Opportunities for health system strengthening to reduce preventable trauma deaths in the Western Cape Province, South Africa: Findings from an expert panel review

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Background. Injuries are a leading cause of death and disability worldwide, and disproportionately affect young persons (aged 15 - 49 years) residing in low- and middle-income countries. Panel reviews of trauma deaths are an effective way to identify areas for improvement within a health system.
Objectives. To assess the preventability of trauma deaths that had contact with the health system, and the associated panellists' recommendations for improvements.
Methods. A comprehensive review of injury-related deaths identified by an epidemiological study was conducted in the Western Cape Province of South Africa in April 2022. Panellists identified contributing factors and opportunities for improvement for each case. Investigators assigned a thematic code to each opportunity for improvement, and codes were categorised and mapped into a matrix organised according to the applicable level of the health system and the descriptive category for improvement.
Results. Twenty-three multidisciplinary expert panellists reviewed 90 injury deaths that occurred in 2021. The largest proportion of deaths was from firearms (30%), and 41 (45%) of the 90 cases were found to be preventable or potentially preventable. The median time from injury to death was 41.4 hours for rural injuries, compared with 12.9 hours for urban injuries.
Conclusion. Key recommendations from the panel included training in basic trauma resuscitation, and increased access to patient monitoring, operating theatres, radiology and intensive care beds. Panellists further recommended implementation of injury primary prevention strategies in the community.

Keywords: trauma, interpersonal violence, preventable trauma death review, injury-related death, health system improvement

S Afr Med J 2026;116(4):e3030. https://doi.org/10.7196/SAMJ.2026.v116i4.3030

Injury deaths disproportionately affect young persons, and account for >2 million deaths annually in people aged 15 - 49 years.[1] It is estimated that an additional 10 million people per year worldwide are disabled from injuries.[2] Road traffic injuries and interpersonal violence are among the top 20 causes of death globally, and have a high socioeconomic impact on people living in low- and middle-income countries (LMICs): the individuals injured as well as the health system as a whole.[1,2]

South Africa (SA) is an upper-middle income country that shoulders a particularly large burden of injury-related death and disability.[3] Almost half of injury-related deaths within SA are from intentional injuries, with road traffic injuries accounting for an additional 25%.[3] Gang violence, access to firearms and alcohol have all been found to be major contributing factors toward intentional injuries.[3,4] Alcohol is a compounding factor in motor vehicle injuries, with almost half of all motor vehicle-related deaths within SA involving alcohol-intoxicated drivers.[5]

The trauma referral pathway in the Western Cape Province of SA includes three major tiers: district, regional and tertiary hospitals. Rural district hospitals are staffed by medical officers and family medicine specialists with limited access to point-of-care laboratories and X-rays.[6] Regional hospitals and some urban district hospitals are predominantly staffed by medical officers or emergency medicine registrars, with an on-call emergency medicine consultant. These hospitals have 24-hour access to general surgical capabilities and weekday access to computed tomography (CT) and ultrasound. Tertiary hospitals have specialty trauma and surgical services as well as 24-hour access to diagnostics. Emergency medical services (EMS) transports patients to the nearest facility, where the patient is evaluated and stabilised and transferred to higher levels of care as needed.[7]

Data from high-income countries show worse outcomes for rural v. urban motor vehicle injuries.[8,9] One SA study found increased mortality in rural gunshot head-injured patients (36% rural v. 9%

urban mortality).[10] Another SA study found the odds of death for elderly trauma patients was 2.5 times higher in rural v. urban areas.[11] Explanations for worse outcomes in rural injured patients are multifactorial, including potentially prolonged response times and longer times to arrival at a tertiary centre. However, there are limited data exploring and identifying the underlying factors that may contribute to worse outcomes in rural injured patients.

A multidisciplinary approach is required to strengthen trauma care in LMIC health systems, and proposed solutions must address the spectrum of care, including prehospital response, emergency resuscitation, definitive operative management and critical care.[12] Multidisciplinary expert panel reviews are an effective and efficient strategy to identify modifiable factors contributing to preventable trauma deaths. The qualitative and quantitative data that emerge from these reviews inform strategies for health systems strengthening. Recommendations may focus on improvements to care processes, such as the approach to triage, and addressing critical resource shortages, with the ultimate goal of reducing deaths from preventable causes.[12]

In 2022, a multidisciplinary panel of clinicians within the Western Cape Province convened to review a cohort of trauma deaths with the goal of determining preventability and making recommendations for the health system. Here we present findings from that panel, with a focus on deaths that occurred after contact with the health system, either a government ambulance or a government health facility. The detailed methods and results from the 2022 panel review, inclusive of trauma deaths that had no contact with the health system, were published separately.[13] The objective of this article is to assess the preventability of trauma deaths that had contact with the health system, and the associated panellists' recommendations for improvements within the health system.

Methods

Setting

The Epidemiology and Outcomes of Prolonged Trauma Care (EpiC) study enrolls injured patients from the 'Eastern' trauma referral pathway in the Western Cape, which includes both the Cape Winelands District Municipality (rural) and the City of Cape Town Municipality (metro). Within the referral pathway, injured patients progress through a tiered health system, including the rural sites Ceres District Hospital, Worcester Regional Hospital, Western Cape Government EMS (WCG EMS) bases and Worcester Forensic Pathology Service Laboratory, and the urban sites Tygerberg Hospital (trauma referral centre), Khayelitsha District Hospital, WCG EMS bases and Tygerberg Forensic Pathology Service Laboratory. Of note is that by law, all injury-related deaths have an autopsy performed, with a detailed postmortem report.[14]

Inclusion and exclusion criteria

All decedents captured by the EpiC study between 1 January 2021 and 31 December 2021 were eligible for panel review. The EpiC study, and consequently this panel, excluded the following categories of decedents:[15]

- age <18 years
- prisoners
- injury from stings
- envenomations
- toxicological exposures
- drownings
- received care at a non-study site
- transported via private EMS (non-WCG EMS)
- made first contact with the health system >24 hours after sustaining the injury.

While the full panel review also included a subset of decedents who were declared dead-on-scene (non-EpiC), this article focuses only on decedents who survived long enough to make contact with the health system, either a government ambulance or a government health facility.

Study design

This was a multi-methods study in which patient data from clinical cases were analysed quantitatively and expert panel recommendations were analysed qualitatively.

The preventable death panel was hosted as an in-person technical meeting over a 2-day period in April 2022. The multidisciplinary expert panel included 23 clinical providers practising within the Western Cape, representing a broad range of specialties, including paramedics and physician specialists in family medicine, emergency medicine, trauma surgery, neurosurgery, intensive care and burns and forensic pathology. Experts represented both the metro and Winelands regions, and all tiers of facility care from district to tertiary. The 23 panellists were invited because they worked within the facilities from which the death cases were drawn, and also because they possessed the relevant clinical expertise.

Prior to the meeting, panellists were each assigned 8 - 10 cases to review and provided with the complete medical records, including prehospital and hospital clinical notes, and radiology, laboratory and postmortem reports. On the day of the preventable death review, panellists were divided into two groups, intentionally assigned to ensure balanced representation of specialists and location of practice. Panellists then presented the clinical course, including the postmortem findings, of each case to the group. Full medical records were available for reference during the panel review. Preventability was categorised as: preventable; potentially preventable; non-preventable; non-preventable with improved care; or indeterminate, defined using previously reported international guidelines and within the context of the local health system (Appendix Table S1). Panellists voted on a category of preventability for each case, with consensus required, which was defined *a priori* as 80% agreement. After each vote, panellists also engaged in a robust discussion to identify actionable opportunities for improvement. Research personnel took detailed notes on factors contributing to the death, and recommendations made.

Data analysis

Quantitative analysis

Patient and injury characteristics were analysed using descriptive statistics. Frequencies and percentages were reported for categorical variables; medians and interquartile ranges were reported for continuous variables. We performed Fisher's exact tests to compare urban and rural deaths for the entire cohort. Mann-Whitney tests were used to compare continuous characteristics for urban and rural injuries. Time from injury to health system event was used to calculate median times to events, including death. Patients with a missing time of injury were excluded from our reporting on median time from injury to EMS arrival and hospital arrival. Time of hospital arrival was used for patients with missing injury event time as a data substitution method to enable calculation of a median time to operating theatre (OT), to help reduce bias due to the small number of patients receiving operative interventions and dying, given this was the primary outcome for all cases. All analyses were conducted using SAS software (version 9.4, SAS Institute Inc., USA).

Qualitative analysis

A rapid qualitative analysis of factors contributing to death and recommendations for improvement was performed using the detailed notes from the expert panel's discussion on each case. A matrix

of health system levels and strategic domains was developed with stakeholder input before the mortality review (Appendix Table S2). Notes were reviewed by two co-investigators (JD, NM), and descriptive codes were mapped to the matrix and consolidated into themes by consensus, and analysed by a system level of recommendation.[16]

Ethical approval

Study activities were approved by the Health Research Ethics Committee at Stellenbosch University (ref. no. N20/03/036), the individual health facilities, the Western Cape Provincial Health Research Committee, the Colorado Multiple Institutional Review Board (COMIRB) and the Defense Health Agency Research and Development Office of Human Research Oversight (OHRO). A waiver of informed consent was used for this study, as approved by Stellenbosch University Human Research Ethics Committee.

Results

The EpiC study identified 109 health system deaths that were eligible for expert panel review. Nineteen were excluded owing to incomplete clinical records at the time of review. A total of 90 health system cases were reviewed by the expert panel. The median age of decedents was 32 years, and most were male (86%) (Table 1). The majority (*n*=76, 84%) of injuries occurred in the Cape Town metro region, and 14 (16%) occurred in the Cape Winelands rural region. There were comparable proportions of blunt injuries (44%) and penetrating injuries (42%). Firearms were the leading mechanism of injury, leading to 30% of deaths. Other leading fatal mechanisms of injury included: vehicular, including pedestrian v. auto (23%); interpersonal blunt trauma, including community assault (18%); and interpersonal penetrating trauma, including stabs (17%) (Table 1).

Preventability

Of all 90 health system deaths reviewed, 41 (45%) were considered preventable or potentially preventable. One death was classified as indeterminate owing to a lack of clinical documentation. All reviewed cases reached consensus during panel voting. There was no significant difference in the proportion of preventable plus potentially preventable deaths when comparing urban (46%) v. rural (43%) injured patients (Table 1).

Time to death

Injury time was available in 73 (81%) of the reviewed cases. Of those, 68 (93%) were transported by EMS. For patients with injury times, the median time to scene contact with EMS was 0.4 hours in urban and 0.6 hours in rural injuries. Time from injury to hospital arrival was longer in urban (1.5 hours) than rural (0.7 hours) injuries. Among patients with a known injury time, the median time from injury to

Table 1. Characteristics of cohort with comparison of urban v. rural location of injury (*N*=90)

Characteristic	Contact with health system, *n* (%)*	Urban injury, *n*=76, *n* (%)*	Rural injury, *n*=14, *n* (%)*	*p*-value
Age, median (IQR)	31.7 (27.1 - 51.5)	32.6 (27.9 - 39.4)	30.6 (26.0 - 43.3)	0.66†
Sex				0.12‡
Male	77 (85.6)	64 (84.2)	13 (92.9)	
Female	13 (14.4)	12 (15.8)	1 (7.1)	
Injury force type				0.13‡
Blunt	40 (44.4)	35 (46.1)	5 (35.7)	
Penetrating	38 (42.2)	31 (40.8)	7 (50.0)	
Blunt and penetrating	5 (5.6)	5 (6.6)	0 (0.0)	
Others	7 (7.8)	5 (6.6)	2 (14.3)	
Injury mechanism				0.09‡
Firearm	27 (30.0)	23 (30.3)	4 (28.6)	
Stab/cut	15 (16.7)	12 (15.8)	3 (21.4)	
Struck/hit	16 (17.8)	12 (15.8)	4 (28.6)	
Vehicular injury	21 (23.3)	21 (27.6)	0 (0.0)	
Others	11 (12.2)	8 (10.5)	2 (21.4)	
Physiological cause of death				0.96‡
Catastrophic tissue destruction	16 (17.8)	14 (18.4)	2 (14.3)	
Central nervous system	19 (21.1)	15 (19.7)	4 (28.6)	
Haemorrhage	19 (21.1)	17 (22.4)	2 (14.3)	
Multiple organ failure	19 (21.1)	16 (21.1)	3 (21.4)	
Other§ and comorbidities	17 (18.9)	14 (18.4)	3 (21.4)	
Preventability				0.29‡
Preventable	10 (11.1)	9 (11.8)	1 (7.1)	
Potentially preventable	31 (34.4)	26 (34.2)	5 (35.7)	
Non-preventable with improvements in care	26 (28.8)	19 (25.0)	7 (50.0)	
Non-preventable	22 (24.4)	21 (27.6)	1 (7.1)	
Indeterminate	1 (1.1)	1 (1.3)	0 (0.0)	

IQR = interquartile range.
*Unless otherwise indicated.
†Mann-Whitney test.
‡Fisher's exact test.
§Other includes airway, breathing, lung (i.e. penetrating lung injury impairing airway and breathing with haemorrhage), cardiac tamponade, tension pneumothorax, pulmonary embolism, full thickness burn/incineration, physiological collapse, sequelae of injury, other (including iatrogenesis).

death was longer in rural injuries (41.4 hours) than urban injuries (12.9 hours) (Fig. 1, Appendix Table S3). Eleven (12%) patients had a surgical procedure: median time to the OT was 12.3 hours for urban injuries v. 2.3 hours for one rural decedent who had surgery at the rural regional facility.

Health system location and cause of death

Among deaths with a known injury time (*n*=73), timing of death after injury followed a bimodal distribution, with the largest proportion (33%) occurring within 6 hours of injury, followed by (28%) occurring >48 hours after injury. Among deaths that occurred >6 hours after injury, nine (15%) occurred in the emergency centre at the first facility. Three (3%) deaths that occurred between 24 and 48 hours after injury were in the second facility emergency centre, and one death that occurred after 48 hours was in the first facility emergency centre (EC) (Fig. 2).

Among all health system deaths, almost half (*n*=41, 46%) occurred in the EC, followed by 31 (34%) in the intensive care unit (ICU), 10 (11%) in the ward, 6 (7%) during EMS transport and 2 (2%) in the OT (Fig. 2). Deaths that occurred in the EC were most frequently due to haemorrhage (*n*=13, 32%), compared with deaths in the ICU and ward that were most frequently due to multi-organ failure and sepsis (*n*=12 (39%) and *n*=4 (40%), respectively) (Table 2).

Health system recommendations for improvement

The qualitative matrix used to code the panel recommendations was organised into health system categories, including providers, hospital units, facilities and community. Within each major category, core themes emerged regarding recommendations for improvement (Fig. 3). Each of the core recommendations was reflected in the panel discussions on multiple cases, and felt to be a significant contributing factor in the death, regardless of preventability.

At the provider level (e.g. doctors and nurses), the first core recommendation was training in basic trauma resuscitation, and implementing standard protocols focusing on head injuries, haemorrhage and crush injury. These recommendations were based on common qualitative codes addressing opportunities for improvement that included gaps in early resuscitation and lack of timely recognition of life-threatening injuries. There were multiple cases that identified a lack of knowledge by healthcare providers in early resuscitation, and poor recognition of abnormal vital signs. Additionally, the panel recommended protocols, strategies and training that will empower and enable providers to identify patients who are appropriate for palliative care. This specific recommendation is driven by the panel's recognition of the burden on the health system from many severe injuries that experience delays in diagnosis, and the need to provide prognostication and standard palliative care protocols in settings with limited diagnostic tools.

Strengthening team-based care was an overarching recommendation at the hospital unit level, including the EC, ICUs and wards. For the EC, the discussion focused on a lack of ability to monitor patients, as well as inadequate staffing. Another frequent recommendation was to improve prehospital notification by EMS to the EC to allow the receiving hospitals to better prepare for receiving critically injured patients. Panellists noted that this system does exist, but is not used consistently.

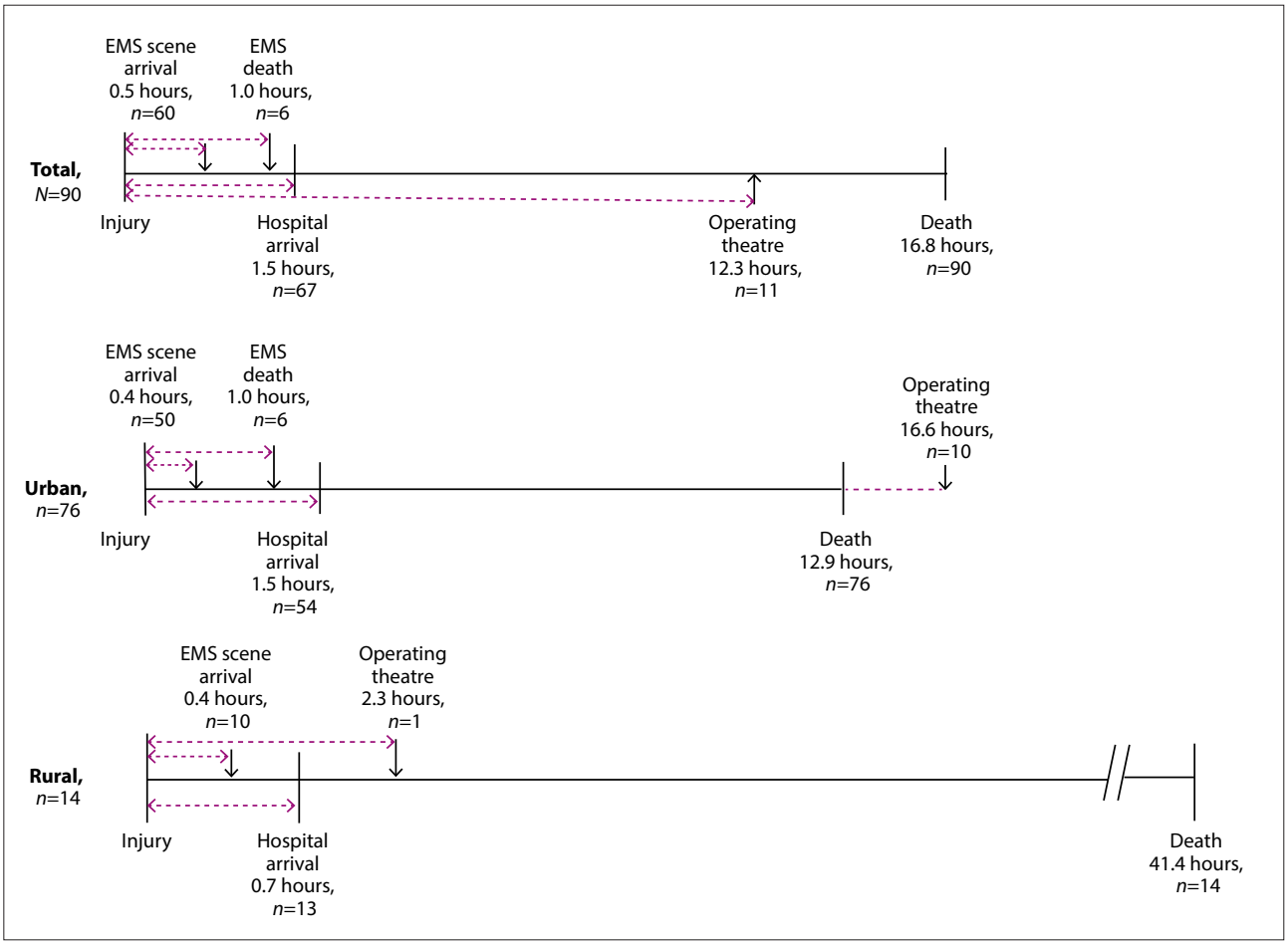

Fig. 1. Injury time to hospital arrival and death in urban v. rural injuries. (EMS = emergency medical services.)

At facility level, the panellists discussed the need to improve access to radiology (X-ray and CT) at both the district and the tertiary level. There are often significant delays in diagnosis when patients require transfer from district and regional hospitals, and further delays when the patients arrive at the tertiary hospital and wait for diagnostic imaging. Once this diagnostic imaging has been obtained, the panel also cited limited access to specialist care, particularly neurosurgery and critical care. The panellists felt that decreasing the time to radiology and specialist care could relieve unnecessary referrals and lessen the case burden at the tertiary facilities through earlier diagnosis and risk stratification.

There was unanimous agreement among the panellists that primary prevention of traumatic injuries is key in reducing deaths from injury. The panel noted that inadequate road safety or interpersonal violence played a role in almost every death reviewed. Community-based interventions to improve road safety, particularly for pedestrians, are needed. The panellists recognised the need to engage additional stakeholders, including public health specialists, to generate actionable recommendations and interventions to reduce the burden of interpersonal violence.

Discussion

This multidisciplinary expert panel review of adult trauma deaths from a cross-section of the Western Cape's Eastern trauma referral drainage zone was the first in the region. In summary, of the 90 cases reviewed, 45% were considered preventable or potentially preventable, with the largest proportion of deaths occurring within 6 hours of injury. Key areas for improvement included medical team knowledge and communication, timely access to diagnostic testing and definitive surgical care, formation of palliative care protocols for end-of-life care and implementation of primary prevention strategies in the community. The quantitative and qualitative findings, when considered together, signal actionable opportunities for health system strengthening to help avert future trauma deaths.

Regarding hospital-based interventions, the panel recommended improving quality of care by targeting early resuscitation guidelines

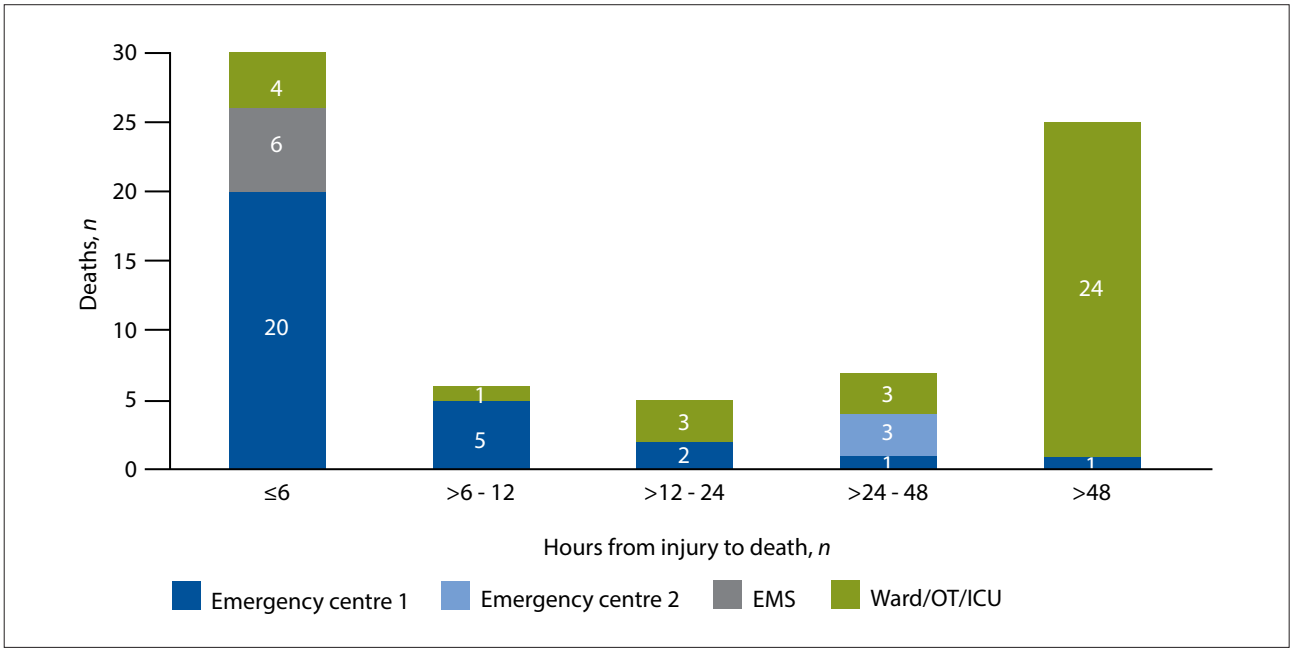

Fig. 2. Health system unit where death occurred, and hours since injury. (EMS = emergency medical services; OT = operating theatre; ICU = intensive care unit.)

Table 2. Health system location of death and timing or physiological cause of death

	Location of death, *n* (%)				
Variable	**EMS**	**EC**	**OT**	**ICU**	**Ward**
Time to death from contact with health system, hours					
≤6	6 (100.0)	25 (61.0)	1 (50.0)	5 (16.1)	0 (0.0)
>6 - 12	0 (0.0)	6 (14.6)	1 (50.0)	1 (3.2)	0 (0.0)
>12 - 24	0 (0.0)	7 (17.1)	0 (0.0)	2 (6.5)	0 (0.0)
>24 - 48	0 (0.0)	2 (4.9)	0 (0.0)	4 (12.9)	1 (10.0)
>48	0 (0.0)	1 (2.4)	0 (0.0)	19 (61.3)	9 (90.0)
Physiological cause of death					
Catastrophic tissue destruction	1 (16.7)	8 (19.5)	0 (0.0)	7 (22.6)	0 (0.0)
Central nervous system	0 (0.0)	8 (19.5)	0 (0.0)	9 (29.0)	2 (20.0)
Haemorrhage	3 (50.0)	13 (31.7)	1 (50.0)	2 (6.5)	0 (0.0)
Multi-organ failure + sepsis	0 (0.0)	2 (4.9)	1 (50.0)	12 (38.7)	4 (40.0)
Other and comorbidities	2 (33.3)	10 (24.4)	0 (0.0)	1 (3.2)	4 (40.0)

EMS = emergency medical services; EC = emergency centre; OT = operating theatre; ICU = intensive care unit.

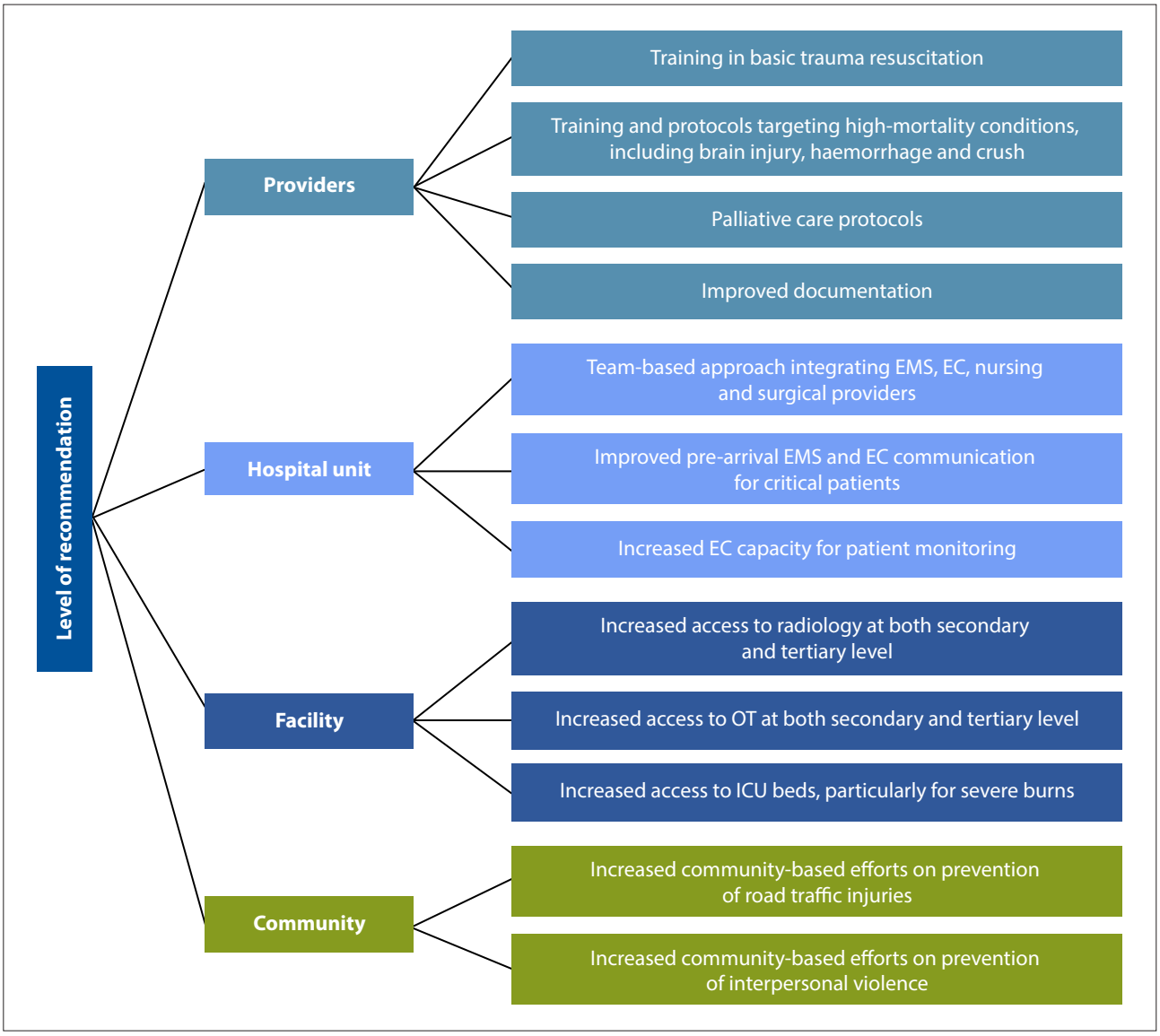

Fig. 3. Key recommendations from the panel. (EMS = emergency medical services; EC = emergency centre; OT = operating theatre; ICU = intensive care unit.)

and recognition of the decompensating patient, with a focus on a team-based approach. This aligns with recommendations for all health systems from a White Paper by the International Federation for Emergency Medicine, which advocates for education initiatives among frontline providers with an emphasis on protocols for resuscitation and emergency response.[17] While SA has a strong emergency medicine physician training system, rural and regional hospitals are often staffed with non-specialist providers who may benefit from further education on trauma resuscitative care.

Early resuscitative care is a team approach and places an emphasis on nursing training and staffing for effective team-based management.[17] There is large support around the World Health Organization-supported basic emergency care course in successful knowledge transfer and application in LMICs.[18] Because trauma resuscitation is dynamic in nature, a patient arriving with normal vital signs can quickly decompensate, requiring a rapid response for stabilisation. Monitoring systems must be in place to alert the provider teams, to ensure quick and effective resuscitation of the acutely decompensating patient, especially in ECs, where 46% of deaths occurred in the present study. An expert panel in Ghana developed consensus trauma care audit filters using the Delphi technique, and emphasised the use of physical examination and serial re-assessments along with a rapid and targeted referral process once transfer need is established.[19] The Ghana panellists placed particular importance on team-based communication surrounding these transfers.[19] These recommendations are relevant to all health systems, and particularly those in LMICs with limited resources.

Regarding diagnostics and surgical interventions, the panel suggested increased access to diagnostic imaging as well as definitive surgical services at strategic locations within the tiered hospital system to promote the greatest impact on patient care. While SA has a robust trauma system to provide definitive management at their tertiary centres, the referral system acts like a funnel, moving patients from stabilisation sites, where access to diagnostic imaging and definitive operative care is lacking, into the tertiary care locations. This was most notable among the 21% of patients who died from central nervous system injuries. For example, a patient sustaining a blunt intracranial injury who arrives at a district hospital after business hours may be unable to have a CT scan or operative management such as a craniotomy performed, but instead must be transferred to the tertiary centre for

imaging and management, thus leading to a prolonged time from injury to definitive care. This is one potential explanation for the increased time to death in rural v. urban injuries. Urban injuries potentially had a shorter time to diagnostics, facilitating a timely decision regarding intervention, compared with the rural setting, where there is prolonged time to diagnostics leading to the transfer of patients with unidentified catastrophic injuries. Additionally, the high volume of undifferentiated transfer patients often strains the resources available at tertiary care centres. This highlights the opportunity for improvement in making diagnostic imaging and access to definitive care more widely available in district and rural hospitals, thus offloading the demand on tertiary centres and distributing resources more equitably within the system. More guidance is needed on the type of resources needed at different levels in the health system, to guide not only the Western Cape system but all tiered systems globally.

Regarding palliative care, at least one in five of this study's decedents died from catastrophic tissue destruction, which is non-survivable and warranted palliative care. Panellists suggested the creation of formal, system-wide palliative care protocols to improve end-of-life care, while decreasing the burden on the healthcare system due to unnecessary transfers. This is a very difficult and ethically challenging proposal, and would need multifactorial input from healthcare providers, medicolegal experts and hospital administration to facilitate. The most common reasons to shift to palliation from pursuing life-saving care include a poor prognosis or impending death.[20] This allows focus on enhancing quality of life, comfort and relief from suffering for both patient and family.[20] The decision to shift to palliation must also consider resource limitations and the current patient burden requiring those resources.[20] Despite these conversations being highlighted in both the pandemic era as well as in the disaster response arena, the availability of literature surrounding palliative care in trauma in LMICs is relatively sparse, and offers an opportunity for future research.

The panellists were in unanimous agreement that targeting primary prevention is a key factor to reducing deaths from injuries. There were several areas of emphasis for public health interventions, including interpersonal violence, gun violence, substance use and vehicle injuries. Owolabi *et al*.[21] examined perceived barriers to care in SA and identified multiple social determinants, including healthcare access, neighbourhood and environmental factors, social and community context, education and economic stability, as direct barriers to patients seeking and receiving care. Barriers relevant to trauma care include safety concerns, high crime rates, absence of social support and alcohol use.[21] Another study found that health disparities in SA are fuelled by differences in three domains: knowledge and education; social protection and employment; and housing and infrastructure.[22]

Study limitations

Decedents presented in this analysis were limited to those meeting EpiC study inclusion criteria who presented to the health system alive and within 24 hours of injury. Some decedent cases were not reviewed by the expert panel owing to missing clinical records. The authors did not identify a pattern (e.g. facility or date range) for the missing records. The cohort used for this review and analysis does not reflect all injury decedents receiving or seeking care in the Western Cape. Injury time was not available for all decedents reviewed, and initial time of contact with the health system was used as a surrogate. Analyses using health system contact time instead of time of injury are described as such; however, this may have introduced bias into the results by underestimating the true time intervals.

Conclusion

In this expert panel review of decedents in 2021 from a trauma referral pathway in the Western Cape Province, SA, nearly half of the deaths were classified as preventable or potentially preventable. Identified areas for health system strengthening included provider knowledge on early resuscitation and team communication, increased access to diagnostic imaging, formation of palliative care protocols targeting end-of-life care and primary prevention interventions at a community level to reduce overall deaths from injury.

Data availability. The data used for this study are available upon reasonable request to the corresponding author.

Declaration. None.

Acknowledgements. We would like to express our gratitude to the members of our expert panel for contributing their expertise, time and passion on the panel: Dr Nadiya Ahmed; Dr Jacob Botes; Dr Kathryn Chu; Dr Marisa Crous; Dr Shaheem de Vries; Dr Riaan Duvenage; Dr Zahier Ebrahim; Dr Elaine Erasmus; Dr Heike Geduld; Dr Shaun Gilbert; Dr Lesley Hodsdon; Dr Hendrick Lategan; Mr Michael Lee; Mr Peter Lesch; Dr Marcel Loubser; Dr Denise Lourens; Dr Suzan Mukonkole; Mr Wayne Smith; Dr Zandre Smith; Dr Elmin Steyn; Dr Grace Simon; Dr Neil van Hoving; and Dr Janette Verster. We would like to thank and acknowledge the EpiC study research staff who helped collect data for this process: Dr Andre Swanepoel; Dr Anronel Stofberg, Sr Willemiena Minnaar; Dr Arifa Kamroodien-Cader; Dr Saeeda Benjamin; Dr Shariefa Williams; Dr Gadija Khan; Mr Fabio Moreira; Ms Daisy Inglis; and Ms Chandni Patel.

Author contributions. JD and N-KM-M conceptualised the work. SB, MR and CD assisted with curation of the primary records. JF created the final dataset, analysed the data and prepared tables and figures. JD and N-KM-M performed the qualitative analysis. JD drafted the first version of the manuscript. HG, ES, HL, LH, SdV, JV, SM and KD assisted with the investigation and provision of resources, facilitated data collection across the participating hospitals in SA, and provided input on the local clinical context and interpretation of findings. All authors made substantial contributions to the acquisition of the data. All authors reviewed, edited and approved of the final version of the manuscript and attested to their contributions and the accuracy of the manuscript.

Funding. Epidemiology and Outcomes of Prolonged Trauma Care (EpiC) is funded by the US Defense Health Agency (award numbers W81XWH-19-20055 (to NKMM, JD, SdV, HL) and W81XWH-20-20042 (to N-KM-M, JD, SdV, HL)). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflicts of interest. None.

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Received 6 February 2025; accepted 15 May 2025.