

# Clinical Characteristics of Invasive Extraintestinal Pathogenic *Escherichia coli* Disease Among Older Adult Patients Treated in Hospitals in the United States

## KEY FINDINGS STATEMENTS

- This study identified nearly 20,000 patients aged ≥60 years who had an invasive extraintestinal pathogenic *Escherichia coli* disease (IED) encounter in the United States; more than half had microbiological confirmation of *E. coli* from blood or normally sterile body sites, while the remaining patients had microbiological confirmation of *E. coli* from urine with signs of sepsis
- IED was associated with an acute burden during the initial encounter; 96.5% required hospitalization (mean duration of stay of 6.9 days) with nearly one-third of patients requiring intensive care unit (ICU) admission and 75% of them being transferred to the ICU on the same day as admission. Most cases were community acquired
- In the 12 months following the initial IED encounter, patients had substantial all-cause medical resource utilization and considerable in-hospital mortality

## CONCLUSIONS

- This study described the course of IED in a large representative sample of older adult patients in US hospitals
- IED may lead to poor outcomes even after the initial encounter is resolved
- These findings emphasize the need for increased awareness and surveillance of IED and its consequences and the potential benefit of preventative measures

## Acknowledgments & Disclosures

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## INTRODUCTION

- Extraintestinal pathogenic *E. coli* (ExPEC) can infect normally sterile body sites and lead to invasive ExPEC disease (IED), also known as invasive *E. coli* disease<sup>1,2</sup>
- IED comprises sepsis (including urosepsis), bacteremia, peritonitis, meningitis, and other infectious syndromes<sup>1,2</sup>
- The risk of IED increases progressively beyond 60 years of age,<sup>3</sup> and can lead to severe outcomes, including death, particularly among older adults more likely to have antibiotic-resistant infections<sup>4</sup>
- E. coli* is a leading cause of community-acquired sepsis, a main reason of hospitalization and death in the United States<sup>1,5,6</sup>

## OBJECTIVE

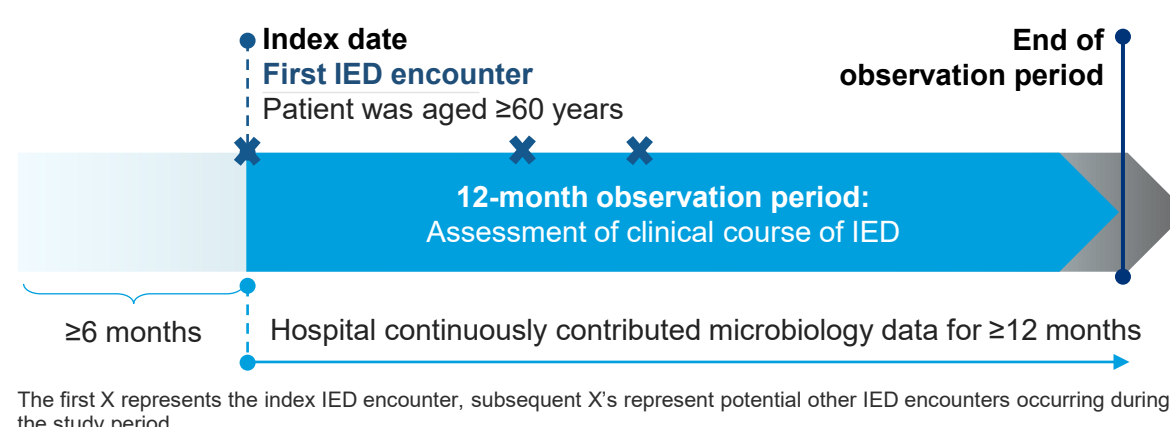
- To describe and characterize the short-term as well as the longer-term outcomes following an IED encounter among patients ≥60 years old hospitalized in the United States

## METHODS

### Data source and study design

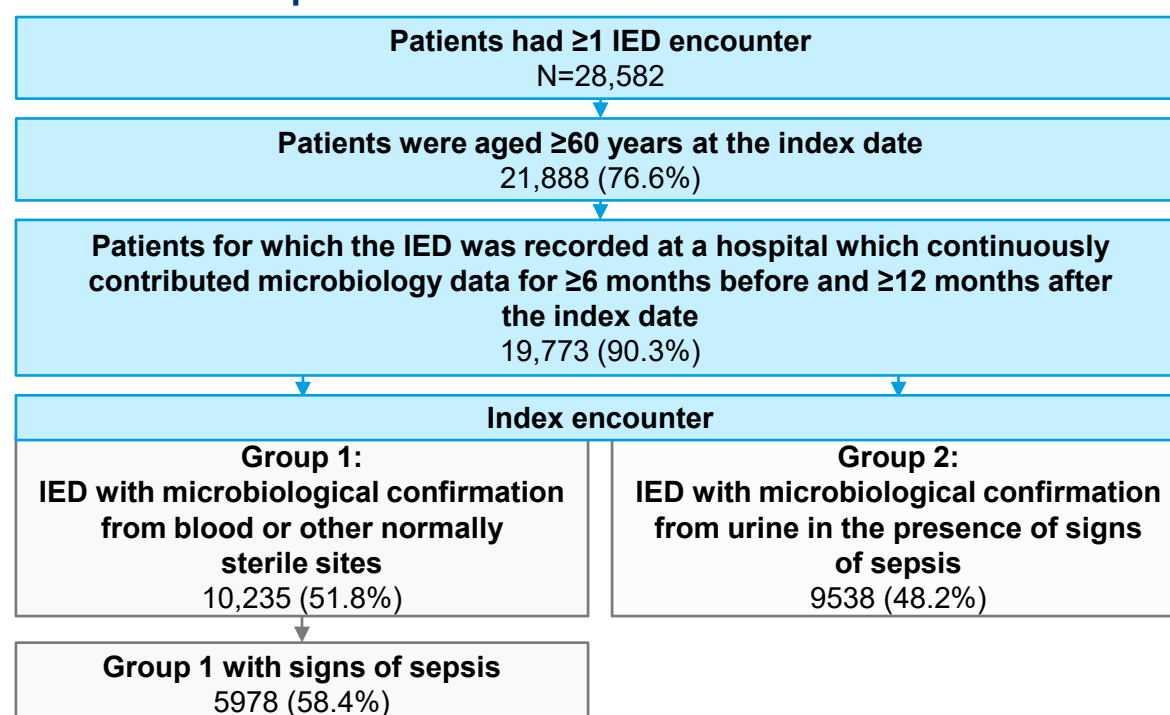
- This retrospective study (Figure 1) used de-identified hospital data from the Premier Healthcare Database (October 1, 2015 to March 31, 2020)
  - Medical resource utilization and cost burden of IED from this study have been previously presented<sup>7</sup>

### FIGURE 1: Study design



- The index encounter was defined as the first encounter with a positive *E. coli* culture in blood or other normally sterile body site (group 1) or a positive *E. coli* culture in urine with urinary tract infection (UTI) and signs of sepsis<sup>8</sup> (group 2), in the absence of other pathogens
- Eligible patients ≥60 years old with ≥1 IED hospital encounter were included (Figure 2)

### FIGURE 2: Sample selection



Group 1 was defined by a positive *E. coli* culture in either blood or in any other normally sterile body site and hospitalization with signs of SIRS or sepsis (as per the CDC's clinical surveillance definition), and no positive culture for other bacteria or fungal pathogens. The CDC's clinical surveillance definition for sepsis utilizes an algorithm defined by C Rhee et al.<sup>8</sup> and details and diagnosis codes were updated using CDC's Hospital Toolkit for Adult Sepsis Surveillance (March 2018); the algorithm was validated using medical records from 510 randomly selected hospitalizations. Group 2 was defined by a positive *E. coli* culture in urine with signs of sepsis (as per the CDC's surveillance definition) and a diagnosis of UTI, with no positive culture for *E. coli* in blood or normally sterile body sites, and no positive culture for other bacteria or fungal pathogens. CDC, Centers for Disease Control and Prevention; SIRS, systemic inflammatory response syndrome.

### Study outcomes and statistical analysis

- Patient, hospital, and IED characteristics, including characterization of antimicrobial resistance of *E. coli* isolates, were descriptively reported for the index encounter
- Medical resource utilization, IED recurrence, and in-hospital mortality were descriptively reported during the index encounter and over the 12-month observation period (excluding the index encounter)

## RESULTS

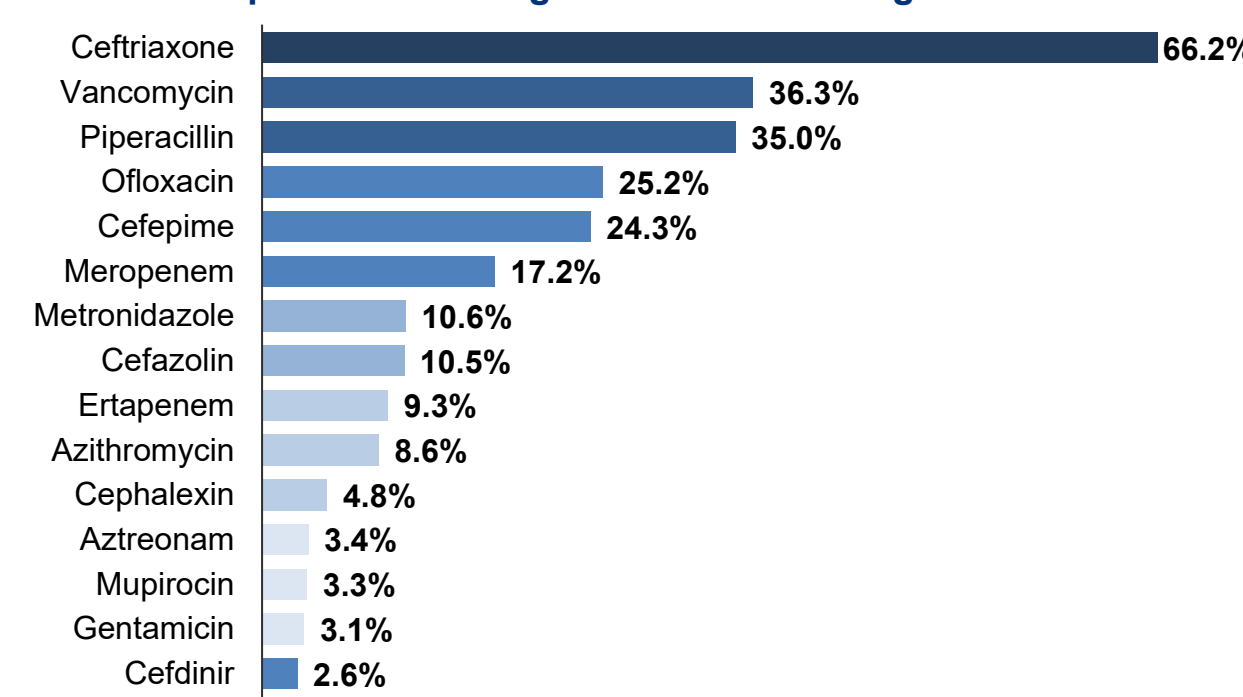
## RESULTS

### TABLE: Patient, hospital, and index IED encounter characteristics

|  | All patients (N=19,773)     |
|--|-----------------------------|
| <b>Patient characteristics</b>                         |                             |
| Age, mean ± SD (median), y                             | 76.8 ± 8.9 (77.0)           |
| Female, n (%)  | 13,321 (67.4)               |
| <b>Race, n (%)</b>                                     |                             |
| White  | 16,234 (82.1)               |
| Black  | 1799 (9.1)                  |
| Asian  | 646 (3.3)                   |
| Other  | 909 (4.6)                   |
| Unknown  | 185 (0.9)                   |
| <b>Selected comorbidities<sup>a</sup>, n (%)</b>       |                             |
| High blood pressure                                    | 15,849 (80.2)               |
| Renal disease  | 6529 (33.0)                 |
| Congestive heart failure                               | 5803 (29.3)                 |
| Chronic pulmonary disease                              | 5036 (25.5)                 |
| Dementia   | 4465 (22.6)                 |
| CCI score, mean ± SD (median) ≥3, n (%)                | 2.5 ± 2.1 (2.0) 8398 (42.5) |
| <b>Hospital characteristics</b>                        |                             |
| Number of beds, n (%)                                  |                             |
| 0–199  | 4978 (25.2)                 |
| 200–499  | 8763 (44.3)                 |
| ≥500   | 6032 (30.5)                 |
| <b>Region, n (%)</b>                                   |                             |
| Midwest  | 4721 (23.9)                 |
| Northeast  | 3271 (16.5)                 |
| South  | 11,046 (55.9)               |
| West   | 735 (3.7)                   |
| <b>IED characteristics</b>                             |                             |
| Onset of IED, n (%)                                    |                             |
| Hospital onset   | 1125 (5.7)                  |
| Community onset  | 18,648 (94.3)               |
| Healthcare-associated community-acquired               | 4787 (25.7)                 |
| Nonhealthcare-associated community-acquired            | 13,861 (74.3)               |
| <b>Type of encounter, n (%)</b>                        |                             |
| Inpatient stay   |                             |
| Inpatient stay   | 19,084 (96.5)               |
| Duration of inpatient stay, mean ± SD (median), days   | 6.9 ± 5.7 (5.0)             |
| Emergency room visit                                   | 554 (2.8)                   |
| Outpatient hospital visit                              | 135 (0.7)                   |
| ICU admission, n (%)                                   |                             |
| ICU admission  | 6405 (32.4)                 |
| Duration of ICU stay, mean ± SD (median), days         | 3.7 ± 4.1 (2.0)             |
| Transferred to ICU on the same day as admission, n (%) | 4774 (74.5)                 |
| Mechanical ventilation, n (%)                          | 1710 (8.6)                  |

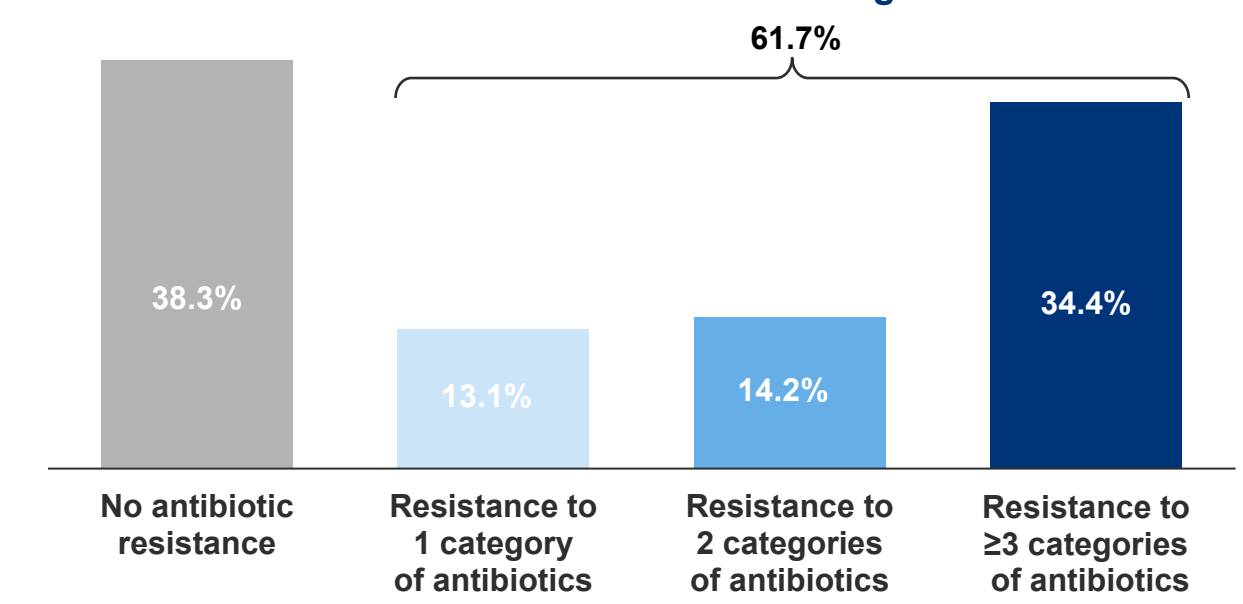
<sup>a</sup>The top 5 most common comorbidities are presented. CCI, Charlson Comorbidity Index.

### FIGURE 3: Top 15 antibiotic agents received during the index encounter

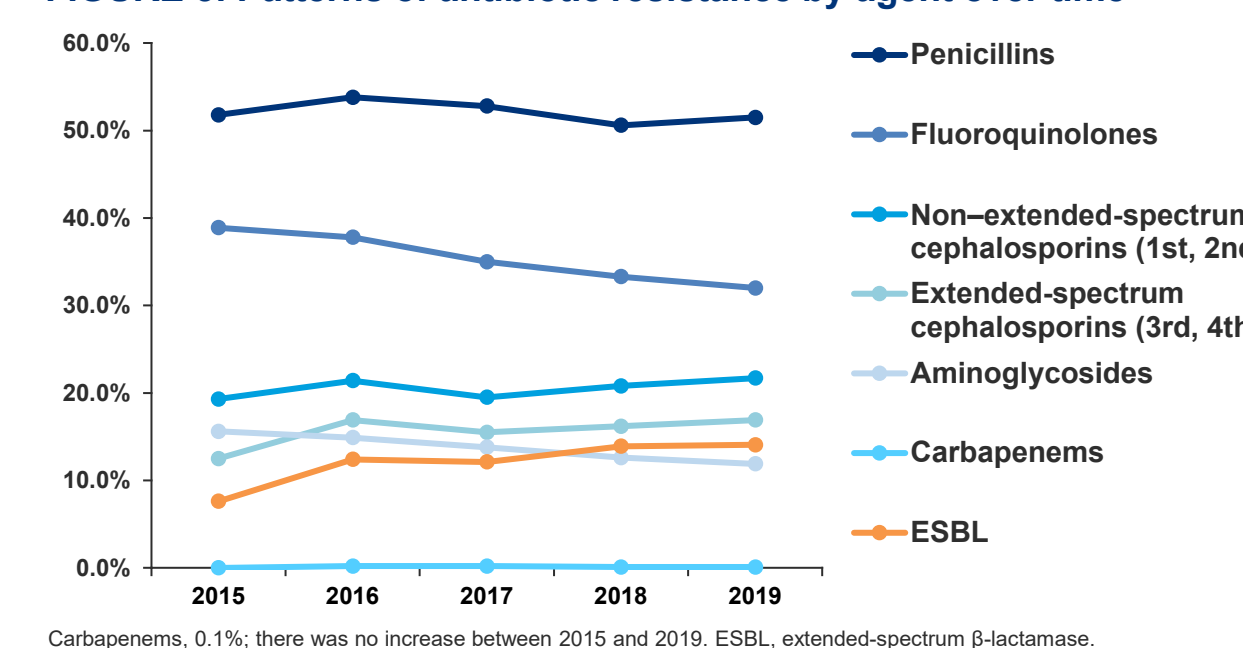


Patients may or may not be receiving some of these antibiotics at the same time.

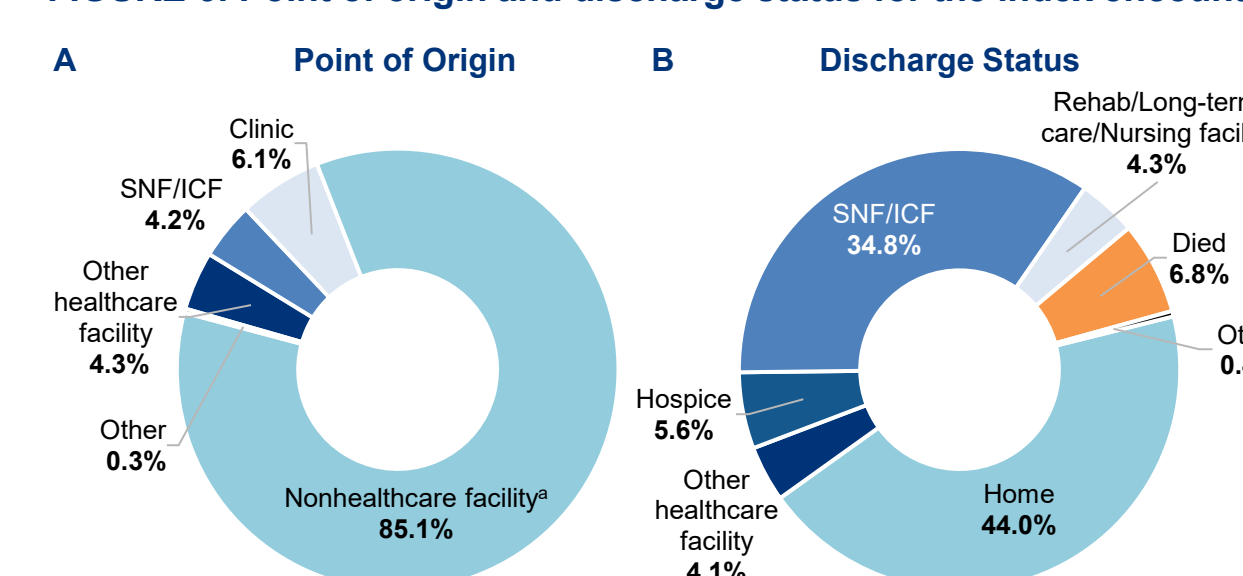
### FIGURE 4: Patterns of antibiotic resistance during the index encounter



### FIGURE 5: Patterns of antibiotic resistance by agent over time

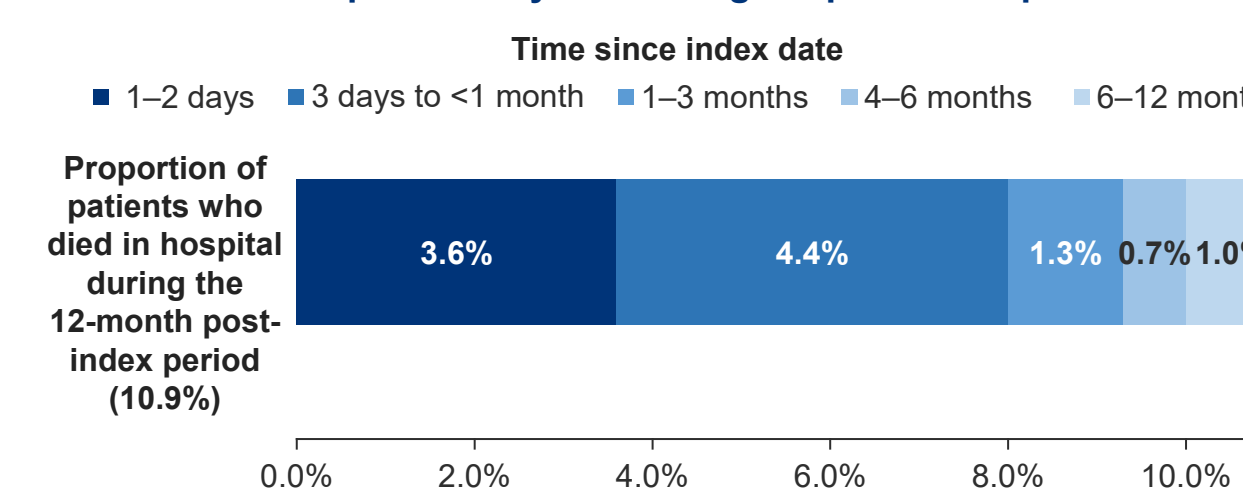


### FIGURE 6: Point of origin and discharge status for the index encounter

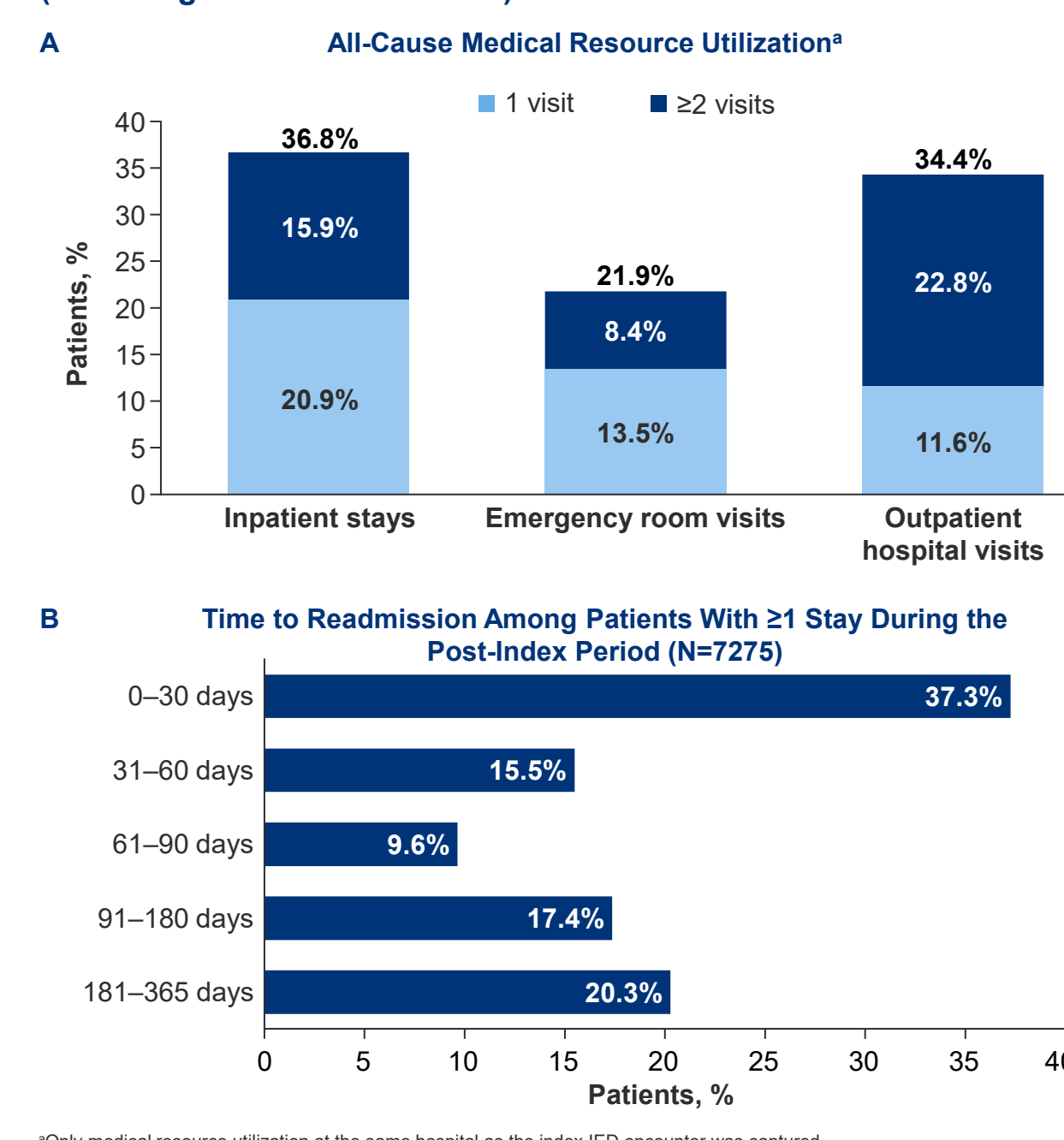


<sup>a</sup>Nonhealthcare facility point of origin indicates that the patient was not transferred from another healthcare facility (eg, originated from home, prison, or other nonhealthcare institution). ICF, intermediate care facility; SNF, skilled nursing facility.

### FIGURE 7: In-hospital fatality rate during the post-index period



### FIGURE 8: Medical resource utilization during the post-index period (excluding the index encounter)



<sup>a</sup>Only medical resource utilization at the same hospital as the index IED encounter was captured.

### Study sample and patient, hospital, and IED characteristics

- A total of 19,773 patients with IED were identified: 10,235 patients (51.8%) were classified in group 1, among whom 5978 (58.4%) had signs of sepsis, and 9538 patients (48.2%) were classified in group 2 (Figure 2)<sup>7</sup>
- Mean age was 76.8 years and 67.4% were female (Table)
- Most index encounters involved community-onset (94.3%) rather than hospital-onset (5.7%) IED and required hospitalization (96.5%); mean duration, 6.9 days; 32.4% of patients were admitted to the ICU (mean duration, 3.7 days)
- During the index encounter, patients received a mean of 2.9 antibiotic agents and 30.1% received ≥4 agents (data not shown)
  - The 3 most prevalent were ceftriaxone (66.2%), vancomycin (36.3%), and piperacillin (35.0%; Figure 3)
- Most *E. coli* isolates showed resistance to ≥1 antibiotic category (61.7%), and 34.4% were classified as multidrug resistant<sup>9</sup> (ie, ≥3 categories; Figure 4)
- The proportion of *E. coli* isolates resistant to most of the antibiotic categories was stable between 2015–2019, though a decreasing trend for fluoroquinolones (37.8–32.0%,  $P<0.001$ ) and aminoglycosides (15.6–11.9%,  $P=0.002$ ) was observed (Figure 5)

### Clinical outcomes post IED

- Most encounters originated in a nonhealthcare facility (85.1%); following discharge, 34.8% of patients were transferred to a SNF/ICF and 44.0% were discharged to their home (Figure 6A and Figure 6B)
- In-hospital fatality rate for all patients was 6.8% during the index encounter (Figure 6B) and reached 10.9% at 1 year post index (Figure 7)
  - The in-hospital fatality rate was similar for group 2 vs group 1 IED during the index encounter (7.0% vs 6.6%,  $P=0.219$ ), but was larger for group 2 IED at 1 year post index (12.2% vs 9.7%,  $P<0.001$ )
- 1 year post index, 2.4% of patients had an IED recurrence (data not shown) and 36.8% were readmitted to the hospital for any reason, 37.3% within the first 30 days of discharge (Figure 8A and Figure 8B)<sup>7</sup>

### LIMITATIONS

- IED encounters were identified from microbiology data and diagnosis/procedure codes; misclassification of IED cannot be excluded
- The Premier Healthcare Database is limited to IED encounters occurring in a hospital setting. Medical services received outside of the hospital where the IED encounter was recorded and pharmacy prescription fills were not captured
- The incidence of antibiotic resistance may have been underestimated because in real-world clinical practice, specimens are not tested for resistance to all possible antibiotics
- Death was identified based on discharge status such that deaths occurring outside of the hospital were not captured

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