FRACTURES IN WOMEN ACROSS LOW- AND MIDDLE-INCOME COUNTRIES

UNDERSTANDING THE GLOBAL LANDSCAPE OF FRACTURES IN WOMEN, AND THE IMPACT OF SEX ON HOSPITAL ADMISSION DELAYS, ACROSS 17 LOW- AND MIDDLE-INCOME COUNTRIES

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment of the Requirements for the Degree Master of Global Health

McMaster University MASTER OF SCIENCE (2018) Hamilton Ontario (Global Health)

TITLE: Understanding the Global Landscape of Fractures, and the Impact of Sex on Hospital Admission Delays, in Women Across 17 Low- and Middle-Income Countries.

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NUMBER OF PAGES: 78

LAY ABSTRACT:

Fractures represent life-threatening injuries within Low- and Middle-Income Countries (LMICs), and globally are a top-ten leading cause of death and disability. Within LMICs, due to gender inequalities, women may be restricted from receiving hospital care following an injury. We investigated the most common types of fractures in women within LMICs and determined that women most frequently experienced fractures due to old age. We further examined whether women were delayed in reaching a hospital after sustaining a fracture, and found that sex did not significantly play a role in determining delay. Instead, injury associated factors, such as the type and severity of the fracture influenced whether a patient was delayed. In addition, transferring patients between hospitals was the most common reason for delay. As a result, policymakers in LMICs should explore strategies to treat the high burden of fractures in the elderly and improve communication between hospitals to reduce delays.

ABSTRACT:

Musculoskeletal trauma including fractures, represents a significant burden of disease for Low- and Middle-Income Countries (LMICs). Within LMICs, women possess reduced agency to make health care decisions and represent a vulnerable population. In this thesis, I aimed to characterize priority fractures among women within LMICs, and investigated whether women were delayed in hospital admission following an orthopaedic trauma. In Chapter 1, I introduce and review the existing literature on injury burden, health care deficiencies, and gender inequities within LMICs.

In Chapter 2, we analyzed regional distributions of fracture burdens across 9,934 female orthopaedic trauma patients across 17 LMICs. Half of our study patients were ≥ 60 years old. We determined that the major burden of orthopaedic trauma among women within LMICs were fractures among the elderly. Fracture burden in Africa was notably different. A majority of patients were between the ages 18-59, and common fractures included tibia/fibula and femur fractures.

In Chapter 3, we analyzed 26,910 orthopaedic trauma patients across 17 LMICs to determine whether women were delayed in hospital admission by >24 hours. After controlling for confounds, sex was not a significant predictor of delay. We found that instead, the severity and type of fracture influenced the delay of patient’s hospital admission. Closed fractures, falling-related injuries, pelvic, spine and hip fractures were associated with increasing delay. Irrespective of sex and region, inter-hospital referrals accounted for nearly half of the reasons patients were delayed.

These two chapters highlight regional trends in orthopaedic burden sustained by women, pointing to the high frequency of fragility fractures. In addition, this thesis identifies critical gaps within LMICs' health care systems infrastructure, demonstrating the need for improved hospital referral systems and ambulatory services. This analysis will enable policymakers, and future researchers to target interventions to address the rising global burden of injuries especially among women.

ACKNOWLEDGEMENTS:

I would like to show my deepest gratitude and appreciation to all the people who supported and enabled me to pursue and succeed in my thesis research endeavours. I would like to thank Dr. Mohit Bhandari for his unwavering mentorship, inspiration, and support. In spite of all the difficulties, Dr. Bhandari was always willing and able to sit down and discuss my progress and provide me with the insights and resources needed to continue on and succeed. I would like to equally thank Dr. Jason Busse who was unequivocally helpful in providing expertise on statistics and educating me on how to approach a clinical study from an evidence-based medicine approach. He further enabled me analyze my data with the highest standards. I would like to thank Dr. Sheila Sprague for serving on my committee and for providing me with instrumental feedback and support in analyzing my research. I would like to thank Dr. Baumann, and Dr. Ladouceur for agreeing to sit on my defence committee and to provide a wealth of global health expertise.

It would truly not have been possible to complete this thesis work without Chuan Silvia Li. I would like to give my deepest thanks to Sylvia for her unwavering help and friendship throughout this process. In addition to helping me brainstorm ideas for my thesis and serving as the INORMUS project manager, Sylvia helped me with learning statistics, in addition to integrating me into the culture of the Bhandari team. In addition, I would like to thank Dr. Kim Madden for all her support with learning statistics and preparing me for my committee meetings and defense.

I would like to thank the whole team from the McMaster Global Health Department. During my time with the program, I have learned so much about using a global health approach to work in teams and conduct research. I would like to thank David Hill for his unending help in providing me with professional development opportunities and guiding me through the administrative processes to successfully complete my degree.

I would like to thank every member of the INORMUS team for which my research, and my thesis could not be possible without. Truly, the INORMUS team represents the ideal goal of what can be achieved through collaboration.

Finally, I would like to thank my friends and family. My mother, and father have been the most supportive, and inspirational people I know in my life. I also want to thank my brother for his unconditional support, and always pushing me forward. I am forever thankful for your love, support and motivation that you have provided me with my entire life. I especially want to thank Joseph Silburt, who has been incredibly supportive throughout this process, always willing to brainstorm ideas and offer advice. For me, this has been a long and transformative journey which I could not have succeeded if not for the all the collective help of those around me.

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LIST OF ABBREVIATIONS:

DALYs – Disability Adjusted Life Years

EMS – Emergency Medical Services

GBD – Global Burden of Disease

HICs – High Income Countries

IMEESC – Integrated Management for Emergency and Essential Surgical Care

INORMUS – INternational ORthopaedic MUlticenter Study in fracture care

LMICs – Low- and Middle-Income Countries

RTIs – Road Traffic Injuries

SDGs – Sustainable Development Goals

SAGE - Study on global AGEing and adult health

UN – United Nations

WHO – World Health Organization

DECLARATION OF ACADEMIC ACHIEVEMENT

The content of this thesis, and all studies within have been completed by myself, Panthea Pouramin. Each study enclosed were designed as secondary studies from data collected as part of the INternational ORthopaedic MUlticenter Study in fracture care (INORMUS). With the guidance, and contributions of Dr. Mohit Bhandari, Dr. Jason Busse, Dr. Sheila Sprague, and Chuan Silvia Lee, I designed, analyzed, and wrote the manuscripts for the enclosed studies. Contributions for data collection are credited in particular to Chuan Silvia Lee, and the INORMUS team as a whole.

CHAPTER 1: Introduction to Injury Burden in LMICs

Injuries represent a major unaddressed burden within Low-and Middle-Income Countries (LMICs) and cause more deaths than malaria, tuberculosis, and HIV/AIDS combined (World Health Organization, 2010). Broadly defined, injuries, are described as a bodily exposure to energy (e.g. mechanical) that exceeds the threshold of physiological tolerance (e.g. a bone fracture), or, as a deficiency in vital elements (e.g. lack of oxygen while drowning) (Baker, O'Neill, Ginsburg, & Li, 1992). However, a focus on injuries, including musculoskeletal injuries have lagged behind as a public health issue (Conway, Coughlin, Caldwell, & Shearer, 2017) and is considered a neglected epidemic within LMICs (C. N. Mock, Adzotor, Conklin, Denno, & Jurkovich, 1993).

The Global Burden of Injuries

In 2013, injuries caused 247.6 million disability-adjusted-life-years (DALYs), accounting for 10.1% of the global DALY burden (Haagsma et al., 2016). Approximately 90% of mortality and related burden are experienced within LMICs. Nearly 5 million individuals are killed every year as a result of injuries (Haagsma et al., 2016; Murray et al., 2012). Globally, road traffic injuries (RTIs) (29.3%), self-harm (14.0%), and falls (12.0%), account for the greatest DALY burden. In 2013, falls accounted for 1,455 injuries per 100,000 people, and 154.5 million injuries overall, while RTIs accounted for 1,118 injuries per 100,000 people and 97 million injuries overall (Haagsma et al., 2016). Road traffic accidents represent the most deadly injuries, accounting for 1.4 million deaths (20.7 deaths per 100,000 people) in 2013 compared to 556,000 (7.8 deaths per 100,000 people) by falls (Haagsma et al., 2016).

Patients who do survive an injury are often burdened with life-altering disabilities. For every individual who is killed by injury-related trauma, there are three to eight more disabled (Beveridge & Howard, 2004; Kobusingye, Guwatudde, & Lett, 2001). Common non-fatal fractures include the patella, tibia, fibula, femur, ulna, and radius (C. Mock & Cherian, 2008). In Ghana, over 78% of injury-related disabilities were found to be the result of body extremity injuries (C. Mock, Boland, Acheampong, & Adjei, 2003). Approximately, half of children who travel to hospitals with non-fatal injuries sustain a long-term disability (WHO, 2008). Low-cost improvements in orthopaedic care and rehabilitation can substantially reduce the burden of injuries(C. Mock et al., 2003).

To address the global burden of injuries, and especially RTIs, the World Health Organization in partnership with the United Nations launched the Decade of Action for Road Safety (2011-2020) in over 100 countries. This initiative aims to prevent 5 million road traffic associated deaths by 2020. Likewise, the UN's sustainable development goals (SDGs), a set of established targets and indicators for sustainable global development, mirrors the need to reduce RTIs through SDG 3.6. Interventions are particularly needed within South East Asia and Africa which combined account for over half of global RTIs (Paniker, Graham, & Harrison, 2015). A complete understanding of the true burden of injuries requires contextualizing the social and economic realities of LMICs to illuminate the indirect human costs of injuries.

Injuries and the Intersection with Poverty and Sustainable Development

In the absence of socialized medicine, households face severe financial costs due to injuries. Conceptually, in receiving treatment a patient must pay for transport costs, treatment costs, and overcome lost wages as a result of an inability to work (Alam & Mahal, 2014; Wesson, Boikhutso, Bachani, Hofman, & Hyder, 2014). Across 22 studies analyzing injury patients, the median cost associated with direct medical expenses was estimated to be $291, or 15% of GDP per capita (Wesson et al., 2014). However, across 6 studies which factored direct non-medical costs (e.g. transport and administrative costs), and indirect costs (e.g. income lost due to lack of work), the median expenses were measured to be $4,085 or 97% of per capita GDP (Wesson et al., 2014). Globally 150 million people suffered a financial catastrophe, and 100 million people became newly impoverished as a result of health care expenditures (Xu et al., 2007). The high out of pocket costs of care and associated lost income can further dissuade patients from seeking care (Alam & Mahal, 2014).

Injury-related mortality exacerbates poverty experienced by families through a loss of income generation or other familial responsibilities (McIntyre, Thiede, Dahlgren, & Whitehead, 2006). Similarly, nonfatal injuries restrict a patient's ability to rejoin the labour force, and create a reliance on familial care (Alam & Mahal, 2014; Wesson et al., 2014). A death of working age family member reduced income by 25% and 40% in Vietnam and Kenya respectively (Wagstaff, 2007; Yamano & Jayne, 2004). Likewise, non-fatal adverse health impacts reduced employment and income (Alam & Mahal, 2014). Low socioeconomic also increases the risk of injury related mortality. For example, fatalities per vehicle strongly correlates with reducing socioeconomic status (Kopits & Cropper, 2005). As such, injury patients within LMICs face a self-perpetuating cycle of psychological trauma and financial costs (Chandran, Hyder, & Peek-Asa, 2010).

Globally, the lost human labour, and resources required to ameliorate victims of injuries creates a substantial economic burden, especially within LMICs. Nearly half of injury-related mortality occurs in individuals aged 15 to 44 years during their most economically productive years (Nilsen, Hudson, & Lindqvist, 2006). Overall, the economic costs of RTIs alone are estimated to be between 1-5% of an LMIC's GDP per year (Blair et al., 2017). Beyond the immediate financial costs, disease and disability within a family can have intergenerational consequences (Alam & Mahal, 2014). In South Africa, mortality of an adult caused children to drop out of school to work (Yamauchi, Buthelezi, & Velia, 2008). Furthermore, catastrophic health expenses impact childhood nutrition (Alam & Mahal, 2014; Vera-Hernández & Martínez, 2008). Thus, injuries perpetuate a cycle of poverty, entrenching future generations.

Injury Prevention and Surgical Solutions in LMICs

To reduce the burden of injury, LMICs must employ surgical and prevention strategies. As countries continue to develop, more individuals will have access to vehicles which will cause greater levels of fatalities (Kopits & Cropper, 2005). Within LMICS, RTI fatalities are expected to increase from 1.25 million deaths globally in 2015 to 2 million per year in LMICs alone (Wegman, 2017). At the same time, RTIs are reducing in HICs (Kopits & Cropper, 2005; Wegman, 2017). Funding towards improving injury burden is inadequate and is in part casually a result of misperceptions around injuries being the result of individuals' carelessness or bad luck (C. Mock & Cherian, 2008). It is estimated that if injury victims in LMICs possessed the health care and surgical infrastructure of HICs, injury burden could be reduced by between 1 and 2 million deaths, 21% of total injury burden, and a total 52.3 million DALYs (Higashi et al., 2015; C. Mock, Joshipura, Arreola-Risa, & Quansah, 2012).

Improving care necessarily requires improvements in access to health care services. LMICs rely on an interconnected network of hospitals and community health care workers. Community health care workers act as the first line of care and surveillance (Meara et al., 2015), playing an important role in directing patients who need care to primary hospitals. Primary hospitals typically have few doctors and capacity to treat only basic injuries and diseases within a catchment area of between 10,000 and 30,000 patients (Hanche-Olsen, Alemu, Viste, Wisborg, & Hansen, 2012). For surgical procedures or other specialty services, patients are referred from primary centres to first level (district) hospitals which are ideally equipped with operating theatres and anesthesia services (Hanche-Olsen et al., 2012; Meara et al., 2015). Patients are further referred to secondary and tertiary hospitals for more specialized surgeries (Hanche-Olsen et al., 2012; Meara et al., 2015).

There are three types of delay that impair receiving timely treatment (Meara et al., 2015). The First Delay occurs when patients do not seek immediate treatment for their injuries, for example, as a result of a preference to seek traditional healers (World Health Organization, 2002). The Second Delay occurs when patients are unable to reach a hospital due to an inability to organize transportation, or a lack of nearby hospitals, among others. The Third Delay occurs when hospitals are delayed in administering care, for example due to insufficient hospital resources or delays in patient referrals. Of significant necessity in ameliorating injury is developing strategies to reduce all three types of delay (Meara et al., 2015). Three priorities include improving hospital quality and surgical availability, creating centralized emergency medical services, and reducing the costs of health care (Meara et al., 2015; Okoroh, Chia, Oliver, Dharmawardene, & Riviello, 2015).

The Deficiency of Hospital and Human Resources in LMICs

Within LMICs, a lack of trained hospital staff and resources are a significant source of mortality and morbidity for trauma patients (Latifi et al., 2016). Resources are lacking at all hospital levels (primary, secondary, tertiary) with many primary hospitals unable to accommodate basic procedures (Chokotho et al., 2015; Spiegel, Nduaguba, Cherian, Monono, & Kelley, 2015). To outline the substantial need, across eight African countries, only 400 surgeons, and 40 orthopaedic surgeons are available for 200 million people. Based on proximity to surgical theatres alone, as many as 2 billion people do not have access to surgical care (Funk et al., 2010). However, considering socioeconomic and other factors, it is estimated currently that 4.8- 5.3 billion people are lacking access to surgical care that is timely, safe, and affordable (Alkire et al., 2015). An estimated 143 million additional surgeries are needed each year to achieve unmet needs, with Africa experiencing the greatest levels need (Alkire et al., 2015).

The Lancet Commission on Global Surgery 2030 established a target of 5000 surgeries per 100,000 people to significantly reduce this unmet burden (Alkire et al., 2015; Meara et al., 2015). Based on current growth patterns, nearly 50% of LMICs will achieve the goal of 5000 surgeries for 100, 000 people by 2030 (Verguet et al., 2015). In spite of this shortfall, determining surgical priorities may help in reducing burden, and to date, at least 44 surgical procedures have been deemed essential (Bickler & Spiegel, 2010). In fact, to better enable procedures within LMICs, the World Health Organization (WHO) has created the Integrated Management for Emergency and Essential Surgical Care (IMEESC) toolkit which has been implemented within 24 LMICs. This comprehensive training package includes videos that teach emergency and trauma care, splinting and casting techniques, and management of open fractures among others traumas (World Health Organization, 2012). Integral to the development of these, and future strategies are accurate clinical data on orthopaedic needs, and the utility of current procedures.

Ambulatory Services in LMICs

A majority of patients die prior to hospital admission, thus necessitating the need for better first response and ambulatory services (Hanche-Olsen et al., 2012). Currently, these services are broadly inadequate within LMICs (Berendes, Heywood, Oliver, & Garner, 2011). For example, a pilot study in Malaysia demonstrated that 80% of trauma patients attending a hospital arrived by private non-emergency transportation rather than ambulatory services (Hauswald & Yeoh, 1997). Likewise in India, only 36.5% of spinal trauma patients used ambulatory services to reach a hospital (Aleem et al., 2017).

Improving ambulatory and administrative services for trauma care within LMICs can substantially improve health outcomes. In Mexico, increasing the number of ambulatory stations reduced emergency response time, and in combination with increasing educational training of trauma care, decreased mortality rates by almost half (Arreola-Risa et al., 2000). Similarly, in Thailand, improved ambulance-hospital communication through radios, and improved patient reporting/monitoring efforts, decreased mortality across all admitted trauma patients from 6.1% to 4.4% (Chardbunchachai, Suppachutikul, Santikarn, & Jungsatitkul, 2002).

LMICs must also ensure first-responders are properly trained to facilitate streamlined interconnection between pre-hospital admission and triage within the hospital network (Kuzma, Lim, Kepha, Nalitolela, & Reynolds, 2015). A dearth of formal training and developed EMS is a common problem among LMICs in general (C. Mock, 2009). A study in Thailand demonstrated pre-hospital admission emergency medical services (EMS) workers had no formal training (Church & Plitponkarnpim, 1998). However, in lieu of properly funded ambulatory services, training community members in first-aid has shown promise in improving pre-hospital mortality outcomes (Jayaraman et al., 2009; C. Mock, 2009). To this effect, it is critical that first responders hold a position of trust within the community due to social and cultural barriers. 38% of trauma patients in Tanzania would only trust a community member or neighbor to deliver them to a hospital, and only 29% would trust a trained layperson (Kuzma et al., 2015). Social barriers included a fear of getting robbed while unconscious (Kuzma et al., 2015).

Inter-Hospital Referrals within LMICs

In most LMICs, there is a lack of protocols for inter-hospital transfers, as well as almost no protocols for patients to bypass primary and district hospitals and transit directly to tertiary centers (Sethi, Aljunid, Sulong, & Zwi, 2000). Within sub-Saharan Africa, delivering patients directly to tertiary hospitals reduced hospital admission time 2-fold, and the odds of mortality 4-fold (Boschini, Lu-Myers, Msiska, Cairns, & Charles, 2016). When transporting patients between hospitals, ambulances are often unavailable, or insufficiently equipped (Balikuddembe, Ardalan, Khorasani-Zavareh, Nejati, & Kasiima, 2016), and over-referrals can cause delays, mortality, and great financial cost for patients (Abebe, Teshome, & Bekele, 2016). Further deficiencies include delayed or misdiagnosis of patients (Kuzma et al., 2015). Common reasons for referral include a lack of specialist capacity, and the unavailability of beds (Abebe et al., 2016). In addition, patients typically have to pay for transportation and surgical services, and a lack of insurance can facilitate delays (Kuzma et al., 2015). Therefore, the creation of a comprehensive and integrated referral system is essential towards improving care within LMICs.

Injury Prevention Strategies within LMICs

A public health strategy should focus both on the prevention of injuries, and the treatment of patients. A lack of resources within LMICs has caused these two goals to compete with each other for resources. As such, policymakers may determine that prevention programs, which are aimed at everyone, are more beneficial compared to funding resources towards treating only the injured within the LMICs (Beveridge and

Howard, 2004). Of primary concern is improving road traffic safety and a significant literature has explored cost-effective interventions to reduce RTIs. In Uganda, efforts towards increasing police presence on important roads within the city of Kampala proved to be effective in decreasing RTI related deaths by 17% (D. Bishai, Asiimwe, Abbas, Hyder, & Bazeyo, 2008). Within Thailand, a law requiring mandatory helmet usage by motorcyclists decreased head-related injuries mortalities by 20.8% (Ichikawa, Chadbunchachai, & Marui, 2003). Speed bumps are a further example of a cost-effective intervention, with estimations of 1 DALY prevented for between $5-$12 (D. M. Bishai & Hyder, 2006). Therefore, prevention and treatment can be implemented using supportive research via legislation, law enforcement, increasing public awareness and road improvements (Staton et al., 2016).

Injuries and Sustainable Development Goal 5: Gender Equality

The majority of injury burden is experienced by men (Langer et al., 2015; Vos et al., 2017). The highest proportion of injury deaths among women was in young or elderly females, while in men, injuries were most common between the ages of 15-44 years old (World Health Organization, 2008). Some evidence points to the injury burden in women to be underreported (Buvinić, Medici, Fernández, & Torres, 2006). Furthermore, in the context of ensuring equitable access to treatment, further emphasis needs to be placed on ensuring women receive equal access to care. Across all forms of disease burden, women suffer greater levels of DALYs (Vos et al., 2017). Furthermore, women have reduced capacity to make health care decisions (Osamor & Grady, 2016) and cultural norms often prevent women from seeking or receiving treatment (Langer et al., 2015). This inequality is also mirrored in children, with boys more often seeking care for common childhood infections (e.g. malaria, diarrhea) whereas girls suffer higher fatality rates as a result of not seeking care (Nair et al., 2015).

Within LMICs, women's gender roles can expose them to disease risks. As the main purveyor of carrying water, women are at risk of sustaining spine and head trauma (Geere et al., 2018). Generally, a substantial focus on women's health in LMICs has been targeted surrounding their sexual and reproductive health. Yet, with an aging population, whereby 2050, over 22% of the global population will be 60 years or older (United Nations Population Fund & International, 2012), a focus on osteoporosis, of which women are at higher risk, is of key importance (Langer et al., 2015).

Within LMICs, due to the important role of women as caregivers and supporting their families, it is paramount they receive equitable care. Notably, in farming households in Kenya, the mortality of a female spouse resulted in 30% of children leaving the household, whereas, the death of a male head of the household resulted in no change (Yamano & Jayne, 2004). While underappreciated, women work long hours, and play a critical role in maintaining the family and household. As such, indirect costs of health care (i.e. lost working hours) can often be greater when women are hospitalized due to the difficulty in compensating for women's roles (McIntyre et al., 2006).

Research Question and Objectives

According to Margaret Chan, the Director General of WHO, "…the real need is to close the data gaps, especially in low and middle-income countries, so that we no longer have to rely heavily on statistical modelling for data on disease burden."(Chan, 2012) This thesis seeks to remedy two existing gaps present in addressing global injury burden: providing prospective clinical data, and identifying present gaps in health care focusing on women within LMICs.

Research Question: Across 17 Low and middle-income countries, between the years 2014-2017, (1) what are the regional distribution of fracture burden within women, and (2) do women experience delays in comparison to men, when seeking hospital care for their fractures?

Across the 17 LMICs we analyzed, our **objectives** were:

1) To describe regional differences in demographics, health care system characteristics, and fracture types sustained by female patients.
2) Assess the association between sex and delay to hospital admission (admission time > 24 hours) among orthopedic trauma patients across 17 LMICs.
3) Identify the significant reasons for hospital admission delay.

Data was collected from the INternational ORthopaedic MUlticentre Study (INORMUS), a global, multicenter, observational study to evaluate and assess global trends in fracture burden and health care infrastructure in LMICs. Data and analyses for 17 LMICs are presented in chapters 2 and 3 as manuscripts. In Chapter 2, we analyze demographic, fracture characteristics, and the status of health care is analyzed for 9,934 patients. In Chapter 3, within 26,910 patients, we analyze sex differences in delays for reaching a hospital following an orthopaedic trauma and the reasons for these delays. In Chapter 4, conclusions are summarized, and future directions are delineated.

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Chapter 2: A Multicentre Observational Study on the Distribution of Orthopaedic Fracture Types across 17 Low- and Middle-Income Countries.

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At the time of writing, this manuscript was under review for publication at OTA International.

Abstract:

Objectives: To describe the regional distribution of fractures sustained by women and health care system characteristics across 17 Low and Middle-Income Countries (LMICs).

Methods: We analyzed demographic and injury characteristics in 9,934 female patients who sustained a musculoskeletal fracture. Data for 17 LMICs was collected from the ongoing INternational ORthopaedic MUlticentre Study in fracture care (INORMUS), an observational cohort study. We explored for differences in the types of fractures reported among patients from 5 regions (China, Africa, India, Other Asia, and Latin America) using a Chi-square analysis.

Results: Half of our study population (49.5%) was ≥60 years of age. Across all regions, 58.3% of patients possessed health insurance. Only 29.1% of patients were transported for care after sustaining a fracture by ambulance. Falling was the most common mechanism of injury (64.6%). Hip fractures were the most common fracture, accounting for 26.9% of all fractures, and 45.8% of fractures among women ≥60 years old. Tibia/fibula fractures were the most common fractures in patients aged 18-39 (22.0%), and 40-59 (17.8%). Regionally, we found, a majority of patients in Africa were working age, and sustained high proportions of tibia/fibula (21.9%) and femur fractures (14.0%). Foot/ankle fractures were disproportionately common in Latin America (24.3%). The distribution of spine fractures varied across the regions studied and was most common in China (18.9%) and underrepresented elsewhere.

Conclusion: Across all regions, the most significant source of fracture burden was in the elderly, and included common fragility fractures, such as hip fractures. Patients in Africa; however, tended to be working age, and suffered greater levels of lower extremity fractures.

Background:

Injuries, broadly originating from traffic accidents, falls, drowning, and violence, among others, are a leading cause of disability-adjusted life years (DALYs) globally (Vos et al., 2017), and account for over 5 million deaths annually worldwide. Over 90% of injury burden occurs within Low- and Middle- Income Countries (LMICs) (Hofman, Primack, Keusch, & Hrynkow, 2005). As such, international institutions, including the United Nations through the Decade of Action on Road Safety (2011-2020), have recognized a global need to reduce the health and economic burdens associated with injuries (Hofman et al., 2005).

Worldwide, road traffic injuries (RTIs) result in 1.25 million fatalities per year, 90% of which are in LMICs (World Health Organization, 2015). High-Income countries (HICs) have responded by mobilizing medical and public resources and have had success in reducing mortality (Wegman, 2017). By comparison, LMICs have experienced an increase in injury-related deaths and disability, and by 2020 road traffic mortalities are expected to increase to two million per year (Wegman, 2017). This has been attributed to a lack of resources for trauma care, and a rise in motorized vehicle use in LMICs (World Health Organization, 2011). It has been estimated that approximately two million lives could be saved globally from injuries through improvements in access to trauma care (Mock, Joshipura, Arreola-Risa, & Quansah, 2012). Improvements are especially needed in pre-hospital care through increased access to ambulatory services and first responders (Mock et al., 2012).

In addition to the impact of vehicular injuries, an emerging challenge for LMICs is addressing the rise in osteoporotic fractures. It is estimated that 158 million individuals aged 50 and older are at high risk of sustaining an osteoporotic fracture, and this number is expected to double worldwide by 2040, a majority of which will occur in LMICs (Odén, McCloskey, Kanis, Harvey, & Johansson, 2015; Zengin et al., 2017). The increase in osteoporotic fractures can be explained in part by a combination of factors including advances in medicine, urbanization, and continued development leading to increased lifespans and an aging population (Pisani et al., 2016).

The health burden associated with injuries strongly intersects with sustainable development. Mortality and long-term disabilities incurred by orthopaedic trauma can exacerbate poverty (Agarwal-Harding, von Keudell, Zirkle, Meara, & Dyer, 2016). Overall, an estimated 2.5% of GDP will be lost in LMICs by 2030 due to a lack of surgical services (Alkire, Shrime, Dare, Vincent, & Meara, 2015). While men suffer greater levels of injury-related DALYs (Vos et al., 2017), in the context of sustainable development, ensuring women receive equitable surgical care is an important priority for achieving global sustainability efforts, including the Sustainable Development Goals (SDGs) (Shawar, Shiffman, & Spiegel, 2015). Women suffer greater levels of all-cause disease burden (Vos et al., 2017), and in LMICs, women have reduced agency to make health care decisions (Osamor & Grady, 2016). Within LMICs, women fulfill important household duties including retrieving water, which can increase the risk for orthopaedic fractures, including head, neck and spine injuries (Geere et al., 2018). Understanding the orthopaedic injury distribution in women will support their long-term health, enable their participation within society, and by doing so, support sustainable development efforts (e.g. SDG 3: Good Health and Wellbeing, and SDG 5: Gender Equality).

In this work, we provide data on orthopaedic fractures across 17 LMICs as part of the INternational ORthopaedic MUlticenter Study in fracture care (INORMUS). We build on international monitoring efforts including the Global Burden of Disease (GBD) study (Vos et al., 2017) and Study on global AGEing and adult health (SAGE) (Stewart Williams et al., 2015) and use prospective observational clinical data to analyze regional trends in demographics, health system, and fracture characteristics. Our primary objective was to describe the regional distribution of fractures sustained by female patients across 17 LMICs. Our secondary objective was to describe regional trends of demographic and health care system characteristics across these 17 LMICs.

Methods:

INORMUS is a global, multicenter, observational study to evaluate and assess global trends in fracture burden and how they relate to demographics. A comprehensive list of objectives and study methods have been published previously (INORMUS Investigators, 2015). In this secondary study, we analyzed all female patients enrolled before December 2017. We included 5 regions defined as China, Africa (Uganda, Kenya, Nigeria, Botswana, Ghana, South Africa, and Tanzania), India, Other Asia (Pakistan, Nepal, Vietnam, Thailand, The Philippines, and Iran) and Latin America (Venezuela, and Mexico).

Ethics

All protocols were approved by the McMaster University Research Ethics Board and each clinical site's Ethics committee. Data were collected with informed consent, and aggregated as de-identified data, with patients identified through identification numbers.

Selection Criteria and Data Collection

Eligible patients were those 18 years of age and older, who were admitted to a participating hospital within three months of sustaining an orthopaedic trauma. Specifically, trauma included a fracture, dislocation, or fracture dislocation of the appendicular skeleton (i.e. upper and lower extremities, shoulder girdle, and pelvic girdle) or spine. Patients were enrolled through a direct emergency department referral. If patients met the eligibility criteria, study personnel obtained informed consent and collected demographic and clinical data. Follow-up was conducted after 30 days following hospital admission. Patients discharged from the hospital prior to 30 days, were followed up at their one-month clinical visit, or alternatively, by telephone. The primary outcome of the INORMUS study includes the incidence of significant complications (i.e. mortality, reoperation, infection) within 30 days from hospital admission. The secondary outcomes include system and patient characteristics and their relation to clinical complications.

Selection of Factors

For this study, we analyzed only the most severe orthopaedic fracture sustained by an enrolled patient. Hip fractures include fractures of the proximal femur. Foot/ankle fractures include plafond, malleolus, talus, calcaneus, and foot fractures. Wrist fractures include fractures of the distal ulna and distal radius. Arm fractures include fractures of the proximal and midshaft humerus, middle radius, and middle ulna. Elbow fractures include fractures of the distal humerus, olecranon, proximal radius, and proximal ulna. Demographic and injury fracture characteristics were selected *a priori* based on previous literature findings and a pilot study (Aleem et al., 2017; INORMUS Investigators, 2015). In chi-square analysis (Table 3), femur, tibia/fibula, ankle/foot, and patella/other were re-coded as 'lower extremity'. Likewise, arm, elbow and clavicle/other were re-coded as 'upper extremity'.

Statistical Analysis

To uncover age-specific fracture burden, we performed a chi-square analysis comparing fracture location with age. To evaluate how different health care system measures vary with fracture location, we performed chi-square analysis comparing fracture location to the method of transportation to the hospital, and location admitted to hospital from. For all analysis, significance was assessed using an $\alpha = 0.001$ to safeguard against spurious associations. All analysis was conducted using SPSS version 25.

Results:

Patient Demographics

From an initial screen of 9,971 females, in the analysis, we included 9,934 female patients who reported information regarding their orthopaedic fracture and hospital admission. In total, patients were included from 39 participating hospitals across 17 LMICs in Asia, Africa, and Latin America. A complete list of hospitals, regions, and countries are included in Appendix B. Across all regions, 49.5% of female orthopaedic patients were aged 60 years and older (Table 1, Figure 1). China had the highest proportion of patients over 60 years old, (62.3%) while Africa had the lowest (26.5%) (Table 1, Figure 1). Generally, patients were of low income, with only 31.5% reporting incomes greater than $6,000. Patients in Latin America (0.17% income > $6000) reported the lowest incomes (Table 1, Figure 1). Female patients were commonly unemployed or homemakers (52.6%). Africa (37.0% homemaker/unemployed) demonstrated the lowest levels of unemployment while, India (75.5%), and Latin America (77.0%), demonstrated the highest (Table 1, Figure 1). The majority of patients received some education, with only 15.0% of patients across all regions receiving no education. In India, patients were the least educated (28.1% no education) (Table 1, Figure 1). Patients generally lived in urban settings (69.6%), with Other Asia representing the least urban region (49.5% urban) (Table 1, Figure 1).

Fracture Distribution

Regional differences in fracture type are compared in Table 1. Hip fractures were the most common overall (26.9%), and in China (29.1%), India (28.7%), Other Asia

(32.8%), and Latin America (29.0%). Notably, only 14.6% of patients in Africa sustained hip fractures. Instead, patients in Africa experienced high levels of tibia/fibula fractures (21.9%) and disproportionately high levels of femur fractures (14.0%). Similarly, patients in Other Asia sustained high levels of tibia/fibula fractures (18.7%). Within Latin America, foot fractures were especially common (24.3%). Spinal injury burden was highly stratified, with patients in China suffering the highest levels (18.9%) and few patients outside of China suffering spine fractures. Falling was the most common mechanism of injury (64.7%), especially in China (73.5%) and Latin America (79.6%). Transportation accidents accounted for 26.6% of fractures and was highest in Other Asia (40.2%) and Africa (39.6%).

Table 2 outlines fracture locations and mechanisms of injury disaggregated by age. Tibia/fibula (age < 40: 22.0%; age 40 – 59: 17.8%), and foot fractures (age < 40: 19.9%; age 40 – 59: 16.0%) were the most common fractures in women under 60 years old (Table 2). In women aged 60 and older, hip fractures comprised 45.8% of fracture types (Table 2). In women aged 40-59, and especially ≥60, falling was the most common mechanism of injury, accounting for 55.6%, and 82.4% of the fracture burden respectively. In women aged 18-39 years old, transportation accidents were the most common mechanism of injury.

Health Care Characteristics

Across all regions, 58.4% of patients possessed health insurance with India having the lowest level of possessing insurance (22.3%) (Table 1, Figure 1). Across all regions, only 29.2% of patients used an ambulance to reach a hospital following an injury, with

Other Asia having the highest usage (51.2%) (Table 1, Figure 1). Private vehicles (55.9%) were the predominant method of transportation to the hospital. Notably, in Africa, 36.0% of patients used public or other forms of transportation to reach the hospital (Table 1). Across all regions, 26.4% of patients were referred from a different hospital. Referrals were highest in Other Asia (44.7%), and Latin America (45.2%) (Table 1). Table 4 disaggregates ambulance use, and the location patients were being admitted from, by fracture location. Patients who sustained a pelvic fracture most often used an ambulance (53.1%). Likewise, referrals were proportionally most common for pelvic (40.1%) fractures.

A visual summary of key regional differences in patient demographic and fracture trends are included as Figure 1, and overall fracture proportions are demonstrated in Figure 2.

Discussion:

In this work, our data provide a global perspective on the distribution of fractures sustained by women in LMICs. We identified a significant role for aging, with nearly half of our patients ≥60 years old. Within this subgroup, hip fractures (45.8%) were the most common fracture type, indicative of osteoporosis (Cummings & Melton, 2002). Overall, falling was the most common mechanism of injury (64.7%), and accounted for 82.4% of fractures in patients ≥60 years old. Together this suggests a high burden of fragility fractures (Haagsma et al., 2016). In women aged 18-59 years old, the most common fractures were of the tibia/fibula and foot/ankle fractures. Regionally, we found higher proportions of tibia/fibula (21.9%) and femur fractures in Africa (14.0%). Foot/ankle fractures were disproportionately high in Latin America (24.3%). Women in China suffered high frequencies of spinal fractures (18.9%); however, this appears to be a result of a lack of observed spinal fractures in other regions (1.4%). In analyzing health systems, we found significant regional variance in insurance coverage, ranging from 85% having insurance in Latin America, to only 18% in Africa. Only one-third of patients across all regions utilized an ambulance in reaching a hospital.

Fractures in the Elderly

Our findings support previous work emphasizing the importance of fragility, and osteoporotic fractures within LMICs (Zengin et al., 2017). Osteoporosis is commonly associated with fractures of the hip, wrist, and spine, which are generally sustained as a result of falling (Cummings & Melton, 2002). It is estimated that globally, 26% and 20% of osteoporotic fractures in patients aged ≥60 years old are hip, and wrist fractures respectively (Johnell & Kanis, 2006; Zhou et al., 2016). By contrast, our results demonstrate almost twice as many hip fractures, and one third as many wrist fractures in women aged ≥60 years old. We must interpret these findings cautiously. Within LMICs, primary care facilities often lack surgical services (Spiegel, Nduaguba, Cherian, Monono, & Kelley, 2015). Therefore, while primary facilities may be more capable of setting wrist fractures, complex surgical procedures (e.g. lower extremity fractures) are likely to be referred to larger facilities (Abebe, Teshome, & Bekele, 2016). Supporting this conjecture, proportionately fewer patients were admitted from other hospitals for wrist fractures. Our data suggests LMICs must address a substantial burden of hip fractures among female patients, the one-year mortality of which is estimated to be 20% (Melton, 2003).

The observed regional enrichment of spine fractures within China should be treated with caution. We considered the influence of hospital selection bias (e.g. hospitals specializing in neurotrauma patients); however, we did not find sufficient evidence for such a bias across included hospitals in China. Moreover, our results are consistent with previous reports. Spinal fractures have been estimated to occur within 16.1% of global fracture burden among women aged ≥60 years old and 11% of fractures in women in China aged ≥65 (Chen et al., 2017; Johnell & Kanis, 2006). However, vertebral fractures are significantly underdiagnosed and it is estimated that worldwide, vertebral fractures are present in 32% of osteoporotic women, and 22.6% in women aged ≥60 years old in China (Cui et al., 2017; Delmas et al., 2004). It has been difficult to estimate the spinal fracture burden within LMICs due to, for example, a lack of prospective neurotrauma registries (Rubiano, Carney, Chesnut, & Puyana, 2015). Our finding that 1.4% of patients outside of China experience spinal fractures is significantly lower than anticipated (Johnell & Kanis, 2006), and may be the result of insufficient health care infrastructure (Mabweijano J, 2015). More focused research is needed to ensure spine injuries are being treated in LMICs.

Africa Demonstrates more Working Age Fractures

Women in Africa showed notable differences in fracture burden. In contrast to a more elderly, homemaker/unemployed population in China, India, Other Asia, and Latin America, patients in Africa were younger, and nearly two-thirds were employed. A pilot surveillance study conducted at a tertiary centre in South Africa similarly found 54%, and 77% of female patients were between the age of 20-39, and 20-59 years old, respectively, a similar distribution to our data (Schuurman et al., 2011). We found patients in Africa showed higher levels of femur and tibia/fibula fractures, and the lowest levels of fall-related injuries. The fact that more working age-women in Africa are sustaining fractures has implications on indirect costs (e.g. from lost work), and poverty (Yamano & Jayne, 2004).

The Need for Improved Hospital Transportation Services

Most fatalities following an orthopaedic trauma occur before a patient reaches the hospital (Hanche-Olsen, Alemu, Viste, Wisborg, & Hansen, 2012). Our finding of low utilization of ambulatory services is consistent with previous work by INORMUS investigators where 36.5% of patients used ambulatory services in India (Aleem et al., 2017). Early operation increases survival rates (Fehlings et al., 2012). In general, ambulance use appears to relate to a lack of mobility, with wrist and upper extremity injuries demonstrating the lowest ambulatory use, while patients suffering hip and pelvic fractures use ambulances with the highest frequency. It is further notable, that women in Africa used public/other transportation nearly as much as private vehicles, necessitating interventions to improve transportation.

Health Insurance

The observed stratification of health insurance across LMICs represents an important barrier of women accessing health care resources. In LMICs, the high cost of care combined with an inability to work creates a fear of financial insecurity (Grimes, Bowman, Dodgion, & Lavy, 2011). In Uganda, over half of adults who received care for trauma experienced financial catastrophe as a result of their treatment (MacKinnon, St-Louis, Yousef, Situma, & Poenaru, 2018). A lack of insurance also impedes efficient emergency medical services, such as inter-hospital referrals (Kuzma, Lim, Kepha, Nalitolela, & Reynolds, 2015; Meara et al., 2015a), of which one-quarter of patients in our study utilized, thus, resulting in poorer health outcomes (Abebe et al., 2016; Meara et al., 2015b). As a result, within LMICs, a lack of insurance may prevent care, and exacerbate poverty in patients who recover.

Limitations

Despite the fact that hospitals were selected to be inclusive of the general population, the potential for a sampling error remains a limitation as ultimately patients were not sampled in a systematic way. Furthermore, we cannot account for differences in how countries' health care systems distribute patients across their hospital networks which vary significantly due to inadequate health care infrastructure. As such, while the patients included in the study represent a population of patients who seek treatment for their injuries, our conclusions may not be generalizable to women who do not seek treatment for their injuries or seek treatment from non-major hospitals (e.g. traditional healers).

Conclusion:

Across all regions, we found a high proportion of hip fractures, and in general, fracture burden was sustained by elderly patients. Patients in Africa; however, were primarily working age, sustained a higher proportion of lower extremity fractures, and disproportionately sustained femur fractures. Foot/ankle fractures were disproportionately high in Latin America. Notable deficiencies in health care systems include a low frequency of ambulance use. In addition, health insurance coverage was low among women in Africa, India, and Other Asia. Our research provides prospective clinical data which aligns with efforts to ameliorate the burden of fractures within LMICs.

Figures and Tables:

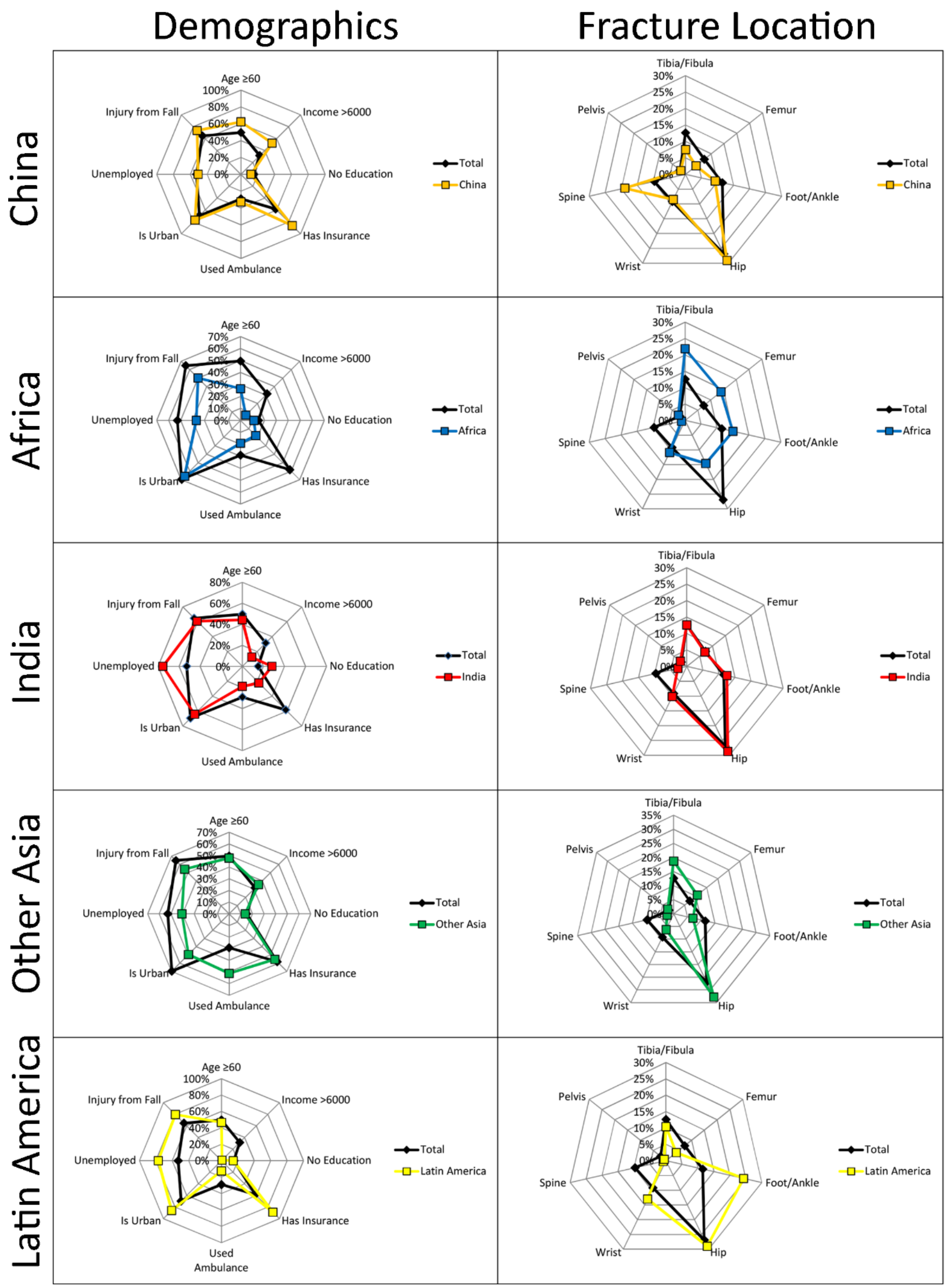

Figure 1: A summary of key demographic and fracture data for each region. The pooled trends of all regions are denoted by the ‘total’

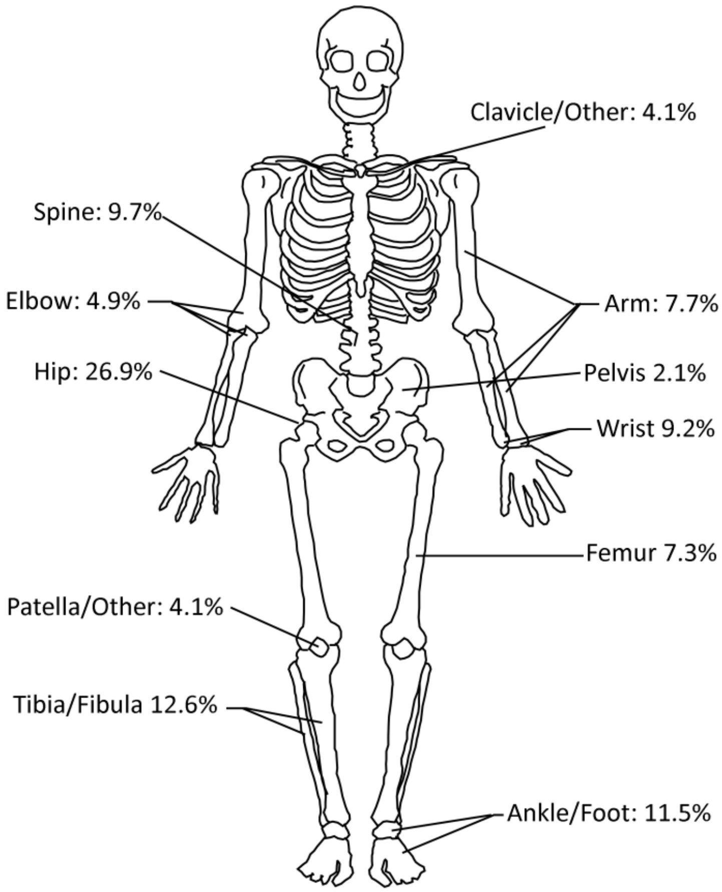

Figure 2: A visual summary of observed proportions of fracture types pooled across all regions in female orthopaedic trauma patients.

Table 1: Baseline demographics, health care, and fracture characteristics of female fracture patients disaggregated by region.

	China	Africa	India	Other Asia	Latin America	Total
Total:	4,449 (44.8%)	1,882 (18.9%)	1,721 (17.3%)	1,304 (13.1%)	578 (5.8%)	9,934 (100%)
Age						
18-39	472 (10.6%)	781 (41.5%)	495 (28.8%)	319 (24.5%)	150 (26.0%)	2,217 (22.3%)
40-59	1,206 (27.1%)	601 (32.0%)	466 (27.1%)	361 (27.7%)	158 (27.3%)	2,792 (28.1%)
≥60	2,771 (62.3%)	499 (26.5%)	760 (44.2%)	624 (47.9%)	270 (46.7%)	4,924 (49.6%)
Has Insurance	3,837 (86.2%)	339 (18.0%)	384 (22.3%)	721 (55.3%)	513 (88.8%)	5,794 (58.3%)
is Urban	3,428 (77.1%)	1,244 (66.1%)	1,105 (64.2%)	645 (49.5%)	496 (85.8%)	6,918 (69.6%)
Income						
Unknown	864 (19.4%)	1,022 (54.3%)	739 (42.9%)	109 (8.4%)	338 (58.5%)	3,072 (30.9%)
2000<	590 (13.3%)	516 (27.4%)	634 (36.8%)	272 (20.9%)	196 (33.9%)	2,208 (22.2%)
2001-6000	667 (15.0%)	226 (12.0%)	132 (7.7%)	460 (35.3%)	38 (6.6%)	1,523 (15.3%)
>6000	2,328 (52.3%)	118 (6.3%)	216 (12.6%)	463 (35.5%)	6 (1.0%)	3,131 (31.5%)
Education						
No Education	529 (11.9%)	210 (11.2%)	483 (28.1%)	180 (13.8%)	83 (14.4%)	1,485 (15.0%)
Up to High School	3,030 (68.1%)	1,327 (70.5%)	798 (46.4%)	808 (62.0%)	408 (70.6%)	6,371 (64.2%)
Post-Secondary	890 (20.0%)	344 (18.3%)	438 (25.5%)	316 (24.2%)	87 (15.1%)	2,075 (20.9%)
Transport To Hospital						
Ambulance	1,459 (32.8%)	359 (19.1%)	325 (19.0%)	666 (51.2%)	72 (12.5%)	2,881 (29.1%)
Private Vehicle	2,473 (55.6%)	842 (44.9%)	1,250 (73.2%)	506 (38.9%)	474 (82.0%)	5,545 (55.9%)
Public Transport / Other[a]	516 (11.6%)	676 (36.0%)	133 (7.8%)	129 (9.9%)	32 (5.5%)	1,486 (15.0%)
Location Administered From						
Injury Site	1,699 (38.2%)	829 (44.2%)	565 (33.0%)	243 (18.7%)	97 (16.8%)	3,433 (34.6%)
Other Hospital	812 (18.3%)	632 (33.7%)	338 (19.8%)	582 (44.7%)	261 (45.2%)	2,625 (26.5%)
Home / Other[b]	1,937 (43.5%)	416 (22.2%)	807 (47.2%)	476 (36.6%)	220 (38.1%)	3,856 (38.9%)
Occupation						
Agriculture/Industry	909 (20.4%)	307 (16.3%)	126 (17.3%)	286 (21.9%)	13 (2.2%)	1,641 (16.5%)
Unemployed/Homemaker	2,261 (50.8%)	696 (37.0%)	1,299 (75.5%)	530 (40.6%)	445 (77.0%)	5,231 (52.7%)
Other[c]	1,279 (28.7%)	879 (46.7%)	295 (17.2%)	488 (37.4%)	120 (20.8%)	3,061 (30.8%)
Fracture Location						
Hip	1,290 (29.1%)	257 (14.6%)	480 (28.7%)	415 (32.8%)	165 (29.0%)	2,607 (26.9%)
Femur	182 (4.1%)	246 (14.0%)	117 (7.0%)	135 (10.7%)	24 (4.2%)	704 (7.3%)
Tibia/Fibula	333 (7.5%)	385 (21.9%)	210 (12.6%)	236 (18.7%)	59 (10.4%)	1,223 (12.6%)
Ankle/Foot	413 (9.3%)	263 (15.0%)	209 (12.5%)	88 (7.0%)	138 (24.3%)	1,111 (11.5%)
Patella/Other	219 (4.9%)	44 (2.5%)	87 (5.2%)	28 (2.2%)	15 (2.6%)	393 (4.1%)
Wrist	375 (8.5%)	191 (10.9%)	170 (10.2%)	79 (6.2%)	74 (13.0%)	889 (9.2%)
Arm	293 (6.6%)	160 (9.1%)	144 (8.6%)	108 (8.5%)	46 (8.1%)	751 (7.7%)
Elbow	182 (4.1%)	103 (5.9%)	99 (5.9%)	59 (4.7%)	31 (5.4%)	474 (4.9%)
Clavicle/Other[d]	226 (5.1%)	45 (2.6%)	68 (4.1%)	53 (4.2%)	8 (1.4%)	400 (4.1%)

Spine	839 (18.9%)	20 (1.1%)	46 (2.8%)	30 (2.4%)	5 (0.9%)	940 (9.7%)
Pelvis	82 (1.8%)	45 (2.6%)	42 (2.5%)	34 (2.7%)	4 (0.7%)	207 (2.1%)
Mechanism of Injury						
Transport	809 (18.2%)	745 (39.6%)	503 (29.2%)	523 (40.2%)	59 (10.2%)	2,639 (26.6%)
Fall	3,272 (73.5%)	943 (50.1%)	1,043 (60.6%)	706 (54.2%)	460 (79.6%)	6,424 (64.7%)
Other[e]	368 (8.3%)	193 (10.3%)	175 (10.2%)	73 (5.6%)	59 (10.2%)	868 (8.7%)

a: includes on-foot, rickshaw or other
b: includes local doctor, nursing home, or other
c: includes entertainment, service, public service, health care, education, business, police, military, or other
d: includes scapula, or other
e: includes struck, lifting, intentional, or other

Table 2: Fracture locations disaggregated by age.

	Age			
Fracture	18-39	40-59	≥60	Total
Hip	73 (3.4%)	305 (11.2%)	2238 (45.8%)	2616 (%26.9)
Femur	206 (9.7%)	177 (6.5%)	321 (6.6%)	704 (%7.2)
Tibia/Fibula	465 (22.0%)	485 (17.8%)	284 (5.8%)	1234 (%12.7)
Ankle/Foot	421 (19.9%)	436 (16.0%)	254 (5.2%)	1111 (%11.4)
Patella/Other	76 (3.6%)	159 (5.8%)	160 (3.3%)	395 (%4.1)
Arm	192 (9.1%)	230 (8.4%)	329 (6.7%)	751 (%7.7)
Wrist	207 (9.8%)	311 (11.4%)	373 (7.6%)	891 (%9.2)
Elbow	157 (7.4%)	169 (6.2%)	149 (3.0%)	475 (%4.9)
Clavicle/Other[a]	149 (7.0%)	163 (6.0%)	89 (1.8%)	401 (%4.1)
Spine	93 (4.4%)	218 (8.0%)	632 (12.9%)	943 (%9.7)
Pelvis	78 (3.7%)	70 (2.6%)	59 (1.2%)	207 (%2.1)
Mechanism of Injury				
Falling	801 (37.8%)	1514 (55.6%)	4026 (82.4%)	6341 (65.2%)
Transport	1001 (47.3%)	914 (33.6%)	636 (13.0%)	2551 (26.2%)
Other[b]	315 (14.9%)	294 (10.8%)	226 (4.6%)	835 (8.6%)
Total	2117 (100.0%)	2722 (100.0%)	4888 (100.0%)	9727 (100.0%)

Fracture vs. Age: chi-square 2525.7, p-value < 0.001.
Mechanism of Injury vs. Age: chi-square 1444.5, p-value < 0.001.
a: includes scapula, or other
b: includes struck, lifting, intentional, or other

Table 3: Fracture location compared with method of transport to hospital, and location admitted to hospital from.

	Hip	Other Lower[a]	Wrist	Other Upper[b]	Spine	Pelvis	Total
Method of Transport to Hospital							
Ambulance	937 (35.8%)	1096 (31.8%)	114 (12.8%)	336 (20.6%)	249 (26.4%)	110 (53.1%)	2842 (29.2%)
Private Vehicle	1458 (55.8%)	1787 (51.9%)	538 (60.4%)	958 (58.7%)	613 (65.0%)	87 (42.0%)	5441 (55.9%)
Public Transportation / Other[c]	219 (8.4%)	559 (16.2%)	238 (26.7%)	338 (20.7%)	81 (8.6%)	10 (4.8%)	1445 (14.9%)
Location Admitted to Hospital From							
Injury Site	625 (23.9%)	1482 (43.0%)	349 (39.2%)	615 (37.7%)	216 (22.9%)	89 (43.0%)	3376 (34.7%)
Other Hospital	639 (24.4%)	1049 (30.5%)	149 (16.7%)	472 (28.9%)	162 (17.2%)	83 (40.1%)	2554 (26.2%)
Home/Other[d]	1352 (51.7%)	912 (26.5%)	392 (44.0%)	545 (33.4%)	565 (59.9%)	35 (16.9%)	3801 (39.1%)
Total:	2616	3443	890	1632	943	207	9731

Method of Transport to Hospital vs. Fracture: chi-square 490.1, p-value < 0.00001.
Location Admitted to Hospital From vs. Fracture: chi-square 711.1, p-value < 0.00001.
a: includes femur, tibia/fibula, ankle/foot, patella or other
b: includes arm, elbow and other upper scapula, clavicle, or other.
c: includes on-foot, rickshaw or other
d: includes local doctor, nursing home, or other

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CHAPTER 3: Do Women Experience Greater Delays in Treatment following Musculoskeletal Trauma in Low-and Middle-Income Countries? A Multicenter Prospective Observational Study

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Abstract:

Background: Delay can be defined as First Delay (e.g. cultural and financial barriers to seeking treatment), Second Delay (e.g. wanting to seek treatment but unable to transit to a hospital) and Third Delay (e.g. hospital related administrative or treatment delays). There is limited information to inform the association between sex and hospital admission delay of trauma patients in Low- and Middle-Income Countries (LMICs).

Outcomes: Our primary outcome was the association between sex and delay to hospital admission (admission time > 24 hours) among orthopedic trauma patients in LMICs.

Methods: We explored sex differences in hospital admission time, and delayed hospital admission, among trauma patients in China, Africa, India, Other Asia, and Latin America. We constructed logistic regression models, adjusted for 12 factors (i.e. region, age, education, employment, urban living, health insurance, hospital referral, method of transport, number of fractures, sustaining an open fracture, the mechanism of injury, and fracture location) to explore the association between sex and hospital admission delay.

Results: We identified 26,910 eligible orthopedic trauma patients across 17 LMICs, of which 16,976 (63.1%) were men and 9,934 (36.9%) were women. Significantly more women experienced delayed admission to hospital in comparison to men (27.5% women vs. 22.0% men, $p < 0.0001$); however, sex was not associated with delayed admission in our adjusted regression model ($p=0.122$). Factors associated with faster admission included: open fractures (OR 0.458, 95%CI 0.410 to 0.511; $p < 0.001$); employment (OR 0.837, 95%CI 0.779 to 0.899; $p < 0.001$); ambulance transport (OR 0.414, 95%CI 0.383 to 0.448; $p<0.001$) and other modes of transportation (OR 0.766, 95%CI 0.697 to 0.841; p <

0.001) relative to private vehicles; and transport relative to falling injuries (OR 0.632, 95%CI 0.585 to 0.684; $p < 0.001$).

Factors associated with delayed admission were older age (OR 1.007, 95%CI 1.005 to 1.009; $p < 0.001$); inter-hospital referrals (OR 3.310, 95%CI 3.085 to 3.550; $p < 0.001$); residing in India (OR 1.479, 95%CI 1.344 to 1.628; $p < 0.001$), other Asia (OR: 1.911, 95%CI 1.727 to 2.115; $p < 0.001$), or Latin America (OR: 1.988, 95%CI 1.719 to 2.298; $p < 0.001$) relative to China, and hip (OR: 1.205, 95%CI 1.096 to 1.325; $p < 0.001$); and spine (OR: 2.580 95%CI 2.303 to 2.910; $p < 0.001$) and pelvic fractures (OR: 1.568, 95%CI 1.301 to 1.890; $p < 0.001$) when compared to lower extremity fractures. The most common reason for delay was a result of inter-hospital referrals (45.1%).

Conclusion: Sex was not associated with time to hospital admission among orthopedic trauma patients in LMICs. Inter-hospital referrals represent the main reason for hospital admission delay.

Background:

Orthopaedic injuries are a leading cause of mortality and disability worldwide, accounting for 11.2% of global disability adjusted life years (DALYs) and 5 million deaths, 90% of which are in Low- and Middle-Income Countries (LMICs) (Hofman, Primack, Keusch, & Hrynkow, 2005; Murray et al., 2012). Broadly defined, injuries include musculoskeletal trauma sustained, for example, from falling or road traffic accidents. Addressing the burden of injury within LMICs is a key global endeavour, and has been the subject of international efforts including the Decade of Action on Road Safety (2011-2020) which aims to reduce the global burden of road traffic accidents by half. In addition to improving access to surgical and other health care resources, hospitals within LMICs must work towards reducing systemic delays which prevent timely treatment (Meara et al., 2015). A majority of mortality occurs before a patient reaches the hospital, (Mock, Arreola-Risa, & Quansah, 2003) and faster treatment of orthopedic trauma can substantially improve outcomes (Boschini, Lu-Myers, Msiska, Cairns, & Charles, 2016).

Within LMICs, there are three major types of delay in receiving hospital treatment (Meara et al., 2015). The First Delay occurs when patients stall in seeking hospitalized health care treatment as a result of socioeconomic and cultural factors. Key reasons can include a lack of finances, poor education, or a distrust of the health care system (Grimes, Bowman, Dodgion, & Lavy, 2011; Meara et al., 2015). In addition, rather than seeking care at hospitals, patients often turn to trusted, community based traditional healers (DeJong, 1991). The Second Delay occurs when patients who have a desire to seek hospital care are unable to as a result of an inability to find transportation or traverse long distances to reach a hospital (Meara et al., 2015). Within LMICs, median distances for hospitals are between 30-35km (Meara et al., 2015). The Third Delay results from an inability of hospitals to provide health care services. Across LMICs, first level hospitals are often ill-equipped to address complex surgeries (Chokotho et al., 2015; Spiegel, Nduaguba, Cherian, Monono, & Kelley, 2015), and such must refer patients to higher level secondary and tertiary level hospitals (Hanche-Olsen, Alemu, Viste, Wisborg, & Hansen, 2012; Meara et al., 2015). Due to a lack of a centralized referral system, a lack of ambulances, and no guarantee that a receiving hospital can address an incoming patient's needs, referrals and a general lack of health care resources across all levels are a substantial source of patient delay(Abebe, Teshome, & Bekele, 2016; Kuzma, Lim, Kepha, Nalitolela, & Reynolds, 2015; Meara et al., 2015).

Within LMICs, due to social roles, women have less agency to seek care for their health care needs (Osamor & Grady, 2016). Furthermore, established societal roles and culture can prevent women from seeking care as has been documented for antenatal care (Finlayson & Downe, 2013; Langer et al., 2015). In this study, we used data from the INternational ORthopaedic MUlticenter Study in fracture care (INORMUS) to analyze the association between sex and hospital admission delay across 17 LMICs.

Methods:

INORMUS is a global, multicenter, observational study to evaluate and assess global trends in musculoskeletal injury burden and its demographic, and health care system causes. An outline of study objectives and methods have been published previously (INORMUS Investigators, 2015). In this secondary study, from an initial subset of 27,028 patients enrolled before December 2017 we analyzed 26,910 patients. Patients were grouped into five regions: China, Africa (Uganda, Kenya, Nigeria, Botswana, Ghana, South Africa, and Tanzania), India, Other Asia (Pakistan, Nepal, Vietnam, Thailand, The Philippines, and Iran) and Latin America (Venezuela, and Mexico).

Ethics

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, with patients identified through unique numbers.

Selection Criteria and Data Collection

To be included in the study, patients must have been admitted to a participating hospital within three months of sustaining an orthopaedic trauma and be 18 years of age or older. 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. Recruitment and enrollment of patients was conducted via direct emergency department referrals. Patients who met the eligibility criteria consulted with study personnel to provide informed consent, in addition to demographic and clinical data. Patients were followed up after 30 days following hospital admission. If patients were discharged prior to 30 days, they were followed up at their one-month clinical visit or in the absence of a follow-up visit, by telephone.

Selection and Coding of Variables

Demographic, injury, and health care system factors were selected *a priori* based on previous literature, and a pilot study (Aleem et al., 2017; INORMUS Investigators, 2015). Fracture types refer only to the single most severe fracture sustained by a patient. Other lower extremity fractures include fractures of the femur, tibia, fibula, ankle, foot, and patella, and other. Other upper extremity fractures include fractures of the humerus, proximal and middle radius, proximal and middle ulna, clavicle, scapula or other. A hospital admission delay was defined as a delay greater than 24 hours.

Comparing Time to Hospital Admission Across Sex, and Regions

The Shapiro-Wilk test was used to assess the normalcy of the time to hospital administration for patients pooled across all regions (Table A1). If data was not sufficiently normal distributed, we used non-parametric testing which does not rely on an assumption of normalcy. An independent samples Mann Whitney-U test was used to assess differences in the time to hospital admission between men and women with data disaggregated by region. A pooled region analysis of time to hospital admission between men and women was also conducted. Chi-square analysis was used to analyze proportional differences in delayed hospital admission between men and women with data disaggregated by region. A pooled regional analysis between men and women was similarly assessed. A Bonferroni correction was applied to p-values, a corrected $\alpha = 0.0083$ was used.

Binary Logistic Regression

We used binary logistic regression analysis to explore the association of sex with hospital admission delay. We adjusted our model with 12 additional variables: (1) region, (2) age, (3) education, (4) employment, (5) urban living, (6) health insurance, (7) referred from hospital, (8) method of transport, (9) number of fractures, (10) open fracture, (11) mechanism of injury, and (12) fracture type, selected *a priori* based on literature highlighting key determinants. Income was excluded as a variable from the model as it surpassed a threshold of 10% missing data, which can introduce bias(Bennett, 2001).

Briefly, socioeconomic and demographic factors (e.g. region, sex, age, education, employment, urban living, health insurance) have been previously described as barriers to health care access(Grimes et al., 2011; Harris et al., 2011; Yaffee et al., 2012). Transportation, and inter-hospital referrals are additional sources of delay(Boschini et al., 2016; Meara et al., 2015). Finally, the type and severity of the fracture can influence hospital admission(Boufous, Finch, Close, Day, & Lord, 2007). Predictor variables were entered using forced simultaneous entry. Cramers V statistic was used to assess if our variables were highly correlated. No pairings of our input variables exceeded our elimination threshold of 0.7. For all analysis, significance was assessed using an $\alpha = 0.001$ to safeguard against spurious associations. All analysis was conducted using SPSS version 25.

Results:

Sex Differences in Fracture Types

From an initial screen of 27,028 patients, 26,910 were included for analysis including 16,976 men and 9,934 women. Across all regions, women were predominantly over the age of 60 (49.6%) years old while men were commonly between the ages 18-39 years old (50.5%). Across all regions, women suffered most from fall-related injuries (64.7%) while men sustained injuries through transportation (49.5%). Non-hip lower extremity fractures (e.g. tibia/fibula) were the most common (44.9%) and especially among men (48.3% men vs. 34.5% women). Notably, women sustained disproportionately more hip fractures (13.5% men vs. 26.9% women) and spine fractures (5.3% men vs. 9.5% women) in comparison to men. (Table 1)

Women Took longer to Reach the Hospital Than Men Following an Orthopaedic Trauma

The time to hospital admission was not normally distributed with a pronounced right-bound skew (Table A1), consequently, non-parametric analysis was conducted. Across all regions, women took a significantly longer time ($p < 0.001$) to reach the hospital with women being delayed by a median of one hour (6 hours men vs. 7 hours women; Table 2). Similarly, 27.5% of women were delayed by > 24 hours, compared with 22.0% of men ($p < 0.001$; Table 3). Women in Other Asia experienced the greatest inequality in terms of hospital admission time with women experiencing a median four-hour delay compared to men (8 hours men vs. 12 hours women; Table 2). A similar disparity was observed in the proportion of women in Other Asia who were delayed by > 24 hours (25.9% men delayed vs. 35.7% women delayed, $p < 0.001$; Table 3). Both men (39.2%) and women (42.9%) most frequently experienced delayed hospital admission in Latin America (Table 3).

Injury and Health Care System Characteristics are Major Determinants of Delay

Our adjusted logistic regression analysis model found that sex was not a significant predictor of delayed hospital admission (OR 0.946, 95%CI 0.881 to 1.02; $p = 0.122$). Factors associated with reduced delay included open fractures (OR 0.458, 95%CI 0.410 to 0.511; $p < 0.001$), employment (OR 0.837, 95%CI 0.779 to 0.899; $p < 0.001$), the use of ambulances (OR 0.414, 95%CI 0.383 to 0.448; $p<0.001$) and other modes of transportation (OR 0.766, 95%CI 0.697, 0.841; $p < 0.001$) instead of private vehicles, and transport injuries relative to falling injuries (OR 0.632, 95%CI 0.585 to 0.684; $p < 0.001$).

Increased delays were associated with aging (OR 1.007, 95%CI 1.005 to 1.009; $p < 0.001$), inter-hospital referrals (OR 3.310, 95%CI 3.085 to 3.550; $p < 0.001$), hip (OR 1.205 95%CI 1.096 to 1.325; $p < 0.001$), spine (OR 2.580, 95%CI 2.303 to 2.910; $p < 0.001$), and pelvic fractures (OR 1.568, 95%CI 1.301 to 1.890; $p < 0.001$) when compared to lower extremity fractures. Regionally, compared to China, India (OR 1.479, 95%CI 1.344 to 1.628; $p < 0.001$), Other Asia (OR 1.911, 95%CI 1.727 to 2.115; $p < 0.01$), and Latin America (OR 1.988, 95%CI 1.719 to 2.298; $p < 0.01$) increased delay. (Table 4)

Reason for Delay

The most common reason for delay was inter-hospital referral (Fig. 1), which was disproportionately high in men (50.0% men vs. 37.7% women) and most frequent in Other Asia (51.1%). Notably, 18.5% of men, while nearly twice as many women (33.3%) were delayed due to believing their injury would heal on its own and was the most common reason for delay in China (48.8%). Patients in India were disproportionately delayed due to delays in the emergency department (24.3%). Patients in Latin America disproportionately reported an unwillingness to go to hospitals or concerns about cost as their primary reason for delay (15.5%), while this reason was relatively less common in other regions.

Discussion

We found that nearly one-quarter of trauma patients in LMICs experienced > 24 hours delays for admission to hospital; however, sex was not a significant predictor of delay. The type and severity of the fracture, hospital referrals, ambulance usage, and region were the most significant predictors of delay. Typically, more severe fractures, including open fractures and fractures sustained by transport accidents, reduced the odds of delay; likely reflecting an urgency of needing care. Aging, as well as hip and spine fractures, increased the odds of delay. Hip and spine fractures are common in the elderly, and thus, our data supports a conjecture whereby across LMICs, the elderly are delayed in hospital admission. We also found that pelvic fractures increased the odds of delay by 1.5-fold. Pelvic fractures are dangerous as they require complex surgeries, and have been established to increase the risk for catastrophic blood loss leading to high mortality rates between 7.6% and 19% (Gehlbach et al., 2012; Lee & Porter, 2007). This reflects an important gap which should be addressed by LMICs health systems networks.

The Need for an Improved Referral System

Our data support existing calls to implement centralized referral systems and increase ambulatory services to improve care within health systems of LMICs (Grimes et al., 2011; Kuzma et al., 2015; Meara et al., 2015). Within LMICs, primarily only secondary and tertiary hospitals are equipped to perform surgeries (Meara et al., 2015; Spiegel et al., 2015). Absent effective emergency medical services, typically patients will attend local hospitals, which are under-resourced, or incapable of treating fractures, and then must be referred to larger secondary or tertiary centers(Roy et al., 2010). A prior study of trauma patients in sub-Saharan Africa found that inter-hospital referrals increased median hospital admission time nearly four-fold, and increased the odds of mortality two-fold (Boschini et al., 2016). In our data, 31.5% of patients were referred from another hospital, and only 33.4% of patients utilized ambulatory services. These findings are consistent with previous observations (Aleem et al., 2017). Being referred from another hospital increased the odds of delay three-fold, while when compared to private vehicles, ambulances reduced the odds of delay by half. Across all regions, half of patients cited hospital transfers as the reason for their delay.

Regional Priorities to Address Delay

In addition to the need for improving inter-hospital referrals, believing an injury would heal on its own, and delays in the emergency room were additional common reasons for delay. Nearly half of patients in China believed their injury would heal on its own and suggests a need to further educate populations to seek hospital care for their injuries. Within India, one in five delayed patients were delayed in the emergency department. Hospitals in India are understaffed and under-resourced, sometimes with only a single doctor available to oversee emergency or other wards(Bajpai, 2014). Improving emergency room management within India would promise to improve health outcomes for a significant portion of patients. Overall, patients in Latin America experienced the greatest levels of delay, with two in five patients being delayed by one day. Currently, few prospective data sources exist to estimate pre-hospital delay within Latin America (Peck et al., 2017). Our data suggests the need to improve pre-hospital infrastructure is substantial and supports existing efforts to delineate and address this burden (Peck et al., 2017).

Spine Injuries and Delay

Our data demonstrate that spine fractures are associated with increased delay in hospital admission. We speculate a role for osteoporotic vertebral fractures. Caused by low trauma events, the presentation of osteoporotic vertebral fractures exists along a spectrum, ranging from painful, to un-noticeable, with pain gradually subsiding over weeks (El Maghraoui et al., 2009; Francis et al., 2004). Between two-thirds and three-quarters of osteoporotic vertebral fractures are undiagnosed, and may be clinically silent (Ballane, Cauley, Luckey, & El-Hajj Fuleihan, 2017). We conjecture that patients who sustain only the most severe pain immediately seek treatment, a finding observed among vertebral fractures in Moroccan women (El Maghraoui et al., 2009). However, vertebral fractures are serious and severely restrict a patient's quality of life (Wong & McGirt, 2013), increase the risk for further fractures (Gehlbach et al., 2012), and mortality (Cooper, Atkinson, Jacobsen, O'Fallon, & Melton, 1993). In a HIC setting, vertebral fractures increased primary care visitations 14-fold compared with controls, demonstrating the need for treatment (Dolan & Torgerson, 1998).

Health Insurance and Delay

We found a fear of financial calamity did not play a substantial role in delay. Across all regions, a fear of hospitals/costs accounted for only 7.2% of reported reasons for delay and was highest in Latin America, where interestingly, possession of health insurance was among the highest (83.8%). Likewise, holding health insurance did not impact the odds of delay. We must treat this interpretation with caution. Financial problems primarily act as a First Delay barrier (Meara et al., 2015), and as such, we are likely missing a substantial population who choose not to seek care from hospitals at all due to perceived costs (Grimes et al., 2011). It is estimated that up to 80% of patients seek out traditional healers instead of seeking hospital care (World Health Organization, 2002). Regardless of delay, we found over half of patients in this study did not possess health insurance. It is estimated worldwide 100 million patients will be pushed into poverty as a result of health care costs, and this remains an important policy concern (Xu et al., 2007).

Limitations

A key limitation of this study is sampling bias. As we can only observe patients who choose to attend a hospital, we are unable to quantify patients who do not attend a hospital. In addition, we cannot rule out that an over or under-representation of hospitals specializing in specific fracture types (e.g. neurotrauma) skew the delay for specific fracture types. Moreover, we may be underestimating the overall number of patients who would require inter-hospital referrals but died prior to hospital admission, and hence inclusion within this study. This study only employed open fractures as a metric of fracture severity and did not measure other measures of injury severity and type which could better explain some sources of delay.

Conclusion

In this study of 26,900 trauma patients across 17 LMICs, we found that one-quarter of patients were delayed more than a day to be admitted to a hospital, and over half of delays were due to inter-hospital referrals. Sex was not a significant predictor of delay. Our findings support the need for better referral and EMS systems to reduce hospital admission delays in LMICs.

Figures and Tables:

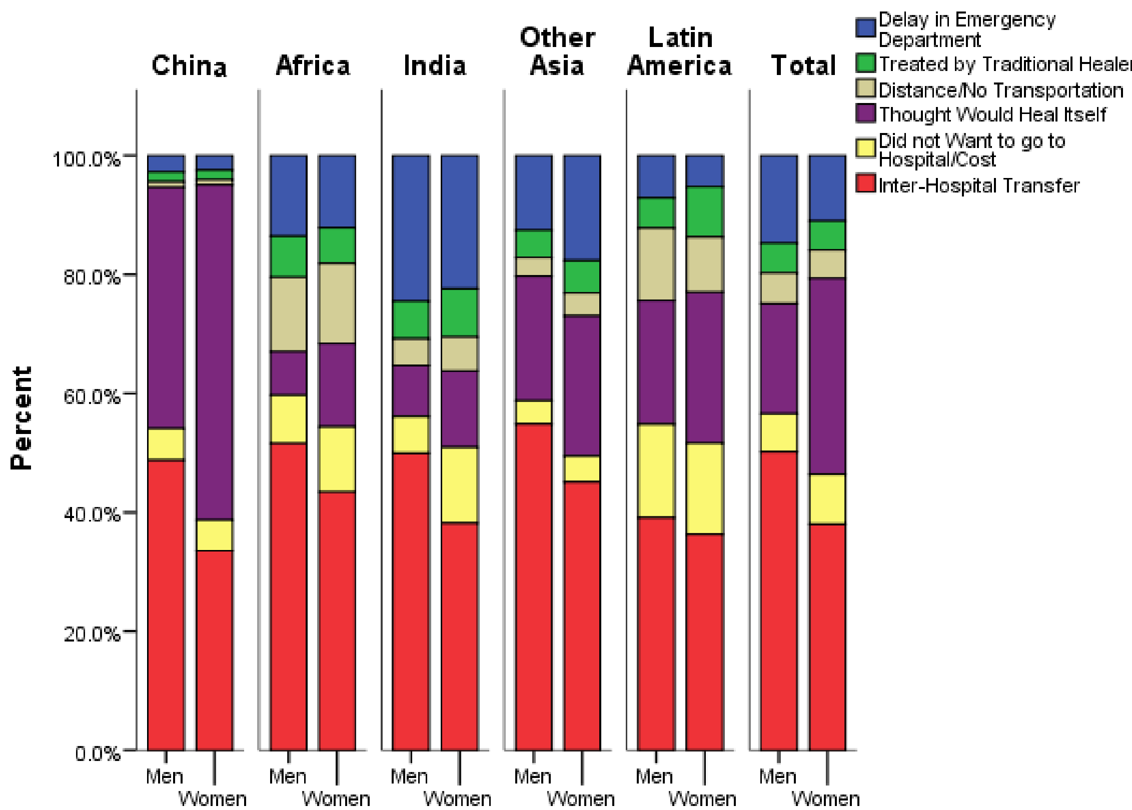

Figure 1: Reasons for hospital delay of greater than 24 hours disaggregated by sex and region.

Table 1: Baseline demographic data of study participants disaggregated by sex

	Male	Female	Total
Total	16976	9934	26910
Region			
China	4721 (27.8%)	4449 (44.6%)	9170 (34.1%)
Africa	4968 (29.3%)	1882 (18.9%)	6850 (25.5%)
India	4340 (25.6%)	1721 (17.3%)	6061 (22.5%)
Other Asia	2444 (14.4%)	1304 (13.1%)	3748 (13.9%)
Latin America	503 (3.0%)	578 (5.8%)	1081 (4.0%)
Age			
18-39	8575 (50.5%)	2217 (22.3%)	10841 (40.2%)
40-59	5417 (31.9%)	2792 (28.1%)	8224 (30.5%)
>60	2983 (17.6%)	4924 (49.6%)	7931 (29.4%)
Income			
Unknown	4513 (26.6%)	3072 (30.9%)	7592 (28.1%)
<2000	5126 (30.2%)	2208 (22.2%)	7348 (27.2%)
2000 - 6000	2956 (17.4%)	1523 (15.3%)	4511 (16.7%)
>6000	4379 (25.8%)	3131 (31.5%)	7539 (27.9%)
Education			
No Education	989 (5.8%)	1485 (15.0%)	2485 (9.2%)
Up to Highschool	11195 (66.0%)	6371 (64.2%)	17620 (65.3%)
Post-Secondary	4788 (28.2%)	2075 (20.9%)	6886 (25.5%)
Is Employed	13683 (80.4%)	4730 (47.4%)	18413 (68.2%)
Is Urban	10852 (63.9%)	6918 (69.6%)	17824 (66.0%)
Has Health Insurance	7145 (42.1%)	5794 (58.3%)	13013 (48.2%)
Referred from another hospital	5832 (34.5%)	2626 (26.4%)	8458 (31.5%)
Transport to Hospital			
Ambulance	6070 (36.0%)	2881 (29.1%)	8992 (33.5%)
Private Vehicle	7831 (46.4%)	5545 (55.9%)	13387 (49.8%)
Other[a]	2981 (17.7%)	1486 (15.0%)	4478 (16.7%)
>1 Orthopaedic Fracture	2969 (17.6%)	976 (9.8%)	3969 (14.8%)
Open Fracture	3265 (20.1%)	737 (7.6%)	4023 (15.5%)
Mechanism of Injury			
Transport	8398 (49.5%)	2639 (26.6%)	11058 (41.0%)
Fall	5921 (34.9%)	6424 (64.7%)	12391 (45.9%)
Other[b]	2645 (15.6%)	868 (8.7%)	3522 (13.1%)
Fracture Location			

Hip	2188 (12.8%)	2616 (26.2%)	4804 (18.5%)
Other Lower Extremity	8232 (48.3%)	3444 (34.5%)	11676 (44.9%)
Wrist	1044 (6.1%)	890 (8.9%)	1934 (7.4%)
Other Upper Extremity	3449 (20.3%)	1632 (16.4%)	5081 (19.6%)
Spine	897 (5.3%)	943 (9.5%)	1840 (7.1%)
Pelvic	447 (2.6%)	207 (2.1%)	654 (2.5%)

a: includes on-foot, rickshaw or other
b: includes struck, lifting, intentional, or other

Table 2: Distributional Differences in the days to Hospital Administration between Men and Women. P-values were calculated using a Mann Whitney U test and adjusted for multiple comparisons using a Bonferroni correction

	China		Africa		India		Other Asia		Latin America		Total	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Median	0.208	0.250	0.167	0.208	0.250	0.292	0.333	0.500	0.917	1.000	0.250	0.292
25 Percentile	0.125	0.125	0.083	0.083	0.083	0.083	0.125	0.167	0.250	0.365	0.083	0.125
75 Percentile	1.000	1.083	0.625	1.000	1.000	2.000	1.083	4.000	3.000	4.000	1.000	1.500
Maximum	90	92	86	84	92	90	90	91	67	90	92	92
adj. P-Value	<0.001		<0.001		0.034		<0.001		0.297		<0.001	

Table 3: The percentage of men and women within each region delayed by more than 24 hours. Statistical Comparisons between men and women are conducted within each region using a Chi-Square test, p-values were Bonferroni corrected.

	Men	Women	adj. P-Value
China	1052 (22.3%)	1143 (25.7%)	0.001
Africa	775 (15.6%)	366 (19.4%)	0.001
India	1063 (24.6%)	510 (29.7%)	<0.001
Other Asia	632 (25.9%)	465 (35.7%)	<0.001
Latin America	197 (39.2%)	248 (42.9%)	1
Total	3726 (22.0%)	2740 (27.5%)	<0.001

Table 4: A binary logistic regression predicting hospital admissions delay of greater than 24 hours, using demographic and injury factors. p < 0.001 were considered significant (denoted by '*')

	OR	lower CI	upper CI	p-value
Region				
Africa vs. China	0.849	0.764	0.944	0.002
India vs. China	1.479	1.344	1.628	<0.001*
Other Asia vs. China	1.911	1.727	2.115	<0.001*
Latin America vs. China	1.988	1.719	2.298	<0.001*
Is Female	0.946	0.881	1.015	0.122
Increasing Age	1.007	1.005	1.009	<0.001*
Increasing Education	0.927	0.873	0.985	0.014
Is Employed	0.837	0.779	0.899	<0.001*
Is Urban	0.922	0.860	0.988	0.022
Has Health Insurance	0.976	0.905	1.052	0.522
Referred From Another Hospital	3.310	3.085	3.550	<0.001*
Method of Transportation to Hospital				
Ambulance vs. Private Vehicle	0.414	0.383	0.448	<0.001*
Public Transport / Other[a] vs. Private Vehicle	0.766	0.697	0.841	<0.001*
> 1 Fractures	0.930	0.847	1.020	0.125
Open Fracture	0.458	0.410	0.511	<0.001*
Mechanism of Injury				
Transport vs. Fall	0.632	0.585	0.684	<0.001*
Other[b] vs. Fall	0.843	0.760	0.936	0.001
Fracture Type				
Hip vs. Other Lower	1.205	1.096	1.325	0.0001*
Wrist vs. Other Lower	1.178	1.044	1.329	0.008
Other Upper vs. Other Lower	1.093	1.003	1.191	0.043
Spine vs. Other Lower	2.589	2.303	2.910	<0.001*
Pelvic vs. Other Lower	1.568	1.301	1.890	<0.001*

a: includes on-foot, rickshaw or other
b: includes struck, lifting, intentional, or other

Appendix A:

Table A1: Metrics of distribution normalcy for hospital admission time disaggregated by region and sex

	China		Africa		India		Other Asia		Latin America	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Shapiro-Wilks P-Value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Skewness	6.4	5.8	8.9	8.2	5.9	5.0	5.8	5.1	4.9	5.0
Kurtosis	59.4	45.8	94.0	87.8	41.1	29.1	40.1	32.6	29.0	31.0

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CHAPTER 4: Thesis Conclusions and Future Directions

The burden of orthopaedic trauma in LMICs is enormous and represents a barrier for sustainable development. Due to existing gender inequities which entrench women as a vulnerable population, ensuring women are included in policy and research efforts to address orthopaedic trauma is essential. In a low-resource setting, efficiently distributing limited resources is necessary towards improving care. In this thesis, we identified regionally stratified priority fractures sustained by women and employed a sex lens in identifying critical deficiencies within current LMIC health care systems.

In chapter 2, we determined that the largest fracture burden facing women were among the elderly, especially hip fractures. However, among younger populations, tibia/fibula fractures were the most common. We illuminated regional differences for addressing fracture burden. This included that women in Africa were more commonly working age and sustained high levels of tibia/fibula and femur fractures. Foot/ankle fractures presented more frequently in Latin America, and spinal fractures were notably underrepresented outside of China. Deficiencies in health care systems were of particular interest, and included the low usage of ambulances globally, and a lack of health insurance, especially within Africa, India, and Other Asia. These distributional differences will aid towards targeting medical training and resources to corresponding high-volume areas.

In chapter 3, we found that sex was not a primary factor in determining hospital delay. Instead, the types and severity of injuries best predicted delay, including, hip, spine, closed fractures, and fractures caused by falling. Furthermore, we demonstrated a considerable need for improving ambulatory and referral systems within LMICs. Inter-hospital transfers represented the most commonly cited reason for delay. Regionally, the odds of delay were highest in India, Other Asia, and Latin America. Collectively, our data provide some of the first multi-national quantifications of hospital admission delay and suggests LMICs could substantially reduce burden by improving their referral systems.

Limitations

A major limitation of this thesis results from sampling error as ultimately patients were not sampled in a systematic way. Thus, the patients observed may be biased by the choice of hospitals included in this study. Also, we cannot observe patients who do not choose to seek treatment at a hospital. The inter-regional nature of this analysis further complicates our interpretations. We cannot rule out that some factors, for example, health insurance, represent different quantities in different regions. Thus, it is important to recognize the conclusions presented in this study may not fully reflect the whole population within all 17 LMICs, but instead provides a snapshot of the treatment priorities, and health care deficiencies of hospitals within similarly situated LMICs.

Future Directions

In the future, work should be done to quantify the impact of identified health system deficiencies on DALYs and mortality within orthopaedic trauma patients. In addition, it would be prudent to analyze how treatments of orthopaedic trauma vary globally, and the impact of these variations on cost and efficacy. Finally, while this thesis began to investigate sex-based inequalities, the question of whether women in LMICs are disadvantaged in receiving treatment for orthopaedic trauma remain incomplete. Further studies are warranted to elucidate if men and women are differentially treated once admitted to hospitals, or, are at greater risk for adverse outcomes. In addition, future research should be focused on analyzing the population of men and women who sustain injuries but do not seek treatment at hospitals. Ultimately, the goal of this thesis, and global surgery more broadly, is to ensure equitable and efficacious treatments for all. I am hopeful the work presented here will serve as a catalyst to support future research efforts, and ultimately evidence-based policies and clinical practices.

Appendix B:

Table B1: List of hospitals in study separated by country and region.

Hospital	Country	Region
Beijing Chaoyang Hospital	China	China
Langfang People's Hospital	China	China
Langfang Aidebao General Hospital	China	China
Second Bethune Hospital of Jilin University	China	China
Tianjin Hospital	China	China
Beijing Anzhen Hospital	China	China
Harbin Medical University Second hospital	China	China
Shenyang Orthopaedic Hospital	China	China
Hanzhong People's Hospital	China	China
Shanghai No.10 People's Hospital	China	China
Xiamen University affiliated First Hospital	China	China
The 2nd affiliated hospital of Wenzhou Medical University	China	China
Mulago Hospital	Uganda	Africa
Rift Valley Provincial General Hospital	Kenya	Africa
Kenyatta National Hospital	Kenya	Africa
Kiambu District Hospital	Kenya	Africa
AIC Kijabe Hospital	Kenya	Africa
Ondo State Trauma and Surgical Centre	Nigeria	Africa
National Orthopedic Hospital, Enugu	Nigeria	Africa
Princess Marina Hospital	Botswana	Africa
KATH, Kumasi	Ghana	Africa
Chris Hani Baragwanath Hospital	South Africa	Africa
Charlotte Maxeke Johannesburg Academic Hospital	South Africa	Africa
Helen Joseph Hospital	South Africa	Africa
KCMC - Kilimanjaro Christian Medical Centre	Tanzania	Africa
Sancheti Institute of Orthopaedics	India	India
Noble Hospital	India	India
Bharati Vidyapeeth University Medical College	India	India
Datta Meghe Institute of Medical Sciences	India	India
AIIMS	India	India
CMC Vellore	India	India
CMC Ludhiana	India	India
Indian Institue for Spinal Care	India	India
IGMC & RI	India	India
St. John's Medical College	India	India
Post Graduate Institute of Medical Education and Research	India	India

Baptist Christian Hospital	India	India
NHL Medical College	India	India
Northwest General Hospital & Research	Pakistan	Other Asia
Lumbini Medical College	Nepal	Other Asia
Cho Ray Hospital	Vietnam	Other Asia
Viet Duc Hospital	Vietnam	Other Asia
Ramathibodi Hospital	Thailand	Other Asia
Khon Kaen Hospital	Thailand	Other Asia
Philippine General Hospital	The Phillipines	Other Asia
University of Tehran	Iran	Other Asia
Hospital Civil de Guadalajara	Mexico	Latin America
Hospital Universitario de Caracas	Venezuela	Latin America

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