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Challenges to improved animal rabies surveillance: Experiences from pilot implementation of decentralized diagnostic units in Chad

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ABSTRACT

Better surveillance is desperately needed to guide rabies prevention and control to achieve the goal of zero dog-mediated human rabies by 2030, defined by the World Health Organization (WHO) and partners in 2015. With the help of funding from the Vaccine Alliance (GAVI) learning agenda, we implemented animal rabies surveillance based on One Health communication, improved accessibility of diagnostic testing and facilitated sample transport to increase case detection in three regions of Chad. Through the project, rabies surveillance, previously only available in N'Djaména, was extended to selected provincial rural and urban areas. Nine decentralized diagnostic units (DDU) were established, hosted by veterinary district agencies (VDA) in four different administrative regions. Four additional VDAs in the study area were reinforced with facilitation of sample collection and transport. Staff from all these 13 veterinary facilities were trained in sample collection and diagnostics. DDUs performed Rapid Immunodiagnostic Tests (RIDT) providing a preliminary result before samples were sent to the central laboratory in N'Djamena for confirmation with the standard Florescent Antibody Test (FAT). Within the project period from June 2016 to March 2018, 115 samples were reported by veterinary facilities in the study areas compared to 63 samples received from outside the study area, the vast majority of them originating from the capital city N'Djaména (N=61). Eighty nine percent of all 178 samples reported to IRED during the project period tested positive. Most of the samples originated from dogs (92%). Other confirmed rabies positive animals observed were cats, a donkey and a pig. Although surveillance of animal rabies was the focus, four human saliva samples were also submitted for diagnosis. We observed high differences in reporting rates between the four study regions. This could be attributable to differences in rabies epidemiology but are also influenced by the distance to the central laboratory in N'Djaména, the cultural background and the level of public awareness. The possibility for local testing through RIDT was very welcomed by local veterinary staff and preliminary insights suggest a positive influence on One Health communication and PEP initiation. However, these aspects as well as the relative impact of local testing on sample collection in comparison to reinforcement of sample collection and transport alone, need to be further investigated. Challenges encountered related to poor infrastructure (buildings, appliances, materials) and low logistic capacity (lacking means and material for transport and communication) of veterinary services in Chad. In addition, veterinary personnel lack experience in data management. Together with staff turnover, this leads to a need for repeated training. Major shortcoming of the approach was the high cost per sample and limited sustainability beyond the project timeframe.

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1. Introduction

Of the 59′000 human rabies deaths estimated to occur annually around the globe (Hampson et al., 2015)(Hampson et al. 2015), over 95% are due to infection through dog bites (WHO, 2016a). Despite the high burden of rabies, the disease remains neglected in most African and Asian countries (Taylor et al., 2017). The cycle of neglect is driven by lack of data resulting in low resource allocation, exacerbating the problem of ineffective surveillance that cannot generate reliable data, which is urgently needed for better control and prevention (Nel, 2013; Taylor et al., 2015, Franka and Wallace, 2018). In Africa, the data situation is especially deplorable. While it is known that rabies is endemic in the dog population and infection risk for humans is high across the entire continent, most countries provide no official data on number of human deaths, and existing data differs greatly from estimated case numbers (WHO, 2016b). In eastern and southern Africa, human rabies was estimated as underreported by 95% (Dodet, 2009a). Human deaths are only one indicator for the burden of rabies. Other important information needed to estimate the true disease burden are the extent of human exposure, vaccine demand for post-exposure prophylaxis (PEP), cost of animal vaccination and economic losses to the livestock and veterinary sector. In December 2015, the World Health Organization (WHO), together with the Global Alliance for Rabies Control (GARC), the Food and Agricultural Organization (FAO) and the World Organization for Animal Health (OIE) initiated the "Agenda towards elimination of dog mediated human rabies by 2030" (WHO, 2016a). Improving the data situation on animal and human rabies cases and bite incidence as an indicator for exposure is an important objective of this agenda (Scott et al., 2017; WHO, 2017). The Pan-African Rabies Control Network (PARACON) was established to consolidate expertise and communicate results across Africa (Scott et al., 2015). While sub-regional and international efforts are a key factor for visibility and advocacy on the global scale, efforts on the national and sub-national level are necessary to increase effectiveness and inclusiveness of surveillance and improve the quality of shared data. Surveillance is a crucial component for all stages towards elimination, including proof of burden, prevention of human rabies, monitoring of control measures, and, finally, verifying and maintaining absence of disease (Franka and Wallace, 2018). Currently no African country has achieved the detection probability of 10% which is necessary to prove absence of rabies after successful initiation of an elimination program (Townsend et al., 2013; WHO, 2016b). Challenges to surveillance are weak public health and veterinary services in many rabies endemic countries and aspects related to disease epidemiology, the nature of the reservoir population and public awareness. Rabies incubation periods can vary greatly and are asymptomatic, followed by only a short symptomatic infectious state before the fatal outcome. Rabies suspicious animals often disappear or are killed without any follow-up (Lechenne et al., 2017). Serological surveys and random sampling of animals are only of limited use and are not cost-effective to establish disease burden (Franka and Wallace, 2018). Surveillance therefore relies on targeted approaches through investigation of bite cases (Townsend et al., 2013; Hampson et al., 2016). Active follow-up of potential exposure requires close collaboration between the human health facility where a bite victim seeks help and the veterinary facility responsible for animal quarantine and testing (Lechenne et al., 2017; Undurraga et al., 2017). However, this type of One Health collaboration, termed Integrated Bite Case Management (IBCM), has not yet been successfully implemented on a large scale. Another obstacle is the low accessibility of diagnostic testing. In most countries rabies diagnosis is only performed in a single central laboratory, which is challenging for sample transport and conservation and leads to long delays between sampling and a diagnostic result (Dodet, 2009b; Banyard et al., 2013). Improved rabies surveillance depends on increased diagnostic access through: 1) sensitization of the public to increase awareness and perceived usefulness of testing; 2) adequate training and efficient collaboration of veterinary and human health staff; 3) decentralization of laboratory facilities to improve geographical access; 4) improved transport networks and 5) reporting systems able to adequately respond to case detection.

This study attempted to improve surveillance through pilot implementation of these five key components in three different regions in Chad and to increase the number of reported animal rabies cases.

1.1. Country context

In the entire country of Chad, which extends over 1,280,000 km^2, there is only one rabies diagnostic laboratory, in the capital N'Djaména, run by the Institut de Recherches en Elevage pour le Développement (IRED) a public veterinary research facility under the ministry of livestock. Since 1999, this central laboratory was regularly reinforced through several research projects conducted by a tripartite partnership between IRED, Swiss Tropical and Public Health Institute (Swiss TPH) and the Centre de Support en Santé International (CSSI). In 2000, the central laboratory renovation included provision of a fluorescence microscope to perform the Fluorescent Antibody Test (FAT), one of the accredited tests for rabies diagnosis (WHO, 2018). This enabled various in-depth research projects involving animal rabies diagnosis (Kayali et al., 2003; Dürr et al., 2008; Lechenne et al., 2016; Zinsstag et al., 2017), but surveillance coverage remained limited to the capital city and the close periurban vicinity.

In 2016, the Vaccine Alliance (GAVI)[1] learning agenda funded a research project to assess rabies burden and vaccine demand in West and Central Africa (Léchenne et al., 2021), providing the opportunity to extend surveillance from N'Djaména into three pilot regions.

2. Materials and Methods

2.1. General project background

Improving One Health collaboration was one core objective of the GAVI funded research project. To trigger a bottom up initiative for better veterinary and human health communication, to better identify true exposure, increase case detection and gain more reliable burden data, we applied a decentralization approach to bring animal rabies diagnosis closer to remote health facilities. Decentralizing animal rabies surveillance was one of three components of the research project on estimating the rabies burden. The other two components were a large scale bite case study in 8000 households and a health facility based study to collect data on bite cases and PEP treatment in public health services (Madjadinan et al. 2020). The study zone comprised three different study areas: the region of Logone Occidentale in the South of Chad with high dog numbers and a predominantly Christian/Animist background; the region of Ouaddaï in the North of the country with a much lower dog to human ratio and an Islamic cultural background (Anyiam et al., 2017). The third area comprised a 100 km radius around N'Djamena which covered parts of the region Chari Baguirmi and Hadjer Lamis in central Chad (Fig. 1). Each study area has approximately 700'000 inhabitants (INSEED, 2009), but there are extreme differences in geographical size (Fig. 1) so population density varies from approximately 18 (Chari Baguirmi and Hadjer Lamis) to 77 (Logone Occidentale) inhabitants per km^2. During the study period, all health districts of the study area received human rabies vaccine to ensure constant availability. A basic training session for supervisors and agents of participating health and veterinary facilities took place prior to the study start (Mbaipago et al., 2019). Public sensitization throughout the study included regular radio broadcasts, leaflets and posters distributed in health and veterinary

[1] GAVI is an international organization collaborating with WHO, UNICEF, World Bank and the Bill &Melinda Gates Foundation. Its aim is to improve access to childcare immunization in the poorest regions of the world by providing vaccines free of charge to eligible countries.

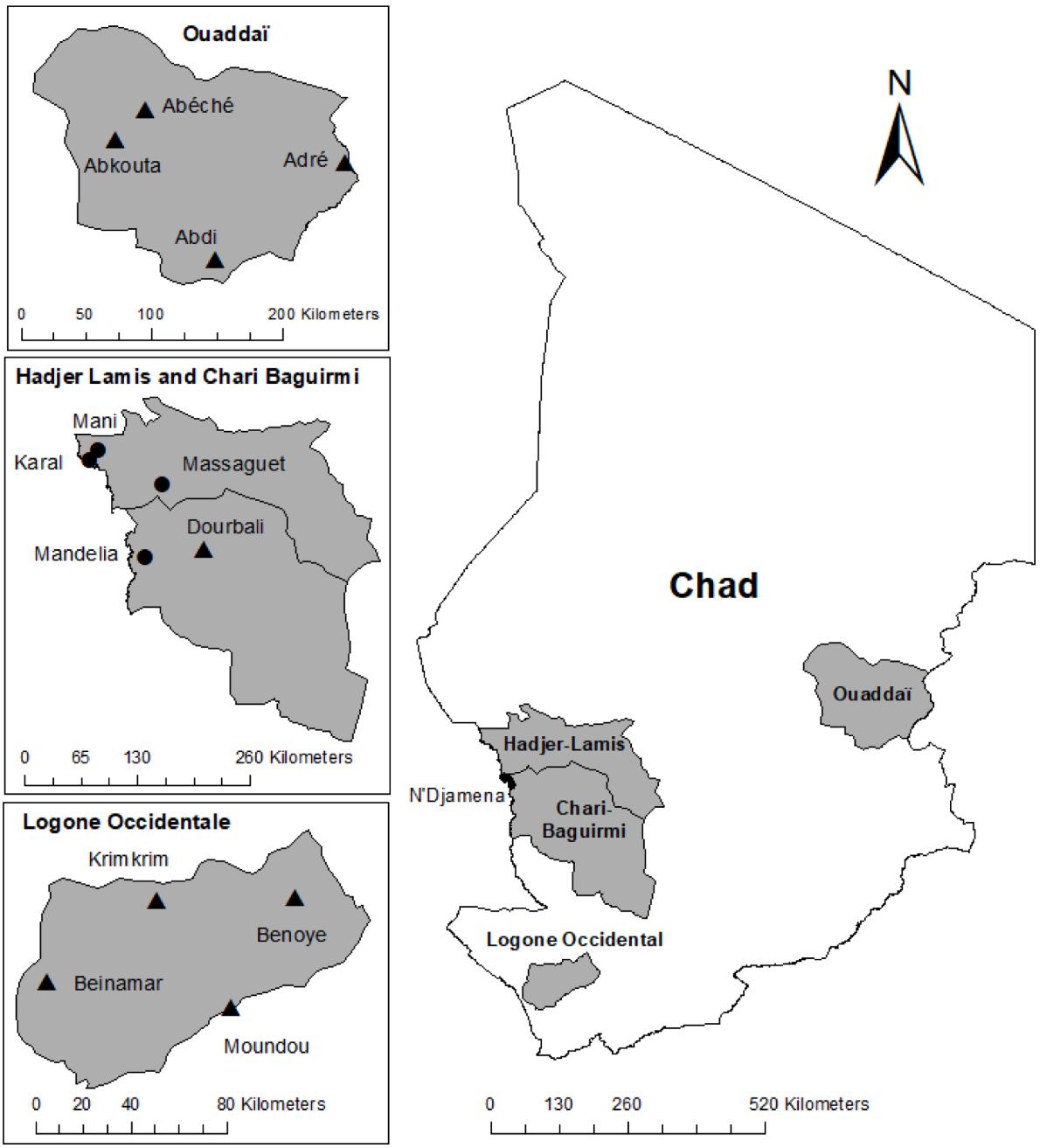

Fig. 1. Map of Chad with the study regions highlighted in grey. The three study areas are depicted enlarged to the left. Locations of decentralized diagnostic units (DDU) are highlighted as black triangles in the respective map of the study areas. Reinforced veterinary district agencies are highlighted as black dots.

facilities and media coverage of training and dissemination workshops. In addition, we established a toll-free phone hotline to facilitate communication with bite victims and public services (Mbaipago et al., 2020). Data collection lasted from June 2016 through March 2018.

2.2. Establishing decentralized diagnostic units

Veterinary staff at participating veterinary facilities in the study zone participated in the joint rabies workshops with human health workers in June 2016 (Ouaddai and Logone Occidentale) and August 2016 (Hadjer Lamis and Chari Baguirmi). A detailed description of the workshops is in Mbaipago et al. (2019). The supervisors of the veterinary district agencies (VDA) of the study areas attended an additional two-day in-depth training on rabies diagnosis at the IRED central rabies laboratory end of August 2016. This training included lectures on theoretical aspects of rabies diagnosis, guidance on biosafety and hands-on practical lessons where participants performed dissection, rapid immunodiagnostic test (RIDT) and FAT. Before the training, all veterinary workers were immunized against rabies. Because of staff turnover, training had to be repeated in Abéché, the capital of the Ouaddaï region mid-term for 5 new veterinary workers. Decentralized Diagnostic Unit (DDU) were created in nine of thirteen VDA in the study zone. The selected locations included all four VDA in the region of Logone Occidentale (Moundou, Beinamar, Benoye and Krim Krim) and all four in the region of Ouaddaï (Abéché, Abdi, Abkouta and Adré). Since the third study area was located close to N'Djaména only one DDU was created: Dourbali in Chari Baguirmi (Fig. 1). The remaining four VDAs in this study area (Massaguet, Mandelia, Mani, Karal) were strengthened through reinforcement of staff mobility (motorbike repair), training, sample collection and transport (tubes, cooler boxes) (Fig. 1).

Installation of the DDUs took place during field missions undertaken from October to November 2016 following identification of suitable buildings on the premises of the respective VDA. Each installation was planned and supervised by the rabies focal point person of the central laboratory. To dispose of potentially infected animal carcasses, 3m deep incineration pits (2m below ground with a 1m wall above ground) with lockable lids were constructed near each unit. The DDUs were equipped with the RIDT, the Anigen Rapid Rabies Tests (Bionote Inc.). This test was previously used at IRED and validated at the Pasteur Institute in Paris, France (Lechenne et al., 2016). The test methodology was modified from the manufacturer's recommendation as described in Lechenne et al. (2016). Since the RIDT is not an accredited rabies test, results must not be used for treatment decisions in bite victims (WHO, 2018).

In addition to RIDT, DDUs received furniture (table, stool), registry and data sheets, sampling and transport material (tubes, surgical kit, cooler boxes), protective material (gloves, filter masks, lab coats, plastic apron, boots, caps and goggles) and other consumables (antiseptics, petrol). In order to facilitate investigation of suspicious cases, defective motorcycles of managing veterinary officers were repaired. Since veterinary and public health services generally don't dispose of a landline the communication is done through the mobile network. Besides challenges related to network coverage this entailed also the risk that veterinary and human health workers have insufficient phone credit to make calls. This was countered by establishing a toll free hotline described in detail in Mbaipago et al. (2019). First reporting of a suspected case was generally received through this hotline. The hotline agent then provided the link between the calling veterinary agent and the closest participating health facility with vaccine in stock. Once link was made the two concerned services were either calling themselves directly or in case of lack of credit continued to communicate through the hotline agent.

2.3. Sampling, documentation and transport

Suspected rabid animals were reported directly by owners or bite victims or referred to a veterinary facility by health workers. According to legal regulations in Chad, veterinary officers must observe a biting animal for 14 days. If the animal remains alive during this period, the owner receives a document to certify the rabies-free status. Since veterinary facilities are not equipped with kennels, the animals are usually kept at home during the observation period. Suspect cases which were killed (usually by the owner prior to contacting a veterinary agent) or died during observation were analysed with the RIDT at a DDU before sending a sample for confirmation of the test result to the IRED central laboratory. Samples collected by a reinforced VDA or another veterinary structure were sent directly to IRED after sampling. Sampling was done by removing brain stem through the atlanto-occipital route using a surgical kit or faecal sample spoon. With this sampling method, the skull does not need to be opened so risk of contamination of the surrounding area is lower. A pea-sized piece of the sample was used to perform the RIDT, with the remainder put into a tube and sent to IRED on ice in a sealed cooler box using public transport agencies. Veterinarians received 9 USD per sample diagnosed as an incentive, which also covered shipment costs of 3.5 USD per sample including return of empty cooler boxes. For samples tested by RIDT at a DDU when results were not listed as doubtful or missing, only the FAT was performed at IRED. All other samples were tested in parallel with RIDT and FAT at IRED. Two different reporting sheets were used for the study: An animal bite questionnaire to document all case related information, such as history, animal status, owners and bite victim information; and a diagnostic sheet where details of the sample and diagnostics performed were noted, including a section to be filled in by the central laboratory at time of confirmation. Both sheets would be sent to IRED with submitted samples. The animal bite case form included a section for certification of the observation and/or test result to be handed out to the animal owner at the end of observation/testing. The project documentation forms and their correct use were covered in-depth during the training sessions. Regardless of preliminary RIDT outcome, all bite victims were counselled to seek free PEP at a participating health facility. Treatment could be discontinued when negative RIDT result was confirmed by FAT or if an animal was alive after the 14 day observation period. If any of the two tests yielded a positive result PEP was recommended to be continued since in a previous study false negative FAT results at IRED had occurred (Lechenne et al., 2016).

2.4. Implementation assessment

Several evaluation parameters and performance indicators were used to measure the success of decentralization. They relate to 1) increase of surveillance; 2) test results and RIDT performance; 3) cost implications; 4) sample transport and documentation and 5) impact on One health communication.

The increase of samples collected during the project period both in comparison to number of samples received from the project regions in previous years and samples received from non-project regions during the study highlights the impact on case detection. Triggered by the start of the other study activities on household and health facility level, first samples from the study regions were reported and sent to IRED prior to installation of DDUs. In consequence, all samples received at IRED from project and non-project areas during the overall project period from June 2016 to March 2018 were included in our results. To illustrate the increase of case detection, we also analyzed the IRED electronic registry for details of cases received from the study areas prior to June 2016.

Test results compared between the DDU and the central laboratory provide information regarding the reliability of RIDT for use in decentralized facilities. To compare RIDT performance in DDUs to performance at IRED, we compared the concordance between RIDT and FAT performed both at IRED and the concordance between RIDT result from DDU and FAT result at IRED.

Cost per sample analysed compared between different DDUs was based on the sum of all fixed and variable costs per DDU divided by the total number of samples analysed by the DDU in the time period from instalment to project end. Fixed and variable cost of a DDU were defined as follows:

- Fixed cost per DDU: Sum of basic and advanced training cost per person + mean installation cost + fixed material cost (e.g. cooler boxes)
- Variable cost per DDU: sum of sample transport and incentive cost + cost for sample diagnosis including RIDT and sampling material multiplied by the number of samples analysed with RIDT at the DDU

To compare cost per sample between DDUs and reinforced VDAs we summed up the variable and fixed cost per type of structure and multiplied this amount with the total number of the respective structures. This amount was then divided by the total number of samples received from the respective type of structure after instalment. Fixed and variable cost of a reinforced VDA were defined as follows:

- Fixed cost per reinforced VDA: Sum of basic and advanced training cost per person + cost of motorbike repair + fixed material cost
- Variable cost per reinforced VDA: Sum of sample transport and incentive cost + cost for sampling material and sample diagnosis without RIDT multiplied by the number of samples received from the reinforced VDA

Cost of the rabies hotline was not included in the analysis, because it was impossible to disentangle calls related to sample collection and diagnosis from other calls related to bite cases without sampling of the suspect animal.

The time to first test result at a DDU and quality of sample documentation provides an indicator of the performance of DDUs, whereas

transport time, time to confirmation and quality of samples upon receipt at IRED provide information on feasibility of the logistical approach chosen for submission of specimens. Lastly, we evaluated the impact of decentralization on One Health communication between the human health and veterinary sector. Indicators for this communication are rate of sampling among all registered suspect animal rabies cases on health facility level during the project period and comparison of initiated PEP among patients exposed to confirmed rabies cases and patients exposed to suspect rabid animals without laboratory confirmation. Health facility data used for this comparison is published in Madjadinan et al., (2020).

3. Results

3.1. Impact on surveillance

The IRED electronic registry dates back to 2005. From then until the start of decentralization, few samples were reported from outside N'Djaména and the vicinity. The only sample received from Logone Occidentale prior to the study period came from Moundou in January 2013. The only recorded sample from the region of Ouaddaï was submitted from Abéché in November 2011. Between 2006-2015, the region of Chari Baguirmi and Hadjer Lamis submitted eight samples. These historic samples were all from dogs, with all but one, from Chari Baguirmi, diagnosed positive. In the first half of 2016, almost all samples tested at IRED came from N'Djaména, with the exception of one from Koundoul and one from Djermaya which are both very close to the capital.

A first sample from Abéché was submitted to IRED immediately after the joint rabies workshop in this region, but reporting did not increase markedly before the in-depth diagnostic training on the 30.August 2016 during which the veterinary agents received transport material such as cooler boxes and documentation material (animal bite case form). Reinforcement of VDAs and installation of DDUs was undertaken between 19.10.-21.11.2016 starting in Logone Occidentale, followed by the region of Ouaddaï and finally the project area around N'Djaména (Hadjer Lamis, Chari Baguirmi). In total, 115 samples were reported to IRED from June 2016 to March 2018 by a veterinary facility in the project areas of which 114 originated from the project regions (table 1). Nine of the 115 samples (8%) were reported by a designated DDU during the time period from in-depth training to installation of DDU, which took on average 2 months. After installation until the project end in March 2018, 77 samples (67%) were reported by a DDU and were subject to peripheral testing prior to sending to the central laboratory in N'Djaména. The remaining 29 samples (25%) arrived through a reinforced VDA or another veterinary structure in the project areas. The majority of samples were reported from Logone Occidentale (55.5%; N=64), followed by Hadjer Lamis and Chari Baguirmi with 28.5% (N=33) (table 1). Ouaddaï region accounted for only 16% (N=18) of samples. Most samples were analysed and/or sent from the DDU in Moundou (43.5%, N=50), followed by the DDU of Abkouta (11.5%, N=13) and KrimKrim (5%, N=6). The remaining 45 samples came either from other DDUs (N=17, 15%), from a reinforced VDA (N=20, 17 %) or another veterinary structure in the project area (N=9, 8%) (table 1).

In the same period 63 samples were received at IRED from outside the study regions (table 1). The majority of these samples originated from N'Djaména (95%, N=61) and only two (5%) were received from regions outside the capital not covered by the project: one from Mongo in the Guera region and one from Sarh in the Moyen Chari region. The majority of all 178 samples reported to IRED during the project period including those from outside the project area were collected from dogs (92%, N=163), followed by cats (3%, N=6), donkeys from Ouaddai (1%, N=2), and a pig from Logone Occidentale (0.5%, N=1). For two brain specimens, species information was missing. In addition to animal brain samples, four human saliva samples were collected, three from Logone Occidentale and one from N'Djaména. Most of the animals showed at least one typical symptom of rabies, such as sudden change of behavior, increased aggression, hypersalivation, appetite loss or paralysis. Only three dogs showed no signs of rabies, but two of these tested rabies positive. Seventy-seven percent of animals were killed (N=137) and 11% (N=20) died during the time of observation. For 11% of cases this information was missing. Vaccination status of animals was known for only 50% of animals. The majority were not vaccinated against rabies (41%, N=72), while outdated vaccination (> 1 year ago according to Chadian regulation) was reported in 13 animals (7%). Only three animals, all dogs, had a valid vaccination certificate. One of these dogs tested positive despite reported vaccination.

3.2. Test results and performance

Of the 77 samples collected by a functional DDU, 75 (95%) got tested with RIDT prior to sending to the central laboratory (table 2). One did not get tested at the DDU of Dourbali for unknown reasons and one sample from a donkey was not tested by the DDU of Adré nor sent to IRED, because the responsible veterinarian did not know that it is possible to perform rabies diagnostics on equids. The remaining samples received from the project area were not tested by a DDU either because they were submitted to IRED by a veterinary facility other than a DDU

Table 1
Overview of samples collected by origin, type of structure and project period.

Region	Samples origin	Total Nr. of samples arrived at IRED through a DDU	Arrived from a DDU before installation	Reported from a DDU after installation	Arrived through a reinforced VDA	Arrived through another veterinary structure
Ouaddaï	18	16	1*	17	0	0
Logone Occidentale	63	64	8	56	0	1
Hadjer Lamis	18	0	NA	NA	12	6
Chari Baguirmi	15	5	1	4	8	2
Total project area	114	85	10	77	20	9
Guéra	1					1
Moyen Chari	2**					1
N'Djaména	61					61
Total non-project area	64					63
Overall total	**178**	**85**	**10**	**77**	**20**	**72**

* this sample arrived before in-depth diagnostic training and was triggered by the local basic training

** one of these samples arrived at IRED through the DDU of Moundou and is counted in the total number arrived at IRED through a DDU for the region of Logone Occidentale

(N=29) or collected by a designated DDU prior to actual instalment (N=9). One dog sample was unfortunately lost during transport from DDU to IRED, due to a traffic accident. This resulted in a total of 85 samples received at IRED from DDUs (table 1), which is 48% of all 176 samples received at IRED for testing during the project period. The majority of samples were tested positive by FAT (N=157, 89%) among them 145 dog samples, all 6 cat samples, the pig sample, the donkey sample, 3 human saliva samples and one sample with missing species information. Three dog samples could not be analyzed with either RIDT or FAT due to decomposition (N=1) or desiccation (N=2). Dried samples resulted from burning the dog carcass before consumption.

Concordance between RIDT and FAT was generally very good, but higher for RIDT performed at IRED (table 2). Overall, only 5 of 173 RIDT results were not concordant between RIDT and FAT. In two of these cases, the specimen was human saliva, which is not within the test manufacturer specifications. In both cases, the RIDT test was negative, but the FAT result positive. A third specimen tested negative by RIDT but positive by FAT was a pig brain sample, which is also not within manufacturer recommendation for RIDT use. The remaining two samples with non-concordant results were dog brain specimens. Both showed a positive result by FAT, but one tested negative and one produced an invalid result with RIDT. For each DDU, the number of samples reported by species, the number of RIDT tests applied by result, and the comparison with FAT test results are shown in table 2.

3.3. Cost implications

Three days were sufficient to create a DDU and the average cost to install a DDU was 1'270 USD. In comparison a reinforced VDA cost 200 USD. In-depth diagnostic training was much more costly (345 USD/participant) than the basic training course (85.5 USD/participant) mainly because participants had to travel to N'Djaména. Follow-up diagnostic training in the provinces cost 137 USD per participant.

Material cost for sampling and transport amounted to approximately 180 USD per DDU and reinforced VDA. The fixed cost amounted to 1'880 USD for a DDU and 810 USD for a reinforced VDA. The cost of one rapid rabies test kit was 5 USD and cost of FAT at IRED is 9 USD. Shipment cost per sample together with incentive for the vet amounts to an additional 9 USD per sample for both a DDU and a reinforced VDA. Therefore cost per sample sums up to 23 USD for a DDU and 18 USD for a reinforced VDA.

Cost per sample compared between a DDU versus a reinforced VDA averaged 249 USD and 180 USD respectively. Cost per sample compared between different DDU reveals the extreme range of 66 USD for Moundou with a total of 44 samples analysed and 2'213 USD for Abdi who analysed only one single sample. The investment in the DDU of Adré did not result in any sample received.

3.4. Sample documentation and time to result at DDU

Despite the material provided for documentation, many samples sent from a DDU or a reinforced VDA had missing or incomplete reporting sheets. Over 1/4 (N=19, 25.5%) of all 75 samples received from a DDUs after its installation were missing the diagnostic and the animal observation sheet, while 7 samples (9.5 %) were lacking only the diagnostic sheet. Of all 105 samples received from either a DDU or a reinforced VDA from in-depth training to project end, 41% (N=43) were lacking the animal bite reporting sheet. Most of the missing data could be obtained by calling the respective veterinary agent through the established rabies hotline. Nonetheless, for 10 samples only animal species and location were noted, but all other information was missing including RIDT result (table 2), which is 13% of all samples tested by a DDU. For other samples important background information were missing, such as number of people bitten and/or treated (21 missing observations), date of sample analysis and/or sending (33 missing observations), and animal background such as vaccination status and owner status (18 missing observations). Complete information was provided for only 37% of samples from the project areas (43/115)

Over 80% (N=49) of samples with information on date of testing (N=60) were analysed with RIDT at the DDU on the day of arrival, while 13% (N=8) occurred on the day following arrival. Maximum time elapsing between arrival at a DDU and RIDT result was 3 days.

3.5. Sample transport and time to confirmation

Most of the 113 samples received from the project areas (94%, N=106) arrived at IRED in good condition. Only seven samples were recorded as decomposed, of which three came from Logone Occidentale and four from Ouaddaî. In five of these cases, the sample had already arrived at the DDU in a decomposed state. Transport was attributed to decomposition for two samples from the Ouaddaï region, which took 2 and 5 days respectively to reach the IRED. Despite the deteriorated state, a positive FAT result was obtained for all seven decomposed samples.

Mean transport time for samples from Logone Occidentale, based on reported sending date was 2 days (45 observations, SD 1.7, min 1, max 8,). For Ouaddaï, mean transport time was 4 days (7 observations, SD 1.7, min 2, max 7). Samples sent from the regions of Chari Baguirmi and Hadjer Lamis, both neighboring N'Djaména, usually arrived at IRED the same day of posting (19 observations, SD 0, min 0, max 0,). One dog sample was lost during transport but earlier tested negative with RIDT at the veterinary post in Abdi.

Time to confirmation with FAT was dependent on location of DDU and time of transport, and was observed as long for Logone Occidentale (mean 15 days, 61 observations, SD 16.8, min 0, max 66). The DDU in Moundou was equipped with a refrigerator with a small freezer compartment and samples were stored for a period before sending them in bulk to IRED. For Ouaddaï, time to confirmation averaged 5 days (12 observations, SD 2, min 3, max 9). RIDT results from Dourbali were usually confirmed within 24 hours (mean 0.85, SD 0.9, min 0, max 3, 5 observations). The time lag from result on the DDU level to confirmation did not influence treatment, as PEP was initiated even when RIDT result was negative, continuing for cases with positive RIDT and negative FAT result as explained above.

3.6. Impact on PEP and One Health collaboration

Of 119 people reported bitten by a laboratory confirmed rabid animal from the project areas 107 were reported to have initiated PEP. This translates into a PEP coverage of 90% among exposure victims of positive animals, which is slightly higher than the observed PEP coverage of 85% for all reported bite patients on health centre level during the same period in the same regions (Madjadinan et al., 2020). Unfortunately, for 18 positive samples information regarding number of people bitten was missing, and in 21 cases information on whether PEP was initiated was missing. Since the reporting on laboratory level did not include follow up of bite patients it is unknown if all patients reported to initiate PEP completed the required 4 injections (Updated Thai Red Cross scheme).

Similar to the weak data quality from the veterinary level, issues with accuracy of reporting were also observed on the health facility level, making it difficult to match animal cases to bite patients and establish true exposure. For example, in Logone Occidentale there were 33 patient files collected in health facilities where it was noted that laboratory diagnosis was made, but 46 animal samples were reported from Moundou from the respective DDU. Overall, laboratory diagnosis was reported in the patient files on the health centre level in 53 cases (Madjadinan et al., 2020). Compared to a 114 animal samples reported from the study areas this translates into a maximum reporting rate of 46.5% (53/114). Considering that some patients might have been bitten by the same animal, the reporting rate might be even lower. Thus, over 50% of cases with a laboratory diagnosis did not specify the result in the patient files registered in health facilities.

Although surveillance increased by project activities through

Table 2
Samples received and tested by the different diagnostic entities and specie with comparison of results between RIDT and FAT

			Rapid test results at DDU					Rapid test results at IRED				Confirmation				Concordance RIDT/FAT		
Diagnostic facility	Specie	No. Samples collected	No. RIDT	Positive RIDT	Negative RIDT	invalid RIDT	missing result	No. RIDT	positive RIDT	negative RIDT	invalid RIDT	No. FAT	positive FAT	negative FAT	invalid FAT	RIDT at DDU/ FAT	RIDT at IRED/ FAT	comments
Abdi	Dog	1	1	0	1	0	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	sample lost in transport
Abeche	Dog	3	2	1	0	0	1	3	3	0	0	3	3	0	0	100%	100%	one sample collected prior to installation
Abkouta	Dog	11	11	8	1	0	2	5	5	0	0	11	11	0	0	89%	100%	1 false negative RIDT at DDU
	Other	2	2	1	0	0	1	2	1	1	0	2	1	1	0	100%	100%	donkey (1), missing information (1)
Adré	Donkey	1	0	0	0	0	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	sample not tested and not sent to IRED
Beinamar	Dog	3	3	2	0	0	1	1	1	0	0	3	3	0	0	100%	100%	
	Pig	1	1	0	1	0	0	0	0	0	0	1	1	0	0	0%	NA	1 false negative RIDT at DDU
Benoye	Dog	4	3	3	0	0	0	1	1	0	0	4	4	0	0	100%	100%	one sample collected prior to installation
Krim Krim	Dog	6	5	5	0	0	0	1	1	0	0	6	6	0	0	100%	100%	one sample collected prior to installation
Moundou	Dog	41	35	29	1	1	4	10	9	1	0	41	39	2	0	97%	100%	1 invalid RIDT at DDU tested positive with FAT, 6 samples collected prior to installation
	Cat	5	5	5	0	0	0	1	1	0	0	5	5	0	0	100%	100%	
	missing species	1	1	1	0	0	0	0	0	0	0	1	1	0	0	100%	NA	
	Human saliva	3	3	0	2	0	1	1	1	0	0	3	2	1	0	50%	100%	1 false negative RIDT at DDU
Dourbali	Dog	5	3	3	0	0	0	2	2	0	0	5	5	0	0	100%	100%	One sample collected prior to installation
Total peripheral		**87**	**75**	**58**	**6**	**1**	**10**	**27**	**25**	**2**	**0**	85	**81**	**4**	**0**	**94%**	**100%**	
IRED central	Dog	89	NA	**89**	74	12	3	89	74	12	3	NA	100%					
	Cat	1		**1**	1	0	0	1	1	0	0	NA	100%					
	Human saliva	1		**1**	0	1	0	1	1	0	0	NA	0%					1 false negative RIDT
Overall		**178**	**75**	**58**	**6**	**1**	**10**	**118**	**100**	**15**	**3**	**176**	**157**	**16**	**3**	**94%**	**99%**	

establishment of DDUs and intensified One Health collaboration, potentially many rabies cases were still missed. Data from the health facility survey published in Madjadinan et al. (2020) shows that among the 1'540 registered bite cases the animal was reported killed or dead in 681 cases. Some of these bite cases might have been inflicted by the same animal. It is therefore impossible to know the true number of animals missed for diagnosis. Applying the average number of 2 exposed patients observed among the registered cases on the laboratory level, we estimate that about 340 samples could potentially have been collected (681/2), compared to 114 animal samples with exposure history actually received for testing. This translates to a sampling rate of around 33% (114/340) among reported dead animals on health center level. A more conservative estimate, assuming that each dead animal corresponds to a single patient, would translate into a sampling rate of 18% (114/681).

4. Discussion

The expansion of rabies epidemiological surveillance into three regions of Chad enabled a marked increase in reporting of animal rabies cases and fostered intersectoral collaboration at the level of local human and veterinary health workers. A knowledge, attitudes and practices (KAP) study among human medical and veterinary staff in Logone Occidentale identified a lack of institutional capacity for rabies control and revealed that improving surveillance and establishing diagnosis capability was desired by personnel working in both sectors (Mindekem et al., 2018). This study therefore responded to an expressed need and aimed at empowering local veterinary services. The surveillance capacity of selected veterinary facilities was enhanced at the staff level through training of their agents. Additional enhancement occurred at the infrastructure and material level and in the level of communication and mobility. Empowerment of veterinary workers on these three different levels, combined with increased incentive to report cases, enabled sample collection from areas of Chad where cases were not previously reported. Sample reporting was driven by a parallel bite case study on health centre level and the projects facilitation of communication between the human health and veterinary workers to identify rabies suspect cases. A program to enhance rabies surveillance in Haiti through a holistic, integrative approach yielded similar promising success (Wallace et al., 2015).

Advantages of acquiring better rabies burden data are manifold. Besides substantiating alarmingly high rabies-endemicity in the country, phylogenetic analysis of collected viral specimens will provide insight into the long-distance spread of the disease, which is useful to plan a national dog mass vaccination campaign. The regional difference in reported number of animal rabies cases, together with the incidence of bite cases reported in Madjadinan et al. (2020) can be used to identify areas of high rabies risk, which in turn can inform distribution of PEP vaccine. However, our example also reveals considerable challenges to be anticipated before choosing a decentralized approach. We show that decentralization comes at a high cost especially in areas where reporting remains low despite capacity enhancement as observed in our case in the northern study area of Chad. Investment into training of veterinary staff and improved sample transport is less expensive than peripheral testing shown by cost comparison with the reinforced VDAs. Unfortunately, our research setting does not allow to directly compare the impact on sampling rate between the peripheral testing approach or the approach based solely on supporting sample collection and transport. The areas in which DDUs were installed differed greatly from areas in which VDAs were only reinforced, especially in regard to epidemiological, cultural and geographical background. The Christian dominated Southern Chad has a much higher dog population density than the Islamic Northern regions which potentially results in a higher rabies incidence and higher case reporting. The fact that the two regions bordering N'Djaména had higher reporting rates than the Ouaddaï with a similar cultural background highlights the impact of distance to the central laboratory. Reporting numbers were also extremely different between the urban DDU in Moundou and the other three rural DDUs in the same region. Besides lower rabies incidence and geographical distances other factors such as lacking public awareness in rural areas and potential cultural obstacles to sample taking in an Islamic society might result in a low sampling rate. Therefore the context needs to be taken into consideration for the choice of approach.

Animal rabies diagnosis relies solely on identification of virus in brain material and can, therefore, only be done post-mortem. Rapid sample decomposition influencing the test result and absence of cooling and transport capacities, create a demand for rapid diagnosis. Decentralization of rabies diagnosis or efficient sample transport is therefore crucial for an effective surveillance system. Positive effects of diagnosis decentralization were proven for control of bluetongue in Europe (Zientara et al., 2015). Similarly numerous examples exist for the potential of point of care testing to improve diagnosis and treatment of infectious diseases (Pai et al., 2012; Drain et al., 2014), HIV (Wynberg et al., 2014), and malaria in particular (Boyce et al., 2018). In our case transport did not substantially affect sample quality and only one sample was lost due to transport. This highlights the potential of an efficient sampling and transport strategy even in the absence of peripheral testing possibilities.

For our study the use of the RIDT was a key component of the decentralised surveillance network. Although the RIDT result was still further confirmed by FAT, the feedback received from the veterinarians was very positive. The higher percentage of initiated PEP among patients of positive tested animals also indicates a potential positive impact of a test result on treatment initiation. In our opinion research should be intensified towards a reliable rapid test that can be used for treatment decision to increase perceived benefit of testing to bite victims and dog owners and thus increase public demand for animal rabies diagnosis. We also noted that possibility to perform a test on local level provided an incentive for collaboration between veterinary and human health services. Some heads of health centers wanted the project to establish the test at their facility, which shows the importance and positive perception of rapid test availability. While it would be possible to equip laboratories in provincial health delegations and train human health workers to perform the RIDT, we feel that it is important to keep this capacity within the veterinary services to empower them and obtain balanced capacity between the two sectors necessary for effective One Health communication. Empowerment of veterinary services, currently marginalized in Africa in general and in Chad in particular, is important to achieve sustainable control of rabies and other zoonotic diseases. The need for a One Health approach was well appreciated among human and animal health workers in Chad (Mbaipago et al., 2019). Improving infrastructure, safety, and service capacity and creating a communication system with timely responses are invaluable for increasing work force motivation, which is sorely needed in developing countries (Chaudhury et al., 2006; Willis-Shattuck et al., 2008). New tools such as the RIDT could play the role of a catalyst to collaboration and potentially motivate better work performance. In view of the plan to eliminate dog mediated human rabies by 2030, there is a need to increase the number of well-trained and motivated veterinary personnel (Wallace et al., 2017b). Both peripheral testing and feedback through a communication system (in our case a hotline) potentially increases recognition, which is identified as highly influential for work morale, since individuals feel their work is valued and their contribution can make a difference. A qualitative study among selected participating animal and human health workers as well as among dog owners and patients is currently under way to evaluate the project implementation tools and communication.

At the endemic stage that Chad is facing, improved diagnosis and One Health communication can help reduce vaccine demand through application of IBCM (Undurraga et al., 2017). Later, effective surveillance capable of detecting at least 10% of occurring rabies cases is required to prove absence of disease during an elimination program (Townsend et al., 2013; Hampson et al., 2016). Although we did not

empirically assess the case detection rate achieved during our study, comparison between the number of reported bite cases and the number of positive animal rabies cases observed in the same period suggests that the project achieved a reporting rate well over this threshold in health facilities. Since many victims do not seek help after a bite, sensitization is an important component of effective surveillance. Identified challenges to One Health communication related to lack of experience in reporting, conflicting priorities, unequal distribution of resources between the two sectors and lack of logistical and technical capacities. Other programs to enhance rabies surveillance need to carefully evaluate the capacity of local veterinary services and the knowledge level of veterinary and human health staff to adequately budget cost for initial and continued training and infrastructural support.

Our results show that enhancement of animal rabies surveillance can also trigger reporting of human rabies cases. For the human saliva samples collected, doubtful results were obtained because the specimen material is unsuitable both for RIDT and FAT testing. Unfortunately, due to cultural reasons it was not possible to obtain brain material in these cases. The project did not provide training and material for skin biopsy collection.

A major shortcoming of the project is the attempted but limited sustainability. For long-term sustainability of a surveillance network and national control programs, governmental commitment must be secured. Our project triggered a bottom-up momentum, which led to short-term higher awareness, improved reporting, increased One Health collaboration and better prevention. Of equal importance, and vital to sustainability, is an enforced top-down pressure on governmental bodies, such as ministries of health and livestock, to create communication platforms at higher administrative levels and prioritize rabies control on the national and sub-regional levels. Positive examples of the power of combined community and institutional approaches are documented in Asia (Lapiz et al., 2012) and Latin America (Wallace et al., 2017a).

In 2015, IRED encouraged intersectoral collaboration for rabies control on the ministerial level and organized a consultation meeting to define the process to develop and implement a national strategic plan. Several ministries (Ministry of Communication, Public Health, Territorial Administration, Livestock, Environment and Education) were invited. In addition, representatives of technical international partners such as WHO, FAO, OIE, United Nations Children Fund (UNICEF), Merial and the Commission Economique du bétail, de la Viande et des Ressourves Halieutiques (CEBEVIRAH) were invited. The initiative was, unfortunately, not taken up by the concerned entities for various reasons including competing priorities, lack of perceived importance and lacking resources. A drafted national rabies control plan exists but is to date the sole initiative of the core tripartite research consortium (Swiss TPH, IRED, CSSI). The results of the GAVI funded project provide a first estimate of the extent of the rabies burden in Chad, which hopefully leads to better visibility of the problem by concerned ministries.

Similar projects in Côte d'Ivoire and Mali have led to the establishment of local One Health committees and adoption of national rabies action plans in both countries (Léchenne et al., 2021). However, the costs of an integrated animal rabies elimination program including dog vaccination, access to PEP for all bite patients in need, efficient surveillance and improved education and awareness, cannot solely be borne by the national budget of a developing country with many competing health priorities. Therefore additional, alternative funding sources and strategies should be considered such as Development impact bonds (Aniyam et al., 2017). To improve cost-efficiency of rabies surveillance, synergies should be used with existing national programs for the control of other zoonotic diseases. As such the investment into infrastructure, training, transport and One Health communication is justified through the horizontal strengthening of surveillance and control of Zoonosis in general and will make the rabies elimination agenda sustainable beyond its achieved goal.

5. Conclusion

Decentralization of rabies surveillance in Chad together with reinforcement of sample collection, sample transport, training of veterinarians and facilitated One Health communication led to a significant boost in rabies case reporting allowing for the first time to assess occurrence of animal rabies in selected regions of Chad outside the capital city. Together with other results of the GAVI funded project, this serves as a basis for identifying high-risk areas and further planning of a national rabies control action plan. Despite the positive results achieved, we identified critical shortcomings of the projects decentralized surveillance strategy related to cost, training and sustainability. The biggest challenges observed are the weak infrastructure of public veterinary services, lacking data reporting and management skills of veterinary workers compromising data quality, the high staff turnover in the participating facilities leading to a need for continued training and the high cost per sample, particularly when peripheral testing is applied in areas with low sampling rate. Cost-effectiveness will depend upon epidemiological parameters, geographical and cultural background and factors related to the existing capacity of veterinary services. The best strategy to improve animal rabies surveillance will therefore vary according to the background of an area or country. The relative contribution of decentralization compared to the other capacity strengthening measures could not be assessed by the study. Further research is needed to evaluate the potential positive effect of peripheral testing on public demand of rabies diagnosis, as catalyst for One Health communication and motivation factor for local veterinary services. In the absence of a more in-depth study our experiences provide a basis for reflection for the choice of strategy to improve animal surveillance in other African countries for the agenda towards elimination of dog mediated human rabies by 2030 (Minghui et al., 2018).

Author statement

KN analysed the presented data and wrote the paper together with ML. RMi, NM, AM, EM contributed to the study and the data collection. AO and RMo were the local study coordinators on the veterinary and the human medical side, respectively. RN was the local study PI on the animal health side. RMi and JH provided critical feedback on the manuscript. JZ and ML supervised the research project.

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