

## Perspectives on snakebite envenoming care needs across different sociocultural contexts and health systems: A comparative qualitative analysis among US and Brazilian health providers

Eleanor Strand<sup>a</sup>, Felipe Murta<sup>b,c,d</sup>, Anna Tupetz<sup>a</sup>, Loren Barcenás<sup>a</sup>, Ashley J. Phillips<sup>a</sup>, Altair Seabra Farias<sup>b,c</sup>, Alícia Cacau Santos<sup>b,c</sup>, Gisele dos Santos Rocha<sup>b,c</sup>, Catherine A. Staton<sup>a</sup>, Flávia Regina Ramos<sup>b,c,d</sup>, Vinícius Azevedo Machado<sup>b,c</sup>, Fan Hui Wen<sup>e</sup>, João R.N. Vissoci<sup>a</sup>, Jacqueline Sachett<sup>b,d,f</sup>, Wuelton Monteiro<sup>b,c,d,1,\*</sup>, Charles J. Gerardo<sup>a,1</sup>

<sup>a</sup> Department of Emergency Medicine, Duke University School of Medicine, Durham, NC, United States

<sup>b</sup> Escola Superior de Ciências da Saúde, Universidade do Estado do Amazonas, Manaus, Brazil

<sup>c</sup> Diretoria de Ensino e Pesquisa, Fundação de Medicina Tropical Dr. Heitor Vieira Dourado, Manaus, Brazil

<sup>d</sup> Programa de Pós-Graduação Em Enfermagem, Universidade Federal de Santa Catarina, Florianópolis, Brazil

<sup>e</sup> Instituto Butantan, São Paulo, São Paulo, Brazil

<sup>f</sup> Diretoria de Ensino e Pesquisa, Fundação Alfredo da Matta, Manaus, Brazil

### ARTICLE INFO

Handling Editor: Dr. Denise Tambourgi

#### Keywords:

Snakebite envenoming  
Antivenom  
Implementation science  
Access to care  
Care delivery  
Health professionals

### ABSTRACT

With the advancements in therapeutics and available treatment options, almost all deaths and permanent disabilities from snakebite envenoming (SBE) are preventable. The challenge lies in implementing these evidence-based treatments and practices across different settings and populations. This study aims to compare data on provider perceptions of SBE care across health systems and cultural contexts to inform potential implementation science approaches. We hypothesize different health systems and cultural contexts will influence specific perceived needs to provide adequate snakebite care within central tenets of care delivery (e.g., cost, access, human resources). We previously conducted exploratory descriptive studies in the US and Brazil in order to understand the experience, knowledge, and perceptions of health professionals treating SBE. In the US, in-depth interviews were performed with emergency physicians from January 2020 to March 2020. In BR, focus group discussions were conducted with health professionals from community health centers at the end of June 2021. The focus group discussions (BR) were originally analyzed through an inductive thematic analysis approach. We conducted a secondary qualitative analysis in which this codebook was then applied to the interviews (US) in a deductive content analysis. The analysis concluded in August 2022. Brazil participants were physicians (n=5) or nurses (n=20) from three municipalities in the State of Amazonas with an average of three years of professional experience. US participants were emergency physicians (n=16) with an average of 15 years of professional experience. Four main themes emerged: 1) barriers to adequate care on the patient and/or community side and 2) on the health system side, 3) perceived considerations for how to address SBE, and 4) identified needs for improving care. There were 25 subthemes within the four themes. These subthemes were largely the same across the Brazil and US data, but the rationale and content within each shared subtheme varied significantly. For example, the subtheme “role of health professionals in improving care” extended across Brazil and the US. Brazil emphasized the need for task-shifting and -sharing amongst health care disciplines, whereas the US suggested specialized approaches geared toward increasing access to toxicologists and other referral resources. Despite similar core barriers to adequate snakebite envenoming care and factors to consider when trying to improve care delivery, health professionals in different health systems and sociocultural contexts identified different needs. Accounting for, and understanding, these differences is crucial to the success of initiatives intended to strengthen snakebite envenoming care. Implementation science efforts, with explicit health professional input, should be applied to develop new and/or adapt existing evidence-based treatments and practices for SBE.

\* Corresponding author. Fundação de Medicina Tropical Dr. Heitor Vieira Dourado, Manaus, Brazil

E-mail address: [wueltonmm@gmail.com](mailto:wueltonmm@gmail.com) (W. Monteiro).

<sup>1</sup> Equal contribution as last co-authors.

<https://doi.org/10.1016/j.toxcx.2022.100143>

Received 14 November 2022; Accepted 25 November 2022

Available online 9 December 2022

2590-1710/© 2022 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### Abbreviations

BR	Brazil
SBE	Snakebite envenoming
US	United States
WHO	World Health Organization

## 1. Introduction

Since the late 1890s, several antivenoms and clinical management strategies have been developed and proven effective against snakebite envenoming (SBE) (Pucca et al., 2019; Gutiérrez et al., 2007; Silva and Isbister, 2020). However, SBE remains a neglected tropical disease with significant morbidity and mortality (Snakebite envenoming, 2020). Annually, an estimated 5.4 million snakebites occur worldwide—half of which are envenomings—and result in up to 138,000 preventable deaths and over 400,000 preventable amputations and/or other permanent disabilities (Snakebite envenoming, 2020).

Such a large, persistent burden of disease despite efficacious, evidence-based treatments and practices is referred to as the know-do gap (Theobald et al., 2018; What is Implementation Science, 2022). Despite having efficacious treatments, the burden of SBE differs across settings. WHO's prevention and control strategy recommends engaging with communities during the implementation of evidence-based interventions (Longbottom et al., 2018; Gutiérrez et al., 2010, 2015, 2021; Gutiérrez, 2014). However, such interventions often miss the need for engaging local health providers (Tupetz et al., 2022; Rocha et al., 2022; Bala et al., 2020) and adaptation to their sociocultural context (Evans et al., 2019; Chu and Leino, 2017; Duda et al., 2021), increasing the know-do gap. Understanding the role of sociocultural context and health professionals' perceptions of SBE care needs is critical to ensure interventions function as intended (Escoffery et al., 2018).

To date, although studies have investigated the perceptions of SBE care needs (Sapkota et al., 2020; Ooms et al., 2021; Barnes et al., 2021), no studies have compared settings and highlighted the contextual similarities and differences between high- and low-resource settings for SBE. In this study, we will compare perceptions of health care providers the United States and Brazil based on their unique differences in terms of the health systems, resource level, SBE burden, universal standard of care, treatment accessibility, and SBE epidemiological surveillance (Table A1). In brief, the United States (US) is a high-income country in North America with a mixed health system. Antivenom is often available, albeit cost challenges (Tupetz et al., 2022). The US does not have a universal clinical practice guideline (though Lavonas et al., 2011 is commonly used among emergency physicians) nor a standardized SBE surveillance system. In contrast, Brazil (BR) is a low- and middle-income country in South America with a universal health system and higher SBE burden than the US. While BR has a universal clinical practice guideline from the Ministry of Health (Guia de Vigilância Epidemiológica, 2009) and a standard surveillance system, antivenom availability and patient time-to-care is a challenge (Cristino et al., 2021).

We previously conducted exploratory descriptive studies in the US and BR to develop and validate a clinical practice guideline for community health centers (Rocha et al., 2022) and understand factors influencing clinical decision making in antivenom administration (Tupetz et al., 2022), respectively. The objective of this study was to use these qualitative datasets to comparatively analyze health provider perceptions regarding how to improve SBE clinical care across the US and BR. We hypothesized different health systems and sociocultural contexts would influence specific perceived needs to provide adequate SBE care within the central tenets of care delivery (e.g., cost, access, human resources).

## 2. Methods

Our study was a secondary qualitative analysis. Data collection, study populations, and ethical approvals were previously described by Tupetz et al., 2022 and Rocha et al., 2022. This study was reported according to the Consolidated Criteria for Reporting Qualitative Research (COREQ) guidelines (Tong et al., 2007).

### 2.1. Study design

In BR and the US, exploratory descriptive studies were conducted to understand experience, knowledge, and perceptions of health providers treating SBE (Tupetz et al., 2022; Rocha et al., 2022). In BR, focus group discussions (FGD) were conducted with health providers from community health centers at the end of June 2021. FGDs took place in Manaus, State of Amazonas, at the Fundação de Medicina Tropical - Dr. Heitor Vieira Dourado (FMT-HVD). FMT-HVD is a tertiary referral hospital known for treatment of SBE and other tropical and infectious diseases. In the US, in-depth interviews were performed with emergency physicians from January 2020 to March 2020. Interviews were conducted in the states of North Carolina, Missouri, New York, Florida, Michigan, New Mexico, and Texas.

### 2.2. Research team and reflexivity

Research team and reflexivity for data collection were previously described by Tupetz et al., 2022 and Rocha et al., 2022. The research team for our secondary analysis included a research assistant (ES); a licensed physical therapist (AT); a clinical research and snakebite envenoming expert (WMM); and two qualitative experts with PhDs (JRN, FM). The study team had no prior relationship with the participants.

### 2.3. Participant selection and recruitment

Participant selection and recruitment were previously described by Tupetz et al., 2022 and Rocha et al., 2022. To summarize, in BR, health professionals from the municipalities Careiro da Várzea, Ipixuna, and Boa Vista do Ramos, in the state of Amazonas, who completed 75% of a five-day SBE training workshop at FMT-HVD were invited to participate. Participants provided written consent and FGDs were conducted with a maximum of 10 participants per group. In the US, 16 participants, who were physicians working in emergency departments (ED) in academic, teaching, and community hospitals across the United States, were recruited using snowball sampling (Sadler et al., 2010).

### 2.4. Data collection procedures

Data collection procedures were previously described by Tupetz et al., 2022 and Rocha et al., 2022. To summarize, in BR, a semi-structured guide was developed by the research team and piloted prior to data collection (Appendix B). An experienced moderator conducted the focus groups according to the guide in a quiet, comfortable room at FMT-HVD. Similarly, in the US, interviews followed a semi-structured interview guide developed and piloted by the research team (Appendix C). Due to the COVID-19 pandemic, interviews were conducted over a secure video conferencing platform. In both BR and the US, field notes were taken throughout data collection.

### 2.5. Data analysis

In this study, we conducted an independent secondary analysis in which we applied the codebook developed by Rocha et al., 2022 to the US data in a deductive content analysis. An independent researcher (ES) coded the US data. Codes were reviewed by another qualitative researcher who collected the US data (AT) and the two researchers who

developed the BR codebook (WMM, FM). Codes were organized under the identified themes from the Brazil FGDs. The codebooks were then merged, and subthemes sorted into Brazil-specific, USA-specific, or both categories. Analysis concluded August 2022.

## 2.6. Ethics statement

This study is approved by the covered by the Research Ethics Committee of the Universidade do Estado do Amazonas (UEA) (CAAE: 35855820.2.0000.5016) in BR and the Duke Health Institutional Review Board (Pro00103272) in the US. Written (BR) and/or verbal (BR, US) informed consent was obtained from all participants.

## 3. Results

Four main themes emerged: 1) barriers to adequate care from the patient and/or community perspective and 2) from the health system perspective, 3) perceived considerations for how to address SBE, and 4) identified needs for improving care. There were 25 subthemes within the four themes. Participant demographics are presented first, followed by each theme and their subthemes.

### 3.1. Participant demographics

**Brazil** Out of the 50 health professionals who attended the five-day workshop, 25 consented to participate in focus groups discussions. There were a total of three focus groups with seven, nine, and seven participants, respectively. Participants were physicians (n = 5) and nurses (n = 20) working at healthcare facilities from three municipalities: Careiro da Várzea (n = 17), Ipixuna (n = 4), and Boa Vista do Ramos (n = 4). Age ranged from 24 to 64. Mean professional experience was three years.

**US** Of the 69 emergency physicians emailed with an interview invitation, 29 responded. Seven declined to participate and six did not respond after providing initial informed consent. 16 were interviewed. Two participants identified as female and 14 as male. Age ranged from 33 to 69 (median of 43).

Almost all participants (n = 15) were trained in an emergency medicine residency program. One was trained in a pediatric residency program. For additional training, participants completed toxicology (n = 4), pediatric emergency (n = 2), hyperbaric medicine (n = 1), and global health (n = 1) fellowships. Professional experience was almost evenly distributed across 0–10 years (n = 6), 10–20 years (n = 5), and 20+ years (n = 5). Number of SBEs professionals had ever treated, in contrast, favored 1–10 bites (n = 5) and 11–50 bites (n = 5), with two professionals under 10 bites and four above 50 bites. Brazil and US participants are compared in [Table 1](#).

### 3.2. Barriers to adequate snakebite envenoming care

Barriers to adequate care from the patient and/or community perspective and the health system perspective were major themes throughout the interview and focus group transcripts. The patient and/or community barriers theme had four subthemes and the health system barriers theme had seven subthemes. These subthemes reflected central tenets of care delivery, such as protocol, human resources, and cost.

Six of the subthemes were identical in the individual ([Tupetz et al., 2022](#)) and joint analyses of the Brazil focus groups and US interviews: the lack of awareness and transportation subthemes from the patient and/or community perspective theme, as well as the irregular anti-venom supply, lack of perceived competence, lack of training and/or education, and lack of specialized staff subthemes from the health system perspective theme. The raw data, however, revealed significant nuances within these subthemes between Brazil and the US.

**Table 1**  
Brazil and US participant characteristics.

	Brazil participants (n = 25)	US participants (n = 16)
Age range in years	24–64	33–69
Sex (male)	8	14
Profession		
Physician	5	16
Nurse	20	–
Average years of experience	3	15

#### 3.2.1. Patient and/or community perspective

From the patient and/or community perspective, the lack of awareness subtheme refers to misconceptions among the public regarding SBE care. Both the Brazil and the US data describe patients attempting to suck venom out of the bite or applying a tourniquet to the affected limb.

*“I know that there’s literature out there on immediate treatment, such as sucking, trying to suck the venom out of the wound. There’s devices that can suck the venom out of the wound as well. There’s tourniquets, and devices to slow the venous blood flow of the venom through the vasculature. So, I think that most of those need to be done pretty quickly after the snakebite and are applicable to what we do in the Emergency Department”* (P6, physician, US).

A nuance emerges in how lack of awareness impacts the decision to seek care. Only Brazil participants noted patients tended not to recognize snakebites as an urgent health concern.

*“The patient was bitten and died, because ... firstly, he did not communicate to his family that he had been bitten, [and] secondly, he went to drink”* (P12, nurse, Careiro da Várzea, Brazil).

The other shared subtheme, transportation, refers to the time it takes patients to reach health facilities. Brazil and US participants identified rural and/or indigenous populations as the most disadvantaged in terms of transportation. Unlike in the US, however, Brazil participants emphasized that the general population (in the Amazon region) also experiences regular barriers to transportation.

*“Most [patients] that come to us ... more than 12 hours [after] the occurrence of the event. It is very rare to get patients who were bitten within one hour, two hours. Usually, time from the bite is more than 24 hours or 48 hours”* (P19, nurse, Ipixuna, Brazil).

An additional nuance concerned who was responsible, the patient or the health system, for transporting patients with acute care conditions to the health system. Brazil participants discussed transportation as the responsibility of the patient, whereas US participants stressed the pre-hospital care system and ambulance transport.

*“We probably have ... about 10% to maybe 20% of what we actually need as far as pre-hospital transport and vehicles. So, I think transportation is a ... huge problem for our population”* (P5, physician, American Indian reservation, US).

In Brazil, most participants describe transport in reference to the river network, whereas transport in the US is largely land-based via roads.

*“For all snakebites, [patients] seek care from us first, as many do not have the resources to go directly to the hospital ... so, as we have a speedboat ambulance, this takes you directly from the clinic to the hospital”* (P25, physician, Boa Vista do Ramos, Brazil).

Brazil and the US each had an additional, independent subtheme within the patient/community barriers theme. Brazil participants explained how the existence of traditional medicine impedes adequate care, as many patients either seek traditional care prior to modern and/or health facilities use traditional knowledge and methods, such as applying black stone.

*“For example, in the village, they scrape the bark of the jabuti and put it on top [of the wound]. They say it has an anesthetic effect”* (P10, nurse, Careiro da Várzea, Brazil).

In contrast, US participants identified cost as a major barrier for the patient. Participants stressed financial harms from the cost of antivenom (largely due to lack of transparent pricing from manufacturers, hospitals, and insurance companies) could be worse than the physiological harm of the venom. In nonfatal cases, the decision to administer antivenom often rests on informal cost-benefit analyses between these potential harms.

*“To me, it does depend ... based on that, if it’s a leg versus an arm, where you really may not be able to work for three weeks, um, or, you know, a little kid that can’t use crutches versus an adult that could get around on crutches. So, yeah, it’s really kind of the cost of the medication, not that the medication doesn’t work. It’s really the cost of it versus how much benefit you’re going to see because again, eventually, your [recovery is] going to come out to the same point”* (P14, physician, USA).

### 3.2.2. Health system perspective

Under the health system perspective theme, the subthemes lack of education/training and lack of perceived competence were similar in Brazil and the US. Both sets of health professionals noted the management of SBE and administration of antivenom was either only briefly or not included in their formal clinical training programs. Most did not feel comfortable treating patients with SBE without supervision or further guidance.

*“If you trained in facilities where you don’t see snakebites often ... you can be uncomfortable with just, kind of, the algorithms to treat a patient. I think that [is] probably the majority of it. And beyond that, it would have to do with just, institutional, you know, where do you turn to? Do you call Poison Control? Do you have a protocol? So on and so forth. Those two things combined, I think, make physicians uncomfortable treating them”* (P2, physician, US).

The irregular antivenom supply subtheme refers to antivenom access and distribution. Both Brazil and US participants noted the unequal distribution of antivenom across health facilities, but access was only discussed as a challenge in Brazil—with the exception of American Indian or Alaskan Native reservations in the US. Otherwise, while not stored in most health facilities, antivenoms are normally accessible quickly by flight or other transport across the United States.

There are additional nuances in the lack of specialized staff. When discussing lack of trained or specialized providers, Brazil participants are referring to physicians as a whole. Most community health centers in and around the Amazon have irregular physician staffing and are largely staffed with nurses.

*“There is a room where we have three beds ... often there was no doctor. It wasn’t the nurses who were there; it was the nursing assistant”* (P17, nurse, Careiro da Várzea).

US participants, on the other hand, refer to lack of physicians with specialized training in envenomation and/or lack of toxicologists. In the same vein, dependence on referral and consult is a subtheme specific to the US. Almost all US participants described either referring care to specialized facilities or facilitating clinical decision-making with outside resources, notably Poison Control, in-house toxicologists or pharmacists for antivenom dosage, and/or personal connections to specialists.

*“We would call the Poison Control Center. For sure. And possibly a toxicologist. And if there were questions about building up the antivenom for some reason, based on labs or something like that, we would talk to our pharmacists”* (P7, physician, US).

The other US-specific subtheme was the lack of a standard or official protocol for treating snakebite envenoming (see [Table A1](#) for context).

A Brazil-specific subtheme of equipment needs includes the infrastructure of the health facility where the participant works. Several participants mentioned structural issues with their building; lack of medicines, including antivenom; and lack of or broken equipment.

### 3.3. Considerations for future interventions

Considerations for how to address snakebite envenoming was a significant theme in both the Brazil and US data. These subthemes reflect what providers believe should be considered when trying to improve SBE care.

One subtheme, role of the community, was specific to Brazil. Only the Brazil study participants extended activities of the health system to communities, suggesting education and awareness initiatives. This relates to nuances in the role of health professionals subtheme. Brazil participants viewed themselves as the potential agents of such initiatives to improve acute care of SBE.

*“So, in each community, we have a community health agent. There are some areas that have nursing assistants. So, [we can] take this information to the team as a whole, so that they can take this information to the community; it’s the transmission of information to carry forward”* (P1, nurse, Careiro da Várzea, Brazil).

In the same vein, Brazil study participants expressed interest and willingness to receive additional training in SBE care. No US participants suggested further required training. Most noted the breadth of information emergency physicians need to know is already extensive and not all emergency physicians commonly treat SBE based on high or low SBE prevalent areas.

*“So, I think we have so many problems in emergency medicine, so many knowledge gaps and things that we know how to treat ... I would really deemphasize snake bites ... This is something we need to know how to look up, but with all the other things that we are tasked with, I think this is really a non-issue and something we not should not be emphasizing. I would remove that from the education—just teach residents how to find that information when they need it”* (P6, physician, US).

An additional nuance to note is the composition of the snakebite care team; 20% of Brazil participants were physicians versus 100% of US participants. Related to the role of health professionals, the approach to improving care in the health system subtheme differs between Brazil and the US. Most Brazil participants emphasized capacity building in the community health center network (primary), whereas US participants suggested improving specialized care (tertiary).

The last subtheme, perception of SBE as a clinical condition, also varies between Brazil and the US. Brazil participants generally considered the treatment of SBE as more complex. This was likely due to the higher number of snake species, and consequently higher number of antivenoms, in the Brazilian Amazon (see [Table A1](#) for context). Unlike in the US, identification of the snake species is usually necessary to initiate the appropriate treatment in Brazil. In the US, the decision of which antivenom is moot and was not discussed. USA participants only discussed the decision of whether to administer antivenom.

### 3.4. Identified needs from the provider perspective

The fourth and final theme from the data was explicitly identified needs to improve treatment of SBE. Unlike the previous themes, identified needs largely differed between Brazil and the US, only overlapping



in two of the ten subthemes.

The two shared subthemes were a case reporting system and a standard clinical practice guideline. Brazil and US participants described existing, but underutilized, case reporting systems and suggested provider awareness initiatives and/or policies to enforce the use of these systems.

In terms of a clinical practice guideline, Brazil participants referenced the Ministry of Health guideline and/or were trained in a recently developed guideline specific to community health centers (Rocha et al., 2022). In the US, some participant EDs had an institutional snakebite envenoming protocol in place, whereas others were not aware of any existing guidelines. Most of the participants referred to Lavonas et al., 2011 or Poison Control for guidance (Lavonas et al., 2011).

#### 3.4.1. Brazil-specific subthemes

Only Brazil participants identified a need for community education and initiatives to raise awareness on first aid practices; communication channels for providers; and specific training needs. To prevent snakebites and improve prehospital care, participants suggested education and training initiatives for the community and for other health professionals.

*“We health professionals are going to carry out this continuing education process with our community health agents and other people in the community, because now we have a base; we have a tool, a protocol”* (P18, nurse, Careiro da Várzea, Brazil).

Participants noted opening communication channels between providers would facilitate such continuing education amongst themselves. Communication channels were described as safe spaces for providers to share experiences treating snakebite envenomings, ask questions, and learn from each other—a similar concept to medical case debriefings.

Participants also identified specific areas in which they, and their colleagues, would benefit from additional training. These areas included identification of snakes; premedication regimens to prevent early adverse reactions; use of antibiotics; epidemiologic approach to diagnosing the type of envenomation; wound care; and patient follow-up needs.

*“What’s the point of sending the serum there and not having trained professionals to be able to administer the serum correctly?”* (P10, nurse, Careiro da Várzea, Brazil)

#### 3.4.2. US-specific subthemes

Only US participants identified the need for transparency regarding the cost of antivenom, specifically the patient facing financial burden; rigorous, unbiased studies and cost-effective analyses to inform clinical decision-making; and improvements to consultation resources, notably Poison Control, to serve as the gold-standard for snakebite management practices.

Transparency regarding the cost of antivenom was discussed in relation to manufacturers, hospitals, and insurance companies. Some participants advocated for government regulation or subsidies to decrease the cost; one noted antivenom should fall under the Orphan Drug Act (eCFR, 2022). Most participants felt decreasing the cost of antivenom would remove financial versus physiological harm decision-making in nonfatal cases and likely improve patient outcomes.

*“If you’re going to charge twenty thousand dollars per vial of antivenom, that is very beneficial to [the patient], that’s a big problem. Globally, the use of antivenom potentially costs, you know, 20, 30 dollars, a hundred dollars, per vial. I understand that there’s a need for innovation and drug development costs that go into it. I think it’s a huge system wide problem that this orphan drug costs so much money”* (P10, physician, US).

Along the same lines, participants expressed interest in studies examining the long-term effects and functional outcomes of administering versus not administering antivenom in nonfatal cases. The current

literature was perceived as insufficient and/or untrustworthy in terms of studies funded by pharmaceutical companies.

*“And again, not that it’s not good science, but it still is a red flag anytime a study is driven by a very high profit pharmaceutical study that has very, very high stakes for ... for obtaining further profit with a positive. Like if this [antivenom], if it really does help chronic pain ... I try to have a pretty healthy level of skepticism about these pharma studies”* (P3, physician, US).

Alongside rigorous, unbiased data, participants described the need for cost-effective analyses to inform decision-making in nonfatal snakebite envenoming cases.

*“I think there is probably a threshold above which costs would become an issue. And it solely would depend on if the patient has to pay out of pocket for that [antivenom]. You can put them into debt for the rest of their life. I don’t know what that threshold would be. I would hope that there would be a cost-effectiveness analysis somewhere in the antivenom literature that would help to inform that”* (P6, physician, US).

Outside of cost, participants recommended improving consultation resources, from mobile applications to the Poison Control Center.

*“Well, I think the better idea is ... I mean, I don’t know how good Poison Control is at [advising snakebite treatment]. But, you know, people who do research in this, using their information and educating Poison Control centers. Because that is where I think most physicians are going to turn”* (P2, physician, US).

#### 3.5. Summary of BR-US comparison across themes and subthemes

Our descriptive thematic analysis resulted in four themes and 25 subthemes (Fig. 1). Subthemes under three themes—barriers to adequate SBE care on the patient and/or community side (theme one) and the health system side (theme two), and perceived considerations for how to address snakebite envenoming (theme three)—largely overlapped across BR and US. However, while the majority of subthemes were the same, the rationale and content within each shared subtheme varied significantly, as discussed above. In contrast to these three themes, almost all of the subthemes under the fourth theme, identified needs, did not extend across the Brazil and US data.

## 4. Discussion

This study analyzed previously collected focus group (BR) and in-depth interview (US) data on health provider perceptions regarding the clinical care of SBE. We hypothesized different health systems and sociocultural contexts between BR and the US would influence perceived needs for improving SBE care delivery. Our results were consistent with this hypothesis.

Despite similar core barriers to adequate snakebite envenoming care and factors to consider when trying to improve care delivery, health professionals in different health systems and sociocultural contexts identified different specific needs. These differences can be abstracted into 1) the system level approach (top-down versus bottom-up) interventions should work within to improve care, 2) the actor responsible for intervention development/adaptation and implementation, and 3) the healthcare delivery model the interventions should reflect.

Health professionals in the US and BR discussed care needs and provided suggestions within dichotomous system level approaches: top-down versus bottom-up (Sabatier, 1986). Needs identified by US health providers—a unified standard of care, government antivenom regulation, insurance cost transparency—reflect a lack of national policy and infrastructure for SBE. The minimal literature on SBE as a public health problem in the US aligns with this finding (Jaramillo et al., 2019). In contrast, health providers in BR highlighted the need to enforce existing infrastructure, such as the Ministry of Health clinical practice guideline.

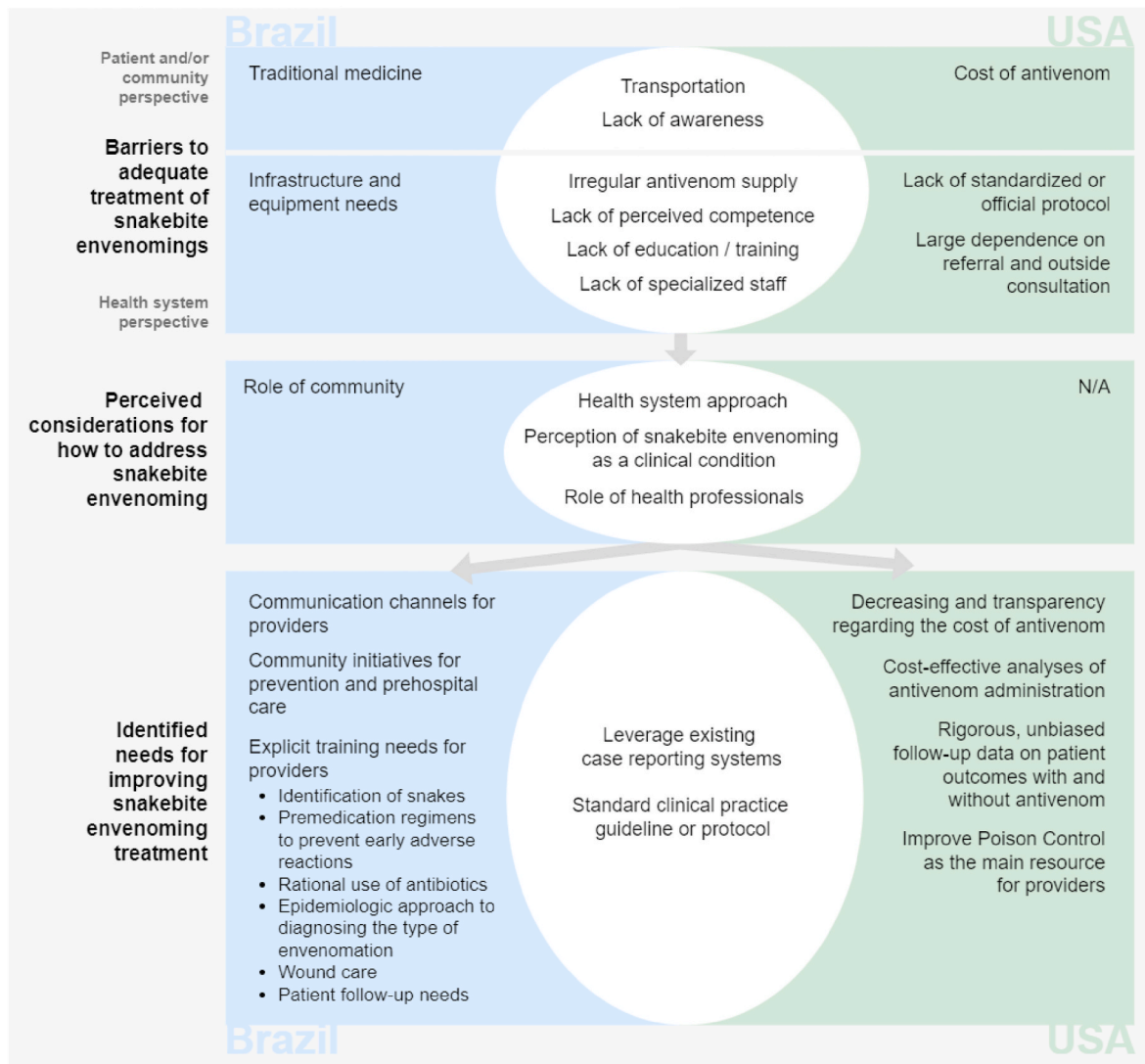


Fig. 1. Themes and subthemes across the Brazil and US data.

System deficits in the US, not BR, is an exception to longstanding, misguided divisions in global health (e.g., Global North versus Global South) (Khan et al., 2022) and stands in contrast to a 2018 global analysis of snakebite vulnerability that concluded public health policy and SBE infrastructure are largely challenges for low- and middle-income countries (LMIC) (Longbottom et al., 2018). Costa Rica is also a notable exception to this perception. BR and Costa Rica have long histories of antivenom research and development and public-private partnerships with other Latin American countries to reduce SBE burden (Schiaffino Salazar, 2021).

Related to the top-down versus bottom-up juxtaposition, the US and BR differed in which main actor should be leading the efforts for improving SBE care—the health system or the health provider? US participants stressed the most pressing issue was within the health system, referring to the cost of antivenom and clinical care. High costs of care is a prevalent, persistent problem in the US (Gupta et al., 2019) and disproportionately impacts indigenous, rural, low-income, and racial/ethnic minority populations (Ye and Rodriguez, 1982; Abdus et al., 2015; Rural Health Snapshot, 2017; Liddell and Meyer, 2022). While almost all US snakebite victims are able to reach care, the above populations likely face financial toxicity as a result (Tupetz et al., 2022).

A recent analysis found an association between morality and poverty in SBE on a global scale (Harrison et al., 2009). In BR, cost is not a patient problem, but time-to-care for rural, indigenous, and agricultural

populations result in disproportionate SBE burden (Schneider et al., 2021a). Further, within rural areas, SBE fatality rate in indigenous populations is 3.5 times higher than their nonindigenous counterparts (Schneider et al., 2021b). These are health system issues, but health providers in BR emphasized improving care through provider training and education. BR has an extensive community health center network in the Amazon; the gap in SBE care largely surrounds ensuring sufficient, quality human resources, education on clinical management practices (Rocha et al., 2022), and equipment (Beck et al., 2022).

In terms of health care delivery models, BR and US health providers discussed SBE treatment within a task-shifting model (van Schalkwyk et al., 2020) or specialized care model, respectively. This difference is related to human resource availability and reflected in who tends to care for SBE patients: nurses in BR and doctors in the US. Physicians as the primary caretaker of SBE patients in the US is consistent with other high-resource settings (Boniol et al., 2022). The leader of the care team in low-resource settings varies. For example, several South Asian countries are similar to BR in their shortage of doctors at primary or community health centers (Mukherjee and Mackessy, 2021), whereas SBE care is distributed almost equally between nurses and doctors in Kenya, Uganda, and Zambia (Ooms et al., 2021).

Our study highlights the need for a multidimensional analysis of the health system when introducing SBE care packages to new contexts and/or adapting existing resources. Implementation science approaches can

facilitate and guide these processes. These approaches should prioritize the input of local professionals—if not health providers, then other agents of change and decision-makers (e.g., community leaders, traditional medicine practitioners). Accounting for, and understanding, sociocultural and resource differences is crucial to the success of initiatives intended to improve care access and quality. This study demonstrated that implementation science is necessary to close the know-do gap by 2030, as outlined in the WHO prevention and control strategy ([Snakebite envenoming, 2020](#)). Such SBE initiatives would be more effective, sustainable, and feasible than efforts without an implementation science focus.

## 5. Limitations

This study has limitations that should be considered when interpreting the results. The BR data includes more nurses than physicians. Our analysis might have benefited from additional physician input, along with nurse assistants, who are often primary care providers in community health clinics and involved in SBE care. However, while physician input would have increased multidisciplinary representation, the majority of SBE patients in BR are treated by nurses, especially in remote areas where physicians are not available 24/7. Additionally, FGDs were conducted within the context of a five-day workshop focusing on SBE treatment, which could have prompted the participants to focus on training needs. Lastly, conclusions drawn from these data are not generalizable beyond clinics in and around the Amazon. However, this limitation is amenable, since the disease burden is concentrated around this region in the country.

The US interviews reflect only the emergency physicians' perspectives. While our analysis would likely have benefited from input further along the care continuum, such as outpatient or follow-up care providers, emergency care physicians are the first point of contact for the majority of SBE patients and managing the continuum of care. Some participants might have known the primary investigator (PI). We thus adhered to a strict deidentification protocol, and the PI was not involved in data collection and analysis. Lastly, the data is largely based on a maximum variation sample in terms of setting. This gives a window of insight into several contexts, but not a deep-dive into each. SBE burden and resources are highly dependent on context; a clinic on an American Indian reservation is vastly different from an urban hospital. However, for the purpose of the study, a variety of healthcare facilities within the US healthcare system provided valuable insight into system-level challenges.

## 6. Conclusion

This study sought to analyze the perceptions of health professionals regarding snakebite envenoming care across two different health systems and sociocultural contexts, the Brazil and the United States. Despite similar core barriers to adequate SBE care and factors to consider when trying to improve care, health professionals in different health systems and sociocultural contexts identified different specific needs. Accounting for, and understanding, these differences is crucial to the success of initiatives intended to strengthen SBE care. Implementation science approaches—with an explicit focus on health care provider and community engagement—should be applied when developing new or adapting existing evidence-based practices for SBE. Such efforts would reduce the disease burden on the health system, providers, and patients, and move the field toward the WHO goals for 2030.

## Credit author statement

Conceptualization (ES, AT, JRNV, WM, FM, CJG); Methodology (ES, AT, WM, FM, LKB, JRNV); Data curation (ES, AT, LKB); Validation (AT, WM, FM, JRNV, AJP, CJG); Formal analysis (ES, AT, LKB, WM, FM, PS, ASF, GSR, FRR, VAM, FHW); Investigation (AT, LKB, PS, ASF, GSR, FRR, VAM, FHW); Writing-original draft preparation (ES, AT, WM); Project administration (ES, AJP); Fund acquisition (WM, CJG, CAS, JS, FR); Writing – review & editing (ES, AT, WM, JRNV).

## Funding

J.S., F.R. and W.M.M. were funded by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq productivity scholarships). W.M. was funded by Fundação de Amparo à Pesquisa do Estado do Amazonas (PRÓ-ESTADO, call 011/2021 - PCGP/FAPEAM, call 010/2021 - CT&I ÁREAS PRIORITÁRIAS, call 003/2022 - PRODOC/FAPEAM, and POSGRAD) and by the Ministry of Health, Brazil (proposal No. 733781/19-035). F.M. is funded by Fiocruz (Inova scholarship). CJG receives research funding and research reported in this publication was partly supported by the Fogarty International Center of the National Institutes of Health under Award Number R21TW011944. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The underlying US-based qualitative study was funded by BTG Specialty Pharmaceuticals. The US study team (JRNV, CJG, LKB, AJP, AT) received funding for salary support of this investigator-initiated research project.

## Ethics statement

The Brazil study was approved by the Research Ethics Committee of the Universidade do Estado do Amazonas (UEA) (CAAE: 35855820.2.0000.5016). The USA study was approved by the Duke Health Institutional Review Board (Pro00103272). Written (BR) and/or verbal (BR, USA) informed consent was obtained from all participants involved in these studies.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Charles J Gerardo reports financial support was provided by National Institutes of Health. Wuelton Monteiro, Jacqueline Sachett, and Flavia Regina Ramos report financial support was provided by Conselho Nacional de Desenvolvimento Científico e Tecnológico. Wuelton Monteiro reports financial support was provided by Fundação de Amparo à Pesquisa do Estado do Amazonas and the Brazilian Ministry of Health. Felipe Murta reports financial support was provided by Fiocruz. Wuelton Monteiro and Joao RN Vissoci have served in an editorial capacity for Toxicon:X.

## Data availability

Data will be made available on request.

## Acknowledgments

We would like to thank all health care professionals who participated in this research.

## Appendix A

The table below is a more detailed examination of SBE in Brazil versus the United States.

**Table A1**  
Snakebite envenoming incidence and care factors in Brazil versus the US.

	Brazil	United States
<b>Health system</b>	Brazil has one of the largest universal public healthcare systems in the world, known as the Sistema Único de Saúde (SUS). SUS aims to decentralize access to healthcare through its network of community health centers (CHC). SUS provides primary care coverage to 90% of municipalities, roughly 70% of the population, and reaches most remote areas of the country—including the Brazilian Amazon. Indigenous communities have an independent health system (Sistema Único de Saúde, 2022).	The US has no universal healthcare system or coverage. Healthcare can be defined as a mixed system, with publicly funded programs (Medicare, Medicaid) and privately funded market coverage (insurance). In 2019, about 56% of the population was privately insured, 35% was publicly insured, and 9% (roughly 30 million people) was uninsured (Health Insurance Coverage of the, 2020). Disparities in healthcare access and outcomes exist along racial, ethnic, and economic lines (Wasserman et al., 2019). Alaskan Native and American Indian communities are sovereign entities and have an independent universal healthcare system (About IHS, Indian Health, 2022).
<b>Types of health facilities with antivenom</b>	In Brazil, in 2021, antivenom treatment was available in 2190 public health units in 2004 municipalities (36% of the 5568 Brazilian municipalities) and Brasília, in the Federal District. In the Amazon region, 553 registered health units provide AV, located in 490 municipalities (63.5% of the municipalities in this region) of the nine states (Citeli et al., 2018). In some regions with indigenous and riverside communities, especially in the Brazilian Amazon, the long distances to the hospital delay the antivenom access of snakebite patients (Beck et al., 2022).	Antivenoms for rare or exotic snakes (often pets) are usually stored in zoos (Basse et al., 2022). Antivenoms are available in select hospitals, but almost always available by flight or other transport unless there is a severe weather event (Tupetz et al., 2022). Antivenom within the indigenous health system is more difficult to obtain (Tupetz et al., 2022).
<b>Antivenoms available and manufacturers</b>	All snake antivenoms are provided free from the Ministry of Health (Wen et al., 2015). Due to the great biological diversity of snakes, six AV F (ab') <sup>2</sup> (equine) are produced in Brazil: <ul style="list-style-type: none"> <li>• <i>Bothrops</i> antivenom.</li> <li>• <i>Crotalus</i> antivenom.</li> <li>• <i>Bothrops-Crotalus</i> antivenom.</li> <li>• <i>Bothrops-Lachesis</i> antivenom.</li> <li>• <i>Micrurus</i> antivenom.</li> </ul> All snake antivenoms are produced by four public manufacturers (Beck et al., 2022): <ul style="list-style-type: none"> <li>• Instituto Butantan (São Paulo)</li> <li>• Fundação Ezequiel Dias (Belo Horizonte)</li> <li>• Instituto Vital Brazil (Rio de Janeiro)</li> <li>• Centro de Produção e Pesquisa de Imunobiológicos (Curitiba)</li> </ul>	<ul style="list-style-type: none"> <li>• Crotalidae polyvalent immune Fab (ovine) is manufactured by BTG Specialty Pharmaceuticals through a multinational manufacturing process and imported to the US.</li> <li>• Crotalidae immune F (ab')<sup>2</sup> (equine) is manufactured by Bioclon Institute in Mexico and imported to the US by Rare Disease Therapeutics.</li> </ul>
<b>Snake species and associated symptoms</b>	<ul style="list-style-type: none"> <li>• The <i>Bothrops</i> genus (lancehead pit vipers) is responsible for ~90% of snakebite envenomings in Brazil. The venom has coagulant, hemorrhagic, and proteolytic or acute inflammatory effects, which results in systemic (bleeding and acute renal failure) and local (pain, swelling, blisters, ecchymosis, necrosis) manifestations (Guia de Vigilância Epidemiológica, 2009).</li> <li>• <i>Crotalus durissus</i>, the South America rattlesnake, is responsible for ~8% of the snakebite envenomings in Brazil. The venom has neurotoxic and myotoxic effects, causing pain and mild edema in the bite site as well as blurred vision, myasthenic facies, palpebral ptosis, myalgia, muscle weakness, acute renal failure, and rhabdomyolysis (Guia de Vigilância Epidemiológica, 2009).</li> <li>• <i>Lachesis muta</i> (bushmaster) venom has coagulant, hemorrhagic, proteolytic, and neurotoxic effects, resulting in the same manifestations as <i>Bothrops</i>. Some patients present with vagal syndrome (Guia de Vigilância Epidemiológica, 2009).</li> <li>• <i>Micrurus</i> genus (coral snakes) venom has neurotoxic effects, leading to nausea, vomiting, paresthesia, slurred speech, double vision, ptosis, muscle twitching, weakness, paralysis, and respiratory failure (Guia de Vigilância Epidemiológica, 2009).</li> </ul>	<ul style="list-style-type: none"> <li>• Crotaline (pit vipers) are responsible for ~96% of SBE in the US (Greene et al., 2021). The venom has systemic (bleeding, gastrointestinal, cardiovascular) local (pain, swelling, blisters, ecchymosis, necrosis), and occasionally neurotoxic manifestations. <ul style="list-style-type: none"> <li>◦ <i>Agkistrodon contortrix</i> (copperhead) snakes are responsible for 45–50% of crotaline envenomings (Greene et al., 2021).</li> <li>◦ The <i>Crotalus</i> and <i>Sistrurus</i> genera (i.e., rattlesnakes) cause 30–40% (Greene et al., 2021).</li> <li>◦ <i>A. piscivorus</i> (cottonmouths) cause 10–15% (Greene et al., 2021).</li> </ul> </li> <li>• Elapids from the <i>Micrurus</i> and <i>Micruroides</i> genera (coral snakes) are responsible for ~3% of SBEs (Greene et al., 2021). The venom is neurotoxic and can result in nausea, vomiting, paresthesia, slurred speech, double vision, ptosis, muscle twitching, weakness, paralysis, and respiratory failure.</li> <li>• Exotic or non-native snakes from zoos or private homes are responsible for ~1% of envenomings (Greene et al., 2021).</li> </ul>
<b>Most affected populations</b>	Indigenous communities (Monteiro et al., 2020); rural and riverine populations (Salazar et al., 2021)	Indigenous and minority communities; rural populations
<b>Epidemiological surveillance</b>	Mandatory reporting of incidence and mortality to the Information Technology Department of the SUS (DATASUS) (DATASUS, 2022).	No standardized, mandatory reporting system for snakebite envenomings. One ICD-10 code represents SBE (TCD-63: Toxic effect of snakebite venom). Data can be pulled from hospital systems, notably the Agency for Healthcare Research and Quality's National Emergency Department Sample (NEDS), to determine epidemiology, but are likely an underestimation and limited to patients seen in emergency departments (Greene et al., 2021). In addition, the National Poison Data System (NPDS) (i.e., Poison Control) logs the calls it receives and releases annual statistics (Poison Statistics, 2022). The military has the only official case reporting system: the Defense Medical Surveillance System (DMSS) (Brief Report, 2021).
<b>Incidence</b>	15 snakebite envenomings per 100,000 persons (36% in Amazon region; ~55 cases per 100,000 persons (DATASUS, 2022).	1.6 snakebite envenomings per 100,000 persons (Chippaux, 2017).
<b>Mortality</b>	0.4 deaths from snakebite envenoming per 100 persons (0.6 in Amazon region) (DATASUS, 2022).	0.002 deaths from snakebite envenoming per 100,000 persons (Chippaux, 2017).

(continued on next page)



**Table A1** (continued)

	Brazil	United States
<b>Official treatment guideline</b>	Yes. The current guideline is from the Ministry of Health ( <a href="#">Guia de Vigilância Epidemiológica, 2009</a> ). An additional clinical practice guideline specific to CHCs was recently developed ( <a href="#">Rocha et al., 2022</a> ).	No official guideline, but Lavonas et al. developed a commonly used unified treatment algorithm for crotaline envenomings ( <a href="#">Lavonas et al., 2011</a> ).

## Appendix B

Overview of focus group discussion guide for the BR study.

1. Who here has treated someone that has been bitten by a snake? Can you tell us about your experience?
  - a. Place of treatment (at the hospital or elsewhere)
  - b. Severity of the cases
  - c. Complications/outcomes
  - d. Use of antivenom
  - e. Traditional remedies and self-care procedures observed
  - f. Where the knowledge that was used in the treatment of these cases came from
2. What subjects most interest you in this training course?
  - a. Specific topics/classes
  - b. Added knowledge
  - c. Conduct in practice
  - d. Subjects that are more difficult to understand
3. How can this care practice guideline (CPG) contribute to the medical assistance you will provide in the future?
  - a. Feel more prepared/confident
  - b. Possibility of applying the CPG in the municipality where I work
4. What suggestions would you give for improving the CPG?
  - a. Contents to be added, deleted or improved
  - b. Need for structure and presentation improvements

## Appendix C

Overview of interview guide for the US study.

1. Please introduce yourself to us.
2. Have you ever treated a snakebite before?
  - a. If so, how many snakebite patients do you typically treat in a year?
  - b. What is the most prominent snake envenomation types you treat in this facility?
3. How would you usually approach treating a snakebite patient?
  - a. Can you provide an example?
4. From a more general point of view, not specifically this one case, what usually informs your decision-making process?
  - a. What factors are influencing your decision? (snake type, bite location, time since bite etc)
  - b. Are there any workplace policies related to snakebite treatment?
  - c. Is there a consistent guideline followed in your institution? How does the proposed treatment policy look like?
  - d. What are other alternative treatment options in snake bite envenomation patients?
  - e. How much were snake bite treatments covered in your residency, and how does the current training of residents look for the management of snake bite envenomation?
5. Based on your experience, how effective are the current procedures for treating envenomation patients?
  - a. What is the most effective treatment?
6. How do you feel about using antivenom as part of your treatment? Why?
7. As you probably know, there is an ongoing controversy about what the best and most appropriate approaches are to manage snake bites. What case would you make personally, to convince the people that would disagree with your usual approach?
8. Why do you think there is this ongoing debate about the usage of antivenom to treat snake bites?
9. How can we solve this debate?
10. Is there anything else that you think we have missed, and you would like to add, before we stop the recording?

## References

- Abdus, S., Mistry, K.B., Selden, T.M., 2015. Racial and ethnic disparities in services and the patient protection and affordable care Act. *Am. J. Publ. Health* 105 (Suppl. 5), S668–S675. Nov.
- About IHS. Indian health service (IHS) [internet]. About IHS [cited 2022 Aug 15]. Available from: <https://www.ihs.gov/aboutihs/>.
- Bala, A.A., Jatau, A.I., Yunusa, I., Mohammed, M., Mohammed, A.K.H., Isa, A.M., et al., 2020. Development and validation of antisnake venom knowledge assessment tool (AKAT) for healthcare practitioners. *Toxicon X* 8, 100064. Dec 1.
- Barnes, K., Ngari, C., Parkurito, S., Wood, L., Otundo, D., Harrison, R., et al., 2021. Delays, fears and training needs: perspectives of health workers on clinical management of snakebite revealed by a qualitative study in Kitui County, Kenya. *Toxicon X* 11, 100078. Sep 1.
- Basse, J., Ruha, A.M., Baumgartner, K., Mullins, M.E., Greene, S., Wax, P.M., et al., 2022. Clinical presentations, treatments, and outcomes of non-native snake envenomations

- in the United States reported in the North American snakebite registry [Internet] *J. Med. Toxicol.* <https://doi.org/10.1007/s13181-022-00912-4>. Sep 29 [cited 2022 Oct 14]; Available from:
- Beck, T.P., Tupetz, A., Farias, A.S., Silva-Neto, A., Rocha, T., Smith, E.R., et al., 2022. Mapping of clinical management resources for snakebites and other animal envenomings in the Brazilian Amazon. *Toxicol X* 16, 100137. Dec 1.
- Boniol, M., Kunjumen, T., Nair, T.S., Siyam, A., Campbell, J., Diallo, K., 2022. The global health workforce stock and distribution in 2020 and 2030: a threat to equity and ‘universal’ health coverage? *BMJ Glob Health* 7 (6), e009316. Jun 27.
- Brief report: medical encounters for snakebite envenomation, active and reserve components, U.S. Armed forces, 2016–2020 [Internet] *Military Health System*, 2021 [cited 2022 Aug 15]. Available from: <https://health.mil/News/Articles/2021/06/01/Brief-Report-June-2021>.
- Chippaux, J.P., 2017. Incidence and mortality due to snakebite in the Americas. *PLoS Neglected Trop. Dis.* 11 (6), e0005662. Jun 21.
- Chu, J., Leino, A., 2017. Advancement in the maturing science of cultural adaptations of evidence-based interventions. *J. Consult. Clin. Psychol.* 85, 45–57.
- Citeli, N., Magalhaes, M., Cavalcante, M., Bochner, R., 2018. Lista dos Polos de Soro para atendimento de acidentes ofídicos no Brasil [Internet]. SINITOX [cited 2022 Oct 10]. Available from: <https://sinitox.icict.fiocruz.br/polos-de-soro-para-acidentes-ofidicos>
- Cristino, J.S., Salazar, G.M., Machado, V.A., Honorato, E., Farias, A.S., Vissoci, J.R.N., et al., 2021. A painful journey to antivenom: the therapeutic itinerary of snakebite patients in the Brazilian Amazon (The QUALISnake Study). *PLoS Neglected Trop. Dis.* 15 (3), e0009245. Mar 4.
- Datasus - Ministry of health [internet] [cited 2022 Aug 15]. Available from: <https://datasus.saude.gov.br/>.
- Duda, R., Monteiro, W.M., Giles-Vernick, T., 2021. Integrating lay knowledge and practice into snakebite prevention and care in central Africa, a hotspot for envenomation. *Toxicol X* 11, 100077. Sep 1.
- eCFR. 21 CFR Part 316 – orphan drugs [Internet] [cited 2022 Sep 2]. Available from: <https://www.ecfr.gov/current/title-21/part-316>.
- Escoffery, C., Lebow-Skelley, E., Haardoerfer, R., Boing, E., Udelson, H., Wood, R., et al., 2018. A systematic review of adaptations of evidence-based public health interventions globally. *Implement. Sci.* 13 (1), 125. Sep 26.
- Evans, R.E., Craig, P., Hodinott, P., Littlecott, H., Moore, L., Murphy, S., et al., 2019. When and how do ‘effective’ interventions need to be adapted and/or re-evaluated in new contexts? The need for guidance. *J. Epidemiol. Community Health* 73 (6), 481–482. Jun 1.
- Greene, S.C., Folt, J., Wyatt, K., Brandehoff, N.P., 2021. Epidemiology of fatal snakebites in the United States 1989–2018. *Am. J. Emerg. Med.* 45, 309–316. Jul 1.
- Guia de Vigilância Epidemiológica, 7th Ed [Internet]. Ministério da Saúde, Secretaria de Vigilância em Saúde, Departamento de Vigilância Epidemiológica. Report No.: 7 ed. Available from: [https://bvsms.saude.gov.br/bvs/publicacoes/guia\\_vigilancia\\_epi\\_demologica\\_7ed.pdf](https://bvsms.saude.gov.br/bvs/publicacoes/guia_vigilancia_epi_demologica_7ed.pdf).
- Gupta, R., Harmon, J., Conway, P.H., 2019. The next frontier in reducing costs of care: patient affordability. *NEJM catal* [internet]. Aug 22 [cited 2022 Oct 13]; Available from: <https://catalyst.nejm.org/doi/full/10.1056/CAT.19.0625>.
- Gutiérrez, J.M., 2014. Reducing the impact of snakebite envenoming in Latin America and the Caribbean: achievements and challenges ahead. *Trans. R. Soc. Trop. Med. Hyg.* 108 (9), 530–537. Sep 1.
- Gutiérrez, J.M., Lomonte, B., León, G., Rucavado, A., Chaves, F., Angulo, Y., 2007. Trends in snakebite envenomation therapy: scientific, technological and public health considerations. *Curr. Pharmaceut. Des.* 13 (28), 2935–2950.
- Gutiérrez, J.M., Williams, D., Fan, H.W., Warrell, D.A., 2010. Snakebite envenoming from a global perspective: towards an integrated approach. *Toxicol X* 56 (7), 1223–1235. Dec 15.
- Gutiérrez, J.M., Burnouf, T., Harrison, R.A., Calvete, J.J., Brown, N., Jensen, S.D., et al., 2015. A call for incorporating social research in the global struggle against snakebite. *PLoS Neglected Trop. Dis.* 9 (9), e0003960. Sep 17.
- Gutiérrez, J.M., Maduwage, K., Iliyasa, G., Habib, A., 2021. Snakebite envenoming in different national contexts: Costa Rica, Sri Lanka, and Nigeria. *Toxicol X* 9–10, 100066. Jul 1.
- Harrison, R.A., Hargreaves, A., Wagstaff, S.C., Faragher, B., Laloo, D.G., 2009. Snake envenoming: a disease of poverty. *PLoS Neglected Trop. Dis.* 3 (12), e569. Dec 22.
- Health insurance coverage of the total population [internet]. KFF [cited 2022 Aug 15]. Available from: <https://www.kff.org/other/state-indicator/total-population/>.
- Jaramillo, J.D., Hakes, N.A., Tennakoon, L., Spain, D., Forrester, J.D., 2019. The “T” of snakebite injury in the USA: fact or fiction? *Trauma Surg Acute Care Open* 4 (1), e000374. Oct 1.
- Khan, T., Abimbola, S., Kyobutungi, C., Pai, M., 2022. How we classify countries and people—and why it matters. *BMJ Glob Health* 7 (6), e009704. Jun 1.
- Lavonas, E.J., Ruha, A.M., Banner, W., Beberta, V., Bernstein, J.N., Bush, S.P., et al., 2011. Unified treatment algorithm for the management of crotaline snakebite in the United States: results of an evidence-informed consensus workshop. *BMC Emerg. Med.* 11 (1), 2. Feb 3.
- Liddell, J.L., Meyer, S., Healthcare needs and infrastructure obstacles for a state-recognised indigenous tribe in the United States. *Health soc care community* [internet] [cited 2022 Oct 13];n/a(n/a). Available from: <https://onlineibrary.wiley.com/doi/abs/10.1111/hsc.14031>.
- Longbottom, J., Shearer, F.M., Devine, M., Alcoba, G., Chappuis, F., Weiss, D.J., et al., 2018. Vulnerability to snakebite envenoming: a global mapping of hotspots. *Lancet* 392 (10148), 673–684. Aug 25.
- Monteiro, W.M., de Farias, A.S., Val, F., Neto, A.V.S., Sachtet, A., Lacerda, M., et al., 2020. Providing antivenom treatment access to all Brazilian Amazon indigenous areas: ‘every life has equal value. *Toxins* 12 (12), 772. Dec 5.
- Mukherjee, A.K., Mackessy, S.P., 2021. Prevention and improvement of clinical management of snakebite in Southern Asian countries: a proposed road map. *Toxicol X* 200, 140–152. Sep 1.
- Ooms, G.I., van Oirschot, J., Waldmann, B., von Bernus, S., van den Ham, H.A., Mantel-Teeuwisse, A.K., et al., 2021. The current state of snakebite care in Kenya, Uganda, and Zambia: healthcare workers’ perspectives and knowledge, and health facilities’ treatment capacity. *Am. J. Trop. Med. Hyg.* 104 (2), 774–782. Feb.
- Poison statistics [internet] [cited 2022 Sep 2]. Available from: <https://www.poison.org/poison-statistics-national>.
- Pucca, M.B., Cerni, F.A., Janke, R., Bermúdez-Méndez, E., Ledsgaard, L., Barbosa, J.E., et al., 2019. History of envenoming therapy and current perspectives. *Front Immunol* [Internet] [cited 2022 Sep 12];10. Available from: <https://www.frontiersin.org/articles/10.3389/fimmu.2019.01598>.
- Rocha, G. dos S., Farias, A.S., Alcântara, J.A., Machado, V.A., Murta, F., Val, F., et al., 2022. Validation of a culturally relevant snakebite envenomation clinical practice guideline in Brazil. *Toxins* 14 (6), 376. May 28.
- Rural health Snapshot [Internet]. Sheps Center. [cited 2022 Oct 13]. Available from: <https://www.shepscenter.unc.edu/product/rural-health-snapshot-2017/>.
- Sabatier, P.A., 1986. Top-down and bottom-up approaches to implementation research: a critical analysis and suggested synthesis. *J. Publ. Pol.* 6 (1), 21–48. Jan.
- Sadler, G.R., Lee, H.C., Lim, R.S.H., Fullerton, J., 2010. Recruitment of hard-to-reach population subgroups via adaptations of the snowball sampling strategy. *Nurs. Health Sci.* 12 (3), 369–374. Sep 1.
- Salazar, G.K.M., Cristino, J.S., Silva-Neto, A.V., Farias, A.S., Alcântara, J.A., Machado, V.A., et al., 2021. Snakebites in “Invisible Populations”: a cross-sectional survey in riverine populations in the remote western Brazilian Amazon. *PLoS Neglected Trop. Dis.* 15 (9), e0009758. Sep 9.
- Sapkota, S., Pandey, D.P., Dhakal, G.P., Gurung, D.B., 2020. Knowledge of health workers on snakes and snakebite management and treatment seeking behavior of snakebite victims in Bhutan. *PLoS Neglected Trop. Dis.* 14 (11), e0008793. Nov 30.
- Schiaffino Salazar, F., 2021. Snakebites in the Global Health Agenda of the Twenty First Century: A South to South Collaborative Effort [Internet] [Thesis]. Johns Hopkins University [cited 2022 Oct 13]. Available from: <https://jscholarship.library.jhu.edu/handle/1774.2/64108>.
- Schneider, M.C., duk, Min K., Hamrick, P.N., Montebello, L.R., Ranieri, T.M., Mardini, L., et al., 2021a. Overview of snakebite in Brazil: possible drivers and a tool for risk mapping. *PLoS Neglected Trop. Dis.* 15 (1), e0009044. Jan 29.
- Schneider, M.C., Vuckovic, M., Montebello, L., Sarpy, C., Huang, Q., Galan, D.I., et al., 2021b. Snakebites in rural areas of Brazil by race: indigenous the most exposed group. *Int. J. Environ. Res. Publ. Health* 18 (17), 9365. Jan.
- Silva, A., Isbister, G.K., 2020. Current research into snake antivenoms, their mechanisms of action and applications. *Biochem. Soc. Trans.* 48 (2), 537–546. Mar 20.
- Sistema Único de Saúde (SUS): estrutura, princípios e como funciona [Internet]. Ministério da Saúde [cited 2022 Oct 10]. Available from: <https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/s/sus-estrutura-principios-e-como-funciona/sistema-unico-de-saude-sus-estrutura-principios-e-como-funciona>.
- [Internet] Snakebite Envenoming: A Strategy for Prevention and Control, 2020. World Health Organization, Geneva [cited 2022 Aug 10] p. 70. Available from: <https://apps.who.int/iris/handle/10665/355282>.
- Theobald, S., Brandes, N., Gyaopong, M., El-Saharty, S., Proctor, E., Diaz, T., et al., 2018. Implementation research: new imperatives and opportunities in global health. *Lancet* 392 (10160), 2214–2228. Nov 17.
- Tupetz, A., Barcenas, L.K., Phillips, A.J., Vissoci, J.R.N., Gerardo, C.J., 2022. BITES study: a qualitative analysis among emergency medicine physicians on snake envenomation management practices. *PLoS One* 17 (1), e0262215. Jan 7.
- van Schalkwyk, M.C., Bourek, A., Kringos, D.S., Siciliani, L., Barry, M.M., De Maeseneer, J., et al., 2020. The best person (or machine) for the job: rethinking task shifting in healthcare. *Health Pol.* 124 (12), 1379–1386. Dec 1.
- Wasserman, J., Palmer, R.C., Gomez, M.M., Berzon, R., Ibrahim, S.A., Ayanian, J.Z., 2019. Advancing health services research to eliminate health care disparities. *Am. J. Publ. Health* 109 (S1), S64–S69. Jan.
- Wen, F.H., Monteiro, W.M., Silva, AMM da, Tambourgi, D.V., Silva, IM da, Sampaio, V.S., et al., 2015. Snakebites and scorpion stings in the Brazilian Amazon: identifying research priorities for a largely neglected problem. *PLoS Neglected Trop. Dis.* 9 (5), e0003701. May 21.
- What is implementation science?. Implementation Science at UW [Internet]. [cited 2022 Sep 13]. Available from: <https://impsciuw.org/implementation-science/learn/implementation-science-overview/>.
- Ye, W., Rodriguez, J.M., 1982. Highly vulnerable communities and the Affordable Care Act: health insurance coverage effects, 2010–2018. *Soc. Sci. Med.* 270, 113670, 2021 Feb.
- Tong, A., Sainsbury, P., Craig, J., 2007. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care.* 19 (6), 349–357 Dec.