

## Background

- Unlike in Gram-positive bloodstream infection (BSI), incidence and risk factors of complications in Gram-negative BSI (GN-BSI) are not well defined
- There is no established criteria to aid in diagnosis or work-up of complications in GN-BSI
- A recent study identified five early clinical failure criteria (ECFC) that were associated with increased risk of 28-day mortality or prolonged hospitalization<sup>1</sup>
- Association between ECFC and risk of complications has not been examined

### Early Clinical Failure Criteria (ECFC) evaluated at 72-96 hours following BSI

SBP <100 mmHg or vasopressor use	HR >100 beats/min	RR ≥22 breaths/min	Altered mental status	WBC count >12,000 mm <sup>3</sup>
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## Aims/Objectives

- Primary:** Assess incidence of complications within 90 days of GN-BSI
- Secondary:** Determine predictors of complicated GN-BSI

## Methods

- Retrospective cohort study
- Hospitalized adult patients with monomicrobial GN-BSI at Prisma Health-Midlands hospitals in SC between 1/1/2012 and 6/30/2015
- Complications of GN-BSI were defined as infective endocarditis, septic arthritis, osteomyelitis, spinal infections, deep-seated abscesses, and recurrent GN-BSI within 90 days of initial episode
- Clinical and microbiological variables were assessed as potential risk factors for complications, including initial response to antimicrobial therapy within first 72-96 hours using early clinical failure criteria (ECFC)
- Kaplan-Meier analysis and multivariate Cox proportional hazards regression were used to examine incidence and risk factors of complicated GN-BSI, respectively

## Results

- 752 patients with GN-BSI were included in analysis
- Median age was 66 years; one-half were women [Table 1]
- Urinary tract was most common source of GN-BSI [Table 2]
- Escherichia coli* was most common bacteria [Figure 1]
- 79 patients developed complications within 90 days of GN-BSI with an overall incidence of complications of 13.9% [Figure 2]
- Median time to identification of complications was 5.2 days from index GN-BSI (interquartile range 1-28 days)
- Incidence of complications was notably higher in BSI due to *Serratia* species, *Proteus mirabilis*, and *Pseudomonas aeruginosa* than other bacteria (log-rank p < 0.001) [Figure 3]
- Independent risk factors for complications included early clinical failure criteria, non-urinary source, presence of indwelling prosthetic devices, BSI due to *Serratia* species, *P. mirabilis* or *P. aeruginosa*, and persistent GN-BSI [Table 3]
- Risk of complications increased from 6% in absence of risk factors to >33% in presence of 3 or more risk factors [Figure 4]

## Results

Table 1. Baseline Demographics & Clinical Characteristics

Variable	(N= 752)
Age, median (IQR)	66 years (55-77)
Male, n (%)	372 (49.4)
White, n (%)	346 (46)
African American, n (%)	377 (50.1)
Charlson comorbidity index, median (IQR)	2 (0-3)
Pitt bacteremia score, median (IQR)	2 (1-3)
Hospital-acquired GN-BSI, n (%)	184 (24.5)

Table 2. Source of Gram-Negative BSI

Site	(N= 752)
Urinary tract, n (%)	378 (50.2)
Biliary tract, n (%)	42 (5.5)
Gastrointestinal tract, n (%)	52 (6.9)
Respiratory tract, n (%)	40 (5.3)
Central venous catheter, n (%)	66 (8.7)
Skin and soft tissue, n (%)	33 (4.3)
Other, n (%)	12 (1.5)
Unknown, n (%)	129 (17.1)

Figure 1. Microbiology of Gram-Negative BSI

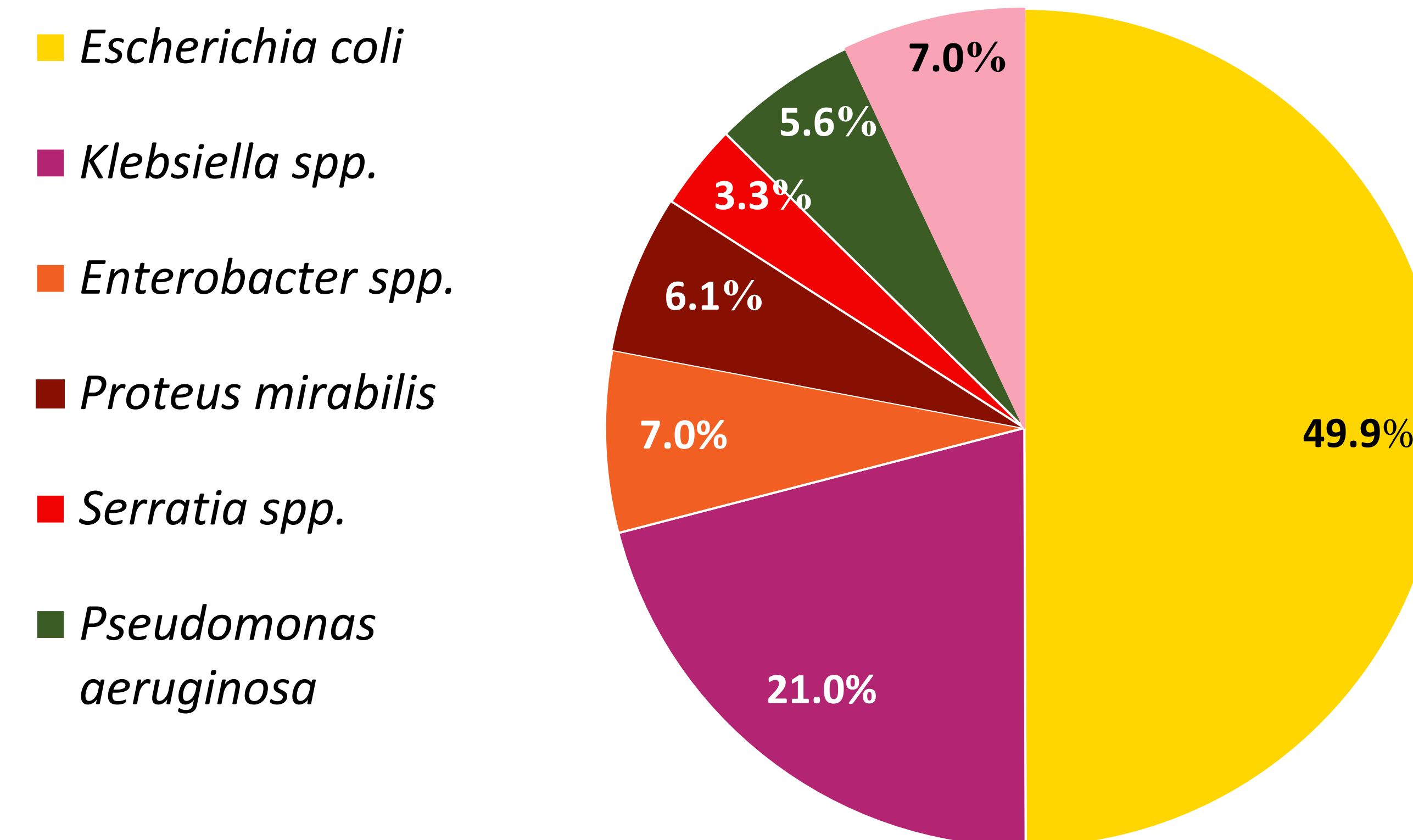


Figure 2. Complications of Gram-Negative BSI (# of events)

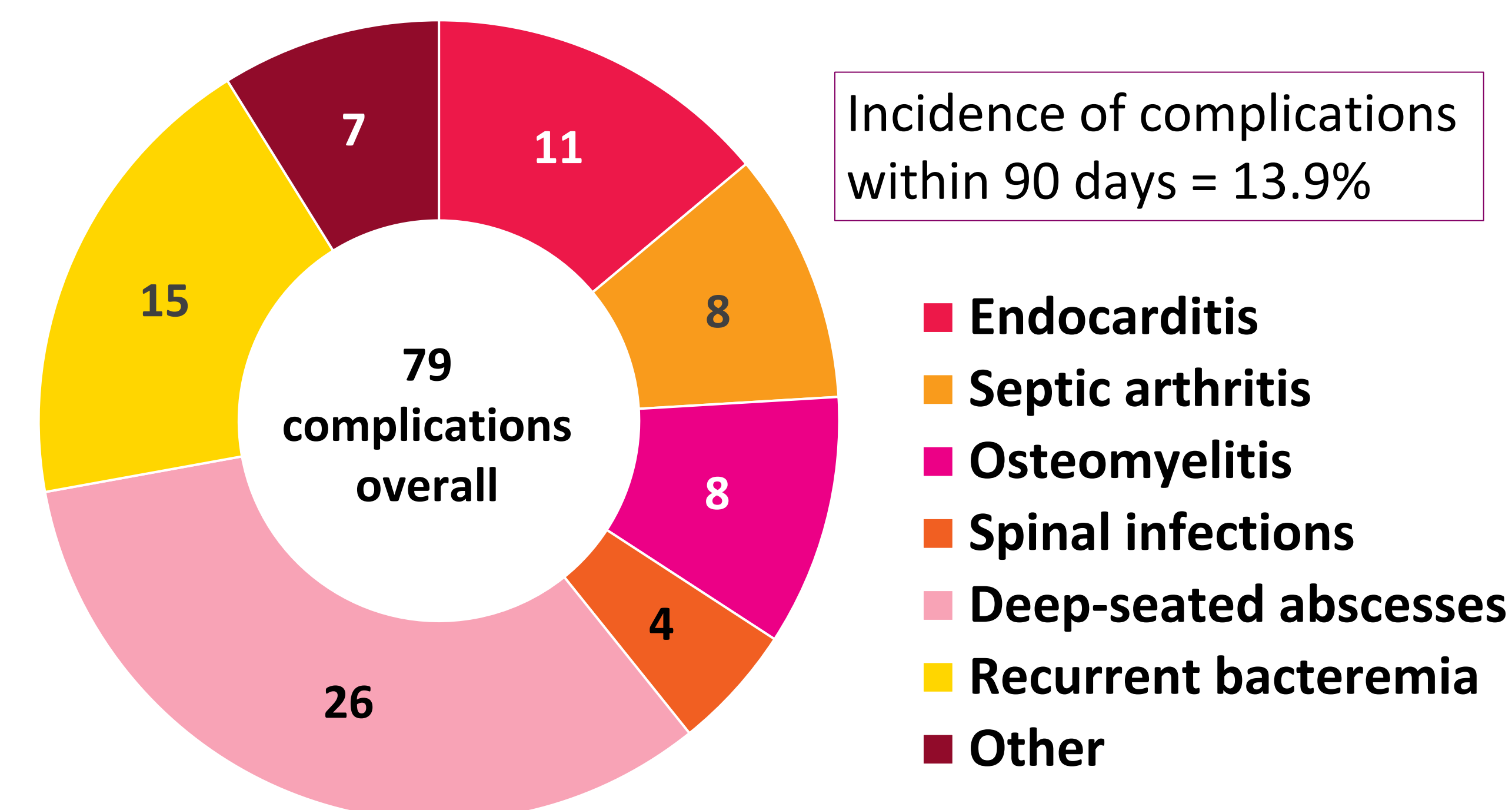


Table 3. Independent Risk Factors for Development of Complications

Independent variable	Hazard ratio	(95% Confidence interval)	P-value
Early clinical failure criteria (per point)	1.19	(1.03, 1.36)	0.02
Non-urinary source	2.04	(1.22, 3.43)	0.007
<i>Pseudomonas</i> , <i>Proteus</i> , or <i>Serratia spp.</i>	1.73	(1.02, 2.94)	0.04
Presence of prosthesis	1.68	(1.05, 2.69)	0.03
Persistent bacteremia	2.92	(1.24, 6.86)	0.01

Figure 3. Incidence of Complications by Pathogen

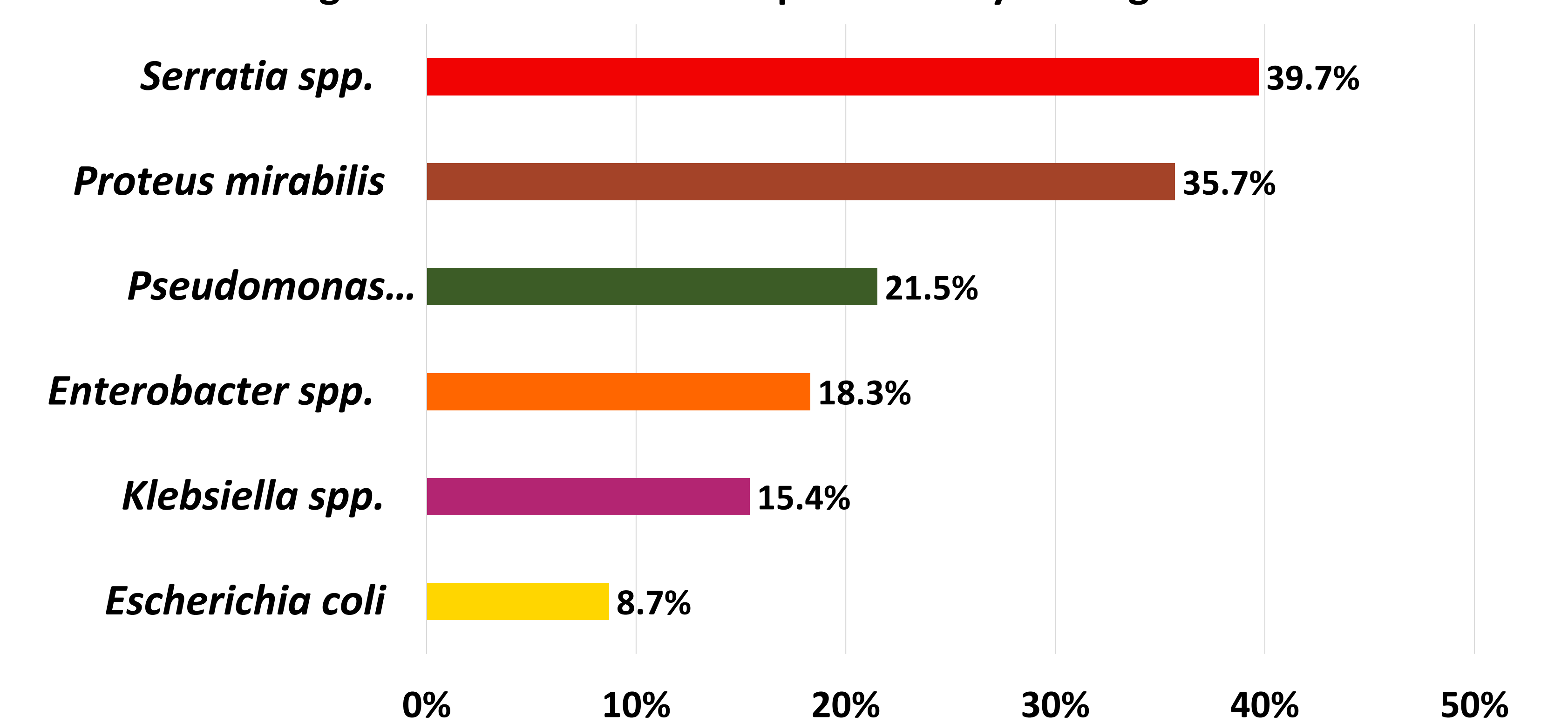
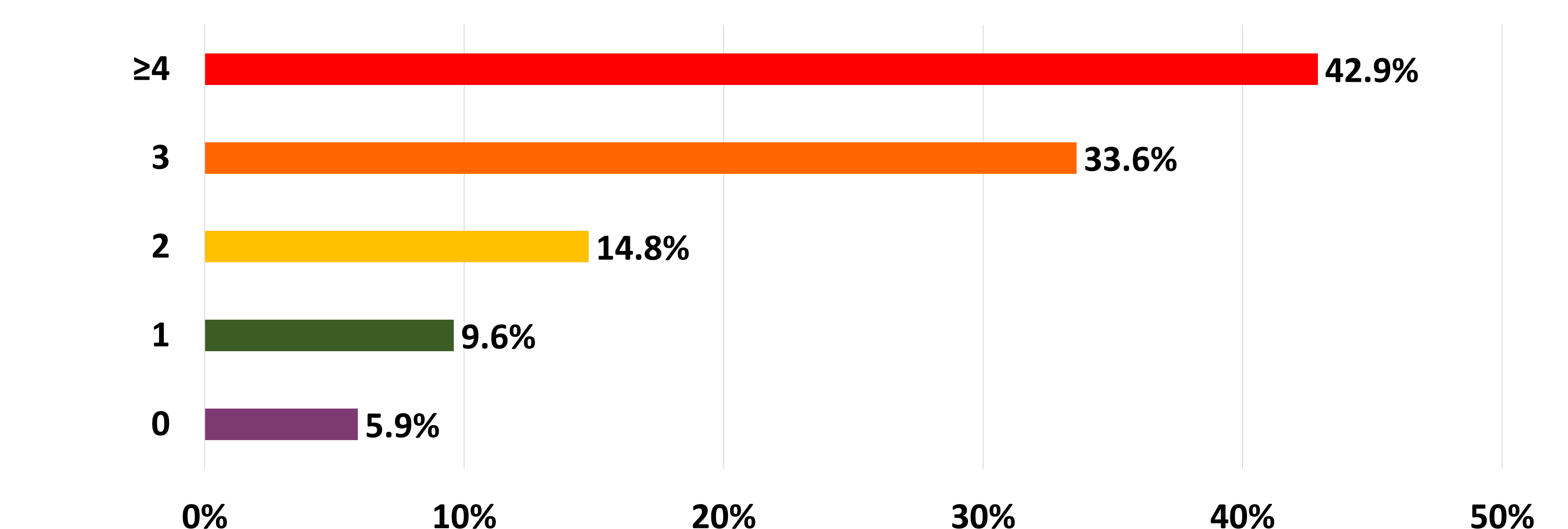


Figure 4. Risk of Developing Complications Based on Number of Risk Factors



## Conclusions

- At least 13.9% of patients develop complications within 90 days of GN-BSI
- Risk of complications may be predicted by specific host and microbiological factors, initial response to antimicrobial therapy, and follow-up blood culture results
- Stratification of patients based on these risk factors may aid in identifying patients requiring further diagnostic work-up for early detection of complications

## Reference

- Rac H, et al. Evaluation of early clinical failure criteria for gram-negative bloodstream infections. *Clin Microbiol Infect* 2020;26:73-77. doi:10.1016/j.cmi.2019.05.017

