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A tale of three pandemics: Shining a light on a hidden problem

Simon Matthew Graham [a,b,c,d,e,i,*], *Maritz Laubscher* [c,d], *David G. Lalloo* [e,f], *William James Harrison* [g,i], *Sithombo Maqungo* [c,d,h]

[a] *Institute of Population Health, University of Liverpool, Liverpool, UK*
[b] *Liverpool Orthopaedic and Trauma Service, Liverpool University Teaching Hospital Trust, Liverpool, UK*
[c] *Division of Orthopaedic Surgery, Groote Schuur Hospital, Cape Town, South Africa*
[d] *Orthopaedic Research Unit (ORU), University of Cape Town, Cape Town, South Africa*
[e] *Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK*
[f] *Malawi-Liverpool-Wellcome Trust Clinical Research Programme, UK*
[g] *Department of Orthopaedic and Trauma Surgery, Countess of Chester Hospital, Chester, UK*
[h] *Division of Global Surgery, University of Cape Town, Cape Town, South Africa*
[i] *AO Alliance Foundation, Davos, Switzerland*

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ABSTRACT

An "epidemic" is an event in which a disease, infectious or non-infectious, is *actively* spreading within a population and designated area. The term "pandemic" is defined as "an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people".

The global response to the COVID-19 pandemic has not been seen since the outbreak of Human Immunodeficiency Virus in the early eighties. But there is another unseen pandemic running alongside the current COVID-19 pandemic, which affects a vast number of people, crossing international boundaries and occurring in every single country worldwide. The pandemic of traumatic injuries.

Traumatic injuries account for 11% of the current Global Burden of Disease, resulting in nearly 5 million deaths annually and is the third-leading cause of death worldwide. For every trauma-related death, it is estimated that up to 50 people sustain permanent or temporary disabilities. Furthermore, traumatic injuries occur at disproportionately higher rates in low- and middle-income countries, with approximately 90% of injuries and more than 90% of global deaths from injury occurring these countries.

Injuries are increasing worldwide, crossing international boundaries and affecting a large number of people, in the same manner Human Immunodeficiency Virus did in the 1980's and COVID-19 is today. The tremendous global effort to tackle the COVID-19 and Human Immunodeficiency Virus pandemics has occurred whilst ignoring the comparable pandemic of injury. Without change and future engagement with policy makers and international donors this disparity is likely to continue.

Introduction

An "epidemic" is an event in which a disease, infectious or non-infectious, is *actively* spreading within a population and designated area. The term "pandemic" is defined as "an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people".[1] Therefore classical definition of a pandemic includes nothing about population immunity,

* *Corresponding author*. Institute of Population Health, University of Liverpool, Liverpool, UK.
E-mail address: S.M.Graham@liverpool.ac.uk (S.M. Graham).
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virology, microbiology or disease severity, but relates to geographic spread of a disease.[1]

The global response to the COVID-19 pandemic has not been seen since the outbreak of Human Immunodeficiency Virus (HIV) in the early eighties. But there is another unseen pandemic running alongside the current COVID-19 pandemic, which affects a vast number of people, crossing international boundaries and occurring in every single country worldwide.

The current pandemic: COVID-19

On 31 December 2019, the World Health Organizaton's (WHO's) Country Office in the People's Republic of China picked up a media statement by the Wuhan Municipal Health Commission from their website on cases of "viral pneumonia" in Wuhan, People's Republic of China.[1] On 11 February 2020, WHO announced, in the *International Classification of Diseases*, "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" as the name of the new virus causing the outbreak. This name was chosen because the virus was genetically related to the coronavirus responsible for the 2003 outbreak of severe acute respiratory syndrome (SARS). Subsequently, WHO announced "COVID-19" as the name of this new disease associated with SARS-CoV-2 infection. COVID-19 was declared a global pandemic by WHO on 11 March 2020 and their Director-General reported that Europe had become the epicentre of the pandemic, with more reported cases and deaths than the rest of the world combined, excluding the People's Republic of China.[1] To date there have been over 90 million reported cases of COVID-19 and over 2 million deaths worldwide.[2]

SARS-CoV-2 spreads through contact, and longer-range transmission via aerosols, especially in conditions where ventilation is poor.[3] Its high infectivity, combined with the susceptibility of unexposed populations to a new virus, creates conditions for rapid transmission. As a result, it spread to every corner of the earth in a matter of months.

With the threat of overwhelming health services, COVID-19 has heavily impacted all aspects of medical practice worldwide, including orthopaedic and trauma surgery. As well as postponement of elective orthopaedic services, the management of emergent and urgent surgical cases has been affected.[4,5] There has been a continuous need to address and apply daily new information and to integrate it into our routine surgical practices, including multiple new and changing guidelines, pathways and policies. Furthermore, the orthopaedic literature has never seen such an influx of scientific publications in one single area within such a short space of time. In the last 6 months (August 2020 to January 2021), there have been have been five published papers, two editorials and one infographic on topics related to COVID-19 and orthopaedic surgery in our leading United Kingdom (UK)-based orthopaedic journal, the *Bone and Joint Journal*.[5–12] In fact, since the start of the pandemic in March 2020, there have been 60 published paper, annotations or infographics across the *Bone and Joint Journal* and *Bone and Joint Open Journal* platforms (search 12th January 2021). This is a highly commendable achievement by the orthopaedic community, that reflects our endeavour to provide the best care for our patients, driven by evidence-based medicine.

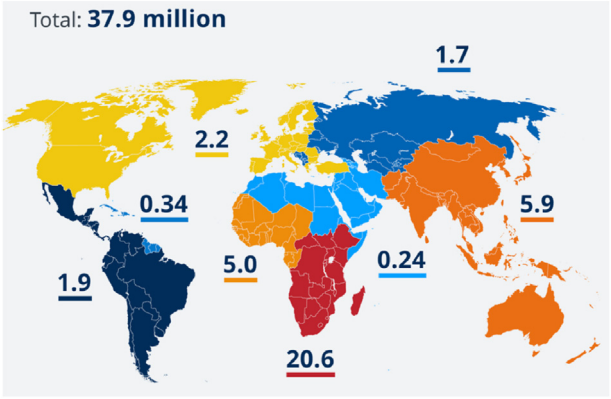

Fig. 1 – The estimated number of people living with HIV around the world in 2018 – World Health Organization.[21] Numbers represent the individual number of people.

The pandemic is still in various stages in different countries and despite the roll-out of a vaccine throughout the UK, the world has a long way to go before life returns to anything resembling "normal".

The forgotten pandemic: Human Immunodeficiency Virus

During the current global COVID-19 pandemic, it is easy to forget that this is not the first time that the world has been gripped by such a pandemic caused by a virus. In the 1980s, a mysterious illness swept throughout the world, resulting in those afflicted becoming emaciated, prematurely ageing and often developing dark purple lesions on their arms and faces, due to a relatively rare and aggressive form of cancer called Kaposi's sarcoma. Physicians were baffled, and fear spread through society. Almost without fail, patients experienced a rapid downhill course and death, as their doctors vainly treated one opportunistic infection after another.

The outbreak of acquired immunodeficiency syndrome (AIDS) officially began on 5 June 1981, when the United States Centers for Disease Control and Prevention (CDC) reported unusual clusters of pneumocystis pneumonia caused by a form of *Pneumocystis carinii*, in five homosexual men in Los Angeles.[13] In June 1982, a report of a group of cases among gay men in Southern California suggested that a sexually transmitted infectious agent might be the cause, and the syndrome was initially termed "GRID", or gay-related immune deficiency.[14] Health experts soon realized, however, that nearly half of the people identified with the syndrome were not homosexual men. The same opportunistic infections were also reported among individuals suffering from haemophilia, intravenous drug users (heroin users), and Haitian immigrants – leading some researchers to call it the "4H" disease.[15] By August 1982, CDC renamed the disease as AIDS.[16]

The isolation of HIV enabled development of the first blood test in 1985,[17] and Margaret M. Heckler, then US Secretary of Health and Human Services, predicted in 1984 that a vaccine

against HIV would be available within 2 ;years. However, it was over 15 years until anti-retroviral therapy (ART) was introduced for treatment of HIV and, over 35 years on, no vaccine is in sight.[18,19] By contrast, this highlights the tremendous achievement of the rapid approval of the Pfizer and AstraZeneca vaccines against COVID-19 within 10 months of a global pandemic being declared by WHO.

Technically, according to WHO the HIV outbreak is now a "global epidemic" rather than a pandemic, although it has been argued otherwise by some researchers.[20] Globally, an estimated 36.9 million people were living with HIV in 2017.[21] (Fig. 1) Ninety-one percent of the people living with HIV are from a low- or middle-income country (LMIC).[22] Sub-Saharan Africa (SSA), particularly southern Africa, has the highest global burden of HIV, with 70.8% of HIV-infected people on the planet living in this region, but no region is spared.[21]

Following the introduction of ART in 1997, the course and nature of disease in individuals infected with HIV changed, with an increased duration of asymptomatic infection, and consequently, patients with HIV are attaining close to normal life spans.[18,19] With increases in the number of people globally having access to ART, the number of people dying from HIV is decreasing. Therefore, although infection rates have been shown to be going down in some countries,[21] the number of people actually living with HIV is not, and the prevalence is even increasing in some areas of South Africa.[23]

HIV and its treatment have both been shown to result in a number of musculoskeletal manifestations, including a reduction in bone mineral density (BMD), bone mineralisation and bone turnover, causing osteoporosis as well as osteonecrosis, particularly of the femoral head.[24–29] Concerns regarding potential problems with HIV-positive patients undergoing fracture fixation were first brought to light in the mid-1990s.[30] It was suggested that "early experience showed that closed fractures healed normally, the risk of sepsis during osteosynthesis was increased and most open fractures became septic".[30] Over the next 25 years, basic science research suggested that HIV infection may be associated with delayed union and non-union of fractures.[31] A number of small underpowered clinical research studies highlighted that caution should be used when considering the use of internal fixation in managing HIV-positive individuals following a fracture and that the removal of all such implants in HIV-positive individuals should be considered.[30,32–35] Other researchers have disputed these high risks of implant and wound infection.[36–39] However, in high-income countries (HICs), such as the UK and United States, some textbooks and websites used by surgeons to provide the basis of orthopaedic and fracture care knowledge report that HIV increases the risk of non-union[2] (orthobullets.com, accessed 11.1.20) and results in problems of wound infections[40] (Miller – Review of Orthopaedics, 6th edition 2012) following fracture surgery. Newer editions of some textbooks have updated this information[41] (Miller – Review of Orthopaedics, 7th edition 2016) but this has still resulted in circulation of conflicting information.

Despite inconsistent evidence, few researchers have thoroughly investigated the true effect of HIV on fracture healing and the subsequent risk of implant sepsis and wound infection. Therefore, although in the modern world of evidence-based medicine, up until recently our current opinions of the best approach to the management of a fracture in an individual who is HIV positive have been based on "expert opinion", "case reports" and underpowered studies rather than higher levels of evidence. Recently, the HIV in Orthopaedic Skeletal Trauma (HOST) Study (ClinicalTrials.gov Identifier: NCT03131947),[42] funded by the Wellcome Trust, confirmed that HIV is not an independent risk factor for the development of delayed union, non-union or infection following fracture surgery.[61]

The delay in undertaking adequate research into the impact of HIV on fracture surgery can most likely be explained by the fact that 90% HIV cases are in LMICs. The prevalence of HIV across South Africa is 18.9%[43,44] but much lower in the UK (0.17%).[45] If nearly 20% of the trauma patients presenting for fracture surgery in the UK were HIV positive, would it have taken over 25 years since concerns were first raised by the orthopaedic community to bring this level of evidence to light? This highlights another health problem which is 90% distributed in LMICs and causes a far greater global impact than the HIV pandemic. It also accounts every year for more than twice the annual deaths that the COVID-19 pandemic has sadly accounted for in the last twelve months. This is the hidden global pandemic of injury.

The hidden pandemic: injury

Traumatic injuries account for 11% of the current Global Burden of Disease (GBD), resulting in nearly 5 million deaths annually.[46] By 2022, traumatic injuries will be the third-leading cause of death worldwide. For every trauma-related death, it is estimated that up to 50 people sustain permanent or temporary disabilities.[47,48] The leading cause of injury is from road traffic collisions and the number of road traffic injuries and deaths have been increasing over the last three decades.[49] Therefore, injury is increasing worldwide, crossing international boundaries and affecting a large number of people, in the same manner HIV did in the 1980's and COVID-19 is today.

Traumatic injuries occur at disproportionately higher rates in LMICs, with approximately 90% of injuries and more than 90% of global deaths from injury occurring these countries.[47,50,51] Nearly one billion people sustain traumatic injury that requires health-care treatment annually, resulting in more than 220 million disability-adjusted life years (DALYs) lost each year in LMICs.[47] With the majority of injuries occurring in young working aged males, this results in a significant socioeconomic impact not only on the patient, but also their family and community in LMIC. Population-based surveys have demonstrated that nearly 1% of the population in some countries in sub-Saharan Africa suffer from injury-related disability.[52,53] Musculoskeletal injuries account for the majority of these injuries, with over 130 million musculoskeletal bone fractures per year and 78% of injury-related disabilities due to musculoskeletal extremity injuries.[47]

Despite this large burden of death and disability from traumatic injury, there has been little policy, research or funding invested in addressing this clearly neglected worldwide problem. The amount of funding, infrastructure and research devoted to traumatic injury is infinitesimally small in comparison to other significant global health problems, such

as HIV/AIDS (excluding orthopaedic surgery and HIV!), malaria and TB, despite injuries causing more deaths than these communicable diseases combined.[47,54] (Fig. 2) As a result, little is known about the burden, health-care provisions and health-care systems or the longer-term consequences and wider impact of traumatic injuries in LMICs.

To give a true picture of the disparity in the burden of disease and provisions available to treat traumatic injuries, it is helpful to consider simple comparisons. Malawi, a low-income country in sub-Saharan Africa, has some of the highest rates of road traffic injuries compared to anywhere else in the world and serves a population of 18 million people. It has just 14 orthopaedic trauma surgeons, 11 of whom are in regular clinical practice. The department of orthopaedic surgery at Liverpool University Teaching Hospital Trust, which does not even serve the entire population of Liverpool (population 496,784), has 52 orthopaedic consultants. It does not take an epidemiologist or health economist to do the maths to see the disparity in services and provision for trauma care.

Considerable progress has been made in the treatment of traumatic injuries in HICs, owing to a combination of injury prevention and improved trauma care. As a result, the rates of traumatic injury have been decreasing in HICs.[48] In contrast, rates of traumatic injury-related death and disability have been steadily rising in the majority of LMICs.[52]

Evidence indicates that well-organized trauma care can save lives and reduce morbidity once injury has occurred.[55,56] Much of the evidence from HICs relates to organizational and administrative aspects that could be implemented with limited input of new material resources: these include planning of systems for trauma management (e.g. regulation to designate trauma centres, pre-hospital triage protocols, and transfer criteria), and verification and accreditation of trauma care services.[57,58] Furthermore, WHO has also highlighted that improving the organization, planning and access to trauma systems, including prehospital, hospital-based and after-care and rehabilitation can save lives and reduce morbidity resulting from traumatic injuries.[1,59,60] It is now essential that these health-care improvements are translated to low-income settings, in order to make positive steps towards improving the outcome of individuals suffering from traumatic injuries across the world and progress towards the Sustainable Development Goals set out by the United Nations in 2015, especially Goal 3: "Ensure healthy lives and promote well-being for all at all ages".

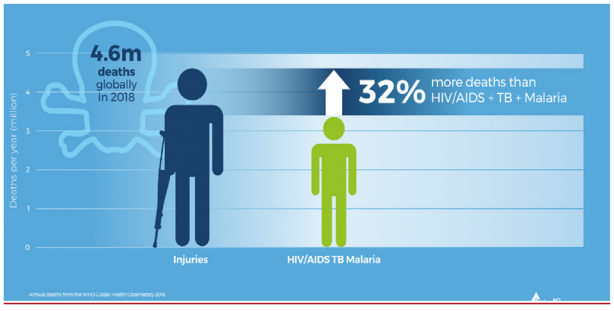

Fig. 2 – Deaths from injuries far outnumber deaths from communicable diseases. From the WHO Global Health Observatory 2018.

Conclusion

It can be easy to ignore something that we cannot see, does not impact us in our daily lives and we cannot fix with a hammer. Whose responsibility is it to highlight and bring to the forefront the neglected global issue of trauma and injuries? There is no Bill and Melinda Gates Foundation dedicated to eradicating injuries from the planet. There are no celebrities like Madonna or Angelina Jolie advocating for improved trauma care and prevention in LMICs. As a global orthopaedic community, are we perpetuating injustice for our fellow citizens living in countries less fortunate than our own? Only we can answer that, but the tremendous global effort to tackle the COVID-19 and HIV pandemics has occurred whilst ignoring the comparable pandemic of injury. Without change and future engagement with policy makers and international donors this disparity is likely to continue.

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