

Outcomes Among Patients with *Staphylococcus aureus* Bacteremia in the Veterans Affairs Healthcare System

Ellyn Ercolano Russo, MS¹, Sara Gale, PhD, MPH², Nicholas Lewin-Koh, MS², Yinong Young-Xu, ScD, MS, MA¹, Daniel Gottlieb, MS¹, Yuliya Halchenko, MA¹, Melicent Peck, MD, PhD²

¹Clinical Epidemiology Program, Veterans Affairs Medical Center, White River Junction, VT; ²Genentech, Inc., South San Francisco, CA

INTRODUCTION

- Staphylococcus aureus* (*S. aureus*) causes approximately 20% of all bloodstream infections in hospitals across the United States, with persistent bacteremia despite appropriate antibiotic therapy occurring in up to 40% of individuals and a 30-day mortality rate after diagnosis of approximately 20% [1-4].
- Despite being a leading cause of bacteremia, there is limited current data about the epidemiology of *S. aureus* bacteremia (SAB).
- The primary purpose of this study is to better understand the demographics, microbiological, and clinical outcomes among a group of patients with SAB.

METHODS

Study design: Retrospective, population-based cohort study.

Data source: Veterans Health Administration electronic medical records available through the Corporate Data Warehouse.

Study population: Inpatient adult Veterans aged 18 years or older with at least one *S. aureus*-positive blood culture (index date) between January 2006 and December 2015 were categorized as having uncomplicated SAB (at least one positive *S. aureus*-positive blood culture), complicated SAB (at least two *S. aureus*-positive blood cultures drawn at least 48 hours apart), or persistent SAB (at least two *S. aureus*-positive blood cultures drawn at least 96 hours apart). Patients with endocarditis were identified by the presence of a primary or secondary ICD-9-CM discharge diagnosis code of 421.

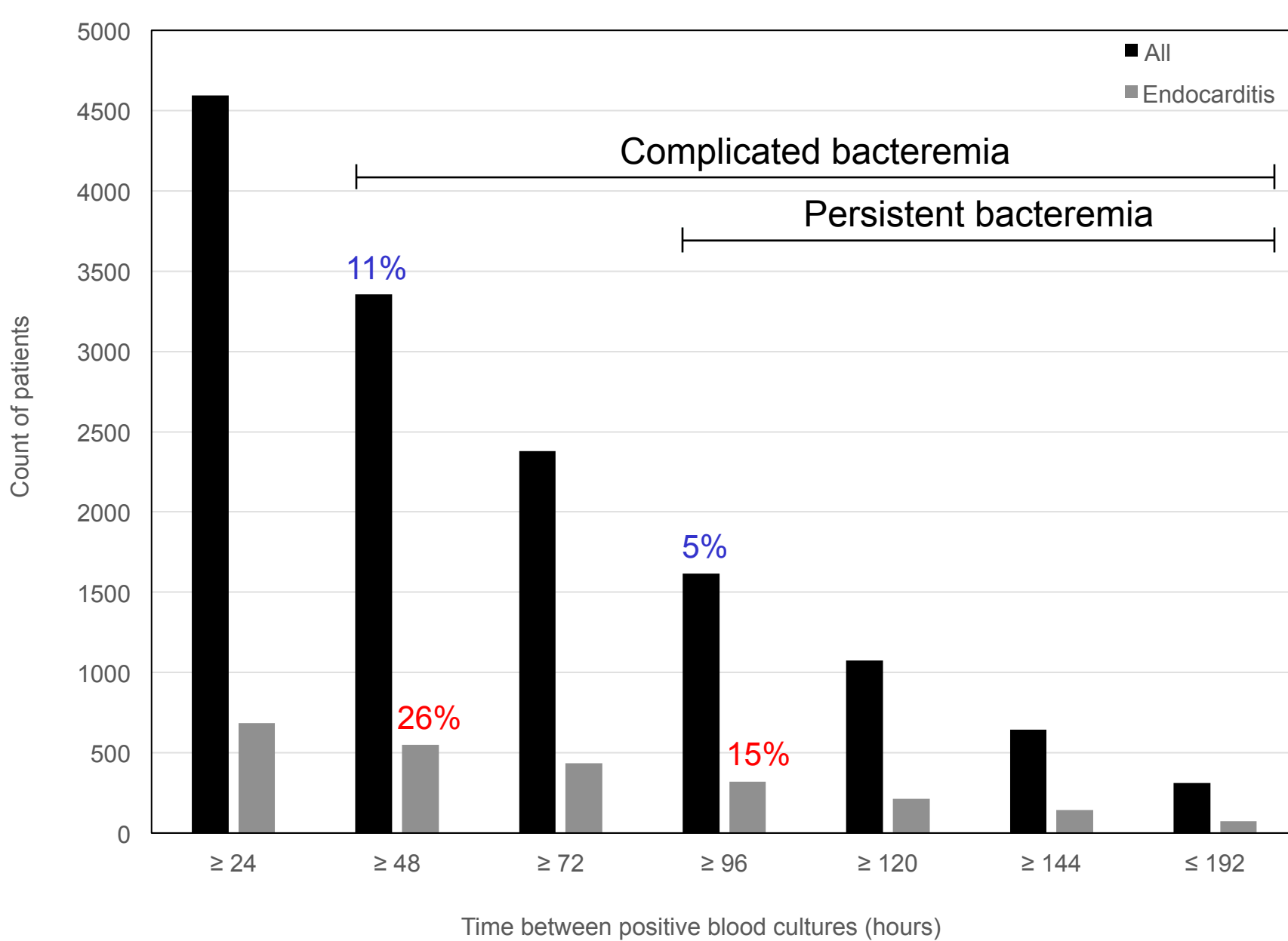
Statistical analyses: We compared demographics, co-morbidities, and outcomes between bacteremic groups and antibiotic treatment regimens among all patients with SAB.

Demographics

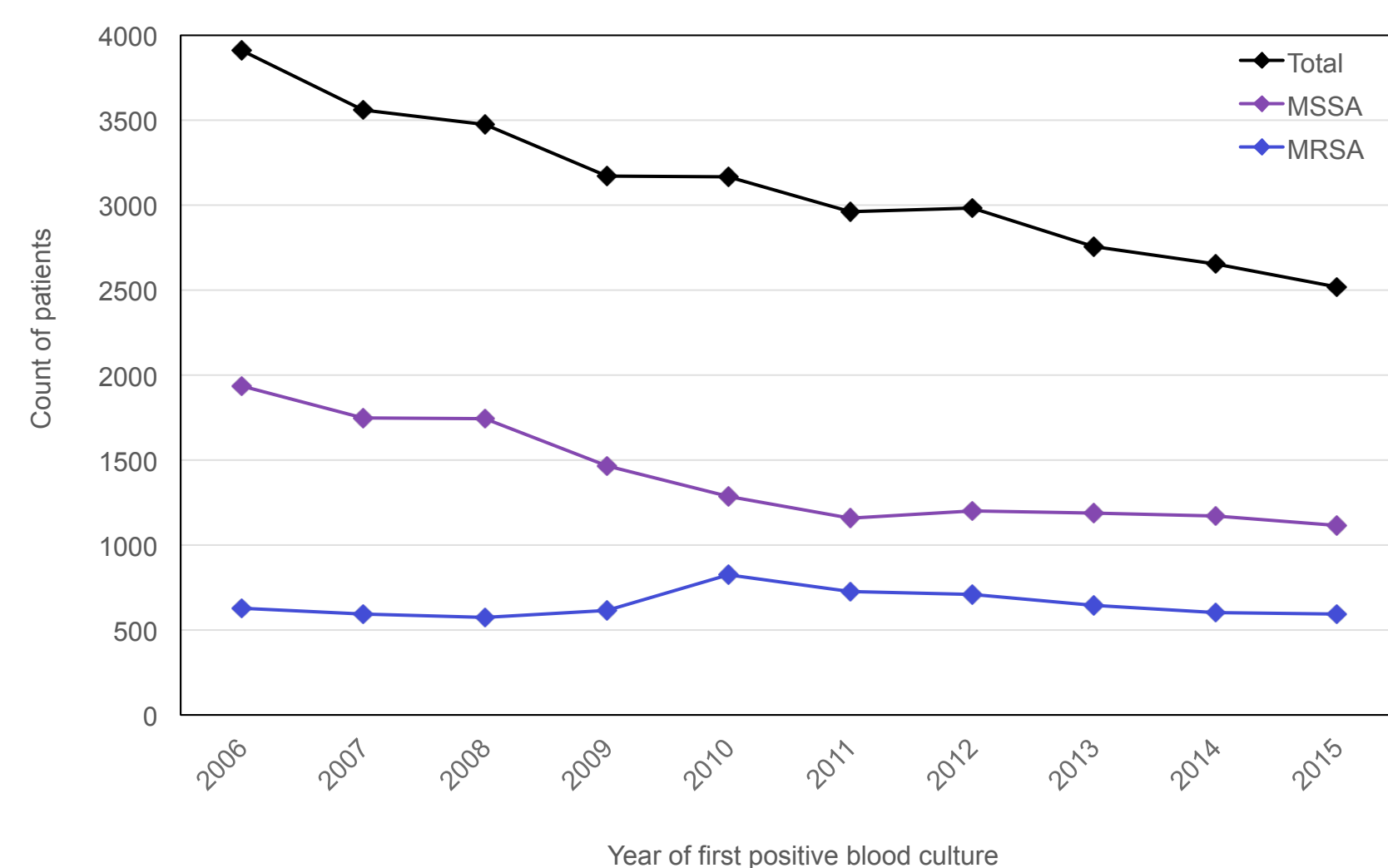
Variable	All		Uncomplicated		Complicated		Persistent		Endocarditis	
	N	Percent	N	Percent	N	Percent	N	Percent	N	Percent
All	31,161	100%	27,806	89%	3,355	11%	1,617	5%	2,115	7%
Age, continuous	Mean (SD)		66 (12)		65 (12)		66 (12)		64 (13)	
Age, categorical										
18-30	183	1%	162	1%	21	1%	7	1%	30	1%
31-40	384	1%	345	1%	39	1%	14	1%	42	2%
41-50	1,926	6%	1,710	6%	216	6%	102	6%	162	8%
51-60	8,017	26%	7,077	25%	940	28%	456	28%	609	29%
61-70	9,994	32%	8,889	32%	1,105	33%	534	33%	652	31%
71-80	5,244	17%	4,688	17%	556	17%	270	17%	339	16%
80+	5,413	17%	4,935	18%	478	14%	234	14%	281	13%
Sex										
Male	30,389	98%	27,115	98%	3,274	98%	1,583	98%	2,058	97%
Race										
White	20,003	64%	17,992	65%	2,011	60%	941	58%	1,365	65%
African-American	6,469	21%	5,628	20%	841	25%	412	25%	418	20%
Hispanic	2,121	7%	1,569	6%	252	8%	144	9%	155	7%
Other	1,503	5%	1,345	5%	158	5%	83	5%	97	5%
Unknown	1,065	3%	971	4%	93	3%	37	2%	80	4%
Smoking										
Yes	5,888	19%	5,277	19%	611	18%	279	17%	409	19%
Alcoholism										
Yes	4,288	14%	3,844	14%	444	13%	213	13%	325	15%
Substance Misuse / Abuse										
Yes	3,197	10%	2,801	10%	296	9%	198	12%	295	14%
Homelessness										
Yes	1,238	4%	1,085	4%	153	5%	63	4%	100	5%

- 6% of patients with uncomplicated SAB and 16% with complicated SAB had *S. aureus* endocarditis.
- Compared to all patients with SAB, patients with endocarditis were younger (40% vs 34% were ≤ 60 years), more likely to use IV drugs (5% vs 3%), and have complicated bacteremia (26% vs 11%, $p < 0.001$).

Time Between *S. aureus*-positive Blood Cultures



S. aureus Susceptibility



- For all SAB, infections were 21% MRSA, 45% MSSA and 34% unknown.
- There was an increasing trend in MRSA rates in complicated (24%) and persistent (26%) SAB compared to uncomplicated SAB (21%).

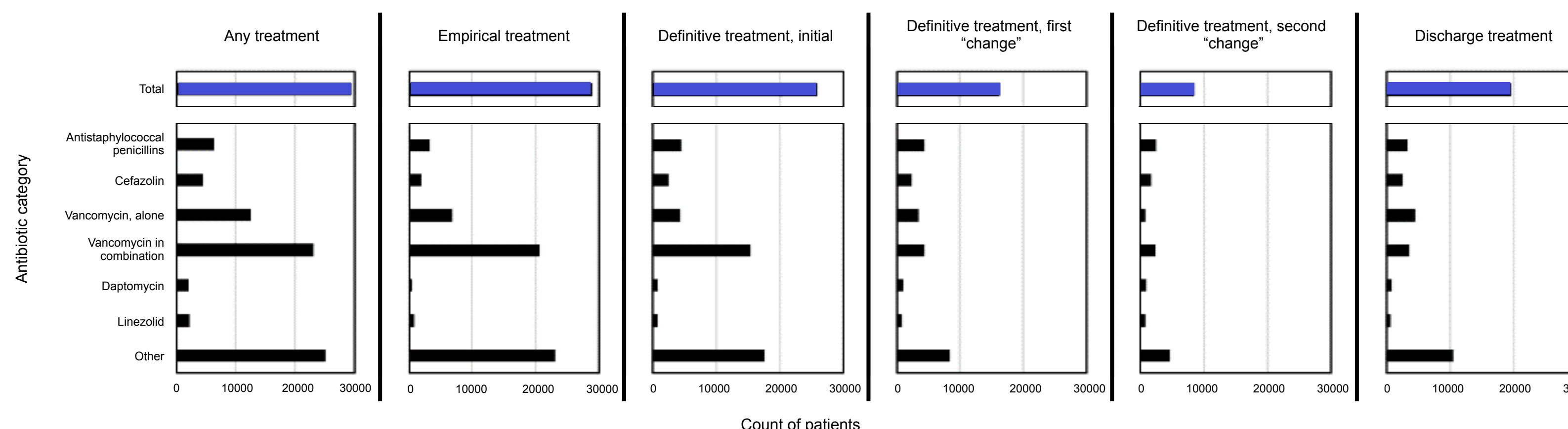
RESULTS

Clinical Characteristics

Variable	All		Uncomplicated		Complicated		Persistent		Endocarditis	
	N	Percent	N	Percent	N	Percent	N	Percent	N	Percent
All	31,161	100%	27,806	89%	3,355	11%	1,617	5%	2,115	7%
Comorbidity										
Congestive heart failure	7,859	25%	6,978	25%	881	26%	430	27%	559	26%
Diabetes	14,936	48%	13,244	48%	1,692	50%	854	53%	967	46%
IV drug use within past year	868	3%	748	3%	120	4%	57	4%	104	5%
Native valve heart disease	2,245	7%	1,991	7%	254	8%	132	8%	247	12%
Prosthetic heart valve	43	1%	35	1%	8	1%	4	1%	8	1%
Permanent pacemaker	11	1%	11	1%	0	-	0	-	1	1%
Prosthetic joint	3	1%	2	1%	1	1%	1	1%	0	-
In-dwelling catheter	500	2%	460	2%	40	1%	16	1%	45	2%
History of endocarditis	142	1%	117	1%	25	1%	16	1%	43	2%
History of osteomyelitis	3,401	11%	3,057	11%	344	10%	160	10%	238	11%
History of SAB	1,828	6%	1,626	6%	202	6%	103	6%	123	6%
Infection onset from hospital admission										
Community (≤ 48 hours)	23,641	76%	21,012	76%	2,629	78%	1,292	80%	1,764	83%
Hospital (> 48 hours)	7,520	24%	6,794	24%	726	22%	325	20%	351	17%
<i>S. aureus</i> -positive blood cultures... ≥ 48 hours apart	3,355	11%	0	-	3,355	100%	1,617	100%	548	26%
<i>S. aureus</i> susceptibility										
MRSA	6,508	21%	5,708	21%	800	24%	416	26%	424	20%
MRSA Vanc MIC ≥ 2	333	1%	281	1%	52	2%	26	2%	25	1%
MRSA Vanc MIC ≤ 1	6,012	19%	5,279	19%	733	22%	381	24%	388	18%
MSSA	14,006	45%	12,680	46%	1,326	40%	579	36%	884	42%
Unknown	10,647	34%	9,418	34%	1,229	37%	622	38%	807	38%
Sites of infection										
Heart (endocarditis)	2,115	7%	1,567	6%	548	16%	320	20%	2,115	100%
Lung (community-acquired pneumonia)	6,023	19%	5,432	20%	591	18%	301	19%	442	21%
Ventilator-associated pneumonia	73	1%	68	1%	5	1%	4	1%	5	1%
Bone (osteomyelitis)	4,102	13%	3,594	13%	508	15%	261	16%	303	14%
Joint (septic arthritis)	239	1%	187	1%	52	2%	21	1%	33	2%
Hardware (implanted prosthetic material)	960	3%	794	3%	166	5%	89	5.5%	154	7%
Skin (abscess, cellulitis)	6,997	22%	6,391	23%	606	18%	297	18%	419	20%
Wound	587	2%	517	2%	70	2%	34	2%	41	2%
Urine (urinary tract infection)	5,605	18%	4,924	18%	681	20%	340	21%	379	18%
Metastatic sites of infection										
Septic pulmonary emboli	313	1%	221	1%	92	3%	47	3%	108	5%
Systemic emboli	148	1%	118	1%	30	1%	14	1%	58	3%
Antibiotic therapy										
Any	30,616	98%	27,282	98%	3,334	99%	1,606	99%	2,110	100%
TTE performed	15,983	51%	13,671	49%	2,312	69%	1,120	69%	1,733	82%
TEE performed	4,802	15%	3,705	13%	1,097	33%	599	37%	947	45%
ICU admission	13,814	44%	12,049	43%	1,765	53%	924	57%	1,073	51%
Length of stay, Mean (SD)	10 (21)		10 (21)		10 (14)		11 (16)		11 (17)	
Length of stay, Mean (SD)	21 (41)		20 (42)		26 (28)		29 (27)		25 (28)	
Discharge disposition										
Home	16,980	54%	15,388	55%	1,593	47%	716	44%	1,031	49%
Rehabilitation or skilled nursing facility	6,941	22%	6,135	22%	805	24%	400	25%	590	28%
Death	4,246	14%	3,674	13%	572	17%	314	19%	285	13%
Other	1,281	4%	1,105	4%	176	5%	90	6%	127	6%
Unknown	1,713	6%	1,504	5%	209	6%	97	6%	82	4%

- Patients with SAB were older (66% were ≥ 60 years) and commonly had congestive heart failure (25%) and diabetes (48%).
- ICU admission and hospital length of stay were highest in patients with complicated SAB and endocarditis versus uncomplicated SAB (53% vs 43% and 51% vs 43%, $p < 0.001$; 26 vs 20 days and 25 vs 20 days, $p < 0.001$).

Antibiotic Treatment Regimens



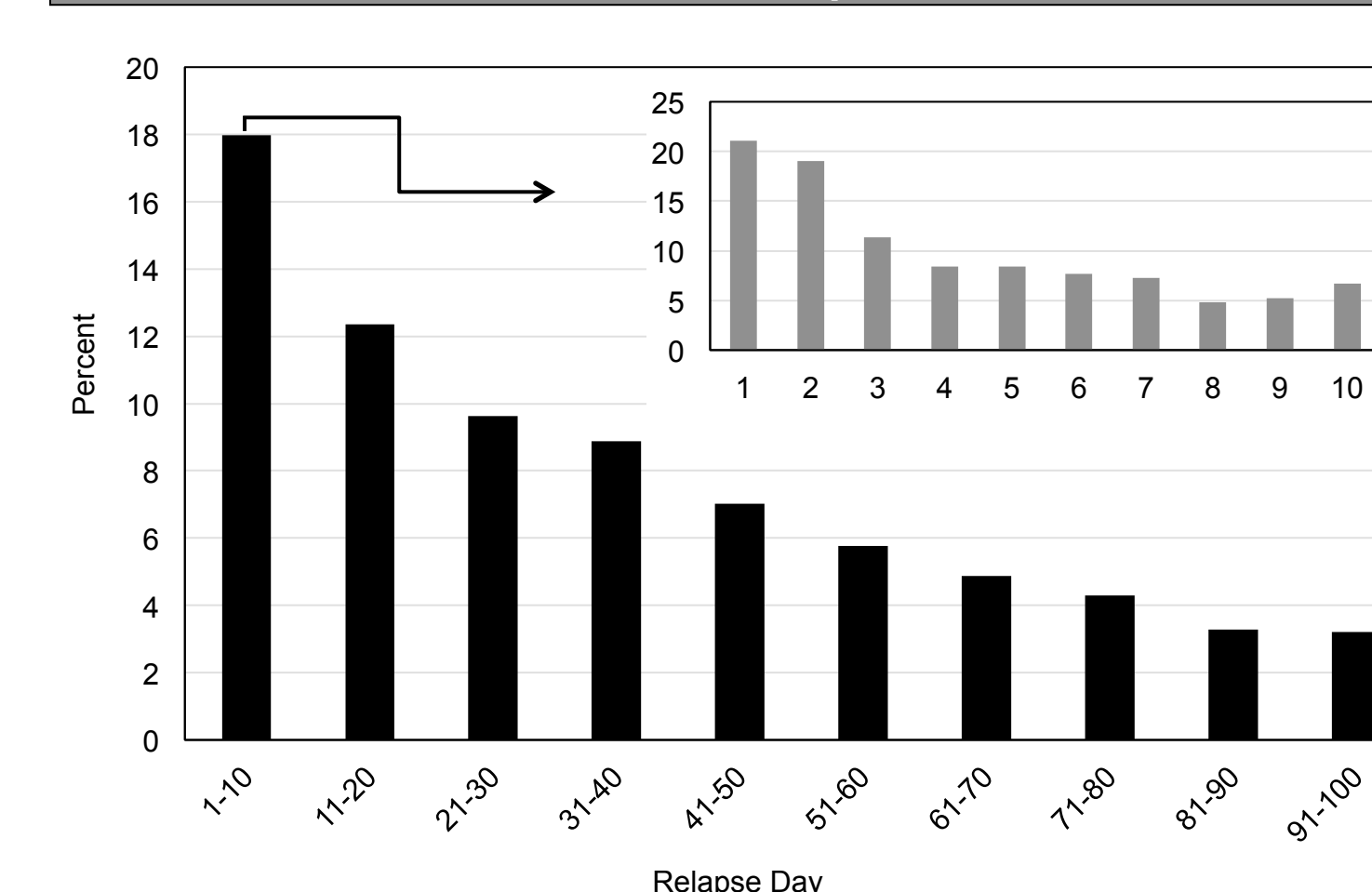
Empirical treatment period: Two days prior to five days following the first *S. aureus*-positive blood culture collection date.

Definitive treatment period: Five days following the first *S. aureus*-positive blood culture collection date to the date of hospital discharge. If a patient died or was discharged from the hospital within five days following the first *S. aureus*-positive blood culture specimen collection date, no definitive treatment period was defined.

Discharge treatment period: Up to sixty days following the date of hospital discharge. For patients that died during this time, the period ended at the date of death.

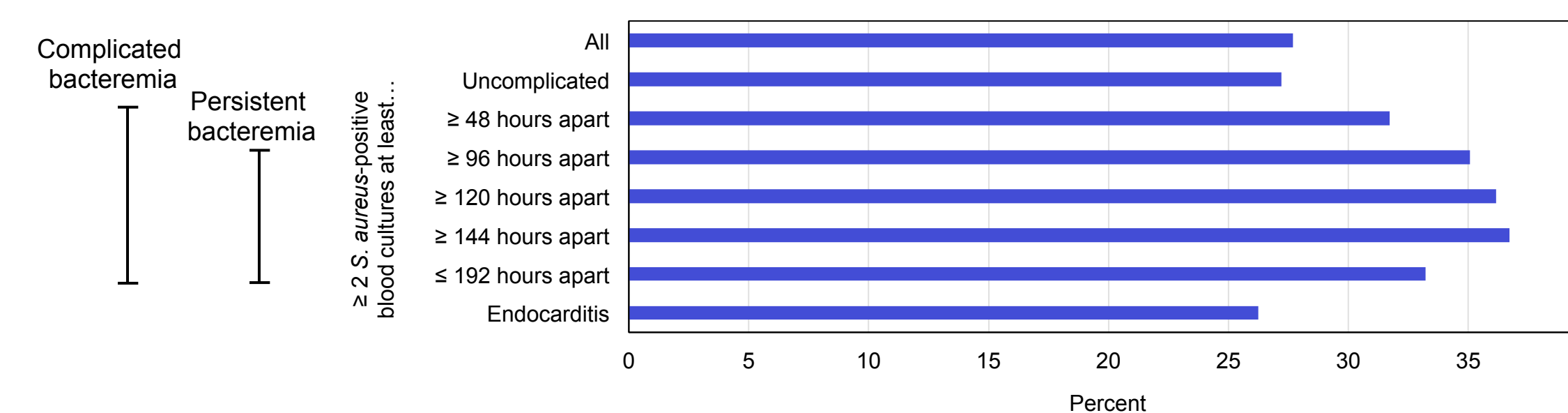
Antibiotics were recorded for which at least two distinct doses were administered. Subsequent consecutive doses of the same antibiotic administered to the patient less than five days apart were considered part of the original antibiotic.

Relapse of *S. aureus* Bacteremia

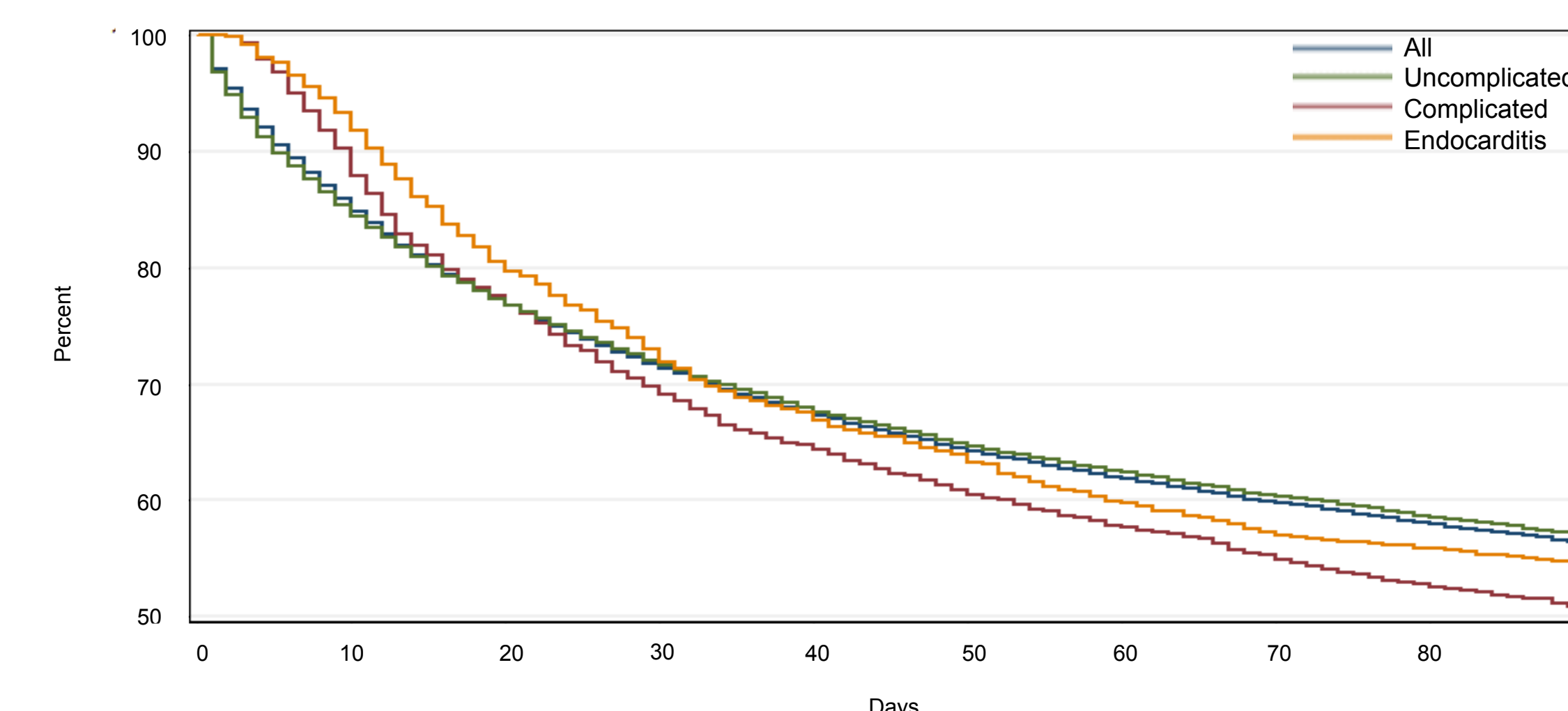


- Relapse Day 1 is defined as SAB 72 hours after the first negative blood culture; SAB relapse cases are recorded through Day 365.
- 2,703 (9%) of all patients had a SAB relapse.
- 40% of relapses occurred within 30 days of the first negative blood culture.
- 23% of SAB relapses occurred more than 100 days from the first negative blood culture.

Mortality Within 90 Days of First *S. aureus*-Positive Blood Culture



Time to Mortality Within 90 Days of First *S. aureus*-Positive Blood Culture



- Patients with complicated SAB and *S. aureus* endocarditis had an initial delayed onset of mortality, but by 90 days mortality was higher for both groups than in uncomplicated SAB.

CONCLUSIONS

- Despite well-established treatments, morbidity and mortality remain high for patients with SAB, especially those with complicated bacteremia and endocarditis.
- Understanding differences in demographics, comorbidities and outcomes will identify SAB populations that may benefit from novel antibiotic therapies.

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