Burden of Invasive Extraintestinal Pathogenic *E. coli* Disease Among Older **Adult Patients** Treated in Hospitals in the United States

KEY FINDINGS STATEMENTS

- This analysis of nearly 20,000 patient records from the Premier Healthcare Database revealed that IED is associated with significant medical resource utilization and all-cause medical costs, which were largely driven by inpatient
- Microbiological confirmation of *E. coli* from a normally sterile body site was found in more than half of the patients, while the remaining had microbiological confirmation of *E. coli* in urine with signs of sepsis
- Nearly all patients with an IED encounter required treatment in an inpatient setting, with one third of patients requiring admission to an intensive care unit

CONCLUSIONS

- IED is associated with a substantial clinical and economic burden both during the initial encounter and over the following year
- The majority of IED cases were community-acquired and mortality associated with IED is considerable
- The significant medical costs experienced beyond the initial IED event indicate that the burden of IED does not conclude at the end of the index hospitalization and point to a long-term impact of the disease
- The results of this study provide pertinent information to stakeholders and policy makers and suggest an unmet need for preventive measures against IED in order to mitigate the high burden associated with the disease

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Disclosures

LH-P, JG, BB, ACE, and **NK** are employees of Janssen; MG-L, RB, and **MC** are employees of Analysis Group Inc., which received funding from Janssen for this research

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All patients

INTRODUCTION

- Extraintestinal pathogenic Escherichia coli (E. coli; ExPEC) comprises a pathogenic group of *E. coli* strains possessing the ability to colonize and infect normally sterile body sites and cause severe invasive ExPEC disease (IED), including bacteremia and sepsis
- In the United States (US), E. coli is a leading cause of community-onset sepsis, particularly among older adults³
- Sepsis is one of the most serious consequences of ExPEC in terms of severity and mortality rate, 4 with nearly 2 million cases of sepsis arising in the US each year and almost 30,000 patient deaths as a result⁵
- Incidence of IED continues to rise, and this increase is exacerbated by aging populations and a high prevalence of antimicrobial-resistant E. coli strains
- However, little is known about the specific burden of IED in US hospitals

OBJECTIVES

To describe medical resource utilization and cost burden of IED during the initial IED index encounter, as well as over a 12-month follow-up period, in older adults in the US

METHODS

Data source

 De-identified data from the Premier Healthcare Database (October 1, 2015) to March 31, 2020) were used

Study design

• A retrospective design was used to conduct this study (**Figure 1**)

Figure 1. Study Design



- The first documented IED encounter was defined as the index encounter
- IED encounters were identified based on a positive *E. coli* culture (**Figure 2**; IED encounters that met the definition for both Group 1 and Group 2 were classified in Group 1)

Figure 2. Definition of IED

1: IED with microbiologica
nation from blood or other
nation from blood or othe normally sterile sites

- A positive culture of E. coli in a
- normally sterile site ≥1 sign of SIRS, or signs of sepsis, as per the CDC's clinical surveillance
- No positive culture for other bacteria or fungal pathogens

Group 2: IED with microbiological presence of signs of sepsis

- A positive culture of E. coli in urine • Sepsis, as per the CDC's clinical surveillance definition*
- ≥1 diagnosis for UTI No positive culture for E. coli in a normally sterile site

N=9,538 (48.2%)

- No positive culture for other bacteria or fungal pathogens
- The sepsis clinical surveillance definition utilizes an algorithm defined by Rhee et al. (2017),4 and details and diagnosis codes were updated using the CDC's Hospital Toolkit for Adult Sepsis Surveillance (March 2018). The algorithm was validated using medical records from 510 randomly selected hospitalizations, which were stratified into those that did and did not meet sepsis surveillance criteria.

CDC. Centers for Disease Control and Prevention: IED. invasive extraintestinal pathogenic E. coli disease; SIRS, systemic inflammatory response syndrome

• Eligible patients ≥60 years old with ≥1 IED hospital encounter were included

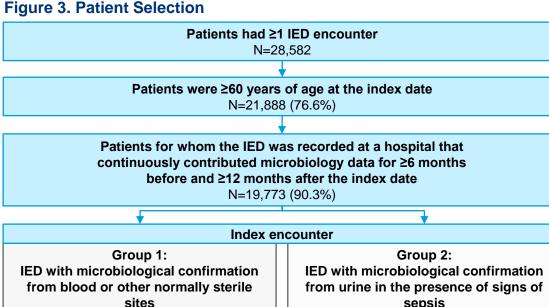


Table 1. Patient and Hospital Characteristics on the Index Date

Characteristics	N=19,773
Patient characteristics	
Age, mean ± SD (median)	76.8 ± 8.9 (77.0)
Sex, n (%)	
Female	13,321 (67.4)
Male	6,451 (32.6)
Unknown	1 (0.0)
Race, n (%)	
White	16,234 (82.1)
Black	1,799 (9.1)
Asian	646 (3.3)
Other	909 (4.6)
Unknown	185 (0.9)
Comorbidities	
CCI score, mean ± SD (median)	2.5 ± 2.1 (2.0)
≥3, n (%)	8,398 (42.5)
Selected comorbidities, n (%)*	
Chronic pulmonary disease	5,036 (25.5)
Congestive heart failure	5,803 (29.3)
Dementia	4,465 (22.6)
Renal disease	6,529 (33.0)
High blood pressure	15,849 (80.2)
Hospital characteristics	
Number of beds, n (%)	
0–199	4,978 (25.2)
200–499	8,763 (44.3)
≥500	6,032 (30.5)
Region, n (%)	
Midwest	4,721 (23.9)
Northeast	3,271 (16.5)
South	11,046 (55.9)
West	735 (3.7)

CCI, Charlson Comorbidity Index; n (%), number (percentage) of patients with the defined characteristic; SD, standard deviation More than 1 option could apply (i.e., categories are not mutually exclusive)

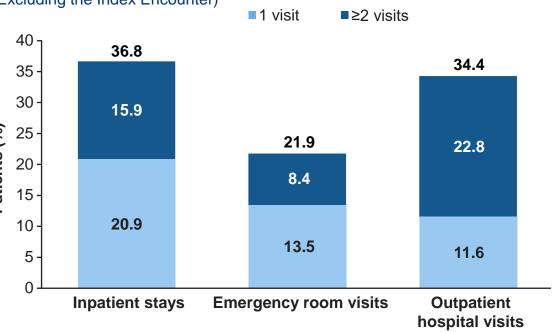
Table 2. Characteristics of the Index Encounter

Characteristics	N=19,773
Onset of IED, n (%)*	
Hospital-onset	1,125 (5.7)
Community-onset	18,648 (94.3)
Health care-associated community-acquired	4,787 (25.7)
Non-health care-associated community-acquired	13,861 (74.3)
Point of origin, n (%)	
Transfer from other health care facility	856 (4.3)
Non-health care facility	16,820 (85.1)
Clinic	1,212 (6.1)
SNF/ICF	821 (4.2)
Other	64 (0.3)
Discharge status, n (%)	
Home	8,695 (44.0)
Hospice or rehabilitation/long-term care/nursing facility	1,961 (9.9)
SNF/ICF	6,864 (34.8)
Death	1,348 (6.8)
Other (including other health care facility)	905 (4.6)
Type of encounter, n (%)	
Inpatient stay	19,084 (96.5)
Duration of inpatient stay, days, mean \pm SD (median)	$6.9 \pm 5.7 \ (5.0)$
1–5 days, n (%)	9,927 (52.0)
6–10 days, n (%)	6,399 (33.5)
11–15 days, n (%)	1,573 (8.2)
>15 days, n (%)	1,185 (6.2)
Emergency room visit	554 (2.8)
Outpatient hospital visit	135 (0.7)
ICU admission, n (%)	6,405 (32.4)
Duration of ICU stay, days, mean \pm SD (median)	3.7 ± 4.1 (2.0)
Transferred to ICU on the same day as admission, n (%)	4,774 (74.5)
In-hospital death at 1-year post-index, n (%)	2,156 (10.9)
Time from index date to death, days, mean \pm SD (median)	43.1 ± 80.3 (6.0)
IED recurrence rate at 1-year post-index, n (%)	477 (2.4)

was available; n (%), number (percentage) of patients with the defined characteristic; SD, standard deviation; SNF, skilled nursing facility Hospital-onset IED was defined as the presence of positive or presumptively positive *E. coli* culture from a normally sterile site or urine collected ≥3 days after the initial admission to the hospital, when the infection was not present at admission; community-onset IED was defined as a positive or presumptive care-associated if any of the following conditions were met: (i) a documented procedure code for anesthesia, surgery, hemodialysis, chemotherapy, or other injections within 30 days of the index encounter; (ii) a hospitalization for ≥2 days within 90 days of the index encounter; (iii) transferred from a nursing home

Figure 4. Medical Resource Utilization and Time to Inpatient Readmission **Following Index Encounter Discharge**

A. All-Cause Medical Resource Utilization in the 12-Month Follow-Up Period (Excluding the Index Encounter)



B. Time to Readmission Among Patients With ≥1 Stay (N=7,275)

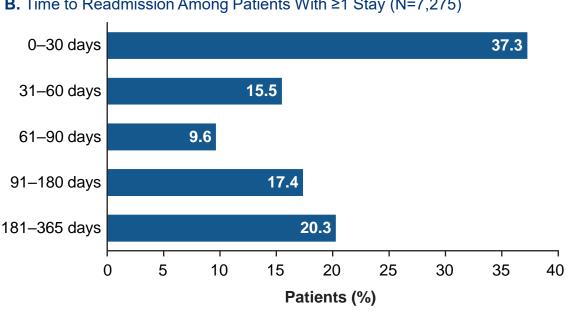
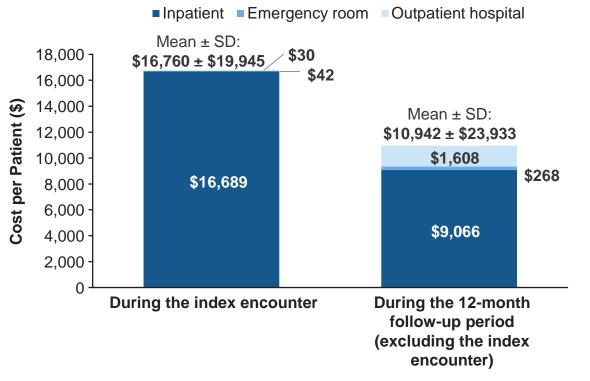
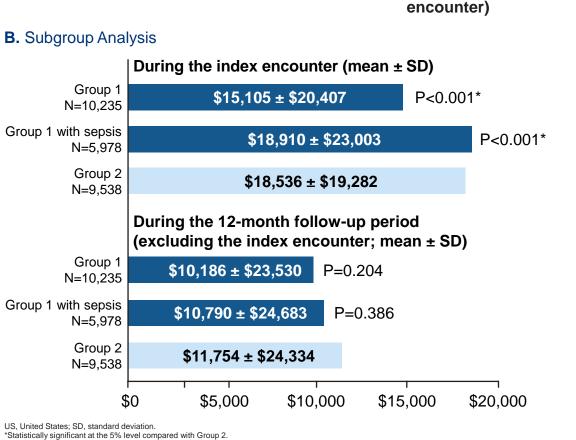


Figure 5. All-Cause Medical Costs per Patient (2021US\$) in the Overall **Population and Among Subgroups**

A. Overall Population





Study outcomes and statistical analysis

- Descriptive patient, hospital, and index IED characteristics were reported for the index encounter
- Medical resource utilization and costs (2021 US dollars [\$]) per patient from a hospital's perspective were evaluated separately for the index encounter and over the 12-month follow-up period (excluding the index encounter)
- In a subgroup analysis, costs were stratified and compared by type of IED (i.e., Group 1 and Group 1 with sepsis vs Group 2) using Wilcoxon rank-sum tests for the continuous variables and Chi-square tests for the categorical

RESULTS

Study sample, patient characteristics, and characteristics of the index

- A total of 19,773 patients with IED were identified, including 10,235 patients (51.8%) with microbiological confirmation of *E. coli* from a normally sterile site (i.e., Group 1; including 5,978 [58.4%] in Group 1 who had signs of sepsis) and 9,538 patients (48.2%) with microbiological confirmation of *E. coli* from urine with signs of sepsis (Group 2)
- Mean age was 76.8 years and 67.4% were female (Table 1)
- Most index encounters were community-onset (94.3%) rather than hospitalonset (5.7%), with approximately 25% of community-onset encounters being healthcare-associated
- Following discharge, only 44.0% of patients went back to their home whereas 34.8% were discharged to a skilled nursing facility or an intermediate care
- In-hospital fatality rate was 6.8% during the index encounter and reached 10.9% at 1-year post-index, with an average time to death of 43.1 days following the index date (**Table 2**)

Medical resource utilization

- The most frequent type of hospital encounter at the index encounter was an inpatient stay (96.5%; mean duration of 6.9 days), with 32.4% of patients requiring transfer to an intensive care unit (mean duration of 3.7 days;
- During the 12-month follow-up, 2.4% of patients had an IED recurrence (Table 2) and 36.8% were re-hospitalized for any reason (Figure 4A):
- Among those who had another inpatient admission following their index encounter, 37.3% were readmitted within the first 30 days of discharge (Figure 4B)

Medical costs

 Average all-cause medical costs amounted to \$16,760 during the index encounter and \$10,942 during the 12-month follow-up, both largely driven by inpatient costs (Figure 5A)

Subgroup analysis

Compared with Group 1, IED encounters from Group 2 were associated with higher all-cause medical costs during the index encounter (\$18,536 vs \$15,105, P<0.001); this difference was less pronounced during the 12month follow-up (\$11,754 vs \$10,186, P=0.204; **Figure 5B**) and when Group 1 was limited to encounters where IED was associated with signs of sepsis (\$18,536 vs \$18,910, P<0.001)

LIMITATIONS

- IED encounters were identified based on information available from microbiology laboratory tests, diagnosis codes, and procedure codes; accordingly, some patients may have been misclassified as having, or not having, IED. Nonetheless, for the identification of sepsis, this study relied on the Centers for Disease Control and Prevention clinical surveillance definition, which has been validated previously
- The Premier database is limited to IED encounters that occurred in a hospital setting, and medical services received outside of a given hospital were not captured
- Further, because some patients died before the end of the 12-month followup period, annualized estimates of medical resource utilization and costs may have been impacted for these patients

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N=10,235 (51.8%)

Group 1 with signs of sepsis

N=5,978 (58.4%)

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