

## ARTICLE



# National emergency department trends for endogenous endophthalmitis: an increasing public health challenge

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**BACKGROUND/OBJECTIVE:** To characterize incidence rates and identify risk factors for admission and mortality in patients with endogenous endophthalmitis (EE) in the United States (US).

**SUBJECTS/METHODS:** Patients with EE were identified using the Nationwide Emergency Department (NEDS) Database from 2006 to 2017 in this cross-sectional study. Subjects were required to have diagnoses of both endophthalmitis and septicaemia using contemporary International Classification of Diseases diagnosis codes. Incidence rates, mortality rates and demographics were evaluated. Risk factors for admission and mortality were identified using weighted logistic regression analysis.

**RESULTS:** A total of 6400 patients with EE were identified. Incidence increased from 0.10 (95% confidence interval [CI]: 0.07–0.12) per 100,000 in the US population in 2006 to 0.25 (95% CI: 0.21–0.30) in 2017 ( $p < 0.05$ ). Most were female (55.4%), insured with Medicare (53.5%), were in the first income quartile earnings (29.3%) [bottom 25% income bracket], lived in the South (40.5%), and presented to metropolitan teaching hospitals (66.6%). Mortality increased from 8.6% (95% CI: 3.8–18.3%) in 2006 to 13.8% (95% CI: 9.7–19.2%) in 2017 ( $p = 0.94$ ). Factors predicting admission included older age (odds ratio [OR] 32.59; [95% CI 2.95–359.78]) and intravenous drug use (OR 14.90 [95% CI: 1.67–133.16]). Factors associated with increased mortality included: human immunodeficiency virus infection/immune deficiencies (OR 2.58 [95% CI: 1.26–5.28]), heart failure (OR 2.12 [95% CI: 1.47–3.05]), and hepatic infections/cirrhosis (OR 1.89 [95% CI: 1.28–2.79]). Pneumonia and renal/urinary tract infections (UTI) were associated with both increased hospital admission [(pneumonia OR 9.64 (95% CI: 1.25–74.35,  $p = 0.030$ ), renal/UTI OR 4.09 (95% CI: 1.77–9.48)] and mortality [(pneumonia OR 1.64 (95% CI: 1.17–2.29,  $p = 0.030$ ), renal/UTI OR 1.87 (95% CI: 1.18–2.97)]. Patients with diabetes mellitus (DM) had decreased odds ratio for mortality (OR 0.49 [95% CI: 0.33–0.73]).

**CONCLUSION:** EE has increased in incidence throughout US. The two systemic factors that conferred both an increase in mortality and admission were pneumonia, and renal/UTI. Additional exploration of the potential protective association of DM with decreased mortality in this context is needed.

Eye (2023) 37:1123–1129; <https://doi.org/10.1038/s41433-022-02080-9>

## INTRODUCTION

Endogenous endophthalmitis (EE) comprises approximately 2–8% of all cases of endophthalmitis [1]. The eye becomes a secondary site of inoculation with hematogenous spread of infection from elsewhere. Since it is relatively infrequent, there have been few large-scale studies evaluating EE. Furthermore, symptoms are non-specific, with blurred vision as the most common presenting ocular symptom [2]. The diagnosis is missed in a substantial number of cases, with reports citing numbers ranging from 16% to 63% [3, 4]. Meanwhile, EE can have a rapid, debilitating course resulting in profound visual impairment. Thus, universal routine screening paradigms have been introduced for patients with bloodstream infections as a means for early identification and treatment (e.g., *Candida* species), but without proven success [5, 6]. Clinical suspicion for EE in the appropriate context for patients with systemic infections needs to be high; awareness of demographics patterns, and admission and mortality trends may therefore help dictate clinical management and elucidate patient outcomes.

There have been several studies limited to single centres evaluating demographics and mortality trends in patients with EE [7–11]. However there are a paucity of other studies that have used national databases to study EE, and none have focused on admission or mortality data [12, 13]. The primary goal of our study is to characterize patients who present to the emergency department (ED) with EE and evaluate risk factors for admission and mortality by examining these characteristics using data from a national database of EDs in the United States (US). We also assessed demographics, incidence, and temporal trends.

## MATERIALS/SUBJECTS AND METHODS

### Data source

The Nationwide Emergency Department Sample (NEDS) is the largest all-payer ED database in the US, and was developed by the Healthcare Cost and Utilization Project to provide both regional and national estimates of ED care [14]. This database consolidates

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Received: 1 November 2021 Revised: 20 April 2022 Accepted: 21 April 2022

Published online: 29 April 2022

**Table 1.** International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes.

ICD Definition	ICD-9 Code	ICD-10 Code
Endophthalmitis	360.00, 360.01, 360.02, 360.13, 360.19	H44.001, H44.002, H44.003, H44.009, H44.011, H44.012, H44.013, H44.019, H44.121, H44.122, H44.123, H44.129, H44.19
Septicaemia	00.31, 022.3, 038.0–038.9, 054.5, 659.3–659.33, 771.81, 785.52, 998.02, 995.92	R65.20, R65.21, A40.0–A40.9, A41.0–A41.9, A54.86, A02.1, A22.7, B00.7, O86.04, P36.0–P36.9, O85.0, O04.87, O07.37, O08.82, T81.44XA, T81.44XD, T81.44XS
Diabetes Mellitus	250.0–250.31	E08.0–E13.0
HIV/Immune Deficiency	H042.0–H044.9, 27.90–27.93	B20.0–B20.9, D80.0–D80.9
Heart Failure	428.0–428.9, 402.01, 402.11, 402.91	I50.0–I50.9
Pneumonia	011.61–011.66, 115.15, 115.95, 003.22, 011.60–011.66, 115.15, 115.95, 48.0–48.7, 99.731, 99.732	J09–J18, P23.0–P23.9, A01.03, A02.22, A54.84, B01.2, B06.81, B77.81, J82–J84, B05.2, J85.1, A37.9, A37.01, A37.11, A37.81
Endocarditis	036.42, 074.22, 093.20, 098.84, 112.91, 115.04, 115.94, 115.14, 42.1–42.49	I38, I39, M32.11, M32.82, A39.51, A52.03, B33.21, B37.6, I01.1, I33.0–I33.9
IV Drug Use	304.0–305.9	F10–F19
Gastrointestinal Comorbidities	52.0–56.0	K0.0–K6.0
Renal/Urinary Tract Infections	59.0–59.9	N0–N3
Hepatic Infections/ Cirrhosis	57.0–57.39	K7–K8

the State Inpatient Databases and State Emergency Department Databases including both patients seen in the ED and subsequently admitted to the hospital, as well as visits that do not result in admission. The database contains roughly 145 million ED visits from 990 hospitals across 36 states nationwide, approximating a 20% stratified sample of hospital-owned EDs. NEDS uses discharge data and elements derived from International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and ICD, Tenth Revision, Clinical Modification (ICD-10-CM). This study was performed with the approval of the Johns Hopkins University School of Medicine Institutional Review Board and in accordance with the Declaration of Helsinki.

### Study population

All cases with an ICD-9-CM and ICD-10-CM code corresponding to endophthalmitis were identified. Selection of cases also required septicaemia as a diagnosis for increasing rigor of capturing EE. These codes used for identification of EE are listed in Table 1.

### Study measures

Secondary variables were also identified using ICD-9-CM and ICD-10-CM codes. Data related to patient, visit, institution, and outcomes were evaluated. Demographic variables consisted of age, gender, insurance status, and income quartile. Institution variables included region, metropolitan status, teaching designation, and trauma centre designation. Visit variables encompassed median cost adjusted for inflation and month. Outcome variables included admission status and mortality. The database only coded mortality if it occurred within the same visit as the presentation, including both death during ED stay or death occurring during the length of admission.

### Data analysis

Nationwide estimates were determined using sample weights provided by NEDS. Weights were provided in the database using discharge level weights that are provided in the database to represent the relative proportion of the total US inpatient hospital population for each record, allowing for calculation of national estimates. Annual incidence of such visits was calculated using census data; the total number of EE cases during the study period

was divided by the total US population in the same period. Standard descriptive statistical methods were used for assessing demographics, and characteristics related to visit and institution. A univariate and multivariate weighted logistic regression model was used to determine demographic and visit characteristics associated with both hospital admission and mortality. Variables in this analysis included age (grouped into  $\leq 20$ , 21–40, 41–60, 61–80,  $\geq 81$ ), sex, household income, primary payer, patient location, hospital region, teaching status of hospital, and the following comorbidities: diabetes mellitus (DM), human immunodeficiency virus (HIV)/immune deficiencies, heart failure, pneumonia, endocarditis, intravenous drug use (IVDU), gastrointestinal infections, renal/urinary tract infections, and cirrhosis/hepatic infections. Weighting was used throughout to identify these variables to account for changes in sampling procedure during this time period. Statistical significance was set at  $p < 0.05$ .

## RESULTS

### Demographics and baseline characteristics

In total, there were 29,400 patients with any endophthalmitis diagnosis code (Table 1) identified from 2006 to 2017. This group was further refined to 6400 patients who were identified as having EE using a diagnosis code consistent with septicaemia, of whom 6307 patients were admitted (98.5%) (Table 1). Demographic data are shown in Table 2. Most (55.4%) patients were female, the majority (53.5%) were insured with Medicare, and the median age was 62 years (interquartile range [IQR]: 49–75). The income quartile distribution was evenly distributed with most patients living in the Southern region (40.5%). Most patients presented to non-trauma centre (42.3%), metropolitan teaching hospitals (66.6%).

### National trends in incidence, cost and mortality

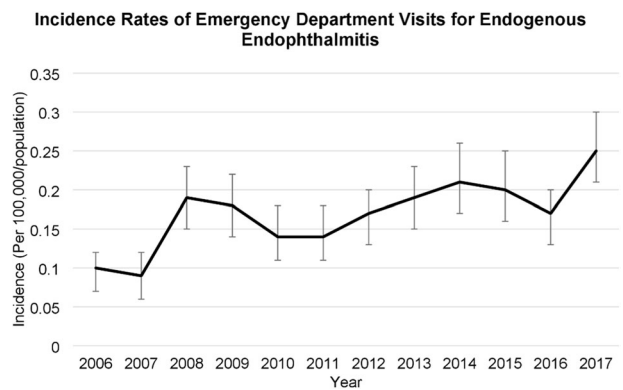
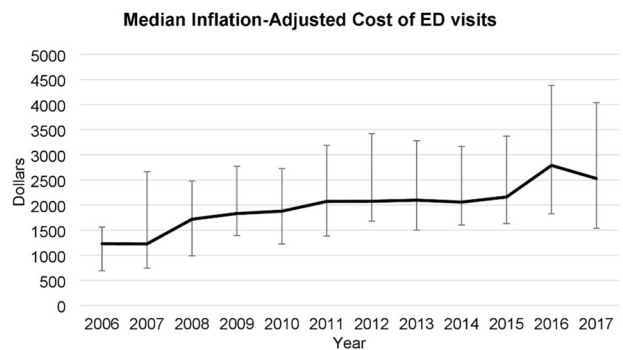
Incidence of EE increased from 0.10 (95% CI: 0.07–0.12) in 2006 to 0.25 (95% CI: 0.21–0.30) in 2017 ( $p < 0.05$ , Fig. 1). The median inflation-adjusted cost of ED visits for EE increased from \$1229 (IQR: \$690–\$1563) in 2006 to \$2529 (IQR: \$1538–4038) in 2017 but was statistically insignificant ( $p = 0.23$ ) (Fig. 2). There was no seasonal variation in the distribution of ED visits for EE ( $p = 0.46$ ).

**Table 2.** Demographics of Endogenous Endophthalmitis Visits to Emergency Departments in the United States (weighted), 2006–2017.

Sex	
Female	3544 (55.4)
Male	2856 (44.6)
Age	
0–20	123 (1.9)
21–40	492 (7.7)
41–60	2196 (34.3)
61–80	2345 (36.6)
>81	1242 (19.4)
Year	
2006	284 (4.4)
2007	271 (4.2)
2008	570 (8.9)
2009	550 (8.6)
2010	446 (7.0)
2011	451 (7.0)
2012	522 (8.1)
2013	604 (9.4)
2014	685 (10.7)
2015	655 (10.2)
2016	535 (8.3)
2017	827 (12.9)
Insurance	
Medicare	3422 (53.5)
Medicaid	1230 (20.3)
Private	1151 (18.0)
Self-Pay	336 (5.3)
No Charge	41 (0.6)
Other	144 (2.3)
Income Quartile	
First	1830 (29.3)
Second	1589 (25.5)
Third	1444 (23.1)
Fourth	1380 (22.1)
Region	
Northeast	1140 (17.8)
Midwest	1106 (17.3)
South	2589 (40.5)
West	1564 (24.4)
Hospital Teaching Status	
Metropolitan Non-teaching	1815 (28.4)
Metropolitan teaching	4263 (66.6)
Non-Metropolitan	323 (5.0)
Hospital Trauma	
Level	
Non-trauma Centre	2708 (42.3)
Level 1	1670 (26.1)
Level 2	779 (12.2)
Level 3	511 (8.0)
Mortality	822 (12.9)
Admission	6307 (98.5)

**Table 2.** continued

Comorbidities	
Diabetes	2389 (37.3)
HIV/AIDS/Immune Deficiency	203 (3.2)
Heart Failure	1342 (21.0)
Pneumonia	1695 (26.5)
Endocarditis	1021 (15.9)
IV Drug Use	844 (13.2)
Gastrointestinal Infections	1808 (28.3)
Renal/Urinary Tract Infections	4551 (71.1)
Hepatic Infections/Cirrhosis	1114 (17.4)

**Fig. 1** Incidence rates of emergency department visits for endogenous endophthalmitis. Incidence rates (error bars represent 95% confidence interval [CI]) of emergency department visits for endogenous endophthalmitis from 2006 to 2017 have been increasing per 100,000 from 0.10 (95% CI: 0.07–0.12) in 2006 to 0.25 (95% CI: 0.21–0.30) in 2017 ( $p < 0.05$ ).**Fig. 2** Median inflation-adjusted cost of ED visits. Median inflation-adjusted cost of ED visits (error bars represent interquartile range [IQR]) for EE has increased from \$1229 (IQR: \$690–1563) in 2006 to \$2529 (IQR: \$1538–4038) in 2017 ( $p = 0.23$ ).

Overall mortality rate was 12.9% and increased from 8.6% (95% CI: 3.8–18.3%) in 2006 to 13.8% (95% CI: 9.7–19.2%) in 2017 ( $p = 0.94$ ).

### Systemic risk factors

On multivariate analysis, factors associated with hospital admission included older age, specifically  $\geq 81$  years (odds ratio [OR] 32.59; [95% confidence interval (CI)]: 2.95–359.78]), and patients with the following comorbidities: pneumonia (OR 9.64 [95% CI: 1.25–74.35]), IVDU (OR 14.90 [95% CI: 1.67–133.16]), and renal/urinary tract infections (OR 4.09 [95% CI: 1.77–9.48]), (Table 3).

**Table 3.** Predictors of admission and mortality among patients coming to emergency department with Endogenous Endophthalmitis as the primary diagnosis (weighted).

	Admission		Mortality	
	Multivariate, Adjusted (Odds ratio, 95% confidence interval)	P value	Multivariate, Adjusted (Odds ratio, 95% confidence interval)	P value
Age (reference 0–20 years)				
21–40	1.51 (0.20–11.48)	0.691	2.40 (0.40–14.50)	0.340
41–60	9.25 (1.54–55.43)	0.015	3.56 (0.73–17.32)	0.115
61–80	18.93 (1.64–217.85)	0.018	5.02 (1.08–23.29)	0.039
≥81	32.59 (2.95–359.78)	0.004	2.84 (0.56–14.36)	0.208
Sex (reference men)				
Women	0.46 (0.19–1.14)	0.095	1.17 (0.84–1.62)	0.361
Primary Payer (reference Medicare)				
Medicaid	1.54 (0.28–10.41)	0.658	0.99 (0.60–1.64)	0.980
Private Insurance	1.37 (0.27–6.87)	0.703	0.71 (0.43–1.17)	0.176
Self Pay	0.12 (0.02–0.66)	0.015	0.65 (0.28–1.51)	0.312
No charge	1		1.00	
Other	0.11 (0.02–0.64)	0.014	1.07 (0.33–3.45)	0.905
Comorbidities (reference not having the comorbidity)				
Diabetes	2.10 (0.66–6.62)	0.207	0.49 (0.33–0.73)	<0.001
HIV/AIDS/Immune Deficiency	1		2.58 (1.26–5.28)	0.010
Heart Failure	0.92 (0.21–3.96)	0.909	2.12 (1.47–3.05)	<0.001
Pneumonia	9.64 (1.25–74.35)	0.030	1.64 (1.17–2.29)	0.004
Endocarditis	5.79 (0.96–34.90)	0.055	0.92 (0.58–1.44)	0.704
IV Drug Use	14.90 (1.67–133.16)	0.016	0.74 (0.41–1.32)	0.308
Gastrointestinal Infections	1		1.00 (0.69–1.43)	0.988
Renal/Urinary Tract Infections	4.09 (1.77–9.48)	0.001	1.87 (1.18–2.97)	0.008
Hepatic Infections/Cirrhosis	1.68 (0.19–15.00)	0.641	1.89 (1.28–2.79)	<0.001

Factors associated with mortality included HIV/immune deficiencies (OR 2.58 [95% CI: 1.26–5.28]), heart failure (OR 2.12 [95% CI: 1.47–3.05]), pneumonia (OR 1.64 [95% CI: 1.17–2.29]), renal/urinary tract infections (OR 1.87 [95% CI: 1.18–2.79]), and hepatic infections/cirrhosis (OR 1.89 [95% CI: 1.28–2.79]). DM was associated with a decreased risk for mortality (OR 0.49 [95% CI: 0.33–0.73]), (Table 3).

## DISCUSSION

There have been few multi-centre investigations examining EE across all regions of the country [15–17]. Previous studies have involved other databases utilizing Medicare insurance billing data for all inpatients (not patients through the emergency department), such as the National Inpatient Sample, but have not evaluated risk factors for mortality or admission [17]. This analysis evaluates risk factors associated with admission and mortality for EE using a large national database evaluating patients presenting to the ED. While the subgroup of IVDU-associated EE has recently been identified as increasing in incidence, our analysis shows that EE at-large has increased regardless of the underlying source [12]. Additionally, multiple comorbidities each demonstrated varying associations with admission or mortality in the setting of EE. These data may be useful in identifying those at higher risk and guiding management early in their clinical presentation.

Incidence rates for EE has been increasing, and the rise in IVDU only explains a subset of this change [12]. We presume a component of this elevation can be attributed to the overall rise of sepsis by 8.7% over the past two decades [18]. Explanations for

growing sepsis rates include the increasing average age of the US population, thereby also increasing susceptibility to more comorbidities and predisposition to systemic infections [19, 20]. Additionally, there has been a greater use of antibiotics resulting in higher rates of antibiotic-resistant infections that also increases the rates of systemic infections [21]. Furthermore, with new advances in medicine, including immunotherapy, chemotherapy, and organ transplantation, there are increasing numbers of patients who are immunocompromised and more susceptible to systemic infections [22]. Finally, recent guidelines have increased surveillance for both sepsis and endophthalmitis, and not necessarily with improved outcomes [5, 6]. Hyperattentive screening paradigms could be contributing to the overdiagnosis of EE in those with non-specific retinal findings (e.g. Roth spots, cotton wool spots, haemorrhages) explained by underlying comorbidities, rather than infection from the bloodstream [6, 23].

The median inflation-adjusted cost of ED visits for EE increased over 11 years, although without statistical significance. A prior study by Friedman et al., evaluated mean inflation-adjusted charge for ED visits for all eye complaints using the NEDS database and found the cost was \$1266 for emergent visits and \$631 for nonemergent visits; these emergency visit expenses appear comparable to those in our study found with EE [24]. Although the study only compared visits from 2006 to 2011, an increase of \$36/visit per year was identified, consistent with the non-significant increase in median cost we noted from 2006 to 2017 in our study [24]. A prior study evaluating EE in the setting of IVDU using the National Inpatient Sample, a large Medicare database, noted the median inflation-adjusted cost per

hospitalization was \$13,560 which also increased over recent years [15]. This expenditure reflects the entire hospital course in contrast with our analysis which accounts only for services rendered during the ED visit. Therefore, it remains important in future studies to determine the cumulative financial burden of EE that extends beyond the ED, and including the respective hospital course, as well as any surgery, follow-up and other medical services following the initial evaluation and management for complications from this disease.

The mortality rate in our study was 12.9%. Other studies evaluating mortality outcomes in patients with EE have noted a range from as low as 4%, to rates closer to our findings at 10% [2, 8]. Studies that cite lower numbers such as 4% by Jackson's group included only patients with bacterial EE and excluded patients with fungal EE (shown to have higher mortality rates, as high as 30%) [2, 6, 25]. Higher rates in our study can be explained by inclusion of both bacterial and fungal EE as well as the inherent bias of using a database derived from ED visits. Patients with EE presenting to the ED might present at a later and more severe stage of the disease process in comparison to patients presenting to an ophthalmology clinic. Furthermore, the median age of our population was 62 which is older than the mean age of patients (52) in Jackson et al.'s study, and therefore our population may have been more susceptible to age-related comorbid conditions [2]. While statistically insignificant, the trend towards increased mortality over time suggests that the risk of mortality may be increasing. This finding could be attributed to the factors highlighted above including an aging population, increased use of immunotherapy, and emergence of novel, more virulent pathogens [25]. Regardless, optimizing systemic antimicrobial management for the septicemia is imperative for treating EE as well as increasing odds for survival of these patients [6, 26].

HIV/immune deficiencies, heart failure, pneumonia, renal/urinary tract infections and hepatic infections/cirrhosis were associated with mortality with immune deficiency having the highest odds ratio for mortality. All of these conditions either result in primary dysfunction of the immune system or predispose individuals to unsustainable, high metabolic demands by which sepsis imposes on human physiology [27]. Studies that have examined mortality in patients with sepsis have noted that patients with primary infections of certain origins such as respiratory or gastrointestinal systems were more likely to have higher rates of organ dysfunction than patients with other sources of sepsis [28]. Furthermore, certain immune deficiencies predispose to septicemia with particular organisms. For example, impaired neutrophil function predisposes to infection with *Apergillus* which portends a more severe course [11]. The compounding factor of immune dysfunction with vulnerability to certain pathogens can help explain why these comorbidities were identified to increase mortality [2, 29, 30]. Further investigation with specific analysis on microbiologic data can further help elucidate these associations.

The two risk factors in our study that increased both mortality and admission were the presence of pneumonia and renal/UTI comorbidities. These two risk factors were also noted to have high prognostic prediction for mortality in Weng et al.'s systemic analysis of endophthalmitis (which included both exogenous and endogenous causes) using a health care database from a Taiwanese population [31]. Although the exact mechanism to explain these associations has yet to be elucidated, there are several postulations to explain this association. Commonly isolated organisms with chronic dialysis include *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas (P.) aeruginosa*, and *Serratia marcescens* which may all be on the rise [23, 32]. In particular, dialysis patients were at higher risk for infection with *P. aeruginosa* than a control group, and showed a more severe septicemic course [33]. Furthermore, dialysis patients are more likely to have external vascular access which is also a risk factor for

bacteremia [34]. Poor prognosis in patients with pneumonia can reflect the overall severity of the patient's septicemia, as septicemia associated with respiratory tract infections has been shown to have higher mortality rates than other systemic comorbidities [28, 35].

In our study, IVDU and endocarditis were associated with increased rate of admission but did not confer an increased risk of mortality. Although we did not stratify the age of our cohort based on comorbidities, we presume these two risk factors did not confer an increased risk of mortality as patients who partake in IVDU and develop septicemia as a consequence tend to be younger. This concept is supported by several case series examining endophthalmitis with IVDU; the mean age in both these series were approximately mid-30s in years and had no reported mortality [36, 37].

DM here was associated with a decrease in mortality. This observation has been noted both in studies evaluating endophthalmitis and in studies looking at mortality trends in patients with sepsis [31, 38]. The mechanism to explain this association remains unclear. Studies have compared coagulation pathways and expression of inflammatory cytokines between patients with DM and patients without DM during sepsis, but no difference between the two cohorts have been identified [39–42]. One hypothesis possibly explaining the improved outcomes in patients with DM is the immune response to hyperglycaemia. Patients with DM chronically experience hyperglycaemia, and appear to have a decreased inflammatory response in this setting; in patients without DM, short term hyperglycaemia is an independent risk factor for mortality from significantly increased cytokine levels in response to this elevated glucose [43–46]. Furthermore, DM diminishes immune function by affecting multiple pathways including polymorphonuclear leukocyte migration and activation, and downregulation of signalling pathways involved in the immune system [47–50]. It is unclear how these multimodal effects of DM affect patients during sepsis and thus warrant further investigation.

Although this study drew from a large, nationally representative sample for a relatively rare disease process, there are inherent limitations from using a database. First, since the NEDS database is derived from coding in medical records, it is susceptible to missing data, errors in documentation, and unverified clinical findings. Furthermore, there is not a specific diagnostic code for EE. We derived our sample size from including patients with both a diagnosis of septicemia and endophthalmitis. By eliminating patients without both of those diagnoses, we might have missed some patients in our cohort, and furthermore we might have erroneously included patients with a diagnosis of septicemia and endophthalmitis not related to the sepsis if patients concurrently had both diagnoses. However, our approach in requiring two distinct diagnostic codes (specifically endophthalmitis and sepsis) was expected to add rigor, and one that buffers the robustness of this analysis, while minimizing the error of including patients who did not have EE. Another limitation inherent to the database is that each visit represented one admission and patients were not able to be followed longitudinally. Therefore, patients who are discharged and return to the ED could be represented more than once, and patients who passed away from EE but after discharge were not included in the mortality data in this study. Next, the database focuses on systemic variables and does not include more granular data such as ophthalmic function (e.g. visual acuity), microbiological or other clinical data to confirm diagnosis of EE, or severity of illness and presentation limiting some of the outcomes and interpretations that can be drawn. Since the database includes patients who first present to the ED it might not be representative of patients who are diagnosed with EE after being admitted in the hospital for sepsis. Finally, hospitals without an ophthalmology service in their hospital might have missed cases of EE.



## CONCLUSION

EE, regardless of underlying source, has recently increased in incidence throughout the US. Explanations for this increase include an aging population, advances in medical care increasing the numbers of immunocompromised individuals, and hyperattentive screening paradigms. The two systemic factors that conferred both an increase in mortality and admission were pneumonia, and renal/UTI. These factors predispose to infections with more virulent organisms and have been shown to act as independent markers for worse prognosis in patients with sepsis. Finally, DM was shown to be associated with decreased mortality, which has also been identified in other studies evaluating both sepsis and endophthalmitis. This association warrants further investigation to elucidate how glycaemic regulation affects immune function and has the potential to influence how glucose is managed in patients with sepsis during times of such high metabolic demand. In conclusion, EE will continue to present as an increasing diagnostic and therapeutic challenge; identification of patient demographics, prognostic factors and visit characteristics may serve to improve current management paradigms.

## SUMMARY TABLE

What was known before

- Endogenous endophthalmitis (EE) comprises approximately 2–8% of all cases of endophthalmitis.
- The eye becomes a secondary site of inoculation with hematogenous spread of infection from elsewhere.

What this study adds

- EE has increased in incidence throughout US.
- The two systemic factors that conferred both an increase in mortality and admission were pneumonia, and renal/UTI.
- Additional exploration of the potential protective association of DM with decreased mortality in this context is needed.

## DATA AVAILABILITY

The data that support the findings of this study are available from the Nationwide Emergency Department Sample (NEDS) but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of NEDS.

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#### AUTHOR CONTRIBUTIONS

Each author contributed to the manuscript as follows: design and conduct of the study (LT, JC, AWS, FAW, MPB); collection, management, analysis, and interpretation of the data (LT, JC, MPB); preparation, review, or approval of the manuscript and decision to submit for publication (LT, JC, AWS, FAW, MPB).

#### FUNDING

This research was supported by unrestricted grants including Research to Prevent Blindness to the Wilmer Eye Institute (Baltimore, MD, USA) as well as from the VitreoRetinal Surgery Foundation in Edina, MN, USA (LT, MPB) and the Kogod Family (MPB).

#### COMPETING INTERESTS

The authors declare no competing interests.

#### ADDITIONAL INFORMATION

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