

SNAKEBITE ENVENOMING

**A strategy for prevention
and control**



**World Health
Organization**

SNAKEBITE ENVENOMING

A strategy for prevention and control

Snakebite envenoming: a strategy for prevention and control

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FOREWORD



Dr Tedros Adhanom Ghebreyesus

Director-General

World Health Organization

Snakebites are a significant risk to health and well-being for 5.8 billion people around the world, and for those affected carry a high financial burden that often cannot be met.

In the homes of families exposed to this threat snakebites are a cause of considerable fear and anxiety. The consequences of being bitten by a snake extend beyond the impact on health and drive families further into poverty, undermining their futures and trapping them in debt.

Last year, the 71st World Health Assembly adopted a comprehensive resolution calling for a coordinated response to the address the global burden of snakebite envenoming. WHO has developed a comprehensive strategy to fulfil our mandate to direct and coordinate global action on snakebite, as requested by Member States in the resolution.

The strategy places countries at the centre, sets priorities, focusses on outcomes and impact, and is aligned with targets set in WHO's 13th General Programme of Work and the Sustainable Development Goals. It is a clear plan of action across all aspects of snakebite envenoming, and many of the elements in this approach will not only help to reduce snakebites, but to improve and strengthen health systems.

The people most affected by snakebite are often those with the least access to services and medicines. The most powerful force for reducing the impact of snakebite envenoming is therefore for countries to commit to universal health coverage, based on strong health systems and people-centred primary health care. Engaging communities and national and international partners is also essential.

I urge all policy-makers and managers in countries, as well as our international partners, to work with WHO to implement this strategy and achieve sustained prevention and control of this disease that affects many of the world's most vulnerable people.

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We are grateful to Mike Turner, Kirstie Eaton and Rebecca Holland from the Wellcome Trust for their support and assistance in hosting a planning meeting in London on 28–29 June 2018. Ms Liz Baltesz acted as meeting facilitator, and Stuart Ainsworth, Tommaso Bulfone and Andrea Nickerson served as rapporteurs.

The WHO Secretariat members Bernadette Abela-Ridder, Naoko Obara (NTD), Emma Cooke, Claudius Micha Nübling, François-Xavier Lery and Carmen Rodriguez-Hernandez (RHT) oversaw the preparation of the document, which was drafted by Dr Williams and Dr Abela-Ridder with editorial support from Professor Warrell. Tim Reed and Mieke Bakz from Health Action International provided additional support in drafting the final strategy. WHO regional and headquarters staff provided additional review. Anne-Marie Labouche provided layout and design. A number of interns assisted the Working Group during their time at WHO.

The background of the image is a blurred forest scene with green foliage and brown tree trunks. On the right side, a portion of a person's arm and shoulder is visible, showing dark skin. The text is centered in the upper half of the image.

CHILDREN ARE ESPECIALLY
VULNERABLE TO SNAKEBITE
ENVENOMING AND OFTEN
BECOME DISABLED OR DIE.



EXECUTIVE SUMMARY

“The large majority of the victims of snakebite are politically voiceless: subsistence farmers and the rural poor, displaced populations, and children. It is up to the international community to be their voice.”

Kofi Annan Foundation, February 2017

A disease whose time has come

Snakebite envenoming is a neglected tropical disease (NTD) that is responsible for enormous suffering, disability and premature death on every continent. As over 5.8 billion people are at risk of encountering a venomous snake, it is not surprising but no less tragic that almost 7400 people every day are bitten by snakes, and 220–380 men, women and children die as a result ¹ (1, 2), adding up to about 2.7 million cases of envenoming and 81 000–138 000 deaths a year. The economic cost of snakebite envenoming is unmanageable in most countries, as it affects not only the victims but often their entire families, particularly in poor communities (3) in low- and middle-income countries that do not have social security.

As work towards achieving the objectives of UHC2030 (<https://www.uhc2030.org/>) accelerates, immediate action is needed to reduce the burden of suffering of some of the world's most disadvantaged communities, and

countries around the globe have appealed for a coordinated response. Following a recommendation by WHO's Strategic and Technical Advisory Group for Neglected Tropical Diseases (4) and a resolution on snakebite envenoming adopted by the Seventy-first World Health Assembly in 2018 (5), WHO has added this disease to its list of category A NTDs. It has now developed a strategy to reduce mortality and disability from snakebite envenoming by 50% before 2030. This document describes the strategy for action in countries, supported by regional collaboration, that will save lives and prevent needless suffering.

A comprehensive strategy

For millions of men, women and children around the world, the risk of snakebite is a daily concern as they go about their everyday activities – walking to school, tending gardens, herding livestock, fetching water or simply going to the toilet – where a misplaced step, a momentary lapse of concentration or being in the wrong place at the wrong time can be fatal. Reducing the problem starts with improving community education about the risk and encouraging them to seek health care and ensuring intensified case management for every patient. First aid, effective, affordable treatment provided by well-trained medical staff and rehabilitation will allow many

victims to return more quickly to good health and productive lives.

The core of the strategy is the goal for all patients to have better overall care, so that the numbers of deaths and cases of disability are reduced by 50% before 2030.

For this to be achieved, four strategic aims will be pursued.

Empower and engage communities

Prevent snakebite envenoming and increase use of treatment through education, training and facilitation. Research will be conducted to determine the sociocultural, economic, political and geophysical influences on perceptions of snakebite and treatment-seeking by populations at risk and the results used to change behaviour, policy and practice.

Ensure safe, effective treatment Build a stable, sustainable market for safe, effective antivenoms at reasonable cost and assured access to treatment. The production and quality of snakebite treatments must meet internationally accepted standards, through cooperation among academia, industry and public and private institutions for innovation and modernization. The current crisis in the supply of antivenoms should be addressed by WHO by creating a revolving stockpile of antivenoms proven to be effective, so they can be sent where they are needed.

Strengthen health systems

The principles of the WHO Health Systems Framework should be used to integrate more effective prevention, treatment and management of snakebite envenoming into national health systems, national health plans and policy frameworks.

Increase partnerships, coordination and resources

Strong collaboration will be required for this comprehensive plan of action, and advoca-

cy will be necessary to build a global coalition to drive change, generate investment, implement projects and accelerate research into new therapies, diagnostics and medical interventions. Country capacity-building and knowledge exchange will be emphasized. The strategy will require transformational public-private investment, with long-term commitment by partners and governments.

A multifocal incremental response by countries

The strategy is based on existing resources, skills and experience while looking ahead to next-generation solutions. A central objective is to strengthen national health systems to provide solutions at community level. Access to treatment will be improved, renewing communities' confidence in early treatment with safe, effective, affordable medicine. Innovative research will address clinicians' needs for better diagnosis and treatment. Better case management – from first aid, through hospital care, to post-discharge rehabilitation – will help victims to resume healthy, productive lives.

The strategy will be tested in 2019–2020 in 10–12 countries with a high burden of snakebite envenoming and urgent need of a solution. Countries will be supported in designing and implementing locally relevant plans and in participating in regional initiatives. During the scaling-up phase in 2021–2024, a further 35–40 countries will be involved, as resources increase and experience demonstrates the effectiveness of the strategy. During full roll-out in 2025–2030, all countries will be able to integrate the strategy into their public health agendas.

The strategy will be reviewed and adapted regularly to ensure that it meets the needs of countries. Through advocacy, WHO will build a sustainable global coalition committed to ensuring that the targets and milestones are achieved to halve the numbers of snakebite deaths and cases of disability by 50% by 2030.

FOR MILLIONS OF MEN, WOMEN AND CHILDREN AROUND THE WORLD, THE RISK OF SNAKEBITE IS A DAILY CONCERN AS THEY GO ABOUT THEIR EVERYDAY ACTIVITIES WHERE A MISPLACED STEP, A MOMENTARY LAPSE OF CONCENTRATION OR BEING IN THE WRONG PLACE AT THE WRONG TIME CAN BE FATAL.

The cost of implementing the four strategic objectives between 2019 and 2030 will be spread over three phases

Timeframe	2019–2020	2021–2024	2025–2030
Empower and engage communities	US\$ 0.65 m	US\$ 8.97 m	US\$ 17.19 m
Ensure safe, effective treatments	US\$ 4.29 m	US\$ 15.58 m	US\$ 29.86 m
Strengthen health systems	US\$ 1.89 m	US\$ 13.26 m	US\$ 21.80 m
Increase partnerships, coordination and resources	US\$ 2.13 m	US\$ 7.63 m	US\$ 13.51 m
	-----	-----	-----
Total	US\$ 8.96 m	US\$ 45.44 m	US\$ 82.36 m



Costs of implementation

WHO's budget will be used to deliver solutions in the field. Thus, 54.1% will be for activities in countries where snakebite is a public health problem, with regional support and collaboration (17.1%). The cost of work by WHO technical departments will account for the remaining 28.8% of the budget. The number of countries involved will increase over the next 11 years as resources are mobilized and capacity built. The success of the programme during the first 2–4 years will determine whether support can be found for the full 12-year strategy.

During the pilot phase, we will prepare a detailed work plan and, in parallel, a strong, evidence-based investment case to demonstrate the cost-effectiveness and the cost-benefit of interventions, as compelling arguments for investment, support, participation and commitment. The projected budget will be updated as the strategy advances and as economic and geopolitical circumstances evolve.

Countries should mobilize domestic and international resources to achieve sustainable financing and implementation of their control programmes, with strong technical support from WHO. National costs and the cost of commodities to be deployed from revolving antivenom stockpiles are not included in the budget; however, as antivenom production is strengthened, the current costings will probably become redundant. WHO will prepare an investment case for the commodities required to operate the stockpiles and will work with governments and other partners to obtain effective, quality-assured products for distribution.

⁽ⁱ⁾ Longbottom J, Shearer FM, Devine M, Alcoba G, Chapuis F, Weiss DJ, Ray SE, Ray N, Warrell DA, Ruiz de Castañeda R, Williams DJ, Hay SI, Pigott DM. Vulnerability to snakebite envenoming: a global mapping of hotspots. *Lancet*. 2018; 392(10148):673-684.

In humans and animals, snake venom can precipitate multi-organ or multi-system disease

Damage to eyes leading to blindness after contact with spat venom from spitting cobras



Indirect toxin effects on brain and **pituitary gland** tissue



Damage to nerves and **blockage of neuro-muscular transmission** leading to paralysis of muscles including those vital to airway protection and breathing



Myocardial ischaemia, **direct damage**, and cardiovascular effects



Direct and indirect effects on liver function



Acute kidney injury that **can kill** or lead to chronic renal health problems in survivors



Direct muscle cell destruction by myotoxins



Pregnant mother and fetus may suffer due to bleeding and placental dysfunction, and from direct effects of toxins



Haemorrhage due to damaged blood vessel walls, **consumption of clotting factors** and degraded platelets



Local tissue damage including swelling, oedema and necrosis due to destructive effects of some snake venoms and **secondary effects on blood supply**

Leaking capillaries throughout the body caused by direct and indirect effects of toxins

Toxin effect on mineral balance causing low serum sodium concentration



ACTION TO REDUCE AND CONTROL THE EFFECTS OF SNAKEBITE ENVENOMING

Snakebite envenoming is a medical emergency that results from contact with snake venoms, which are complex mixtures of toxins that are injected when a snake bites or when venom is sprayed into the eyes and onto mucosal surfaces as a defence strategy. Snake venoms are evolutionarily adapted to kill prey rapidly by targeting and negating the function of various cell receptors. In humans and animals, this can precipitate multi-organ or multi-system disease that can cause (depending on the species of snake and the classes of toxins in the venom) haemorrhage, prolonged disruption of thrombosis and haemostasis, neuromuscular paralysis, tissue necrosis, generalized muscle breakdown, cardiotoxicity, acute kidney injury, hypovolaemic shock and other effects (6).

WHO recognized snakebite envenoming as an NTD in 2017 and acknowledged that, although data are incomplete, the mortality and morbidity associated with this disease, particularly in tropical and sub-tropical regions, have been underestimated and that a coordinated international response is necessary. WHO also recognized that, because of decades of inattention to this disease, the fundamental systems, resources and tools required to reduce and control the burden have either lagged behind or disappeared

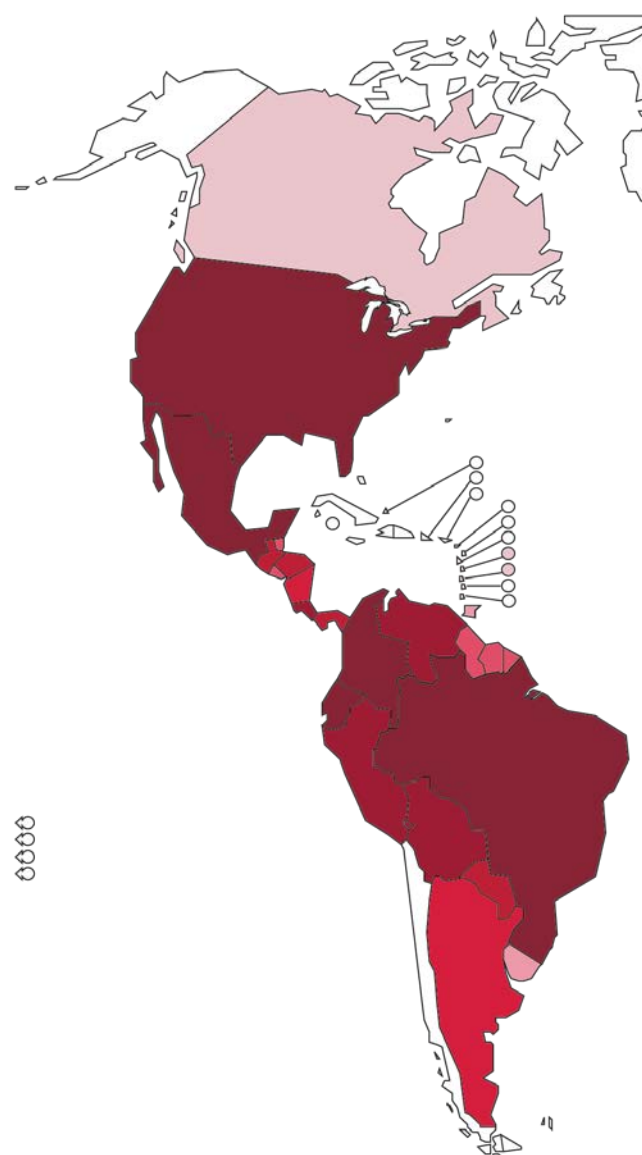
altogether. The situation in sub-Saharan Africa is of particular concern. With limited production of antivenom products in only one country, the region depends almost entirely on importation of antivenoms manufactured in other parts of the world, most of which are marketed with no evidence of their safety or effectiveness. Antivenom production was abandoned by some companies in the 1980s and 1990s, and a crisis point was reached in 2015 when a manufacturer of antivenoms for Africa and the Middle East also ceased production, citing competition from less expensive, unproven products. Similar crises are emerging in Asia. Without urgent reshaping of the market, greater regulatory control and other measures, a public health emergency is imminent.

Disease burden and social and socioeconomic effects

As for other NTDs, it is difficult to estimate morbidity, disability and mortality globally, for a number of reasons. First, snakebite is most prevalent in impoverished agricultural and herding communities in low- to middle-income countries, who have poor access to health care and where health ministries do

not collect specific data. An attempt to quantify deaths due to snakebite envenoming by WHO in 1954 based on inadequate data arrived at 30 000–40 000 deaths per annum. More recent attempts with better (although still incomplete) data provide broad estimates of 81 000–138 000 deaths resulting from 1.8–2.7 million cases of envenoming and up to 5.4 million snakebites (6). The Institute for Health Metrics and Evaluation estimated that there were 79 000 deaths due to bites from venomous animals in 2016, with an uncertainty range of 56 800–89 400 (7), which is lower than in most other studies (1, 2). An estimated 400 000 people a year suffer permanent disability, including blindness, extensive scarring and contractures, restricted mobility and amputation after snakebite envenoming (8), and the psychological effects of snakebite are under-recognized. In Sri Lanka, snakebite envenoming had long-term psychological sequelae, the prevalence of post-traumatic stress disorder being similar to that observed after the 2004 tsunami in Asia or major road traffic accidents (9).

Snakebite envenoming typically affects predominantly poor, rural communities in tropical and sub-tropical countries throughout the world. WHO recognizes 109 species of venomous snakes as category 1, of highest medical importance, in the countries in which they occur. At least another 142 species are regarded as category 2 (medically important but to an uncertain degree) because exact epidemiological or clinical data are lacking and/or they are less frequently implicated in envenoming cases because of their activity cycles, behaviour, habitat preferences or occurrence in areas remote from large human populations. Despite their abundance (see Fig. 1), the majority of the most medically important species in each region belong to a few genera. For example, the 25 category-1 species recognized in the African region belong to five genera, and the 30 category-1 species in the Americas belong to only four genera.



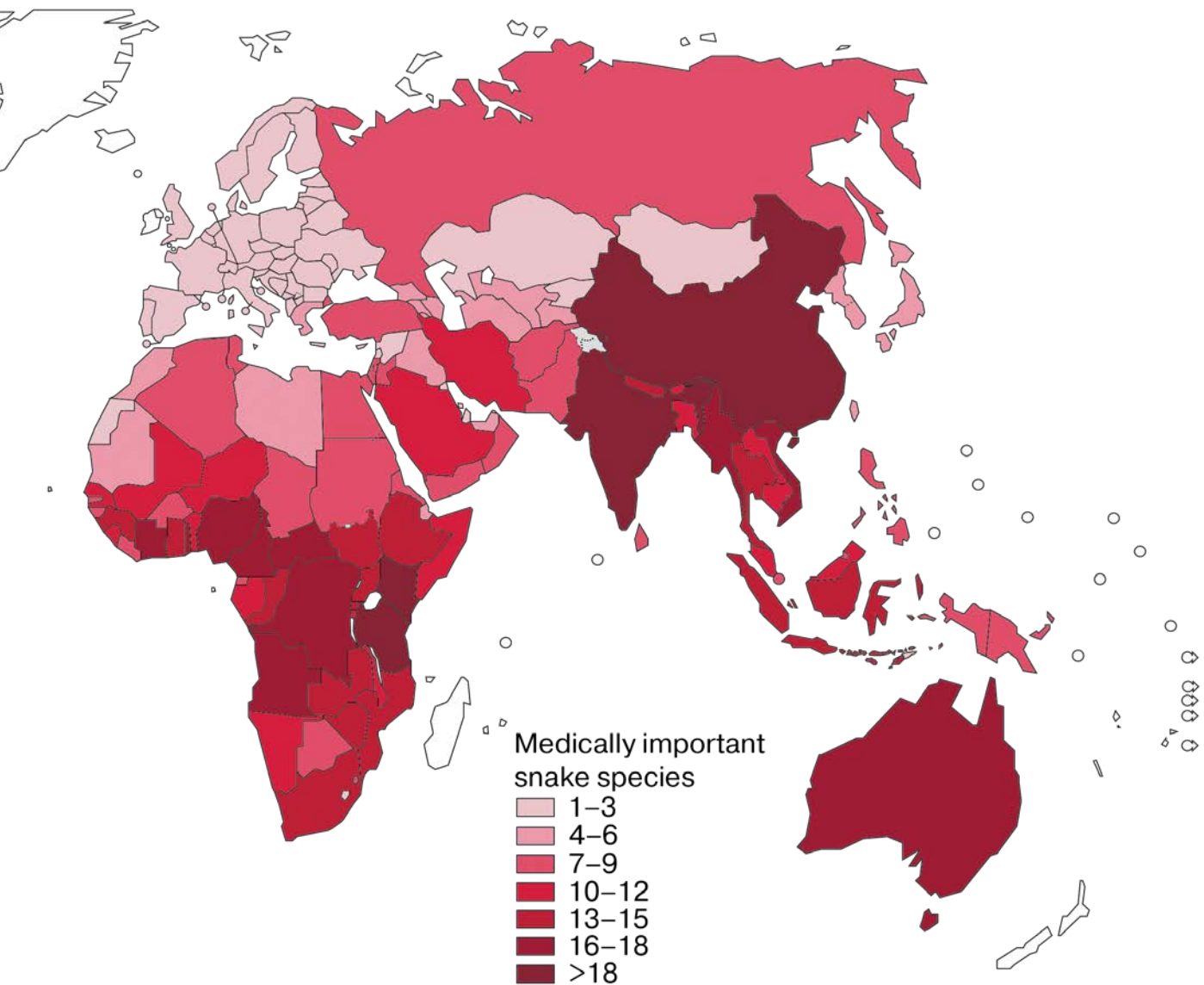


Fig. 1. **Worldwide distribution of medically important snake species, with the relative abundance of species in each country.**

Medically important snake species in WHO regions



Region of the Americas

Bothrops asper

Common names: Fer-de-lance or Terciopelo



African Region

Bitis arietans

Common name: Puff adder



Eastern Mediterranean Region

Naja haje

Common name: Egyptian cobra



South-East Asia Region

Daboia russelii

Common name: Russell's viper



European Region

Vipera berus

Common name: European viper



Western Pacific Region

Calloselasma rhodostoma

Common name: Malayan pit viper

Snakebite envenoming typically affects predominantly poor, rural communities in tropical and sub-tropical countries throughout the world.

A large body of literature demonstrates a strong association between low socioeconomic status or poverty and a high burden of snakebite envenoming and death. Rural hunter-gatherers, agricultural workers, working children (10–14 years of age), families living in poorly constructed houses and people with limited access to education and health care are all particularly vulnerable (3, 10–12). In West Africa, 16 low- to middle-income countries have at least 3500–5350 deaths annually, equivalent to 1.2 deaths/100 000 population per annum (95% CI: 0.9–1.4/100 000) (13). In just one Nigerian hospital, 6687 people were treated for snakebite envenoming over 3 years (14), and in Burkina Faso 114 126 cases of snakebite were reported over 5 years (15). While the data are incomplete, 20 000–32 000 people in sub-Saharan Africa die each year from snakebites (2). A study in India provided a direct estimate of 1.4–2.8 million snakebites a year, which resulted in at least 46 000 fatalities (16). In Bangladesh, the estimated annual incidence of snakebite was 589 919 and 6041 deaths (17). Snakebite results in large numbers of disability-adjusted life years (DALYs) in Africa, due to factors such as the size and density of both human and snake populations. Overall, 320 000–330 000 DALYs are lost to snakebite envenoming annually in West Africa (7, 13), which is more than those lost due to dengue, echinococcosis, intestinal nematode infestations, leishmaniasis, trachoma and trypanosomiasis (13).

Snakebite envenoming has many consequences for victims and their families. It often makes poor people poorer, because of the high treatment costs and loss of income. In sub-Saharan Africa, a dose of effective antivenom alone can cost US\$ 55–640, with an average cost of US\$ 124 per dose (18). In India, the cost of initial treatment has been reported to be as high as US\$ 5150 and long-term cost of US\$ 5890 (19). Some victims have suffered financial losses equivalent to 3.6 years' income, and others have sold land worth up to 14 years of income. Some families have to remove their children from education because of lost income following snakebite envenoming or so that the children can work to contribute to the family income or care for a disabled snakebite victim. In Zimbabwe, the average cost of hospitalization of an envenomed patient was US\$ 225 per day, before treatment was given (20). In Bangladesh, nearly 75% of snakebite victims spent their savings on treatment, and over 60% had to borrow to meet the costs (21).

Treatment

Immunotherapy with antivenom preparations from animals, containing either immunoglobulin G or its derivative fractionation products, F(ab')₂ or Fab, has been the main treatment for snakebite envenoming for over 120 years. Antivenoms that are manufactured according to the highest standards, that comply with good manufacturing practice and undergo rigorous preclinical and clinical evaluation before registration are very effective, especially if administered early in an adequate dose (22).

In many regions, however, appropriately manufactured, quality-assured products are not available or accessible, due partly to poor control and regulation of preparations (23, 24). In many places, there are no minimum specifications for the potency, efficacy, dose or safety of antivenom products. Weak health systems and regulatory frameworks let un-

safe, ineffective products enter markets, with no preclinical or clinical evaluation before registration (25, 26). One consequence of such fragile systems is that inferior products have become ubiquitous, particularly in sub-Saharan Africa and in Asia, so that competitors that are rigidly regulated have had to abandon production (27). The weakness of the market also discourages investment in research to improve current treatments and in development of a next generation of antivenoms at lower cost and with greater safety and efficacy.

Apart from antivenom treatment, victims usually also require a range of health services, as antivenom neutralizes accessible venom components but does not reverse the damage to organ systems, as some toxins that are sequestered inside cells are inaccessible to antivenom immunoglobulins. Effective treatment therefore involves both antivenom and other interventions, such as cardiorespiratory and/or fluid resuscitation, airway intubation, mechanical ventilation, haemodialysis, wound debridement, reconstructive surgery, physiotherapy and other rehabilitation services. Improving the outcomes of patients will require strengthening health systems, improving access to essential medicines, eliminating substandard antivenoms and other medicines, strengthening diagnosis and treatment, improving regulatory capacity and ensuring effective distribution of antivenoms and monitoring their use and safety.

The need to involve wound care experts, rehabilitation services, prosthetic limb manufacturers, oculists and others who can contribute to recovery and rehabilitation has long been ignored. Similarly, the psychological consequences of snakebite envenoming, including post-traumatic stress disorder and chronic depression, should be prioritized. Operational research is necessary as a basis for robust clinical guidelines, assessment algorithms and other resources to ensure the chain of care, from evidence-based first aid in the community or by first responders to treat-

ment with antivenom and other drugs, surgical and medical care of local tissue injury, better treatment of organ or system sequelae such as acute kidney injury and recovery and rehabilitation. The aim should be to restore function so that snakebite victims can return to healthy productive lives.

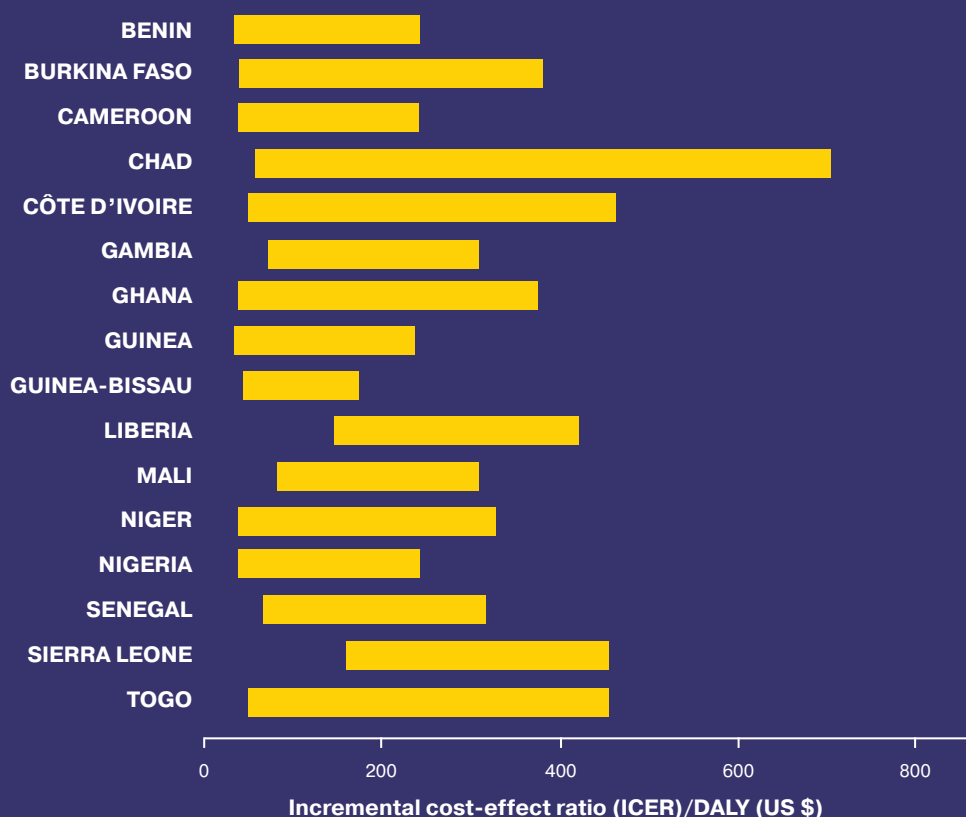
Challenges to improving the quality, safety and cost-effectiveness of antivenoms

The practical challenges to reducing the burden of snakebite envenoming and bringing it under long-term control throughout the world epitomize many of the obstacles to ensuring healthy lives and well-being for everyone at all ages under United Nations Sustainable Development Goal (SDG) 3 and the aspiration of achieving universal health coverage by 2030 (28). National and sub-national supplies of good-quality antivenoms are not enough, as, in many countries, poor-quality products and the absence of effective treatment have eroded confidence in conventional health care. Strong engagement with communities and health workers is necessary to encourage victims to seek care early, which will require a coordinated health promotion strategy.

Decades of neglect and inaction in the systems, tools and safeguards required to ensure access to safe, effective treatment have resulted in the collapse of the largely under-regulated, under-supported market for antivenoms, because of low demand and a glut of poor-quality products, while millions of victims have suffered unnecessarily. At least three million effective treatments are required each year, yet important challenges remain to ensuring that the antivenoms on the market are safe, effective and affordable. WHO is taking steps to establish the quality of antivenoms on the sub-Saharan African market and will work with manufacturers to collect evidence of their safety and effectiveness. The programme should be extended to other

Box 1.**Case study of the cost-effectiveness of antivenom treatment in West Africa**

The incremental cost-effectiveness ratio associated with making antivenom available for each death averted in 16 West African countries (29) ranged from US\$ 1997 in Guinea-Bissau to US\$ 6205 in Liberia and Sierra Leone, while the cost per DALY averted ranged from US\$ 83 in Benin to US\$ 281 in Sierra Leone. The probability that treatment with antivenom would be cost-effective was 97.3–100.0%. These estimates compare favourably with the cost-effectiveness of other commonly funded health interventions and indicate that a relatively modest cost can substantially reduce mortality and losses in DALYs. In Nigeria, the country with the highest burden of snakebite envenoming in West Africa, the incremental cost-effectiveness ratio was US\$ 92.56 per DALY averted and US\$ 2160.33 per death averted. These sums were far lower than Nigeria's gross domestic income per capita at the time (US\$ 2742), confirming that antivenom treatment is highly cost-effective.



regions where there are similar doubts about products and a thorough, independent investigation and validation are required.

The issue of treatment cost should be investigated operationally, by simulations of production system cost–efficiency and evaluations of cost–effectiveness, to develop pricing models that will convince countries, partners and donors to support investment in these essential medicines. **Box 1** shows the results of a study of the cost–effectiveness of antivenoms for snakebite in 16 countries in West Africa in 2016 (29).

Small-scale production results in high costs, which are a disincentive to investment. In a study of products in sub-Saharan Africa in 2012, the number of effective treatments was estimated to represent only 2.5% of those needed (18). In 2010–2011, approximately

83 000 treatments were supplied at an average cost of US\$ 124 per treatment, irrespective of their effectiveness. The most effective product at that time cost US\$ 640 per treatment (but only 1250 treatments could be supplied by the manufacturer), a cost that is unsustainable for large-scale supply. The cost of treatment for other NTDs is much lower. For example, post-exposure prophylaxis for rabies costs as little as US\$ 12 per treatment. It is difficult to convince countries and donors to accept the much higher costs of antivenoms, and providing the necessary quantity will require substantial market growth and increased industrial production. Facilitating improved access to academic research outcomes, new technology and technical assistance can help manufacturers to eliminate unnecessary costs, streamline and modernize production and deliver products at more affordable prices.

IN AMAZONAS FOR EVERY SNAKEBITE DEATH UP TO 10 SURVIVORS ARE LEFT WITH PERMANENT DISABILITY, INCLUDING AMPUTATIONS.



RATIONALE FOR THE STRATEGY

Our approach is based on the conviction that empowered communities with well-functioning health systems that have access to safe, effective medicines can effectively prevent and control snakebite envenoming. Once a community recognizes the value of prevention, avoidance of risks and early medical care for snakebite envenoming, the outcomes will improve. More people will seek help sooner, will suffer less and will be more likely to survive and recover. Community education to promote better health-seeking behaviour and prevention of injury, training of health workers, stronger health systems and access to good-quality medicines will benefit everyone and contribute to achieving the SDGs.

When health professionals are taught fundamental clinical skills, they not only diagnose and treat snakebite envenoming better but also improve their entire practice of medical care. Likewise, improvements in health systems for the management of snakebite benefit the health needs of everyone. Snakebite envenoming is a multi-organ system disease that requires holistic management and expertise in many areas of medicine. Better access to medicines, training and provision of basic equipment and laboratory and other services will increase the return on investment and bring some of the most vulnerable people closer to universal health coverage.

Snakebite envenoming is preventable.

The risk for snakebite envenoming can be reduced through community education and often through measures for preventing other diseases. Use of bed nets to prevent transmission of mosquito-borne diseases can also reduce the risk of bites from snakes entering houses at night (30). Encouraging people to protect their feet, ankles and lower legs by wearing boots protects them not only from snakebites but also from infection by soil-transmitted helminths, bacteria and fungi, podoconiosis and trauma associated with walking or working barefoot.

Snakebite envenoming is treatable.

The means for treating snakebite envenoming are available, and, by ensuring that those who are bitten have access to safe, effective, affordable medicines, the toll of death and disability caused by snakebites can be substantially reduced. Technological support, investment and training can rapidly improve the production and regulation of antivenoms. This will not only result in better snakebite treatment but will also improve the safety and quality of other biotherapeutics, such as for diphtheria,



WEST AFRICAN
CARPET VIPERS ARE
THE MAJOR CAUSE
OF SNAKEBITES IN
THE BRONG AHAFO
REGION OF GHANA

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Box 2

Case study in Ghana

At Yeji, on the shores of Lake Volta in the north of the Brong Ahafo Region of Ghana, snakebite was one of the 10 main reasons for hospital admission, and the case fatality rate was 11.1% (31). A case review system, a new treatment strategy and new antivenoms were introduced and the effects monitored for 33 months. The case fatality rate fell to 1.3%, the number of admissions increased by 50%, the time between bite and admission was reduced by 40%, and the proportion of patients who required wound debridement dropped from 6.9% to 2.2%.

The interventions for achieving these changes were simple: **apply a standard protocol to the treatment of all patients, introduce staff training, monitor compliance, and use effective antivenoms.**

Our approach is based on the conviction that empowered communities with well-functioning health systems that have access to safe, effective medicines can effectively prevent and control snakebite envenoming.

tetanus and rabies, and of other drugs and equipment necessary to treat infections and circulatory, respiratory and renal failure. **Box 2** provides a case study of how outcomes can be improved even with few resources.

Investment in prevention and treatment of snakebite envenoming saves victims from poverty and reduces health inequality.

Most victims of snakebite envenoming live in impoverished, vulnerable communities with poor health indicators. Most are inhabitants of rural areas in tropical and sub-tropical regions of Africa, the Middle East, Asia, Oceania and Latin America, where a bite by a venomous snake can lead to death or to months (or years) of depression, disability and economic destitution. Without access to effective treatment, many victims lose their livelihoods, savings and property. A debilitating snakebite may leave an agricultural worker fit only to beg and be supported by his or her family. Their immediate and even extended families may have to share and endure the economic consequences, marginalization and stigmatization. Investment in antivenoms can relieve the suffering of the victims and their families and give them a chance to recover, rebuild their lives and resume their roles as productive members of their communities.

Investment in improving the prevention of snakebites and controlling the incidence of

envenoming is part of achieving SDG 1, to “end poverty in all its forms”, and the commitment of Member States to “leave no one behind”. It also contributes to the goals of SDG 3, to “ensure healthy lives and promote well-being for all at all ages” and, specifically, SDG 3.3, that “by 2030, end the epidemics of ... neglected tropical diseases”, and SDG 3.8, to “achieve universal health coverage ... and access to safe, effective, quality and affordable essential medicines and vaccines for all” (28).

WHO based its 13th Global Programme of Work on a commitment to leave no one behind (32). The right to the highest attainable standard of health as expressed in WHO’s Constitution underpins all WHO’s work. WHO is committed, at all levels of engagement, to gender equality, equity and rights-based approaches to health to enhance participation, build resilience and empower communities. Investment in antivenoms will meet these commitments and WHO’s goals of ensuring that one billion more people have health coverage, one billion more people’s lives are made safer, and one billion more lives are improved. It will accelerate progress to achieving universal health coverage by 2030 so that all people have a safer, healthier, fairer world in which to live productive, fulfilling, active lives.

The prevention and treatment of snakebite envenoming is a model of collaboration for “One health”.

Snakebite envenoming also causes substantial economic losses by disabling and killing livestock and working animals. Engagement with communities to prevent human snakebites may increase their awareness of the little-known problem of fatal and debilitating snakebites among valuable domestic livestock. Coordination between human and veterinary health systems to reduce the impact of snakebite envenoming on communities is a model for other “One health” collaborations.

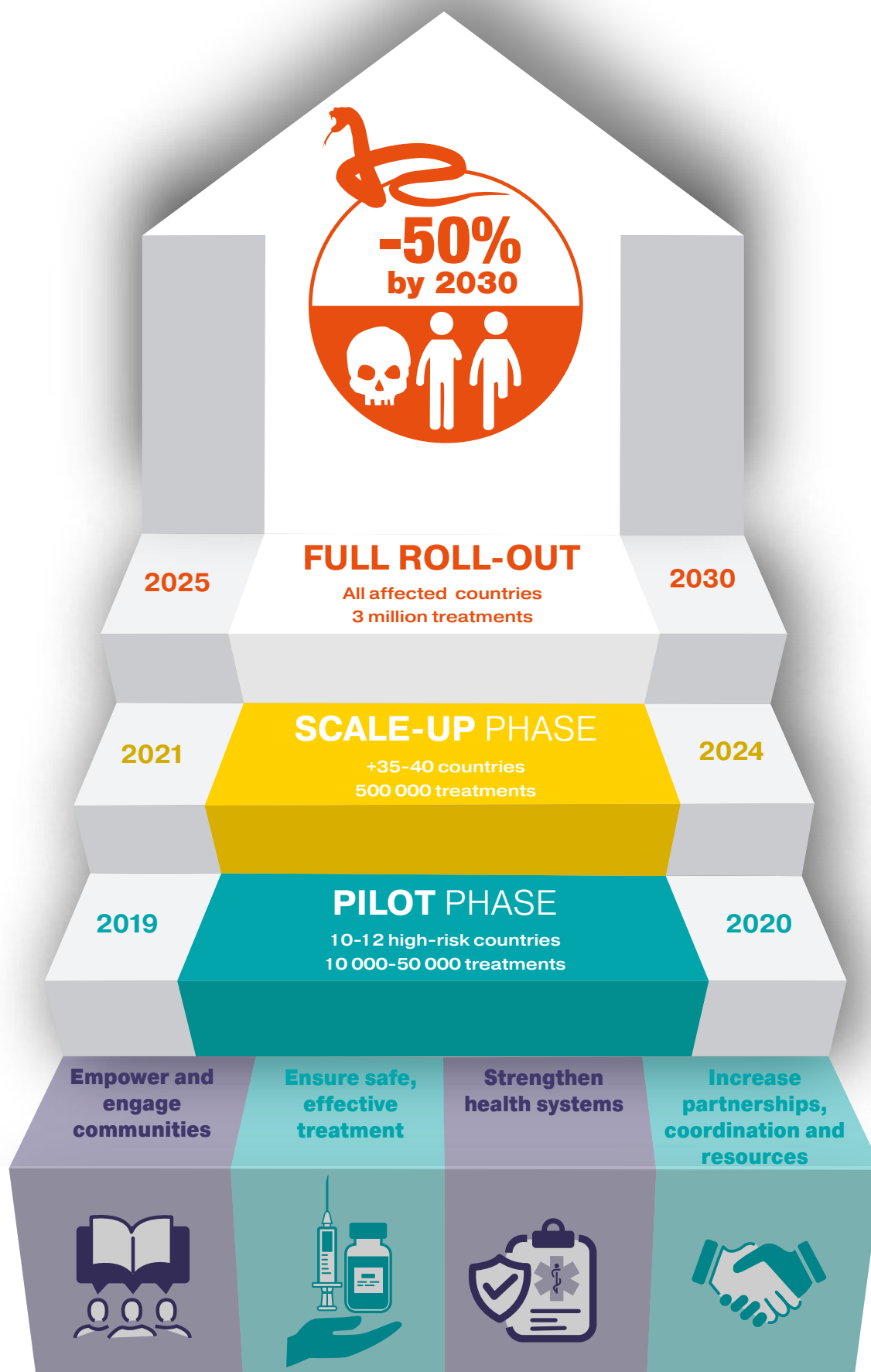


Fig. 2. **Strategic objectives, target and implementation phases**

STRATEGY FOR PREVENTION AND CONTROL OF SNAKEBITE ENVENOMING

The strategy is a coordinated, evidence-based approach to the control of snakebite envenoming, with technical support, the availability, accessibility and affordability of safe, effective treatments, technical cooperation among Member States and strengthening of their capacity to deal with this disease in a multifocal manner.

Target, strategic objectives and activities

The goal of the strategy is to prevent and control snakebite envenoming in order to halve the numbers of deaths and cases of disability that it causes by 2030. The four strategic objectives, illustrated in **Fig. 2**, are:

Empower and engage communities: Through education, communication, training and facilitation, give communities the tools and capability to make informed decisions to prevent snakebites and improve the outcomes of those who are affected.

Ensure safe, effective treatment: In line with SDG 3.8 and 3B, ensure that safe, effective, affordable, accessible treatments for snakebite envenoming are available to all the people who need them.

Strengthen health systems: Within established frameworks and in line with SDG 3.8 and 3B–D, build strong national health systems to ensure that the resources, information and health personnel required for the control of snakebite envenoming are available and accessible.

Increase partnerships, coordination and resources: Use advocacy, data, collaboration and partnerships to build a transformational, multi-stakeholder alliance to find solutions and generate public–private investment for sustained success.

The next sections briefly describe the tasks involved, examples of expected outcomes and information on the rationale for each task. Some of the practical results of the strategy are expected to be:

- **availability of safe, effective treatments:** 50 000 for snakebite envenoming by the end of 2020, increasing to 500 000 by 2024 and full coverage with 3 million by 2030;
- **restoration of a sustainable market for snakebite treatment:** a long-term supply of well-regulated, safe, effective treatments and conditions to ensure an

increase of at least 25% in the number of competent manufacturers by 2030;

- **cost mitigation to reduce the debilitating financial impact of treatment:** better understanding of the barriers to treatment, rehabilitation and reintegration and research and policy on mitigating the costs of treating snakebite envenoming by 2030;
- **integration of treatment of snakebite envenoming into national health plans in all affected countries:** including surveillance systems, policy frameworks, research priorities, health system components, community and civil society mechanisms for effective prevention and control; and
- **long-term sustainability and strong collaborative partnerships for effective control:** strong cases for medium- and long-term investment to ensure resources for the control of snakebite envenoming and enduring multilateral partnerships to ensure the sustainability and success of control.

As the strategy is implemented, additional tasks and priorities will be identified, in consultation with partners and countries, and flexibility will be necessary to ensure that the strategy remains responsive and appropriate locally, nationally, regionally and globally.

Implementation phases

The roadmap will be rolled out in three phases, starting with a pilot phase (2019–2020) in 10–12 high-burden countries to demonstrate the robustness and adaptability of the plan and of both individual and collective interventions. As the programme evolves and resources become available, it will be scaled up (2021–2024) by extending implementation to another 35–40 countries. In the full roll-

out phase (2025–2030), support to control snakebite envenoming will be extended to all countries that require it. Some of the outcomes to be achieved during these phases are listed below.

PILOT PHASE (2019–2020)

- A risk–benefit assessment of antivenom products in Africa and Asia will be completed to ensure that at least three quality-assured, appropriate antivenoms are accessible in each region.
- A pilot project to design and test an initial antivenom stockpile programme will be initiated, to deliver 10 000–50 000 effective treatments in 10–12 countries with a high burden of snakebite. Models based on WHO revolving stockpiles of vaccine (33) will be tested. A small-scale pilot project will be conducted to test the model, and the findings will be used to improve it for wider use.
- Countries will be encouraged to integrate training on snakebites into the professional development and in-service training of health workers and to provide opportunities for them to improve the prevention, diagnosis, treatment and management of the disease as part of overall investment in health systems.
- WHO will identify and engage with a wide range of potential partners and stakeholders and prepare a framework to coordinate investment and mobilize resources for national and regional initiatives.
- Countries will be called upon to include snakebite envenoming and other NTDs in national and regional health plans. WHO will encourage countries to adopt the undertakings in resolution WHA71.5 and to add snakebite envenoming to their lists of notifiable diseases in order to collect and report more complete, accurate data.

The goal of the strategy is to prevent and control snakebite envenoming in order to halve the numbers of deaths and cases of disability that it causes by 2030.

- Research priorities will be promoted to ensure that the clinical tools required to tackle the disease become available.
- Community-level snakebite education programmes in countries will be supported with technical guidance and learning materials.

SCALE-UP PHASE (2021–2024)

- Risk–benefit assessments of antivenom products for the remaining regions of the world will be completed, so that at least three quality-assured, appropriate antivenoms are accessible in every region of the world.
- Another 35–40 countries will be included, and the antivenom stockpile programme will expand as demand increases, with the aim of delivering a minimum of 500 000 effective treatments by 2024.
- Investment in clinical research, clinical tools and translation of research results into practice and policy will begin to deliver results.
- WHO will work with countries, partners and donors to apply strategies to reshape regional antivenom markets.
- WHO will support low- to middle-income countries in developing policy frameworks to encourage investment in viable new manufacturing capacity in order to meet regional demand for quality-assured antivenoms.

FULL ROLL-OUT PHASE (2025–2030)

- All countries will have access to the tools and interventions of the strategy.
- Better market conditions will attract new manufacturers, increasing the number of companies producing high-quality antivenoms by 25% and delivery of 3 million effective treatments a year globally by 2030.
- Integration of snakebite envenoming into national health plans will ensure that all victims who suffer disability are afforded equal, equitable access to rehabilitation and that the UHC2030 and SDG objectives for access to medicines are achieved.
- A new generation of products will become available that are more effective, safe and affordable for treatment of the local and systemic effects of envenoming.

*THE RISK OF SNAKEBITE
ENVENOMING CAN BE REDUCED
THROUGH COMMUNITY EDUCATION.*



EMPOWER AND ENGAGE COMMUNITIES

Snakebite envenoming hurts communities. Victims of snakebite are typically young, healthy, productive members of their communities, until they are bitten. They may be heads of families who contribute to food production, raise children, care for the sick and elderly and lead the life of their towns, villages and hamlets. The strategy emphasizes the importance of engaging with communities to encourage better education about risks and avoidance to prevent snakebites and health care-seeking behaviour. The aim is to empower communities to be more proactive in a holistic approach that integrates snakebite awareness into programmes to prevent environmental, zoonotic and other diseases.

Ensure active community engagement and participation.

In many regions and communities, there are no quantitative or qualitative indicators of the burden and impact of snakebite envenoming for measuring the success of interventions. Systematic baseline data will be obtained about the burden of snakebite envenoming, its impact on communities and the effects of interventions over time. Applying new tools for community-acquired data collection will complement health systems data.

Effective control of snakebite envenoming is possible only if the affected communities are active participants. A bottom-up approach is more likely to succeed than an initiative from outside. Community participation, with the support from local leaders, civil society and health and social activists, will improve the outcomes of snakebite envenoming.

Improve the prevention, reduce risk and increase avoidance of snakebite envenoming.

Qualitative research should be conducted on community knowledge, perceptions, socio-cultural and spiritual understanding and depiction of snakes and snakebite envenoming. Prevention, risk-reduction and avoidance initiatives can then be designed and planned with strong community participation. Community consultation and research are essential for understanding their views on snakebite envenoming and using the information to design strategies that can be tested with affected communities. Strategies that work in one setting may not work in others.

Operational research will be conducted to evaluate snake avoidance and snakebite prevention strategies in communities. Research results will be used to validate affordable,

context-appropriate prevention activities and interventions, including targeted community education.

Research on human–animal interfaces and ecological and environmental risk factors to understand the ecology of venomous snakes will inform prevention and risk-reduction approaches. Studies will also be done to obtain a more accurate assessment of the economic burden of snakebite envenoming including the impact on domestic animals and livestock. Reducing the cost of snakebite envenoming to communities due to loss of livestock should be included in community approaches to snakebite envenoming control.

Ensure effective first aid and ambulance transport to hospital.

Guidelines, training and education will be prepared for community first responders to ensure that local communities have the basic skills and knowledge for pre-hospital care and life support until medical assistance is available. Most victims of snakebite envenoming have to travel considerable distances to access primary health care; appropriate community response to snakebite envenoming can reduce mortality and change community perceptions of snakebite envenoming and its treatment.



TEACHING COMMUNITIES HOW TO PROVIDE SAFE, EFFECTIVE SNAKEBITE FIRST AID IS FUNDAMENTAL TO ACHIEVING BETTER OUTCOMES.

The strategy emphasizes the importance of engaging with communities to encourage better education about risks and avoidance to prevent snakebites and health care-seeking behaviour.

Snakebite envenoming is a potentially life-threatening emergency, and emergency responders must be appropriately trained to recognize the signs and symptoms of envenoming and of associated medical issues that may be a threat to life during transport, such as severe shock, haemorrhage, airway obstruction or respiratory paralysis. The training of ambulance personnel who transport cases of snakebite envenoming will be improved in order to reduce pre-hospital mortality and complications. Pre-hospital mortality is reduced measurably if there is appropriate transport. Supervised, appropriately qualified ambulance transport services are an essential part of a well-designed, functioning health system and should be available to everyone in a community who has to be transported urgently to an appropriate health care facility.

Accelerate development of pre-hospital treatment.

Time is critical after snakebite envenoming: the longer the delay before treatment, the poorer the outcome. Improving first-aid treatment, developing and validating effective strategies and introducing new drugs to interrupt the natural progress of the disease until the victim reaches hospital will save many thousands of lives every year and reduce the incidence and severity of sequelae. Investment in research on pre-hospital treatment, including first aid, and pre-hospital therapeutics will be improved.

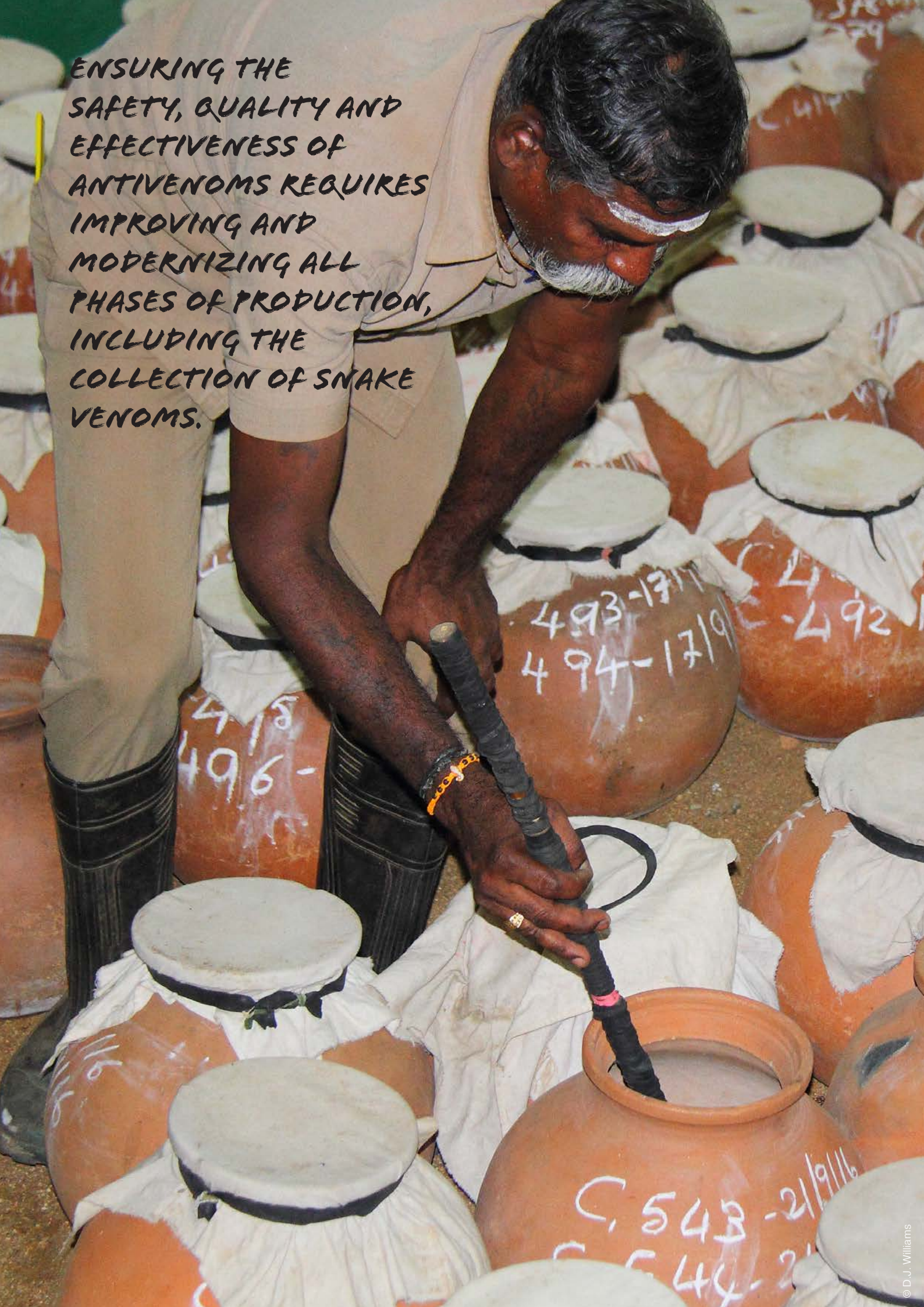
Improve health care-seeking behaviour.

In many communities affected by snakebite envenoming, 60–80% of victims rely on traditional medicine or spiritual healers for treatment, often with poor outcomes. In order to change or modify poor health-seeking behaviour, the factors that influence these treatment decisions must be understood. Treatment choices should be investigated to understand why they persist within communities and how future choices in communities can be positively influenced. Engaging with traditional medicine practitioners and other influential community members to encourage them to support better health care-seeking behaviour and/or act as first responders will result in greater use of allopathic medicine and better outcomes.

Research on socio-cultural and economic factors affecting outcomes

Understanding the social, cultural, economic and spiritual context of snakebite envenoming across communities is essential to improving outcomes. This operational research is important because of the degree to which these influences impact the outcome after snakebite envenoming varies considerably depending on the context and cultural dynamics. Identifying the issues that contribute to poor outcomes such as pre-hospital mortality, chronic morbidity and substantial economic loss at national and subnational level will enhance local programme specificity and success.

**ENSURING THE
SAFETY, QUALITY AND
EFFECTIVENESS OF
ANTIVENOMS REQUIRES
IMPROVING AND
MODERNIZING ALL
PHASES OF PRODUCTION,
INCLUDING THE
COLLECTION OF SNAKE
VENOMS.**



ENSURE SAFE, EFFECTIVE TREATMENT

In order for people to be successfully treated and recover from snakebite envenoming they require access to good-quality antivenoms, and all of the other aspects of medical treatment that may be necessary.

Antivenom is the first choice for treatment of systemic snakebite envenoming. It must be well designed and formulated and adhere to international standards for the manufacture of sero-therapeutic medicines to ensure their safety and effectiveness. Lack of safe, effective antivenoms in many parts of sub-Saharan Africa and South and South-East Asia is the primary cause of the continuing high rates of death and disability among tropical snakebite victims. Without urgent, strategic investment to improve and strengthen production, control and regulation of snake antivenom products, promote greater collaboration between industry and academia and restructure the current fragile market to increase supply, large parts of the world may soon face increasing shortages. One aim of the strategy is to make sure that by 2030 everyone who needs antivenom has access to an affordable, safe, effective product. New and emerging technologies may revolutionize the treatment of snakebite envenoming, and investment in research to deliver “next-generation” treatments is important.

In addition to antivenom, victims require additional medical care and interventions that can vary according to the circumstances of the individual case. Factors such as the type of snake involved, the length of time between the bite and presentation to health care and the severity of envenoming can influence the need for other types of medical treatment. It is also important that innovative research is supported to investigate, optimize and rationalize treatment of snakebite envenoming to improve outcomes. Advances in the medical treatment of snakebite envenoming, and treatment of long-term sequelae (physical and psychological) are possible, but require investment in clinical research and translation of that research into practice. Activities that prospectively test new protocols, or undertake clinical trials of antivenoms, medical interventions and drug combinations will be prioritized. The data generated will provide the evidence needed to design and deliver clinical guidelines and protocols for integration into national health worker training programmes, and will indicate how infrastructure and health systems need to be strengthened and changed by countries and regions.

New and emerging technologies may revolutionize the treatment of snakebite envenoming, and investment in research to deliver “next-generation” treatments is important.

Make safe, effective treatments available, accessible and affordable to all.

Global risk–benefit assessments of antivenom products will be conducted so that at least three quality-assured, appropriate antivenom treatments are recommended in each WHO region. The assessments will indicate which products are suitable for use on the basis of risk vs benefit and the issues in antivenom production that must be addressed.

Direct WHO action is needed to restore confidence in the use of antivenoms and reshape regional antivenom markets. To counteract the current failure of the antivenom market in sub-Saharan Africa, WHO-recommended products will be provided through a revolving supply facility, with an antivenom stockpile programme established, initially for countries in sub-Saharan Africa, to deliver 10 000–50 000 treatments from the pilot stockpile in 2019–2020, up to 500 000 treatments a year by 2024 and contribute to the delivery of up to 3 million treatments a year by 2030. The outcome should be greater confidence, which will generate demand and extend the availability, accessibility and affordability of WHO-recommended antivenoms.

Weak manufacturing leads to poor-quality products that are ineffective and unsafe.

Poor-quality products undermine market confidence, thus contributing to market fragility and potential collapse. Initiatives will be taken to strengthen antivenom manufacture and encourage innovation and modernization. Strong manufacturers with quality-assured products will contribute to re-establishment of a sustainable antivenom market.

When patients and their families undergo financial hardship in order to obtain antivenom, use decreases and markets become fragile. Patient outcomes worsen due to lack of proper treatment and socioeconomic and productivity loss costs to communities increase. Cost-mitigation schemes will be established to remove financial barriers, increase appropriate treatment-seeking behaviour and result in better clinical and socioeconomic outcomes by reducing the numbers of deaths, disability, socioeconomic hardship and loss of productivity.

Local political will and financial investment are critical to the success of health interventions, such as improving the availability, affordability and accessibility of quality-assured antivenoms. Long-term sustainability requires local participation in solutions to ensure the supply of safe, effective antivenoms. The strategy will encourage political buy-in and commitment by national governments to establish local policies and programmes for the regulation, supply and distribution of antivenoms cost-mitigation and surveillance. New public–private partnerships will emerge for antivenom production in low- and middle-income countries, contributing to reaching the target of a 25% increase in the number of manufacturers by 2030.

Improve control and regulation of antivenoms.

Many regulatory agencies, drug control laboratories and health authorities lack the technical capacity to adequately regulate and control the safety, effectiveness and quality of

the antivenoms marketed in their countries. In many countries, products that are not suitable for use are marketed, with poor clinical outcomes. Poor-quality products undermine market confidence, thus contributing to market fragility and potential collapse.

The strategy will provide guidance, norms, standards and technical support on antivenoms to regulatory agencies, drug control laboratories and health authorities to build their capacity to evaluate, license and monitor antivenoms in all regions. WHO training and laboratory services will support countries in comprehensive assessment of application dossiers for product registration and marketing approval and also in evaluation of compliance with good manufacturing practice and validation of product quality and applicability. Inappropriate, unsafe or ineffective products will be removed from markets and replaced with products that meet appropriate standards of safety, effectiveness and quality.

Introduce prequalification for antivenoms.

Target product profiles are not available for most of the antivenom products marketed in WHO regions, which has resulted in many antivenoms that are inadequate for their intended use. This contributes to poor outcomes and loss of confidence by users. WHO will work with technical partners to establish minimum specifications for antivenom products manufactured for specific purposes (e.g. broad-spectrum coverage against a range of snake species) by 2020. Target product profiles and minimum specifications will be introduced in 2021 as essential prerequisites for introduction of a formal WHO antivenom prequalification scheme.

Reference standards for venoms and antivenoms are essential for reliable, reproducible evaluation of antivenom products submitted for prequalification. WHO will establish a new process for the preparation and validation of

these materials as a further precursor to WHO prequalification, in collaboration with technical partners and national drug control laboratories and health authorities. The process for production and validation of reference materials will be established by the WHO Expert Committee on Biological Standardization (ECBS) in 2019; adoption of technical specifications for individual venom and antivenom reference standards endorsed by the ECBS in 2020–2022; and production of reference standards for WHO antivenom prequalification will start in 2023–2024. A WHO antivenom prequalification programme will then be established.

Prequalification helps national regulatory agencies and other organizations to make good-quality medicines available to those who need them. It also allows purchasers, donors and users to be confident that medicines are safe, effective and made to high standards. Some organizations support the procurement only of prequalified medicines. Introduction of prequalified antivenoms will contribute substantially to rehabilitating the antivenom market and ensuring its sustainability. Manufacturers will have access to antivenom prequalification in 2023–2024, and products that meet the standards will be available for procurement. The demand for prequalified antivenoms will stimulate the market, increasing the supply, affordability and sustainability of well-designed, safe, effective, affordable antivenoms. Prequalification facilitates inclusion of antivenom products in programmes for financing medicines.

Encourage investment in innovative research on new therapeutics.

Lack of investment restricts the ability of manufacturers to improve production, undertake research and development and finance essential improvements to their infrastructure. Relatively modest investment into strengthening manufacturing and the development and validation of new products is essential to



WHO WILL EVALUATE ANTIVENOM PRODUCTION TO ENSURE THAT SAFE AND EFFECTIVE PRODUCTS ARE AVAILABLE IN ALL REGIONS OF THE WORLD.

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overcome the current supply crisis. Investment in delivering new treatments that can be brought to the market now will immediately reduce mortality, morbidity and disability. The strategy will stimulate investment for rapid delivery of new treatments for snakebite envenoming in regions that currently lack effective products. If manufacturers are able to access capital to modernize production infrastructure, introduce new technologies and invest in research, new products will be introduced in adequate quantities to overcome the immediate chronic shortages, with measurable reductions in indicators.

Most manufacturers lack the resources for innovative research, and academic research on antivenoms is often poorly aligned with the

needs of industry. Support for partnerships and collaboration between academia and industry to strengthen, innovate, improve and expand the production, quality control and preclinical and clinical testing and pharmacovigilance of antivenoms and other treatments could lead to rapid improvements in access to safe, effective antivenoms. The strategy will include support for innovative and collaborative research between industry and academia. Research and development into new products, processes and other areas will accelerate, with support from research funding agencies.

Several exciting avenues of research have strong potential to deliver innovative therapeutics with better safety, efficacy and cost-effectiveness in the medium to the long term, but

most currently lack investment to be commercially viable. Support will be provided to research and development into new technologies and innovative treatments to revolutionize the management of snakebite envenoming. Research funding agencies and other stakeholders will be encouraged to increase investment in strategic research on new technologies and therapeutics. New therapeutic candidates will be identified so that drug development pipelines can deliver these next generation treatments by 2030.

Integrate health worker training and education.

Health workers receive little if any training in diagnosing and treating snakebite envenoming, and many have limited opportunities for in-service professional development of clinical practice. Training packages should be integrated into health worker curricula at all levels to improve the management of snakebite envenoming. Locally relevant training packages will be prepared for all health wor-

kers to increase their knowledge and practical clinical competence. Improved management of snakebite envenoming and overall improvements in clinical practice will benefit all patients.

Working health professionals require regular in-service training in clinical skills for the management of snakebite envenoming. Many rural health workers lack regular in-service training. The skills relevant to snakebite envenoming are often multiple, and training therefore improves overall clinical practice. A number of workforce training measures adopted by Member States would directly improve and standardize treatment and recovery.

Snakebite envenoming is poorly covered in most of the tertiary and vocational training curricula for health professionals. Graduates are often poorly equipped to manage snakebite envenoming, and most have limited experience. Integration of clinical toxinology into training programmes will improve patient care and treatment at all levels. Integration of



**TEACHING HEALTH
WORKERS TO
PROPERLY TREAT
SNAKE BITES
PROVIDES THEM WITH
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CUTTING CLINICAL
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education on the prevention and treatment of snakebite into medical, nursing and other schools, colleges and university curricula will make health professionals better qualified and more confident of their ability to manage snakebite envenoming. Such efforts would benefit from clinical toxinology becoming a recognized medical speciality coordinated by a professional college or association as a formal qualification.

Few resources are available to help health professionals improve the care and treatment of snakebite envenoming. The availability of appropriate guidelines, resources and other tools will improve clinical practice. Guidelines, resources and learning tools will be developed to improve and standardize the prevention, clinical diagnosis, treatment, recovery and rehabilitation of snakebite patients.

Improve clinical decision-making, treatment, recovery and rehabilitation.

The success of treatment can be evaluated only if the clinical criteria for different envenoming syndromes are specified, yet these are not available in many countries. Furthermore, lack of clear clinical end-points that define the effectiveness of treatment for these syndromes confounds objective assessment of treatment success or failure and comparisons of effectiveness across different health care settings and locations. Standardized, objective clinical criteria will be defined for envenoming syndromes in consensus documents with clear clinical end-points for treatment effectiveness. Health workers will be better able to diagnose snakebite envenoming objectively and identify specific clinical syndromes, which will improve case management. Standardized tools will be available to support decision-making and improve treatment outcomes, allowing more reliable analysis and comparison of data.

Current point-of-care diagnostic tests for snakebite envenoming could be made more

accurate and reliable, which will reduce treatment delays and improve patient outcomes. A framework will be developed for delivering innovative new point-of-care diagnostic tools.

Post-acute care and services for disability support and rehabilitation have long been neglected. Critical pathways should be reframed to include these elements of treatment and recovery. Adoption of such measures by Member States will directly improve and standardize treatment and recovery, and more patients will have access to care and support during recovery.

Awareness will be raised about the rehabilitation needs of snakebite victims, and strategies will be found to increase access to rehabilitation services to accelerate recovery. Rehabilitation care providers will provide the necessary services that will hasten recovery and a return to a productive life for snakebite envenoming patients who have experienced disability.

Current medical management focuses mainly on treatment in the acute phase and management in other phases such as post-discharge are often not included in the training of health professionals. The importance of after-care should be included in management protocols to ensure that all snakebite patients are followed up. Follow-up will increase participation in care and rehabilitation during recovery, reducing morbidity and disability. More comprehensive snakebite envenoming management protocols, medical and health worker training curricula, guidelines and tools will be prepared.

STRENGTHEN HEALTH SYSTEMS

Snakebite envenoming is a serious medical emergency, but most health systems are unable to provide the services, personnel, medicines and technologies required to manage it effectively. Improving snakebite treatment means strengthening the entire health care system, so that it will benefit everyone. Better disease surveillance and reporting systems, strong regulatory and policy frameworks, well-trained staff working in well-equipped health facilities are necessary to improve the outlook for victims of all diseases, including snakebite.

For many, the costs of antivenom, other treatments and hospitalization are beyond their financial means. In countries such as India and Bangladesh, these costs have been shown to drive people further into poverty and debt (19, 21). The strategy encourages the establishment of initiatives to defray such costs. Including snakebite treatment in professional insurance schemes (e.g. farm insurance) or, preferably, making treatment free of charge, as in India, should be a priority (34). In countries where governments pay compensation for deaths and injuries caused by wild animals, more efficient, cost-effective use of this funding might be the provision of access to effective treatment, such as antivenom or ambulance services, and reimbursement of health care expenses.

Strengthen community health services.

Primary health care services for snakebite envenoming must be improved to ensure that facilities have the capacity and resources to manage life-threatening medical emergencies associated with snakebite envenoming and are appropriately staffed. Strengthening primary health care capacity, performance and resources will increase the number of services that can provide initial treatment of snakebite envenoming, including administration of antivenom and other life-saving interventions.

Snake antivenoms are only one of the essential medicines that may be needed in the treatment of snakebite envenoming. Health facilities require many other drugs, items of medical equipment and consumables to treat snakebite envenoming and the full range of other medical conditions with which people present. Ensuring that all facilities have access to these products will advance progress towards universal health coverage by 2030. The strategy will improve access to medicines, medical products and consumables, with measurable improvement in access to essential medicines, including antivenoms, and all other medical drugs, equipment and consumable items.



THE STRATEGY
ENCOURAGES THE
ESTABLISHMENT OF
INITIATIVES TO DEFRAY
TREATMENT COSTS.

**Facilitate research and policy
development to reduce treatment costs.**

Most victims of snakebite envenoming are at or below the poverty index, and the cost of treatment can be financially crippling, with long-term effects on whole families. Better understanding of the economic costs of snakebite envenoming and approaches to including it as a disease eligible for coverage by public and private health finance schemes will reduce the economic harm. Research will be

conducted on the direct and indirect costs of treatment and recovery for victims of snakebite envenoming and into models for financing and cost-mitigation schemes by public and private agencies.

Inclusion of snakebite envenoming in schemes for equitable access to health care, which remove the burden of poor families, will encourage more victims to seek medical treatment, resulting in better outcomes and reducing the long-term financial impacts.

Snakebite envenoming should be included in private and public health care funding mechanisms in countries and as an approved condition in rural or agricultural health insurance programmes.

Governments in some countries have schemes to reduce or eliminate high treatment costs for snakebite envenoming. Extending the number of countries that prioritize a reduction or elimination of user-pays barriers to access to antivenoms will contribute to achieving universal health coverage and influence health care-seeking behaviour, thus reducing the burden of snakebite envenoming on communities. Economic models will be developed to make a strong case for government support of programmes to reduce financial and social vulnerability at the time of treatment and throughout recovery.

Improve infrastructure, services and health facilities.

Strong health systems are fundamental to improving treatment of snakebite envenoming. Rural primary health services, district secondary, sub-national and national tertiary health services can all improve treatment and recovery after snakebite envenoming and should be strengthened in line with SDG3 and UHC2030. Targeted investment will be sought to build-up peripheral infrastructure and in-

crease access to effective health care, including transport, communications and support services, to improve access to health care for all citizens.

Many regulatory agencies, drug control laboratories and health authorities lack the technical capacity to adequately regulate and control the safety, effectiveness and quality of antivenoms marketed in their countries. The solution will be to improve their capacity to undertake normative, regulatory and laboratory activities to improve access to safe, effective quality-assured antivenoms and other medicines.

Innovative, validated systems for the procurement, distribution and surveillance of antivenoms are important to overcome current logistical, infrastructure and communications difficulties in remote rural communities. Pragmatic investment in research for emerging technologies should be encouraged, such as low-cost portable cold-chains, delivery systems and mobile surveillance and reporting tools. Research will be conducted for better implementation, monitoring and evaluation of innovative interventions to improve distribution systems and post-marketing surveillance of safety and effectiveness for antivenoms in health facilities and communities. New approaches will be introduced for the procurement, distribution and surveillance of antivenoms.

Stronger, more effective supply chains and surveillance systems will ensure that antivenoms are accessible to all who need them. Better procurement and distribution will reduce stock outages in rural areas, and better surveillance will identify problems in quality and product safety more rapidly. National drug procurement, distribution and surveillance systems will be improved.

Snakebite envenoming is rarely reported either sub-nationally or nationally in most countries. Better data collection and analy-

Improving snakebite treatment means strengthening the entire health care system, so that it will benefit everyone.

sis are essential for resource allocation and investment. Common tools and applications and clearly defined minimum data set requirements, should be defined for assessing the burden of the disease in the health system and communities. Support will be provided to improve the capacity of health systems to collect, compile and analyse data on snakebite envenoming. The success of the measure will be determined by the number of countries that use new or repurposed data collection tools and applications to monitor and assess the burden of snakebite envenoming and the number that contribute data on snakebite envenoming to the WHO Global Health Observatory.

Include snakebite envenoming in national and sub-national health plans.

Snakebite envenoming must be addressed to meet the SDGs and UHC2030. Integration of snakebite envenoming into health plans ensures inclusivity and recognition that, as for other NTDs, control of snakebite envenoming is essential to improve the lives of the world's poor.

Overall improvements in health systems benefit everyone. In some regions, the effects of some types of snakebite envenoming require additional resources, and some countries will require support. For example, long-term renal injury is a disproportionately prevalent consequence of envenoming by certain snake species in some countries, which requires substantial investment in specialist care and medical consumables. National and sub-national level programmes to meet specific needs and requirements should be supported by programmes, tools and resources.

Enhance monitoring and surveillance of the disease burden.

Inclusion of snakebite envenoming as a notifiable disease will hasten accumulation of accurate data on disease burden for accu-

rate modelling of the economic, health and social impacts of the disease. This will ensure that appropriate resources are allocated and distributed to the countries and regions in which the problem is most severe and will accelerate implementation of the strategy for control of snakebite envenoming. More accurate sub-national, national, regional and global estimates of the burden of snakebite envenoming the resources required and priority areas will be identified.

Snakebite envenoming, like many other NTDs, is significantly under-reported, partly because a large proportion of cases are not registered in health systems. The most accurate data are those acquired from both health systems and communities, with various tools and applications. Ensuring that data are standardized, comparable and reliable requires investment in data collection methods, tools and applications. Robust, standardized applications, software packages, tools and disease surveillance systems will be developed to improve the collection, storage, analysis and reporting of snakebite envenoming.

Measurement of the burden of snakebite envenoming requires application of a standardized minimum set of definitions, agreed by consensus, harmonized epidemiological parameters, surveillance methods and agreement to contribute data to a common global repository. This is essential to ensure that data are comparable at sub-national, national, regional and global levels. Internationally agreed standards will be established for surveillance, guidance and harmonization of strategies for snakebite envenoming. A minimum data set and definitions and standardization of common epidemiological parameters will be agreed, with a snakebite envenoming data repository within the WHO Global Health Observatory and inclusion of queries on snakebite envenoming in the questionnaire for the Global Burden of Disease and other health surveillance projects. Agreed reporting parameters will then be incorporated into

Most of the antivenoms used today have not been tested in formal clinical trials, and the evidence for the safety and effectiveness of some is weak.

sub-national and national health plans and disease surveillance programmes.

Foster research on the ecology, epidemiology, clinical outcomes and therapeutics of snakebite envenoming.

In most countries affected by snakebite envenoming, the quality and reliability of data are poor. In order to implement programmes and measure their effectiveness, a series of benchmarks should be established based on research in communities and health systems. Sub-national and national baseline data will be published to establish benchmarks against which programmes can be evaluated. Integration of consolidated baseline data into the Global Health Observatory will allow establishment of regional benchmarks. Improving the quality of data from countries or regions where surveillance is particularly weak will ensure that gaps in knowledge about the burden of snakebite envenoming are filled and that regional assessments are accurate and reliable.

There is substantial disparity between data acquired in communities and those acquired from health systems, mainly because many victims of snakebite envenoming do not present to health services. Research integrating data from these two sources will provide a more accurate assessment of the overall burden. Combined evaluation of data acquired in communities and in health systems will raise the priority of this disease and increase resource allocation.

The current “gold standard” for testing the efficacy of antivenoms is in laboratory animals *in vivo*. New testing procedures to reduce or eliminate the use of live animals in such research will meet international commitments to the principles of “replacement, reduction and refinement” and may be more relevant and cost-effective. The strategy will encourage research into preclinical models of antivenom safety and efficacy. New preclinical tests for the safety and efficacy of antivenoms that adhere to new principles of animal testing will improve the quality and reliability of preclinical test data and reduce the costs of quality control testing.

Most of the antivenoms used today have not been tested in formal clinical trials, and the evidence for the safety and effectiveness of some is weak. Investment in pragmatic, cost-effective clinical studies of snakebite envenoming will improve understanding of the disease in different countries and regions and associated with different species of venomous snake, in addition to providing good evidence about specific antivenom products. Incorporation of cost data in clinical studies will allow better resource allocation by health ministries. The strategy emphasizes support for preclinical and clinical research, including clinical trials, to improve understanding of snakebite envenoming and the effectiveness, safety and affordability of treatment. One outcome might be establishment of field centres for snakebite envenoming clinical research and sentinel clinical trial sites, with publication of well-designed clinical studies of the safety, effectiveness and costs of treatments or medical interventions. The data could be used to inform policy, procurement, clinical care and resource allocation decisions at sub-national and national level.

The risk of snakebite envenoming is higher in populations in frequent contact with venomous snakes, such as those in certain agricultural occupations, or who engage in high-exposure activities. Understanding of



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the ecology and epidemiology of these interactions can be used to frame interventions to reduce or eliminate these risks. Additional resources will be directed to areas in which the incidence of snakebite envenoming is high because of occupational, environmental or behavioural factors. Epidemiological research will be undertaken on the distribution and factors associated with snakebite envenoming in high-risk populations to identify occupations, behaviour and other factors responsible for risk and exposure. The data will be used for risk mitigation, prevention or elimination strategies and interventions.

The incidence of snakebite envenoming is rarely uniform throughout a country or a region. The distribution of venomous snake varies according to ecological, geographic and environmental parameters. Climate, human population density, transport networks, land use and habitat should all be better understood. Research with geospatial and other tools can build a more accurate picture of the distribution of the incidence of snakebite envenoming and the reasons for it, and this can be used directly to guide resource allocation and the design and use of interventions. The outcomes might include production of sub-national, national and regional maps of snakebite envenoming incidence and other metrics. Better geospatial understanding of the determinants of snakebite envenoming will improve resource allocation and the prioritization of interventions, leading to new strategies for prevention and control at all levels.

Operational research on the challenges to be overcome to reinvigorate and rebuild a sustainable market for antivenoms in regions such as sub-Saharan Africa will make it possible to plan interventions and strategies for implementation, development of a business case and resource planning. Additional research will be conducted on the supply and demand of health, socioeconomic factors, the economics of antivenom production and barriers to efficiency, the antivenom market, needs, affordability and cost-effectiveness. Analysis will be conducted to better understand the market for antivenoms and the forces that affect access and affordability. Tools will be found to acquire data on the cost-effectiveness of antivenoms, and economic analyses will be made of antivenom production processes and recommendations to improve and rationalize production, reduce costs and increase product quality and efficacy. "Forward-needs" assessment tools will be developed to improve forecasting and resource planning by procurement agencies.

INCREASE PARTNERSHIPS, COORDINATION AND RESOURCES

Transformation of the strategic objectives into effective outcomes will require strong partnerships among WHO, Member States, development partners, donors and other stakeholders. The strategy will build such partnerships through advocacy, supported by robust data, consensus and effective coordination, monitoring and reporting. We will build a sound investment case for the strategy overall and for its key activities. This will involve collecting and analysing data from countries about the burden of snakebite envenoming and how it changes over time with the interventions proposed in this strategy. Robust health economics analyses of the cost–benefits and cost–effectiveness of certain actions should persuade countries and development partners to support the strategy and its implementation.

Greater visibility and recognition of the disease burden, coupled with strong investment to sustain the strategy and achieve its objectives will be essential. The focus will be on integrating snakebite envenoming into public health programmes and into the health plans of affected countries.

The incidence of snakebite is affected by various socioeconomic factors. While seeking to reduce the overall impact of snakebite enve-

noming, the strategy will encourage national health authorities to identify and engage with relevant stakeholders, such as ministries of agriculture, fisheries and natural resources, and perhaps assign them roles in implementation of the strategy, especially in reducing the incidence of snakebite and promoting early health-seeking in the communities they serve.

Support governance and leadership.

Snakebite envenoming is one of the many health problems facing the world's poorest citizens in some of the least developed countries. It is a disease strongly associated with poverty and affects millions of people each year. Ensuring that snakebite envenoming is integrated into aspirations for universal health coverage and the SDGs will ensure that efforts to control snakebite envenoming are accelerated and prioritized, so that all affected individuals and communities have access to good-quality essential health services without suffering financial hardship. The task will be to encourage country coordination to integrate snakebite envenoming with other health activities for ensuring universal health coverage through better management of resources. Snakebite envenoming should therefore be integrated into national

health plans, regulatory systems and activity frameworks, and policies should be adopted to improve affordable, equitable access to essential health services for people affected by snakebite envenoming.

Supporting countries with tools for snakebite envenoming will help them to accelerate progress towards meeting the overall objectives of UHC2030 and the SDGs for better health outcomes for everyone. Health policy to improve the guidance, standards, norms and monitoring and evaluation frameworks is essential for achieving UHC2030 and the SDGs. Countries should incorporate snakebite envenoming into their SDG and UHC2030 agendas and identify the actions necessary to meet those objectives, with published reports of updated assessments and progress to achieving the targets.

Most countries in which snakebite envenoming is prevalent face similar development challenges. Many have weak regulatory frameworks and, particularly for antivenoms, limited capacity to regulate these essential medicines effectively. Greater regional cooperation in the regulation of antivenoms, with technical support from WHO, will strengthen their systems multilaterally. Strong regional regulatory frameworks should be established for accountable, evidence-based health systems and cooperative intersectoral partnerships between countries and other stakeholders. Regional regulatory pathways for the registration, evaluation and control of antivenoms will measurably improve access to quality-assured, appropriate antivenoms. Common registration pathways result in reduced costs and streamlined application processes for manufacturers of antivenoms, thus facilitating wider market penetration of products.

Promote advocacy, effective communication and productive engagement.

Strong advocacy is necessary to build a coalition of partners and stakeholders to operationalize the strategy and raise the necessary resources and the profile of the disease sufficiently for sustainable change. Broad advocacy about snakebite envenoming should be conducted to raise the awareness of all stakeholders. Advocacy and communication can result in tangible, measurable outcomes, including resource allocation and initiation of projects in countries. A strong coalition of countries, development partners and stakeholders will be established and extended over time.

Engagement with communities can be improved by use of validated tools and information resources tailored to contexts (e.g. language, cultural, social) and delivered by local “champions”, advocacy groups and activists. A toolkit will be adopted to provide partners with effective communications, training and learning solutions to ensure that the core messages are standardized and consistent across communities and countries. Tools and information resources will be prepared, with standard core messages that can be adapted to different contexts. Networks of local partners will be established and empowered to engage with communities. The outcome will be measured as improvements in use of prevention and risk-mitigation strategies.

Effective snakebite envenoming communication and engagement is based on maximization of opportunities afforded by various forms of media, communication outlets and stakeholders in industry, business and government agencies linked to or serving populations at risk. Provision of health promotion information on snakebite envenoming to communities can increase the effectiveness of campaigns and other activities. Health promotion strategies can be disseminated

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through mass and social media, educators, agribusiness, industry, labour unions, employers and governments. A comprehensive communications strategy for snakebite envenoming will be prepared, with core media materials and resources. Regional health promotion will be conducted in collaboration with countries, with targeted activities for high-risk communities.

The strategy is central to WHO's response to World Health Assembly resolution WHA71.5, and active engagement with Member States and other stakeholders is essential to implementing the resolution. Information about the strategy and progress being made will encourage its uptake in other countries and provide an incentive for other stakeholders to engage and participate. More dialogue between WHO regional and country offices, Member States and focal points will raise the profile of snakebite envenoming and advance the activities in the strategy. Member States should allocate resources to support implementation of the strategy by WHO. Engagement with other stakeholders can lead to productive collaboration on projects and allocation of resources to support WHO activities.

Enhance integration, coordination and cooperation.

WHO will integrate its snakebite envenoming prevention and control programme into its General Programme of Work to ensure that the activities are aligned with its objectives and aims. It will also be aligned with relevant regional and country health systems and partners. One of the outcomes will be an increase in the number of WHO programmes that incorporate snakebite envenoming activities in their activities in the General Programme of Work.

WHO will identify synergies with other public health programmes and leverage partnerships to maximize the impact and use of resources by addressing the overall health needs of affected communities and integrating snakebite envenoming into other programmes, rather than working in isolation and potentially duplicating efforts. Multifocal partnerships will be formed to deliver coordinated solutions, identify synergies in human and animal health programmes and provide technical support for the integration of snakebite envenoming into existing health programmes. The outcomes should be measurable increases in international collaboration and cooperation among countries and development partners, and productive cooperation between WHO with other public health or disease-specific initiatives that address common challenges.

Build strong regional partnerships and alliances.

Countries in some regions have the same requirements for antivenom and face similar technical and health systems challenges. WHO will work with countries to find cooperative activities for addressing common issues and deliver solutions to shortages of antivenom and problems with supply, production or quality. WHO will also work with neighbouring countries with the same venomous snakes

and the same challenges to clinical care and treatment to find regional solutions. It will collaborate to establish regional cooperation projects for improved antivenom production and create antivenom stockpiles, training and technical support. These activities should result in partnerships and regional collaboration to improve and sustain adequate supplies of effective antivenoms. Regional technical assistance and training programmes will improve prevention and control of snakebite envenoming and sustain reductions in morbidity, disability and mortality. Other bilateral and multinational projects and partnerships will also promote the objectives of the strategy.

Coordinate data management and analysis.

WHO will use the Global Health Observatory and other resources to establish a central repository for data on snakebite envenoming that is open and accessible to all interested parties. This will ensure that data are collated and available for analysis and that the results can be extracted and used for evidence-based decision-making. Essential data will be captured, analysed and stored in accessible repositories. Standardized national, regional and global data on snakebite envenoming will be deposited in the Global Health Observatory, and data analyses will be published regularly to inform decision-making.

The 11th edition of the International Classification of Diseases (ICD-11) contains global health information, in which clinical and epidemiological parameters and causes are coded. It can provide data that can be used to understand the etiology of snakebite envenoming and its outcomes. By ensuring that snakebite envenoming is correctly classified in this resource and encouraging increased use of ICD-11 for coding presentations of snakebite envenoming to health services better-quality hospital-acquired data will be obtained.

Establish a strong, sustainable investment case.

There are currently few high-quality data on which to base a strong health economics argument to prioritize funding for snakebite envenoming. Addressing this deficiency is essential to finding the resources to implement the strategy and to fund commodities such as antivenoms. A strong investment case should be prepared to ensure adequate resources for the programme, based on robust data and analysis of cost-benefit and cost-effectiveness. Data can be analysed and modelled to prepare an investment case for countries and funding partners to fund specific strategic projects, activities and human resources.

The business case for the prevention and control snakebite envenoming will be supported by data demonstrating the economic and health benefits of integration of snakebite envenoming into health systems, by combining control of this disease with that of other NTDs, which are often prevalent in the same communities affected by snakebite envenoming. Implementation research should be conducted to demonstrate the benefits of integration with the control of other NTDs and medical conditions. This will stimulate new partnerships and collaboration with other health groups and progress to the elimination or control of several NTDs and other health and development issues in affected communities.

In addition to the resources required by WHO to implement the strategy, funding will also be required to purchase and distribute commodities, finance national prevention and control activities, regional cooperation, research investments and capital to fund manufacture of therapeutics and other activities. Coordination of investment and resource mobilization and a framework to track, monitor and coordinate activities among all stakeholders will allow WHO to monitor and evaluate implementation of the strategy nationally, regionally

and globally and create a dynamic network of stakeholders as the strategy moves towards its 2030 goals. A framework will therefore be established to coordinate investment, resource mobilization, collaboration, knowledge exchange, engagement and implementation at country and regional levels. WHO will maintain a clear view of progress towards the 2030 goals and make use of information to update and modify the strategy according to the progress made and the opportunities, obstacles and challenges encountered. Strong coordination mechanisms will be established to ensure that resources are used strategically, with minimum duplication, and that stakeholders have access to information that stimulates partnership and collaboration. Resource wastage will be minimized and opportunities for collaboration, knowledge exchange, investment and improved resource maximized.

One reason for considering snakebite envenoming as an NTD is the substantial disparity between the extent of the problem and investment in research. WHO recognizes that research is fundamental to effective control of NTDs such as snakebite envenoming. Investment by research funding bodies and other agencies in a range of topics to inform decision-making, improve surveillance, change behaviour, deliver new treatments or improve understanding of the clinical effectiveness and safety of antivenoms will contribute significantly to achieving the objectives of the strategy. Funding for research on snakebite envenoming will be sought in accordance with the priorities highlighted in this strategy and particularly to improve existing antivenom production technologies and products. Funding agencies should commit themselves to increase support for research on snakebite envenoming and to deliver solutions to specific problems, including modernization and improvement of current antivenom production technology and antivenom products.

PLANNING, MONITORING AND EVALUATION

WHO, in collaboration with partners, will prepare a framework for planning, monitoring and evaluation for critical assessment of the strategy over time. As the plan is to deliver local solutions in the countries in which snakebite envenoming is a problem, monitoring and evaluation should be part of national plans. These activities will require collection of baseline data in order to measure progress in programme activities and work plans tailored to the objectives of each country. Progress towards the objectives will be measured regularly, and annual reports will be issued and made publicly available.

For each of the four strategic objectives, we will prioritize a pathway of change for short-, medium- and long-term outcomes. The tasks to be undertaken in pursuit of these objectives will deliver both independent and interconnected results, synergistically strengthening each other and progress towards the 12-year target. While the pathways to the objectives are non-linear and outcomes will probably be reached at different times, they complement and support the overall goals, such as improved antivenom products, better trained health workers and health facilities with resources to manage snakebite envenoming, which are essential for ensuring that community engagement to change health care-seeking be-

haviour will succeed. Likewise, greater use of allopathic health services and of antivenom resulting from community engagement will increase the demand for antivenom and the reversal of the current vicious circle that has precipitated the current crisis in antivenom supply in sub-Saharan Africa and other regions.

The planning, monitoring and evaluation framework will be prepared during the initial phase of the strategy and updated throughout the programme. As baseline data and data on progress improve, the framework will become a composite of general elements and context-specific components.

Planning

WHO will prepare outcome-based work plans for implementation of the phases of the strategy. Interventions will be planned in context-specific frameworks, and a “SMART” (specific, measurable, achievable, relevant, time-bound) approach will be used to achieve short-, mid- and long-term outcomes. Each component will be integrated into a risk mitigation matrix, and actions taken to ensure that risks are appropriately managed. Timelines, budgets and deliverables will be mapped and resources identified and secured. Planning will be updated annually or as necessary.

Monitoring

A monitoring framework will be prepared, with indicators for each outcome to track progress through a range of data sources and appropriate verification methods. Reports and data will be collected and aggregated regularly to track overall and context-specific progress.

Evaluation

WHO will evaluate progress towards objectives and outcome targets, with particular attention to the relevant indicators of SDG 3 and WHO's Thirteenth General Programme of Work 2019–2023 (and subsequent Programmes of Work). Evaluations will be made at the end of each phase of the strategy to clearly understand progress and achievements nationally, regionally and globally to achieving the goal.

WHO will prepare an adaptable template of the theory of change to enhance implementation of the strategy by matching context and assumptions with a logic model for mapping the sequence of steps, actions or milestones for short-, medium- and long-term outcomes. Application of the theory of change will strengthen planning, monitoring and evaluation and ensure that the best approaches are used to achieve the outcomes and objectives.

WHO will work with countries and partners in a structured approach to defining baseline data requirements and the processes for acquiring and analysing the information. Various types of data will be required to measure progress, which will be acquired with standard research methods, tools and applications based on consensus. They include:

- accurate data on burden of disease (i.e. incidence, morbidity, disability and mortality) for geographically defined subnational, national and regional areas;
- access to data on antivenoms and other commodities used in the treatment of snakebite envenoming;
- data on community prevention, health care-seeking behaviour and sociocultural perceptions of snakebite events and their consequences;
- analysis of the capacity and needs of national and local health systems;
- analysis of gaps in antivenoms produced by good manufacturing practice;
- assessments of the clinical skills and knowledge of health workers; and
- evaluation of the shortfalls in regulatory agency capacity, training and resources.

MANAGING RISK

WHO will use a robust model of risk mitigation in the programme, to identify risks, assess their likelihood and possible consequences and then find strategies to minimize or eliminate them (**Fig. 3**). Internal factors within WHO that might affect implementation of the strategy will be evaluated and measures put in place to address them. The risks will be reas-

sessed regularly. WHO will also use validated risk assessment tools to manage external factors that may represent risks to the overall strategy or to individual components by identifying them early and reducing or removing their likelihood. Partners and stakeholders will be consulted regularly.

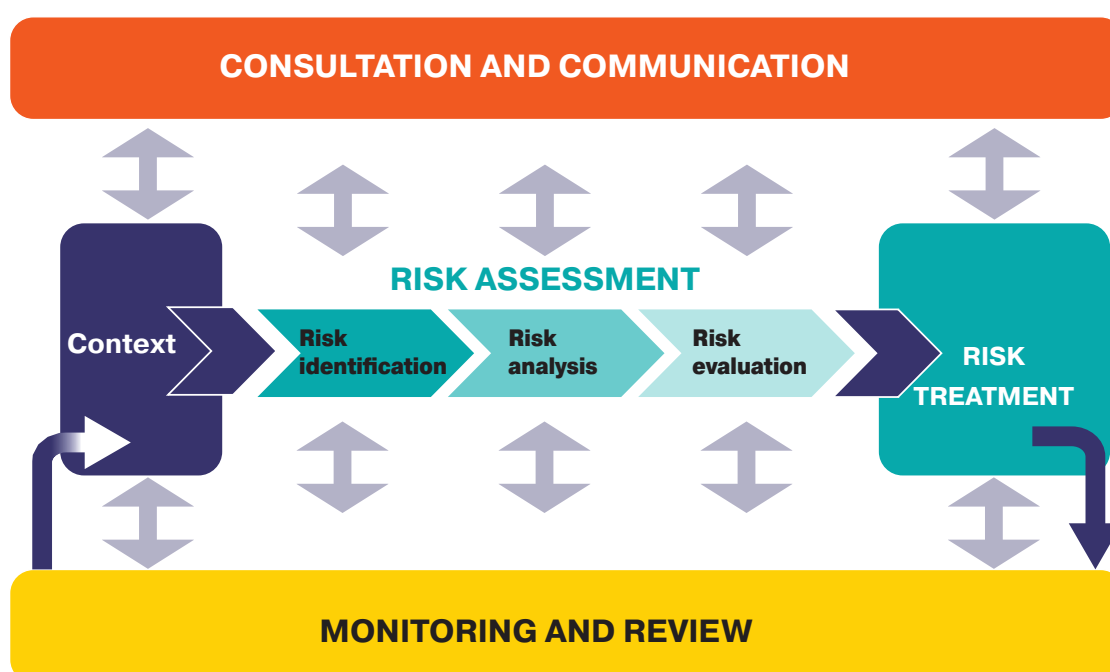


Fig. 3. **Model of risk mitigation for snakebite envenoming strategy**

In assessing risks, WHO will use a matrix to identify the likelihood (probability) that a risk will arise and evaluate the severity of the consequences and the effect on the programme overall or on a specific project (Table 1). The urgency with which specific risks are addressed will be based on risk ratings, the highest priority being given to events that combine the highest likelihood with the greatest impact. Consultation, monitoring and regular review will ensure that risks are managed pragmatically and strategically.

With partners and other stakeholders, WHO will ensure that the strategy is technically sound at all times and addresses the objectives to effect lasting, sustainable change. Regular progress reviews and consultation with experts in relevant fields will ensure that risks are managed effectively.

Table 1. Matrix of likelihood of a risk and the severity of its consequences

Likelihood		Consequences	
1	Rare	1	Negligible
2	Unilkely	2	Minor
3	Possible	3	Moderate
4	Likely	4	Major
5	Expected	5	Severe

COSTS

WHO activities between 2019 and 2030 will require US\$ 136.76 million in direct support. The budget is incremental and annual costs will increase as the strategy is extended and more countries are included (Fig. 4). A key consideration in estimating the budget was that actions are conducted with strong parallel regional coordination and collaboration. Consequently, 54% of the total budget over 12 years is for work in countries and 17% for regional activities (Fig. 5).

Prevention and control of snakebite envenoming will be integrated into broader national and sub-national health plans and into programmes for improving health objectives and meeting needs. This approach will reduce duplication and maximize the impact in all affected countries. A detailed case for the value of investment will be prepared in the first year of the programme. Regular planning, monitoring and evaluation and biannual budget reviews will ensure that the strategy remains responsive and adapted to economic and other circumstances.

PILOT PHASE (2019–2020): WHO will require US\$ 8.96 million in 2019–2020 for the pilot phase, in which communities and health systems will be strengthened in 10–12 countries where snakebite envenoming is a public health problem. **Highlights:** Approximately

US\$ 2.85 million will be used to assess the safety and effectiveness of currently available antivenoms, to set up a trial antivenom stockpile for sub-Saharan African countries where access to antivenom is very limited and to improve antivenom manufacture, innovation and modernization. Another US\$ 1.21 million will be used to improve the treatment of snakebite envenoming from first-aid before admission to hospital through discharge and subsequent return to normal life. Encouraging the development of new therapeutics, improving disease burden surveillance and ensuring coordinated data management and analysis will require US\$ 1.84 million, and preparing and validating a strong, sustainable investment case for the programme to give donors confidence to support the interventions will cost US\$ 0.57 million.

An economic model for supplying up to 500 000 effective antivenom treatments a year to sub-Saharan Africa will be designed during the pilot phase. Additional funding for a supply of antivenom commodities will probably be sought from donors and governments in the affected regions. The cost of supplies for the trial antivenom stockpile of 50 000 treatments for the 10–12 trial countries is expected to be US\$ 6.0–7.2 million.

Fig. 4. **Funding requirements** during the three phases of the strategy, for regions, countries and WHO technical divisions



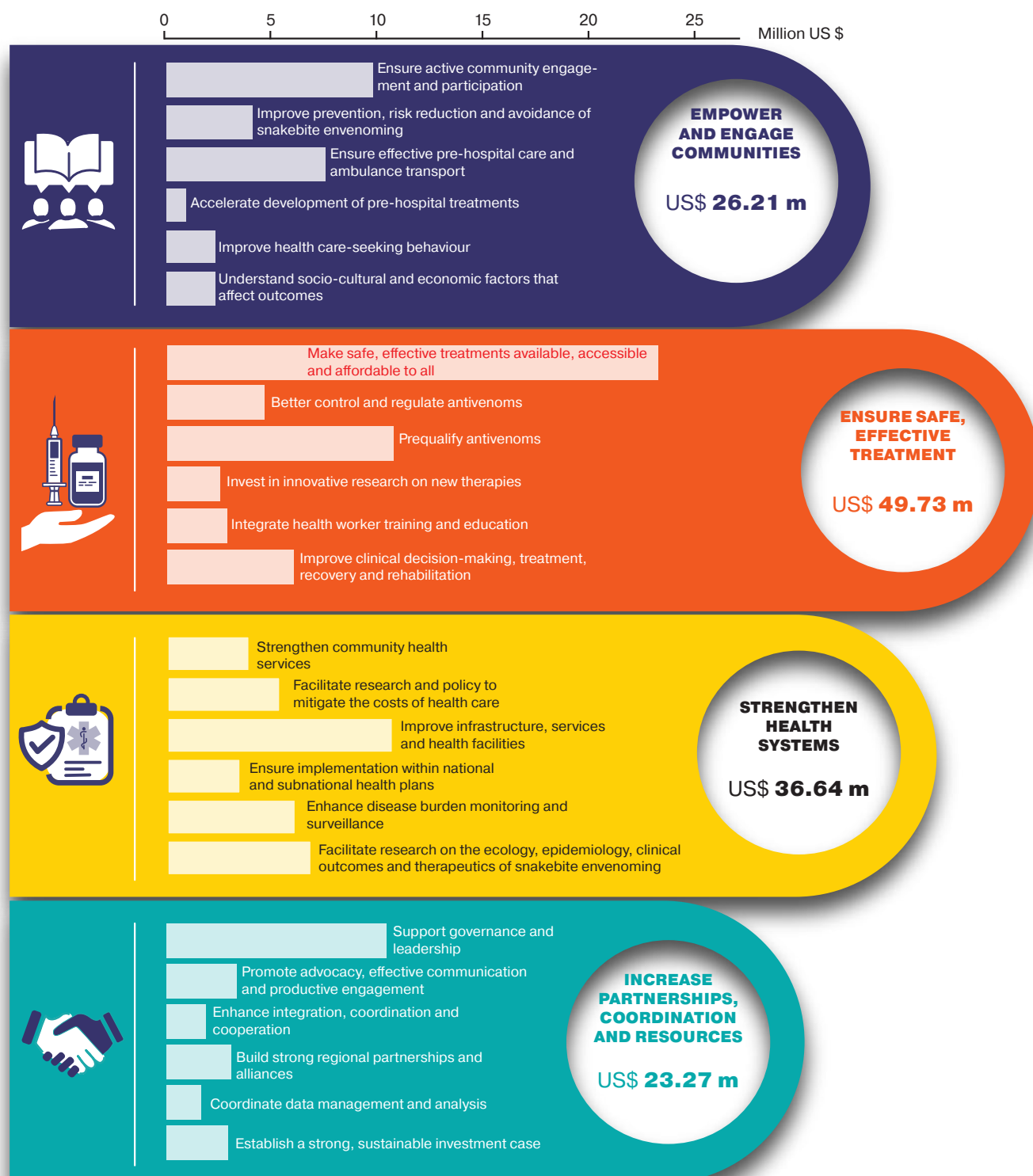


Fig. 5. **Total programme cost to 2030: US\$ 136.76 million**

SCALE-UP PHASE (2021–2024): As another 35–40 countries are added to the programme, an additional US\$ 45.44 million will be required. **Highlights:** US\$ 6.71 million will be for community engagement, US\$ 8.49 million for health systems and US\$5.29 million for monitoring, surveillance and analysis of the burden of snakebite envenoming to ensure that data continue to improve, for accurate forecasting of priorities, resources and activities. WHO will continue to ensure that antivenoms and other treatments are safe, affordable and accessible, including a prequalification programme for products and additional commitment to access to antivenom stockpiles. These activities will require US\$ 11.47 million over 4 years. Improvements to first-aid and hospital treatment for snakebite, development of new treatments and health worker training and support will require US\$ 6.37 million. US\$ 0.80 million will be spent to ensure a sound investment case that reflects current circumstances. Monitoring and evaluation of activities to meet all four objectives will provide the data necessary for effective planning and review. US\$ 6.35 million will be required for increasing programme governance and leadership for the extended investment and greater communication, engagement, integration and partnership development over the 4-year period.

FULL ROLL-OUT PHASE (2025–2030): Community activities and health system improvement will be extended to up to 80 more countries during this period, requiring the commitment of another US\$ 82.36 million. WHO recognizes that significant changes may occur in global, regional and even national economic and geo-political circumstances during the 6-year period; consequently, this costing is only an estimate based on current predictions of global inflation and expected programme progress. Planning, monitoring and evaluation of the phases of the strategy and a commitment to regular updating of the investment case and the programme strategy will help to ensure that they are dynamically responsive to any change. The mid- to long-term budget will be adjusted accordingly over time. **Highlights:** WHO's work with communities and health systems in all the affected countries will ensure advancement towards the SDGs and achievement of universal health coverage. Community activities will cost an estimated US\$ 11.35 million and health systems strengthening another US\$ 14.62 million. A full-scale WHO prequalification scheme for antivenoms and other activities to ensure the safety, quality and effectiveness of these essential medicines will cost US\$ 23.61 million. As the impact of the investment is seen, a sustainable supply of effective products will become available in all regions of the world. Disease monitoring, surveillance and analysis will require funding of US\$ 8.08 million, maintaining the momentum of the global partnership will require US\$ 11.15 million and sustaining better first-aid, and medical care, training and introduction of new therapeutic solutions will account for US\$ 12.09 million).

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A close-up photograph of two young Indigenous Australian children. They are wet, with water droplets on their skin and hair. The child on the left is smiling broadly, showing their teeth, and pointing their right index finger towards the camera. The child on the right is looking directly at the camera with a neutral expression, also pointing their right index finger towards the camera. The background is a blurred natural setting, possibly near water.

THE CORE OF THE STRATEGY IS THE GOAL FOR
ALL PATIENTS TO HAVE BETTER OVERALL
CARE, SO THAT THE NUMBERS OF DEATHS AND
CASES OF DISABILITY ARE REDUCED BY 50%
BEFORE 2030.



FOR MILLIONS OF MEN, WOMEN AND CHILDREN
AROUND THE WORLD, THE RISK OF SNAKEBITE
IS A DAILY CONCERN AS THEY GO ABOUT THEIR
EVERYDAY ACTIVITIES WHERE A MISPLACED STEP,
A MOMENTARY LAPSE OF CONCENTRATION OR
BEING IN THE WRONG PLACE AT THE WRONG TIME
CAN BE FATAL.



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