Sphingomonas koreensis Investigation and Management of Nosocomial Reservoir

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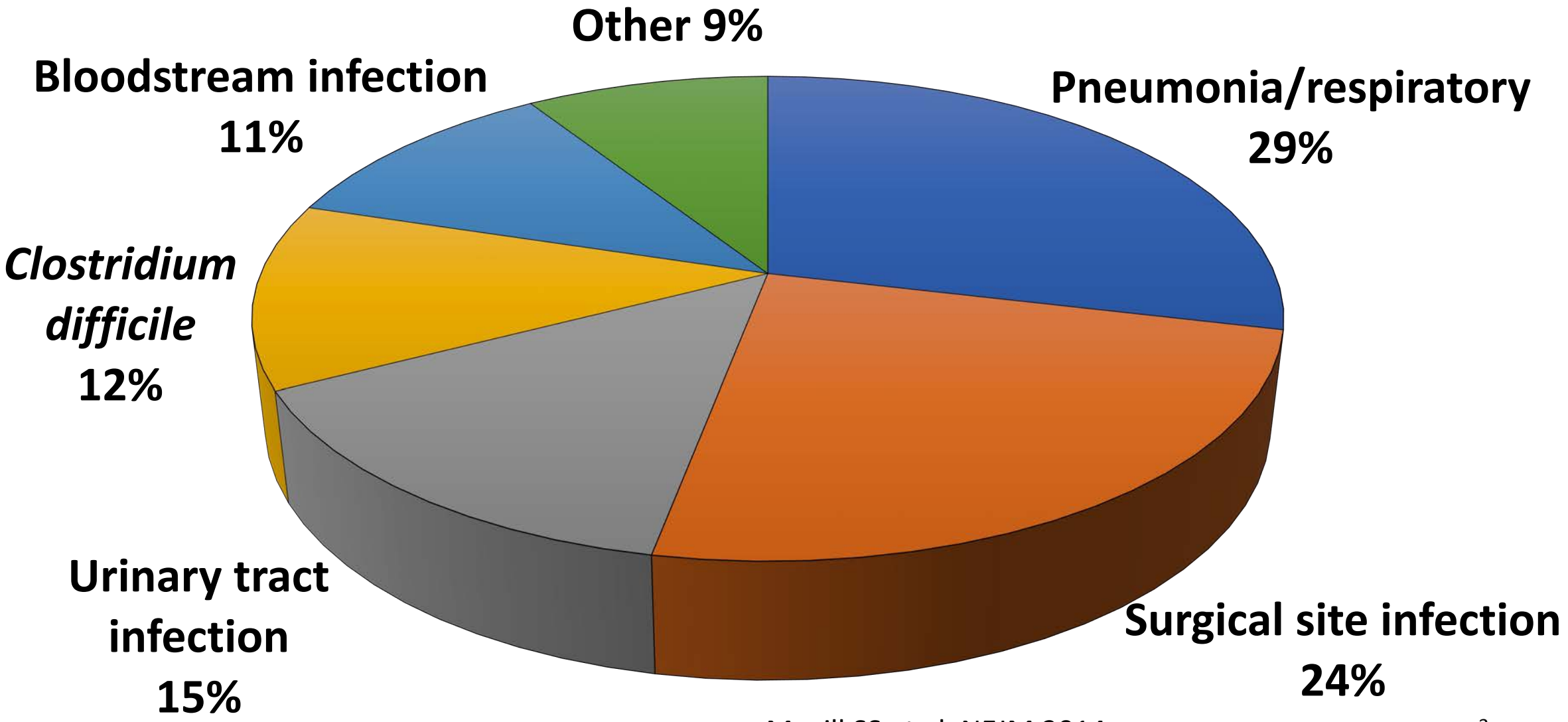
Objectives

- Describe the investigation into *S. koreensis* infections in Clinical Center patients.
- Describe the integration of trans-NIH efforts to eliminate a hazard in the Clinical Center.

Nosocomial Infections in the United States



Magill SS et al, NEJM 2014

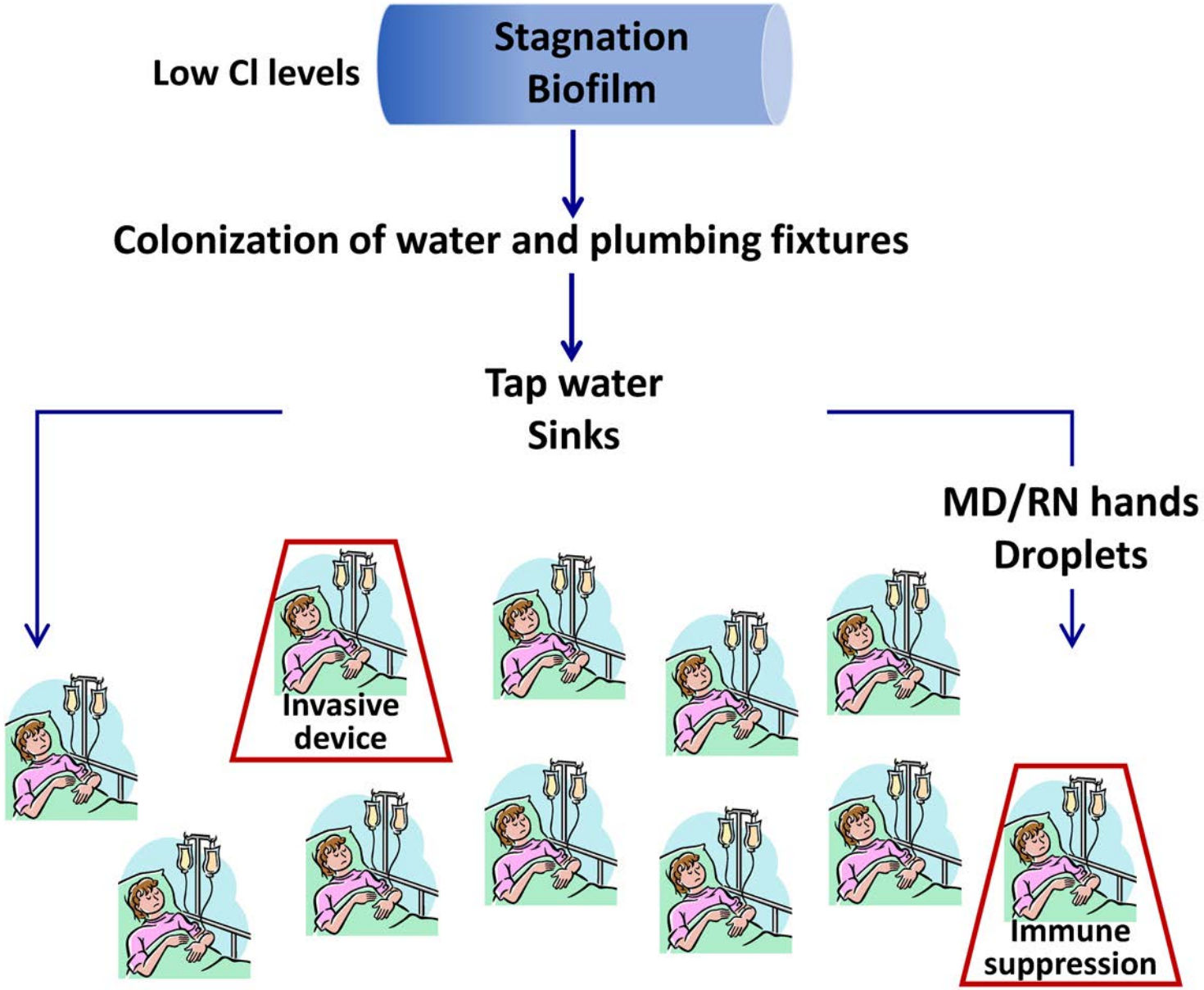
How Pathogens Get into Hospital Water

Municipal water system

Hospital water distribution system

Point-of-use plumbing

Nosocomial Transmission of Waterborne Pathogens

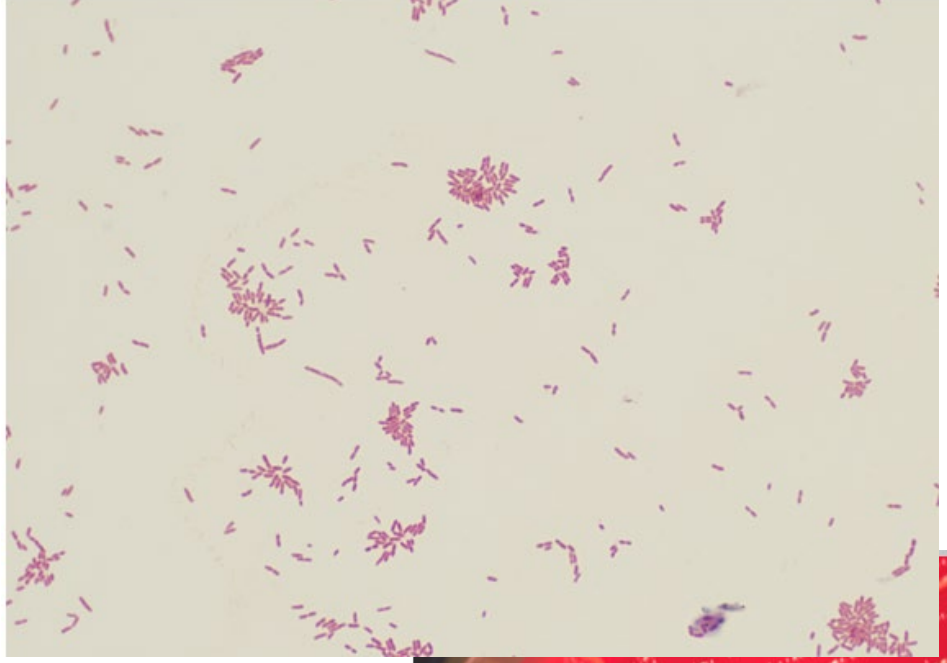


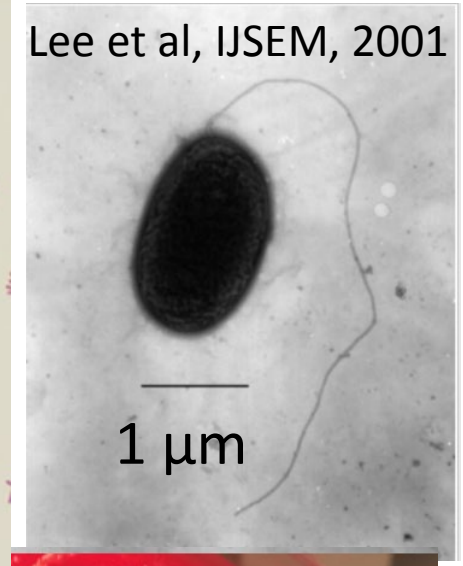
Case

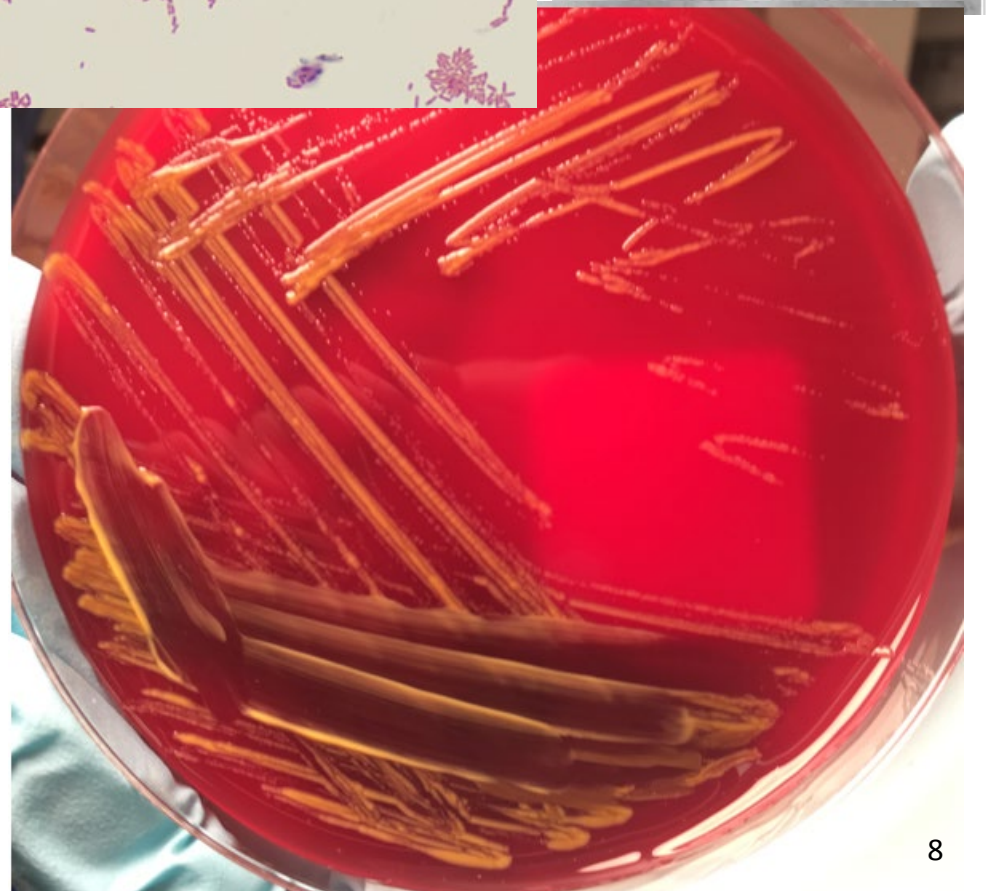
- 20-year-old man with congenital immunodeficiency s/p stem cell transplant, intubated with pneumonia
- Blood cultures grew *Sphingomonas koreensis* (86 hours)
  - Resistant: carbapenems, cephalosporins, aminoglycosides, piperacillin/tazobactam
  - Susceptible: ciprofloxacin and trimethoprim/sulfamethoxazole
- Treated with multiple antibiotics but died three days later.

What is *Sphingomonas*?

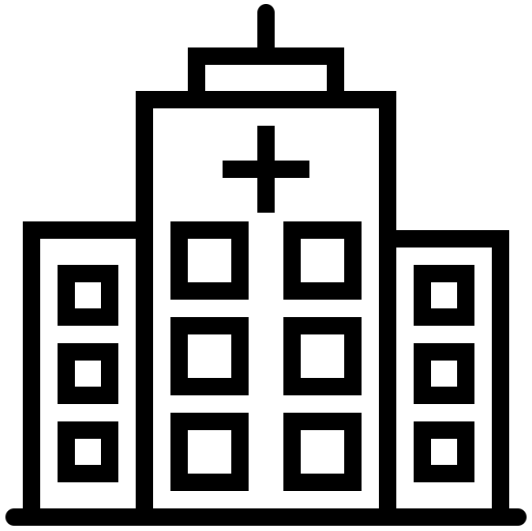
- Gram-negative rod bacteria
- Yellow, opaque colonies
- Ubiquitous
- Found in water in low concentration
  - Tap water
  - Mineral water
  - Distilled water
- Sphingolipids in cell wall
- “Low pathogenicity”
- Survive in nutrient poor conditions







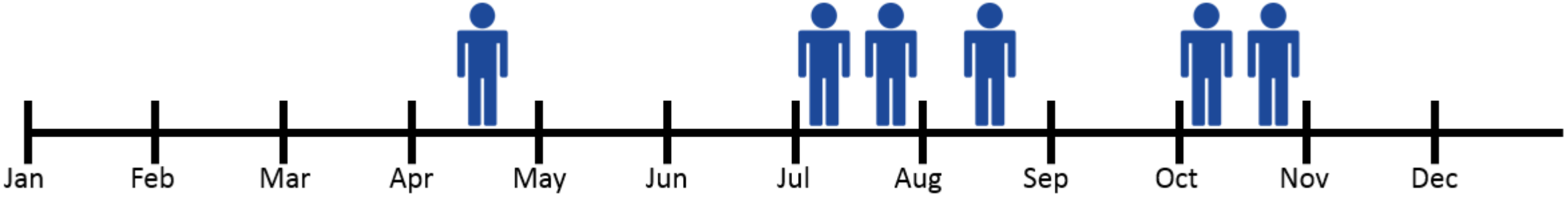
How it all started...



NIHCC

6 patients with clinical cultures of *Sphingomonas* spp.

- Blood (4)
- Bile drainage
- CSF
- Bronchoalveolar lavage
- Tracheal aspirate



2016

4/6 Patients in 2016 Unusually Resistant

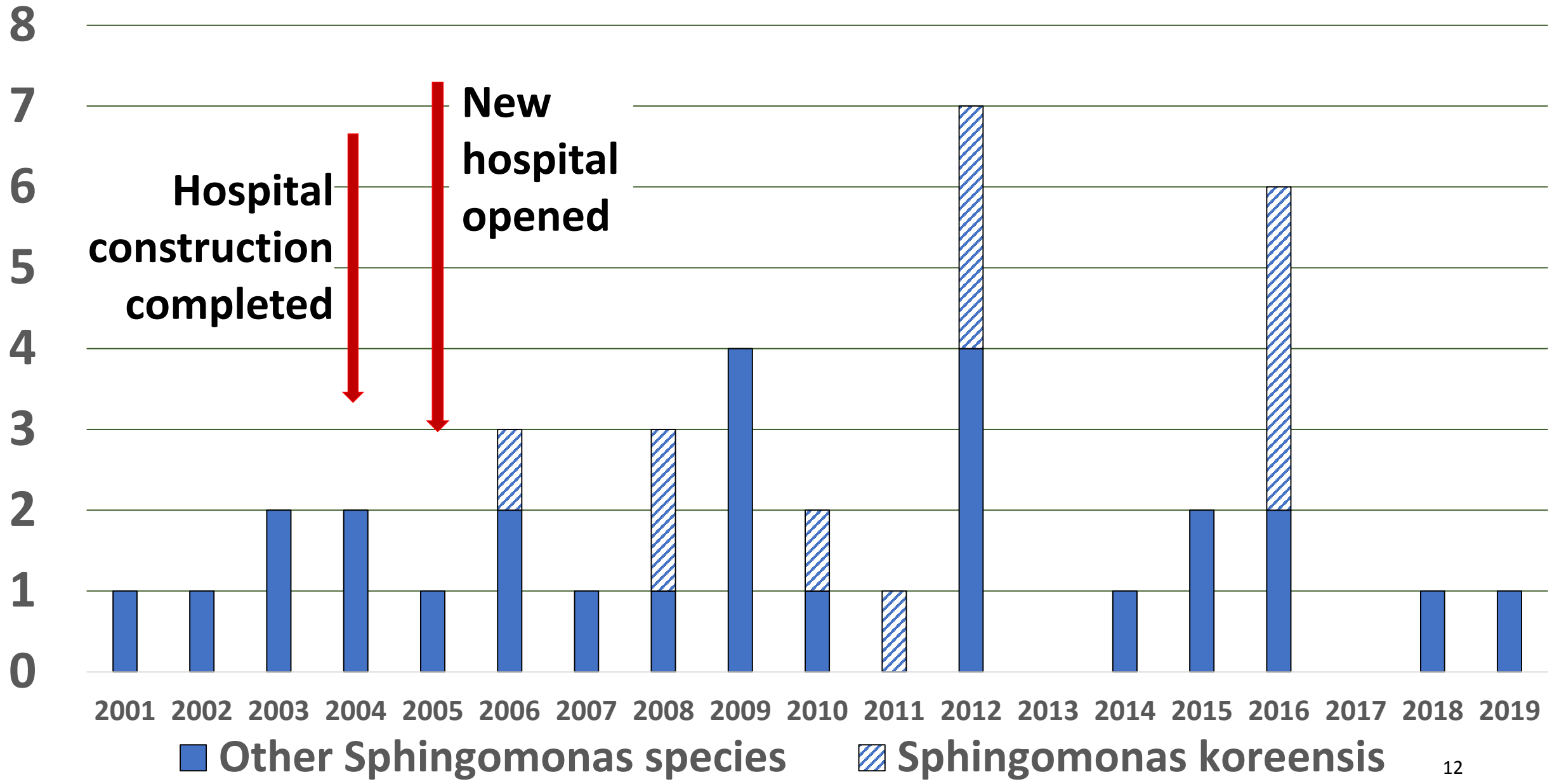
Aminoglycosides	Amikacin	**R**
	Gentamicin	**R**
Monobactam	Aztreonam	**R**
Cephalosporins	Cefepime	**R**
	Ceftazidime	**R**
Carbapenems	Imipenem	**R**
	Meropenem	**R**
β-lactam combinations	Piperacillin/tazobactam	**R**
Fluoroquinolones	Ciprofloxacin	S/I/R
	Levofloxacin	S/I/R
Folate pathway inhibitors	Trimethoprim/sulfamethoxazole	S

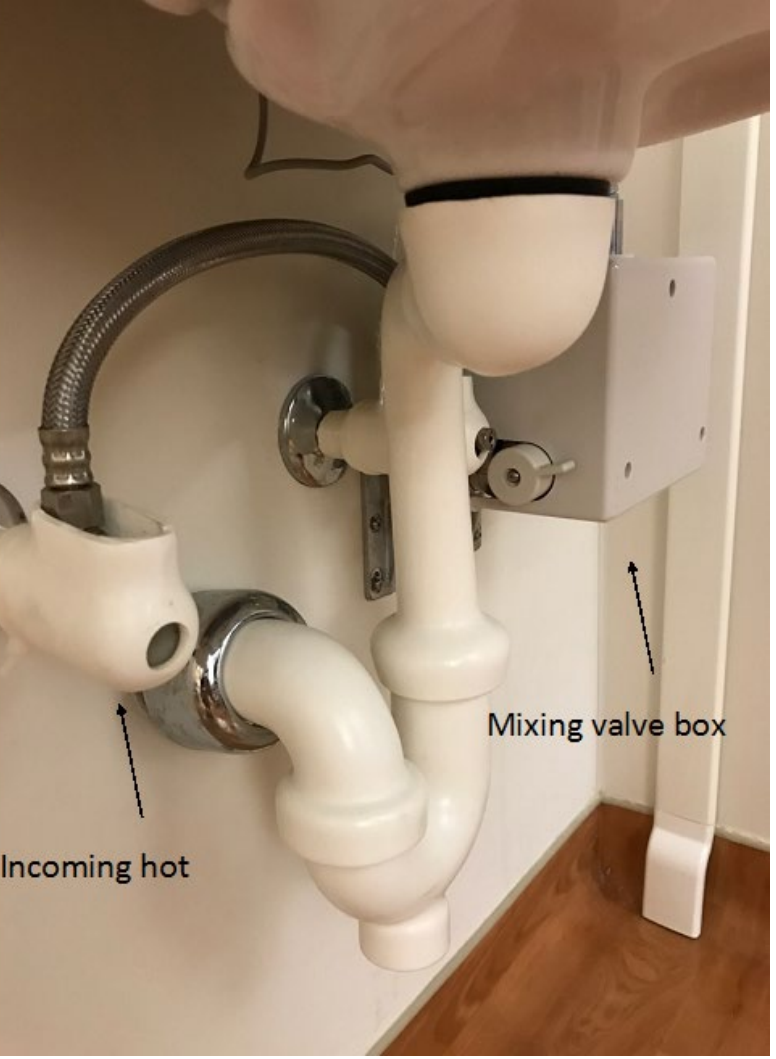
Antibiotic Resistance Key: R = Resistant, **S** = Sensitive, **I** = Intermediate

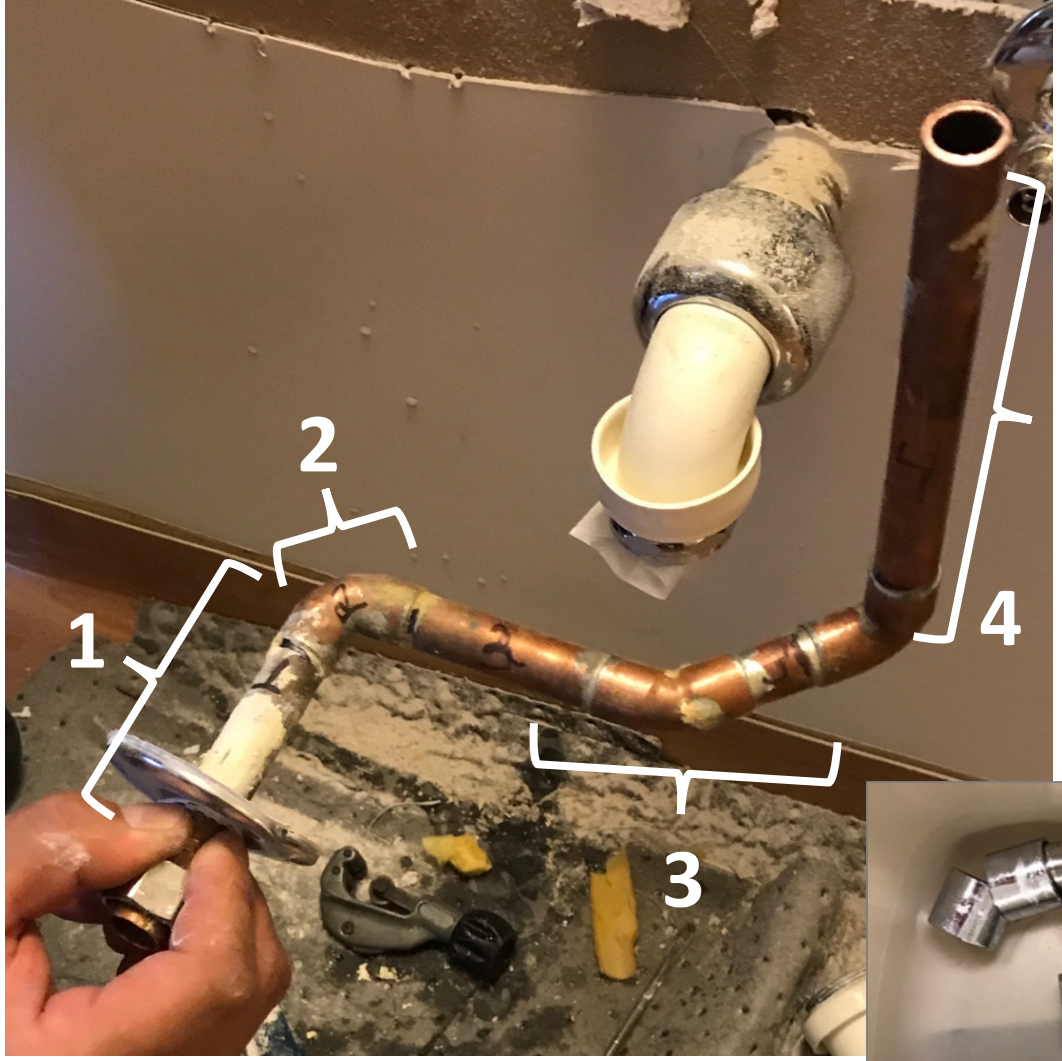
Clinical Micro Isolate Bank

- Review of clinical isolates 2001 through 2016
- 89 isolates *Sphingomonas* spp. reported to the medical record
- 66 available and viable from frozen stock
- 37 unique patients and 5 environmental sources
- Identification confirmed by mass spectrometry and sequencing

37 unique patient isolates




Mixing valve box
Incoming hot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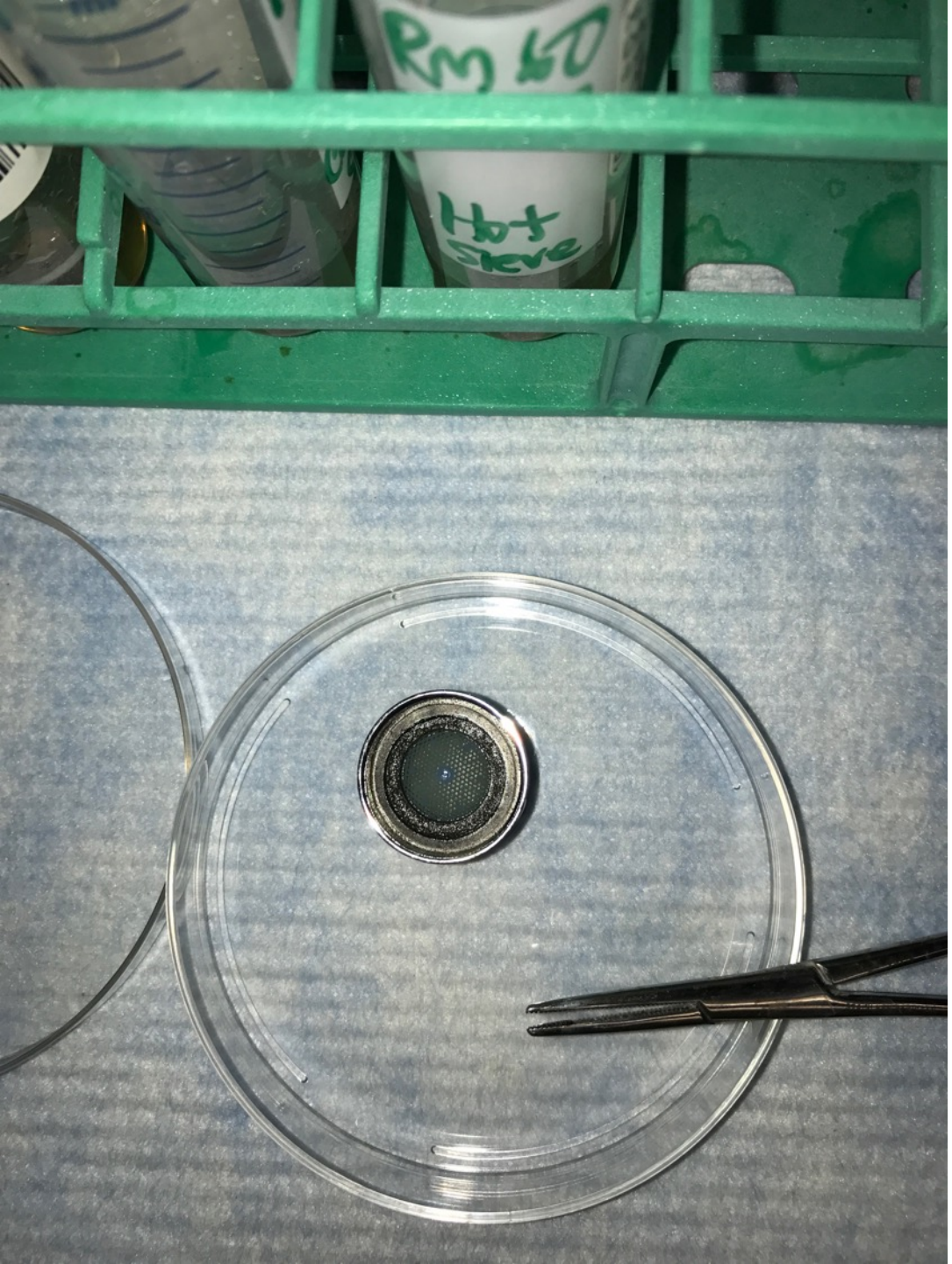

Faucet aerator with visible brown-black biofilm on rubber gasket

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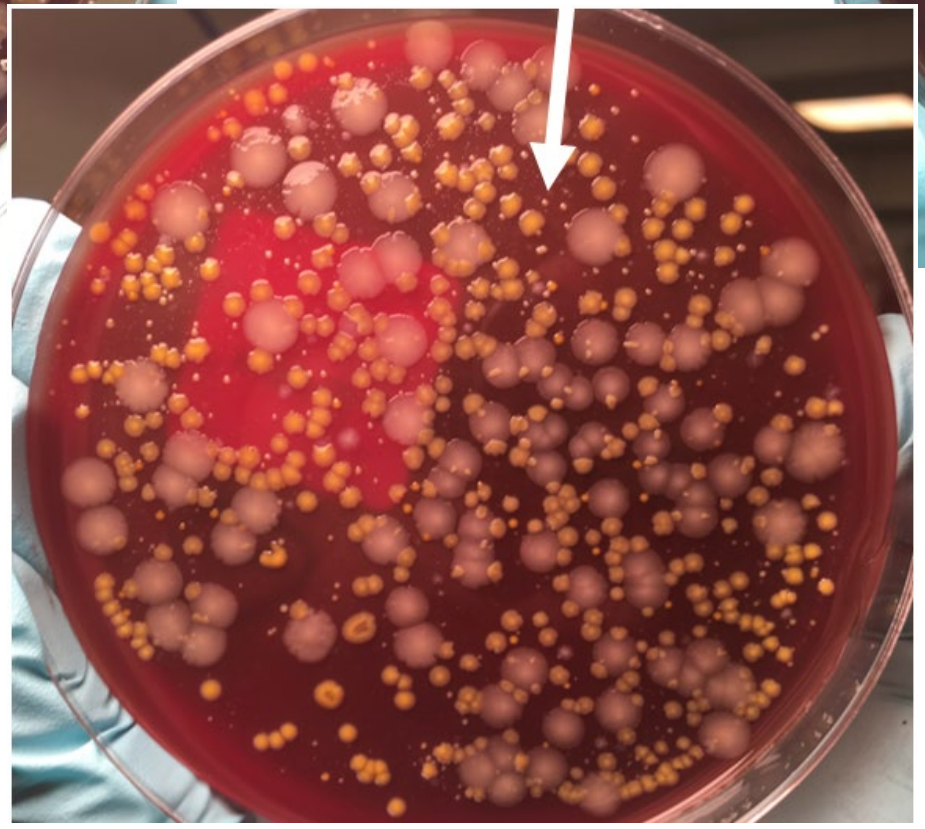
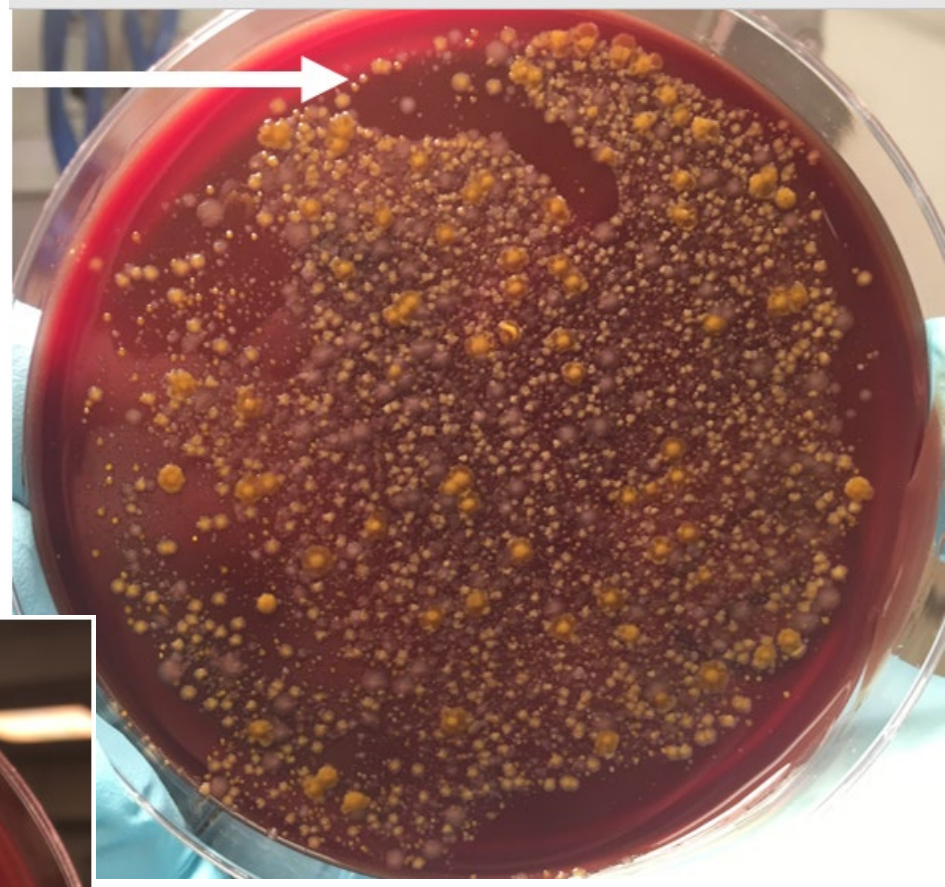
Culture positive for *S. koreensis*

Cloudy, stagnant water with heavy growth of *S. koreensis*
DOMESTIC HOT WATER
DOMESTIC COLD WATER

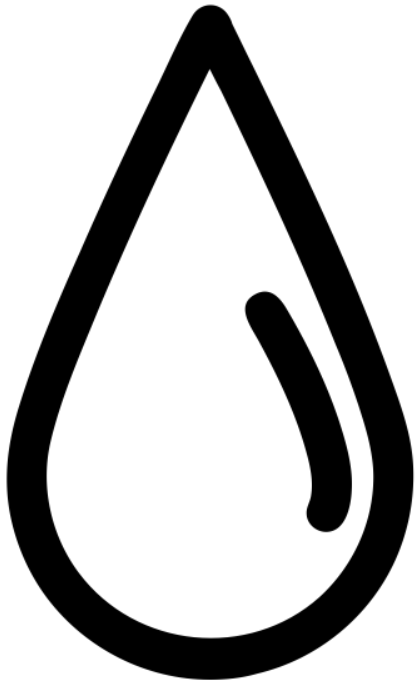


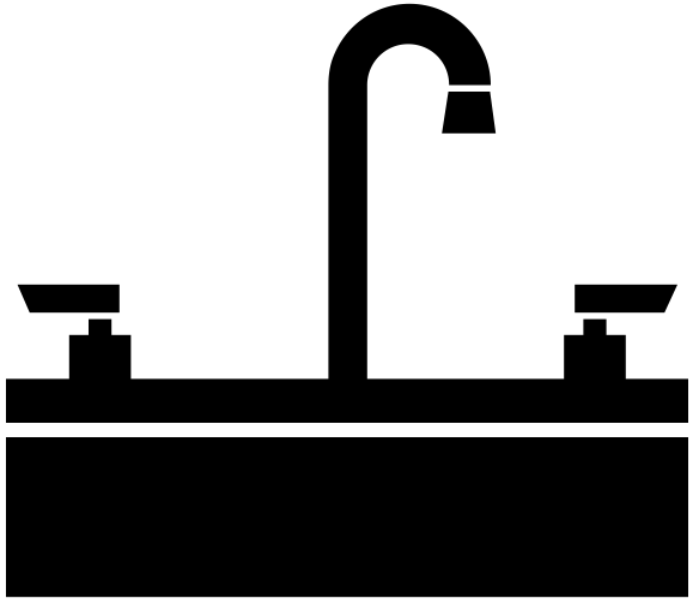


THANK YOU!!
Microbiology techs
Sterility Lab techs

3 water samples
- Diversity
- Heterogeneity

Environmental Surveillance (Oct 2016 – Dec 2017)



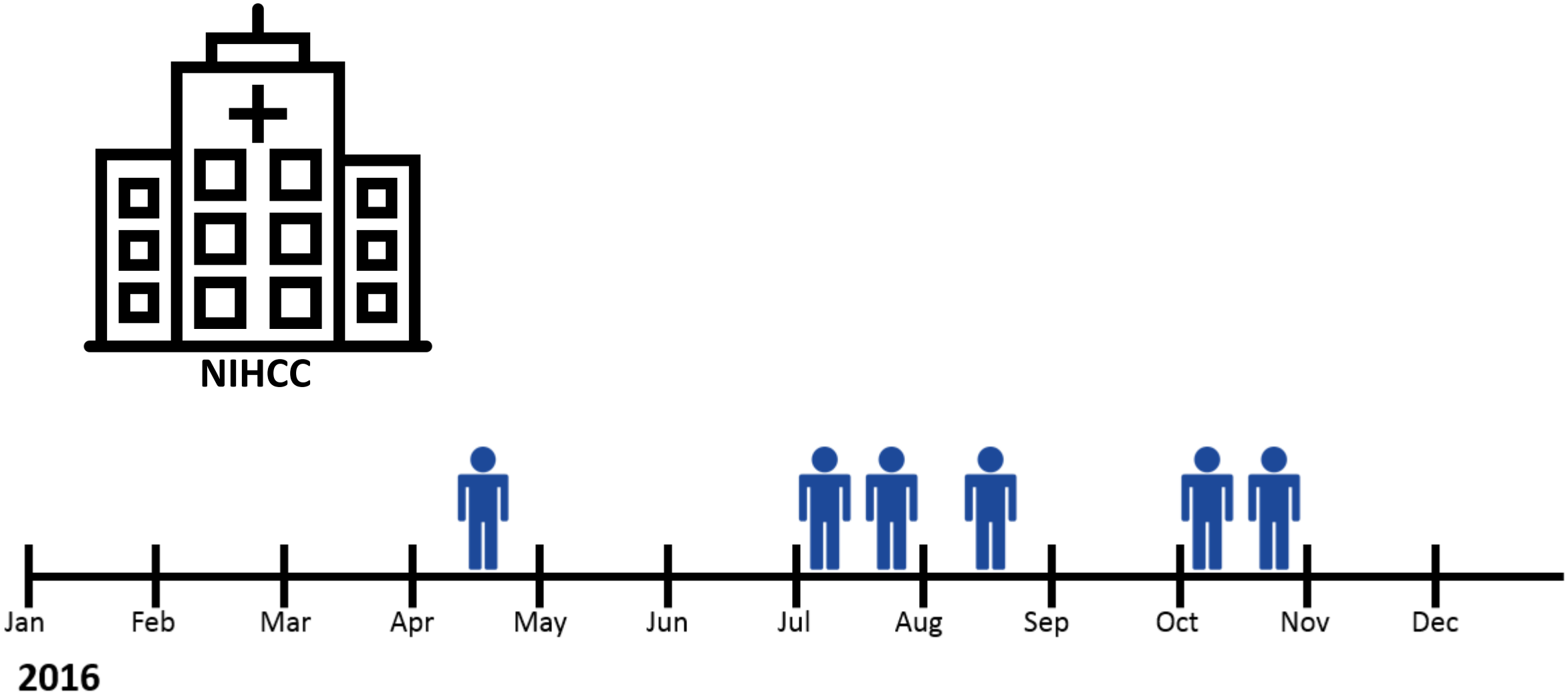


54 ***S. koreensis*** **Isolates**

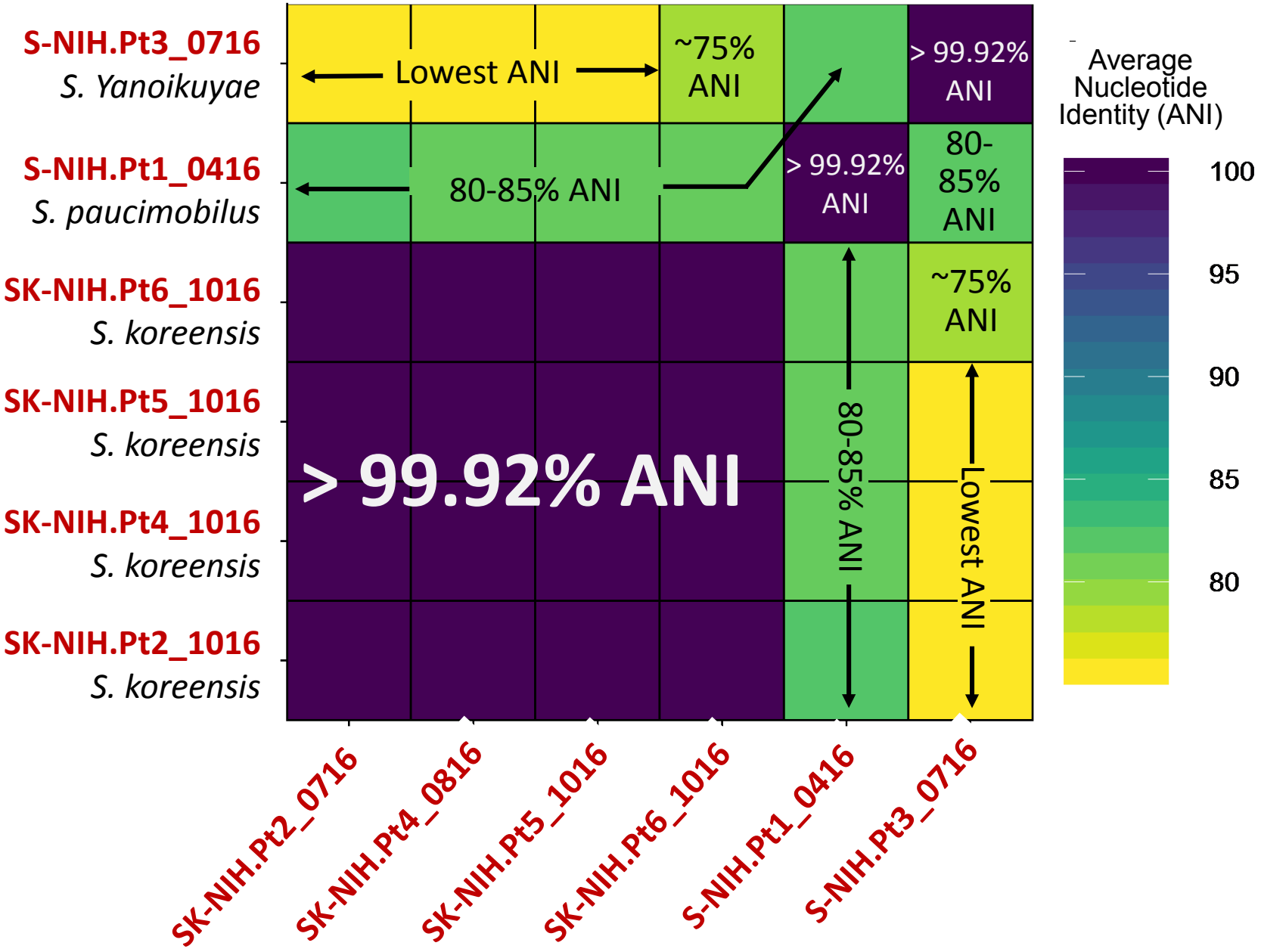
17 Patient Rooms

22 Sinks

Sphingomonas cases in 2016

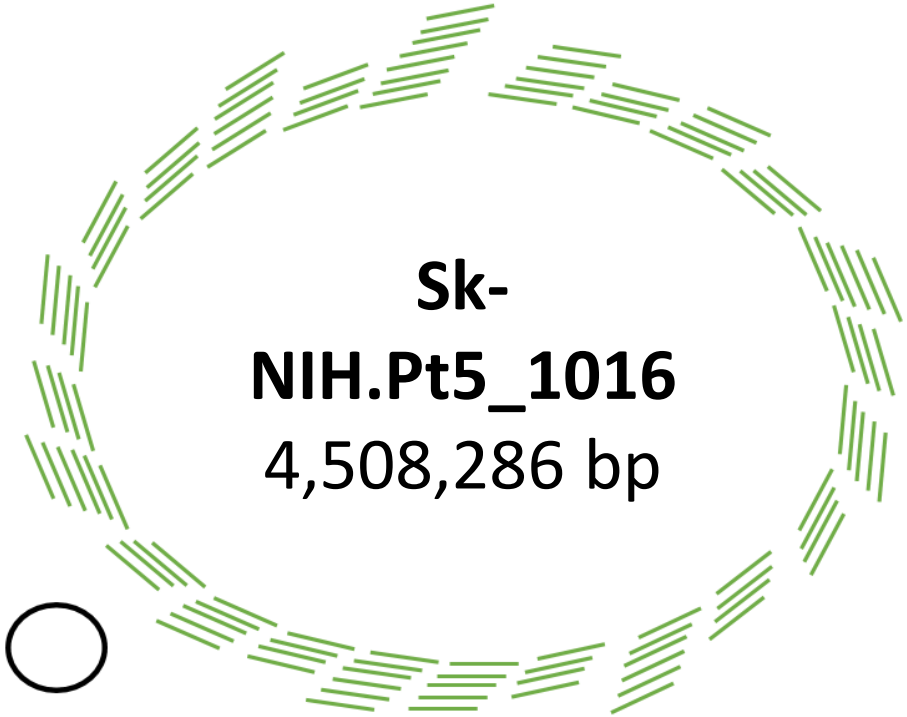


Genomic Comparison of 2016 *Sphingomonas* Patient Isolates



Achieving a higher level of resolution with complete long read genomic sequencing

PacBio Sequel II



Plasmid
310,952 bp

	# of DNA base pair differences
Sk-NIH.Pt2_0716	16
Sk-NIH.Pt4_0816	11
Sk-NIH.Pt6_1016	40
Sk-NIH.Pt7_0906	16
Sk-NIH.Pt8_0208	11
Sk-NIH.Pt9_0208	14
Sk-NIH.Pt10_0210	17
Sk-NIH.Pt11_0411	21
Sk-NIH.Pt14_0112	23
Sk-NIH.Pt16_1112	17
S. koreensis sink isolates	12-29 (range)

Genomic Findings...

- *Sphingomonas koreensis* has a 4,508,286 base pair genome
- Of 20 sequenced NIHCC patient *Sphingomonas* isolates, 12 were genetically HIGHLY related *S. koreensis.* These clinical isolates differed by only 11-40 basepairs even though patients span a decade.
- All *S. koreensis* isolates were highly antibiotic resistant. No classical antimicrobial resistance gene was found by sequencing. Suggests intrinsic resistance.
- All 40 genomes of *S. koreensis* isolated from water and sinks differed from patient isolates by only 12-29 basepairs of DNA.

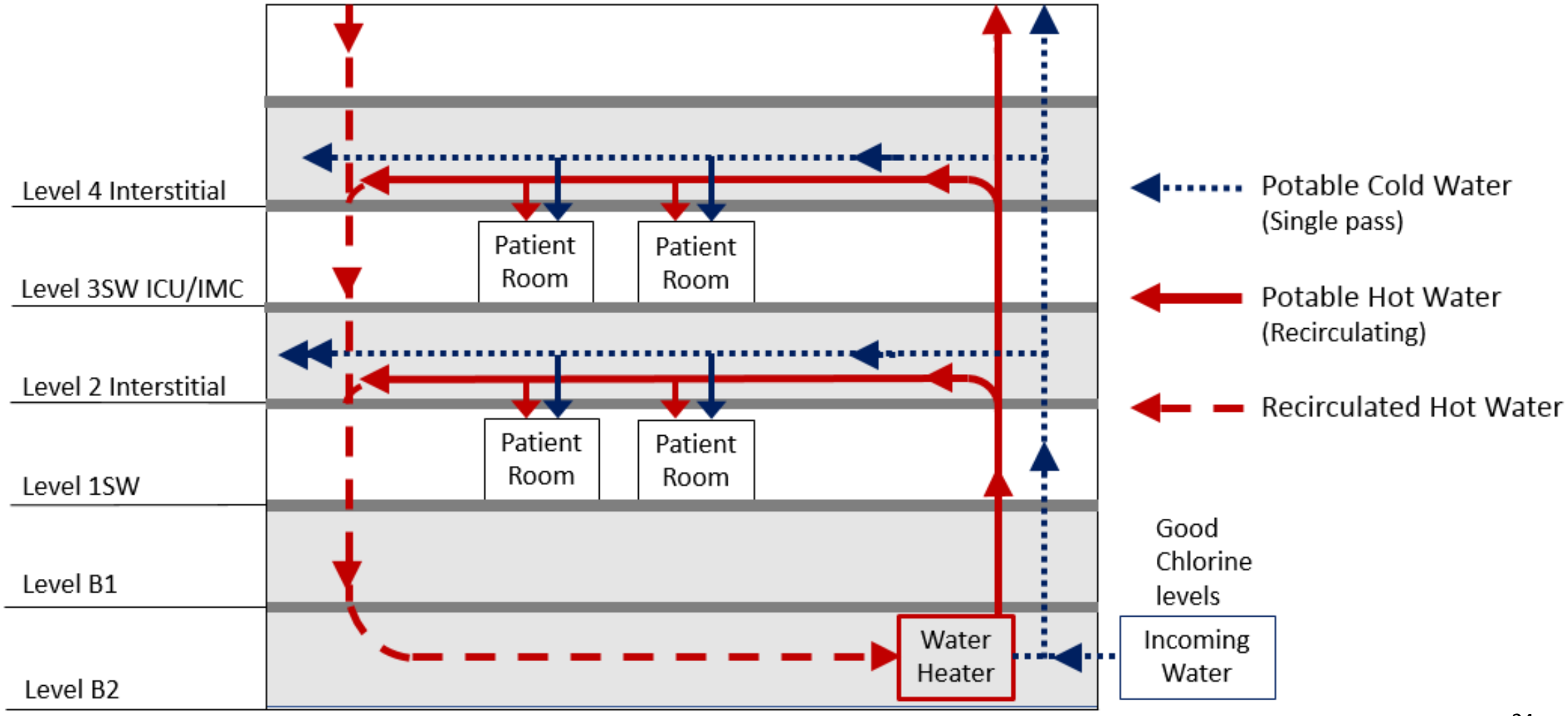
Genomic Findings, continued...

- Identical *S. koreensis* strains were found in adjoining rooms that shared water pipes.
- *S. koreensis* isolates obtained from NY State Health Department (Wadsworth) and CDC differed by 145 and 30,000 basepairs respectively. These are genetically distinct from NIHCC strains.
- Genomic and epidemiologic data, including the identification of highly clonal clinical *S. koreensis* isolates from 2006-2016 and contemporaneous, highly genetically related isolates in the water supply, suggests diffuse point sources resident in the NIHCC.

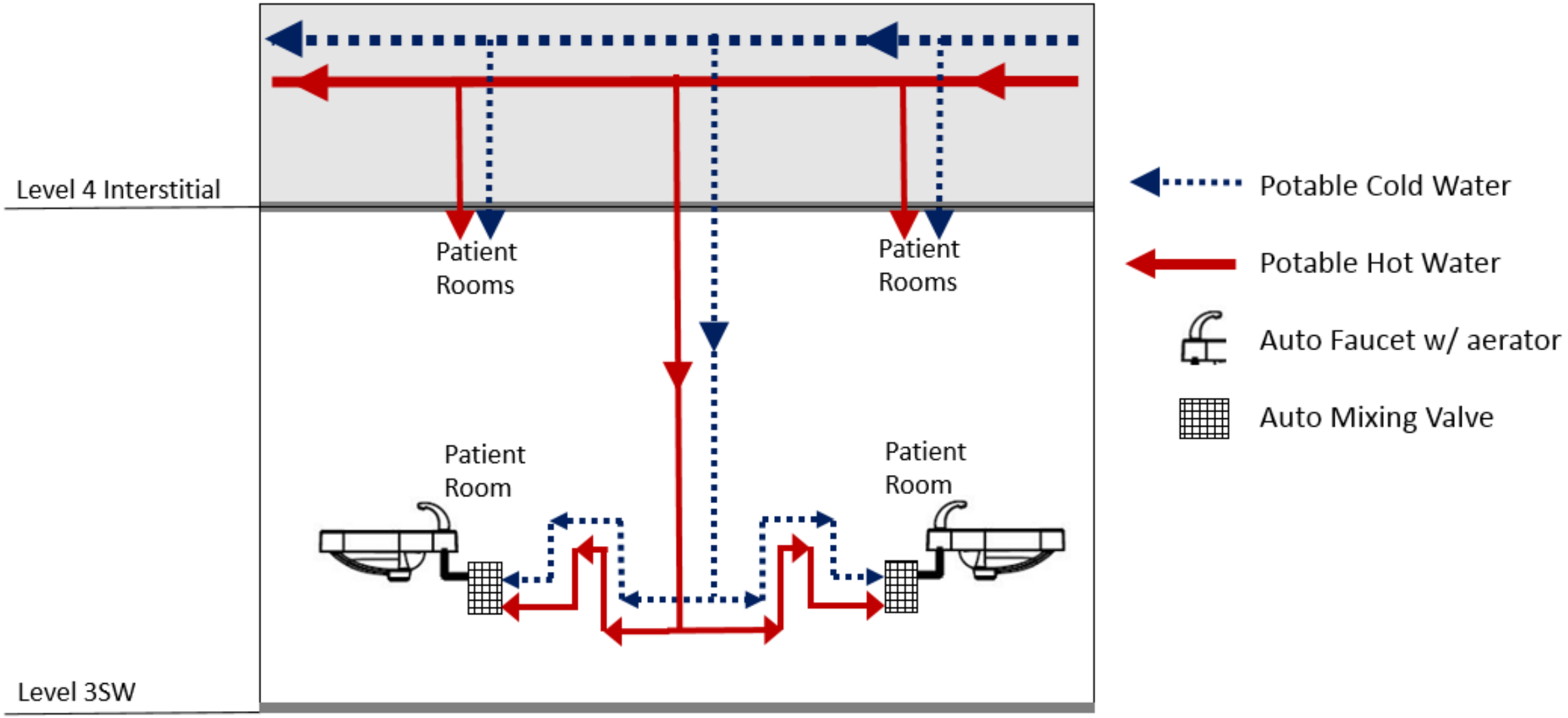
CRC Potable Water System

Control of
Opportunistic Waterborne Pathogens

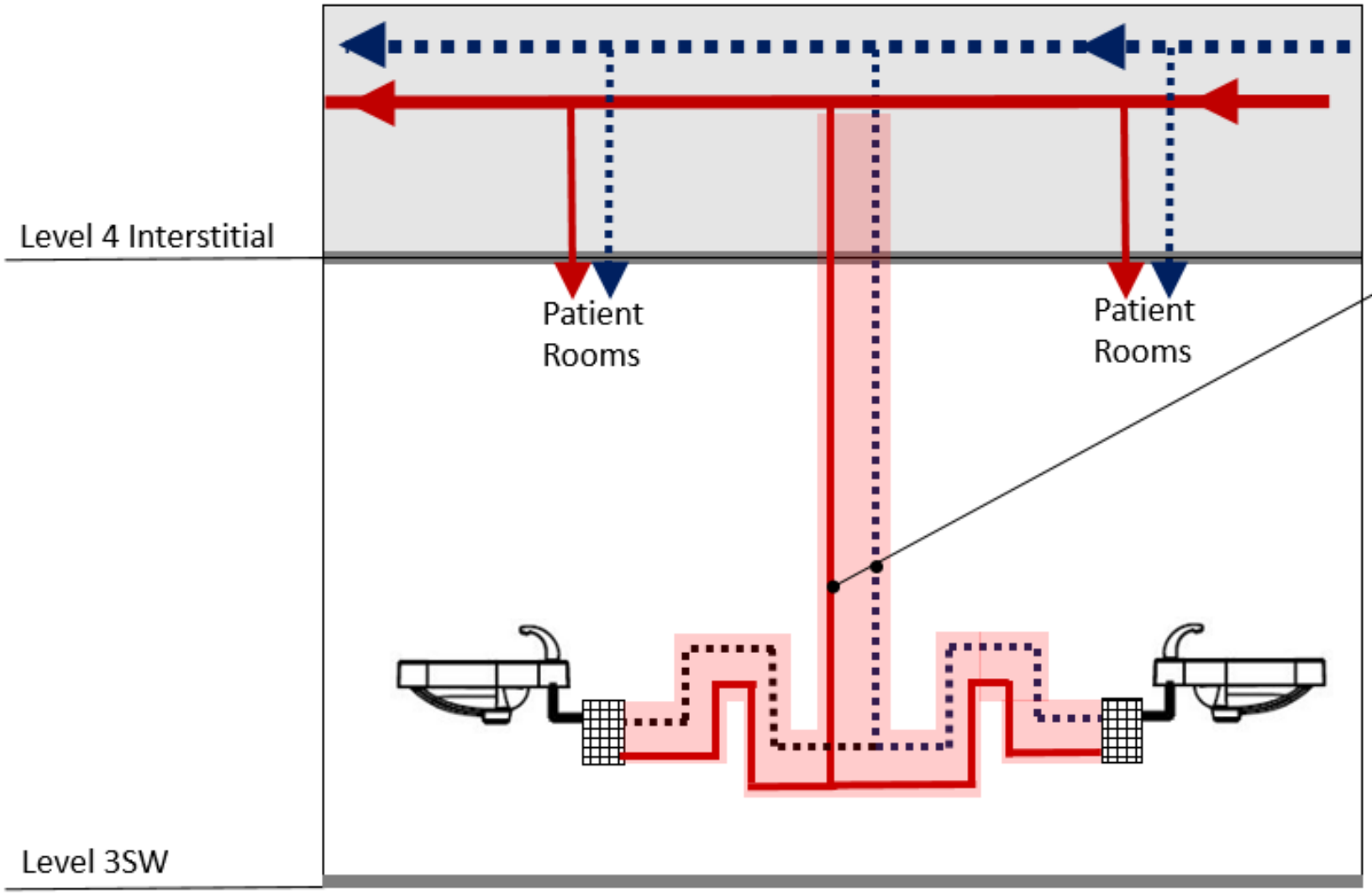
Building Water Distribution



ICU/IMC Piping



ICU/IMC Piping



Deadleg Pipe

- Flow only when sink(s) are in use
- Approx. 30’ in length

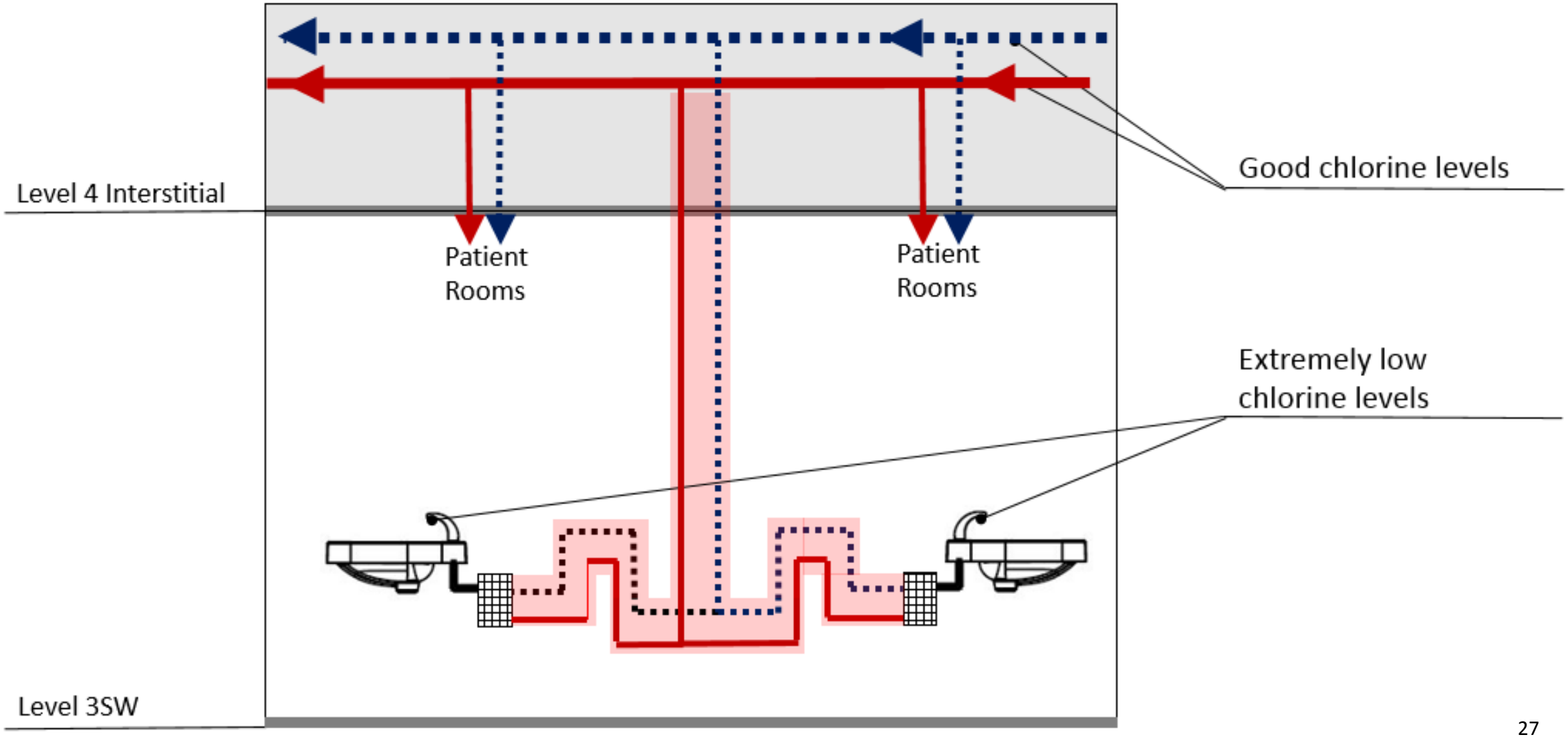
Leads to:

- Stagnant Water
- Biofilm

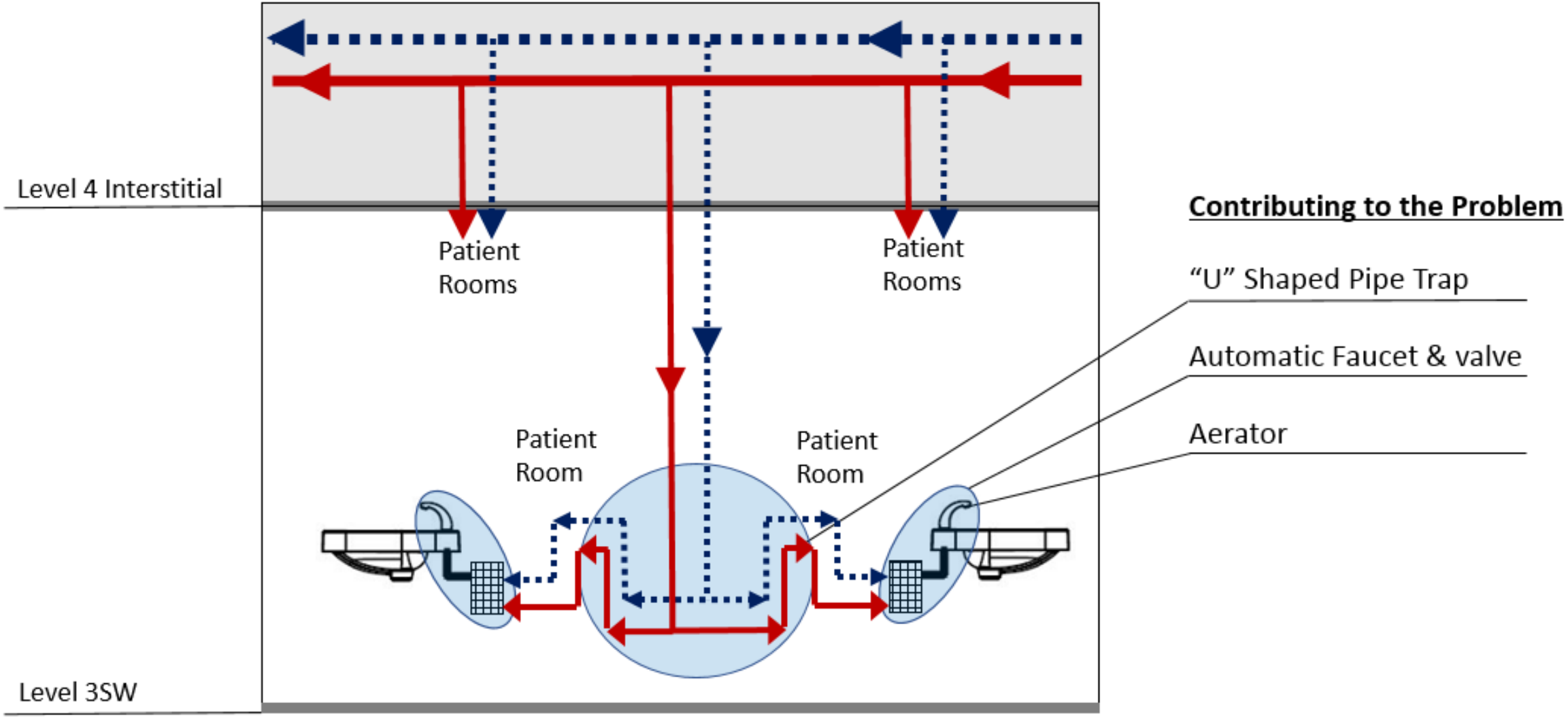
Leads to:

- Chlorine Dissipation

ICU/IMC Piping



ICU/IMC Piping



Findings

CDC/WHO: Maintain Free Chlorine Levels ≥ $0.5^{mg/L}$

Investigation

- Building incoming: Good
- Point of use (sinks): Unacceptable
- Hot water system:
  - Less free chlorine than cold water
  - Heat = Increased chlorine dissipation
  - Recirculation = Increased water age

Infrastructure

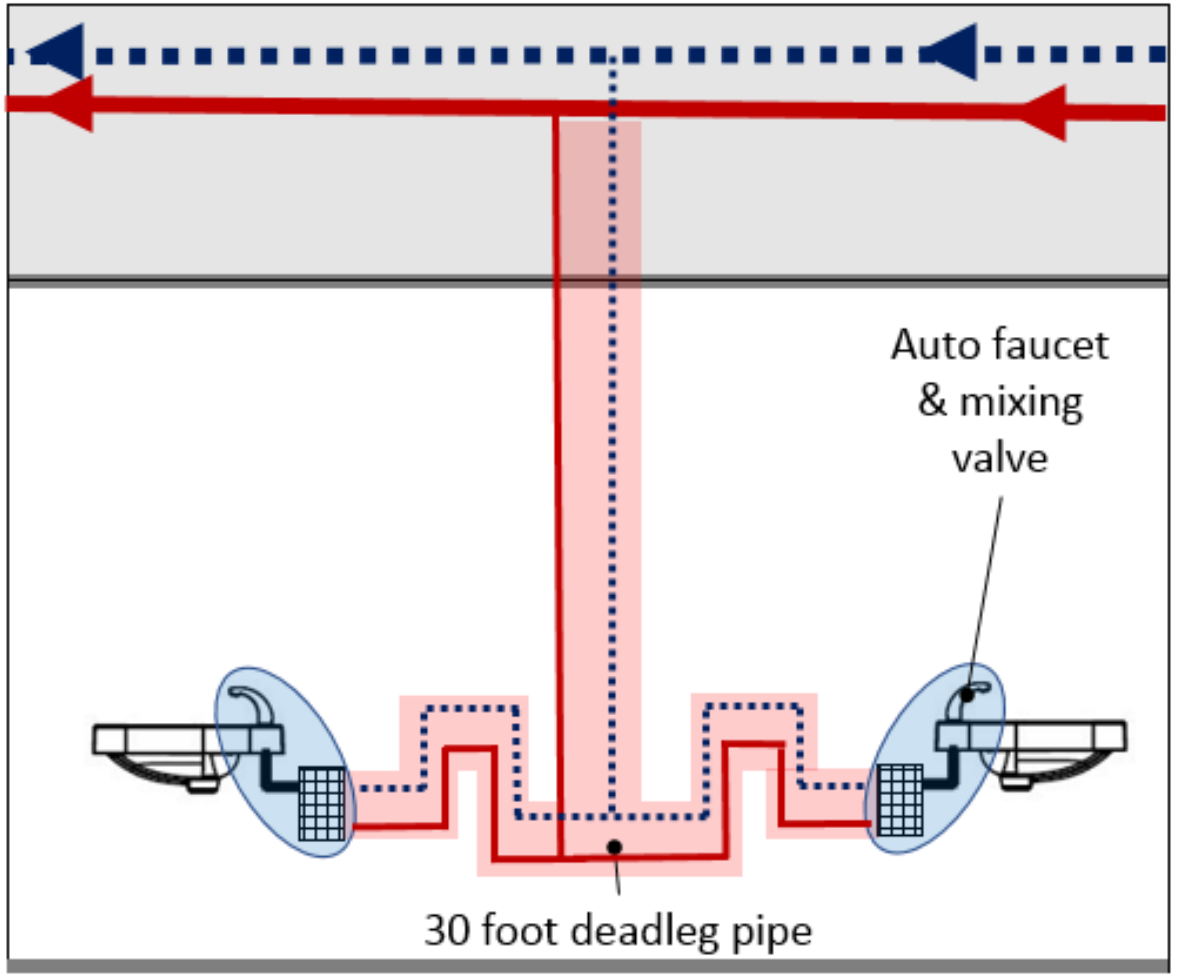
- Deadleg pipe
  - Stagnant water
  - Biofilm
- Automatic faucets & mixing valves
  - Low Flow - creates safe harbor for pathogens
  - Complex components – more places to shelter pathogens
- Aerator
  - Another surface for pathogen growth

Solutions

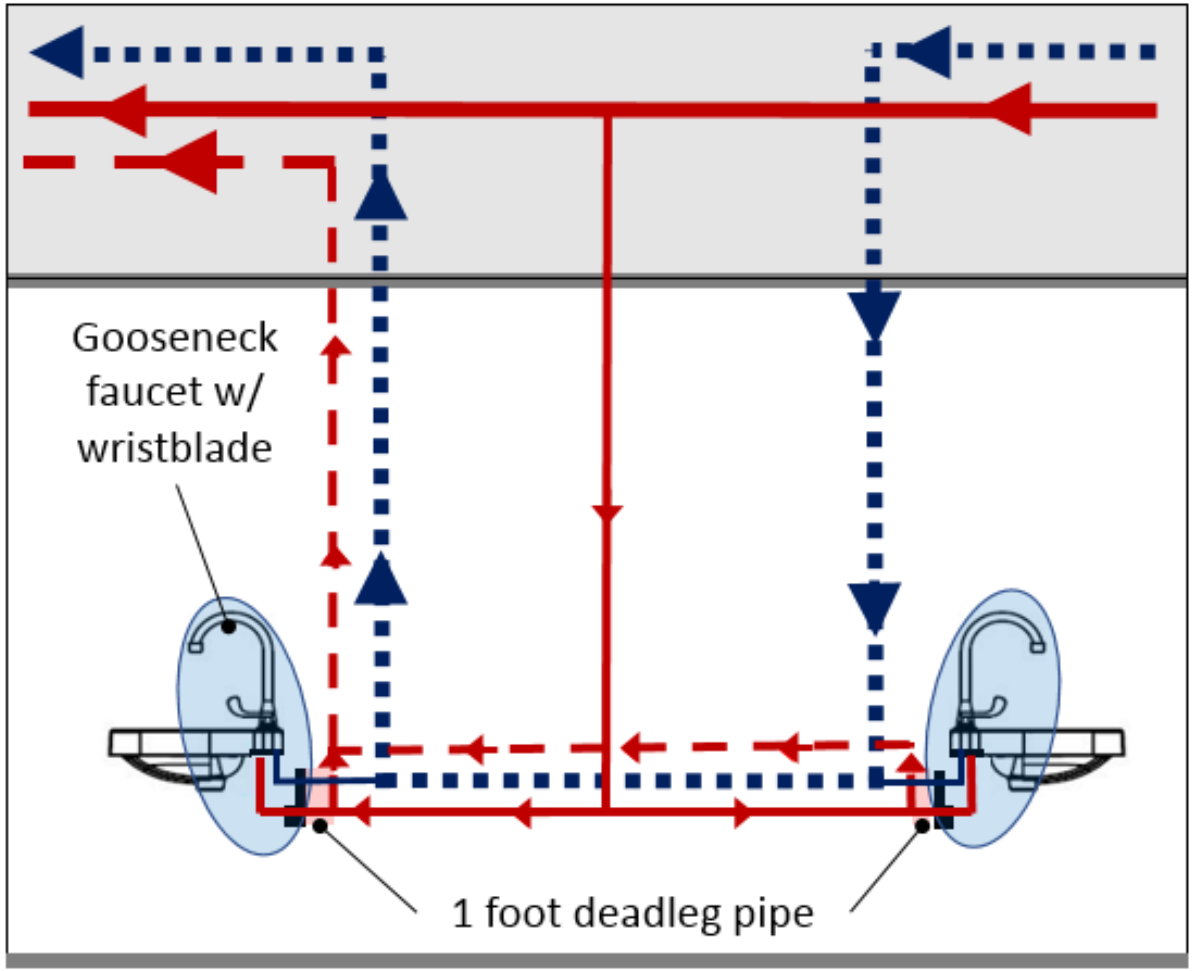
- Aerator Removal:
  - Increase water usage
  - Reduce pathogen collection areas
- Re-engineer distribution piping to patient room sinks
  - Reduce stagnant water
- Replace automatic faucets & mixing valves:
  - Increase water usage
  - Reduce pathogen collection areas

Changes

Before



After



Changes

Before

Auto faucet & mixing valve

After

Gooseneck faucet w/ wristblade

Data Comparison

Before

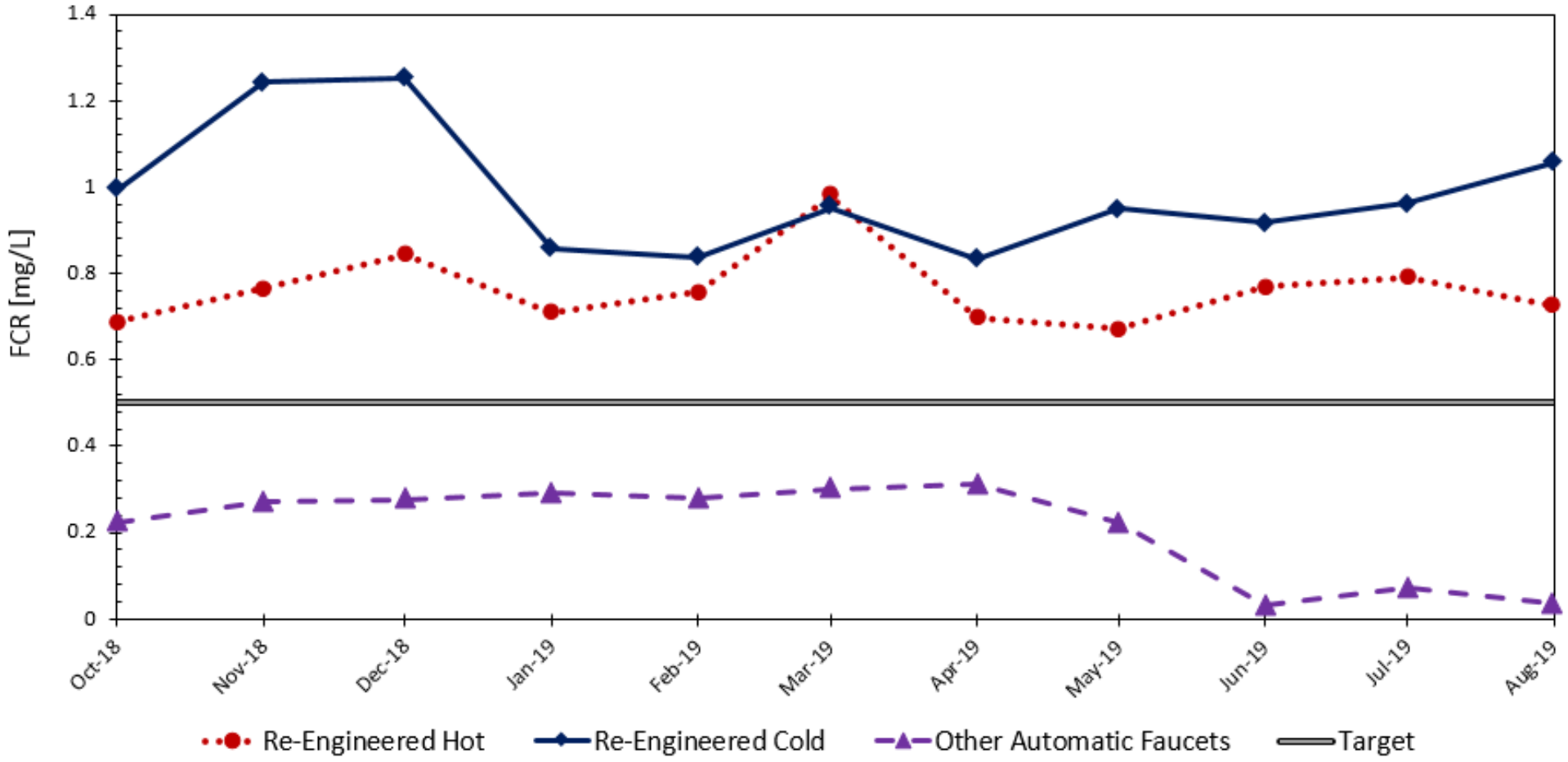
- Average chlorine levels:
  - Automatic: 0.27 mg/L
- Four faucet & water cultures
  - All Positive: *S. koreensis*

After

- Average chlorine levels:
  - Hot: **0.76** mg/L
  - Cold: **0.99** mg/L
  - Control: 0.21 mg/L (*from other automatic faucet in ICU/IMC*)
- Four Faucets tested
  - **All Negative:** *S. koreensis* for 12 months

Comparison

Average Free Chlorine Residual



Projects

Current

- Re-pipe 22 ICU/IMC inpatient rooms with re-engineered solution
  - Phased implementation (two rooms at a time)
  - Expected completion: March 2020

Future (Capital Improvement Fund)

- CRC main distribution improvements
  - Replace aging hot water heaters: increase hot water reliability
    - Temperatures >140°F minimize pathogen growth
  - Potable water filter installation: reduce sediment & potential biofilm growth
  - Expected duration: 6 months
- Re-pipe additional 114 inpatient rooms in the CRC
  - All potential immunocompromised patient locations
  - Expected duration: determined by hospital census

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Investigation of a Cluster of *Sphingomonas koreensis* Infections

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