



Proposed standard method for testing the efficacy of antimicrobial urinary catheters

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Acknowledgements

BURROUGHS
WELLCOME
FUND 

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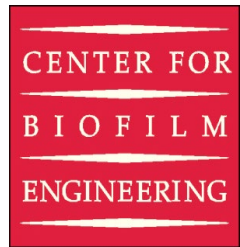
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CAUTI Rates

- 2009-2014: CAUTI was the only HAI to not see a reduction in infection rates between
- 2015-2016: Nationally, acute care hospitals report decrease CAUTI rates ~7%

	States better than 2015 baseline	States worse than 2015 baseline
Acute Care Hospitals	22	5
Inpatient Rehab Facilities	2	8
Long Term Acute Care Hospitals	6	6

SHEA/IDSA

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY MAY 2014, VOL. 35, NO. 5

SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent Catheter-Associated Urinary Tract Infections in Acute Care Hospitals: 2014 Update

III. Approaches that should not be considered a routine part of CAUTI prevention

1. Do not routinely use antimicrobial/antiseptic-impregnated catheters (quality of evidence: I).

I. High

Highly confident that the true effect lies close to that of the estimated size and direction of the effect. Evidence is rated as high quality when there is a wide range of studies with no major limitations, there is little variation between studies, and the summary estimate has a narrow confidence interval.

Assess Biofilm Prevention

The goal of this project was to develop and validate a standard quantitative in vitro method that will assist FDA regulators in evaluating the efficacy of surface modified urinary catheters.

CDC Infection Criteria

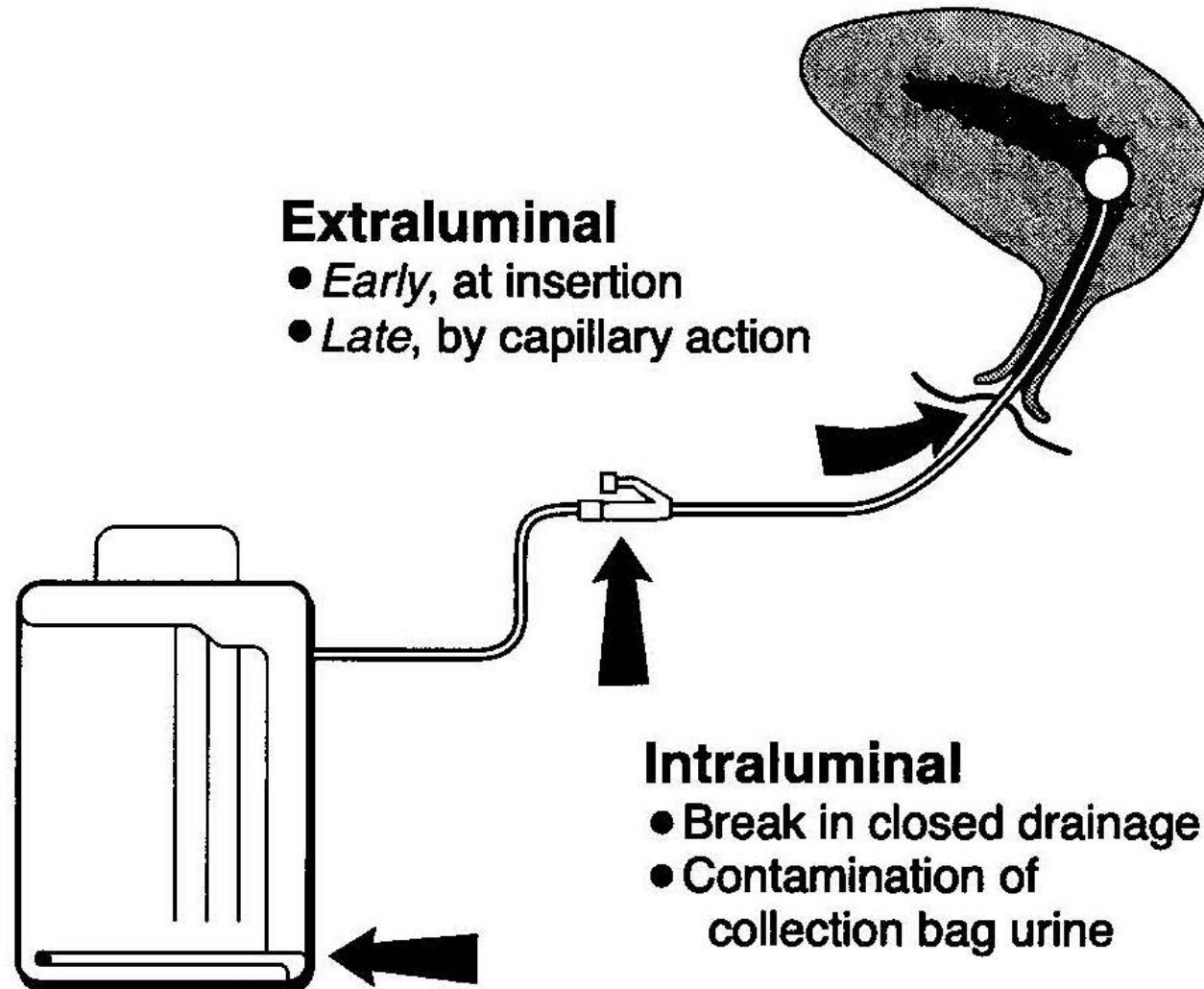
1. Patient had an indwelling urinary catheter that had been in place for **> 2 days**.
2. Patient has at least one of the following signs or symptoms.
 - Fever(>38° C)
 - Suprapubic tenderness
 - Urinary urgency
 - Urinary frequency
 - Dysuria
3. Patient has a urine culture with no more than two species of organisms identified, at least one of which is a bacterium of **10⁵ CFU/ml**.

CAUTI Microorganisms - Top 5

January 2011-December 2014

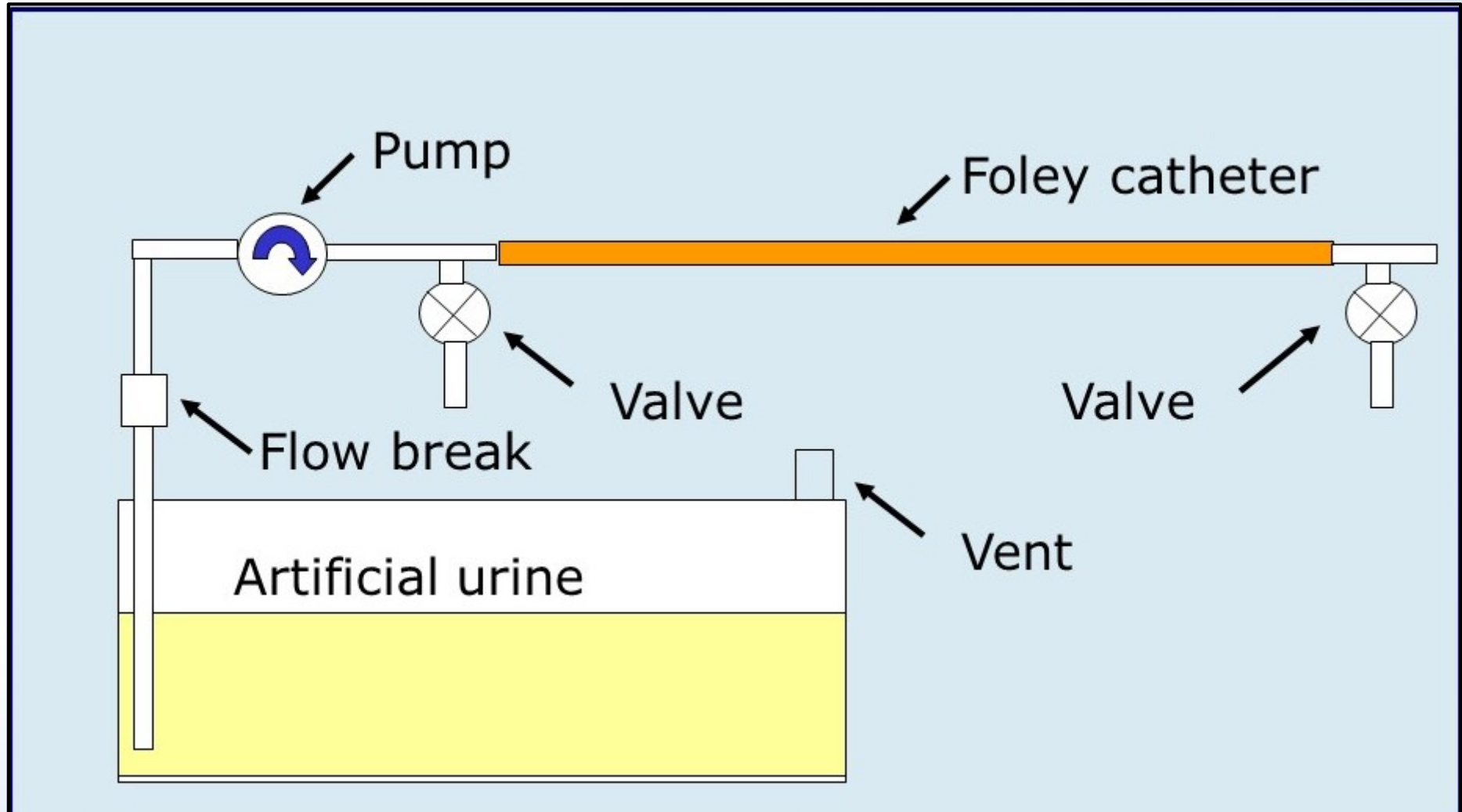
Pathogen	Percent of Pathogenic Isolates	Rank
<u><i>Escherichia coli</i></u>	23.9	1
<i>Candida albicans</i>	11.7	2
<i>Pseudomonas aeruginosa</i>	10.3	3
<i>Klebsiella spp.</i>	10.1	4
<i>Enterococcus faecalis</i>	7.0	5

Routes of Infection

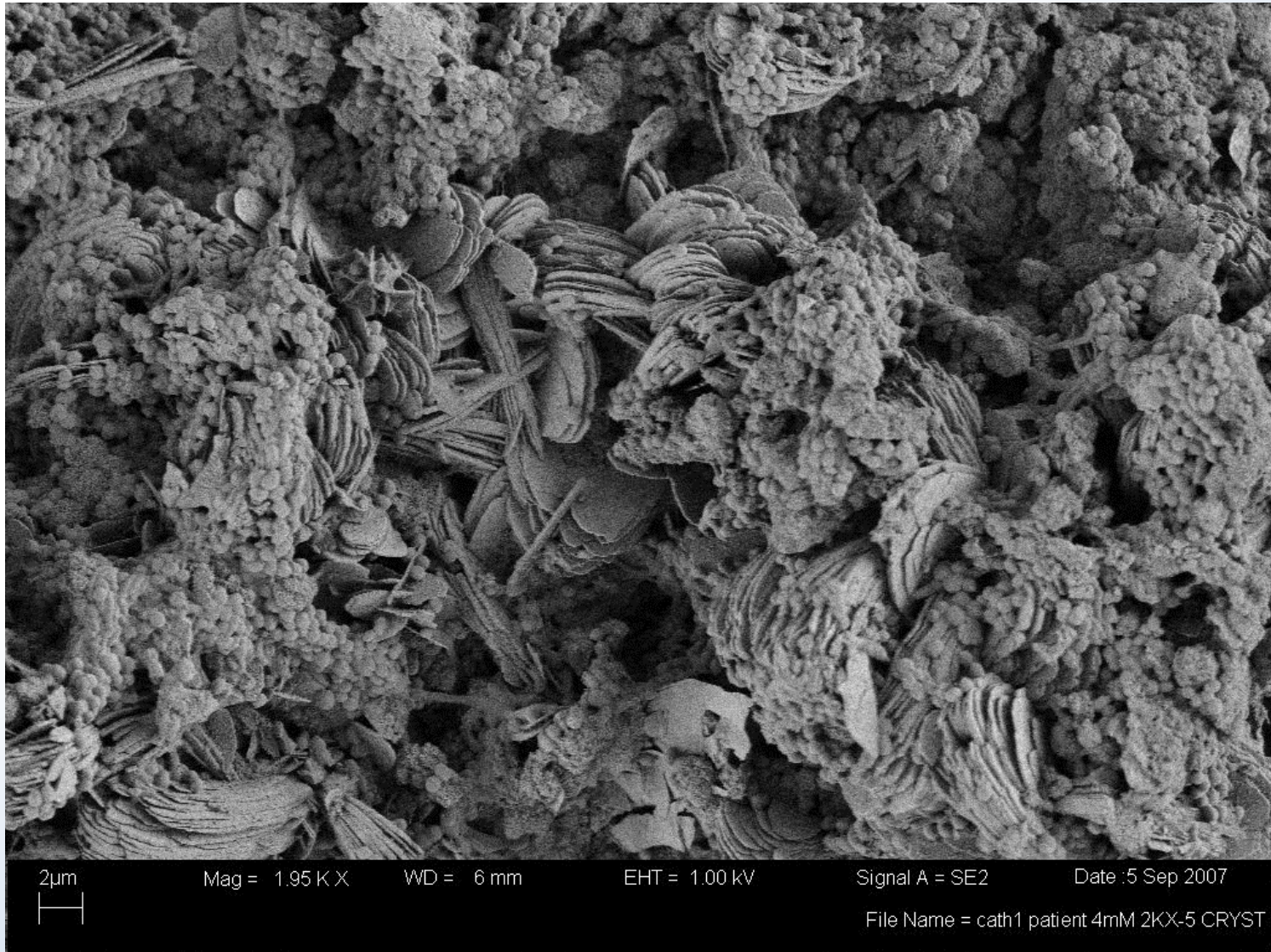


Maki and Tambyah, 2001

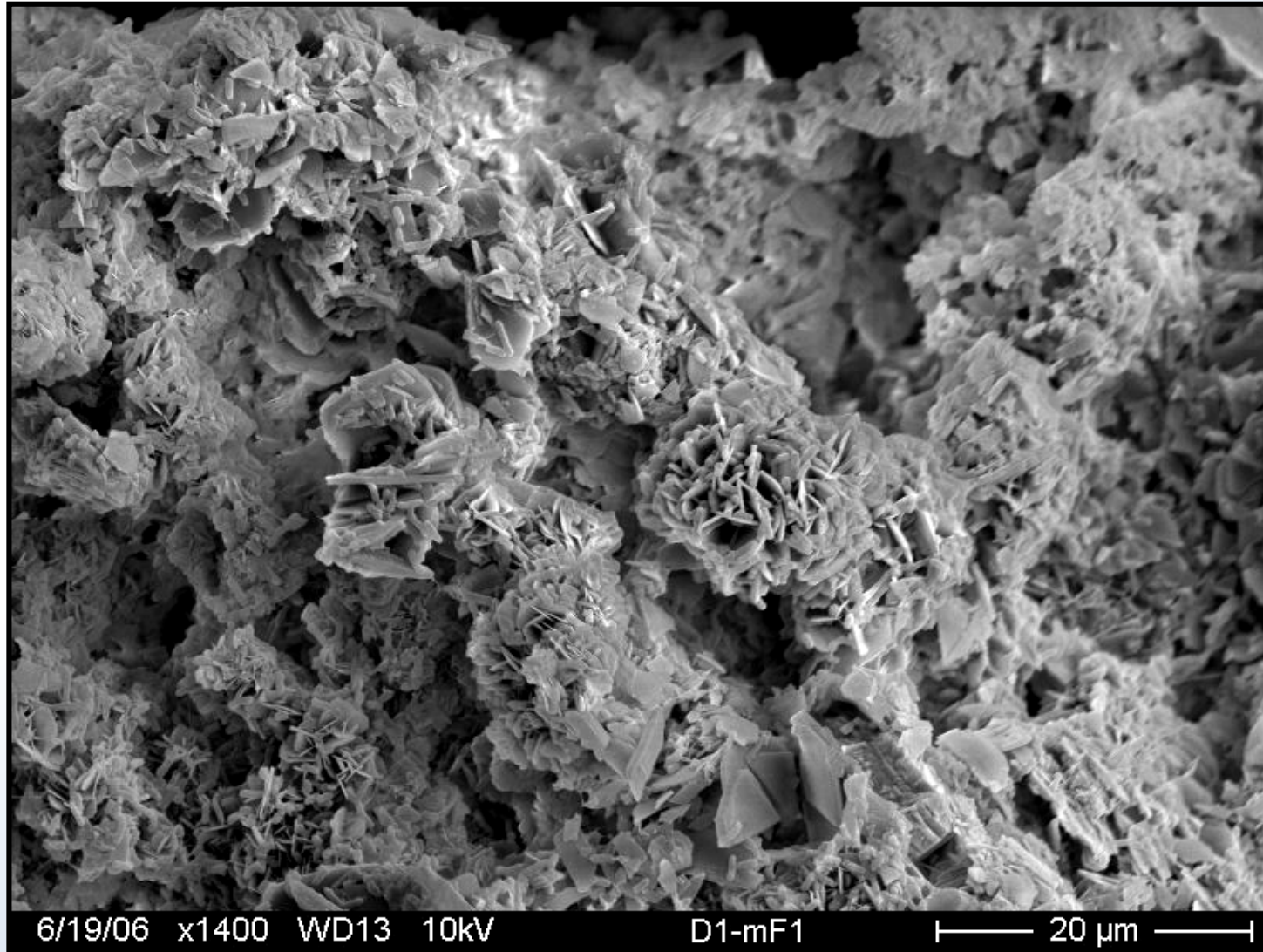
In vitro Urinary Catheter Model



Patient Urinary Catheter



In vitro Urinary Catheter Model



The 7 R's for Standard Methods

- **Reasonableness** (expense, lab techniques)
- **Relevance** (lab outcome ~ field/clinical outcome)
- **Repeatability** (intra-laboratory, SDr)
- **Resemblance** (controls similar between experiments)
- **Responsiveness** (detect changes)
- **Reproducibility** (inter-laboratory, SDR)
- **Ruggedness** (unaffected by slight changes)

The 7 R's

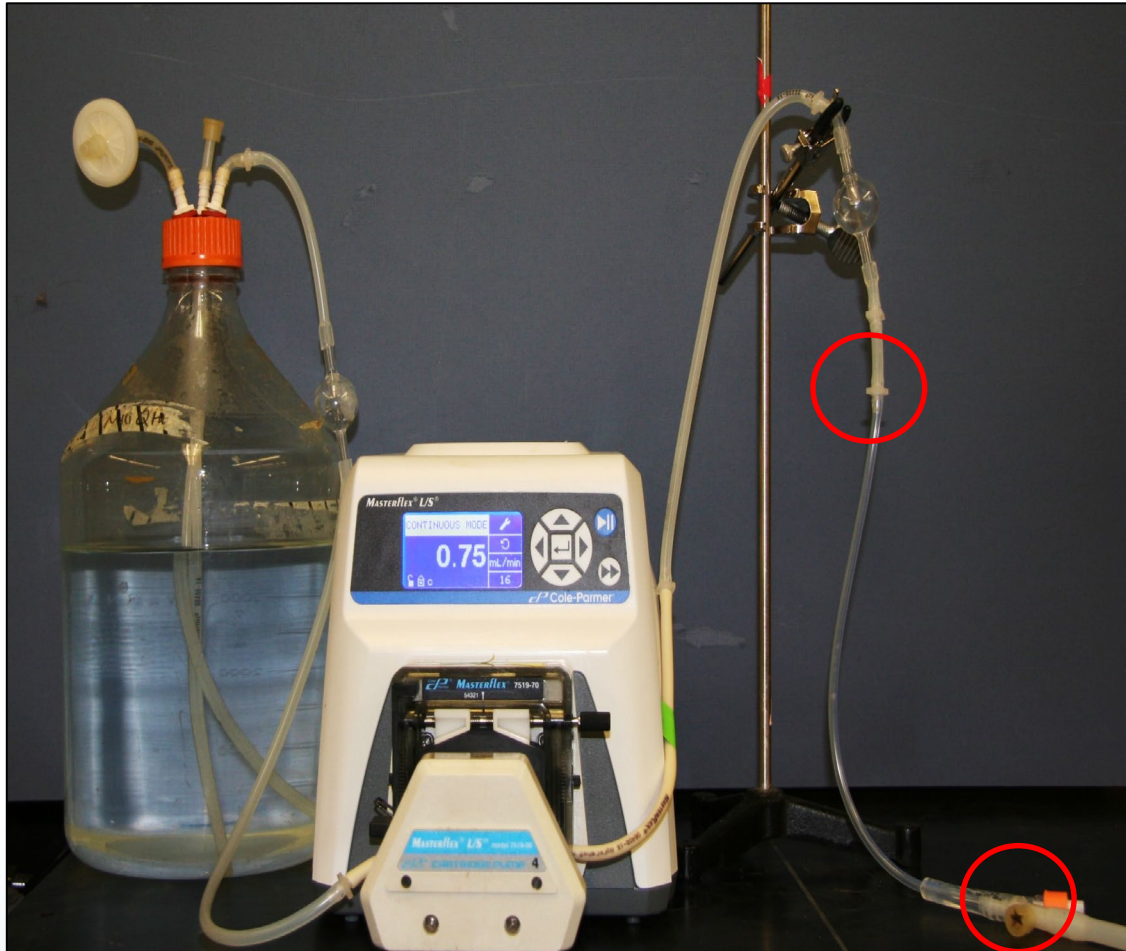
- Reasonableness (expense, lab techniques)
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- Reproducibility (inter-laboratory, SD_R)
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Intraluminal Catheter Model



- *Escherichia coli* ATCC 53498
- Artificial Urine Medium
- 16 French, silicone, 2 way Foley
- 0.75mL/min
- 37°C

Intraluminal Catheter Model



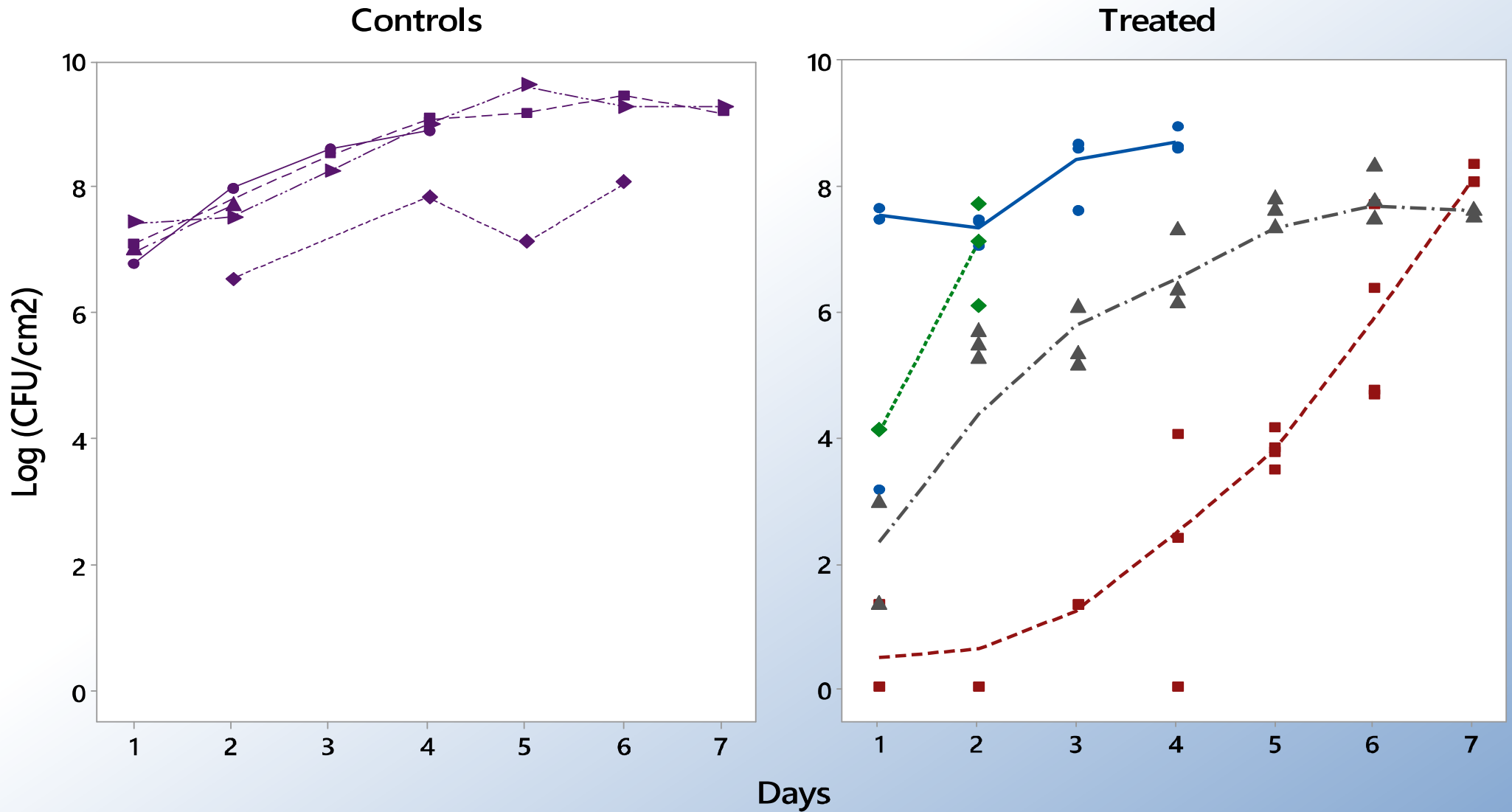
Day One:

- Run sterile AUM through catheter for 2 hours
- Inoculate catheter with 10^3 CFU/mL of UPEC

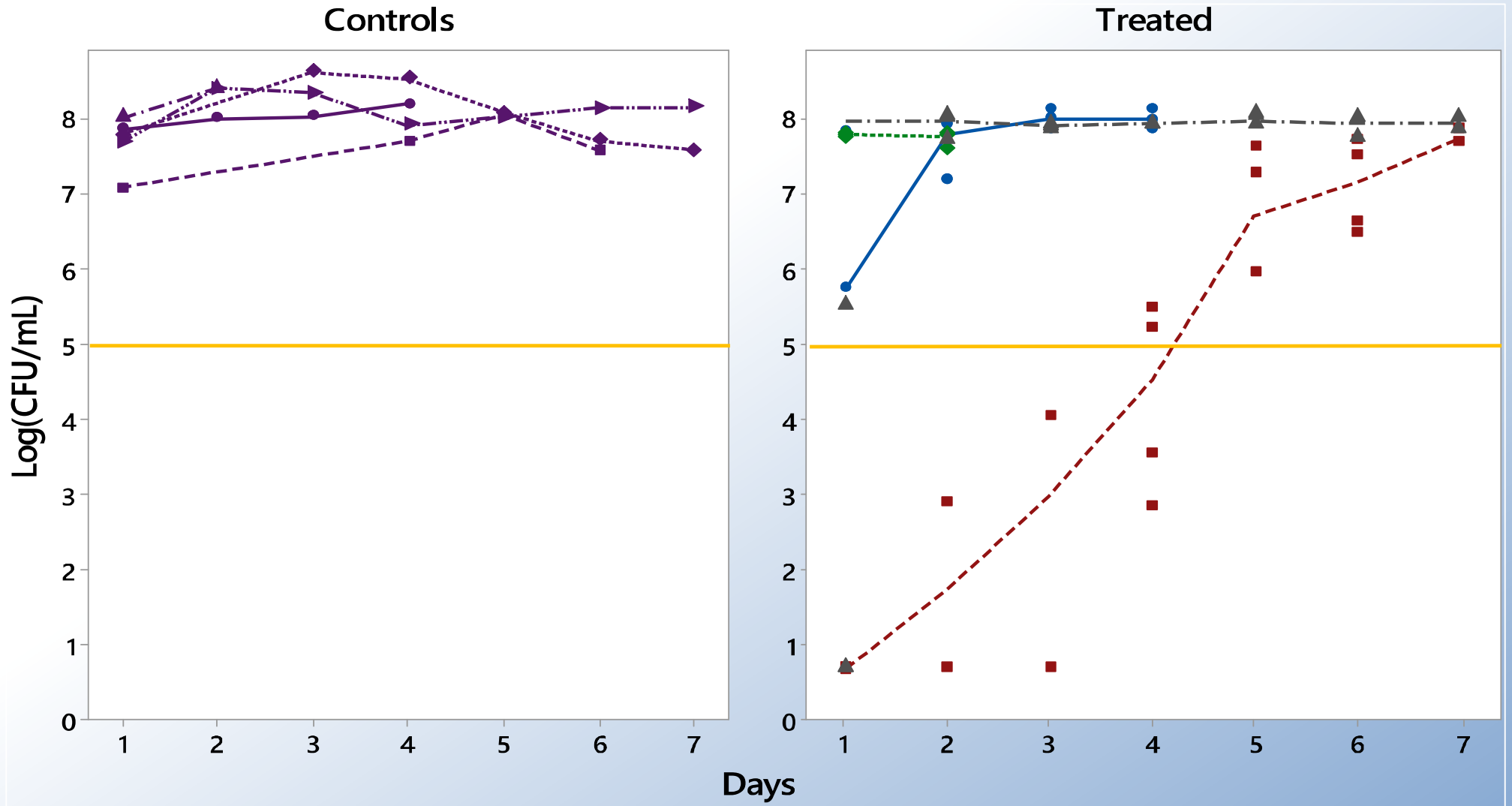
Daily

- Collect Samples
 - Effluent
 - Catheter segment
- Disaggregate through vortex and sonication series
- Plate for viable cell counts

Catheter Segment Samples



Effluent Counts



Repeatability

Independent repeats of the same experiment in the same laboratory produce nearly the same response

Acceptable repeatability: $SDr < 1.0$

Repeatability

Time Point	Catheter Samples		Effluent Samples	
	Mean Log (CFU/cm ²)	St Dev	MeanLog (CFU/ml)	St Dev
24	7.07	0.28	7.98	0.36
48	7.42	0.62	8.55	0.24
72	8.46	0.19	8.63	0.29
96	8.69	0.58	8.39	0.36

Control Catheter Samples CSDr = 0.79

Control Effluent Samples CSDr = 0.29

Ruggedness

A standard laboratory method is said to be rugged if the outcome is unaffected by slight departures from the protocol.

**Statistical tool: *mixed effects* regression or ANOVA
(e.g., repeated measures regression or ANOVA)**

Operational Parameters

- Inoculum Concentration: 10^2 , **10^3** , 10^4 CFU/mL
- Incubator Temperature: 34, **37**, 40 °C
- Flow Rate: 0.25, **0.75**, 1.25 mL/min
- pH of AUM: 6, **6.5**, 7
- Biofilm Removal Technique: **Sonicate**, Scrape

Ruggedness

Run	Inoc (CFU/mL)	Temp (°C)	Flow (mL/min)	pH	Removal
1A	10 ⁴	34	0.25	7	sonicate
1B	10 ²	40	1.25	6	scrape
2A	10 ²	40	0.25	6	sonicate
2A	10 ⁴	34	1.25	7	scrape
3A	10 ²	40	1.25	7	scrape
3B	10 ⁴	34	0.25	6	sonicate
4A	10 ²	34	1.25	7	sonicate
4A	10 ⁴	40	0.25	6	scrape
5A	10 ²	34	0.25	7	scrape
5B	10 ⁴	40	1.25	6	sonicate
6A	10 ²	34	0.25	6	scrape
6B	10 ⁴	40	1.25	7	sonicate
7A	10 ²	40	0.25	7	sonicate
8B	10 ⁴	34	1.25	6	scrape
9A	10 ²	34	1.25	6	sonicate
9B	10 ⁴	40	0.25	7	scape

Ruggedness

Control Catheter Samples, log(CFU/cm²)

Sample Points	Factor	Low pH, 6	High pH, 7
8 hours	Inoculum	0.69	0.93
	Temperature	0.08	-0.05
	Flow	0.13	0.54
24 hours	Inoculum	0.63	1.15
	Temperature	0.41	-0.07
	Flow	1.05	2.85
48 hours	Inoculum	0.45	1.19
	Temperature	0.23	-0.35
	Flow	1.09	3.37

Method is rugged with respect to parameter if effect is less than +/- 0.30 log

Rugged

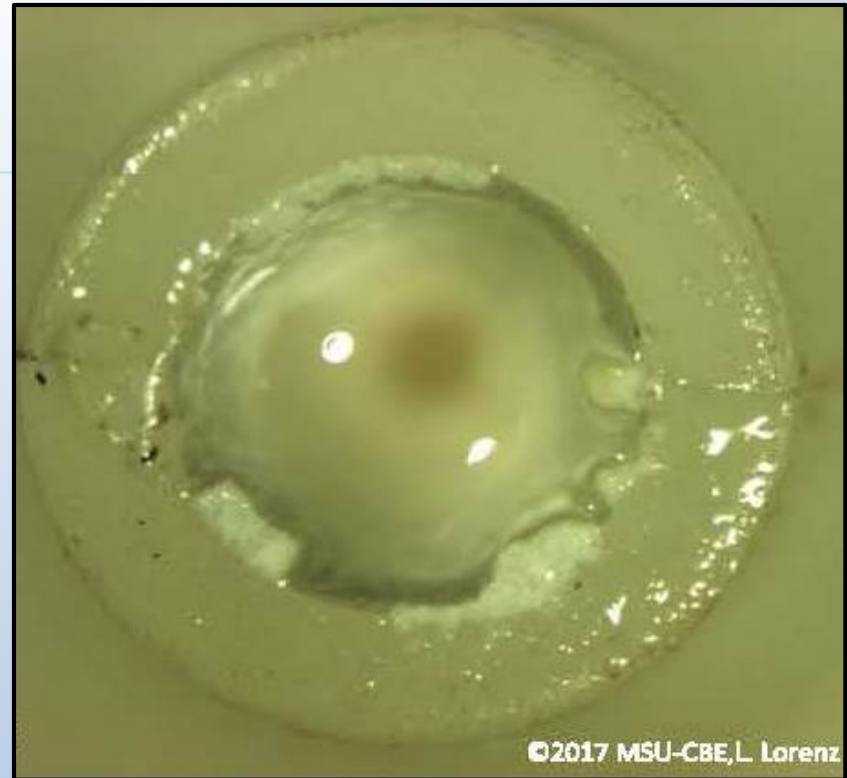
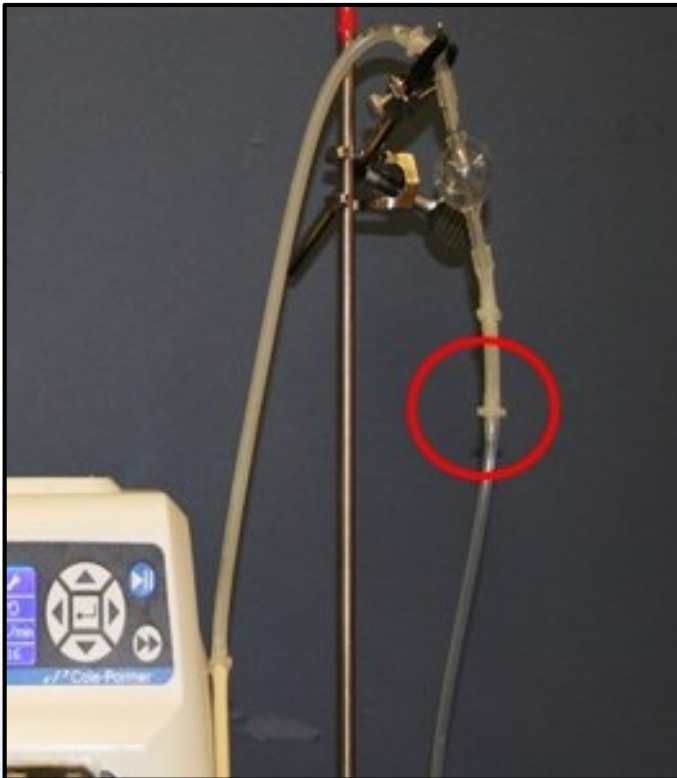
- No standard for ruggedness has been set
 - +0.30
- Ruggedness Testing
 - Never performed
 - Key for developing a method predictive of clinical outcomes

Changes to SOP

- Scraping vs sonication
 - Improved removal (increased plate counts)
- pH
 - Increased effect with time
 - UPEC: pili expression

Changes to SOP

- Connector may have been a source for bacteria
 - Higher SD in effluent compared to segment data



Conclusions

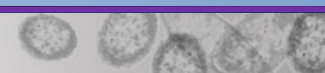
- Validated an Intraluminal Catheter Model (ICM)
- Increase ICM ruggedness
 - Optimization of AUM (pH)
 - Change biofilm harvesting
- Future
 - Test other relevant uropathogens
 - Develop and validate an extraluminal model

Reproducibility of antimicrobial test methods





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Patient Catheter

