AMR in Manitoba and Canada – What can we expect?

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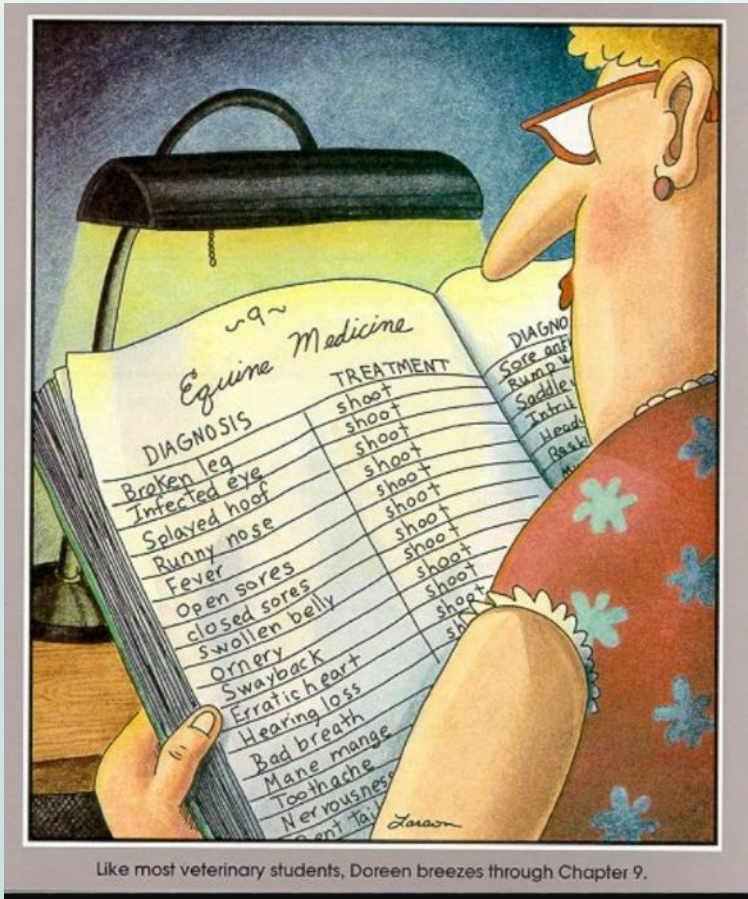
Manitoba

OBJECTIVES

- Overview of the emerging threat AMR poses to medicine and society
- Snapshots of Manitoban and Canadian AMR
- Overview of Canadian and international initiatives



Like most veterinary students, Doreen breezes through Chapter 9.

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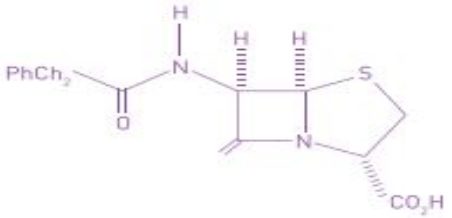
WHO AMR REPORT



What you need to know

WHO's first global report on antimicrobial resistance, with a focus on antibiotic resistance, reveals that it is no longer a prediction for the future. Antibiotic resistance - when bacteria change and antibiotics fail - is happening **right now**, across the world

The report is the most comprehensive picture to date, with data provided by 114 countries

Looking at 7 common bacteria that cause serious diseases from bloodstream infections to gonorrhoea

High levels of resistance found in all regions of the world

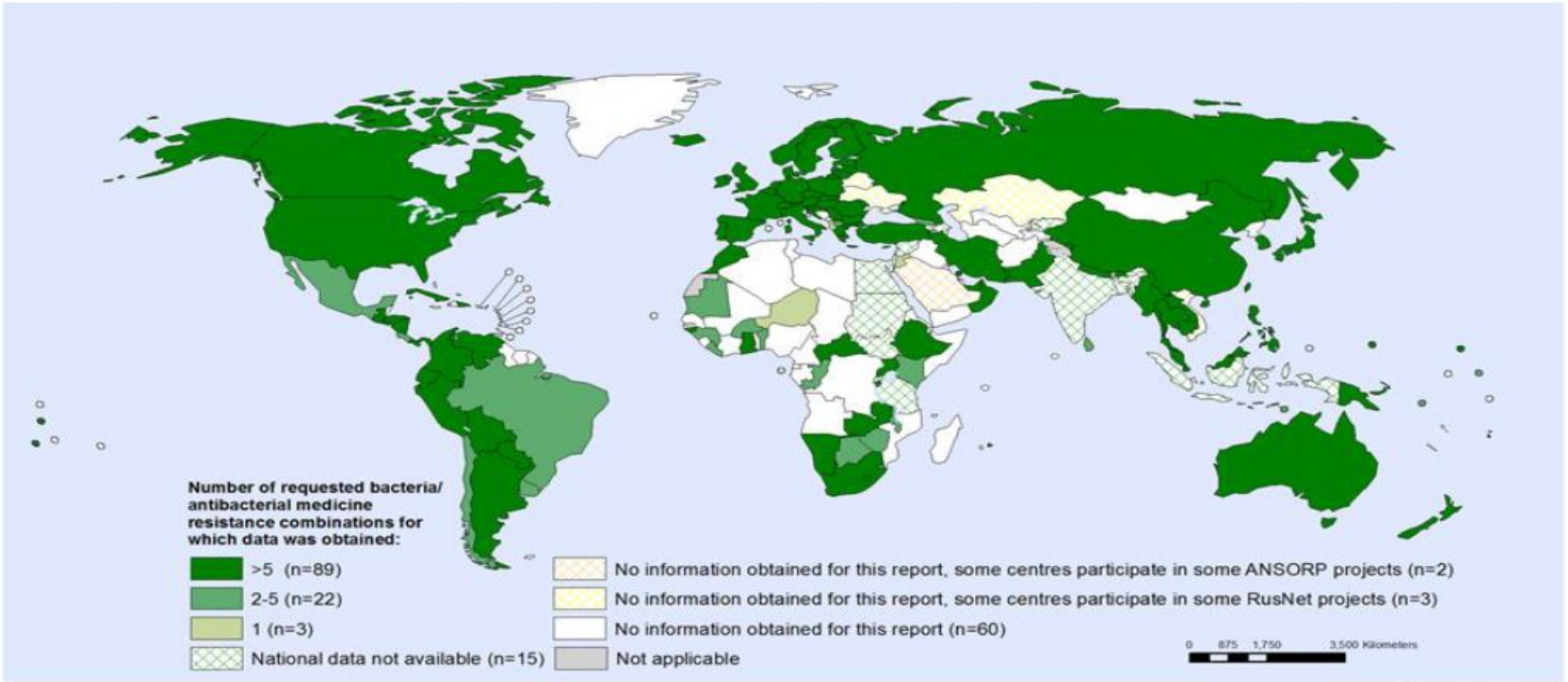
Significant gaps exist in tracking of antibiotic resistance

Over the last 30 years, no major new types of antibiotics have been developed

Source: http://www.who.int/drugresistance/documents/surveillancereport/en/

INTERNATIONAL AMR PATTERNS

Available National Data* on Resistance for Nine Selected Bacteria/Antibacterial Drug Combinations, 2013



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

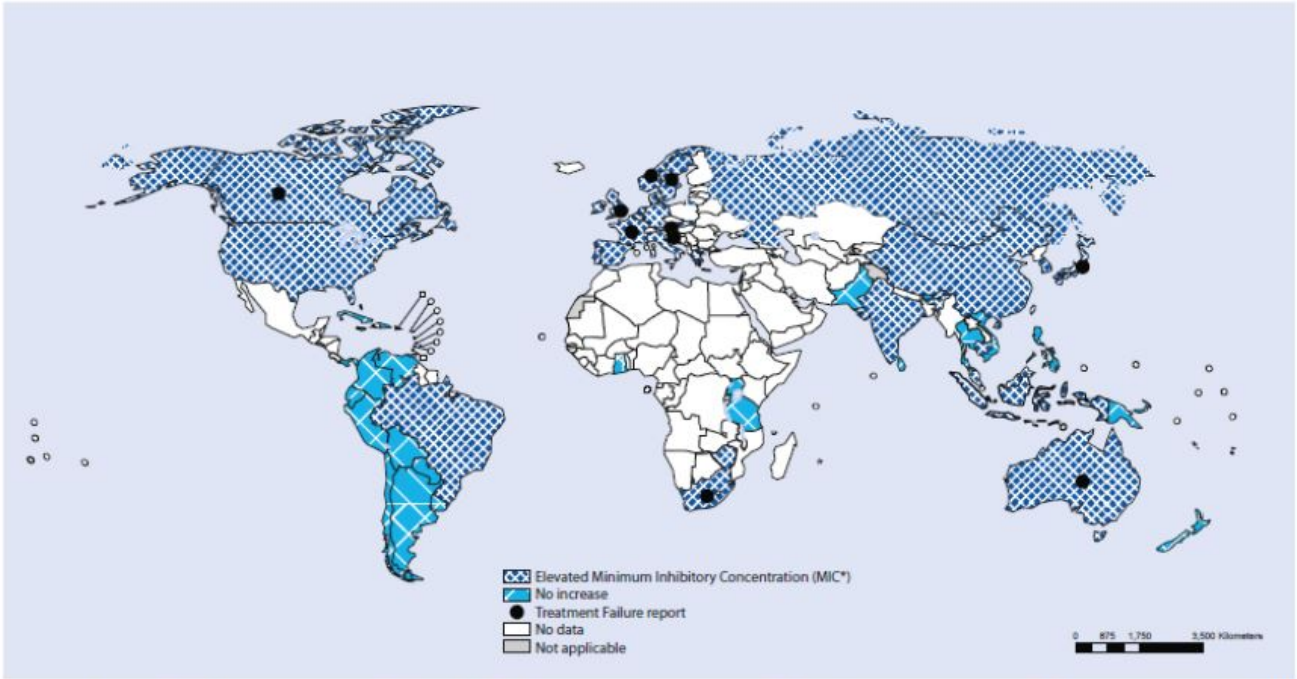
World Health Organization

*National data means data obtained from official sources, but not that data necessarily are representative for the population or country as a whole

STI RESISTANCE

Neisseria Gonorrhoeae

Detection of decreased susceptibility to 3rd generation cephalosporin and treatment failures up to 2010



* Note: cefixime >0.25µg/L or ceftriaxone >0.125µg/L. The definition of decreased susceptibility to third-generation cephalosporins differs across AMR testing methods. Countries are shaded where there has been any report of decreased susceptibility within their jurisdiction.

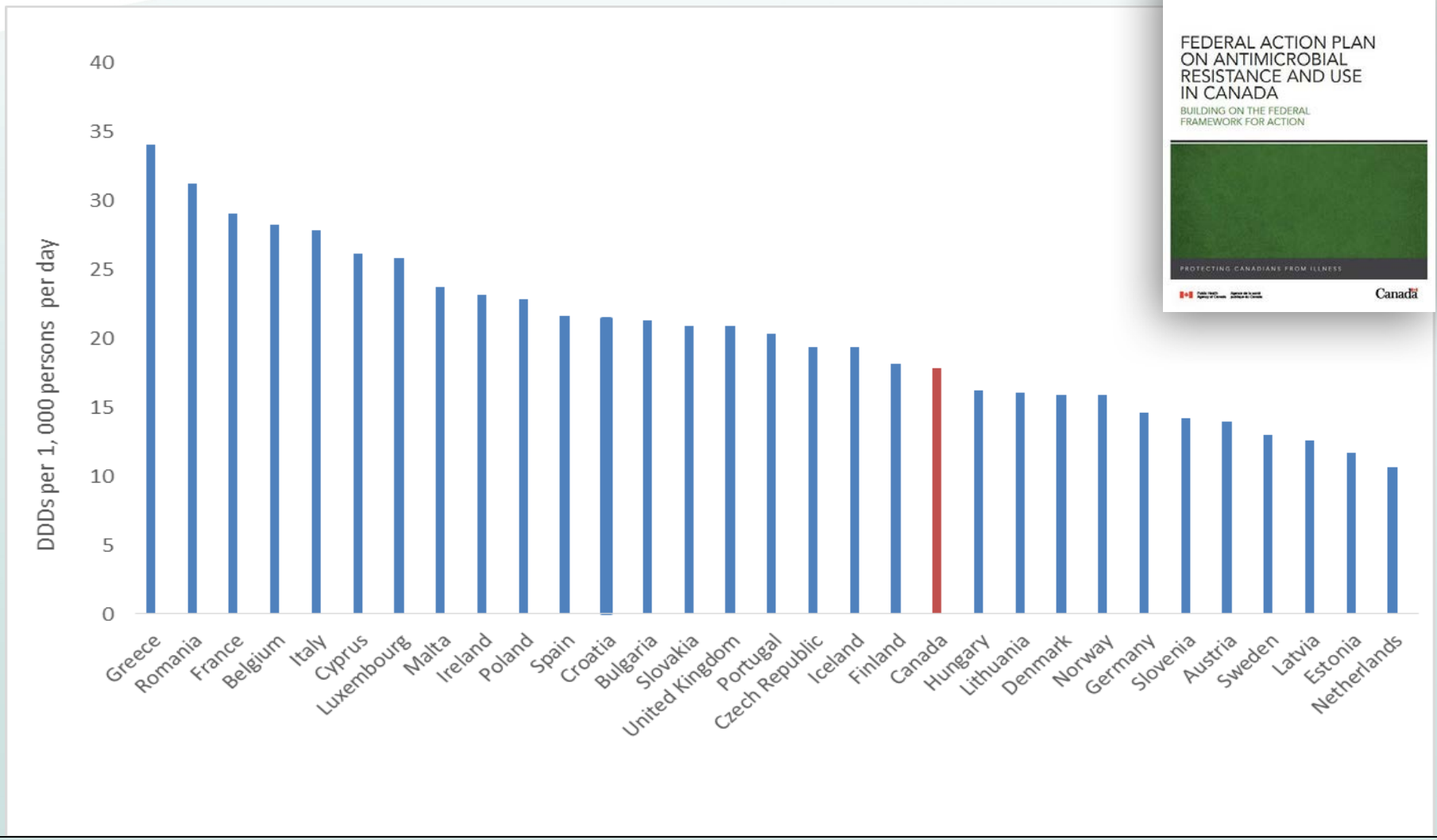
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

World Health Organization

Be a virus, see the world.

Outpatient antimicrobial use (defined daily dosage (DDD) per 1,000 persons per day) reported in Canada and in 30 European countries



Source: https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/federal-action-plan-antimicrobial-resistance-canada.html

ANTIBIOTIC USE

Manitoba

Table 14: Total consumption for the top 10 antimicrobials* dispensed by community pharmacies (DDDs per 1,000 inhabitants) in Canada, 2007 to 2014

Antimicrobial	Rank	2007	2008	2009	2010	2011	2012	2013	2014
Amoxicillin	1	1597.2	1624.1	1641.8	1691.4	1836.3	1768.9	1758.9	1843.5
Amoxicillin and enzyme inhibitor	4	244.5	262.0	271.6	239.0	314.7	333.9	368.5	405.8
Azithromycin	7	284.4	288.0	289.4	282.7	370.6	367.7	308.9	310.3
Cephalexin	6	342.6	348.6	337.4	330.0	354.1	358.7	368.9	371.1
Ciprofloxacin	5	439.6	442.8	425.2	434.4	444.1	428.2	405.8	390.8
Clarithromycin	2	982.5	997.6	1009.0	985.6	1028.8	965.6	830.6	743.0
Doxycycline	3	313.0	336.6	346.9	411.5	449.9	477.8	510.1	548.0
Minocycline	9	371.6	370.9	349.2	374.4	357.8	319.6	299.4	275.4
Nitrofurantoin	8	211.7	226.4	241.9	256.2	271.4	284.5	283.8	292.5
Sulfamethoxazole and trimethoprim	10	287.5	285.2	282.8	279.3	274.9	254.1	248.3	245.3
TOTAL		**3477.4**	**5182.2**	**5195.2**	**5284.5**	**5702.6**	**5559**	**5383.2**	**5425.7**

33%

* Ranked from greatest to least DDDs at the national level in 2014.

FEDERAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE AND USE IN CANADA
BUILDING ON THE FEDERAL FRAMEWORK FOR ACTION

Prevalence of Common Resistance Isolated Genotypes

Phenotype	N	% Total
MRSA	391/1,850	**21.1%**
VRE	5/385	**1.2%**
ESBL *E. coli*	123/2,965	**4.1%**
ESBL *K. pneumoniae*	10/628	**1.6%**

- Bacteriology of Top Urinary Organisms in Canadian ED's – 61% E. coli
- 98% susceptible to Nitrofurantoin
- Bacteriology of Top Wound Organisms in Canadian ED's – 42.1% S. aureus (MSSA)
- 98% susceptible to Doxy

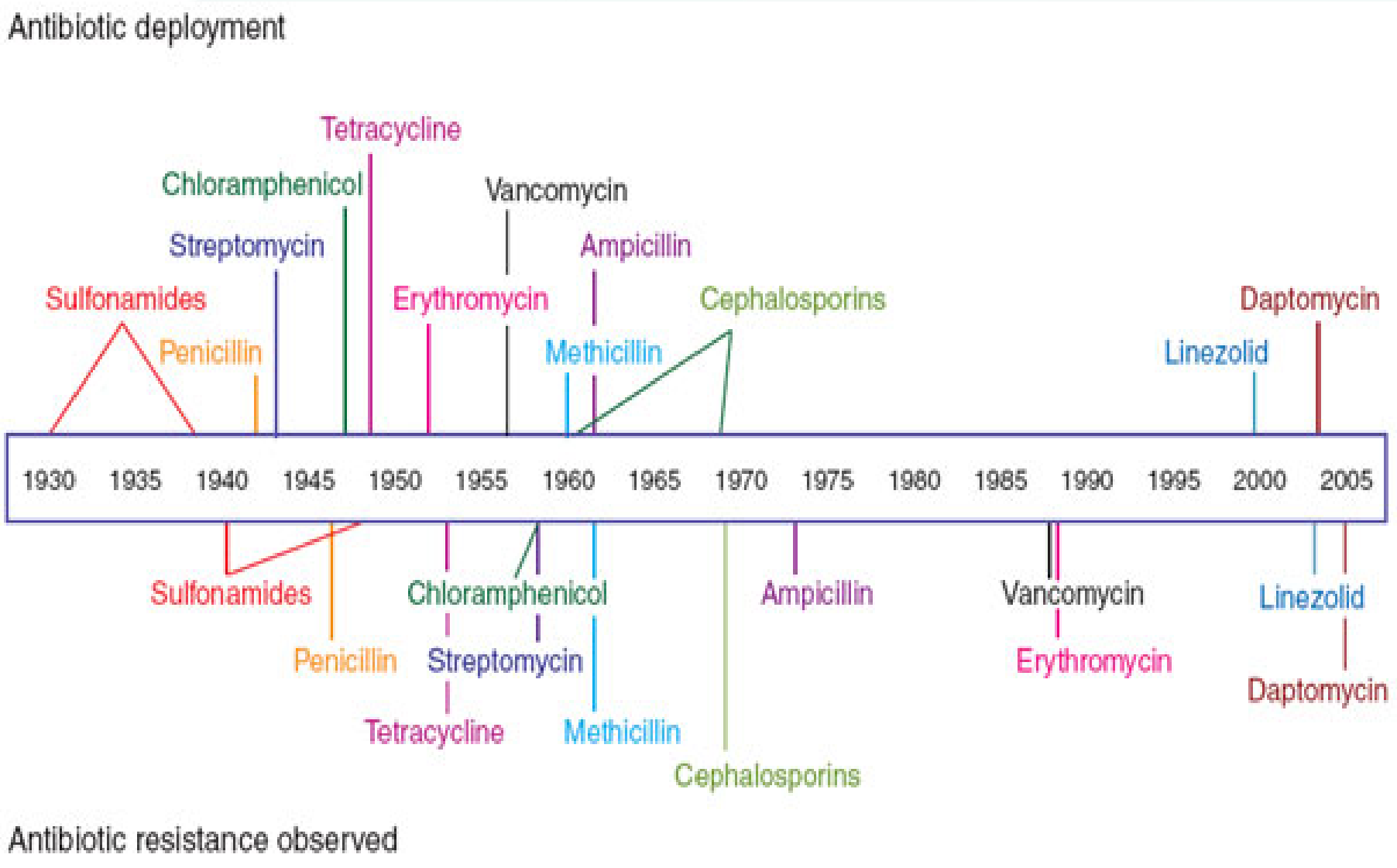
Source: CANWARD 2007-11 Study, Zhanel, G. et al. J Antimicrob Chemother. 2013 May;68 Suppl 1:i7-22. doi: 10.1093/jac/dkt022

MB STI RESISTANCE

- 354 clinical samples tested from 2012 to 2016
- 12 molecular strain types all resistant to azithromycin were found among 74 (21%) PCR-positive syphilis patients
- One patient was infected by two different strain types nine months apart
- http://www.gov.mb.ca/health/publichealth/cdc/**protocol**/syphilis.pdf - NO AZITHRO USE

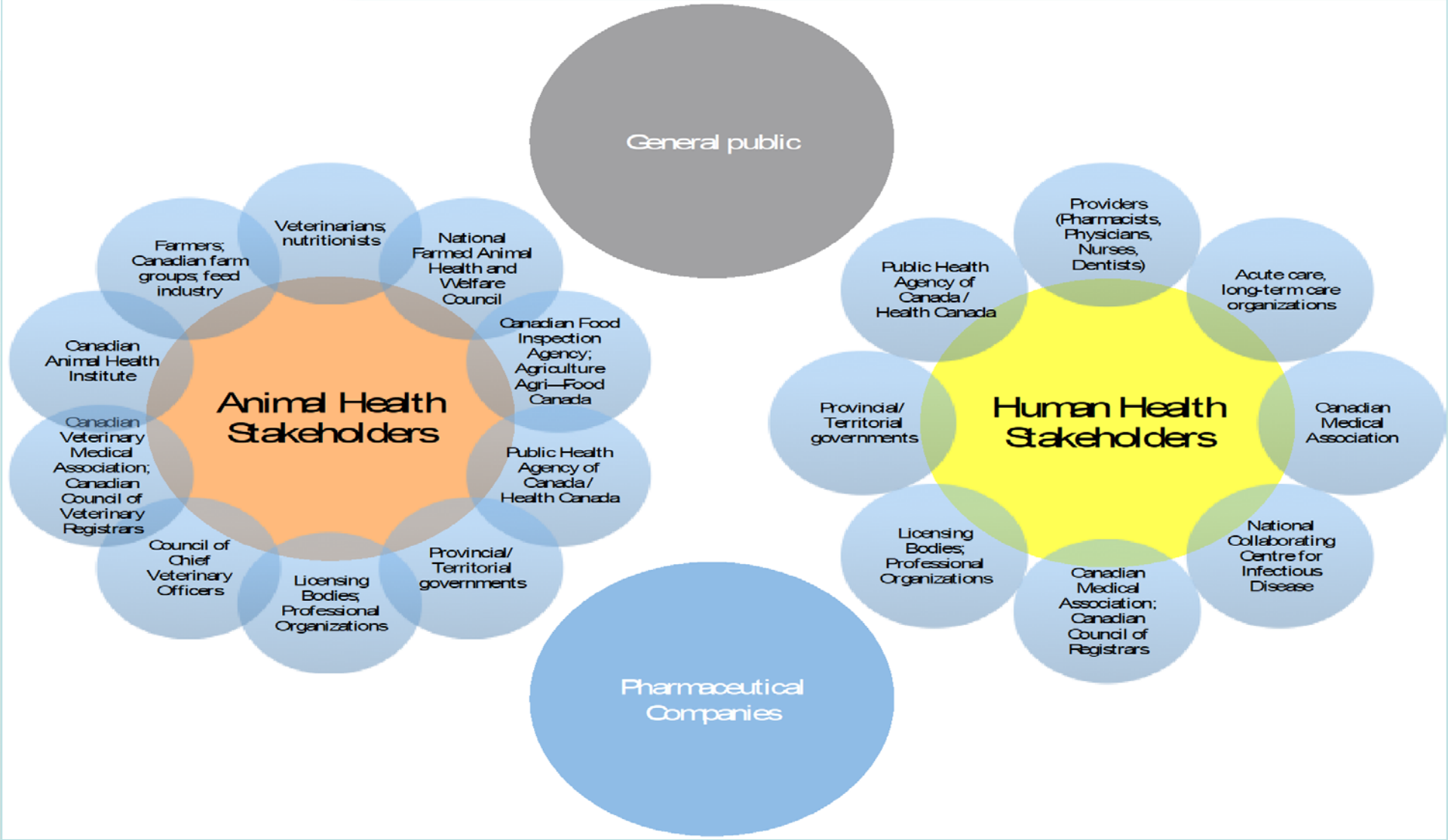
Source: Molecular typing and macrolide resistance of syphilis cases in Manitoba, Shuel M, et al. Sexually Transmitted Diseases, Publish Ahead of Print, DOI:10.1097/OLQ.0000000000000734

AMR DEVELOPMENT



Source: Nature Chemical Biology; 2007; 3: 541-548

AMR STAKEHOLDERS



Source: National AMR Stewardship Task Group Report for PHAC, January 2017

EPIDEMIOLOGY OF AMR

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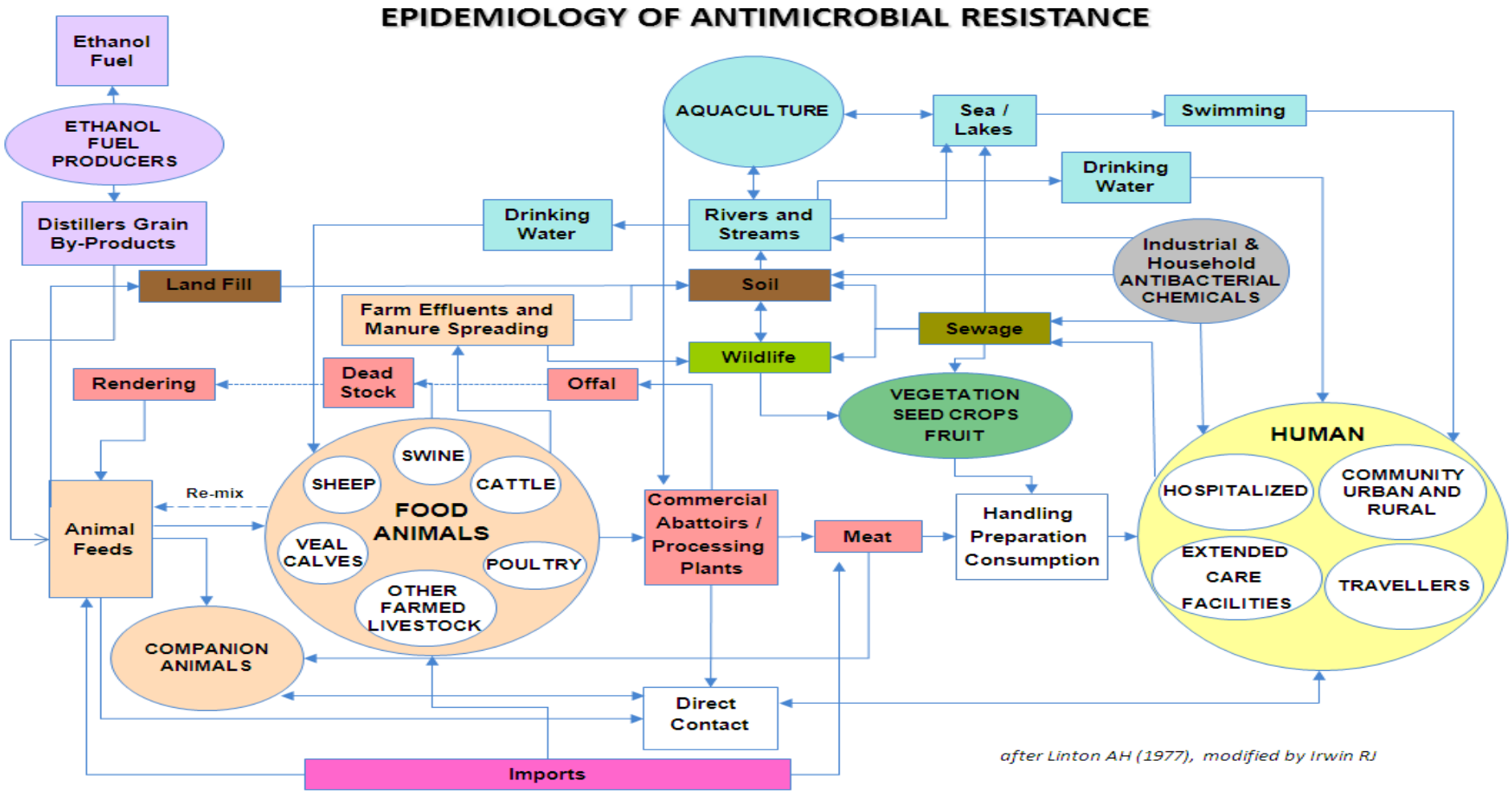


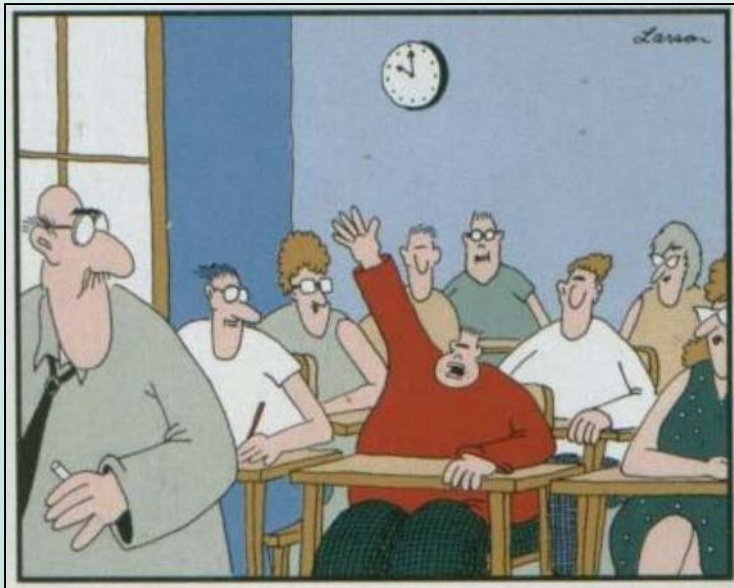
Source: https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars/background.html

Reasons for Inappropriate Prescribing

- Inadequate diagnosis, or lack of diagnostic facilities/resources
- Compliance with patients' inappropriate demand or pressure to prescribe antibiotics
  - Patient satisfaction
- Fear of adverse outcomes, or litigation
- Influence from senior colleagues
- Lack of knowledge
  - Incorrect selection, dose, duration, and route of antimicrobial rx
- Financial gain/pressure from pharmaceutical industry

CONCLUSIONS

- Antimicrobial resistance is real and here in MB
- We are **ALL** responsible for addressing the causes and the solutions
- Addressing this requires participation from all stakeholders
- Can we lose our social license to practice if we ignore this issue?



"Mr. Osborne, may I be excused? My brain is full."

Children's Hospital
Health Sciences Centre Winnipeg

Antimicrobial Stewardship

Improving Antimicrobial Prescribing

(May the Forces Be with You…)

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University of Manitoba

Affiliated with the
University of Manitoba

An operating division of the
Winnipeg Regional Health Authority
Office régional de la santé de Winnipeg

Objectives

- Understand antimicrobial stewardship & rationale for ASPs
- Discuss aspects of ASPs relevant to the different settings
- Review the experience from an inpatient ASP at Children's Hospital

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What fruit helped save lives in WWII and change modern medicine?

- A. Watermelon
- B. Kiwi fruit
- C. Cantaloupe
- D. Spartan apples
- E. Hawaiian pineapples

Zoho Docs

SEARCH

The New York Times

Inquiry Opens Into How a Network of Marines Shared Illicit Images of Female Peers

U.S. Frees Visa-Holding Afghan Family It Detained for 4 Days

RETRO REPORT
For Yale Law Group Fighting Trump's Travel Ban, Echoes of 1991

RETRO REPORT
Trump and the Battle Over Sanctuary In America

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U.S.

Anne Miller, 90, First Patient Who Was Saved by Penicillin

By WOLFGANG SAXON JUNE 9, 1999

Anne Sheafe Miller, who made medical history as the first patient ever saved by penicillin, died on May 27 in Salisbury, Conn. She was 90.

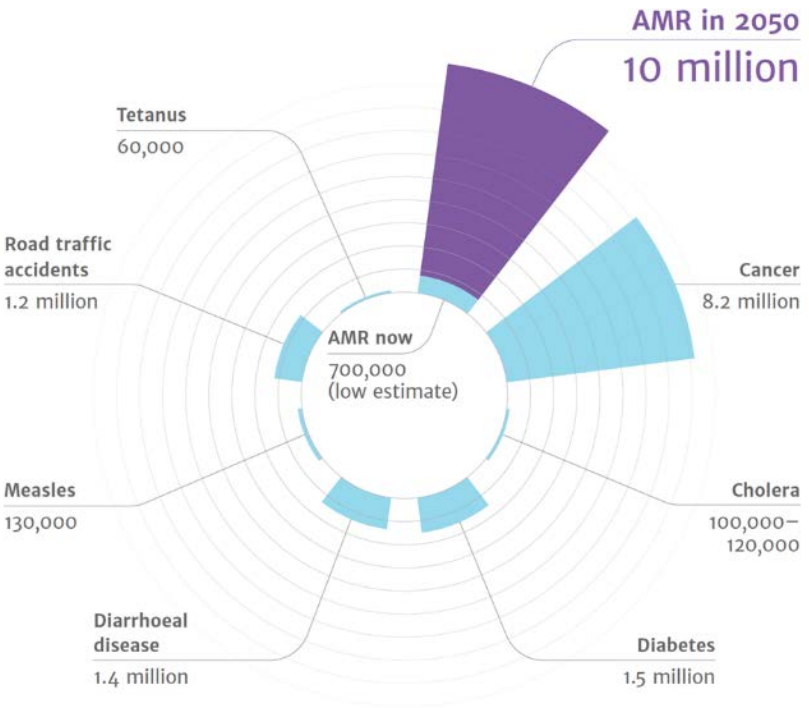
In March 1942, Mrs. Miller was near death at New Haven Hospital suffering from a streptococcal infection, a common cause of death then. She had been hospitalized for a month, often delirious with her temperature spiking to nearly 107, while doctors tried everything available, including sulfa drugs, blood transfusions and surgery. All failed.

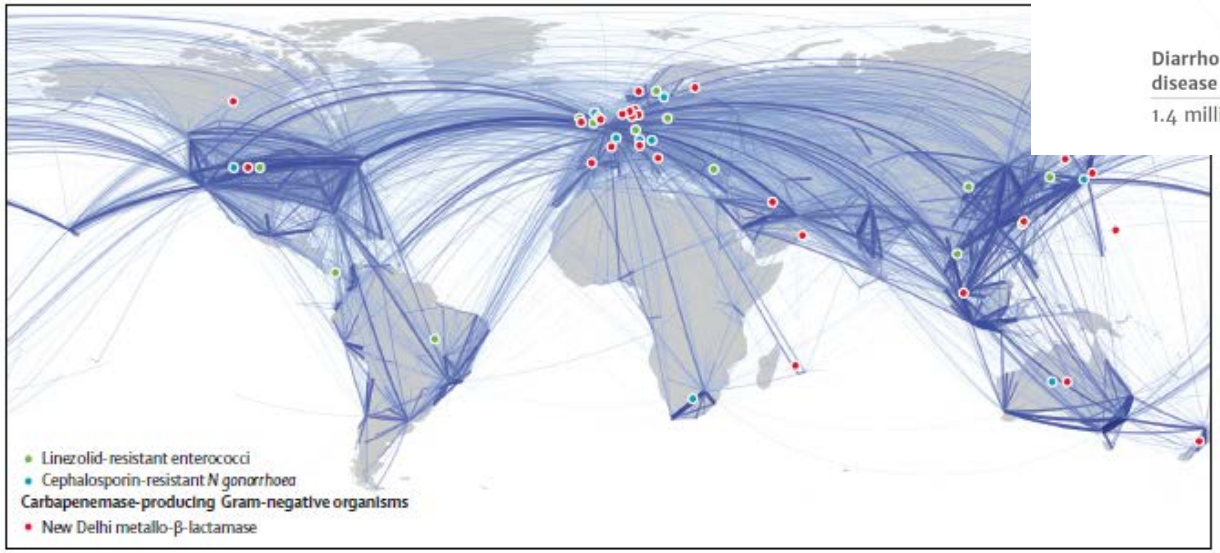
As she slipped in and out of consciousness, her desperate doctors obtained a tiny amount of what was still an obscure, experimental drug and injected her with it. Her hospital chart, now at the Smithsonian Institution, registered a sharp overnight drop in temperature, and by the next day she was no longer delirious and soon was eating full meals, one of her doctors reported.

Mrs. Miller's life was saved, and so eventually were the lives of all those previously felled by infections of bacteria like streptococci, staphylococci

http://www.nytimes.com/1999/06/09/us/anne-miller-90-first-patient-who-was-saved-by-penicillin.html

In the News for the Wrong Reasons





https://www.washingtonpost.com/news/to-your-health/wp/2016/05/26/the-superbug-that-doctor
dreading-just-reached-the-u-s/?utm_term=.a6ce70aa33f0

Audience Question

- Antimicrobials are over-prescribed to children in Canada
- A. Strongly agree
- B. Agree
- C. Neutral
- D. Disagree
- E. Strongly disagree

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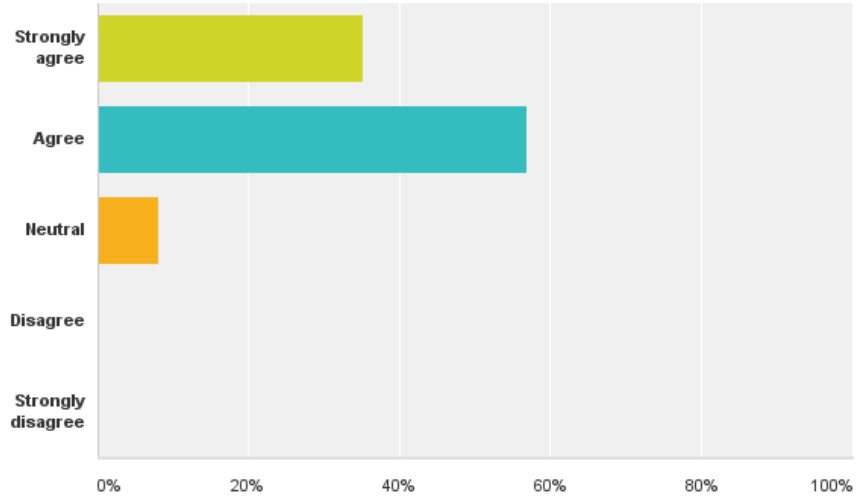
Winnipeg Pediatricians

Q14 Overall, antibiotics are over-prescribed to children in Canada.

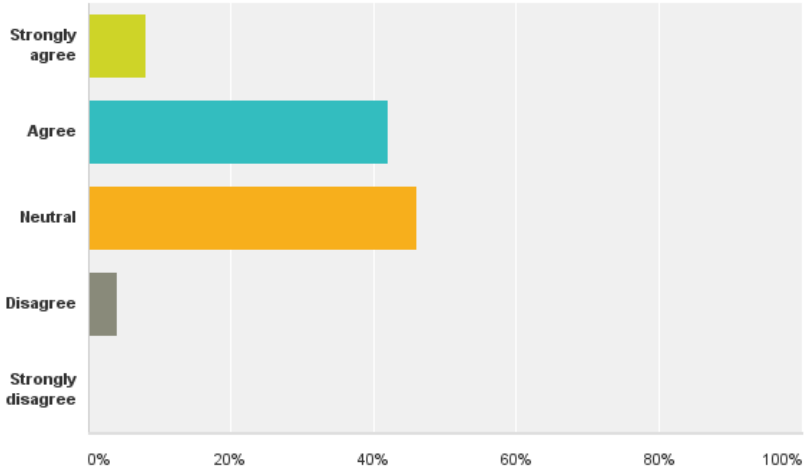
Answered: 74 Skipped: 2



~91% Agree

Q15 Overall, antibiotics are over-prescribed to children at Children's Hospital in Winnipeg.

Answered: 74 Skipped: 2



~50% Agree

Affiliated with the University of Manitoba

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ASP – A Helping Hand

- *A system which optimizes the use of antimicrobial agents*
- Promotes safety, quality of care
- Apply to your setting (hospital vs. clinics)

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Why ASPs?

- Inappropriate use of antimicrobials HARMS patients
  - "Antimicrobial chemotherapy"
- Collateral Damage

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Why ASPs?

- Clostridium difficile disease
  - Increasing in hospitalized kids
  - 10X increase in community-onset
  - Hospital-onset C.diff infections:
    - ↑ risk of mortality OR 6.73 (3.77-12.02)
    - ↑ length of stay – 5.5 days (4.5-6.5 days)
    - ↑hospital costs - $93K ($80-107K)
- ADEs
  - 20% of all pediatric ADE presenting to ER
  - TMP-SMX – 13 cases/100K admissions in 2013 (tripled)

Kim J Pediatrics 2008 122:1266
Sammons J Clin Inf D 2013;57
Goldman JL Pediatrics 2013

ASP Strategies

Strong Recommendations

- Prospective-audit with feedback
- Pre-authorization
  - Aka ID approval required
- IV to oral conversion programs
- Interventions to ↓use of Abx associated with high risk of C. diff
- Dedicated PK monitoring program

Outcomes

- Need to measure something
- Process vs. Outcome metrics
- Process Metrics
  - health care service provided to, or on behalf of, a patient
  - E.g. guideline compliance, how Abx are used, DDD vs DOT vs LOT, costs

Outcomes

- Outcome metric
  - Health state of a patient resulting from health care
  - Reflect the cumulative impact of multiple processes of care
  - E.g. length of stay, mortality, ICU admission rates,
    - *C.diff* rates, adverse drug events
    - Antimicrobial resistance rates

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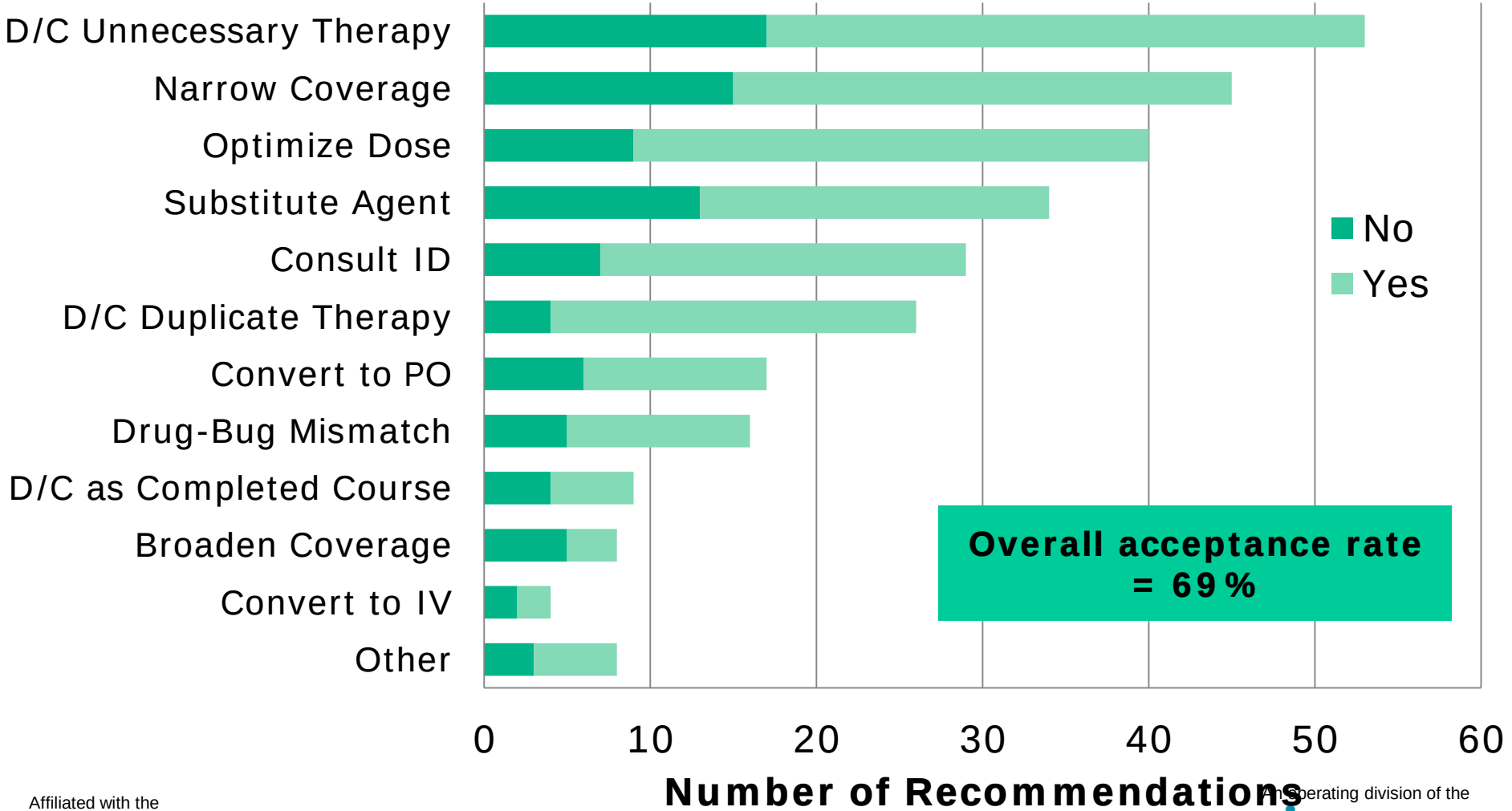
A Pilot ASP at Children's Hospital

- Grant from Child Health Advisory Committee (CHAC)
- 12 months (July 2013 – July 2014)
- 0.6 FTE pharmacist (Ms. Ashley Walus)
- Prospective Audit with Feedback
  - M/W/F
  - Elm/Oak/Pine/PICU
  - All systemic antimicrobials
- Note in chart when agreement


D/C Unnecessary Therapy
Narrow Coverage
Optimize Dose
Substitute Agent
Consult ID
D/C Duplicate Therapy
Convert to PO
Drug-Bug Mismatch
D/C as Completed Course
Broaden Coverage
Convert to IV
Other
No
Yes
Overall acceptance rate = 69%
0
10
20
30
40
50
60
Number of Recommendations

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	Elm	Oak	Pine	PICU
Cases (#) median (range)	6 (0 – 11)	6 (1 – 12)	6 (1 – 16)	4 (1 – 8)
Time (mins) median (range)	8 (0 – 30)	10 (1 – 30)	10 (1 – 30)	5 (0 – 30)

Table 1: Patient cases per ASP Shift

Pre-ASP Apr 2011 – Sept 2013	During ASP Oct 2013 – June 2014	P-value
4.0	3.5	0.49

Table 2: Median Length of Stay

Ambulatory ABx

- Est. 50 million Abx Rx annually
  - ~20% of all visits
  - ~50% (24.6 million) received broad-spectrum (azithromycin)
  - 70% for respiratory conditions
    - 23% for respiratory conditions not needing abx…

Pediatrics 2011;128:1053–1061

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Education?

WARNING: Antibiotics don t work for viruses like colds and the flu. Using them for viruses will **NOT** make you feel better or get back to work faster.

Antibiotics are strong medicines. Keep them that way. Prevent antibiotic resistance. Antibiotics don't fight viruses—they fight bacteria. Using antibiotics for viruses can put you at risk of getting a bacterial infection that is resistant to antibiotic treatment. Talk to your healthcare provider about antibiotics, visit **www.cdc.gov/getsmart**, or call **1-800-CDC-INFO** to learn more.

Taking antibiotics for viral infections such as a cold, a cough, or the flu will **NOT**.
- Cure the infection
- Keep other people from catching it
- Help you feel better

CDC FDA

GET SMART

GET SMART
Know When Antibiotics Work
www.cdc.gov/getsmar

Choose wisely.

Antibiotics aren't always the right tool for the job.

Choosing Wisely NL | Choosing Wisely Canada

Antibiotics aren't effective in treating most coughs, colds or flus. Be #healthcareful – talk to your doctor about what you need, and what you don't. To learn more, visit **choosingwiselynl.ca**

Antibiotic Resistance Twitter Chats
November 18, 2014

Join @CDC_eHealth
3 pm EST
#SaveAbx

Join the 24 hour global chat
#AntibioticDay

www.cdc.gov/getsmart/week

CDC

Affi

University of Manitoba

Office régional de la santé de Winnipeg

A Psychological Dilemma?

Box. The Imbalance in Factors Related to Antibiotic Prescribing

Factors Driving Antibiotic Prescribing: Immediate and Emotionally Salient

- Belief that a patient wants antibiotics
- Perception that it is easier and quicker to prescribe antibiotics than explain why they are unnecessary
- Habit
- Worry about serious complications and "just to be safe" mentality

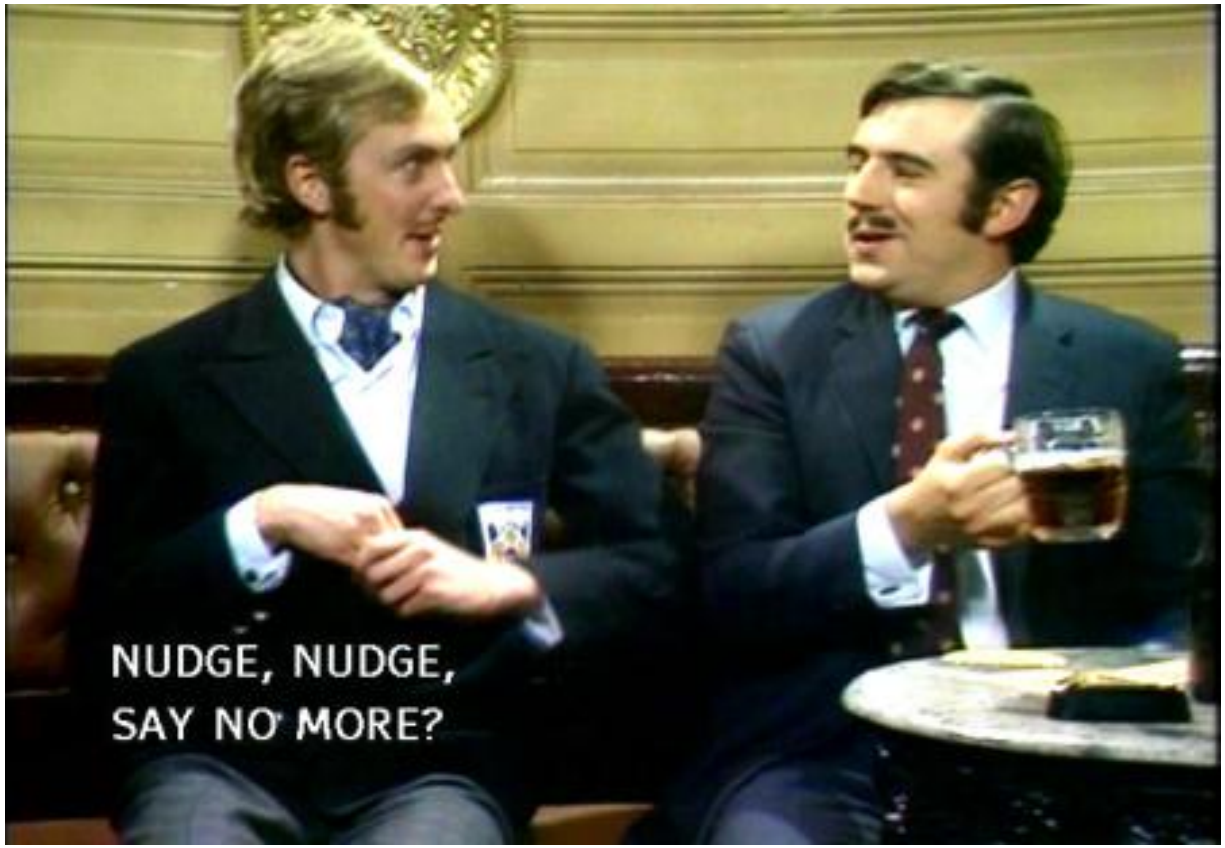
Factors Deterring Antibiotic Prescribing: More Remote and Less Emotionally Salient

- Risks of adverse reactions and drug interactions
- Recognizing the need for antibiotic stewardship
- Desire to deter low-value care and decrease unnecessary health care spending
- Prefer to follow guidelines

Mehrotra A et al JAMA IM 2016 Sept 19

How do we tip the balance?

How about a little nudge?



Meeker D et al. *JAMA Inter Med* 2014;174(3);425

- 5 Los Angeles community clinics, adult patients
- Randomized to either:
  - Signed-commitment-poster in exam room x 12 weeks
  - vs. no poster in office
- Lay-person explanation to why using less Abx
- Baseline & intervention period Abx data analysis
- Patients with an acute respiratory infection (ARI) diagnosis
  - frame with one influenza season
- Looked at ARI Dx for which Abx inappropriate and appropriate

~20% ↓ Inappropriate Use

- MDs & NPs; in practice x 17.6 years

Table 4. Changes in Adjusted Rates[a] of Inappropriate Antibiotic Prescribing for ARIs

	Poster Condition		Control Condition	
Characteristic	Baseline	Final Measurement	Baseline	Final Measurement
Inappropriate prescribing rate, % (95% CI)	43.5 (38.5 to 49.0)	33.7 (25.1 to 43.1)	42.8 (38.1 to 48.1)	52.7 (44.2 to 61.9)
Absolute percentage change, baseline to final measurement (95% CI)	−9.8 (0.0 to −19.3)		9.9 (0.0 to 20.2)	
Difference in differences between poster condition and control (95% CI)	−19.7 (−5.8 to −33.04)[b]			

Abbreviation: ARI, acute respiratory infection.

[a] Adjusted for demographic characteristics and insurance status.

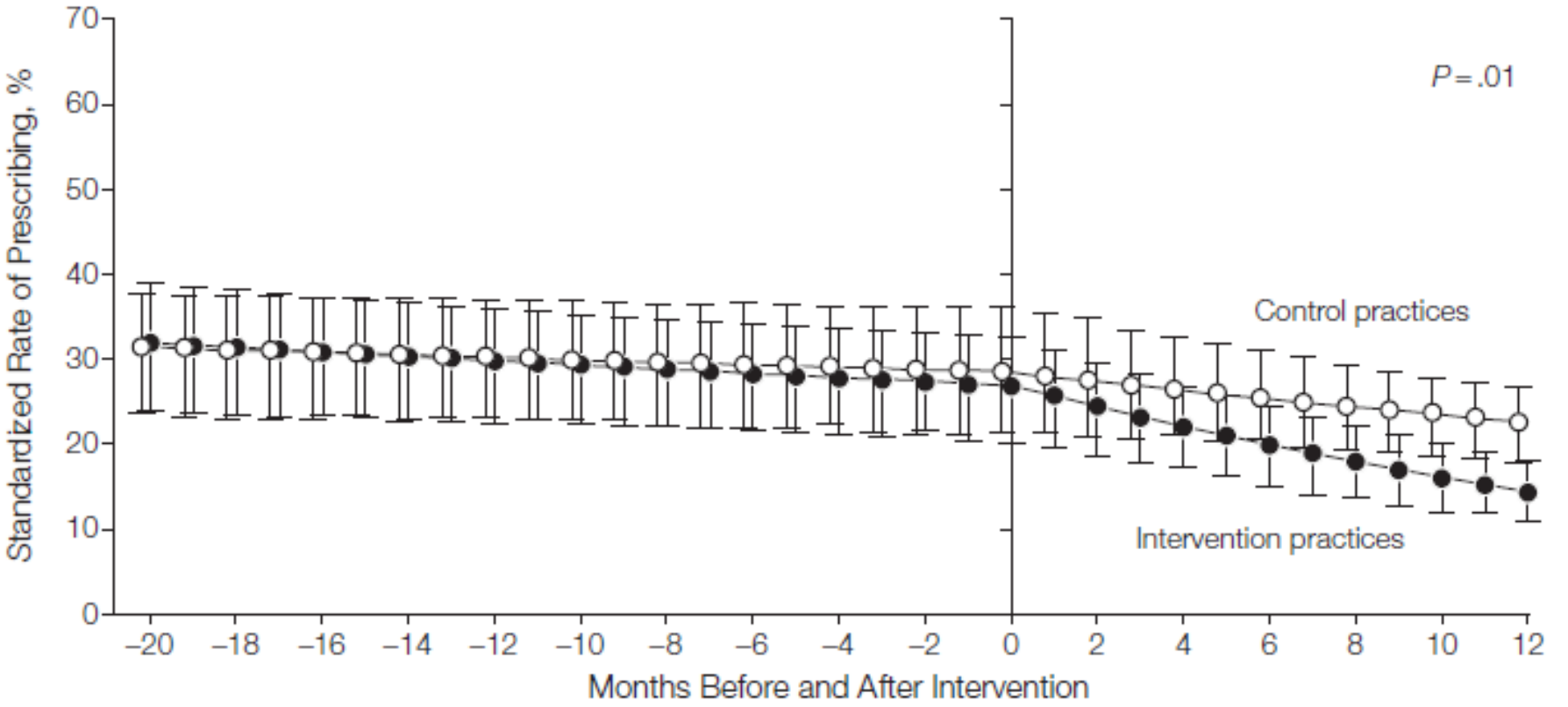
[b] P=.02 for the difference.

Outpatient Audit & Feedback

- Network of 25 primary care pediatric practices
  - 9 control vs. 9 intervention groups
  - Common EMR
- Clinical education sessions q4 months + 1 year personalized, quarterly audit & feedback on Abx Rx's
- Broad vs. narrow spectrum use
  - pneumonia; sinusitis; pharyngitis; "viral infection"

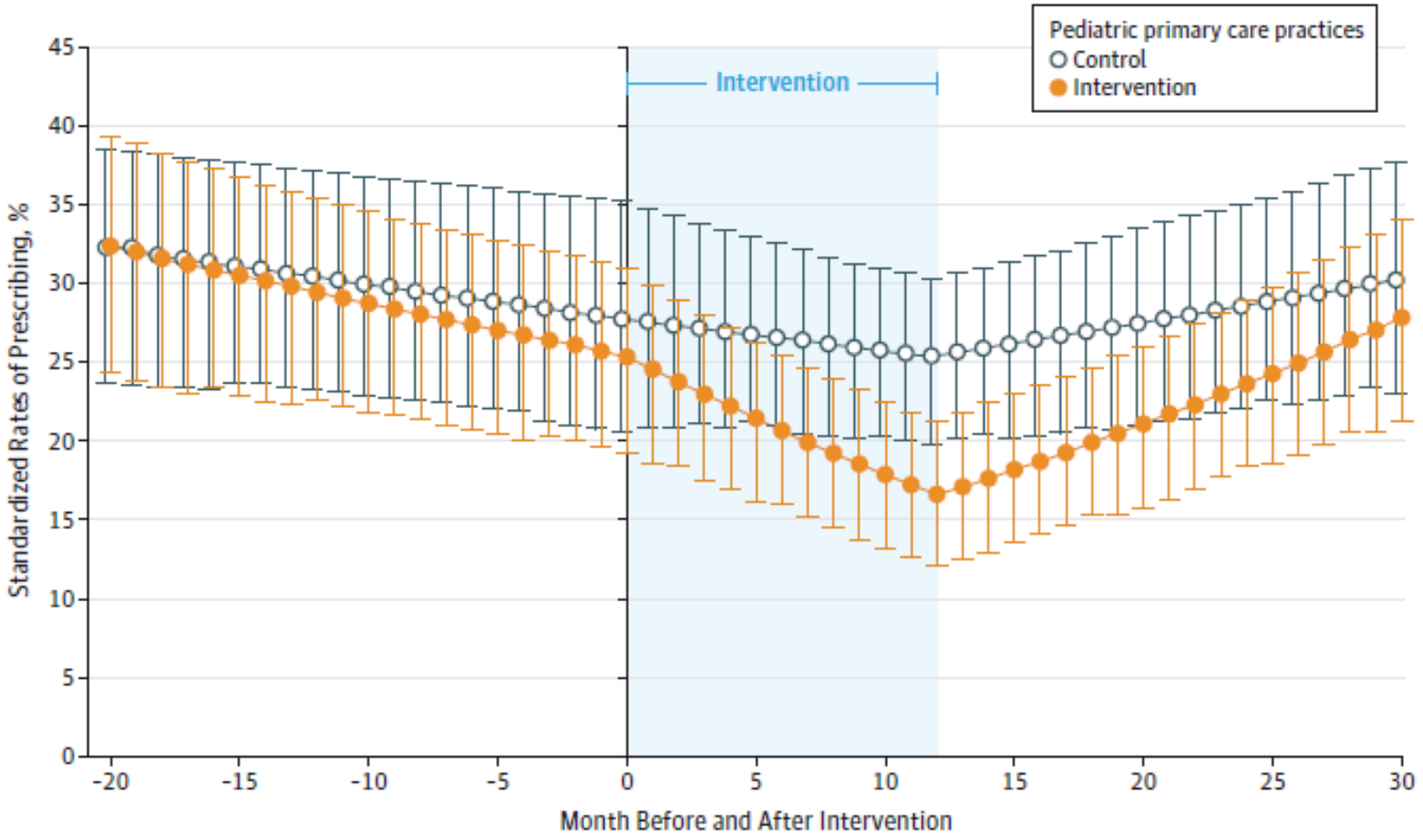
Gerber JS et al. JAMA 2013;309(22):2345-2352

Figure 2. Standardized Rates of Broad-Spectrum Antibiotic Prescribing at Acute Care Office Visits Over Time



Durability & A Lasting Impression

Figure. Standardized Rates of Broad-Spectrum Antibiotic Prescribing Before, During, and After Audit and Feedback



Pediatrician Perceptions

- Ignoring of reports; distrust
  - Didn't believe them
  - Data integrity
- "Gaming" behaviour
  - Adding bacterial Dx codes during ARTI
- Liked idea of guidelines, just not following them…
- Parental pressure
- Perceptions of antibiotic overuse
  - *It's not me, it's them…*

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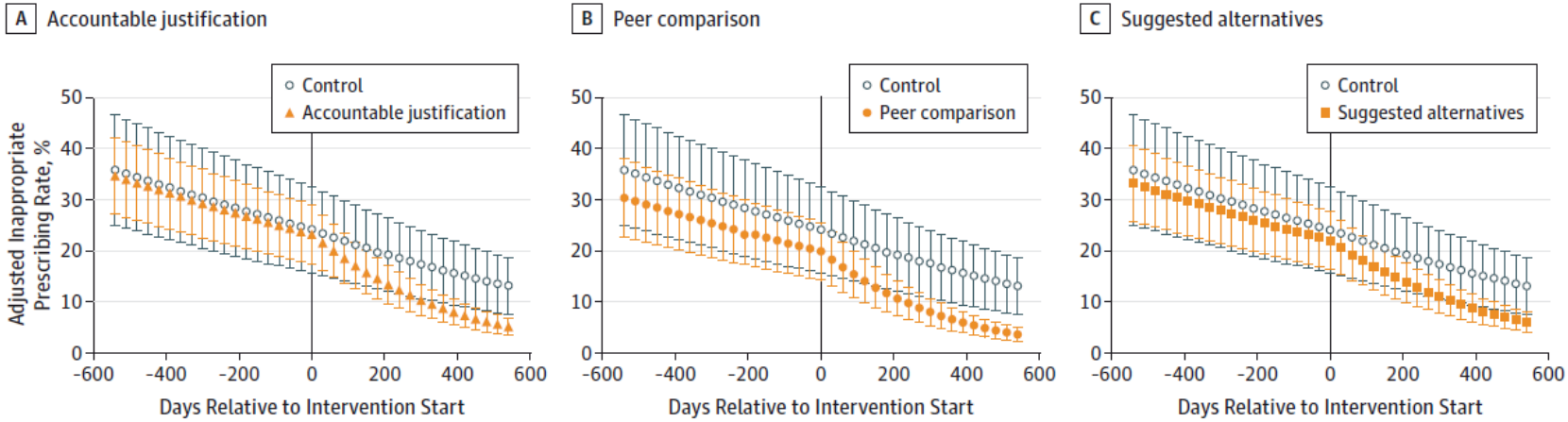
Another Nudge in the Right Direction

Meeker D et al. JAMA 2016;315(6);562-70

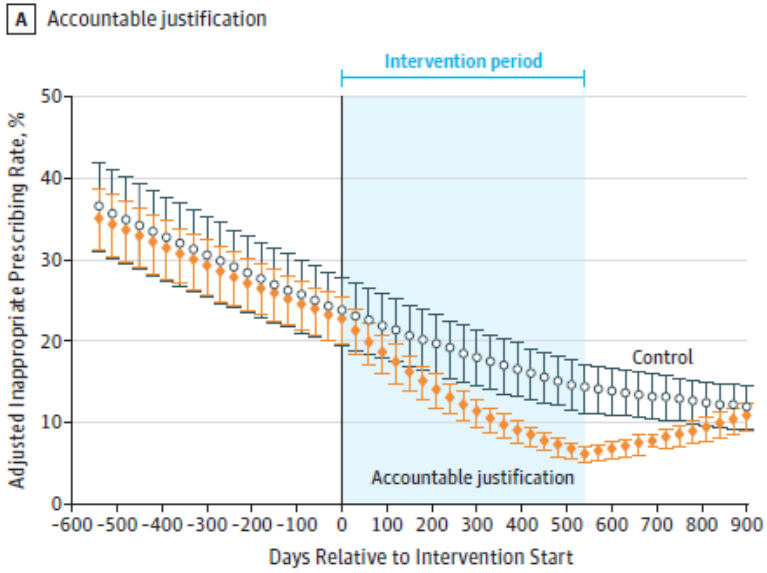
- RCT in 47 clinics, ~250 MDs
- Rx rates for Abx-inappropriate visits
- Effect of 3 behavioral interventions
  - Suggested alternatives
  - Accountable justification
  - Peer comparison
- 0,1,2,or 3 of these

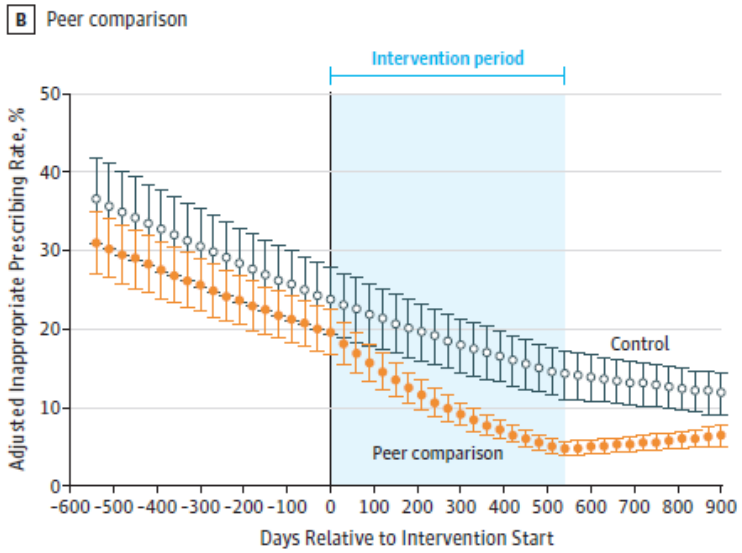
- Decreased in all groups
- Significant only in accountability + peer comparison group

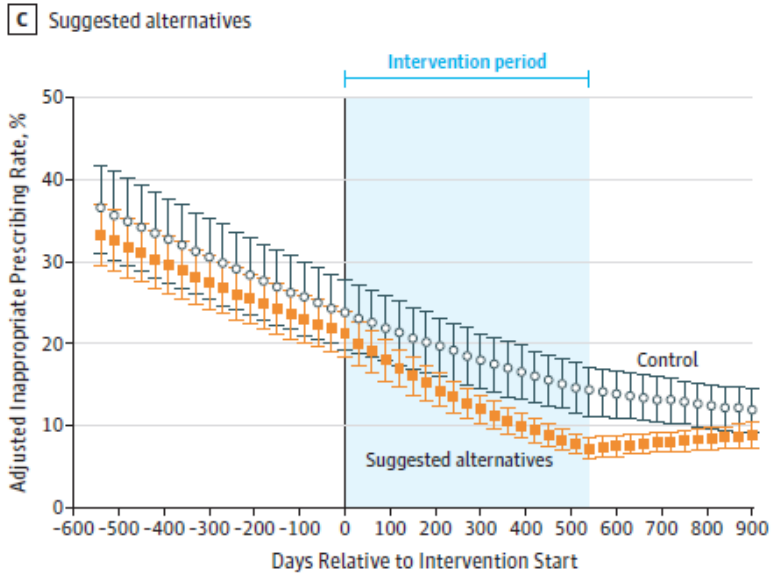
Figure 2. Adjusted Rates of Antibiotic Prescribing at Primary Care Office Visits for Antibiotic-Inappropriate Acute Respiratory Tract Infections Over Time



Prescribing rates for each intervention are marginal predictions from hierarchical regression models of intervention effects, adjusted for concurrent exposure to other interventions and clinician and practice random effects. Error bars indicate 95% CIs. Model coefficients are available in eTable 3 in Supplement 2.


A Accountable justification
Intervention period
Adjusted Inappropriate Prescribing Rate, %
50
40
30
20
10
0
Control
Accountable justification
-600 -500 -400 -300 -200 -100 0 100 200 300 400 500 600 700 800 900
Days Relative to Intervention Start


B Peer comparison
Intervention period
Adjusted Inappropriate Prescribing Rate, %
50
40
30
20
10
0
Control
Peer comparison
-600 -500 -400 -300 -200 -100 0 100 200 300 400 500 600 700 800 900
Days Relative to Intervention Start


C Suggested alternatives
Intervention period
Adjusted Inappropriate Prescribing Rate, %
50
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Control
Suggested alternatives
-600 -500 -400 -300 -200 -100 0 100 200 300 400 500 600 700 800 900
Days Relative to Intervention Start

Table 1. Tips on Counseling Patients About Antibiotics

Communication strategy	*Examples*
Explanation for why antibiotics are not needed	"This is a nasty cold, so antibiotics won't make you better faster." "The strep test is negative, meaning your sore throat is caused by a virus, and antibiotics won't help."[14] "You have a chest cold, and antibiotics won't help." *Tip for clinicians: Patients are less likely to expect antibiotics for "chest colds" than for "bronchitis."[15] Always combine explanations for why antibiotics are not needed with positive treatment recommendations. Patients are willing to hear that antibiotics are not needed if the message is combined with how to help them feel better.*[14]
Positive treatment recommendations	"Taking ibuprofen and drinking plenty of fluids will help you feel better." "Honey can actually soothe your child's cough and help her sleep better."[14]
Contingency plan	"If you are not better in three or four days, call or come back and we can reassess the need for antibiotics then." "If your child is still sick in a week or if he develops a fever, come back and see me."[13]
Delayed antibiotic prescriptions	"Your child has an ear infection that will likely clear up on its own. If the ear still hurts in two days or gets worse, call or come back and we will recheck the ears." "Your child has an ear infection that will likely clear up on its own. Just in case it doesn't, here is an antibiotic prescription. Fill this prescription in two days if the ear still hurts, or earlier if your child gets worse. Feel free to call me with any questions."[16-18] *Tip for clinicians: When using delayed prescriptions, write an expiration date on the prescription (e.g., five to 10 days in the future) so that the prescription can be filled only during the watchful waiting period and not a few months later.*[17]

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Conclusions

- **Antimicrobial "chemotherapy"**
  - **misuse = harm**
- **ASPs are successful in lowering inappropriate Abx use safely**
- **Tailor an ASP to your needs**
  - **Low-hanging fruit**
- **A blend of:**
  - **Education**
  - **Behavioural economic techniques**
  - **Communication Strategies**
- **May need a few nudges…**