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Delays in hospital admissions in patients with fractures across 18 low-income and middleincome countries (INORMUS): a prospective observational study.

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## Delays to Hospital Admission in 31,255 Fracture Patients Across 18 Low-Middle Income Countries: A Prospective, Observational Study

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### Abstract

**Background**—The *Lancet* Commission on Global Surgery (LCoGS) established the Three Delays Framework categorizing delays in accessing timely surgical care into delays in seeking, reaching, and receiving care. Globally, knowledge gaps regarding delays for fracture care, and the lack of large prospective studies informed the rationale for our multi-country observational study. We investigated hospital admission delay as a surrogate for accessing timely fracture care and explored factors associated with delayed hospital admission.

**Methods**—We prospectively enrolled fracture patients across 49 hospitals in 18 low- and middleincome countries (LMICs), categorized into China, Africa, India, South and East Asia, and

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Contributions:

PP, SL, and MB designed the analysis plan for this sub-study. PP, SL, SS, JB, and MB, contributed towards the statistical analysis. PP and MB drafted the manuscript, SL and MB provided overall management, and support throughout the project. MB, RI, PJD, SS, SL, JJ contributed design and management of INORMUS. SL, SS and JJ contributed to overseeing the collection and management of the clinical data. PJD, RI, JJ, JB, SS, and SL contributed to the second draft of the manuscript, providing input and critical review. All authors reviewed and approved the manuscript.

Declaration of Interests

The authors declare no financial or other conflicts of interest.

Latin America. Eligible patients were 18 years old, admitted within 3 months of sustaining an orthopaedic trauma. We collected demographic injury data, and time to hospital admission. We defined delays as >2-hours for open fractures (in accordance with the LCoGS) and >24-hours for closed fracture patients. Reasons for delay were collected for admissions >24-hours. We conducted logistic regression analysis to identify predictors of >2-hours, and >24-hours in open and closed fracture patients, respectively. This study was registered with ClinicalTrials.gov (NCT02150980).

**Findings:** Between January 2014 and May 2019, we enrolled 31,255 consecutive fracture patients, of which most were male (63.8%), with a median age of 45 years (interquartile range: 31, 62) and lower limb fractures (46.5%) were most common. Of 5,256 open fracture patients, 3,778 (71.9%) did not reach the treating hospital within 2-hours. Of 25,999 closed fracture patients, 7,141 (27.5%) were delayed by >24-hours. Latin America possessed the greatest proportion of delay (88.7% open fracture patients; 44.7% closed fracture patients). Interfacility referrals (47.7%), and Third Delays (50.5%), were the most common reasons for delay, while delays in reaching care were the least common (5.4%). As compared to other modes of transportation (e.g., walking, rickshaw), ambulances led to delay in transporting open fracture patients to a treating hospital (aRR 0.68, 99% CI 0.47–0.93). Closed spine (aRR 2.47, 99% CI 2.17–2.81) and pelvic (aRR 1.35, 99% CI 1.10–1.66) fracture patients were most likely to experience >24-hour delay to hospital admission.

**Interpretation**—Within LMICs, timely hospital admission remains largely inaccessible, especially among open fracture patients. Reducing hospital-based delays in receiving care, and in particular, improving interfacility referral systems improving interfacility transfers represent the most significant levers for reducing hospital admission delays.

**Funding**—National Health and Medical Research Council of Australia (APP1084967), Canadian Institutes of Health Research (MOP133609), McMaster Surgical Associates, Hamilton Health Sciences.

#### Keywords

Pre-hospital network; Low-and Middle-Income Countries; Injuries; Delay; Fractures

#### Introduction

Injuries worldwide account for >10% of global disability-adjusted life years, 90% of which occur in low- and middle-income countries (LMICs).<sup>1,2</sup> Deficiencies in the prehospital network contribute significantly to injury mortality and morbidity,<sup>3</sup> and 4 of 5 injury-related deaths occur before patients are admitted to a hospital.<sup>4</sup> Approximately 54% of 45 million annual all disease premature deaths in LMICs can be addressed by improving emergency care systems.<sup>5</sup> The *Lancet* Commission on Global Surgery (LCoGS) determined that essential surgical care facilities should be available within 2-hours for patients with severe injuries, including open fractures. Surpassing this benchmark increases the risk for complications and mortality.<sup>3</sup> Treatment timing thresholds for closed fractures range broadly, from 6-hours for long bone fractures to 24-hours for closed hip fractures.<sup>6</sup>

The LCoGS developed the Three Delays Framework for categorizing delays in accessing timely surgical care.<sup>3</sup> The First Delay, "the delay in seeking care", occurs when a patient stalls in seeking formal healthcare treatment due to, for example, a lack of finances, or distrust in the healthcare system.<sup>3,7</sup> The Second Delay, "the delay in reaching care", occurs when patients who have a desire to seek hospital care are impeded from doing so. This could result from travelling long distances or a lack of transportation.<sup>3</sup> The Third Delay, "the delay in receiving care", are a result of hospital-based deficiencies, such as a lack of capacity to provide care.<sup>8</sup>

Underscored by the World Health Organization (WHO), there is a lack of emergency medical systems (EMS) data,<sup>9</sup> and a need for prospective studies to address critical gaps on understanding delays in fracture care in LMICs. In response to this call, the international multicenter orthopaedic study of fracture care (INORMUS) represents, to date, the largest prospective observational study to quantify hospital admission delays in fracture patients. Similar to previous work<sup>10</sup>, we assessed hospital admission time as a pre-requisite, and surrogate for timely care. To identify priorities for improving access to care, our objectives were three-fold: 1) determine the frequency of 2-hour and 24-hour hospital admission delay in open and closed fracture patients, respectively; 2) apply the Three Delays Framework to categorize admission delays of >24-hours by First, Second, and Third Delays; 3) identify predictors of delayed hospital admission.

#### Methods

#### Study design and participants

INORMUS is an ongoing multicenter, observational study evaluating global trends in musculoskeletal injury and healthcare systems. The current study included 31,255 patients enrolled between January 2014 and May 2019 from 49 hospitals in 18 countries. Patients were grouped into 5 regions: China, Africa (Uganda, Kenya, Nigeria, Ghana, South Africa, Tanzania, Cameroon, and Ethiopia), India, South and East Asia (Pakistan, Nepal, Vietnam, Thailand, The Philippines, Iran), and Latin America (Venezuela, and Mexico).

Our protocol was approved by the McMaster University Research Ethics Board and each clinical site's Ethics Committee. Data was collected with informed consent, and aggregated as de-identified data. This study was registered with ClinicalTrials.gov (NCT02150980).

#### **Eligibility Criteria and Data Collection**

Inclusion criteria consisted of admission to a participating hospital within 3 months of sustaining an orthopaedic trauma and 18 years of age. Trauma was defined as a fracture, dislocation, or fracture dislocation of the appendicular skeleton (i.e., upper and lower extremities, shoulder girdle, and pelvic girdle) or spine. At each admitting hospital, eligible patients were identified through direct emergency department referrals. Patients were approached by study personnel (e.g., nurses, physicians, residents, and research coordinators) to acquire written and informed consent which was provided by all included patients. Upon inclusion, the orthopaedic team at the hospital conducted a history and physical examination of the patient and recorded their findings via a case report form.

Additional methodological details have been previously published.<sup>11,12</sup> Among all fracture patients approached, 3415 (9.6%) refused to participate or did not meet inclusion criteria. In this sub-study, only patients who sustained a fracture were analyzed.

#### **Definition of Delays in Open and Closed Fracture Patients**

The primary outcome was to evaluate the number of open and closed fracture patients who were delayed in admission to a treating hospital by >2-hours, and >24-hours, respectively. During the clinical assessments, for both in- and out-patients were asked when their injury occurred, from which the time to admission at the treating hospital was determined. In accordance with the LCoGS framework, delay in admitting open fracture patients to a treating hospital was defined as taking >2-hours from the time of injury.<sup>3</sup> Admission delay in closed fracture patients was defined as presenting to a treating hospital >24-hours after sustaining a fracture. The delay threshold of >24-hours represents a conservative time point by which many closed fractures are at an increased risk for adverse outcomes and has been previously used as a hospital admissions benchmark.<sup>6,13,14</sup>

#### **Definition and Application of the Three Delays Framework**

Our secondary outcomes were the reasons for delay to hospital admission inclusively among open and closed fracture patients which were stratified according to First, Second, and Third Delays of >24-hours.

In all patients delayed by >24-hours, we collected data on the primary reason for delay, including: 1) fear of hospitals, 2) treated by traditional healer, 3) fear of costs, 4) believing the injury would heal itself, 5) did not want to go to hospital, 6) unavailable transportation, 7) distance to hospital, 8) interfacility referral, 9) delay in emergency department, and 10) other reasons. Reasons for delay 1–5 were categorized into First Delay, defined as a delay in seeking care. Reasons 6 and 7 were recoded as the Second Delay, defined as a delay in reaching care. Lastly, reasons 8 and 9 were categorized as the Third Delay, defined as a delay in receiving care. These categories are in accordance with the LCoGS.<sup>3</sup> In alignment with previous research, because interfacility referrals occur when the transferring hospital is unable to provide care, we defined it as Third Delay.<sup>8,15,16</sup> However, assessing the time to treatment was beyond the scope of this analysis.

#### **Selection and Coding of Variables**

We analysed demographic (age, sex, level of education, occupation, income, living location, region); pre-hospital network (health insurance coverage, method of transportation, location transported from); and injury-related factors (fracture location, mechanism of injury, open fracture grade, number of fractures sustained). We selected variables *a priori* based on previous qualitative and quantitative literature, themes derived from the LCoGS and the WHO EMS model, and our pilot studies.<sup>3,5,14,16–19</sup> Demographic and socio-economic factors impact a patient's willingness or financial capacity to access hospital care. Indicators of the pre-hospital network, including access to transportation and interfacility referrals, impact the timeliness of hospital admission. Finally, the type and severity of the fracture can influence the impetus to seek treatment, the mobility of the patient, and the capacity of hospitals to provide treatment.<sup>3,5,14,16–19</sup>

We only report the most severe fracture sustained by a patient, as determined by the treating surgeon, based on clinical experience. Fractures were categorized as hip, lower limb, upper limb, spine, and pelvic. The lower limb includes the femur, tibia, fibula, ankle, foot, patella, or other. The upper limb includes the humerus, radius, ulna, clavicle, scapula, or other.

#### Sample Size

INORMUS was originally powered with 40,000 patients for the primary outcome of quantifying fracture patient mortality.<sup>11,12</sup> This resulted in outstanding power for this substudy. Considering the frequency of admission time >2-hours among all patients is  $>50\%^{19}$ , and the frequency of open fractures is  $15\%^{18}$ , we estimated a minimum sample size of 2,800 fracture patients to obtain the 420 open fracture patients required to power this analysis.<sup>20</sup> Given that one-sixth of patients were delayed by >24-hours in previous work<sup>18</sup>, we estimated that a robust regional model of >24-hour delay in closed fracture patients would require a minimum sample size of 1500 patients.<sup>20</sup>

## Determining Factors Associated with Delayed Admission in Open and Closed Fracture Patients

In accordance with objective 3, we constructed 2 separate adjusted binary logistic regression models to predict hospital admission delay of >2-hours in open fracture patients (model 1) or >24-hour in closed fracture patients (model 2). For both models, the independent variables were region, age, employment, urban living, health insurance, interfacility referral, method of transportation, number of fractures, mechanism of injury, and fracture location. However, for model 1, spine and pelvic fractures were aggregated into a single category, 'Other', due to their low frequency in open fracture patients. Previous literature has quantitatively or qualitatively ascribed the contribution of the included demographic, health-systems, and fracture variables towards delay, or adverse surgical outcomes.<sup>3,5,14,16–19</sup> We did not include income as an independent factor, as >10% of participants did not report their income.<sup>21</sup> A table of hypothesized associations is included in Appendix A. For all models, independent variables were entered using forced simultaneous entry. We calculated adjusted Odds Ratios (aOR) but converted these to adjusted Risk Ratios (aRR) with 99% confidence intervals (99% CI) to facilitate interpretation. To do so, an estimated baseline risk of admission delay was used to convert odds ratios to relative risk (Supplemental methods).

#### **Statistical Analysis**

We present categorical variables as proportions and continuous variables as median and inter-quartile range (IQR) due to non-normal distributions. Between-group differences in categorical variables were assessed using the chi-square test. Between-group differences for continuous variables were assessed using the Kruskal-Wallis test when >2 groups, and the Mann-Whitney U test when 2-groups. Given our large dataset, and to avoid spurious associates, p<0.01 was considered significant. Missing cases were infrequent (<1%) and excluded from analyses.

#### **Role of the Funding Source**

Funding sources had no role in the design, conduct, analysis or writing of the report. The corresponding author had full access to all data in the study and had the final responsibility to submit for publication.

#### Results

#### Study Population:

Of 31,255 patients, 19,937 (63.8%) were men and 11,318 (36.2%) were women. Regionally, 9,121 (29.2%) participants were from China, 7,775 (24.9%) from Africa, 8,736 (28.0%) from India, 4,476 (14.3%) from South and East Asia, and 1,147 (3.7%) from Latin America (Table 1). Men were of working age (median: 39 years old [y/o]; IQR: 28–53 y/o) and commonly sustained tibia/fibula (23.8%), hip (12.9%), and femur (12.6%) fractures. Women were older (median: 58 y/o; IQR: 41-72 y/o) and commonly sustained hip (26.0%), tibia/ fibula (14.2%), and wrist (8.8%) fractures (Supplemental Table 1).

#### Frequency of 2-hour and 24-hour delay in open and closed fracture patients

Of 5,256 open fracture patients, 3,778 (71·9%) were delayed by >2-hours, with a median hospital admission time of 5-hours (IQR: 2–14 hours). Of 25,999 closed fracture patients, 7,141 (27·5%) were delayed by >24-hours with a median hospital admission time of 7-hours (IQR: 3–36 hours). Overall, patients in Latin America (88·7% open fractures delayed; 44·7% closed fractures delayed) experienced the greatest proportions of hospital admission delay. Patients in China (61·4%) and Africa (22·2%) experienced the least open, and closed fracture delays, respectively (Figure 1). Ambulances were used by 45·3% and 30·6% of open and closed fracture patients, respectively (Table 2). In 7 of 18 countries (38·8%), 50% of open fracture patients used an ambulance (Supplemental Table 2).

#### Identifying First, Second, and Third Hospital Admission Delays of >24-hours.

Most commonly interfacility referrals (47.7%) and believing the injury would heal itself (23.2%) were the primary reasons for delay. China, had a high frequency of patients believing the injury would itself (48.9%). Of note, only 4.3% patients reported concerns about cost as the primary reason for their delay (Figure 2). In aggregate, Third Delays were the most common (50.5%) followed by First (39.3%) and Second (5.4%) delays. First Delays were the lengthiest, (median: 6 days; IQR: 2.9–13 days), with seeking treatment from a traditional healer incurring the longest delays (median: 8 days, IQR: 4–17 days) (Supplemental Figure 2).

#### **Risk Factors of Hospital Admission Delay**

We delineated risk factors of 2-hour and 24-hour hospital admission delay for open and closed fracture patients, respectively (Table 3). Increasing age elevated the risk of delay for both open (aRR 1.005, 99% CI 1.001–1.009) and closed (aRR 1.008, 99% CI 1.006–1.011) fracture patients. Delay was strongly associated with region. Compared to China, open (aRR: 1.67, 99% CI 1.31–1.95) and closed (aRR 1.87, 99% CI 1.56–2.23) fracture patients in Latin America were more likely to be delayed, while closed fracture patients in Africa

(aRR 0.85, 99% CI 0.75–0.97) were at decreased risk for delay. Sex did not predict delay in open or closed fracture patients. However, when subcategorizing by First and Third delays (Supplemental Table 3), women were at increased risk for Third delays >24-hours (aRR 1.15, 99% CI 1.07–1.23).

Among injury-related factors, patients with open upper limb fractures (aRR 0·87, 99% CI 0.76-0.98) were associated with less risk for 2-hour delay versus those with open lower limb fractures. Closed spine (aRR 2·47, 99% CI 2·17–2·81) and pelvic (aRR 1·35, 99% CI 1·10– 1·66) fractures were associated with greater risk for 24-hour delay. Standing fall injuries were further at-risk for 24-hour delay (aRR 1·44, 99% CI 1·32–1·57). Subcategorizing by the type of delay, (Supplemental Table 3), spine (aRR 3·21, 99% CI 2·70–3·81) and pelvic (aRR 0·56, 99% CI 0·35–0·91) fractures strongly increased, and decreased, respectively, the risk for First Delay. Moreover, spine (aRR 1·67, 99% CI 1·49–1·87), pelvic (aRR 1·74, 99% CI 1·52–1·98), and hip (aRR 1·22, 99% CI 1·13–1·32) fractures increased the risk for Third delay.

The healthcare network likewise influenced delay. Health insurance reduced the risk for 2-hour (aRR 0.87, 99% CI 0.76-0.99) and 24-hour (aRR 0.88, 99% CI 0.80-0.96) delay in open and closed fracture patients, respectively (Table 3). Subcategorizing by the type of delay (Supplemental Table 3), health insurance reduced the risk for Third (aRR 0.79, 99% CI 0.73–0.85), but not First (aRR 0.88, 99% CI 0.77–1.00) delay. Ambulances were associated with less risk than private vehicles (aRR 2.61, 99% CI 2.39–2.85), public transportation (aRR 2.29, 99% CI 2.01-2.60), and other modes of transportation (aRR 1.54, 99% CI 1·22–1·95) for 24-hour delay in closed fracture patients. However, other modes of transportation (e.g., walking, rickshaw) reduced the risk of delay in open fracture patients versus ambulances (aRR 0.68, 99% CI 0.47–0.93). Indeed, 77.0% of open fracture patients who used an ambulance were delayed by >2-hours, compared to 42.1% who used other methods of transportation (P<0.0001; Supplemental Figure 1). This trend extended to 2-hour delay in general. In analyzing open and closed fracture patients combined, other modes of transportations reduced the odds of 2-hour delay (aRR 0.73, 99% CI 0.63-0.84) compared to ambulances (Supplemental Table 4). Interfacility referrals were associated with a greater risk of delay for both open (aRR 2.02, 99% CI 1.95-2.08) and closed (aRR 3.25, 99% CI 3.02-3.50) fracture patients.

#### Discussion

Our international prospective observational study found a significant gap in timely admission to a treating hospital in open and closed fracture patients. Seven in 10 patients with open fractures failed to reach the LCoGS target of hospital admission within 2-hours, and 1 in 4 closed fracture patients were delayed >24-hours. Regionally, patients in China and Africa were the least delayed, whilst patients in Latin America were the most. Two-thirds of patients did not use ambulances. Third Delays accounted for half of patients delayed by >24-hours which was largely a result of interfacility referrals, the most common reason for delay. First Delays accounted for 4 in 10 patients and were the lengthiest.

This study was strengthened by a large sample size of 31,255 patients from 49 hospitals in 18 LMICs and by using prospective consecutive sampling. Limitations include that hospitals were not evenly distributed and were mostly reserved to larger trauma centers. Consecutive sampling may under-represent minority populations. Given that we only observed patients who attended a hospital, our analysis suffers from Berksonian bias, and thus, the magnitude of First and Second Delays are likely underestimated. Our threshold for assessing the reasons for delay, >24-hours, is conservative and may not be clinically suitable for all fractures. Furthermore, other reasons may better describe delays present on shorter timescales. Although there are few cases, patients admitted long after their injury may be subject to some recall bias. Furthermore, we were unable to consider the total distance travelled by patients nor can we quantify the time it took patients to be admitted to an initial referring hospital. Finally, the conversion from ORs to RRs may overestimate the risk.<sup>22</sup> Nevertheless, this study addresses a large gap concerning fracture epidemiology within LMICs and is the largest to date to ascertain the sources of delay using the Three Delays framework.

Due to a lack of clinical registry data in LMICs, current measurements of healthcare access use modeling strategies. Estimates have ranged from 2·2 billion lacking access to surgical theatres in LMICs, to 4·8 billion lacking access to timely affordable care globally.<sup>23,24</sup> By contrast, Ouma et al. estimated that 71% of patients in Sub-Saharan Africa live within 2-hours of a hospital, implying a theoretical access to timely care.<sup>10</sup> As only 5% of delays were Second Delays, our study supports that proximity is not the primary barrier to access.<sup>25</sup>

Instead, we found that interfacility referrals represented the greatest contributor towards delay. Interfacility referrals are often precipitated by a lack of facility resources and specialist capacity. Indeed, Nkurunziza et al. showed that across 3 district hospitals in Rwanda, half of referred patients were delayed by >2-days before being transferred due to lacking resources and protocols.<sup>16</sup> Moreover, inadequate triage protocols, and poor communication with ambulances result in the transportation of patients to ill-equipped hospitals<sup>9,16,26,27</sup> Interfacility referrals delay treatment and lead to poor clinical outcomes.<sup>9,16,19,27</sup> We echo others who call for strengthening district hospital resources, referral protocols, and centralising EMS dispatch services.<sup>9,16,27</sup>

Reducing delays of >2-hours will require improving the timeliness of ambulances. Previous estimates on ambulance usage within LMICs have ranged widely from 4% to 67%.<sup>8,17,28</sup> Our data establishes a baseline that 45·4% of open fracture patients and 33·1% of all patients used an ambulance. The WHO determined that in 37% of LMICs, ambulances transported the majority of seriously injured patients.<sup>29</sup> Similarly, we found that in 38·8% of countries, ambulances transported >50% of open fracture patients. In addition, we found that other methods of transportation, including walking and rickshaws, were faster than ambulances for reaching treating hospitals over shorter timeframes (i.e., <2-hours). Indeed, patients who sustained upper limb open fractures were at less risk for delay, suggesting a role for patient mobility in reducing delay. Patients who used other modes of transportation methods could have travelled shorter distances. Moreover, ambulance transportation may disproportionately suffer from unmeasured confounds such as congestion, or poor infrastructure. Nevertheless, our data aligns with previous descriptive field work illustrating how taxis and rickshaws

often supplant ambulances as a first-line of transportation  $^{14,30}$  and highlights a need to improve ambulance dispatch services.<sup>9</sup>

Notably, patients who sustained hip, spine, and pelvic fractures were at an increased risk for 24-hour, and Third Delays. Clinically, in LMICs, spine and pelvic fractures are difficult to diagnose because of lacking x-rays and trained personnel. Thus, our data may reflect a deficiency by facilities to diagnose these fractures.<sup>14</sup> In addition, while sex did not affect 2-hour or 24-hour delay, women were at risk for Third Delay. This suggests a gender bias within the healthcare system in LMICs which can potentiate long-term consequences for women's development. Thus, hospitals should take active measures to mitigate these inequities.

Universal health insurance is a commonly cited solution for increasing access to care within LMICs.<sup>3</sup> While health insurance overall reduced delay, it did not reduce First Delay. Consistent with this finding, <5% of patients reported a 'fear of cost' as a major reason for their delay. Instead, health insurance reduced Third Delays, supporting a previously described role in reducing bureaucratic hospital barriers to care.<sup>14,16</sup> Nevertheless, we acknowledge that patients who cannot afford care may not be represented in our sample. Furthermore, admitted patients may still experience financial calamity due to treatment costs.

While Sub-Saharan Africa is traditionally viewed as amongst the most marginalized regions for surgical access<sup>31</sup>, we found that patients in Africa experienced among the least delay. This discrepancy can, in part, be attributed to the fact that 6 of the 7 African countries included in our study met the LCoGS benchmark that >80% of patients live within 2-hours of a hospital.<sup>10</sup> Our data instead emphasizes a need for improving access to care in Latin America, a region under-represented in global studies.<sup>32</sup> In trying to understand these deficiencies, Mexico, for example, represents an urbanized country with a high frequency of road-traffic injuries, yet has an underfunded and understaffed EMS system.<sup>33</sup> Regionally, we also found that a high proportion of patients in China believed their injuries would 'heal on their own'. Thus, it is important to consider regional nuances when shaping future healthcare policies.

In summary, to address the LCoGS and WHO targets for global access to surgical care, we demonstrate that across 18 LMICs, 71.9% open fracture and 27.5% closed fracture patients, were delayed in hospital admission. To ameliorate delays of >2-hours, ambulatory services must be improved. Additionally, reducing delays associated with interfacility transfers are critical. A priority lies in improving the capacity for hospitals to diagnose and admit hip, spine, and pelvic fracture patients, who were at an increased risk for 24-hour and Third Delay. Our data affirms that improving the pre-hospital network in LMICs represents an important lever for improving access to fracture care.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

#### Acknowledgements:

This research was funded by the National Health and Medical Research Council of Australia (APP1084967), Canadian Institutes of Health Research (MOP133609), and McMaster Surgical Associates, and Hamilton Health Sciences.

We would like to acknowledge Diane Heels-Ansdell for her valuable contribution and advice regarding statistical analyses. We would also like to acknowledge Behnam sadeghirad and Li Wang for their expertise and insights.

#### **Data Sharing Statement:**

Data dictionaries pertaining to individual patient data will not be made available for sharing upon publication.

# Table: List of INORMUS investigators separated by their first and last namefor submission to Pubmed.

First Name	Last Name
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Zichao	Jia
Jianzhong	Yang
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Peng	Zhang
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Donghai	Liu
Yinghua	Ma
Yanguo	Qin
Jincheng	Wang
Dan	Luo
Xinlong	Ma
Jianxiong	Ma
Haobo	Jia
Shuangshuang	Cui
Zhihu	Zhao
Lin	Fu
Hongqiang	Jiang
Jianwei	Lv
Sanbao	Hu

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Shisheng He	
Xinyu Cai	
Gejun Liu	
Gang Rui	
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Pingfang Shi	
Hua Chen	
Te Wang	
Qingqing Wang	
Linzhen Xie	
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DeanOtsyenoJumaWakhayangaDesmondnziokaVeraleaDeograciaOwendeRuthLucindeBrian NgureKariukiDennisKanauMaureenMaranaMoureenMaranaMalariynNyabutiPatriciaOdongoAbrahamOdongoPaulMarealleAbrahamGodingoPaulSinauAbrahamBishaPaulSinauPausSinauPausSinauPausSinauPanasGodreguPanyo BonaneGodreguMurilaJohnsonMosesKimaniKinuthiaFeruAnagersFirthSinau <td< th=""></td<>
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Ananias Poopedi Machuene
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Michael Mara
Geoffrey Chege Mwangi
Anthony Muchiri Maina
David Wamae
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First Name	Last Name
Peter	Watson
Ezra Mitei	Kiptoo
Olufemi Olukemi	Temiloluwa
Adeyeye Adeolu	Ikechukwu
Ige Oluwole	Olugbenga
Ojodu Ishaq	Bamidele
Oladimeji Oladipupo	Akanbi
Panchu	Subramania n
Olivia L	Mosweu
Samuel	Hailu
Geletaw	Tessema
Bahiru	Bezabih
Birhanu	Ayana
Hiwot	Hailu
Betelhem	Zewdneh
Hana	Tesfaye
Sosena	Tadesse
Samuel	Tesfaye
Dominic	Konadu- Yeboah
Vincent	Ativor
Peter	Konadu
Dominic	Awariyah
Raphael	Quartey
Raphael	Kumah- Ametepey
Saani	Osman
Robert Ekow	Quansah
Peter	Trafton
David	Anyitey- Korkor
Michael	Leat
Johnny	Sobotie
Godwin	Opuni
Kwasi	Kusi
Twimasi	Baah
Felicia	Agbenorwu
Phyllis	Osei- Donkor
Paul	Okyere
Bernice	Mensah
Doris Akuoko	Sarpong
Priscilla	Opoku

First Name	Last Name
Michael	Segbefia
Paa Kwesi	Baidoo
Gerald	Omzia
Emmanual Chino	Juidobi
Caistan Uwataranya	Nwodiniawa
Cajetan Uwatoronye	inwadinigWe
Uloma	Oguzie
Emina Bami	Kesiena
Henry Tanyi	Ndasi
Nietiayurk Aminake	Ghislain
Mala Irine	Shey
Ikose John	Nanje
Parag	Sancheti
Ashok	Shyam
Madhav	Borate
Sampat Dumbre	Patil
Sachin	Karkamakar
Shailesh	Patil
Abhijeet	Ranaware
Shadab	Tamboli
Manish	Gandhalikar
Rohini	Tupe
Vishal	Choudhary
Avanti	Joshi
Sanjay	Patil
Tejas	Gandhi
Chintamani	Latkar
Gopal	Pundkare
Sandeep	Shrivastava
Pradeep K	Singh
Sanjay	Deshpande
Sumit	Baheti
Ravi	Mittal
Vijay	Sharma
Vinoo Mathew	Cherian
Thilak Samuel	Jepegnanam
Vijay T K	Titus
Manasseh	Nithyananth
Palapattu R J V C	Boopalan
Viju Daniel	Varghese
Justin	Arockiaraj
Vinu Mathew	George

First Name	Last Name
Anupam	Mahajan
Ritesh	Pandey
Bobby	John
Jeewan S	Prakash
Harvinder Singh	Chhabra
Rajesh	Sharawat
Ritabh	Kumar
Pushkar	Chawla
Rashmi	Yadav
Rajagopalan	N.
Naveen	Nair
Rajkumar S	Amaravathi
Srinivasalu	Santhanago pa
Anoop	Pilar
Keith Behram	Tamboowala
Mandeep S	Dhillon
Sarvdeep S	Dhatt
Asolie	Chase
Neel M	Bhavsar
Rameez	Musa
Darshan	Shah
Sunil	Chodavadiy ah
Pankaj G	Patel
Raja Irfan	Qadir
Syed Imran	Bukhari
Khushnood Ali	Baz
Subin	Byanjankar
Ruban Raj	Joshi
Rajeev	Dwivedi
Jay Raj	Sharma
La Ngoc	Quang
Nguyen Duc	Chinh
Vu Bao	Hong
Panhon	Sa- ngasoongso
Norsten	ng Kulachota
noratep	Sirierootroor
Norachart	ux
Wanjak	Pongsamakt hai
Irewin Alagar	Tabu
Paula Veronica	Reyes

First Name	Last Name
Jenna	González
Iardinne	Caiquep
Joni Mitchell Robles	Bituin
Mohammadreza	Golbakhsh
Mashyaneh	Haddadi
Soheil	Saadat
Mohammadreza	Zafarghandi
Clotilde Fuentes	Orozco
José de Jesús Martínez	Ruíz
Gustavo Armando Tafoya	Arreguin
Paola Alejandra Alvarez	Lopez
Adan Cervantes	Gomez
Fatima Nohemi Franco	Bravo
Eugenia de los Angeles Reyes	Arias
Ileana Guadalupe Canales	Navarro
Mizael Dennis	Pérez
Rodrigo Salcedo	López
Daniel de Jesús Enciso	Carrillo
Diego Abraham Estrada	Téllez
Miguel Oscar Hernandez	Camacho
Iridia Guadalupe Pellegrini	Verdizco
Cesar Eduardo Pinedo	Flores
Igor A Escalante	Elguezabal
Ennio Antonio	Rizzo
Jean Michel	Hovsepian
Victor	Rodriguez
Manuel Malaret	Baldo
Andres	Serrano
Carlos G	Sanchez Valenciano
Edgar Efren Mercado	Salcedo
Fryda	Medina
Gerardo	Aguilar
Jorge	Rubio-Avila
William Dias	Belangero
José Ricado Lenzi	Mariolani

First Name	Last Name
Bruno	Livani
André	Lugnani
Felipe	Rossi
Angela	Katayama
Fernando	Baldy
Vinícius Ynoe	de Moraes
Fabricio	Fogagnolo
Kodi Edson	Kojima
Jorge dos Santos	Silva
Marco Kawamura	Demange
Fernando Brandão de Andrade e	Silva
Adriana Carvalho Gomes da	Silva
Nelson	Elias
Dino Aguilar	Martinez
Fernando	Contreras
Mario	Garuz
Jose Eduardo	Quintero
Gavino	Merchan
Christian Lozano	Lurita
David Torres	Manrique
Jorge Hurtano	Fernandez
Sergio Iriarte	Vincenti
Alfredo Pozzo	Bobarin
Dalton Salinas	Sanchez
Julio Segoiva	Altieri
Antonio	Barquet
Daniel	Rienzi
Carlos	Amanquez
Georges	Beauvoir
Iván J Salce	Cutipa
José Eduardo Grandi	Ribeiro
Hernando Cuevas	Ochoa
Hernando Cuevas	Cano
Adriana Vaca	González
Nubia Itzel Gonzalez	Gutierrez
Sylvester	Ndayisaba
Titus	Amone
Samuel Remmy	Odong
Andrew	Pollak
Robyn	Norton
Jing	Zhang

First Name	Last Name
Theodore	Miclau III
Saam	Morshed
Madeline C.	MacKechnie
Qiushi	Wang
Shiwen	Tian
Nutan	Jadhav
Vijay	Shetty
Ritabh	Mittal
Tagakou Jules	Mbula
Samrawit	Esayas
Jose Guadalupe Alfaro	Garcia
Gustavo Cedric Enciso	Dumuin

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#### **Research in Context:**

#### Evidence before this study

Approximately 80% of injury-related mortalities occur before the patient is admitted to the hospital. Thus, an emphasis is needed to focus on the pre-hospital network and timely admissions. We searched PubMed for relevant articles using the search terms including "hospital admission delay" or "hospital delay" or admission delay" combined with "injury" or fracture" which provided 21 results. No studies have directly assessed the frequency of hospital admission delay in fracture patients in low- and middle- income countries. Two studies which retrospectively analysed trauma related deaths in India and Ghana demonstrated that hospital admission delay was a significant factor in preventable deaths. Five studies linked morbidity and mortality resulting from non-fracture injuries to delays in hospital admission in a single country. We have further identified 3 studies which more broadly measured access to surgical services using statistical modelling, and generally suggest poor access to surgical care that is timely, and affordable. Given the paucity of clinical data to inform on observed trends in timely access to hospital admission, and the lack of studies focused on identifying the reasons for delay, our study is the first to provide a comprehensive clinical perspective of timely access to hospital admission.

#### Added value of this study

We have undertaken, to our knowledge, the largest prospective observational clinical study to date to investigate hospital admission delay among orthopaedic fracture patients, or, apply the Lancet Three Delays Framework in order to understand the major reasons for hospital admission delay in low-and middle-income countries (LMICs). Given the global target for 80% of a population to have access to surgical care within 2-hours of an injury, our study shows that 7 in 10 of open fracture patients failed to reach the hospital within this time frame. Among closed fracture patients, 1 in 4 were delayed by >24-hours. In assessing hospital admission delays of >24-hours among all patients, delays in receiving care (i.e., Third Delay), and in particular, interfacility referrals, accounted for over half of delays. Thus, our analysis provides a clinically observed assessment of gaps in the pre-hospital network and the state of global fracture care targets in LMICs.

#### Implications of all the available evidence

Our clinical data demonstrates that LMICs are lagging far behind in achieving global targets for accessing orthopaedic care, and are failing at the first step of the emergency-care system, i.e., transporting patients to a treating hospital in a timely manner. In particular, developing and improving interfacility referral protocols and systems is a critical hospital-based lever for decreasing admission delays. Our data further provides baseline clinical indicators of the pre-hospital network collected from 18 LMICs and will provide a reference point for future research and targets.

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#### Figure 1:

Hospital admission delay disaggregated by sex and region in all patients (A), where delay is defined as >24 hours, and open fracture patients (B), where delay is defined as >2 hours. Time is reported as the log10 transformation of days to hospital admission.

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#### Figure 2:

The reasons for hospital admission delay of > 24 hours disaggregated by sex (A) and the distribution of hospital admission times for each reason for delay disaggregated by sex (B). Time is reported as the log10 transformation of days to hospital admission.

#### Table 1:

Baseline demographic and clinical characteristics of patients included in the study

	Men		Women		Total	
	16800	63.0%	9865	37.0%	26665	100%
alcohol	1252	7.5%	150	1.5%	1402	5.3%
Health Insurance						
Private	1048	6.2%	512	5.2%	1560	5.9%
Government	6028	35.9%	5238	53.1%	11266	42.3%
None	9721	57.9%	4115	41.7%	13836	51.9%
Education						
no education	979	5.8%	1477	15.0%	2456	9.2%
up to elemen tary	3681	21.9%	2476	25.1%	6157	23.1%
up to secondary	7404	44.1%	3869	39.2%	11273	42.3%
post-secondary	4732	28.2%	2040	20.7%	6772	25.4%
Occupation						
agriculture	2777	16.5%	1251	12.7%	4028	15.1%
service	3202	19.1%	783	7.9%	3985	14.9%
business	2748	16.4%	902	9.1%	3650	13.7%
homemaker/unemployed	2190	13.0%	4885	49.5%	7075	26.5%
student	1103	6.6%	309	3.1%	1412	5.3%
industrial	2422	14.4%	384	3.9%	2806	10.5%
education	367	2.2%	240	2.4%	607	2.3%
other	1988	11.8%	1110	11.3%	3098	11.6%
Transportation to Hospital						
ambulance	5947	35.6%	2831	28.8%	8778	33.1%
private vehicle	7481	44.8%	5419	55.0%	12900	48.6%
public transport	2462	14.7%	1238	12.6%	3700	13.9%
other	824	4.9%	357	3.6%	1181	4.4%
Administered to Hospital From						
Iniury Site	7362	44.0%	3418	34.7%	10780	40.6%
Home	2754	16.5%	3448	35.0%	6202	23.3%
Other Hospital	5749	34.4%	2607	26.5%	8356	31.4%
Other	859	5.1%	374	3.8%	1233	4.6%
Mechanism of Injury						
standing fall	3117	18.6%	5108	51.8%	8225	30.9%
fall from height	2757	16.4%	1281	13.0%	4038	15.1%
pedestrian RTI	1674	10.0%	909	9.2%	2583	9.7%
other RTI	6633	39.5%	1713	17.4%	8346	31.3%
struck/lifting	1161	6.9%	349	3.5%	1510	5.7%

	Men		Women		Total	
	16800	63.0%	9865	37.0%	26665	100%
Other	1454	8.7%	505	5.1%	1959	7.3%
Open Fractures						
closed	12884	80.0%	8911	92.4%	21795	84.7%
low grade open	2110	13.1%	478	5.0%	2588	10.1%
high grade open	1101	6.8%	251	2.6%	1352	5.3%
Fractures						
hip	2158	13.4%	2586	26.8%	4744	18.4%
femur	1916	11.9%	698	7.2%	2614	10.2%
tibia/fibula	3532	22.0%	1208	12.5%	4740	18.4%
ankle malleolus	846	5.3%	702	7.3%	1548	6.0%
ankle plaflond	146	0.9%	74	0.8%	220	0.9%
foot	956	5.9%	327	3.4%	1283	5.0%
patella/other lower	740	4.6%	389	4.0%	1129	4.4%
prox humerus	396	2.5%	389	4.0%	785	3.1%
arm	842	5.2%	358	3.7%	1200	4.7%
elbow	757	4.7%	473	4.9%	1230	4.8%
wrist	1031	6.4%	884	9.2%	1915	7.4%
other upper	1420	8.8%	404	4.2%	1824	7.1%
spine	897	5.6%	939	9.7%	1836	7.1%
pelvic	445	2.8%	207	2.1%	652	2.5%
>1 Fracture	2944	17.6%	971	9.9%	3915	14.9%
Is Urban	10710	63.8%	6859	69.5%	17569	65.9%
Country						
China	4719	28.1%	4447	45.1%	9166	34.4%
Africa	4879	29.0%	1866	18.9%	6745	25.3%
India	4256	25.3%	1673	17.0%	5929	22.2%
Other Asia	2444	14.5%	1302	13.2%	3746	14.0%
Latin America	502	3.0%	577	5.8%	1079	4.0%
Age [years] (Median, IOR)	39	(28–53)	59	(42-73)	41	(31–62)

#### Table 2:

A binary logistic regression predicting either 24-hour delay in all patients, or 2-hour delay in open fracture patients.

	2	24-Hour Delay [All Patients]				2-Hour Delay [Open Fracture Patients]				
	OR	Lower CI	Upper CI p-value		OR	Lower CI	Upper CI	P-value		
Mechanism of Injury										
standing fall (ref)										
fall from height	0.811	0.731	0.899	< 0.001	1.177	0.711	1.948	0.526		
pedestrian RTI	0.805	0.699	0.927	0.003	1.012	0.629	1.627	0.962		
other RTI	0.765	0.69	0.849	< 0.001	0.831	0.535	1.289	0.408		
Struck/Lifting	0.759	0.644	0.896	0.001	1.416	0.852	2.353	0.180		
Other	1.003	0.869	1.157	0.970	0.757	0.479	1.194	0.231		
Is Employed	0.945	0.869	1.028	0.191	0.973	0.762	1.242	0.824		
Has Insurance	0.905	0.836	0.979	0.013	0.891	0.74	1.072	0.222		
Increasing Education	0.927	0.889	0.965	< 0.001	0.965	0.873	1.068	0.494		
>1 Injury	0.968	0.878	1.068	0.518	0.896	0.751	1.069	0.222		
Open Fracture	0.468	0.417	0.525	< 0.001	n/a	n/a	n/a	n/a		
Is Urban	0.981	0.91	1.056	0.606	0.793	0.671	0.937	0.007		
Fracture Location										
Lower Limb (ref)										
hip	1.08	0.976	1.194	0.136	1.27	0.59	2.734	0.542		
wrist	1.087	0.955	1.238	0.204	1.165	0.782	1.736	0.453		
Upper Limb	1.063	0.97	1.165	0.192	0.72	0.586	0.885	0.002		
spine	2.202	1.942	2.498	< 0.001	0.241	0.04	1.469	0.123		
pelvis	1.582	1.298	1.928	< 0.001	1.221	0.33	4.517	0.764		
Is Female	0.869	0.805	0.937	< 0.001	0.733	0.594	0.905	0.004		
Region										
China (ref)										
Africa	0.924	0.826	1.034	0.169	0.653	0.496	0.86	0.002		
India	1.395	1.256	1.55	< 0.001	0.747	0.564	0.99	0.042		
Other Asia	1.515	1.361	1.686	< 0.001	1.423	1.078	1.878	0.013		
Latin America	1.855	1.596	2.156	< 0.001	2.743	1.607	4.683	< 0.001		
Increasing Age	0.999	0.997	1.002	0.568	1.003	0.997	1.009	0.325		
Transportation to Hospital										
Ambulance (ref)										
private vehicle	1.771	1.627	1.927	< 0.001	0.914	0.763	1.094	0.326		
public transport	1.821	1.613	2.057	< 0.001	0.64	0.492	0.832	0.001		

	24-Hour Delay [All Patients]				2-Hour Delay [Open Fracture Patients]			
	OR	Lower CI	Upper CI	p-value	OR	Lower CI	Upper CI	P-value
other	1.461	1.188	1.797	< 0.001	0.553	0.381	0.802	0.002
Administered to Hospital From								
injury site (ref)								
home	13.216	11.763	14.849	< 0.001	5.749	3.703	8.926	< 0.001
other hospital	13.542	12.104	15.15	< 0.001	6.716	5.587	8.073	< 0.001
other	8.683	7.34	10.272	< 0.001	1.6	1.155	2.217	0.005
Alcohol Involved	0.734	0.623	0.864	< 0.001	1.105	0.832	1.466	0.491

#### Table 3:

A binary logistic regression predicting either first delay or third delay of > 24-hours in all fracture patients.

		Firs	t Delay		Third Delay					
	OR	Lower CI	Upper CI	p-value	OR	Lower CI	Upper CI	p-value		
Is Female	0.873	0.788	0.966	0.009	0.936	0.855	1.024	0.149		
>1 Injury	0.539	0.449	0.646	< 0.001	1.253	1.131	1.389	< 0.001		
Is Urban	0.862	0.775	0.96	0.007	0.795	0.73	0.865	< 0.001		
Injury Location										
Lower Limb (ref)										
Hip	1.069	0.932	1.225	0.340	1.178	1.045	1.327	0.007		
Wrist	1.233	1.034	1.469	0.019	1.035	0.889	1.204	0.658		
Upper Limb	1.239	1.085	1.414	0.002	1.096	0.988	1.215	0.085		
Spine	3.563	3.067	4.141	< 0.001	1.565	1.333	1.838	< 0.001		
Pelvis	0.798	0.534	1.19	0.268	2.002	1.642	2.44	< 0.001		
Open Fracture	0.182	0.139	0.239	< 0.001	0.567	0.5	0.643	< 0.001		
Is Employed	0.736	0.659	0.822	< 0.001	1.072	0.967	1.189	0.185		
Has Health Insurance	1.048	0.934	1.176	0.423	0.873	0.797	0.956	0.003		
increasing Education	0.893	0.843	0.946	< 0.001	0.986	0.94	1.035	0.575		
Mechanism of Injury										
standing fall (ref)										
fall from height	0.56	0.488	0.643	< 0.001	0.775	0.685	0.878	< 0.001		
pedestrian RTI	0.282	0.222	0.357	< 0.001	0.68	0.584	0.792	< 0.001		
other RTI	0.388	0.334	0.451	< 0.001	0.687	0.611	0.773	< 0.001		
Struck/Lifting	0.611	0.489	0.763	< 0.001	0.613	0.504	0.745	< 0.001		
Other	1.081	0.898	1.3	0.410	0.769	0.643	0.92	0.004		
Region										
China (ref)										
Africa	0.676	0.57	0.8	< 0.001	1.033	0.909	1.174	0.617		
India	1.871	1.619	2.162	< 0.001	1.585	1.405	1.788	< 0.001		
Other Asia	1.758	1.505	2.055	< 0.001	2.323	2.057	2.622	< 0.001		
Latin America	2.594	2.145	3.136	< 0.001	2.753	2.293	3.306	< 0.001		
Increasing Age	1.009	1.006	1.013	< 0.001	0.999	0.996	1.002	0.505		
Alcohol Involved	0.971	0.758	1.244	0.817	0.631	0.517	0.769	< 0.001		

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