Development of a national web-based antibiogram tool

Teagan Zeggil, PharmD; Dylan Dobbyn, BHSc, PharmD; Brendan Kudrowich, PharmD; Nathan P. Beahm, BSP, PharmD

Case

A 30-year-old man presents to your pharmacy with a prescription for ciprofloxacin 500 mg oral twice daily for 7 days that was given to him by his physician. The patient tells you that he has been experiencing dysuria and increased urinary frequency for the past 2 days. After your assessment, you agree that this patient requires antibiotics, but you are uncertain whether ciprofloxacin is the most appropriate antimicrobial. You check your references[1-3] and realize that it is advised to assess local susceptibility rates of *Escherichia coli* to fluoroquinolones when considering them for a urinary tract infection (UTI). You learn that ciprofloxacin is recommended as empiric therapy only if the local resistance rates are lower than 10%.[1-3] How would you determine your local resistance rates to *E. coli*?

Introduction

Antimicrobial resistance rates are an important consideration when deciding on empiric antibiotic treatment. Resistance rates may have regional differences due to antimicrobial use patterns and patient populations. Resistance rates may also vary across time, with it being possible to see significant shifts in resistance rates from one year to the next.[4,5] Regional susceptibilities are commonly published as antibiograms annually to guide antibiotic therapy decisions.

An antibiogram is a summary of antimicrobial susceptibilities in bacterial isolates tested by a microbiology laboratory. Once a sufficient sample size has been collected, the susceptibility of a given organism can be predicted based on the aggregate data collected. To test susceptibility, the microbiology laboratory determines the isolates' minimum inhibitory concentration (MIC) to different antibiotics. The MIC is used to determine whether the antibiotic-pathogen combination should be labelled as susceptible (S), susceptible dose-dependent (S-DD), intermediate (I) or resistant (R), based on predetermined breakpoint thresholds that have been recommended by organizations such as the Clinical and Laboratory Standards Institute (CLSI)[6] or the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[7] Of note, the S-DD threshold is not commonly used at present and tends to be reserved for certain antimicrobial-pathogen combinations. This method is used to classify individual isolates, which are then used to help determine antibiogram susceptibility. The susceptibilities of these individual isolates are then combined to create the antibiogram. The more isolates of a given organism that are tested and included in the antibiogram, the more reliable will be the resultant susceptibility percentage. The susceptibility percentage for an organism that was isolated and tested fewer than 30 times within an antibiogram's reporting period is typically regarded as unreliable.

An antibiogram may use the aforementioned labels to demonstrate the susceptibility of a pathogen-antimicrobial pairing. However, antibiograms will more commonly use colour-coded representations of susceptibility and/or list the percentage of isolates that were susceptible. Generally, for colour-coded antibiograms, the colours indicate the range of susceptibility of the tested organisms and the reliability of using that antimicrobial-pathogen combination. Green corresponds to a range of susceptibilities indicating that the isolates are reliably tested as susceptible. Red indicates a range of susceptibilities that are commonly around or less than 50% susceptible and specify that the combination antimicrobial-pathogen is likely unreliable. Yellow corresponds to the range between green and red where the isolates are more inconsistently susceptible. The percentages represent the number of isolates collected that are susceptible to the antimicrobial in question. These antibiograms commonly have legends that inform the reader of the

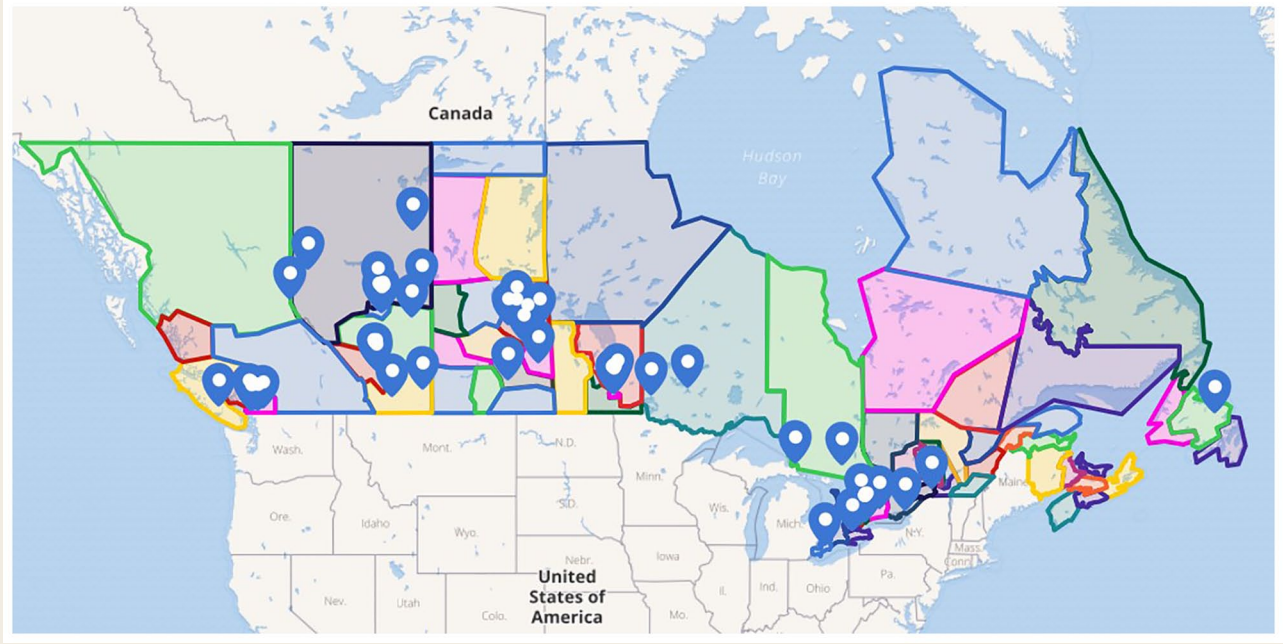
DOI:10.1177/17151635221101343

FIGURE 1 An example of an antibiogram for a hypothetical region/facility

	Total	Amikacin	Ampicillin	Ampicillin + Sulbactam	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone	Ciprofloxacin	Doxycycline	Ertapenem	Gentamicin	Levofloxacin	Linezolid	Meropenem	Nitrofurantoin	Oxacillin	Piperacillin + Tazobactam	Tobramycin	Trimethoprim + Sulfamethoxazole	Vancomycin
Citrobacter Freundii	47							71	80		100	93	93		100	98			90	78	
Citrobacter koseri	43			93	81			98	93		100	98	98		100	95			98	100	
Coagulase negative Staphylococcus species	168									87		88		100		98	50			53	100
Enterobacter (Klebsiella) aerogenes	64							80	85		95	100	97		100	23			100	97	
Enterobacter cloacae complex	98							76	86		93	92	96		100	64			93	80	
Enterococcus faecalis	376		100							29				99		99					
Escherichia coli	2982	100	53	81	60			92	72	67	100	92	77		100	96			92	73	
Klebsiella oxytoca	61			78	6			95	92		100	97	94		100	89			97	94	
Klebsiella pneumoniae	642			87	76			95	76	100	100	98	84		100	42			97	77	
Klebsiella species	33			100	94			100	94		100	97	100		100	88			100	82	

Less than 60% | Between 60% and 90% | 90% and above

FIGURE 2 Zoomed out view of the Antibiogram Canada application



https://maphub.net/CREAC/Antibiogram-Canada

thresholds used to determine the assigned colour-coding. See Figure 1 for a sample antibiogram.

Creating antibiograms requires planning, and the publication of antibiograms should be timely to give clinicians access to accurate susceptibility data. Although there are guidelines for the standardized development of antibiograms,[8] variability can occur between laboratories or regions with regard to development and presentation of antibiogram data. This can result in differences in reporting styles, organisms and antimicrobials analyzed, or access to accurate resistance information. The utility of an antibiogram diminishes if it is not easily accessible and updated based on the most current data. Additionally, some clinical practice guidelines indicate local susceptibility thresholds for situations where certain agents could be considered empirically. For example, the Infectious Diseases Society of America (IDSA) guidelines for uncomplicated UTI suggest that fluoroquinolones may be empirically prescribed only when resistance rates in uropathogens do not

exceed 10%.[1] Similarly, the IDSA guidelines for community-acquired pneumonia suggest that macrolides should be used for monotherapy in the outpatient setting only when their susceptibility in *Streptococcus pneumoniae* is greater than 75%.[9] Antibiograms can be generated for multiple purposes: guiding clinician antimicrobial selection; tracking antimicrobial resistance rates between wards, regions, and institutions or over time; and predicting outbreaks or potential resistant organisms.[10] In fact, it is ideal for antibiograms to differentiate by care setting where possible, because the resistance rates can be considerably different between these, even in the same region. From the perspective of antimicrobial stewardship, antibiograms should be used in selecting empiric therapy against a particular pathogen to optimize outcomes and prevent further resistance. Antibiograms can be used to guide empiric therapy or can be useful in culture-directed therapy if susceptibility data are pending. Once culture-derived susceptibilities become available, these data should be used to derive therapy decisions over population antibiogram data.

If an antimicrobial-pathogen pair has not been reported on an antibiogram, this does not necessarily mean that the combination has not been analyzed. Susceptibility data for unreported antimicrobial-pathogens combinations may be found in some instances by contacting the microbiology laboratory or sometimes can be inferred from other tested agents. Selective reporting of antimicrobial susceptibilities is an antimicrobial stewardship effort, as it may discourage use of more broad-spectrum antibiotics that have lower resistance rates in pathogens or the use of other agents that are not typically considered first- or second-line for infections caused by those pathogens. Although an antibiogram denotes susceptibility between an antimicrobial and pathogen, the clinical context and pharmacokinetic parameters of the antibiotic must still be considered.

Due to variable reporting or other barriers, clinicians may find it difficult to access accurate local resistance data to guide their prescribing decisions and assist in adhering to antimicrobial stewardship principles. Enhanced knowledge of local resistance rates will theoretically reduce inappropriate antibiotic use, which in turn could lead to better economic and patient-centred outcomes.

Although fluoroquinolones have largely become less favourable for the treatment of UTIs for several reasons,[11,12] fluoroquinolones remain commonly prescribed for this indication,[13] with guidelines indicating them as reasonable alternatives empirically when local resistance rates are below a certain threshold,[1,2] as mentioned above. We previously collected antibiogram data from across the 10 Canadian provinces for the purposes of looking at trends in resistance of *E. coli* to fluoroquinolones (The Ciprofloxacin Resistance Rates in *Escherichia coli* Across Canada [CREAC] Study).[14] With these data, we also aimed to create a free, accessible, user-friendly tool to provide clinicians with easy access to information about the resistance patterns in their region.

Tool development

Antibiograms were collected directly from online publications or web applications, such as Firstline.[15] If antibiograms could not be found through these channels, the health authorities and hospitals were directly contacted. When contacted to provide antibiogram data, a site or region had the option to opt out of having its antibiogram published on the tool. Ethics approval was not required because the data collected either had been previously published or were intended for public or clinician use and were already in aggregate form without any patient identifiers. The intention of data collection was to assess *E. coli* resistance to ciprofloxacin; however, during this phase we also collected completed antibiograms. We collected 591 antibiograms in total from various regions across Canada (see Table 1 for breakdown). After screening for incomplete or duplicate antibiograms, we analyzed 588 antibiograms. As depicted in Table 1, antibiograms were more easily attained in the Western provinces and were less accessible in the Eastern provinces.

The map was created from an established map-designing website, maphub.net. The app can be found at **https://maphub.net/CREAC/Antibiogram-Canada**. Health zones were drawn onto the map to match provincial designations (Figure 2). Of note, Saskatchewan was divided based on the previously designated health zones according to the study period analyzed in the CREAC study (2015-2019). The most current antibiogram data available from the source at the time of collection, June 2020, were posted onto the corresponding geographic area on the interactive map along with the respective source website when available.

Tool application

When a health region is selected, the latest antibiogram data collected from that region are made visible. Pins are placed when hospital or specific long-term care antibiograms are obtained and the data are unique to a single site (Figure 3). When available, the image of the full antibiogram is attached to the region or pin for ease of reading (Figure 4). The link to a region's publicly available antibiograms is provided in each available region, which will provide clinicians with information on how to find regional antibiograms and may provide historical data. The tool also has a search function that allows the user to search for a particular health region or hospital instead of selecting it from the map.

Discussion

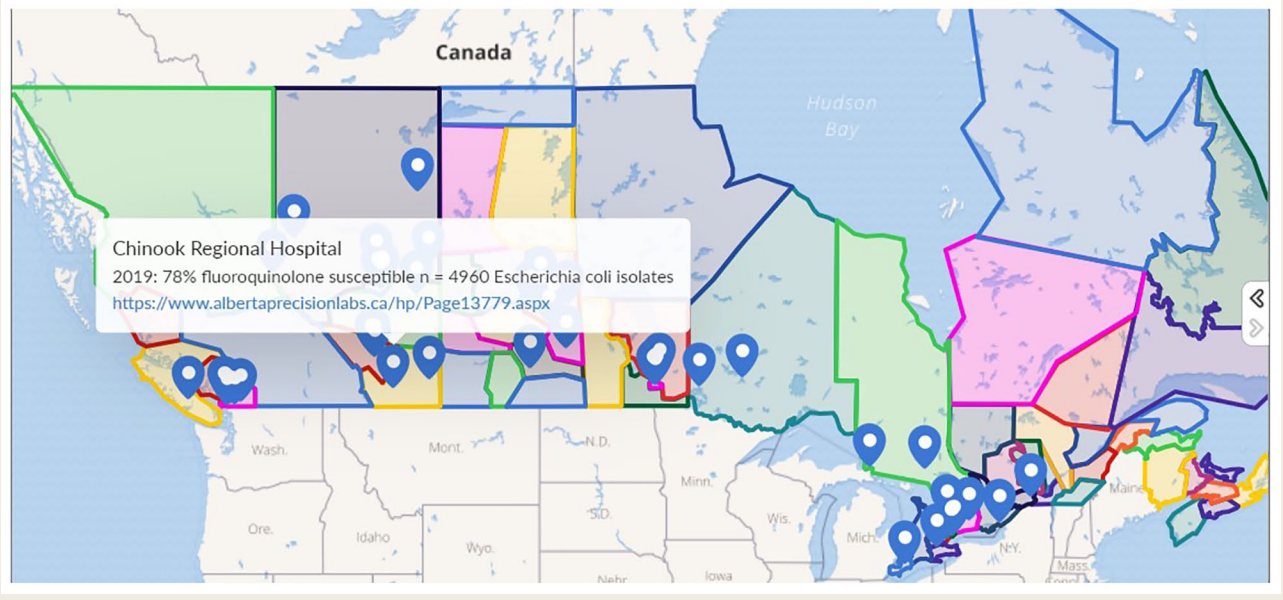
This tool is a region-specific resource that enables clinicians to access local susceptibility data more easily. Although the information collected was primarily focused on one organism and one antimicrobial, we simultaneously collected information on other pathogens whose susceptibilities were reported. Therefore, we were able to construct a tool that shared the collected antibiograms within each health zone of all the provinces to ultimately enhance access to these resources. This tool may

TABLE 1 Number of antibiograms obtained per province per year

	Year					
Province	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
British Columbia		2	3	3	3	15
Alberta		16	17	17	26	22
Saskatchewan		3	13	20	22	12
Manitoba		18	20	20	20	20
Ontario	4*	11	44	45	61	30
Quebec	1*	1	3	2	2	
New Brunswick		1		2	1	2
Nova Scotia		4	6	32	32	
Newfoundland and Labrador		2	2	2	1	3
Prince Edward Island	2*		2			2

*Where 2015 data were not available, but 2014 data were available, the 2014 data were used in lieu of 2015 because these were the susceptibility data that would be clinically referenced for the year 2015 at that site. In the tool, only the most recently published data were demonstrated in order to maintain relevance.

FIGURE 3 Screenshot of the Antibiogram Canada app showing data from Alberta



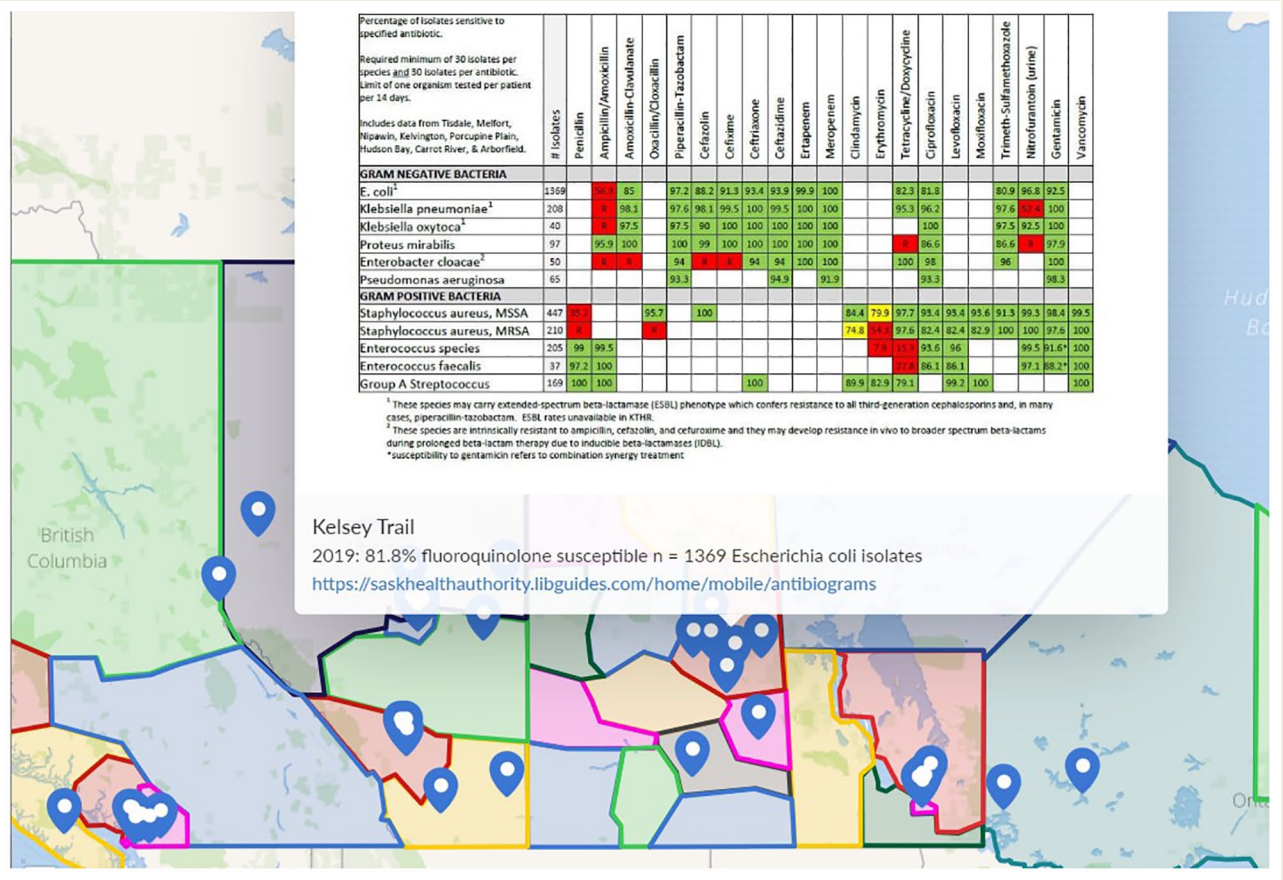
https://maphub.net/CREAC/Antibiogram-Canada

also serve as a proof of concept for future cross-jurisdiction sharing of susceptibility data.

This tool may provide more benefit to clinicians in regions where antibiogram data are more difficult to attain. For example, some of the Atlantic provinces have recently started to develop antibiogram programs to track susceptibility rates. Because these are generally less used or accessible in those regions, our tool may improve accessibility and the ability to make informed therapeutic decisions. We do recommend that, wherever possible, clinicians learn how to obtain or access their local antibiogram data; another potential use for this tool is to point clinicians in the direction of how to do so for themselves.

Urban centres tend to have more accessible data than rural centres. This is likely attributable to the presence of antimicrobial stewardship programs, higher isolate counts and institutional microbiology programs that are familiar with antibiogram development and are better resourced for this

FIGURE 4 Antibiogram image from the (former) Kelsey Trail Health Region, Saskatchewan



https://maphub.net/CREAC/Antibiogram-Canada

development. Urban centres are also more likely to treat complex or seriously ill patients who may reside there or may have been referred from rural communities. These patients are more likely to have experienced failure with initial therapies or may receive broader spectrum antibiotics. Larger patient populations, more complicated infections and higher antibiotic utilization tend to increase resistance rates in urban populations. Although these factors contribute to the robustness of the data in urban centers, they also indicate that it may be inappropriate to generalize urban data to rural settings and emphasize the need for accessible rural data. We have attempted to address this with the development of our tool.

Limitations

For many regions, we were unable to attain a comprehensive data set with every hospital or health zone. This may be due to an inability to access the data from a particular region, or it may indicate that a particular region has not produced any antibiogram data. In these instances, however, one may be able to cautiously use data from neighbouring regions with similar populations under the assumption that they would have similar resistance rates.

For the purposes of this web application, we decided that only the most recent data would be posted on the interactive map. This was done to keep the interface user friendly and avoid crowding with less relevant data. Although trends can be important to consider, we believe that the most up-to-date information is of more value for a tool such as this. Therefore, clinicians who seek information on resistance trends would need to look elsewhere to obtain that information. Because the data were originally collected to analyze *E. coli* resistance to ciprofloxacin, some pins or regions on the map may demonstrate only that specific pathogen-antimicrobial data. It is important to note that in select populations (e.g., more complicated infections), other uropathogens may be more likely to be causative than in less complicated infections, for which *E. coli* is by far the predominant pathogen. Where applicable, for many of the regions where only *E. coli* was provided on the map, additional antibiogram data may be found by clicking on the source link.

Last, the study period that was analyzed in the CREAC study assessed the years 2015-2019. Therefore, the map was created with the most recently published antibiogram (usually 2019, but in some cases 2018 or earlier) from the time of data collection. Since that period, some regions may have made more recent antibiogram data available. However, even with outdated antibiograms, our application will still be beneficial

and informative as it may teach clinicians where to access this information for themselves. Resistance rates often do not change drastically from one year to the next, so the susceptibilities listed could be expected to portray a reasonably accurate estimate of local resistance rates.

Case resolution

After your assessment of your patient (including additional information that you have gathered), you agree that the prescription is indicated, but you are concerned about whether ciprofloxacin is the best choice. You recall that *E. coli* is the most prevalent pathogen in urinary tract infections so you decide to refer to your local antibiogram to assess ciprofloxacin susceptibility in *E. coli*. The antibiogram informs you that 72% of local *E. coli* isolates are susceptible to ciprofloxacin, which falls beneath the IDSA threshold of susceptibility of less than 10% resistant. You decide to adapt the prescription to another agent with more reliable susceptibility and a better tolerability profile. One week later, the patient returns to your pharmacy after he has completed his course of antibiotics to thank you, as his symptoms have resolved and he did not experience any adverse effects with his therapy. ■

From the Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta. Contact nathan.beahm@ualberta.ca.

Author Contributions: *T. Zeggil collected and inputted data into the web application, wrote the initial draft of the manuscript and edited subsequent drafts of the manuscript. D. Dobbyn collected and inputted data into the web application and reviewed and edited all drafts of the manuscript. B. Kudrowich collected and inputted data into the web application and reviewed and edited early and late drafts of the manuscript. N.P. Beahm initiated and supervised the project and reviewed and edited all drafts of the manuscript. All authors approved the final draft of the manuscript.*

Declaration of Conflicts of Interest: *No author declared any conflicts of interest.*

Funding: *The authors received no financial support for the research, authorship and publication of this article.*

ORCID iD: *Nathan P. Beahm https://orcid.org/0000-0002-5095-8570*

References

1. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52:e103-20.

2. Beahm NP, Nicolle LE, Bursey A, et al. The assessment and management of urinary tract infections in adults: guidelines for pharmacists. *Can Pharm J (Ott)* 2017;150:298-305.

3. Blondel-Hill E, Fryters S. *Bugs & Drugs*. Alberta Health Services. c1998-2020. Available: https://bugsanddrugs.org/ (accessed Jun. 26, 2021).

4. Reynolds R. Antimicrobial resistance in the UK and Ireland. *J Antimicrob Chemother* 2009;64(suppl 1):i19-23.

5. Gauthier TP, Justo JAJ. *Five important things to know about hospital antibiograms*. April 6, 2018. Available: https://www.idstewardship.com/five-important-things-know-hospital-antibiograms/ (accessed Jun. 26, 2021).

6. *Clinical and Laboratory Standards Institute*. c2021. Available: https://clsi.org/ (accessed Jun. 26, 2021).

7. *The European Committee on Antimicrobial Susceptibility Testing*. c2021. Available: https://eucast.org/ (accessed Jun. 16, 2021).

8. Lacy MK, Klutman NE, Horvat RT, et al. Antibiograms: new NCCLS guidelines, development and clinical application. *Hosp Pharm* 2004;39:542-53.

9. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia: an official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200:e45-67.

10. Pakyz AL. The utility of hospital antibiograms as tools for guiding empiric therapy and tracking resistance: insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy* 2007;27:1306-12.

11. Chao YS, Farrah K. *Fluoroquinolones for the treatment of urinary tract infection: a review of clinical effectiveness, cost-effectiveness and guidelines*. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019.

12. Food and Drug Administration. FDA Drug Safety Communication: FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together. *Drug Safety and Availability* 2016:1-2. Available: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-advises-restricting-fluoroquinolone-antibiotic-use-certain (accessed Jun. 26, 2021).

13. CADTH Technology Review. *Fluoroquinolone prescribing and use in Canadian primary care practice*. May 2017. Available: http://www.ncbi.nlm.nih.gov/books/NBK487515 (accessed Jun. 26, 2021).

14. Dobbyn D, Zeggil T, Kudrowich B, Beahm NP. Ciprofloxacin resistance rates in Escherichia coli across Canada (CREAC): a longitudinal analysis 2015-2019. *Int J Antimicrob Agents* 2022;59(3):106532.

15. Firstline. *Spectrum Mobile Health Inc*. c2016-2021 Available: https://app.firstline.org/. (accessed Jun. 26, 2021).