When a Cluster Becomes an Outbreak — The Multistate Perspective

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InFORM Conference: Cluster vs. Outbreak
Signal and Noise

- Epidemiologists have to evaluate all the data at their disposal to determine what to investigate.

- **Clusters** represent all the “noise” that we have to sort through:
  - PFGE/WGS clusters
  - Restaurant/venue sub-clusters
  - Consumer complaints

- **Outbreaks** are the “signal” that we’re trying to find:
  - Individuals whose illnesses are causally linked to a common source
  - These are the illnesses that *we can do something about and learn from*
Signal and Noise

- Total of 340 clusters shown here as blue dots
  - 20, or 6%, determined to be outbreaks
- We can dial up or down the number of clusters by raising or lowering our threshold to investigate
- But we can also affect how many are determined to be outbreaks
  - What data are we using to group the illnesses together as a cluster?
  - How vigorous was the epi investigation?
ORPB Definitions for Multistate Investigations

- **Cluster**
  - Two or more potentially related enteric illnesses
  - Reported to federal, state, or local health officials
  - That results in monitoring for additional illnesses or active epidemiologic follow-up by ORPB
Multistate Outbreaks: Pathway From Cluster to Outbreak

PulseNet

State/Local Report

Regulatory Agency Report

Weekly Triage Meeting

Cluster Investigated

No Investigation
Deciding What to Investigate

The decision about what to investigate depends on:

- How recent are the illnesses?
- Does it appear to be ongoing?
- Is the investigation localized and being handled by a local/state agency?
- Which pathogen is involved?

<table>
<thead>
<tr>
<th>E. coli</th>
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<tbody>
<tr>
<td>TW</td>
</tr>
<tr>
<td>1710MNEXH-1, E. coli 0157:H7 detected by CDC:</td>
</tr>
<tr>
<td>XbaI: EXH01.6994 (i+/i-):</td>
</tr>
<tr>
<td>BlnI: EXHA26.5137 (i+/i-):</td>
</tr>
<tr>
<td>Secondary Enzyme Rank:        4869 out of 5018</td>
</tr>
<tr>
<td>Combo Frequency:  /=</td>
</tr>
<tr>
<td>60 Days:  60 Days: AZ, MN (5)</td>
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<tr>
<td>Notes:  10/26: Unique pattern combination. Unique XbaI pattern. Only one other isolate outside of outbreak with BlnI pattern in national database uploaded 10/10</td>
</tr>
<tr>
<td>Outbreak Code: 1710MNEXH-1</td>
</tr>
<tr>
<td>Organism: E. coli 0157:H7</td>
</tr>
<tr>
<td>Primary Pattern #: EXH01.6994</td>
</tr>
<tr>
<td>Secondary Pattern #: EXHA26.5137</td>
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<tr>
<td>Epi Update:</td>
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Cluster Investigated

Outbreak: Unknown Vehicle

Outbreak: Suspect Vehicle

Outbreak: Confirmed Vehicle

No Investigation

Not an Outbreak

No Investigation

Not an Outbreak

No Investigation

Not an Outbreak
Deciding Which Clusters Are Outbreaks

- Outbreak — An enteric disease cluster with supporting data indicative of a common source
  - Temporal, geographic, demographic, dietary, travel, food history, or other information suggesting case-patients share similarities
  - The subtype of the pathogen has had a strong historical association with a specific vehicle
Categorizing Multistate Outbreaks

- Outbreak: Unknown Vehicle
  - Supporting data indicative of a common source
  - No epi, lab, or traceback data pointing to a specific vehicle

- Outbreak: Suspect Vehicle
  - 1 leg of evidence (epi, lab, or traceback) points to a specific vehicle

- Outbreak: Confirmed Vehicle
  - 2 or more legs of evidence (epi, lab, or traceback) point to a specific vehicle
Example

- **Cluster** – STEC O157 infections with an uncommon PFGE pattern in 11 states with no unusual demographics or common food types/preferences

- **Outbreak: Unknown Vehicle** – STEC O157 infections centered in the Pacific Northwest; young median age; many reports of “healthy foods”

- **Outbreak: Suspect Vehicle** – STEC O157 infections centered in the Pacific Northwest; romaine lettuce is reported significantly more often than expected and no other vehicles of interest

- **Outbreak: Confirmed Vehicle** – STEC O157 infections centered in the Pacific Northwest; romaine lettuce is reported significantly more often than expected with common brands reported; traceback shows the lettuce was all harvested from one field
Why Do We Care About These Definitions?

- Tracking “success”
  - Using all clusters as a denominator for calculating a solve rate is not ideal
  - Many PFGE clusters are not “solvable” because they don’t have a common source or have multiple sources

- Identifying gaps in process or prevention
  - Unknown outbreaks are outbreaks we think we could have solved but didn’t
  - Suspect outbreaks are important to report so that more difficult to solve food types are less under reported
  - Confirmed outbreaks represent data with the most confidence about the vehicle and are the best chance to work toward finding a root cause
WGS Impact on Multistate Clusters and Outbreaks

- Will exclude unrelated illnesses that had previously been included in PFGE clusters
- Will break up what had previously been large PFGE clusters into multiple smaller WGS clusters
- Will detect clusters that were never previously detected by PFGE
WGS Impact on Multistate Clusters and Outbreaks
WGS Impact on Multistate Clusters and Outbreaks

- WGS will give us much more confidence that illnesses in a cluster are all linked in some way
- But it will also help show that some PFGE clusters were just “noise
- This will likely have the effect of substantially increasing the proportion of clusters that represent true outbreaks
- Great, right!?
How will we prioritize in the face of this new volume of clusters/outbreaks?
Conclusions

- Cluster triage and investigation are tools we use to find outbreaks

- Outbreaks are groups of illnesses that we can take public health action on:
  - Stop the current outbreak
  - Understand how illnesses occurred to prevent similar outbreaks

- Having consistent definitions for these can help identify gaps in process or prevention

- WGS will likely substantially increase the number of clusters detected, but also the prior probability that the illnesses represent a true outbreak
  - Is does every WGS cluster represent an outbreak?