

Antimicrobial Resistant *Neisseria gonorrhoeae* in Canada: a National Perspective

Antibiotic Awareness Week Webinar - November 16, 2012

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PROTECTING CANADIANS FROM ILLNESS



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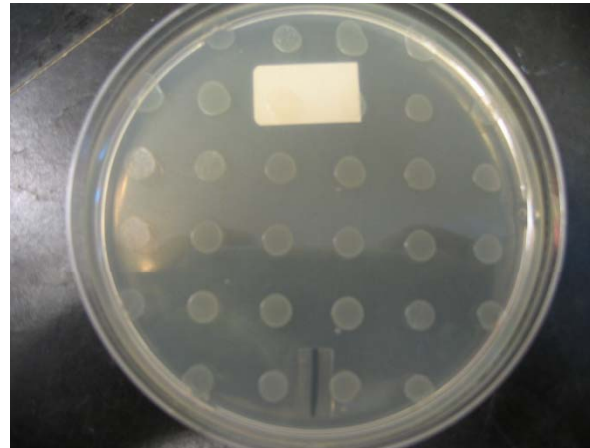
Background

- NML program is a passive surveillance system monitoring antimicrobial susceptibilities of *Neisseria gonorrhoeae* (GC) since mid-80's – 35000 isolates
- As infection rates increase fewer cultures are available for testing due to an increase in Nucleic Acid Amplification Tests (NAAT) for diagnosis
- Worsening *Neisseria gonorrhoeae* drug resistance will compromise effective treatment and disease control efforts.

International Attention

- There is an increase in the global prevalence of antimicrobial resistant (AMR) *Neisseria gonorrhoeae* (GC) and of specific concern emerging resistance to third generation Cephalosporins.
- The WHO has identified AMR-GC as a global health issue since the MICs for Cephalosporins and Azithromycin continues to increase.
- On June 6, 2012 the World Health Organization (WHO) released the “*Global action plan to control the spread and impact of antimicrobial resistance in Neisseria gonorrhoeae*”.
 - http://whqlibdoc.who.int/publications/2012/9789241503501_eng.pdf

Agar Dilution Method for Determination of Minimum Inhibitory Concentration (MIC) using Clinical and Laboratory Standards Institute (CLSI) method.

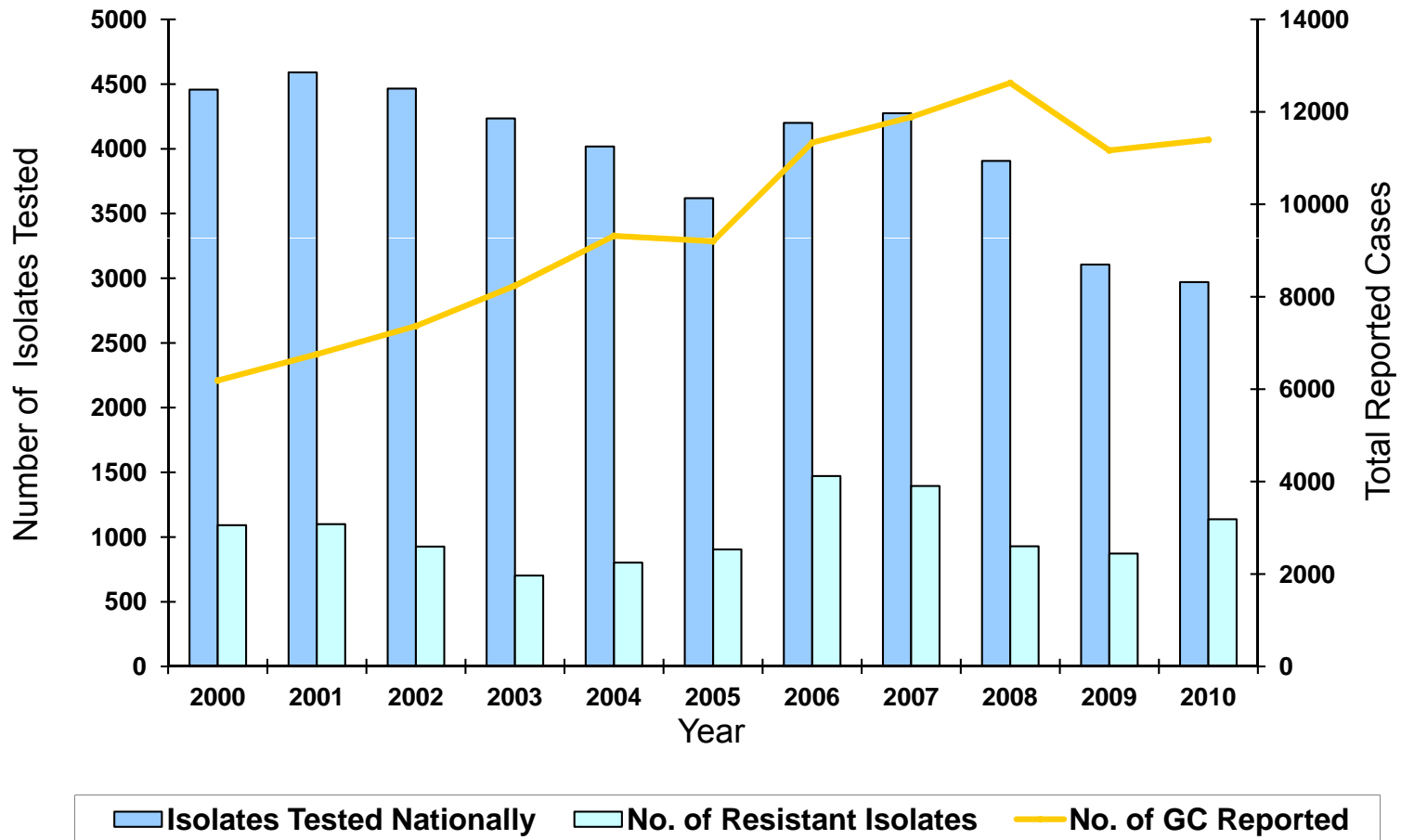


Penicillin - Tetracycline - Erythromycin -
Spectinomycin - Ciprofloxacin - Ceftriaxone
Cefixime - Azithromycin

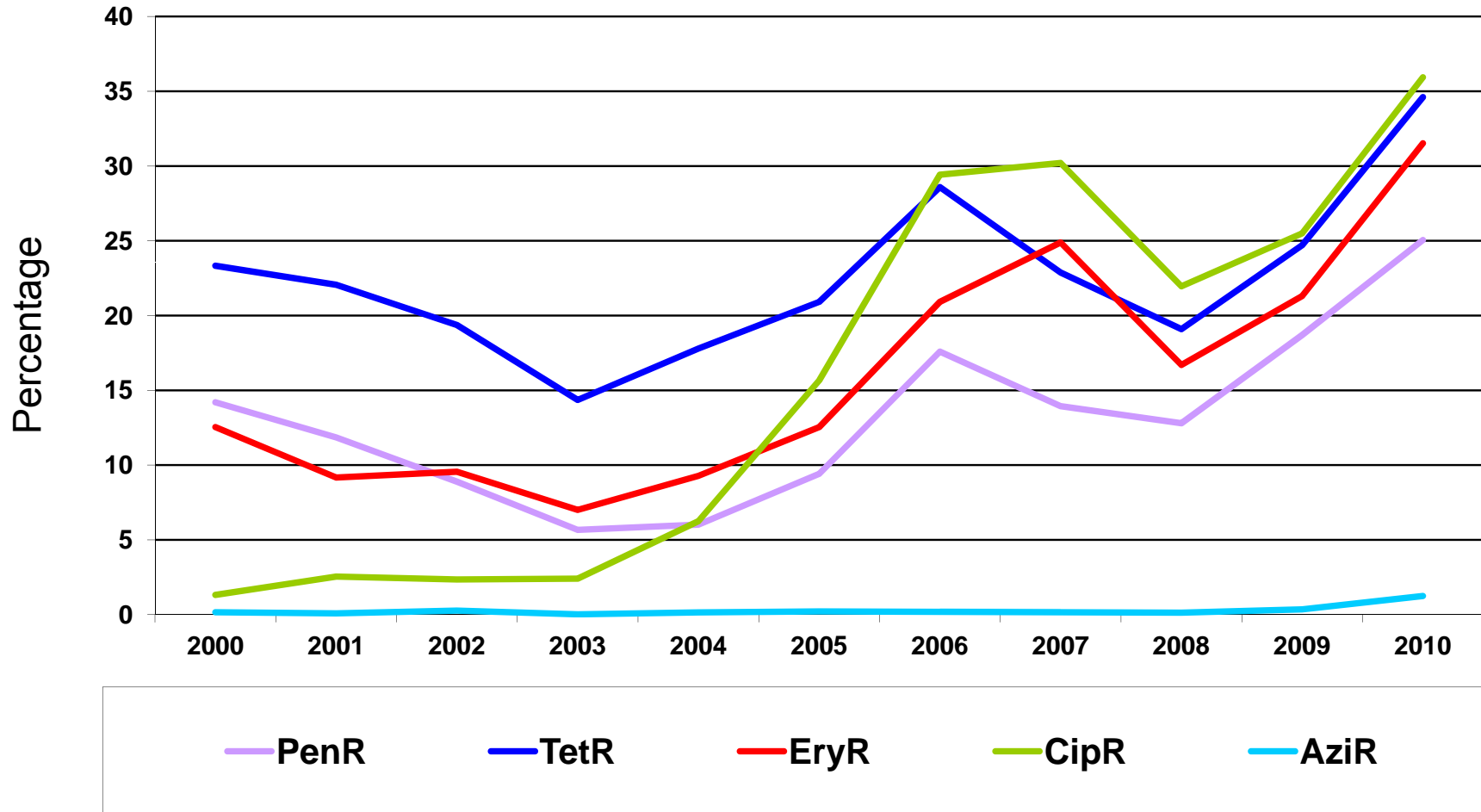
Neisseria gonorrhoeae Antimicrobial Resistance Characterization Definitions

	Characterization	Definition
PPNG	Penicillinase Producing <i>Neisseria gonorrhoeae</i>	Pen MIC \geq 2.0 mg/L, β -lactamase positive, β -lactamase plasmid (3.05, 3.2 or 4.5 Mdal plasmid)
TRNG	Tetracycline Resistant <i>Neisseria gonorrhoeae</i>	Tet MIC \geq 16.0 mg/L, 25.2 Mdal plasmid, TetM PCR positive
CMRNG	Chromosomal Mediated Resistant <i>Neisseria gonorrhoeae</i>	Pen MIC \geq 2.0 mg/L, Tet MIC \geq 2.0 mg/L but \leq 8.0 mg/L, and Ery MIC \geq 2.0 mg/L
Probable CMRNG	Probable Chromosomal Mediated Resistant <i>Neisseria gonorrhoeae</i>	One of the MIC values of Pen, Tet, Ery = 1 mg/L, the other two \geq 2.0 mg/L
PenR	Penicillin Resistant <i>Neisseria gonorrhoeae</i>	Pen MIC \geq 2.0 mg/L, β -lactamase negative
TetR	Tetracycline Resistant <i>Neisseria gonorrhoeae</i>	Tet MIC \geq 2.0 mg/L but \leq 8.0 mg/L
EryR	Erythromycin Resistant <i>Neisseria gonorrhoeae</i>	Ery MIC \geq 2.0 mg/L
CipR	Ciprofloxacin Resistant <i>Neisseria gonorrhoeae</i>	Cip MIC \geq 1.0 mg/L
AzR	Azithromycin Resistant <i>Neisseria gonorrhoeae</i>	Az MIC \geq 2.0 mg/L
SpecR	Spectinomycin Resistant <i>Neisseria gonorrhoeae</i>	Spec R \geq 128 mg/L
CxNS	Ceftriaxone Non-susceptible <i>Neisseria gonorrhoeae</i>	Cx MIC \geq 0.5 mg/L
CeNS	Cefixime Non-susceptible <i>Neisseria gonorrhoeae</i>	Ce MIC \geq 0.5 mg/L

Neisseria gonorrhoeae Isolates in Canada, 2000 to 2010



Antimicrobial Susceptibility of *Neisseria gonorrhoeae* Isolates Tested in Canada Between 2000-2010

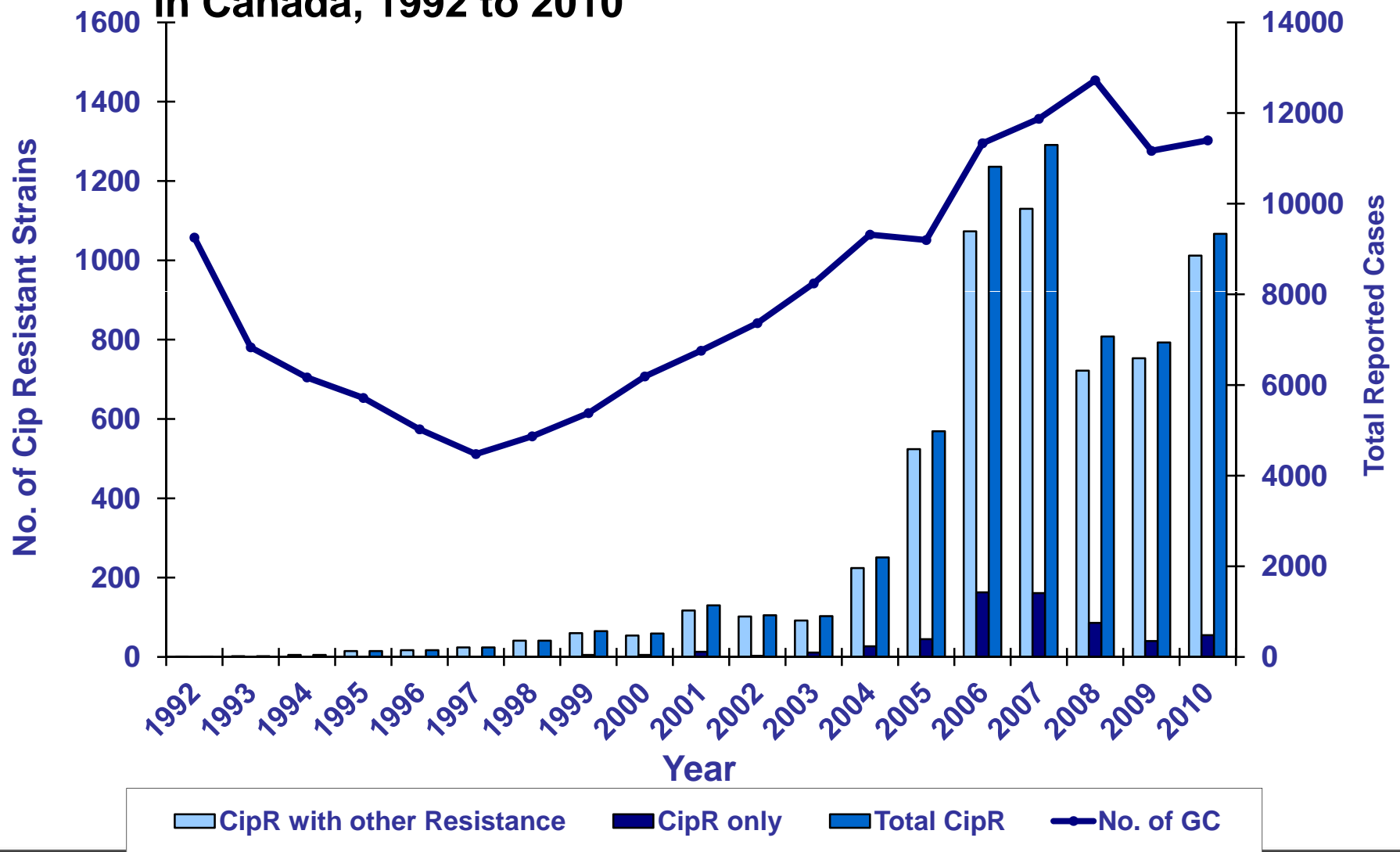


Percentage based on total number of isolates tested nationally

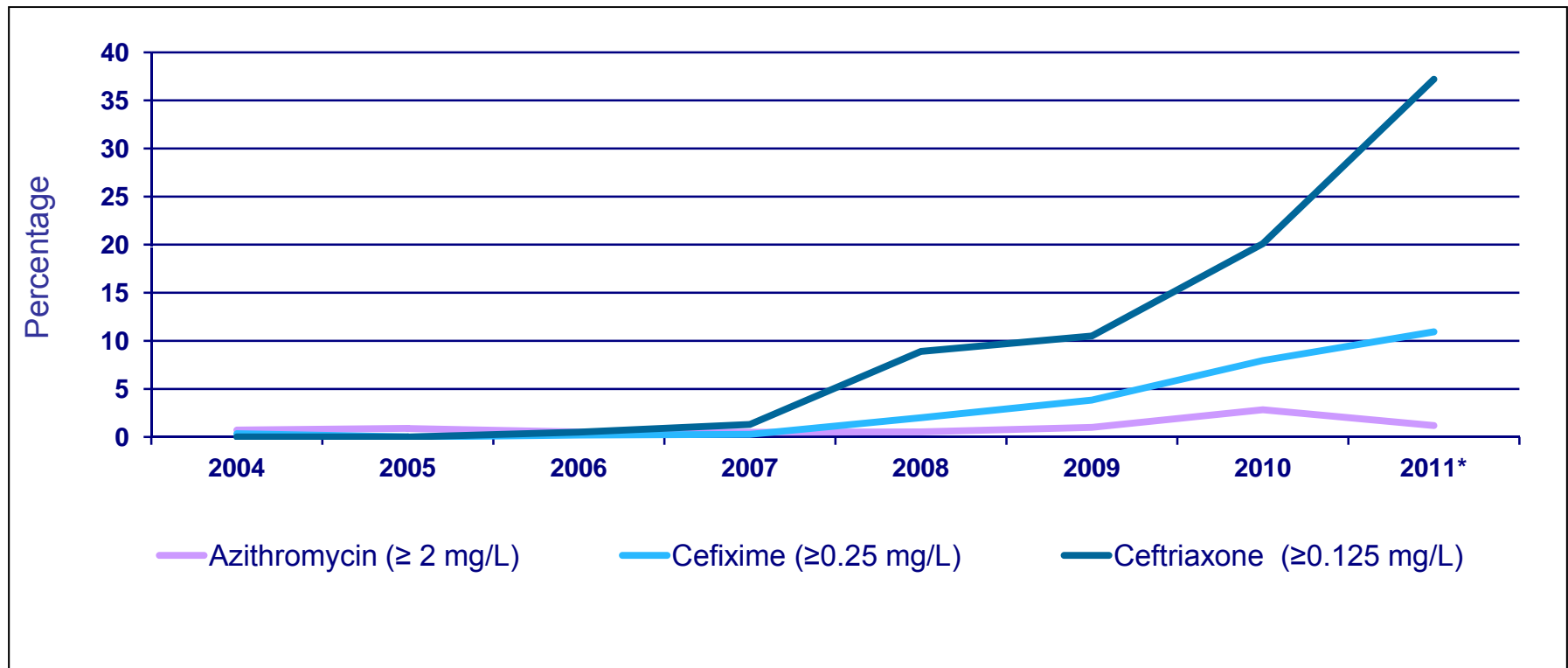
AMR emergence in *Neisseria gonorrhoeae* over time

- 1970's - more chromosomal penicillin resistance and penicillinase producing GC (PPNG)
- 1980's – spectinomycin resistant GC
- 1990's – fluoroquinolone resistant GC
- 2000's – 3rd generation cephalosporins?

Ciprofloxacin Resistant *Neisseria gonorrhoeae* Strains in Canada, 1992 to 2010



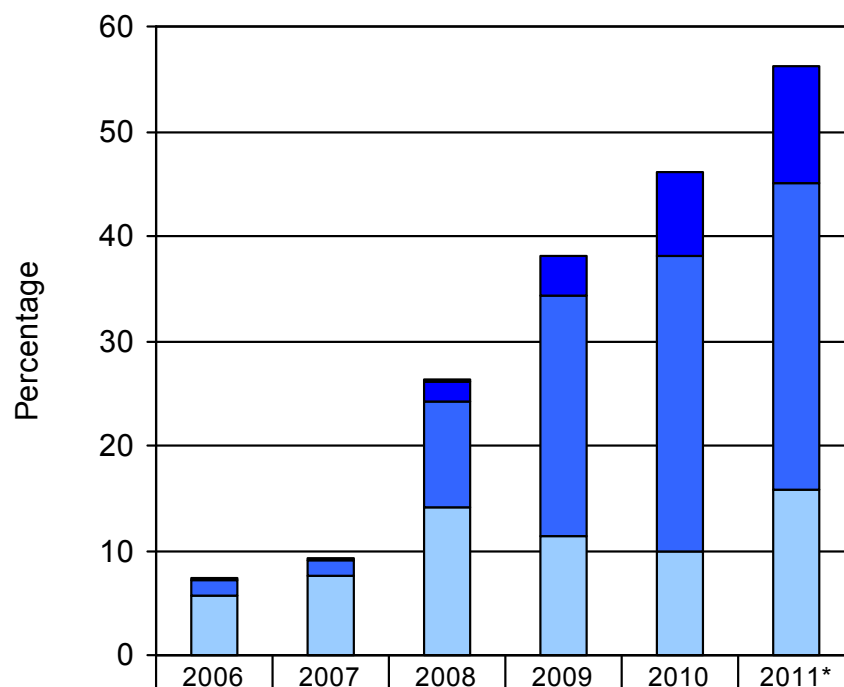
***Neisseria gonorrhoeae* Isolates with Decreased/Non Susceptibility to Cefixime and Ceftriaxone and Resistance to Azithromycin, 2004 and 2011**



Cefixime and Ceftriaxone Includes MICs using WHO Criteria for Decreased Susceptibility to Cephalosporins (2012): Cefixime ≥ 0.25 mg/L and Ceftriaxone ≥ 0.125 mg/L
Azithromycin Includes MICs Resistant ≥ 2.0 mg/L

*preliminary data as of November 1, 2012

Trends of **Cefixime** Susceptibilities of *Neisseria gonorrhoeae* Isolates Received by NML from 2006 to 2011



Note – a steady increase of isolates with MIC=0.25 mg/L between 2007 and 2011

*preliminary data as of August 31, 2012

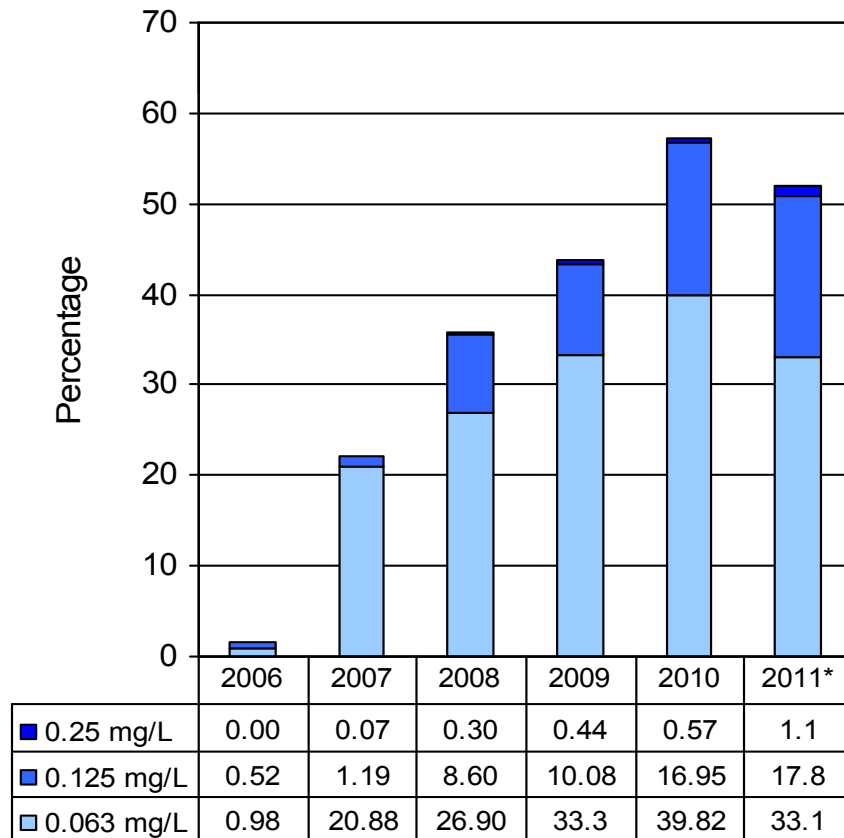
	2006	2007	2008	2009	2010	2011*
■ 0.5 mg/L	0.00	0.07	0.11	0.00	0.00	0.00
■ 0.25 mg/L	0.20	0.21	1.90	3.83	7.95	11.2
■ 0.125 mg/L	1.31	1.47	10.03	22.89	28.14	29.2
■ 0.063 mg/L	5.76	7.61	14.20	11.39	9.98	15.8

Percentages were calculated using the total number of viable isolates (both resistant and susceptible isolates) tested by NML as the denominator (N).

Total Isolates Tested at NML

2006	2007	2008	2009	2010	2011
1528	1432	947	912	1233	833*

Trends of **Ceftriaxone** Susceptibilities of *Neisseria gonorrhoeae* Isolates Received by NML from 2006 to 2011



Note – a steady increase of isolates with MIC=0.125 mg/L between 2007 and 2011

Isolates with MIC=0.25 increased from 0.07% to 1.1% between 2007 and 2011

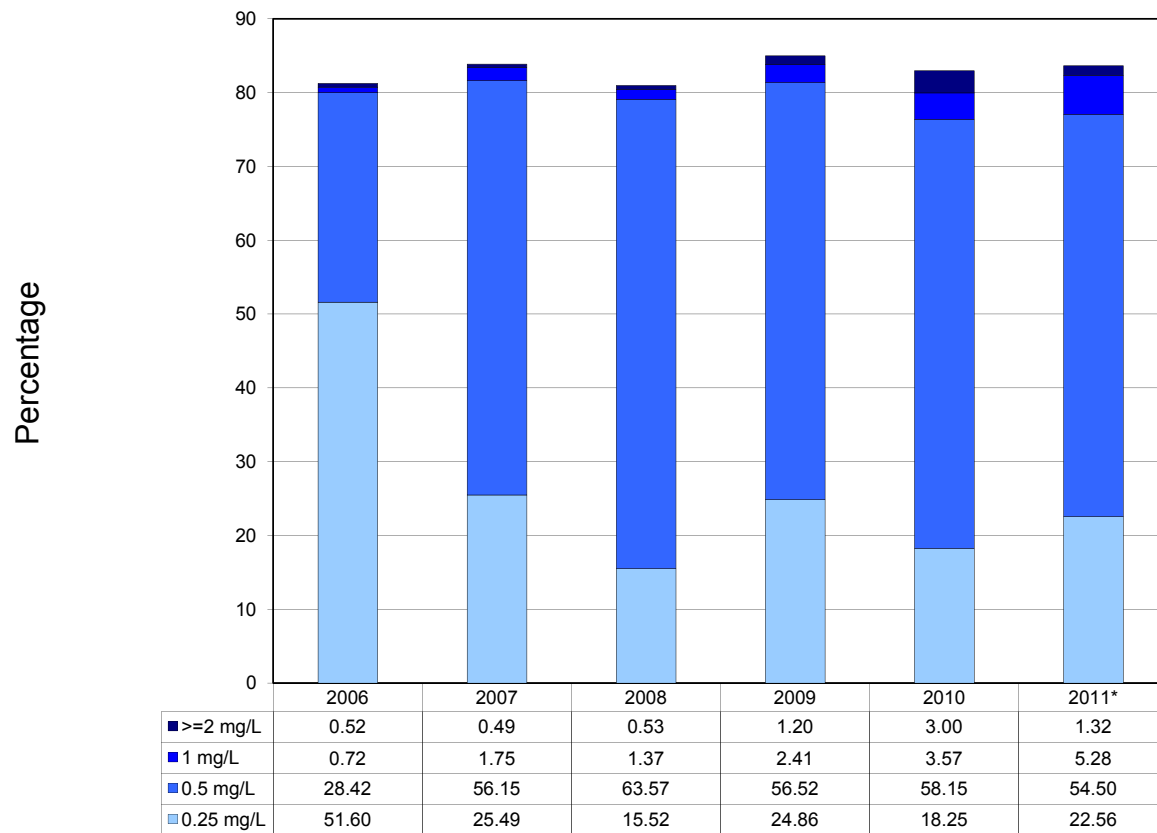
*preliminary data as of August 31, 2012

Percentages were calculated using the total number of viable isolates (both resistant and susceptible isolates) tested by NML as the denominator (N).

Total Isolates Tested at NML

2006	2007	2008	2009	2010	2011
1528	1432	947	912	1233	833*

Trends of **Azithromycin** Susceptibilities of *Neisseria gonorrhoeae* Isolates Received by NML from 2006 to 2011



Note – a steady increase of isolates with MIC=1.0 mg/L between 2006 and 2011

Isolates with Resistant MIC=2.0 fluctuate from 0.5% in 2006 to a high of 3.0% in 2010.

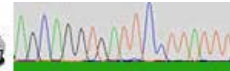
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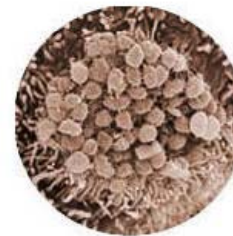
http://www.ng-mast.net/



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PLEASE NOTE: We are migrating to faster servers and there may be minimal disruption for the next 24 hours - apologies for inconvenience

Neisseria gonorrhoeae



- ▣ [Organism Specific Information](#)
- ▣ [N. gonorrhoeae Links](#)
- ▣ [Download Alleles | STs](#)
- ▣ [NRDB allele assignment](#)
- ▣ [Starting your own NG-MAST study?](#)
- ▣ [Contact Curator](#)
- ▣ [Administration](#)

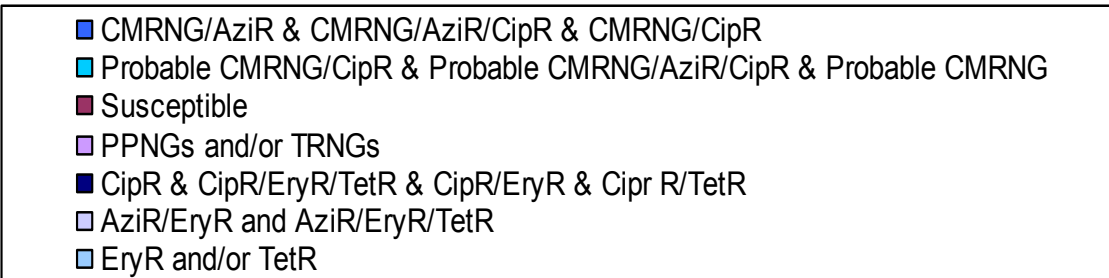
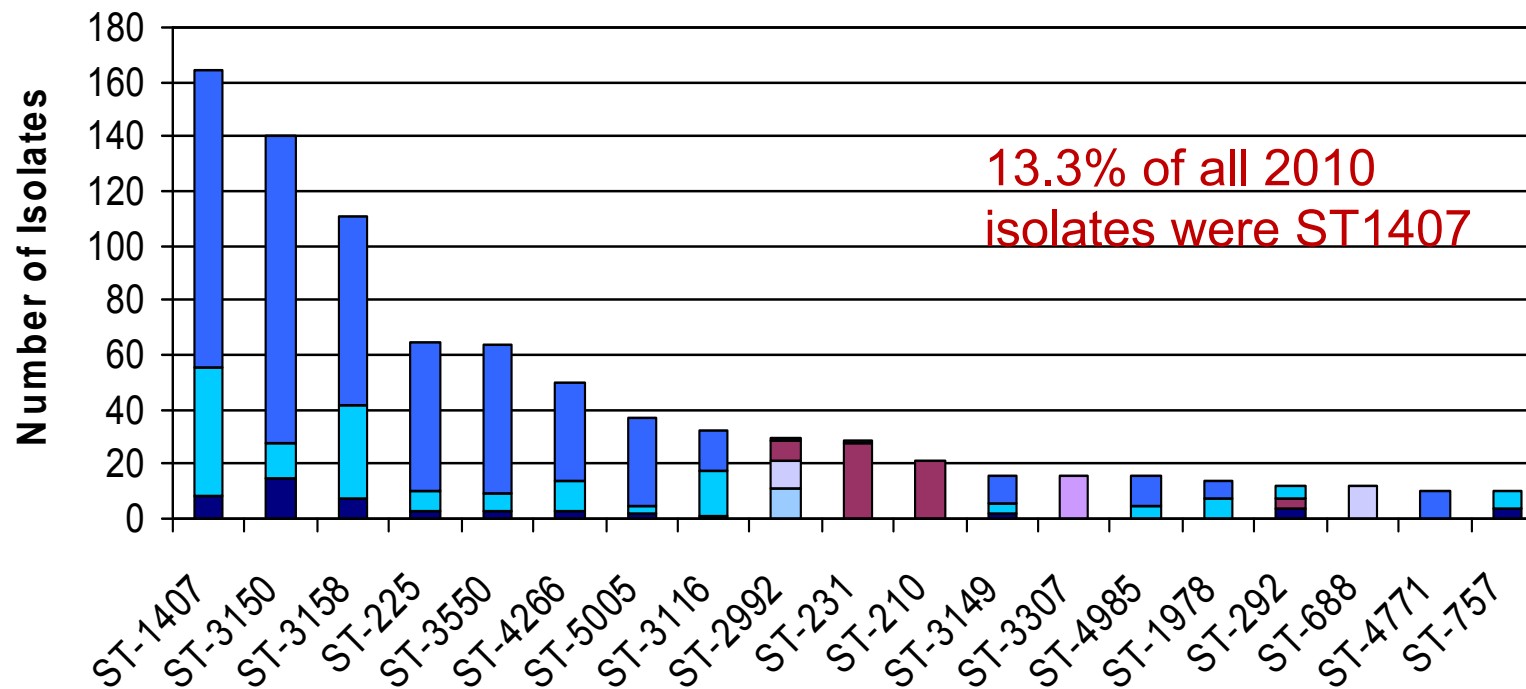
Query global sequence and ST database

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Martin IM, Ison CA, Aanensen DM, Fenton KA, Spratt BG. Rapid Sequence-Based Identification of Gonococcal Transmission Clusters in a Large Metropolitan Area. *J Infect Dis.* 2004 Apr 15;189(8):1497-1505.

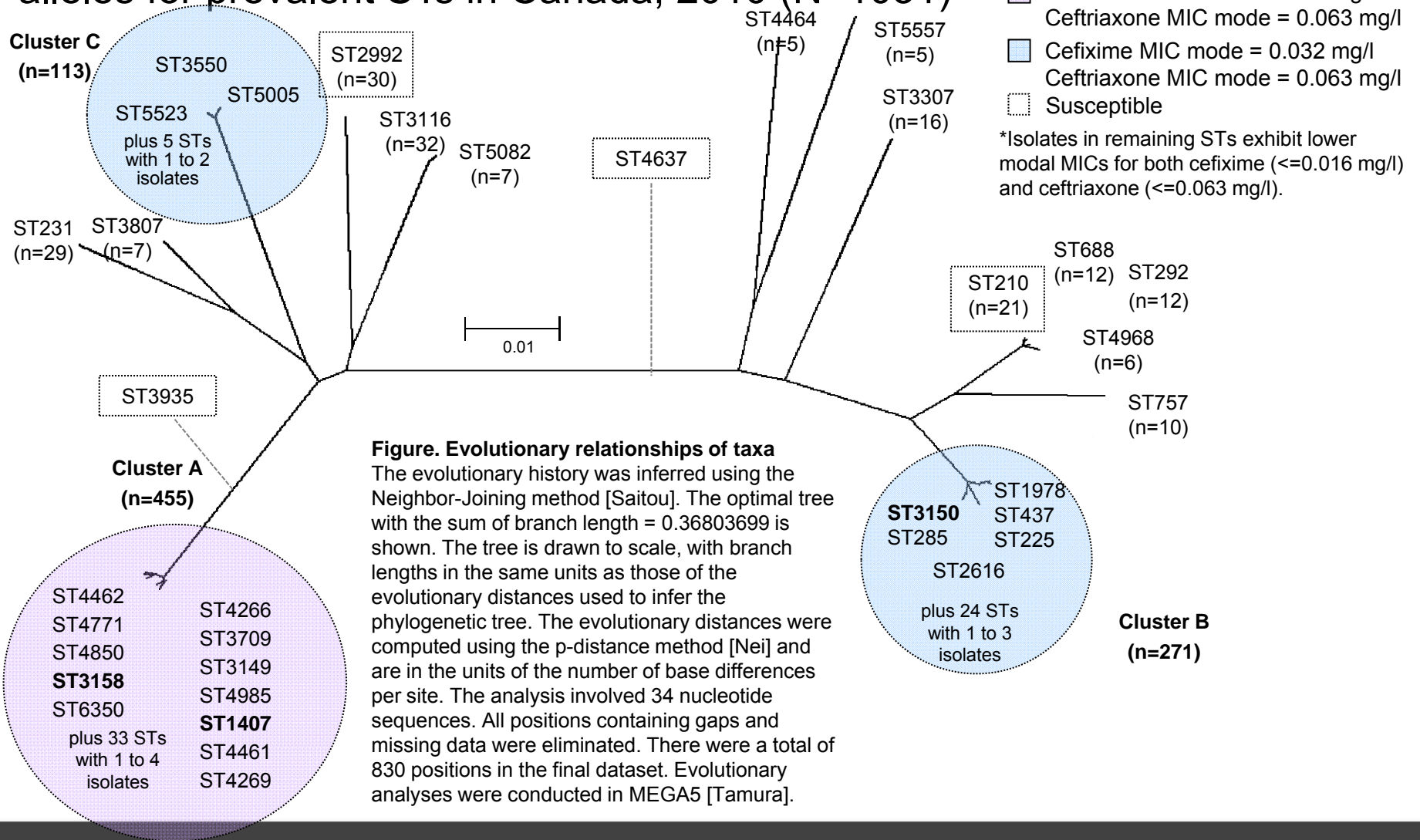
The NG-MAST databases and website are hosted at the Department of Infectious Disease Epidemiology, Imperial College London and are funded by The Wellcome Trust

Distribution of Resistance Characterizations within *Neisseria gonorrhoeae* NG-MAST Sequence Types, 2010; N=849*



*The remaining isolates (n=384) are dispersed among 230 sequence types (STs) containing 1 to 9 isolates each and exhibit a variety of resistance/susceptibility patterns.

Phylogenetic reconstruction of concatenated sequences of *por* and *tbpB* alleles for prevalent STs in Canada, 2010 (N=1031)



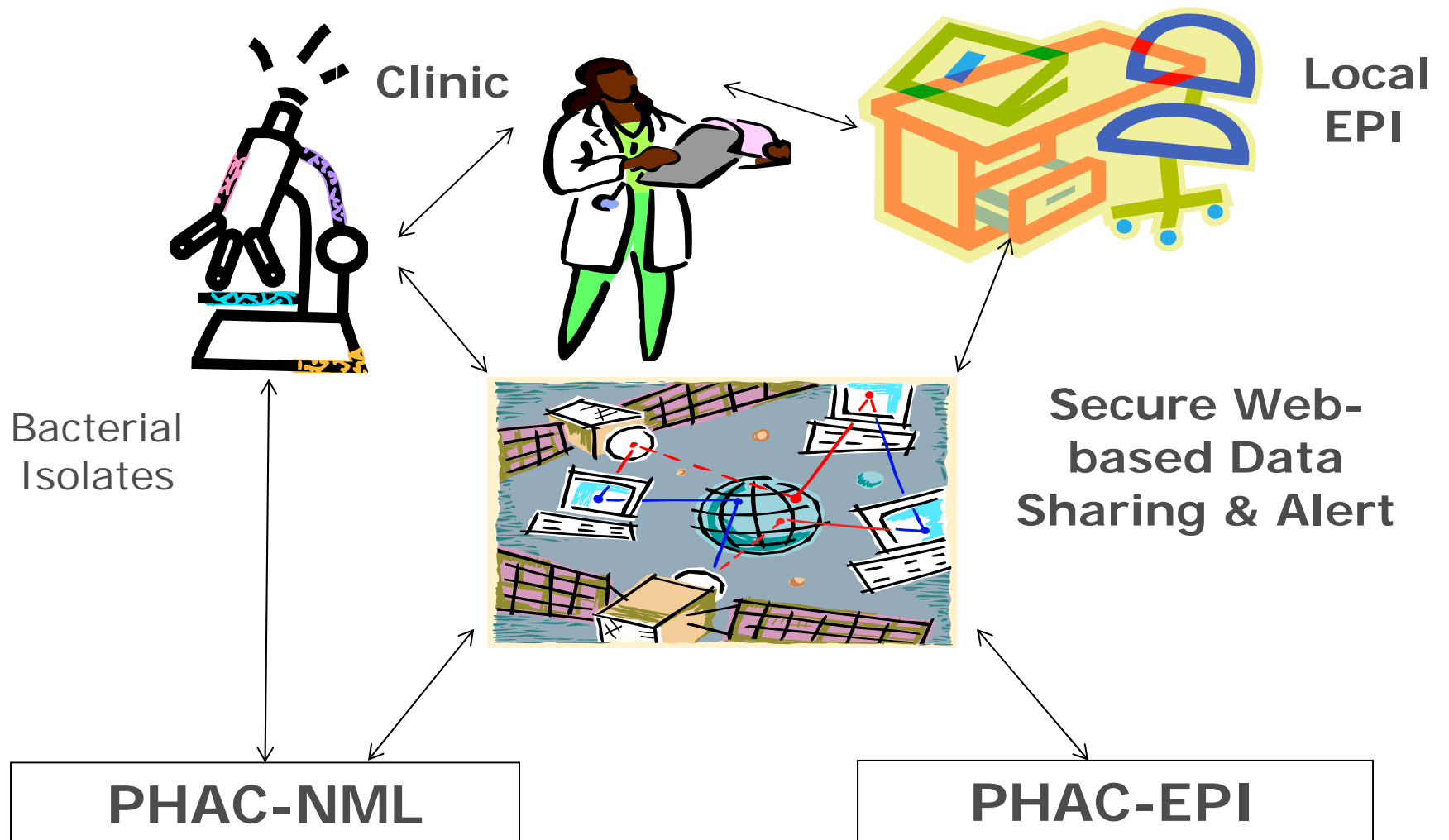
International ST1407

- First identified in Scotland in 2007 and accounted for 15.4% of all typed isolates
- Also reported in Austria, France, Norway, Spain, Netherlands, Sweden, California, Australia, Japan, UK
- Japan study 6.7% of all tested isolates (n=242) ST1407 (Tanaka, 2011)
- Slovenia 2011 pharyngeal ceftriaxone treatment failure (Unemo, 2012)
- France 2011 urethral cefixime treatment failure (Unemo, 2012)

Proposal – Sentinel Site Surveillance Program to Improve Gonorrhea Antimicrobial Resistance (AMR) Assessment in Canada

- Integrated laboratory, clinical and epidemiologic data
- Standardized sampling framework and susceptibility testing panels
- Objectives
 1. To assess the trends of *N. gonorrhoeae* antimicrobial resistance and treatment failure in Canada in order to develop population-level public health interventions and inform STI Treatment Guidelines
 2. To use NG-MAST typing to characterize both antimicrobial susceptible and resistant strains of gonorrhea in order to understand the spread of strains in Canada

Proposed Data and Isolate Flow for *Neisseria gonorrhoeae* Sentinel Site Surveillance System



Canadian Network for Public Health Intelligence (CNPHI) and the Laboratory Reporting Collaboration Centre

- Currently being used by the NML *Neisseria gonorrhoeae* laboratory, allows sharing of test result data with our provincial partners in a timely fashion
- A secure web-based platform which facilitates data and information exchange in an efficient and convenient manner
- Additional functionality by allowing our clients to access:
 - » Current real-time data
 - » Annual summary reports
 - » Sample testing statuses
 - » New on-line cluster analyzer

Acknowledgements

Canadian Provincial Public Health Laboratories

British Columbia Centre for Disease Control

Provincial Laboratory of Public Health Alberta

Saskatchewan Disease Control Laboratory

Cadham Provincial Laboratory

Public Health Laboratories, Public Health Ontario

Laboratoire de santé publique du Québec

Queen Elizabeth II Health Science Centre

New Brunswick Regional Hospitals

Newfoundland Public Health Laboratory

Streptococcus and STI Unit:

Walter Demczuk

Averil Griffith

Gary Liu

Pam Sawatzky

Ravinder Singh

For more information visit our website: <http://www.nml-lnm.gc.ca/eb-be/strepSTI-eng.htm>