Hospitalized Infections in People with Osteoarthritis: A National U.S. Study

Jasvinder A. Singh, MBBS, MPH[1,2,3]; John D. Cleveland, MS[2]

[1]Medicine Service, VA Medical Center, 510, 20th street South, FOT 805B, Birmingham, AL 35233, USA; [2]Department of Medicine at School of Medicine, and [3]Division of Epidemiology at School of Public Health, University of Alabama at Birmingham, 1720 Second Ave South, Birmingham, AL 35294-0022, USA

Emails and Addresses of Authors:

Jasvinder A. Singh: Jasvinder.md@gmail.com

John Cleveland: jcleveland@uabmc.edu

Address for both authors**:** University of Alabama at Birmingham, Faculty Office Tower 805B, 510 20th Street S, Birmingham, AL 35294-0022, USA.

Correspondence: Jasvinder A. Singh, MBBS, MPH, University of Alabama at Birmingham, Faculty Office Tower 805B, 510 20th Street S, Birmingham, AL 35294-0022

Phone: 205-934-8158 Fax : 205-996-9685 E-mail: Jasvinder.md@gmail.com

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ORCID ID: 0000-0003-3485-0006

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Abstract

Objective: To study the incidence, time-trends and outcomes of serious infections in people with osteoarthritis.

Methods: We used the 1998-2016 U.S. National Inpatient Sample data. We examined the epidemiology of five hospitalized, i.e., serious infections (opportunistic infections (OI), skin and soft tissue infections (SSTI), urinary tract infection (UTI), pneumonia, and sepsis/bacteremia) in people with osteoarthritis, using recommended weights. We performed multivariable-adjusted logistic regression analyses to analyze factors associated with healthcare utilization (hospital charges, length of hospital stay, discharge to non-home setting), and in-hospital mortality.

Results: Of all serious infection hospitalizations, 46,708,154 were without osteoarthritis, and 3,258,416 had osteoarthritis. Respectively, people with OA were 16 years older, more likely to be female (52% vs. 65%), White (59% vs. 70%), have Deyo-Charlson index score ≥2 (41% vs 51%), Medicare (54% vs. 80%), and less likely to receive care at an urban teaching hospital (45% vs. 39%). Serious infection rates /100,000 NIS hospitalizations increased from 1998-2000 to 2015-2016: OI from 4.5 to 7.2; SSTI, 48.3 to 145.8; UTI, 8.4 to 104.6; pneumonia, 164.0 to 224.3; sepsis, 39.4 to 436.3. In multivariable-adjusted analyses, older age, higher Deyo-Charlson score, sepsis, Northeast region, urban hospital and medium or large hospital bed size were significantly associated with higher healthcare utilization outcomes and in-hospital mortality; and Medicaid insurance, non-White race, and female sex with higher healthcare utilization.

Conclusions: Serious infection rates have increased in people with osteoarthritis. Association of demographic, clinic and hospital variables with serious infection outcomes identifies potential targets for future interventions.

Key Points

1. Rates of serious infections in people with osteoarthritis have increased in the last 2 decades.
2. Our findings of the association of demographic, clinic and hospital variables with serious infection outcomes in people with osteoarthritis identifies potential targets for future interventions.

Introduction

Osteoarthritis (OA) is the most common of all joint disorders, and is one of the leading causes of disability in the U.S. (1). The prevalence of OA increases with age, such that 50% in individuals >60 years of age have OA (2). In the U.S., OA was the fourth leading cause for hospitalization in 2009 (3).

Serious infections in osteoarthritis is an understudied area. The rate of serious infections in people with OA may be increased due to the association of OA with autoimmune rheumatic diseases (e.g. rheumatoid arthritis, lupus), reduced mobility in OA that is associated with higher rate of urinary infections (4), and increasing rates prosthetic joint infections in people undergoing knee or hip arthroplasty for which OA is the cause in >80% of the cases (5). Most studies of hospitalized infections in OA are limited to people who underwent total knee or hip arthroplasty (6, 7). This is a subset of people with OA, and people undergoing knee/hip arthroplasty are hospitalized for the elective surgery, i.e., arthroplasty. In a study comparing RA to OA, 23% of RA vs. 27% with OA or soft tissue rheumatism developed at least one infection (8). This study was performed in 1986 (pre-biologic era), infection diagnosis was based on patient interview, and the recall period was short leading to a possibility of misclassification error including both underestimation and overestimation of the frequency of infections (8). Therefore, our study objectives were to fill this knowledge gap by examining the healthcare utilization or inpatient mortality associated with serious infection hospitalizations in a national sample of people with OA in a nationally representative sample.

Our specific aims were to: (1) assess the rates of five hospitalized serious infections in the people with OA in the U.S. and their time-trends; (2) estimate healthcare utilization and in-patient mortality associated a serious infection hospitalization; and (3) analyze the factors associated with healthcare utilization and in-hospital mortality in people with OA hospitalized with a serious infection.

Methods

Data Source and Study Cohort Selection

We performed a study of five, common serious infection hospitalizations in people with OA in the U.S. NIS 1998-2016 sample. The NIS is a 20% stratified sample of discharge records from all participating community hospitals from all participating states in the U.S. that includes all-payers, including those without insurance (9). Thus, it represents all hospitalizations in the U.S. The U.S. NIS is a de-identified inpatient healthcare database that is publicly available. The Institutional Review Board at the University of Alabama at Birmingham (UAB) approved this study (UAB X120207004). All investigations were conducted in conformity with ethical principles of research. The IRB waived the need for an informed consent for this database study.

We identified five serious infections based on the presence of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes in the primary diagnosis position for hospitalization: (1) opportunistic infections (OI; 010.xx –018.xx, 031.xx, 078.5, 075.xx, 053.xx, 112.4, 112.5, 112.81, 112.83, 130.xx, 136.3, 117.5, 027.0, 039.xx, 117.3, 114.xx, 115.xx, or 116.0); (2) skin and soft tissue infections (SSTI; 040.0, 569.61, 681.xx, 682.xx, 785.4, 728.86, or 035.xx); (3) urinary tract infection (UTI; 590.xx); (4) pneumonia (003.22, 481.0, 513.0, 480.xx, 482.xx, 483.xx, 485.xx, or 486.xx); and (5) sepsis/bacteremia (038.xx or 790.7), as previously (10, 11). These codes were valid, with positive predictive values of 70% to 100% in people with rheumatoid arthritis (12). With the coding system change to ICD-10-CM in 2015 in the U.S., we used the ICD-10-CM codes for serious infections for the 2015-2016 data (**Appendix 1**). Composite infection was defined as any of the serious infection occurring as primary diagnosis for hospitalization.

We identified osteoarthritis (OA) based on the presence of an International Classification of Diseases, ninth or tenth revision, clinical modification (ICD-9-CM or ICD-10-CM) codes in a non-primary (i.e. secondary) position during the index hospitalization, 715, M15, M16, M17, M18 or M19. A previous

study showed sensitivity of 55-57% and specificity of 75-100% and positive predictive values from 63-100% to using a diagnostic code approach for OA (13, 14).

Covariates

The covariates/confounders of interest included age, sex, race, serious infection type (OI, SSTI, UTI, pneumonia, sepsis), median household income, the insurance payer, hospital characteristics (region, location/teaching status, bed size) and Deyo-Charlson comorbidity index, a validated medical comorbidity measure that includes 17 comorbidities; higher score indicated more comorbidity load (15).

Study Outcomes

For descriptive analysis (aim 1), we estimated the rate of hospitalization for each serious infection as the primary diagnosis, with OA listed in the non-primary position (secondary position).

We examined in-hospital mortality and healthcare utilization as study outcomes for the remaining analyses. Healthcare utilization included: (1) total hospital charges above the median for each calendar year; (2) the length of hospital stay above the median of 3 days; and (3) discharge to non-home settings (rehabilitation or an inpatient facility).

This categorization using NIS medians for dichotomizing variables (>3 days stay, >median hospital charge) was made on an *a priori* clinical decision to aid clinical interpretation of results of these outcomes. Additionally, both variables had a heavily right skewed distribution, which made them most appropriate to be analyzed with logistic regression, to avoid undue influence of extreme values on a linear regression.

Statistical Analyses

We followed the survey analysis procedures that account for the weights, clusters and strata as defined in NIS, including the modified weights with the change in sampling in 2012 (16). We used the "trend" discharge weights for 1993–2011 NIS files to minimize the effects of the redesign on estimated trends since our study period crossed the 1998 and 2012 data year. We used the trend weight (TRENDWT) in place of the original discharge weight (DISCWT) for years prior to 2012 to create national estimates for trend analysis that are consistent with the 2012 NIS data onward. The new trend weights are available for download (https://www.hcup-us.ahrq.gov/db/nation/nis/trendwghts.jsp) on the HCUP-US Web site. We used the SAS procedure surveyfreq, surveymeans, and surveylogistic to perform this analysis.

We compared the summary statistics using chi-square or student's t-test. We calculated incidence rates per 100,000 NIS claims and analyzed for trends over time using the Cochran Armitage test. We used the SAS procedure freq to perform this analysis.

We performed multivariable-adjusted logistic regression analyses for each study outcome, adjusting for all covariates listed in the section above. Covariates included age, sex, race, serious infection type (OI, SSTI, UTI, pneumonia, sepsis), median household income, the insurance payer, hospital characteristics (region, location/teaching status, bed size) and Deyo-Charlson comorbidity index. We used the SAS procedure surveylogistic to perform this analysis. Sensitivity analyses adjusted the main model for calendar year. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. We used SAS 9.3 (Cary, N.C.) for all analyses.

Results

Characteristics and outcomes of people with vs. without osteoarthritis admitted with serious Infection

Among people hospitalized with serious infections, there were 3,258,416 people with OA and 46,708,154 without OA in national estimates that used recommended weights. Compared to people

with serious infections without OA, those with OA were 16 years older, more likely to be female (52% vs. 65%), White (59% vs. 70%), have Deyo-Charlson index score ≥2 (41% vs 51%), Medicare (54% vs. 80%), and less likely to receive care at an urban teaching hospital (45% vs. 39%) (**Table 1**). Compared to people with serious infections without OA, those with OA were more likely to be discharged to non-home settings (25% vs. 35%), less likely to die in-hospital (6.3% vs. 4.6%), and as likely to have hospital charges above the median (57% vs. 57%) (**Table 1**).

Characteristics of people with each serious infection and OA

People with SSTI were 5-6 years younger than people with other serious infections (**Appendix 2**). Females constituted 64% to 81% and Whites, 65% to 72% of each serious infection cohort. 37-43% people with serious infection and OA were hospitalized in Southern U.S., 32%-45% at an urban teaching hospital and more than half at a large bed size hospital (**Appendix 2**). In-hospital mortality ranged from 0.3-0.5% for UTI or SSTI to 9.9% for sepsis. We noted that 46% of sepsis patients and 25% to 33% with other serious infections were discharged to non-home settings. Mean total hospital charges ranged from $21,306 for UTI to $49,065 for sepsis.

Rate of serious infections in people with OA over time

The frequency of each serious infection increased in people with OA (**Appendix 3**). Rates of all serious infections increased in the general population over time except for pneumonia and OI (**Appendix 4**). Rates of each of the serious infections /100,000 NIS claims increased significantly in people with osteoarthritis from 1998-2000 to 2015-2016 (increase): OI from 4.5 to 7.2 (1.6-fold); SSTI, 48.3 to 145.8 (3-fold); UTI, 8.4 to 104.6 (12.5-fold); pneumonia, 164.0 to 224.3 (1.4-fold); sepsis, 39.4 to 436.3 (11-fold); and composite infection, from 264.6 to 918.2 (3.5-fold) (**Appendix 5; Figure 1;** $p<0.0001$ each). We noted similar trends when using a different denominator of OA hospitalizations (OA as non-primary

diagnosis), except that OI and pneumonia rates declined over time; composite infection serious infection rate increased from 8.6% in 1998-2000 to 14.1% in 2015-2016 of OA hospitalizations with OA as non-primary diagnosis (**Appendix 5; Figure 1**). Unadjusted length of hospital stay and in-hospital mortality decreased, and total hospital charges increased for serious infections from 1998-2000 to 2015-2016 (**Appendix 6**).

Multivariable-adjusted correlates of healthcare utilization and mortality for serious infections in OA

In multivariable-adjusted analyses, we found that older age, higher Deyo-Charlson index score, sepsis, Medicare payer, Northeast region, urban teaching or non-teaching hospital and medium or large hospital bed size were each associated with higher healthcare utilization outcomes and in-hospital mortality (**Table 2**). For example, compared to age <50 years, those ≥80 years had higher OR of discharge to care facility, 6.48 (95% CI, 6.20, 6.78), hospital stay >median, 1.40 (95% CI, 1.36, 1.44) and in-hospital mortality, 6.06 (95% CI, 5.32, 6.90**; Table 2).** Compared to Deyo-Charlson index of 0, score ≥2 was associated higher OR of discharge to care facility, 1.38 (95% CI, 1.36, 1.40), hospital stay >median, 1.53 (95% CI, 1.51, 1.55) and in-hospital mortality, 1.65 (95% CI, 1.59, 1.71; **Table 2).** Medicaid insurance payer, non-White race, and female sex were associated with higher healthcare utilization only (**Table 2**). Sensitivity analyses adjusted additionally for calendar year confirmed all findings with minimal/no attenuation of OR; calendar year was associated with significantly lower odds of hospital charges >median, length of hospital stay >median and in-hospital mortality, but was not associated with discharge disposition (**Appendix 7**).

Discussion

We compared the characteristics of people with OA versus without OA in this national study of a large cohort of people with OA hospitalized with a primary diagnosis of a serious infection. We used NIS-

recommended weights in obtaining national estimates and rates. In the cohort with serious infections and a secondary diagnosis of OA, we examined the epidemiology and outcomes of the five serious infections. We described the factors associated with healthcare utilization and in-hospital mortality. We made several observations that merit further discussion.

We found that compared to people with serious infections without OA, those with OA were 16 years older with more medical comorbidity, and were more likely to be female, White, have Medicare and receive care at a rural hospital. Not surprisingly, those with OA were more likely to be discharged to non-home settings, 24% vs. 35%, respectively, which may be related to their older age and higher comorbidity and Medicare's benefits for discharge to a rehabilitation/healthcare facility. People with OA and serious infections were less likely to die in-hospital, 6.3% vs. 4.6%, respectively.

The overall rates of serious infections (composite) in people with OA increased over the study period from 264/100,000 NIS hospitalizations in 1998 to 918/100,000 in 2016, a 3.5-fold higher rate, in contrast to a 1.7-fold increase in serious infection hospitalizations in the general NIS population over the same period. This higher rate of increase in serious infections in OA cohort compared to that of the general NIS sample may be due to the differences in the two cohorts in age and comorbidity, i.e., people with OA were older and sicker compared to their counterparts. Some differences may be related to increasing rates of prosthetic infections in people undergoing knee or hip arthroplasty (5). Increasing rates of use of biologics and glucocorticoids in other concomitant rheumatic conditions in OA, such as rheumatoid arthritis, lupus etc. may have contributed. In a study of the 1993-2003 NIS, hospitalizations for serious infections more than doubled in people with RA, mostly due to 3-fold increase in sepsis rate, but SSTI, UTI and OI rates decreased over time (10). A similar increase in sepsis rate over time in OA may have also occurred, but can not explain the increases in other serious infections.

Relative increases in rates/100,000 NIS hospitalizations of sepsis and UTI of 11-12.5 fold exceeded those of pneumonia at 1.4-fold. Many of these time-trends in each serious infection

hospitalization were in parallel to those in the general NIS cohort, although the relative increases were higher in OA versus non-OA cohorts. These are important observations that can inform the policymakers with regards to the relative contribution of these serious infections to the overall morbidity burden of serious infection in OA cohort in the U.S.

Our findings of the association of patient, comorbidity and hospital variables with higher healthcare utilization outcomes and in-hospital mortality, add to the current knowledge. We observed independent associations of older age, higher Deyo-Charlson index score, sepsis, Northeast region, Medicare insurance payer, urban teaching or non-teaching hospital and medium or large hospital bed size with higher healthcare utilization outcomes and in-hospital mortality. Additionally, Medicaid insurance payer, non-White race, and female sex were associated with higher healthcare utilization only. This knowledge can help in better prognostication of healthcare utilization and mortality in people hospitalized with serious infections in OA that have these risk factors.

We found that the unadjusted length of hospital stay and in-hospital mortality decreased, and total hospital charges increased for serious infections from 1998-2000 to 2015-2016. These findings are in parallel to the similar time-trends in the overall NIS sample.

Several study limitations must be considered while interpreting our findings. Misclassification bias was minimized by the use of valid codes for serious infection (10-12, 17, 18) and osteoarthritis (13, 14) with high positive predictive values, but is possible, since we used the ICD-codes. A separate validation of codes in the NIS is not possible, since no medical records, laboratory and imaging tests and medications are available in the NIS. Misclassification might have biased our results towards the null. The absence of measures of disease severity and extent, and imaging tests in the NIS limits analyses of OA disease subgroups, which could provide valuable insight. These questions need to be examined in future studies, which use other datasets that provide these data. The unit of analysis in NIS is hospitalizations, not people. A greater increase in the rate of sepsis over time versus pneumonia and

other serious infections may at least partially be due to upcoding pneumonia and other infections being coded as sepsis diagnosis in the more recent years (19-21). We used a completed cases sample for our multivariable-adjusted analyses and exclusion of incomplete cases may have biased our results. However, of the almost 3.2 million eligible serious infection hospitalizations in people with RA, 93% to 98% were included in the multivariable-adjusted analyses, which minimizes this bias. We dichotomized hospital stay and charges, which may have limited our ability to detect changes; however, these allowed a more clinically meaningful interpretation of results and we noted several significant associations with our current approach.

Our study strengths include the use of the U.S. national data, inclusion of several important confounders of healthcare utilization and mortality, and a large sample size.

In conclusion, we found that people hospitalized with a primary diagnosis of a serious infection and a secondary diagnosis of OA differed in important ways from people hospitalized with serious infections, but no OA. We found that the rate of serious infections increased from 1998 to 2016 in people with OA. The rate of increase in each serious infection in people with OA varied across the serious infections, being the lowest for pneumonia and highest for UTI and sepsis. We found that over time in people with OA and serious infection, the unadjusted length of hospital stay and in-hospital mortality decreased, and the total hospital charges increased. Several patient, comorbidity and hospital characteristics were associated with higher healthcare utilization and in-hospital mortality. Our study provides data for the serious infection hospitalization burden for people with OA. Several novel findings from our study can lead to the development and testing of interventions to improve outcomes of serious infection hospitalizations in OA.

Abbreviations:

NIS, National Inpatient Sample

HR, Hazard ratio

CI, confidence interval

SD, standard deviation

SE, standard error

OA, osteoarthritis

UTI, urinary tract infection

SSTI, skin and soft tissue infections

OI, opportunistic infections

CCS, Clinical Classifications Software

UAB, University of Alabama at Birmingham

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification

Author contributions: Jasvinder A. Singh designed the study, developed study protocol, reviewed analyses and wrote the first draft of the paper. John D. Cleveland performed the data abstraction and data analyses. All authors revised the manuscript, read, and approved the final manuscript.

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of Care Committees, the Chair of the ACR Meet-the-Professor, Workshop and Study Group Subcommittee and the co-chair of the ACR Criteria and Response Criteria subcommittee. JDC has no conflicts. There are no non-financial competing interests for either author.

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Authors Information:

Jasvinder A. Singh: Jasvinder.md@gmail.com

John Cleveland: jcleveland@uabmc.edu

Address for both authors: University of Alabama at Birmingham, Faculty Office Tower 805B, 510 20th Street S, Birmingham, AL 35294-0022, USA.

Availability of Data and materials: These data are easily available from the Agency for Healthcare Research and Quality (AHRQ's) "Healthcare Cost and Utilization Project (HCUP)" and can be obtained after completing an on-line Data Use Agreement training session and signing a Data Use Agreement. The contact information for requesting the data is as follows:

HCUP Central Distributor

Phone: (866) 556-4287 (toll-free)

Fax: (866) 792-5313

E-mail: HCUPDistributor@ahrq.gov

Figure Title and Figure legend

Figure 1. Rate of hospitalized infection in people with osteoarthritis per 100,000 total NIS claims (1A) and per 100,000 overall osteoarthritis claims (1B)

Figure 1 legend

The y-axis shows rate per 100,000 hospitalization claims. The denominator for 1A was all NIS claims and for 1B claims with osteoarthritis as a non-primary (or secondary) diagnosis. The study cohort had a primary diagnosis of one of the hospitalized infections of interest.

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Table 1. Demographic characteristics of infection hospitalizations in people with versus without osteoarthritis (OA)

	Any Hospitalization in people **with OA** diagnosis (n= 6,640,693*)	Serious Infection hospitalization in people **without OA** (n=46,708,154*)	Serious Infection hospitalization in people **with OA** (n=3,258,416*)
Age, Mean (SE); Median	73.0 (0.03); 74.8	58.7 (0.09); 63.7	75.1 (0.03); 77.1
Age category			
<50 years	1,955,351 (6.08%)	13,938,324 (30.07%)	144,347 (4.45%)
50 - <65 years	6,223,753 (19.35%)	9,457,702 (20.40%)	538,309 (16.61%)
65 - 79 years	11,902,974 (37.01%)	12,176,601 (26.27%)	1,111,384 (34.29%)
≥80 years	12,079,521 (37.56%)	10,778,643 (23.25%)	1,446,991 (44.65%)
Sex			
Male	10,728,960 (33.36%)	22,340,303 (48.22%)	1,118,888 (34.53%)
Female	21,428,319 (66.64%)	23,984,951 (51.78%)	2,121,736 (65.47%)
Race			
White	21,389,350 (66.50%)	27,497,186 (59.30%)	2,261,686 (69.78%)
Black	3,070,053 (9.55%)	5,085,488 (10.97%)	257,590 (7.95%)
Hispanic	1,598,330 (4.97%)	4,046,213 (8.73%)	175,664 (5.42%)
Other/Missing	6,104,736 (18.98%)	9,740,081 (21.01%)	546,113 (16.85%)
Deyo-Charlson Score			
0	7,796,316 (24.24%)	15,010,295 (32.37%)	673,534 (20.78%)
1	8,207,134 (25.52%)	12,024,008 (25.93%)	913,367 (28.18%)
≥2	16,160,294 (50.24%)	19,339,287 (41.70%)	1,654,313 (51.04%)
Income Category			
0-25th percentile	8,318,330 (26.38%)	12,090,341 (26.71%)	889,336 (27.97%)
25-50th percentile	8,816,928 (27.96%)	12,399,653 (27.40%)	905,655 (28.48%)
50-75th percentile	7,663,994 (24.31%)	10,862,479 (24.00%)	755,089 (23.75%)
75-100th percentile	6,730,793 (21.35%)	9,905,646 (21.89%)	629,460 (19.80%)
Insurance			
Private	5,069,319 (15.79%)	10,578,781 (22.86%)	378,109 (11.68%)
Medicare	24,279,386 (75.61%)	24,878,546 (53.77%)	2,597,031 (80.24%)
Medicaid	1,734,792 (5.40%)	6,913,725 (14.94%)	173,718 (5.37%)
Other	603,564 (1.88%)	1,455,988 (3.15%)	46,523 (1.44%)
Self	426,151 (1.33%)	2,444,533 (5.28%)	41,283 (1.28%)
Hospital Location/Teaching			
Rural	5,291,083 (16.49%)	6,481,258 (14.72%)	551,438 (17.91%)
Urban Non-teaching	13,400,262 (41.77%)	17,919,939 (40.70%)	1,336,070 (43.40%)
Urban Teaching	13,386,218 (41.73%)	19,630,903 (44.58%)	1,190,903 (38.69%)
Discharge Status			
Rehabilitation or skilled nursing facility (SNF)	9,170,864 (29.24%)	10,594,684 (24.73%)	1,072,873 (34.92%)
Home	22,190,318 (70.76%)	32,245,769 (75.27%)	1,999,149 (65.08%)
Length of Stay in days			
≤3	14,857,065 (46.19%)	19,001,734 (40.98%)	1,119,995 (34.55%)
>3	17,306,680 (53.81%)	27,371,856 (59.02%)	2,121,219 (65.45%)
Died during hospitalization	607,104 (1.89%)	2,929,186 (6.32%)	149,883 (4.63%)
Length of Stay in days: Mean (SE); median	5.2 (0.01); 3.3	6.0 (0.01); 3.7	5.7 (0.01); 4.0

Total hospital charges (US $)			
≤median	12,430,982 (38.65%)	19,750,315 (42.59%)	1,405,007 (43.35%)
>median	19,732,763 (61.35%)	26,623,275 (57.41%)	1,836,207 (56.65%)
Total hospital charges in US $: mean (SE); median	31,324 (166); 18,626	34,872 (169); 16,754	31,085 (180); 17,942
1998-2000	12,510 (160); 8,360	11,709 (192); 8,063	18,474 (343); 9,629
2015-2016	49,808 (414); 31,983	54,383 (444); 28,862	45,242 (406); 27,977

SE, standard error; $, dollar

Median total charges by year: 1998, $5,775; 1999, $6,060; 2000, $6,723; 2001, $7,504; 2002, $8,601; 2003, $9,732; 2004, $9918; 2005, $10,816; 2006, $12,078; 2007, $13,001; 2008, $13,983; 2009, $14,814; 2010, $15,560; 2011, $17,815; 2012, $19,654; 2013, $21,166; 2014, $22,343; 2015, $23,678; 2016, $25,261

* All the rates and frequencies are national level estimates based on the sampling weights as recommended by the NIS

Table 2. Multivariable-adjusted correlates of healthcare utilization and mortality for serious infections in OA in a national U.S. sample*

	Hospital charges >median	Discharge to care facility	Length of Hospital Stay >median	In-hospital Mortality
	Adjusted odds ratio (95% CI)			
Age category				
<50 years	Ref	Ref	Ref	Ref
50 - <65 years	**1.04 (1.01, 1.07)**	**1.66 (1.59, 1.74)**	**1.17 (1.14, 1.20)**	**1.89 (1.66, 2.16)**
65 - 79 years	1.01 (0.98, 1.04)	**2.71 (2.59, 2.83)**	**1.25 (1.22, 1.29)**	**3.16 (2.78, 3.60)**
≥80 years	0.94 (0.92, 0.97)	**6.48 (6.20, 6.78)**	**1.40 (1.36, 1.44)**	**6.06 (5.32, 6.90)**
Sex				
Male	Ref	Ref	Ref	Ref
Female	**1.02 (1.01, 1.03)**	**1.18 (1.16, 1.19)**	**1.11 (1.09, 1.12)**	1.01 (0.99, 1.04)
Race/ethnicity				
White	Ref	Ref	Ref	Ref
Black	**1.17 (1.15, 1.19)**	**1.10 (1.08, 1.13)**	**1.17 (1.15, 1.20)**	1.03 (0.98, 1.07)
Hispanic	**1.71 (1.67, 1.76)**	**0.73 (0.71, 0.75)**	**1.08 (1.06, 1.11)**	**0.92 (0.87, 0.97)**
Other/missing	0.98 (0.97, 0.99)	**0.88 (0.87, 0.89)**	1.02 (1.00, 1.03)	1.02 (0.98, 1.06)
Deyo-Charlson score				
0	Ref	Ref	Ref	Ref
1	**1.27 (1.25, 1.29)**	**1.10 (1.08, 1.11)**	**1.24 (1.22, 1.26)**	**1.15 (1.11, 1.20)**
≥2	**1.53 (1.51, 1.55)**	**1.38 (1.36, 1.40)**	**1.53 (1.51, 1.55)**	**1.65 (1.59, 1.71)**
Income category				
0-25th percentile	**0.94 (0.92, 0.96)**	1.00 (0.98, 1.02)	**1.03 (1.01, 1.04)**	0.97 (0.93, 1.01)
25-50th percentile	**0.92 (0.91, 0.94)**	0.99 (0.97, 1.01)	**1.04 (1.02, 1.06)**	0.97 (0.94, 1.01)
50-75th percentile	**0.93 (0.92, 0.95)**	1.01 (0.99, 1.02)	1.01 (0.99, 1.02)	**0.94 (0.90, 0.97)**
75-100th percentile	Ref	Ref	Ref	Ref
Primary Infection Diagnosis				
Sepsis	Ref	Ref	Ref	Ref
OI	**0.86 (0.82, 0.90)**	**0.48 (0.45, 0.50)**	**0.92 (0.87, 0.96)**	**0.32 (0.28, 0.36)**
SSTI	**0.42 (0.42, 0.43)**	**0.44 (0.44, 0.45)**	**0.64 (0.63, 0.65)**	**0.04 (0.03, 0.04)**
UTI	**0.37 (0.36, 0.38)**	**0.48 (0.46, 0.49)**	**0.36 (0.36, 0.37)**	**0.05 (0.04, 0.06)**
Pneumonia	**0.70 (0.70, 0.71)**	**0.48 (0.48, 0.49)**	**0.73 (0.72, 0.74)**	**0.31 (0.30, 0.32)**
Insurance payer				
Medicare	**1.19 (1.17, 1.22)**	**1.79 (1.75, 1.83)**	**1.25 (1.22, 1.27)**	**0.89 (0.85, 0.94)**
Medicaid	**1.29 (1.25, 1.32)**	**1.55 (1.49, 1.60)**	**1.23 (1.20, 1.27)**	0.96 (0.88, 1.04)
Other	**1.13 (1.08, 1.18)**	**1.28 (1.21, 1.36)**	1.05 (1.00, 1.09)	**1.63 (1.47, 1.81)**
Private	Ref	Ref	Ref	Ref
Self	**1.15 (1.09, 1.21)**	**0.72 (0.66, 0.78)**	1.01 (0.97, 1.06)	**1.18 (1.02, 1.37)**
Hospital Region				
Northeast	Ref	Ref	Ref	Ref
Midwest	**0.74 (0.73, 0.76)**	0.99 (0.97, 1.01)	**0.76 (0.75, 0.78)**	**0.85 (0.82, 0.89)**
South	**0.88 (0.87, 0.90)**	**0.76 (0.74, 0.77)**	**0.84 (0.83, 0.85)**	**0.94 (0.90, 0.97)**
West	**1.09 (1.07, 1.11)**	**0.74 (0.73, 0.76)**	**0.61 (0.60, 0.62)**	**0.93 (0.89, 0.97)**
Hospital Location/Teaching				
Rural	Ref	Ref	Ref	Ref
Urban Non-teaching	**2.36 (2.32, 2.40)**	0.99 (0.97, 1.01)	**1.27 (1.25, 1.30)**	**1.06 (1.02, 1.10)**
Urban Teaching	**2.02 (1.99, 2.05)**	**0.88 (0.87, 0.90)**	**1.14 (1.12, 1.16)**	**1.06 (1.02, 1.10)**
Hospital Bed size				
Small	Ref	Ref	Ref	Ref

Medium	**1.37 (1.35, 1.39)**	0.97 (0.95, 0.99)	**1.16 (1.14, 1.18)**	**1.07 (1.03, 1.11)**
Large	**1.82 (1.79, 1.85)**	**0.91 (0.90, 0.93)**	**1.31 (1.29, 1.33)**	**1.17 (1.13, 1.22)**

CI, Confidence Interval; Ref, reference category

* All the rates and frequencies are national level estimates based on the sampling weights as recommended by the NIS

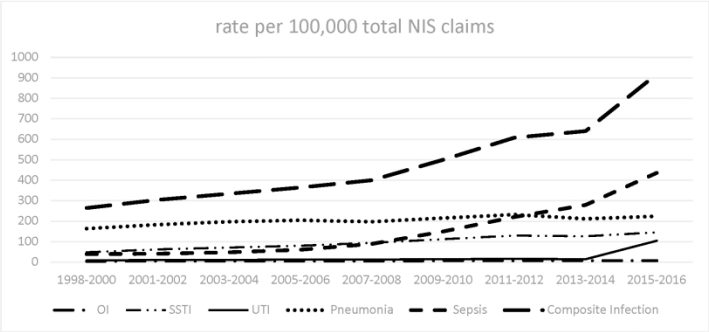

Figure 1A.

Figure 1. Rate of hospitalized infection in people with osteoarthritis per 100,000 total NIS claims (1A) and per 100,000 overall osteoarthritis claims (1B)

Figure 1 legend

The y-axis shows rate per 100,000 hospitalization claims. The denominator for 1A was all NIS claims and for 1B claims with osteoarthritis as a non-primary (or secondary) diagnosis. The study cohort had a primary diagnosis of one of the hospitalized infections of interest.

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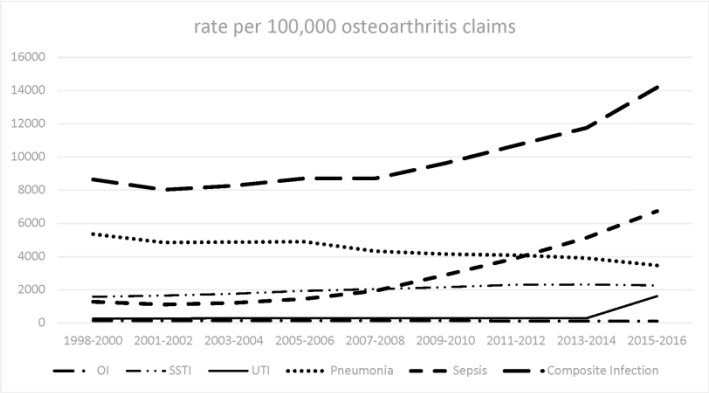

Figure 1B.
same as above

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