

Clinical and Economic Burden of Invasive *Escherichia Coli* Disease Among Commercially Insured Adult Patients in the United States

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KEY FINDINGS AND CONCLUSIONS

- Among adults, invasive *E. coli* disease adds significant clinical and economic burden, with total healthcare costs substantially higher than matched controls, and with inpatient cost representing 86% of total cost. Average total costs among invasive *E. coli* disease cases were \$8,645 PPPM for 1 year follow-up.
- 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 study utilized a large sample of administrative claims data spanning across commercial payers and geographical regions, representing 87% of insured patients in the U.S.
- Information available from laboratory data such as microbiological and diseases-specific parameters used to identify IED cases were not available in the claims database. This could have resulted in misclassification of IED cases.
- 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.
- Socioeconomic factors such as race, income, and employment status were not available.

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 *E. coli* disease (IED), including bacteremia and (uro) sepsis. [1-3]
- IED has been found to be associated with high morbidity and mortality translating in substantial healthcare resource utilization and costs. [1-5]
- Even though older adult patients (>60 years old) are known to be at higher risk of IED, little is known about the healthcare burden associated with IED among younger age groups, primarily covered under commercial insurance plans in the U.S.

OBJECTIVES

- This study aims to describe the clinical and economic burden of IED among commercially insured adults in the United States.

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 U.S. healthcare system.
- This database provides comprehensive capture of inpatient (IP), outpatient (OP), emergency department (ED), office visits, and pharmacy claims for adult patients enrolled in commercial insurance plans with ability to continuously track patients as they move across insurance plans and channels.

Study Sample

- 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 18-64 years of age and had commercial insurance on the index date.
- Patients had continuous data capture (≥1 medical or pharmacy claim) in the 12 months prior to index date (Baseline period) and following index date.

Cohorts

- Patients were assigned to the following cohorts based on IED diagnosis.
 - IED patients: had ≥1 claim(s) with diagnosis codes indicating IED during Identification period.
 - Non-IED patients: no medical claims indicating IED during Baseline and Identification periods.

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 propensity score matched IED and non-IED patients.
- 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 (CI).

RESULTS

Patient Population

Figure 1 and 2:

- After selection criteria were applied, a total of 7,588 IED cases and 525,736 non-IED patients were identified.
- After adjustment using PSM, the sample included 6,889 IED cases and 6,889 non-IED controls.

Figure 1. Definition for Invasive *E. coli*

The definition of IED was assigned based on the mapping of International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes to Systematized Nomenclature of Medicine terms for the two 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

Patients with IED diagnosis; index date is the date of the first IED diagnosis Jan 1, 2018 – Dec 31, 2018 N = 99,697	Patients with commercial insurance on pseudo-index date N = 2,287,921
Patients with commercial insurance N = 16,706	Continuous data capture in the 12 months pre-index N = 857,536
Patients aged 18-64 N = 14,604	Patients aged 18-64 N = 677,330
Continuous data capture in the 12 months pre-index N = 11,949	No medical claims indicating IED prior to index date N = 477,205
No medical claims indicating IED prior to index date (incident IED cases) N = 9,452	No medical claims indicating IED during the identification period Jan 1, 2018 – Dec 31, 2018 N = 677,159
Continuous data capture through the earliest of 12 months post-index or death N = 7,588	Continuous data capture through the earliest of 12 months post-index or death N = 525,736

IED: invasive *E. coli* disease

Study Outcomes

Table 1:

- The IED patients were older (52.4 vs. 44.8, p<0.0001), included more females (68.5% vs. 57.5%, p<0.0001), and had a higher CCI score (2.5 vs. 0.2, p<0.0001) when compared to the non-IED cohort.
- The majority of IED and non-IED patients were in the South region (40.6% and 41.2%, respectively) followed by Midwest region (26.5% and 22.7%, respectively).

Table 1: Descriptive Baseline Characteristics for non-matched 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	7,588		525,736				
Age (Mean)	52.44	11.23	44.79	13.47	61.68	<.0001	
Sex							
	Male	2,392	31.52%	223,335	42.48%	22.84	<.0001
	Female	5,196	68.48%	302,396	57.52%	22.84	<.0001
U.S. Geographic Region							
	Northeast	1,265	16.67%	92,611	17.62%	2.51	0.0320
	Midwest	2,010	26.49%	119,543	22.74%	8.72	<.0001
	South	3,062	40.35%	217,894	41.45%	2.22	0.0551
	West	1,245	16.41%	92,876	17.67%	3.35	0.0043
	Unknown	6	0.08%	2,812	0.53%	8.25	<.0001
Charlson Comorbidity Index	CCI Score	2.47	3.03	0.22	0.80	101.32	<.0001
Diagnoses included in CCI Score:							
	Myocardial infarction (MI)	314	4.14%	1,800	0.34%	25.86	<.0001
	Congestive heart failure	730	9.62%	3,335	0.63%	41.61	<.0001
	Peripheral vascular disease	692	9.12%	3,869	0.74%	39.48	<.0001
	Cerebrovascular disease	501	6.60%	3,599	0.68%	31.98	<.0001
	Dementia	61	0.80%	188	0.04%	11.90	<.0001
	COPD	1,493	19.68%	18,892	3.59%	51.81	<.0001
	Connective tissue disease/rheumatic disease	411	5.42%	3,851	0.73%	27.39	<.0001
	Peptic ulcer disease	154	2.03%	914	0.17%	17.85	<.0001
	-Liver disease – mild	927	12.22%	5,941	1.13%	45.56	<.0001
	Liver disease – moderate or severe	200	2.64%	323	0.06%	22.46	<.0001
	Renal disease	1,114	14.68%	4,488	0.85%	53.47	<.0001
	Diabetes mellitus without complications	2,343	30.88%	24,832	4.72%	72.75	<.0001
	Diabetes mellitus with complications	1,141	15.04%	6,207	1.18%	52.48	<.0001
	Cancer (Includes: leukemia, lymphoma, and other malignancy)	1,129	14.88%	7,519	1.43%	50.69	<.0001
	Metastatic carcinoma	445	5.86%	1,016	0.19%	33.55	<.0001
	HIV/AIDS	69	0.91%	647	0.12%	10.99	<.0001
	Paraplegia and hemiplegia	331	4.36%	639	0.12%	28.94	<.0001

COPD: chronic obstructive pulmonary disease; IED: invasive *E. coli* disease; SD: standard deviation; UTI: urinary tract infection

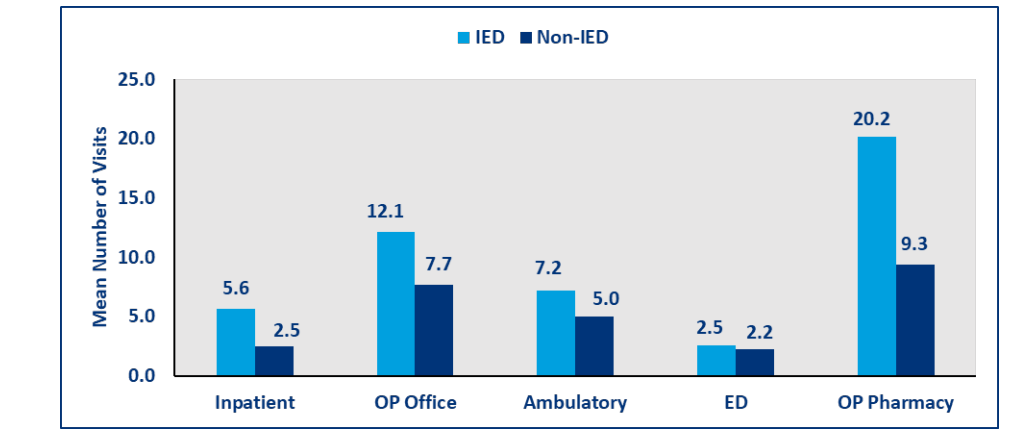
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Figure 3 and 4:

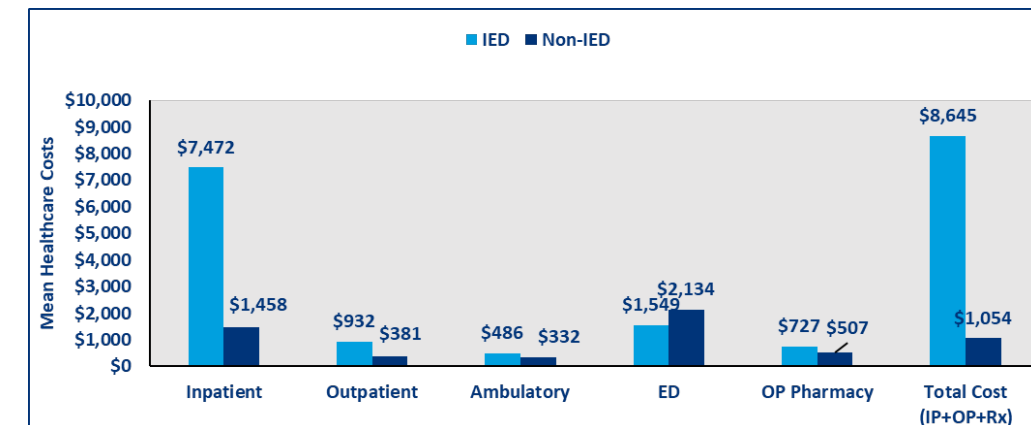
- IED patients had significantly higher mean HCRU per patient per year (PPPY) in the follow up when compared with matched non-IED, with OP pharmacy visits (20.2 vs 9.3, p-values<.0001), followed by OP office (12.1 vs 7.7, p-values<.0001), ambulatory (7.2 vs 5.0, p-values<.0001), inpatient (5.6 vs 2.47, p-values<.0001) and ED visits (2.5 vs. 2.2, p-value=0.631).
- Mean all cause costs per patient per month (PPPM) were significantly higher among IED patients compared to matched non-IED patients (\$8,645 vs \$1,054, p-values<.0001) and the difference was primarily driven by IP costs among IED patients (\$7,472 vs \$1,458, p-values<.0001) versus matched controls.

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

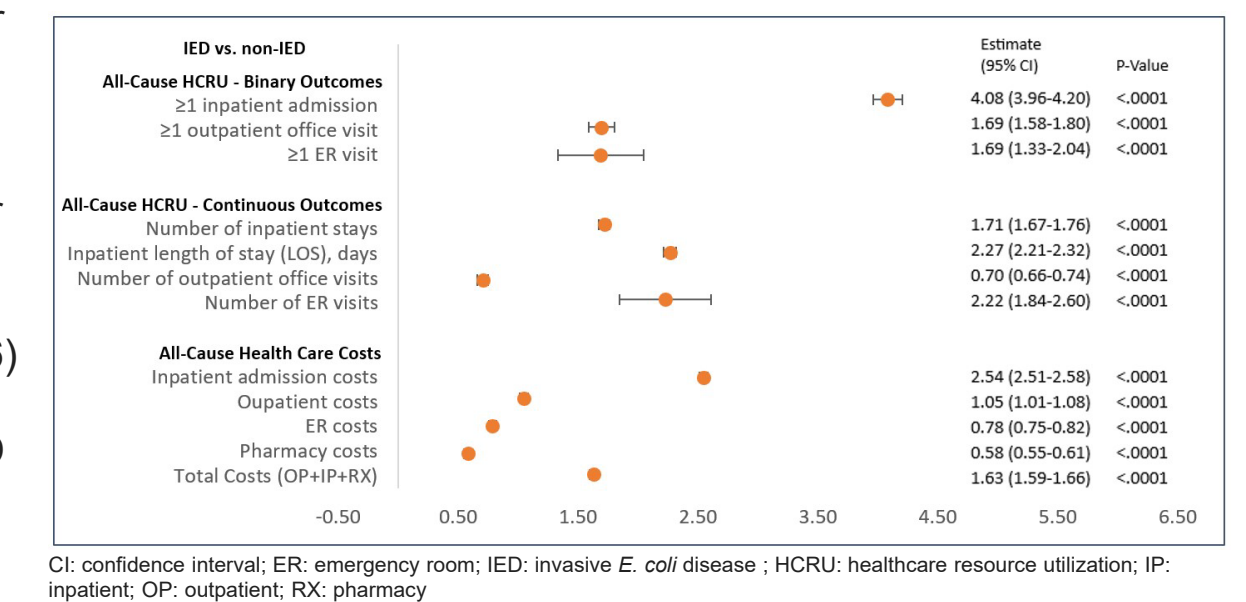


ED: emergency department; IED: invasive *E. coli* disease; OP: outpatient; PPPM: per patient per month

Figure 5:

- Relative risk of inpatient admission among IED patients was 4.08 (CI: 3.96-4.2) times higher than in matched non-IED patients.
- Similarly, the risk of outpatient (1.69, CI: 1.58-1.8) and emergency department (1.69, CI: 1.33-2.04) visits was significantly higher among IED patients when compared with non-IED patients.
- The risk for longer length of stay (2.27, CI:2.21-2.32) and increased number of emergency department visits (2.22, CI: 1.84-2.6) was significantly higher among IED patients than for non-IED patients.

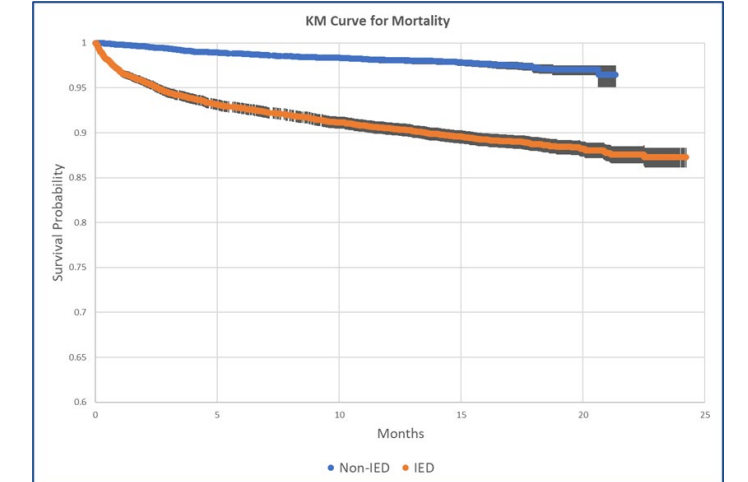
Figure 5: Multivariate Regression Models Comparing HCRU and Costs Among IED vs Non-IED Patients



CI: confidence interval; ER: emergency room; IED: invasive *E. coli* disease; HCRU: healthcare resource utilization; IP: inpatient; OP: outpatient; RX: pharmacy

- The risk for increased inpatient admission costs (2.54, CI: 2.51-2.58), and outpatient costs (1.05, CI: 1.01-1.08) was found to be significantly higher among IED patients.
- Figure 6: Not only was the median time to death shorter among IED patients (90 vs 177 days, p-values<.001), but significantly more patients with IED died compared to non-IED patients (760 vs 158).
- Adjusted hazard ratio for mortality were 4.73 (CI: 4.73, 3.99, p-values<.001) among IED patients when compared with matched non-IED patients.

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



IED: invasive *E. coli* disease; KM: kaplan meier

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