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A population-based epidemiological and health economic analysis of fracture-related infection

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Aims

The aim of this study was to perform the first population-based description of the epidemiological and health economic burden of fracture-related infection (FRI).

Methods

This is a retrospective cohort study of operatively managed orthopaedic trauma patients from 1 January 2007 to 31 December 2016, performed in Queensland, Australia. Record linkage was used to develop a person-centric, population-based dataset incorporating routinely collected administrative, clinical, and health economic information. The FRI group consisted of patients with International Classification of Disease 10th Revision diagnosis codes for deep infection associated with an implanted device within two years following surgery, while all others were deemed not infected. Demographic and clinical variables, as well as healthcare utilization costs, were compared.

Results

There were 111,402 patients operatively managed for orthopaedic trauma, with 2,775 of these (2.5%) complicated by FRI. The development of FRI had a statistically significant association with older age, male sex, residing in rural/remote areas, Aboriginal or Torres Strait Islander background, lower socioeconomic status, road traffic accident, work-related injuries, open fractures, anatomical region (lower limb, spine, pelvis), high injury severity, requiring soft-tissue coverage, and medical comorbidities (univariate analysis). Patients with FRI had an eight-times longer median inpatient length of stay (24 days vs 3 days), and a 2.8-times higher mean estimated inpatient hospitalization cost (AU$56,565 vs AU$19,773) compared with uninfected patients. The total estimated inpatient cost of the FRI cohort to the healthcare system was AU$156.9 million over the ten-year period.

Conclusion

The results of this study advocate for improvements in trauma care and infection management, address social determinants of health, and highlight the upside potential to improve prevention and treatment strategies.

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Introduction

Fracture-related infection (FRI) is a potentially devastating complication following fracture management.[1,2] The risk of developing FRI is classically reported as 2% for closed fractures,[3] and up to 50% for open fractures depending on the associated soft-tissue injury.[4,5] Healthcare costs of treating patients with FRI are immense due to the potential requirements for additional operations and long durations of antibiotic treatment. Inpatient costs have been reported to be between two and six times that of uninfected trauma patients.[6,7]

Previous epidemiological, risk factor, and economic studies have often been limited by their methodology. These limitations include the use of only a single centre, small sample sizes, or a sole focus on a specific anatomical location.[8] Recently this limitation has begun to be addressed, with a population-based epidemiological study

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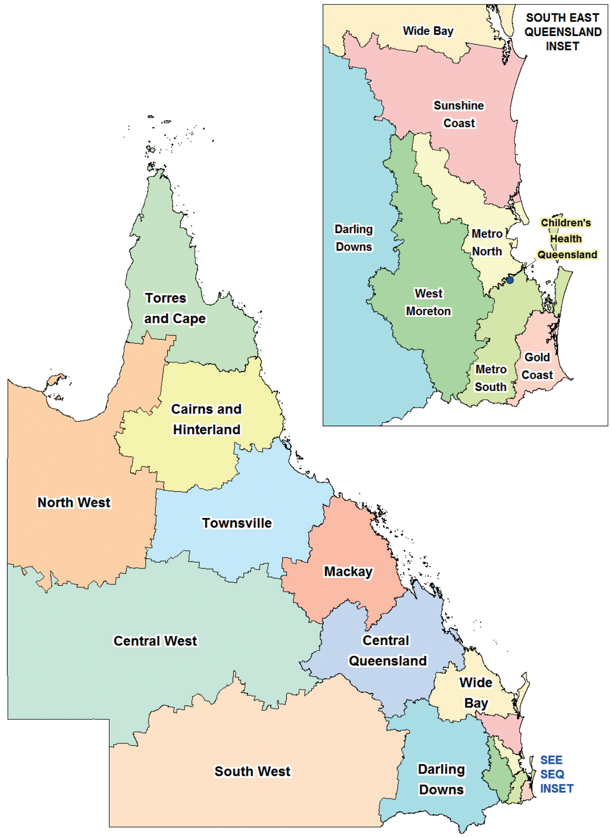

Fig. 1

Map of Queensland showing all 16 Hospital and Health Service (HHS) Districts governed by Queensland Health.[14] Queensland is a state in Australia that has an area of 1.7 million km^2 and a decentralized population of 5.24 million people.[15] In the 2016 census, the median age was 37 years, sex split was 49.4% male and 50.6% female, and 4.0% were of Aboriginal or Torres Strait Islander background.[16] The population is decentralized with 63% residing in a major city, 20% inner regional, 14% outer regional, 2% remote, and 1% very remote.[17] Universal healthcare is available in the public system, with an additional private sector (encompassed by Queensland Health).

examining age and sex trends in FRI.[9] This study highlighted an increasing incidence of FRI from 1.05% to 1.25% over the previous decade, particularly affecting those of older age, however the lack of linked clinical or health economic data hampers its utility.

Record-linkage is the process of merging records that correspond to the same person between datasets. This methodology has been used with impact for periprosthetic joint infection (PJI),[10] but not for FRI. Our aim was to create the first population-based linked dataset of FRI to describe the epidemiological burden and compare healthcare costs with uninfected trauma patients.

Methods

Study design and data source. This is a retrospective cohort study performed within all public and private hospitals in Queensland, Australia (Figure 1). This was done in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplementary Table i). This study uses routinely collected, state-wide, hospital administrative data contained within the Queensland Hospital Admitted Patients Data Collection (QHAPDC).[11] For data to be captured within QHAPDC, trained clinical coders from each public and private hospital review the patient's medical record following their discharge, and code their principal diagnosis (PD), any other diagnoses (OD) relevant to the admission, and any injury event information (mechanism, place, activity being undertaken) according to the International Classification of Disease and Related Health Problems, 10th revision, Australian modification (ICD-10-AM).[12] Procedures performed during each episode of care are coded according to the Australian Classification of Health Interventions (ACHI).[12] Based on the assigned diagnostic and procedure codes, an Australian Refined Diagnosis Related Groups (AR-DRG) classification is also assigned, and can be used in estimating the average inpatient cost per episode.[13] These coded data are cleaned and audited

Table I. Demographic characteristics of operatively managed orthopaedic trauma patients with and without the development of fracture-related infection.

Characteristics	Total cohort	No FRI	FRI	p-value
Patients, n	111,402	108,627	2,775	
Median age, yrs (IQR)	46 (24 to 71)	46 (24 to 71)	49 (29 to 69)	0.009*
Sex, n (%)				< 0.001†
Male	59,957	58,204 (97.1)	1,753 (2.9)	
Female	51,445	50,423 (98.0)	1,022 (2.0)	
ARIA+, n (%)				< 0.001†
Major city	64,389	62,952 (97.8)	1,437 (2.2)	
Inner regional	26,794	26,102 (97.4)	692 (2.6)	
Outer regional	16,004	15,485 (96.8)	519 (3.2)	
Remote	1,610	1,547 (96.1)	63 (3.9)	
Very remote	1,298	1,246 (96.0)	52 (4.0)	
Unknown	1,307	1,295 (99.1)	12 (0.9)	
Indigenous status, n (%)				< 0.001†
Indigenous	3,665	3,494 (95.3)	171 (4.7)	
Non-Indigenous	105,364	102,779 (97.5)	2,585 (2.5)	
Not stated	2,373	2,354 (99.2)	19 (0.8)	
SEIFA, n (%)				< 0.001†
1 (most disadvantaged)	16,952	16,438 (97.0)	514 (3.0)	
2	23,876	23,212 (97.2)	664 (2.8)	
3	27,109	26,373 (97.3)	736 (2.7)	
4	22,634	22,124 (97.7)	510 (2.3)	
5 (most advantaged)	17,417	17,106 (98.2)	311 (1.8)	
Unknown/overseas	3,414	3,374 (98.8)	40 (1.2)	

*Mann-Whitney U test.
†Chi-squared test.
ARIA+, Accessibility and Remoteness Index of Australia; FRI, fracture-related infection; IQR, interquartile range; SEIFA, socioeconomic indexes for areas.

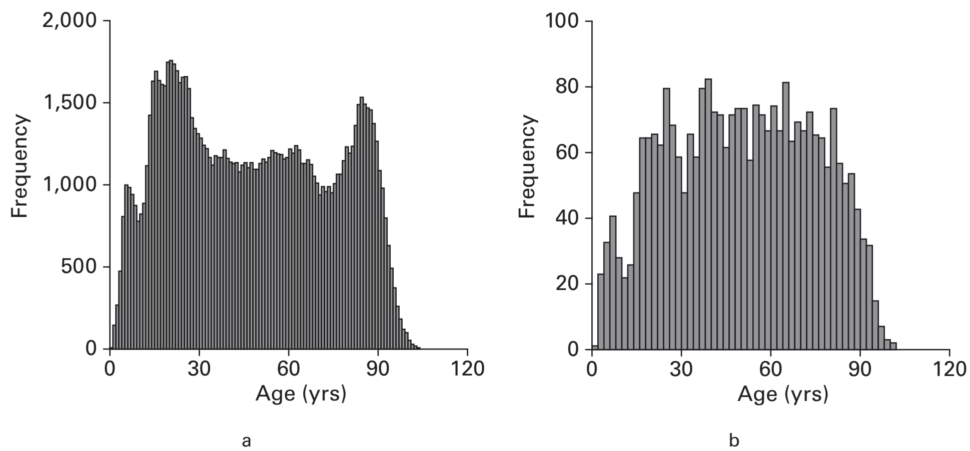

Fig. 2

Histogram contrasting the bimodal distribution of a) all trauma patients who had an implant in Queensland to b) the more normally distributed (left-skewed) population affected by fracture-related infection.

by the State health department and are ultimately compiled into QHAPDC.

Cohort identification. All inpatient episodes with a PD related to injury (ICD-10-AM Chapter 19; S00 – T98) between 1 January 2007 and 31 December 2016 were linked, via a unique patient identifier, by the Statistical Services Branch, Queensland Health. The first episode of care where the PD related to injury and a patient underwent internal fixation of a fracture or arthroplasty was defined as the index episode of care (see Supplementary Table ii for relevant ACHI procedure codes). A follow-up period of two years was observed for the development of FRI. Admissions or readmissions unrelated to the initial trauma or FRI were excluded from analysis based on diagnosis codes and use of a patient-linked dataset.

Table II. Injury and clinical characteristics of orthopaedic trauma and fracture-related infection in Queensland.

Characteristics	Total cohort	No FRI	FRI	p-value
Injury factors				
External cause, n (%)				< 0.001
Falls	61,051	59,731 (97.8)	1,320 (2.2)	
Road traffic accident	16,913	16,266 (96.2)	647 (3.8)	
Struck by person/object	7,205	7,050 (97.8)	155 (2.2)	
Machinery	2,400	2,320 (96.7)	80 (3.3)	
Animal-related	2,265	2,201 (97.2)	64 (2.8)	
Other specified	7,726	7,373 (95.4)	353 (4.6)	
Unspecified	13,842	13,686 (98.9)	156 (1.1)	
Assault-related fracture, n (%)				0.682
Yes	1,546	1,505 (97.3)	41 (2.7)	
No	109,856	107,122 (97.5)	2,734 (2.5)	
Work-related fracture, n (%)*				< 0.001
Yes	7,287	7,062 (96.9)	225 (3.1)	
No	104,115	101,565 (97.6)	2,550 (2.4)	
Injury severity, n (%)				< 0.001
High threat to life	31,459	30,529 (97.0)	930 (3.0)	
Low threat to life	79,943	78,098 (97.7)	1,845 (2.3)	
Surgical factors				
Open fracture, n (%)†				< 0.001
Yes	10,775	10,128 (94.0)	647 (6.0)	
No	100,627	98,499 (97.9)	2,1278 (2.1)	
Main anatomical fracture location, n (%)‡				< 0.001
Upper limb	49,386	48,531 (98.3)	855 (1.7)	
Lower limb	58,294	56,592 (97.1)	1,702 (2.9)	
Pelvis	842	790 (93.8)	52 (6.2)	
Spine	569	548 (96.3)	21 (3.7)	
Fracture procedure, n (%)§				< 0.001
ORIF only	87,862	85,733 (97.6)	2,129 (2.4)	
Closed reduction and percutaneous fixation only	11,993	11,706 (97.6)	287 (2.4)	
Arthroplasty only	9,765	9,553 (97.8)	212 (2.2)	
More than one procedure type	1,782	1,635 (91.8)	147 (8.2)	
Number of surgeries, n (%)¶				0.030
One	99,429	97,091 (97.6)	2,338 (2.4)	
More than one	11,973	11,536 (96.4)	437 (3.6)	
Soft-tissue coverage, n (%)**				< 0.001
Yes	1,514	1,295 (85.5)	219 (14.5)	
No	109,888	107,332 (97.7)	2,556 (2.3)	
Comorbidities, n (%)**				
Presence of a comorbidity				< 0.001
None††	81,907	80,409 (98.2)	1,498 (1.8)	
One or more	29,495	28,218 (95.7)	1,277 (4.3)	
Obesity				< 0.001
Not obese	111,012	108,280 (97.5)	2,732 (2.5)	
Obesity	390	347 (89.0)	43 (11.0)	
Heart failure				< 0.001
No heart failure	108,746	106,110 (97.6)	2,636 (2.4)	
Heart failure	2,656	2,517 (94.8)	139 (5.2)	
PVD				< 0.001
No PVD	110,848	108,126 (97.5)	2,722 (2.5)	
PVD	554	501 (90.4)	53 (9.6)	
COPD				< 0.001
No COPD	109,290	106,637 (97.6)	2,653 (2.4)	
COPD	2,112	1,990 (94.2)	122 (5.8)	
Diabetes				< 0.001
No diabetes	105,567	103,092 (97.7)	2,475 (2.3)	
Diabetes	5,835	5,535 (94.9)	300 (5.1)	

Continued

Table II. Continued

Characteristics	Total cohort	No FRI	FRI	p-value
CKD				< 0.001
No CKD	108,482	105,873 (97.6)	2,609 (2.4)	
CKD	2,920	2,754 (94.3)	166 (5.7)	
Malignancy				0.030
No malignancy	110,558	107,813 (97.5)	2,745 (2.5)	
Malignancy	844	814 (96.4)	30 (3.6)	
Smoking				< 0.001
Non-smoker	92,365	90,396 (97.9)	1,969 (2.1)	
Smoker	19,037	18,231 (95.8)	806 (4.2)	
Depression				< 0.001
No depression	110.830	108,119 (97.6)	2,711 (2.4)	
Depression	572	508 (88.8)	64 (11.2)	

*Based on Activity coded as U73.0 within the index hospitalization.
†Based on ODs recorded within the index hospitalization.
‡Based on PD recorded for the index hospitalization. 2.1% (n = 2,311) of the cohort did not have their fracture location coded in their PD, and are therefore not included in this table.
§Based on Australian Classification of Health Interventions codes recorded for the index hospitalization. A patient may have more than one of these procedures.
¶Prior to the development of FRI.
**Based on ODs recorded within the index hospitalization (see Supplementary Table iv).
††'None' means none of the comorbidities specified in the table were present. A patient may have other pre-existing conditions, such a liver disease or other psychological diagnoses (e.g. post-traumatic stress disorder).
CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; FRI, fracture-related infection; OD, other diagnosis; ORIF, open reduction and internal fixation; PD, principal diagnosis; PVD, peripheral vascular disease.

Identification of FRI. Patients were defined as having a FRI if there was an episode of care with a PD or OD for infection/inflammatory reaction due to internal orthopaedic prosthetic devices, implants, or grafts (ICD-10-AM range T84.4 to T84.7) within two years of their trauma surgery. Where no episode meeting the definition of a FRI was found within two years of the index hospitalization, the patient was classified as not having a FRI.

Data management and variables. All acute care hospitalization episodes for each patient were grouped into encounters to reproducibly organize the linked dataset.[18] Episodes are largely analogous to episodes in the UK system, and encounters (groups of episodes) are analogous to spells in the UK when they occur in a single facility; however, for our study we use encounters more broadly to include all facilities which the patient moved through in the single healthcare experience, i.e. initial referring hospital and definitive care hospital are included in the one encounter if the patient experienced the care in a continuous block. All demographic, injury, and acute care clinical details were extracted from the index hospitalization.

Demographic data included age, sex, geographical location of residence, and identification as Aboriginal and/or Torres Strait Islander. The patient's postcode was used to determine the Accessibility and Remoteness Index of Australia (ARIA+), which is used as both a measure of health accessibility in Australia and for dividing Australia into five categories of remoteness (major city, inner regional, outer regional, remote, very remote).[19] Injury details included the mechanism of injury, whether the injury was assault- or work-related, and the ICD-based injury severity score (ICISS), where high threat to life is defined as ICISS $\leq$ 0.941.[20,21] Clinical variables included whether there was an open fracture, anatomical location involved, type of surgery, need for soft-tissue coverage (ACHI codes in Supplementary Table iii), and comorbidities. The fracture site for each person was ultimately determined by the patient's PD code from their index admission. Any additional fractures were not reported in the descriptive statistics. Comorbidities included were based on the Charlson Comorbidity Index, plus those routinely included in risk factor studies for surgical site infection, such as smoking (Supplementary Table iv).[22] These included heart failure, peripheral vascular disease, chronic obstructive pulmonary disease (COPD), diabetes mellitus, chronic kidney disease, malignancy, obesity (BMI > 30 kg/m^2), smoking, and depression.

Health economic measures included the median number of hospitalization episodes per patient, total length of stay over all hospitalizations related to the index admission, and an estimate of inpatient hospitalization costs using AR-DRGs. The estimated cost for each AR-DRG is calculated by multiplying the National Efficient Price (NEP), set annually by the Independent Health and Aged Care Pricing Authority (IHACPA),[23] by a weight determined by IHACPA for each specific AR-DRG. The NEP is a benchmark that represents the average cost of delivering public hospital services in Australia and aims to ensure fairness and consistency in funding allocation across the country. The NEP considers various factors such as healthcare costs, patient needs, and hospital efficiency. This method for estimating inpatient costs was used for both public and private hospitals. For FRI patients, the AR-DRGs for the index and all subsequent hospitalization episodes related to the infection were added together to obtain a total estimated cost. For patients without FRI, only the AR-DRGs for the index hospitalization episodes were relevant. For this study, the average cost for each AR-DRG was calculated using published price weights,[23] and the NEP for the 2023 to 24 financial year, which was $6,032. Due to the study dataset being based on AR-DRG version 5

Table III. Outcome measures (length of stay and hospitalization costs) for operatively managed orthopaedic trauma patients with and without fracture-related infection.

Variable	Total cohort	No FRI	FRI
Median number of episodes (IQR)	1 (1 to 2)	1 (1 to 2)	3 (2 to 4)
Median length of stay, days (IQR)	4 (1 to 10)	3 (1 to 9)	24 (9 to 51)
Inpatient cost per patient, AU$			
Median (IQR)	11,769 (8,994 to 27,803)	10,592 (8,994 to 26,154)	41,869 (22,771 to 78,829)
Mean (SD)	20,689 (20,650)	19,773 (18,858)	56,565 (43,343)
Total inpatient cost	2,304,835,032	2,147,867,181	156,967,851

FRI, fracture-related infection; IQR, interquartile range; SD, standard deviation.

(v5), and the 2023 to 24 reference tables based on AR-DRG version 11 (v11), a correspondence between versions was needed (Supplementary Table v). Most AR-DRGs remained unchanged, but where the levels of complexity for a certain condition had been expanded/consolidated from v5 to v11, the most appropriate v11 AR-DRG was chosen based on both the category description and the v11 price weight that was most like the v5 price weight. This approach is appropriate for ensuring a conservative estimate of inpatient costs.

Statistical analysis. Descriptive statistics were used to describe the state-wide burden of disease by demographic, injury, clinical, and outcome factors. Median (interquartile range (IQR)) or mean (standard deviation (SD)) was used for continuous variables and counts (percentages) were used for categorical variables. Univariate analyses were undertaken to compare factors between the FRI and uninfected groups using the non-parametric Mann-Whitney U test for continuous variables, and chi-squared test for categorical variables. All analyses were undertaken using SPSS v. 23 (IBM, USA).

Results

There were 111,402 orthopaedic trauma patients operatively managed during the study period. The median age was 46 years (IQR 24 to 71), with age having a bimodal distribution (Figure 2a). Males comprised 59,957 patients (53.8%) of the total cohort. Most patients (64,389; 57.8%) resided within a major city, and 3,665 (3.3%) were of Aboriginal and/or Torres Strait Islander background. The most disadvantaged socioeconomic status category accounted for 16,952 patients (15.2%; Table I).

Of these 111,402 patients, 2,775 (2.5%) developed a FRI within two years following the index surgery (Table I). The median age for those with FRI was 49 years (IQR 29 to 69), with the age distribution being more uniformly distributed (Figure 2b). The incidence of FRI was 2.9% in males and 2.0% in females ($p < 0.001$, chi-squared test). Almost half of patients with FRI resided outside of a major city (1,338; 48.2%), whereas only 36.6% of the Queensland population reside in this area.[17] The incidence of FRI was 2.2% in a major city, with this percentage being significantly higher with increasing rurality (3.9% in remote areas, 4.0% very remote; $p < 0.001$, chi-squared test). Similarly, the incidence of FRI for patients residing in areas of high socioeconomic advantage was 1.8%, becoming significantly higher with higher disadvantage (most disadvantaged = 3.0%; $p < 0.001$, chi-squared test). Among Aboriginal and/or Torres Strait Islander peoples, the incidence of FRI was 4.7%, significantly higher than non-Indigenous Australians (2.5%; $p < 0.001$, chi-squared test).

Table II describes the clinical factors investigated and the risk of developing FRI. Regarding injury mechanism, patients involved in a road traffic accident had the highest incidence of FRI (n = 647 (3.8%); $p < 0.001$, chi-squared test).

In 10,775 patients (9.7%), the fracture was an open/compound injury, with FRI occurring in 6.0% of these patients (compared to 2.1% in closed fractures; $p < 0.001$, chi-squared test). FRI was highest following pelvic injuries (6.2%). More than one procedure type during the index admission was recorded for 1,782 patients (1.6%), with 8.2% of these developing FRI ($p < 0.001$). A single surgery was performed in 99,429 patients (89.3%), while 11,973 (10.7%) required more than one operation. Patients requiring more than one operation had a higher incidence of FRI (3.6%) compared to those with a single surgery (2.4%; $p < 0.001$, chi-squared test). Soft-tissue coverage was required in 1,514 (1.4%) patients, with 14.5% developing FRI; this was significantly higher than those not requiring soft-tissue coverage (2.3%; $p < 0.001$, chi-squared test).

No medical comorbidities were recorded in 81,907 patients (73.5%), while 29,495 (26.4%) had one or more. Patients with one or more comorbidity had a higher incidence of FRI (4.3%) compared to those with no comorbidities (1.8%; $p < 0.001$, chi-squared test).

Table III describes the length of stay and the cost therewith related to FRI (Table III). The FRI group had a significantly higher number of inpatient episodes (median 3 (IQR 2 to 4)) compared to the uninfected group (median 1 (IQR 1 to 2); $p < 0.001$, Mann-Whitney U test), a significantly longer length of hospital stay (median 24 days (IQR 9 to 51)), and an inpatient cost per patient that was 2.8 times higher (mean AU$56,565 (SD 43,343)) than the uninfected group (mean AU$19,773 (SD 18,858)) ($p < 0.001$, Mann-Whitney U test)). The total estimated inpatient cost of the cohort with FRI to the healthcare system was AU$156.9 million over the ten-year period.

Discussion

The most important aspect of this study is that this is the first population-based analysis using linked data to explore the epidemiology and health economics of FRI. There were 111,402 patients operatively managed for orthopaedic trauma in the ten-year period, with 2,775 of these (2.5%) complicated by FRI. Increased age, sex (male), rural/remoteness, Aboriginal and/or Torres Strait Islander background, and lower socioeconomic status were all significantly associated with the complication of FRI. Sustaining an injury in a road traffic accident, a work-related mechanism, and high injury severity were significantly associated with FRI. Open fractures, those requiring reoperation, and soft-tissue coverage were significantly more likely to develop FRI. The presence of comorbidities, including obesity, heart failure, PVD, COPD, CKD, diabetes, smoking, and depression were significantly associated with FRI. Patients with FRI had more hospitalization episodes, eight-times longer median inpatient length of stay (24 days vs 3 days), and 2.8-times higher average direct inpatient hospitalization costs per patient (AU$56,565 vs AU$19,773) compared with uninfected patients. The total estimated inpatient cost of the cohort with FRI to the healthcare system was AU$156.9 million over the ten-year period.

Demographic data in this study highlight the role of cultural and socioeconomic disadvantage in the development of FRI. Increasing age of patients suffering from FRI has previously been described,[9] which is likely due to an ageing population as well as medical comorbidities; however, the role of osteoporosis has recently been described through preclinical research.[24] Poorer health outcomes due to socioeconomic disadvantage have also been described for type 2 diabetes, among other medical conditions.[25] Poorer access to health services, particularly culturally safe health services, in regional areas may contribute to these findings. This lack of health services may in turn result in delays in open fracture management, and the need for interhospital transfers for definitive soft-tissue coverage.

The infection rate of 2.5% in this study is consistent with the expected rate from the literature.[3,9] The associations found between FRI and open fracture, multiple surgeries, and need for soft-tissue coverage are consistent with a systematic review that specifically investigated tibial shaft fractures.[26] External-cause data demonstrates the influence of the mechanism of injury such as road traffic accident, work-related injuries, and higher injury severity on the development of FRI. The association of FRI with medical comorbidities and smoking is consistent with the risk of infection following elective joint replacement.[27] It is likely that these factors are causative in the development of FRI, especially given the methodology in this study only recorded associated diagnoses in the original presentation for trauma. Unlike elective surgery, the urgency of trauma surgery limits the ability to optimize these comorbidities in the preoperative period.

This study highlights the large health economic cost of treating patients with FRI. These patients use a large volume of healthcare resources, staying in hospital eight times longer than uninfected patients and costing almost three times as much in direct inpatient costs. These results support the results of a previous single-centre case series that estimated the cost of FRI to be two to six times that of uninfected patients.[6,7] Notably, the 75th percentile for length of stay and cost in the FRI group, at 51 inpatient days and AU$78,829, respectively, suggests a substantial portion of patients are difficult to treat, such as failing an initial debridement procedure or requiring complex limb reconstruction surgery. The costs of managing the FRI cohort in this study are comparable to that of PJI demonstrated in an Australian study with a median inpatient cost of AU$34,800.[28] Given the high volume and the comparable cost of FRI, it is therefore surprising that the resources applied to optimizing care following elective arthroplasty, such as joint registries to monitor revision and infection rates, do not exist for trauma care. Furthermore, the unmeasured costs, such as lost productivity due to prolonged morbidity for these patients with FRI, will be enormous.

The results of this study should now be used to advocate for improvements in trauma care, addressing both demographic/social determinants of health and modifiable clinical variables. The International Consensus Meeting on Musculoskeletal Infection highlighted a number of strategies to prevent and treat FRI, such as smoking cessation, nutritional optimization, local antibiotic therapy, topical decolonization of methicillin-resistance *Staphylococcus aureus*, early administration of prophylactic antibiotics for open fractures, and early soft-tissue coverage.[2]

The main strength of this study is the comprehensive analysis of a linked database encompassing all patients treated in both public and private hospitals, using administrative, clinical, and health economic data. These databases are established prospectively by trained clinical coders, and therefore are objective with less risk of selection biases. The rate of FRI at 2.5% for all operatively managed orthopaedic trauma validates our methodology, as this is a rate consistent with prior literature.[3]

Although the data were prospectively collected, the retrospective nature of the investigation for FRI is a limitation of this study. It is likely that the use of administrative codes applied to the diagnostic criteria prospectively would conservatively diagnose FRI with the potential to underestimate the proportion of patients affected, as has been demonstrated in the PJI literature.[10,29] Infecting organisms with low virulence, such as *Cutibacterium acnes*, which may not produce pus and may not result in raised inflammatory markers, and are more likely to be culture-negative without prolonged culture,[30] are possible false negatives in this study. Late-acute infections arising after two years from the index surgery would also be false negatives in this study; while this has been demonstrated to be a significant mode of presentation in PJI,[31] this is poorly described in FRI and perhaps another potential source of underestimated results. In identifying the index admission, we used the PD code to specify that the admission was for treatment of an acute injury, plus the procedure code to specify that surgical intervention of a fracture was performed in that same admission. There is a possibility of misclassifying a small proportion of readmissions as index admissions due to the reliance on this administrative coding, particularly in the first year of observation (2007), however the magnitude of this misclassification would not substantially affect the overall interpretation of the results. Comorbidities in this study are likely understated, as they would only be recorded as an associated diagnosis by clinical coders if they were actively being treated during the hospital admission. The healthcare-associated costs in this study were estimated through AR-DRGs, which is an average measure used to reimburse hospitals for inpatient care, and may be less accurate for complex cases than using actual hospital costs specific to each identified episode of inpatient care. These costs likely underestimate the total costs of treating FRI, given estimates using AR-DRGs do not include outpatient and emergency care costs, as well as costs associated with loss of productivity and other societal costs. The methods used describe the inpatient healthcare-associated costs of treating trauma patients with and without FRI, but the lack of a matched-control group for possible confounding variables means that the difference in costs is not necessarily entirely attributable to the development of infection. Performing the first population-based analysis of FRI using linked data was methodologically challenging to establish the database, and as a consequence of this, the timeliness of the data is a limitation of the study. Given this study was conducted in Queensland, Australia, the generalizability of the findings may be limited in more centralized populations, those with smaller geographical distances, or developing economies.

This is the first population-based analysis of the epidemiological and health economic burden of FRI. There were 111,402 patients operatively managed for orthopaedic trauma in ten years, with 2,775 of these (2.5%) complicated by FRI. The development of FRI was significantly associated with: older age, male sex, residing in rural/remote areas, identifying as Aboriginal and/or Torres Strait Islander, and lower socioeconomic status, road traffic accidents, work-related injuries, open fractures, anatomical region (lower limb, spine, pelvis), high injury severity, requiring soft-tissue coverage, and medical comorbidities. Patients with FRI have an eight-times longer average inpatient length of stay and 2.8-times higher average estimated inpatient hospitalization costs. The results of this study should advocate for improvements in trauma care and infection management, address social determinants of health, and highlight the upside potential to introduce prevention and treatment strategies.

Take home message

- Fracture-related infection is a condition of social disadvantage with rural, lower socioeconomic status, and people of an Aboriginal and/or Torres Strait Islander background being disproportionately affected.
- There is a large health economic burden of fracture-related infection that highlights the need for further resource allocation for optimization of trauma care and the prevention of infectious complications.

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