



# Eosinopenia and binary toxin increases mortality in hospitalized patients with *Clostridioides difficile* infection

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## BACKGROUND

- C. difficile* toxin causes clinical disease
  - Toxin A, toxin B
  - Binary toxin (CDT)
- CDT+ strains cause increased severity, nonhome discharge, mortality, and recurrence of *C. difficile* infection (CDI)
- CDI due to a CDT+ strain is associated with a decrease in peripheral eosinophils of mice
- Fewer eosinophils increased CDI mortality in mice and humans

## SPECIFIC AIM

To assess the combined effect of peripheral eosinophil count and CDT presence on inpatient mortality following CDI diagnosis using univariate and multivariable analysis

## METHODS

### Study design / population

- Retrospective, cohort study
  - Training cohort
    - Houston, TX
    - August 1, 2015 – July 31, 2018
    - 13 hospitals
  - Validation cohort
    - National Veterans Affairs database
    - October 1, 2002 – September 30, 2014
    - 8 hospitals
- Inclusion criteria:
  - Age ≥18 years
  - Diagnosed with CDI
  - Specimen ribotype/CDT data available

### Covariates and outcomes

- Laboratory analytes measured at the time of CDI diagnosis (± 24 hours)
  - White blood cells (WBC)
  - Serum eosinophil count
  - Serum albumin level
  - Serum creatinine (SCR)
- Primary outcome: inpatient mortality

### Statistical analysis

- Cohort stratification based on eosinophil count: (0.0 cells/μL vs. > 0.0 cells/μL)
  - Further stratified to show combined effect with CDT

### Baseline characteristics

- Binary/categorical variables: χ<sup>2</sup> or Fisher's exact test
- Continuous variables: Student's t-test or Wilcoxon rank-sum test

### Primary outcome: inpatient mortality

- Multivariable logistic regression
  - Selection using univariate analysis (P<0.20)
  - Backwards elimination (P>0.05) using partial likelihood ratio test

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Figure 1. Patient selection flow chart (Houston cohort)

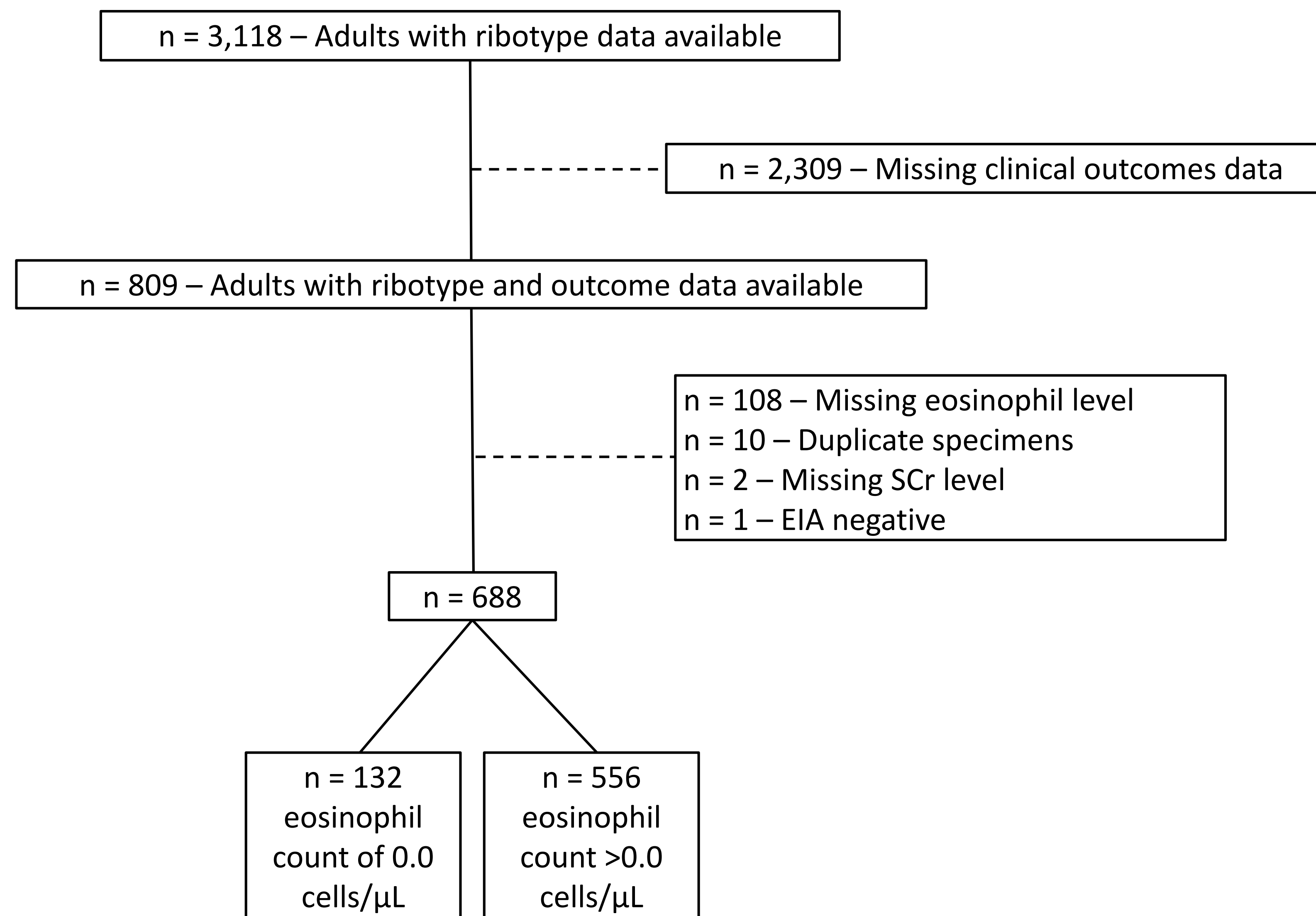


Table 1. Comparison of patient demographics, comorbidities, and laboratory parameters between eosinophil count groups

Covariate	Houston cohort			Validation cohort		
	Eosinopenia (n = 132)	Eosinophils present (n = 556)	P value	Eosinopenia (n = 67)	Eosinophils present (n = 723)	P value
Age, mean (±SD), y	65.5 (18.7)	63.7 (17.7)	0.32	67 (12.2)	66 (12.5)	0.33
Female, no. (%)	71 (53.8)	318 (57.2)	0.48	3 (4.4)	38 (5.3)	0.78
Race/ethnicity, no. (%)			<b>0.04</b>			
White, non-Hispanic	94 (71.2)	320 (57.6)		43 (67.2)	459 (65.9)	0.84
Black, non-Hispanic	18 (13.6)	114 (20.5)		19 (29.7)	186 (26.7)	0.61
Hispanic	14 (10.6)	98 (17.6)		2 (3.1)	25 (3.6)	0.84
Asian	2 (1.5)	7 (1.3)		0 (0.0)	26 (3.7)	<b>0.03</b>
Other	4 (3.0)	17 (3.1)		0 (0.0)	0 (0.0)	N/A
CCI, median (IQR)	2 (1-3)	2 (1-4)	0.09	3 (2-5)	3 (1-6)	0.79
SOT, no. (%)	8 (6.1)	57 (10.3)	0.14	2 (3.0)	6 (0.8)	0.16
HSCT, no. (%)	0 (0.0)	1 (0.2)	1.00	0 (0.0)	0 (0.0)	N/A
WBC, median (IQR), cells/μL	12.3 (8.7-20.0)	10.7 (7.3-15.8)	<b>0.001</b>	15.4 (10.5-22.0)	10.6 (7.4-15.1)	<b>&lt;0.001</b>
SCR, median (IQR), mg/dL	1.07 (0.78-1.70)	1.06 (0.75-2.00)	0.88	1.4 (1.0-2.3)	1.2 (0.9-1.9)	0.12
Albumin, mean (±SD), g/dL	3.1 (0.8)	3.1 (0.7)	0.98	2.7 (0.9)	2.9 (0.6)	0.31
Severe CDI, no. (%)	73 (55.3)	289 (52.0)	0.49	61 (91.0)	512 (70.8)	<b>&lt;0.001</b>
Testing method, no. (%)			0.78			N/A
NAAT	129 (97.7)	538 (96.8)		67 (100)	723 (100)	
EIA	3 (2.3)	18 (3.2)		0 (0.0)	0 (0.0)	
HO-CDI, no. (%)	40 (30.3)	204 (36.7)	0.17	56 (83.6)	450 (62.2)	<b>&lt;0.001</b>
Recurrent CDI, no. (%)	16 (12.1)	54 (9.7)	0.41	0 (0.0)	0 (0.0)	N/A
History of CDI, no. (%)	36 (27.3)	136 (24.5)	0.50	0 (0.0)	0 (0.0)	N/A
CDT + ribotype, no. (%)	14 (10.6)	95 (17.1)	0.07	13 (19.4)	214 (29.6)	0.07

## RESULTS

Figure 2. Stratified analysis demonstrating the combined effect of eosinopenia and infection with a binary toxin strain on inpatient mortality

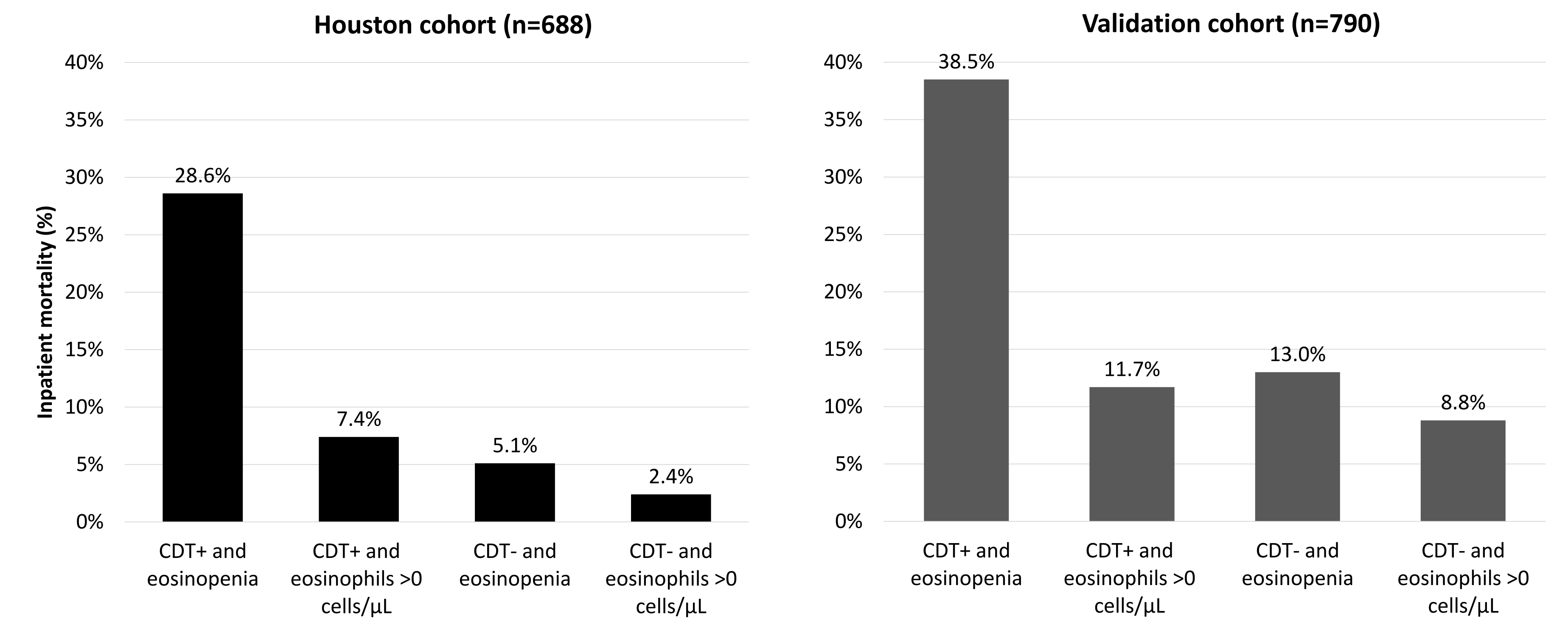


Table 2. Stratified univariate analysis of primary and secondary outcomes

Outcomes	Eosinopenia / CDT present		Eosinopenia / CDT present		Eosinopenia / CDT present	
	Yes / Yes (n=14)	No / Yes (n=95)	Yes / No (n=118)	No / No (n=461)	Yes / Yes (n=13)	No / Yes (n=214)
<b>Houston cohort</b>						
Inpatient mortality, n (%)	4 (28.6)	7 (7.4)	6 (5.1)	11 (2.4)		
30-day recurrence, n (%)	0 (0.0)	5 (5.3)	3 (2.5)	22 (4.8)		
90-day recurrence, n (%)	3 (21.4)	20 (21.1)	5 (4.2)	55 (11.9)		
ICU admission, n (%)	4 (28.6)	13 (13.7)	24 (20.3)	57 (12.4)		
Higher LOC at discharge, n (%)	7 (50)	23 (24.2)	44 (37.3)	128 (27.8)		
Colectomy, n (%)	0 (0.0)	0 (0.0)	3 (2.5)	4 (0.9)		
<b>Validation cohort</b>						
Inpatient mortality, n (%)	5 (38.5)	25 (11.7)	7 (13.0)	45 (8.8)		
30-day recurrence, n (%)	1 (7.7)	8 (3.7)	0 (0.0)	17 (3.3)		
90-day recurrence, n (%)	3 (23.1)	13 (6.1)	0 (0.0)	26 (5.1)		
ICU admission, n (%)	0 (0.0)	9 (4.2)	1 (1.9)	7 (1.4)		
Higher LOC at discharge, n (%)	8 (66.7)	54 (29.7)	16 (32.0)	88 (19.5)		
Colectomy, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		

Table 3. Univariate and multivariable analysis for predictors of inpatient mortality post *Clostridioides difficile* infection diagnosis

Covariate	Houston cohort				Validation cohort			
	Univariate analysis		Multivariable analysis		Univariate analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
<b>Eosinopenia + CDT</b>	10.8 (3.2-37.0)	<0.001	7.8 (1.9-33.2)	0.005	5.7 (1.8 – 17.8)	0.003	6.1 (1.5-23.9)	0.009
Age	1.02 (0.99-1.04)	0.14			1.01 (0.99 – 1.03)	0.19		
CCI	1.19 (1.02-1.39)	0.02	1.23 (1.01-1.48)	0.04	1.11 (1.04 – 1.19)	0.002	1.09 (1.01-1.17)	0.02
SOT	0.73 (0.17-3.14)	0.67			9.0 (2.2-36.8)	0.002		
WBC	1.05 (1.03-1.08)	<0.001	1.03 (1.00-1.06)	0.02	1.02 (1.01-1.04)	0.005	1.01 (0.99-1.03)	0.18
Scr	1.02 (0.88-1.19)	0.76			0.96 (0.81-1.15)	0.67		
Albumin	0.15 (0.07-0.33)	<0.001	0.18 (0.08-0.43)	<0.001	0.48 (0.34-0.68)	<0.001	0.53 (0.37-0.77)	<0.001
Severe CDI	1.65 (0.75-3.64)	0.21			17.4 (4.3 – 71.6)	<0.001		
HO-CDI	2.95 (1.36-6.40)	0.01			0.91 (0.57 – 1.47)	0.71		

## CONCLUSION

Hospitalized patients with CDI caused by a binary toxin strain and concomitant eosinopenia were nearly eight times more likely to die in the hospital than patients that did not meet these criteria.