

# Clinical and Economic Burden of Invasive *Escherichia Coli* Disease Among Medicare Insured Patients

## KEY FINDINGS AND CONCLUSIONS

- Invasive *E. coli* disease adds significant clinical and economic burden in Medicare patients, with total healthcare costs substantially higher than for matched controls.
- This study found that invasive *E. coli* disease had substantial impact on morbidity and mortality.
- These findings highlight the need for novel preventive measures, early diagnosis and effective treatment strategies for invasive *E. coli* disease.

## STRENGTHS AND LIMITATIONS

- This is one of the first claims-based retrospective studies to have implemented an ICD-10 diagnosis codes-based algorithm for IED identification.
- Laboratory data that are often used to identify IED cases were not available and the use of an ICD-10 diagnosis codes-based algorithm may have led to some misclassification.
- This study used a preliminary PSM to adjust for differences in baseline characteristics and assess incremental burden associated with IED by comparing matched cases and controls. Further evaluation and validation of diagnosis categories used in PSM is ongoing.
- Low-income subsidy (LIS) information was not available for Medicare enrollees, thereby, we were not able to adjust for LIS status in this study.
- The presence of a diagnosis code on a medical claim does not indicate a positive presence of disease, as the diagnosis code may be incorrectly coded or included as rule-out criteria rather than the actual disease.

## INTRODUCTION

- Escherichia coli* (*E. coli*) is a diverse gram-negative bacterial species associated with gastrointestinal infections and extraintestinal pathologies. [1-2]
- Extraintestinal pathogenic *E. coli* may cause invasive *E. coli* disease (IED), and may include sepsis, bacteremia, peritonitis, and/or meningitis, and is associated with high morbidity and mortality. [1-4]
- The underlying mechanism of IED remains unclear but older adults are found to be at an increased risk. [5-6]
- Little is known about healthcare burden associated with IED among high-risk populations such as older adults (≥65 years) in the US.

## OBJECTIVES

- This study aims to describe patient characteristics and clinical and economic burden of IED among Medicare patients.

## METHODS

### Data Source

- This study was conducted using STATinMED RWD Insights database, which is an all-payer medical and pharmacy claims data source covering approximately 80% of the US healthcare system. This database provides comprehensive capture of inpatient, outpatient, emergency department, office visits, and pharmacy claims for adult patients enrolled in Medicare Fee-for-Service and Advantage plans with ability to continuously track patients as they move across insurance plans and channels.

### Study Sample

- Study population consisted of adult patients with medical claims indicating IED (Figure 1) between January 1, 2018, and December 31, 2018 (Identification period), with no medical encounters indicating IED in the 12 months before the index date (Baseline period).
- Index date was defined as the date of first claim with indication of IED.
- Patients were ≥65 years and had Medicare insurance at index date.
- Patients had continuous data capture (≥1 medical or pharmacy claim) both in the 12 months prior to index date (baseline period) and 12 months post-index (follow-up period).

### Cohorts

- Patients were assigned to the following cohorts based on IED diagnosis.
  - IED patients (cases): Had ≥1 claim(s) with diagnosis codes indicating IED during Identification period.
  - Non-IED patients (controls): No medical claims indicating IED during baseline and Identification period.

### Study Outcomes

- Outcomes were captured during the follow-up period spanning from the index date until the earliest of death, 12 months post-index date, or the end of the study period, i.e., December 31, 2019.
- All-cause healthcare resource use (HCRU) and costs were examined during the follow-up period. HCRU was reported as per patient per year (PPPY) and costs were reported as per patient per month (PPPM). Costs were adjusted to 2020 U.S. dollars using the medical care component of the Consumer Price Index (CPI).
- Time to all-cause death was compared between matched IED and non-IED patients.

### Statistical Analysis

- Baseline demographic and clinical characteristics were evaluated using descriptive statistics, before the matched analyses were performed.
- Preliminary propensity score matching (PSM) was implemented with 1:1 nearest neighbor matching algorithm to adjust for differences in selected baseline patient characteristics – age, gender, Charlson Comorbidity Index (CCI) score, urinary tract infection (UTI), and pyelonephritis, with further evaluation and validation of diagnosis categories used in PSM ongoing.
- Generalized linear models (GLMs) were used to compare all-cause HCRU and costs between matched IED and non-IED patients.
- Time to all-cause death was compared between cohorts using Kaplan-Meier analyses with log-rank tests and Cox proportional hazards models reporting hazard ratios with 95% confidence intervals.

## RESULTS

### Patient Population

#### Figure 1 and 2:

- After selection criteria were applied, a total of 32,247 IED cases and 283,779 non-IED patients were identified.
- After adjustment with PSM, the sample included 29,041 IED cases and 29,041 non-IED controls.

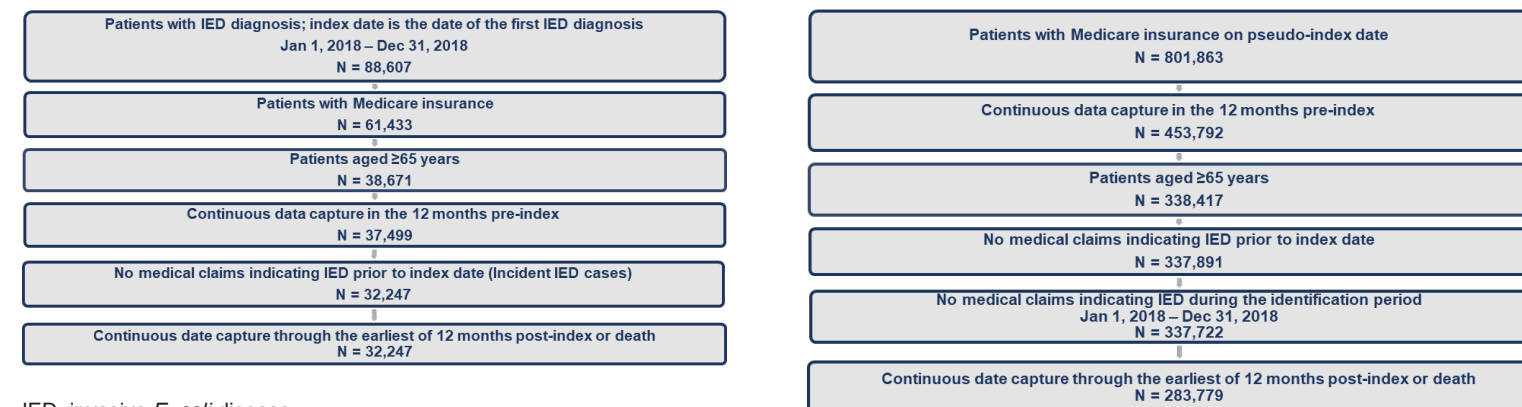
Figure 1. Definition for Invasive *E. coli* Disease

The definition of IED was assigned based on the mapping of International Classification of Diseases, 10<sup>th</sup> Revision, Clinical Modification (ICD-10-CM) codes to Systematized Nomenclature of Medicine terms for the following definitions: A or [(B+C) without D], with no more than a 10-day gap between claims.

Where:

A = Invasive disease due to *E. coli*  
 B = Infection due to *E. coli*  
 C = Invasive disease due to unspecified gram-negative bacteria, unspecified bacteria or unspecified cause  
 D = Infection due to other gram negative or positive bacteria or fungus

Figure 2. Patient Selection



IED: Invasive *E. coli* disease

### Study Outcomes

#### Table 1:

- The IED cohort was generally older (76.7 vs. 74.2, p <0.0001), included more females (62.7% vs. 57.1%, p <0.0001), and had a higher Charlson Comorbidity Index score (3.6 vs. 1.1, p <0.0001) when compared to the non-IED cohort.
- The majority of IED and non-IED patients were in the South region (35.5% and 40.1% respectively) followed by Midwest region (25.1% and 23.0%, respectively).
- 83% (n=26,671) of IED cases were identified in the inpatient setting and among these, 29.0% (n=7,725) cases required ICU care.

Table 1: Descriptive Baseline Characteristics for IED and non-IED Cohorts

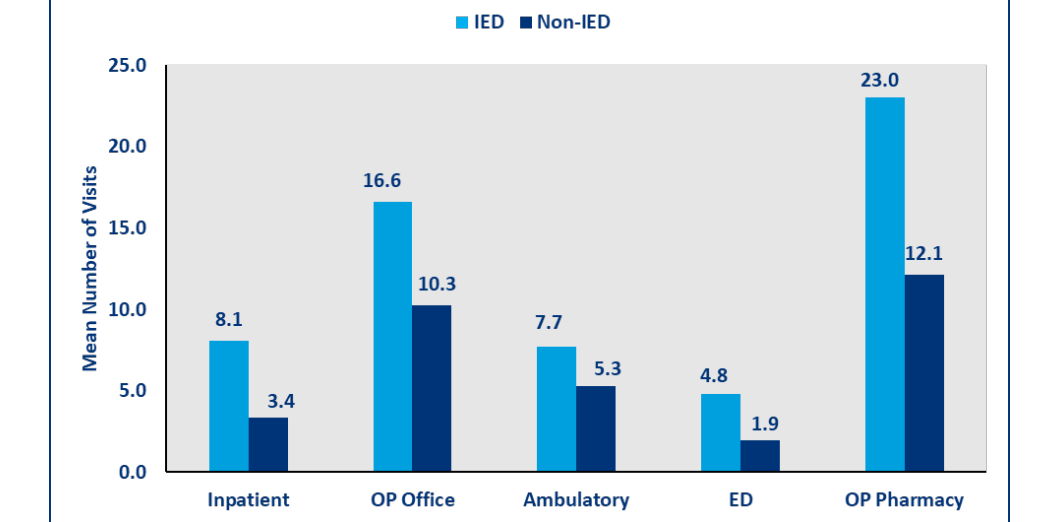
Baseline Table	IED Cohort (Reference)		Non-IED Cohort		Standardized Mean Difference	P-value
	N/Mean	%/SD	N/Mean	%/SD		
Sample Size	32,247		283,779			
Age (Mean)	76.68	5.93	74.15	6.02	42.43	<.0001
Sex						
Male	12,044	37.35%	121,891	42.95%	11.45	<.0001
Female	20,203	62.65%	161,888	57.05%	11.45	<.0001
U.S. Geographic Region						
Northeast	6,071	18.83%	47,138	16.61%	5.81	<.0001
Midwest	8,084	25.07%	65,320	23.02%	4.80	<.0001
South	11,434	35.46%	115,370	40.65%	10.72	<.0001
West	6,653	20.63%	52,826	18.62%	5.08	<.0001
Unknown	5	0.02%	3,125	1.10%	14.61	<.0001
Charlson Comorbidity Index						
CCI Score	3.64	3.24	1.12	1.86	95.32	<.0001
Diagnoses included in CCI Score:						
Myocardial infarction	3455	10.71%	6665	2.35%	34.35	<.0001
Congestive heart failure	8916	27.65%	18235	6.43%	58.84	<.0001
Peripheral vascular disease	7051	21.87%	20328	7.16%	42.68	<.0001
Cerebrovascular disease	5829	18.08%	16733	5.90%	38.18	<.0001
Dementia	4414	13.69%	8273	2.92%	39.81	<.0001
Chronic obstructive pulmonary disease	9362	29.03%	31887	11.24%	45.51	<.0001
Connective tissue/rheumatic disease	1,944	6.03%	6,295	2.22%	19.25	<.0001
Peptic ulcer disease	874	2.71%	1,741	0.61%	16.46	<.0001
Liver disease – mild	2427	7.53%	6106	2.15%	25.24	<.0001
Liver disease – moderate or severe	464	1.44%	550	0.19%	13.87	<.0001
Renal disease	9,522	29.53%	24,109	8.50%	55.64	<.0001
Diabetes mellitus without complications	13048	40.46%	51461	18.13%	50.61	<.0001
Diabetes mellitus with complications	8,006	24.83%	20,989	7.40%	48.80	<.0001
Cancer	5913	18.34%	20109	7.09%	34.27	<.0001
Metastatic carcinoma	1,519	4.71%	2,232	0.79%	24.18	<.0001
HIV/AIDS	54	0.17%	275	0.10%	1.94	0.0002
Paraplegia and hemiplegia	1116	3.46%	1383	0.49%	21.50	<.0001
Type of IED care						
Identified in the Inpatient setting	26,671	82.71%				
Required ICU care	7,725	23.96%				

CCI: Charlson comorbidity index; ICU: intensive care unit; IED: Invasive *E. coli* disease; SD: standard deviation; UTI: urinary tract infection

### Figures 3 and 4:

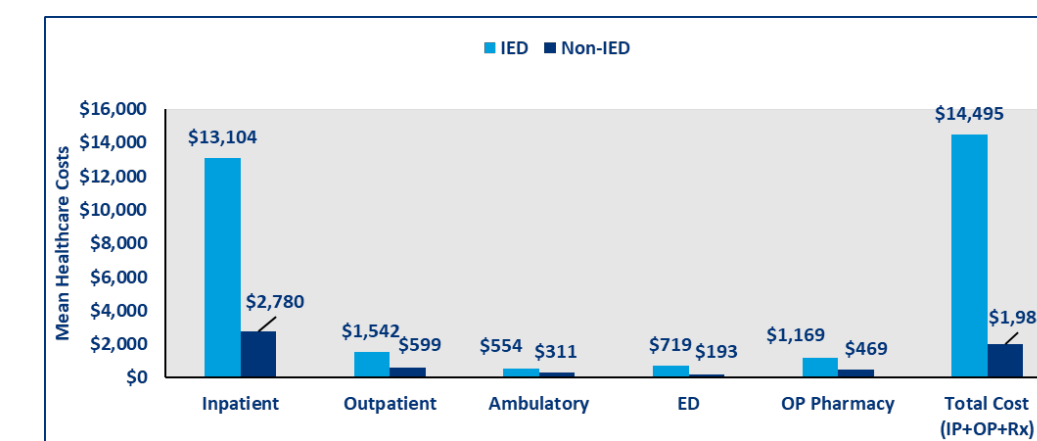
- IED patients had significantly higher mean visits per patient per year (PPPY) in the follow up when compared with matched non-IED, with outpatient (OP) pharmacy visits (23.0 vs 12.1, p-value ≤.0001), followed by OP office (16.6 vs 10.3, p-value ≤.0001), ambulatory (7.7 vs 5.3, p-value ≤.0001) and ED visits (4.8 vs 1.9, p-value =0.631).
- All cause costs per patient per month (PPPM) were significantly higher among IED patients compared to matched non-IED patients (\$14,495 vs \$1,988, p-value ≤.0001) and the difference was primarily driven by IP costs among IED patients (\$13,104 vs \$2,780, p-value ≤.0001). The mean length of stay (LOS) per inpatient (IP) visit was higher among non-IED patients (3.47 vs 3.34 days).

Figure 3: All-Cause Healthcare Resource Use in the Follow-up (mean), PPPY, for IED vs Matched Non-IED Patients



ED: emergency department; IED: Invasive *E. coli* disease; OP: outpatient; PPPY: per patient per year

Figure 4: All-Cause Healthcare Costs (mean), PPPM, for IED vs Matched Non-IED Patients

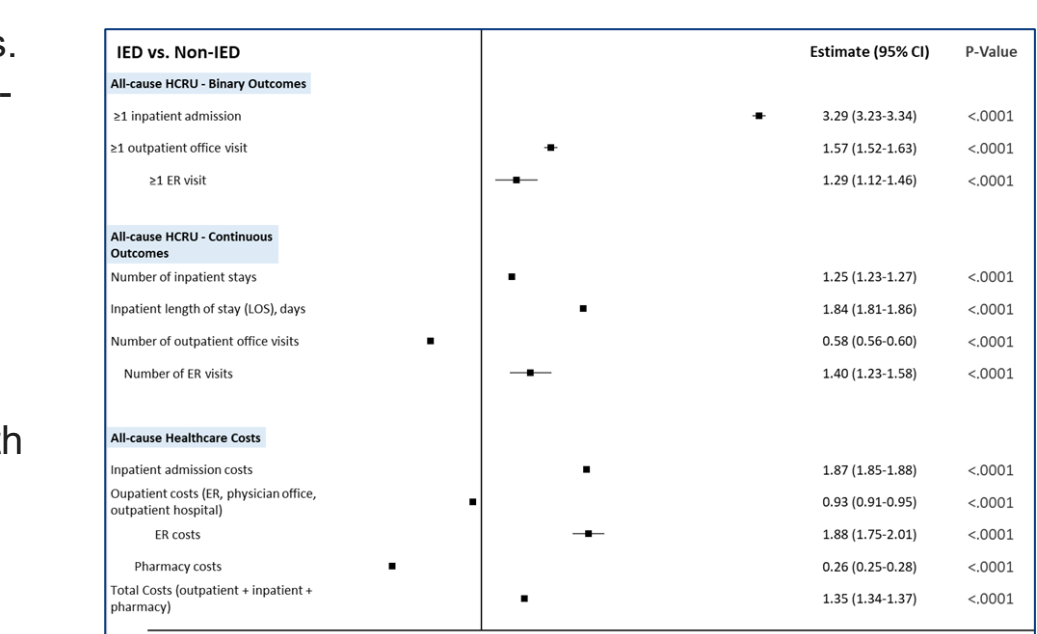


ED: emergency department; IED: Invasive *E. coli* disease; IP: inpatient; OP: outpatient; PPPM: per patient per month; Rx: pharmacy

### Figure 5:

- Relative risk of IP admission among IED patients was 3.29 times (CI: 3.23-3.34) higher than non-IED patients.
- Similarly, the risk of OP and emergency department (ED) visit was significantly higher among IED patients. (Risk of OP: 1.57, CI: 1.52-1.63 and, risk of ER: 1.29, CI: 1.12-1.46) visits was significantly higher among IED patients when compared with non-IED patients.
- The risk for longer IP length of stay IED patients was 1.25 (CI: 1.23-1.27) times that of non-IED patients.
- The risk for increased IP admission costs (1.87, CI: 1.85-1.88) and ED costs (1.88, CI: 1.75-2.01) was found to be significantly higher among IED patients.

Figure 5: Multivariate Regression Models Comparing HCRU and Costs Among IED vs non-IED Patients

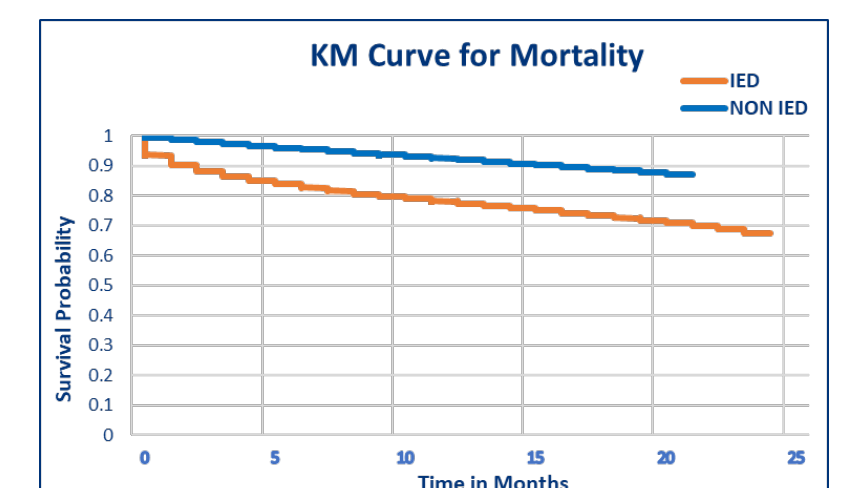


CI: confidence interval; ER: emergency room; IED: Invasive *E. coli* disease; HCRU: healthcare resource utilization

### Figure 6:

- Median time to death from index date was shorter among IED patients (173.4 vs 229.5 days, p-value ≤.001).
- Adjusted hazard ratio for mortality was 2.84 (CI: 2.72, 2.97, p-value ≤.001) among IED patients when compared with non-IED patients.

Figure 6: Survival Analysis Comparing Time to Mortality Among IED and Non-IED Patients



IED: Invasive *E. coli* disease; KM: Kaplan Meier

## References

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## Acknowledgments and Disclosures

This study was funded by Janssen Global Services. AEK, LHP, JG, BB are employees of Janssen Pharmaceutical Companies of J&J. NK was an employee of Janssen Pharmaceutical Companies of J&J at the time of this work. SV and RS were employees of STATinMED at the time of this work.