Genomic Surveillance for Outbreak Detection and Control in Healthcare

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Disclosures

- Consulting with GSK, Merck, Pfizer, Sanofi, and CSL Seqiris on epidemiology and vaccine prevention of infectious diseases
- Funding from NIH and CDC on studies of epidemiology and genomic epidemiology of infectious diseases
- Views expressed are mine and not those of the University of Pittsburgh or UPMC
- Spoiler alert: I’m not going to be talking about antimicrobial stewardship!

Objectives

- To understand
  - The mechanics of performing genomic surveillance in healthcare
  - How genomic surveillance leads to improvements in patient safety
  - The economic benefits of genomic surveillance in healthcare

Genomic Surveillance for Hospital Outbreak Detection

- Introduction
- Results of Enhanced Detection System for Hospital-Acquired Transmission
  - Phase 1: Retrospective genomic surveillance: Proof of concept
  - Phase 2: Real-time genomic surveillance
- Other EDS-HAT applications
- Barriers to implementation
- Summary

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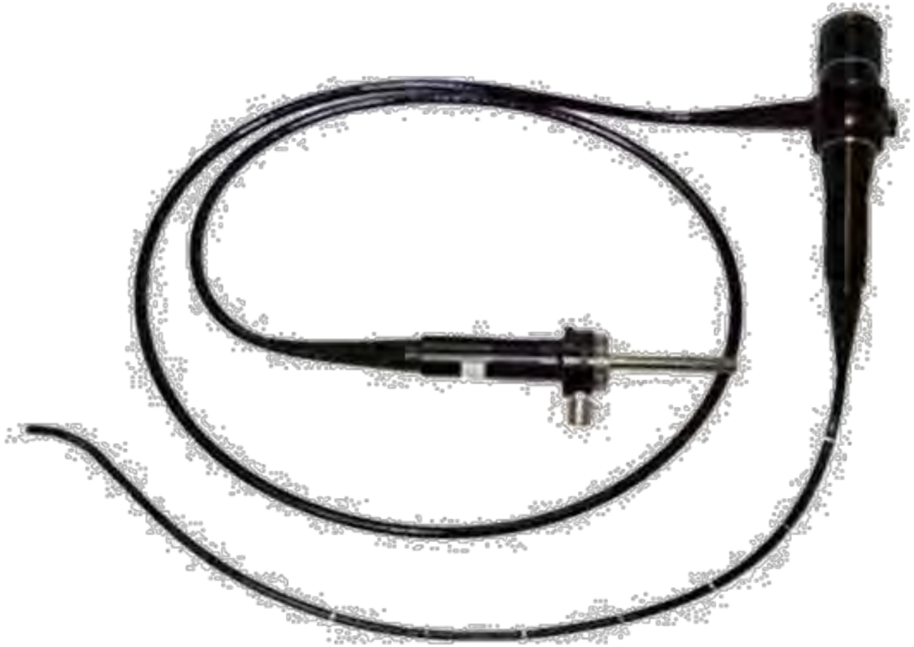
Hospital Associated Infections (HAIs) in the U.S.

- 722,000 infections per year
- 98,000 deaths per year
- $30 billion+ system costs
- 7-10% of patients will develop HAI

The tipping point: UPMC ERCP scope outbreak, 2012

- Caused by *K. pneumoniae*
- 17 cases over 14-months
    - 12 bloodstream infections
    - 5 deaths
    - Reactive WGS: Contaminated scopes
    - Took over a year to detect!
- If detected early?
    - Prevention of 14 cases, 9 BSIs, 3 deaths
    - Cost of treating bacteremias alone: $164,000



Marsh et al. PLoS One 2015. PMID 26637170

And it wasn’t just us. . .

Office of Public Affairs
U.S. Department of Justice

PRESS RELEASE **December 10, 2018**

Olympus Medical Systems Corporation, Former Senior Executive Plead Guilty to Distributing Endoscopes After Failing to File FDA-Required Adverse Event Reports of Serious Infections

Olympus to pay $85M after pleading guilty to fraudulently selling scopes linked to superbug spread

By **Tina Reed** · Dec 10, 2018 5:50pm

Los Angeles Times

Olympus told its U.S. executives no broad warning about tainted medical scopes was needed, despite superbug outbreaks

“The current paradigm for hospital outbreak detection and investigation is based on methodology first developed over 150 years ago”

“This method (of looking for geotemporal clustering) may misidentify transmission where it has not occurred or miss transmission when it has”

Translation: We’re guessing, not detecting

Peacock SJ et al. Microbiology 2018. PMID: 30052172
Houlihan CF et al. J Infect Dis 2018;218:1485. PMID: 29873767

Definitions for how whole genome sequencing (WGS) is used

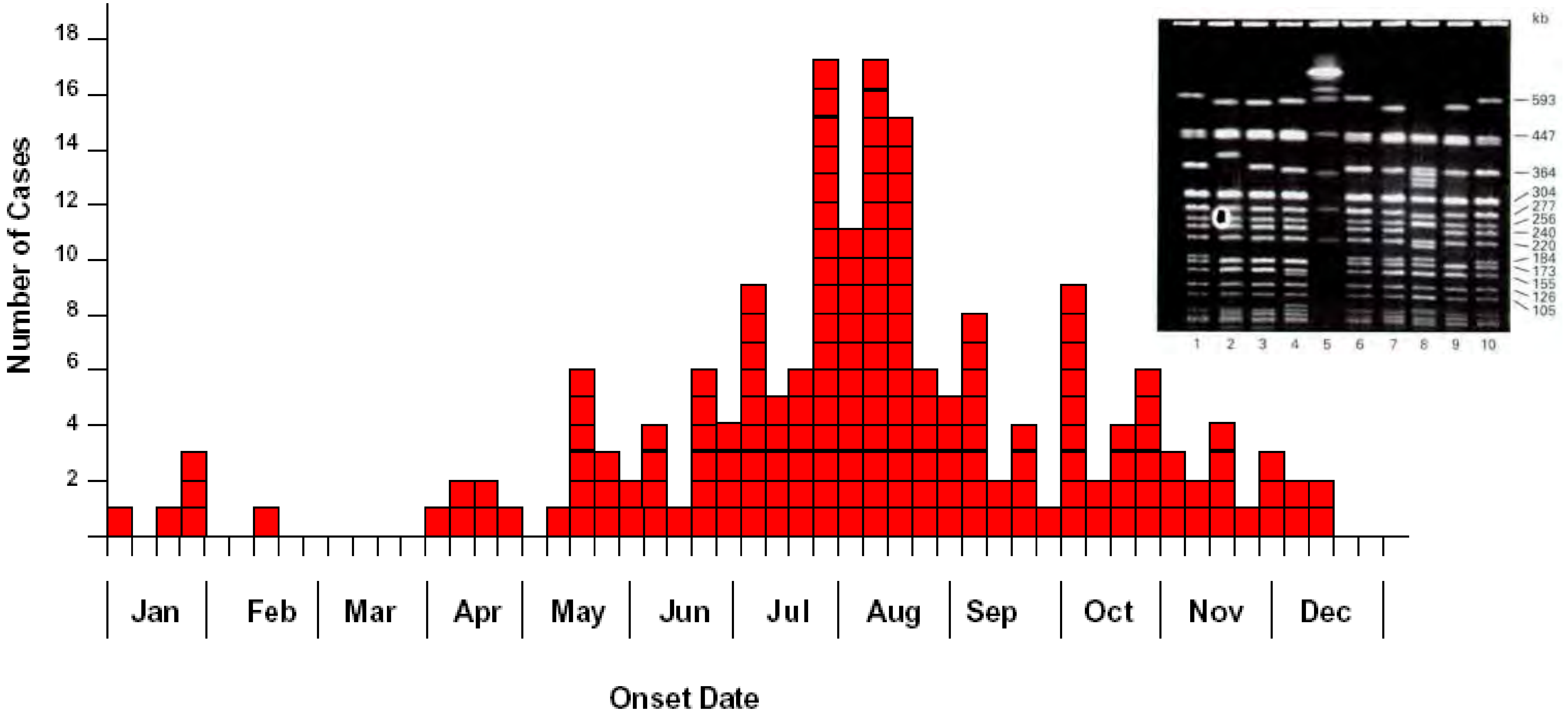
- Reactive WGS (traditional approach):
  - WGS in response to a suspected outbreak to confirm or refute
  - Purpose: Outbreak investigation

- Genomic surveillance
  - Routine WGS of all clinical isolates
  - Purpose: Outbreak detection

How are healthcare outbreaks detected now?

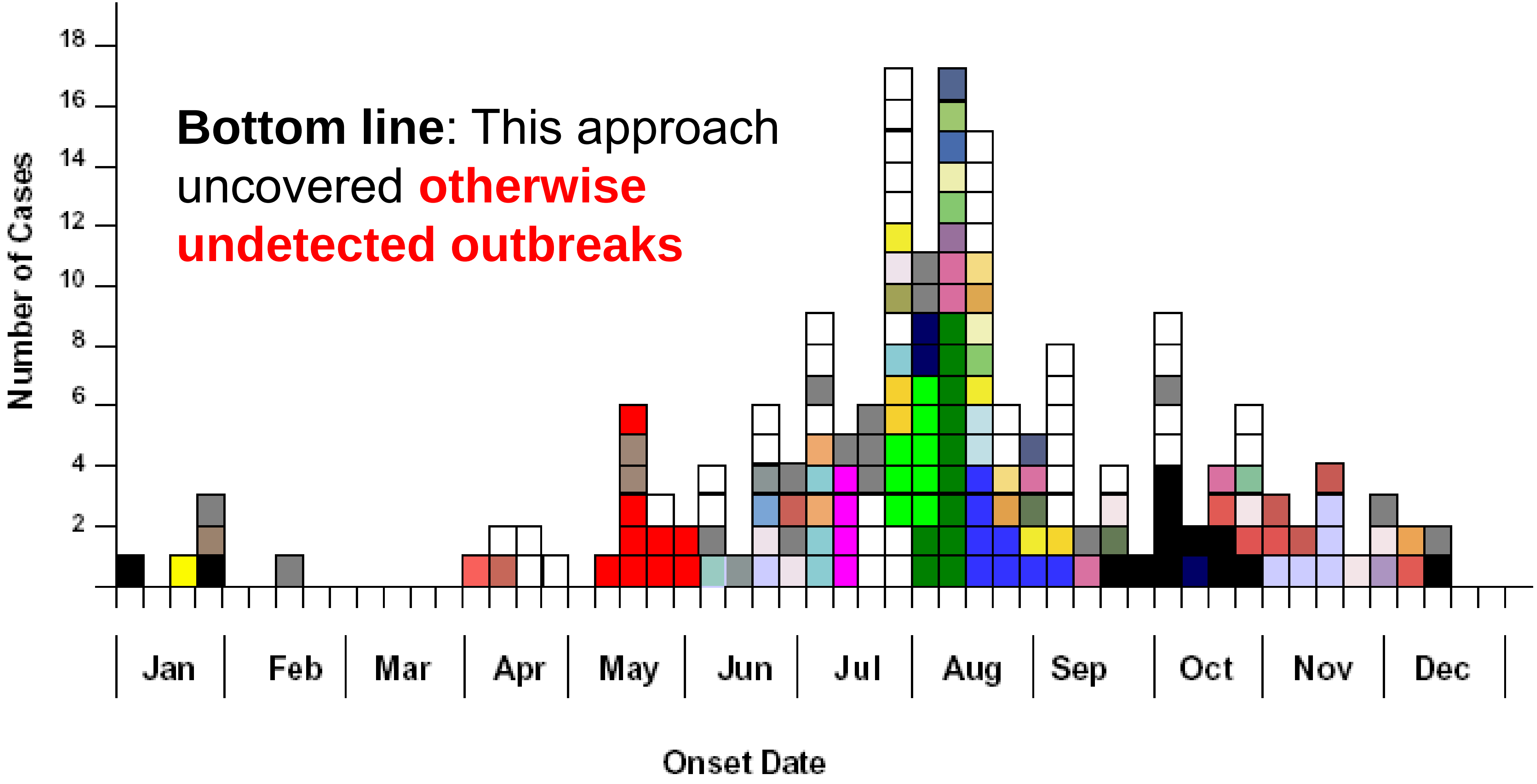
- Select pathogen monitoring
- Line lists of infections
- Astute healthcare workers noticing increase of infections (often geotemporal clustering)
- Sudden appearance of unusual pathogen
- Reactive WGS in some settings
- Bottom line: This approach misses many outbreaks, delays recognition of others, and falsely identifies “outbreaks” that aren’t confirmed

The origins of bacterial genomic surveillance: Routine PFGE of *E. coli* O157:H7, Minnesota Department of Health, 1995



Bender JB et al. N Engl J Med 1997. PMID 9241128

The origins of bacterial genomic surveillance: Routine PFGE of *E. coli* O157:H7, Minnesota Department of Health, 1995

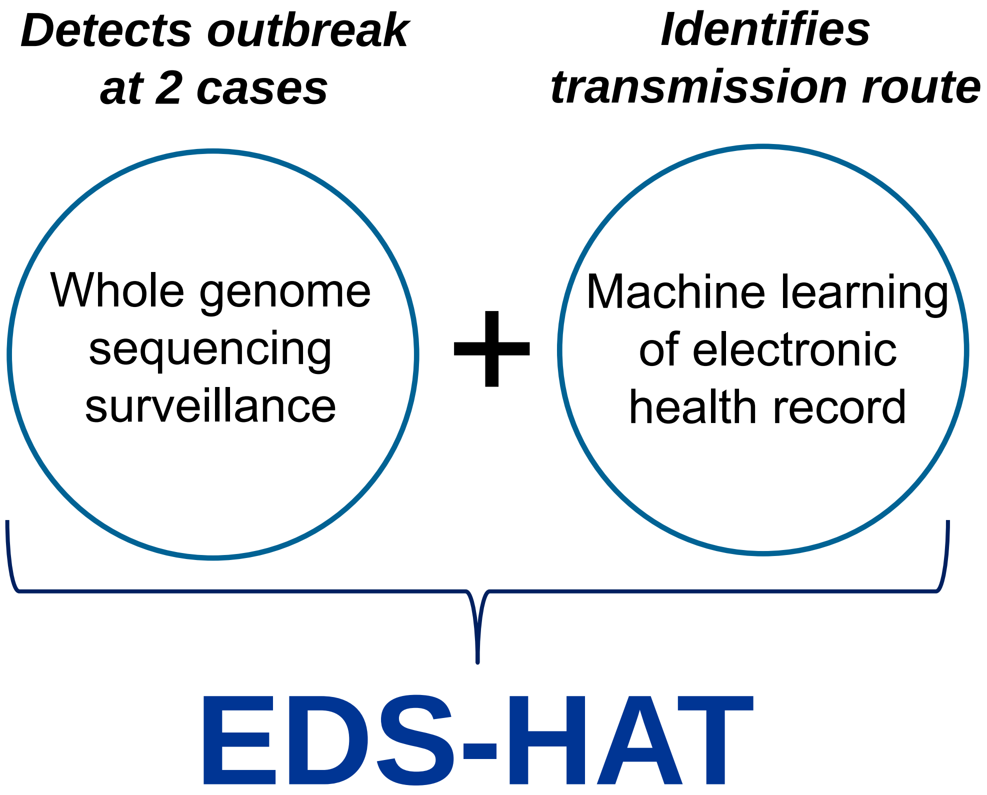


Bottom line: This approach uncovered **otherwise undetected outbreaks**

Bender JB et al. N Engl J Med 1997. PMID 9241128

http://www.cdc.gov/pulsenet/

Enhanced Detection System for Healthcare-Associated Transmission (EDS-HAT)



Detects outbreak at 2 cases

Whole genome sequencing surveillance

+

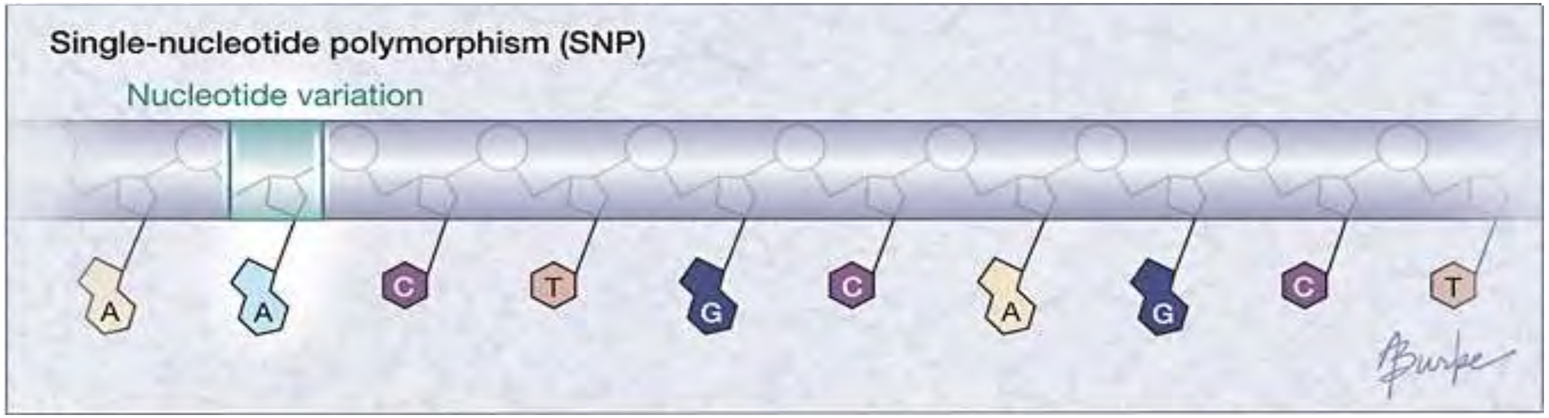
Identifies transmission route

Machine learning of electronic health record

EDS-HAT

Whole genome sequencing: What’s a SNP?

- Genomes of most bacterial species consist of 2-7 million nucleotides (adenine/cytosine/thymine/guanine)
- Rapid bacterial evolution results in single nucleotide polymorphisms (SNPs)



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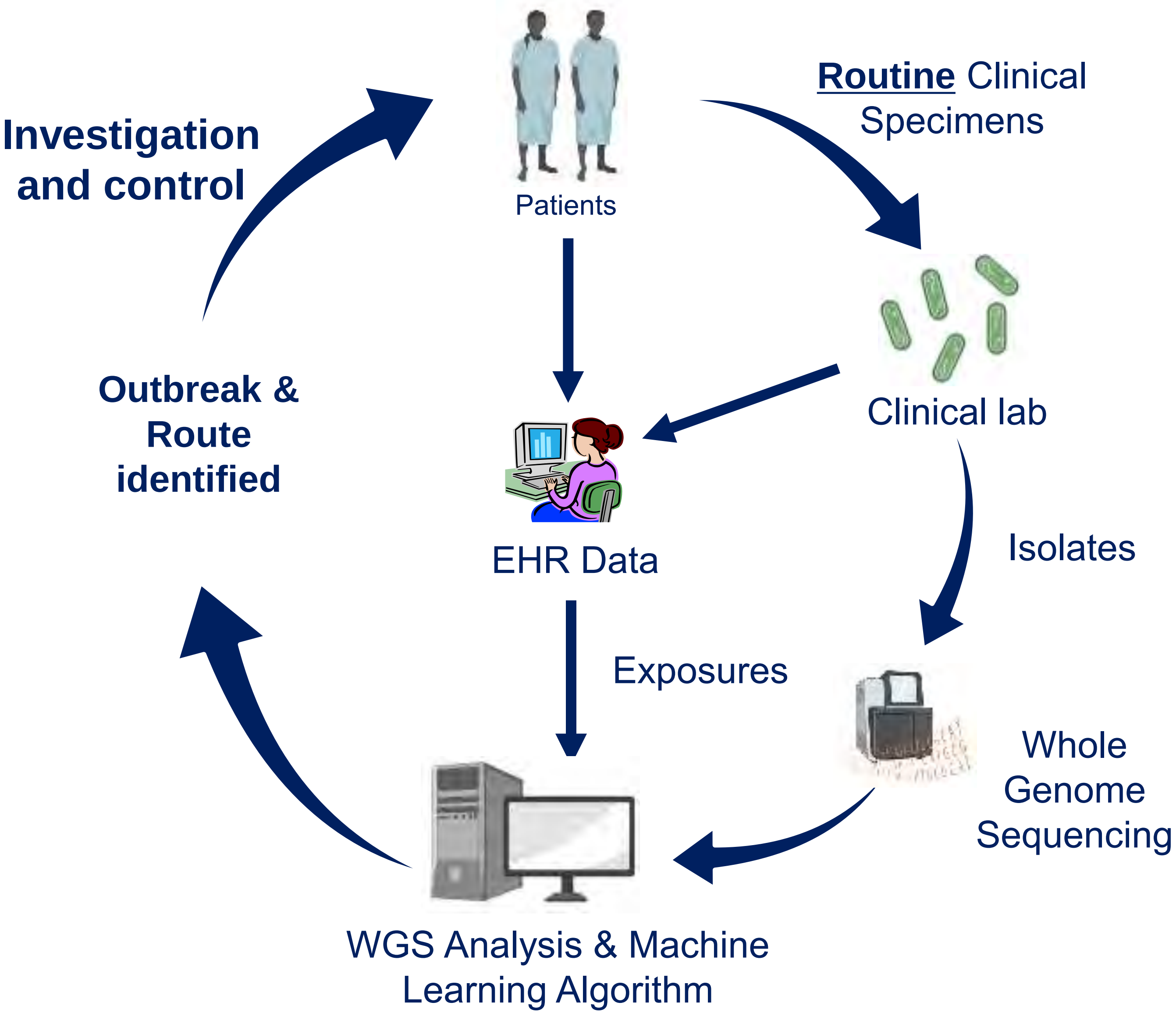

Patients

Routine Clinical Specimens

Clinical lab

Isolates

Whole Genome Sequencing

WGS Analysis & Machine Learning Algorithm

EHR Data

Exposures

Outbreak & Route identified

Investigation and control

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EDS-HAT 2-Year Retrospective Proof-of-Concept Analysis

Clinical Infectious Diseases

MAJOR ARTICLE

Whole-Genome Sequencing Surveillance and Machine Learning of the Electronic Health Record for Enhanced Healthcare Outbreak Detection

Alexander J. Sundermann,[1,2,3] Jieshi Chen,[4] Praveen Kumar,[5] Ashley M. Ayres,[6] Shu-Ting Cho,[2] Chinelo Ezeonwuka,[1,2] Marissa P. Griffith,[1,2] James K. Miller,[4] Mustapha M. Mustapha,[1,2] A. William Pasculle,[7] Melissa I. Saul,[8] Kathleen A. Shutt,[1,2] Vatsala Srinivasa,[1,2] Kady Waggle,[1,2] Daniel J. Snyder,[9] Vaughn S. Cooper,[9] Daria Van Tyne,[2] Graham M. Snyder,[2,6] Jane W. Marsh,[1,2] Artur Dubrawski,[4] Mark S. Roberts,[5,8] and Lee H. Harrison,[1,2,3]

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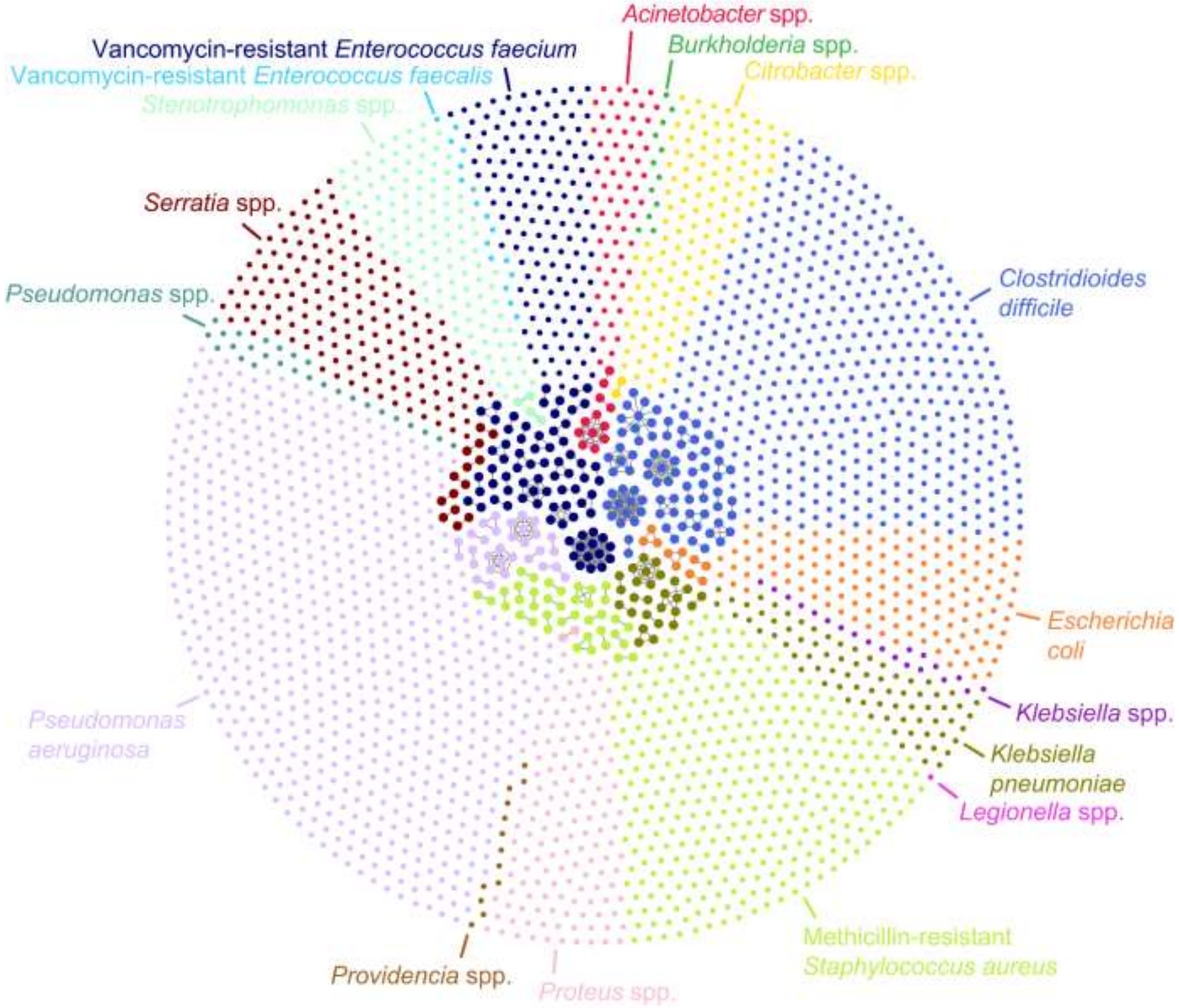
Sundermann AJ et al. Clin Infect Dis 2022. PMID 34791136

EDS-HAT 2-Year Retrospective Proof-of-Concept Analysis: WGS of 3,165 isolates



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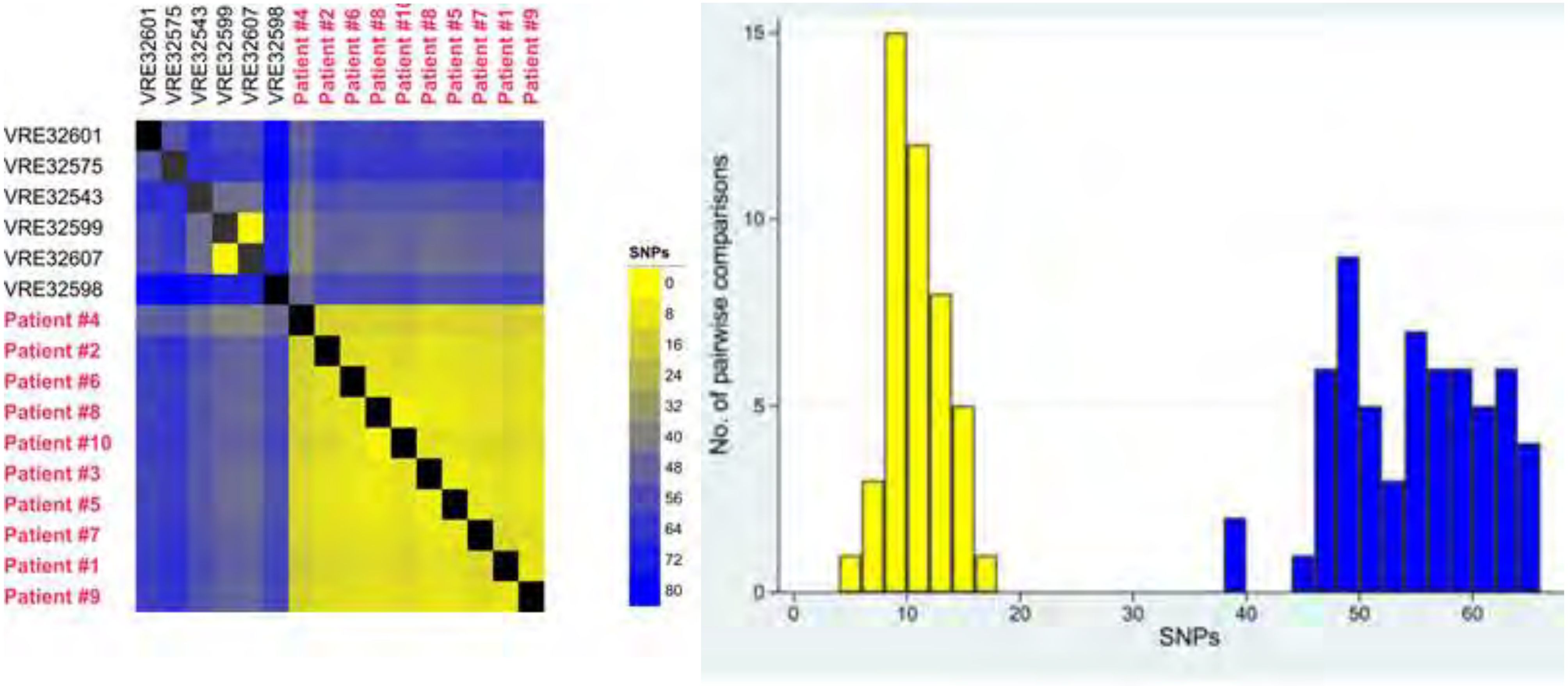
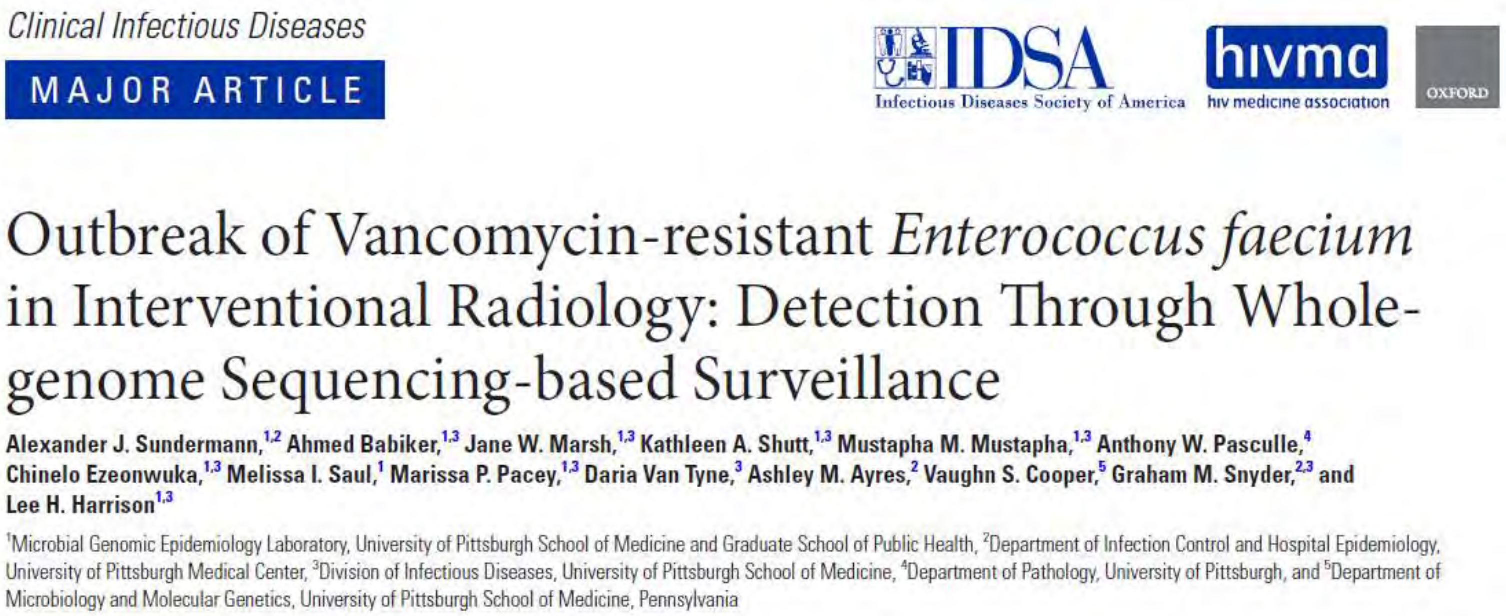
EDS-HAT: Detection of previously unrecognized outbreak



Sundermann AJ et al. Clin Infect Dis 2022. PMID 34791136

Notable Outbreak Detected by Genomic Surveillance: Ten cases of VRE in Interventional Radiology



Clinical Infectious Diseases

MAJOR ARTICLE

Outbreak of Vancomycin-resistant *Enterococcus faecium* in Interventional Radiology: Detection Through Whole-genome Sequencing-based Surveillance

Alexander J. Sundermann,[1,2] Ahmed Babiker,[1,3] Jane W. Marsh,[1,3] Kathleen A. Shutt,[1,3] Mustapha M. Mustapha,[1,3] Anthony W. Pasculle,[4] Chinelo Ezeonwuka,[1,3] Melissa I. Saul,[1] Marissa P. Pacey,[1,3] Daria Van Tyne,[3] Ashley M. Ayres,[2] Vaughn S. Cooper,[5] Graham M. Snyder,[2,3] and Lee H. Harrison[1,3]

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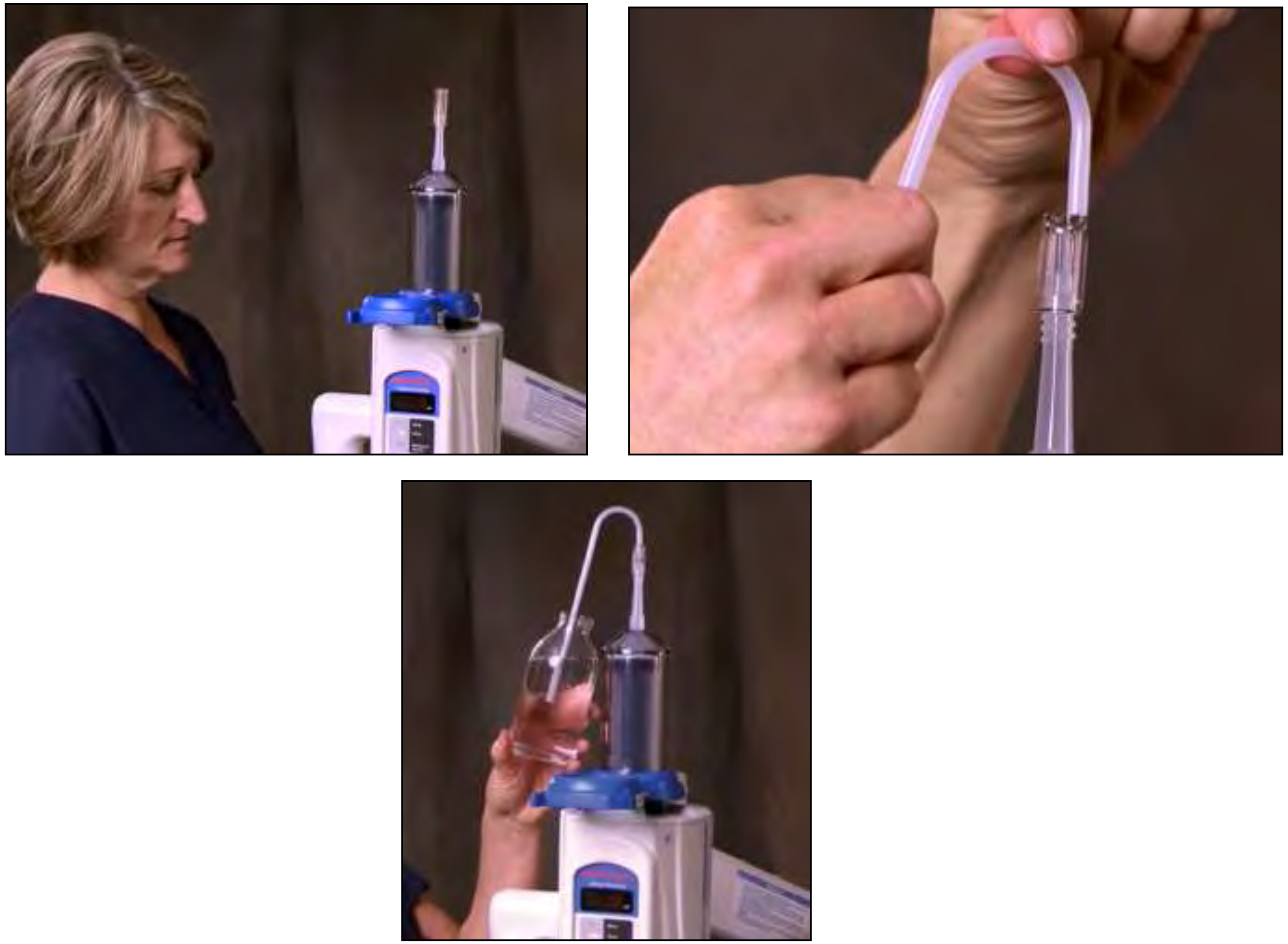
Loading the Automatic "Sterile" Contrast Injector: Screen Shots from Manufacturer's Training Video



- Outbreak undetected by traditional methods
- Novel transmission route
- We don't know when it started
- Patients on **8 different nursing units**
- IR practices observed, procedure stopped before contrast injection
- Extensive education about safe practices
- Outbreak ended immediately

Sundermann AJ et al. Clin Infect Dis 2022. PMID 34791136

EDS-HAT 2-Year Retrospective Analysis: Notable Outbreaks Not Detected by Routine IP Practice

- VRE outbreak associated with interventional radiology and injection of sterile contrast
- *Pseudomonas aeruginosa* outbreak associated with gastroscopy
- Outbreaks of multiple pathogens at an imbedded chronic care facility
- Outbreaks of multiple pathogens on an intensive care unit
- *C. difficile* outbreaks associated with wound care
- MRSA infections associated with electroencephalography

Sundermann AJ et al. Clin Infect Dis 2022. PMID 34791136

EDS-HAT 2-Year Retrospective Analysis: Traditional IP practice

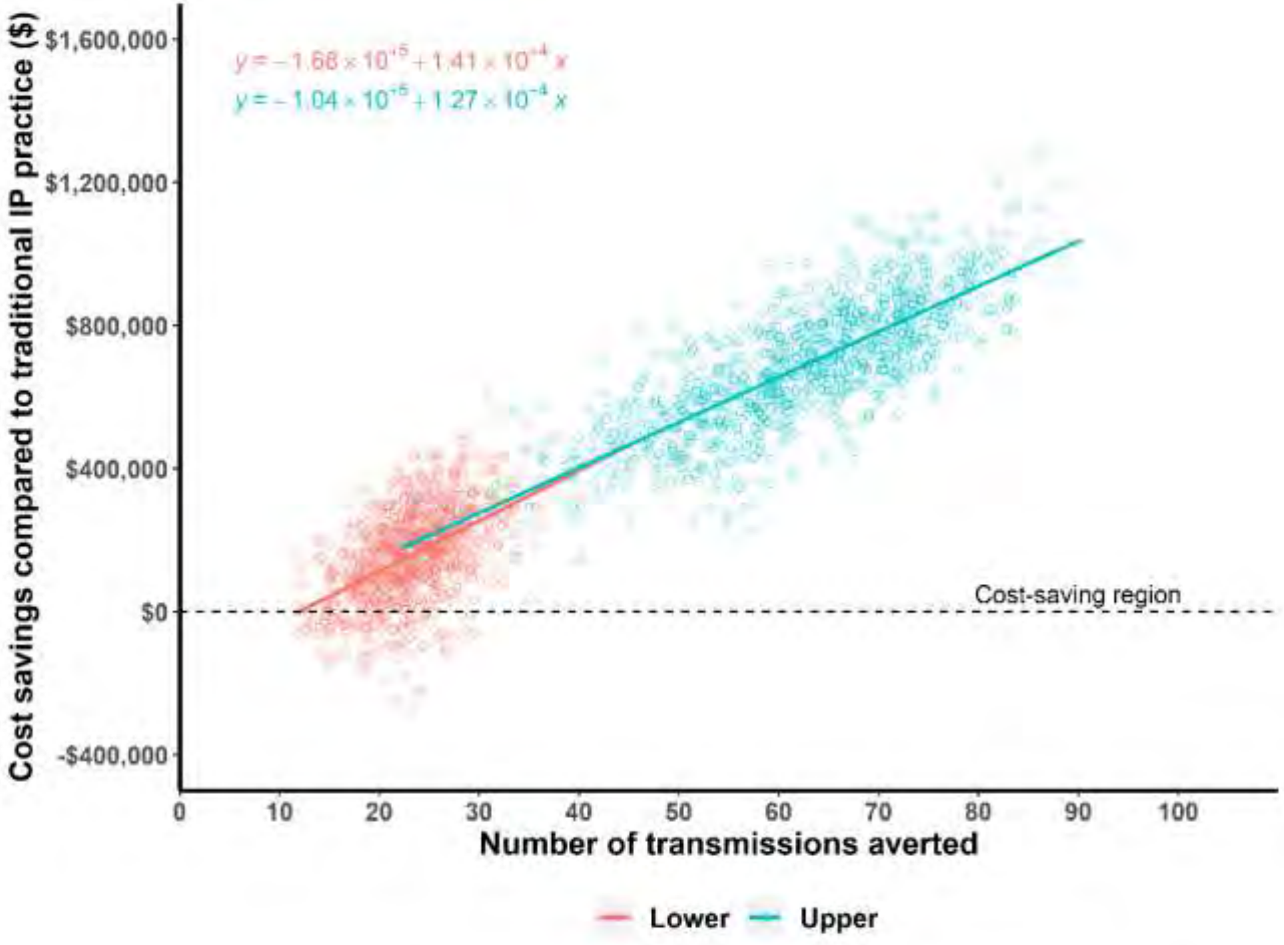
During the same time that **EDS-HAT was running in the background**:

- 15 **reactive sequencing** requests for suspected and potentially actionable outbreaks involving 133 patients
- Only 5 (3.8%) patients from 2 clusters genetically related
- **Conclusion**: Reactive sequencing missed most outbreaks identified by EDS-HAT and created multiple false alarms

Sundermann AJ et al. Clin Infect Dis 2022. PMID 34791136

EDS-HAT Retrospective Analysis: Clinical and Economic Impact

- EDS-HAT may have prevented 25 to 63 transmissions if run in real-time
- Overall cost savings ~$700,000
- EDS-HAT cost-saving in >99% of simulations



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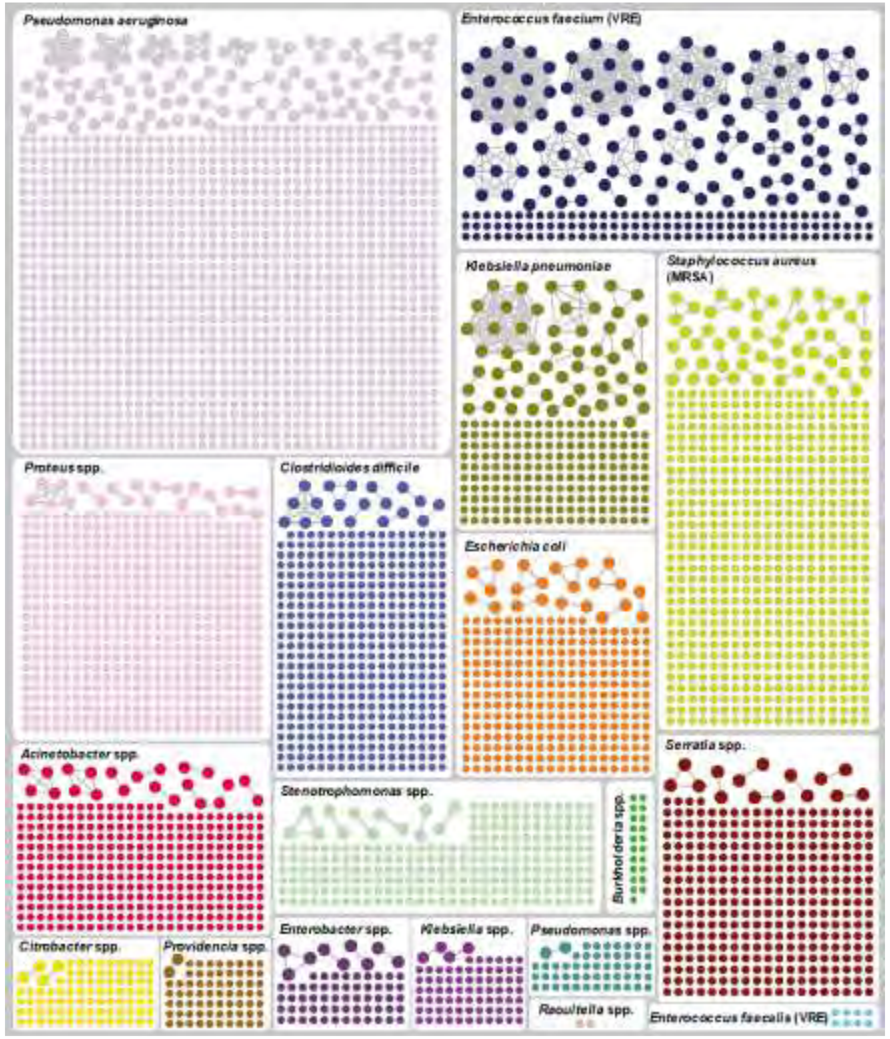
EDS-HAT 2-Year Real Time Analysis

Initiated November 2021

- 3,921 unique patient isolates
- 476 (12.1%) related in 172 clusters
- Clusters 2-16 patients
- Median turnaround time 15 days
- 61.3% identified epidemiological links



Sundermann AJ et al. Clin Infect Dis. 2025. PMID 40302215

EDS-HAT 2-Year Real Time Analysis

Notable outbreaks

- 9 endoscope clusters: All detected at and limited to 2 patients
- 3 clusters with shared ventilators
  - 2 clusters: each with same ventilator, same ICU
  - 1 cluster: same ventilator, two ICUs (ventilator had been relocated)
- Three patients with *P. aeruginosa* infection, same ICU bed
- Cluster of 7 patients with VRE infection from wound care across multiple nursing units (multiple *C. difficile* clusters in retrospective study*)*
- No additional IR outbreaks

Incidental findings

- Multiple clusters from outside facilities
- National artificial tears *P. aeruginosa* outbreak: 2 patients

Sundermann AJ et al. Clin Infect Dis. 2025. PMID 40302215

EDS-HAT 2-Year Real Time Analysis: Clinical and Economic Impact

Approach

- Compared real-time period to two-year retrospective period (when no interventions [except IR outbreak])
- Transmission route specific
- Compared size of outbreaks within the same route during retrospective period
- Probabilistic sensitivity analysis

Sundermann AJ et al. Clin Infect Dis. 2025. PMID 40302215

EDS-HAT 2-Year Real Time Analysis: Clinical and Economic Impact

Results

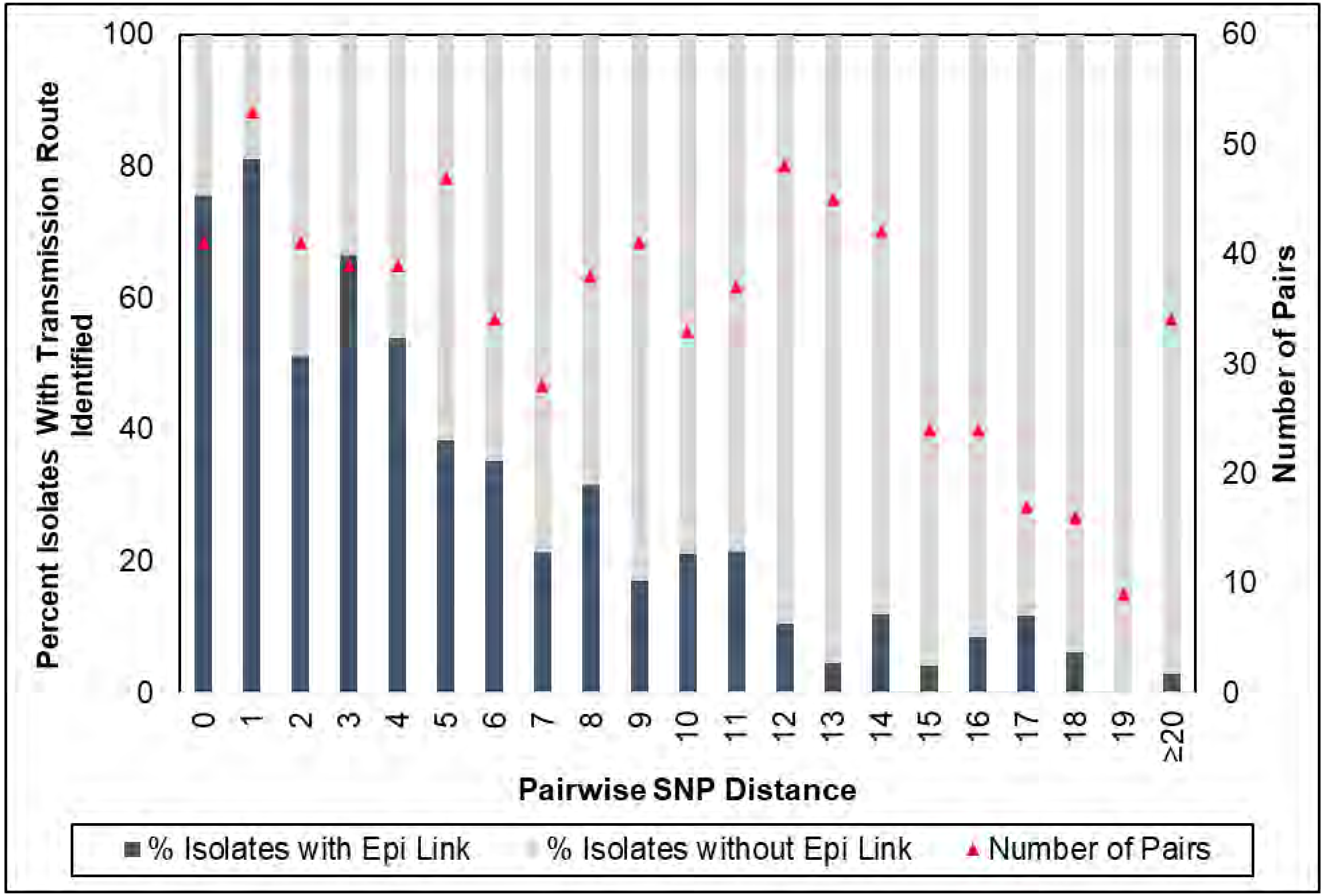
- 62 prevented infections (2.5th-97.5th percentile: 22-126 infections prevented)
- Net cost savings of $695,706 (2.5th-97.5th percentile: $26,383-$1,769,390)
- 3.2-fold return on investment
- These benefits in setting of several years of EDS-HAT resulting in strengthening of IP&C measures

Sundermann AJ et al. Clin Infect Dis. 2025. PMID 40302215

SNP & Epidemiological Links

- Significant association between lower SNP distance and presence of epi link

- Conclusion: possibly overcalling clusters



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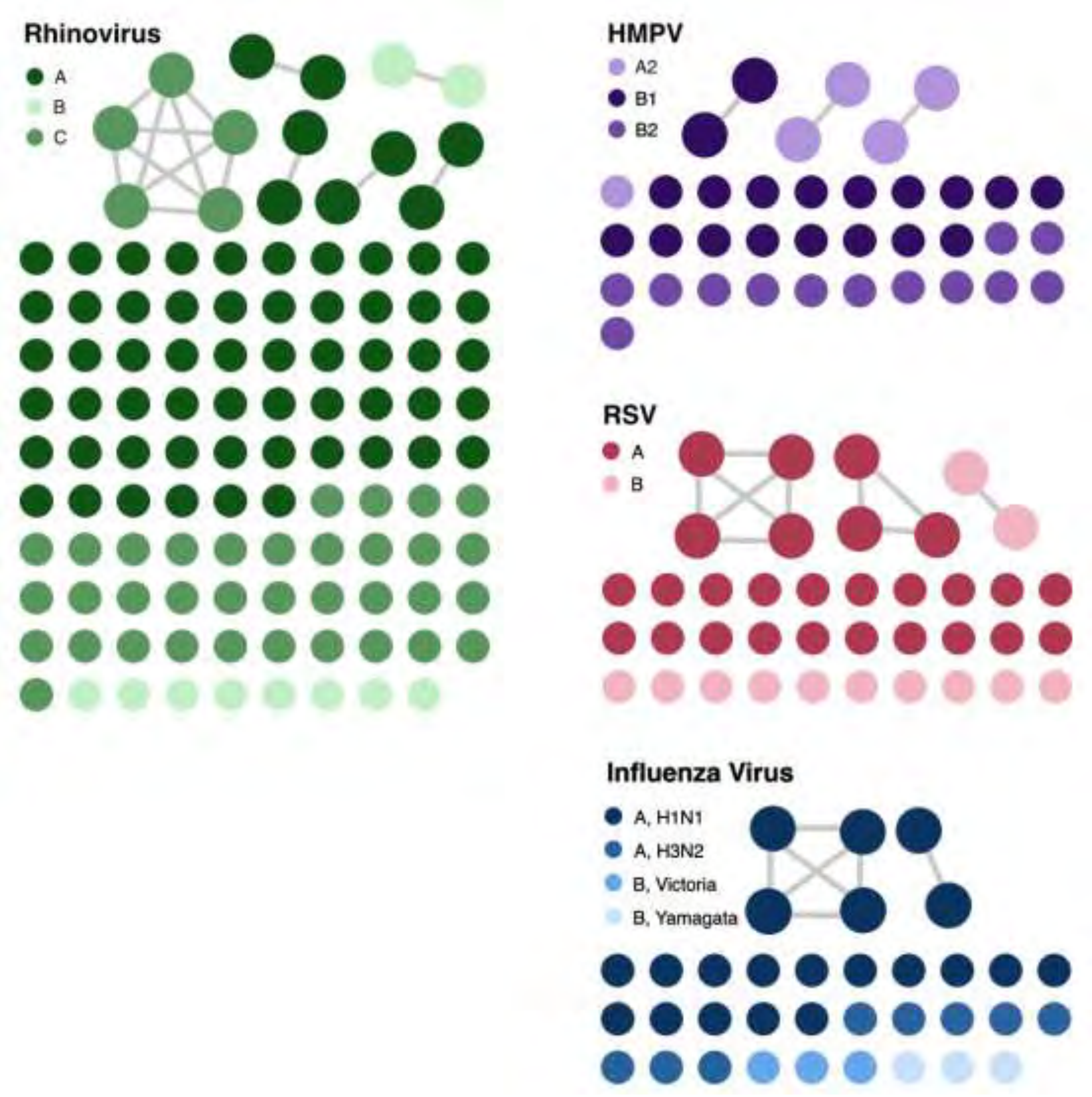
Other EDS-HAT applications under investigation

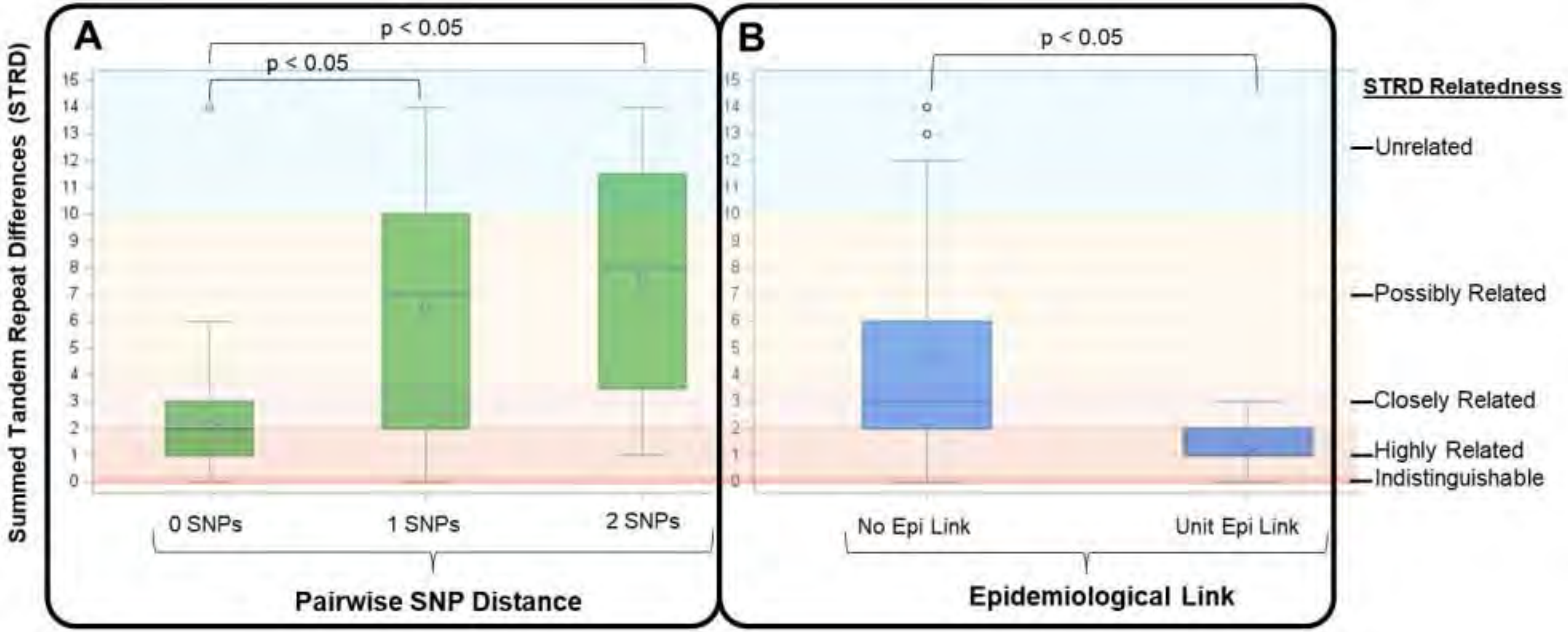
- Explore incorporation of
  - Respiratory viruses
  - Non-tuberculous mycobacteria
  - Environmental surveillance cultures
  - Short-read sequencing for tracking plasmids in the hospital
  - Non-teaching hospitals
  - VIGIA: Pilot study of genomic surveillance in two Brazilian teaching hospitals
- EDS-HAT Lite: Leverage artificial intelligence to identify outbreaks using routinely available microbiologic and EHR data
- Enhanced genomic methods for *C. difficile* using *in silico* MLVA

Retrospective genomic surveillance for respiratory viruses at three UPMC hospitals, 2018-2020



Srinivasa VT et al. medRxiv 2025. PMID 40313286

MLVA for *C. difficile*: Summed tandem repeat differences, by SNP distance (Panel A) and whether epidemiologic link identified (Panel B), for isolates with 0-2 SNP differences



- Conclusion: *in silico* MLVA provides more discriminatory power than SNPs alone

Sundermann AJ et al. medRxiv 2024. PMID 39371154

Prediction:

Genomic surveillance will eventually become
a routine part of U.S. healthcare

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This is best thing since sliced bread,

but how do we get it at our hospital?

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

Check for updates

| Editor's Pick | Genomics and Proteomics | Commentary

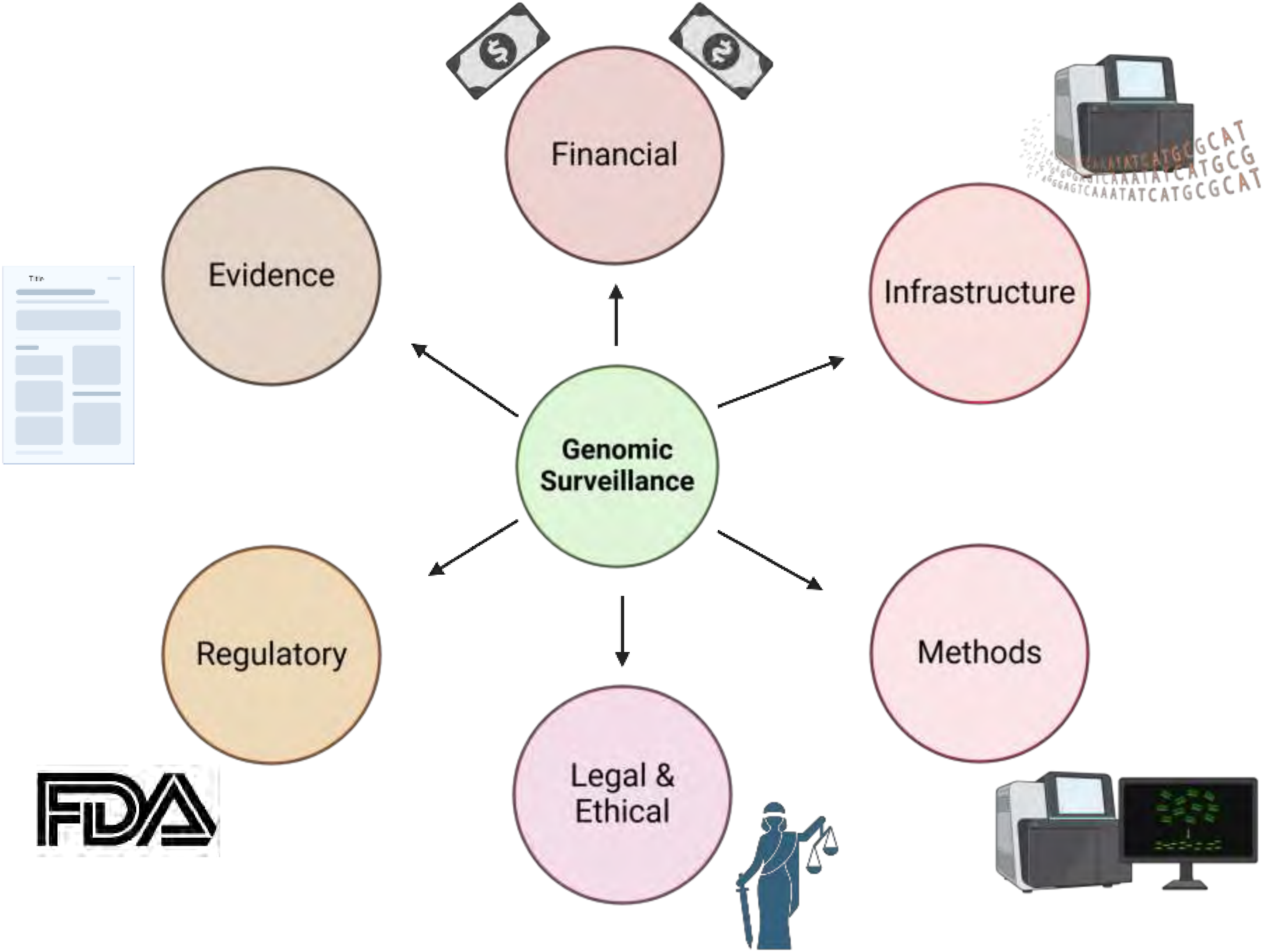
Pathogen genomics in healthcare: overcoming barriers to proactive surveillance

Alexander J. Sundermann,[1,2] Rossana Rosa,[3] Patrick N. A. Harris,[4,5,6] Evan Snitkin,[7,8] Waleed Javaid,[9] Nicholas M. Moore,[10] Mary K. Hayden,[10] Krisandra Allen,[11] Kyle Rodino,[12] Sharon J. Peacock,[13] Lilian M. Abbo,[3,14] Lee H. Harrison[1,2,15]

AUTHOR AFFILIATIONS See affiliation list on p. 11.

ABSTRACT Pathogen genomic surveillance in healthcare has the potential to enhance patient safety by detecting outbreaks earlier, thereby reducing morbidity and mortality. Despite benefits, there are barriers to adoption, including cost, expertise, and lack of standardized methodologies and incentives. This commentary advocates for 1) investment from healthcare payors, public health, and regulatory bodies and 2) additional research on genomic surveillance for improving patient outcomes and reducing infections. Effective implementation will require strategic investment and cross-sector collaboration.

Sundermann AJ et al, Antimicrob Agents Chemother 2025. PMID 39636107



Genomic Surveillance

Financial

Infrastructure

Methods

Legal & Ethical

Regulatory

Evidence

Evidence: Studies

Area	Current Status for Genomic Surveillance	Considerations	Future Directions
Evidence	• Multiple studies showing surveillance finds previously unrecognized outbreaks and with interventions can reduce infections, deaths	• Causal evidence in reducing HAIs • Differences in fungal, viral, or bacterial approaches • Cost-effectiveness	• Additional, independent analysis showing benefit and outcomes • Detailed modeling analysis for single centers and broader communities

Sundermann AJ et al, Antimicrob Agents Chemother 2025. PMID 39636107

Financial

Area	Current Status for Genomic Surveillance	Considerations	Future Directions
Financial	• Studies showing support for net cost-savings by averted infections	• Different healthcare institution type • In-house versus outsourced capacity • Consistent funding opportunities	• Analysis on impact by institution type • Listing of resources available to institutions

Sundermann AJ et al, Antimicrob Agents Chemother 2025. PMID 39636107

Infrastructure

Area	Current Status for Genomic Surveillance	Considerations	Future Directions
Infrastructure	• Variability in access and knowledge for genomics	• Necessary equipment and laboratory space • Dedicated staff Competencies in analysis • Trained infection prevention departments capable of making interventions	• Analysis on optimal practices • Programs to train individuals on analysis and interventions

Sundermann AJ et al, Antimicrob Agents Chemother 2025. PMID 39636107

Methods

Area	Current Status for Genomic Surveillance	Considerations	Future Directions
Methods	• No consensus on optimal methodology for genomics	• Consistent methods across multiple centers • Bioinformatic pipeline methods • Identifying genetically related pathogens	• Professional society guidance on optimal analysis methods

Sundermann AJ et al, Antimicrob Agents Chemother 2025. PMID 39636107

Legal, Ethical, Regulatory

Area	**Current Status for Genomic Surveillance**	**Considerations**	**Future Directions**
Legal & Ethical	• No guidance or professional society documents on legal, ethical, or regulatory guidelines	• Data-security, privacy, and storage • Considerations in patient disclosure • Equitable access	• Discussions and analysis on best practices
Regulatory		• Laboratory certification • Development of billing or reimbursement models	• Discussions with regulatory bodies on potential future pathways

Sundermann AJ et al, Antimicrob Agents Chemother 2025. PMID 39636107

Next steps? Low hanging fruit?

- Continue to generate evidence
- Professional society acknowledgement
- Approaching payers

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Summary

EDS-HAT/genomic surveillance

- Prevents infections
- Saves healthcare costs
- Is superior to traditional outbreak detection methods
- Goes far beyond geotemporal clustering
- Is a real-time quality improvement tool that improves patient safety
- A nationwide system would have benefits in addition to those seen in individual hospitals
- There are barriers to widespread implementation

EDS-HAT Team

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UPMC

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Thank you!

University of Pittsburgh

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