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# Assessing the practicalities of joint snakebite and dog rabies control programs: Commonalities and potential pitfalls

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ABSTRACT

Both rabies and snakebite primarily affect underserved and impoverished communities globally, with an estimated 200,000 people dying from these diseases annually, and the greatest burden being in Africa and Asia. Both diseases have been neglected and have thus been denied appropriate prioritization, support, and interventions, and face many of the challenges common to all neglected tropical diseases (NTDs). In line with the call for integrated approaches between NTDs in the recent NTD Roadmap, we sought to build upon previous conceptualizations for an integrated approach by identifying the commonalities between snakebite and rabies to explore the feasibility of an integrated approach. While multiple areas for potential integration are identified, we highlight the potential pitfalls to integrating rabies and snakebite programs, considering the nuances that make each disease and its intervention program unique. We conclude that health system strengthening, and capacity building should be the focus of any integrated approach among NTDs, and that by strengthening overall health systems, both rabies and snakebite can advocate for further support from governments and stakeholders.

## 1. Introduction

The 2021–2030 roadmap for neglected tropical diseases (NTDs) emphasizes a move from disease-specific to integrated approaches towards the reduction, elimination, or eradication of the 20 listed diseases or disease groups (WHO, 2020). This approach is borne of the experiences and lessons learnt from implementing the first road map (2012 London Declaration) and is seen as critical for building country ownership and leadership. It is also envisioned as a potentially cost-effective approach to ending the neglect of these diseases and contributing to the achievement of the 2030 Sustainable Development Goals (SDGs), specifically SDG 3.3.5 (United Nations Statistics Division, 2021). Due to their neglected nature, and the limited funding, recognition and support available, there has been a concerted drive within the NTD community to investigate areas where partnership and joint ventures between NTDs could be explored and exploited. While some NTDs may be less clearly compatible, there are others that seem to lend themselves to a concerted or integrated approach. One such example that we investigate in this perspective piece is that of snakebite envenomation and rabies virus exposures.

Snakebite envenomation and rabies virus exposures have similar exposure and treatment pathways that make them unique compared to many other NTDs. Both diseases are prominent in underserved communities where access to healthcare is limited, if at all available, and both result in severe outcomes if left untreated (Feder et al., 2012; The Lancet, 2019). The logistical constraints surrounding the supply of

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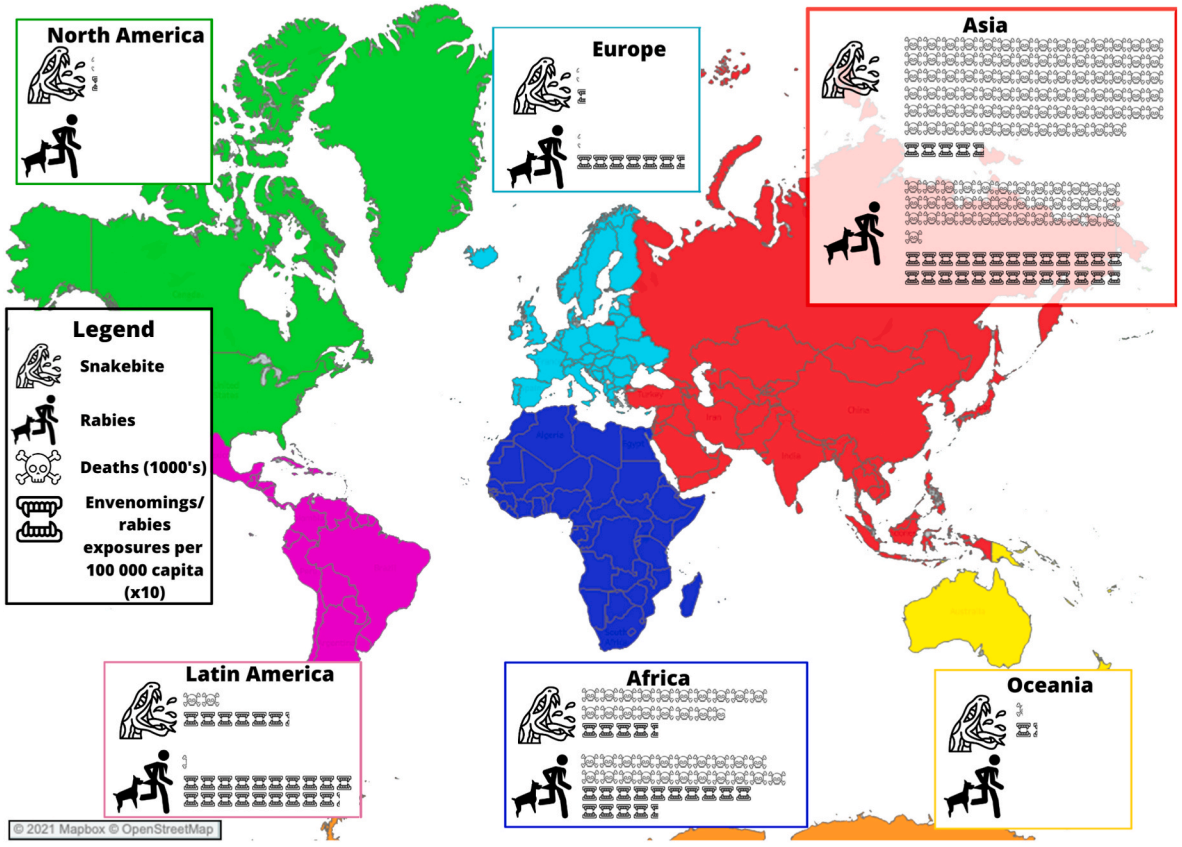


**Fig. 1.** The annual global burden of dog-mediated rabies and snakebite, including the number of human deaths and incidence per 100,000 capita. Burden data taken from (Hampson et al., 2015b; Kasturiratne et al., 2008) with the snakebite burden data from India updated from (Suraweera et al., 2020). Dog bites per capita relate only to rabies risk, thus in dog-rabies free countries, the dog bite incidence is recorded as zero (e.g., North America).

on-demand biologicals is a major limiting factor to both diseases, requiring either complex decentralized stockage, or consistent supply at centralized health facilities. Here we examine potential mutually beneficial opportunities for the prevention and treatment of snakebite envenomation and rabies virus exposures. We provide insight and considerations as to the practicality and feasibility of a joint approach, and our potential concerns of the ramifications of such partnerships using various seemingly opportunistic areas for collaboration.

## 2. Burden

Deaths from snakebites and rabies mainly occur among populations with poor or inaccessible healthcare, and without readily available antivenom, rabies vaccines and rabies immunoglobulins. While both diseases have economically insignificant vectors in terms of production, they inflict a high economic burden due to the loss of livestock (Bolon et al., 2021; Hampson et al., 2015b). Their true global burden remains largely unknown, owing to inadequate surveillance data on snakebites and rabid dog bites, and their outcomes (Longbottom et al., 2018; Taylor et al., 2017). Snakebite envenoming is estimated to result in between 67, 000 and 137,000 (mean 102,000) deaths annually, in addition to approximately 400,000 survivors who suffer severe morbidity after exposure (Chippaux, 1998; Gutiérrez et al., 2017; Kasturiratne et al., 2008; Suraweera et al., 2020). Rabies is estimated to result in 25, 000–159,000 deaths annually (predicted 59,000) (Hampson et al., 2015b; Knobel et al., 2005), with no significant burden relating to morbidity due to its exceptionally high case fatality ratio - apart from the psychological morbidity from those able to receive treatment after an exposure. Although these estimates are primarily based on modelling and from studies that are more than 5 years old, they point to a significant burden that is greatest in Africa and Asia (Fig. 1). A good understanding of the burden of each at high resolution (sub-nationally) is critical for decision-making and advocacy. To understand this, we require reliable data on the exposures (bites), their risk (species of biting snakes, status of biting animal), access to therapies (antivenom, rabies immunoglobulins and vaccines), and outcomes of these bites (morbidity - including psychological morbidity - and mortality) (Williams et al., 2011). Although the data required for each are different, there are key similarities in the health system needs required to address these problems.

## 3. Surveillance

Bite case reporting and investigation are critical and foundational aspects of surveillance for both rabies exposures and snakebite envenoming. For this reason, it is important that both snakebite envenomation and human and animal rabies are notifiable diseases under national legislation. However, snakebites and dog bites occur in the community and are often captured by surveillance systems only if the bite patients visit health facilities. While there are some exceptions to this – as is the case with comprehensive community surveys or active surveillance – these remain the exception. Where there is poor healthcare seeking behavior and inaccessible healthcare, these community cases will likely remain unreported. The key community level information required includes: the occurrence, location, and details surrounding the incident, a risk assessment, and the determination of appropriate treatment. For snakebite, the critical detail is the identification of the species of the snake that determines whether the snake is venomous and which antivenom and/or supportive therapy is required. This risk assessment should be immediate where possible, and the information should be provided to healthcare providers upon presentation for care or should be assessed by healthcare providers upon presentation

of supporting evidence. For rabies, a risk assessment is required based on the category of exposure, the presence/absence of the disease in the area and thorough bite investigations to attempt to locate and monitor/diagnose the biting animal – all of which inform decisions on use and administration of rabies vaccines and/or rabies immunoglobulins (WHO, 2018). Although the type of information required for each disease is different, there are obvious areas of synergy, including who and what tools are used to collect and disseminate this information at the community level.

Effective, active surveillance systems often require costly infrastructure and the presence within communities of a trained workforce that is actively seeking cases. The infrastructure for data collection and reporting itself - such as mobile phones, toll-free numbers, digital surveillance systems (servers, Information Technology support and maintenance, analysis, the potential use of Artificial Intelligence, and others) – lends itself to shared capacity and thus shared costs in most situations, especially considering that these are recommended to be notifiable diseases and should thus form part of the larger public health system in each country (OIE, 2019; World Health Organization, 2019a). However, while infrastructure and resources can be shared, there should be careful consideration for the structure of any joint surveillance systems, as it is critical that any mutual surveillance systems for these two conditions be able to accurately distinguish data elements. This is crucial as surveillance data are often used for program monitoring and evaluation by local, national, and international organizations, thus having potential ramifications on burden, support, and interventions for both diseases.

## 4. Event reporting and community response

A key component of health strategies in many countries endemic for NTDs is the community health strategy that uses community-based workers or volunteers to help monitor multiple health indicators. These workers play a critical role and can contribute positively to the impact of health intervention programs, as has been evidenced in Nepal (Panday et al., 2017). Field-based investigation of snake envenoming and rabies virus exposures benefit both the community and the bite victim, as rapid identification of venomous snake species and rabies suspect dogs in a home or community reduces the risk of further human and domestic animal exposures. Furthermore, identification of the snake species and a rabies risk assessment of the offending animal play an important role in determining if expensive and oft-limited vaccines and biologics are required (World Health Organization, 2018, 2019a). In both instances, the One Health approach remains critical, with open and rapid communication and data flow among the various sectors involved, including – but not limited to – human and animal health and environmental management. These field-level investigations require community-level animal health experts with unique skills in animal species identification, capture, and sample collection. In many upper-income countries, these field-level operations are carried out by Animal Control Professionals/community health workers (CHWs), who are highly skilled and usually employed by local or national government. In many developing countries, CHWs exist, but are often employed by specific projects, typically using international financial aid, or alternatively, through volunteer programs (Olaniran et al., 2017). The added challenge of programs supported through international aid or volunteer programs is that these programs remain transient, with the longevity of success being entirely reliant on the longevity of funding and support if local capacity is not developed during the program. CHWs are often responsible for all community public health interventions, ranging from maternal health to infectious disease control. Understanding that CHWs are responsible for numerous routine health monitoring and reporting activities, it may be unrealistic to expect them to take on additional responsibility for zoonotic disease control and animal health activities (Philips et al., 2008). As highlighted previously, urgency in assessing the animal threat and ensuring appropriate care for those exposed is of utmost importance for preventing deaths due to these two conditions. As such, we propose a parallel model to the CHW to address animal health and zoonotic disease events. This new class of zoonotic and animal health community workers could be trained to report and surveil both rabies and snakebite, among other zoonotic and neglected tropical diseases. Such a model could truly reflect the spirit of One Health, embracing the specialty of animal and human health, and environmental professionals while establishing an environment in which these professionals can serve community needs.

## 5. Information and education

Routine childhood immunizations benefit from standardized intervals of vaccine administration that enable providers and parents to prepare medical visits well in advance. In addition, the consistency, regularity, and clarity of standardized messaging in plain language, coupled with adequately equipped health professionals, results in routine childhood immunizations achieving a near 90% coverage in at-risk populations globally. On the contrary, the vast majority of the global population will never experience a rabies virus exposure or snakebite envenomation. Therefore, for the population that is unfortunate enough to experience one of these events, both the victim and the health professional may be less familiar with the appropriate post-exposure health actions. It is for this reason that education and awareness for both diseases remain critical components to their successful control and/or elimination.

Both snakebite and rabies education and awareness initiatives have a strong focus on animal bite prevention and wound care if bitten. Whilst the behavior of animals may differ, the behavior of people when interacting with any wild or unknown animal should remain consistent, and the basic information surrounding the procedure following a bite (whether from a snake or a dog) is the same. Considering this, joint education initiatives – especially in more remote, poor, or underserved communities – could be beneficial in reducing costs associated with transport, personnel and training, and other administrative and logistical costs such as venue rental. As the messages are similar – standing still and “be like a tree” to avoid animal bites and seeking timely and adequate treatment (including potential hospitalization) after an exposure – interventions for both diseases could benefit from a joint basic bite prevention education program. In particular, the challenges faced by victims seeking treatment with traditional remedies need to be addressed with inclusive education programs that target traditional healers and the community in a considered, yet practical manner (Schioldann et al., 2018; Yalemebrat et al., 2016). By jointly emphasizing and addressing the urgent needs for adequate medical treatment for both snakebite and rabies exposure to traditional healers in a mutually respectful and beneficial manner, and by ensuring their participation in raising awareness and ensuring appropriate health-seeking behavior, a stronger case can be made to ensure that victims receive the required treatment in a timely manner.

Beyond the basic education messaging, the diseases begin to rapidly distinguish themselves, including the differing requirements for wound management recommendations (wound washing, treatment with Iodine/antiseptic solution, and tetanus treatment is recommended for rabies, while for venomous snakebites no wound washing is recommended), post-exposure prophylaxis and antivenom, as well as the duration of treatment. For these reasons, we suggest that joint education initiatives focusing on bite prevention and general health-seeking behavior are feasible and can be targeted, in particular, towards young school-going children within their school curriculum, whilst extensive awareness, advocacy and inclusion programs for traditional healers should also be pursued. Easily accessible and understandable media should be used for children, such as comics, cartoon series and booklets that focus on a child’s daily interactions where they may encounter these afflictions. Beyond this, more specific and detailed messaging is required – especially for health workers – as the differences between the two diseases could make joint messaging challenging and

potentially confusing.

## 6. Procurement, distribution, and storage of biological treatments

Each year infectious disease vaccination programs prevent over two million deaths; the vast majority of these vaccinees are children (World Health Organization, 2019b). Such massive distribution of vaccines has largely been achieved through routine immunization practices that rely on synchronized schedules to enable pre-planned administration, often based on the person's age. Many vaccines are distributed and administered through childhood immunization programs to prevent diseases such as diphtheria, tetanus, and pertussis, among others. By having global standards for childhood immunization, these vaccines benefit from shared systems for distribution, cold chain, consumables, and locations for distribution. A highly beneficial common thread for many vaccines is that they can be pre-planned and utilize shared basic infrastructural resources and communication strategies.

In contrast, a relatively small number of biologicals are administered as post-exposure prophylaxis, as in the case of rabies vaccine, and as specific treatment of envenoming in the case of snake antivenom. The demand for biologicals that are administered after an exposure is inherently more difficult to predict and appropriate distribution plans that would ensure timely access for all exposed individuals are not necessarily straightforward to design. Due to the unpredictable need for these types of biologicals, they often do not benefit from the shared infrastructure of routinely administered vaccines. Each year an estimated 20 million people are treated for an animal bite requiring either rabies vaccine or snake antivenom, and an additional 200,000 people die due to a lack of access to the necessary life-saving biologicals (WHO, 2020). Despite not benefitting from the EPI (Expanded Program on Immunization) and its infrastructure in most countries, there is potential for shared capacity and overall health system strengthening through joint efforts among NTDs that require post-exposure treatment. International health agencies should develop standardized pathways for the centralized delivery and implementation of NTD vaccines and biologicals to utilize immunization program infrastructure and support exploratory case studies examining successful examples where EPI and NTD programs operate jointly. While at the international level, procurement and delivery of rabies vaccines, RIG and antivenom have been improved through joint initiatives such as the OIE vaccine bank, as well as the PAHO Revolving Fund and the Strategic Fund in the Latin America region (Pan American Health Organization, 2021a, 2021b), there remains a lack of in-country capacity and infrastructure to deliver these biologicals to the victim.

While many specificities among diseases may be incompatible, the basic health infrastructure requirements for the delivery of biologicals after exposure remain consistent. For example, the maintenance of cold chain, logistical supply based on ever-changing demand, personnel capacity and training, and feasible and realistic access to treatment facilities in terms of both government capacity and patient accessibility. Two primary models exist in terms of post-exposure treatment for diseases such as rabies and snakebite envenomation: 1) a decentralized model where the victim has access to the appropriate biologicals and treatment within their locality, or 2) a centralized treatment facility with a suitable patient transport system in place. Both models have been explored and the latter is most often employed by countries, simply due to the challenges of supply and demand, as well as the general shortage of availability of biologicals in most of the affected countries (for both diseases). While a centralized system addresses the challenges of supply and demand, the patient transport system (such as a reliable ambulance service that services remote and underserved communities) is the aspect of this approach that remains lacking. A shared patient transport system - such as the volunteer motorcycle transport system piloted in Nepal to transport snakebite victims to the relevant health facility (Sharma et al., 2013) - is something that could be explored as a joint capacity building exercise that not only addresses the need of both diseases, but also contributes to overall health system strengthening.

Similarly, the decentralized model has also been explored and could potentially benefit from innovative thinking to overcome challenges associated with the varying and sporadic supply and demand requirements (Briggs and Moore, 2020). For example, a program testing the delivery of biologicals to remote underserved communities was undertaken using drones to deliver blood to clinics based on a mobile phone reporting and response system (Glauser, 2018; Ling and Draghic, 2019). While such innovative systems may not be feasible to individual disease intervention programs due to the high costs and specialized technical requirements, joint programs that address the needs for multiple diseases and public health services could generate sufficient demand to make its implementation both feasible and practical. An additional caveat to this system would be the need for trained health professionals capable of safely administering the biologicals to the victim under appropriate medical supervision in each of the decentralized facilities, further reinforcing the need for improved capacity-building in remote or underserved communities.

Lastly, because of the challenges faced with predicting supply and demand, and the relatively low demand for post-exposure treatments (hyperimmune antivenoms and rabies immunoglobulins) compared with other large-scale productions and preventative treatments (such as antiretroviral therapies), there remains a global shortage for the production of both snake hyperimmune antivenoms and rabies immunoglobulins. To address this, the combined production of both these treatments could be undertaken, as was explored several years prior (WHO, 2007). However, an initiative such as this would require substantial time, investment, and advocacy to undertake and would not pose the short- or medium-term solution needed to address the current shortages experienced in light of the 2030 goals for both diseases. On the contrary, a joint procurement model of WHO-assessed or approved biologicals could be investigated. This joint procurement system could follow a similar structuring to the OIE vaccine banks (OIE, 2021), resulting in optimal pricing, reduced logistical costs and constraints, and the surety of accessing high-quality biologicals. By combining biologicals for snakebite and rabies control, the logistical costs and constraints, as well as procurement challenges, can be addressed at the national level.

## 7. Control measures

One key area where these two NTDs differ is in their control. Some species of snakes are inherently and uncontrollably venomous. The elimination of venomous species has been attempted in several countries (e.g., 19th century India, 20–21st century Japan) but has never succeeded and, for ecological reasons, should not be attempted. Therefore, snakes (including venomous ones) are important contributors to ecosystems and should not be de-venomed or eradicated. In contrast, rabies virus has a parasitic and fatal relationship with all the host species (mammals) that it infects. Given that rabies virus ecology offers no benefits to any species, a strong argument for its elimination can be made. Understandably, there are considerable efforts underway to implement rabies virus control programs on a population level in various affected species, with a particular focus on dogs due to the significant public health impact of dog-mediated rabies. These efforts rely primarily on vaccination of susceptible species over a certain period (typically 5–10 years) until the virus is eliminated from the population. Conversely, the main preventive strategies for snakebite envenoming are education and avoidance. So long as the snakes are endemic species in the ecosystem, this operation needs to continue in perpetuity. Herein lies a major challenge for program synergies: dog-mediated rabies control has a targeted intervention to eliminate the virus that should last a fixed number of years if applied successfully, whereas snake envenoming has no such goal of eliminating the toxin, and lifesaving preventive programs will always be necessary. While other rabies virus

## Box 1

In light of the recent NTD roadmap, we provide insight and considerations as to the practicality and feasibility of a joint approach between snakebite and dog rabies control programs:

- The need for improved coordination among NTDs is evident to address resource, support, and awareness constraints.
- Joint snakebite and dog bite prevention education programs are practical and feasible.
- We propose a novel, One Health-focused class of zoonotic disease and animal health specialist community health workers to address community disease events.
- Shared infrastructure, including production and delivery of biologicals, can address challenges associated with delivery to under-served communities.
- Simplistic approaches to fully integrate NTD programs are unlikely to succeed, due to the nuances required to successfully address the needs of each disease.
- Overall capacity building and health system strengthening is key to any joint NTD initiative and should be prioritized.

variants exist in sylvatic populations, and with current knowledge these variants are not likely to be eliminated (e.g., rabies in bats), these variants pose a lesser public health impact in comparison to the current impact and burden of dog-mediated rabies. Thus, in terms of global advocacy, awareness, and public health impact, the focus for rabies elimination remains on dog-mediated rabies. These differences in the investment needs over time may present challenges in advocating for sustained support from governments for a combined program. While snakebite will require perpetual investment, a clear goal for dog-mediated rabies elimination can (and has) been set, and governments should work towards that goal (Abela-Ridder et al., 2016). Given a scenario for potential re-introduction of rabies into a rabies-free population/geographical area, the maintenance phase of rabies mass vaccination programs in target species (primarily dogs, but also in terrestrial wildlife vectors) is important but challenging in terms of advocacy and sustained funding. Nevertheless, it remains plausible as there is a clear financial and health benefit after the disease has been eliminated. Thus, for stakeholders, joint programs may be less appealing and potentially confusing if the measures of success for each program are not clearly outlined.

## 8. Costs

The concept of cost-sharing and synergistic programs for NTDs is not novel. Some opportunities presented here would very likely present a cost-effective synergistic approach to preventing human deaths due to these two conditions. However, neither of these systems have yet shown a large-scale synergistic approach that was cost-effective and sustainable in a lower income setting. This may be due to their unique methods of prevention and control, or it may be that appropriate synergies have not yet been identified. Either way, these are two programs that lack adequate funding for control, and any attempt to combine funds, infrastructure, or human capital needs to be approached in a sensitive manner that ensures mutual benefit to both conditions.

## 9. Conclusion

With fewer than 9 years before the global targets set for the SDGs, the "Zero by 30" target for dog-mediated human rabies elimination, and the target to halve the numbers of deaths and cases of disability due to snakebite envenoming, there is a clear need for increased vigor and impetus towards achieving these goals. In an attempt to address the funding challenges associated with all NTDs, there has been renewed encouragement throughout the NTD community to explore means of inter-disease collaboration (Malecela and Ducker, 2021; WHO, 2020). While we wholeheartedly recognize and support the need for both intra- and inter-disease collaboration, we urge that such partnerships be carefully considered with respect to benefits and potential unexpected ramifications of such joint initiatives. In the case of rabies and snakebite for example, we have described potential synergies inclusive of joint bite prevention education initiatives. However, we have also pointed out nuances that require disease-specific interventions to effectively and efficiently control and/or eliminate snakebite and rabies, respectively.

The NTD roadmap calls for "a move away from siloed, disease-specific programs to cross-cutting perspectives centered on the needs of patients and communities", suggesting that where possible, different NTD programs should work collaboratively (WHO, 2020). We have explored the potential for improved collaboration and the integration of several aspects critical to the success of both rabies and snakebite intervention programs, including education, surveillance, the production and procurement of biologicals, and treatment. While some potential means of resource-sharing exist - such as joint basic bite prevention education programs - the majority of the needs for each disease remain unique and nuanced, suggesting that simplistic approaches to fully integrate NTD programs are unlikely to succeed. However, it remains clear that there is a need for a joint approach to health system strengthening and capacity-building within the NTD sector. By working collaboratively on these overarching needs, overall public health can be improved through the control and elimination of NTDs, especially in the poor and underserved communities that are both most affected by NTDs and have the most need for health system strengthening that contributes towards Universal Health Coverage (UHC). Considering that NTDs such as rabies and snakebite predominantly affect the poorest and most under-served communities, the greatest contributions (and thus justifications for such interventions) rely on improving UHC in these affected areas. It remains clear that health system strengthening is key to the successful implementation of any NTD intervention and by synergizing efforts, each NTD – whether rabies and snakebite, or any other – should investigate means in common localities where health system strengthening can be supported in a collaborative manner. For example, by improving overall access to biologicals through a joint procurement and a strengthened delivery mechanism from a centralized facility to remote and under-served areas, challenges associated with the inaccessibility of treatment for any NTD in that locality can be addressed. Typically, health system strengthening is costly and thus may be too much for any individual program to bear, but through joint efforts, it may be feasible to address these overarching and common challenges in specific target locations. While acting alone, the decentralized delivery of rabies vaccine, for example, to a remote clinic via drone would likely be infeasible due to the relatively low demand for this service daily in most areas. But by coalescing the needs of multiple NTDs into a single system, the benefits of economy of scale become more apparent as the demand for biologicals to be delivered to the desired location would increase based on the demand of multiple

NTDs (and other health requirements) in those areas.

By addressing NTDs in a sustainable manner through shared health system strengthening, the NTD community would not only address SGD 3.3.5 aspiring to reduce the number of people requiring interventions against NTDs but would also significantly contribute towards the achievement of SDG 3.8 that aims to achieve UHC, ensuring that no one is left behind.

## Author contributions

T.P.S, S.S., R.M.W. and S.M.T – Conceptualization, Writing original draft. All authors – Writing, review, and editing.

## Ethical statement

Ethical approval was not required.

## Credit author statement

**Scott, Terence P:** Conceptualization, Writing - Original draft preparation **Sharma, Sanjib K:** Conceptualization, Writing - Original draft preparation **Wallace, Ryan M:** Conceptualization, Writing - Original draft preparation **Nel, Louis H:** Writing- Reviewing and Editing **Adhikari, Samir K:** Writing- Reviewing and Editing **Abela-Ridder, Bernadette:** Writing- Reviewing and Editing **Thumbi, S.M:** Conceptualization, Writing - Original draft preparation.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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