**GEORGETOWN PUBLIC HOSPITAL CORPORATION**



**MEDICAL INTERSHIP PROGRAMME**

**RESEARCH PROPOSAL**

**Title:**

***A Retrospective study on the occurrence of malunion, delayed-union and non-union in the tibial shaft secondary to fractures in Orthopedics Department at Georgetown Public Hospital Corporation*** ***from 30th June 2017 to 30th June 2022.***

***Incidence of malunion, delayed union and non-union following tibial shaft fracture at GPHC from 2017 to 2022: A retrospective analysis.***

**Researcher**: **Renessa Amanda Henry** (BSMD, Medical Intern).

**Supervisor: Dr. Stephen Budhram**

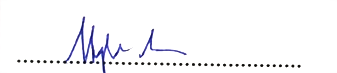
**Name of Head of Department: Dr. Hyder Khan**

I hereby certify that approval has been given for **Renessa Amanda Henry** to conduct the proposed research, **‘A Retrospective study on the occurrence of malunion, nonunion and delayed union in the tibia shaft secondary to tibial shaft fractures among patients admitted to the Orthopedics Department at Georgetown Public Hospital Corporation during the time period of 30th June 2017 to 30th June 2022,’** within the **Department of Orthopedics, Surgery.**



**Dr. Stephen Budhram, MD, Dip Ortho and Traumatology**

**Medical Registrar**

**(Research Supervisor)**

**Dr. Hyder Khan**

**(Head of Department Orthopedics)**

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# Project summary

Literatures searches has shown that fracture healing complications are common in patients with fractures. Studies show that the most common healing complication are non-union, malunion and delayed union with incidences of 6.8%, 0.7% and 0.6% respectively.(1) Patients’ quality of life is affected post operatively with additional burden to the healthcare system.

The study aims to determine the incidence and risk factors of fracture healing complications: malunion, non-union and delayed union of the tibial shaft secondary to fractures tibial shaft fractures among patients that were admitted to the Orthopedic Department at the Georgetown Public Hospital Corporation (GPHC). This will enable healthcare providers to better identify the group of patients that are at an increased risks for the development of such complications.

This goal will be achieved by using a retrospective cohort quantitative approach. It will include collection of data of all patients that were admitted to the Orthopedics Department at GPHC from 30th June 2017 to 30th June 2022 with fractures to the tibial shaft. General information about patients’ sex, age, gender, race and comorbidities will be documented as well as time of injury, time of presentation to hospital setting whether to clinic or accident and emergency department and the type of treatment that was first given to the patient at the time of presentation. The patients will be followed over a period of at least 8 weeks to assess whether their fractures healed without complications or whether they had complications by using their clinic charts. Information about outcome will be recorded either as good: no healing complications, or bad: malunion, non- union or delayed union.

At the completion of this project it is expected that data will be known about the rate of incidence of malunion, nonunion and delayed union associated with fractures of the tibial shaft, the results of which will be used to determine the percentage incidence of fracture healing complications secondary to fractures of the tibial shaft and identify the specific groups of patients that are at an increased risk of suffering from fracture healing complications: malunion, nonunion and delayed union at the time of presentation so that we can be able to prevent rather than treat these complications early on.

**Question**

What is the incidence and risk factors of fracture healing complications (malunion, non-union and delayed union) among patients previously admitted to the Orthopedics department at GPHC for fractures to the tibial shaft during the period 30th June 2017 to 30th June 2022?

# General Information

## Research Title

A Retrospective study on the occurrence of malunion, delayed-union and non-union in the tibial shaft secondary to fractures in Orthopedics Department at Georgetown Public Hospital Corporation from 30th June 2017 to 30th June 2022.

## Investigator

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## Research Site

Orthopedic Department at Georgetown Public Hospital Corporation (GPHC)

## Institute

* Georgetown Public Hospital Corporation
* Medical Internship Programme

## Introduction and Rationale

The rate of incidence of tibial shaft complications secondary

The tibia is one out of two long bones that is located in the lower part of the lower extremity. The tibia is the longer thicker medial bone that bears most of the weight of the body. Lateral to this is the fibula which is smaller and functions to support the ankle and stabilize the ankle joint and lower leg.

Tibial shaft fractures can be due to either low energy impact (torsional injury) or high energy impact (MVC, falls sporting injuries). This research will be focusing on fractures strictly of the tibial shaft and fibula. These fractures can be classified according to:

* Location: proximal third, mid third or distal third
* Open vs closed: bone breaks through skin and exposed, no break in skin
* Simple vs complex: 2 fragments, more than 2 fragments
* Displaced vs non displaced: out of line with other fragment(s), in line with other fragment(s)

Diagnosis is made via physical examination and x-rays of the lower extremity. Clinical features include:

* Pain
* Tenderness
* Erytherma
* Edema
* Inability to weight bear
* Neurovascular compromise

Investigations include: AP and Lateral views of affected limb. Full length. Joints above and below.

Treatment options depend on the classification of the fracture.

For simple non-displaced closed fractures in children immobilization in a short or long leg case for three to four weeks in toddlers and six to ten weeks in older children is sufficient. In adults the treatment of tibial fractures varies slightly from that of children. For minimally displaced closed midshaft tibial fractures, either conservative management via casting can be done. However the patient or surgeon may choose surgical management in the form of intramedullary nailing as it decreases the time it takes for the patient to return to full functional status and also increases the chances of the patient being able to do so.

Operative management for tibial shaft fractures includes intramedullary nailing, plating and external fixation. Intramedullary nailing is more commonly used for midshaft tibial fractures, plating for proximal and distal fractures and external fixation is generally used for damage control such as open fractures with compromised soft tissue injury.

In the case of open fractures, the first treatment regimen is to start the patient on antibiotics and give a tetanus shot to prevent infection. Afterwards the wound is cleaned to remove debris and bone fragments. Depending on the size of the wound, amount of tissue damage, extent of bone injury and presence or absence of vascular compromise and nerve injury, surgery may be necessary. Surgical treatment options include:

ORIF: Open reduction and internal fixation. Can be done with plate and screws or intramedullary fixation lock vs non-locking. Repositions and physically connects the bones.

External fixation: can be done with pins. Involves stabilizing the bones from the outside.

Other methods include wire fixation to hold the bones in place until they heal.

In certain procedures where the fixation method is not stable enough the limb can be immobilized by a cast or back slab (plaster of paris), brace or splint, which can be either above the knee or below the knee.

Following the fracture, healing begins. The mechanism of fracture healing is an intricate and fluent process consisting of four steps:

1. Hematoma formation
2. Fibrocartilaginous callus formation
3. Bony callus formation
4. Bone remodeling

There are many complications of bone healing as a certain environment must be present in order for bone healing to occur, the complications that will be mentioned in this research however would be:

* Malunion: when a fractured bone heals in an abnormal position, resulting in impaired function of the limb or bone. Can be crooked, rotated, shortened, etc.
* Nonunion: fracture that does not unite within 9-12 months, or extension of the healing process beyond the expected rate.
* Delayed union: absence of radiographic progression of healing or the instability of a fracture upon clinical examination between 4 to 6 months after injury.

There are multiple factors which affect fracture healing. These factors can be divided into local and systemic factors.

Local factors:

* Fracture characteristics- movement, misalignment, extensive damage and soft tissues caught within fracture ends can lead to delayed or non-union
* Infection
* Blood supply

Systematic factors:

* Advanced age
* Obesity
* Anemia
* Endocrine disorders
* Steroid administration
* Malnutrition
* Smoking

These factors have significant mortality and morbidity. It is important that patients with fracture healing complications receive treatment as it can result in disruption of weight bearing activities to the affected limb. This can intern disrupt the normal day to day functions of the patient. Usually, treatment is to restore the alignment, provide stable fixation, bone graft and/or bone transport. The use of bone graft substitutes for stimulating bone repair and filling bone defects is also possible. Though treatment regimens exist however, it would be better to be able to identify the risk groups that are at a higher risk for developing fracture healing complications as “prevention is better than cure”.

While rotating in the orthopedics department at GPHC it was observed that these fracture healing complications were common among patients that previously sustained fractures to the tibia. Another observation made was that there were no specific age group, gender or historical risk factors in which these complications were common in. Thus, it would be reasonable to conduct such a study to better understand the incidence, and the relationship among risk factors, age and gender as it relates to these fracture healing complications.

Over the years there has been a vast majority of research done on this topic in different parts of the world, however there a research gap in Guyana as it relates to these fracture healing complications. having such research done in Guyana will allow physicians to be aware about the incidence of these complications among our population.

## Literature **review**

Tibial shaft fractures are the most common long bone fractures(3). The peak incidence is in young men, with a second peak in the elderly population. The commonest mechanisms are falls, sporting and transport accidents, with higher energy mechanisms seen more commonly in younger patients, for example as a result of soccer or motorcycle collisions. (3)

Fracture healing is a complex mechanism that is affected by multiple biological, mechanical, local and systemic factors.(4) The most common fracture healing complication of the tibia is non-union.(1) There are multiple modifiable and non-modifiable factors associated with healing(4), some of which may have positive and some of which have negative effects on healing. Over the years these factors have been studied multiple times. Factors that have an impact on fracture healing include age, sex, mechanism of injury, location of fracture, classification of fracture (simple vs comminuted, open vs closed, transverse vs spiral, complete vs, incomplete, displaced vs un-displaced), NSAID use, opioid use, alcohol consumption, smoking history and status, physical status. Multiple studies have been done on the effects of these factors and many more.

In the year 2018 a retrospective cohort study was done by C. L. Ekegren to determine the rate, cost and predictors of two-year readmissions for surgical management of healing complications following fractures of the femur, tibia and humerus. The sample size used was 3886. Of these 315 patients (18.1%) were readmitted for fracture healing complications. The most common healing complication was non-union- 264 patients (6.8%). Malunion- 29 patients (0.7%) and delayed union- 22 patients (0.6%). Most admissions were of the male gender, younger, from rural areas, sustained fractures that resulted from high energy impact and were being compensated. Patients who also sustained non- orthopedic injuries such as head injuries and injuries of the abdomen and chest also had higher rates of readmissions for fracture healing complications. (1)

Another retrospective cohort study done in the USA in 2016 by K. O’Halloran with a smaller sample size of 386 patients also showed similar results to the before mentioned study but more factors were studied. This study took into consideration 35 variables, 14 of which were found to have an impact on fracture healing. The fracture healing complication looked at in this study was that of non-union, however the results are applicable to the task as the mechanisms are similar. The results of the study were used to create the NURD SCORE- Nonunion risk determination score. The NURD score was intended to be used as a predictor towards the outcome of tibial shaft fractures at the time of definitive fixation. Seven factors were included in the score, each of which had a different point value if present. These factors are: flaps- 5 points, compartment syndrome- 4 points, chronic conditions- 3 points, open fracture- 2 points, male gender-one point, grade of American Society of Anesthesiologist Physical Status and percent cortical contact- one point each. These factors were proven to have negative impacts on fracture healing. Spiral fractures and low energy injuries were also included in the score and were given negative one points each. Reason for this is because these two factors were predictive of union. Further conclusion of this study was that a NURD score of zero-five (0-5) was indicative of a two (2) percent chance of non-union, a score of six to eight (6-8) was indicative of a twenty-two (22) percent chance of non-union, a score of nine to eleven (9-11) was indicative of forty-two (42) percent and a score of twelve (12) and more than twelve (12) was indicative of a sixty-one percent chance of non-union.(5)

Another factor that has a negative impact on fracture healing would be smoking. This is supported by a metanalysis and systemic review observational study that was done in 2021 by A. Mahajan, N. Kumar and B. Gupta. The studied showed that tobacco smoking is associated with an increased risk of non-union and delayed union in the tibial shaft post fracture.(4) Similar results were reported in a systemic study by Tian et al., which reported that the prevalence of tibial fracture non-union was significantly higher in smokers as compared to non-smokers, p=0.111. The reason for this as discussed in the literature was because of a concept referred to as the “Diamond concept” introduced by Giannoudis et al. The concept states that successful fracture healing is dependent on three factors in the biological environment at the fracture site: availability of osteoinductive mediators, osteogenic cells, an osteoconductive matrix and mechanical stability, smoking has a negative impact on all these biological factors, thereby impairing fracture healing. (6)

The same study stated that heredity is another very important factor when it comes to the prevalence of non-union. (6)

Other influencing factors that were revealed by the study to have negative impacts on fracture healing included increased age (>60), DM, Opioid use, middle and distal tibial fracture, Gustilo Anderson score grades IIIB and IIIC, AO classification C, BMI greater than forty (>40) and NSAID use. Also, according to the study, open reduction had a higher rate of tibial fracture non-union than closed reduction. Reasoning for this is because closed reduction can better protect the blood supply and soft tissue than open reduction. (6)

NSAID use can have negative impacts on fracture healing. As referenced by the study done by Pountos, I et al.(7) Another study which is an inception cohort study by T. Buchheit et al, in the USA in 2016 not only support the claim that NSAID use can be associated with increased risk of fracture healing complications but also studied the relationship of fracture healing with other drugs. The study was done with a sample size of 309,330 fractures. It stated that antibiotics, anticoagulants and bisphosphonates were associated with a significantly higher risk of non-union when used acutely, insulin and diuretic use were associated with a slightly lower risk and oral contraceptive pills were also with an even lower risk. Acute use of non-opioid medications such as anticonvulsants or butalbital significantly increased the risk of fracture non-union as well as chronic use of prescription NSAIDs. Anticonvulsants used chronically and benzodiazepines used acutely also increased the risk. Both acute and chronic use of opioid significantly increased the risk of non-union. However, there was a substantial difference in healing when comparing acute and chronic opioid user. Chronic opioid use was associated with twice the risk of non-union than acute opioid use. (2)

In conclusion, a vast number of studies have been done worldwide focusing on the risk factors of non-union, delayed union and malunion. Most of the studies referenced have similar conclusions as to the factors that increase the risks of fracture complications. However more studies have been done on non-union as compared to the lesser two and no studies have been done in Guyana focusing on the factors associated with fracture healing. As such this study is proposed so that our physicians in Guyana can be better prepared and aware about which patients are at greater risk of developing fracture healing complications at the time of presentation. Future plans and parameters will be put into place to significantly deal with the results of the study.

## Objectives

1. To determine the incidence rate of fracture healing complications: malunion, non-union and delayed union, of the tibial shaft secondary to fractures among patients that were previously admitted to the orthopedics department at GPHC between the period of 30th June 2017 to 30th June 2022.
2. To determine whether or not there has been an increase or decline in the occurrence of malunion, nonunion and delayed union of the tibial shaft secondary to factures during this period.
3. To identify the factors that have the most influence on the occurrence of fracture healing complications in patients that were previously diagnosed with fractures of the tibial shaft.

# Methodology

## Study Design

### Study Type

This study can be described as a retrospective cohort study that uses quantitative methods for the collection and analysis of data.

### Population and Study Setting

The source population in this study include persons who were admitted to GPHC with a diagnosis of fractures of the tibial shaft during 30th June 2017 to 30th June 2022 that fit the inclusion criteria and will be taken from the admissions to the Orthopedics Department located at GPHC either through accident and emergency or clinic. Using Yamane formulae to calculate sample size- a sample size of 254 will be used, with the source population (N) being 700 and margin or error (E) being 0.05.

### Sampling

The entire source population will be used to calculate incidence and the sample population will be represented as the patients that have the fracture complications understudy in this research. Data collection and analysis on the risk fractures will be collected from the sample population.

### Inclusion and Exclusion Criteria

Inclusion criteria:

All patients that were admitted to the Orthopedics Department at GPHC for fractures of the tibial shaft, during the time period of 30th June 2017 to 30th June 2022, who were admitted to and followed up at the orthopedics clinic afterwards will be included in this study. The first admission for these patients would have occurred inclusive of and onwards from the 30th June 2017.

Exclusion criteria:

* Patients that had fractures related to bone disorders: brittle bone disease, osteogenesis imperfecta, osteoporosis, malignancies affecting bone density, will be excluded from the study
* Patients that were not admitted to the orthopedic clinic after discharge will be excluded from the study as there would be no way of following up a patient if they were not admitted to the clinic after discharge.
* Patients that were admitted to the emergency room with fractures of the tibial shaft as well as other injuries that resulted in death soon after will also be excluded from the study.

### Data Collection Tool

The data for this research will be obtained from secondary sources, this will be the patients’ ward charts stored at the records department and also their charts from the Orthopedics clinic at GPHC.

## Procedure

* Ethical approval will be sought from the Institutional Review Board (IRB) at the Ministry of Public Health (MOPH), Guyana, before commencement of data collection.
* Once ethical approval is granted, permission will be requested from the Director of GPHC, the Head of Department for Orthopedics and the Research supervisor to gain access to the patients’ chart from the records department and Orthopedics clinic at GPHC to conduct data collection.
* The data for this research will be collected from the patients’ admission charts and clinic charts. They will be entered onto a spreadsheet created on IBM SPSS version 26.
* All the charts that satisfy the inclusion criteria for a fracture of the tibial shaft will be included in this study.
* The information about whether the patients had fracture healing complications: malunion, non-union or delayed union will be recorded and used to determine incidence or these fracture healing complications.
* Information about risk factors will be collected from the charts in which the patients had the fracture healing complications under study in this research.
* The data that will be collected from admission charts are as follows:
  + The age, gender and ethnicity of all patients will be recorded.
  + Risk factors
    - Presence of comorbidities or previous injuries and whether controlled or uncontrolled.
    - BMI
    - Presence or absence or previous injury to affected limb
    - Absence/ presence of trauma or type of impact whether low, moderate or high energy impact.
    - Fracture classification
    - Location of fracture
    - Previous injuries
    - Drug history
    - Alcohol and smoking history
    - Treatment regimen
    - Treatment regimen and operative procedures that were used:
* The patients will be followed over a period of at least 6 months after discharge and initial treatment or until discharge from the clinic to assess on further risk factors by retrieving their clinic charts. The following data will be obtained from their clinic charts:
  + - Presence or absence of injury after initial insult.
    - Was the patient on any medication (recreational or pharmacological) during the fracture healing period.
    - Alcohol use?
* For any variable where the data is not recorded in the charts, it will be entered as missing data.
* The data collected will be tabulated and represented graphically for analysis and interpretation.

## Safety considerations

To maintain the confidentiality of patient’s information no name, date of birth and address will be recorded. The only demographic information of vital importance to this study includes the age, gender and ethnicity. Each of the charts will be given a researcher generated code to enter data. The code will comprise of a serial number (001, 002, 003, 004, ….) and the date of admission for fracture. The registration number will be taken to link researcher generated code for the anticipation to correct error during the data collection process. During the process of this project, the information will be kept on a password protected personal computer to which only the researcher has access to. Upon completion of the project, the registration number will be discarded to further maintain confidentiality of patient’s information.

## Project Duration and Follow Up

This project is expected to be completed within a period of 35 weeks commencing on March 14th 2022 and completing on November 14th 2022. It will be divided into three sections:

1. The planning and research proposal section
2. The data collection and entry section
3. The data analysis and interpretation section

|  |  |  |
| --- | --- | --- |
| **Date** | **Sections** | **Plan** |
| **PLANNING AND RESEARCH PROPOSAL: March 14th , 2022 – June 30th, 2022** | | |
| March 14th – April 4th 2022. | Choose a research topic | * Choose within a department and topic of interest. * Review of previous researches done * Identify a topic * Consult with a supervisor |
| April 4th – May 2nd 2022 | Introduction and Literature review | * Research on the facts of the topic * Research for similar researches done before. * Compile |
| May 2nd – May 30th 2022 | Methodology and other sections | * Complete all the remaining sections * Compile the proposal |
| June 1st – June 30th 2022 | Review | * Submit to supervisor for review * Make corrections as advised * Submit completed proposal to DMPS\* |
| **DATA COLLECTION AND ENTRY: July 1st – September 30th** | | |
| July 1st – July 31st | Approval to begin data entry | * Submit proposal to IRB for approval * Submit to head of department of Orthopedics for permission to gain access to patients’ chart * Seek approval letter from supervisor to gain access to patient’s chart at records. |
| August 1st - September 30th | Data collection | * Daily visits to the record department will be done to collect the data from the charts * Plans will be made to have an assistant to aid with data collection * Data will be entered onto IBM SPSS version 26 |
| **DATA ANALYSIS AND INTERPRETATION: October 1st – November 30th** | | |
| October 1st – October 15th | Data analysis | * Using the IBM SPSS version 26 and Microsoft Excel, graphical and table representations will be done for analysis |
| October 16th – October 30th | Data interpretation | * Interpretations will be made * Discussion will be drafted comparing previous researches with the findings of this one |
| October 31st- November 14th | Compilation, review and finalize | * The preliminary final report will be compiled * It will be submitted to the supervisor to be reviewed * Necessary corrections will be made * The final report will be completed |
| November 30th | Submission | * The final report will to DMPS office |

\* DMPS – Director Medical and Professional Services.

## Data Management and Statistical Analysis

For the entry of data, a code book will be created for all the variables required. (See appendix 1) This will guide the entry of data into IBM SPSS version 26 spreadsheet. The researcher will use a sheet for data collection at the records department and then transpose this onto the IBM SPSS version 26. She will use an assistant to review data entered from sheets to ensure quality assurance.

After collection of data and assurance of quality data, the confounding variables in the research will be identified and adjusted. Bivariate and multivariate regression analyses will be used to determine which variables are significant risk factors associated with these fracture healing complications.

Using IBM SPSS version 26, analysis of data will be done. Tables, pie charts, bar graphs and histograms will be used to represent the data collected. …..

## Quality Assurance

To ensure the data collected has no errors, an assistant will be of vital importance during the process of data collection and entry. In both process the assistant will be utilized to review the data collected and entered for any mistakes. This is to ensure the quality of the data collected is true of the population.

# Expected Outcome of the Study

Upon completion of this project, the following outcomes are expected:

1. **Awareness of results to the medical community**: Through presentations to the Surgical department and Orthopedics, the results will be disseminated to the doctors and nurses, so as to make aware of the current percentage incident rate regarding malunion, nonunion and delayed union of the tibial shaft secondary to fractures at GPHC.
2. **Implementation to patient Management**: Knowing the major risk factors will allow doctors to identify the specific risk groups in the population. Therefore, they can further manage those patients by tracking the most common risk factors. Since the information will be well known, facts can be given to the patients to make them better understand the importance of controlling their risk factors.

# Dissemination of Results and Publication Policy

After completing the data analysis and final report, the results of the study will be disseminated firstly to the staff within the Department of Orthopedics at Georgetown Public Hospital Corporation.

Further plans will be made to public the report in Guyana.

# Problems anticipated

During this project, a number of factors are anticipated that can affect the final result. These include:

1. **Missing information from charts:** some charts may not contain all the information required. This may be due to incomplete history taking from the admitting physician, a result of the patient being a poor historian, or withholding of information by the patient. These missing data will be accommodated for by making a record option as missing data.
2. **Legibility of writing:** even with information present, the writing in the charts may not be legible for the researcher to understand. Contact with the admitting physician will be made to accommodate for this whenever possible. If there is failure to obtain information the data will be entered as illegible, meaning that it is present but not understood.

# Ethical consideration

Confidentiality of patients’ information will be maintained by not entering the patients’ names and deleting all registration codes from the data entry file after completion of the project. This project will be reviews by the Institutional Review Board to obtain approval before commencing data collection. Permissions from the Head of Department for Orthopedics and the Supervisor will also be obtained. Any suggested changes will be made.

# References

1Ekegren, C.L. et al. (2018) Incidence, costs and predictors of non-union, delayed union and mal-union following long bone fracture, MDPI. Multidisciplinary Digital Publishing Institute. Available at: https://www.mdpi.com/1660-4601/15/12/2845 (Accessed: March 11, 2023).

2Buchheit, T. et al. (2018) Opioid exposure is associated with nonunion risk in a traumatically injured population: An inception cohort study, Injury. Elsevier. Available at: https://www.injuryjournal.com/article/S0020-1383(18)30225-0/fulltext (Accessed: March 12, 2023).

3Rudge, will, Newman, kevin and Trompeter, A. (214AD) (PDF) fractures of the tibial shaft in adults - researchgate, fractures of the tibial shaft in adults . Elsevier. Available at: https://www.researchgate.net/publication/263968706\_Fractures\_of\_the\_tibial\_shaft\_in\_adults (Accessed: March 12, 2023).

4Mahajan, A., Kumar, narinder and Gupta, B. (2021) Delayed Tibial Shaft Fracture Healing Associated with Smoking: A Systematic Review and Meta-Analysis of Observational Studies Conducted Worldwide, Pubmed. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8507831/pdf/ijerph-18-10228.pdf. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8507831/pdf/ijerph-18-10228.pdf (Accessed: March 12, 2023).

5O'Toole, R.V. *et al.* (2020) *NURD 2.0: Prediction of tibial nonunion after intramedullary nail fixation at any time within 3 months after injury*, *Injury journel* . Available at: https://www.injuryjournal.com/article/S0020-1383(20)31057-3/fulltext (Accessed: March 12, 2023).

6Tian, R. *et al.* (2020) *Prevalence and influencing factors of nonunion in patients with tibial fracture: Systematic review and meta-analysis - Journal of Orthopaedic Surgery and research*, *BioMed Central*. BioMed Central. Available at: https://josr-online.biomedcentral.com/articles/10.1186/s13018-020-01904-2 (Accessed: March 12, 2023).

7Pountos, I. *et al.* (2012) *Do nonsteroidal anti-inflammatory drugs affect bone healing? A critical analysis*, *TheScientificWorldJournal*. U.S. National Library of Medicine. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3259713/ (Accessed: March 12, 2023).