

---

Is clinical practice  
in agreement with  
current INESSS  
antibiotic use  
recommandations:  
Evaluation-  
associated  
challenges

April 24th, 2017



# The revolution...and its « unpredictable » drawbacks

**MAISON** du lundi au et à 12 h 1  
PARTICIPE **597-3700**

**BREAKING NEWS** Get the latest news updates all day, everyday [stcatharinesstandard.ca](#)

**HEALTH: Another senior in poor condition**  
**C. diff patient dies**

Le 5 août 2004  
**Bactérie C. difficile : peut-on contrer l'épidémie?**  
exprimez-vous sur le sujet | consultez les commentaires

La bactérie *Clostridium difficile* serait à l'origine d'une des

**Bugs resistant to antibiotics 'will kill more than cancer'**

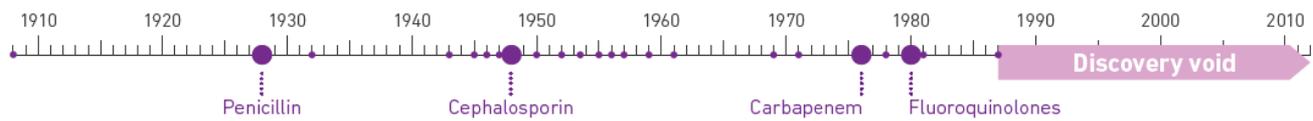
**Next epidemic? Outbreak of drug-resistant bugs**  
World Facing Antibiotics Crunch To Fight Diseases, But Fast-Tracking Medicine Approvals A Concern

**SIGHT RUINED BY ANTIBIOTIC DRUG**  
Declan, 6, 'lucky to survive' allergy

**EXCLUSIF MONTRÉAL**  
**Des superbactéries se propagent dans les hôpitaux**  
NOMBRE DE CAS D'ÉPC\* SIGNALÉS À MONTRÉAL  
39 44 52  
2012\* 2013 2014 2015 2016

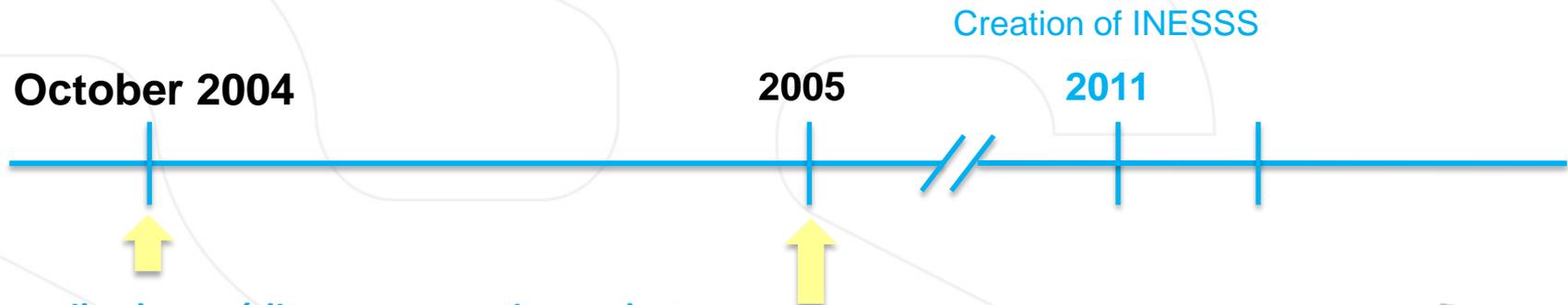
**C. difficile: une épidémie nord-américaine**  
Mise à jour le vendredi 22 octobre 2004 à 22 h 33

La nouvelle souche de la bactérie du *C. difficile* qui sévit au Québec frappe aussi six États américains. Les responsables de la santé publique aux États-Unis sont formelles: l'épidémie s'étend à tout le continent.



# Back on the antibiotic optimal use story in INESSS

- Antibiotic optimal use became a main concern in Quebec following the outbreaks of *Clostridium difficile* occurring in several hospitals and long-term facilities between 2002 and 2004.



Conseil du médicament receives the mandate from health minister to develop recommendations promoting best practices in antibiotic use for common infections in hospital, long-term facilities and primary care.

Development and mass distribution of optimal use guides + Implementation of an extensive educational program





## Impact of a Multipronged Education Strategy on Antibiotic Prescribing in Quebec, Canada

**Karl Weiss,<sup>1</sup> Régis Blais,<sup>2</sup> Anne Fortin,<sup>3</sup> Sonia Lantin,<sup>3</sup> and Michel Gaudet<sup>3</sup>**

<sup>1</sup>Department of Infectious Diseases and Microbiology, Faculty of Medicine, University of Montreal, Montreal, Canada; <sup>2</sup>Department of Health Administration, Faculty of Medicine, University of Montreal, Montreal, Canada; and <sup>3</sup>Conseil du Médicament du Québec, INESSS, Québec City, Canada



# Related costs to antibiotic prescriptions

## Quebec vs other provinces in Canada

- The cost per 1000 population decreased by  $\approx 13\%$  in Quebec between 2007 and 2003 whereas it barely decreased in the other provinces ( $\approx 0,5\%$ )

**Table 3. Costs of Outpatient Antibiotic Prescriptions per 1000 Population in Quebec (QC) and the Other Canadian Provinces (CAN) From 2003 to 2007**

Class of antibiotics	Cost of outpatient antibiotic prescriptions, CAD/1000 population									
	2003		2004		2005		2006		2007	
	QC	CAN <sup>a</sup>	QC	CAN	QC	CAN	QC	CAN	QC	CAN
Cephalosporins	2824	2640	2790	2669	2541	2880	2535	2815	2363	2667
Macrolides	6299	6265	6129	6216	6144	7131	6053	6307	5457	5991
Penicillins	2753	3490	2508	3297	2490	3581	2529	3532	2553	3580
Fluoroquinolones	5177	4327	4958	4201	4214	3934	3995	3759	4080	3946
Others	1486	1915	1692	1972	1602	2069	1639	2214	1684	2366
<b>Total</b>	<b>18 539</b>	<b>18 637</b>	18 077	18 355	16 991	19 595	16 751	18 627	<b>16 137</b>	<b>18 550</b>

**NOTE.** CAD, Canadian dollars.

<sup>a</sup> Canadian provinces other than Quebec.





# Antibiotic consumption per capita

## Quebec vs other provinces in Canada

- The total number of antibiotic prescriptions per 1000 population was 10,5% lower in Quebec in 2007 than in 2003 while it was 1,4% higher in the other provinces

**Table 1. Outpatient Antibiotic Prescriptions per 1000 Population in Quebec (QC) and the Other Canadian Provinces (CAN) From 2003 to 2007**

Class of antibiotics	Outpatient antibiotic prescriptions/1000 population									
	2003		2004		2005		2006		2007	
	QC	CAN <sup>a</sup>	QC	CAN	QC	CAN	QC	CAN	QC	CAN
Cephalosporins	70	92	67	90	61	95	62	94	58	92
Macrolides	134	144	127	135	123	148	122	141	110	137
Penicillins	155	229	143	213	140	229	141	226	141	224
Fluoroquinolones	101	79	101	83	99	88	99	89	101	91
Others	66	99	63	97	57	98	59	102	61	108
<b>Total</b>	<b>526</b>	<b>643</b>	<b>501</b>	<b>618</b>	<b>480</b>	<b>658</b>	<b>483</b>	<b>652</b>	<b>471</b>	<b>652</b>

**NOTE.** <sup>a</sup> Canadian provinces other than Quebec.



# Do we have an impact on outpatient antibiotic prescribing in the province of Quebec?

- Despite limits linked to data source, especially the absence of outpatient clinical data allowing a match between antibiotic and diagnosis, we can conclude that the expected aims were obtained for the policymakers ...
- Nevertheless, question remains for INESSS



**Do we have an impact on antibiotic optimal use with our guides, namely the best antibiotic at the right dosage and duration for the patient?**



Since INESSS creation in 2011, have international guidelines on antibiotic use and context changed?

**HAS**

**NICE**

**SHEA**

**AAO**

**FDA**

**BTS**

**IDSA**

**ASID**

**CSO-HNS**

**CSP**

**ERS-ESCMID**

**AAP**

**HC**

**WHO**

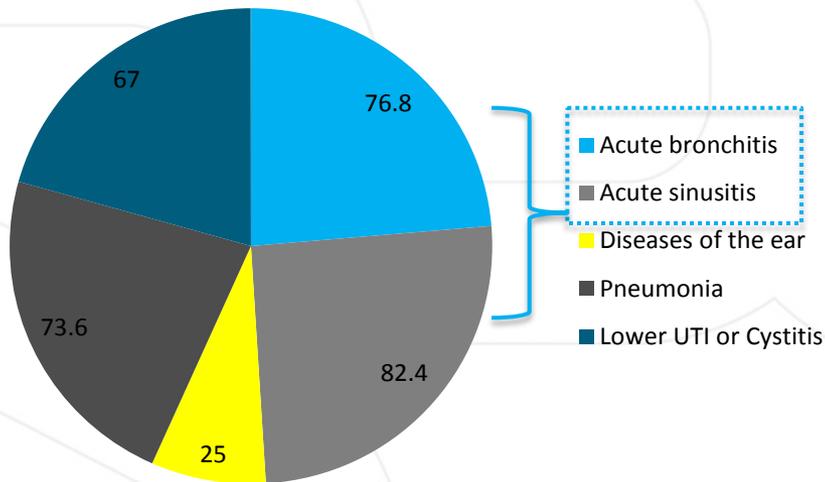
# Is antibiotic optimal use still a matter of concern?

- **Until 2011, trends are observed in International, American and Canadian guidelines as**
- more promotion of preventive interventions;
  - emphasis on the importance of clinical investigation to determine the real need for an antibiotic;
  - keeping broad spectrum antibiotics in second-line treatment especially for uncomplicated infections;
  - limiting the use of fluoroquinolone related to their disabling side effects;
  - reducing antibiotic duration.

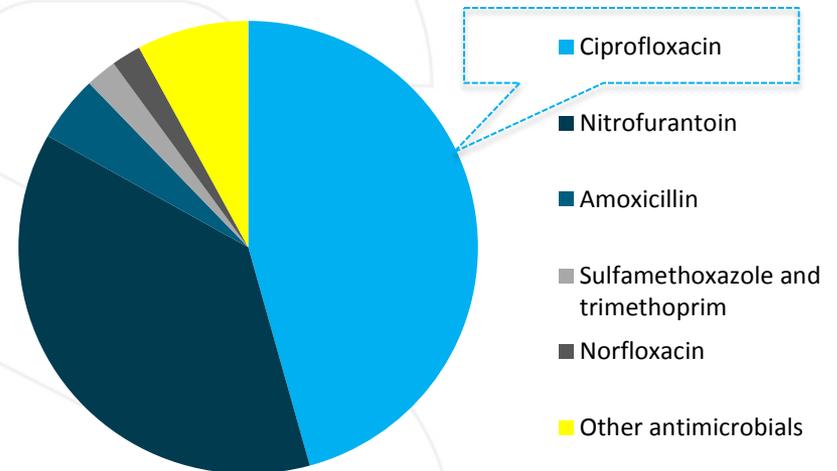
# Is antibiotic optimal use still a matter of concern?

➤ In spite of clinical guidelines, gaps between evidence-based medicine and antibiotic prescribing practices exist.

% of diagnosis with antimicrobial recommendations by office-based physicians in Canada in 2014



Number of antimicrobial recommendations for lower UTI or cystitis by office-based physicians per 10,000 inhabitants



# Is antibiotic optimal use is still a matter of concern?

- Bacterial resistance is still a concern despite local, provincial, federal and international initiatives. The phenomenon increases worldwide including Canada.

## **WHO publishes list of bacteria for which new antibiotics are urgently needed**

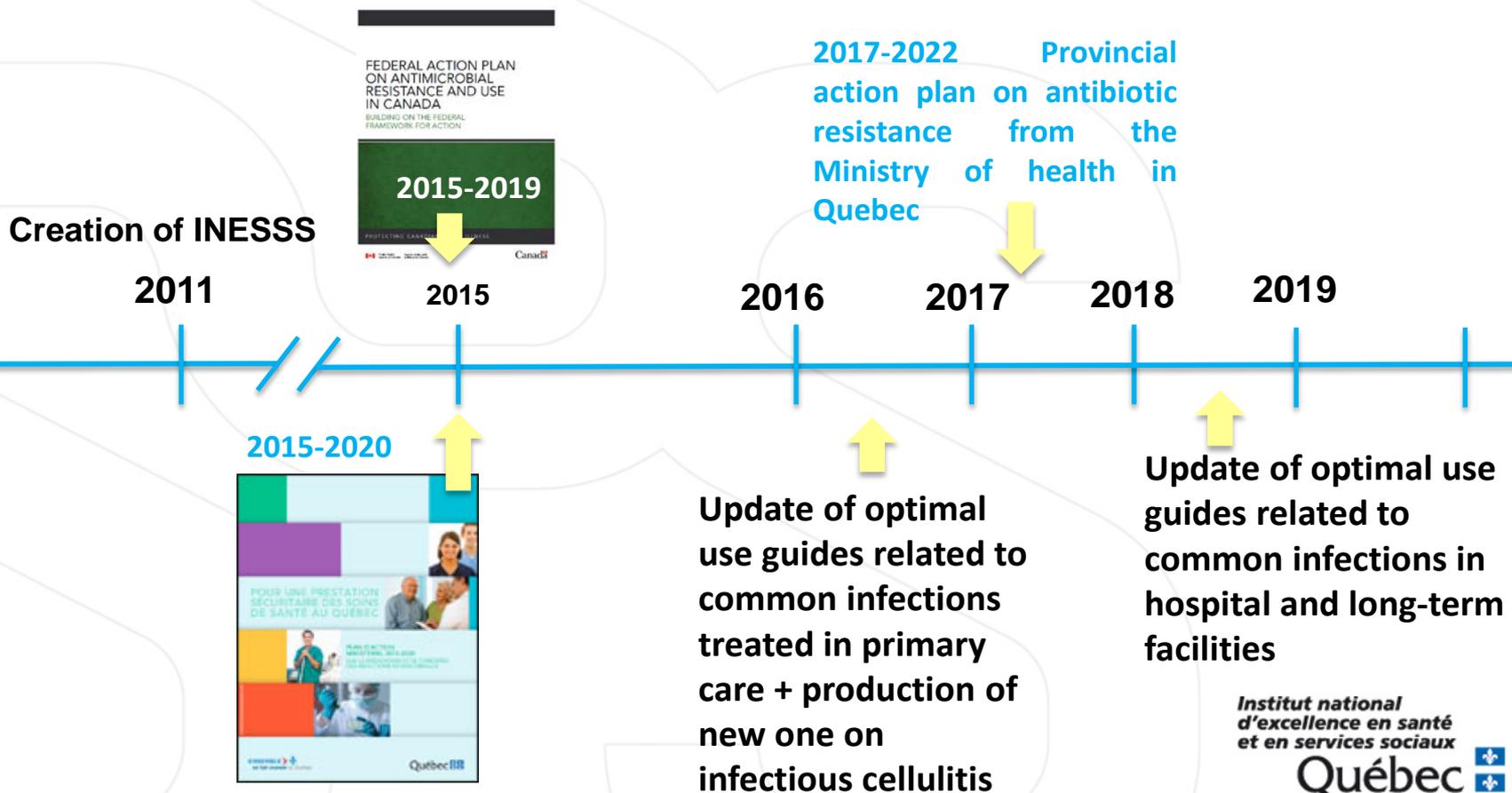
News release

27 FEBRUARY 2017 | GENEVA - WHO today published its first ever list of antibiotic-resistant "priority pathogens" – a catalogue of 12 families of bacteria that pose the greatest threat to human health.

- Unfortunately, no truly novel antibiotics have made it into the market since the mid-1980s, and it took almost two decades for those drugs to be approved for human use.

# Is antibiotic optimal use still a matter of concern?

- Improving and streamlining the use of antibiotics are a national and provincial priority.



# Is antibiotic optimal use still a matter of concern?



**Since INESSS creation in 2011, have international guidelines on antibiotic use and context changed?**



- **It is thus justified to move forward and update our guides.**

# Primarily aims pursued by the antibiotic optimal use guides

1. Support primary care professionals in their diagnosis process and help them ascertain **the genuine need** of prescribing an antibiotic

2. Help care professionals in determining the right adjuvant treatment, and if/when required the best antibiotic at the right dose and the suitable duration, based on patient health condition and characteristics (ex. allergy, comorbidities, risk of bacterial resistance)

3. Generate a standardized care for common infectious diseases, optimize and streamline use of antibiotics, especially to limit development and propagation of bacterial resistance and *C. difficile* infection

4. Promote the appropriate use of antibiotics and limit unjustified health costs because of over, under or misprescriptions

INESSS, professional associations  
facility managers & patient, citizens  
perspectives

Policymakers  
perspectives

# Evaluating the before and after release of updated guides: setting aims and identifying indicators

Searched-aims (INESSS's perspective)	Suggested indicators (outpatient)	Suggested source of data
<p>1. Support primary care professionals in their diagnosis process and help them ascertain <b>the truly need</b> of prescribing an antibiotic</p> <p>2. Help care professionals in determining the right adjuvant treatment, and if/when required the best antibiotic at the right dose and the suitable duration, based on patient health condition and characteristics (ex. allergy, comorbidities, risk of bacterial resistance)</p>	<p><b>Number of updated guides downloaded</b></p> <p><b>Number of patients with a diagnostic-antibiotic match namely on</b></p> <ul style="list-style-type: none"> <li>• class of antibiotics</li> <li>• dose</li> <li>• duration</li> </ul> <p><b>Number of patient with the appropriate antibiotic or dose based on their particular characteristics (ex. allergy to penicillins, age)</b></p> <p><b>Number of patient needing a second-line treatment</b></p> <p><b>Number of patient hospitalized following a failure of community-treatment</b></p> <p><b>Number of mismatched bug-antibiotic</b></p> <p><b>Number of patients with allergy assessed</b></p>	<p>INESSS web server</p> <p><b>Surveys to prescribers and other health professionals</b></p> <p><b>Chart review</b></p> <p>Pharmacy software review</p> <p><b>Quebec administrative database (RAMQ)</b></p> <p><b>IMS Health Canada administrative databases</b></p>

- Source of data
  - Quebec administrative databases (RAMQ)
    - Allow to analyze the global prescribing antibiotics and costs
    - Provide information for welfare and resident who are covered by Quebec's public prescription drug insurance plan
    - BUT do not to provide information for users covered with private insurance
    - And not permit to obtain reliable diagnosis informations to evaluate the appropriate use of antibiotics for outpatient (ex. infection-drug match, appropriate dose and duration).

- Source of data
  - Surveys
    - Rate of participation
    - Information bias risks
- Access to clinical data
  - Chart review require resources, **time** and ethical considerations.

- INESSS new access to administrative data
  - Will permit the linkage of many administrative databases.
  - BUT no access to drugs data in health facilities
- To access all clinical data, INESSS can collaborate with
  - Hospitals
  - Primary care settings
  - Health software providers

## Key points to remember

- Improve and streamline the use of antibiotics are an important patient safety and public health issue as well as a national priority.
- Antibiotic optimal use concerns policymakers, health professionals and patients. To have an impact on clinical practice, stakeholders need to collaborate together to optimize implementation and facilitate the use of INESSS guides.
- To evaluate the impact of optimal use guides the access to all clinical data is an important issue to be addressed by INESSS.
- We are planning on doing so in the next few years.

# Antibiotic-related optimal-use guides and tools available on web site [www.inesss.qc.ca](http://www.inesss.qc.ca)

Community acquired pneumonia, acute exacerbation COPD and acute bronchitis, UTI and infectious cellulitis guides available soon...

Tools for allergy to penicillins

**MÉDICAMENT ANTIBIOTIQUES**  
OTITE MOYENNE AIGÜE (OMA) CHEZ L'ENFANT DE 3 MOIS ET PLUS

**MÉDICAMENT ANTIBIOTIQUES**  
PNEUMONIE ACQUISE EN COMMUNAUTÉ CHEZ L'ENFANT DE 3 MOIS ET PLUS

**MÉDICAMENT ANTIBIOTIQUES**  
RHINOSINUSITE AIGÜE CHEZ L'ENFANT

**MÉDICAMENT ANTIBIOTIQUES**  
PHARYNGITE-AMYGDALECTE CHEZ L'ENFANT ET L'ADULTE

**MÉDICAMENT ANTIBIOTIQUES**  
RHINOSINUSITE AIGÜE CHEZ L'ADULTE

**MÉDICAMENT ANTIBIOTIQUES**  
PHARYNGITE-AMYGDALECTE CHEZ L'ENFANT ET L'ADULTE

**MÉDICAMENT ANTIBIOTIQUES**  
RHINOSINUSITE AIGÜE CHEZ L'ADULTE

**MÉDICAMENT ANTIBIOTIQUES**  
RHINOSINUSITE AIGÜE CHEZ L'ADULTE

**GÉNÉRALITÉS**

**CONSIDÉRATIONS IMPORTANTES**

**AGENTS PATHOGÈNES**

**MESURES PRÉVENTIVES**

**DIAGNOSTIC**

**RHINOSINUSITE AIGÜE**

**POUR POSER LE DIAGNOSTIC DE RHINOSINUSITE AIGÜE, LA PRÉSENCE DE PLUS D'UN SYMPTÔME PRINCIPAL EST NÉCESSAIRE**

**Symptômes principaux:**

- Douleur faciale ou dentaire unilatérale
- Œdème du gonflement nasale
- Rhinorrhée colorée antérieure ou postérieure

**Autres symptômes à considérer:**

- Écoulement
- Hyposmia/hyposmétrie
- Fièvre

**Les examens du nez et de l'arrière-gorge sont appropriés afin de:**

- rechercher, à l'aide d'un otoscope, la présence de sécrétions purulentes entre le nez et la gorge latérale du nez (test moyen).
- vérifier la présence de sécrétions dans l'arrière-gorge.
- La palpation/pression des sinus maxillaires ou frontaux peut être utile au diagnostic.

**INESSS**  
LE SAVOIR PREND FORME

Processus d'aide au diagnostic en cas d'allergie soupçonnée ou confirmée aux pénicillines

**Aide mémoire en cas d'allergie soupçonnée ou confirmée aux pénicillines**

**Outil d'aide à la décision en cas d'allergie soupçonnée ou confirmée aux pénicillines**

**Réaction**

Le risque de réaction croisée est généralement et révélatrice

La réaction (1<sup>re</sup> génération et 2<sup>e</sup> génération) de pénicillines de structure chimique semblant relativement faibles (H)

Les dérivés de structure chimique de 1<sup>re</sup> et 2<sup>e</sup> génération de pénicillines semblent équivalente

Le risque de réaction allergique est faible (estimation: 1-2%)

**Tableau de décision:**

Réaction	Non sévère	Sévère	Très sévère
<ul style="list-style-type: none"> <li>• Éruption maculo-papuleuse</li> <li>• Œdème nasale</li> <li>• Œdème labial</li> <li>• Œdème de Quincke</li> </ul>	<ul style="list-style-type: none"> <li>• Anaphylaxie</li> <li>• Réaction anaphylactique</li> <li>• Allergie aux céphalosporines</li> <li>• Allergie aux carbapénèmes</li> <li>• Anémie hémolytique</li> <li>• Anémie aplasique</li> <li>• DGS (DGS)</li> <li>• SJS/TSS</li> </ul>	<ul style="list-style-type: none"> <li>• Choc anaphylactique</li> <li>• Anoxie ou cyanose</li> <li>• Anémie hémolytique</li> <li>• Anémie aplasique</li> <li>• DGS (DGS)</li> <li>• SJS/TSS</li> </ul>	<ul style="list-style-type: none"> <li>• Choc anaphylactique</li> <li>• Anoxie ou cyanose</li> <li>• Anémie hémolytique</li> <li>• Anémie aplasique</li> <li>• DGS (DGS)</li> <li>• SJS/TSS</li> </ul>

**Tableau de décision:**

Risque de réaction croisée entre les pénicillines	Céphalosporines (C 1, 2, 3, 4)	Carbapénèmes (C 1, 2, 3, 4)
Non sévère	Céphalosporines (C 1, 2, 3, 4) <b>Non sévère</b>	Carbapénèmes (C 1, 2, 3, 4) <b>Non sévère</b>
Sévère	Céphalosporines (C 1, 2, 3, 4) <b>Sévère</b>	Carbapénèmes (C 1, 2, 3, 4) <b>Sévère</b>
Très sévère	Céphalosporines (C 1, 2, 3, 4) <b>Très sévère</b>	Carbapénèmes (C 1, 2, 3, 4) <b>Très sévère</b>

**Administration standard:** Une période d'observation d'au moins 1 heure après l'administration de la 1<sup>re</sup> dose permet d'être convaincu.

**Administration non standard:** Une surveillance rapprochée est recommandée pendant 2 heures après l'administration de la 1<sup>re</sup> dose.

**Administration en cas de réaction allergique:** Une surveillance rapprochée est recommandée pendant 2 heures après l'administration de la 1<sup>re</sup> dose.

**Administration en cas de réaction allergique sévère:** Une surveillance rapprochée est recommandée pendant 2 heures après l'administration de la 1<sup>re</sup> dose.

English versions of antibiotic guides coming soon...



**Institut national d'excellence et en service**

**ALLERGIES MÉDICAMENTEUSES**  
Définitions et manifestations cliniques

**Uтил interactif**

**Thank you**

---

inesss.qc.ca  
[inesss@inesss.qc.ca](mailto:inesss@inesss.qc.ca)

2535, boulevard Laurier, 5e étage  
Québec (Québec) G1V 4M3

2021, avenue Union, bureau 10.083  
Montréal (Québec) H3A 2S9

# Question\_Example with urinary tract infection

Can you give us a concrete example of how INESSS can evaluate if clinician adhere to the updated recommendations?

- *I will give you an example with URINARY TRACT INFECTION.*
- *We can primarily decide to evaluate several periods to look at outpatient practice evolution before the first intervention between 2002 and 2004, after the publication of the first serie of guides between 2005 and 2007, after the first update of guides between 2010 and 2012 and finally after the publication of the current update between mid-2017 and mid-2019.*

# Question\_Example with urinary tract infection

- *Next we can choose ANTIBIOTIC for which recommendation have changed over time either on treatment line, dosage or duration.*
  - *In this particular example we can evaluate the use of fluoroquinolones for uncomplicated urinary tract infection which will pass on second-line treatment in 2017 version. Sulfonamide ,nitrofurantoin and fosfomycine-trométanol , which is on drug's list, covered by Quebec public insurance until 2013, will be positioned in first-line treatment.*
- *We can also verify if modified recommandatrions let some bad outcomes.*
- *To evaluate all of these indicators we can used different method.*
- *We should use Administrative databases administered by the RAMQ. With unique encrypted health insurance number, drug plan admissibility, beneficiary information,prescription and medical services claims databases can be merged.*
- *Next to validate clinical informations like diagnosis we can do chart review and collaborate with partners to reach more data*
- *Finally to verify bad outcome, like complication, we can merge data from MED-ECHO to get information on patient-needed hospitalization.*
- *During interpretation it will be important to take into account factors that can influence antibiotic prescriptions like seasonal variations and infection outbreaks in some area*

## 2005 version

## 2009 version

Treatment of uncomplicated urinary tract infections*			
Antibiotic <sup>†</sup>	Oral dosage	Duration	
<b>Fluoroquinolone</b>			
Ciprofloxacin (Cipro <sup>®</sup> )	250 mg every 12 hours	3 days	
Ciprofloxacin XL (Cipro XL <sup>®</sup> )	500 mg every 24 hours		
Levofloxacin (Levaquin <sup>®</sup> )	250 mg every 24 hours		
Norfloxacin (Norflox <sup>®</sup> generic)	400 mg every 12 hours		
Ofloxacin (Oflox <sup>®</sup> generic)	200 mg every 12 hours		
<b>Sulfonamide</b>			
TMP-SMX (Septra DS <sup>®</sup> generic)	1 tab. every 12 hours	7 days	
TMP (Apo-Trimethoprim <sup>®</sup> )	100 mg every 12 hours		
<b>Other</b>			
Nitrofurantoin (Macrobid <sup>®</sup> )	100 mg every 12 hours		
Nitrofurantoin (Novo-Furantoin <sup>®</sup> )	50-100 mg every 6 hours		
<b>β-lactams</b>			
Amoxicillin-clavulanate potassium (Clavulin <sup>®</sup> )	250 mg every 8 hours or 500 mg every 12 hours	7 days	
Narrow spectrum cephalosporins <sup>‡</sup> ex. : Cefadroxil (Duricef <sup>®</sup> )	500 mg every 12 hours		

## 2017 version

Whereas sulfonamide and nitrofurantoin will be in first-line, fluoroquinolone will be in second-line treatment for uncomplicated urinary tract infection. The duration and dosage will remain similar for all.

## Question

- We could also investigate physician's characteristics associated with INESSS recommendation mismatch to even think about strategies to improve their adherence.

- Why it is difficult for a clinician to change its practice?
  - *Barriers to prescribing antibiotics appropriately can include clinician knowledge gaps about best practices and clinical practice guidelines, clinician perception of patient expectations for antibiotics, perceived pressure to see patients quickly, or clinician concerns about decreased patient satisfaction with clinical visits when antibiotics are not prescribed.*