Treatment patterns, costs, and mortality among Medicare beneficiaries with CIED infection

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Abstract

Background: Cardiac implantable electronic device (CIED) infection is a serious adverse event, but there are limited contemporary real-world data on treatment pathways and associated costs in the Medicare population following diagnosis of CIED infection. Hence, this study evaluates postinfection treatment pathways and associated healthcare expenditures and mortality among Medicare fee-for-service beneficiaries with CIED infection.

Methods: Retrospective cohort analysis of 5,401 beneficiaries who developed a device-related infection in the year following implantation/upgraded CIED (1/1/2010–12/31/2012). Patients were followed-up to 12 months/death following diagnosis of infection and were divided into mutually exclusive groups based on whether they underwent CIED system removal (Group I), or no CIED system intervention (Group II; Group IIA with or Group IIB without infection hospitalization). All-cause healthcare resource utilization/expenditures were also measured.

Results: In the year following infection, 64.1% of patients underwent device extraction, of whom 2,109 (39.0%) had their device replaced (Group IA) and 1,355 (25.1%) had their device extracted without replacement (Group IB); 62.2% of patients were hospitalized and 25.3% of patients died. Mean Medicare payments-per-patient for facility-based services by group were: IA = $62,638 (standard deviation [SD]: $46,830), IB = $50,079 (SD: $45,006), IIA = $77,397 (SD: $79,130), and IIB = $22,856 (SD: $31,167).

Conclusions: Hospitalizations were the largest cost driver; infection-related costs, including cost of extraction/replacement, accounted for >50% of expenditures for patients with surgical/hospital intervention. Management of CIED infection in Medicare beneficiaries is associated with high healthcare expenditures in the year following infection. Additional measures to prevent device infection are needed to improve the outcomes and reduce costs in these patients.

KEYWORDS
CIED infection, healthcare costs, healthcare resource utilization, Medicare

1 | INTRODUCTION

Infection remains a serious complication following cardiac implantable electronic device (CIED) implantation.1–3 The threefold rise in CIED infection rate has surpassed the growth rate of CIED implantation over the past 20 years.4–8 While most CIED procedure costs are paid by Medicare, there are limited contemporary real-world data on treatment pathways and healthcare costs in the Medicare population following the diagnosis of infection. Most research to date has focused on infection-related resource utilization and costs in the inpatient setting. There is limited information about infection treatment pathways and subsequent costs once the patient leaves the hospital. To bridge this gap, the present investigation was conducted to evaluate the postinfection treatment pathways and associated healthcare resource
utilization including hospital, emergency room (ER), and postacute care settings among Medicare fee-for-service (FFS) beneficiaries with CIED infection.

2 METHODS

We performed a retrospective cohort analysis of Medicare FFS beneficiaries who received an initial implantation or replacement (including upgrades) of a CIED between January 1, 2010 and December 31, 2012, and then developed a device-related infection during the 12-month period following the procedure. The study cohort was derived from the 100% Medicare Standard Analytic File Limited Data Set, which includes all facility-level encounters for Medicare FFS beneficiaries, including hospital claims, ER visits, skilled nursing facility (SNF) stays, home health services, and hospice care. Physician office visits and retail/mail order pharmacy claims were not captured. The Medicare Master Beneficiary Summary File was used to determine beneficiary monthly eligibility for Part A/B services, patient demographics, and, where applicable, date of death.

We selected patients who developed CIED infection in the 12-month period following an initial implantation or replacement (including upgrades) of a CIED in the hospital inpatient or outpatient setting (i.e., observation services, same day surgery, or any stay in the absence of a formal admission). The study cohort was required to meet all of the following inclusion criteria: (1) received an initial CIED implantation, device upgrade, or replacement procedure based on ≥1 medical claim with a procedure code of interest in the inpatient or outpatient setting between 1/1/2010 and 12/31/2012 (index selection window); (2) date of the first observed CIED procedure defined the index date; (2) ≥65 years of age at index; and (3) continuously enrolled in Medicare FFS Parts A/B for ≥6 months pre- and ≥12 months postindex or died on/after the index event. Patients were excluded from analysis if any of the following occurred during the index procedure: (1) underwent an additional major cardiac procedure (procedure name and ICD-CM procedure code: closed heart valvotomy: 35.00-35.04; open-heart valvuloplasty w/o replacement: 35.10-35.14; replacement of heart valve: 35.20-35.28; repair of arterial and venous septal defect of the heart with prosthesis or tissue: 35.50-35.55; 35.60-35.62; 35.70-35.72; percutaneous valvuloplasty: 35.96; removal of coronary artery obstruction w/ and w/o stents: 36.03-36.09; aortocoronary bypass for heart revascularization: 36.10-36-19; implantation of prosthetic cardiac support device around the heart: 37.41; heart replacement procedures [mechanical]: 37.52-37.54; or insertion of implantable heart assist system and percutaneous external heart assist device [includes left ventricular assist device and percutaneous ventricular assist device]: 37.62-37.64, 37.66-37.68); or (2) type of index device could not be identified. The index procedure was categorized by: (1) type of procedure (initial implantation vs replacement/upgradation; (2) type of CIED: (i) cardiac resynchronization therapy device with defibrillator (CRT-D), (ii) CRT device without defibrillator (CRT-P), (iii) implantable cardioverter defibrillator (ICD), or (iv) pacemaker (PM); and (3) whether or not the index procedure required hospitalization.

The presence of CIED infection was based on one or more medical claims with a diagnosis of infection and inflammatory reaction due to cardiac device, implant, and graft (ICD-9-CM 996.61) in the 12-month period following the index procedure. Unlike the definition of CIED infection commonly used in the literature, our analysis did not include those nonspecific infection diagnoses which would then require a CIED intervention to prove that the infection was related to the device. We did not want to limit this analysis to a point in time when there was a CIED intervention. Subsequent diagnoses of CIED events occurring after the initial diagnosis and prior to the implantation of a new device were classified as a single case of infection.

Patients were followed for up to 12 months following first recorded date of infection or to date of death, whichever occurred first. Outcomes of interest included all-cause mortality, postinfection device intervention, and healthcare resource utilization and expenditures. Mortality measures included the number who died in the follow-up period, time from index procedure to death, and time from infection to death. All-cause healthcare resource utilization during the follow-up period included number of hospitalizations, ER visits, time from index to first readmission, SNF stays, and use of home health services. Total all-cause Medicare-reimbursed amounts (i.e., the amount Medicare reimburses providers for delivery of care) during the follow-up period were calculated overall and by setting of care (inpatient, outpatient, SNF, home care, and hospice). The Medicare-reimbursed amount includes the Medicare Severity-Diagnosis Related Group amount, teaching, disproportionate share, capital, and outlier payments for all cases; payments from secondary insurers and beneficiary out-of-pocket payments were not captured in the data. Infection-related payments included service claims with ICD-9-CM diagnosis code 996.61 and/or procedure codes indicating device extraction, revision, or replacement.

During the follow-up period, medical claims were reviewed to determine if the index device was revised, removed, or replaced, allowing us to analyze patients based on the intensity of the treatment associated with their CIED infection. Four mutually exclusive categories were analyzed: Group I: CIED system removal; then subdivided into Group IA: Extraction and replacement (most intensive intervention) and Group IB: Extraction of generator/full system and no evidence of device replacement; Group II: No CIED system intervention; then subdivided into Group IIA who experienced at least one infection-related hospitalization or Group IIB no device generator procedure and no infection specific hospitalization (Figure 1). For patients with extraction and/or replacement (Group I), we measured time from infection to extraction, time from infection to replacement, time between extraction and replacement, and setting of care for extraction (inpatient or outpatient).

Baseline characteristics of the cohort included patient age at index, gender, race, and geographic region, Charlson Comorbidity Index Score (Deyo adaptation), evidence of CIED infection (ICD-9-CM 996.61) in the 6 months prior to the initial implantation/replacement, history of advanced chronic kidney disease (i.e., stage 4 or 5), end stage renal disease, or renal insufficiency, congestive heart failure, and diabetes mellitus in the 6-month preindex period or present on admission.
Descriptive and summary statistics are reported. Postinfection resource utilization and Medicare payments were further stratified by infection treatment group. Kaplan-Meier analyses were performed on the infection cohort to measure time to: (1) infection; (2) death; and (3) reimplantation. Bivariate analysis identified differences in baseline and clinical characteristics for patients with major infection versus other and by postinfection intervention group using the \( \chi^2 \) test (for categorical variables) and \( t \)-test for continuous variables. A multivariable Cox proportional hazards model evaluated baseline factors associated with mortality. All statistical tests used a significance level of \( \alpha = 0.05 \).

### 3 | RESULTS

#### 3.1 | Patient characteristics

A total of 5,401 Medicare beneficiaries (mean age 77.4 years; 62.9% male) had evidence of CIED infection in the 12-month period following initial implantation or replacement of a CIED. Baseline characteristics, overall and by infection treatment group, are reported in Table 1. The average time between the index procedure and first facility-based diagnosis of infection was 81 days (median: 48 days) with 60% of infections identified within 30 days following the index procedure. The treatment patterns of CIED infections were analyzed based on the intensity of the treatment (Figure 1). A total of 64.1% (n = 3,654) of patients underwent extraction or removal of their CIED system (Group I). Of these, 2,109 (39.0%) had their device replaced (Group IA) and 1,355 (25.1%) had their device extracted without replacement (Group IB). In Group IIA, there were 163 (3.0%) who did not have evidence of any revision or replacement but experienced at least one infection-related hospitalization, while Group IIB consisted of 1,774 patients (32.8%) who did not have any device-related intervention and did not experience any infection-related hospitalizations. Group IIB patients may have been hospitalized for other reasons, not related to infection or the device.

#### 3.2 | Timing from infection to device extraction

Of those with device extraction (Groups IA and IB), the time from first observed diagnosis of CIED infection to extraction varied based on whether the extraction procedure was performed during a hospitalization versus as an outpatient procedure. Among the 56.3% of patients in Groups IA and IB who were hospitalized for the extraction, the mean time between diagnosis of infection and extraction was 5.4 days (standard deviation [SD]: 5.9) with a total length of stay of 10.8 days, while those patients who underwent extraction in the outpatient setting, the mean time from diagnosis to intervention was approximately 60 days (Table 2).

#### 3.3 | Healthcare resource utilization and Medicare expenditures

There was substantial healthcare resource utilization for the entire infection cohort. This included both utilization related and unrelated to the infection. In the 12-month period following infection, 43% of the entire group of patients had at least one ER visit (not resulting in hospital admission) and 62% were hospitalized (Figure 2). Patients with infections experienced on average 1.5 (SD: 1.8) hospitalizations with 11.0 (SD: 17.7) total hospital days in the year following infection (Table 3). All groups of patients utilized both ED and hospital resources including those who had no postinfection-related hospitalization or device intervention (Group IIB). For those with infection-related resource utilization (Groups I, IIA), most of their healthcare utilization was related to treatment of infection.

Mean total all-cause Medicare payments per patient in the 12-month period following infection for facility-based services by group were: IA = $62,638 (SD: $46,830), IB = $50,079 (SD: $45,006), IIA = $77,397 (SD: $79,130), and IIB = $22,856 (SD: $31,167).
TABLE 1  Demographics and clinical characteristics of Medicare FFS patients with CIED infection, overall and by intervention group

|                      | All study patients (N = 5,401) | IA: Generator / System removed and replaced (N = 2,109) | IB: Generator / System removed but not replaced (N = 1,355) | IIA: No device procedure but 1+ infection-specific hospitalization (N = 163) | IIB: No device procedure and no infection-specific hospitalization (N = 1,774) |
|----------------------|-------------------------------|---------------------------------------------------|------------------------------------------------|------------------------------------------------|------------------------------------------------|
| Age at index (Column %) |                               |                                                   |                                                   |                                                   |                                                   |
| 65–74 years          | 37.6%                         | 39.7%                                             | 37.5%                                             | 35.6%                                             | 35.3%                                             |
| 75–84 years          | 43.9%                         | 42.6%                                             | 43.0%                                             | 42.3%                                             | 46.4%                                             |
| 85+ years            | 18.5%                         | 17.7%                                             | 19.5%                                             | 22.1%                                             | 18.3%                                             |
| Age (Mean, SD)       | 77.4 (7.4)                    | 77.1 (7.4)                                        | 77.5 (7.5)                                        | 77.9 (7.8)                                        | 77.8 (7.2)                                        |
| Gender (Column %)    |                               |                                                   |                                                   |                                                   |                                                   |
| Female               | 37.1%                         | 31.5%                                             | 37.0%                                             | 35.6%                                             | 43.8%                                             |
| Male                 | 62.9%                         | 68.5%                                             | 63.0%                                             | 64.4%                                             | 56.2%                                             |
| Race                 |                               |                                                   |                                                   |                                                   |                                                   |
| White/Caucasian      | 88.3%                         | 89.8%                                             | 87.5%                                             | 81.6%                                             | 87.9%                                             |
| Other race/races     | 11.7%                         | 10.2%                                             | 12.5%                                             | 18.4%                                             | 12.1%                                             |
| U.S. geographic region (Column %) |                           |                                                   |                                                   |                                                   |                                                   |
| Midwest              | 24.3%                         | 22.5%                                             | 25.0%                                             | 25.8%                                             | 25.8%                                             |
| Northeast            | 17.1%                         | 17.7%                                             | 16.8%                                             | 22.7%                                             | 16.2%                                             |
| South                | 43.5%                         | 44.5%                                             | 44.1%                                             | 35.6%                                             | 42.7%                                             |
| West                 | 15.0%                         | 15.3%                                             | 14.0%                                             | 16.0%                                             | 15.4%                                             |
| CCI score (Column %) |                               |                                                   |                                                   |                                                   |                                                   |
| 0                    | 29.0%                         | 31.1%                                             | 26.3%                                             | 20.9%                                             | 29.5%                                             |
| 1                    | 19.8%                         | 20.9%                                             | 20.3%                                             | 16.0%                                             | 18.5%                                             |
| 2                    | 16.9%                         | 17.2%                                             | 16.8%                                             | 16.6%                                             | 16.5%                                             |
| 3 or more            | 34.3%                         | 30.8%                                             | 36.6%                                             | 46.6%                                             | 35.5%                                             |
| CCI score (Mean, SD) | 2.1 (2.2)                     | 1.9 (2.1)                                         | 2.3 (2.3)                                         | 2.7 (2.5)                                         | 2.2 (2.3)                                         |
| History of CKD (% Yes) | 4.5%                         | 3.1%                                             | 4.9%                                             | n/a                                              | 5.7%                                              |
| History of CHF (% Yes) | 20.0%                        | 20.2%                                             | 20.7%                                             | 19.6%                                             | 19.3%                                             |
| History of diabetes (% Yes) | 10.5%                     | 9.7%                                             | 9.9%                                             | 12.9%                                             | 11.6%                                             |
| Type of index procedure (Column %) |                           |                                                   |                                                   |                                                   |                                                   |
| Initial implantation | 81.2%                         | 79.6%                                             | 83.6%                                             | 74.8%                                             | 81.9%                                             |
| Replacement/Upgrade  | 18.8%                         | 20.4%                                             | 16.4%                                             | 25.2%                                             | 18.1%                                             |
| Hospitalized for index procedure (% Yes) | 63.5%                     | 62.1%                                             | 65.5%                                             | 69.3%                                             | 63.2%                                             |
| Type of CIED received at index (Column %) |                           |                                                   |                                                   |                                                   |                                                   |
| PM                   | 56.8%                         | 54.1%                                             | 57.0%                                             | 56.4%                                             | 60.0%                                             |
| CRT-D or CRT-P       | 22.2%                         | 25.3%                                             | 19.1%                                             | 23.3%                                             | 20.7%                                             |
| ICD                  | 21.0%                         | 20.6%                                             | 23.9%                                             | 20.2%                                             | 19.3%                                             |

CCI = Charlson Comorbidity Index; CHF = congestive heart failure; CIED = cardiac implantable electronic device; CKD = chronic kidney disease; CRT-D = cardiac resynchronization therapy device with defibrillator; CRT-P = cardiac resynchronization therapy device without defibrillator; SD = standard deviation.

Medicare payments were highest among patients who did not receive a device revision or replacement following infection but experienced at least one infection-related hospitalization (Group IIA). Hospitalizations were the largest cost driver (Figure 3). Infection-related payments as percentage of total payments varied from 52% to 65% among patients who required surgical intervention or hospitalization (Groups IA, IB, IIA) (Figure 3). Overall, across all treatment groups, infection-related payments accounted for more than half of all payments in the year following CIED infection.

### 3.4 Mortality

A total of 25.3% of patients (n = 1,369) died during the follow-up period (IA: 16.9%, IB: 34.2%, IIA: 55.2%, IIB: 25.9%). Unadjusted mean time from first recorded diagnosis of infection to death was 105.5 days (SD: 104.8) (Kaplan-Meier curves presented in Figure 4). Unadjusted mortality was highest among patients who did not receive a device revision or replacement following infection (Group IIA). Via multivariable modeling, older age, complex comorbidities, and lack of device
### TABLE 2  Timing between first observed diagnosis of CIED infection and device extraction, by setting for extraction procedure (includes Groups IA/IB)

| Setting for extraction procedure | Number of patients | Mean days (SD) |
|---------------------------------|--------------------|----------------|
| All patients with a postinfection extraction procedure | 3,464 | 30.9 (56.7) |
| Time from first observed diagnosis of infection and CIED extraction performed in outpatient setting | 1,515 | 63.9 (73.2) |
| Time from first observed diagnosis of infection and CIED extraction performed during hospitalization | 1,949 | 5.3 (5.8) |
| Days between hospital admission for infection and surgical intervention* | 1,901 | 5.4 (5.9) |
| Days between surgical intervention and hospital discharge* | 1,901 | 5.6 (6.3) |
| Total length of stay* | 1,901 | 10.8 (8.9) |

Note: *Procedure date were not reported in some cases. Results shown for patients with valid procedure date. Visibility into diagnosis of infection and extraction based on facility-based medical claims; claims for physician office visits were not available for analysis. Abbreviations as in Table 1.

### FIGURE 2  All-cause and infection-related ER visits and hospitalizations during follow-up period, by intervention group. Legend: IA: Generator/system removed and replaced; IB: Generator/system removed but not replaced; IIA: No device procedure but 1+ infection-specific hospitalization; IIB: No device procedure and no infection-specific hospitalization. ER = emergency room [Color figure can be viewed at wileyonlinelibrary.com]

intervention were associated with poorer survival (Table 4). The median survival time was 225 days. Patients with full system replacement (Group IA) survived 345 days versus 116 days for patients who did not receive any device intervention (Group IIA).

In sensitivity analyses, we evaluated differences in all-cause Medicare payments per patient by time to extraction (Figure 5) and time to death (results not shown). The highest costs were observed in those patients whose extraction was delayed more than 180 days following first observed diagnosis of infection. Mean Medicare payments were higher for patients who died in the 6- to 12-month period following infection versus patients who survived the full 12-month study period ($91,281 vs $44,990, respectively).

### 4 | DISCUSSION

The present study analyzed the treatment patterns and costs associated with CIED infection in a Medicare population in the year following diagnosis across the inpatient, ED, and postacute care settings based on treatment intensity. The major findings of this study are: (1) Most patients with CIED infection (64.1%) were treated with system extraction or removal. However, there were a substantial number of patients (32.8%) who did not undergo any further CIED procedures postinfection diagnosis and had no infection-related hospitalizations. (2) The mortality in the first-year postinfection was high (25.3%) but appeared to be much lower in those who had their system removed and replaced (16.9%). (3) There was substantial healthcare resource utilization, both inpatient and outpatient, in all groups of patients with CIED infection, regardless of the postinfection classification group. This included the group of patients who had no device intervention or infection-related hospitalization. (4) Infection-related payments, particularly hospitalizations, were responsible for most of the cost to Medicare in the first year following CIED infection. (5) Payments appeared highest in those whose device extraction and system removal was delayed.
In our analysis, the majority of Medicare beneficiaries with CIED infection were managed with device extraction, consistent with current guidelines for the management of CIED infection. Of these, 56% (n = 1,949) were hospitalized for the extraction, while 44% (n = 1,515) were managed in the outpatient setting. Group IIA (infection-related hospitalization but no CIED intervention) had the highest rate of comorbidities and mortality, suggesting that these patients were not healthy enough to undergo device extraction procedures. There were 1,774 (32.8%) Group IIB patients (the group with the lowest intensity of infection treatment) who underwent no revision or replacement surgery nor had a postinfection-related hospitalization. This group of patients likely had local surgical site infection. In a previous study of MarketScan patients with CIED infection (including both commercially insured [i.e., employer-based and self-insured plans] and Medicare supplemental coverage), we found that 38.4% of patients with initial CIED implants and 47.2% of those with replacement implants were treated with the lowest intensity level of treatment (no infection-related inpatient admission or device-related intervention).

Incremental costs at 12 months were $16,651 in those with initial implants versus $26,851 in those with replacement implants when compared to a group without infection in the MarketScan study. These patients were similar to our Group IIB patients and likely had surgical site infection or localized cellulitis. The lower average costs observed in this study versus the MarketScan study is likely due to two factors. First, Medicare reimbursed amounts are typically lower than commercial payments. For example, average Medicare DRG payment for FY2013 implantation of a PM ranges from $12,921 without complication to $16,893 with complication.

A recent evaluation of cost to revise or repair CIED lead in a commercially insured population found that procedures to revise or repair leads were associated with increased inpatient hospitalization costs (mean $19,959 for PM, $24,885 for ICD, and $46,229 for CRT-D; P = 0.048). Second, our definition of infection-related cost required ICD-9-CM code 996.61 or a procedure code indicating device revision, removal, or replacement. This could potentially underestimate the total cost related to CIED infections if subsequent encounters associated with sequelae no longer carried the infection diagnosis. Despite these differences, it is clear that there are substantial costs involved in treating patients with even minor CIED infection. An analysis of only in-hospital expenditures at the time of CIED infection diagnosis underestimates the true costs of treating all patients with CIED infection.
There are limited data on the optimal timing between diagnosis of CIED infection and device intervention. The American Heart Association/American College of Cardiology guidelines do not comment on the appropriate timing of lead extraction while the British guidelines recommend lead extraction be performed as soon as possible but within 2 weeks of a diagnosis of infection. The British guidelines state that there is no specific evidence on which to base this recommendation. Our study supports the recommendation that early and complete device removal has been associated with improved outcomes. In our study, median survival time from the detection of infection was longer for patients who underwent full system extraction and replacement versus patients receiving limited or no intervention. Among patients with infection, our results suggest longer survival time for patients with the most intensive intervention (i.e., Group I).

Total Medicare all-cause payments were generally lower for patients who underwent full system extraction and replacement versus patients who underwent extraction more than 30 days after diagnosis of infection. Medicare payments were more than double for patients who died in the 6- to 12-month period following infection versus patients who did not die during the 12-month study period, further highlighting that there are significant costs associated with treating CIED infection beyond the initial hospitalization.

These data suggest that all patients with CIED infection, including those with minor infection, incur significant treatment costs. Hospitalizations were the largest cost driver among patients with infection in this current investigation and infection-related costs, including cost of extraction and replacement, accounted for more than half of total costs. Comparative data on financial costs associated with managing CIED infection are modest, despite the fact that there are ample reports focusing on the increasing rate of CIED infections. Sohail et al. analyzed hospital payments for 5,817 admissions during calendar year 2007 for CIED infection. Incremental costs were $14,360 to $16,498 depending upon the type of CIED. Our analysis extends these observations to include additional Medicare payments including additional hospitalizations, services, and procedures performed in a hospital outpatient setting, ER visits, SNF stays, home health services, and hospice care within 1 year following infection. When one considers that there are over 4 million PMs and ICDs currently in use in the United States, the costs associated with managing CIED infection are significant. Strategies to reduce CIED infection will yield significant savings in healthcare expenditures.

Most CIED infections occurring early following the CIED implant procedure are related to local pocket infection. Therefore, strategies to reduce risk of surgical site infection such as chlorhexidine skin preparation at the time of surgery, reduction of *S. aureus* skin colonization, preoperative antibiotic prophylaxis, and use of an antibiotic impregnated envelope at the time of surgery may reduce the risk for subsequent CIED infection.
TABLE 4  Adjusted risk of mortality in 12-month postinfection period (Cox proportional hazards model)

| Reference group | Comparator | Hazard ratio | 95% Hazard ratio Confidence limits | P-value |
|-----------------|------------|--------------|-----------------------------------|---------|
| Extraction/Group = Group IIB No device procedure and no infection-specific hospitalization | IA: Generator/System removed and replaced | 0.58 | 0.50 0.67 | <0.0001 |
| | IB: Generator/System removed but not replaced | 1.35 | 1.19 1.54 | <0.0001 |
| | IIA: No device procedure but 1+ infection-specific hospitalization | 2.11 | 1.68 2.64 | <0.0001 |
| Age = 65–74 years | 75–84 years | 1.40 | 1.24 1.59 | <0.0001 |
| | 85+ years | 2.22 | 1.91 2.57 | <0.0001 |
| Sex = Male | Female | 0.77 | 0.69 0.87 | <0.0001 |
| Race = White | Non-Caucasian/Other race(s) | 1.06 | 0.91 1.24 | 0.4500 |
| CCI Score = 0 | 1 | 1.39 | 1.14 1.71 | 0.0014 |
| | 2 | 1.90 | 1.55 2.32 | <0.0001 |
| | 3 or more | 2.93 | 2.46 3.49 | <0.0001 |
| Index device = Pacemaker | ICD, CRT-D, or CRT-P | 1.21 | 1.08 1.36 | 0.0011 |
| Index procedure = Initial implantation | Replacement or revision of existing device | 1.43 | 1.24 1.63 | <0.0001 |
| Index procedure required hospitalization = Yes | Index procedure did not require hospitalization | 0.69 | 0.60 0.79 | <0.0001 |

Abbreviations as in Table 1.

FIGURE 5  Sensitivity analysis of mean all-cause Medicare payments in 12-month postinfection period, by time to device extraction, among intervention groups IA and IB. Legend: IA: Generator/system removed and replaced; IB: Generator/system removed but not replaced [Color figure can be viewed at wileyonlinelibrary.com]

4.1 | Limitations

A few limitations should be considered when interpreting the findings of this analysis. First, our definition of infection focused on a single diagnosis code (996.61). While this code is believed to capture the majority of CIED infections, it is possible that infections coded differently (i.e., under a broader, systemic infection code), would be missing from this analysis. Additionally, this code is also used for seemingly superficial infections that do not result in inpatient treatment or device revision as well as deep pocket infections that require device removal. The superficial infections are generally not included as serious adverse events reported in clinical trials or in surgical site infection quality metrics. Furthermore, since this work utilized Medicare medical institutional claims data, we were unable to confirm CIED infections through laboratory results, physician office visits, or use of antibiotic
treatment. Sensitivity analyses were conducted using the 5% sample of the Medicare claims which includes physician office visit data (due to large volume of claims, physician office data are not made available to researchers using the 100% sample files). The proportion of beneficiaries with infection increased by 61% when physician visit claims were added, but the overall sample size was too small to report meaningful results. This suggests that event rates based exclusively on hospital claims likely underestimate the true rate of infection and baseline comorbidities. Second, this study did not include any Medicare payments directly to physicians for noninstitutional outpatient treatment (i.e., office visits and office-based procedures), nor any costs related to medication use outside of the hospital setting. Therefore, our study likely underestimated the true cost of treating CIED infection in the Medicare population.

5 | CONCLUSION

Management of CIED infection in the year following diagnosis in Medicare beneficiaries is associated with high resource utilization and healthcare expenditures, even among patients with less intensive treatment. Infection-related costs account for more than half of overall Medicare payments in patients who required surgical/hospital intervention. Mortality in the year following infection is high and median survival is longer among those who underwent full system extraction with or without device replacement. Improved measures to prevent device infection are needed to reduce the considerable resource utilization in these patients. Any economic analysis of CIED infection must take into account that there are substantial expenditures following the initial diagnosis of infection.

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REFERENCES

1. Uslan DZ, Tleyjeh IM, Baddour LM, et al. Temporal trends in permanent pacemaker implantation: A population-based study. Am Heart J. 2008;155:896–903.

2. Mond HG, Irwin M, Ector H, Proclemer A. The world survey of cardiac pacing and cardioverter-defibrillators: Calendar year 2005 an International Cardiac Pacing and Electrophysiology Society (ICPES) project. Pacing Clin Electrophysiol. 2008;31:1202–1212.

3. Kurtz SM, Ochoa JA, Lau E, et al. Implantation trends and patient profiles for pacemakers and implantable cardioverter defibrillators in the United States: 1993-2006. Pacing Clin Electrophysiol. 2010;33:705-711.

4. Voigt A, Shalaby A, Saba S. Continued rise in rates of cardiovascular implantable electronic device infections in the United States: Temporal trends and causative insights. Pacing Clin Electrophysiol. 2010;33:414–419.

5. Greenspon AJ, Patel JD, Lau E, et al. 16-year trends in the infection burden for pacemakers and implantable cardioverter-defibrillators in the United States 1993 to 2008. J Am Coll Cardiol. 2011;30:1001–1006.

6. Prutkin JM, Reynolds MR, Bao H, et al. Rates of and factors associated with infection in 200,909 Medicare implantable cardioverter-defibrillator implants: Results from the National Cardiovascular Data Registry. Circulation. 2014;130:1037–1043.

7. Baddour LM, Epstein AE, Erickson CC, et al. Update on cardiovascular implantable electronic device infections and their management: A scientific statement from the American Heart Association. Circulation. 2010;121:458–477.

8. Sohail MR, Henriksen CA, Braid-Forbes MJ, et al. Mortality and cost associated with cardiovascular implantable electronic device infections. Arch Intern Med. 2011;171:1821–1828.

9. CMS. Available at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/Inpatient2013.html. Accessed February 21, 2018.

10. Sohail MR, Eby EL, Ryan MP, et al. The incidence, treatment intensity and incremental annual expenditures for patients experiencing a cardiac implantable electronic device infection: Evidence from a large US payer database one-year post implantation. Circ Arrhythm Electrophysiol. 2016;9 pii:003929.

11. CMS. Inpatient Charge Data FY 2013. Available at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Medicare-Provider-Charge-Data/Inpatient2013.html. Accessed February 17, 2018.

12. Nichols CI, Vose JG, Mittal S. Incidence and costs related to lead damage occurring within the first year after a cardiac implantable electronic device replacement procedure. J Am Heart Assoc. 2016 Feb 12;5 pii:002813.

13. Sandoe JA, Barlow G, Chambers JB, et al. Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. J Antimicrob Chemother. 2015;70:325–359.

14. Le KY, Sohail MR, Friedman PA, et al. Impact of timing of device removal on mortality in patients with cardiovascular implantable electronic device infections. Heart Rhythm. 2011;8:1678–1685.

15. Darouiche RO, Jr, Wall MJ, Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. N Engl J Med. 2010;362:18–26.

16. Kallen AJ, Wilson CT, Larson RJ. Perioperative intranasal mupirocin for the prevention of surgical-site infections: Systematic review of the literature and meta-analysis. Infect Control Hosp Epidemiol. 2005;26:916–922.

17. Kolek MJ, Dresen WF, Wells QS, et al. Use of an antibiotic envelope is associated with reduced cardiac implantable electronic device infections in high-risk patients. Pacing Clin Electrophysiol. 2013;36:354–361.

18. Mittal S, Shaw RE, Michel K, et al. Cardiac implantable electronic device infections: Incidence, risk factors, and the effect of the AegisRx antibacterial envelope. Heart Rhythm. 2014;11:595–601.