



Decentralization of snakebite antivenom treatment to indigenous community health centers in the Brazilian Amazon: From demand to the first treatment (the SAVING Program)

WUELTON MARCELO MONTEIRO
Fundação de Medicina Tropical Dr. Heitor Vieira Dourado
Universidade do Estado do Amazonas

GOVERNO FEDERAL
MINISTÉRIO DA SAÚDE
BRASIL
UNIÃO E RECONSTRUÇÃO

SAVING



INSTITUTO BUTANTAN
A serviço da vida



LSTM
LIVERPOOL SCHOOL
OF TROPICAL MEDICINE

FVS-RCP

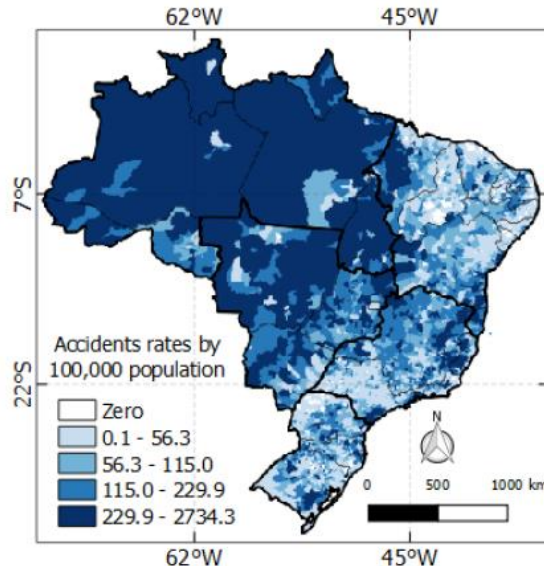


FMT-HVD





Bothrops atrox



SBEs IN THE BRAZILIAN AMAZON: AN OVERVIEW

- 50 cases/100,000 inhabitants;
- 5 times higher than in the Extra-Amazonia;
- ~90% caused by *B. atrox*. (Monteiro et al., 2020)

- Costs per year: US\$8 million (Magalhães et al., 2020)

- Systemic complications:

Systemic bleeding: 15% (Oliveira et al., 2019)

Acute kidney injury: 13% (Alves et al., 2018)

Thrombotic microangiopathy: 11% (Bentes et al., in preparation)

- Local complications (Sachett et al., 2018):

Secondary bacterial infections: 40%

Permanent disabilities: 5%

- Case-fatality: 0.6% (Souza et al., 2018)

Risk factors: Time to care >6 hrs, age ≥61 years, Indigenous status, lack of AV administration

Causes of death (n=127): AKI (29.1%), acute respiratory failure (28.3%), sepsis (24.4%), circulatory shock (21.3%), systemic bleeding (including hemorrhagic strokes) (15%)

SNAKE ANTIVENOMS IN BRAZIL

- horse-derived F(ab')₂ Igs

- 4 producers:

Bothrops AV

Bothrops-Lachesis AV

Crotalus AV

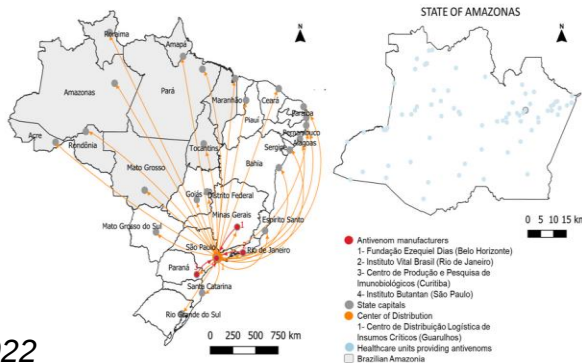
Bothrops-Crotalus AV

Micrurus AV

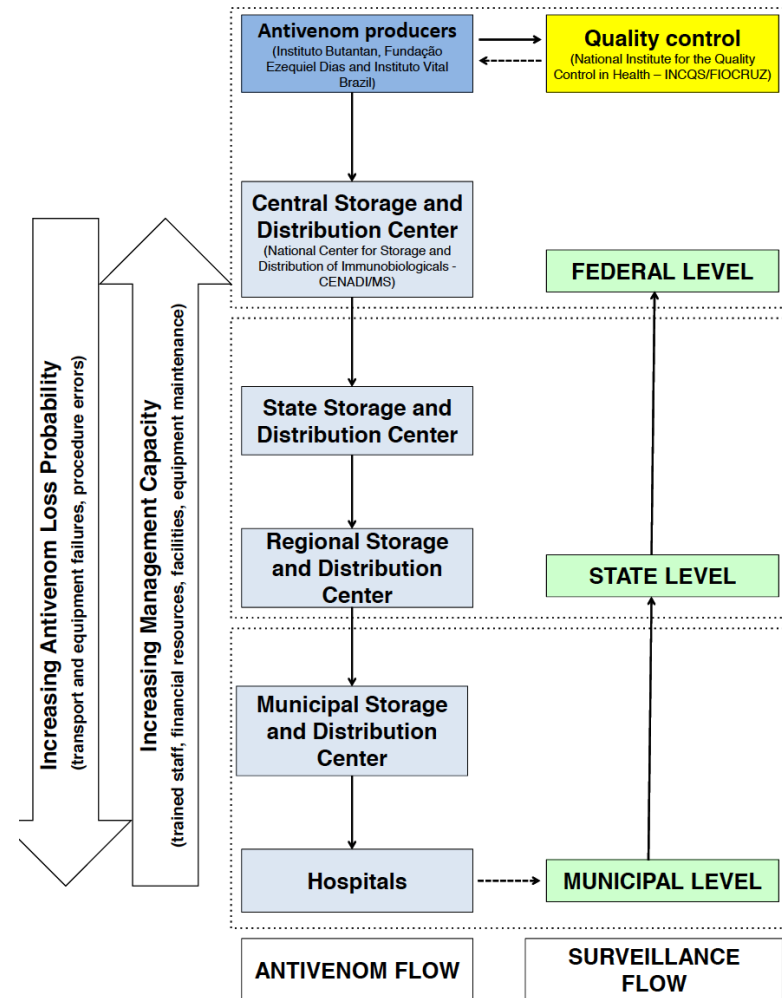
- Free of charge (MoH)

- 2,200 hospitals (2021)

- >300,000 vials/year



Beck et al., 2022



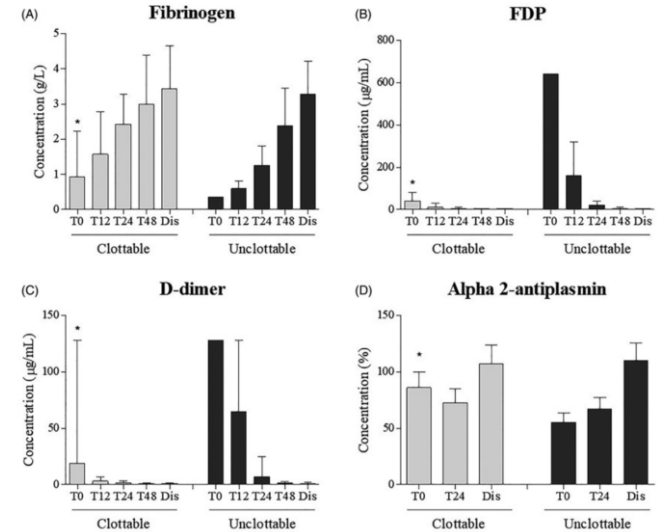
SNAKE ANTIVENOMS IN BRAZIL



BASIC RESEARCH

Bothrops snakebites in the Amazon: recovery from hemostatic disorders after Brazilian antivenom therapy

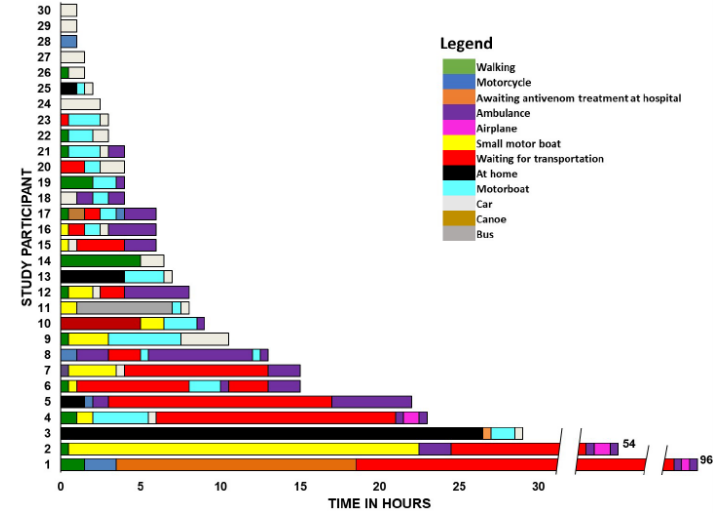
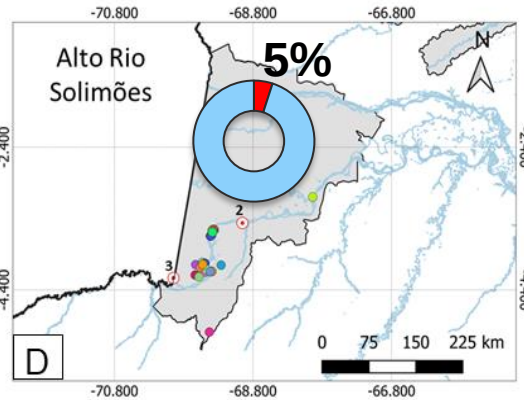
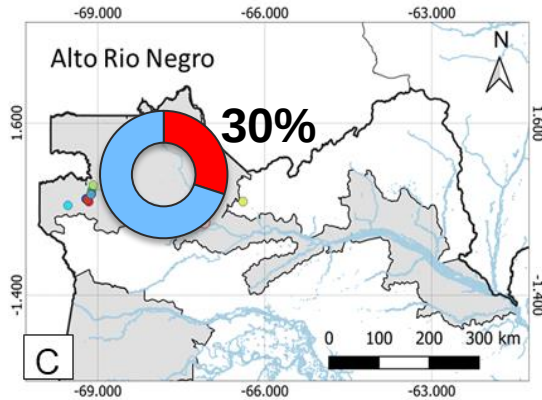
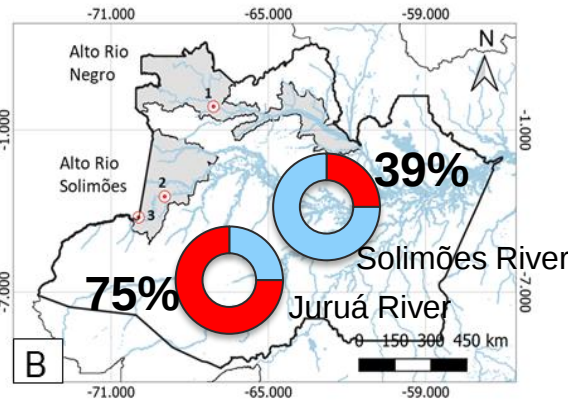
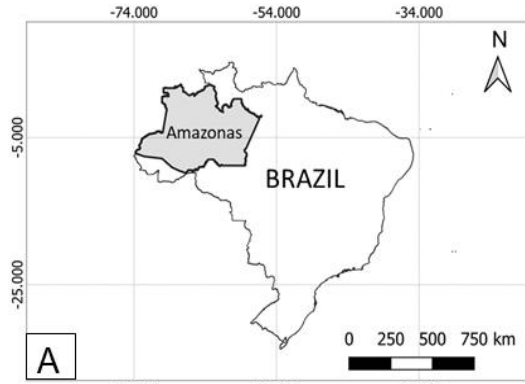
Sâmella Silva de Oliveira^{a,b}, Eliane Campos Alves^{a,b}, Alessandra dos Santos Santos^a, Elizandra Freitas Nascimento^a, João Pedro Tavares Pereira^a, Iran Mendonça da Silva^{a,b}, Jacqueline Sachett^{a,b}, Hiochelson Najibe dos Santos Ibiapina^{a,b}, Lybia Kássia Santos Sarraf^a, Jorge Carlos Contreras Bernal^{a,b}, Luciana Aparecida Freitas de Sousa^c, Mônica Colombini^c, Hedyamar Oliveira Marques^d, Marcus Vinicius Guimarães de Lacerda^a, Ana Maria Moura-da-Silva^c, Hui Wen Fan^e, Luiz Carlos de Lima Ferreira^a, Ida Sigueko Sano Martins^a and Wuelton Marcelo Monteiro^{a,b,e}



~10% of early adverse events (pruritus/urticaria)

(Soares et al., 2022)

INDIGENOUS HEALTH SYSTEM AND ACCESS INEQUALITIES



SBES IN THE BRAZILIAN AMAZON: CLINICAL ASPECTS



DECENTRALIZING ANTIVENOMS TO INDIGENOUS AREAS

Demands from
Indigenous
leaders/Indigenous
Health Districts
(2019)

Fundação de Vigilância em
Saúde do Amazonas
(responsible for SBE surveillance and
AV distribution in the state)

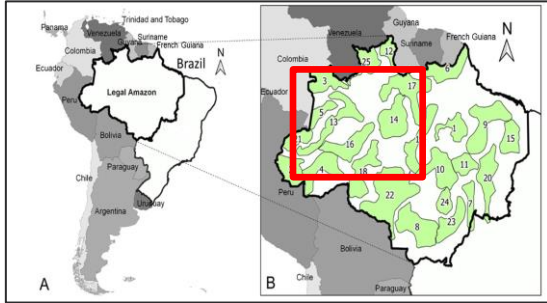
Brazilian Ministry of Health
(Venomous Animals Technical Group
AND
Indigenous Health Secretariat)

AV decentralization technical group:

1. FVS-AM (coordination)
2. MoH (Venomous Animals Technical Group and Indigenous Health Secretariat)
3. Amazonas Tropical Medicine Foundation
4. Seven DSEIs
5. Butantan Institute
6. Duke University



TG Meetings
AND
Professional Engagement
(Manaus, February 24-28, 2020)



SAVING

Snake Antivenom Immunoglobulins
NEED TO BE GUARANTEED



- 1) Develop a decentralized antivenom distribution program, optimized by the geographic location of SBEs and CHC facilities in a low resource area.
- 2) Conduct a formative intervention using a culturally relevant SBE care package.
- 3) Conduct an economic evaluation of various of the model of decentralized antivenom delivery.
- 4) Implement the decentralized antivenom distribution program in indigenous CHCs.

Demand-Informed Treatment Locations		
AIM 1		SAVING Program Technical Group Institution
AIM 2	PHASE I	Development and Validation of a Minimum Requirements Checklist for SBE Treatment
	PHASE II	Selection of the Indigenous Health Units
AIM 3	PHASE I	Development and Validation of a Culturally-Relevant CPG
	PHASE II	Training and Proficiency Evaluation of the Health Staff
Deliver of the Antivenoms to indigenous CHCs		
AIM 4	PHASE I	Estimates of Patient-Centered Clinical Outcomes
	PHASE II	Estimates of Implementation Outcomes
	PHASE III	Cost-effectiveness of the Decentralized Care Model

SAVING

Snake Antivenom Immunoglobulins
NEED TO BE GUARANTEED



AIM 1

Demand-Informed Treatment Locations

182 CHCs, 220,000 inhabitants, 1691 villages

- Technical group meeting (2019) – list of potential CHCs able to treat SBEs from the 7 DSEIs:

2 CHCs per Indigenous District (14 CHCs)

CHC coverage

Number of SBEs in the area – last 3 years

Electricity (AV storage)

Ability to transport patients

Presence of physicians

- Development, validation and application of a checklist – 80 essential items

Human resources

Equipment

Supplies

Medicines (Serrão-Pinto et al., 2024)



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Contents lists available at ScienceDirect

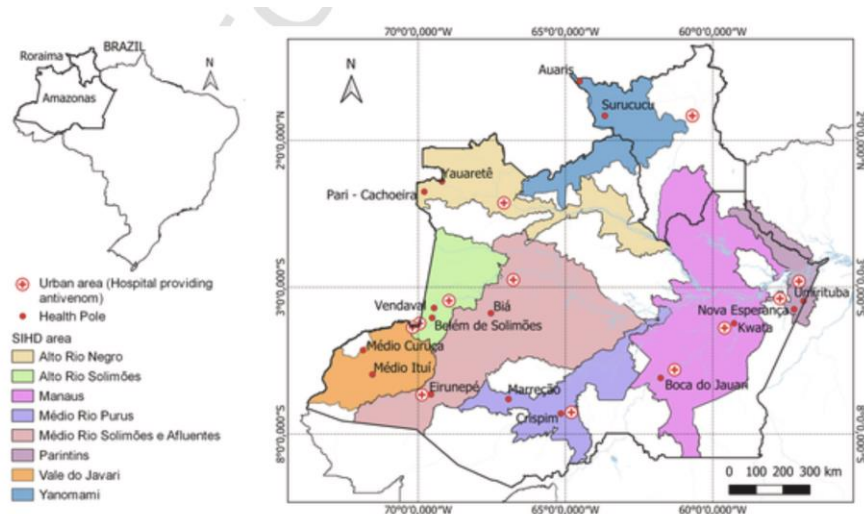
Toxicon

journal homepage: www.elsevier.com/locate/toxicon



Capacity of community health centers to treat snakebite envenoming in indigenous territories of the Brazilian Amazon

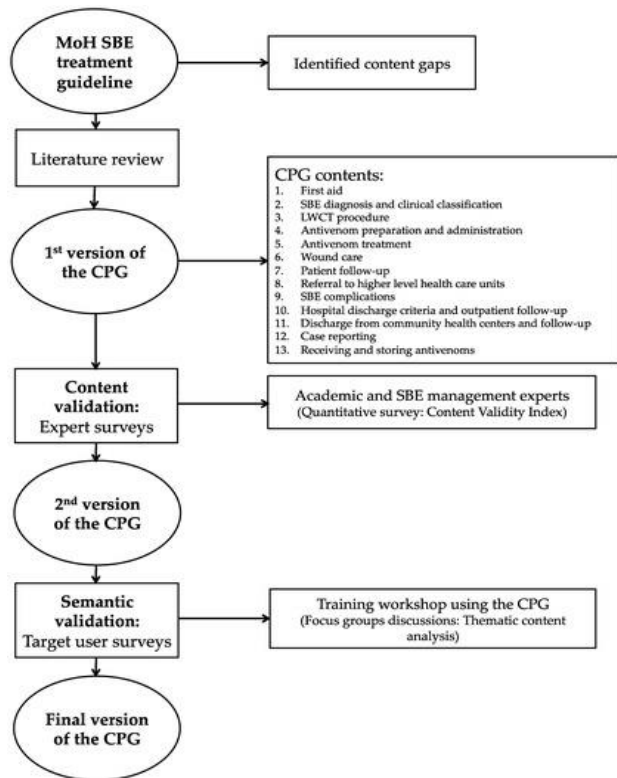
André Sachett^{a,b}, Eleanor Strand^c, Thiago Serrão-Pinto^{a,b,d}, Alexandre da Silva Neto^{a,b},
Thais Pinto Nascimento^{a,b}, Sewbert Rodrigues Jati^{a,b,e}, Gisele dos Santos Rocha^{a,b},
Sediel Ambrósio Andrade^a, Fan Hui Wen^f, Manuela Berto Pucca^g, João Vissoci^c,
Charles J. Gerardo^c, Jacqueline Sachett^{a,b}, Altair Seabra de Farias^{a,b}, Wuelton Monteiro^{a,b,g}



(Sachett et al., 2024)

AIM 2

Development and Validation of a Culturally-Relevant CPG



Article

Validation of a Culturally Relevant Snakebite Envenomation Clinical Practice Guideline in Brazil

Gisele dos Santos Rocha ^{1,2}, Altair Seabra Farias ^{1,2}, João Arthur Alcântara ^{1,2}, Vinicius Azevedo Machado ^{1,2}, Felipe Murta ^{1,2}, Fernando Val ^{1,2}, Joseir Saturnino Cristino ^{1,2}, Alicia Cacao Santos ^{1,2}, Mena Bianca Ferreira ^{1,2}, Leonardo Marques ^{1,2}, Yasmim Vieira Rocha ^{1,2}, André Sachett ^{1,2}, Mailma Costa Almeida ^{1,2}, Aline Alencar ^{1,2}, Lisele Brasileiro ^{1,2}, Érica da Silva Carvalho ^{1,2}, Pedro Ferreira Bisneto ^{1,2,3}, Marcus Lacerda ^{1,2,4}, Anna Tupetz ⁵, Catherine A. Staton ⁵, João R.N. Vissoci ⁵, Elizabeth Teixeira ¹, Charles J. Gerardo ⁵, Fan Hui Wen ^{6,†}, Jacqueline Sachett ^{1,2,7,†} and Wuelton Monteiro ^{1,2,*,†}



FG with target users during CPG validation

SPECIFIC AIMS – SAVING PROJECT

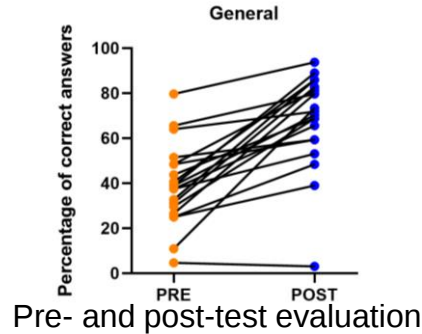
(Snake Antivenom Immunoglobulins Need to be Guaranteed)

AIM 4

PHASE I

Training and Proficiency Evaluation of the
CHCs Staff

June 27-1st July, 2022



April 23-24, 2024



Barriers identified:

- Lack of training in SBE treatment during technical or university courses
- Concerns on the turnover of human resources in the health units, and irregular antivenom and medicines supply
- Community education - awareness within the community

(Murta et al., 2023)

SPECIFIC AIMS – SAVING PROJECT

(Snake Antivenom Immunoglobulins Need to be Guaranteed)

AIM
4

PHASE
II

Deliver of the Antivenoms to Indigenous
CHCs



AIM 4

Implementation Targets



Pharmacovigilance report

República Federativa do Brasil Ministério da Saúde		SISTEMA DE INFORMAÇÃO DE NOTIFICAÇÃO DE DOENÇAS ACIDENTES POR ANIMAIS RECENTOS		Nº _____
CASO CONFIRMADO: Paciente com evidências clínicas de enfermidades, específicas para cada tipo de animal, independentemente de animal inoculador do agente ou não, diagnosticado em: _____				
CASO SUSPEITO: Paciente com sintomas sugestivos de enfermidades, independentemente de animal inoculador do agente ou não, diagnosticado em: _____				
NÃO RECORREDO: Paciente com sintomas sugestivos de enfermidades, independentemente de animal inoculador do agente ou não, diagnosticado em: _____				
1 - Tipo de Notificação 2 - Intervalo				
1) ☐ Telemática		2) ☐ Aparentemente		
ACIDENTES POR ANIMAIS RECENTOS		X ☒ 3 - Data de Notificação X ☒ 4 - Data de Referência		
4) ☒ 1) Município de Notificação		5) ☐ 2) Município de Referência		
6) Unidade de Saúde (ou outra fonte noticiadora)		7) Data de Primeira Sintomatologia		
8) Nome do Paciente		9) ☐ 3) Data de Primeira Consulta		
10) ☐ 4) Sexo ☐ 5) Idade		11) ☐ 6) Nome do Animal		
12) ☐ 7) Estado Civil ☐ 8) Grau de Instrução		13) ☐ 9) Profissão		
14) ☐ 10) Tipo de Lesão ☐ 11) Tipo de Contato		15) ☐ 12) Tipo de Lesão		
16) ☐ 13) Tipo de Contato ☐ 14) Tipo de Lesão		17) ☐ 15) Tipo de Lesão		
18) ☐ 16) Município de Referência		19) ☐ 17) Data de Referência		
20) ☐ 18) Bairro		21) ☐ 19) Localidade (ou, se possível, ...)		
22) ☐ 20) Endereçamento (rua, casa, ...)		23) ☐ 21) Data de Referência		
24) ☐ 22) Gênero		25) ☐ 23) CEP		
26) ☐ 24) Telefone		27) ☐ 25) Nome do Animal		
28) ☐ 26) Nome do Animal		29) ☐ 27) Nome do Animal		
30) ☐ 28) Nome do Animal		31) ☐ 29) Nome do Animal		
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126) ☐ 124)				

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Qualitative outcomes: Patients' satisfaction and health professionals' acceptability.



FIRST ANTIVENOM TREATMENT IN AN INDIGENOUS CHC IN BRAZIL

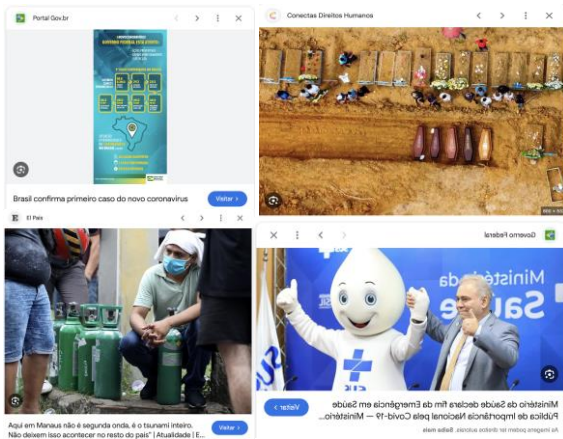


“Let me tell you this one. The little girl was about to find out almost 48 hours after the bite. We found out later in the afternoon, when they informed me and I sent the team there because the father didn't want to bring her to the health post. A mess. We took the antivenom, 12 vials, and went to the girl's house. When we got there she was in severe condition, bleeding everywhere. On the finger, in a cut, which he had about 3 days ago. Just after she had already taken the antivenom, the 12 ampoules, the bleeding stopped. The team was all amazed. We are following her here at the health post.”

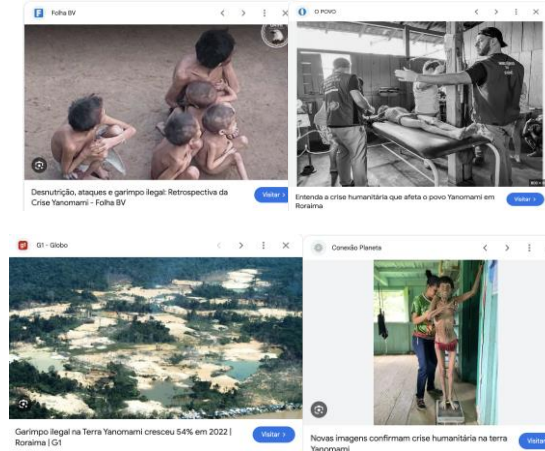
Manoel Gomes Filho, RN

TG First Meeting (Manaus, February 24-28, 2020)

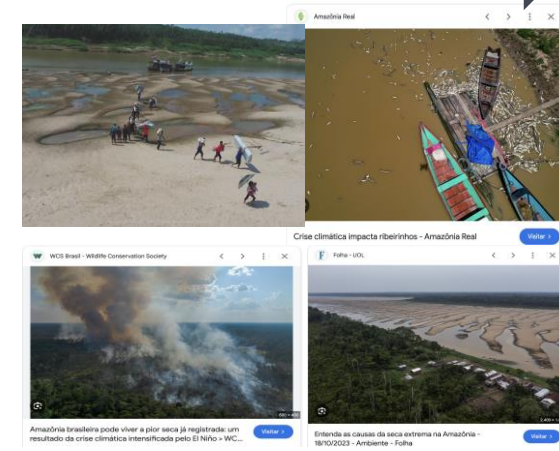
AV distribution to the first 3 CHCs (October 2023)



- Feb 16, 2020 - first COVID-19 case in Brazil
- Manaus as the pandemics' epicenter
- Resource allocation to COVID-19
- Restriction of access in the Indigenous areas
- Apr 22, 2022 – Decree of the end of the Public Health Emergency of National Importance in Brazil



- Yanomami humanitarian crisis
- Malaria
- Malnutrition
- Severe respiratory syndromes
- Violence
- Mercury poisoning
- January 21, 2023 - Federal Government declares state of public calamity in the Yanomami land



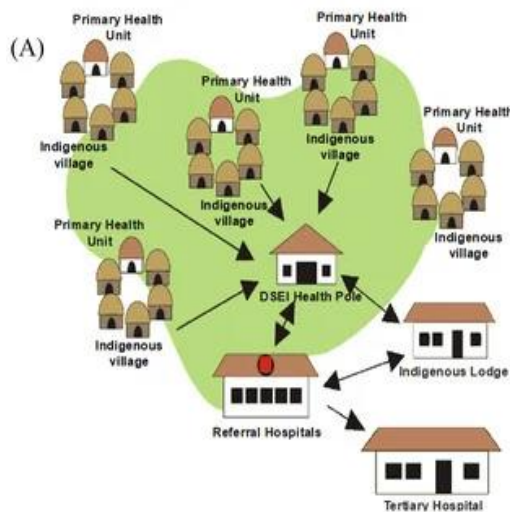
- 2023 extreme drought in the Amazonia
- Diarrheic and respiratory diseases
- Food crisis
- Low river navigability
- Poor access to health system
- Compromised delivering of food and medicines
- September 29, 2023 – Amazonas Government declares emergency state



Reference	MR/Y006259/1
Applicant	Monteiro, Wuelton Marcelo Monteiro
Title	Implementation of a Culturally Tailored Decentralization Programme for Snakebite Treatment in Indigenous Communities In The Brazilian Amazonia ; Tropical Medicine Foundation (FMT-HVD); Duration (Months): 48; Grant Type: Research Grant



AJURI Program (*Ajuri* means 'working together' in Tupi)



Cluster randomized trial

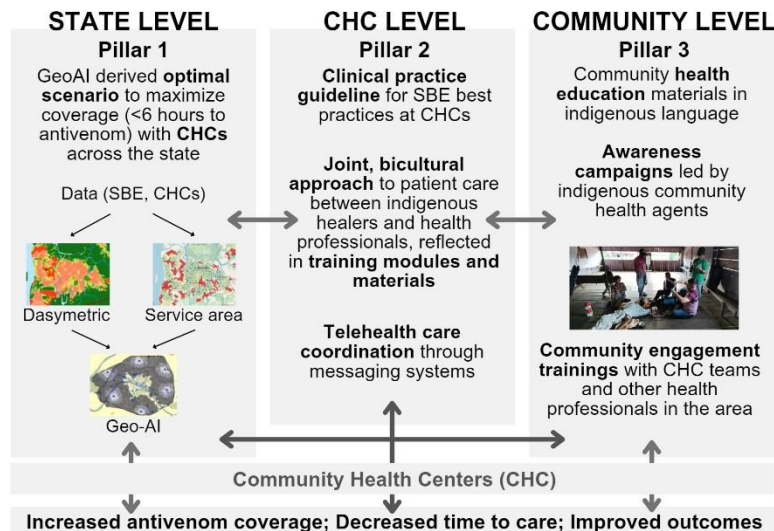


Figure 3. Outline of intervention components to be linguistically and culturally adapted to develop AJURI: an antivenom decentralization strategy for the indigenous population in the Brazilian Amazon. The word **AJURI** means "working together" in which indigenous communities come together to help each other build homes, farm, and more.

Hypothesis: AJURI lowers time from SBE to antivenom and reduces the envenoming impact on morbidity compared to usual care.

Outcomes: Case severity on admission; AV-related early reactions; functionality and lethality; protocol fidelity; cultural mediators and moderators; adoption, implementation, and sustainability outcomes.

Current situation: Final ethical evaluation.
Possible starting: Oct 2024

Wuelton Monteiro
wueltonmm@gmail.com

