The epidemiology of fracture-related infections in Germany

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The epidemiology of fracture-related infection (FRI) is unknown, which makes it difficult to estimate future demands and evaluate progress in infection prevention. Therefore, we aimed to determine the nationwide burden’s development over the last decade as a function of age group and gender. FRI prevalence as a function of age group and gender was quantified based on annual ICD-10 diagnosis codes from German medical institutions between 2008 through 2018, provided by the Federal Statistical Office of Germany (Destatis). The prevalence of FRI increased by 0.28 from 8.4 cases per 100,000 inhabitants to 10.7 cases per 100,000 inhabitants between 2008 and 2018. The proportion of fractures resulting in FRI increased from 1.05 to 1.23%. Gender distribution was equal. Patients aged 60–69 years and 70–79 years comprised the largest internal proportion with 20.2% and 20.7%, respectively, whereby prevalence increased with age group. A trend towards more diagnoses in older patients was observed with a growth rate of 0.63 for patients older than 90 years. Increasing rates of fracture-related infection especially in older patients indicate an upcoming challenge for stakeholders in health care systems. Newly emerging treatment strategies, prevention methods and interdisciplinary approaches are strongly required.

In trauma surgery, reduction and internal fixation is applied to restore skeletal integrity. One of the major complications after fracture fixation utilizing metallic fracture fixation devices, is implant related infection, which in general requires surgical treatment Depending on several factors, at least one, but often two or even multiple staged surgeries are needed for eradication of infection and finally bony consolidation. In the literature, rates of developing a posttraumatic infection are reported to be around 1–2% for closed fractures ranging up to exceeding 30% for Gustilo-Anderson type III open tibia fractures. Considering studies showing that incidences of long bone fractures increase, numbers of infection complications can be expected to rise as well.

Depending on injury severity, success rates only vary between 70–90% with a recurrence of the infection in 6–9% of the patients. Among others, consequences are significantly reduced patient-reported quality of life and multiplied healthcare costs up to 6.5 times. Hence, much effort has been made in prevention approaches.

However, current socioeconomic calculations are based on small patient numbers and the exact prevalence of fracture-related infection is unknown. Therefore, it remains difficult to estimate future demands foresee developments and evaluate the progress in infection prevention methods. To this end, we aimed at determining the nationwide burden and analysing recent trends in fracture-related infections.

Material and methods

Data consisting of annual ICD-10 diagnosis codes from German medical institutions between 2008 through 2018 was provided by the Federal Statistical Office of Germany (Destatis). The ICD-10 code “T84.6, infection and inflammatory reaction due to internal fixation device” was used to identify patients aged 20 years or older diagnosed with FRI. A detailed breakdown of these data by age group and gender was performed. Prevalence rates were calculated based on Germany’s historical population aged 20 years or older provided by Destatis. Here, the number of inhabitants in each of the 16 German federal states was considered by year of birth for each year of the period 2008 through 2018. The deadline of each year was December 31. The proportion of FRI was calculated based on total numbers of fracture diagnoses. Here, the ICD-10 codes shown in Table 1 were used (Table 1). Data were analyzed using the statistical software SPSS Version 26.0 (IBM, SPSS Inc. Armonk, NY, USA).

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Results

In 2018, a total number of 7253 FRI cases were listed in Germany. In comparison to 5556 cases in 2008, the overall prevalence substantially increased with a growth rate of 0.28 from 8.4 cases per 100,000 inhabitants to 10.7 cases per 100,000 inhabitants. Accordingly, the proportion of fractures resulting in FRI increased from 1.04 to 1.23% (Table 2).

The internal gender distribution was equal with 50.8% male cases and 49.2% cases in 2018, whereby the prevalence of FRI was slightly higher in the male population (11.1 cases per 100,000 inhabitants) than for the female population (10.3 cases per 100,000 inhabitants) (Fig. 1, Table 3).

Regarding the prevalence for distinct age groups, cases per 100,000 inhabitants steadily increased with age. For 2018, 35 cases were calculated per 100,000 per inhabitants aged 90 years or older, 24.9 cases per 100,000 per inhabitants aged 80–89 years and 19.5 cases per 100,000 per inhabitants aged 70–79 years, whereas only 3.4 cases were estimated per 100,000 per inhabitants aged 20–29 years and 4.1 cases per 100,000 per inhabitants aged 30–39 years. Relative to the year 2008, a trend towards more FRI diagnoses in older patients can be observed. Highest growth rates were found for patients aged 90 years or older (0.63) and patients aged 70–79 years (0.28) (Table 4, Fig. 2).

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### Table 1. Used ICD-10 code to calculate total numbers of fractures with descriptions.

| ICD-10 code | Description                  | ICD-10 code | Description                  |
|-------------|------------------------------|-------------|------------------------------|
| S32.1       | Sacrum fracture              | S72.0       | Femur neck fracture          |
| S32.2       | Coccyx fracture              | S72.1       | Peritrochanteric femur fracture |
| S32.3       | Ilium fracture               | S72.2       | Subtrochanteric femur fracture |
| S32.4       | Acetabulum fracture          | S72.3       | Femur shaft fracture         |
| S32.5       | Pubis fracture               | S72.4       | Distal femur fracture        |
| S32.6       | Ischium fracture             | S82.0       | Patella fracture             |
| S32.8       | Fracture of other parts of pelvis | S82.1       | Proximal tibia fracture      |
| S42.0       | Clavicle fracture            | S82.2       | Tibia shaft fracture         |
| S42.1       | Scapula fracture             | S82.3       | Distal tibia fracture        |
| S42.2       | Proximal humerus fracture    | S82.4       | Fibula shaft fracture        |
| S42.3       | Humerus shaft fracture       | S82.5       | Medial malleolus fracture    |
| S42.4       | Distal humerus fracture      | S82.6       | Lateral malleolus fracture   |
| S52.0       | Proximal ulna fracture       | S92.0       | Calcaneus fracture           |
| S52.1       | Proximal radius fracture     | S92.1       | Talus fracture               |
| S52.2       | Ulna shaft fracture          | S92.2       | Other tarsal bone(s) fracture|
| S52.3       | Radius shaft fracture        | S92.3       | Metatarsal bone(s) fracture  |
| S52.5       | Distal radius fracture       |             |                              |
| S62.0       | Scaphoid fracture            |             |                              |
| S62.1       | Carpal bone fracture         |             |                              |
| S62.2       | First metacarpal bone fracture|             |                              |
| S62.3       | Other metacarpal bones fracture|            |                              |

### Table 2. Historic development of population and fracture-related infection prevalence from 2008 through 2018.

| Year | Total numbers | German population 20 years or older | Prevalence per 100,000 inhabitants | Growth rate (relative to 2008) | Fractures total numbers | Proportion of FRI |
|------|---------------|-------------------------------------|------------------------------------|-------------------------------|------------------------|------------------|
| 2008 | 5556          | 66,346,045                          | 8.4                                | –                             | 534,131                | 1.04             |
| 2009 | 6091          | 66,400,066                          | 9.2                                | 0.10                          | 578,897                | 1.05             |
| 2010 | 6503          | 66,549,975                          | 9.8                                | 0.17                          | 553,012                | 1.18             |
| 2011 | 6800          | 65,398,514                          | 10.4                               | 0.24                          | 547,319                | 1.24             |
| 2012 | 6735          | 65,665,089                          | 10.3                               | 0.22                          | 556,766                | 1.21             |
| 2013 | 6985          | 65,943,867                          | 10.6                               | 0.26                          | 547,683                | 1.28             |
| 2014 | 6882          | 66,677,665                          | 10.3                               | 0.23                          | 562,294                | 1.22             |
| 2015 | 7206          | 67,097,676                          | 10.7                               | 0.28                          | 568,598                | 1.27             |
| 2016 | 7024          | 67,440,230                          | 10.4                               | 0.24                          | 580,975                | 1.21             |
| 2017 | 7228          | 67,540,025                          | 10.7                               | 0.28                          | 585,891                | 1.23             |
| 2018 | 7253          | 67,724,921                          | 10.7                               | 0.28                          | 587,612                | 1.23             |
Regarding the constituent ratio, explaining the internal proportion of infection, in 2018 patients aged 70–79 years comprised the largest cohort with 20.7%, followed by patients aged 60–69 years (20.2%) and patients aged 50–59 years (19.3%). Comparing the age distribution as a function of gender, it becomes apparent that older patients were predominantly female. For instance, 6.30% of female cases were aged 90 years or older compared to 1.11% male cases, 23.47% female patients aged 80–89 years versus 8.58% male cases in this increment and 24.64% women aged 70–79 years in relation to 16.89% men of this age. In the age increments 50–59 years, more male cases were registered than female cases (23.60% versus 14.84%). The same applied for patients aged 40–49 years with 13.17% male cases compared to 6.05% affected women (Fig. 3).

Discussion

In this population-based study, trends in the epidemiology of fracture-related infections were described and prevalence was analyzed as a function of gender and age group. To the best of our knowledge, this study is the first one describing the nationwide burden of FRI.

A literature review estimated that fracture-fixation device infections comprise < 5% of all implant associated infections\textsuperscript{14}, whereas a single center cohort study at Geneva University Hospital pooling clinical data on orthopaedic infections reported that 24% of all cases involved osteosynthetic material\textsuperscript{15}. In general, prevalence data on FRI vary in the literature. For instance, a multi-center study carried out in India included 787 participants with tibia fractures, estimating the incidence of infection as 1.6% for closed fractures and 8.0% for open fractures\textsuperscript{16}, whereas Metsemakers and colleagues found an infection rate of 3.4% in a cohort of 358 patients with tibia fractures\textsuperscript{8}. Blonna et al. reported an infection rate of 4% out of 452 proximal humeral fractures and Ovaska et al. identified 5% of 1923 consecutive ankle fractures to be infected\textsuperscript{17,18}. One study carried out in Brazil found...
an infection rate of 13.24%, examining 142 patients with open fractures at various anatomical locations, whereas another one reported 18.8% infections in 133 patients with open fractures19,20. Additionally, a review on open femoral shaft fractures treated with intramedullary nailing estimated an infection rate of 6%, whereas another review reported infection rates in the range of 0.9–11.6% comparing outcomes of open tibial fractures21,22. In light of the diversity of findings, describing the nationwide burden of FRI seems useful. Here, an overall FRI rate of 1.23% was estimated for the year 2018 based on calculated total numbers of fracture cases, which is lower than previously reported. Differences might be explainable by the distinct considered fracture types and sites, heterogeneity in the study design as well as center-specific treatment procedures.

Further, our analysis revealed that the prevalence of FRI increased with a rate of 0.28 from 8.4 cases per 100,000 inhabitants to 10.7 cases per 100,000 inhabitants between 2008 and 2018. The distribution of male and female cases was equal in our analysis, whereas research increasingly addresses immune response gender differences23,24. The observed trend towards more FRI diagnosis in older patients possibly reflects demographic changes such as population decline and aging, which challenge the healthcare system not only in Germany. In consideration that prevention strategies and improved treatment algorithms for optimal patient care moved into focus of orthopedic research2,10,25, the increase of infection rates over the last decade seems surprisingly high. This might be attributable to heightened prevalence of obesity, which has risen substantially and the fact that Germany is rated among the countries with the highest prevalence of tobacco use in Europe26,27. Further, an extrapolation of hospital-based data to the German population revealed 16,742 severely injured persons per year and at least 5.8 million German inhabitants have received a medical diagnosis of type 2 diabetes, which may contribute to rising FRI numbers28–30.

Table 4. Historic development from 2008 through 2018 of all fracture-related infection cases as a function of age group. Data is shown as total numbers, percentage and prevalence per 100,000 inhabitants of the considered age group.

| Year | 20–29 years Total (percentage), prevalence | 30–39 years Total (percentage), prevalence | 40–49 years Total (percentage), prevalence | 50–59 years Total (percentage), prevalence | 60–69 years Total (percentage), prevalence | 70–79 years Total (percentage), prevalence | 80–89 years Total (percentage), prevalence | 90 years or older Total (percentage), prevalence |
|------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| 2008 | 274 (4.9), 2.8                           | 393 (7.1), 3.8                           | 753 (13.6), 5.4                         | 969 (17.4), 8.6                         | 1136 (20.4), 12.1                       | 1146 (20.6), 15.2                       | 756 (13.6), 21.8                        | 129 (2.3), 21.5                        |
| 2009 | 319 (5.2), 3.2                           | 363 (6.0), 3.6                           | 821 (13.5), 5.9                         | 1035 (17.0), 9.0                        | 1208 (19.8), 13.1                       | 1355 (22.2), 17.3                       | 859 (14.1), 24.1                       | 131 (2.2), 21.0                        |
| 2010 | 324 (5.0), 3.3                           | 368 (5.7), 3.8                           | 827 (12.7), 6.0                         | 1137 (17.5), 9.7                        | 1326 (20.4), 14.7                       | 1491 (22.8), 18.3                       | 888 (13.7), 24.3                       | 142 (2.2), 21.8                        |
| 2011 | 321 (4.7), 3.3                           | 385 (5.7), 4.1                           | 836 (12.3), 6.3                         | 1251 (18.4), 10.6                       | 1291 (19.0), 14.6                       | 1587 (23.3), 19.0                       | 973 (14.3), 26.8                       | 156 (2.3), 24.2                        |
| 2012 | 283 (4.2), 2.9                           | 384 (5.7), 4.0                           | 823 (12.2), 6.4                         | 1244 (18.5), 10.3                       | 1271 (18.9), 14.2                       | 1593 (23.7), 18.9                       | 926 (13.7), 25.3                       | 211 (3.1), 31.7                        |
| 2013 | 378 (5.4), 3.9                           | 373 (5.3), 3.9                           | 804 (11.5), 6.5                         | 1284 (18.4), 10.4                       | 1259 (18.0), 14.0                       | 1716 (24.6), 20.0                       | 971 (13.9), 26.4                       | 200 (2.9), 29.0                        |
| 2014 | 322 (4.7), 3.3                           | 360 (5.2), 3.7                           | 710 (10.3), 6.0                         | 1285 (18.7), 10.1                       | 1289 (18.7), 14.1                       | 1715 (24.9), 20.1                       | 975 (14.2), 25.6                       | 226 (3.3), 31.6                        |
| 2015 | 292 (4.1), 2.9                           | 422 (5.9), 4.2                           | 735 (10.2), 6.4                         | 1382 (19.2), 10.6                       | 1370 (19.0), 14.4                       | 1647 (22.9), 20.0                       | 1110 (15.4), 27.7                       | 248 (3.4), 34.5                        |
| 2016 | 371 (5.3), 3.7                           | 474 (6.7), 4.6                           | 686 (9.8), 6.2                         | 1320 (18.8), 10.0                       | 1361 (19.4), 13.8                       | 1579 (22.5), 19.7                       | 1102 (14.4), 24.1                       | 221 (3.1), 29.5                        |
| 2017 | 345 (4.8), 3.5                           | 459 (6.4), 4.4                           | 659 (9.1), 6.1                         | 1438 (19.9), 10.8                       | 1370 (19.0), 13.6                       | 1588 (22.0), 20.2                       | 1114 (15.4), 25.3                       | 255 (3.5), 33.8                        |
| 2018 | 333 (4.6), 3.4                           | 435 (6.0), 4.1                           | 701 (9.7), 6.7                         | 1399 (19.3), 10.4                       | 1463 (20.2), 14.2                       | 1502 (20.7), 19.5                       | 1154 (15.9), 24.9                       | 266 (3.7), 35.0                        |

Growth rate (2018 relative to 2008) 0.23 0.07 0.25 0.21 0.17 0.28 0.14 0.63

Figure 2. Development of FRI prevalence from 2008 to 2018 as a function of age group in 10-year increments.
Our study shows several limitations. First, the ICD-10 codes do not allow a differentiation regarding anatomical localization, classification of fractures as well as surgical treatment strategies. Further, it was not possible to derive individual features of the patients and risk factors such as obesity, smoking and comorbidities. Also, no statement about underlying pathogens causing the infection can be made. Finally, analyzing large registry data does not allow to apply in every treated case the FRI diagnosis criteria recently described by a consensus group.31. This downside goes hand in hand with the upside of analyzing a complete data set, since all patients treated for FRI, which is in general an inpatient procedure have been coded by the OPS-code T84.6.

In conclusion, in light of a strong increase especially in elderly patients, prevention strategies, improved treatment strategies and an interdisciplinary treatment approaches are strongly required.

**Data availability**
The datasets analysed during the current study are available from the corresponding author on reasonable request.

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**Figure 3.** (A) Development of the internal proportion of male FRI cases divided by age group. (B) Development of the internal proportion of female FRI cases divided by age group.
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V.A. conceptualized the study, M.R. and N.W. analysed the data and wrote the main manuscript text, S.L. prepared Figs. 1, 2 and 3. All authors interpreted the data, reviewed, and approved the manuscript.

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