Need for a harmonised approach for surveillance of antimicrobial resistance (AMR) in animals – the Canadian experience

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Carolee Carson, Rebecca Irwin, Brent Avery, Anne Deckert, David Leger, Rita Finley
SURVEILLANCE INFORMATION IS COMPELLING

...a need for a harmonized approach...

harmonization enables comparisons & integration
Outline

1. **Why** do you want surveillance information?

2. **Understand the system** (ecology, population distribution, stakeholders)

3. Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)
Surveillance

- **Ongoing** analysis, interpretation & feedback of systematically collected data using methods distinguished by their **practicality, uniformity & rapidity** rather than total accuracy or completeness

- Main purpose is to detect changes in trends (e.g. time, space) in order to **initiate investigative or control measures** (Last, 1995)

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**Harmonization**

- Sample or data collection (AMR, antimicrobial use, animal, human)
- Laboratory methods
- Data analysis & metrics
- Communication
Why do you want surveillance information?

CIPARS Objectives

• Unified approach to monitor trends in AMR & antimicrobial use in humans & animals
• Generate timely reports
• Generate data to facilitate the assessment of the public health impact of antimicrobials used in human & agricultural sectors
• Allow accurate international comparisons with other countries that use similar surveillance systems
Understand the system – ecology

after Linton AH (1977), modified by Irwin RJ
Understand the system – stakeholders

- Federal Gov’t
- Regional Gov’t
- International
- Industry–Pharmaceutical
- Public Health
- Industry-Farming
- Universities
- Veterinary

Policy Community
Policy Network
Antimicrobial Resistance

- Human population
  - Medical visit
  - Local laboratory
  - Provincial/territorial laboratory
    - NML

- Animal population
  - Sentinel farm
  - Abattoir
  - Retail meat
    - Sick animals
    - Healthy animals
    - Provincial or private animal health Laboratories
      - LFZ

CIPARS

Data Integration

PICRA

Antimicrobial Use

- Physician diagnosis
- Hospital purchases
- Pharmacy sales
- Sentinel farm questionnaire
- Kilograms of antimicrobials distributed for use in animals

1 National Microbiology Laboratory, Winnipeg, MB
2 Laboratory for Foodborne Zoonoses, Guelph, ON and Saint-Hyacinthe, QC
3 Canadian Integrated Program for Antimicrobial Resistance Surveillance, Public Health Agency of Canada
4 Programme Intégré canadien de surveillance de la résistance aux antimicrobien, Agence de la santé publique du Canada
5 IMS Health Canada, Inc.
6 Canadian Animal Health Institute (CAHI)
Retail Surveillance

- Chicken, pork, beef, & turkey
- *Salmonella*, generic *E. coli*, *Campylobacter*
- Implemented in different provinces, implementation date varied over time
- Provincial estimates
- Census division selection & sample allocation weighted by human population

Harmonization Considerations:

- Active or passive surveillance?
- Meat ‘species’? Product?
- Bacterial species? Culture methods?
- Where geographically?
- Store types?
Abattoir Surveillance

- Cattle, pigs, broiler chickens
- *Salmonella*, generic *E. coli*, *Campylobacter*
- Implemented in fall of 2002
- National estimates, federally inspected abattoirs
- Abattoir selection & sample allocation weighted by slaughter volume
- Caecal samples

Harmonization Considerations:

- Active or passive surveillance?
- Animal species?
- *Animal origin (domestic or imported)*?
- Bacterial species?
- *Where geographically (raised or slaughtered)*?
- *Sample type*?
Farm Surveillance

- Pigs – grower-finisher hogs
- *Salmonella*, generic *E. coli*
- Implemented in 2006 (5 major pork producing provinces)
- Herds allocated per province proportional to number of grower-finisher units in each province
- Each herd sampled once per year
  - Herd questionnaire
- Broiler chickens in 2013

Harmonization Considerations:

- Active or passive surveillance?
- Animal species?
- *Animal production stage*?
- Bacterial species?
- Where geographically?
- *Sample type*?
More harmonization

Laboratory Methods

• Isolation, serotyping, phage typing, susceptibility testing
  • Sensititre™ (automated broth microdilution)

• Data Management
  • Centralized database – data integrity, access, timeliness

• Breakpoints - Clinical Laboratory Standards Institute (CLSI)

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>n</th>
<th>% R</th>
<th>Distribution (%) of MICs (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>280</td>
<td>0.0</td>
<td>≤ 0.015 0.03 0.06 0.12 0.25 0.5 1 2 4 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>80.00 18.21 0.36 0.36 1.07</td>
</tr>
</tbody>
</table>

Harmonization Considerations:

• What type of testing?
• What antimicrobials?
• Data access & ease of changes?
• Breakpoints?

1.43% above ECOFF
0% Resistant
0% Resistant
Reporting - examples

Categorization of antimicrobials based on importance in human medicine

- Amoxicillin-clavulanic acid
- Ceftiofur
- Ceftriaxone
- Ciprofloxacin
- Amikacin
- Ampicillin
- Cefoxitin
- Gentamicin
- Kanamycin
- Nalidixic acid
- Streptomycin
- Trimethoprim-sulfamethoxazole
- Chloramphenicol
- Sulfooxazole
- Tetracycline

Percentage of isolates resistant and 95% confidence interval

n=230
Reporting - examples

The graph shows the percentage of isolates resistant to various antibiotics over the years from 2003 to 2009. The antibiotics include Ampicillin, Ceftiofur, Gentamicin, Nalidixic acid, Streptomycin, Tetracycline, and Trimethoprim-sulfamethoxazole. The x-axis represents the number of isolates and year, while the y-axis represents the percentage of isolates resistant.

The graph highlights an increase in the percentage of isolates resistant to Ampicillin and Ceftiofur from 2003 to 2009, with a significant rise in the latter years.
### Reporting - examples

<table>
<thead>
<tr>
<th>Bacterial species</th>
<th>Number (%) of isolates / Salmonella total</th>
<th>Susceptible to all antimicrobials</th>
<th>Resistant to A2C-AMP</th>
<th>Number (%) of isolates / Salmonella total</th>
<th>Susceptible to all antimicrobials</th>
<th>Resistant to A2C-AMP</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Salmonella</em> Enteritidis (n = 44)</td>
<td>93/44 (98%)</td>
<td>59/44 (98%)</td>
<td></td>
<td></td>
<td>93/44 (98%)</td>
<td>59/44 (98%)</td>
</tr>
<tr>
<td><em>Salmonella</em> Heidelberg (n = 50)</td>
<td>23/50 (46%)</td>
<td>23/50 (46%)</td>
<td>9/50 (18%)</td>
<td>43/230 (19%)</td>
<td>43/230 (19%)</td>
<td></td>
</tr>
<tr>
<td><em>Salmonella</em> Typhimurium (n = 8)</td>
<td>5/8 (63%)</td>
<td>5/8 (63%)</td>
<td>1/8 (13%)</td>
<td>1/230 (&lt; 1%)</td>
<td>1/230 (&lt; 1%)</td>
<td></td>
</tr>
<tr>
<td>Other serovars (n = 128)</td>
<td>35/230 (15%)</td>
<td>26/230 (11%)</td>
<td></td>
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</tr>
</tbody>
</table>
Communication

- Annual Reports
- Short Reports
- Antimicrobial Use Reports
- Surveillance Bulletins
- *Ad hoc* Reports - stakeholders
- *Salmonella* Quarterly Reports
- Peer-reviewed papers
- Risk profile
- Multi-commodity stakeholder meeting

**SURVEILLANCE BULLETIN**

Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)

Emergence of Ciprofloxacin-Resistant *Campylobacter* in Retail Chicken in British Columbia and Saskatchewan

CIPARS has identified an emerging trend (> 10% prevalence) in ciprofloxacin-resistant *Campylobacter* isolated from retail chicken in the provinces of British Columbia and Saskatchewan (Figure 1). This is in contrast to Canadian studies and CIPARS data from previous years and other provinces where the prevalence was less than 4% (1).
Ceftiofur resistance in *Salmonella* Heidelberg in 2003

- **Ceftiofur**
- **Ceftriaxone**
- **Ciprofloxacin**
- **Amikacin**

Legend:
- **Québec Retail Chicken (n=20)**
- **Québec Human S. Heidelberg (n=167)**
- **Ontario Retail Chicken (n=19)**
- **Ontario Human S. Heidelberg (n=172)**

Percentage of isolates resistant

CIPARS
Context

Ceftiofur (Category I)

- Can be used in many animal species, but **NOT** licensed for chicken in Canada
- Used extra-label for the control of *E. coli* omphalitis

*Salmonella* Heidelberg

Frequent: Top 3 serovars in humans in Canada since 1995

Invasive: Can cause septicemia, myocarditis, extra-intestinal infections, & death

Treatment concern: Resistance to ceftiofur = resistance to ceftriaxone; a drug of choice for treatment of pregnant women & children
Ceftiofur resistance in *Salmonella* Heidelberg isolates from retail chicken & people

Voluntary withdrawal of ceftiofur use

Release of CIPARS Report

Partial resumption in ceftiofur use

Number of *Salmonella* Heidelberg isolates from retail chicken, humans, year and province

CIPARS
Summary

• Surveillance information is compelling - need for harmonization
  • Need to understand *why* you want surveillance
  • Need to *understand the system*
  • Need commitment from funding agencies

• What to harmonize?
  • Sample & data collection, laboratory methods, data analysis & reporting metrics, communication

• CIPARS ceftiofur-resistant *Salmonella* Heidelberg data
  • Example of integration of harmonized regional & temporal data highlighting the effects of an intervention
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Health Canada - Veterinary Drugs Directorate
Agriculture and Agri-Food Canada

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Retail Meat Surveillance Participants
Farm Surveillance Participants

Canadian Animal Health Institute
Intercontinental Medical Statistics

Provincial Public Health Laboratories
Provincial Animal Health Labs
Other collaborating laboratories