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Canadian Nosocomial Infection Surveillance Program

Antimicrobial Utilization (AMU) Protocol

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BACKGROUND

There is a well-documented association between antimicrobial (or antibiotic) use and the emergence of antimicrobial resistant pathogens (AMR) (Canton R 2011). Antimicrobial stewardship, which includes the appropriate selection, dosing, route, and duration of antimicrobial therapy, is an important component of infection control and patient safety. Effective antimicrobial stewardship and comprehensive infection prevention and control programs have been shown to limit the emergence and transmission of AMR including, but not limited to, Methicillin-resistant Staphylococcus aureus (MRSA), Vancomycin-resistant Enterococcus (VRE) and Carbapenem-resistant Gram-negative organisms (Lawes T 2016, Molina 2017).

National data on AMU in Canadian hospitals are limited. Taylor et al. reported on the prevalence of AMU within a network of Canadian hospitals from 2002 and 2009 (Taylor 2015). These data provide cross-sectional antimicrobial dispensing results from 28 and 44 hospitals, respectively. Data collected in the Canadian Drug Store and Hospital Purchases (CDH) Dataset (administered by IQVIA) captures the national quantity of antimicrobials purchased by the hospital sector (i.e., acute-care, long-term care, government redistribution centers, and government facilities), but relies on proprietary projection methods and does not directly measure antimicrobial dispensation.

To address this knowledge gap, the Canadian Nosocomial Infection Surveillance Program (CNISP) antimicrobial usage study collects AMU data from participating sentinel sites. Since CNISP collects AMU data directly from CNISP hospital pharmacies, CNISP AMU data is more robust than other sources of AMU information representing consumption in acute care hospitals. These data are analyzed using Defined Daily Doses (DDDs) or days-of-therapy (DOTs) for pediatrics as per the World Health Organization's guidelines, allowing for comparisons within Canada and internationally.
Since CNISP collects data on both AMU and AMR, by linking the AMU and AMR data, CNISP will be able to estimate the magnitude and impact of AMU and AMR in tertiary acute care hospitals in Canada. CNISP uses these data to monitor trends and provide valuable information to health care providers and policy makers to aid in the control of AMR and the promotion of appropriate antimicrobial use.

OBJECTIVES

1. Estimate national and regional antimicrobial utilization (AMU) and provide benchmarks based on data received through participating CNISP hospitals.
2. Estimate rates of antimicrobial utilization by specific ward-type (including ICU and non-ICU wards; medical, surgical, combined, ICU and other ward types)
3. Evaluate trends and patterns of AMR across Canada and identify whether a correlation between CNISP AMU data and CNISP AMR data can be established.

METHODS

Site Eligibility

Sites that are able to provide the following mandatory fields (also outlined in Table 1) are eligible to participate in CNISP's AMU surveillance.

1. **Numerator:** Acute-care inpatient antimicrobial usage (separated by adult and pediatric populations, by parenteral and oral administration routes, and by ICU and non-ICU ward types.
2. **Denominator:** Patient-day denominators by ward type (please use the same ward types/groups of wards as your numerator data).

Surveillance Design

AMU surveillance is ongoing and optional for hospitals participating in CNISP.

CNISP collects annual AMU data for all inpatients at participating hospitals. The AMU data may be separated by individual hospital ward or by groups of wards. For each hospital ward or group of wards that are used to submit AMU data to CNISP, participating hospitals must also provide an associated patient-day denominator for that ward or group of wards.

CNISP collects information on antibiotic use among acute adult and pediatric inpatients. This surveillance includes the following antimicrobials:

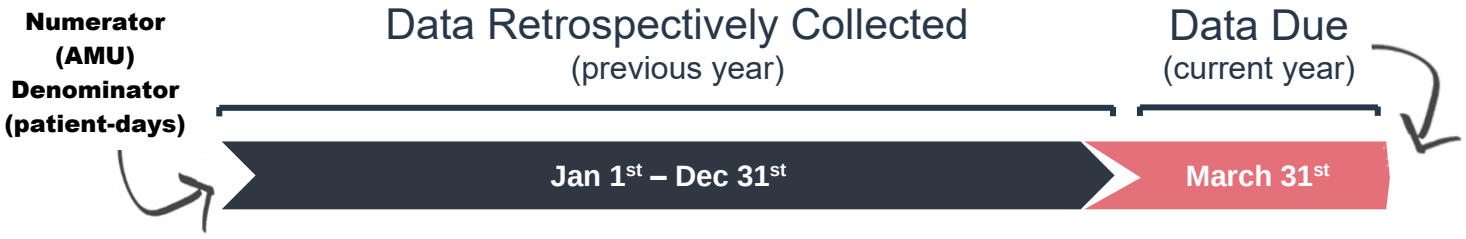
- All systemic antibacterials (all 'J01' ATC codes)
- Metronidazole oral ('P01AB01' ATC code)
- Vancomycin oral ('A07AA09' ATC code)

Full list of the included ATC codes: APPENDIX 3 –ATC CODES AND DDDS FOR ALL SYSTEMIC ANTIMICROBIALS.

Surveillance period

Data are retrospectively collected. Annual calendar-year data are due by March 31st of the subsequent year.

> **Example:** Data from January 1st 2021 to December 31st 2021 are due by March 31st 2022 as part of the 2022 Surveillance period.



If you have any questions please do not hesitate to contact us cnisp-pcsin@phac-aspc.gc.ca

Numerators

Inpatient antimicrobial usage

AMU separated by adult and pediatric populations, by parenteral and oral administration routes, and by ICU vs non-ICU wards. Pediatric AMU data is collected in days of therapy. Sites may submit adult AMU data as 'quantities of antimicrobial used' (e.g., in grams/MU) and/or as defined daily doses (DDD); it is requested that sites submit quantity data so that changes in DDD values can be accounted for over time. Please note that:

a) ER patients that are admitted as inpatients are to be included in the 'other' or 'Non-ICU' category (depending on your data submission format) for both the AMU and patient days data.
b) Units/wards designated as Long-term Care (LTC) units should not be included in the AMU or patient days data.

Denominators

Patient-day denominators

Patient-days for all ward/ward groups used for submitting the above AMU data.

Table 1: Mandatory and Requested Data Elements

	Variable	Adults	Pediatrics	Description of variable	Notes
Antimicrobial usage	**Drug name**	MANDATORY	MANDATORY	Generic drug name for drugs meeting **inclusion criteria:** - All systemic antibacterials (all 'J01' ATC codes excl. inhaled powders/solutions) OR - Metronidazole oral ('P01AB01' ATC code) OR Vancomycin oral ('A07AA09' ATC code)	
	ATC code	REQUESTED	REQUESTED	ATC code	
	Dose form or route	MANDATORY	MANDATORY	Identify dose form or route: *Parenteral (i.e., intravenous, intramuscular, intradermal or subcutaneous), or oral*	
	Quantity of antimicrobial used (preferred) AND/OR **Defined Daily Doses (DDDs)**	MANDATORY		**Defined Daily Doses (DDDs):** • The assumed average maintenance dose per day for a drug used for its main indication in adults" as specified by the WHO[1] **Quantity of antimicrobial used:** Weight of drug used (grams, mgs, or million units)	• If providing DDDs, please use **Appendix 1** for consistency. Please note that 2019 data should be converted using the 2019 ATC Index. • If providing DDDs is not feasible, strength and quantity information can be provided instead (e.g. Provide quantity of antimicrobial used).
	Unit of measure	MANDATORY		Unit used for antimicrobial usage measure (*DDDs, grams, milligrams, or million units*)	If number of 'tablets' is provided, include dosage information.
	Days of Therapy (DOTs)	REQUESTED	MANDATORY	The duration of antimicrobial usage. The number of days that a patient receives an antimicrobial agent (regardless of dose). Any antibiotic dose that is received during a 24-hour period represents 1 DOT. The DOT for a given patient on multiple antibiotics will be the sum of DOT for each antibiotic that the patient is receiving.	• For patients that are transferred during the day to a new unit, the DOT is not split. The DOT for that day is recorded for the ward where the patient was transferred from and the following day the DOT is associated with the new ward.
	Length of Therapy (LOTs)		REQUESTED	The number of days that a patient receives systemic antimicrobial agents, irrespective of the number of different drugs.	- LOT will be lower than or equal to DOT because each antibiotic received is its own DOT.
	Antimicrobial Free-Days		REQUESTED	The number of days that antimicrobial agents were NOT received during a given period on a given hospital unit.	- AFD is calculated irrespective of the number of antimicrobial agents received.
Pop.	**Age group**	MANDATORY	MANDATORY	*Adult or Pediatric* • Where possible to separate individual patients by age, adults are defined as patients ≥18 yrs of age and pediatric patients are those < 18 yrs of age. • Where not possible to separate individual patients by age, wards may be separated based on the age group of the majority of patients.	
Ward information	**ICU vs Non-ICU**	MANDATORY	MANDATORY	Identify ward type: *Non-ICU, ICU, CCU, PICU, PCICU, or NICU* ICU includes stand-alone medical, surgical or any ICUs with a combination of patient types e.g. med/surg; trauma/surgical; neuro, surgical, trauma, burn etc.	- Please provide data for CCU separately from ICU data. - Ward categories must be mutually exclusive.
	Ward type[2]	REQUESTED	REQUESTED	Identify ward type where available and applicable for your institution: • *Medical ward* (excluding obstetrics/psychiatry) • *Surgical ward* • *Combined (medical/surgical) ward* • *Hematology-Oncology Unit** • *Transplant Unit* (if possible separate bone marrow transplant and solid organ transplant units)* • *Burn Unit** • *ICU, NICU, PICU,* PCICU or *CCU* • *Other [2] (see notes--->)*	**- Ward categories must be mutually exclusive.** **- If an assigned ward type is inconsistent with its function, categorize it based on its function the majority of the time for the calendar year (e.g. a surgical ward used mainly as a COVID-19 unit should be identified as a medical ward type).** *If not possible to separate antimicrobial usage and/or patient denominator data for the Hematology-Oncology Unit, Transplant Unit, or Burn Unit at your site, please include these units under the appropriate medical, surgical, or combined category. Other includes: Obstetrics; Psychiatry and mental health units; Emergency (if inpatient/i.e., admitted); and other not listed.
	Inpatient-Days	MANDATORY	MANDATORY	Sites will provide inpatient days for January 1, 2019 to December 31, 2019 separated into adult and pediatric, and ward-type specific patient-days.	For each ward type the site is able to calculate antimicrobial usage, a denominator must be provided.

[1] Source: PHO ASP Metrics Examples

[2] Please note that 1. ER patients that are admitted as inpatients are to be included in the 'other' or 'Non-ICU' category depending on your data submission for both the AMU and patient days. 2. Units/wards designated as Long-term Care (LTC) units should not be included in the AMU or patient days.

Data Submission

To meet the objectives of the study, AMU data separated by specific ward-type (see Table 1 for list of mandatory and requested data elements) and the associated patient-day data are requested.

All data must be submitted to CNISP by email (cnisp-pcsin@phac-aspc.gc.ca). AMU and patient-day data are due by March 31st.

Format

Excel format is preferred following one of the example templates found in APPENDIX 2 – EXAMPLE TEMPLATES FOR DATA SUBMISSION.

If another submission format is easier for your hospital site, please contact CNISP (cnisp-pcsin@phac-aspc.gc.ca) to confirm that the format contains the necessary data elements.

For sites that submit ward-level information, please provide us with a data dictionary for your wards so that we can identify the type of ward (for example, indicating whether '6E' is a medical or surgical ward). This data dictionary may be included as a variable in the dataset (preferred) or may be provided as a separate document.

Analysis

PHAC will be responsible for converting data files into a common platform and merging files for analysis. Individual site-specific as well as ICU vs non-ICU, oral vs. parental, regional and national adult rates will be calculated and standardized by 1000 patient days.

For adult surveillance, if sites have not submitted DDDs, PHAC will convert quantities to WHO DDDs (see Table 2). The following drugs are special cases:

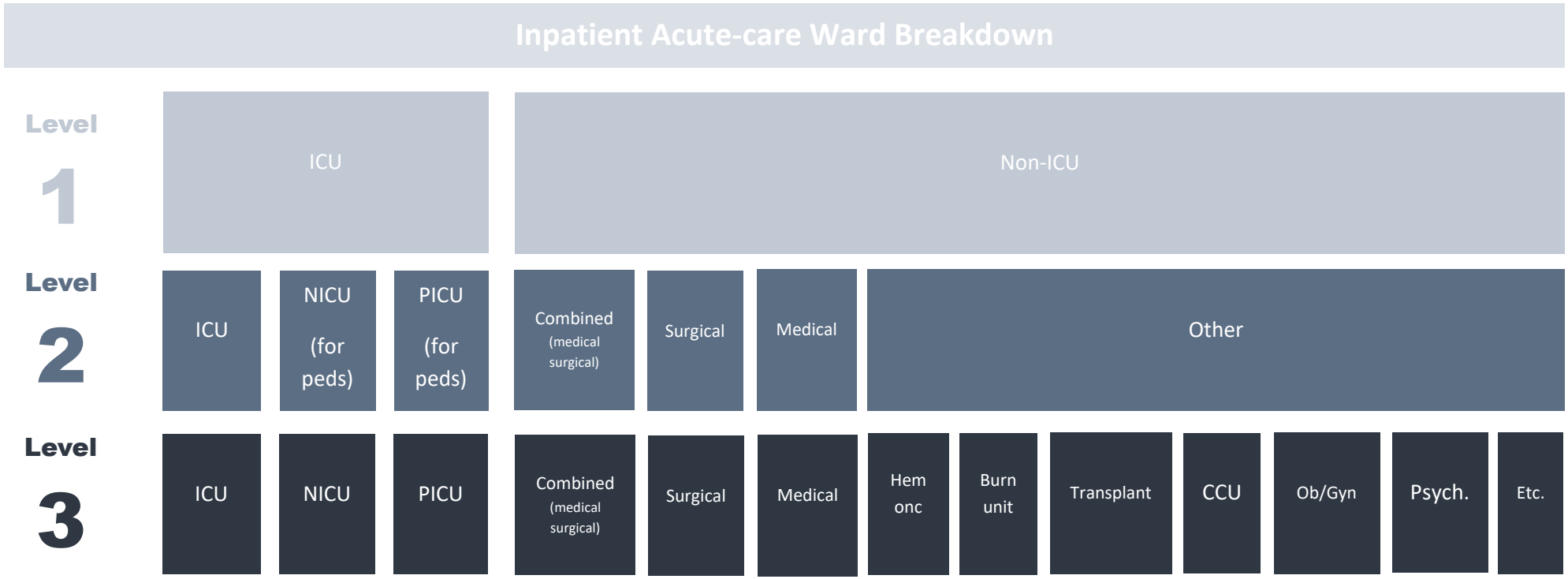
- For benzylpenicillin (J01ECE01), also known as penicillin G, and benzathine benzylpenicillin (J01CE08), data received in million units (MU) will be converted to grams (where 0.6 g = 1 MU), which can then be converted to DDDs using WHO values.
- Methenamine (J01XX05) is further divided into mandelate and hippurate, which have different DDDs: 3 g per DDD and 2 g per DDD, respectively.
- Erythromycin (J01FA01) can also be categorized as either erythromycin and erythromycin ethylsuccinate, both of which have different DDDs: 1 g per DDD and 2 g per DDD, respectively.

Data analysis for pediatric patients will be addressed differently as the dose given to pediatrics is adjusted by weight and there is no single DDD; thus, WHO suggests DOT as the appropriate measure to monitor trends of antimicrobials in children. The rates will be adjusted by the number of patient days in pediatrics sites.

ETHICS

While this surveillance project does not involve any alteration in patient care, ethics approval may be sought at some hospital sites. There are no patient identifiers in this data and data is aggregated with the lowest level of aggregation being at the hospital ward. All data submitted to PHAC is kept strictly confidential.

Appendix 1 – Breakdown by Ward-type



Notes:
If unable to breakdown further than level 1 and you have both adult ICUs, and PICU or NICU, please indicate what types of ICUs are included in your submission.

Notes:
Combined = combined medical/surgical wards
"Other" wards can include any Non-ICU acute-care wards (Psychiatry, Ob/Gyn, etc.)
If possible, breakdown by all individual ward types is appreciated (level 3)

Where possible, please indicate the wards included at all levels. If submitting data at levels 1 or 2, please include a note indicating what wards you submitted data for. E.x. Non-ICU included: Medical, Surgical, combined, and Ob/Gyn wards.

Ward categories must be mutually exclusive.

If an assigned ward type is inconsistent with its function, categorize it based on its function the majority of the time for the calendar year (e.g. a surgical ward used mainly as a COVID-19 unit should be identified as a medical ward type).

Appendix 2 – Example Templates for Data Submission

Sites may submit data in a variety of formats. Some examples of possible submission formats are below. It is preferred that sites submit data in similar formats each year.

Table 2: Example submission format for adult data – hospital calculating DDDs

Ward type	Drug Name	Route	DDD	DOT (optional)	Patient-days for the ward-type
Medical	Ciprofloxacin	P	165		1992
Medical	Ciprofloxacin	O	117		1992
Surgical	Ciprofloxacin	P	195		3941
Surgical	Ciprofloxacin	O	54		3941
ICU	Ciprofloxacin	O	175		545
CCU	Ciprofloxacin	O	175		345
Combined (Medical/Surgical)	Ciprofloxacin	O	180		654
Other - BMT	Ciprofloxacin	O	123		212
Other - Psychiatry	Ciprofloxacin	O	12		697

Table 3: Example submission format for adult data – hospital providing quantity and units

Ward type	Drug Name	Route	Quantity	Units	DOT (optional)	Patient-days for the ward-type
Medical	Amoxicillin	P	455	Gr		1992
Medical	Amoxicillin	O	375	Gr		1992
Surgical	Amoxicillin	P	295	Gr		3941
ICU	Amoxicillin	O	155	Gr		545
CCU	Amoxicillin	O	17500	Mg		345
Combined (Medical/Surgical)	Amoxicillin	O	180	Gr		654
Other - BMT	Amoxicillin	O	123	Gr		212

Table 4: Example submission format for pediatric data – hospital providing DOTs

Ward type	Drug Name	Route	DOT	Patient-days for the ward-type
Medical	Pip-tazo	P	512	1605
Medical	Pip-tazo	O	125	1605
Surgical	Pip-tazo	P	454	3941
Other - Transplant	Pip-tazo	O	545	345
PICU	Pip-tazo	O	455	654
NICU	Pip-tazo	O	212	212
Other - Psychiatry	Pip-tazo	O	24	343

Table 5: Example submission format for adult data – hospitals provide patient days in separate tab

Ward	Drug Name	Route	Quantity	Units
M8	Amoxicillin	P	455	Gr
M8	Amoxicillin	O	375	Gr
SURG	Amoxicillin	P	295	Gr
ICU	Amoxicillin	O	155	Gr
CCU	Amoxicillin	O	17500	Mg
FE	Amoxicillin	O	180	Gr
S9	Amoxicillin	O	123	Gr

Tab 1 – AMU by ward

Ward type	Ward	Patient-days
Medical	M8	1992
Surgical	SURG	3941
ICU	ICU	545
CCU	CCU	345
Combined (Medical/Surgical)	FE	654
Other - BMT	S9	212

Tab 2 – Data dictionary and patient-days

Appendix 3 –ATC codes and DDDs for all Systemic Antimicrobials

2021_AMU_ATC_DDD_conversions.xlsx

References

Canton R, Morosini MI. Emergence and spread of antibiotic resistance following exposure to antibiotics. FEMS Microbiol Rev 2011;35:977-991.

Lawes T, et al. Effects of national antibiotic stewardship and infection control strategies on hospital-associated and community-associated methicillin-resistant Staphylococcus aureus infections across Scotland: a non-linear time-series study. Lancet Infect Dis 2015;15(12):1438-49.

Molina J, et al. Long-Term Impact of an Educational Antimicrobial Stewardship Program on Hospital-Acquired Candidemia and Multidrug-Resistant Bloodstream Infections: A Quasi-Experimental Study of Interrupted Time-Series Analysis. Clin Infect Dis 2017;(Epub)

Taylor G, Gravel D, Saxinger L, Bush K, Simmonds K, Matlow A, Embree J, Le Saux N, Johnston L, Suh K, Embil J, Henderson E, John M, Roth V, Wong A, Canadian Nosocomial Infection Surveillance Program. Prevalence of antimicrobial use in a network of Canadian hospitals in 2002 and 2009. Can J Infect Dis Med Microbiol 2015; 26(2): 85–9.

Revision History

Date	Revisions Made
May 2018	1. Will only accept AMU data as dispensed or administered (not purchased) – have removed this as an option from Appendix 3 – pt-days submission form (p. 11) and clarified it in the numerator data (p. 3) 2. Have asked that CCU data be separated (as an optional variable) (p.4, Appendices 2 & 3) 3. Have asked that type of ICU(s) be specified (if possible) (p.4, Appendices 2 & 3) 4. For co-trimoxazole (J01EE01) WHO does provide the DDD – so have removed this comment (p.4) 5. Have corrected the WHO DDD unit for Trimethoprim/ Sulfamethoxazole (Co-trimoxazole) (parenteral & oral) (p. 7) 6. As the inclusion criteria specified the collection of only systemic antibacterials (J01) the following inhaled powders and solutions have been removed from both the protocol and the data collection form (excel) and the data are no longer required to be submitted Aztreonam J01DF01 Inhaled solution Tobramycin J01GB01 Inhaled solution Tobramycin J01GB01 Inhaled powder Colistin J01XB01 Inhaled solution
October 2018	1. Added hem/onc, transplant, bone marrow transplant, solid organ transplant separations to the other category. 2. Clarified age break point for adults/peds 3. Created table of requested and mandatory variables.
December 2018	1. Added references 2. Removed Appendix 3 and created new example templates
August 2019	1. Updated DDD values to the 2019 WHO values. 2. Clarified the details of the ward transferred 3. Changed ‘due’ date of data to March.
December 2019	1. Updated protocol format 2. Added appendix 1 3. Added Table 5 in appendix 2 4. Updated Surveillance period (removed years), changed submission date from June to March 31st
November 2020	1. Updated DDD values for 2020 2. Added stewardship questions.
January 2022	1. No substantive changes to protocol. Note there were no changes to the ATC DDD conversion values this year.

January 2023	1. Clarified ward type categorization – to be based on function the majority of the calendar year. 2. Note there were no changes to the ATC DDD conversion values this year.
November 2023	1. Updated the working group member list 2. Removed three ASP questions (appendix 4) 3. Updated CNISP email 4. Note there were no changes to the ATC DDD conversion values this year. Note: Addition of the antibacterial(s) relevant to the collaboration with PHAC's AMR access pilot project is now planned for the 2024 surveillance year.
November 2024	1. Updated the working group member list 2. Clarified administration routes included as "parenteral" (intravenous, intramuscular, intradermal or subcutaneous) 3. Note there were no changes to the ATC DDD conversion values this year. Note: We plan to add up to five antibacterials relevant to the collaboration with PHAC's AMR economic incentive pilot project. The protocol will be amended as needed once their names can be disclosed.