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Hospitalized Infections in Patients With Rheumatic Disease Hospitalizations in Alaska, 2015-2018

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Objective. Rheumatic diseases are associated with increased rates of hospitalized infection, but few studies have included Indigenous North American populations. Our objective was to evaluate the association of rheumatic disease diagnosis during a hospitalization with odds of hospitalized infections in Alaska and assess differences by race.

Methods. We used hospital discharge data from the Alaska Health Facilities Data Reporting Program from 2015 to 2018. We identified people with a rheumatic disease diagnosis based on any hospital discharge diagnosis of a set of rheumatic diseases and compared them to people hospitalized but without a rheumatic disease diagnosis. We determined odds of hospitalized infection by rheumatic disease diagnosis status and type, race, and type of infection. Using multivariable modeling, we determined factors associated with hospitalized infection.

Results. Having a rheumatic disease diagnosis other than osteoarthritis was associated with 1.90 higher odds of hospitalized infection overall, whereas people of Alaska Native/American Indian (AN/AI) race with rheumatic disease had 2.44 higher odds. The odds varied by rheumatic disease and were increased in all rheumatic diseases except osteoarthritis (0.73). The most common type of hospitalized infection was sepsis, but opportunistic infections and pneumonia were most associated with a rheumatic disease diagnosis. On multivariable analysis, having a rheumatic disease diagnosis other than osteoarthritis, being of older age, and being of AN/AI race were associated with increased odds of hospitalized infection, with an interaction between race and rheumatic disease status.

Conclusion. This study confirmed the association of hospitalized infections with rheumatic disease diagnosis (other than osteoarthritis) during hospitalization and identified disparities by race.

INTRODUCTION

Rheumatic diseases are associated with an increased risk of serious infections resulting in hospitalization. The risk of infection is increased by certain disease-modifying or immunosuppressive medications used to treat rheumatic diseases, as well as immune dysregulation in certain disease states, and high rates of hospitalization for infections have been described most commonly in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) (1,2). While the risk of serious infection is higher in RA than noninflammatory rheumatic diseases (3), recent studies have also described high rates of hospitalization for serious infections in people with osteoarthritis and gout, for whom long-term immunosuppressive medication is not typically prescribed, compared to individuals without those conditions (4,5). Several studies have described an increase in the rates of hospitalization for serious infections over time with changes in the distribution of types of infection, specifically in RA (6) and SLE (7).

There are disparities in the incidence and prevalence of rheumatic diseases, as well as disparities in the risk of infections in different populations. Indigenous North American (INA) populations have high rates of some rheumatic diseases, including RA, SLE, and spondyloarthritis (8). In addition, studies have described high rates of certain infections and disparities in hospitalizations for infectious diseases in INA populations, including Alaska Native people (9,10). Few studies have examined the rates of hospitalized infections in INA populations with rheumatic disease diagnoses, but one study in a cohort of patients with SLE identified among Medicaid beneficiaries in the US found a high incidence of hospitalizations for serious infections in INA people (2).

Our overall study was designed to evaluate the impact of rheumatic disease on the Alaska Native/American Indian (AN/AI)

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population in Alaska, including a focus on hospitalizations. We previously described the general characteristics of hospitalizations in people with or without a rheumatic disease diagnosis and found that people with a rheumatic disease diagnosis were older and more likely to be of AN/AI race, and that they had more hospitalizations overall with a longer average length of stay and a higher likelihood of having a hospitalization with a primary diagnosis of a musculoskeletal condition (11). In the analysis presented herein, we investigated hospitalized infections in people with rheumatic disease hospitalizations compared to those hospitalized without a rheumatic disease diagnosis in Alaska from 2015 to 2018. Despite the limitations of hospital discharge data sets to identify population-based cohorts of people with rheumatic disease, we hypothesized that higher rates of hospitalized infection would be found in people of all races with a rheumatic disease diagnosis made during a hospitalization compared to people without a rheumatic disease diagnosis. We also hypothesized that the difference would be more pronounced for AN/AI people with a rheumatic disease diagnosis. Finally, we hypothesized that the likelihood of hospitalized infection would differ based on the specific rheumatic disease diagnosed.

PATIENTS AND METHODS

This study was reviewed and approved as expedited research by the Alaska Area Institutional Review Board (IRB; protocol #2019-03-021), including a waiver of consent. In addition to IRB approval, the study was reviewed and approved by the Alaska Native Tribal Health Consortium and participating regional tribal health organizations prior to the research being conducted. Finally, this article's manuscript was reviewed and approved by participating tribal health organizations prior to submission for journal review.

Study population and data source. Data for this study were obtained from the State of Alaska Health Facilities Data Reporting Program (HFDR). The HFDR collects mandated reports on discharge data from hospitals and health care facilities in Alaska, which is used to create the Alaska Inpatient Database. Because only limited outpatient data are available and not as complete as the inpatient data, only inpatient data were used for this study. The data set is deidentified and may be used for population health assessment, research, or health care operations, but it may not be linked with other data sets to identify cohorts of patients. The lack of outpatient data and inability to identify individuals precludes study of true population-based cohorts using this data set. While protected health information is not included in the HFDR, the data set does include demographics provided by the submitting health care facility (age, gender, race, region of residence), as well as discharge diagnoses (primary and all listed), length of stay, in-hospital mortality, and discharge status (to home or other). The HFDR includes data from all regions of Alaska. For this study, we included patients aged 18 and older at the time of the hospital encounter, of any gender and race, and from any region of Alaska. Out of state residents hospitalized in Alaska were excluded from this study because we were interested in Alaska residents and out of state resident characteristics were expected to differ. For data analysis, an individual person's race was determined by the category listed in the HFDR as provided by the submitting health care facility (typically collected from the patient at the time of registration at the facility) and included AN/AI, White, Black, Asian, Native Hawaiian/Pacific Islander, or Other. The HFDR does not include a multiracial category. For comparisons of race, persons with missing race in the HFDR were excluded. In our analyses, we were interested in differences between AN/AI and non-AN/AI people. Because of observed differences between White and other races, our analyses included three categories for race, AN/AI, White, and Other (which combined Black, Asian, Native Hawaiian/Pacific Islander, and Other as listed in HFDR). The HFDR data set from the years of interest only allows for male or female gender to be reported.

Case definitions. First, we identified people with or without a rheumatic disease diagnosis stated during a hospitalization as described previously (11). Once eligibility was determined based on age and Alaska residence, people with rheumatic disease were defined as having at least one hospitalization with any listed diagnosis of a set of rheumatic diseases of interest (primary or any alternate) at any time from 2015 through 2018. People without rheumatic disease had at least one hospitalization during that time period without any listed diagnosis of rheumatic disease. Rheumatic diseases were identified by International Classification of Diseases (ICD)-9 and ICD-10 codes as previously described and included a set of nine categories of conditions (osteoarthritis, gout, RA, spondyloarthritis, SLE or mixed connective tissue disease [MCTD], systemic sclerosis, vasculitis, Sjögren syndrome, and inflammatory myopathy) (11). While we were unable to specifically validate these case definitions in this data set, the ICD-9 and ICD-10 codes were selected based on typical coding for these conditions. In our analyses, we considered people with a rheumatic disease diagnosis of osteoarthritis only separately from those with all other rheumatic disease diagnoses, based on differences in associations with hospitalized infection.

Hospitalized infections were identified based on having a primary diagnosis of one of a set of serious infections during a hospitalization during the study period. These infections were identified based on ICD-9 and ICD-10 codes, as listed in Supplementary Table 1. Serious infections were grouped into five categories: pneumonia, skin and soft tissue infections, urinary tract infections, sepsis, and opportunistic infections.

Statistical analysis. We assessed difference in likelihood of any hospitalized infection among people with a rheumatic disease diagnosis of osteoarthritis only, people with all other rheumatic diseases, and people without any rheumatic disease

diagnosis. We used univariate analysis to compare overall proportion hospitalized and odds of hospitalization stratified by specific patient characteristics, including gender, age, race, type of residence (urban or rural), comorbidities, and total number of hospitalizations of any type during the study period. We also compared the length of hospitalization and hospital discharge status (to home vs. other and to home vs. in-hospital mortality) for hospitalized infections by rheumatic disease diagnosis status. For evaluation of comorbidities, we used the Deyo-Charlson comorbidity index, including a list of 17 comorbid conditions identified by ICD-9 and ICD-10 codes and with associated weights. This was calculated using an R package created to compute comorbidity scores (12).

We evaluated whether the odds of hospitalized infection by the level of these other factors differed between people diagnosed with rheumatic disease (with osteoarthritis or all other rheumatic diseases) and people without any rheumatic disease diagnosis, calculating conditional exact tests, odds ratios, and associated melded confidence intervals (13). We further examined whether there were additional variations in the odds of hospitalized infections by the specific type of rheumatic disease and whether there were variations in the association with rheumatic disease by the category of infection. Because race appears to influence both of these characteristics, we also examined differences by race.

To more accurately understand the modification of odds of hospitalized infection conveyed by a rheumatic disease diagnosis, we constructed multivariable logistic models to adjust for differences in the aforementioned patient characteristics for people with versus without a rheumatic disease diagnosis who did or did not have a hospitalized infection. We considered models with and without interaction terms, balancing complexity of interpretation with accurate representation of the effects of covariates. We developed separate models for osteoarthritis and for all other rheumatic disease diagnoses.

In analyses using patients' reported race, persons (and associated hospitalizations) with unknown race were excluded (less than 5% of hospitalizations). Similarly, persons (and their hospitalizations) whose only hospitalizations were pregnancy related were excluded. Because a person's hospitalizations were not examined until they turned age 18, and because some patients were known to have died during the study period (based on in-hospital mortality as reported in the HFDR), a small number of patients (less than 5%) contributed data for a shorter period than the entire 2015 to 2018 study period. A simple sensitivity analysis did not suggest any meaningful systematic difference in examined characteristics of these few persons with a curtailed examination period.

RESULTS

The characteristics associated with differences in the proportion of hospitalized infections for people with a rheumatic disease diagnosis during a hospitalization compared to people without a rheumatic disease diagnosis are presented in Table 1, stratified by characteristics of the patients. In patients with a rheumatic disease diagnosis other than osteoarthritis, a higher proportion had been hospitalized for infection than people without a rheumatic disease diagnosis, whereas the converse was true for people with an osteoarthritis diagnosis only. The odds ratio of hospitalized infection for people with a rheumatic disease diagnosis other than osteoarthritis compared to people with no rheumatic disease diagnosis was highest in those in the youngest age group (18 to 39 years old), although the absolute number of hospitalizations increased with age. The odds did not differ by gender, but people of AN/AI race had the highest odds of hospitalized infection associated with rheumatic disease (for osteoarthritis and for all other rheumatic diseases), with the set of races categorized as "Other" also having higher odds than those who identified as White. Rural residence was associated with higher odds than urban residence. A comorbidity score of 3 or higher and a longer length of stay had higher odds of hospitalized infection, whereas discharge to home was not statistically different between groups. In-hospital mortality was lower in people with osteoarthritis than people with no rheumatic disease diagnosis, but there was no difference in mortality between people with all other rheumatic disease diagnoses as compared to no rheumatic disease diagnosis.

The proportion and odds of hospitalized infection by type of rheumatic disease are shown in Table 2, with a breakdown by race in Figure 1. The rheumatic disease with the highest odds of hospitalized infection was myopathy, although the number of cases was small. The next highest odds were for SLE/MCTD and vasculitis. The lowest odds of hospitalized infection were with osteoarthritis (odds ratio 0.84; 95% CI: 0.79-0.89), the only condition for which the odds of infection were lower in the setting of a rheumatic disease diagnosis. As presented in Figure 1, the association between types of rheumatic disease and hospitalized infection varied by race, for all conditions except SLE/MCTD ($P = 0.34$). For all conditions with statistically significant differences by race, the lowest proportion of hospitalized infections occurred in people who identified as White, whereas AN/AI people had a higher likelihood of hospitalized infections, and those of other races fell in between White and AN/AI. Figure 1 excludes vasculitis, Sjögren syndrome, myopathy, and systemic sclerosis because each of these conditions have fewer than 75 people with a hospitalized infection.

Differences in the types of hospitalized infections are presented in Table 3. As shown in Table 3, 22.3% of people with a rheumatic disease diagnosis other than osteoarthritis had at least one hospitalized infection compared to 13.1% of those with no rheumatic disease diagnosis (odds ratio 1.90; 95% CI: 1.77-2.03). The most common infectious disease diagnosis was sepsis in all groups. Opportunistic infections and pneumonia were the categories with the most significant differences in odds between people with rheumatic disease diagnoses compared to people without.

Table 1. Hospitalized infections for patients in Alaska with OA, other RD hospitalization, or no RD hospitalization, 2015-2018, overall and stratified by patient characteristics

Characteristic	Hospitalization for infection in people with OA and no other RD (of 10,516)	Hospitalization for infection in people with RD other than OA (of 5316)	Hospitalization for infection in people without RD (of 61,896)	Odds ratio (95% confidence interval) for OA vs. no RD	Odds ratio (95% confidence interval) for RD other than OA vs. no RD
Any ID hospitalization	1047 (10.0%)	1184 (22.3%)	8123 (13.1%)	0.73 (0.68-0.78)	1.90 (1.77-2.03)
Age group					
18-39 y	25 (9.3%)	105 (28.5%)	1797 (10.9%)	0.84 (0.53-1.27)	3.26 (2.56-4.12)
40-64 y	376 (8.5%)	440 (21.0%)	3281 (12.4%)	0.66 (0.59-0.74)	1.88 (1.68-2.10)
65 y or older	646 (11.1%)	639 (22.4%)	3045 (16.0%)	0.65 (0.59-0.71)	1.51 (1.37-1.67)
Gender					
Female	619 (10.5%)	606 (23.8%)	3997 (13.5%)	0.75 (0.69-0.82)	1.99 (1.80-2.20)
Male	428 (9.2%)	578 (20.9%)	4126 (12.7%)	0.70 (0.62-0.77)	1.81 (1.64-2.00)
Race					
White	635 (8.2%)	620 (19.1%)	4490 (12.0%)	0.66 (0.60-0.72)	1.73 (1.58-1.90)
AN/AI	304 (18.2%)	348 (31.5%)	2467 (15.8%)	1.18 (1.03-1.35)	2.44 (2.13-2.79)
Other	89 (10.0%)	200 (23.4%)	950 (13.5%)	0.72 (0.56-0.90)	1.96 (1.64-2.33)
Type of residence					
Urban	722 (10.1%)	807 (22.5%)	5439 (13.5%)	0.72 (0.66-0.78)	1.86 (1.71-2.02)
Rural	325 (9.7%)	377 (21.8%)	2676 (12.4%)	0.76 (0.67-0.86)	1.97 (1.74-2.23)
Deyo-Charlson comorbidity index					
0	104 (2.3%)	57 (9.2%)	2192 (7.9%)	0.28 (0.23-0.34)	1.19 (0.88-1.57)
1-2	337 (9.4%)	314 (16.5%)	2838 (14.0%)	0.64 (0.56-0.72)	1.21 (1.06-1.38)
≥3	606 (24.5%)	813 (29.1%)	3093(22.1%)	1.14 (1.03-1.26)	1.44 (1.31-1.58)
Length of stay of ID hospitalization					
≤3 d	513 (34.0%)	573 (33.7%)	3838 (37.2%)	Reference	Reference
>3 d	998 (66.0%)	1129 (66.3%)	6468 (62.8%)	1.15 (1.03-1.30)	1.17 (1.05-1.31)
Discharge status					
To home	1160 (82.3%)	1282	7669 (81.4%)	Reference	Reference
Other than home	250 (17.7%)	287	1748 (18.6%)	0.95 (0.81-1.10)	0.98 (0.85-1.12)
In-hospital mortality					
Discharge home	1160 (92.5)	1282	7669 (90.0%)	Reference	Reference
Death in hospital	94 (7.5%)	127	851 (10.0%)	0.73 (0.58-0.91)	0.89 (0.73-1.09)

Abbreviations: AN/AI, Alaska Native/American Indian; ID, infectious disease; OA, osteoarthritis; RD, rheumatic disease.

In Table 4, we present four multivariable models investigating associations with hospitalized infection, two for osteoarthritis alone and two for rheumatic disease other than osteoarthritis. These models include rheumatic disease and other characteristics associated with hospitalized infection. The first model for each condition does not include interaction terms, and therefore the odds ratios have a clearer interpretation. The second model for each condition includes relevant interaction terms for race and rheumatic disease, given that there are significant interactions identified. As shown in the first model for rheumatic disease other than osteoarthritis, when adjusted for other factors including age, race, gender, total number of hospitalizations, and death, people

Table 2. Unadjusted odds of hospitalized infection by type of RD for people of all races in Alaska, 2015 to 2018

Type of RD[a]	Number with this rheumatic disease	Number (%) with any hospitalized infection	Odds ratio (95% confidence interval)
None	61,896	8123 (13.1%)	Reference
Osteoarthritis	11,943	1346 (11.3%)	0.84** (0.79-0.89)
Gout	2880	595 (20.7%)	1.72** (1.57-1.89)
Rheumatoid arthritis	1710	420 (24.6%)	2.16** (1.92-2.41)
Lupus or MCTD	384	111 (28.9%)	2.69** (2.14-3.37)
Spondyloarthritis	314	77 (24.5%)	2.15** (1.64-2.80)
Vasculitis	165	46 (27.9%)	2.56** (1.78-3.63)
Sjögren syndrome	145	35 (24.1%)	2.11** (1.40-3.11)
Systemic sclerosis	72	18 (25.0%)	2.21** (1.22-3.82)
Myopathy	45	17 (37.8%)	4.02** (2.06-7.61)

Abbreviations: MCTD, mixed connective tissue disorder; RD, rheumatic disease.
[a]One patient can be in multiple rows if multiple types of RD were diagnosed.
**$P < 0.01$ for all odds ratio calculations.

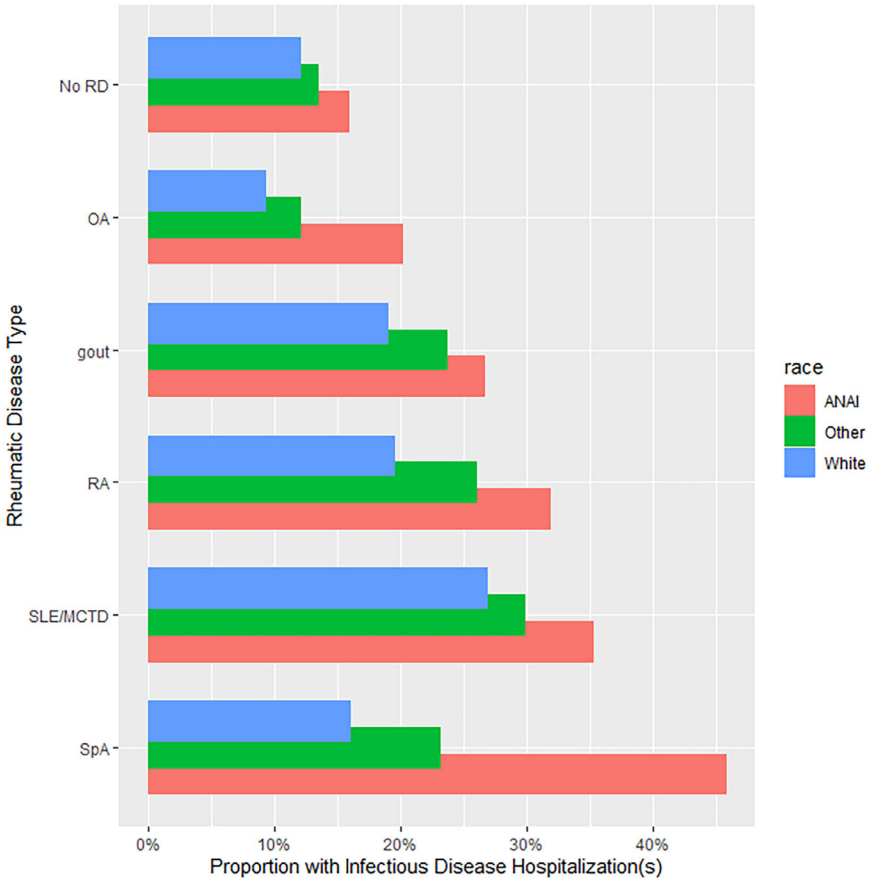

Figure 1. Percentage of patients with any hospitalized infection by rheumatic disease type and by race. This figure excludes vasculitis, Sjögren syndrome, myopathy, and systemic sclerosis because there were fewer than 75 people in each of these groups with a hospitalized infection. Comparisons by race were statistically significant (at $P < 0.01$) for all rheumatic disease types displayed except SLE/MCTD ($P = 0.34$). AN/AI, Alaska Native/American Indian; OA, osteoarthritis; RA, rheumatoid arthritis; RD, rheumatic disease; SLE/MCTD, systemic lupus erythematosus or mixed connective tissue disease; SpA, spondyloarthritis.

with rheumatic disease have 1.37 higher odds of hospitalization overall than people without a rheumatic disease diagnosis. The odds are lower for people of White and other races compared to people of AN/AI race. When adding the interaction term, the odds of hospitalized infection are increased to 1.77 for AN/AI people with rheumatic disease compared to AN/AI people without

Table 3. Odds of hospitalization by type of infection for patients of all races with OA, other RD hospitalization, or no RD hospitalization, 2015 to 2018

Type of infection	Number (%) with one or more hospitalizations for this infection for patients with OA and no other RD (of 10,516)	Number (%) with one or more hospitalizations for this infection for patients with RD other than OA (of 5316)	Number (%) with one or more hospitalizations for this infection for patients without RD (of 61,896)	Odds ratio (95% confidence interval) of one or more hospitalizations for this infection for patients with OA vs. no RD	Odds ratio (95% confidence interval) of one or more hospitalizations for this infection for patients with RD other than OA vs. no RD
Any ID hospitalization	1047 (10.0%)	1184 (22.3%)	8123 (13.1%)	0.73 (0.68-0.78)	1.90 (1.77-2.03)
Pneumonia	100 (1.0%)	93 (1.7%)	521 (0.8%)	1.13 (0.90-1.41)	2.10 (1.66-2.63)
SSTI	57 (0.5%)	86 (1.6%)	563 (0.9%)	0.59 (0.44-0.78)	1.79 (1.41-2.26)
Sepsis	916 (8.7%)	1023 (19.2%)	6870 (11.1%)	0.76 (0.71-0.82)	1.91 (1.77-2.05)
UTI	32 (0.3%)	24 (0.5%)	289 (0.5%)	0.65 (0.44-0.94)	0.97 (0.61-1.47)
OI	17 (0.2%)	31 (0.6%)	127 (0.2%)	0.79 (0.45-1.31)	2.85 (1.86-4.26)

Abbreviations: ID, infectious disease; OA, osteoarthritis; OI, opportunistic infection; RD, rheumatic disease; SSTI, skin and soft tissue infection; UTI, urinary tract infection.

Table 4. Multivariable model of associations with hospitalized infection for people with OA or other RD hospitalization compared to no RD hospitalization in Alaska, 2015 to 2018

Predictor variable	Simple model for OA and no other RD Odds ratio (95% confidence interval) for hospitalized infection	Model accounting for interactions for OA and no other RD Odds ratio (95% confidence interval) for hospitalized infection	Simple model for RD other than OA Odds ratio (95% confidence interval) for hospitalized infection	Model accounting for interactions for RD other than OA Odds ratio (95% confidence interval) for hospitalized infection
RD				
None	Reference	See below	Reference	See below
Any	0.61 (0.57-0.66)	--	1.37 (1.27-1.47)	--
Race				
AN/AI	Reference	See below	Reference	See below
White	0.73 (0.69-0.77)	--	0.73 (0.69-0.77)	-
Other	0.87 (0.80-0.94)	--	0.87 (0.81-0.94)	--
Age				
Under 65 years	Reference	Reference	Reference	Reference
65 years or older	1.31 (1.25-1.38)	1.31 (1.24-1.37)	1.27 (1.21-1.33)	1.27 (1.21-1.34)
Total number of hospitalizations for any condition (for every increase by 1)	1.27 (1.26-1.28)	1.27 (1.25-1.28)	1.24 (1.23-1.26)	1.24 (1.23-1.26)
Death during hospitalization				
No	Reference	Reference	Reference	Reference
Yes	2.79 (2.59-3.01)	2.78 (2.57-3.00)	2.65 (2.46-2.85)	2.65 (2.46-2.85)
Gender				
Female	Reference	Reference	Reference	Reference
Male	0.96 (0.91-1.00)	0.96 (0.91-1.00)	0.95 (0.91-1.00)	0.95 (0.91-1.00)
Race and RD interaction				
AN/AI without RD	Not applicable	Reference	Not applicable	Reference
AN/AI with RD	Not applicable	0.82 (0.71-0.94)	Not applicable	1.77 (1.53-2.04)
White without RD	Not applicable	0.76 (0.72-0.80)	Not applicable	0.76 (0.72-0.80)
White with RD	Not applicable	0.42 (0.32-0.52)	Not applicable	0.92 (0.81-1.02)
Other without RD	Not applicable	0.89 (0.82-0.97)	Not applicable	0.89 (0.82-0.97)
Other with RD	Not applicable	0.52 (0.28-0.75)	Not applicable	1.24 (1.07-1.41)

Abbreviations: AN/AI, Alaska Native/American Indian; OA, osteoarthritis; RD, rheumatic disease.

rheumatic disease, whereas the odds of infection associated with a rheumatic disease diagnosis are not increased as much in those of White or other races. In contrast, the models for osteoarthritis show lower odds of hospitalized infection in people with a diagnosis of osteoarthritis compared to people with no rheumatic disease, and the model accounting for interactions demonstrates that these lowered odds occur in people of all categories of race.

DISCUSSION

In this study, we found that having a rheumatic disease diagnosis other than osteoarthritis during a hospitalization is associated with increased odds of hospitalized infection whereas having a diagnosis of osteoarthritis alone is associated with lower odds of hospitalized infection compared to people with a hospitalization but without a rheumatic disease diagnosis. The association between rheumatic disease diagnosis other than osteoarthritis and hospitalized infection varied by race, age, rural or urban residence, and comorbidities, but not gender. On multivariable analysis, having a rheumatic disease diagnosis other than osteoarthritis, being of older age, being of AN/AI race, having a higher number of total hospitalizations, and in-hospital mortality were associated with increased odds of hospitalized infection. Our most novel finding was that of an interaction between race and rheumatic disease status, such that rheumatic disease other than osteoarthritis increased the odds of hospitalized infection more in AN/AI people than in White people or people of other races. Hospital stays for people with rheumatic disease and infection were longer in people with any rheumatic disease diagnosis (including osteoarthritis) than for people without rheumatic disease but were not more likely to result in in-hospital mortality. The odds of hospitalized infection varied by rheumatic disease

and were highest in myopathy, SLE/MCTD, and vasculitis and lowest in osteoarthritis, although the likelihood of hospitalized infection within most rheumatic disease types also varied by race. The most common type of hospitalized infection overall was sepsis, but opportunistic infections and pneumonia were most strongly associated with a rheumatic disease diagnosis other than osteoarthritis. These findings should be interpreted in the context of the data source, a hospital discharge data set rather than a population-based cohort, and association may not indicate causation.

Our finding that having a diagnosis of a rheumatic disease other than osteoarthritis is associated with hospitalized infection is consistent with other studies. Several studies have recently evaluated characteristics of hospitalized infection using data from the US National Inpatient Sample (NIS) and compared characteristics of people with hospitalized infection and rheumatic disease to those without rheumatic disease. These have included studies of gout (5), RA, SLE (14), Sjögren syndrome (15), systemic sclerosis (16), and vasculitis (17). A recent study of a population-based cohort with systemic sclerosis identified the highest risk of any hospitalization in the first 5 years of disease and found a relative risk of hospitalization for infection of 3.90 compared to people without systemic sclerosis (18). Fewer studies have investigated hospitalized infections in inflammatory myopathy and spondyloarthritis. Most studies focus on a single rheumatic disease rather than considering rheumatic diseases as a whole. One study compared RA to a combination of noninflammatory rheumatic diseases and found a 50% higher risk of infectious disease hospitalization in RA compared to noninflammatory rheumatic diseases (3). One area in which our findings may differ from previous studies is the lower odds of hospitalized infection that we found in osteoarthritis. A study using data from the NIS, similar to those described earlier, found increasing rates of hospitalized infections in people with osteoarthritis (4). This study did not compare rates of infection in people with osteoarthritis to rates of infection in those without osteoarthritis but did find that characteristics of people with osteoarthritis and hospitalized infection differed from people without osteoarthritis: those with osteoarthritis were of older age and were more likely to be of female sex and White race (4). We are uncertain why lower rates of hospitalized infections exist for osteoarthritis compared to people with no rheumatic disease diagnosis even after controlling for demographics and other factors, but one possibility is that people hospitalized with a diagnosis of osteoarthritis in Alaska may have had better overall health than people hospitalized with other diagnoses, as the diagnosis of osteoarthritis may be listed during elective admission for joint replacement surgery. We plan to investigate the characteristics of people who have had joint replacement surgery in future research, but joint replacement did account for at least a quarter of hospitalizations for patients with a diagnosis of osteoarthritis.

Some studies have examined disparities by race in hospitalized infections. In the aforementioned studies using the NIS, race has been categorized as White, Black, Hispanic, and Other/Missing. Disparities in characteristics of hospitalizations (hospital charges, length of stay, and discharge to care facility) and in-hospital mortality by race have been described and have varied by the specific rheumatic disease. For example, in SLE, Black race was associated with an increase in all the health care use metrics of hospitalizations but not in-hospital mortality (14). Few studies have included indigenous populations when considering disparities, but one study found a high incidence rate ratio (1.40) of serious infection among Native American people with SLE compared to White people with SLE in the US (2). Our study adds substantially to the literature on disparities in hospitalized infections in INA populations with rheumatic disease.

Our finding that sepsis is the most common hospitalized infection in patients with or without rheumatic disease is consistent with recent national trends in RA (6), SLE (14), and other conditions. We observed that disparities by race were most significant for opportunistic infections and pneumonia. Disparities in lower respiratory tract infections resulting in hospitalization have been previously described for AN/AI people in Alaska compared to non-AN/AI people (10), but opportunistic infections are less common overall and were not described in the study of infectious disease hospitalizations in Alaska.

This study has a few limitations. First, data were obtained from a hospital discharge data set and do not include outpatient visits. Therefore, rheumatic disease diagnoses were identified based on having that diagnosis coded during an inpatient stay. This may identify patients with more severe disease or more comorbidities than the general population of rheumatic disease patients. As such, using hospitalization data may result in selection bias. Unfortunately, this limitation is inherent in any study using hospital discharge data, as many other rheumatic disease studies do. Second, we considered many rheumatic diseases combined for much of the data analysis although the associations with infection vary in magnitude across rheumatic disease. However, in addition to presenting combined data, we analyzed hospitalized infections for each condition separately, including a breakdown by race within rheumatic disease types. Third, data from this study depend on the coding of rheumatic disease during hospitalization, and if access to rheumatologists is limited, some rheumatic diseases may not be identified at all or may be misdiagnosed. In contrast, it is possible that physicians are more likely to code the rheumatic disease when the infection occurs, which may lead to collider bias. Again, these limitations are inherent in all studies using hospital discharge data. Finally, data from Alaska about hospitalized infections in AN/AI people may not be generalizable to other INA populations. However, published data in these populations are so limited that this study adds substantially to the existing literature.

This study of hospitalizations in Alaska from 2015 to 2018 confirmed the association of hospitalized infections with rheumatic disease diagnoses other than osteoarthritis identified during hospitalization. We confirmed that this association varies by specific rheumatic disease and type of infection and that race interacts with rheumatic disease status to affect the association, with the highest odds of hospitalized infection identified among AN/AI people with a rheumatic disease diagnosis. This study adds significantly to the literature on rheumatic disease impact in INA populations and supports the need for ongoing and future interventions to reduce disparities in infectious disease hospitalizations in these populations, especially when rheumatic diseases are present.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Holck had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Ferucci, Holck.
Acquisition of data. Ferucci.
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