Molecular Surveillance as a Means to Expand an Outbreak Investigation - Massachusetts, 2015-2018

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Abstract #0857

BACKGROUND AND OBJECTIVES

- In mid-2016, the Massachusetts Department of Public Health (MDPH) identified an increase in HIV diagnoses among persons who inject drugs (PWID) in northeastern Massachusetts, most notably in the cities of Lowell and Lawrence.
- This increase was identified primarily through provider notifications and case surveillance investigations.
- With CDC assistance, MDPH began an investigation in 2018 to characterize the outbreak and institute further control measures to prevent additional cases.
- We describe the contributions of molecular HIV surveillance to the investigation through the following objectives:
  1. Assess how molecular surveillance expanded the investigation by linking cases to the investigation that might not have been linked through traditional public health field services
  2. Compare cases initially epidemiologically linked to the investigation to those initially molecularly linked
  3. Understand the dynamics of transmission
  4. Examine the overlaps of molecular and partner services networks

METHODS

Case definition

HIV diagnoses occurring during January 2015 through June 2018 were considered:

- Epidemiologically linked to the investigation through:
  a) residence, homelessness, HIV diagnosis, or HIV care in the cities of Lawrence or Lowell OR
  b) as a named partner of an investigation case.
- Molecularly linked to the investigation if their HIV sequence linked to that of an epidemiologically linked case at a genetic distance threshold of ≤1.5%

Data sources

- Massachusetts HIV surveillance data (enhanced HIV/AIDS Reporting System)
- Massachusetts partner services data (MAVEN)

Analysis

- HIV sequences from all persons with a drug resistance test conducted by CDC or commercial labs since January 2016 were reported as part of routine surveillance and analyzed in Secure HIV-TRACE through pairwise comparisons. Molecular clusters were constructed that contained cases that met the case definition and HIV diagnoses that did not (e.g. diagnoses from before 2015).
- Characteristics of cases initially linked through molecular analysis to those already epidemiologically linked were compared by using Fisher's exact test.
- Partner links between cases and HIV diagnoses that did not meet the case definition were visualized by using MicrobeTrace (http://bit.ly/microbetrace) in a network diagram. Information on molecular cluster membership was overlaid on top.

RESULTS

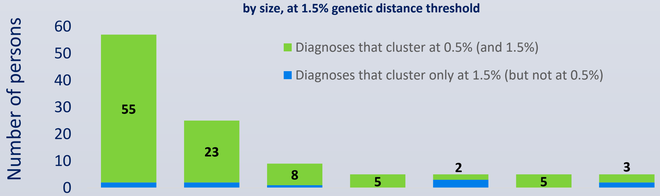
Table 1. Characteristics of cluster cases (n = 129), as of June 2018 by initial method of linkage to investigation

Characteristic	Initially Molecularly Linked (N = 36)	Initially Epidemiologically Linked (N = 93)	P value
Age (median, years)	35	31	0.201
Sex at Birth	Male: 19 (53%)	Male: 55 (59%)	0.555
Race/Ethnicity	White (non-Hispanic): 25 (69%) Black (non-Hispanic): 1 (3%) Hispanic: 10 (28%)	White (non-Hispanic): 62 (67%) Black (non-Hispanic): 3 (3%) Hispanic: 28 (30%)	0.929
Transmission Category	Injection Drug Use[1]: 30 (83%) MSM: 0 (0%) Heterosexual contact: 3 (8%) Other/Unknown: 3 (8%)	Injection Drug Use[1]: 86 (92%) MSM: 1 (1%) Heterosexual contact: 3 (3%) Other/Unknown: 3 (3%)	0.297
Year of HIV diagnosis	2015–2016: 19 (53%) 2017–2018: 17 (47%)	2015–2016: 24 (26%) 2017–2018: 69 (74%)	**0.006**
County of Residence at HIV Diagnosis	Middlesex: 14 (39%) Essex: 9 (25%) Other: 13 (36%)	Middlesex: 44 (47%) Essex: 36 (39%) Other: 13 (14%)	**0.024**
Interviewed by Partner Services	17%	71%	**<0.001**

[1]includes persons who report male-to-male sexual contact and inject drugs

- Initially, 36 (23%) of cases were linked molecularly to the investigation.
- Molecularly linked and epidemiologically linked cases were similar with respect to:
  - age (majority aged <40 years)
  - race/ethnicity (majority white, non-Hispanic)
  - sex at birth (majority male)
  - transmission category (vast majority inject drugs)
- Epidemiologically linked cases were more likely to have been:
  - diagnosed in 2017–2018
  - diagnosed in Middlesex and Essex counties
  - interviewed by partner services
- Of the 129 cases, 27 (21%) were found to have only epi links, 29 (22%) to have only molecular links, and 73 (57%) to have both epi and molecular links

Figure 1. Molecular clusters[2] of at least 5 cases, by size, at 1.5% genetic distance threshold

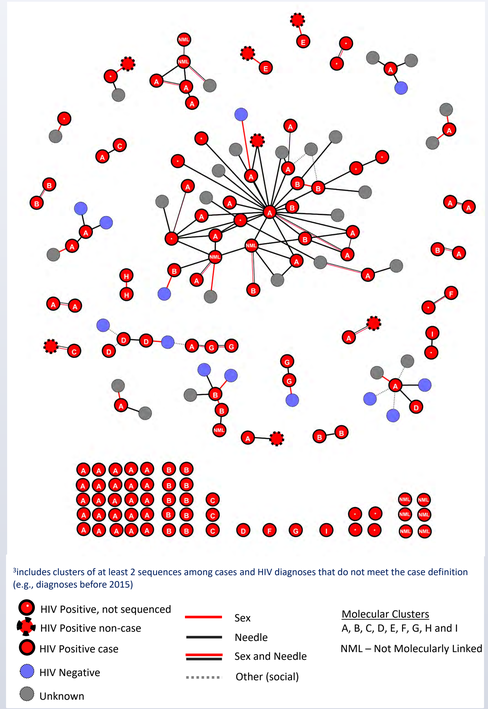


Molecular cluster name	A	B	C	D	E	F	G
Molecular cluster size (1.5%)	57	25	9	5	5	5	5
Molecular cluster size (0.5%)	55	23	8	5	2	5	3

[2]includes clusters of at least 5 sequences among cases and HIV infections that do not meet the case definition (e.g., diagnoses before 2015)

- Presence of seven clusters of size ≥5 suggests multiple introductions of HIV into the community of PWIDs.
- Most individuals in the distinct clusters also linked at the 0.5% threshold, suggesting that much of the HIV transmission likely occurred within the past few years.

Figure 2. Molecular and elicited named partner networks[3]



[3]includes clusters of at least 2 sequences among cases and HIV diagnoses that do not meet the case definition (e.g., diagnoses before 2015)

- The molecular network and the network of elicited named partners overlap but do not mirror each other.
  - Networks elucidated through MDPH partner services include cases from different molecular clusters and cases without any identified molecular links.
  - Many of the molecular cluster members would not have been included in networks elucidated by partner services.
  - Of named partner linkages between persons with sequences, the majority are between persons in the same molecular cluster.
- A substantial proportion of uniquely named partners were HIV-positive (73, 65%), while only 13 (12%) tested HIV-negative and 26 (23%) were not tested.

LIMITATIONS/CHALLENGES

- Molecular analysis requires HIV sequences generated from drug resistance testing for persons with diagnosed HIV. Persons involved in transmission whose infection has not been diagnosed and persons for whom an HIV sequence was not generated or reported to MDPH are not included in the molecular analysis.
- At the time of this investigation, partner services interviews were not routinely conducted for all new HIV diagnoses. Consequently, elicitation of names of partners was hindered. Additionally, some PWID who were interviewed did not report names of partners.

CURRENT STATUS OF INVESTIGATION

- 153 cases had been linked to this investigation by December 31, 2018, of whom
  - 106 (69%) were initially epidemiologically linked and 47 (31%) were initially molecularly linked
  - 81 (53%) had both epidemiologic and molecular links 32 (21%) had only epidemiologic links, and 40 (26%) had only molecular links
- Viral Suppression
  - 94 (61%) were suppressed based on their most recent viral load test during 2018.

CONCLUSIONS

- As of December 2018, the addition of molecular data expanded the number of persons linked to the investigation by 44%, improving prevention opportunities and highlighting the importance of molecular surveillance in HIV outbreak response.
- Similar patterns of risk, demographics and geography between epidemiologically linked and molecularly linked cases indicate that the molecularly linked cases are part of the same risk network as cases originally identified before molecular data were available.
- The presence of multiple molecular clusters among investigation cases suggests multiple introductions of HIV into the community of PWIDs in Northeast Massachusetts.
- The high proportion of cases linking at 0.5% genetic distance threshold suggests sustained transmission within these clusters.

PUBLIC HEALTH IMPLICATIONS

- A substantial proportion of uniquely named partners were HIV-positive, indicating that offering partner service interviews to all persons with newly diagnosed HIV will maximize HIV prevention opportunities both for persons with newly diagnosed infection and their at-risk partners.
- Molecular and elicited named partner networks provide additional information not gathered from either source alone, and highlight the importance of a multi-pronged approach to identifying members of high-risk networks.

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