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Review article

The ethical considerations for emergency care research in low- and middle-income countries: A scoping review of the published literature

Sarah Hirner[a], Colleen Saunders[b], Willem Stassen[b,*]

[a] University of Colorado School of Medicine, Aurora, Colorado USA
[b] Division of Emergency Medicine, University of Cape Town, Cape Town, South Africa

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ABSTRACT

Introduction: Research studies on emergency care in low- and middle-income countries (LMICs) face many ethical considerations, including obtaining valid informed consent from vulnerable patients. This study aims to describe the body of literature related to the ethical considerations associated with emergency care research in low- and middle-income settings.

Methods: A scoping review was conducted to identify literature published between 2000 and 2020 related to ethical considerations associated with emergency care research in the LMIC setting. Titles and abstracts were screened in duplicate, and full texts were reviewed and extracted by the principal author.

Results: In total, 1087 articles were identified and 17 articles were included. Major themes identified in the literature included risk versus benefit assessments, patient vulnerabilities, consent, community engagement, clinical roles, ancillary care provision, and regulation of research. Alternative models of consent are often used in emergency care research, including surrogate consent, community consent, and waiver of consent. Challenges and best practices with these alternative models of consent in LMICs are discussed.

Discussion: Gaps remain in the literature describing the ethics of emergency care research in LMICs, including clear guidelines for protecting vulnerable patients and designing ethical consent processes. Best practices identified include community engagement for designing research studies, identifying acceptable risk profiles, and allocating benefits. Continuous and rigorous assessment of the quality of consent is also needed.

African relevance

- Strong, contextually relevant research will enable the development of resilient emergency care systems in low- to middle-income countries. However, doing research in LMICs (and Africa), and especially in emergency care, comes with a series of complex ethical considerations.
- Describing the ethical considerations previously outlined in association with emergency care research in LMICs is an important first step in providing contextually relevant ethical guidance for researchers.
- Understanding the gaps in the literature will help inform the development of guidelines for ethical engagement and future research.

Introduction

It is estimated that the development of effective emergency care systems may reduce up to half of the deaths and over a third of disability-adjusted life years in low- and middle-income countries (LMICs) [1]. Resolution 60.22 of the World Health Assembly in 2007 highlighted the need for the development of African emergency care systems [2]. Similarly, Resolution 72.16 in 2019 recognises the importance of emergency care as a vehicle for universal healthcare access in LMICs [3]. In order to inform and guide the development of emergency care systems, research that is contextually relevant to the setting in which the healthcare interventions are performed is essential [1,4]. While there remains limited published emergency care research overall, clinical studies focusing on LMICs are even more uncommon [1,4]. Conducting emergency care studies in LMICs presents even more challenges as healthcare resources are strained, and the emergency care system is overburdened. Consequently, research becomes a luxury that emergency care services might not be able to support. Yet, research in these settings is essential as LMICs carry a disproportionately high burden of emergency conditions globally [5].

As the importance of emergency care research in LMICs becomes recognised, it is essential that good quality ethical guidance is provided in order to ensure that the interests of participants are protected. Emergency care research studies in LMICs are often ethically complex. Owing to the patient's (or surrogate's) emotional state, physical symptoms, or cognitive impairment due to injury or illness [6], obtaining informed

* Corresponding author.
E-mail address: willem.stassen@uct.ac.za (W. Stassen).

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consent in an emergency situation is challenging and often impossible [7,8]. For example, a comatose patient is unable to give consent. In an LMIC, it may be difficult to identify a surrogate who can understand the situation well enough to give valid consent due to a lack of research-related jargon; or cultural norms may threaten the validity of consent. For example, people from some cultural backgrounds in South Africa might respond affirmatively to any question requiring a confirmatory response. Although this might indicate agreement, in some cases, it instead indicates respect for a person in authority. [17] Due to the nature of the injury or illness, there may exist a real risk to the patient's well-being should consent or research procedures delay any clinical interventions [8]. This also places the patient at a much higher baseline risk for poor outcomes and serious adverse events, increasing the patient's vulnerability. Vulnerability is also intensified by poor healthcare access, relative poverty, and a high reliance on the limited care available [9].

One of the first logical steps towards providing ethical guidance is to understand the full scope of the ethical considerations associated with such research. The aim of this study is, therefore, to describe and summarise the body of literature related to the ethical considerations associated with the conduct of emergency care research in low- to middle-income settings.

Methods

Study design

We conducted a scoping review of articles published between 1 June 2000 and 31 May 2020 according to an *a priori* developed search strategy to identify literature related to ethical considerations in the conduct of emergency care research in LMICs. Studies published before 2000 were excluded due to feasibility, nascency of emergency care in these settings at the turn of the century, and numerous changes to important research ethics codes (such as the Declaration of Helsinki) since 2000. These changes might thus affect the relevance of studies published before 2000. Results are reported in accordance with the PRISMA Extension for Scoping Reviews (PRISMA-ScR) [10]. A protocol was not registered for this study. This study was considered exempt from ethical review as no human participants were involved, and the literature included was available in the public domain.

Search strategy and eligibility criteria

The search strategy included four elements:

(a) Ethics and ethical considerations
(b) Medical research and clinical trials
(c) Emergency care, including prehospital and facility-based care
(d) Low- and middle-income settings

A search string was developed for each of these elements using appropriate keywords and synonyms, and these elements were combined using Boolean operators (Appendix 1). The search was conducted using Medline (via PubMed), CINAHL, and Web of Science databases.

Articles were limited to English articles describing or dealing with the ethical considerations for any manner of medical research (not limited by study design), completed in the facility-based or out-of-hospital emergency care settings in LMICs. Articles published outside of the emergency care and the LMIC setting, outside of the timeframe (1 June 2000 and 31 May 2020), in languages other than English, or where the full text was not obtainable, were excluded.

After the removal of duplicates, an eligibility assessment was conducted independently by two authors (SH, WS) at the title and abstract level. Disputes were resolved by a third author (CS). Finally, papers were reviewed for inclusion based on the full manuscript, with any uncertainties or ambiguity handled by consensus. The reference lists of any articles included were also interrogated, and eligibility was determined in a similar manner.

Data extraction and analysis

Information from the included full-text articles was extracted by the principal author (SH) into an Excel spreadsheet (Microsoft Corporation, Washington, United States) using an *a priori* data extraction matrix (Appendix 2). Briefly, the extraction matrix included bibliographic details of the full-texts reviewed, study aims, methodological details such as setting, study population, and interventions performed, and a detailed examination of ethical considerations. The extraction matrix was piloted on the first five studies by two authors (SH, WS) independently. The main themes contained in the literature were derived from several initial studies and then revised using data from the extraction process. Hereafter, themes were refined through frequent debriefing sessions between the authors. Regarding the expertise of the authors, SH, CS, and WS have experience in conducting scoping and literature reviews, while CS and WS have experience in qualitative and quantitative research. WS has formal postgraduate education in applied ethics and serves on human research ethics committees.

As is commensurate with scoping review methodology, a formal risk of bias assessment was not performed [10,11]. Further, as most included papers were of conference proceedings, narratives, or commentary, rather than original research, a formal critical appraisal was not performed.

Results

Our search was conducted on 17 May 2020 and resulted in 1087 records for initial review. After removal of duplicates and eligibility screening, 60 full-text articles were deemed relevant (Fig. 1). Ten additional articles were considered through interrogation of the reference lists. Following full-text review, 17 articles were included in this review (Supplementary Table 1).

The majority of articles originated from the United States of America (n = 6; 35%), Kenya (n = 3; 18%), and South Africa (n = 2; 12%). Authors with LMIC affiliations were among the author list in 71% (n = 12) of articles and were first or senior authors in 47% (n = 8) of articles included. Publication dates ranged between 2005 and 2019.

Ethical considerations in emergency care research were grouped into seven main themes (Table 1). These themes included: risk versus benefit assessments, patient vulnerabilities, consent, community engagement, clinical roles, ancillary care provision, and research regulation. Much of the literature dealt with issues related to consent, particularly consent by surrogates, community-level consent, waivers of consent, and consent assessment.

Discussion

This study identified several themes regarding ethical considerations associated with the conduct of emergency care research in low- to middle-income settings, which are discussed in detail below. Where there exist clear gaps in the literature, these are highlighted.

Due to the unique environment of emergency care research in LMICs, elevated baseline risks can skew the risk/benefit profile used to assess traditional clinical research. Greater baseline risks in LMICs stem from more underlying vulnerabilities, such as malnutrition, low literacy, and comorbidities [9]. No clear consensus exists on the acceptable level of risk in emergency care research in LMICs. The literature identifies that researchers are responsible for conducting risk assessment within communities and through continued community engagement; however, best practices for conducting risk assessment are not described in detail [12]. Potential risks to research participants and their communities fall into the categories of physical, psychological, social, and economic. A community's definition of risk may include one or more of these categories and will be influenced by local norms and culture.

Patients in LMICs experience intersecting vulnerabilities due to poverty, healthcare access, and lack of power [13]. Most authors agree

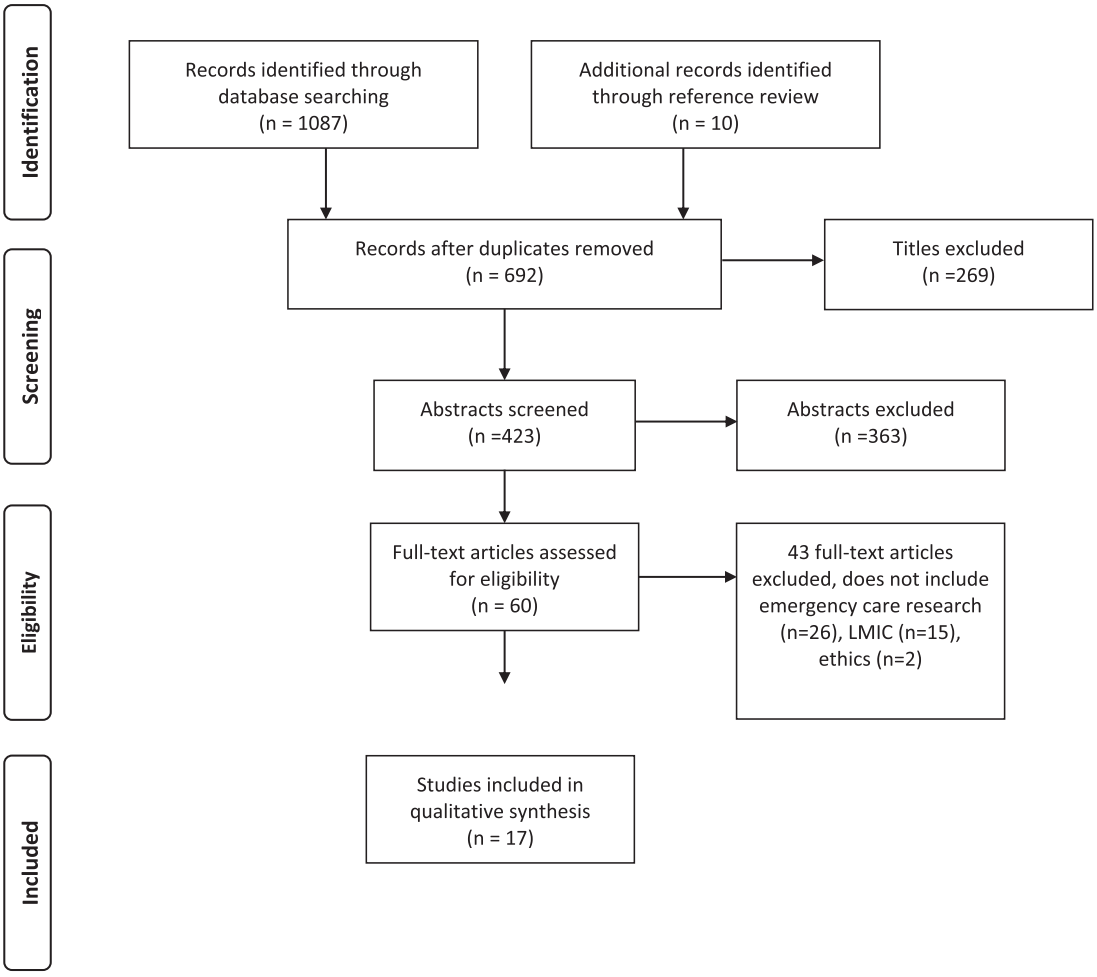

Fig. 1. Flow diagram depicting screening and review process of articles.

that vulnerable participants need to be included in emergency care research. Failure to enrol these populations could undermine study generalisability and result in increased uncertainty in treating those with the greatest need [18]. While most authors expressed concern that vulnerable populations may be exploited and special protections are needed [12,14–16], what constitutes a vulnerable population is not clearly outlined. Studies did not describe how to design and employ special protections, nor did they explore mechanisms of accountability for special protection of vulnerable groups.

Consent is one of the most important considerations for medical research. In order for an individual to give true informed consent, three elements are necessary: voluntariness, full disclosure of risks and benefits, and capacity to consent [28]. The conditions that lead to the need for emergency care can induce stress which may impair the decision-making capacity of patients and their surrogates [12], and in turn, threaten the validity of informed consent by calling into question the voluntary nature of the consent and full disclosure of risks and benefits. The literature reported that patients and surrogates in LMICs face significant barriers to understanding research, including high levels of illiteracy and a lack of research-related terms in vernacular [17]. In addition, cultural norms may threaten the validity of consent [17]. Studies also describe that researchers are responsible for understanding how local language, education, and understanding of disease aetiology and medical research may affect individual and community comprehension of the proposed research and the consent process.

While solutions such as verbal explanations have been proposed, it has also been noted that cultural norms may threaten the validity of consent even when obtained by alternate methods. [22] Since emergency care researchers in LMICs often originate from high-income countries that traditionally have high literacy, use written forms of communication, and have different cultural traditions around consent; these researchers must carefully examine how they give information, how they measure the comprehension of this information, and how responses to questions of consent should be interpreted within the cultural context of the population [12]. The literature fails to describe best practices in designing and assessing methods of consent, yet the authors are of the opinion that participatory methods of designing consent processes are essential in establishing this on a study-by-study basis.

In situations where decisions need to be made quickly, patients can become emotionally and psychologically dependent on health care providers, and the validity of informed consent is further threatened [15,18]. In order to address this challenge, alternative models of consent may be used. Consent may be obtained from a surrogate, obtained from the community, or waived. While the terms deferred, delayed, or retrospective consent are sometimes used to describe consent models, consent cannot be given per se to interventions that have already been applied, and participants can only consent to prospectively including their data within the study[8].

If a patient is unable to provide consent, a surrogate may be asked for consent. While literature reports that using this consent model shows respect for societal structures [19], it may potentially introduce delays to treatment [24]. LMICs more commonly include surrogate consent provisions compared to a waiver of consent provisions, suggesting that these countries may consider surrogate consent preferable to waived consent

Table 1
Themes and key messages identified during descriptive analysis of included literature.

Themes	Key messages	Number of studies	References
Risk versus benefit assessments	How benefits are defined in the context of emergency care research in LMICs varies, and these definitions may make research restrictive. Research participants in LMICs have a greater baseline risk, and there is not a clear consensus on the level of risk acceptable in emergency care research.	5	[9,12,17,18,25]
Patient vulnerabilities	There is an increased prevalence of vulnerable patients in emergency care research in LMICs. Vulnerable patients need to be included in emergency care research in LMICs in order to improve care for these populations.	9	[9,12,13,14,15,16,18,22,23]
Consent		12	[8,9,12,13,14,15,17,18,20,22,26,27]
Surrogate consent	Surrogate decision-makers may experience impaired decision-making capacity due to a high emotional and psychological burden and lack of health literacy and knowledge. A stepwise or continuous consent model may be considered to improve the quality of surrogate consent. There is no clear consensus on who is the most appropriate surrogate decision-maker.	5	[9,12,14,26,27]
Community consent	Community consent allows consent of members that the community denies the right to give consent, which raises questions of the appropriate balance of autonomy and risks/benefits between the individual and the community.	4	[9,14,16,17]
Waived consent	There is international variation in practices and policies regarding waived consent. Conditions for a waiver of consent vary across countries but include that the research could not otherwise be performed and must demonstrate an appropriate risk/benefit profile.	1	[14]
Consent assessment	Assessment of the quality of consent and whether the consent model is appropriate is needed.	2	[12,17]
Community engagement	Communities can be engaged in emergency care research in a variety of ways, and formal structuring of community engagement is helpful. Engagement of communities in planning research activities is important for the fair allocation of benefits and rewards.	9	[1,12,13,14,15,16,20,24,26]
Clinical roles	Therapeutic misconception, when there is a failure to distinguish between research and clinical interventions, can be worsened when clinicians obtain consent for research trials.	4	[9,15,17,18]
Ancillary care provision	Ancillary care provision, or capacity building, can include basic infrastructure for healthcare and training personnel and helps ensure that research is integrated into health systems.	6	[9,12,13,14,15,16]
Regulation of research	Ideally, research will be approved by a local institution, either a research ethics committee or another collaborating institution. There is currently a lack of governance for research ethics, and this role currently falls on the investigator.	5	[9,12,13,16,23]

LMIC: low- and middle-income countries

[9]. However, the literature does not clearly describe whether surrogate consent, community consent, or waived consent is preferable; nor is clear guidance provided on when which might be more appropriate.

Multiple authors noted that identifying appropriate surrogate decision-makers is also a challenge [19]. Complicating this matter is the International Conference for Harmonization Good Clinical Practice (ICH GCP) guidelines which provide yet another opinion on the most appropriate surrogate decision-maker, defining a surrogate as a patient's "legally accepted representative" [26]. However, it is challenging to apply this definition in LMICs, since patients here rarely have a legally acceptable representative [26]. The most appropriate surrogate may be determined by social and cultural norms. For example, data suggest that proceeding with a clinical trial without the father's permission in certain communities can result in domestic violence and households being split [20]. The literature does not propose methods for identifying the most appropriate surrogate decision-maker.

Community consent allows community leaders to make decisions about whether individuals in the community can be included in the research [16]. The literature reports that in some communities, individuals are denied the right to consent due to social structures (for example, where only fathers are allowed to give permission for participation). In these cases, community consent provides a framework for providing consent when the father is not present [12]. It is also described that in some traditional African cultures, it may be more appropriate to obtain consent from the extended family or community rather than the individual [17]. Yet, this model of consent brings into question the appropriate balance of autonomy (between the community and the individual), especially if the research participant is vulnerable within the community [16]. In order to implement community consent, representatives of the community are selected. While studies caution that researchers must carefully plan how to engage communities to develop a research plan that balances risks and benefits between the individual and community, best practices for engaging communities for emergency care research are not described in the literature identified [9,14]. Further, methods for selecting community representatives are not described, neither are methods for resolving conflict between community members nor conflicts between community and participant consent.

Time pressure often makes it difficult to identify a surrogate decision-maker. In this situation, consent to participate in research may be waived. If a patient later regains capacity to consent, assent to include the patient's data in the study may be obtained. In the literature, there is substantial international variation in practices and policies regarding the waiver of informed consent. In some countries, such as Malawi, there are no ethical guidelines dictating the appropriate use of consent waivers. In other countries, such as South Africa, waivers must be approved by a research ethics review committee, with stipulated requirements for consideration of a consent waiver [14]. There appears to be no consensus in the literature regarding what conditions are appropri-

ate for a waiver of consent. In addition, studies fail to specify who is responsible for reviewing and monitoring consent waiver practices.

Literature notes that the quality of consent, including barriers to understanding consent, community governance and structure, and whether the consent model being used is appropriate should be continuously assessed [16, 22]. Studies describe that consent assessment may be carried out by research ethics committees or independent consent monitors [17]. The presence of these committees and monitors in LMICs and their current use is not described.

Community engagement involves a continuous, bidirectional conversation between the communities and researchers that are not from the community and may include local research ethics committees, recognised community leaders, and community partnerships. How to plan community engagement is described as involving a local co-investigator, through national policy, descriptions of plans for community engagement during funding and research ethics committee reviews, guidelines and checklists, and training on community engagement at an institutional level [13,14,21]. Yet again, literature does not describe how to determine which communities are of interest in emergency care research, nor exactly what form the engagement should take.

When clinicians are responsible for consenting participants for research, this may accentuate a patient's misconception that participation in research is likely to provide a benefit. It is noted that in emergency care research, ethical tensions can be intensified by time limitations, which may limit the ability of the researchers to provide detailed information and exacerbate power dynamics between physician-researchers and patients or their proxies [12]. In addition, participants may have no other method to access care (for example, specialist care provided by ancillary health care providers in a low-resource setting). Studies identify that ideally, someone other than investigators should obtain consent [9,17,18]. However, differentiating the roles between investigator and clinician in busy, under-staffed LMIC emergency centres may not be practical nor responsible [9]. Solutions to this issue are not proposed in the literature identified in this review.

Ancillary care provision, building the capacity of a local health system, can help maximise the long-term benefits of research. Specific methods of ancillary care provision are identified, including providing basic health infrastructure [17] and training personnel, including local research ethics committees [14], research staff [16], and health policymakers [22]. Research studies may also provide basic infrastructure for healthcare in LMICs [22]. Literature reviewed recommends that plans to build local health system capacity should be described in the proposal phase of the research, and the research team should provide their own personnel and materials [17]. Studies note that it is important to consider the consequences of withdrawing such personnel and resources upon study completion; however, examples are not given. The most ethical methods of providing ancillary care are not described, nor how best to decide which resources ought to be invested in. The authors again recommend that transparent engagement with communities is essential to facilitate this.

Typically in order to fulfil procedural research, ethics studies involving human participants are and should be approved by a local ethics committee. However, literature shows that local research ethics committees in LMICs may not be available or may be underfunded and suffer from shortages of staff, training, and institutional support [9,16]. If local research ethics committees are not available, approval for research may also be granted from a local collaborating institution and will ideally involve representatives of the participants to be enrolled in the study [13].

The literature does not describe who is responsible for ensuring that research ethics are upheld. Governance is lacking in many LMICs, and some authors believe that local governments are ineffective [15]. The responsibility to understand local ethics (including culture, social norms, and the hierarchy of decision-making) and to ensure that research is conducted ethically falls on the investigator [12]. Mechanisms of accountability or consequences, especially from foreign funders, are not described.

It is possible that some ethical considerations are missing from this review, especially as no grey literature or published policies were included. Risk of bias assessment was not performed since most articles were descriptive in nature. Further, only English papers were reviewed and thus, some literature from LMICs that predominantly do not publish in English may have been excluded.

The ethical considerations of emergency care research in LMICs centre around protecting vulnerable populations. Due to international variation in regulations and lack of governance, the responsibility for designing and implementing ethical research practices falls on the investigator.

Clear guidelines for designing an ethical emergency care research study in the LMIC setting are lacking. However, in order to be considered ethical, a study must demonstrate an acceptable risk-benefit profile, yet the literature does not clearly describe what risks are acceptable in emergency care research in LMICs. Including local research ethics committees and participating in community engagement is considered best practice. By working with local individuals and groups, researchers can identify acceptable risk profiles for the community and plan for fair allocation of benefits.

While the literature acknowledges that patients participating in emergency care research have an increased level of vulnerability, it fails to identify what protections ought to be instituted for these patients. One mechanism for addressing vulnerability is ensuring the validity of consent. Many ambiguities remain around this process, including clear guidelines for a waiver of consent. Best practices for designing consent processes include considerations of how local language, education, and cultural factors may affect consent processes, including the most appropriate alternative methods of consent (surrogate consent, community consent). Developing models for the continuous assessment of the quality of consent have also been identified as best practice. When using alternative models of consent, the most appropriate way to balance autonomy and the risk/benefit between the individual and community remains ambiguous.

Consent is one of the most challenging ethical issues in emergency care research in LMICs. Processes for identifying surrogate decision-makers that are aligned with cultural norms and communication challenges will ideally be identified when designing research studies in LMICs. In addition, it is important for consent processes to consider the psychological dependence that can develop in the emergency care setting. One best practice identified to address this challenge includes having someone other than the investigator obtain consent.

Declaration of Competing Interest

Dr. Willem Stassen is an editor of the African Journal of Emergency Medicine. Dr. Stassen was not involved in the editorial workflow for this manuscript. The African Journal of Emergency Medicine applies a double blinded process for all manuscript peer reviews. The authors declared no further conflicts of interest.

Dissemination of results

No primary data collection was undertaken, and only publications that were publicly obtainable were included in this scoping review. Dissemination is undertaken through open access publication.

Authors' contributions

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual

content: SH contributed 50%, WS 30%, and CS contributed 20%. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.afjem.2021.12.001.

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