Impact Surgery

Original Research Paper

e-ISSN: 3033-4470

The Incidence of Infection Following Open Tibia Fractures in Low-Income Countries: A Systematic Review

Eaton-Brown J[1], Sodhi K[1], Dhaif F[2], Schade A[3], Khatri C[2]

Correspondence: Jacob Eaton-Brown, *Warwick Medical School, Gibbet Hill Campus, The University of Warwick, Coventry CV4 7AL, UK.* Email:Jacob.eaton-brown@warwick.ac.uk

Abstract

Introduction: Open tibial fractures (OTFs) are common in low-income countries (LICs), primarily caused by road traffic collisions. High rates of infection in OTFs contribute to prolonged recovery, disability, and economic loss. Identifying infection rates and causative organisms is essential for improving outcomes and guiding antibiotic treatment in LICs. This systematic review aimed to determine the incidence of surgical site infections (SSIs) following OTF treatment in LICs and identify the most prevalent microorganisms involved.

Methods: Following PRISMA and Cochrane guidelines, a systematic review was conducted using five databases. Eligible studies included randomised controlled trials, cohort studies, and case series investigating OTFs in LICs. Studies with fewer than ten participants, military medical resources, or those from high-income countries were excluded. Data were extracted for infection rates, causative organisms, and treatment modalities, with a meta-analysis performed using a random effects model to calculate incidence in person-years.

Results: Five studies, including two retrospective cohorts, two prospective cohorts, and one RCT, were analysed. The overall infection incidence was 23.21 per 100 person-years (95% CI: 9.19; 58.62). Subgroup analysis showed a slightly lower incidence of 21.88 per 100 person-years for surgical interventions. A high degree of heterogeneity (I^2 = 91%) was noted. Common causative organisms were not consistently reported.

Conclusion: The incidence of SSIs following OTFs in LICs is high, particularly in severe fractures. Establishing a baseline infection rate is critical for future studies to evaluate treatment efficacy and improve outcomes in resource-limited settings. Further research should focus on standardising definitions and reporting of infections to reduce heterogeneity.

1. Warwick Medical School, Gibbet Hill Campus, The University of Warwick, Coventry CV4 7AL, UK

2. Warwick Clinical Trials Unit, University of Warwick, Coventry, CV4 7AL, UK

3. University Hospital Coventry & Warwickshire, Clifford Bridge Rd, Coventry CV2 2DX

Cite as: Eaton-Brown, J., Sodhi, K., Dhaif, F., Schade, A., & Khatri, C. The Incidence of Infection Following Open Tibia Fractures in Low-Income Countries: A Systematic Review: Infection in Open Tibia Fractures in Low-Income Countries. *Impact Surgery*, 1(6), 225–232. https://doi.org/10.62463/surgery.97

Introduction

The impact of trauma on both public health and the economy in low-income countries (LICs) is substantial with disability-adjusted life years now exceeding the combined burden of ischaemic heart disease, cancer, and infectious diseases [1]. Open tibia fractures (OTFs) are the most common long-bone open fracture - comprising two-thirds of open fractures - and are frequently due to road traffic collisions (RTCs) in LICs [2]. Infection rates are high in this injury type, requiring aggressive and early treatment [2]. Therefore, identifying the most prevalent causative organisms is a priority when deciding antibiotic treatment and may improve patient outcomes.

It has been previously shown that 80% of patients with OTFs did not return to work by 12 months post-injury [3]. Complications, such as infection, can lead to re-admission, directly impacting hospital costs and delaying economically active patients from returning to work. Infections following OTFs increase recovery time and significantly decrease health related quality of life in comparison to patients without infection as reported by Doshi et al. [4]. Identifying the incidence of surgical site infections (SSIs) for different surgical treatments will provide further education on early intervention [2]. A baseline incidence rate for SSIs will allow further comparison in future randomised controlled trials (RCTs). Culturing organisms directly from infected OTFs would provide guidance on appropriate antibiotic usage, as 80% of deaths from infectious disease in low and middle-income countries (LMICs) are due to antimicrobial resistance [2].

The World Bank denotes 26 LICs, the majority of which are in Sub-Saharan Africa [5]. OTFs are a leading cause of trauma-related disability, especially in LICs where limited access to treatment resources or delayed presentation are contributing factors [6]. The Gustilo-Anderson classification is a good predictor of the development of complications from OTFs, with higher-grade OTFs being linked to an increased risk of infection and amputation [7]. Relatively low infection rates are reported in type I (0-2%), type II (2.4%), and type IIIA (4%) fractures in contrast with the higher infection rates in type IIIB (52%) and type IIIC (42%) fractures [8].

Good treatment outcomes for open fractures rely upon early antibiotic administration, irrigation and debridement [9]. Surgical fracture fixation can be undertaken either by external fixation, or by internal fixation with an intramedullary nail or plate fixation. Other treatment options include stabilisation with plaster of Paris and amputation. Treatment practices are poorly documented and can vary due to local and regional factors in LICs [10]. Furthermore, multiple infection-causing organisms have been implicated in local and systemic infections following OTFs [11]. This review aimed to determine the incidence of SSIs for different treatment types following OTFs in LICs and identify the most common causative microorganisms.

Methods

This review follows the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) model [12] and the Cochrane Handbook for Systematic Reviews of Interventions [13]. A customised search strategy was developed through consultation with a university librarian. Search criteria (see Appendix 1) were run on five search engines (Embase, Medline, Cochrane, Web of Science, Scopus) and a systematic review was performed by two independent reviewers (JEB and KS). In five studies where partial data is available, authors were contacted to obtain data pertaining specifically to infection in OTFs.

Eligibility criteria

The inclusion criteria for this study consists of RCTs, cohort studies, case-control studies and case series with more than ten participants investigating OTFs with any treatment modality in low-income countries. Only full-text studies published in the English language were included. Studies reporting outcomes for adults (>18 years old) from LICs as defined by the World Bank Atlas method were included [5].

The exclusion criteria removed studies that report results for OTFs treated using military medical resources as these outcomes do not fairly reflect the wider civilian populations in LICs. Studies from middle-income and high-income countries, case series with less than ten participants, case reports, and expert opinions were also excluded.

The terminology for “infection” as defined by the author was used instead of a singular definition. This is due to the variation in descriptions of “infection” in research conducted in LICs. Before quality assessment, an acceptable minimum follow-up time was determined as 90 days post-surgery, as defined by the Centers for Disease Control and Prevention (CDC) criteria for SSIs in procedures that involve prosthetic implants [14].

Outcomes

The primary outcome of the search was to ascertain the post-operative surgical site infection (SSI) in patients with OTFs treated with civilian medical resources. Open fractures were reported in accordance with the Gustilo-Anderson Classification. Additionally, the causative organisms of infection and antibiotic resistance profile were also recorded.

Statistical analysis plan

Data was extracted for SSI. Information on infection-causing organism and treatment types were also sought after. A meta-analysis was performed with a random effects model to calculate incidence in person-years using RStudio™ in order to assess the incidence of infection [15]. All analysis were performed in R using the “readr”, “meta”, “metafor”, “ggplot2” and “repos” packages [15].

Risk of Bias

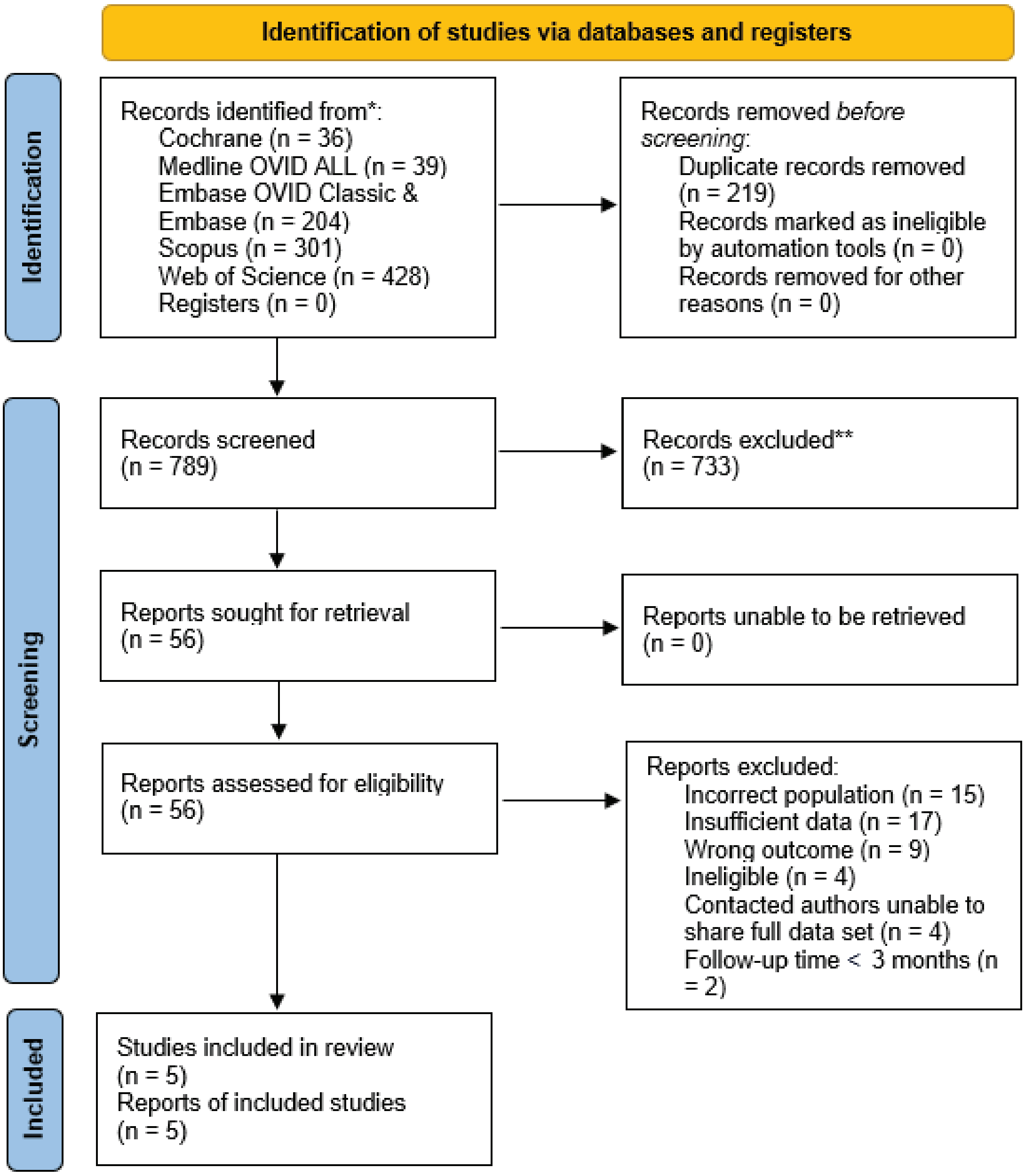
Two reviewers (JEB and KS) independently assessed the risk of bias in the studies included in this systematic review and any areas of disagreement were discussed before submitting the final assessment. The Cochrane Risk of Bias 2 (RoB 2) tool for RCTs [16] was used to assess RCTs and the Newcastle-Ottawa Scale[17] was used to assess the non-randomised trials.

Results

Study Selection

The combined search engines produced 1008 studies from five search engines which were downloaded on to the EndNote™ software [18] for duplicate removal after which the remaining studies were uploaded on to Rayyan™ [19]. 789 studies remained after duplicate removal and two independent reviewers (JEB and KS) subsequently performed a blinded systematic literature review according to the inclusion/exclusion criteria. Any disagreements were resolved with input from the senior author. 56 studies were selected for full text review, as reported in the PRISMA flow chart in Figure 1. 51 of these studies were excluded, four of which were due to lack of available data despite authors being contacted.

Figure 1: PRISMA flow diagram detailing the study selection process [12].



Demographics

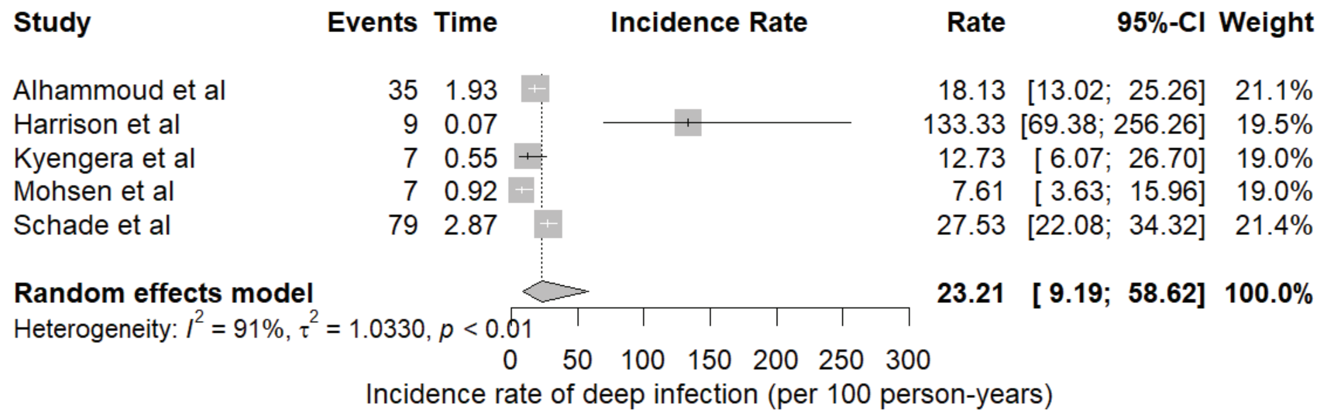
Five studies were included in the review: two retrospective cohort studies, two prospective cohort studies and one RCT. These studies were conducted in Syria, Uganda, Yemen, and two in Malawi. The studies were published after 2019, with the exception of the study by Harrison et al [20]. All studies have a higher proportion of male patients and the average age ranged from 27.5(±11) to 39 (see table 1). Follow up time ranged substantially across studies from one week to one year.

Narrative Results Summary

Alhammoud et al. [21] conducted a retrospective cohort study in Aleppo, Syria, during the Syrian Civil War, finding a significantly higher risk of infection in Grade 3 fractures compared to Grade 2 and Grade 1 fractures. They reported an overall infection rate of 18.1% following external fixation. Harrison et al. [20] conducted a prospective trial in Malawi, observing a significant difference in infection rates between HIV-positive and HIV-negative patients, with an overall infection rate of 33% at 3 months post-operation.

Kyengera et al. [22] provided a comprehensive randomised controlled trial in Uganda comparing intramedullary nailing and external fixation for OTFs. They reported seven deep surgical site infections (SSIs), with slightly more cases in the intramedullary nail group. Additionally, Mohsen [23] conducted a retrospective cohort study in Yemen, reporting a pin-site infection rate of 7.6% within a one-year follow-up period. Schade et al. [10] describe their prospective study in Malawi, noting a high incidence of infection following both OTFs and surgical interventions to treat them.

Figure 2: Meta-analysis of five studies conducted for incidence of infection per 100 person-years against a random effects model in R.



The 'Events' column denotes the number of infections per cohort. The total number of participants included was 632. The 'Time' column describes the person time calculated based on follow-up time and number of participants per cohort. The 'Rate' column is the calculated incidence rate of infection.

Table 1: Demographic data of each study included in the meta-analysis.

Author	Study type	Year	Country	Patients	Controls	Male/Female	Mean age (years)	Follow-up time
Alhammoud[21]	Retrospective Cohort Study	2019	Syria	193	N/A	180/15	27.5±11	1 week - 1 year
Harrison[20]	Prospective Cohort study	2004	Malawi	27	N/A	24/3	34.2	3 months
Kyengera[22]	Randomised Controlled Trial	2022	Uganda	31	24	37/18	39	365 days (IM nail), 136 days (ex-fix)
Mohsen[23]	Retrospective Cohort Study	2019	Yemen	92	N/A	71/21	37.3 ± 10.3	1 year
Schade[10]	Prospective cohort study	2023	Malawi	287	N/A	248/39	34 (IQR 26-45)	1 year
Total				632	24	560/96		

Meta-analysis

The meta-analysis in Figure 2 revealed that the overall incidence of infection across the studies was 23.21 per 100 person-years (95% CI: 9.19; 58.62). The incidence rate ranged from 7.61 [23] to 133.33 [20]. Seven HIV positive patients are included in the Harrison et al cohort [20]. The heterogeneity is indicated by the I^2 value (91%). The p-value (<0.01) generated using the Q-test on R was less than 0.05 and is statistically significant against the null hypothesis.

Sensitivity Analysis

The subgroup sensitivity analysis in Figure 3 was undertaken to determine the rate of infection after surgical intervention by intramedullary nailing or external fixation. It reported a lower overall rate of infection: 21.88 per 100 person years (95% CI: 8.69; 55.10). There was also a statistically significant (p<0.01) high level of heterogeneity in this sensitivity analysis (90%). The RoB 2 tool [16] used to assess randomised controlled trials (table 2).

Discussion

The meta-analysis in this review revealed that the overall incidence of infection following OTFs was 23.21 per 100 person-years (95% CI: 9.19-58.62) using all treatments, and 21.88 per 100 person years (95% CI: 8.69-55.10) when considering only surgical interventions. This indicates that if 100 patients with OTFs are monitored for one year, approximately 23 would develop an infection. A previous study on the incidence of infection in LMICs reports an infection rate of OTFs as 18% over an average of 19.8 months for 15 studies [3], reflecting a similar result to the findings from this systematic review.

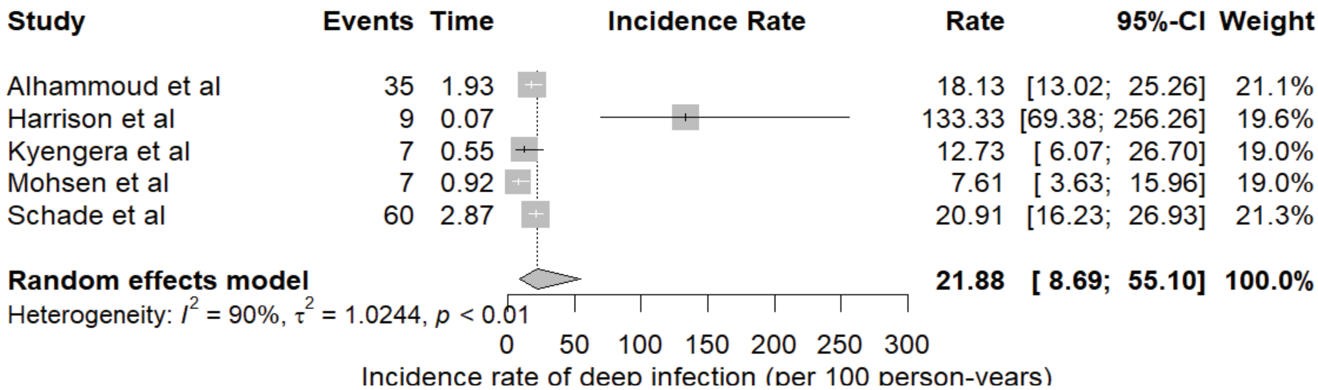
This is useful in establishing a baseline rate of infection for OTFs in LICs. Future treatment practices can be measured against these findings to compare infection rates and improve protocol if infection rates are found to be higher than expected. If infection rates are found to be lower than that established in this study, clinicians are

Table 2: The Newcastle-Ottawa Scale (NOS) assessment of risk of bias in the included Cohort studies in this systematic review.

Author	Study type	Year	Country	Patients	Controls	Male/Female	Mean age (years)	Follow-up time
Alhammoud[21]	Retrospective Cohort Study	2019	Syria	193	N/A	180/15	27.5±11	1 week - 1 year
Harrison[20]	Prospective Cohort study	2004	Malawi	27	N/A	24/3	34.2	3 months
Kyengera[22]	Randomised Controlled Trial	2022	Uganda	31	24	37/18	39	365 days (IM nail), 136 days (ex-fix)
Mohsen[23]	Retrospective Cohort Study	2019	Yemen	92	N/A	71/21	37.3 ± 10.3	1 year
Schade[10]	Prospective cohort study	2023	Malawi	287	N/A	248/39	34 (IQR 26-45)	1 year
Total				632	24	560/96		

The NOS assessment involves assigning stars to each subgroup of the scoring system if it meets the appropriate criteria. Each section in the NOS assessment is assigned a maximum number of stars: Selection (4), Comparability (2), and Outcome (3). These stars relate to numbered categories within each section [17].

Figure 3: Sensitivity analysis of surgical site infections of participants who only received surgical treatment by intramedullary nail or external fixation.



Data for amputation and plaster of Paris was excluded for the sensitivity analysis. Results are displayed as a forest plot on RStudio™ [15] using a random effects model. Incidence of infection is reported per 100 person-years.

urged to share their techniques and practices to lower the rate of infection across populations. However, there are challenges in the implementation of SSI prevention and surveillance in LICs, due to less access to training and resources pertaining to infection prevention [24]. For example, access to technology such as laminar air flow systems is limited due to constraints in infrastructure, expertise, and funding [24]. Nevertheless, studies have suggested that identifying healthcare workers who are empowered to push for infection prevention measures and creating easily understandable and readily available education resources could be a step towards reducing the incidence of SSIs in LICs [25].

However, this meta-analysis does demonstrate a high level of heterogeneity as determined by the I^2 statistic and the large 95% confidence intervals reported. This could be due to a variety of reasons as the included studies differ in many ways. There is a mix of study types, with both RCTs and cohort studies included in the same analysis. Additionally, population sizes vary from 27 in Alhammoud et al. [21] to 287 in Schade et al. [10], and follow-up times vary from three months in Harrison et al. [20] to one year in Alhammoud et al. [21]. The latter reported follow-up times varying from one week to one year. Kyengera et al. [22] conducted follow-ups at different times for the two different treatment types (136 days for ex-fix and one year for IM nail).

The sensitivity analysis helps to assess the robustness of the studies included. The studies are of a similar weighting and there is a high level of heterogeneity (90%). Future RCTs comparing external fixation and intramedullary nail would achieve a lower heterogeneity of results and power more accurate statistical analysis for incidence rate in OTFs.

This review also found there was a noticeably higher proportion of male patients than female patients in the included studies: 560 out of 632 patients (77.5%) were male across all studies. This reflects the finding that OTFs are twice as likely to occur in males than in females and RTCs are the most common cause [26]. There is also a higher rate of RTCs in LMICs, accounting for over 90% of mortalities from RTCs globally [27]. Gunshot wounds were also a major cause of OTFs in this review – a phenomenon more common in wartime - as is reflected in Alhammoud et al. [21]. OTFs inflicted by gunshot wounds provide a different mechanism of injury compared to those sustained in RTCs [28]. Low-velocity gunshot wound OTFs may affect incidence of infection due to increased tissue trauma, entrance and exit wounds [28]. We therefore suggest using the modified Orthopaedic Trauma Society (OTS) Open Fracture Classification System to aid policymakers in providing clear guidance on OTFs inflicted by gunshot wounds [28]. These factors all contribute to economic loss in these countries and burden on limited healthcare systems.

Crucially, our review provides a baseline infection rate for SSIs of OTFs in LICs. This data is essential for designing future RCTs and interventional studies comparing treatment types and infection rates in this population. There are currently very few RCTs on infection in OTFs in LICs. Therefore, future investment in orthopaedic research in LICs should focus on RCTs which aim to identify the most suitable treatment for each Gustilo-Anderson classification. Surgical treatments with the lowest incidence of SSI reduce disability, improve patient outcomes, and hence incur lower economic losses.

This study had limitations. Many studies were excluded for grouping together the results of different types of open fractures (e.g. open femur fractures and OTFs grouped together). Data regarding specific Gustilo-Anderson categorisation was often reported, but infection data was not available for each category of fracture. Microbiological data was also unavailable for causative organisms of infection. Authors of five studies where partial data was available were contacted for data specific to OTFs, but only one study provided data for infection rates, Schade et al. [10]. This highlights an on-going international issue regarding shared scientific data. More studies reporting microbial agents would allow for sub-group analysis of the types of infection associated with different treatment types.

The link between high grade Gustilo-Anderson OTFs and increased incidence of SSIs is well known. The limited data available in the included studies prevented sub-group analysis according to Gustilo-Anderson classification. Furthermore, the variation in fracture classification across studies increased the heterogeneity of the meta-analysis. As a result, there is a chance of reporting bias, in that more severe injuries with higher Gustilo-Anderson classification are likely to be included as they require surgical treatment. Higher grades of open fracture correlate to higher rates of infection, which may confound the incidence of infection after surgical intervention [29].

The Centers for Disease Control and Prevention (CDC) defines surgical site infection as "an infection related to a surgical procedure that occurs near the surgical site within 30 days following surgery (or up to 90 days following surgery where an implant is involved)" [30]. However, in this review, no standardised definition for infection is implemented as no two studies define infection the same way. This is an ongoing point of interest in the literature as a study found that at least 41 different definitions of surgical wound infection have been used [31]. The World Health Organisation (WHO) suggests that using a standardised definition such as the CDC definition could help in producing globally comparable data which can be analysed to further improve health outcomes for patients worldwide [24].

There are some signs of development in the research and treatment of OTFs in LICs. Four of the five included studies were published in the last five years, indicating an increase in the sharing of vital information on treating OTFs in LICs. There is relatively more information on how to treat OTFs in high-income and middle-income countries, but information on how to treat such fractures in more limited resource settings can inform policy and practices across the globe [32]. Further research is required to determine the baseline SSI rate of each Gustilo classification. Authors should attempt to display future infection data for each specific grade and fracture type independently allowing for more specific policies on gold standard treatment.

This systematic review found that the incidence of infection following open tibial fractures in low-income countries was 23.21 per 100 person-years and the incidence of infection following surgical intervention was 21.88 per 100 person years. These findings can be used to power high quality studies investigating incidence of surgical site infections when treating open tibial fractures and ultimately reduce a major source of disability and economic loss in low-income countries.

Conflicts of interest: None declared

References

1. Shanthakumar D, Payne A, Leitch T, Alfa-Wali M. Trauma care in low- and middle-income countries. Surg J. 2021;7(4):e281–5.

2. Mwafulirwa K, Munthali R, Ghosten I, Schade A. Epidemiology of open tibia fractures presenting to a tertiary referral centre in Southern Malawi: a retrospective study. Malawi Med J. 2022;34(2):118–22.

3. Schade AT, Hind J, Khatri C, Metcalfe AJ, Harrison WJ. Systematic review of patient-reported outcomes from open tibia fractures in low and middle-income countries. Injury. 2020;51(2):142–6.

4. Doshi P, Gopalan H, Sprague S, Pradhan C, Kulkarni S, Bhandari M. Incidence of infection following internal fixation of open and closed tibia fractures in India (INFINITI): a multi-centre observational cohort study. BMC Musculoskelet Disord. 2017;18(1):1–10.

5. World Bank Country and Lending Groups – World Bank Data Help Desk. 2023. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.

6. ORCA Study Group. Open tibial shaft fractures: treatment patterns in sub-Saharan Africa. OTA Int. 2023;6(2):e228.

7. Higgin R, Dean M, Qureshi A, Hancock N. Outcomes following the delayed management of open tibial fractures. Injury. 2021;52(8):2434–8.

8. Coombs J, Billow D, Cereijo C, Patterson B, Pinney S. Current concept review: risk factors for infection following open fractures. Orthop Res Rev. 2022;14(November):383–91.

9. Cross WW, Swiontkowski MF. Treatment principles in the management of open fractures. J Am Acad Orthop Surg. 2008;42(4).

10. Schade AT, Sabawo M, Nyamulani N, Mpanga CC, Ngoie LB, Metcalfe AJ, et al. Functional outcomes and quality of life at 1-year follow-up after an open tibia fracture in Malawi: a multicentre prospective cohort study. Lancet Glob Health. 2023;11(10):e1609–18.

11. Islam MS, Islam SS, Parvin S, Manjur M, Islam MR, Halder RC, et al. Current pathogens infecting open fracture tibia and their antibiotic susceptibility at a tertiary care teaching hospital in South East Asia. Infect Prev Pract. 2022;4(1):100205.

12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339(7716):332–6.

13. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, eds. Cochrane Handbook for Systematic Reviews of Interventions, version 6.4. Cochrane; 2023. Available from: www.training.cochrane.org/handbook.

14. Borchardt RA, Tzizik D. Update on surgical site infections: the new CDC guidelines. JAAPA. 2018;31(4):52–4.

15. Posit Team. RStudio: Integrated. Boston; 2023. Available from: http://www.posit.co/.

16. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:1–8.

17. Gierisch JM, Beadles C, Shapiro A, et al. Health disparities in quality indicators of healthcare among adults with mental illness. 2014. Available from: https://www.ncbi.nlm.nih.gov/books/NBK299087.

18. Team EndNote. EndNote. Clarivate; 2023.

19. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan: a web and mobile app for systematic reviews. Syst Rev. 2016;5(1):1–10.

20. Harrison WJ, Lewis CP, Lavy CBD. Open fractures of the tibia in HIV positive patients: a prospective controlled single-blind study. Injury. 2004;35(9):852–6.

21. Alhammoud A, Maaz B, Alhaneedi GA, Alnouri M. External fixation for primary and definitive management of open long bone fractures: the Syrian war experience. Int Orthop. 2019;43(12):2661–70.

22. Kyengera DK, O'Hara NN, Slobogean GP, Howe AL, Blachut PA, O'Brien PJ, et al. Unreamed intramedullary nailing versus external fixation for the treatment of open tibial shaft fractures in Uganda: a randomized clinical trial. J Orthop Trauma. 2022;36(9):E349–57.

23. Mohsen AAH. Open tibia fracture treated by external fixation: our experience in two private hospitals in Aden, Yemen. World Fam Med J. 2019;17(11):44–8.

24. WHO. Global guidelines on the prevention of surgical site infection. 2018. Available from: http://www.who.int/gpsc/ssi-prevention-guidelines/en/.

25. Mehtar S, Wanyoro A, Ogunsola F, Ameh EA, Nthumba P, Kilpatrick C, et al. Implementation of surgical site infection surveillance in low- and middle-income countries: a

position statement for the international society for infectious diseases. Int J Infect Dis. 2020;100:123–31.

26. Nicolaides M, Pafitanis G, Vris A. Open tibial fractures: an overview. J Clin Orthop Trauma. 2021;20.

27. Mapossa JB. Global status report on road safety. N Engl J Med. 2018;372:2499–508.

28. Lunga Z, Laubscher M, Graham SM, Held M, Ferreira N, Magampa R, et al. Optimising the Orthopaedic Trauma Society open fracture classification system: a proposal for modification in the context of high civilian gunshot fractures. Eur J Orthop Surg Traumatol. 2024;34(3):1667–74.

29. Papakostidis C, Kanakaris NK, Pretel J, Faour O, Morell DJ, Giannoudis PV. Prevalence of complications of open tibial shaft fractures stratified as per the Gustilo-Anderson classification. Injury. 2011;42(12):1408–15.

30. Evans HL, Hedrick TL. Overview of the evaluation and management of surgical site infection. Wolters Kluwer. 2024. Available from: https://www.uptodate.com/contents/overview-of-the-evaluation-and-management-of-surgical-site-infection.

31. Bruce J, Russell EM, Mollison J, Krukowski ZH. The quality of measurement of surgical wound infection as the basis for monitoring: a systematic review. J Hosp Infect. 2001;49(2):99–108.

32. Schade AT, Khatri C, Nwankwo H, Carlos W, Harrison WJ, Metcalfe AJ. The economic burden of open tibia fractures: a systematic review. Injury. 2021;52(6):1251–9.