Advanced Molecular Detection and Epidemiology

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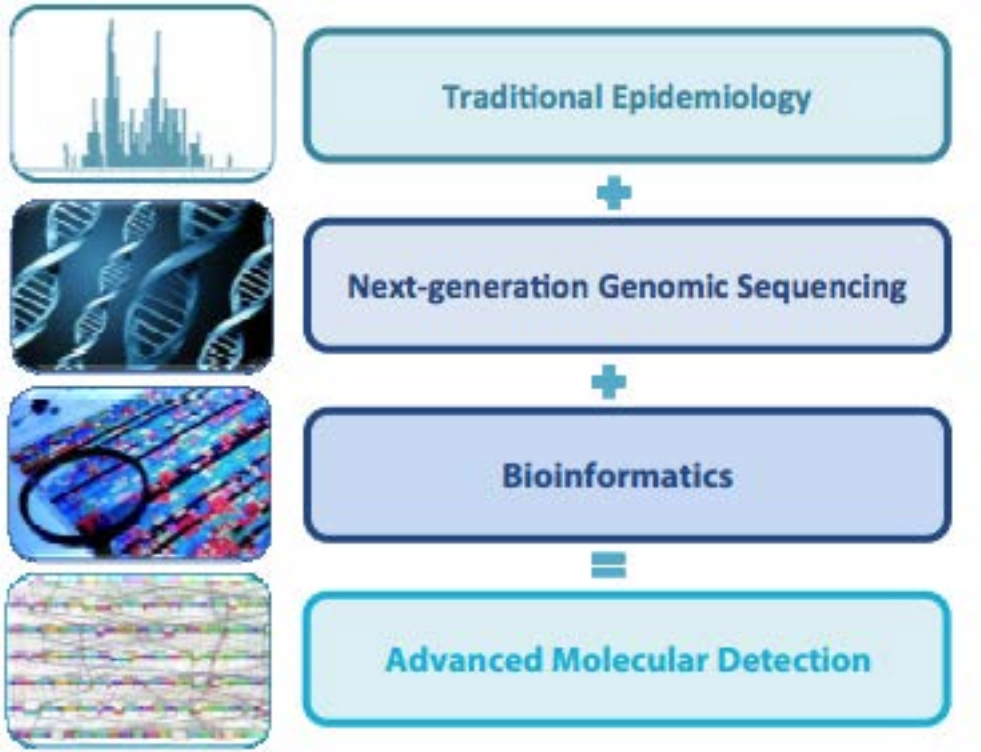
- **No Financial Disclosures**

- **The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.**

Preview

- Impact of incorporating whole genome sequencing (WGS)
- Role of epidemiological data in interpretation of WGS data
- Potential use of Advanced Molecular Detection technology in infection control

What is Advanced Molecular Detection (AMD)?



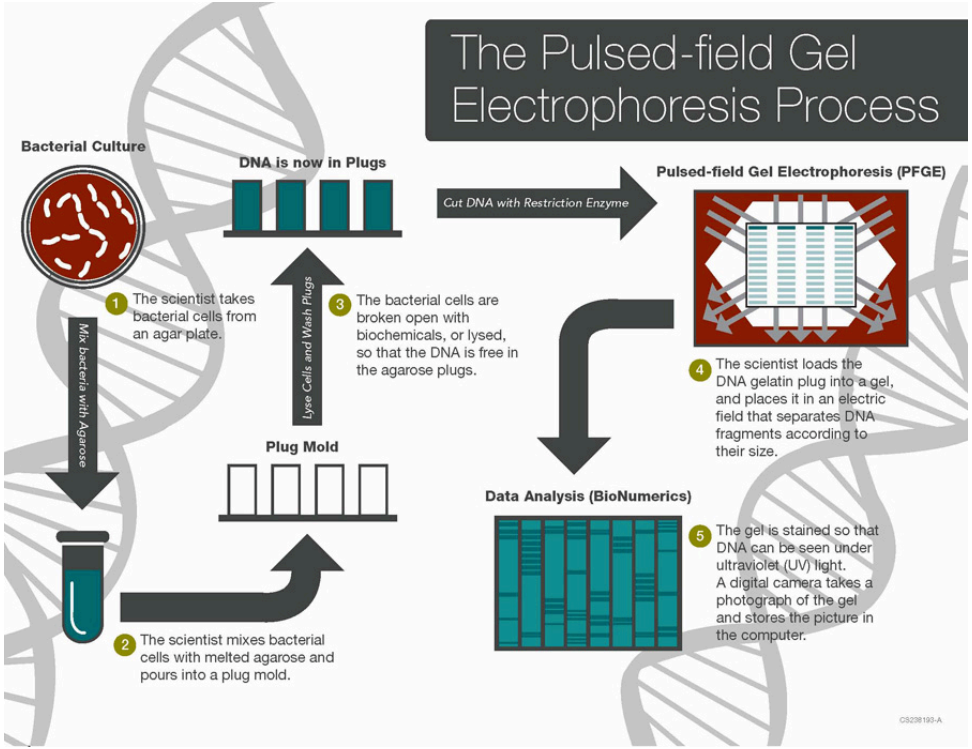
Advanced Molecular Detection (AMD)

- Impact public health
  - Investigate outbreaks
  - Understand antibiotic resistance
  - Diagnose new pathogens
  - Identify control points

- New technologies
  - Next generation sequencing platforms
  - Supercomputers

Pulsed-Field Gel Electrophoresis (PFGE): Strengths

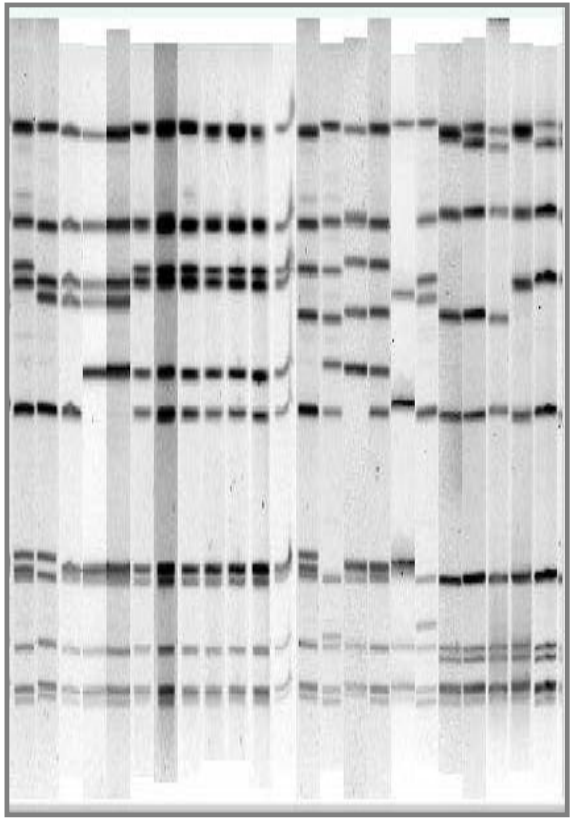
- **Universal subtyping method**
- **Reproducible**
- **Outbreaks**
  - **Flag disseminated foodborne outbreaks (space, time)**
  - **Identify isolates that are <u>likely</u> to have come from a common source**



http://www.cdc.gov/pulsenet/pathogens/protocol-images.html#pfge

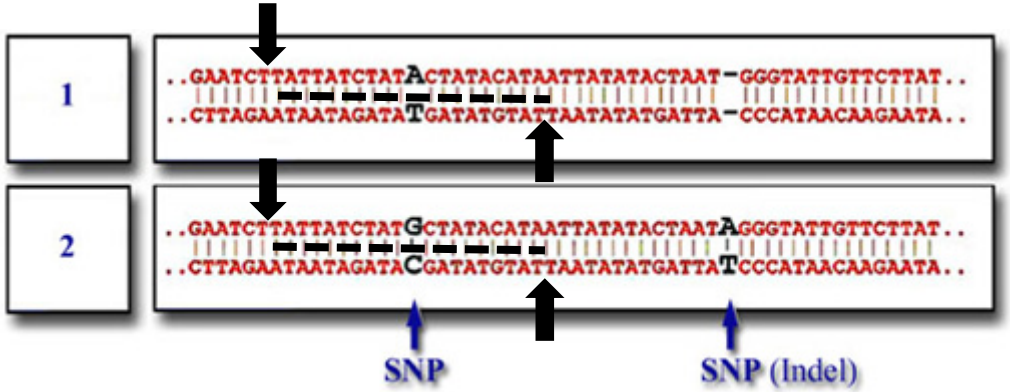
Pulsed-Field Gel Electrophoresis (PFGE): Limitations

- Relatedness is not a true phylogenetic measure
  - Related isolates may have different PFGE pattern
  - Unrelated isolates may have same PFGE pattern
- Cannot discriminate between epidemiologically unrelated isolates
- Information only at the cut sites
- PFGE ≠ WGS

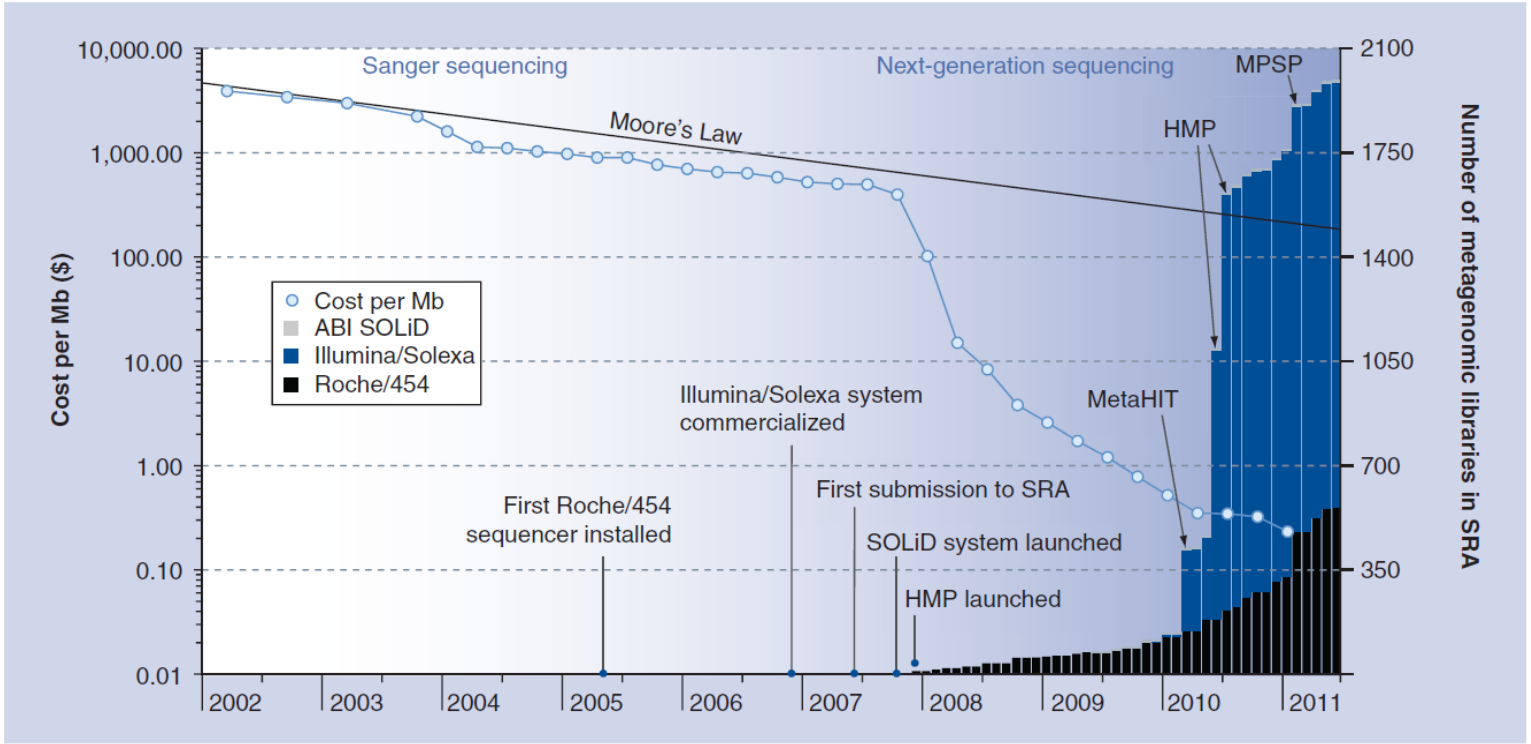


Whole Genome Sequencing (WGS): Strengths

- High resolution sequence data
- Information at every point in the genome
  - True phylogenetic relatedness
  - Transmission path
  - Identify control points



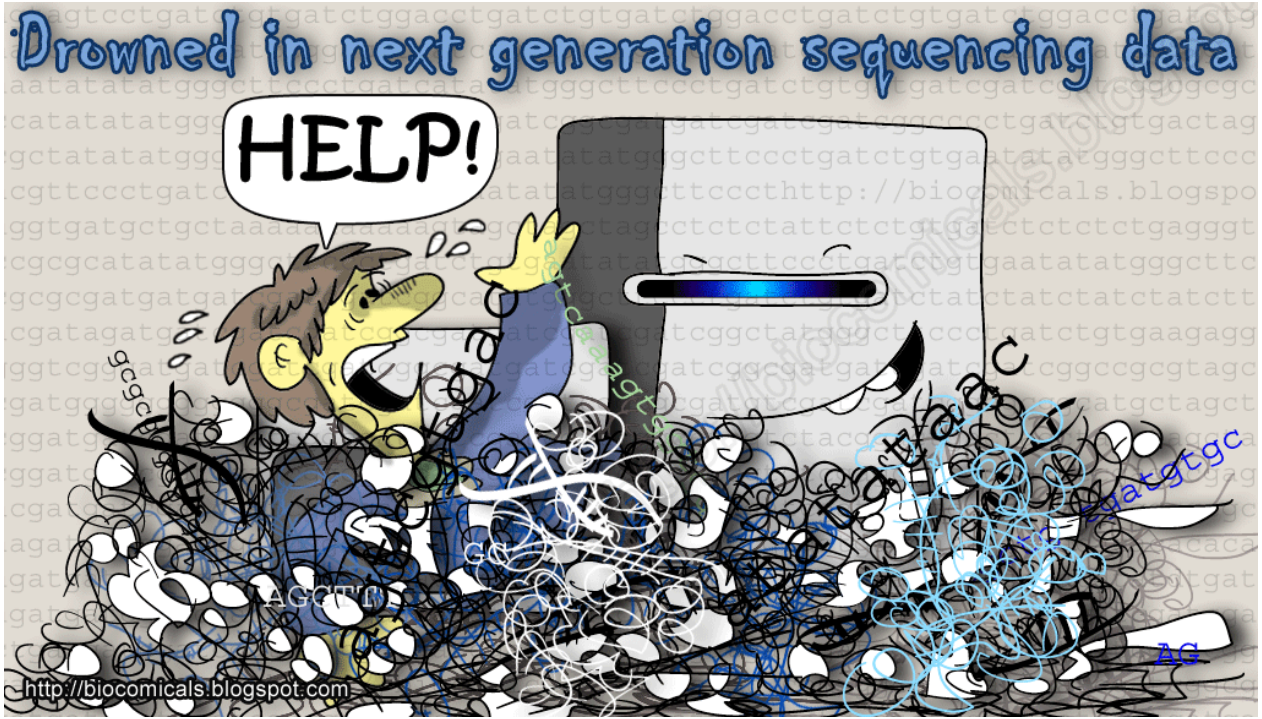
Impact of Next Generation Sequencing



Schmieder and Edwards. Future Microbiol. (2012) 7(1), 73–89

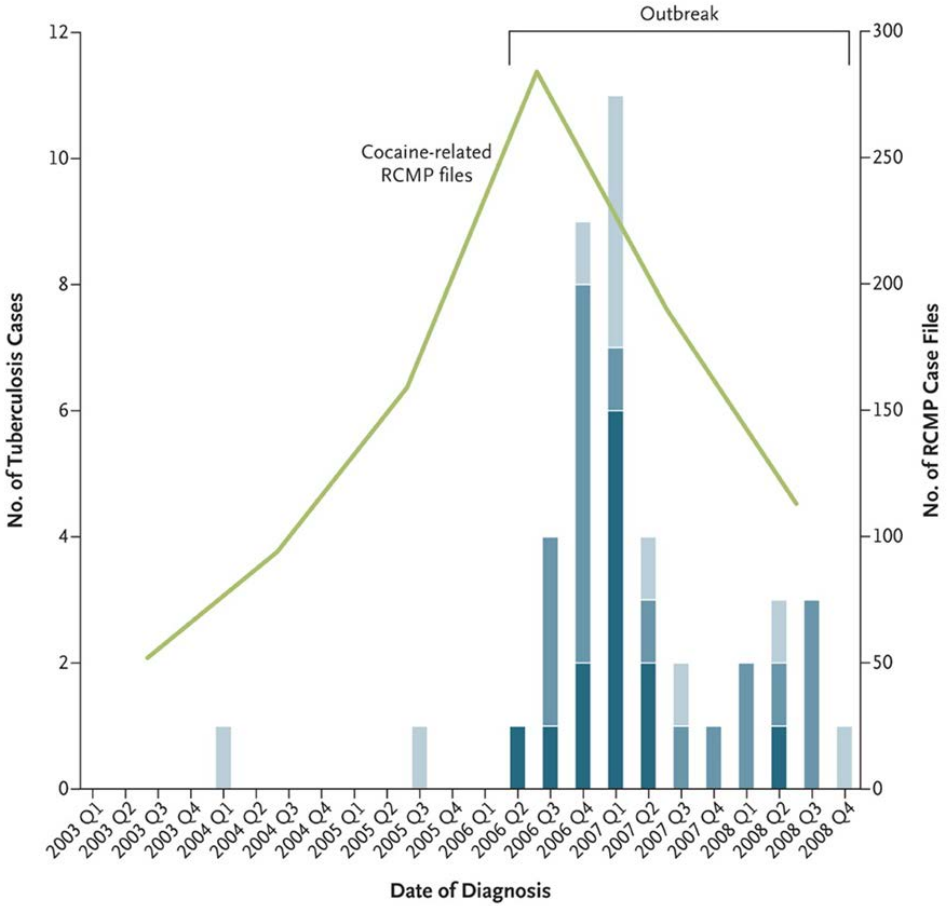
Impact of Next Generation Sequencing

- **Challenges**
  - Data overload
  - Interpretation



Integration of Epidemiology and WGS

Mycobacterium tuberculosis Outbreak



Gardy et al. NEJM 2011; 364:730-739. 24 Feb 2011

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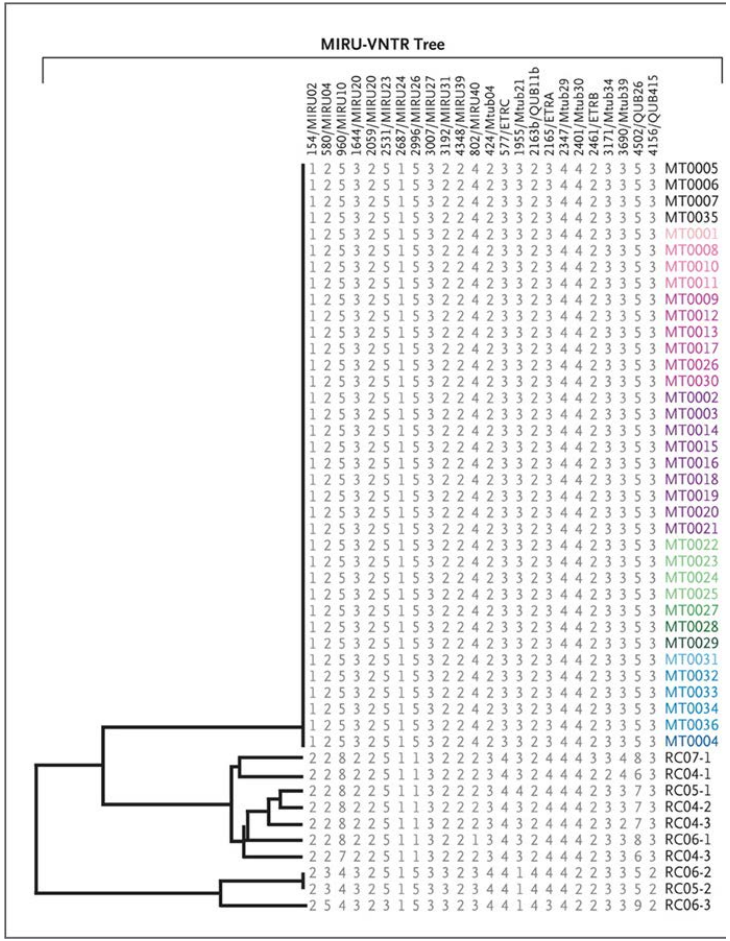

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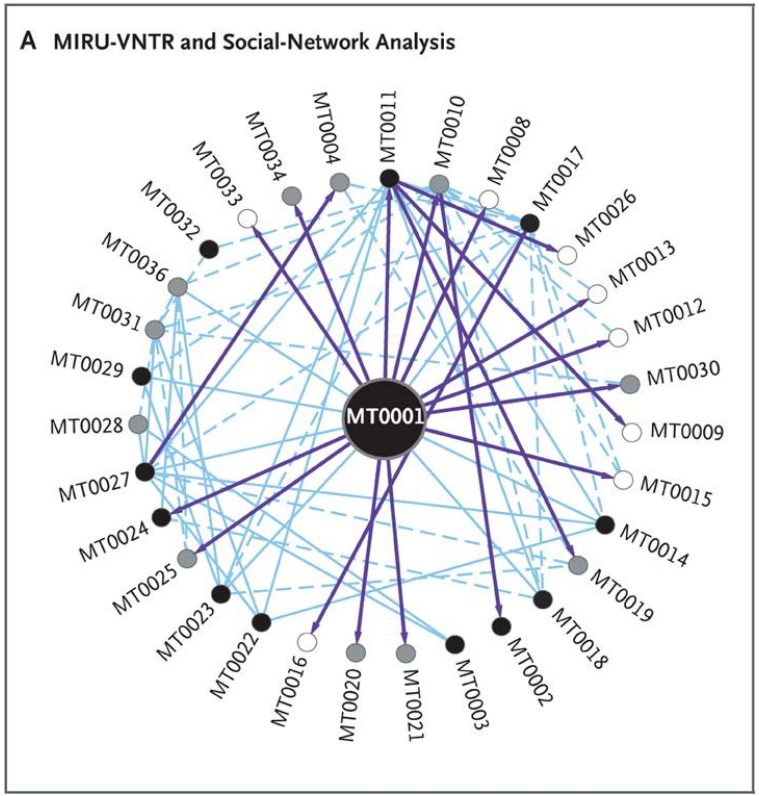

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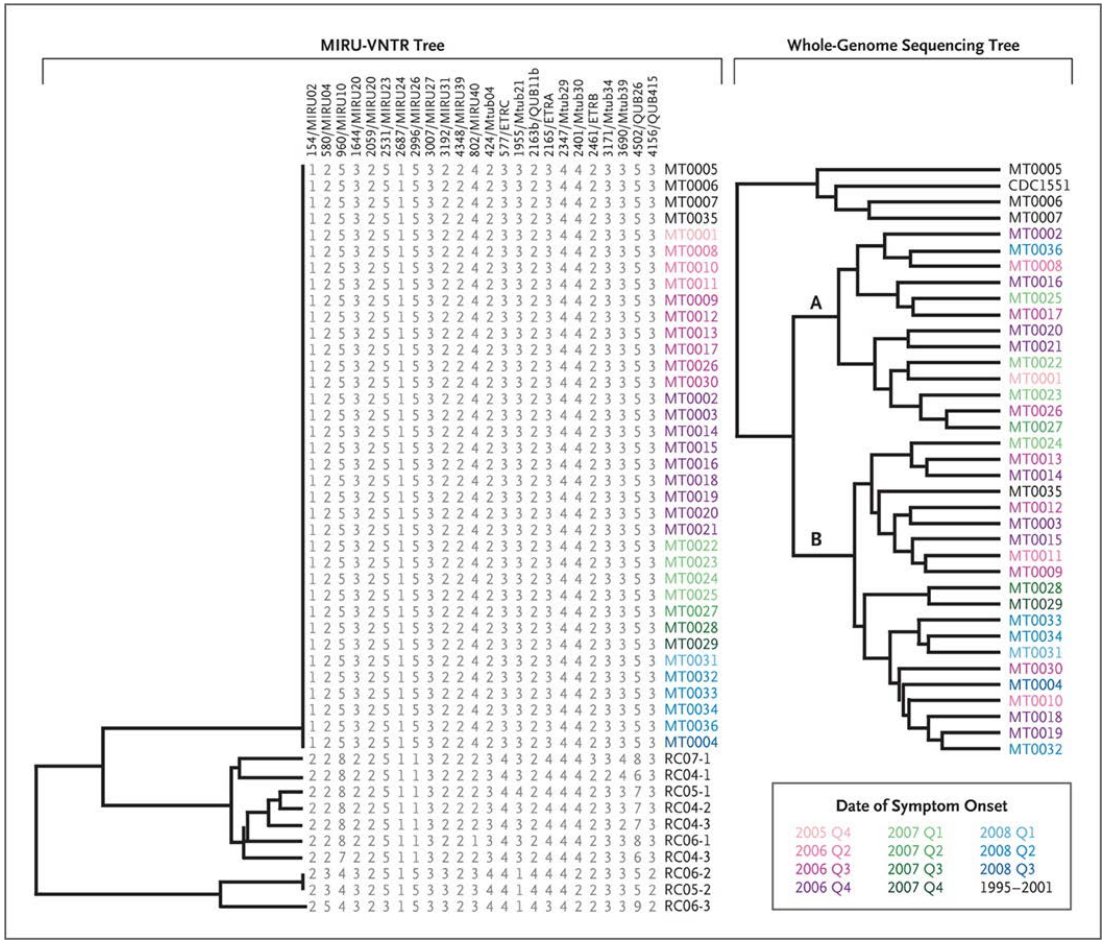

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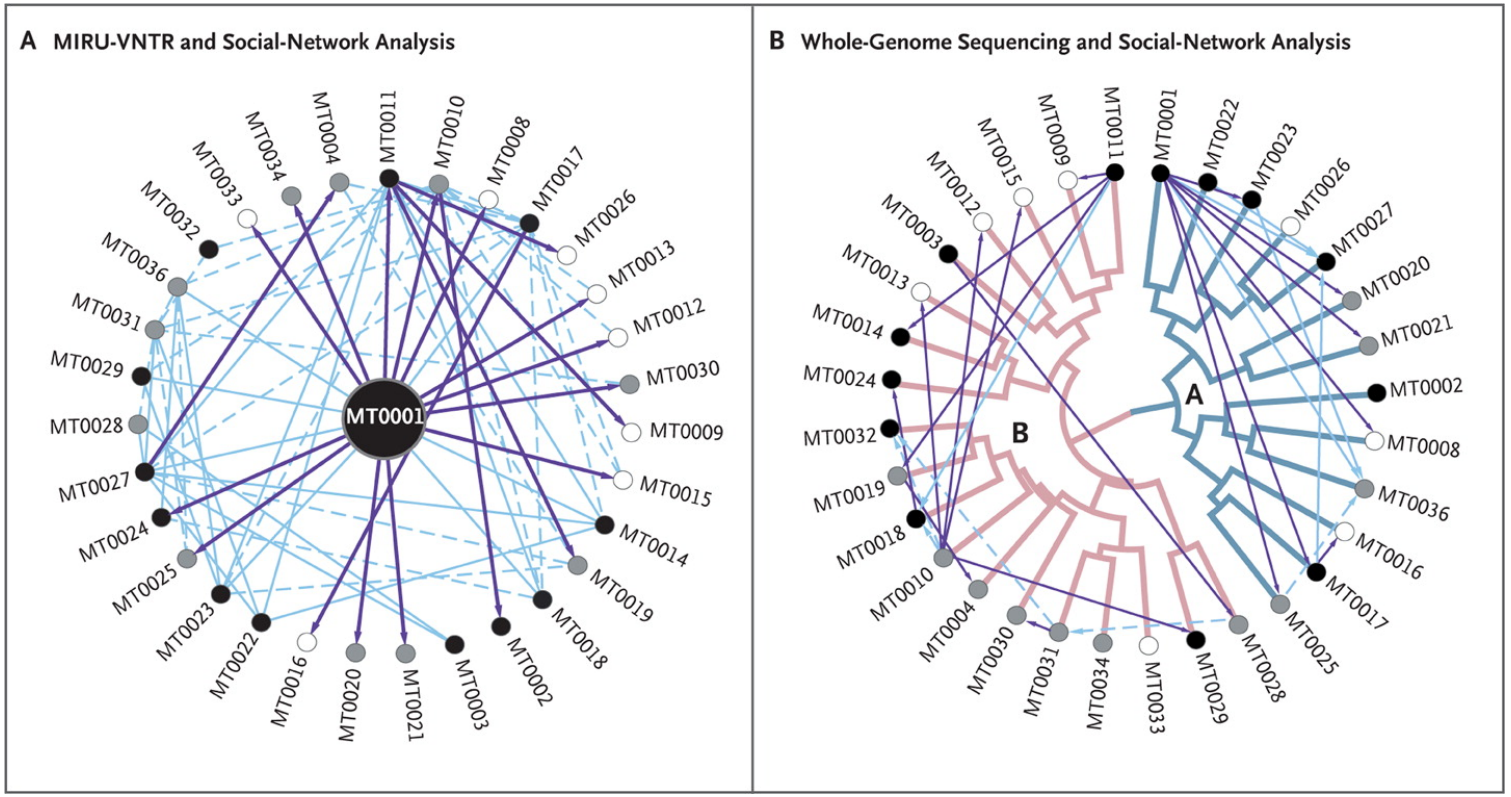


- Identified transmission pathways
- Revealed socioenvironmental factor that led to outbreaks

Gardy et al. NEJM 2011; 364:730-739. 24 Feb 2011

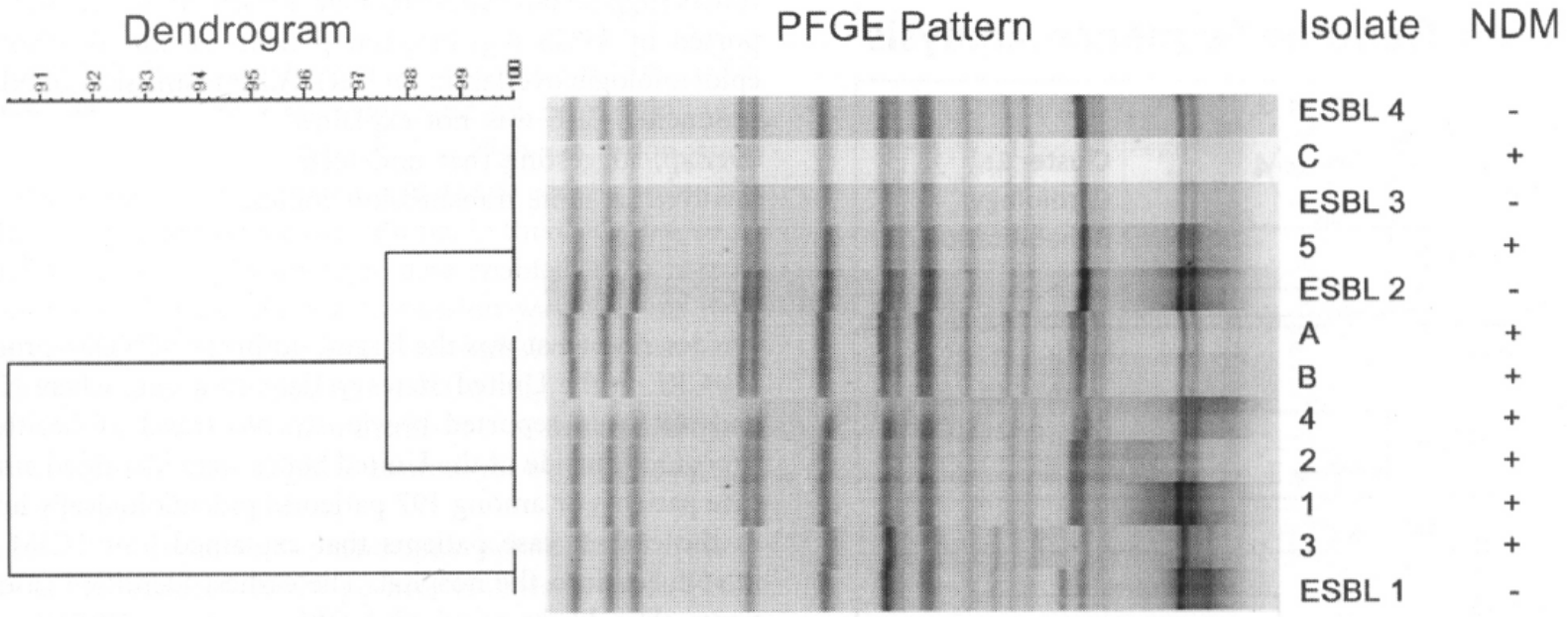
Healthcare-associated infection

Denver, Colorado - 2012

- **8 patients in a single acute care hospital**
- **Carbapenem-resistant *Klebsiella pneumoniae* producing New Delhi Metallo-Beta-Lactamase (NDM)**
- **Laboratory typing**
  - **Pulsed-field gel electrophoresis (PFGE)**
  - **Whole genome sequencing (WGS)**

Epson, et al. ICHE; 35(4): 390-7. April 2014

Denver, Colorado - 2012



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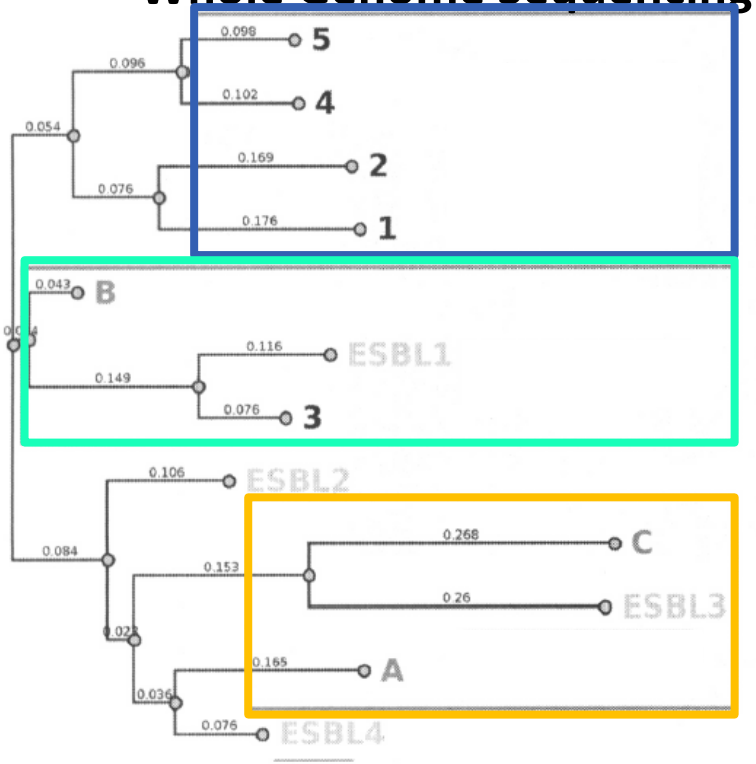

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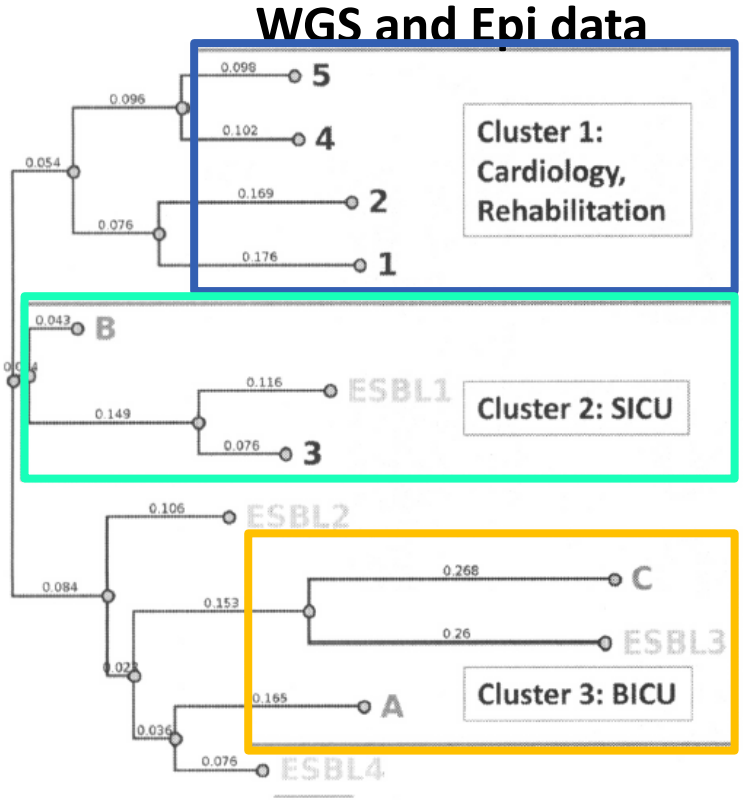

- **Identified 3 areas where improvements in infection control were needed**

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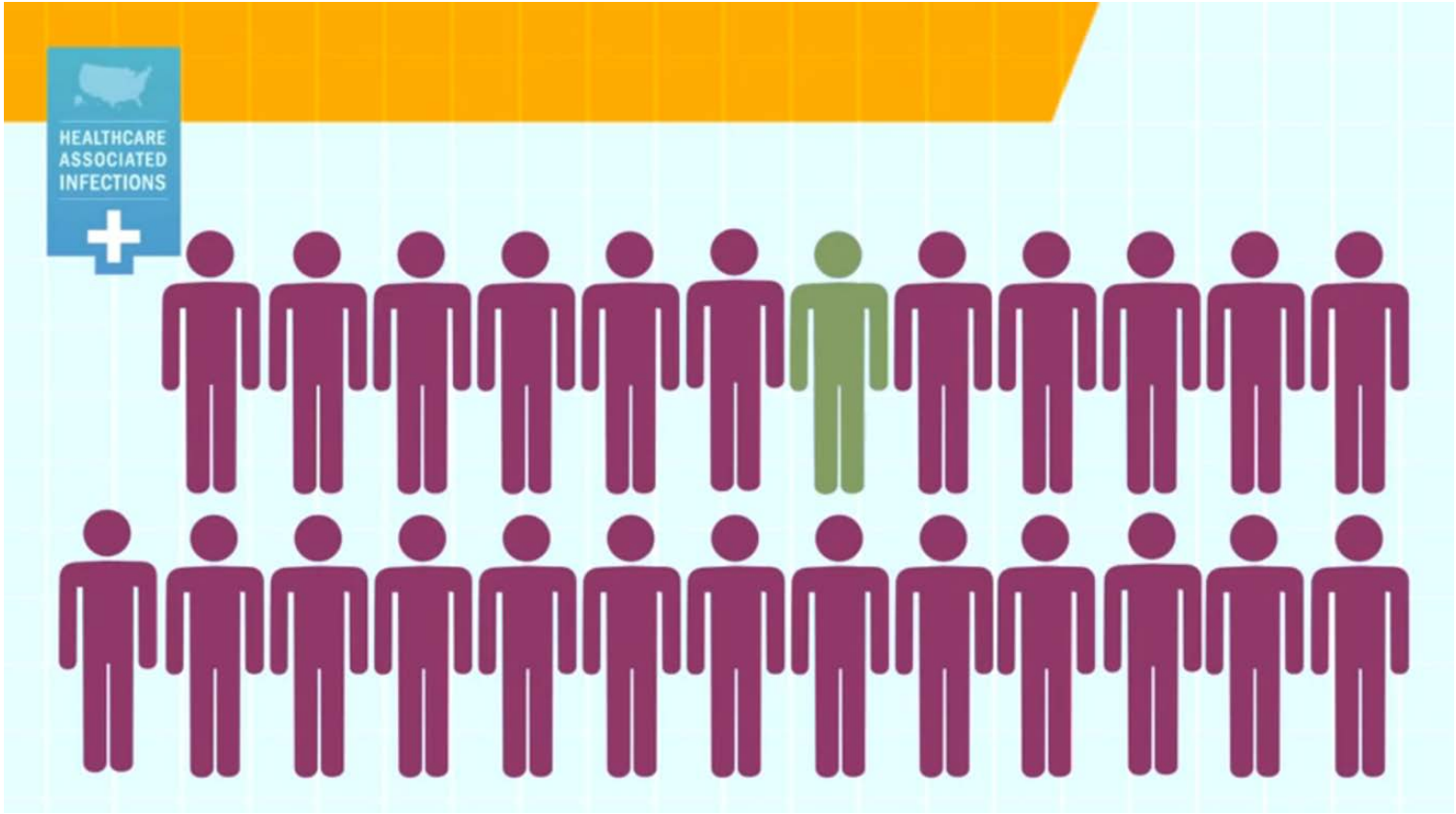
Infection Control and Prevention

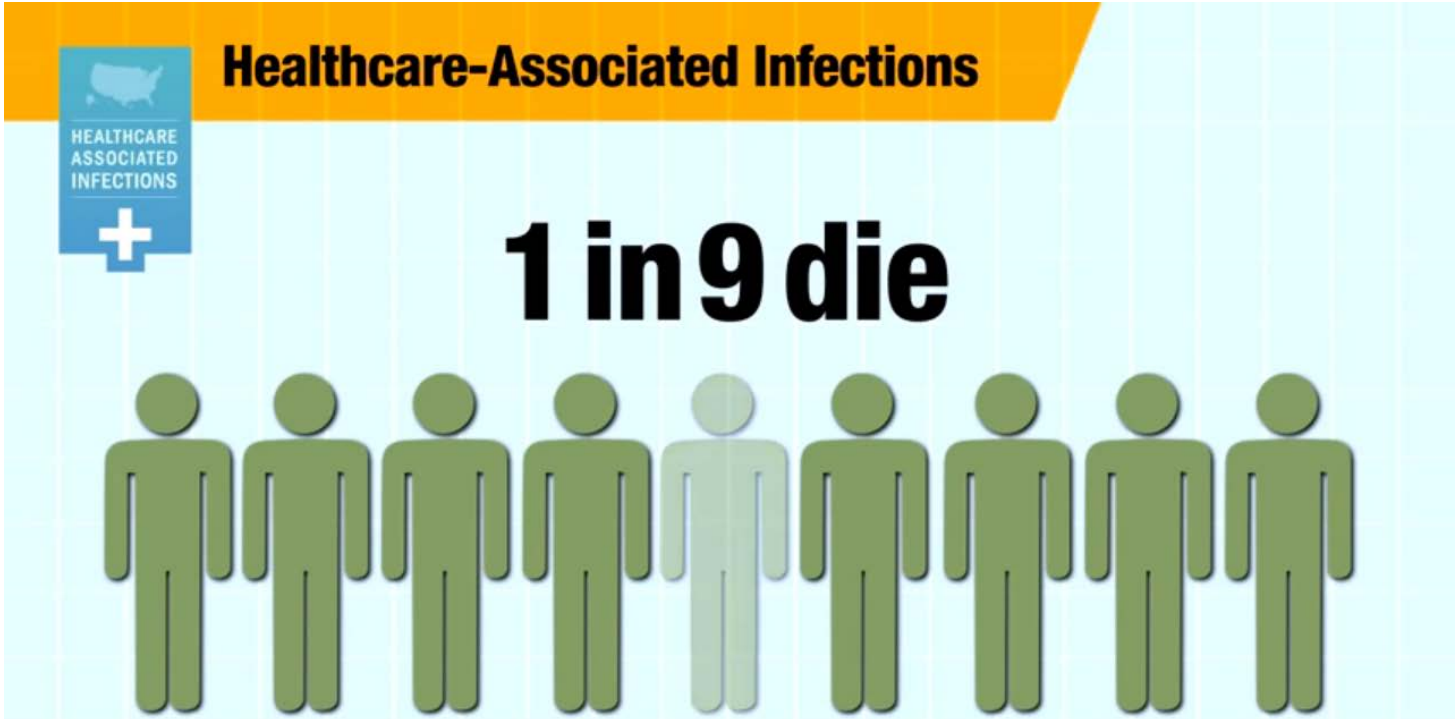
Standard Infection Prevention Strategies

- Standard Precautions
  - Hand hygiene
  - Personal Protective Equipment
  - Respiratory hygiene
  - Medication safety
  - Injection safety
  - Environmental/equipment cleaning and disinfection
- Transmission-based Precautions
  - Contact Precautions (e.g., CDI)
  - Droplet Precautions (e.g., respiratory viruses)
  - Airborne Precautions (e.g., TB, measles)
- Antibiotic Stewardship

On any given day, about 1 in 25 hospital patients has at least one healthcare-associated infection (HAI)

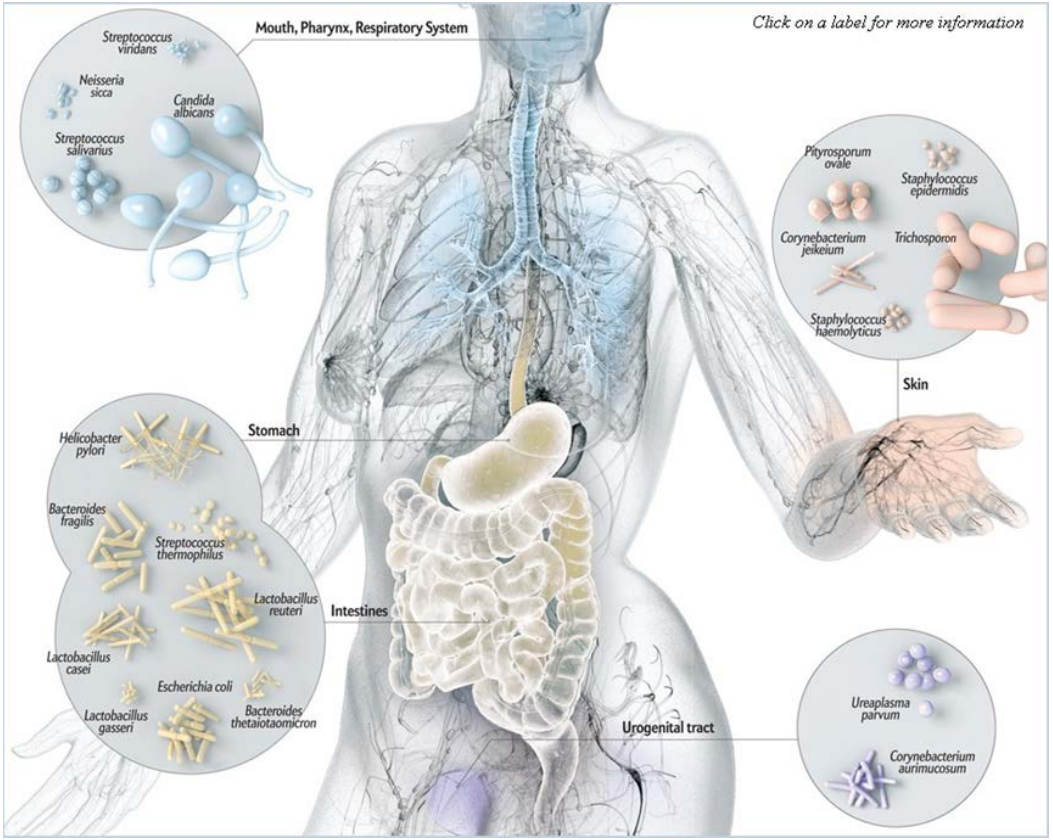


One in every 9 patients who gets a healthcare-associated infection will die during their hospitalization



- **Vital to continue progress in healthcare epi and implementation research**

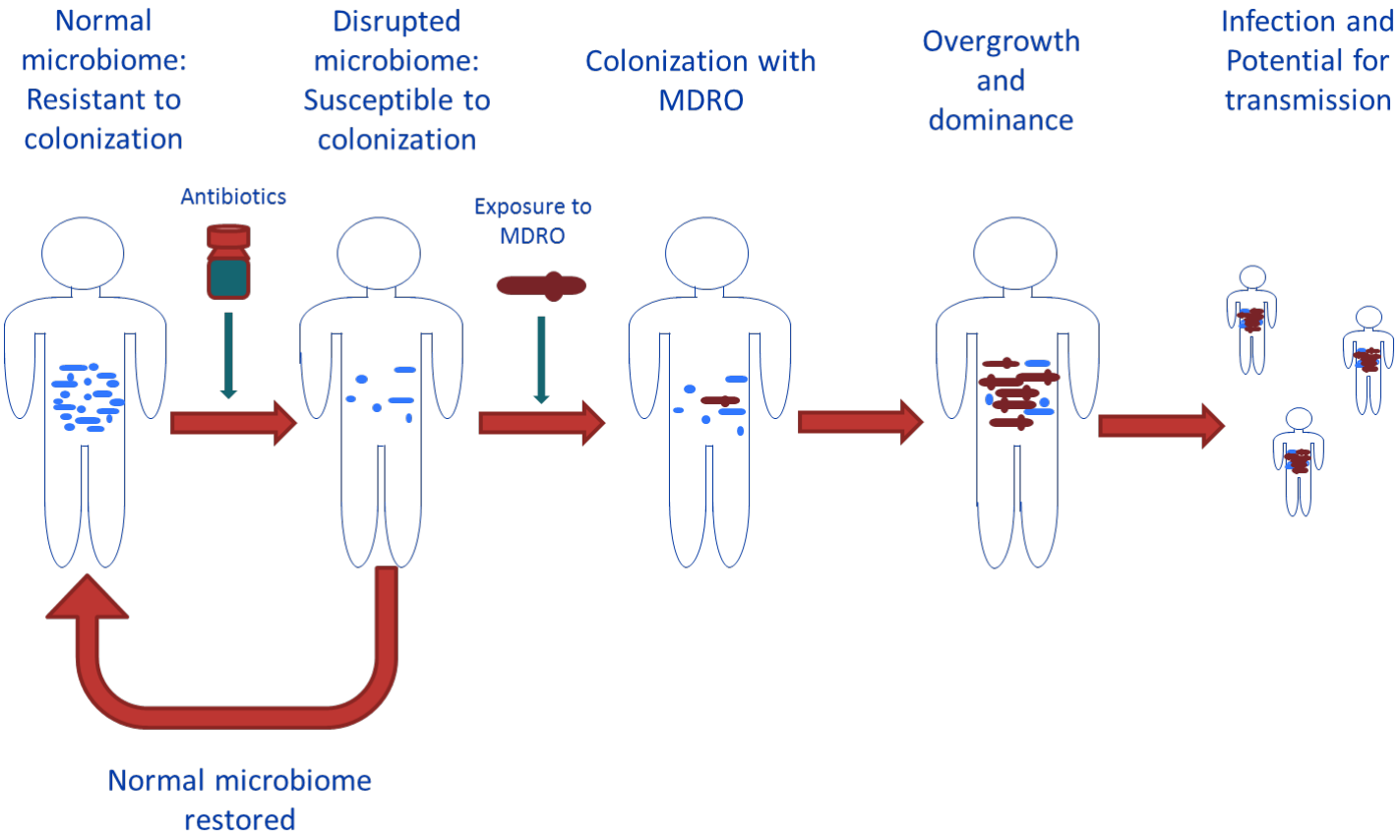
Protective Role of the Microbiota



Microbiome Disruption Indices (MDI)

- CDC working to develop
- Standardized criteria
- Characterize major human microbiomes
  - Lower intestinal microbiome

Causal Pathway from Health to Disease



Halpin, et al. 2016 AJIC

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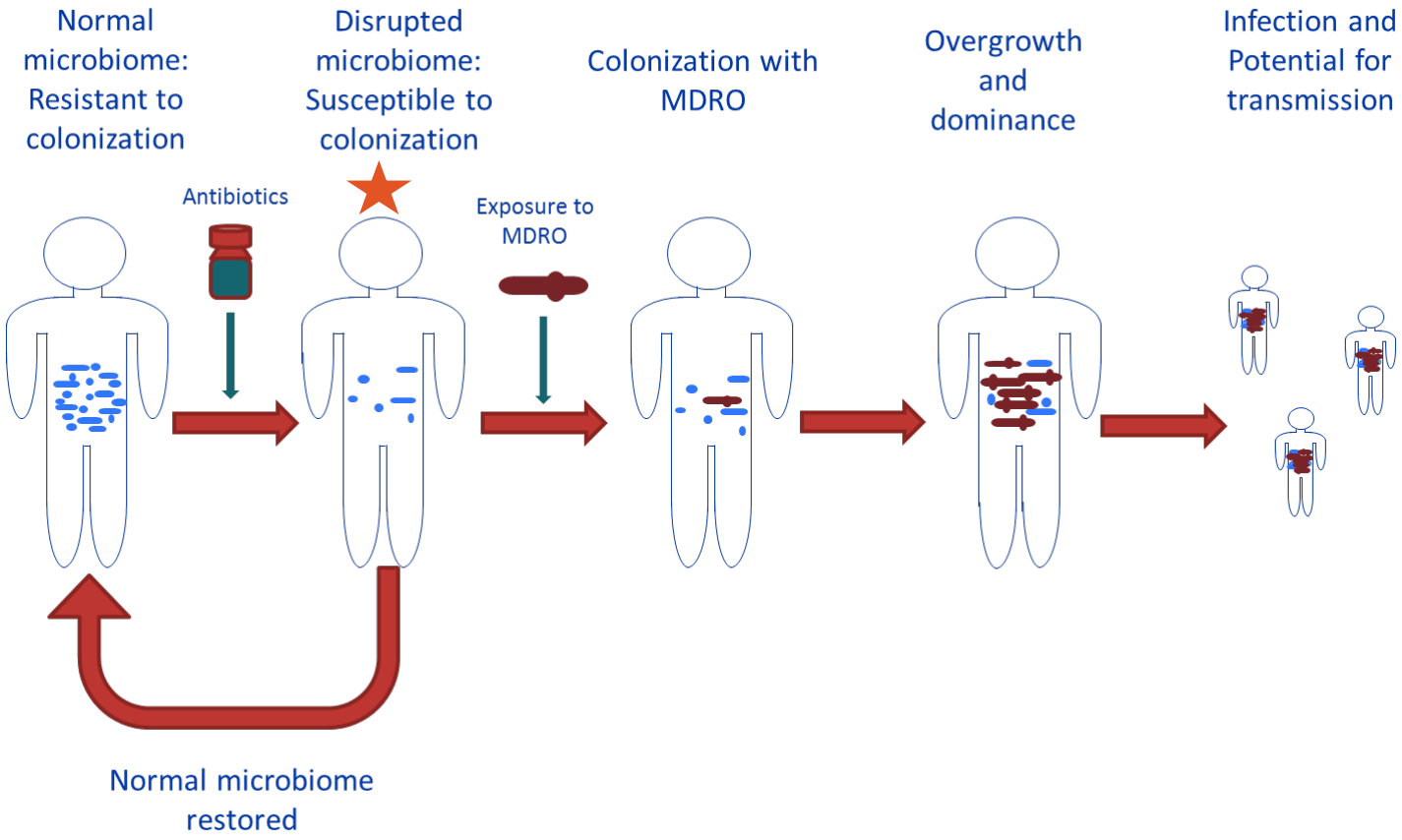

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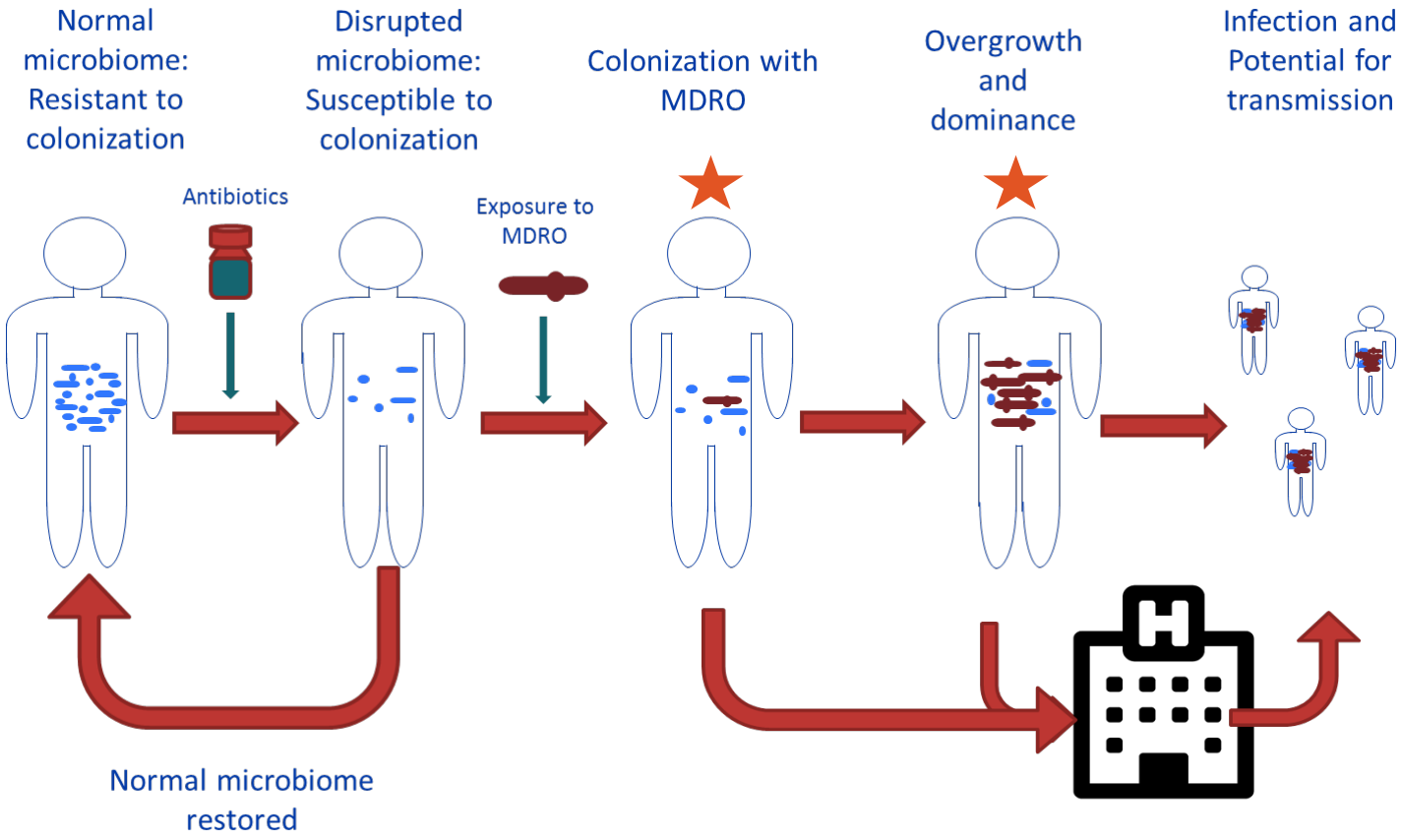

Halpin, et al. 2016 AJIC

Potential MDI

- Potential MDIs
  - Compositional diversity
  - Species richness
  - Presence/absence of protective species
  - Resistome
  - Functional status – metagenomics, metabolomics

Uses for MDIs

- Monitor microbiome
  - When to take remedial action (e.g., fecal microbiota transplant)
  - Antibiotic stewardship/selection
  - Infection control decisions
    - Isolation precautions for when at increased risk for transmitting (colonized, dominated)
    - Reverse isolation precautions for those at high risk for colonization (disrupted)

Uses for MDIs

- Prepare for future FDA-approved microbiome remediation therapies
  - e.g., FMT, synthetic stool, advanced/designer probiotics
- Communicate disruptive potential of drugs, including antibiotics
  - Rating system to gauge relative risks of different agents
  - MDIs determined during approval process and included in package insert

Wrap Up

- Using WGS has already had a substantial impact on our ability to investigate outbreaks
- Collect timely and accurate epi data is crucial
- Interpret WGS in the context of available epi data

Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Antibiotic Resistance Threat Report

- 18 antibiotic resistant pathogens
  - >2 million infections
  - ~23,000 deaths
  - Billions in excess medical costs

- Half are healthcare-associated infections

- Vital to continue progress in healthcare epidemiology and implementation research

Pulsed-Field Gel Electrophoresis (PFGE): Strengths

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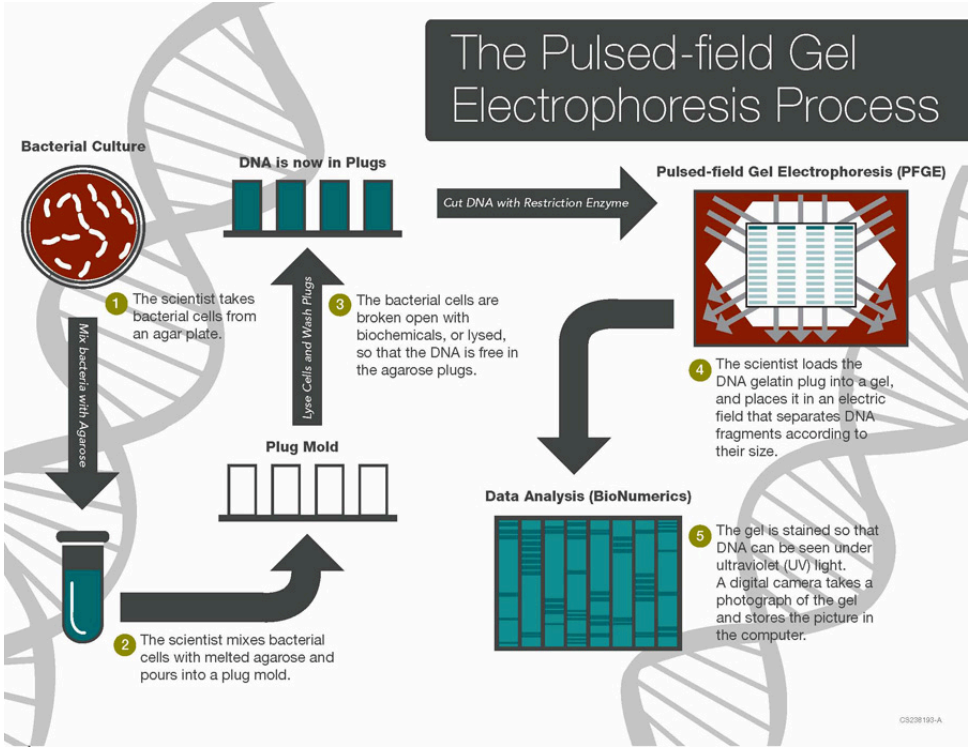

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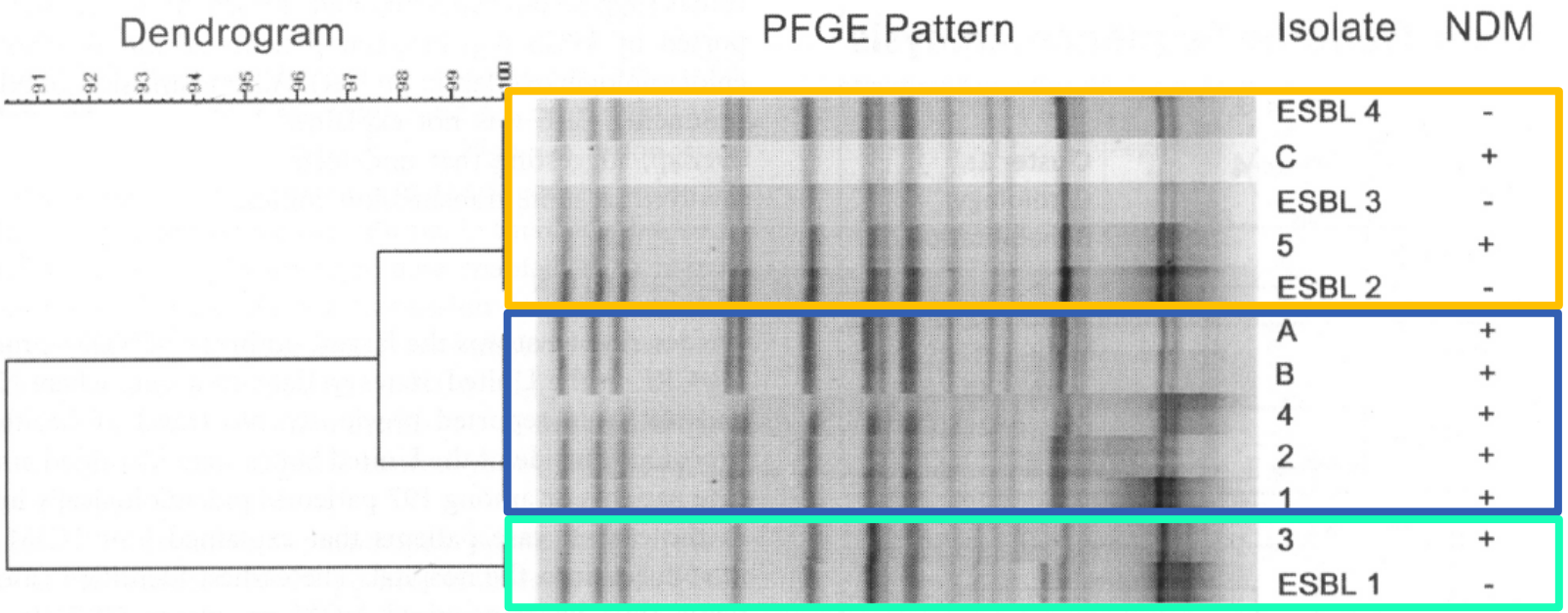

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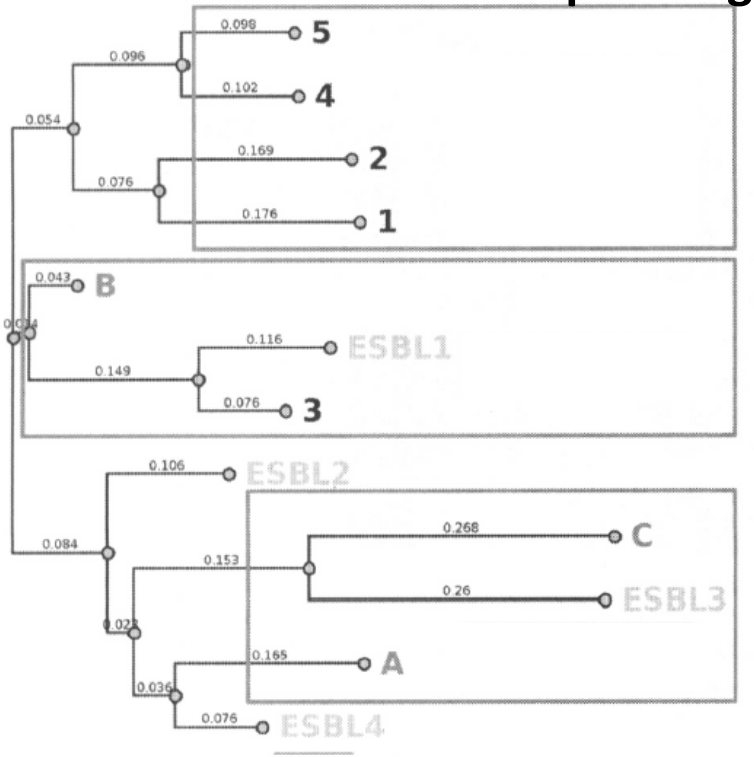

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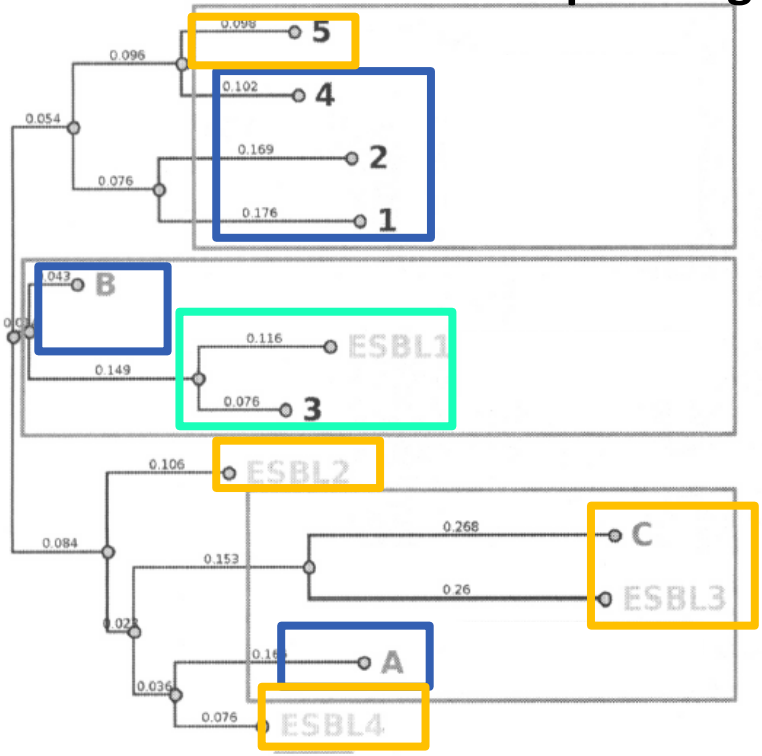

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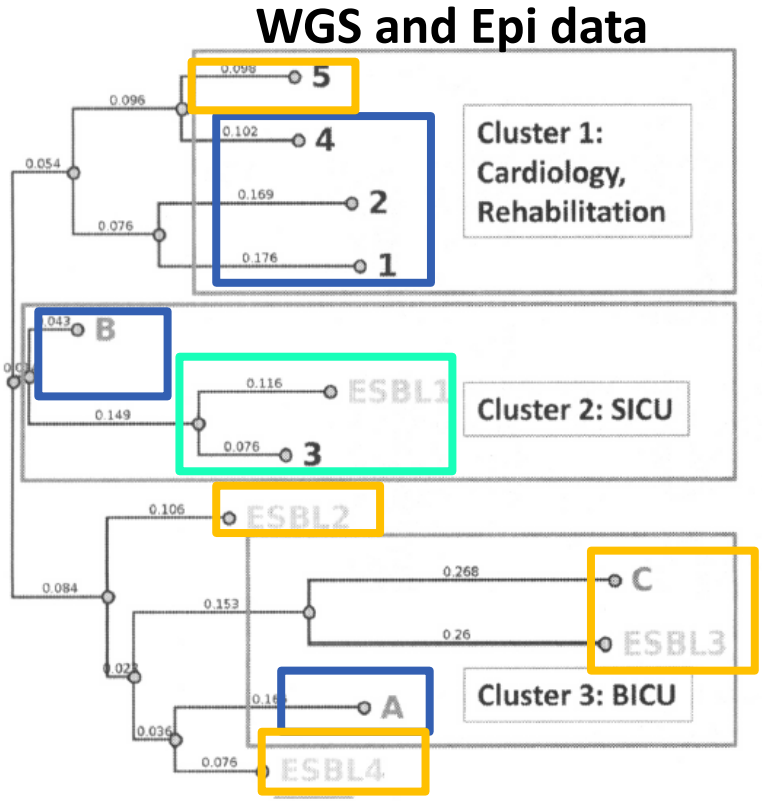

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