Microbiology of Healthcare-associated Infections

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Goals

- Microorganisms causing healthcare-associated infections
- Microbiological tools that can be used to “fingerprint” microorganisms

Properties of Microorganisms

	Size	Growth on Non-Living Media	DNA and RNA	Sensitivity to Antibiotics
Mycotic Agents				
Yeasts	3-15 μm	+	+	+
Molds	2-20 μm	+	+	+
Bacteria	1-5 μm	+	+	+
Mycoplasma	0.1-0.25μm	+	+	+
Rickettsiae	0.3-0.7μm	-	+	+
Chlamydiae	0.1-1.5μm	-	+	+
Viruses	20-300nm	-	-	-

Sources of Healthcare-Associated Pathogens

Weinstein RA. Am J Med 1991:91 (suppl 3B):179S

- Endogenous flora (SSI, UTI, CLABSI): 40-60%
- Exogenous: 20-40% (e.g., cross-infection via contaminated hands [staff, visitors])
- Other (environment): 20%
  - Medical devices/inanimate objects
  - Contact with environmental surfaces (direct and indirect)

Nosocomial Infections

Chain of Infection

- Agent
- Mode of transmission
  - Contact (direct, indirect, droplet spread)
  - Airborne
  - Common-vehicle spread
- Host

Mechanisms of Transmission

- Airborne-true airborne phase in route of dissemination
- Contact-victim has contact with source
  - Direct: Person-to-person (physical contact)
  - Indirect: Person-to-object-to-person (contact with contaminated intermediate object)
  - Droplet: <3 feet (brief passage of infection agent through the air)
- Common-vehicle: Food, water, medical devices (contaminated inanimate vehicles serves as vector of agent to multiple persons)
- Vector-borne

HAI PATHOGENS, NHSN, 2011-2014

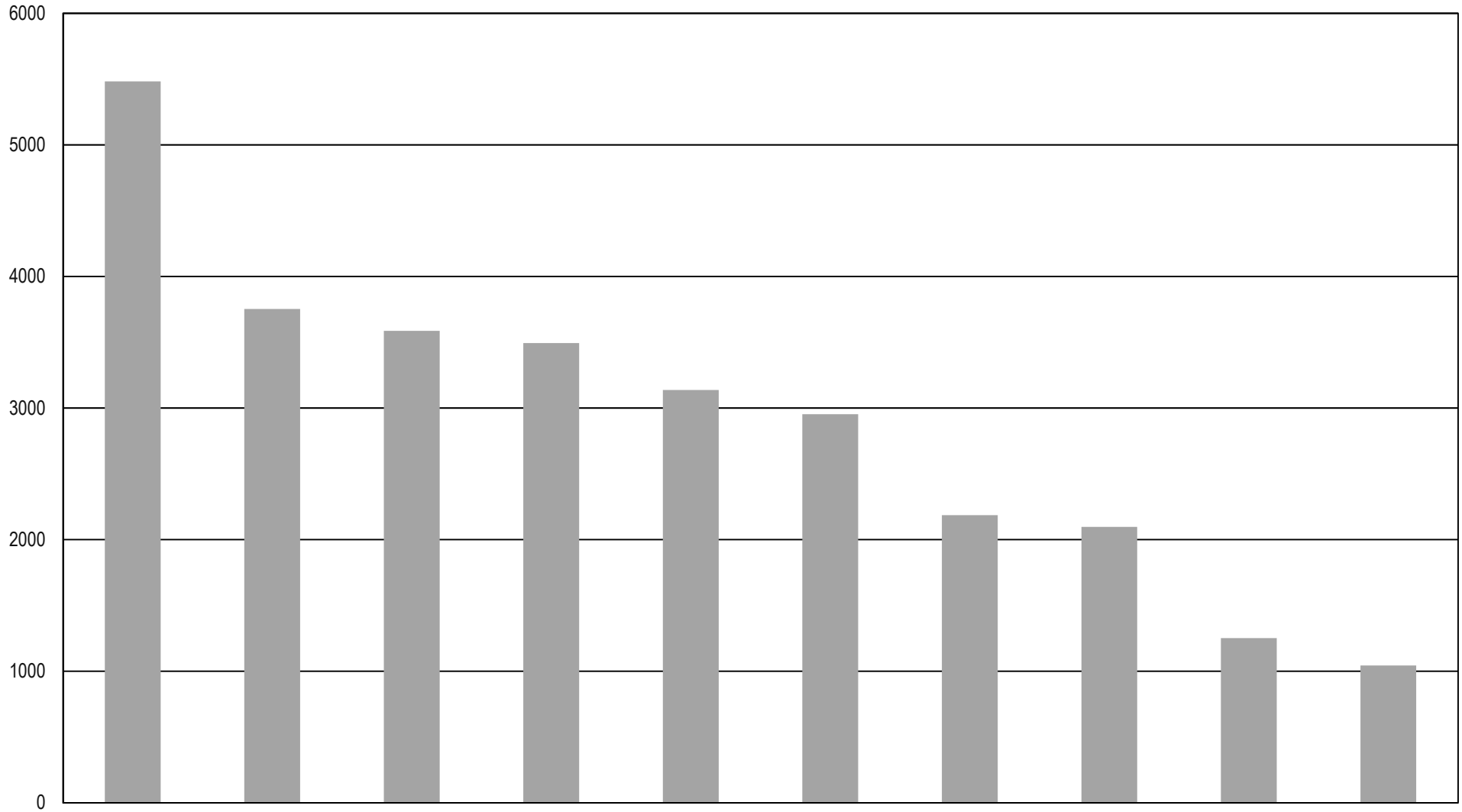
TABLE 4. Distribution and Rank Order of Pathogens Frequently Reported to the National Healthcare Safety Network (NHSN), by Type of Healthcare-Associated Infection (HAI), 2011–2014

	Overall		CLABSI		CAUTI		VAP[a]		SSI	
Pathogen	No. (%) of pathogens	Rank[b]	No. (%) of pathogens	Rank[b]	No. (%) of pathogens	Rank[b]	No. (%) of pathogens	Rank[b]	No. (%) of pathogens	Rank[b]
Escherichia coli	62,904 (15.4)	1	5,193 (5.4)	7	36,806 (23.9)	1	476 (5.4)	6	20,429 (13.7)	2
Staphylococcus aureus	48,302 (11.8)	2	12,706 (13.2)	2	2,515 (1.6)	14	2,179 (24.7)	1	30,902 (20.7)	1
Klebsiella (pneumoniae/oxytoca)	31,498 (7.7)	3	8,062 (8.4)	4	15,471 (10.1)	4	898 (10.2)	3	7,067 (4.7)	6
Coagulase-negative staphylococci[c]	31,361 (7.7)	4	15,794 (16.4)	1	3,696 (2.4)	13	72 (0.8)	13	11,799 (7.9)	3
Enterococcus faecalis[d]	30,034 (7.4)	5	8,118 (8.4)	3	10,728 (7.0)	5	32 (0.4)	21	11,156 (7.5)	4
Pseudomonas aeruginosa	29,636 (7.3)	6	3,881 (4.0)	10	15,848 (10.3)	3	1,449 (16.5)	2	8,458 (5.7)	5
Candida albicans[d]	27,231 (6.7)	7	5,761 (6.0)	6	17,926 (11.7)	2	193 (2.2)	10	3,351 (2.2)	12
Enterobacter spp[c]	17,235 (4.2)	8	4,204 (4.4)	9	5,689 (3.7)	9	727 (8.3)	4	6,615 (4.4)	8
Enterococcus faecium[d]	14,942 (3.7)	9	6,567 (6.8)	5	4,212 (2.7)	11	23 (0.3)	24	4,140 (2.8)	11
Other *Enterococcus* spp.[d]	14,694 (3.6)	10	1,974 (2.0)	14	6,291 (4.1)	7	19 (0.2)	27	6,410 (4.3)	9
Proteus spp.[c]	11,249 (2.8)	11	820 (0.8)	17	6,108 (4.0)	8	125 (1.4)	12	4,196 (2.8)	10
Yeast NOS[e]	10,811 (2.6)	12	763 (0.8)	18	9,443 (6.1)	6	54 (0.6)	16	551 (0.4)	25
Other *Candida* spp.[d]	10,641 (2.6)	13	4,730 (4.9)	8	5,178 (3.4)	10	37 (0.4)	19	696 (0.5)	19
Candida glabrata[d]	8,121 (2.0)	14	3,314 (3.4)	11	4,121 (2.7)	12	12 (0.1)	33	674 (0.5)	20
Bacteroides spp.	7,560 (1.9)	15	515 (0.5)	19	2 (<0.1)	130	2 (<0.1)	72	7,041 (4.7)	7
Other pathogen	51,932 (12.7)		14,130 (14.6)		9,771 (6.4)		2,507 (28.5)		25,524 (17.1)	
Total	408,151 (100)		96,532 (100)		153,805 (100)		8,805 (100)		149,009 (100)	

%MRSA by site: CLABSI, 50.7% (2014); VAP, 42.4% (2012); SSI, 42.6% (2014); CAUTI, 52.0% (2014)

Weiner LM, et al. ICHE 2016;37:1288-1301

Top Ten Pathogens Causing Healthcare-Associated Infections, UNC Hospitals (1980-2008)



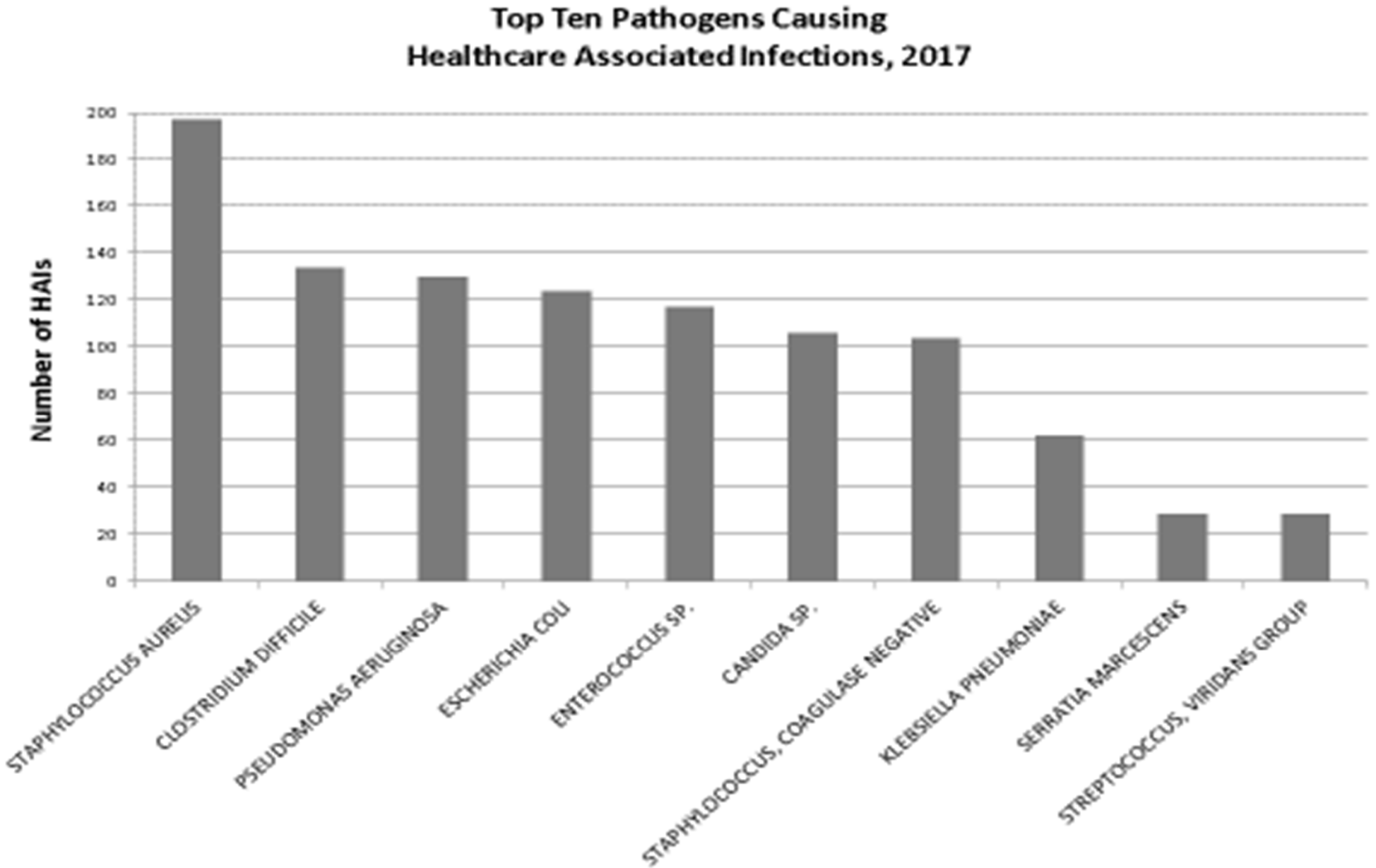
Relative Frequency of HA Pathogens, 1980-2008

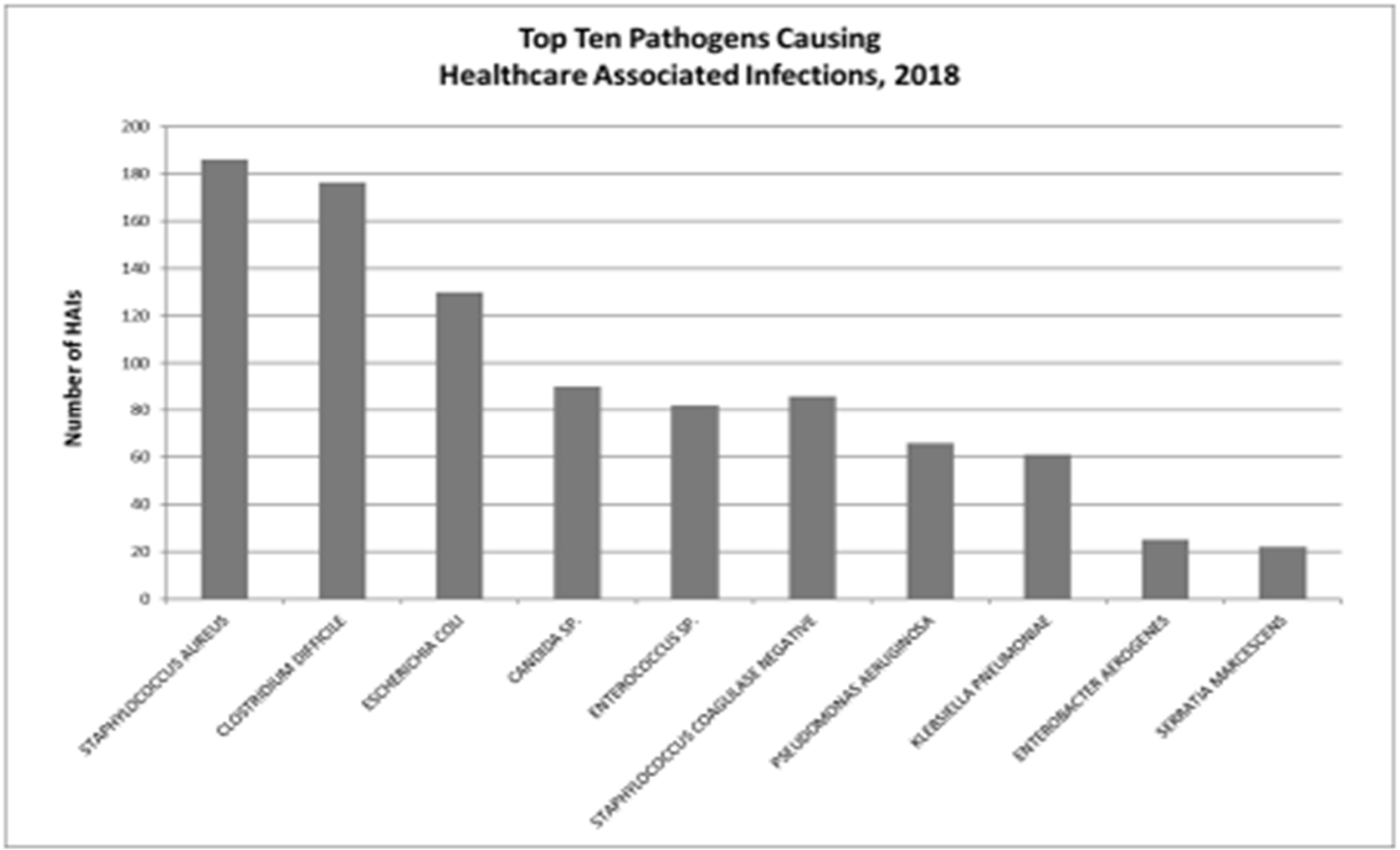
Kang, Sickbert-Bennett, Brown, Weber, Rutala. AJIC, 2012

Table 1

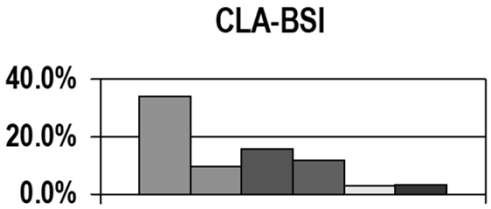
Changes in relative frequency of health care-associated pathogens by time blocks from 1980 to 2008

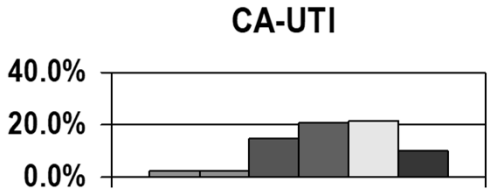
	Total (1980-2008)			Percent of each time blocks						Trend analysis	
Organism	Rank	No.	%	1980-1984	1985-1989	1990-1994	1995-1999	2000-2004	2005-2008	% Change	*P* value
Staphylococcus aureus	1	5,483	15.4	11.8	11.2	16.0	18.2	17.3	15.5	5.3	<.0001
Escherichia coli	2	3,753	10.6	12.6	12.7	11.3	9.2	8.2	11.5	−3.1	<.0001
Coagulase negative staphylococci	3	3,587	10.1	6.9	7.6	8.1	12.7	13.2	9.2	4.8	<.0001
Candida and other yeasts	4	3,494	9.8	7.7	10.4	11.0	10.3	11.1	8.1	3.0	.1890
Enterococcus spp	5	3,138	8.8	8.1	5.8	8.0	8.8	10.2	10.7	3.8	<.0001
Pseudomonas aeruginosa	6	2,954	8.3	9.5	9.5	9.7	8.6	6.7	7.1	−3.1	<.0001
Klebsiella spp	7	2,186	6.2	7.3	7.7	5.9	6.3	4.9	5.7	−2.4	<.0001
Enterobacter spp	8	2,097	5.9	7.2	8.2	6.3	4.8	4.7	5.7	−2.7	<.0001
Other streptococci	9	1,252	3.5	5.0	4.1	2.8	3.6	3.1	2.9	−1.8	<.0001
Clostridium difficile and other anaerobes	10	1,044	2.9	3.3	3.2	2.9	1.5	1.9	5.5	0.8	.0025
Proteus spp	11	946	2.7	5.4	3.9	2.1	1.6	1.9	2.1	−1.8	<.0001
Serratia spp	12	802	2.3	3.8	2.5	2.1	1.8	2.1	1.7	0.8	<.0001
Acinetobacter spp	13	593	1.7	1.2	1.4	2.2	1.4	2.1	1.6	−1.5	.0163
Haemophilus spp	14	494	1.4	1.6	2.5	2.2	1.1	0.9	0.8	−2.0	<.0001
Bacteroides spp	15	349	1.0	2.6	1.6	1.0	0.3	0.4	0.7	−0.8	<.0001
Citrobacter spp	16	325	0.9	1.1	1.1	0.9	0.8	0.9	0.8	0.5	.0488
Group B streptococci	17	324	0.9	1.4	1.3	1.1	0.5	0.6	0.9	−0.3	<.0001
Other	18	2,689	7.6	3.5	5.2	6.2	8.5	10.0	9.5	6.7	<.0001
Total (n)		35,510		5,217	4,336	4,904	6,964	7,999	6,090		

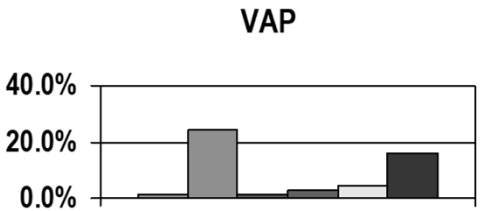

Top Ten Pathogens Causing
Healthcare Associated Infections, 2017
Number of HAIs
200
180
160
140
120
100
80
60
40
20
0
STAPHYLOCOCCUS AUREUS
CLOSTRIDIUM DIFFICILE
PSEUDOMONAS AERUGINOSA
ESCHERICHIA COLI
ENTEROCOCCUS SP.
CANDIDA SP.
STAPHYLOCOCCUS, COAGULASE NEGATIVE
KLEBSIELLA PNEUMONIAE
SERRATIA MARCESCENS
STREPTOCOCCUS, VIRIDANS GROUP

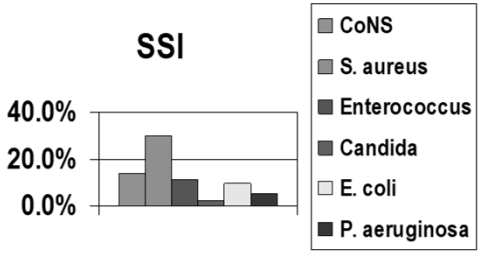

Top Ten Pathogens Causing
Healthcare Associated Infections, 2018
Number of HAIs
200
180
160
140
120
100
80
60
40
20
0
STAPHYLOCOCCUS AUREUS
CLOSTRIDIUM DIFFICILE
ESCHERICHIA COLI
CANDIDA SP.
ENTEROCOCCUS SP.
STAPHYLOCOCCUS COAGULASE NEGATIVE
PSEUDOMONAS AERUGINOSA
KLEBSIELLA PNEUMONIAE
ENTEROBACTER AEROGENES
SERRATIA MARCESCENS

PATHOGENS CAUSING HAIs, NHSN, 2006-2007

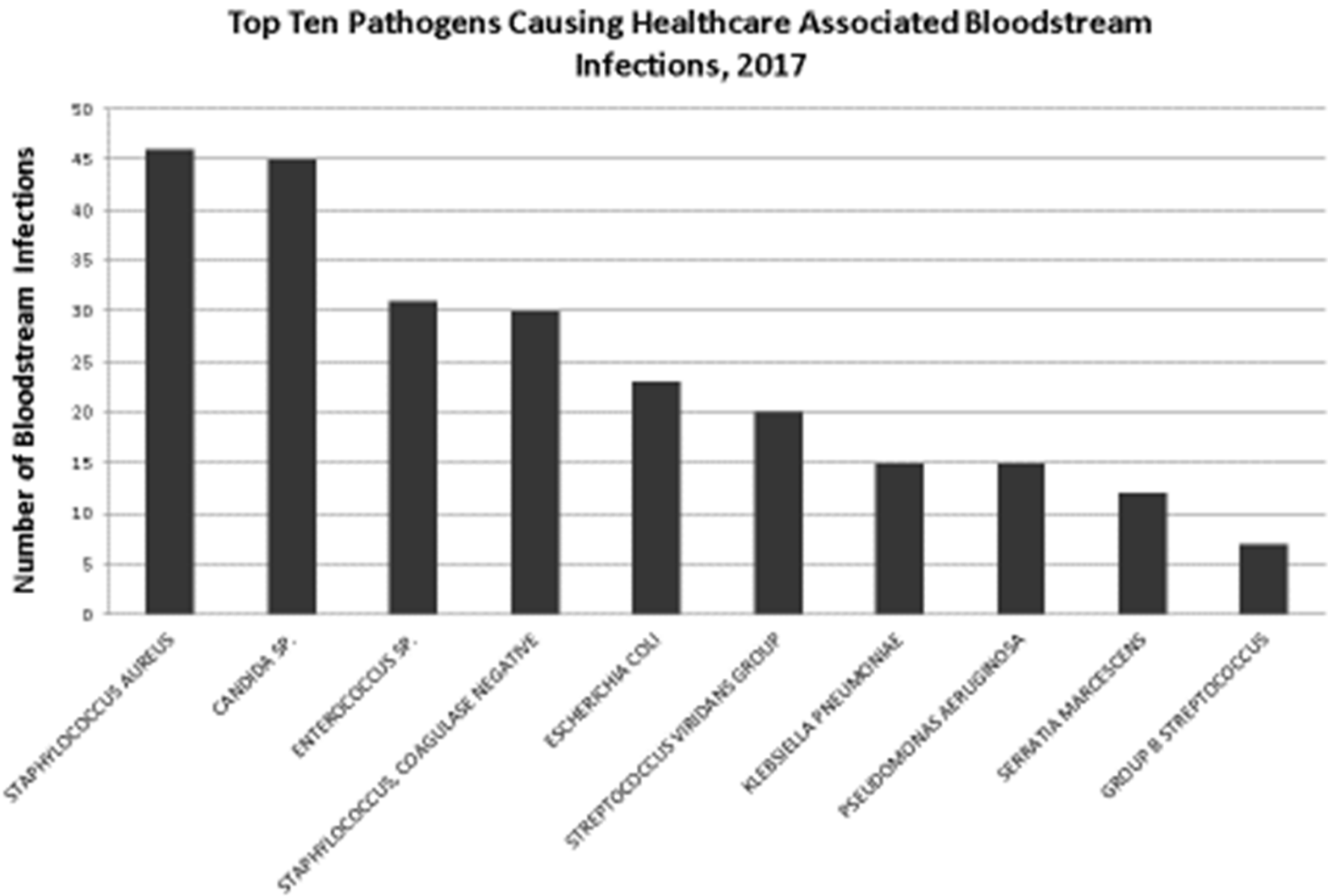


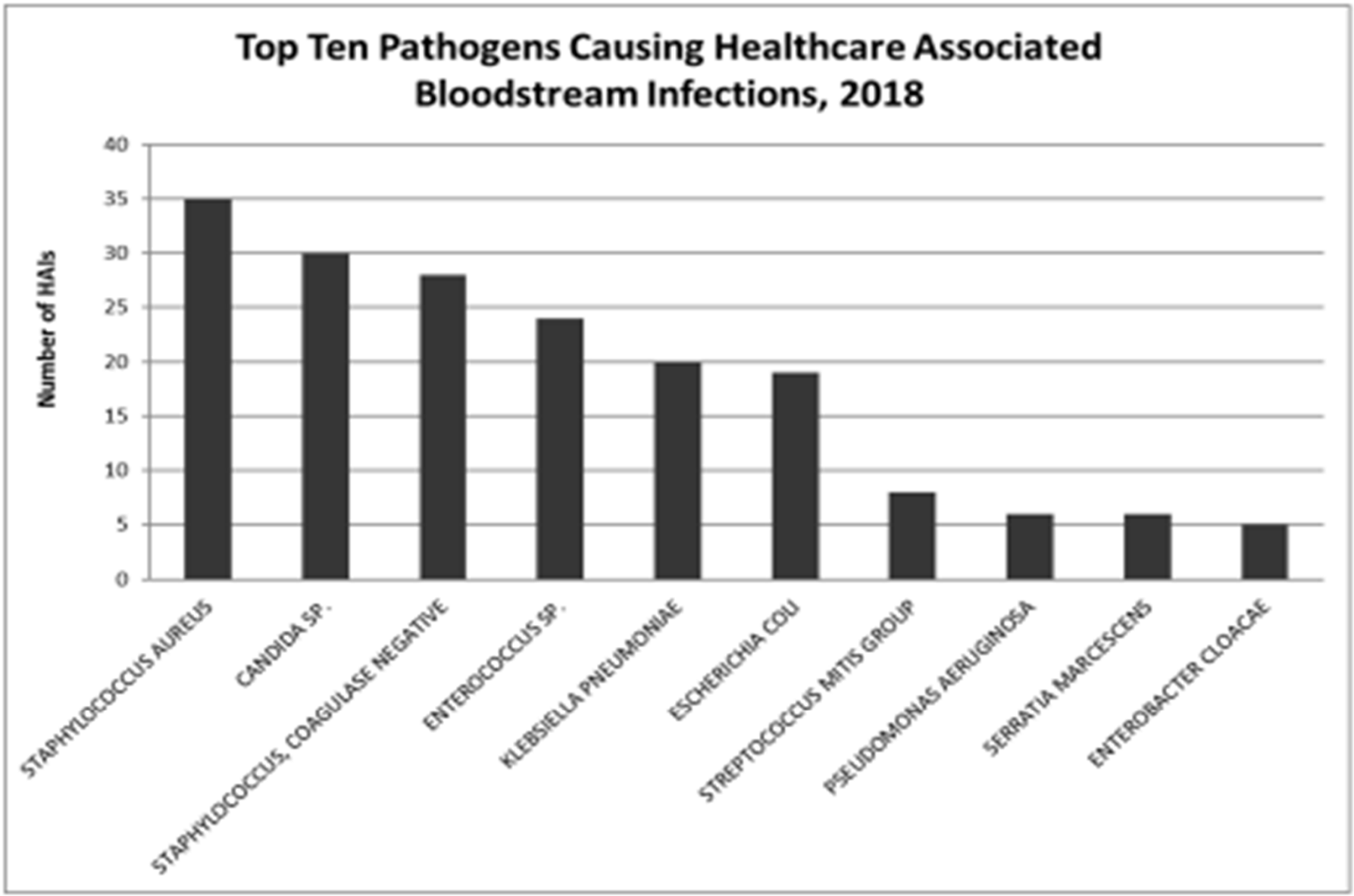


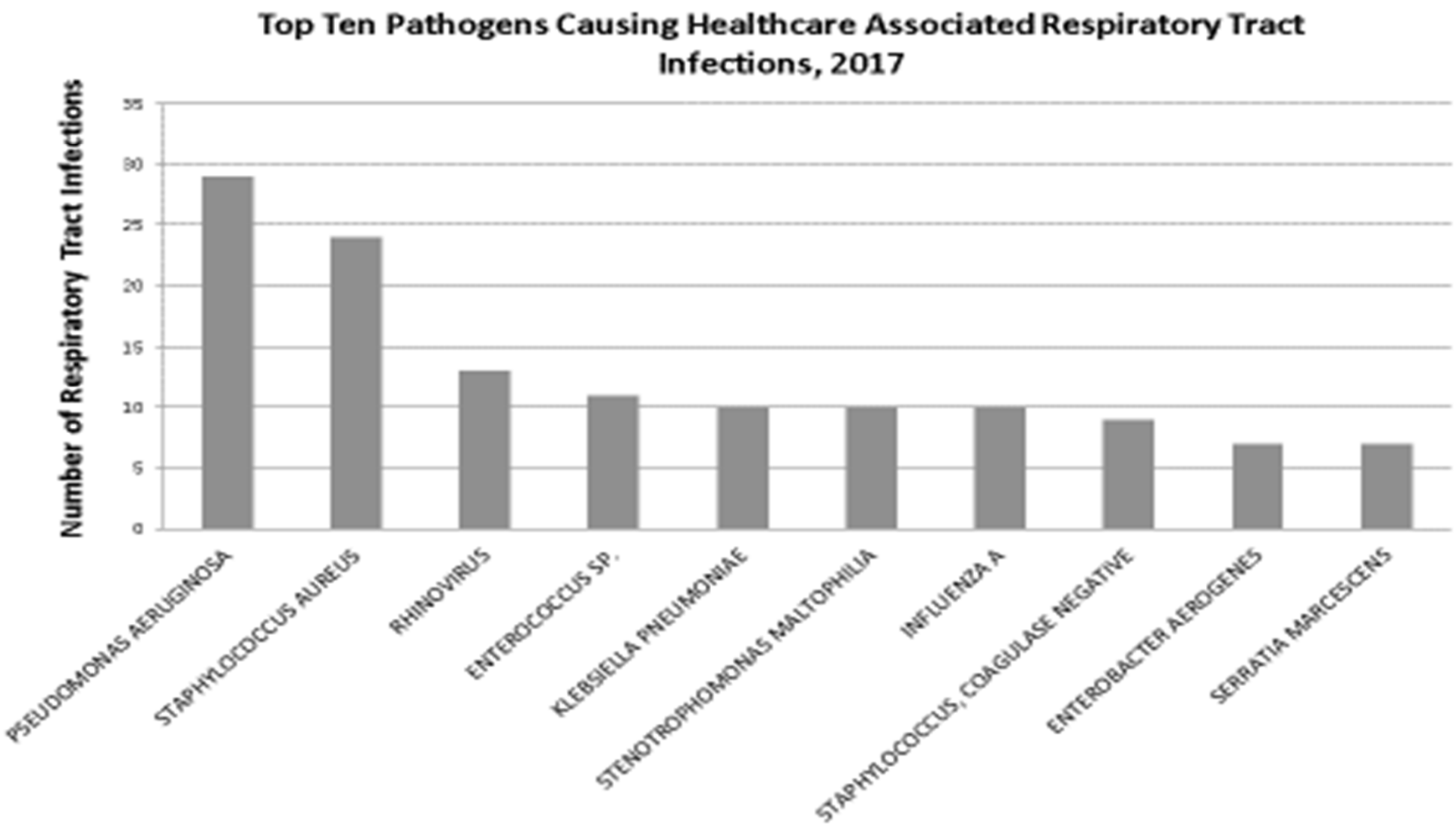


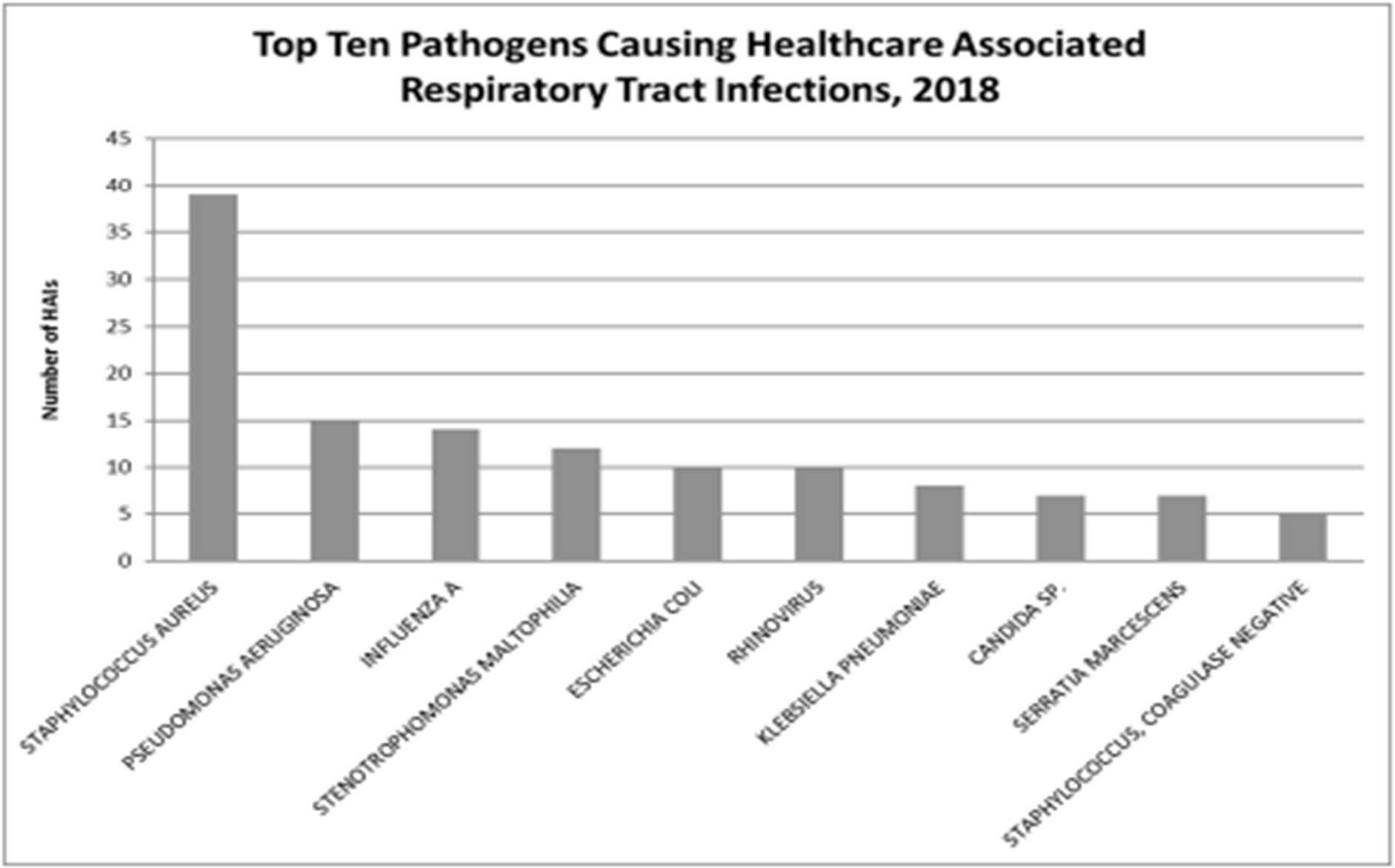


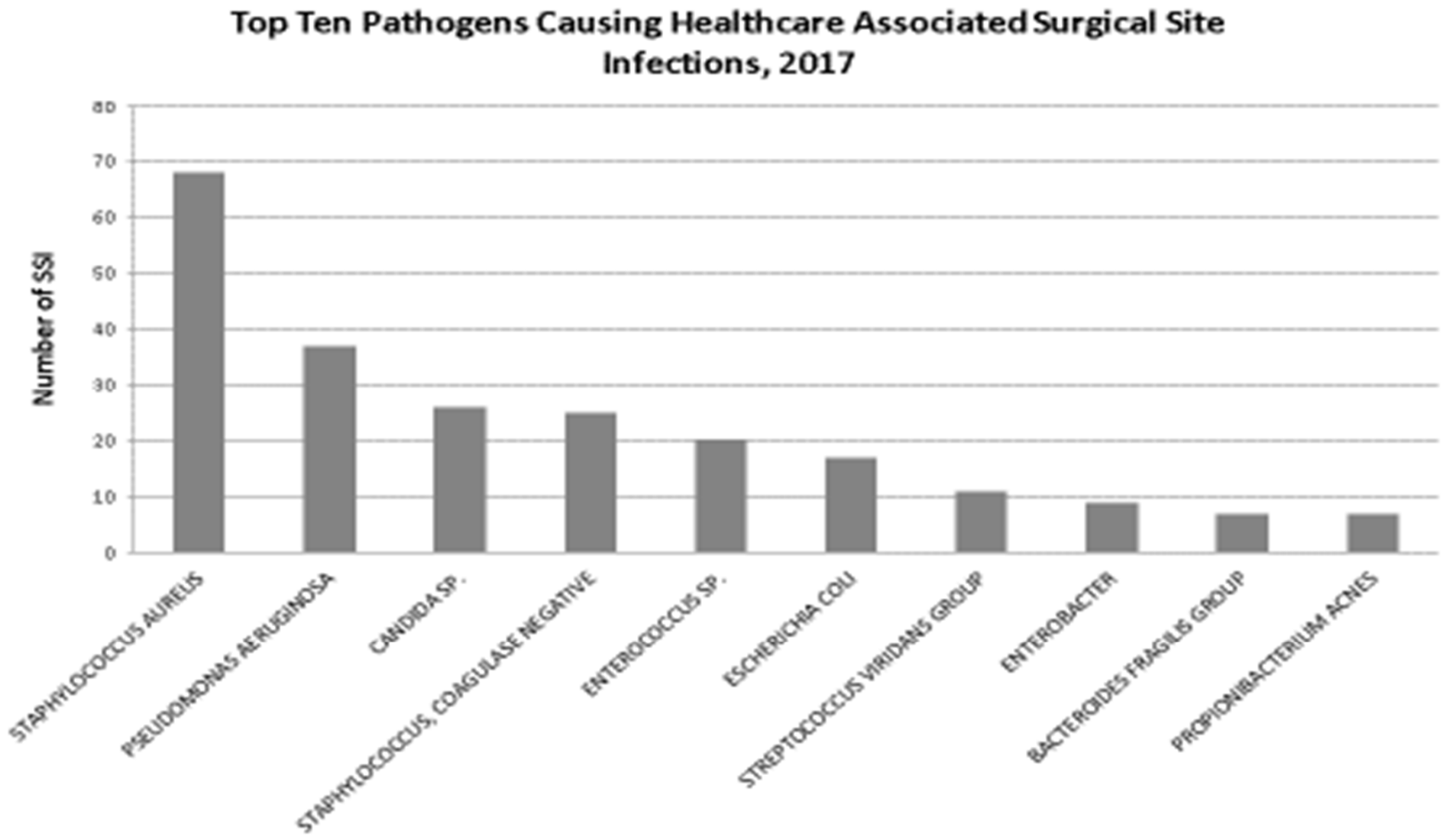
Hidron AI, et al. ICHE 2008;29:996-1011

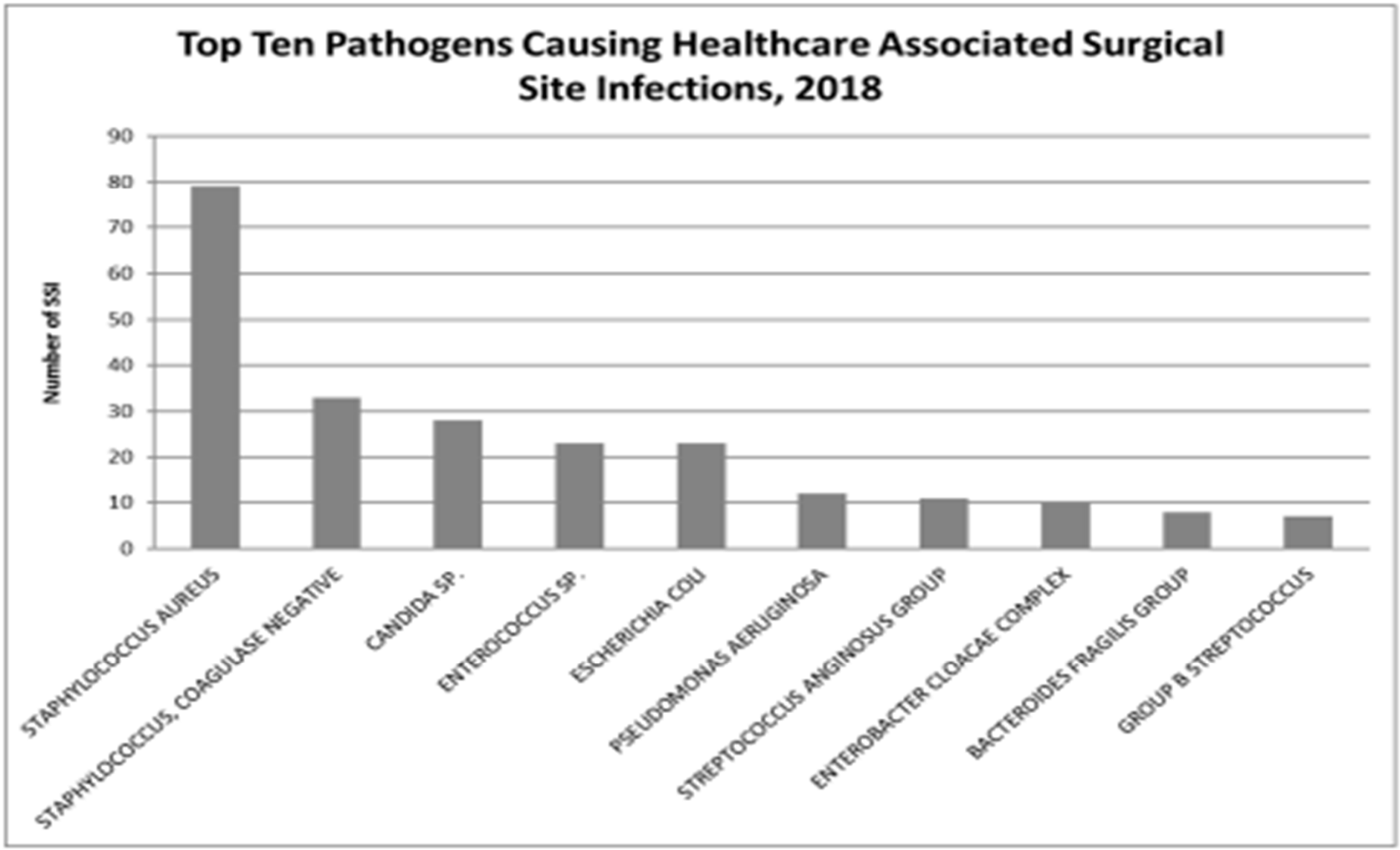

Top Ten Pathogens Causing Healthcare Associated Bloodstream Infections, 2017
Number of Bloodstream Infections
50
45
40
35
30
25
20
15
10
5
0
STAPHYLOCOCCUS AUREUS
CANDIDA SP.
ENTEROCOCCUS SP.
STAPHYLOCOCCUS, COAGULASE NEGATIVE
ESCHERICHIA COLI
STREPTOCOCCUS VIRIDANS GROUP
KLEBSIELLA PNEUMONIAE
PSEUDOMONAS AERUGINOSA
SERRATIA MARCESCENS
GROUP B STREPTOCOCCUS

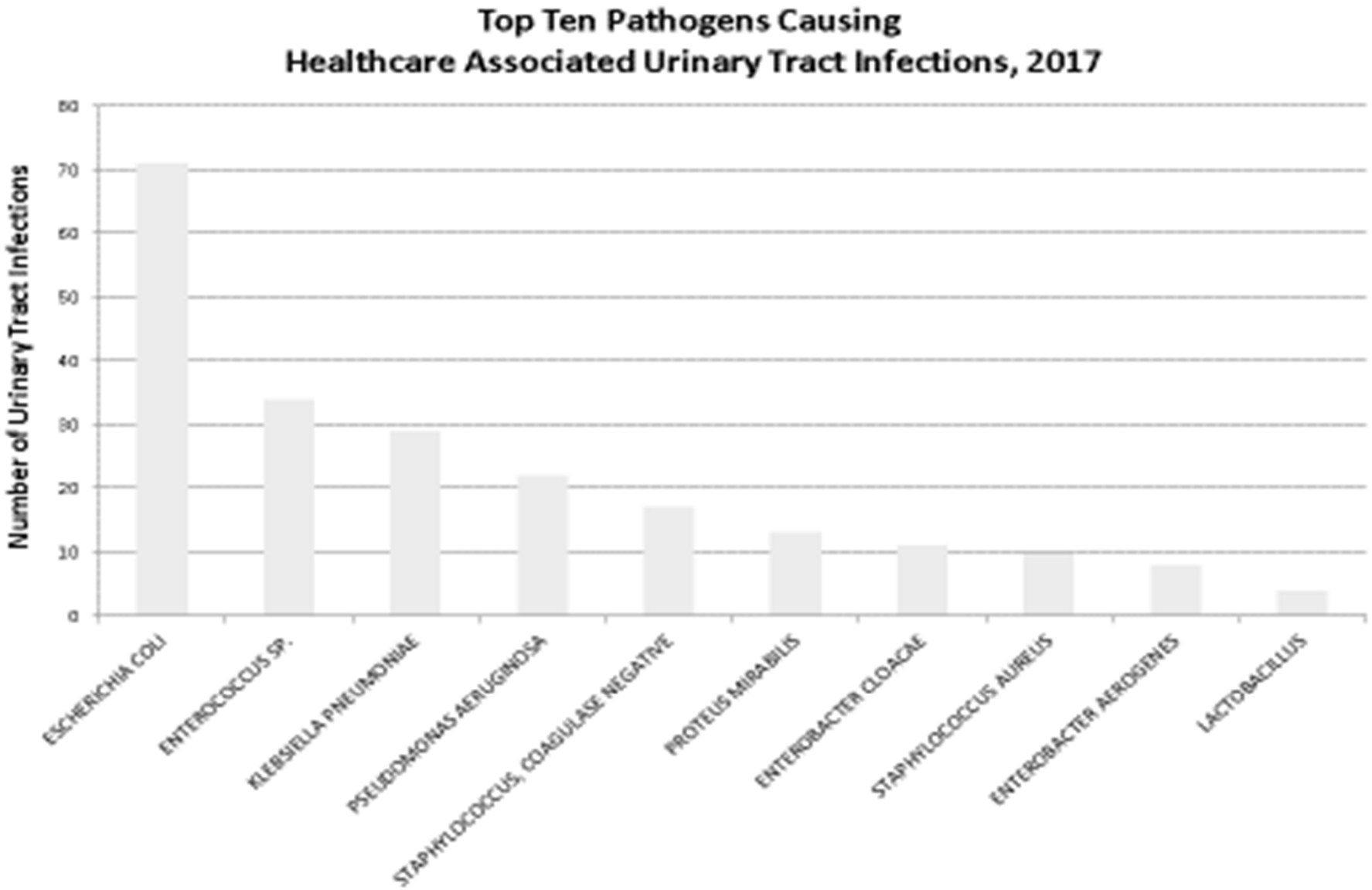

Top Ten Pathogens Causing Healthcare Associated Bloodstream Infections, 2018
Number of HAIs
40
35
30
25
20
15
10
5
0
STAPHYLOCOCCUS AUREUS
CANDIDA SP.
STAPHYLOCOCCUS, COAGULASE NEGATIVE
ENTEROCOCCUS SP.
KLEBSIELLA PNEUMONIAE
ESCHERICHIA COLI
STREPTOCOCCUS MITIS GROUP
PSEUDOMONAS AERUGINOSA
SERRATIA MARCESCENS
ENTEROBACTER CLOACAE

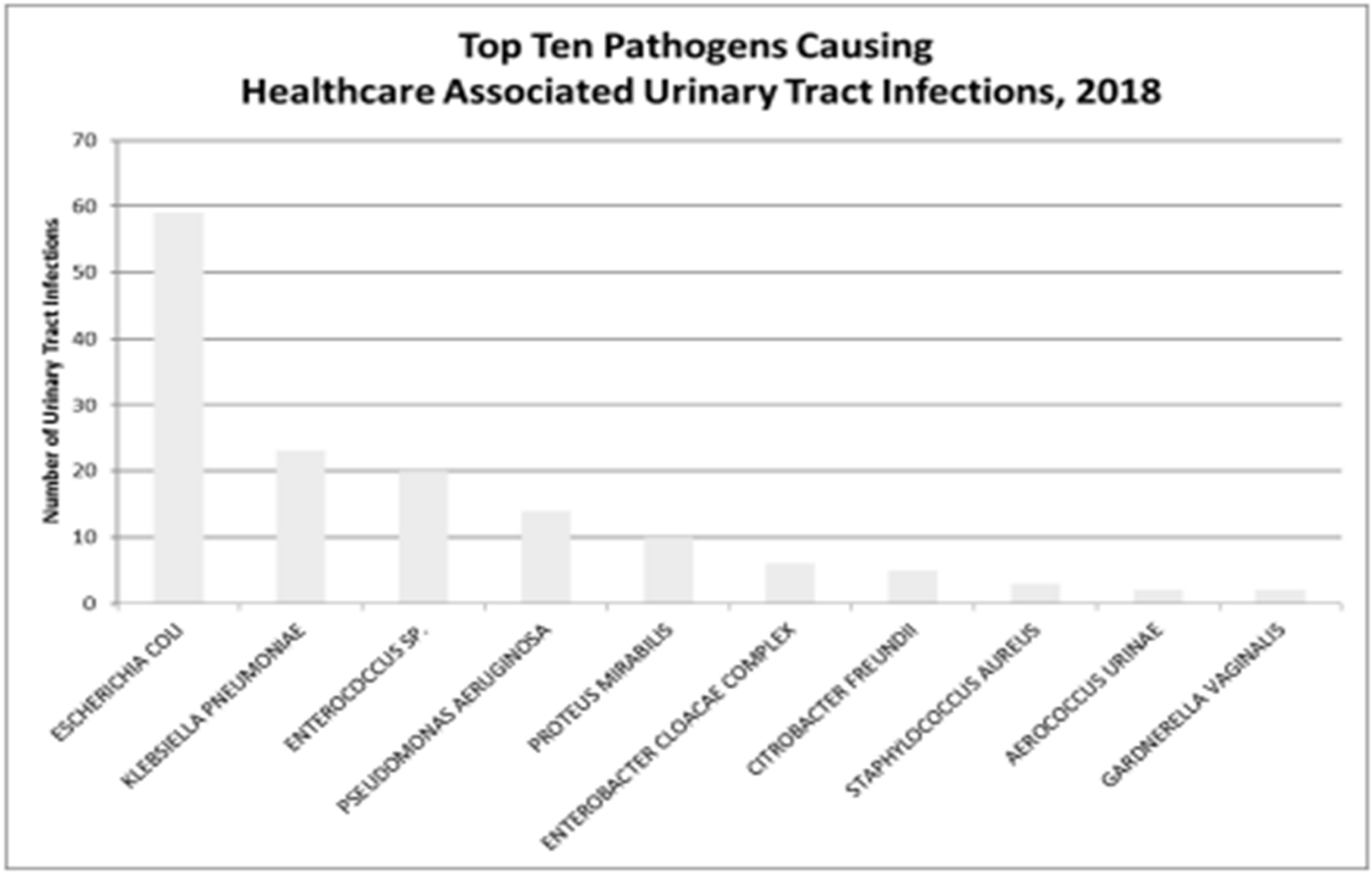

Top Ten Pathogens Causing Healthcare Associated Respiratory Tract Infections, 2017
Number of Respiratory Tract Infections
0
5
10
15
20
25
30
35
PSEUDOMONAS AERUGINOSA
STAPHYLOCOCCUS AUREUS
RHINOVIRUS
ENTEROCOCCUS SP.
KLEBSIELLA PNEUMONIAE
STENOTROPHOMONAS MALTOPHILIA
INFLUENZA A
STAPHYLOCOCCUS, COAGULASE NEGATIVE
ENTEROBACTER AEROGENES
SERRATIA MARCESCENS

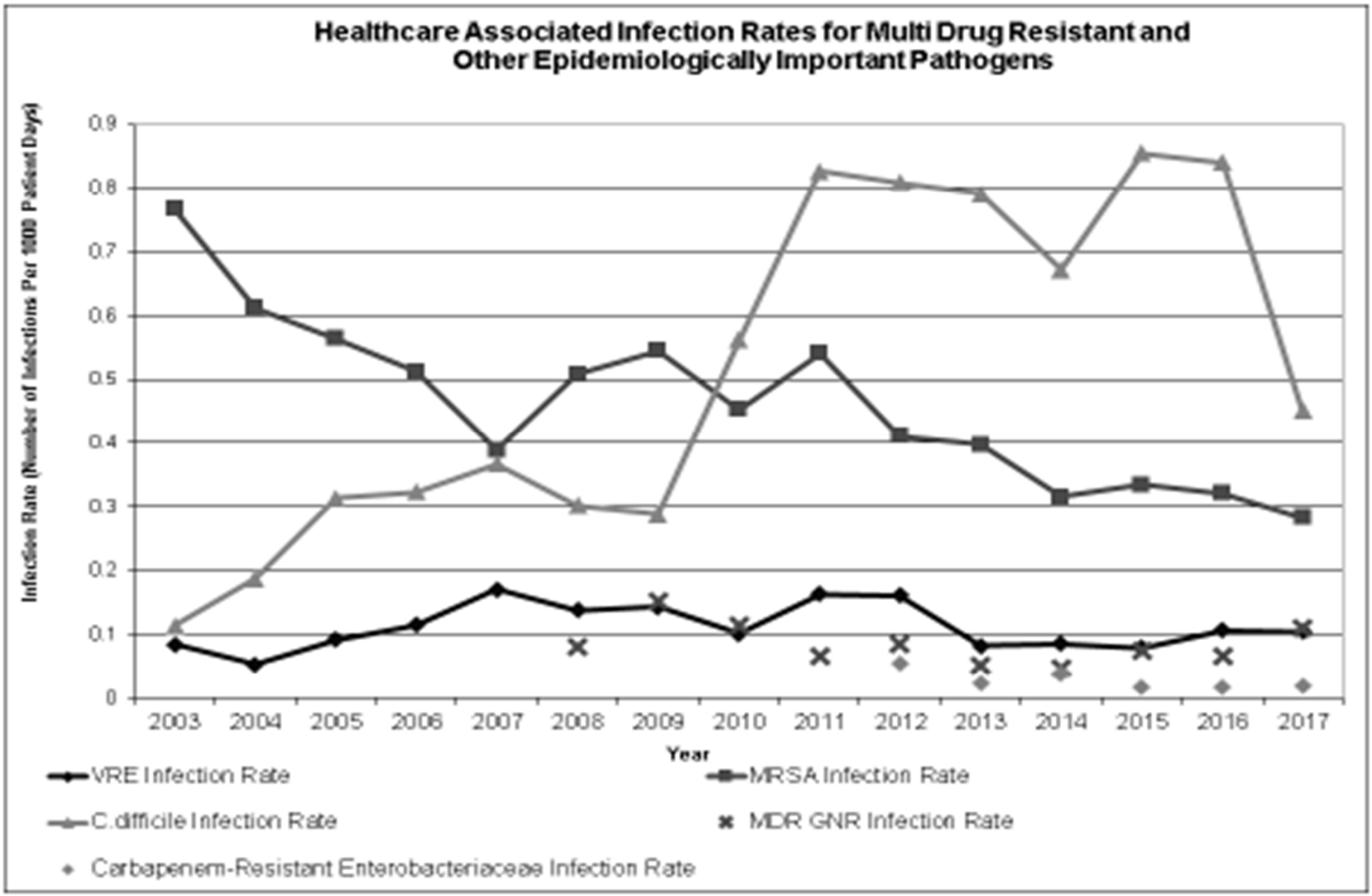

Top Ten Pathogens Causing Healthcare Associated Respiratory Tract Infections, 2018
Number of HAIs
45
40
35
30
25
20
15
10
5
0
STAPHYLOCOCCUS AUREUS
PSEUDOMONAS AERUGINOSA
INFLUENZA A
STENOTROPHOMONAS MALTOPHILIA
ESCHERICHIA COLI
RHINOVIRUS
KLEBSIELLA PNEUMONIAE
CANDIDA SP.
SERRATIA MARCESCENS
STAPHYLOCOCCUS, COAGULASE NEGATIVE

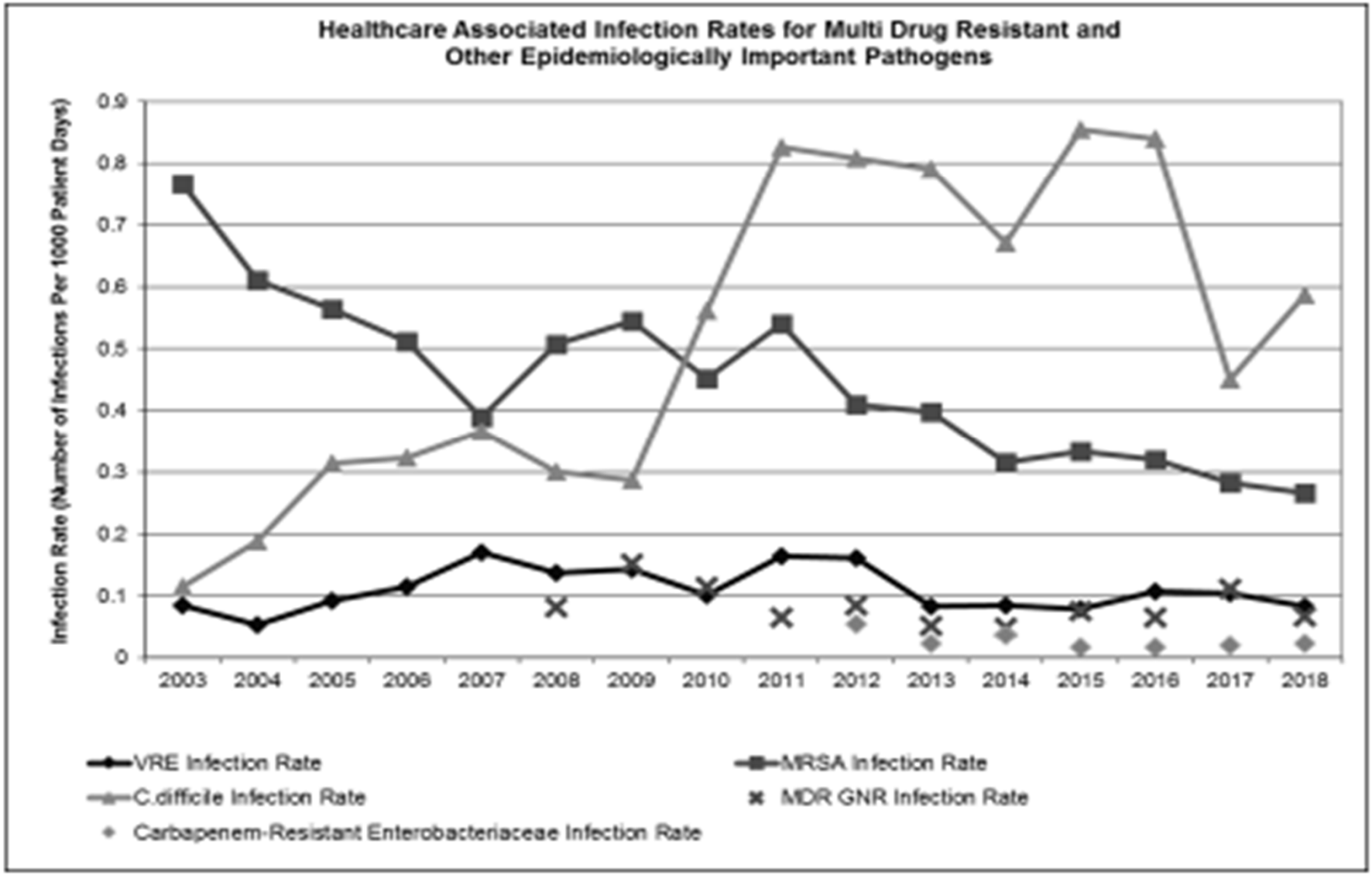

Top Ten Pathogens Causing Healthcare Associated Surgical Site Infections, 2017
Number of SSI
80
70
60
50
40
30
20
10
0
STAPHYLOCOCCUS AURELIS
PSEUDOMONAS AERUGINOSA
CANDIDA SP.
STAPHYLOCOCCUS, COAGULASE NEGATIVE
ENTEROCOCCUS SP.
ESCHERICHIA COLI
STREPTOCOCCUS VIRIDANS GROUP
ENTEROBACTER
BACTEROIDES FRAGILIS GROUP
PROPIONIBACTERIUM ACNES


Top Ten Pathogens Causing Healthcare Associated Surgical Site Infections, 2018
Number of SSI
90
80
70
60
50
40
30
20
10
0
STAPHYLOCOCCUS AUREUS
STAPHYLOCOCCUS, COAGULASE NEGATIVE
CANDIDA SP.
ENTEROCOCCUS SP.
ESCHERICHIA COLI
PSEUDOMONAS AERUGINOSA
STREPTOCOCCUS ANGINOSUS GROUP
ENTEROBACTER CLOACAE COMPLEX
BACTEROIDES FRAGILIS GROUP
GROUP B STREPTOCOCCUS


Top Ten Pathogens Causing
Healthcare Associated Urinary Tract Infections, 2017
Number of Urinary Tract Infections
80
70
60
50
40
30
20
10
0
ESCHERICHIA COLI
ENTEROCOCCUS SP.
KLEBSIELLA PNEUMONIAE
PSEUDOMONAS AERUGINOSA
STAPHYLOCOCCUS, COAGULASE NEGATIVE
PROTEUS MIRABILIS
ENTEROBACTER CLOACAE
STAPHYLOCOCCUS AUREUS
ENTEROBACTER AEROGENES
LACTOBACILLUS


Top Ten Pathogens Causing
Healthcare Associated Urinary Tract Infections, 2018
Number of Urinary Tract Infections
70
60
50
40
30
20
10
0
ESCHERICHIA COLI
KLEBSIELLA PNEUMONIAE
ENTEROCOCCUS SP.
PSEUDOMONAS AERUGINOSA
PROTEUS MIRABILIS
ENTEROBACTER CLOACAE COMPLEX
CITROBACTER FREUNDII
STAPHYLOCOCCUS AUREUS
AEROCOCCUS URINAE
GARDNERELLA VAGINALIS


Healthcare Associated Infection Rates for Multi Drug Resistant and Other Epidemiologically Important Pathogens
Infection Rate (Number of Infections Per 1000 Patient Days)
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Year
VRE Infection Rate
MRSA Infection Rate
C.difficile Infection Rate
MDR GNR Infection Rate
Carbapenem-Resistant Enterobacteriaceae Infection Rate


Healthcare Associated Infection Rates for Multi Drug Resistant and Other Epidemiologically Important Pathogens
Infection Rate (Number of Infections Per 1000 Patient Days)
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
VRE Infection Rate
MRSA Infection Rate
C.difficile Infection Rate
MDR GNR Infection Rate
Carbapenem-Resistant Enterobacteriaceae Infection Rate

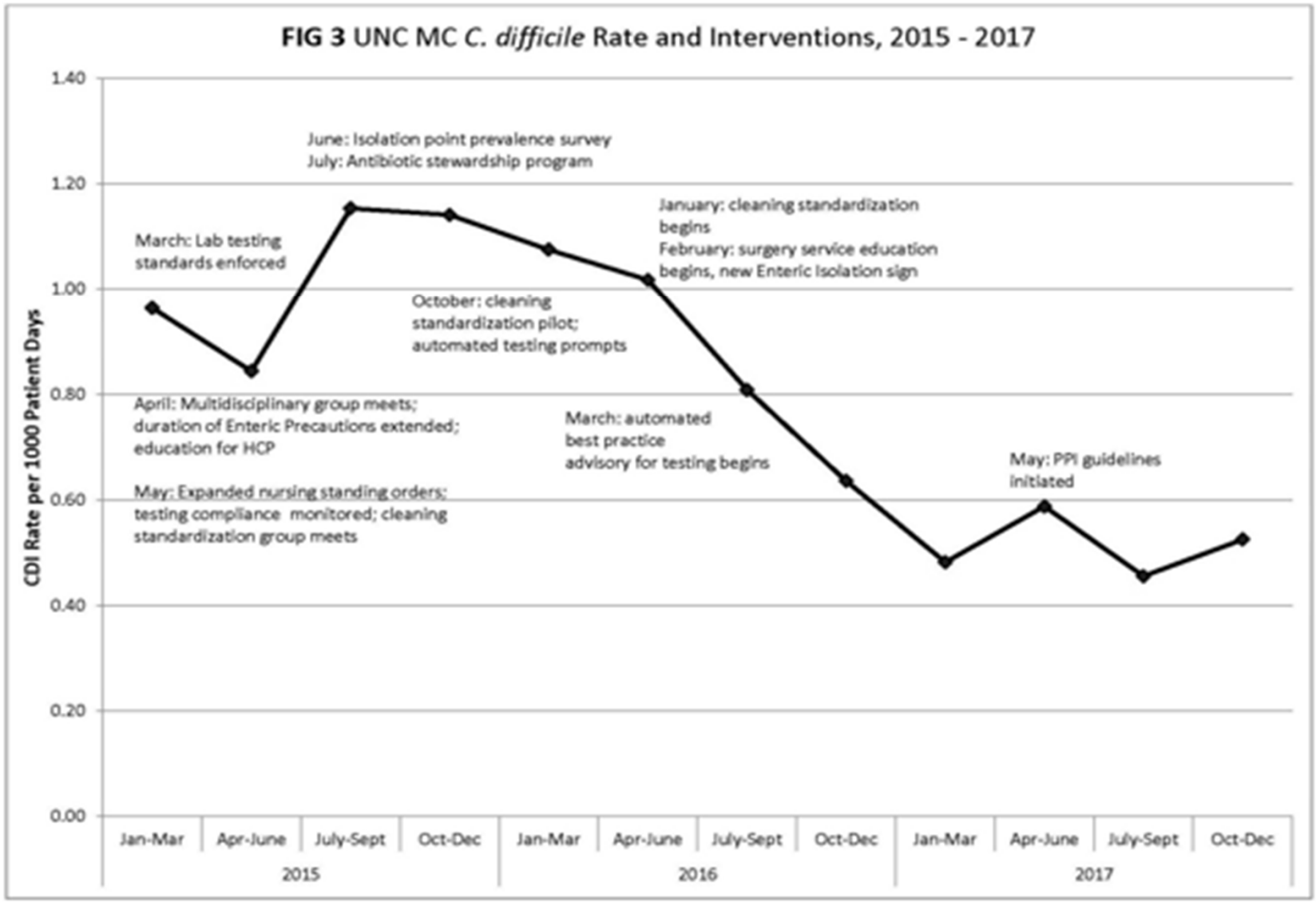


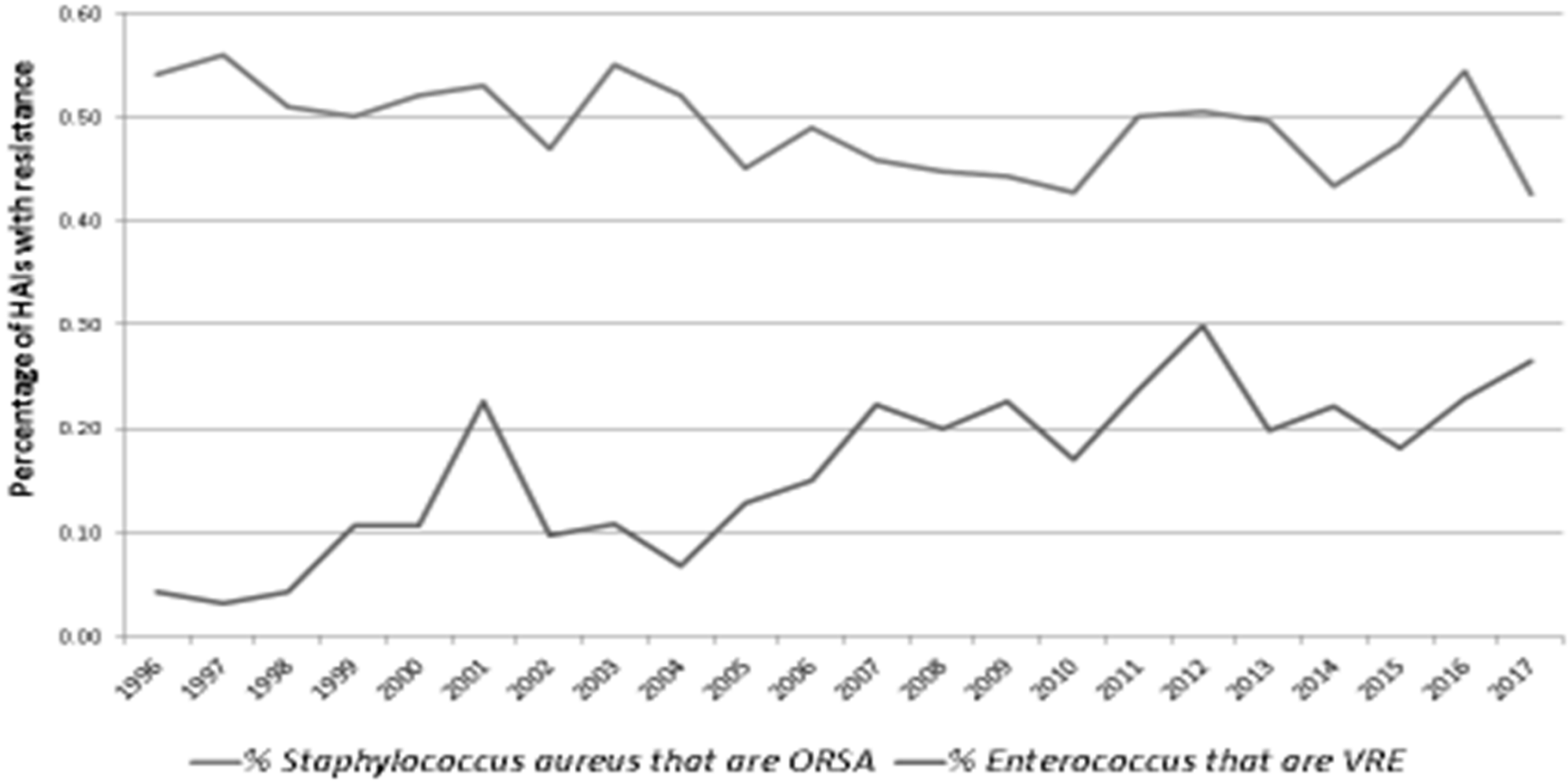
FIG 3 UNC MC C. difficile Rate and Interventions, 2015 - 2017
CDI Rate per 1000 Patient Days
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
March: Lab testing standards enforced
April: Multidisciplinary group meets; duration of Enteric Precautions extended; education for HCP
May: Expanded nursing standing orders; testing compliance monitored; cleaning standardization group meets
June: Isolation point prevalence survey
July: Antibiotic stewardship program
October: cleaning standardization pilot; automated testing prompts
January: cleaning standardization begins
February: surgery service education begins, new Enteric Isolation sign
March: automated best practice advisory for testing begins
May: PPI guidelines initiated
Jan-Mar
Apr-June
July-Sept
Oct-Dec
2015
2016
2017

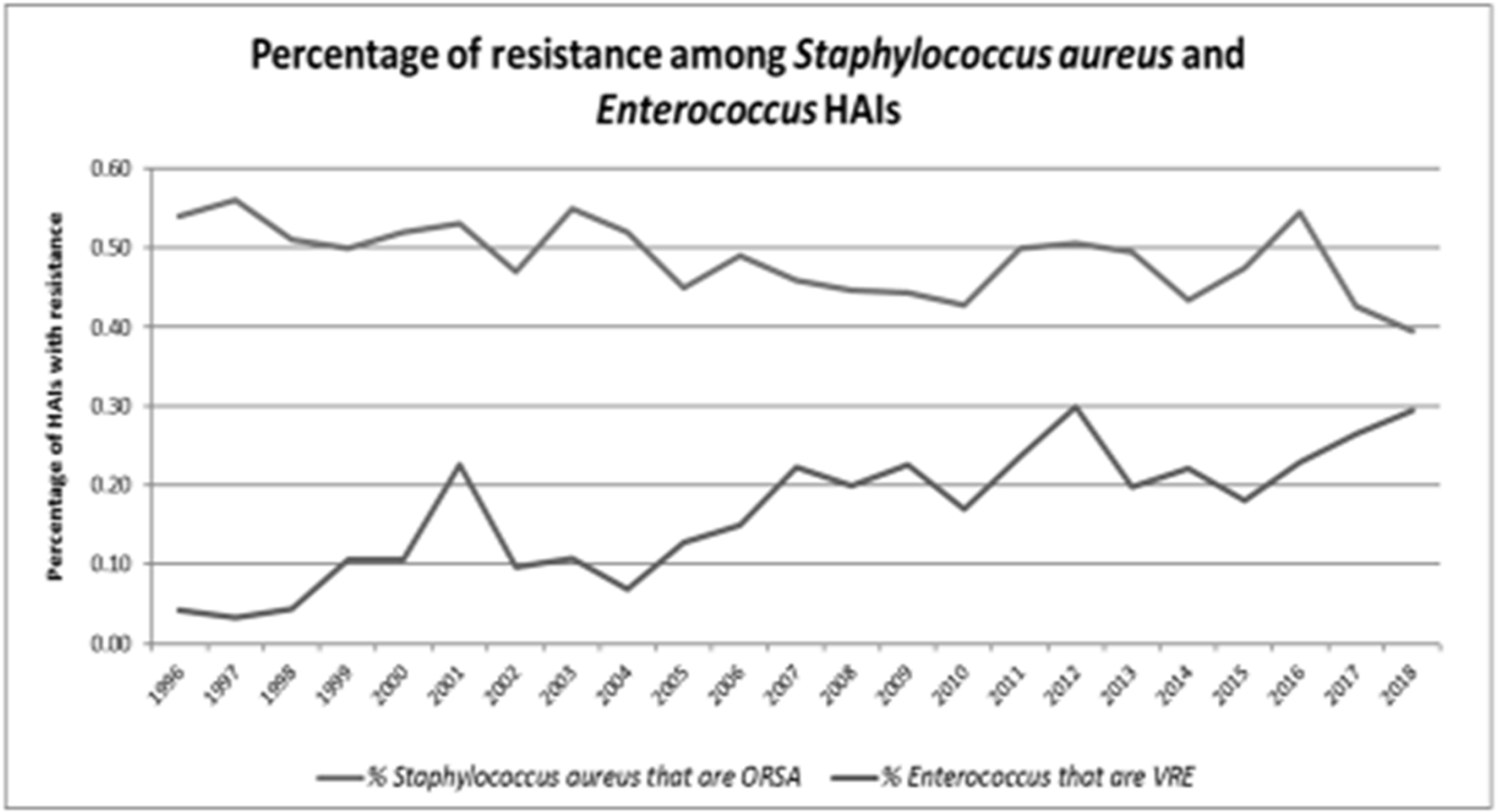
Bundled Approach to Reduce *C. difficile*

(two-step GDH-glutamate dehydrogenase/toxin and NAAT-nucleic acid amplification)

- Diagnostic Stewardship
  - Only unformed liquid stool tested
  - No testing from patients with positive C. difficile test in previous 14 days
  - Testing restricted for patients with negative C. difficile in previous 7 days
  - Discouraged testing patients who received laxatives and/or stool softeners in previous 48 hours
- Enhanced Isolation-to 30 days after cessation of antibiotics
- Environmental C/D-standardized plan; UV
- Antimicrobial stewardship-reduce 3rd/4th generation cephalosporins and fluoroquinolones
- Hand Hygiene-clean in, clean out; immediate feedback

Percentage of resistance among *Staphylococcus aureus* and *Enterococcus* HAIs




Percentage of resistance among *Staphylococcus aureus* and *Enterococcus* HAIs
Percentage of HAIs with resistance
0.60
0.50
0.40
0.30
0.20
0.10
0.00
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
% Staphylococcus aureus that are ORSA
% Enterococcus that are VRE

Pathogens of Epidemiologic Importance

- **Carbapenem resistant**
  - 1 of 8 (12%) *Morganella morganii*
  - 3 of 62 (5%) *Klebsiella pneumoniae*
  - 1 of 21 (5%) *Enterobacter aerogenes*
  - 1 of 26 (4%) *Enterobacter cloacae*

- **Multi-drug resistant**
  - 19 of 130 (14.6%) *Pseudomonas aeruginosa*
  - 6 of 124 (5%) *Escherichia coli*
  - 1 of 62 (1.6%) *Klebsiella pneumoniae*
  - 1 of 5 (20%) *Acinetobacter baumannii*

- **Other drug resistant**
  - 31 of 117 (27%) *Enterococcus* were vancomycin resistant
  - 84 of 197 (43%) *Staphylococcus aureus* were oxacillin resistant

2017

Pathogens of Epidemiologic Importance

- **Carbapenem resistant**
  - 4 of 61 (6.5%) *Klebsiella pneumoniae*
  - 2 of 130 (1.5%) *Escherichia coli*

- **Multi-drug resistant**
  - 11 of 66 (17%) *Pseudomonas aeruginosa*
  - 3 of 61 (5%) *Klebsiella pneumoniae*
  - 5 of 130 (4%) *Escherichia coli*
  - 1 of 4 (25%) *Acinetobacter baumannii*

- **Other drug resistant**
  - 25 of 82 (30%) *Enterococcus* were vancomycin resistant
  - 80 of 186 (43%) *Staphylococcus aureus* were oxacillin resistant

2018

Pathogens of Epidemiologic Importance

- **Others**
  - 134 *Clostridium difficile*
  - 16 Group B *streptococcus*
  - 13 Rhinovirus
  - 10 Influenza A
  - 8 Norovirus
  - 7 Parainfluenza virus
  - 6 Coronavirus
  - 6 Respiratory Syncytial Virus
  - 5 *Haemophilus influenzae*
  - 4 *streptococcus pneumoniae*
  - 2 *Mycobacterium abscessus*
  - 2 *rhizopus*
  - 1 *Mycobacterium chelonae*
  - 1 Aspergillus sp.
  - 1 Rotavirus

2017

Pathogens of Epidemiologic Importance

- **Others**
  - 176 *Clostridium difficile*
  - 22 Group B *streptococcus*
  - 14 Influenza A
  - 10 Rhinovirus
  - 5 Respiratory Syncytial Virus
  - 4 *Haemophilus influenzae*
  - 3 Norovirus
  - 3 *streptococcus pneumoniae*
  - 3 Parainfluenza virus
  - 2 *Mycobacterium abscessus*
  - 2 Aspergillus sp.
  - 1 *rhizopus*
  - 1 *Mycobacterium chelonae*
  - *1 Mycobacterium fortuitum*
  - 1 Coronavirus

2018

Conclusions and Recommendations

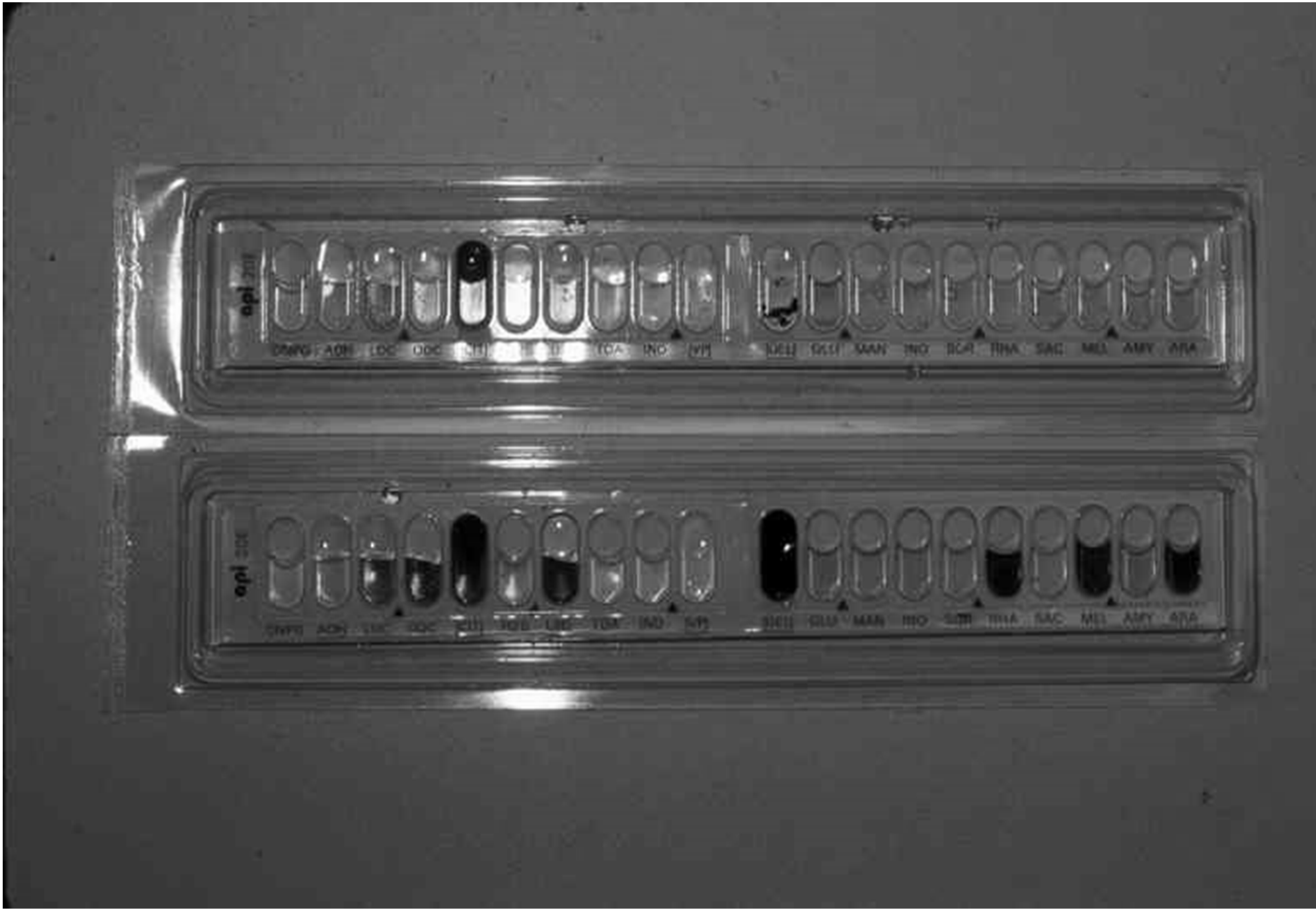
- Nosocomial pathogens recovered at UNC Hospitals are similar in spectrum to nationally reported data.
- The proportion of vancomycin-resistance among *Enterococcus* and the VRE HAI rate slightly increased in 2017 compared to 2016.
- There was a slight decrease in the proportion of oxacillin-resistance among *Staphylococcus aureus* and in the MRSA HAI rate in 2017 compared to 2016.
- HAI rates of MDR Gram negative bacteria and CRE remain low.

Goals

- Microorganisms causing healthcare-associated infections
- Microbiological tools that can be used to “fingerprint” microorganisms

Microbiological Tools That Can Aid an Infection Control Professional

- Biotyping: use of biochemical reactions to differentiate bacteria
- Antibiograms: antimicrobial susceptibility
- Phage Typing: certain bacteria under bacterial phage attachment and subsequent lysis
- Serotyping: whole microorganism or its components can be used as antigenic sources for a variety of serologic schemes
- Molecular Typing: microbial DNA fingerprinting (e.g., PFGE, whole genome sequence analysis)
- MALDI-TOF mass spectrometry for organism ID (peptide map used to search sequence database)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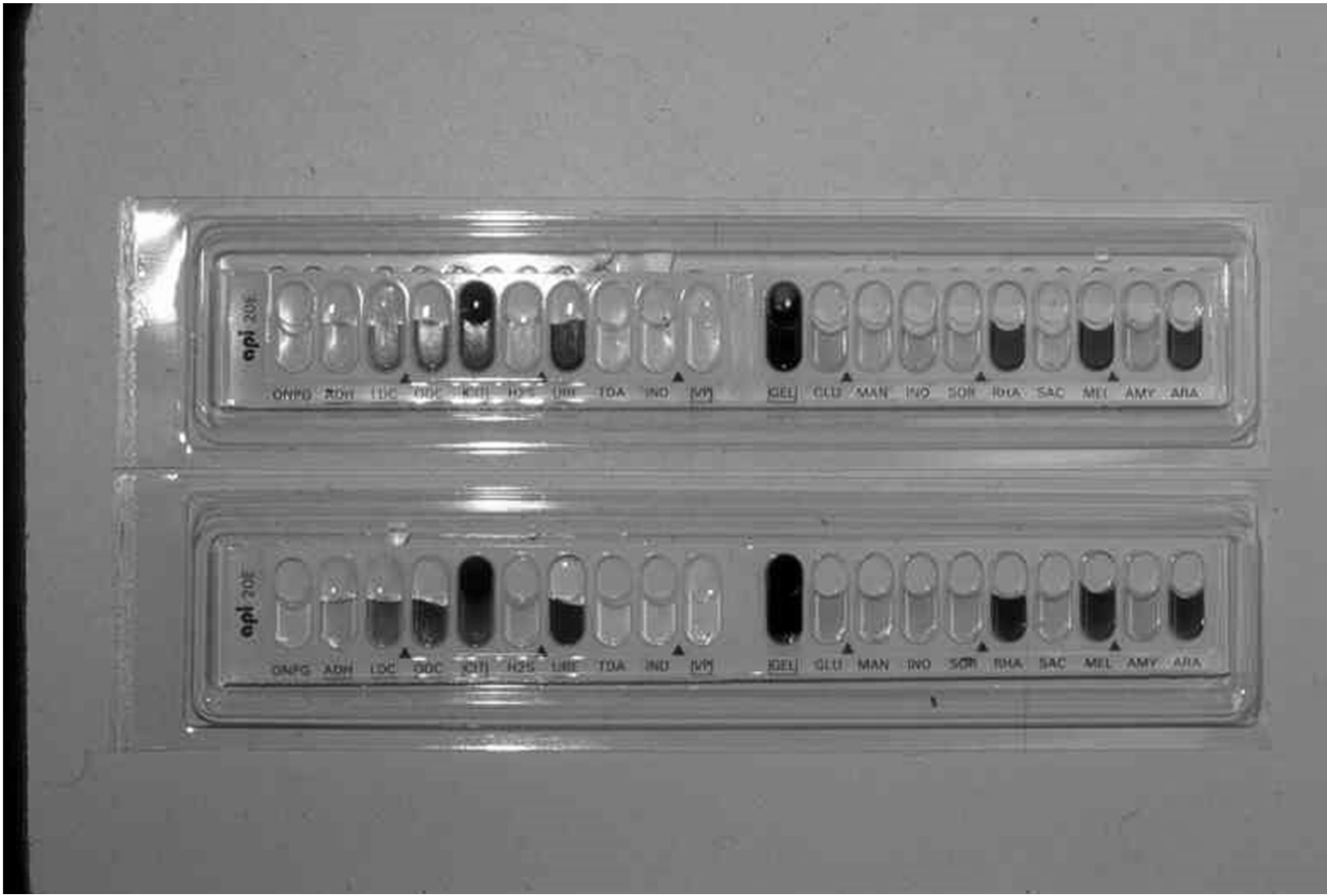
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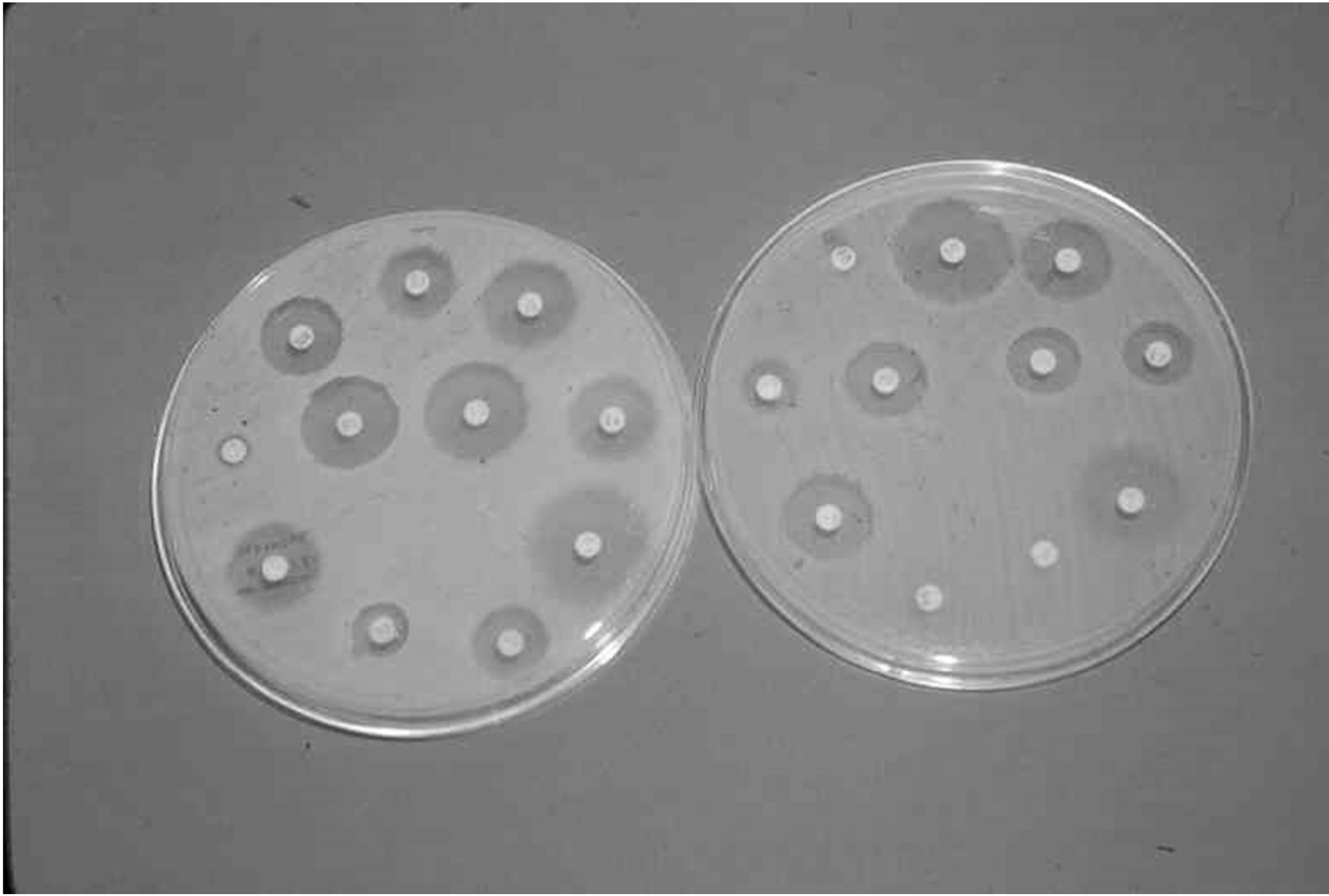

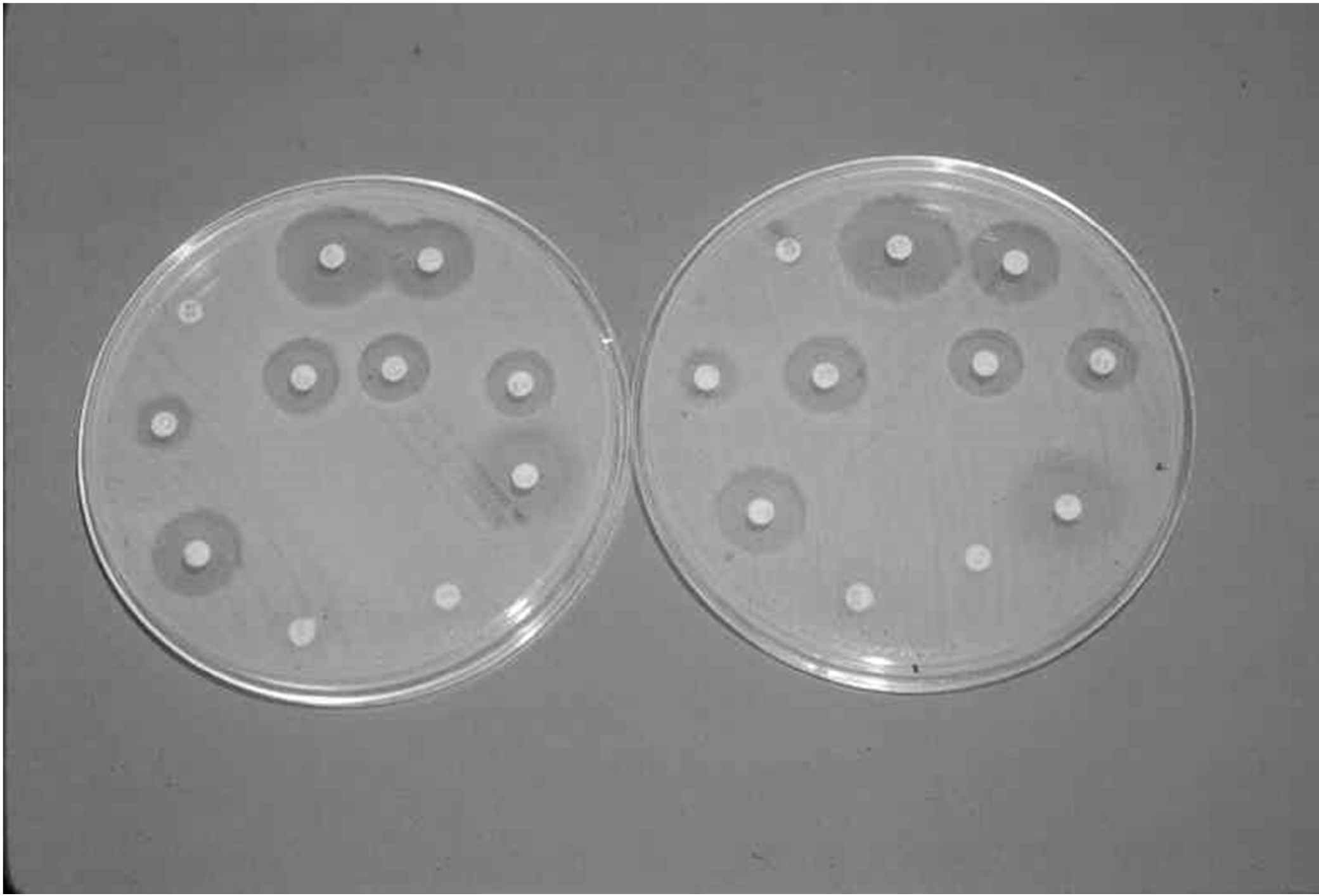


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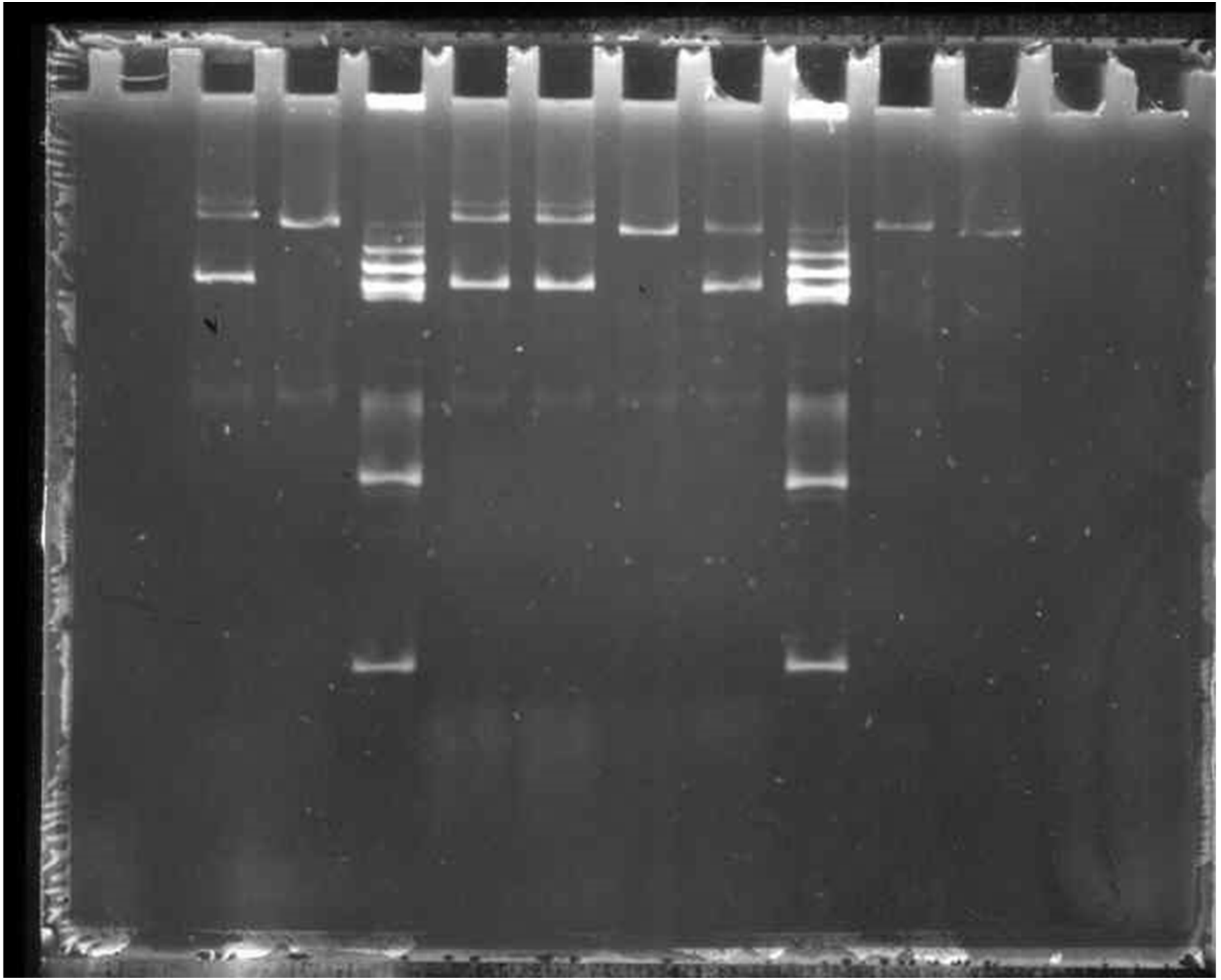


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S. MALTOPHILIA

PCR Tests Done at UNC Health Care

(PCR-multiple copies of segments of DNA used to ID microbes)

- HIV, quantitative
- HCV, quantitative
- HBV, quantitative
- Enterovirus
- HSV 1 and 2
- VZV
- CMV, quantitative and qualitative
- EBV, quantitative
- HHV-6
- BK, quantitative
- Adenovirus
- Parvovirus
- Influenza A/B
- RSV A/B
- Respiratory Viral Panel (12):
  - influenza A (H1, H3)
  - influenza B
  - RSV
  - parainfluenza 1-3
  - Metapneumovirus
  - Adenovirus
  - rhinovirus/enterovirus
- Bordetella *pertussis/parapertussis*
- *Mycobacterium tuberculosis*
- *Chlamydia trachomatis*
- *Neisseria gonorrhoeae*
- *Toxoplasma*