Acta Tropica 215 (2021) 105808

Contents lists available at ScienceDirect

Acta Tropica

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

Increasing rabies data availability: The example of a One Health research project in Chad, Côte d'Ivoire and Mali

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ARTICLE INFO

Keywords:
One Health
Rabies
Translational research
South-South-North partnership
Africa

ABSTRACT

Rabies is a fatal but preventable disease that remains notoriously underreported. Weak data availability hampers advocacy, constitutes a barrier to resource allocation and inhibits effective prevention and control. To gain better insight into the global rabies burden and human vaccine demand several studies were funded through the Vaccine Alliance (GAVI) learning agenda. With the help of this funding, Swiss TPH and local in country partner organizations implemented a One Health research project in Chad, Côte d'Ivoire and Mali to collect data at household, public health facility and veterinary level. This paper describes the implementation of this research project and evaluates its success on amount of information gained, achieved capacity building, impact on knowledge creation and influence on national and international policies. The project was based on the One Health concept and guided by the principles of transboundary research partnerships formulated by the Swiss Academy of Sciences. Data was collected on bite incidents and health seeking from over 24'000 households, on access to treatment of over 8'800 bite cases registered in public health facilities and on the status of over 1'800 rabies suspect animals. Selected country specific datasets have contributed to more than 10 scientific articles so far. On the international level, the multi-level data collection provided a unique set of indicators to inform, along with results from other studies, new WHO rabies immunization recommendations and a vaccine investment case scenario to prevent human rabies. New rabies burden estimates based on the data gathered are published for Mali and will be modelled for the whole West and Central African region. On the national level, the project facilitated communication between animal health and human health workers catalyzing creation of local and national committees and formulation of national action plans for Mali and Côte D'Ivoire. Major challenges arose from lack of data collection and documentation experience of human health and veterinary workers and weak infrastructural capacities of the veterinary and human health systems of the project countries. Through adherence to the principles of transboundary research partnerships, project team members acquired valuable research and networking skills despite language barriers, enabling them to play key roles in the future agenda towards national, regional and global canine rabies elimination. Project external collaborations with local public institutions was facilitated through long-term local partnerships. Both factors enabled success in project implementation and outcomes by identifying and mitigating risks in advance, resolving challenges amiably and enabling mutual knowledge creation as a fructuous ground for sustained commitment. Lack of immediate follow-up funding did not allow to maintain activities beyond the project timeframe. However, the national and international policy

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https://doi.org/10.1016/j.actatropica.2020.105808
Received 23 May 2019; Received in revised form 21 November 2020; Accepted 23 December 2020
Available online 29 December 2020

changes triggered, as well as the strengthened local disease control and research capacities provides sustainable basis for the elimination of dog transmitted human rabies.

1. Introduction

1.1. General project background

In December 2015, the World Health Organization (WHO) and partners agreed to work jointly towards elimination of dog transmitted human rabies by 2030 (Minghui et al., 2018). The main beneficiaries of elimination are underprivileged populations in Africa and Asia, the two continents carrying the highest rabies burden worldwide. Currently, effective rabies prevention and control is hampered by the notorious lack of reliable human and animal surveillance data (Nel, 2013; Taylor et al., 2017; WHO, 2017). Previous rabies burden estimates based on decision tree modeling revealed big discrepancies compared with globally reported mortality data (Hampson et al., 2015; WHO, 2016). The reasons for insufficient and incoherent mortality data are manifold: A majority of rabies victims die at home and thus are not officially registered (Diop et al., 2007; Taylor et al., 2017); rabies deaths might be misdiagnosed as cerebral malaria or another type of encephalitis (Mallewa et al., 2007); laboratory diagnosis is not readily accessible, sample transport is difficult and sample collection is invasive and often not accepted by relatives for cultural reasons (Dacheux et al., 2010). More data exists on bite exposure on a local scale in health facilities and bite treatment centers, but reporting to the national and international level is nonexistent or infrequent and underreporting due to limited access to health facilities or a preference for traditional methods in rural areas is frequent (Tschopp et al., 2016; Mbilo et al., 2017). Another challenge is the loss to follow-up when patients do not return for all required doses of vaccine (Zamina et al., 2019).

Dog-related data are even less available than human related data, because dog owners rarely utilize veterinary services, animals vanish or have unclear ownership and veterinary facilities lack appropriate shelters for observation purposes (Lechenne et al., 2017). The possibility of etiological diagnosis in animal rabies cases is limited to urban centers with a central laboratory facility (Banyard et al., 2013). National veterinary surveillance networks, accessible laboratories and a sample transport system are required to gather reliable epidemiological data. Even in settings where dog and human surveillance are independently efficient, the two data streams are not integrated making it impossible to reliably determine rabies burden. The total cost of rabies to the public sector results from Years of Life Lost (YLL) due to premature deaths and investment into PEP on the human health side, and also cost of animal vaccination and economic losses in the livestock sector following transmission to farm animals.

Recently, awareness of dog rabies in Africa and Asia increased, coordinated by the Partners for Rabies Prevention, initiated by the Global Alliance of Rabies Control (GARC) (Nel et al., 2017) and facilitated through newly established or revitalized regional networks such as the Pan African Rabies Control Network (PARACON) which merged the African Rabies Network Bureau (AfroREB) and the Southern and Eastern African Rabies Group (SEARG). However, the data situation regarding rabies remains deplorable across Africa. Obstacles to more epidemiological insight are found on all levels of surveillance, and the resulting lack of information hinders effective intervention and drives neglect (Nel, 2013). To address this situation PARACON launched the regional African rabies bulletin, an online open access platform, intended to facilitate data reporting, sharing and analysis (Scott et al, 2017). Estimating the extent of the public health burden caused by rabies is a primary objective of the roadmap to interrupt disease transmission from dogs to humans (WHO, 2016). With support from the GAVI learning agenda and WHO several research activities were undertaken to study the rabies burden in Africa and Asia. A model consortium collated the data of the various projects and assessed the extent of human vaccine demand, in view of potential GAVI investment for PEP provision. Swiss TPH, in coordination with local partner institutions, conducted a core project of the GAVI learning agenda in three West and Central African countries. This article presents the methodology of this large-scale study based on the One Health concept (Zinsstag et al., 2015), gives an overview of the implementation outcomes and evaluates its success. The scientific goal of the project was to collect empirical field data on animal bite frequency, the proportion of rabies suspected bites and the proportion of rabies confirmed bites, current coverage of PEP and future health impact of PEP in selected urban and rural study areas of Mali, Chad and Côte d'Ivoire. The collected data contributed to an evidence base for modeling the potential effect of future investment in human rabies vaccine (Hampson et al, 2019a) and new recommendations on PEP (Hampson et al. 2019b). Country specific results of the studies conducted during the project are published in companion papers included in the special issue "Towards rabies elimination in West and Central Africa" published by Acta Tropica. The implementation was guided by the One Health concept and the guide to transboundary research partnership formulated by the Swiss Academy of Science (2012).

The One Health concept is based on the idea that closer cooperation between veterinary and human health services can create added value for both sectors (Zinsstag et al. 2015). Rabies is one of the best examples to illustrate the positive effects of closer collaboration between the human health and veterinary sectors for disease control (Lechenne et al., 2015). Domestic dogs are the important reservoir of classical rabies and play the key role for transmission to humans. Therefore, elimination of rabies in dogs is the only way to achieve a substantial and sustainable reduction of human rabies. Economic studies show that dog rabies control through mass-vaccination and population management is affordable and cost-effective when compared with human post-exposure prophylaxis (PEP) (Fitzpatrick et al., 2014; Mindekem et al., 2017; Hampson et al., 2019b). Despite the success story of South America and the Carribean, where sustained vaccination programs have eliminated dog rabies (Vigilato et al., 2013), financial allocations in Asia and Africa are highest for prevention measures in humans (Shwiff et al., 2013; Léchenne et al., 2015). The high investment into individual human vaccination stands in contrast to the unachieved success in eliminating human rabies on a greater public scale. This illustrates that current access to PEP reaches only a fraction of the true number of exposed victims and does not address the major source of the disease. Better communication between the human health and veterinary sectors through the applied One Health approach of integrated bite case management (IBCM) can improve bite exposure risk assessment leading to more accurate use of PEP and increased animal case detection (Undurraga et al, 2017) leading in turn to a better data situation urgently needed for rabies control advocacy.

The guide to transboundary research partnership was developed by the Swiss Commission for Research Partnerships with Developing Countries (KFPE). The 11 principles formulated by the guide intend to enhance fair and equal research partnerships, based on mutual trust, mutual learning, shared responsibility and shared ownership (Swiss Academy of Science, 2012).

1.2. Specific country context

1.2.1. Chad

Swiss TPH research partnerships with institutions in Chad have been in place for more than 20 years, with first studies on rabies initiated in 2000 at the request of Chadian colleagues. In the following 15 years,

consecutive projects provided detailed insight into many aspects of rabies epidemiology and control, including economic aspects, transmission parameters, surveillance, public sensitization and vaccination effectiveness (Kayali et al., 2003; Durr et al., 2009; Zinsstag et al., 2009; Lechenne et al., 2016a; Laager et al., 2018). N'Djamena, the capital city of Chad, has gradually become an example for elimination of dog rabies in urban Africa and the expected challenges. After positive experiences in N'Djamena, studies at the national level were undertaken to estimate the Chadian dog population and calculate the budget for nationwide dog vaccination (Anyiam et al., 2017; Mbilo et al., 2017). Animal and human rabies surveillance remained limited to the capital city due to lack of provincial diagnostic facilities and absence of a transport network to send samples to the rabies laboratory in N'Djamena.

Chadian public services suffer from generally low resource allocation, worsened by recent financial crises due to low oil prices and a national budget with high expenses for security and defense because of unstable neighbor countries. Health services often depend on external funding sources, which are frequently allocated to vertical programs focused on single diseases rather than a horizontal general health systems strengthening approach. Veterinary services are particularly neglected, seldom comprising more than occasional ruminant vaccination programs and supervision of livestock markets and abattoirs for food safety. Rabies is not a notifiable disease in Chad and, therefore, data is not routinely collected or reported from veterinary and human health services.

1.2.2. Côte d'Ivoire

In Côte d'Ivoire, rabies control is managed by two ministries, the Ministry of Public Health and the Ministry of Agriculture in charge of animal health. Each ministry has a center overseeing rabies control: the veterinary anti-rabies center of the Directorate of Veterinary Services (DSV) and the human anti-rabies center of the National Institute of Public Hygiene (INHP). The veterinary anti-rabies center has two main tasks, surveillance of biting animals by a legal provision and analysis of information related to animal rabies cases. To achieve these tasks nationally there are 19 regional directorates. The human anti-rabies center functions as a reference center for care of exposed people, and communicates and educates communities on avoiding and responding to exposures and oversees epidemiological surveillance of human rabies nationally. It connects to 27 sub-centers of the INHP to cover the whole country. Recently these centers underwent a capacity reinforcement program to increase the rate and quality of reporting (Tiembré et al., 2018). Two laboratories support these centres, the Central Pathology Laboratory at Bingerville and the Institut Pasteur of Côte d'Ivoire. All bite cases inflicted by a potential rabies vector species are considered suspicious in Côte d'Ivoire, and therefore every victim is recommended for PEP. Rabies control in Côte d'Ivoire is challenged by low reporting rates for rabid animals and low animal vaccination coverage. Communities are not sufficiently sensitized and involved in control activities (Tiembré et al., 2014), and competent authorities lack adequate training. Prior studies focused on human aspects of rabies including exposure risk, help seeking and PEP access and compliance (Tiembré et al., 2010; Tiembré et al., 2011; Zamina et al., 2019). There are no data on dog population size.

1.2.3. Mali

In Bamako, human rabies diagnosis is available at the "Laboratoire Rodolph Mérieux" in Bamako, and the central veterinary laboratory (LCV) is equipped with immunofluorescence diagnostic capacity for animals. Only one rabies treatment center exists, situated in Bamako. Outside of Bamako, rural health centers provide consultations for rabies exposure. The health system is composed of community health centers (CSCom), which are close to the populations, and health reference centers (CSRef), which are sub-regional hospitals and tertiary level hospitals. A CSCom covers a population of at least 5000 inhabitants and is the first contact point for rabies exposure.

Cost and geographical access are the main barriers to PEP treatment. Rabies was identified as a priority disease within the framework of the national Integrated Disease Surveillance and Response strategy in 2008 (SMIR), but more needs be done to improve the quality of epidemiological data. Similar to Chad, Bamako the capital city is the most studied area, with information available for animal vaccination coverage and dog population size and an implemented pilot mass vaccination campaign (Mauti et al., 2017a; Muthiani et al., 2015; Mauti et al., 2017b). In preparation for a national control strategy, a phylogenetic analysis of collected viral strains investigated the spatial occurrence of animal rabies (Traore et al., 2016).

2. Methodology

2.1. Project aims

The overall scientific aim of the project was to gain better insight on the rabies burden in the three study countries and to extrapolate the findings to the whole West and Central African region. The funder specific aim was to contribute to a global vaccine demand and cost calculation to inform the GAVI advisory board on the benefits of including human rabies vaccine in a revised investment agenda from 2021. To meet the scientific and funder specific aims the project had three main objectives:

1) establish incidence of rabies exposure, its risk factors and the rabies mortality burden in Chad, Côte d'Ivoire, and Mali;
2) assess access to current PEP, treatment compliance, current cost and unmet demand;
3) estimate the health impact of PEP with regard to timing, number of doses received and inclusion of equine rabies immunoglobulin (ERIG).

The specific indicators to inform the objectives were grouped in exposure risk factors and access factors by data collection level, as depicted in Table 1. In this paper, we only report on the data collected by study level to quantify the success of the project implementation. The analysis and results derived from the collected data are published in country specific research articles collated in the Acta Tropica, special issue entitled "Towards the elimination of dog rabies in West - and Central Africa". They also contributed to an investment case scenario to provide free PEP to GAVI eligible countries (Hampson et al., 2019a) and to inform WHO recommendations on PEP regiments (Hampson et al, 2019b). A paper on rabies burden estimates for West and Central Africa is in preparation. The project implementation goal was to apply a three level One Health approach, collecting data on household, health facility and animal diagnostics level, while strengthening capacity for rabies control in both the veterinary and human health sectors and increasing public rabies awareness. A main goal of the project team was to trigger mutual learning and capacity building among all collaborating partners. Alongside data collection, the project therefore engaged strongly in capacity building: in the human and veterinary sector, internally among the project team members and through method transfer to local stakeholders and international partners. For conducting multi-national research projects, Swiss TPH and partners are committed to the 11 principles of transboundary research partnership (Swiss Academy of Science, 2012). In consequence, these principles guided project implementation alongside the One Health aspect and scientific output requirements.

2.2. Project management and organization

The project builds on more than twenty years of partnership between Swiss TPH and the core in-country partners (Box1). The partnership with Côte d'Ivoire began in 1994 at Centre Suisse de Recherches Scientifiques (CSRS), which is currently a regional hub with large-scale

Table 1
Risk, access and rabies burden indicators gained from data collection on three study levels.

	Household level	Health facility level	Veterinary level	
	Exposure risk	Representative animal bite frequency in urban and rural zones	Health impact of PEP with regard to timing, number of doses, injection method and inclusion of RIG	Animal rabies incidence in rural and urban zones
Proportion of rabies suspect bites among observed animal bites				
Severity and location of animal bites in humans		Proportion of etiologically confirmed rabid animals among the suspected biting animals		
Access	Proportion of people seeking help in a health facility	Availability of PEP and RIG in a rural and urban setting	Proportion of bite cases referred to a veterinary facility	
		Proportion of bite victims of a rabies suspicious animal receiving adequate PEP	Proportion of suspicious animals with certified diagnosis (including negative observation result)	
	PEP compliance and source of funding			
Rabies burden	Proportion of unmet PEP demand Incidence of human rabies deaths Years of life lost (YLL)			

African capacity building activities sustained even through civil unrest (Bonfoh et al., 2011). The project activities in Côte d'Ivoire were led by CSRS and implemented by an interdisciplinary committee with representatives from the Program for Improvement of Animal Health (HPV DSV/PASA), the ministry of animal resources and fishery, the INHP, the laboratory for the support of agricultural development and the University Alassane Ouattara (Sociology lab).

Collaboration between Swiss TPH and the two main partner institutions in Chad, the "Institut de Recherche en Élevage pour le Développement" (IRED) and the "Centre de Support de Santé Internationale" (CSSI) started in 1998. The CSSI is a local Chadian Non-governmental Organization (NGO) focussing on many aspects of human health, whereas the IRED is a veterinary research institution under the umbrella of the ministry of livestock with close links to the national Directorate of Veterinary Services (DSV). During the past 20 years, this tripartite partnership led to the most comprehensive human and animal research in rabies in Sub-Saharan Africa. The director of CSSI is a physician who took medical responsibility for the project studies in Chad and liaised with the Ministry of Health. The head of the animal health division at IRED assured the quality of studies on the veterinary side.

The partnership with the "Laboratoire Centrale Vétérinaire" (LCV) in Mali was established in 2000 and extended in 2009 to the Faculty of Medicine and Odontostomatology of the University of Sciences, Technics and Technologies of Bamako. A medical professor supervised the studies on the human health side and the head of the rabies laboratory at LCV oversaw animal observation and rabies diagnosis.

The project management was structured into two organisational committees, one supervisory and one technical. In each country, technical coordination was ensured by a responsible for the animal health sector and the human health sector, respectively. They were supervised by national project investigators (PI). In Chad the PI role was shared between CSSI and IRED. Regular project coordination meetings among local team members were held in country. The overarching technical committee met regularly either on the occasion of project workshops or online meetings. The technical group was responsible for quarterly reporting to the supervisory committee and to GAVI.

The supervisory committee did not follow a regular meeting calendar, but convened as necessary. Swiss TPH secured overall coordination, high quality data management and analysis through the project statistician. Technology and knowledge transfer to and between Southern partners was a core component of the organizational and administrative process. An external advisory panel (EAP) advised and evaluated study progress. The planning phase of the project began in December 2015 with preparation of sub-contracts and ethical approvals. Official launch of project activities took place in January 2016 and the project period ended in August 2018.

2.3. Study sites

The study sites of the respective countries were chosen according to geographical and cultural context and based on their demographic weight. In Chad, the sites included the region of Logone Occidentale in the south of the country, Ouaddaï in the northeast and a 100 km radius around the capital N'Djamena. Southern Chad consists mainly of Christian dominated communities that raise more dogs than the Muslim communities, predominantly living in central and northern regions of the country. In Côte d'Ivoire, the study sites were Bouaké in the center of the country and San Pedro region bordering the Atlantic Ocean to the South. The chosen study cites in Mali were Bamako region including the capital city and Sikasso region, which is the main agricultural region in Mali, and is located in the south, bordering Côte d'Ivoire, Burkina Faso and Guinea. Sikasso is similar in size to the capital city, Bamako. Some communities in the Sikasso region (Senoufo, Minianka and Bobo) raise dogs for consumption.

2.4. One Health methodological approach

The three data collection levels are inextricably linked for estimating the incidence of ascertained rabid animal bites, the total number of bite exposures in need of PEP, and the risk of developing clinical rabies through inadequate access to PEP, such as low availability, accessibility, affordability, adequacy and acceptability (Obrist et al., 2007). Comparing the risk factor indicators with access factor indicators allows calculation of rabies burden through unmet vaccine demand leading to human deaths and cost in terms of years of life lost (YLL). Indicators for the risk of developing rabies after exposure were defined by the inputs for the decision tree model (Hampson et al., 2015), related to severity and location of the wound, as well as timely access and compliance with adequate PEP.

To boost overall reporting, a public sensitization strategy was designed and implemented in each country, which included conception and distribution of information material, celebration of World Rabies Day (WRD) and media coverage of project activities. By maximizing communication between the public health providers and animal health authorities, we attempted to relate the number of suspected dogs as closely as possible to the number of etiologically confirmed rabid animals. Matching health facility and veterinary data also helped anticipate the level of underreporting.

Data collection for each level, including the level specific period of study activities, is briefly described below.

2.4.1. Household level

The targeted number of households in each country was 8000. The data collection on household level was done through cross-sectional animal bite recall surveys in selected households. The baseline questionnaire included demographic, socio-economic and knowledge related information. Further collection of information on dog ownership and vaccination status allowed estimates of the dog population size and dog immunization coverage in the different study areas. In case of a recalled bite that occurred in the previous 12 months, information on the victim, circumstances, animal status, wound, health seeking and treatment were collected. The first field data collection was done between June and September 2016. At the same time, information leaflets were distributed. Phone contacts were registered where available, which allowed follow-up surveys after 6 and 12 months to register new bite cases and record outcomes of previously registered cases.

2.4.2. Health facility level

Before the project started, registration of bite cases was routinely done by health facilities in Mali and Côte d'Ivoire but not in Chad. PEP treatment in Côte d'Ivoire was fully centralized in anti-rabies centers, but only partly centralized (Bamako area) in Mali. In Chad, PEP treatment was managed by the general decentralized health services. These specific country backgrounds called for slight differences in methodologies between the study countries. In Mali and Côte d'Ivoire, the existing registries were improved, and the data collection process in Côte d'Ivoire was digitalized. In addition to data reported from the anti-rabies centers, the Ivorian study team did a cross-sectional data collection in public health facilities, pharmacies and veterinary facilities in the study zones to assess the rate of underreporting from peripheral health centers to anti-rabies centers. In Mali, data was collected from the anti-rabies center in Bamako and the public health facilities in the Sikasso region during quarterly visits by the study investigators. In Chad, public health facilities in the study area received standardized data sheets, which were sent to the district health office upon completion and collected twice a year by the study team during supervisory missions. The study period for this data component lasted from July 2016 to the end of March 2018. In Mali, bite cases were also collected retrospectively from January to June 2016. Human vaccine for PEP was provided free of charge during the project and health staff of participating facilities attended a general training on rabies control and prevention including bite treatment prior to project implementation. Adequate PEP included thorough wound washing, vaccination with any of the WHO recommended PEP schemes using quality-insured vaccine, and injection of human or equine derived rabies immunoglobulin (RIG) in case of a category 3 exposure. Human RIG is not available in Chad nor is equine RIG (ERIG) licensed for use. Therefore, PEP in Chad only included wound washing and active vaccination. GAVI provided funds for vaccine procurement with the stipulation to use the four-dose Updated Thai Red Cross intradermal (ID) PEP schedule. Prior to the project intramuscular (IM) regiments such as the Essen five dose and the Zagreb three dose schedule was primarily used in all study countries. The ministries of health approved the regime change, and training sessions were given for the newly introduced ID schedule. The two vaccine products used during the project (Rabipur® for Mali and Côte d'Ivoire, Verorab® for Chad) are both licensed for ID use. The ERIG procured by the project (Equirab® by Bharat Serum) was quality tested prior to use and proved efficacious.

2.4.3. Veterinary level

During the same period as the health facility survey, all animals put under observation at veterinary facilities were registered. Due to relatively weak capacity of veterinary services in all study countries, infrastructural, logistical and administrative support for animal rabies surveillance was provided by the project. Similar to training of health staff, all veterinarians involved in observation and diagnosis were trained and pre-immunized against rabies. When an animal died or was killed, ideally laboratory diagnosis was obtained. Access to rabies testing was increased through decentralization of diagnosis and improved sample transport. Peripheral laboratories were established, and personnel were trained to use a commercially available rapid immune diagnostic test (RIDT) (Lechenne et al., 2016b). Because RIDT was not an OIE recognized standard diagnostic test, all brain samples examined with the rapid test were also confirmed by the Fluorescent Antibody Test (FAT) in the respective national reference laboratory. Likewise, PEP for bite victims was not based on the RIDT result but was initiated immediately for all suspect exposures. However, PEP could be discontinued if both test RIDT and FAT showed a negative result. Through collaboration with the Pasteur Institute in Paris (IPP), all positive brain samples underwent PCR and subsequent phylogenetic analysis. More detail on the veterinary level diagnostic methodology can be found in Naïssengar et al., 2021.

2.5. Project evaluation

Implementation success of the project was examined through three evaluation components. A first quantitative success measure was the amount of data and indicators collected on the different study levels. Secondly, the achieved capacity building was assessed with the help of mixed quantitative and qualitative outcomes of the project. To illustrate internal and external capacity building triggered by the project, we divided this evaluation component into 5 sub-sections covering networking, material and infrastructural support, knowledge transfer, public awareness building and valorization of results/securing sustainability. Thirdly, a self-evaluation of the project implementation in light of the 11 principles of transboundary research partnership provided a solely subjective measure. This self-evaluation was done by the main project coordinator and approved by the principle investigators. To compare compliance across principles, we applied a score that shows which principles were represented on a stronger and weaker scale. Because this score was a self-rating based on comparison of components within the project, it cannot be used to compare the project with other partnerships or programs. The highest score does not mean that maximum compliance to the principle was achieved, but rather indicates that this principle was best applied in comparison to the others.

2.6. Ethical statement

Ethical approval was granted by the Ethics Committee of North Western and Central Switzerland (EKNZ), from the respective national ethics committees of Chad (Ministère de l'enseignement supérieur et de la recherche scientifique, Comité National de Bioéthique du Tchad, N°298/PR/MESRS/SG/CNBT/2016), Côte d'Ivoire (Ministère de la santé et de l'hygiène publique, Comité National d'Éthique de la Recherché, N/Réf: 010/MSLS/CNER-kp) and Mali (Ministère de l'enseignement supérieur et de la recherche scientifique, comité d'éthique de la Faculté de Médecine de Pharmacie et d'Odonto-Stomatologie, N°2016/_41/CE/FMPOS). Informed consent was obtained from interviewed people on the household level and from bite victims. Contact information was maintained during the time of bite-case follow-up, with access to the information limited to agents performing follow-up, and deleted after the follow-up period. Vaccine was available free to all bite victims that were registered at a collaborating health facility regardless of consent for study enrolment.

All veterinary personnel involved in sampling rabies cases received pre-exposure prophylaxis (PreP) through the project.

3. Results

3.1. Collected data and gained indicators

In all countries, a large volume of data was collected from all study levels (Table 2). The data collection started in June 2016 and lasted until the end of March 2018, resulting in a data collection period of over 20 months. The extent of data acquired is unique in rabies research, especially on household level. From the household baseline and follow-up surveys, the incidence of bite exposure and risk factors in rural and urban zones and across different cultural backgrounds can be assessed as done for Chad (Madjadinan et al. 2020). Although the recall period at baseline was rather long, it provides the basis for a national and sub-regional rabies burden estimate. For Mali these estimates are already published (Keita et al., 2020). PEP access parameters and exposure incidence observed at household level were used to calculate an investment case scenario (Hampson et al., 2019a). The health facility data provide indicators of access to PEP in regard to availability and compliance on the patient and provider level (Madjadinan et al. 2020, Tetchi et al. 2020a). The health impact of PEP in terms of survival considering injection method, use of RIG, and timing and number of doses received at health facility level are extremely valuable data to inform future treatment recommendations. Data from Côte d'Ivoire were used to evaluate the efficacy of PEP with and without RIG (Gerber et al., 2020) and evaluate the uptake of the Updated Thai Red Cross ID regiment (Tetchi et al., 2020b).

Since it was the first time a research One Health collaboration was attempted in the study regions, mechanisms for data sharing with and between participating facilities were not yet well established. In consequence, a direct link between health facility data and veterinary data was not possible in the majority of cases, which is a shortcoming of the study. Nonetheless, parallel data collection on both levels provides valuable indicators for the incidence of true rabies exposure such as observational and diagnostic results (Naïssengar et al., 2021, Madjadinand et al. 2020 Traoré et al., 2020). The available veterinary surveillance data varied considerably between countries: in Côte d'Ivoire the focus was on animal observation, the Chadian project focused on laboratory diagnosis, and Mali balanced both approaches (Table 2). Animal related data collected during the household survey, such as dog ownership and vaccination status, will contribute to regional and national dog population estimates and informed planning of mass vaccination interventions (Kallo et al. 2020).

3.2. Capacity building

3.2.1. Networking

Communication between project partner institutions during two project workshops Table 3 and four meetings greatly increased South-South exchange of expertise. In-country networks with and between local stakeholders were strengthened through the One Health approach and during the numerous stakeholder workshops and trainings. The northern partner, Swiss TPH, provided links to international partners and collaborators such as PARACON, WHO and the IPP. African research partners and Swiss TPH researchers attended expert meetings and conferences together Table 3. Sharing a network among project partners and collaborators should facilitate future direct exchanges without requiring the Swiss TPH intermediary. New contacts were established, primarily with GAVI but also with private sector vaccine manufacturers such as Glaxo Smith Kline (GSK) and Sanofi Pasteur. Former contacts were strengthened, especially between Swiss TPH and the modeling consortium and between Swiss TPH and IPP.

Table 2
Summary of data collected during study period in three study countries, by study level.

Study level	Database	Chad	Côte d'Ivoire	Mali	Total
Household	Households (HH) visited in baseline survey	8005	8005	8774	24784
	Registered bite cases on HH level at baseline	326	107	36	469
	Registered bite cases in HH during follow-up	113	54	85	252
Health facilities	Bite cases registered in health facilities	1520	3367	4010	8897
Veterinary facilities	Animal observations registered	179	1113	384	1676
	Performed laboratory diagnosis	186	44	34	264

3.2.2. Material and infrastructural support

Increased technical capacity of core project partners included mainly administrative (office equipment) and logistical aspects (Table 3). For the household survey, tablets were procured to facilitate data entry. A server with shared drives for data storage and exchange was created as a data repository for the household level and follow-up data. Infrastructural support was given to veterinary services through provision of dog kennels for observation (Côte d'Ivoire) and renovation of buildings to host peripheral laboratories (Chad) (Naïssengar et al., 2021). Establishing the laboratory facilities also included building incineration pits for contaminated carcasses and repairing motorbikes for the veterinarians in charge. In Côte d'Ivoire, motorbikes procured for the household survey were later donated to the veterinary posts to follow-up suspicious cases. In all study zones in Côte d'Ivoire and in Bamako, human anti-rabies centers were equipped with electronic data repositories. In all study countries, the public health services received a considerable amount of donated vaccine (> 5000 doses per country) and ERIG (600 doses per country, except for Chad) to ensure PEP for all patients registered during the study. Work security was improved through provision of PreP for all veterinary personnel working for the study. The project also provided a large amount of diagnostic material and equipment to the involved rabies laboratories, such as rapid tests, consumables, reagents and microscopes.

3.2.3. Mutual kn owledge transfer:

Project activities were officially launched during an inception workshop in N'Djamena in January 2016, which brought together representatives of the three different country field teams. This workshop was used to exchange and discuss planning details within the project team. Local project launch workshops with national authorities and local stakeholders were then conducted in all study countries (Table 3). These workshops were accompanied or followed by joint training workshops with animal and human health workers. The education material for the general joint rabies prevention trainings was based on the on-line rabies educator certificate provided by GARC (https://rabiesalliance.org/capacity-building/gep). Training sessions on general aspects of rabies control were followed by specific workshops on rabies diagnosis and use of the rapid test, mainly for veterinarians. On the human health side, workshops were organized on use of the Updated Thai Red Cross PEP schedule and ERIG in Côte D'Ivoire and Mali, facilitated by a representative from GSK. In Chad, an instruction document accompanied distribution of vaccine and syringes for ID use and implementation of the correct ID or IM schedule was followed-up during biannual supervisory missions in all health districts of the study zones. In Bouaké and San Pedro, 30 health agents attended training on clinical care and bite-case follow up. For each participating anti-rabies center in Côte d'Ivoire, a person was trained to use Epi Info for continuous data entry of the bite victim questionnaires. Use of tablets during the household survey increased technical capacity of local investigators and interviewers.

Capacity building on the internal level continued throughout the project on various occasions (Table 3). The rabies laboratory focal points of each country met for an exchange workshop in Abidjan in early 2016.

Table 3
Summary of capacity building activities and outcomes, by partnership level.

	Internal (among subcontracted project partners and team)			External in country (among participating public institutions and local stakeholders)			International
	Chad	Côte d'Ivoire	Mali	Chad	Côte d'Ivoire	Mali	
Networking	Inception workshop in N'Djamena in January 2016			Local stakeholder meetings held in all countries in early 2016			PARACON regional meeting for West and Central Africa in Grand Bassam June 2016
	Meeting of project focal points for rabies diagnosis and training on the rapid immuno-diagnostic test (RIDT) in Abidjan March 2016			Joint training workshops for human and veterinary workers mid 2016			WHO rabies expert meeting in Bangkok April 2017 and subsequent meeting on rabies burden modelling
	Project implementation meeting in Grand Bassam June 2016			Establish a free hotline facilitating intersectorial communication	Training workshops for the use of ID schedule for PEP		Partners for rabies prevention meeting in Wolfsberg August 2017 and 2018
	Sharing of progress and results at GAVI advisory board meeting in Geneva March 2017 and 2018			Quarterly supervisory visits to facilities participating in data collection			WHO meeting for progress towards 2030 held in Kathmandu May 2018
	Analysis and paper writing workshop in Abidjan in August 2017			Restitutions workshop held in all countries mid 2018 for dissemination of results			Joint WHO/PARACON meeting on progress towards 2030 in Johannesburg September 2018
	Quality control of rabies diagnosis through contact with WHO rabies reference laboratory at the Institut Pasteur Paris			Stronger link with vaccine providers established; funding and training support aquired for Côte d'Ivoire and Mali			Participation at RIWA conferences held in Abidjan October 2017 and Bamako October 2018
Material and infrastructural support	Project car Equipment of project offices Tablets for household survey data collection Immunofluorescent microscope	Motorbikes for household survey		RIDT, reagents and consumables for rabies diagnosis Vaccine for PEP with syringes and needles for ID use ERIG Establish 9 provincial rabies laboratories	Built kennels for animal observation	Establish 6 provincial rabies laboratories	N/A
	Improved data security through a storage on shared data platform			Motorbikes for veterinary services to facilitate case investigation and sample collection Improved biosafety by creating carcass disposal sites	Donation of computers to Antirabies centers for electronic data storage		
				PreP for veterinary personnel Provision of cooler boxes and payment for sample transport	Refrigerators for vaccine storage in antirabies treatment centers		
Knowledge transfer	Data analysis			General training on rabies prevention and control for health and veterinary workers			Publication of study results in over 10 peer reviewed journals so far
	Paper writing			Use of ID schedule for health workers			Presentation of study results at international conferences and expert meetings
	Survey planning				Use of ERIG for health workers		Sharing of results with rabies modelling consortium
	Improved financial reporting			Laboratory diagnosis for veterinary services			Results influencing GAVI investment agenda
	GCP and patient consent			Documentation and reporting of bite cases and rabies suspicious animal cases	Electronic data entry and Epi Info training for anti-rabies center personnel Rabies prevention training for teachers	Improved documentation and reporting of bite cases for health facilities	
Public awareness building	N/A			Distribution of leaflets and posters Radio broadcasts Coverage of project activities through local media Celebration of World Rabies Day Free hotline			N/A

(*continued on next page*)

Table 3 (*continued*)

	Internal (among subcontracted project partners and team)			External in country (among participating public institutions and local stakeholders)			International
	Chad	Côte d'Ivoire	Mali	Chad	Côte d'Ivoire	Mali	
					Participation of schools in project launch and closing ceremonies		
Valorisation of results and securing sustainability	Several project team members pursue Master and PhD studies with the Afrique One ASPIRE consortium (2 Master Chad, 2 Master CI and 1 PhD CI)		One team member persuing a PhD with Swiss TPH		Several project team members are part of the established national rabies control committees and contributed to the draft of a national rabies action plans		Decision by GAVI to invest in PEP from 2021
	About 20 peer reviewed publications planned (14 in this issue of Acta Tropica)			Small scale vaccination programs undertaken through support by Afrique One ASPIRE			Contribution to new WHO recommendations for rabies immunization published April 2018 and to WHO manual for rabies diagnosis
	Acquiring of sub-grants (Wolfermann Nägeli Foundation, SARECO, Freiwillige Akademische Gesellschaft Basel and Insitut Pasteur Paris) to study the phylogeny of collected viral specimens			Hotline taken up by the Afrique One ASPIRE program activity	Establish provincial and national rabies control committees		Contribution to the modelling of the potential impact of improved provision of PEP through GAVI (Hampson et al.,2019a)
	Draft of a national rabies control plan	Follow-up funding secured through EDCTP for sustainable supply of PEP			SARE assessment through FAO organised stakeholder meeting		Contribution to the modelling to inform prophylaxis regimens for prevention of human rabies (Hampson et al., 2019b)
	Follow-up qualitative data collection undertaken						Data utilized for cost estimate for rabies exposure in West-Africa through a postdoc student from Senegal within the Afrique One ASPIRE consortium

The PARACON meeting in summer 2016 provided an opportunity for a meeting between the respective national coordinators and PIs to discuss implementation approaches. The most important internal training event was the analysis and paper-writing workshop that took place in August 2017, hosted by CSRS in Abidjan.

Finally, knowledge transfer also occurred on the international level through sharing results and expertise within the modelling consortium, with GAVI and to stakeholder bodies such as PARACON, WHO and GARC.

3.2.4. *Public awareness building:*

Public outreach activities were organized during project launch celebrations, annually on WRD, and alongside project restitution meetings in the study zones. An example on WRD in Côte d'Ivoire highlights the diversity of the sensitization activities. The celebration agenda included 1) training 15 teachers in every department of the study regions 2) presentation of the local committees for rabies control 3) a theater competition among pupils 4) radio broadcasts 5) demonstration of dog vaccination and 6) a policy meeting with local authorities. Continued sensitization throughout the project period was done using posters, leaflets, radio spots and broadcasts. There was a live discussion on Chadian national radio with three participants from the project team and a local private veterinarian followed by a phone based question and answer session with the public. This broadcast triggered reporting of two animal rabies cases. Both samples tested positive and the victims, who otherwise would not have sought care received PEP. The project team in Chad established a free phone hotline to give advice in case of animal bites, which was widely used by the public (Mbaipago et al., 2020).

Results dissemination meetings with local authorities and stakeholders were held in all study regions and covered by diverse media channels. The dissemination meetings included summaries of study results from different data collection levels and discussions on how to move forward with the rabies control agenda. Recommendations from the meetings focused on increased engagement of local community leaders and authorities in sensitization and finding continued funding sources. In Côte d'Ivoire, education through schools was identified as an important way to reduce bite cases. The created local rabies committees in Bouaké and San Pedro included among other members journalists and community workers.

3.2.5. *Valorization of results and securing sustainability:*

Along with insights from other studies funded by the GAVI learning agenda and WHO, the results and expertise gained through the project contributed to two major publications by a modelling consortium estimating the impact of a GAVI investment (Hampson et al., 2019a) and showing the advantage of applying an ID PEP scheme (Hampson et al., 2019b). The free availability of vaccine will likely save nearly 500'000 lives over 15 years (Hampson et al., 2019a). Based on the model results, GAVI decided to include human rabies vaccine for PEP in their investment strategy beginning in 2021. By changing to the dose sparing ID schedule, this investment is secured without the need to significantly increase vaccine production (Hampson et al., 2019b).

On the international policy level, the project contributed to the new WHO recommendations for rabies immunization (WHO, 2018a) and the WHO manual for rabies laboratory techniques (WHO, 2018b).

To ensure sustainability of control efforts on the national level beyond the project timeframe, local stakeholders were motivated to form One Health committees. The team in Côte d'Ivoire initiated local intersectoral committees in Bouaké and San Pedro. The objective of the committees is to reinforce joint efforts against rabies. There are 7-11 members in each local committee. They include the responsible heads of the animal and human health sectors, staff of anti-rabies centers, a journalist (communication team), a sociologist and a teacher. A training session for committees was held, and the responsibilities and tasks of

each member of the local intersectoral office were defined. A workshop on the national rabies strategy, held in Grand Bassam in May 2018, concluded that the GAVI funded project enabled Côte d'Ivoire to advance from level 1 of the Stepwise Approach to Rabies Elimination (SARE) to level 2. The SARE tool, established by the Food and Agricultural Organization (FAO) and GARC helps countries evaluate their current status of rabies control and indicates the next activities for further steps towards elimination, providing useful guidelines (Coetzer et al., 2016). During the workshop, a committee was formed to develop a strategic plan based on the SARE assessment. Of five committee members, three were key local leaders in the GAVI funded project. The national program for rabies elimination proposed by the committee was officially presented to the authorities, including the ministry of health and the ministry of livestock, on WRD 2018 and the program was approved and signed by both ministers. Equal success was achieved in Mali, where the project team was involved in developing the first draft of the national rabies control plan, supported by several institutions: the DSV, the LCV, the National Health Directorate, the National Disease Support Centre, the National Animal Health Support Centre and FAO through the Mali branch of the Emergency Centre for Transboundary Animal Diseases (ECTAD). This outcome shows how the project actively triggered policy action by increasing visibility of the rabies problem to a larger scale and building local capacity for a future elimination program. Unfortunately, in Chad it was not possible to initiate a One Health platform on the ministerial level to guide the process of elaborating a national plan. However, a draft plan was prepared by the local project team.

To secure sustained capacity building among project team members and continued research activities, close collaboration was sought with the Afrique One ASPIRE consortium (AOA). Project data contributes to one postdoc, one PhD and four master students within the AOA consortium, and additional research is planned to complement the acquired quantitative information with qualitative data (Table 3). Additionally, a team member from Mali acquired funding for a PhD at Swiss TPH. In collaboration with IPP, follow-up funding was secured to investigate the rabies strains collected during the project in more detail for insight into the spatial dynamics of rabies virus. Major funding by EDCTP was secured for Côte d'Ivoire and Mali to continue research on PEP delivery based on exposure risk assessment of health personnel in communication with the veterinary services. Innovative block chain technology will be used to facilitate intersectoral communication.

3.3. Implementation of the principles of transboundary research partnership

Overall, positive points of compliance with the principles predominated. However, for each of the eleven principles some shortcomings to compliance were identified. The only principle for which negative points outweighed the positive aspects was No. 10 "application of results". Table 4 lists the perceived positive and negative aspects of the project implementation by principle. Fig. 1 illustrates the scores using a spider graph. Highest compliance was achieved for project management, knowledge sharing and transparency focused principles (No. 3, 5, 7 and 9). These principles profited strongly from a very good project team internal communication, responsibility sharing and mutual learning. Compliance to principles with a stronger focus on in-country collaboration with public services and stakeholders are rated slightly lower (No. 2, 4, 6 and 11). Weak participation of both project partners and collaborators in project agenda setting led to a low score for principle No.1. Lowest scores were given for principles with a strong sustainability focus such as No. 8 and 10.

4. Discussion

Given the short timeline of the project, implementation and success were only possible with already established long-term partnerships and trust built over many years. The importance of good personal relationships, mutual respect and openness was highlighted previously in other examples of successful North-South partnerships (Mayhew et al., 2008; Mirzoev et al., 2012). Many of the previous research projects with the same partner organizations were limited to only one country at a time and were therefore restricted to North-South collaboration. However, strong South-South-North partnerships would be preferable to establish sustainable disease research and control capacity in developing countries (Osei-Atweneboana et al., 2012; Cash-Gibson et al., 2015). The parallel implementation of the same research study in three southern countries gave the opportunity to combine existing North-South partnerships into a South-South-North collaboration. The strength of this approach lies in facilitation of South-South capacity exchange, improved access of southern partners to international expert networks and, through the help of southern partners, better access of northern partners to local public entities. Although well-established partnerships already existed on the project internal level, many of the collaborations with public services at the national level were new. Challenges arose on both levels, but in particular, the latter. Thanks to strong partnership roots and established trust, most challenges and risks were navigated well. In the following section, we discuss the partnership's strength to face certain challenges and risks encountered, many of which were identified by other similar partnerships (Cash-Gibson et al., 2015; Varshney et al., 2016). In the second section of the discussion shortcomings to compliance and positive fit with the principles of the transboundary research partnership are addressed.

4.1. Strength, challenges and risks

The general weakness of public services in the sub-Saharan context, especially pronounced in the veterinary sector, posed the biggest challenge to implementation. Although this project vertically focused on one disease, the strong One Health and capacity-building approach strengthened local services in a more sustainable horizontal way. Direct knowledge exchange during workshops was limited to prevention and control of rabies, but contact facilitated between human health and veterinary services potentially triggers better collaboration for control of zoonotic diseases in general. The long data collection period, with continuous feedback from the project team, increased knowledge on reporting and documentation, both paper based and electronic. As an example, the quality of data initially reported from health centers and documented on diagnostic cases in veterinary services was a huge concern in Chad, but quality increased gradually throughout the project. The novel collaborations with local health and veterinary structures also meant that some envisioned methodological approaches had to be revised during implementation. In Chad, real-time reporting of bite cases through the hotline was planned, but many health workers could not make long phone calls because they were very busy with patients and concerned about limited battery charge on phones. In consequence, supervisory missions were intensified. Turnover of staff in veterinary services was another challenge encountered in Chad, requiring a second training round for newly appointed personnel at collaborating veterinary posts. During implementation of ERIG in Côte d'Ivoire, a challenge was encountered regarding the management of category 3 wounds. Health staff found it difficult to infiltrate the whole required volume of ERIG in small wounds located on the fingers or toes. Follow-up training instructed health workers to apply remaining quantity of ERIG intramuscularly distant from the wound in such cases. However, this practice is no longer recommended by the new WHO regulations on rabies immunization published in April 2018 (WHO, 2018a).

These three examples show that considerable flexibility in planning and budget allocation was needed across countries and within country specific project activities. Country partners received generous discretion for budget allocation and implementation approaches. This provided project internal resilience to challenges encountered and allowed for adapting to country specific administrative, cultural and

Table 4
Self-evaluation of project implementation for compliance with the 11 principles of transboundary research partnerships.

	Praise	Critics	Rating
1. Agenda setting	Long term research collaboration in all three countries Activities are based on previous joint experience Research undertaken meets the need identified through previous research projects Local teams had considerable degree of freedom for practical implementation of the research methodology	Research questions defined by GAVI learning agenda Project timeline set by GAVI learning agenda Main research method defined by Swiss TPH to ensure comparability of data	3
2. Interaction with stakeholders	Inception and restitution workshops held with local authorities, human and veterinary services Yearly communication with community stakeholders during World Rabies Day Strong public sensitization component Direct communication with health workers, veterinarians and the public through the rabies hotline in Chad Service capacity building for health centers and veterinary posts Stakeholder platforms established in Côte d'Ivoire and Mali Strong communication with international stakeholder institutions (WHO, PARACON, vaccine providers, OIE, FAO) Regular contact with human and veterinary services during supervisory visits	Data collection requirement dictated by the project methodology No interactive process with stakeholders in regard to analysis and interpretation of results Data acquired is property of project partners In Chad stakeholder involvement was not secured on ministerial level	4
3. Clarified responsibilities	Roles and responsibilities clearly defined between the project partners in sub-contracts Clear organisational structure and shared competencies between different local partners and team members Long term experience with problem solving in case of conflict Clear assignment of responsibilities and duties among project team members	Minor conflicts over hierarchical structure between veterinary and human health project component and supervision	5
4. Account to beneficiaries	Regular joint reporting to funder Contribution and presence of PIs at the yearly meeting of the GAVI advisory board Provision of free PEP Certification of diagnostic results Accounting to health workers and local veterinarians Results shared with a wide research community through conference participation and scientific articles	Research outcome not communicated to the broader public Incomplete follow-up of PEP Delayed financial reporting by local partners	4
5. Promotion of mutual learning	Direct exchange of results and discussion of analysis during a project team workshop in Abidjan August 2017 Insights and experiences shared with the greater rabies expert community Joint workshops for human and animal health workers in all project countries Career support to 4 Master, 2 PhDs and 1 postdoc student Exchange of diagnostic expertise between project countries Joint paper writing	Learning targets not clearly defined within the project Focus is higher on individual than on institutional training and learning	5
6. Enhance capacities	Enhanced diagnostic capacities in all countries Strengthened organisational capacities of partner institutions Enhanced scientific capacities as benefit to all institutions Strengthened communication between the veterinary and human health sectors Improved data reporting in health and veterinary facilities Improved PEP provision Strong South-South exchange of capacities Master and doctoral studies initiated	One health communication largely driven by project team Low quality of documentation and reporting on health and veterinary level in Chad and Mali Training on rabies control and prevention remained a point in time event and is not institutionalized High turnover of staff poses a risk for personnel capacity building Educational component on school level only included in Côte d'Ivoire	4
7. Sharing of data and networks	All data and budget are shared between the main project partners All partners are involved in networking activities Participation of local PIs and study coordinators at international meetings and conferences Initiation of partnership with WHO reference laboratory Long-term partnership creates confidence and trust	Language barriers of local partners for international networking No official complaint and arbitration mechanism	5
8. Dissemination of results	High scientific output and clearly defined publication pipeline Publication in Open Access format Sharing of results with local stakeholders and international community	Dissemination heavily based on peer review publications No written reports for local authorities and collaborating institutions prepared	3
9. Pooling of profits and merits	First authorship granted for African team members Language barrier overcome by translation of articles initially written in French Full transparency and close communication on dissemination issues African team members recognized for authorship in the overall published outcomes of the GAVI Learning Agenda		5
10. Application of results	National rabies action plans designed and approved in Côte d'Ivoire and Mali Small-scale dog vaccination campaigns initiated in Chad and Côte d'Ivoire	No policy impact achieved in Chad	2

(*continued on next page*)

Table 4 (*continued*)

	Praise	Critics	Rating
		Lack of short-term sustainability of improved PEP access through unsecured continued funding for free provision	
	Study results provided input for the new WHO recommendations for rabies immunization	RIDT not available beyond the project period	
		ID schedule for PEP not approved by ministries for use beyond the project period	
11. Secure outcomes	Provincial (Côte d'Ivoire) and national rabies control committees established (Côte d'Ivoire, Mali)	No local financial resources secured	4
	Several project team members are part of national rabies committees and invited as country experts at WHO and PARACON meetings	No direct follow-up project secured	
	Continued training of Master and PhD students	Long term impact of the project remains to be evaluated	
	New project proposals initiated with Mali and Côte d'Ivoire		
	Positive decision of GAVI to invest in PEP from 2021		
	Selected project activities taken up by the Afrique One ASPIRE consortium		

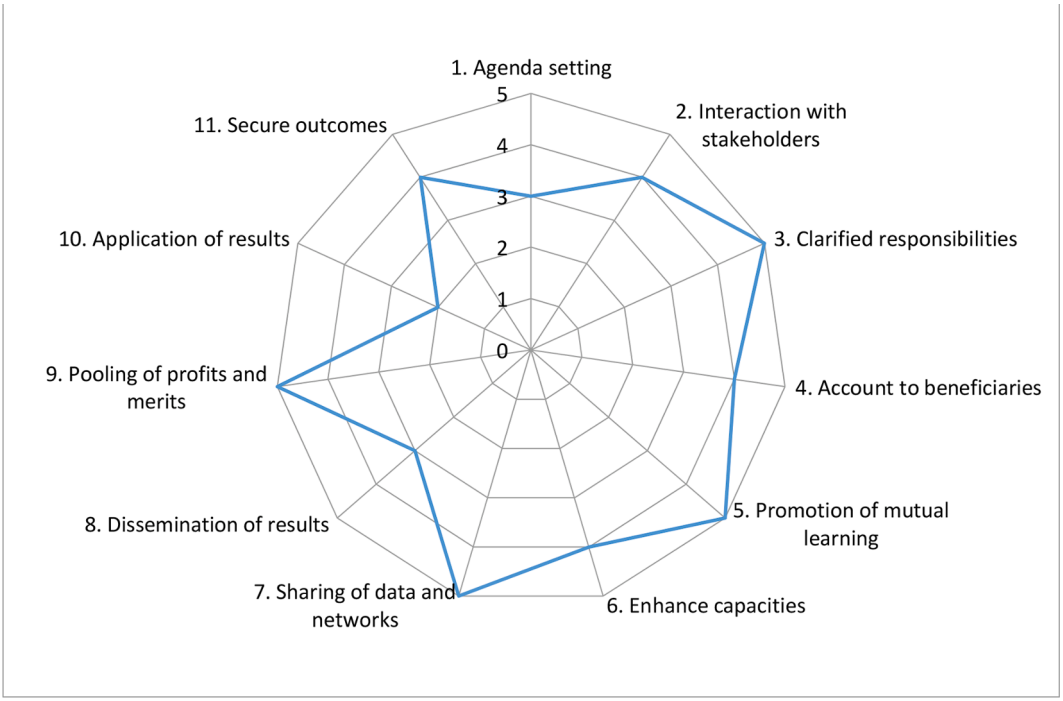

Figure 1. Spider graph of scores for the conversion of each of the 11 principles of translational research partnership by the project.

epidemiological backgrounds. This is illustrated by the comparison of activities on the veterinary study level between Côte d'Ivoire and Chad. Observation of dogs by veterinary services in Côte d'Ivoire proved to be well established and yielded most often a negative outcome. Therefore, the demand for an in-field rapid diagnostic test was not as high as in Chad where veterinary observation is less practiced, and rabies incidence among suspected dogs proved to be quite high (Naïssengar et al., 2021).

Long-lasting partnerships with local institutions and recruitment of mainly local project team leaders were also beneficial in risk mitigation. Risks were encountered on all levels: within the core project team, on the level of collaborating partners and on the project external national level. Team internal conflicts were rare and concerned mainly the hierarchical position of veterinary and human health institutions and team members. These were all solved amiably. Another project internal risk was delayed financial reporting, leading to delayed transfer of funds and project activities. On the level of public services, risks arose through the voluntary nature of the collaboration, which influenced staff motivation, through the variable level of professional skills, and through the non-influence of the project on staff relocation. Public services strikes during the project period were encountered in Mali and Chad. In Chad, the extent of the strike, coupled with a national economic crisis, led to the decision to grant a case reward for reporting bite incidences and animal samples. Working with public services also entailed risk of corruption and personal gain in all three countries, e.g. selling of vaccine and false reporting to earn case rewards. These risks are more quickly and accurately identified and mitigated by local team members than by country external partners. Terrorism is another risk in both Mali and Chad, which restricted travel to certain areas of these countries, especially for Swiss team members, making strong local leadership essential. Other risks that were well anticipated and alleviated through strong local project roots were climate factors affecting logistics, mainly in the rainy season, and communication barriers (internet access, phone network coverage).

On the level of collaboration with international partner institutions, the main challenge encountered was the language barrier between francophone team members and English speaking collaborators. However, the respective local PIs all spoke both French and English and facilitated communication. Language also affected timescale to publication, because many authors wrote their papers in French, with manuscripts subsequently translated to English. This process was important to share profits and merits and build publication capacity and still

achieve high reach for research results, which is stronger for articles published in English.

Another challenge related to analysis of data and publishing was the data management and statistical skill level of local team members. This, along with the language barrier and a growing pressure for fast publication, means that much research undertaken in Africa only involve local partners on the level of data collection. This is identified as a concern of southern partners in Van der Veken et al. (2017). Collaborative research partnerships between low and middle income countries entails risks related to power differences, inadequate authorship guidance and editorial bias towards renowned experts, which provokes discussion about authorship ethics (Smith et al., 2014). In this project, we countered this pattern and enhanced both analytical and writing capacity. Training in other research management skills such as proposal writing and communication with funders was not in the scope of this project but is also an identified skills gap leading to dependency on northern partners to acquire research funds (Van der Veken et al., 2017).

4.2. Compliance to the principles of transboundary research partnership

This evaluation component is not intended as a comparison with other projects, but rather to illustrate differences in level of application of each principle within one project. Another limitation is that the evaluation is only based on the subjective opinion of the project coordination and PIs and does not include consultation with a wider range of team members/project collaborators due to time and financial constraints. It would be preferable to include a feedback component, in the form of a qualitative data collection among all team members and selected local collaborators (Mayhew et al., 2008; Mirzoev et al., 2012; Varshney et al., 2016) to get input and ideas to improve approaches.

In general, the guidelines of the Swiss Academy of Sciences were well applied, but improvements concerning all principles are possible for future projects. Since the data had to be comparable, the main methodology was pre-defined by Swiss TPH. However, as explained above, there was considerable degree of freedom given to the local project teams to address specific contextual situations.

Highest compliance was found for clarified responsibilities, promotion of mutual learning, sharing of data and networks, and pooling of profits and merits. These principles all profited from strong project internal task sharing, focus on capacity building and commitment to shifting leadership to local partners where possible. The latter is essential to build trust through transferring ownership to local partners and strive towards partnerships based on equality of powers. Vertical quantitative programs, in particular, entail the risk of neglecting equity among partners, which is documented to cause frustration and reason to resign (Katisi et al., 2016). Power inequalities among partners can also lead to fear of exploitation by African researchers (Munung et al., 2017).

Second in line are the principles related to communication of results and sustainability, e.g. interaction with stakeholders, accounting to beneficiaries and securing outcome. They were positively impacted by the influence of project outcomes on international recommendations and on the numerous stakeholder workshops and awareness building activities. Agenda setting, dissemination and application of results scored lowest. Because the research topic was dictated by the GAVI learning agenda, the priorities and objectives were prescribed rather than mutually agreed upon. However, rabies prevention was prioritized by local leaders especially from the veterinary sector and community representatives. To prevent a gap between local research needs and priorities set by funders and to profit from an existing reservoir of research capacity, programs should incorporate a reflection step to mutually agree on topics and objectives (Kok et al., 2017).

Although results dissemination among the international expert community and through the planned articles is high, more could have been done to share results with local collaborators and the public nationally, apart from presentations at final stakeholder meetings. For example, informative, succinct reports of the findings by country could be written for district medical offices, veterinary sectors and involved ministries. Throughout the project short newsletters could be distributed to local collaborating partners keeping them informed on the progress of the project. Along with a built-in feedback mechanism this would enable the partners to input the implementation in a constant and dynamic way. Prompt application of results was limited due to limited funds for immediate continued project activities, such as vaccine provision, surveillance and awareness. However, the commitment of GAVI to include human rabies vaccine in their vaccine investment strategy provides hope for the agenda towards zero by 2030(Minghui et al., 2018). Furthermore, the local One Health committees and national action plans triggered by the project, together with the strengthened zoonotic disease control and research capacities in the three countries provides good grounds for the long-term goal to eliminate rabies in domestic dogs.

5. Conclusion

This article describes the implementation of one of the largest One Health research projects in the field spanning all scales from local to national to international level. Despite the tight timeline for planning and implementation, the presented South-South-North research project on rabies burden in West and Central Africa provided impressive results concerning both the amount of data collected and the resulting policy influence at the national and global scale. The project links to several of the Sustainable Development Goals (SDG) such as Good Health and Well-Being (goal 3), Industry, Innovation and Infrastructure (goal 9), Reduce Inequalities (goal 10) and Partnerships for the Goals (goal 17) (United Nations General Assembly, 2015). This success was only possible due to a strongly rooted partnership built on trust, focused on mutual learning and striving towards equity. Challenges and risks encountered during implementation in the field were related to general infrastructural weaknesses of public services in the project countries, veterinary and human health workers inexperienced in data documentation, adverse climatic conditions and low mobile network coverage in some project areas. These challenges were anticipated through the expertise of local project team members and overcome by allowing in-country teams a considerable degree of flexibility concerning budget allocation and methodology. Project internal challenges were related to language barriers, mechanisms of data sharing and analytical skills. The strong internal capacity building approach helped to reach a good integration of African team members in the analysis and paper writing process and as a result strengthened research expertise in sub-Saharan Africa. Communication was strengthened between animal and human health services: A bottom-up movement led to local uptake of the applied One Health approach through creation of joint committees and elaboration of national rabies action plans. This example shows that with good methodological and organizational design, funding for a vertical, disease centered project can strengthen structures and services on a horizontal level, without compromising data quality. Long-term sustainability should be evaluated in the coming years.

Author statement

ML and JZ conceived of the idea to the paper. ML wrote the paper together with AT, BB and JZ. JZ was the main study PI and ML the technical coordinator of the study activities in all three countries. AT was the study PI for Mali, BB the study PI for Côte d'Ivoire, DD and RN were the study PIs for Chad. AO, VK, and AT were the local technical coordinators on the animal health side in Chad, Côte d'Ivoire and Mali, respectively. MT was the technical study coordinator on the human health side in Côte d'Ivoire, AKT assumed this role in Mali and RM in Chad. JH was the project statistician and provided critical feedback on the manuscript.

Declaration of Competing Interest

The authors of the manuscript entitled "One Health research partnership to estimate rabies burden and vaccine demand in Chad, Côte d'Ivoire and Mali" declare that there is no actual or potential conflict of interest in relation to this article. They have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Acknowledgments

We are grateful to all contributors to study, namely all health and veterinary workers for their efforts in data collection, the medical and veterinary officials for their kind administrative support and the big team of interviewers making the household surveys possible. We also thank our colleagues from the IPP for diagnostic assistance. Many thanks go to the GAVI team for their benevolent assistance to the project and the advisory board members for their valuable input. Furthermore, we thank our international partners at WHO and GARC for their great support. The project was mainly funded by GAVI. GSK kindly provided human rabies vaccine for PEP and training support. Monique Léchenne was partly funded by the DELTAS Africa Initiative [Afrique One-ASPIRE /DEL-15-008]. Afrique One-ASPIRE is funded by a consortium of donor including the African Academy of Sciences (AAS) Alliance for Accelerating Excellence in Science in Africa (AESA), the New Partnership for Africa's Development Planning and Coordinating (NEPAD) Agency, the Wellcome Trust [107753/A/15/Z] and the UK government.

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