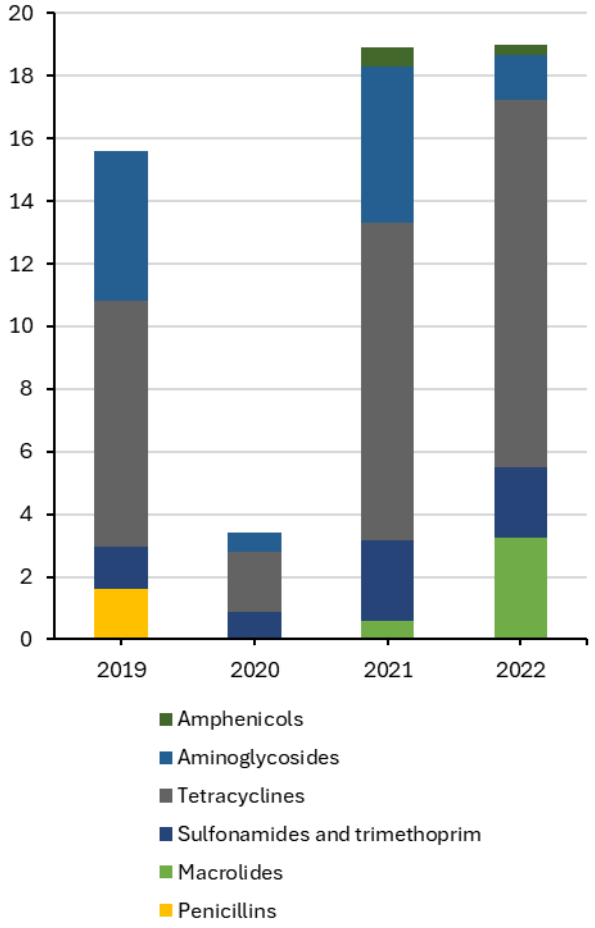
Source: 2019 – 2022 CaDNetASR veterinary dispensing data

AMU per antimicrobial class, stratified by production group

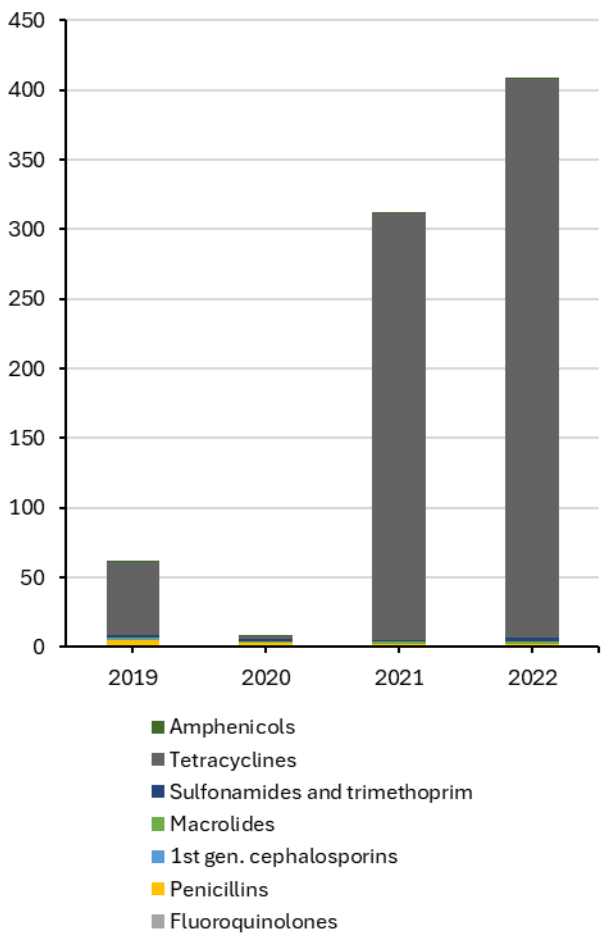
Tetracyclines used mainly in calves and non-lactating cattle

DDDvetCA/1,000 cow-days at risk

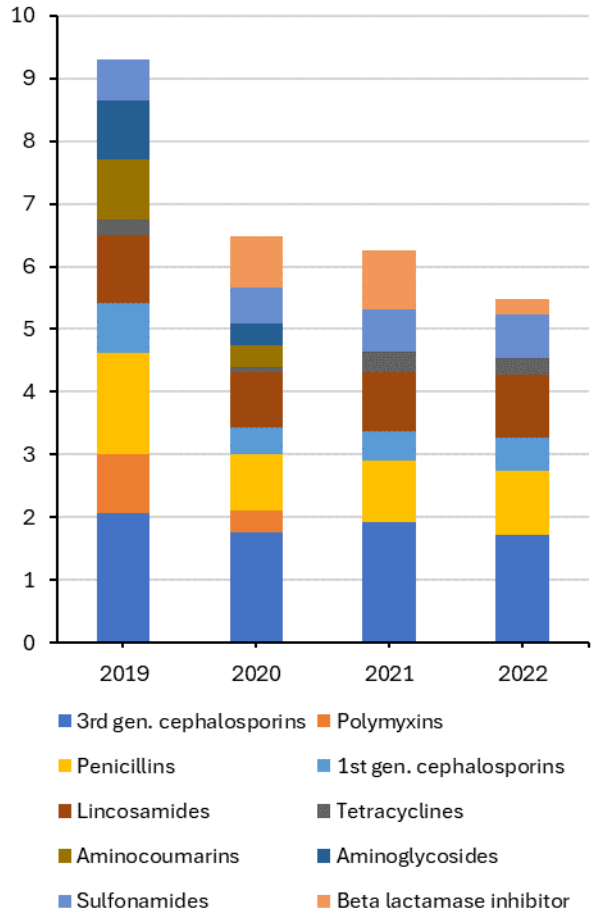
Calves



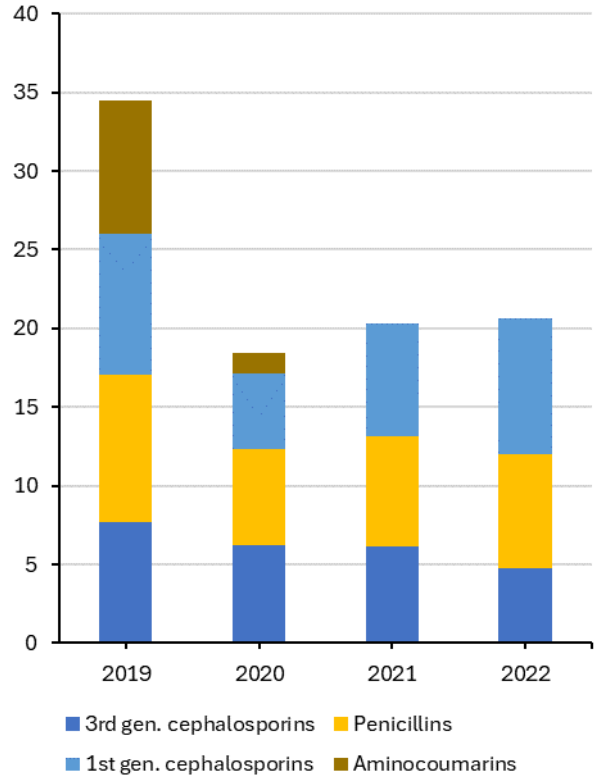
Non-lactating cattle



Lactating cows



Dry cows



Source: 2019 – 2022 CaDNetASR veterinary dispensing data

Veterinary Antimicrobial Sales Reporting: Dairy Cattle

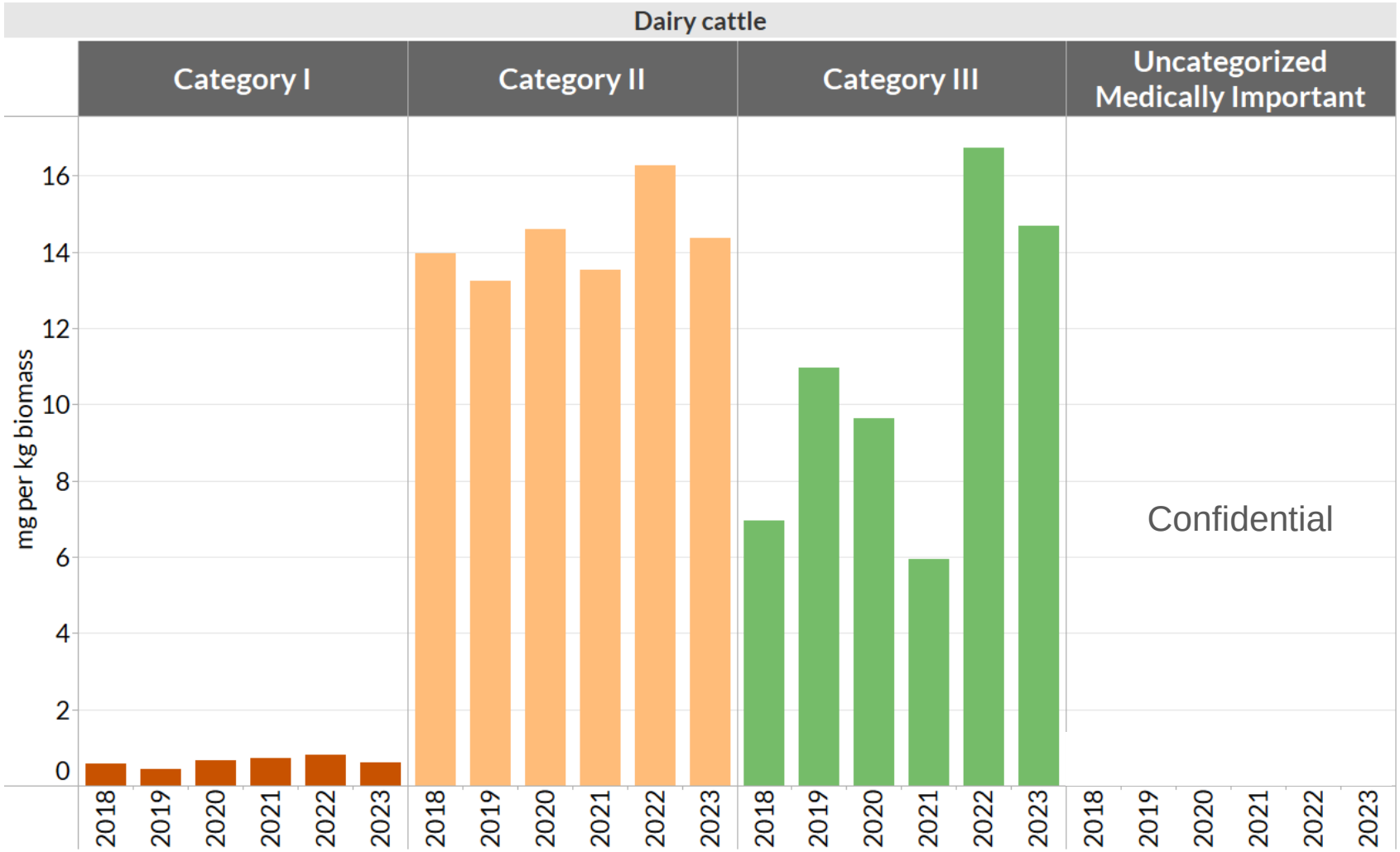
Similar conclusions drawn from VASR data

Sales for dairy cattle are primarily Category II and III antimicrobials.

- Top classes (as of 2023) include tetracyclines, TMS, and penicillins

Sales are primarily for use in feed, followed by use in water and intramammary use.

Category I antimicrobial sales are for intramammary use and use by injection.



*Uncategorized medically important antimicrobial sales not shown due to confidentiality

Veterinary Antimicrobial Sales Reporting: Dairy Cattle

Putting our dairy data into perspective

National veterinary sales data (VASR)

kg sold

1. Pigs
2. Beef cattle
3. Poultry
4. Dairy cattle
5. Aquaculture
6. Cats and dogs
7. Veal calves
8. Horses
9. Small ruminants

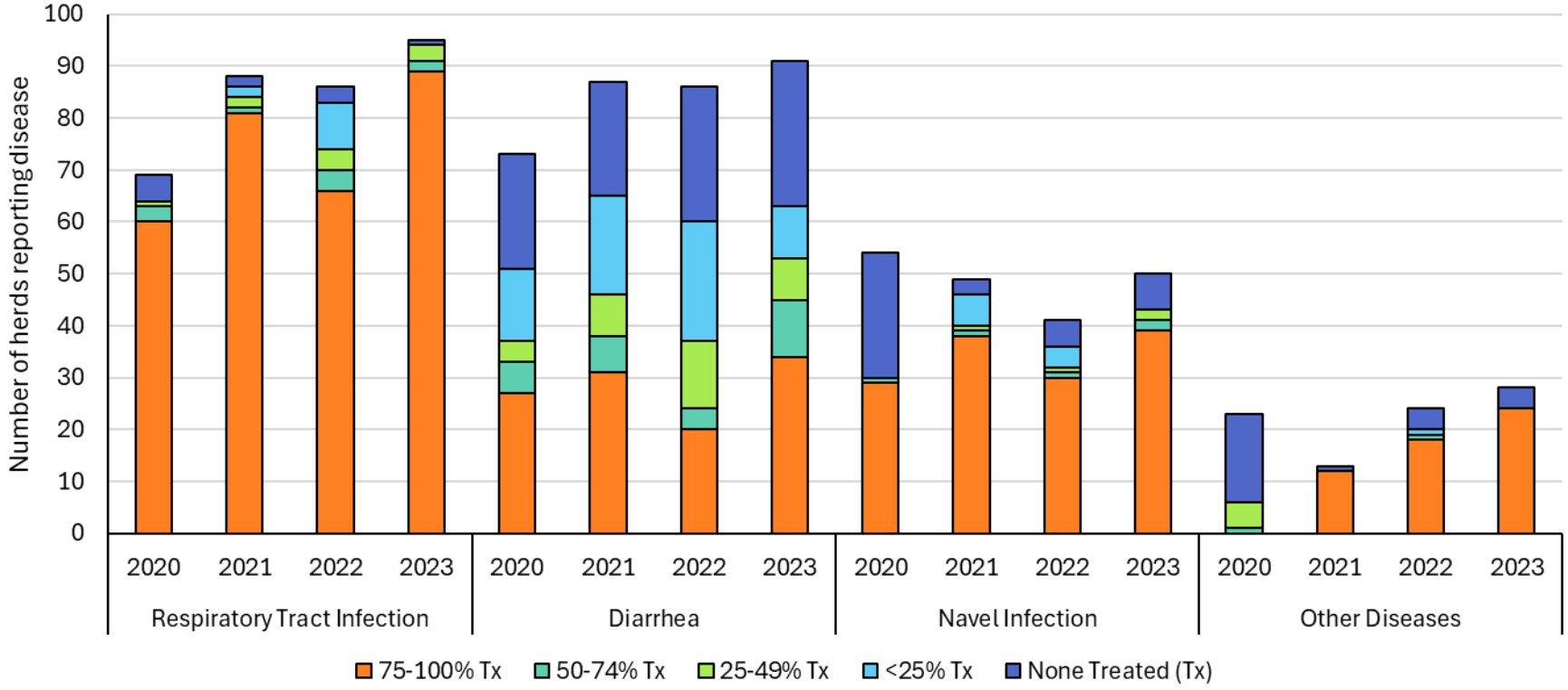
mg/kg biomass

1. Pigs
2. Veal calves
3. Poultry
4. Beef cattle
5. Aquaculture
6. Cats and dogs
7. Dairy cattle
8. Small ruminants
9. Horses

Questionnaire data: reasons for use - calves

Respiratory disease is a major driver of use in dairy calves

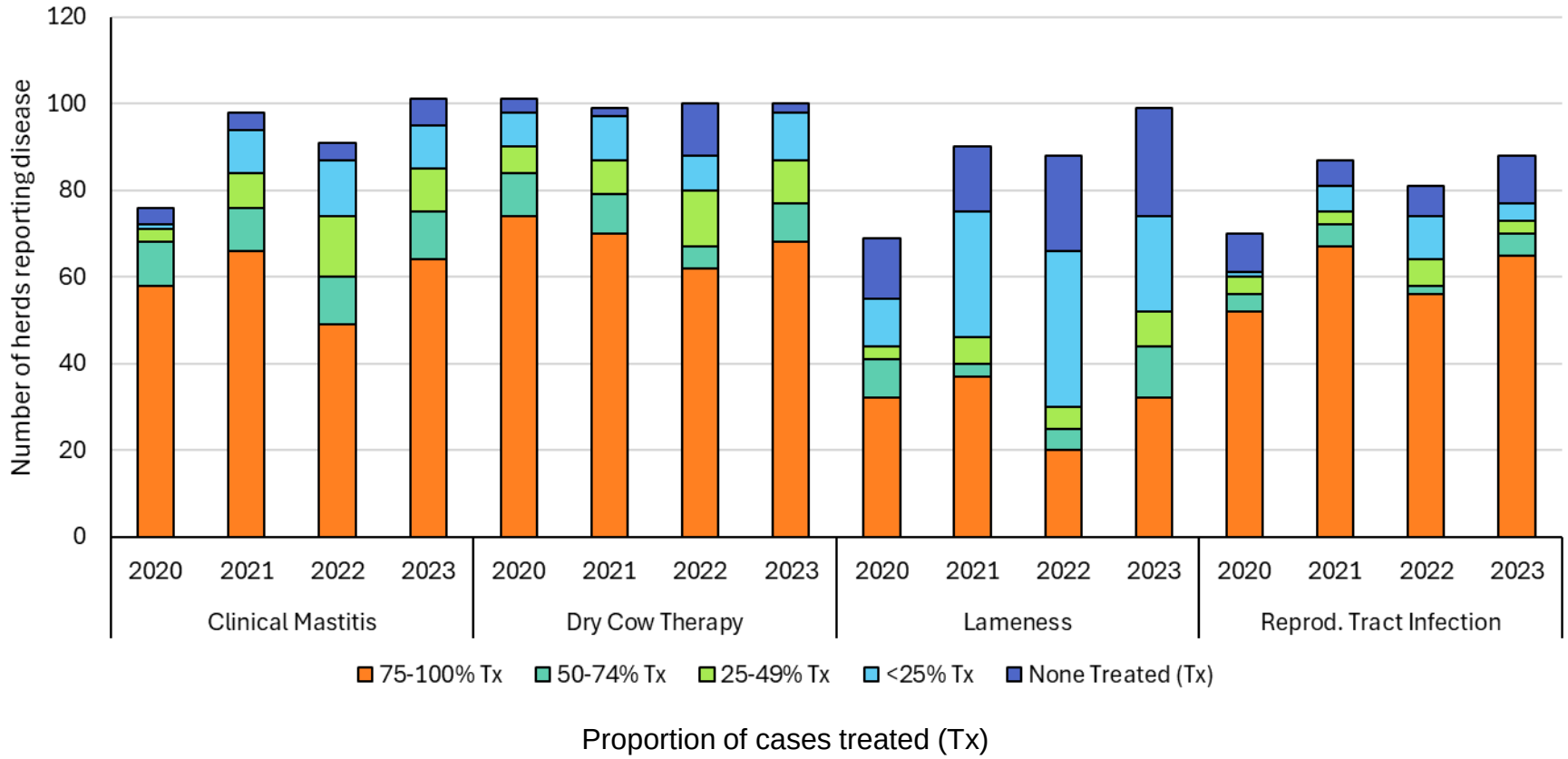
- Respiratory and intestinal infections in calves were reported by a majority of farms



Questionnaire data: reasons for use - cows

Clinical mastitis and dry cow therapy remain drivers of use in cows

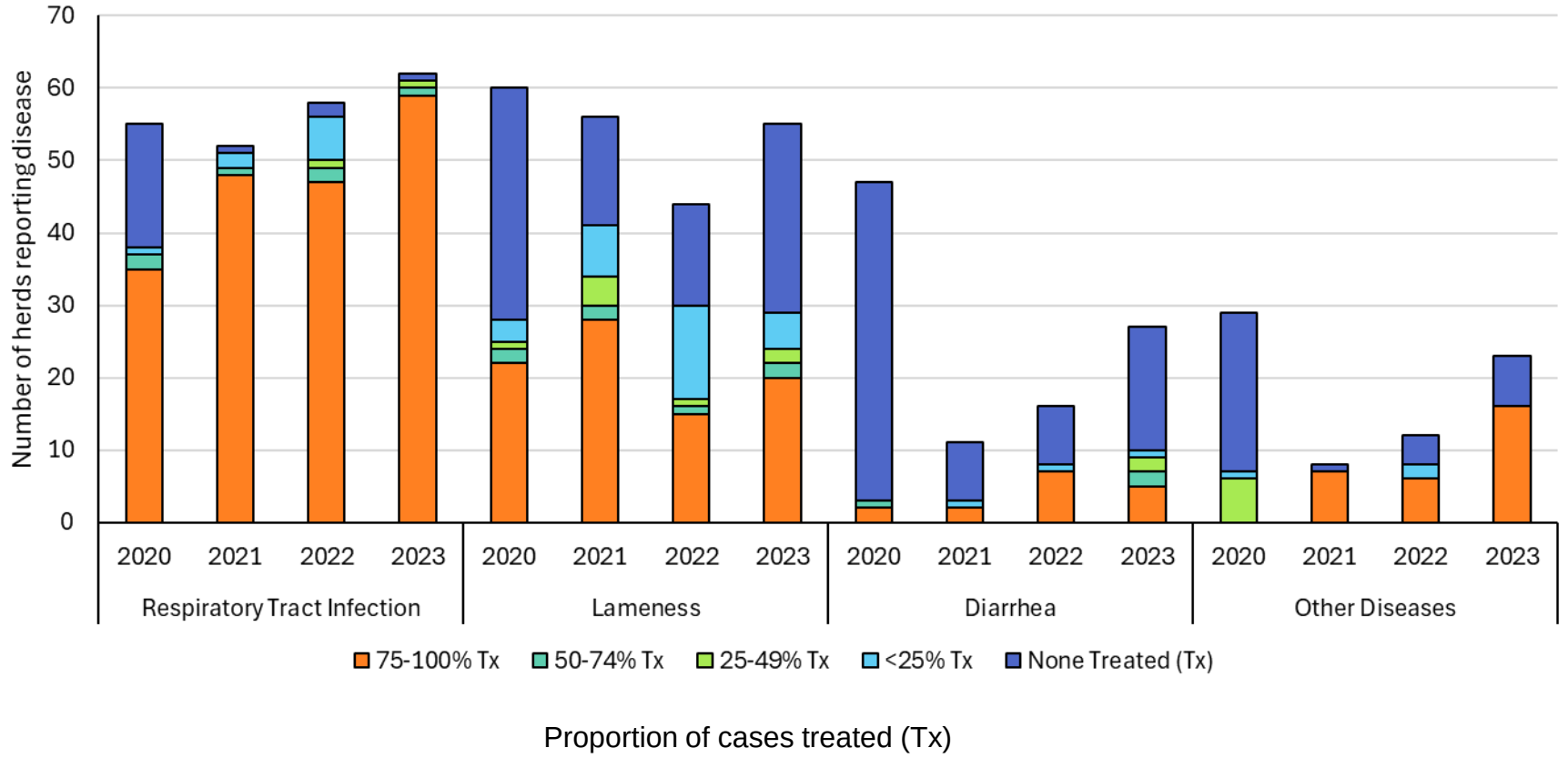
- Clinical mastitis, dry cow therapy, lameness and reproductive tract infections were reported by most farms



Questionnaire data: reasons for use - heifers

Respiratory tract infections remain high drivers of use in heifers

- Lameness and respiratory tract infections were reported by just over half of participating farms



Take-Home Messages – Antimicrobial Use

First presentation of comprehensive results since the start of program

Total category I and II use has fluctuated between 2019 and 2022

Fewer herds used Category I antimicrobials in 2022 (vs. 2019)

Dry cow therapy remains responsible for majority of antimicrobial use

Differences between provinces present

Underreporting of oral tetracyclines prior to 2021 complicates comparisons over time

Accessing feed mill data (including medicated milk replacers) is challenging

Respiratory tract infections most often listed as reason for use across animal groups

Take-Home Messages – Antimicrobial Resistance

E. coli resistance is low with stable trends, but most prevalent in isolates from calves

Low *Salmonella* recovery in 2023. No recovery of *S.* Dublin to date

Emerging ciprofloxacin resistance among *Campylobacter* isolates

Large proportion of bulk tank milk sample isolates resistant to tetracycline

Acknowledgements

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- CaDNetASR contributors
  - Prince Edward Island Laboratory
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Questions?