Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

The Public Health Agency of Canada's Experience with Whole Genome Sequencing Transition: Successes and Pitfalls

Presented at the PulseNet/OutbreakNet East Coast Regional Meeting

Tampa, FL

January 15, 2019

PROTECTING AND EMPOWERING CANADIANS
TO IMPROVE THEIR HEALTH

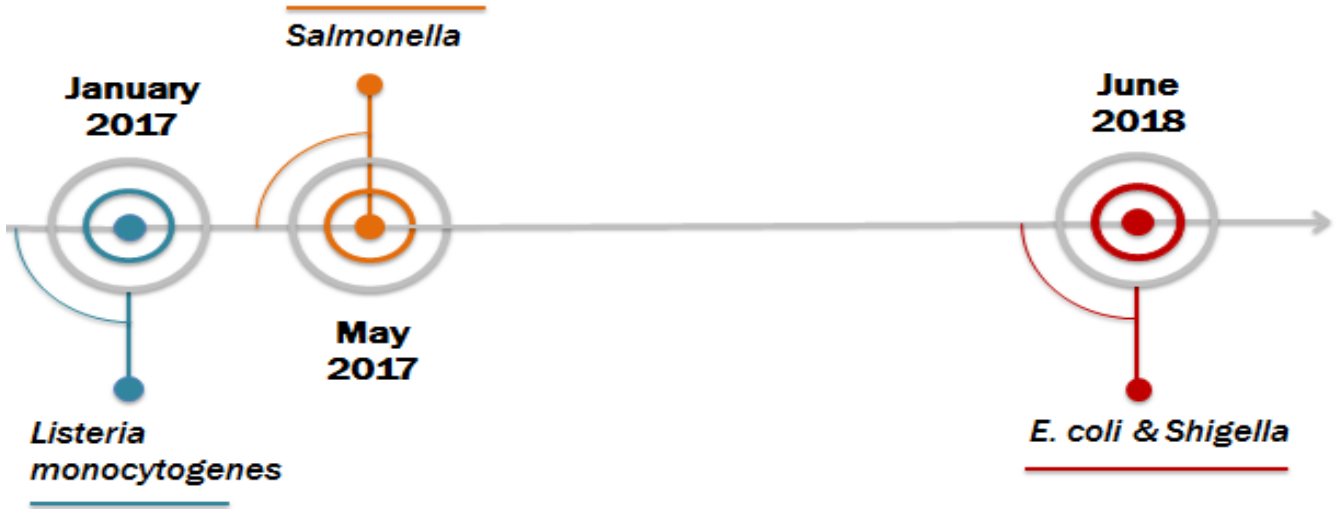
Outline

- Background on whole genome sequencing implementation in Canada
- Successes and pitfalls:
  - Improved resolution
  - Historical analysis for comparison
  - Cluster assessment process
  - Integration of non-clinical isolates
  - Timeliness
  - Collaboration
- Conclusions

Background

- Whole genome sequencing (WGS) for *Listeria*, *Salmonella, E. coli,* and *Shigella* has been implemented in Canada

- Whole genome multilocus sequence typing (wgMLST) is primary tool

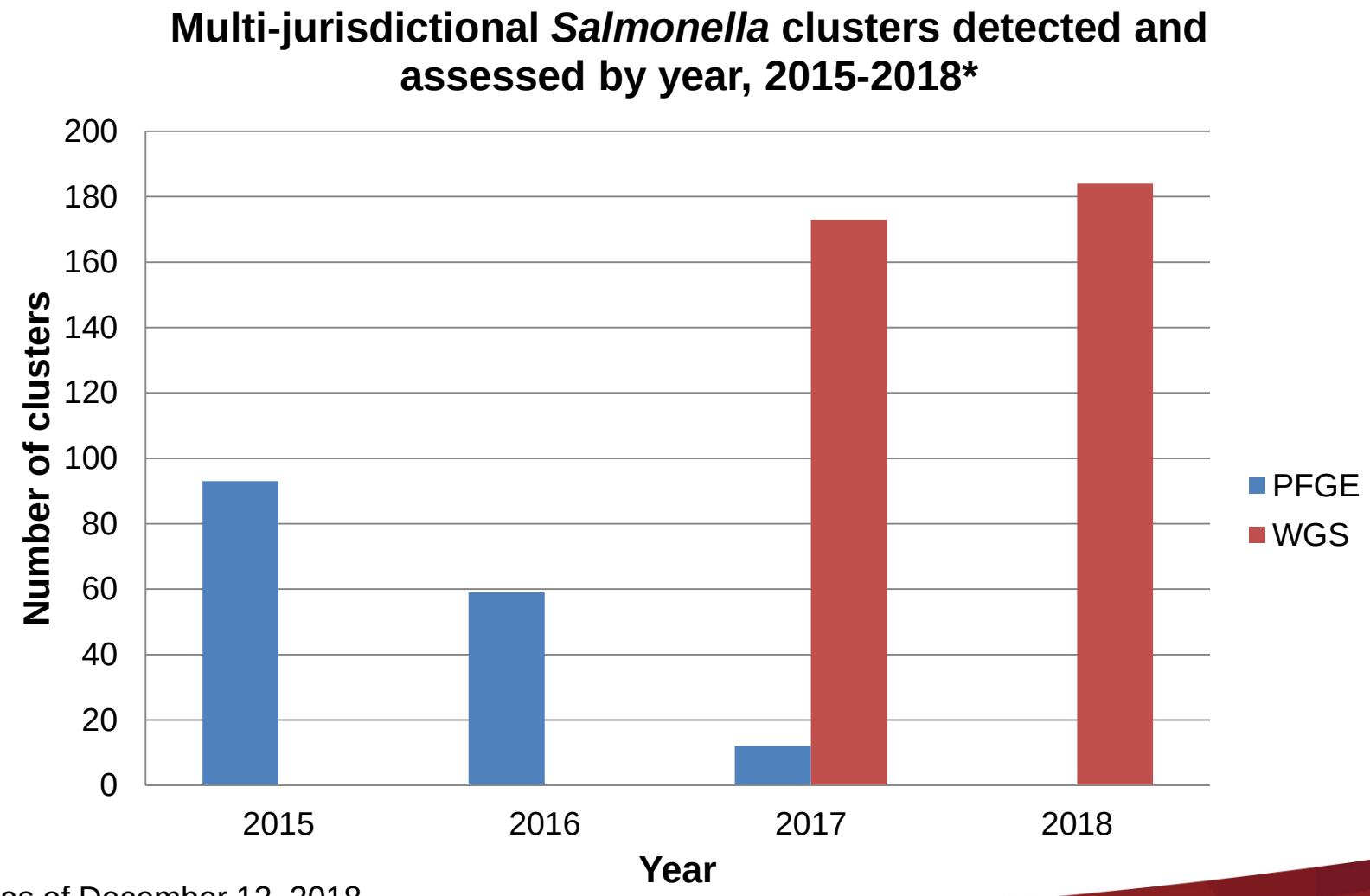


Background - Process

- Centralized analysis at the National Microbiology Laboratory (NML)
  - Provinces/territories (P/Ts) ship isolates for analysis
  - Results shared with P/T labs first & then shared nationally via PulseNet Canada password protected discussion board
  - Decentralization is beginning…

- Current process:
  - Notified each time a new cluster is posted or updated on the PulseNet Canada password protected discussion board
  - Individual clusters shared, the entire *Salmonella* phylogenetic tree is not
  - Regular communication
  - Nothing set in stone, constant tweaking

Success: Improved resolution for common Salmonella serotypes



*Data as of December 12, 2018

Success: Improved resolution for common Salmonella serotypes

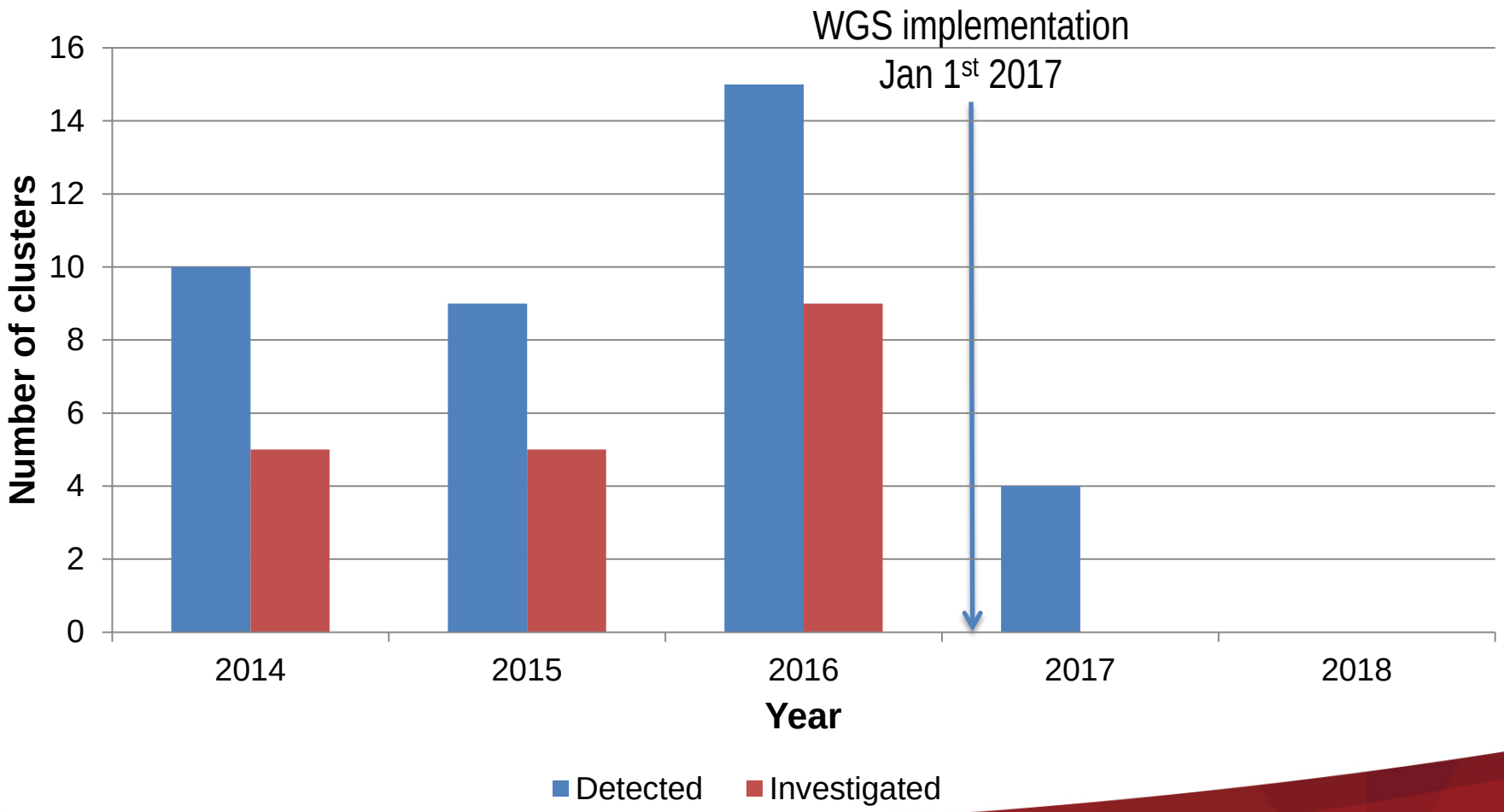
- WGS highlights clusters we could not see through PFGE
  - Breaks large PFGE clusters into smaller WGS clusters

- Especially true for Canada's top three (very common) serotypes

Example: *Salmonella* Enteritidis

Success: Improved resolution for *Listeria monocytogenes*

Multi-jurisdictional *Listeria monocytogenes* clusters detected and investigated by year, 2014-2018*

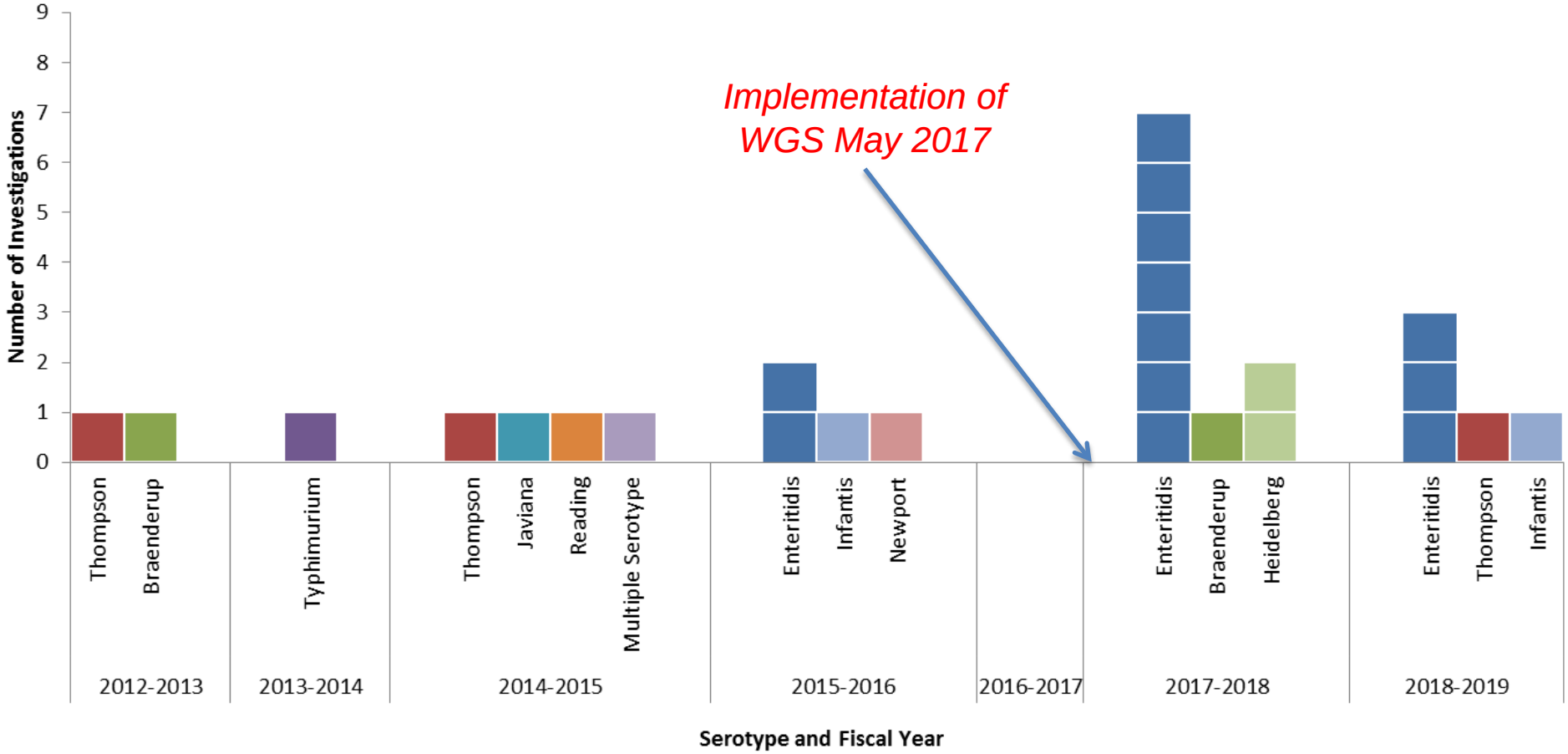


*Data as of December 2018

Pitfall: Very little historical analysis for comparison

- Previously, had significant PFGE database to reference for comparison
  - More than a decade of historical PFGE data
- Little retrospective WGS data to look back
  - Retro1000
  - Past outbreaks, validation study post implementation
- With limited historical analysis, everything looks like an outbreak
  - Led to an increase in national outbreak investigations

Number of multi-jurisdictional *Salmonella* investigations, by serotype, 2012-2018



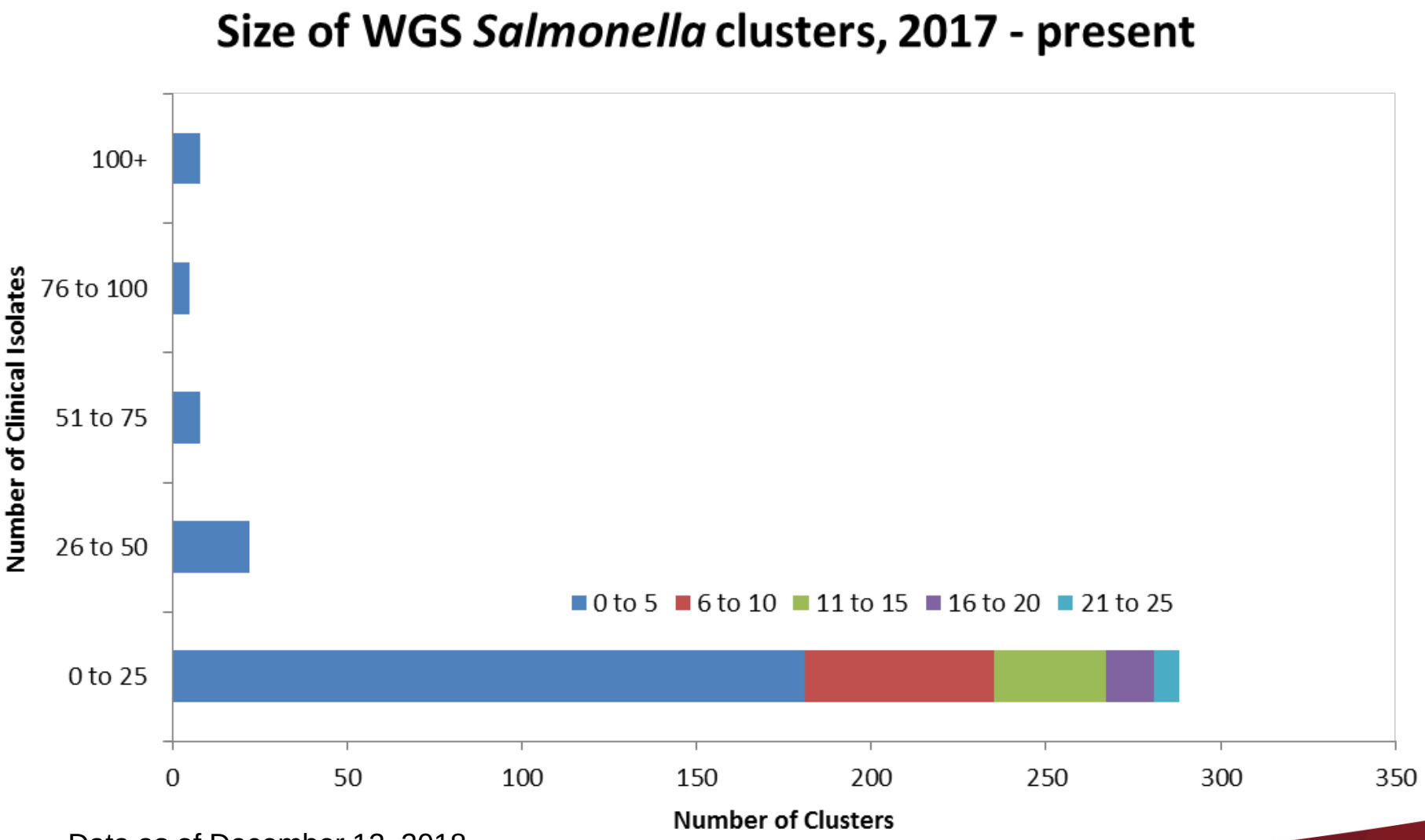
Pitfall → Success: Adaptive cluster assessment process

- Evolution of Cluster Assessment Criteria
  - Previous tools focused on case count thresholds and serotype frequency
  - Tool evolved from strict criteria into a list of considerations when assessing a cluster
    - e.g. serotype frequency, case count, allele ranges, demographic profiles, isolation dates, presence of non-clinical isolates, etc.

- Importance of ongoing collaboration with laboratory and surveillance colleagues
  - Weekly meetings to review WGS data and clusters of interest

- Importance of ongoing collaboration with provincial/territorial epidemiologists
  - Weekly meetings to discuss implementation updates and challenges, lessons learned, upcoming training opportunities, and WGS-related projects

Many small clusters, limited investigation opportunity



Data as of December 12, 2018

How are WGS results assessed?

- When new or updated WGS clusters are posted, the following considerations are used to guide the assessment:

Laboratory considerations:

- Serotype Frequency
- Allele ranges and branching
- Presence of nonclinical isolates
- Nearby clusters
- Surveillance data

Epidemiologic considerations:

- Person: Number of cases, demographic information
- Place: Geographic spread
- Time: Isolation dates
- Previous follow-up completed

- The assessment criteria continues to evolve as our knowledge and experience with WGS increases

Success: Integration of non-clinical isolates

- Non-clinical WGS data provided by the Canadian Food Inspection Agency (CFIA), FoodNet Canada and provincial/territorial laboratories

- Retail, farm & abattoir sampling data from the Canadian Integrated Program for Antimicrobial Resistance (CIPARS) not yet integrated

- The real-time integration of non-clinical samples has helped to:
  - Inform hypotheses
  - Strengthen epidemiological assessments by providing microbiological evidence
  - Understand product distribution
  - Demonstrate the utility of combining non-clinical and clinical isolates in single analysis
  - Inform the classification and prioritization of clusters (e.g. non-domestic travel, chicken)

Success: Integration of non-clinical isolates

Chicken example:

May 1, 2017 to December 12, 2018

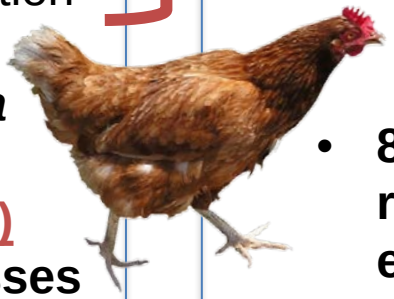
74 multi-jurisdictional WGS clusters include one or more poultry product isolate

3 multi-jurisdictional WGS clusters have strong epidemiologic evidence to implicate poultry as a source of infection

2,777 lab-confirmed *Salmonella* illnesses in the 77 clusters

x 26.1 (underreporting estimate)

72,480 estimated *Salmonella* illnesses



14 multi-jurisdictional *Salmonella* investigations

- **2 associated with raw chicken exposure**
- **4 associated with raw chicken and frozen raw breaded chicken exposure**
- **8 associated with frozen raw breaded chicken exposure**

Success: Integration of non-clinical isolates

Frozen raw breaded chicken product example:

- Definitive association between human illness and contaminated product
- Increased attention on *Salmonella* and chicken exposure in Canada, as a result of an increase in the number of national investigations
- Criteria for product action

Notice to Industry – New requirements to reduce Salmonella to below detectable amounts in frozen raw breaded chicken products

Update: The addition of preservatives approved for use by Health Canada is now permitted to help manufacturers reduce the risk of Salmonella in frozen raw breaded chicken products. Control measure – Option 1 has also been updated in regards to requirements.

July 12, 2018: The Canadian Food Inspection Agency (CFIA) is requiring industry to implement measures at the manufacturing/processing level to reduce Salmonella to below detectable amounts in frozen raw breaded chicken products that are packaged for retail sale.

Frozen raw breaded chicken products include chicken meat products (excludes quail, duck, and turkey) that are manufactured and are:

- raw
- breaded
- frozen
- appear "ready to eat" and
- packaged for retail sale

Frozen raw breaded "stuffed" chicken products are not affected at this time.

These new measures were prompted by the continued link between frozen raw breaded chicken products and outbreaks of food-borne illness. Facilities that manufacture these products must review their processes and implement control measures by **April 1, 2019**.

Pitfall: Decrease in timeliness

- Timeliness has decreased.
  - Previous reporting delay was approximately 21 days for *E. coli* and 28 days for *Salmonella*

- Average reporting delay for *Salmonella* observed through 16 multi-jurisdictional outbreak investigations since WGS implementation was 43 days, range 9 to 103 days.

- Recent *E. coli* outbreak example:
  - Average reporting delay for PFGE: 8 days
  - Average reporting delay for MLVA: 21 days
  - Average reporting delay for WGS: 30 days

- Impact of decentralization on timeliness to be seen

Success: Collaboration, collaboration, collaboration!

- Lab/Epi collaboration
  - Weekly meetings to review new WGS info and clusters
  - Biweekly meetings to discuss WGS operational issues
  - Validation projects to look at allele ranges from past outbreaks

- Federal/Provincial/Territorial epi collaboration
  - Weekly meetings to discuss WGS implementation, decentralization, surveillance work
  - Face to face training/discussions on incorporating WGS info into routine cluster detection and follow up

- Extensive collaboration has been essential to support the ongoing learning process associated with the integration and use of WGS

Conclusion: The more things change, the more they stay the same

- WGS doesn't solve clusters – continued importance of case interview data, especially at first interview

- Limited resources available at the P/T and local level
  - No resource increase with WGS implementation

- Challenge of ongoing clusters
  - in place of large PFGE clusters we now have large WGS clusters

- Use of the same regulatory processes

Summary

- Increase in clusters
- Impact on common serotypes
- Importance of non-human isolates
- Increased collaboration between partners
- Requires adaptive processes
- Issues before WGS remain issues after WGS
- More changes ahead – decentralization!

Thank you!