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Developments in animal health surveillance, volume II

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Published in
Frontiers in Veterinary Science

ISSN 1664-8714
ISBN 978-2-8325-5760-0
DOI 10.3389/978-2-8325-5760-0

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Developments in animal health surveillance, volume II

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Citation
Phiri, B. J., Hernandez-Jover, M., Hidano, A., Martinez Aviles, M., eds. (2024). *Developments in animal health surveillance, volume II*. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-5760-0

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Frontiers | Frontiers in Veterinary Science

TYPE Editorial
PUBLISHED 26 November 2024
DOI 10.3389/fvets.2024.1505140

Check for updates

OPEN ACCESS

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RECEIVED 02 October 2024
ACCEPTED 11 November 2024
PUBLISHED 26 November 2024

CITATION
Phiri BJ, Hernandez-Jover M, Hidano A and Martinez Aviles M (2024) Editorial: Developments in animal health surveillance, volume II. *Front. Vet. Sci.* 11:1505140.
doi: 10.3389/fvets.2024.1505140

Editorial: Developments in animal health surveillance, volume II

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KEYWORDS

surveillance, biosecurity, animal health, epidemiology, disease, detection, incidence, prevalence

Editorial on the Research Topic
Developments in animal health surveillance, volume II

The functions of animal health surveillance include substantiating the absence or distribution of specified disease while facilitating the early detection of exotic or emerging diseases (1). Ideally, surveillance should be timely, sensitive, easy to implement, inexpensive and resource efficient. Fulfilling these functions and attributes is challenging. Specific challenges include limited resources, the ever-lurking threat of disease incursion or spread, underreporting of cases, sustaining motivation for stakeholder participation and the quest to enhance existing surveillance systems. Overcoming these challenges requires continuous effort and novel approaches. Therefore, the goal of the current Research Topic was to collate research-based evidence for solutions or innovative approaches to overcome some of the challenges under different settings.

A useful way to bolster an early warning system is to optimally utilize available resources by using data collected for other purposes. However, the strengths and limitations of such data should be assessed to set the appropriate expectation of their value. Eze et al. examined two utility datasets: a mandatory register (Cattle Tracing System) and a voluntary catalog of fallen stock. Each of the two data sources provided some measure of mortality in the Scottish cattle population. Neither data source was ideal by itself but were complementary. Thus, analyzing and interpreting them in parallel was necessary to produce optimal surveillance outputs. Another possible source of valuable surveillance intelligence is regularly collected on-farm data. In the United States of America, on-farm swine production and disease surveillance data were examined for the prospect of enhancing African swine fever (ASF) surveillance (Schambow et al.). A consultative approach involving a broad range of stakeholders was used to determine the value of the data in enhancing surveillance. Pertinent issues requiring attention to fully realize the value of the data were raised, including data input and sharing, stakeholder expectations, collaboration, labor, and the cost of diagnostic testing. Overall, ordinary on-farm data, along with other types of data, can provide valuable surveillance intelligence when subjected to thorough analysis.

Underreporting of cases is a common phenomenon in many surveillance systems across the world. In Madagascar, underreporting led to the ineffective surveillance of rabies. Resource-deprivation was identified as the main cause of this challenge. Recommended mitigation measures included allocating more resources and/or better utilization of existing ones. For instance, a One-Health approach could be used to pool resources from the veterinary and public health sectors (Dreyfus et al.; Andriamandimby et al.). In France, an innovative holistic and inter-sectoral framework optimized the usage of available resources to enhance the efficiency of animal health surveillance. This was achieved by forming platforms composed of experts from different industries (Dupuy et al.). Newer technology can also help in using available resources efficiently. The Haiti national rabies surveillance program adopted an electronic application for managing its integrated bite case management in 2018. Previously, bite case management was paper based. The newer technology led to superior data quality, improved data completeness, and shortened durations for notifications. Overall, the timeliness of surveillance improved because the flow of data and analysis were quicker compared to the paper-based system. These gains were achieved with minimal increase in operational costs (Schrodt et al.).

Movement of animals is a common pathway for disease spread. Hence, in-depth knowledge of animal movement patterns is very informative in developing targeted surveillance and disease control measures. A description of trade networks for cattle, small ruminants and pigs in Uganda provided useful insights for this purpose. The networks were derived from the 2019–2021 data for animal movement permits. The findings highlighted key nodes that could be targeted to enhance surveillance and inform decision-making regarding infectious animal disease control (Hasahya et al.). Similarly, an analysis of factors influencing seasonal peaks and regional movement patterns of beef cattle in Japan provided useful biosecurity insights. The findings could inform the development of risk-based surveillance measures suited for specific age groups, regions, and seasons (Murato et al.). Identifying influential nodes or factors along disease transmission pathways allows for the application of resources where they will maximize surveillance sensitivity.

Keeping stakeholders actively engaged and participating in surveillance to maintain a vibrant early warning system can be challenging. The Canadian dairy network for antimicrobial stewardship and resistance tackled this difficulty by allowing farmers and veterinarians to visualize data online. Metrics for antimicrobial use were benchmarked in relation to antimicrobial resistance and animal health in dairy herds. This allowed comparisons among participant farms with the view of enhancing antimicrobial stewardship practices on dairy farms in Canada (Fonseca et al.). However, similar bidirectional communication with stakeholders needs to be well-managed. For instance, in situations where outbreak alerts are communicated to stakeholders, the quality and frequency should be well-balanced. Frequent alerts that are not meaningful or irrelevant to stakeholders can damage the credibility of the surveillance system and diminish stakeholder participation. In the United Kingdom, veterinary practitioners were consulted in selecting notification thresholds that were clinically relevant for detecting genuine outbreaks of canine disease (Tamayo Cuartero et al.). Unimpeded communication between surveillance operators and those involved more directly with animals is invaluable for both detecting outbreaks early and influencing appropriate biosecurity practices.

Timely production of surveillance outputs is vital for the success of disease control efforts, particularly for fast-spreading diseases like foot and mouth disease (FMD). Ellis et al. provide evidence that intensive environmental sampling could detect FMDV in a herd more quickly than clinical inspection. Adopting this technique could drastically reduce the cost of FMD control. The authors also evaluated, using a mathematical model, if at-risk farms could be monitored using environmental sampling instead of resorting to pre-emptive culling so that the number of animals culled may be reduced to minimize the socio-economic impact on farmers. Similarly, machine-learning based technology can enhance early detection. The performance of video surveillance system in detecting lameness in dairy cattle was found to be comparable to that of two experienced veterinarians in the United Kingdom. Additionally, the video system was more sensitive than a trained veterinarian in detecting painful foot lesions (Anagnostopoulos et al.). Use of smart technology could not only improve the efficiency of surveillance but also free up resources like veterinary practitioners to perform other functions.

The articles in the current Research Topic provide valuable contributions to the pool of alternatives for improving animal health surveillance. These alternatives include using available resources more holistically, such as adopting a One-Health or inter-sectoral approach. Underreporting can be minimized by implementing surveillance methods that are easy to apply, and the use of smart technology is a feasible option for this purpose, provided it is accepted by key stakeholders. Gaining insights into disease transmission pathways, along with their temporal and spatial influencing factors, enables the implementation of risk-based surveillance. It also allows for the deployment of resources where they are most needed, maximizing the benefits. Maintaining social license and fostering productive stakeholder engagement are crucial for an early warning system to function effectively. Demonstrating to stakeholders that their contribution is valued and relevant is essential in this regard. Practical steps include allowing visualization of a broad perspective derived from the aggregated data that is relevant or helpful to stakeholders. For instance, visualizing geographical variations across a country or having the ability to benchmark farm performance against the geographical averages for variables such as disease incidence or drug usage. Ultimately, animal health surveillance systems around the world have similar functions but vary in capacities and capabilities, yet all aspire to improve.

Author contributions

BP: Writing – original draft, Writing – review & editing. MH-J: Writing – review & editing. AH: Writing – review & editing. MMA: Writing – review & editing.

Acknowledgments

We appreciate the contribution of all participating authors and reviewers. We want to thank Frontiers in Veterinary Science, in Public Health, and in Medicine for the opportunity, all the reviewers for their dedicated time and efforts, all the authors who contributed to the Research Topic, and the external editors who kindly collaborated with us Alasdair James Charles Cook, Kimberly

VanderWaal, Krishna Thakur, Michael Sanderson, Latiffah Hassan, and Francois Louis Roger.

Conflict of interest

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frontiers in Veterinary Science

ORIGINAL RESEARCH
published: 12 January 2022
doi: 10.3389/fvets.2021.799622

Canadian Dairy Network for Antimicrobial Stewardship and Resistance (CaDNetASR): An On-Farm Surveillance System

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Specialty section:
This article was submitted to Veterinary Epidemiology and Economics, a section of the journal Frontiers in Veterinary Science

Received: 21 October 2021
Accepted: 20 December 2021
Published: 12 January 2022

Citation:
Fonseca M, Heider LC, Léger D, Mcclure JT, Rizzo D, Dufour S, Kelton DF, Renaud D, Barkema HW and Sanchez J (2022) Canadian Dairy Network for Antimicrobial Stewardship and Resistance (CaDNetASR): An On-Farm Surveillance System. Front. Vet. Sci. 8:799622. doi: 10.3389/fvets.2021.799622

Canada has implemented on-farm antimicrobial resistance (AMR) surveillance systems for food-producing animals under the Canadian Integrated Program for Antimicrobial Resistance (CIPARS); however, dairy cattle have not been included in that program yet. The objective of this manuscript was to describe the development and implementation of the Canadian Dairy Network for Antimicrobial Stewardship and Resistance (CaDNetASR). An Expert Panel (EP) of researchers was created to lead the development of the dairy surveillance system. The EP initiated a draft document outlining the essential elements of the surveillance framework. This document was then circulated to a Steering Committee (SC), which provided recommendations used by the EP to finalize the framework. CaDNetASR has the following components: (1) a herd-level antimicrobial use quantification system; (2) annually administered risk factor questionnaires; and (3) methods for herd-level detection of AMR in three sentinel enteric pathogens (generic *Escherichia coli*, *Campylobacter* spp., and *Salmonella* spp.) recovered from pooled fecal samples collected from calves, heifers, cows, and the manure pit. A total of 144 dairy farms were recruited in five Canadian provinces (British-Columbia, Alberta, Ontario, Québec, and Nova-Scotia), with the help of local herd veterinarians and regional field workers, and in September 2019, the surveillance system was launched. 97.1 and 94.4% of samples were positive for *E. coli,* 63.8, and 49.1% of samples were positive for *Campylobacter* spp., and 5.0 and 7.7% of samples were positive for *Salmonella* spp., in 2019 and 2020, respectively. *E. coli* was equally distributed among all sample types. However, it was more likely that *Campylobacter* spp. were recovered from heifer and cow samples. On the other hand, it was more common to isolate *Salmonella* spp. from the manure pit compared to samples from calves, heifers, or cows. CaDNetASR will continue sampling until 2022 after which time this system will be integrated into

CIPARS. CaDNetASR will provide online access to farmers and veterinarians interested in visualizing benchmarking metrics regarding AMU practices and their relationship to AMR and animal health in dairy herds. This will provide an opportunity to enhance antimicrobial stewardship practices on dairy farms in Canada.

Keywords: dairy cattle, antimicrobial use, antimicrobial resistance, surveillance, Canada

INTRODUCTION

Antimicrobial resistance (AMR) is a natural phenomenon that occurs when bacteria evolve and no longer respond to antimicrobial drugs that previously were efficacious. Major economic losses and animal health and welfare problems have been described as the consequences of AMR (1, 2). Many AMR commensal and pathogenic bacteria have been described in food animals. For instance, a study conducted in North California demonstrated that all *Salmonella* Newport isolates recovered from dairy cattle fecal samples (symptomatic and asymptomatic animals) were multidrug-resistant (3). Infections caused by *Salmonella* Newport can cause economic losses due to treatment failure and increase mortality rates in animals (4). Many bacterial organisms, including *Salmonella* Newport can be shared between human and animal populations. In humans, AMR can make treatment of bacterial infections more challenging, increase treatment costs, allow for increased disease spread, and increase the risk of mortality in people (5). It is estimated that 700,000 deaths worldwide are caused annually by antimicrobial resistant bacteria and, by 2050, this figure may increase to 10 million (6). For these reasons, AMR is considered one of the major challenges to public health (7).

To address the global problem of AMR, many countries have developed and implemented AMR surveillance systems for humans and animals. A surveillance system can be defined as "a system based on continuous information recording, making it possible to monitor the health status of a given population and the risk factors to which it is exposed, to detect pathological processes as they appear and study their development in time and space, and then to take appropriate measures to control them" (8). The main objectives of an on-farm AMR surveillance system are: (1) to determine the current prevalence of AMR (2) to describe AMR trends; (3) to detect the emergence of new types of resistance; and (4) to track a particular type of resistance (9).

In addition, this surveillance system should be able to provide estimates of the types and amount of antimicrobials used on farms. Evidence (6) suggests associations between using certain antimicrobials in animals with resistance in clinical bacterial isolates from humans (10). Similar to the situation in humans, there is also a strong association between antimicrobial use (AMU) and AMR in the livestock sector (11–14). In the dairy sector, the route of administration and the antimicrobial active ingredient seem to play an important role in the development of antimicrobial resistance. A study conducted in Canada demonstrated that the use of systemic antimicrobials was associated with resistance in non-aureus staphylococci isolated from milk, while intramammary treatments were not (15). However, a study conducted in Ohio found that the use of cephalosporin based dry cow therapy was associated with recovering a greater number of fecal coliform bacteria with reduced susceptibility to cephalothin and streptomycin in dairy cows (16).

Recognizing the interrelationship between AMU/AMR in humans and animals and the need for the standardization of methods between countries (e.g., AMU metrics, target pathogens, etc.), in 2018, the Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), and the World Health Organization (WHO) formed a tripartite alliance (FAO-OIE-WHO) focusing on a "One Health" approach to AMR (17). The "One Health" approach includes surveillance of important AMR organisms and AMU in humans, animals, and the environment.

In support of this One Health approach to AMR, many countries developed surveillance systems to monitor AMU and AMR in food animal agriculture (15). Many of these surveillance systems report the proportion of antimicrobial resistant isolates of *Salmonella* spp., *Campylobacter* spp., and *Escherichia coli* (8), as these pathogens can be transmitted zoonotically through the food chain to humans.

Denmark and the Netherlands have comprehensive AMU surveillance systems (DANMAP and Nethmap-MARAN, respectively) (18). In Canada, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) was developed in 2002 to collect and analyze AMU/AMR data, and report trends in AMU and AMR from human, retail food, and food-producing animals (19). In 2006, CIPARS implemented an on-farm component in grower-finisher pigs; then, in 2013, in broiler chicken and turkey (20), and in 2019, a surveillance system for feedlot cattle was started (21). These national surveillance systems collect AMU data at the farm level to facilitate AMU benchmarking for farms and for developing interventions toward antimicrobial stewardship (AMS).

Reducing AMU in humans and animals is crucial to diminish the burden of AMR and prolong antimicrobial efficacy (22). In Canada, initiatives led by the Canadian Veterinary Medical Association (CVMA) and the Public Health Agency of Canada (PHAC) have created guidelines to improve AMS. The CVMA defines AMS as "multifaceted and dynamic approaches required to sustain clinical efficacy of antimicrobials." In 2017, the PHAC released the document "*Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action.*" The framework's goal was to strengthen the ability to fight AMR in a coordinated, multisectoral and effective manner (23). AMS was one of the components promoted to achieve the goal. However, despite these initiatives, there are still challenges because the coordination of AMS leadership is sparse and inconsistent across the country (23).

In the dairy sector, some factors, such as dairy consumer perception, government requirements, and animal and human health are the main reasons for continuing to work on AMS programs (24). Recognizing the knowledge gap on AMR and AMU in the dairy sector in Canada, the Canadian Dairy Network for Antimicrobial Stewardship and Resistance (CaDNetASR) was developed to help determine and improve AMU stewardship on Canadian dairy farms. This surveillance system will estimate AMU, determine how and why antimicrobials are used on dairy farms, and determine AMR patterns and trends in the Canadian dairy sector. This manuscript aims to describe the development and implementation of a national on-farm surveillance system (CaDNetASR), for an ongoing AMU and AMR data collection on Canadian dairy farms, toward improved AMS in this production sector.

CaDNetASR SURVEILLANCE FRAMEWORK DEVELOPMENT AND IMPLEMENTATION

Research personnel from five veterinary colleges in Canada (University of Prince Edward Island, University of Guelph, University of Saskatchewan, University of Montreal, University of Calgary) and PHAC recognized the lack of information regarding AMU, AMR, and the importance of improving AMS in the Canadian dairy sector. Together they decided to develop a surveillance system to fill the knowledge gap. This diverse group of researchers had expertise in epidemiology, antimicrobial resistance, dairy production medicine, surveillance system development, and public policy.

In order to initiate the development of the surveillance system a 5-year proposal was developed and funded by Dairy Farmers of Canada and Agriculture and Agri-food Canada, under the Dairy Research cluster 3 program, and by PHAC and the University of Prince Edward Island (UPEI). After the initial funding (2018–2022) the intention is to incorporate this system into CIPARS.

An Expert Panel (EP) was created to develop a farm-based surveillance framework for AMU, AMS, and AMR on dairy farms across Canada. The EP was composed of researchers from six Canadian universities (University of Prince Edward Island, University of Guelph, University of Saskatchewan, University of Montreal, University of Calgary, and Memorial University) and veterinary epidemiologists from the PHAC.

In the summer of 2018, members of the EP developed a draft of the surveillance framework. As part of the framework development, it was decided that the surveillance system should be deployed in five regions across Canada. These regions were the communities of Truro/Halifax in Nova Scotia, Montérégie region in Québec, London Middlesex in Ontario, Calgary-East in Alberta, and Fraser Valley in British Columbia, which are part of the sentinel sites from FoodNet Canada, a surveillance system focused on foodborne and waterborne diseases (25).

During the initial development phase of the surveillance framework, a Steering Committee (SC) was created, and the framework was sent to them for comments in January 2019. The SC was composed of relevant stakeholders from provincial and national milk boards (e.g., Dairy Farmers of Canada), veterinary organizations (e.g., Canadian Association of Bovine Veterinarians), PHAC, dairy herd improvement organizations and others. The role of the SC was to provide input on developing the surveillance framework for implementation in 2019 and ensure that the methods to collect farm samples and data were practical and sustainable. In addition, SC members were tasked with disseminating findings from the surveillance system to their respective organizations.

After the initial development of the framework, the EP and the SC, came together for a 2-day meeting whereby the framework was introduced and discussed. Suggestions were offered to improve the quality of data generated and introduce the surveillance system to the Canadian dairy industry. The information generated from this meeting was used to refine and finalize the surveillance framework. A final framework was ready for implementation in the spring of 2019.

For the implementation of the surveillance system, an operation committee was created. The operations committee was composed of all EP members, regional project managers, regional field workers, technicians and graduate students involved in the system. The role of the operations committee was to provide feedback on the operational issues through monthly meetings after the surveillance implementation and contribute to potential refinements of the surveillance system.

Each of the five regions had one regional project manager responsible for overseeing herd selection, the data collection and supervising the regional field workers. The regional field workers scheduled the farm visits and conducted the sampling based on the protocols provided. The surveillance system (CaDNetASR) was implemented in September 2019 and continued for 4 years in the first round of funding. The development and implementation of CaDNetASR is illustrated in **Figure 1**.

CaDNetASR SURVEILLANCE COMPONENTS

The CaDNetASR surveillance includes all the critical components for AMR and AMU surveillance, collecting, analyzing, and reporting AMR and AMU in dairy herds at the farm level. The components of CaDNetASR are described below and are illustrated in **Figure 2**.

Farm Enrollment

As the AMU stewardship was a key component in the surveillance system, the sample size was calculated to estimate an AMU rate with a precision of +/- 0.3 for various antimicrobials based on the assumption that 95% of the farms have AMU rates between 0.001 and 4 ADD/1,000 cows (26). Therefore, the goal was to select 30 farms from each of the five regions to participate in the research project. At implementation in 2019, a convenience sample of 144 dairy farms was enrolled. All regions enrolled 30 farms except Nova Scotia, where only 24 farmers agreed to participate. In 2020, three herds from British Columbia

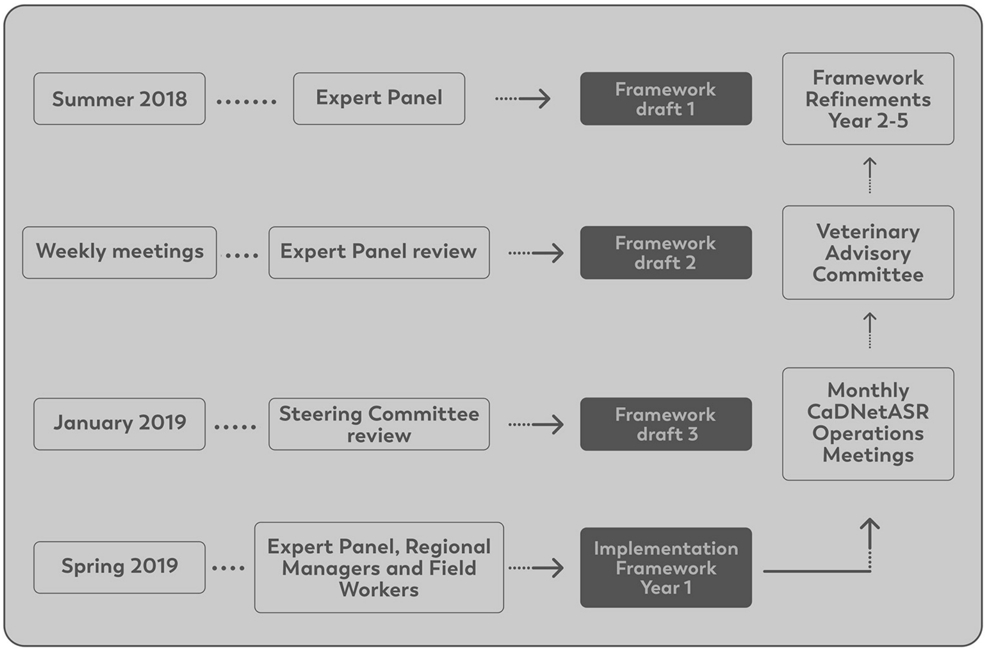

FIGURE 1 | CaDNetASR framework development and implementation.

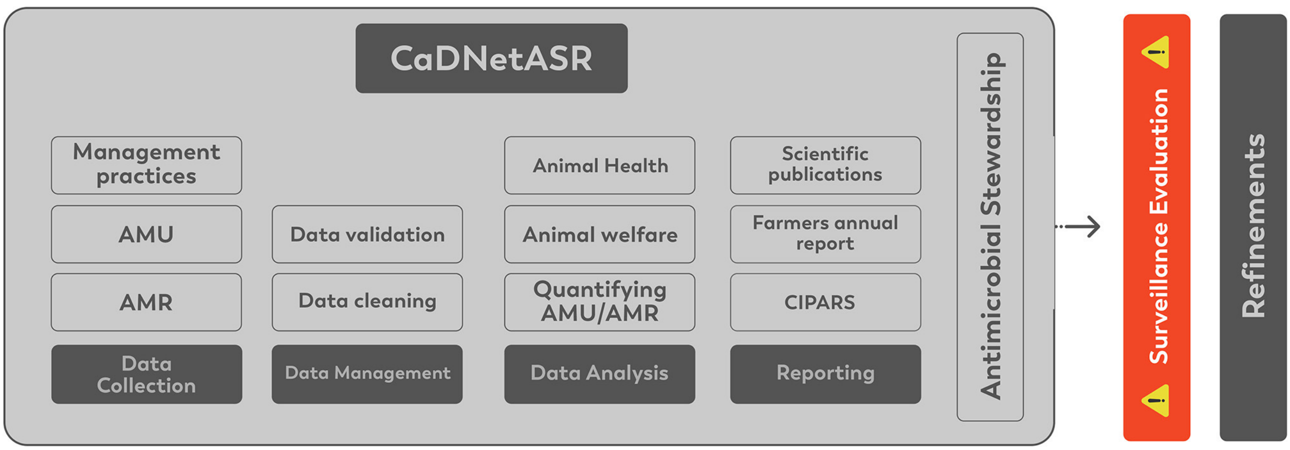

FIGURE 2 | CaDNetASR surveillance system components.

and one herd from Quebec dropped out of the program and were replaced with new herds. Farms should be representative of commercial dairy operations in each region. The following inclusion criteria were considered: (1) farms should be enrolled in ProAction/CQM (national mandatory certification program focused on several aspects of milk production) and DHI (dairy herd improvement organization responsible for milk recording, genetic evaluations and knowledge transfer in Canada); (2) minimum herd size of 50 animals except for Nova Scotia, that was minimum herd size of 40 animals; (3) raise their replacement heifers on-site; (4) Antimicrobial-free, organic or robotic herds should be enrolled proportional to their prevalence in a given region; (5) farmers should be willing to provide/share drug purchase information obtained from their veterinary clinics and feed mills. The only exclusion criteria were farms not planning to continue farming for the next 5 years. To protect the identity of participating farms, each farm was assigned an identifier, and only the regional project managers recorded which farm was linked to the study identifier to maintain anonymity. All producers signed an informed consent form explaining the project objectives and their role as participants, at the beginning of the 1st year, which was reviewed with them annually. The summary of demographic information for the dairy farms enrolled in CaDNetASR is presented in **Table 1**.

TABLE 1 | Summary of demographic information from dairy farms enrolled in CaDNetASR during 2019 and 2020.

	Province				
Characteristic	**British Columbia**	**Alberta**	**Ontario**	**Quebec**	**Nova Scotia**
Farms enrolled	30	30	30	30	24
Herd size* (mean)	175.3	170.4	159.8	86.3	101.1
% Free stall	100.0	96.6	87.1	21.4	62.5
% Tie-stall	0.0	3.3	9.7	74.2	37.5
% Other housing	0.0	0.1	3.2	4.4	0.0
Milking parlor	57.1	76.6	48.4	21.4	37.5
Robotic	42.9	23.4	41.9	12.9	16.7
Milking Pipeline	0.0	0.0	9.7	65.7	45.8
% Holstein	90.7	93.7	97.9	91.9	97.0
% Jersey	6.0	3.6	0.7	0.8	0.7
% Other breeds	3.3	2.7	1.4	7.3	2.3

*Number of lactating cows.

Data Collection, Data Management, and Reporting

On-farm data collection included annual collection of fecal samples, a bulk tank milk sample (BTM), administration of questionnaires to collect herd management practices, AMU, and risk factor information for AMR related projects/questions. The main sections of the questionnaires are presented in **Supplementary Tables 1**, **2**. Regional field workers collected pooled fecal samples from up to five pre-weaned calves, five breeding age heifers and five lactating cows and a single sample from the manure storage system by pooling from three to five different locations in that system. Standardized sampling kits designed by PHAC were sent to each regional project manager.

Samples were stored in a cooler with ice and sent to be processed at the central laboratory. Upon arrival at the laboratory, samples were processed for generic *E. coli*, *Campylobacter spp*., and *Salmonella spp*., in addition to preserving the raw sample following the protocol used by CIPARS (19). A 1 mL aliquot of each sample was saved for potential further processing. If there was growth on any of the three plates, then a single representative bacterial isolate was selected and stored. In 2019, a total of 560 fecal samples were collected and cultured. The proportion of samples positive for each target bacterial species were as follows: *E. coli* - 97.1% (544/560); *Campylobacter* spp.—63.8% (357/560); and *Salmonella* spp.—5.0% (28/560). In 2020, a total of 574 samples were collected and cultured. 94.4% (542/574), 49.1% (282/574), and 7.7% (44/574) of samples were positive for *E. coli*, *Campylobacter* spp. and *Salmonella* spp., respectively. The information is presented in **Table 2**. Susceptibility testing on the stored isolates was done using the broth microdilution system method (Sensititre, ThermoFisher, Mississauga). *E. coli* and *Salmonella* spp. were tested against 14 antimicrobials using the CMV2AGNF plate (27), and *Campylobacter* spp. was tested against eight antimicrobials using the CAMPY AST plate designed by the National Antimicrobial Resistance Monitoring System (28). All results were extracted to a Microsoft Excel (office 16) spreadsheet by the laboratory technicians and uploaded into the central digital platform.

During the initial phase of CaDNetASR, the garbage can audit (GCA) was implemented for a period of 6 months to quantify AMU. The farmers were advised to deposit all the empty antimicrobials vials (bottles, packages, and tubes) in the receptacles, which were placed strategically where antibiotics might be administered around the farm. The contents of the receptacles were collected and recorded by the regional field workers. In addition, the regional field workers collected information on the antimicrobial inventory at the beginning and the end of the GCA period. The quantities of each antimicrobial were later converted to dose-based metric developed for Canadian dairy cattle as published by Lardé et al. (29). For the following years, antimicrobial use will be estimated using veterinary clinic dispensing records. A Veterinary Advisory Committee (VAC) composed of three veterinarians was created to help understand how best to extract information from clinic electronic medical records. The surveillance components on AMU and AMR data are summarized in **Table 3**.

Data are managed through a collaborative and integrated computer system developed to store the data generated by the surveillance system efficiently. All data are standardized, validated, and uploaded to the central digital platform. All information stored in the digital platform is protected by restricted access. The data flow is illustrated in **Figure 3**.

An important component for surveillance systems is knowledge dissemination. There is a diverse group of stakeholders interested in data regarding AMU and AMR in dairy cattle. These include veterinarians, academia, industry, policymakers, producers, government, public, among others. After each year, summary findings on AMU and AMR are being sent to participating producers and their veterinarians (**Supplementary Figure 1**). Reports include benchmarking data on AMU, which allow comparisons within participant farms. The report also includes a summary of AMR in the target pathogens. CIPARS publishes annual reports and will incorporate the dairy cattle data along with other animal species (e.g., pigs, poultry, and turkey). Peer-reviewed publications and abstracts for conferences are being prepared according to data availability.

DISCUSSION

There is increasing pressure on animal agriculture to justify the use of antimicrobials to treat and prevent infections in animals. Antimicrobial use is the main driver of resistance in target and non-target bacteria in food animals, which can potentially pass to humans via the food chain (30). In the United States, almost 70% of respondents from the general public believed that AMU in dairy cattle represented a moderate to high threat to human health (31). In another study in Canada, 28% of the respondents from the general public reported that they prefered not to consume products from animals raised with antimicrobials (32). The development of CaDNetASR provides AMR and AMU

TABLE 2 | Proportion (%) of fecal samples positive for target bacteria processed in 2019[a] and 2020[b].

Target bacteria	Calf		Heifer		Cow		Manure pit	
	2019	**2020**	**2019**	**2020**	**2019**	**2020**	**2019**	**2020**
Generic *E. coli*	97.9	98.6	99.3	99.3	99.3	100.0	92.1	79.7
Campylobacter spp.	31.4	21.5	82.9	66.4	84.3	72.2	56.4	36.4
Salmonella spp.	3.6	3.5	2.1	4.9	2.9	4.9	11.4	17.5

[a]*A total of 140 samples were analyzed by each production phase and manure pit;* [b]*A total of 144 samples were analyzed by each production phase and manure pit.*

TABLE 3 | Summary of the key activities of the CaDNetASR on-farm surveillance system.

Data collection	**Data management**	**Data analysis**	**Data reporting**	**Antimicrobial stewardship**
AMR Annual bulk tank milk and composite fecal samples from: • Pre-weaned calves • Breeding age heifers • Lactating cows • Manure storage	Samples are shipped to one central laboratory and cultured for: • Generic *E. coli* • *Campylobacter* spp. • *Salmonella* spp. • Antimicrobial susceptibility test (MIC) Freeze-dried isolates bank • The results from the laboratory are recorded and uploaded to the central digital platform. All the data is anonymized for privacy protection	Analysis of resistance profiles over time, regions, and sample types	• Annual report with summary AMR results and AMU benchmarking for farmers and veterinarians • Scientific publications • CaDNetASR results integrated with CIPARS reports (integrated surveillance data reporting AMU and AMR trends from animals and humans)	• Development of decision support charts and guidelines for efficient use of antimicrobials • Develop decision support tools and educational material highlighting the importance of the prudent use of antimicrobials • Target interventions on management practices where the use of antimicrobials can be done more responsibly (e.g., dry-cow treatment, udder infections, etc.)
AMU Annual collection of dispensing veterinary records	All AMU data are converted to the dose-based metric (DDD/DCD) and uploaded to the central digital platform after being validated by members of the operations committee. All the data is anonymized for privacy protection	Analysis of AMU converted to DDD and DCD/100 animals/year over time, regions, active ingredients, and administration routes		
Questionnaire Annual data collection on management practices (demographics, animal health, biosecurity, AMU)	Each regional field worker is responsible for recording the questionnaire information into a spreadsheet that is uploaded to the central digital platform after being validated by the regional managers.	The questionnaires will provide information on potential risk factors that can contribute to the development of AMR, which can impact animal health and animal welfare		

information for another major food animal production system in Canada.

Antimicrobial stewardship is a key factor for mitigating the effects of AMR (21) but changing how antimicrobials are used on farms can be challenging. To improve AMS in the food animal industries in Canada, all Medically Important Antimicrobials (MIAs) for veterinary use are sold by veterinary prescription only. Additionally, to support AMS by veterinarians, the CVMA launched the "SAVI" initiative (The Stewardship of Antimicrobials by Veterinarians Initiative). This initiative was supported by the government of Canada and the Canadian Agricultural Partnership. It consists of an electronic platform that has information on AMS and helps veterinary practitioners make informed decisions on AMU in their patients (33). CaDNetASR will support these initiatives by collecting and analyzing AMU and AMR and determining any changes that may be occurring.

AMS initiatives can have significant impacts on AMU and AMR on farms. For example, in the Netherlands there are compulsory and voluntary programs that affect AMS in farm animals, including dairy cattle. The RESET Mindset Model (34) was a stewardship strategy used in the Netherlands in the dairy sector aiming to limit the use of critically important antimicrobials and to ban the preventive use of antimicrobials as in blanket dry cow treatment. This model is

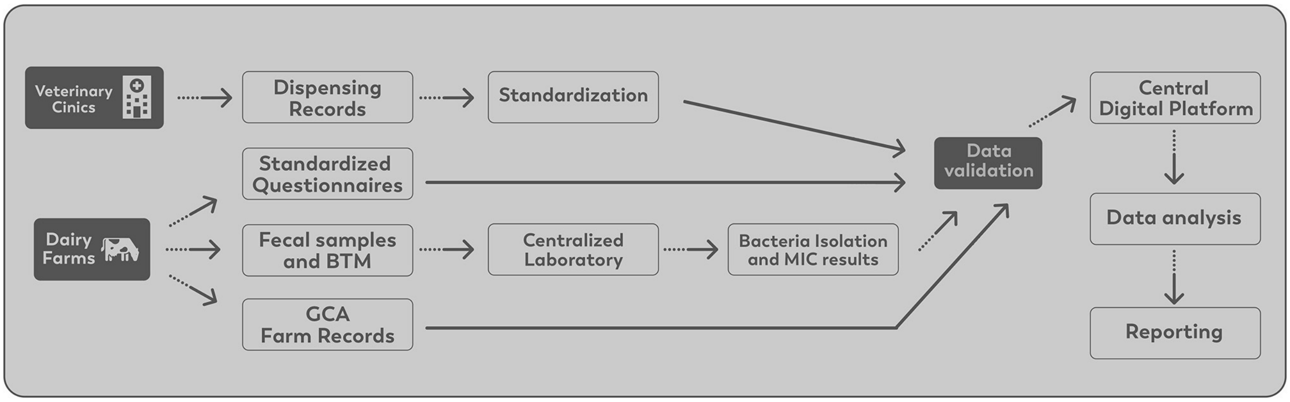

FIGURE 3 | CaDNetASR communication policy and data flow.

a behavioral change intervention aimed at more rational use of antimicrobials by farmers and veterinarians and has proven to be effective at reducing AMU. These programs combined with new regulations have resulted in a 56% decrease in total AMU on participating farms between 2007 and 2012 (35, 36). In Switzerland, interventions targeting management practices on udder health, uterine health, and calf health were implemented on farms that were followed for 3 years. The implementation of these interventions provided knowledge for evidence-based decisions that contributes to better AMU stewardship (37).

Most dairy farms in Canada are in the provinces of Quebec and Ontario, and the production of fluid milk is regulated in Canada using a quota system. Federal and provincial organizations adjust quota to meet expected consumer demand. Milk produced in a province is frequently consumed within the province. Therefore, to ascertain AMR and AMU practices for Canadian dairy herds, it is necessary to conduct surveillance in as many provinces as possible. Each farm is visited annually for sample collection from three different age groups, which can aid in investigating AMR patterns in all stages of dairy production and may help target interventions where they are needed most. Additional data (herd demographic and farm management information) were collected on-farm using two questionnaires. All the information collected is standardized and stored in a central database. In the first 2 years, the questionnaires were administered using standardized spreadsheets that required manual data entry. In the process of validating these data, input errors were found, which had to be corrected. Automated processes for data entry are preferable to manual entry, and in future years, data will be uploaded from a hand-held device directly to a central database without the need for manual data entry.

The primary outcome of CaDNetASR is to inform the Canadian dairy industry, the general public, and policy decision makers on the level of AMU and AMR, and the impact that AMS practices have on AMU and AMR on Canadian dairy farms. Recently, 15 countries collecting AMU data at the farm level were identified (38). Among these countries, 12 have dairy surveillance programs monitoring AMU (**Supplementary Table 3**), and only seven of these countries collect and report AMU at the farm level. A major feature of CaDNetASR is that AMU data is collected at the farm level for dairy cattle. Farm level AMU data results in better estimates of AMU as it can account for the number of exposed animals, exposed time, and biomass on individual farms and allows for benchmarking, which can be used to compare high and low users of antimicrobials (38).

High quality estimates of AMU from surveillance programs are essential to provide reliable results. AMU estimates can be made from a variety of sources. In Denmark, for instance, there is a national, centralized database (VetStat) that collects AMU data at the herd level. The VetStat was implemented in 2000, and the program estimates AMU by collecting antimicrobial dispensing records from pharmacies, veterinarians, and feed mills for individual farms (39). In the Netherlands, estimation of farm level AMU started in 2004 with the implementation of MARAN (Monitoring of Antimicrobial Resistance and Antimicrobial Usage in Animals in the Netherlands). At the implementation, only a sample of farms was part of the program, and the experience gained with MARAN was used as a base for the development of a sectoral quality assuring system that collects AMU data nationally from the different animal sectors in Netherlands (38). In 2010, the Netherlands Veterinary Medicines Authority (SDa) was established to receive and centralize the AMU information from the sectoral systems (veterinary prescriptions) and from national sales (pharmaceutical industry). All the AMU information is reported annually through the MARAN program.

Since 2018, the Veterinary antimicrobial sales reporting system (VASR) system in Canada has provided an annual report regarding the sales of veterinary antimicrobials considered important for human medicine (40). The information gathered by the VASR system provides crude estimates of the amount of antimicrobials used in animals in the different agricultural production sectors. This information is adequate to estimate AMU on a national scale but is not precise enough to estimate AMU at the farm level (41).

Efforts in Canada to improve farm-level estimates of AMU are ongoing. One method that has been used is the GCA, which is considered the reference test for farm-level AMU estimates. GCAs are very labor intensive and time consuming, so other approaches for estimating AMU must be found. In Québec, a recent study investigated different methods of collecting AMU data at the farm level (42). GCA was used as reference method and were compared with information collected through veterinary invoices, information from the Am9lioration de la Sant9 Animale au Qu9bec (ASAQ) Program (Provincial Government), and farm treatment records. It is important to mention, that in Québec, almost 90% of the veterinary clinics providing antimicrobials to dairy farms, use the same office management software (Vet-Expert software), which facilitates data standardization (42).Veterinary invoices were found to have almost a perfect agreement with GCA and proved to be a reliable estimate of AMU. In the CaDNetASR system, the collection of veterinary clinics dispensing records was chosen to estimate farm-level AMU. This will demand standardization because of the variety of software packages used by veterinary clinics in Canada (other than the province of QC). To help with this process, 49 veterinary clinics that provided veterinary services, including sales of antimicrobials, to the 144 enrolled dairy herds were contacted and asked about their clinic software and how their AM sales were tracked. Responses from 23 clinics showed that only eight different electronic software systems were being used. Furthermore, there were also many differences in how sales were reported within each system. Consultations with the VAC helped CaDNetASR administrators understand the challenges associated with AMU data extraction from these different systems and to help determine the best approach to clinic engagement for data provision. Members of this group also provided preliminary herd-level dispensing data, which were helpful in the development of automated routines necessary for the standardization of dispensing record data. This approach to AMU data collection and estimation will improve the quality of the dispensing record data received by CaDNetASR.

AMU data collected by CaDNetASR, was transformed into a dose-based metric, to account for the different dosages among the different active ingredients. The dose-based metric divides the total amount of antimicrobial used (mg) by total animal weight and estimate daily dose for the antimicrobial (43). There is no perfect metric, and the choice of a metric to be used should be made based on the surveillance objectives. Ten countries monitoring AMU at farm level use dose-based metrics to quantify AMU (32) which allow for meaningful and comparable estimates of AMU within the different animal sectors (38). A specific dose-based metric was developed for dairy cattle in Canada (23), and it is being used to estimate AMU in the CaDNetASR (29).

In addition to the amount of AMU on farms it is important to determine which antimicrobial is used as well. Some antimicrobials are more important than others in treating infections in humans and their use in animal agriculture should be minimized and used only when other antimicrobials are known to be ineffective. The WHO publishes a regularly updated document, classifying the antimicrobials according to their human importance (44). In Canada, Health Canada's Veterinary Drugs Directorate (Government of Canada, 2009) has categorized the antimicrobials according to their importance in human and veterinary medicine (45). These classifications can provide meaningful information to be included in the AMS goals, aiming to decrease the usage of highly important antimicrobials for human medicine (46).

CaDNetASR is collecting AMR data from the following organisms: *Salmonella spp*., *Campylobacter spp., and E. coli*. These bacteria were selected because they are important zoonotic pathogens, where AMR is a concern or in the case of generic *E. coli*, it is thought to reflect the reservoir of resistance genes. These bacteria are monitored in other CIPARS' surveillance programs (27) and have been recommended by the European Food Safety Authority (EFSA) (47). By monitoring AMR in these target organisms, it may be possible to determine trends in resistance profiles. Ideally, after AMU interventions have been applied to surveillance farms, AMR in the target organisms will decrease.

Not all countries report AMR in the same organisms. Among the thirteen countries listed in **Supplementary Table 4**, only five provided information regarding AMR in bacterial isolates from dairy cattle in their national reports: Belgium, Denmark, Netherlands, Sweden, and United States. In the United States, NARMS monitors *Salmonella spp*., *Campylobacter spp., Enterococcus* spp., and the indicator *E. coli* from cecal samples of dairy cattle collected at the abattoir (48). In Belgium (FASFC), Denmark (DANMAP), and Sweden (SVARM), only MRSA *Staphylococcus aureus* is targeted for AMR surveillance in dairy cattle. The most common MRSA clone in production animals is the Livestock Associated MRSA (LA-MRSA), which has been associated with pig production (49). In Denmark and Sweden, the prevalence of LA-MRSA in dairy production remains low and it is not thought to be of concern in North America either (50, 51). In Canada, the MRSA in dairy production also has a limited occurrence. A study conducted in 91 herds across six provinces in Canada screened 1802 *Staphylococcus aureus* isolates for MRSA, and only one isolate was positive (0.05%) (52). For this reason, the inclusion of MRSA in CaDNetASR was not considered. In the Netherlands (MARAN), annual surveillance for ESBL-producing *E. coli* from cattle fecal samples is reported. After the 3rd year, CaDNetASR will be reporting recovery of ESBL-producing *E. coli* as well. Monitoring ESBL- producing enterobacteria is of critical importance as they pose a threat to human health (53). To the author's knowledge, CaDNetASR is the only surveillance system for dairy cattle that monitors AMR in enteric bacteria in different production phases and from manure storage.

Another important feature of the CaDNetASR system is the development of an isolate bank. All bacterial isolates will be freeze-dried and stored for future analysis. Although currently WGS is being done only for *Salmonella* spp. isolates, the idea is to expand to other isolates of interest, as it is anticipated that WGS will be routinely done in the future. The isolate bank will allow for the comparison of data from historical isolates to those collected in the future. In some European countries, WGS is being implemented gradually, and it will be mandatory after 2026 (47). The WGS data can be used as a complementary tool to the phenotypic AMR surveillance data and provide more information on the AMR epidemiology. Another new approach used for AMR detection is the use of metagenomics. Shotgun metagenomics allows for the detection of the entire bacterial community in a sample. If using traditional culture methods only cultivable organism will be detected and some important data may be missed (54). In the future, the inclusion of metagenomic approaches to characterize the resistome of a sample will improve the monitoring of the spread of resistance genes and the association between resistance from animals and humans.

CaDNetASR SURVEILLANCE SYSTEM LIMITATIONS

The development of a surveillance system requires an iterative process that will reduce data limitations and biases. Some of these limitations can be interpreted in the context of the main goals of the surveillance system. For instance, dairy farms were recruited by local veterinarians to participate in CaDNetASR. Therefore, the results from these farms should only be extrapolated to the study farms. Participating farmers might be more motivated and might have differing management practices and burdens of AMR compared to non-participating farms. According to the EFSA recommendations (47) samples should come from randomly selected epidemiological units to avoid sampling bias. CaDNetASR enrolled farms were not randomly selected, although, the samples collected within farms, were randomly selected from healthy animals, following the recommendations. Thus, it believed that findings can be extrapolated with caution to similar commercial operations. Data coverage is also a key factor that can affect the interpretation of surveillance results. Ideally monitoring would be conducted on as many farms as possible to obtain more precise results. Although CaDNetASR is not a full coverage system, it includes farms from five different provinces in Canada, and it could be used as a model to expand surveillance in the future.

The cross-sectional design implemented in CaDNetASR can bring disadvantages for supporting causal inferences, however, a major goal of the system is to benchmark AMR / AMU patterns across years and regions rather than making a causal inference. Three other major limitations can be considered for this surveillance system: (1) Yearly sampling. This sampling scheme will limit the possibility of tracking seasonal variability; however, each farm is sampled during the same season, allowing comparisons over time; (2) Sample type. CaDNetASR is based on pooled samples from three different ages of cattle and samples from two areas of the farm (calves, heifers, cows, manure pit and BTM. In the future, CaDNetASR will evolve to genomic methods, detecting pathogens and AMR genes. Pooled individual samples have been recommended, as it provided optimal results measuring AMR genes at herd level (55). But still, the surveillance system might miss resistant bacteria occurring in other environments in the farm (e.g., feed, water) (56, 57) which could lead to a low diagnostic sensitivity. However, the sampling scheme used in CaDNetASR includes three age groups, the manure pit and BTM, which will increase the chances of detecting antimicrobial resistant bacteria; and (3) Number of isolates. CaDNetASR has not established a required number of isolates to make inferences about the proportion of resistant bacteria. The initial years of CaDNetASR will provide the baseline trend information that will be used to develop sample size calculations for the ongoing surveillance.

Limitations can also occur in other two components of data collection in CaDNetASR: AMU and questionnaire information. AMU was initially estimated using a GCA system, which is time-consuming and prone to human errors. For this reason, all data were validated by each regional field worker to minimize errors. However, it is envisioned for the next years the AMU will be quantified using veterinary dispensing records. In Canada, all the antimicrobials are sold only with a veterinary prescription, thus, it is believed that veterinary dispensing records can provide a reliable estimation of AMU at farm level. Inaccurate results can arise from questionnaires when response bias occur in data collected. The questionnaires applied during the visits are long, which can demotivate the responders. However, to avoid that, the answers were entered by the regional field workers, that were also responsible to contact again the farmers to fill missing questions or to revise answers. Thus, this procedure is expected to reduce bias.

CONCLUSIONS

In conclusion, the implementation and ongoing development of CaDNetASR are essential to guide AMS on dairy farms across Canada. It will also contribute to the Canadian program for AMR on animal health and public health. Finally, it will help stakeholders in the agricultural commodity groups to achieve more rational AMU on-farm, maintain and improve animal welfare, and support public health by diminishing AMR's burden.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because confidentiality and data ownership. Requests to access the datasets should be directed to mfonseca@upei.ca.

ETHICS STATEMENT

The animal study was reviewed and approved by University of Prince Edward Island Research Ethics Board on March 7, 2019. Written informed consent was obtained from the owners for the participation of their animals in this study.

AUTHOR CONTRIBUTIONS

MF prepared the initial draft, figures, tables, and appendices. JS and LH contributed with conceptual development and writing of the manuscript. DL, JM, DR, SD, DK, DR, and HB critically revised the manuscript. All authors contributed to the article and approved the submitted version.

FUNDING

This research was supported by a contribution from the Dairy Research Cluster 3 (Dairy Farmers of Canada and Agriculture and Agri-Food Canada) under the Canadian Agricultural Partnership AgriScience Program and the Public Health Agency of Canada.

ACKNOWLEDGMENTS

The authors would like to acknowledge the producers and their veterinarians, the regional field workers, the laboratory technicians, and all the graduate students who participated in the data collection.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2021.799622/full#supplementary-material

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frontiers | Frontiers in Veterinary Science

TYPE Perspective
PUBLISHED 02 December 2022
DOI 10.3389/fvets.2022.1080150

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OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Veterinary Epidemiology and Economics,
a section of the journal Frontiers in Veterinary Science

RECEIVED 25 October 2022
ACCEPTED 18 November 2022
PUBLISHED 02 December 2022

CITATION
Schambow R, Colin Y, Dave W, Schettino DN and Perez AM (2022) Enhancing passive surveillance for African swine fever detection on U.S. swine farms. *Front. Vet. Sci.* 9:1080150. doi: 10.3389/fvets.2022.1080150

Enhancing passive surveillance for African swine fever detection on U.S. swine farms

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As the threat of African swine fever (ASF) introduction into new areas continues, animal health officials and epidemiologists need novel tools for early detection and surveillance. Passive surveillance from swine producers and veterinarians is critical to identify cases, especially the first introduction. Enhanced passive surveillance (EPS) protocols are needed that maximize temporal sensitivity for early ASF detection yet are easily implemented. Regularly collected production and disease data on swine farms may pose an opportunity for developing EPS protocols. To better understand the types of data regularly collected on swine farms and on-farm disease surveillance, a questionnaire was distributed in summer 2022 across multiple channels to MN swine producers. Thirty responses were received that indicated the majority of farms collect various types of disease information and conduct routine diagnostic testing for endemic swine diseases. Following this, a focus group discussion was held at the 2022 Leman Swine Conference where private and public stakeholders discussed the potential value of EPS, opportunities for collaboration, and challenges. The reported value of EPS varied by stakeholder group, but generally participants felt that for swine producers and packers, EPS would help identify abnormal disease occurrences. Many opportunities were identified for collaboration with ongoing industry initiatives and swine management software. Challenges included maintaining motivation for participation in ASF-free areas, labor, data sharing issues, and the cost of diagnostic testing. These highlight important issues to address, and future collaborations can help in the development of practical, fit-for-purpose, and valuable EPS protocols for ASF detection in the swine industry.

KEYWORDS

African swine fever, disease surveillance, enhanced passive surveillance, foreign animal disease, pig, participatory

Introduction

Foreign animal diseases (FADs), such as African swine fever (ASF), cause significant global economic and health burden to the swine industry. ASF is caused by the ASF virus (ASFV), a large, enveloped DNA arbovirus that only affects swine, including domestic pigs and wild boar (1, 2). No treatment or readily approved and available vaccine exist to help mitigate its impact, so identification of infected herds followed by depopulation is primarily used to control disease spread and for eradication. In addition to trade restrictions imposed for ASF-infected countries, infection with the ASFV may cause devastatingly high mortalities in affected farms and wide-scale losses due to culling. In recent years, ASF has spread throughout Africa, Asia, Europe, and to the island of Hispaniola containing Haiti and the Dominican Republic in the Caribbean (3). The ongoing ASF global spread has raised serious concerns of a potential disease introduction into the United States (U.S.). An introduction into the U.S. would immediately halt all swine trade and exports and lead to widespread losses of pigs, with recovery estimated at costing $50 billion over 10 years (4). To prevent such a catastrophic scenario, animal health officials rely on strategies of detection and depopulation to identify, contain, and eradicate ASF outbreaks (5).

Global ASF spread highlights the importance of disease surveillance even in apparently disease-free areas. The availability of high-quality diagnostic tests with targeted active surveillance has substantially decreased the time to confirm suspect ASF cases to hours after sample collection (6–8). However, these systems do not decrease the time for swine producers and veterinarians to identify suspect cases on farms, and the time to identify an initial suspect after the first introduction into a country is highly uncertain (9–11). Achieving high coverage of the population is often difficult and expensive with active surveillance. Passive surveillance of animal populations, whereby disease reporting is initiated directly by animal observers such as farmers or primary veterinarians, is highly valuable for monitoring otherwise unreached populations and for increasing the overall sensitivity of a surveillance system. Passive reporting has been especially critical for initial detections of ASF (12–14), and enhancing these strategies will likely be more effective at early ASF detection. Regularly collected information from swine production systems may help create the foundations for a constant flow of data and associated algorithms monitoring for signals that could indicate a FAD such as ASF. In recent years, many groups have explored methods of syndromic surveillance for diseases and pathogens like ASFV or Porcine Reproductive and Respiratory Syndrome virus (PRRSV) with swine data or with technologies like activity monitors or cameras (15–17). These showed some potential success for decreasing detection time for swine pathogens, and collectively, demonstrate that disease surveillance through swine data monitoring may be possible if appropriate data are available.

Practical considerations of the U.S. swine industry preclude an easily implementable, national surveillance system for ASF and other FADs. In the absence of an animal health emergency that justifies governmental intervention, data sharing with animal health officials is not mandatory for U.S. swine producers, and consequently, accessibility to the data necessary to implement widespread surveillance is limited. In recent years, some voluntary initiatives to manage and control domestic infectious swine diseases in the U.S. have had high participation and success. For example, the Morrison Swine Health Monitoring Program (MSHMP) is a national control project started in 2011 to better understand PRRSV epidemiology in the U.S. (18). The program relies on voluntary participation and has significantly helped in the understanding and control of PRRSV (19, 20). Its success has led to the extension of the program to monitoring of other swine pathogens (18, 21).

To develop an enhanced passive surveillance protocol (EPS) for ASF, a better understanding of the current state of swine data capacity is necessary. Objectives of the work here were to characterize regularly collected swine data and disease surveillance activities on U.S. swine farms, explore how these activities could be used for ASF surveillance, and identify how ongoing swine industry technologies and initiatives for disease preparedness could be collaborative to improve ASF surveillance. We explored through a combination of mixed qualitative methods the types of data and management systems used by swine farmers in Minnesota, one of the top swine producing states in the U.S. We later convened a workshop of researchers, government officials, producers, veterinarians, and management software representatives to discuss the potential for EPS implementation on swine farms. Results collected and assessed here will help to identify next steps and priorities for EPS development and opportunities for collaborations between ongoing ASF surveillance efforts.

Analytical approach

To understand the current state of swine data collection and disease surveillance and to characterize the potential for EPS, two stages of data collection were designed following a modified Delphi approach (22). First, an anonymous questionnaire was developed in Qualtrics to characterize the types of data collected on swine farms and practices for disease surveillance and to give a baseline understanding that would inform future in-person discussions. The questionnaire is available in full in Supplementary File 1. Generally, questions asked about the respondent's swine operation, participation in industry initiatives for FAD-preparedness, the type of software or method used to collect swine farm data, the type and frequency of disease, production, and breeding data collection, and on-farm disease surveillance including diseases routinely tested for, routinely collected specimens, necropsy protocols, and disease investigation triggers. At the end, respondents were able to indicate their interest in participating in a future EPS study through an additional one-question Qualtrics questionnaire, to maintain their anonymity to the first questionnaire. The questionnaire was beta-tested with three purposely-selected MN swine producers or veterinarians for feedback on clarity and

TABLE 1 Characteristics of survey respondents.

Farm type	Number of respondents
Boar stud	3
Farrow-to-finish	3
Finisher	8
Genetic multiplier	1
Gilt Development Unit	1
Nursery	4
Sow	9
Other: Isowean-to-finish	1

structure. A targeted list of individuals was not selected in advance to receive the questionnaire; instead, it was openly distributed through email addresses available from Secure Pork Supply (SPS) program activities in MN and through advertisements in the MN Board of Animal Health, University of MN Swine Extension, and MN Pork Board newsletters. These channels were chosen through discussions with a former swine veterinarian and SPS program leader because they represent main modes of communication and education to MN swine producers and would likely reach a wide audience. Briefly, the SPS program is a voluntary, industry-led initiative promoting the development of on-farm biosecurity plans (23). The University of MN Swine Extension is an educational service for sharing information with swine producers (24). The MN Board of Animal Health is the government agency managing animal health issues and rules within Minnesota (25). Finally, the MN Pork Board is an industry-led board with USDA oversight that supports swine producers within the state and oversees Pork Checkoff activities (26). The questionnaire was kept open from June to August 2022.

The information collected from the questionnaire was used to guide the development of in-person activities at one of the most important swine health outreach events annually organized in the U.S., referred to as the Allen D. Leman Swine Conference in St. Paul, MN. The Leman Swine Conference is an international conference that draws one of the largest groups of academic and professional attendees from across the swine industry to share current swine research. This participatory approach, whereby participants of an ongoing program were involved to help inform research activities, has previously been used in veterinary epidemiology to support the development of risk assessments for foot-and-mouth disease (27). First, an open workshop introducing the EPS approach and related approaches was organized. Talks were presented from USDA, academia, and private industry that focused on analytical tools to support ASF preparedness and surveillance. The objective of that initial open activity was to familiarize the audience with key concepts and ideas to inform the discussion. The following day, a focus group was organized to prompt the review and discussion of collected answers from the initial questionnaire and the potential for EPS protocols on swine farms (28). In total, 74 individuals were invited to participate in the focus group discussion. These individuals represented research/academia, private swine software companies, USDA, NPB, AASV, primary swine veterinary clinics, and private swine farms and companies. Approximately one quarter of the invitees (n = 19) and 4 moderators attended the discussion, which was organized following a world-café format (29). The participants were given a brief introduction of disease surveillance and EPS, which summarized the presentations from the previous day, and a summary of the questionnaire results. Participants were then given the choice to join one of four topics:

1. Do you see value for EPS for the industry (depending on the epidemiological conditions of the country) for FAD detection?
2. What is needed for swine data on farms for a successful EPS system?
3. What are opportunities for collaboration for FAD surveillance and preparedness?
4. What are challenges for EPS implementation?

Each table had approximately 30 minutes to discuss their assigned question as a small group, which was coordinated by a moderator, from the authorial team, to facilitate and record the discussion. Conclusions were then presented for the whole group to discuss. Each moderators' recorded notes were later reviewed and summarized.

Results

Questionnaire summary

Thirty questionnaire responses were received, of which 25 were fully completed and 5 were partially completed. All farm types in the questionnaire were represented, and the majority were sow farms (Table 1). Sixteen respondents reported having multiple production sites (ranging from 1 to 27). Twenty-nine had veterinary access, of which 21 had a veterinarian regularly visit while only 8 visited for specific concerns only (No response = 1). Twelve were enrolled in National Pork Board's online contact tracing platform, though 14 were unfamiliar with it. Three were familiar but unenrolled (no response = 1). Conversely, 23 had a SPS biosecurity plan (no response = 1) and only one was not aware of the program. Disease events were primarily recognized by farm staff (n = 19) or managers/owners (n = 7, no response = 4), and none reported by their veterinarian. Nineteen respondents thought they would recognize signs of a FAD, but five were unsure (no response = 4). Many different factors were reported to trigger further disease investigation, including increased mortality or morbidity (n = 22), changes in feed (n = 15) or water consumption (n = 14), or a "gut feeling" (n = 14, no response = 4). Fifteen felt they could detect a drop in feed consumption within a day, while others estimated within hours ($n = 3$) or a week ($n = 7$, no response $= 5$). Software usage was high ($n = 25$, no response $= 1$). Some used multiple types of software, and only four farms, of which three were finisher farms, used none. All data was primarily collected by farm staff either through hand-written records ($n = 15$) or digital handheld technology ($n = 12$, no response $=$ 1, owner/off-farm staff $= 2$). Nineteen completed this on their own, though some used a management company ($n = 6$) and/or their veterinarian ($n = 3$, no response $= 3$).

Disease event information was collected on 23 farms (no response $= 1$). On sow or boar stud farms, records were always recorded for individual animals, otherwise group records were more common. The most commonly recorded events were sudden death, respiratory, and enteric signs, but this varied some by farm type (Figure 1A). Of these 23 farms, 16 (no response $=$ 2) also recorded a confirmed or presumptive pathogen. Fourteen recorded the occurrence of observed disease events daily, and three recorded multiple days a week or weekly (no response $= 2$). Four had no set schedule of recording observed events. Production records were collected on all farms (Figure 1B, no response $= 4$). The most commonly recorded information was treatment records (antibiotic usage or other veterinary care) and mortality, while the least recorded was movement of workers, feed consumption by pen, and semen quality. Breeding records were collected on 6 sow farms, 3 farrow-to-finish farms, and 1 nursery farm. These all included breeding dates, pregnancy check results, rebreeding events, abortion dates, stillbirths, and mummies. Two farms also recorded abortion cause.

PRRSV ($n = 21$) and porcine epidemic diarrhea virus ($n = 17$) were the most routinely tested domestic diseases, followed by transmissible gastroenteritis virus ($n = 14$), porcine deltacoronavirus ($n = 11$), influenza ($n = 9$), Mycoplasma hyopneumoniae ($n = 7$) and porcine circovirus type 2 ($n = 3$). Five farms did no routine testing (no response $= 4$). Oral fluids ($n = 21$) and blood ($n = 20$) were the most commonly collected specimens. The collection of blood may be for serum collection, but that was not specified or distinguished here. Only 3 recorded diagnostic test results into their management software (no response $= 4$). Fourteen performed routine necropsies by farm staff or veterinarians, though 12 didn't (no response $=$ 4), and those that did only performed them infrequently or during large-scale outbreaks. Nineteen farms felt they would be comfortable necropsying pigs themselves and collecting samples (no response $= 4$), and of these many felt comfortable collecting spleen ($n = 14$), tonsils ($n = 9$), or superficial lymph nodes ($n = 8$).

World-café discussion findings

Discussion covered the potential value and benefits of EPS for the swine industry, data needs for surveillance, opportunities for collaboration, and challenges. The reported value of EPS was highly different by stakeholder. For producers and packers, EPS protocols could be valuable to differentiate domestic and foreign diseases and identify concerning disease trends. They could support ASF case definitions and help identify suspect pigs to target for sampling. For small producers in particular, EPS systems could support awareness of ASF and serve as surveillance tools in resource-limited situations. Prior to an ASF outbreak, these activities would support communication about disease events between farm employees and management. Participants also suggested that collected data could be used to forecast domestic disease outbreaks. With increased usage across many producers and sites, data could potentially be used to create regional risk maps for disease outbreaks that could be informative to swine producers. Veterinarians could increase business from helping their producers implement and maintain these protocols. EPS could be beneficial for government and veterinary diagnostic labs by prioritizing limited testing resources to suspect farms, and by incentivizing development of multiplex diagnostic tests to complement domestic disease surveillance. Participants felt that value to wholesalers and resellers would be limited as they would likely adjust what they sell according to the market trends. Potential incentives for participation included improving the detection of endemic diseases, such as PRRSV, or financial incentives like decreased insurance rates or quicker return to shipping animals in the event of an outbreak.

Many data needs were identified. Daily data collection at the pen or barn-level would be ideal and provide sufficient opportunity for early detection of highly-virulent ASF strains. Weekly collection was suggested as viable for detecting moderately-virulent ASF strains, but premise-level data wouldn't be sensitive enough for early detection. Data would need to be automatically or quickly uploaded to a centralized source for analysis. Participants were concerned that if data were collected *via* hand-written records, it would take up to a week for entry into a database, and the resulting time lag would be too great. Participants also highly emphasized the need for a simple system that could be used daily by on-farm workers with minimal training, especially because farm owners or managers may only visit a given site on a weekly basis. Ideally, data would be collected through mobile apps within software programs producers already own. Easily understood questions, such as a "yes/no" format or checklist, in multiple languages would facilitate collection and increase data quality. Offline software capability would be important because many farms in the U.S. have limited or no access to Internet or cellular services. Finally, standardized data fields would allow for better communication between software and analysis.

Many potential opportunities were reported. Swine management software could be modified for collecting relevant data, assuming a standardized design with producer support were developed. Industry initiatives could also support EPS.

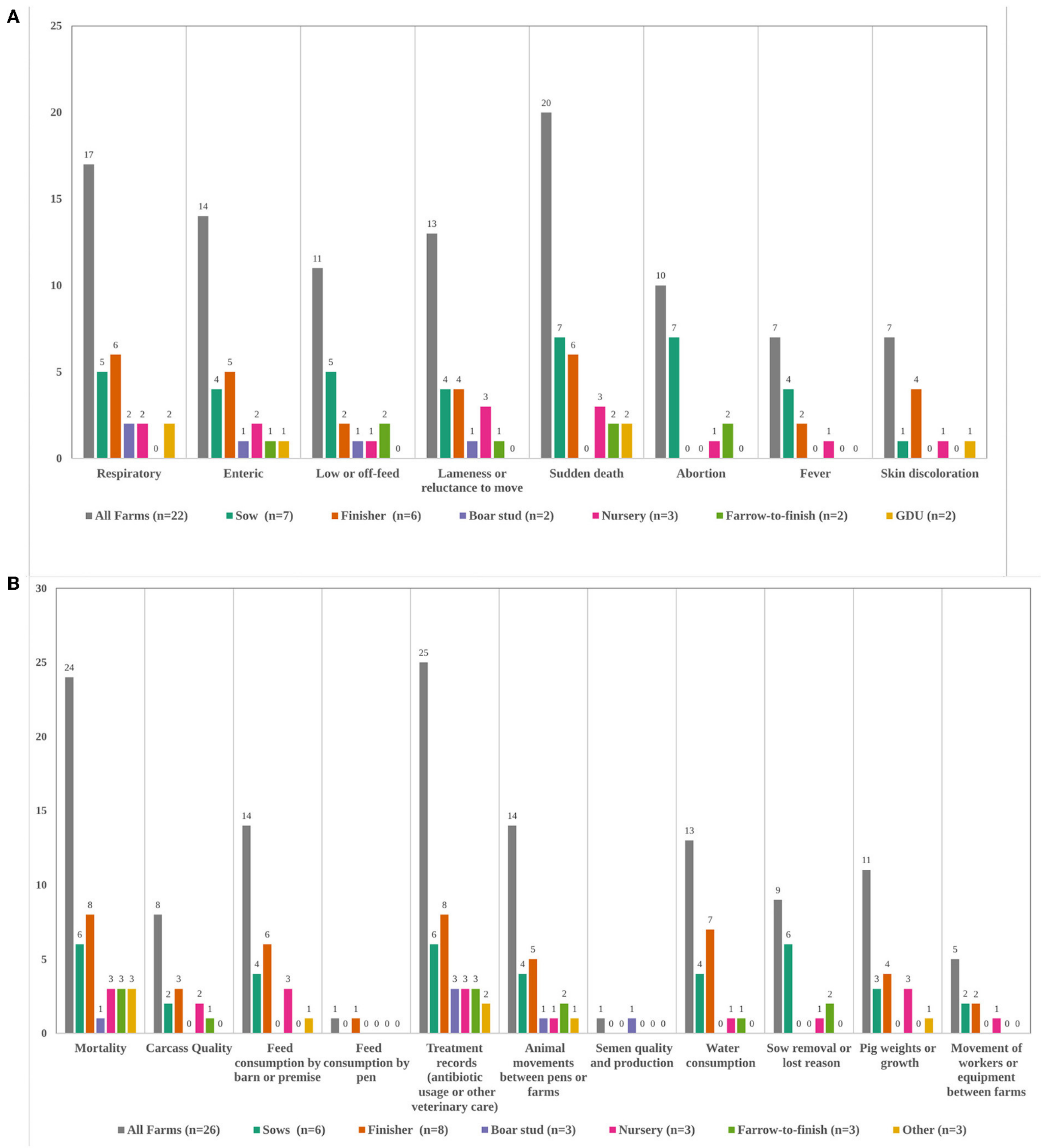

FIGURE 1
(A,B) Types of disease events **(A)** and production data **(B)** recorded on farms, by total and farm type. Total farm number for disease events **(A)** is out of those that answered "Yes" to recording any type of disease information and selected at least one disease event ($n = 22$, no response = 1). No farms reported huddling. For production data **(B)** "other" included 1 gilt development unit, 1 isowean to finish farm, and 1 genetic multiplier. Three sow farms and one nursery farm did not specify what type of production information they recorded. GDU, Gilt Development Unit.

The U.S. Swine Health Improvement Plan (U.S. SHIP) is a USDA-sponsored initiative to improve swine health, biosecurity, traceability, and disease surveillance (30). Data collected by U.S. SHIP or pre-movement testing programs could potentially inform EPS or vice versa. EPS could also support the NPB Pork Quality Assurance program, an initiative to help producers improve their production practices, through supporting visual inspections for disease (31). EPS could also collaborate with USDA's sick pig surveillance program by standardizing case definitions and connecting to findings from National Animal Health Laboratory Network laboratories. Biosecurity and movement data could be incorporated through the Rapid

Access Biosecurity App, an application and service that helps standardize SPS biosecurity plans for producers and animal health officials (32). National swine disease monitoring efforts such as the Swine Disease Reporting System or MSHMP might also be collaborative with on-farm EPS. Precision farming tools, such as audio monitors for coughing and video cameras for huddling, could reduce staffing needs. However, these technologies are often expensive, require specific hardware, and are still under development. Despite this, participants felt these technologies should be explored for EPS.

Finally, participants identified many key challenges for EPS. Employee training and availability were major concerns. Participants reported that many employees have little or no background in swine production. Specific clinical signs, such as hemorrhagic diarrhea, would likely be too difficult for farm staff to identify. Training would need to be simple and accessible for those with different language or educational backgrounds. Otherwise, data quality would likely suffer. Additionally, many farms already experienced staff shortages for regular operations, and more surveillance could be burdensome. Maintaining participation in the absence of an ASF outbreak would also be difficult. While some early adopters would see value in supporting ASF preparedness, many would be hesitant because of a perceived low risk of an ASF introduction on their farm. Participants were also concerned about regulatory or government response to EPS suspect findings and thought that the potential for business disruptions during an FAD investigation would discourage reporting suspect cases in an ASF-free region. A regulatory framework to handle EPS suspects would be important. Participants also felt that some diagnostic testing would likely be necessary, but that prior to an ASF outbreak in the U.S., it would be difficult for farms to justify or afford this additional cost and time. Specimens that could be collected without opening up a carcass or validation of pen-level samples such as oral or processing fluids would help address these concerns. Data sharing and maintaining data privacy were another major challenge. To be effective, participants felt that some data or procedures may need to be communicated and shared between companies, but it would be difficult to coordinate. This would be especially challenging if data were shared with government, and many felt that some producers would not participate in government-led EPS.

Discussion

This work explored current swine data collection and disease surveillance practices and private and public opportunities for enhancing ASF surveillance in the U.S. swine industry. Through the questionnaire and subsequent focus group discussion, many potential strengths and values of EPS protocols were identified, but many challenges and concerns were also recognized. While the questionnaire results indicate that disease surveillance practices are commonly conducted on U.S. swine farms, it is still unclear how much information reaches an electronic database, especially considering that nearly half of farms reported primarily collecting data through hand-written records. To improve data collection, new or existing technologies such as cell phones should be used directly in barns and pens by farm staff. Data could then be automatically uploaded to centralized management software. Management software usage was also high across all farm types, representing an opportunity to embed an EPS utility within the software. Alternatively, features like application programming interfaces (APIs) could centralize data from multiple software sources, so that data entered into a swine management system could potentially be automatically available for a surveillance application, or vice versa. APIs or other software connections are already used in the swine industry to link many types of software, such as for sharing movement or feed information. However, the type of software used by questionnaire respondents varied considerably, which may hinder the development of a uniform, data-monitoring EPS protocol. This view was repeated by participants in the world-café, who emphasized that standardized data collection will be critical for EPS protocols to be implemented across different software. Another technological consideration for EPS is to what extent it would rely on online or cellular access for functionality, as many farms are located in regions with limited connectivity.

Many opportunities for improvement and collaboration in disease surveillance were identified. High diversity in collected records suggests an opportunity to standardize disease data collection across the industry. Important signs of ASF including fever, skin discoloration, and huddling, were the least common to be recorded, but this may be improved through EPS protocols or precision farming technologies. Routine disease surveillance as described in the questionnaire might be an opportunity for implementing ASF surveillance with minimal extra cost to the producer through additional testing on suspect samples or multiplex assays. However, respondents rarely recorded test results into management software, though this may be more easily captured through collecting data directly from veterinary diagnostic laboratories. Notably, necropsies were not consistently performed on farms. In response to this questionnaire finding, participants from the world-café felt that necropsy and specimen collection procedures could be streamlined by not opening the carcass, developing techniques for easier collection of tissues such as lymph nodes, or by diagnostic testing of routinely collected oral or processing fluids. Necropsy findings are critical for surveillance, and improvements might be achieved through collaboration with programs such as the Certified Swine Sample Collector Training (33). EPS protocols should explore how these different specimens and testing schemes could be applied to maximize surveillance sensitivity and balance economic factors.

Some limitations were present in interpreting results from these activities. The questionnaire was only advertised to MN swine producers, and disease surveillance practices identified here might not be commonly shared throughout the U.S. Also, some important parts of the industry, such as small or show herd producers, were not represented in the world-café, so opportunities or challenges unique to these groups could not be collected in detail. This again highlights the need for improved ASF awareness and collaboration with these types of producers, as surveillance within these groups will be critical to protecting the U.S. swine industry. Despite these limitations, results from these activities have demonstrated a potential role for EPS to improve ASF early detection in the U.S. Future EPS protocols will need to be tested on swine farms to identify potential pitfalls in their application and fine-tune detection methods, and overall, any swine disease surveillance plan should be developed as a joint effort between researchers, industry, and, in case of ASF, government and regulatory officials. This work will help direct development of valuable EPS protocols for the U.S. swine industry.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

WD conducted beta-testing and distributed the questionnaire. AP, RS, YC, and WD organized, moderated the focus group discussion, and summarized findings. RS analyzed the questionnaire data and wrote the manuscript. AP and YC edited it. All authors helped draft and revise the questionnaire. All authors contributed to the article and approved the submitted version.

Funding

This work was funded by a cooperative agreement with the United States Department of Agriculture Center for Epidemiology and Animal Health. The findings and conclusions in this publication are those of the author(s) and should not be construed to represent any official USDA or U.S. Government determination or policy.

Acknowledgments

Thank you to USDA-CEAH for their funding and support of this work, and to the public and private industry stakeholders who participated in the questionnaire and discussions and for their ongoing support and engagement.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2022.1080150/full#supplementary-material

SUPPLEMENTARY FILE 1
Swine data collection and disease surveillance questionnaire.

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frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 23 January 2023
DOI 10.3389/fvets.2023.1095293

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OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Veterinary Epidemiology and Economics, a section of the journal Frontiers in Veterinary Science

RECEIVED 11 November 2022
ACCEPTED 03 January 2023
PUBLISHED 23 January 2023

CITATION
Hasahya E, Thakur K, Dione MM, Kerfua SD, Mugezi I and Lee HS (2023) Analysis of patterns of livestock movements in the Cattle Corridor of Uganda for risk-based surveillance of infectious diseases. *Front. Vet. Sci.* 10:1095293. doi: 10.3389/fvets.2023.1095293

Analysis of patterns of livestock movements in the Cattle Corridor of Uganda for risk-based surveillance of infectious diseases

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Introduction: The knowledge of animal movements is key to formulating strategic animal disease control policies and carrying out targeted surveillance. This study describes the characteristics of district-level cattle, small ruminant, and pig trade networks in the Cattle Corridor of Uganda between 2019 and 2021.

Methodology: The data for the study was extracted from 7,043 animal movement permits (AMPs) obtained from the Ministry of Agriculture, Animal Industry and Fisheries (MAAIF) of Uganda. Most of the data was on cattle (87.2%), followed by small ruminants (11.2%) and pigs (1.6%). Two types of networks representing animal shipments between districts were created for each species based on monthly ($n = 30$) and seasonal ($n = 10$) temporal windows. Measures of centrality and cohesiveness were computed for all the temporal windows and our analysis identified the most central districts in the networks.

Results: The median in-degree for monthly networks ranged from 0–3 for cattle, 0–1 for small ruminants and 0–1 for pigs. The highest median out-degrees for cattle, small ruminant and pig monthly networks were observed in Lira, Oyam and Butambala districts, respectively. Unlike the pig networks, the cattle and small ruminant networks were found to be of small-world and free-scale topologies.

Discussion: The cattle and small ruminant trade movement networks were also found to be highly connected, which could facilitate quick spread of infectious animal diseases across these networks. The findings from this study highlighted the significance of characterizing animal movement networks to inform surveillance, early detection, and subsequent control of infectious animal disease outbreaks.

KEYWORDS

Uganda, animal movement, network analysis, surveillance system, epidemiology

1. Introduction

The Cattle Corridor covers about 35% of Uganda's land surface and diagonally stretches from southwestern to northeastern Uganda, with many semi-arid characteristics such as; low and unreliable rainfall, and prolonged drought dominated by pastoral rangelands (1, 2). The region has in the present past experienced numerous outbreaks of foot-and-mouth disease (FMD), lumpy skin disease, contagious bovine pleuro-pneumonia in cattle; *peste des petits ruminants*, contagious caprine pleuro-pneumonia in small ruminants; African swine fever in pigs; trypanosomiasis, brucellosis and anthrax in all ruminants and pigs which has partly been fueled by direct animal movement (3–15).

Direct animal movement through animal trade is a major risk factor for the spread of infectious diseases in animals where adequate biosecurity practices and risk management protocols are not followed or are poorly implemented especially in sub-Saharan Africa (16, 17). For example, the spread of the 2001 foot-and-mouth disease (FMD) epidemic from one part of United Kingdom (UK) to geographically distant regions was facilitated by the movement of animals (18).

Therefore, failure to understand animal movement hinders formulation of specific control strategies in case of infectious animal disease outbreaks (19, 20). The lack of animal movement data in Uganda has made it difficult to quantify key parameters for simulating potential disease transmission and hindered effective planning of control strategies for eradication of transboundary animal diseases (TADs) (15, 21).

Uganda has no formal centralized system for identification and traceability of livestock during movement (22). However, a health certificate (commonly known as animal movement permit; AMP) issued by the district veterinary officer (DVO) is required to move animals between districts and even between countries (23). Therefore, the exploration of data from AMPs can help veterinary epidemiologists in Uganda to understand previous outbreaks, predict epidemic spread, and guide decision-making as far as disease control and prevention in livestock are concerned (24). Network analysis is a useful tool that can be used to evaluate different forms of contact between different points/nodes (such as farms, markets, villages, and districts) in the livestock trade and their frequency, as well as how they may play a potential role in the spread of infectious diseases between animal populations (24–26). There is a correlation between the connectivity and centrality of a node within a network, such as the number of other nodes to which it is linked, with the probability of becoming infected and subsequently infecting other nodes (20).

This study aims to characterize the movement of livestock between districts and evaluate the structure of the livestock trade networks in Uganda using data from the archived AMP booklets. We also discuss the potential impact of such networks on the spread of infectious diseases to inform disease surveillance and control.

2. Materials and methods

2.1. Data collection and source

Secondary data in AMPs from the Cattle Corridor were digitized with permission from Uganda's Ministry of Agriculture, Animal Industry and Fisheries (MAAIF). The DVO used the AMPs to permit the movement of animals as well as record the date, number of animals, species, purpose of movement, source, and destination districts of the livestock. The study area, generally referred to as Cattle Corridor stretches diagonally across Uganda, from the southwest to the northeast (Figure 1). It was selected because it is a hotspot for FMD outbreaks (11, 27). The region also has most of the national cattle and small ruminant herds (about 60% of the national herd) (28).

2.2. Data entry and management

Information from the 2015 to 2021 (n = 18,400) AMP booklets was entered directly into an Excel spreadsheet by eight (8) data clerks and crosschecked by three (3) of the co-authors. The information recorded was: (i) permit number, (ii) date of issuance (i.e., year/month/day), (iii) district of origin, (iv) destination district, (v) species of animal being moved, and (vi) number of animals being moved. Because some districts were missing data in the earlier years, we used data from 2019 to 2021 (n = 7,043 APMs).

The data was ordered by year of AMP issuance and district of origin then grouped into 3-month periods to generate movement data by season, i.e., January to March (first dry season), April to June (first wet season), July to September (second dry season) and October to December (second wet season) for each of the years (29). The animal movement data was also grouped by month to generate monthly networks.

2.3. Data analysis

2.3.1. Network construction

The networks constructed in this study consisted of nodes, which represent districts animals moved to and from connected by links, which represent the movement of animals between two districts. A district in Uganda is an administrative area averaging 800 km^2. The nodes (districts) were linked by edges, which were animal movements weighted by number of shipments between the districts per the temporal window the data was grouped by, i.e., monthly, seasonally, or yearly. A shipment event was a batch of one or more animals from a source to a destination district.

Two types of networks were constituted based on the temporal window (monthly: $n = 30$, seasonally: $n = 10$) for each group of animals (cattle, small ruminants and pigs, respectively) using Ucinet6 (Analytical Technologies, USA) (30). The edges between districts in the network were considered static or constant as was in the data and each edge was weighted by the number of direct shipments between the districts. The networks were one-mode type denoting the farm-to-farm direct movement of animals.

We considered seasonal and monthly networks because these allowed us to pinpoint any short-term changes in the network structure, which would be pertinent to the control of a highly infectious disease such as FMD, and equally helpful in understanding the temporal variability in movement patterns. The networks constructed were visualized using Gephi version 0.9.5 (31).

2.3.2. Network analysis

From the networks constructed, we calculated different centrality measures such as in- and out-degree, betweenness and eigenvector values of the nodes. With the centrality measures known, the roles of different nodes in the spread of diseases as a consequence of livestock trade were established. This was critical in identifying nodes for active surveillance, for example in the case of FMD outbreak or as a potential target for strategic vaccinations.

In-degree centrality denoted the number of districts a particular district was connected to by animal purchase while out-degree was determined by the number of districts a particular district sent animals to. On the other hand, betweenness centrality was the frequency with which a district was in the shortest path between pairs of districts in a network. In terms of epizootic control, districts with high betweenness can be critical because they act as conduits

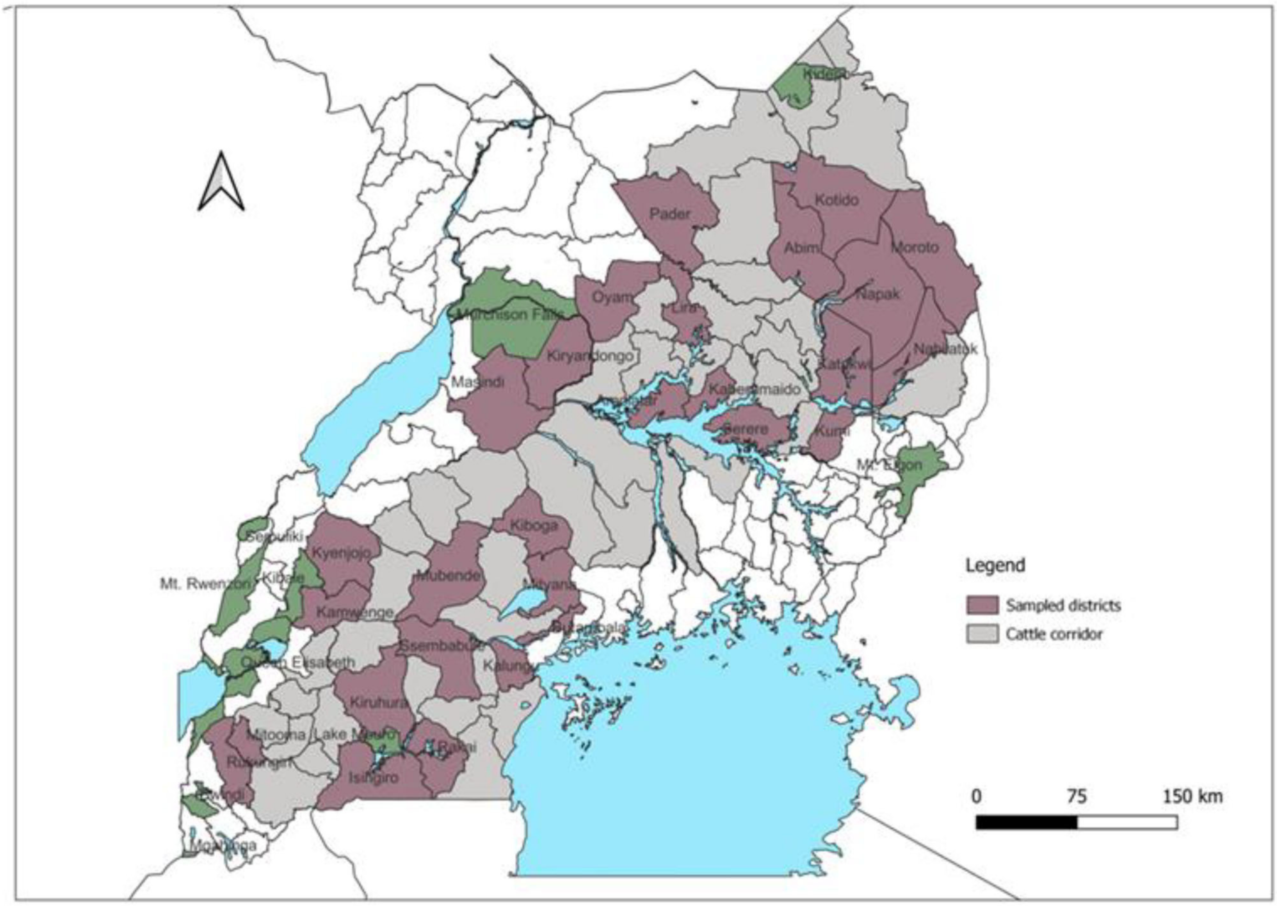

FIGURE 1
Map of Uganda showing the cattle corridor.

that can hasten the spread of a disease to previously unexposed and naïve populations.

We further estimated the network-level characteristics of seasonal and monthly networks for each species by calculating the average path length (APL), average degree, fragmentation, clustering coefficient, density, diameter, and component structure, i.e., the number of components and sizes of the giant strongly or weakly connected components: Giant Strongly Connected Component (GSCC) and Giant Weakly Connected Component (GWCC). The medians were calculated using the "ggplot2" R-package and the figures created using QGIS (32, 33).

We also tested if the generated networks followed small-world and scale-free topologies. A network was considered to have a small-world structure if its clustering coefficient was higher than that calculated from a random network of equivalent size and connections (i.e., with the same number of nodes, edges and density) while its APL was smaller than that of the random network (25, 34). Therefore, to determine if the networks had small-world properties, 100 random networks with the same number of nodes and density as their corresponding empirical networks were generated using Ucinet6. The mean clustering coefficients and average path lengths for the randomly generated networks were then compared with each of their respective opposite empirical networks.

Another useful property of most real-world networks is that the node linkages follow a scale-free power-law distribution. This characteristic is a consequence of two mechanisms: networks spread out continuously by the addition of new nodes, and these new nodes preferring links to other nodes that are already well connected (35). We plotted the fraction of nodes against the in- or out-degree on a logarithmic scale to check if the plots followed the power-law distribution. Spatio-temporal aspects of livestock movements in the cattle corridor were described using tables and graphs.

3. Results

3.1. Temporal trends of animal movements

Of the 7, 043 AMPs (from 2019 to 2021) used in the study, 87.2% were for cattle movement, 11.2% for small ruminants and 1.6% for pigs. For all species, movements were highest in 2019 before the COVID-19-related lockdown occurred, with the highest volume of animals being traded from March to August 2019. Subsequently, animal movement decreased drastically in 2020 and 2021 (Figure 2). Throughout the study period, the number of cattle traded was twice the number of both small ruminants and pigs. The volume

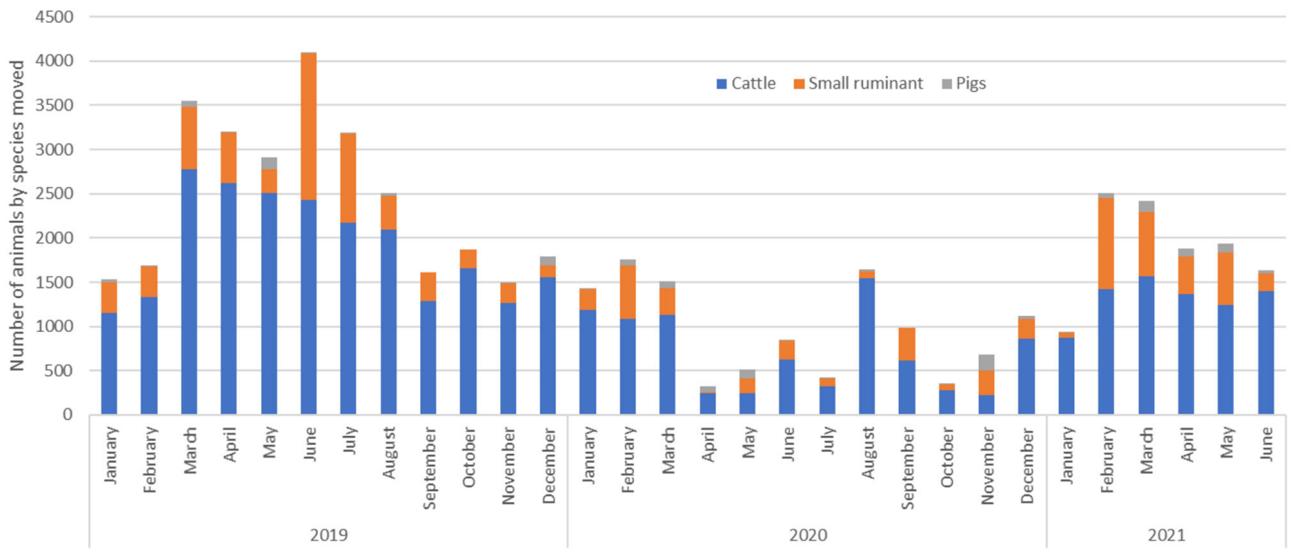

FIGURE 2
The total number of animals shipped in cattle, small ruminant, and pig monthly movements between trading districts in the Cattle Corridor of Uganda from 2019 to 2021.

of pigs moved between districts remained steady throughout the study period.

3.2. Description of the network structure

The results showed that, across all species, edge densities for seasonal and monthly networks were low, but monthly edge densities were lower than seasonal ones except for the pig networks. All seasonal and monthly networks ranged between 2.4–7 and 2.3–5.2% of the possible edges between nodes across all the species for seasonal and monthly networks, respectively (Table 1). All networks were equally fragmented at seasonal and monthly levels, with an average fragmentation index of 0.9 suggesting a high fraction of isolated pairs of nodes in all the networks.

When the direction of the edges was ignored, seasonal networks had more weakly connected components and larger components than monthly networks across all species. In all the seasonal and monthly networks, we found that most of the remaining components contained only a few nodes.

When the direction of the edges was considered, the month with the highest number of components was January 2019 in the bovine networks, with 71 strongly connected components (largest size = 4), while April–June 2019 was the season with the highest number of components, with 86 strongly connected components (largest size = 8) (Table 2).

On average, the APL was shorter in the monthly networks than in seasonal networks across all three species. The monthly pig networks had the shortest mean APL of 1.32 while the seasonal small ruminant network had the highest mean APL (2.78).

The seasonal and monthly networks of cattle and small ruminants followed small-world topologies. The randomly generated networks had lower mean clustering coefficients than the cattle networks for the seasonal and monthly periods at 0.71 and 0.52, respectively. Similarly, the mean APL was much higher for the randomly generated networks than for the seasonal and monthly networks at 6 and 5, respectively. All evaluated pig networks (seasonal and monthly) did not conform to the small-world network topology.

The monthly and seasonal networks for cattle and small ruminants were found to have asymmetric and right-skewed distribution of degrees with long tails, typical degree distributions observed in scale-free networks (35, 36). The monthly and seasonal pig networks did not exhibit typical scale-free characteristics.

3.3. Description of node-level metrics

Ssembabule District was the only district in the cattle seasonal and monthly networks with both highest median in-degree and out-degree (Figure 3). Lira and Kaberamaido districts showed highest median out-degree for seasonal and monthly cattle networks. In all temporal networks across the species studied, most of the districts that exhibited the highest median in-degree index were bordering one of the five neighboring countries, i.e., Democratic Republic of Congo, Kenya, Tanzania, and South Sudan (Figures 4, 5).

Whereas, Oyam District noticeably had the highest median out-degree across all small ruminant seasonal and monthly networks, Kyenjojo and Butambala districts had the highest median out-degree across all temporal pig networks (Supplementary Figures 1–3). The highest median monthly out-degree (19) was observed in cattle networks in Lira District. The median monthly in-degree ranged from 0–3, 0–1, to 0–1 for cattle, small ruminant, and pig networks, respectively. We also noticed that the districts of Lira, Oyam, and Butambala had the highest betweenness for all network types of cattle, small ruminants, and pigs respectively.

4. Discussion

This study was the first of its kind to describe three groups of livestock movements in the Cattle Corridor of Uganda, where we built weighted networks of animal movements. It characterized

TABLE 1 Network-level measures for the cattle, small ruminant, and pig seasonal/monthly movements between trading districts in the Cattle Corridor of Uganda from 2019 to 2021.

Network parameter	Mean (minimum, maximum) measure of the network					
	Cattle networks		Small ruminant networks		Pig networks	
	Seasonal ($n = 10$)	Monthly ($n = 30$)	Seasonal ($n = 10$)	Monthly ($n = 30$)	Seasonal ($n = 10$)	Monthly ($n = 30$)
Density	0.023 (0.019, 0.028)	0.024 (0.017, 0.055)	0.025 (0.017, 0.037)	0.038 (0.02, 0.071)	0.052 (0.014, 0.095)	0.07 (0.04, 0.1)
Nodes	70 (43, 94)	54 (16, 76)	41 (21, 65)	22 (7, 44)	15 (9, 19)	7.4 (5, 11)
Edges	129 (51, 211)	67 (12, 120)	40 (13, 71)	17 (4, 41)	10 (5, 15)	4.7 (3, 8)
Average degree	1.73 (1.19, 2.26)	1.16 (0.74, 1.63)	0.91 (0.57, 1.12)	0.66 (0.14, 0.897)	0.5 (0.1, 0.74)	0.34 (0, 0.7)
Fragmentation	0.9 (0.84, 0.96)	0.92 (0.853, 0.961)	0.89 (0.084, 0.94)	0.89 (0.81, 0.98)	0.9 (0.83, 1)	0.89 (0.83, 0.96)
Average path length	2.56 (1.64, 3.26)	2.29 (1.61, 3.31)	2.78 (1.86, 3.52)	2.22 (1, 3.04)	1.67 (1, 2.5)	1.32 (1, 1.69)
Diameter	6.5 (4, 9)	5.5 (3, 9)	6.5 (4, 9)	5.03 (1, 8)	3.2 (1, 6)	1.82 (1, 3)
Overall clustering coefficient	0.61 (0.16, 1.5)	0.36 (0, 1.4)	0.125 (0, 0.27)	0.076 (0, 0.28)	0 (0, 0)	4.61E + 37 (0, 1E + 38)
Weighted clustering coefficient	0.17 (0.033, 0.37)	0.13 (0, 0.77)	0.067 (0, 0.13)	0.06 (0, 0.23)	0 (0, 0)	0.01 (0, 0.088)
GWCC						
Number	6 (4, 10)	8.96 (4, 16)	10.9 (8, 14)	8.24 (4, 15)	6 (3, 10)	5 (3, 10)
Largest size	72.2 (39, 89)	45.25 (11, 71)	30.8 (13, 53)	13.4 (2, 11)	6.3 (1, 15)	3.5 (1, 8)
GSCC						
Number	71 (39, 86)	49.38 (15, 71)	37.1 (20, 62)	19.3 (7, 41)	11 (6, 19)	8 (5, 11)
Largest size	7 (1, 15)	4.1 (1, 11)	4.4 (1, 10)	2.9 (1, 7)	1.33 (1, 2)	1.1 (1, 2)

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TABLE 2 Seasons and months that exhibited the highest and lowest numbers of GSCCs and GWCCs by network type for cattle, small ruminant, and pig seasonal/monthly movements between trading districts in the Cattle Corridor of Uganda from 2019 to 2021.

Network type	Period with highest number of GSCCs	Period with lowest number of GSCCs	Period with highest number of GWCCs	Period with lowest number of GWCCs
Cattle seasonal networks	April–June 2019	April–June 2020	October–December 2020	July–September 2019
Cattle monthly networks	January 2019	April 2020	January 2021	May 2020
Small ruminant seasonal networks	April–June 2019	July–September 2020	January–March 2019	July–September 2020
Small ruminant monthly networks	June 2019	January 2021	March 2019	July 2020
Pig seasonal networks	April–June 2021	July–September 2020	January–March 2020	October–December 2020
Pig monthly networks	May 2021	December 2020	March 2021	June 2021

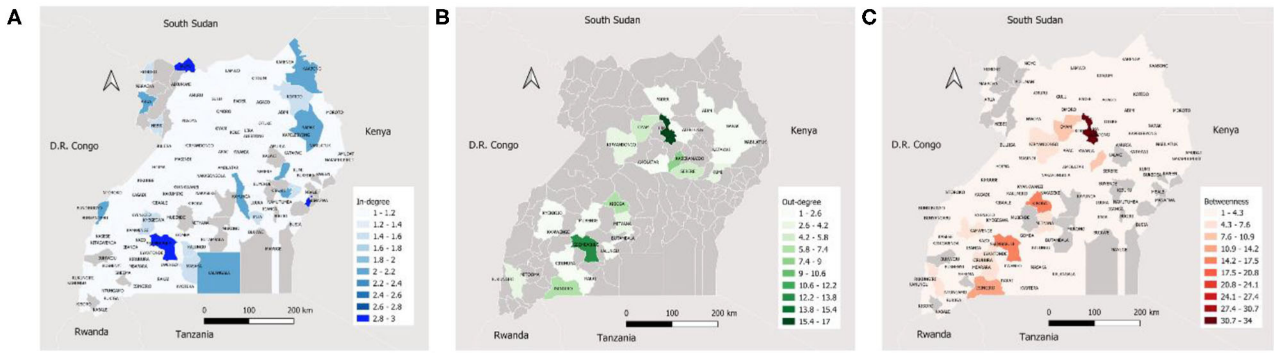

FIGURE 3
Maps showing the median monthly in-degree **(A)**, out-degree **(B)** and betweenness centrality **(C)** in the cattle inter-district movement networks in the Cattle Corridor of Uganda between 2019 and 2021.

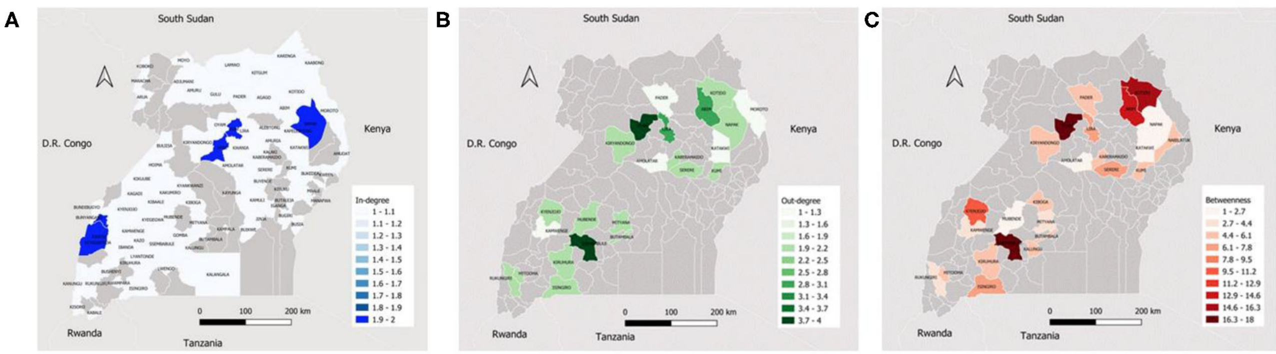

FIGURE 4
Maps showing the median monthly in-degree **(A)**, out-degree **(B)** and betweenness centrality **(C)** in the small ruminant inter-district movement networks in the Cattle Corridor of Uganda between 2019 and 2021.

networks of cattle, small ruminant, and pig movements, which could potentially play a role in the spread of livestock diseases in Uganda.

The seasonal aspect of cattle and small ruminant movement could be related to the fact that from January to March, the Cattle Corridor registered low amounts of rainfall, which translates to shortages of pasture and water, forcing many farmers in the region to depopulate their herds through sale (1). Therefore, many farmers from other regions rush to buy ruminants from the cattle corridor cheaply, resulting in the increased movement of livestock to other districts. This was also observed during another study in the Sahel region, where livestock movements peak prior to the start of the rainy season (37). The additional explanation was that the period between January and March also marks the reopening of schools after the long Christmas holiday. It may suggest that the farmers in the cattle corridor increased sale of animals during this period of the year, especially for small ruminants and pigs to raise money for school fees (38).

The present study revealed the seasonal and monthly livestock trade networks to be compacted networks with many smaller clusters which were intertwined by limited long-distance links. We found

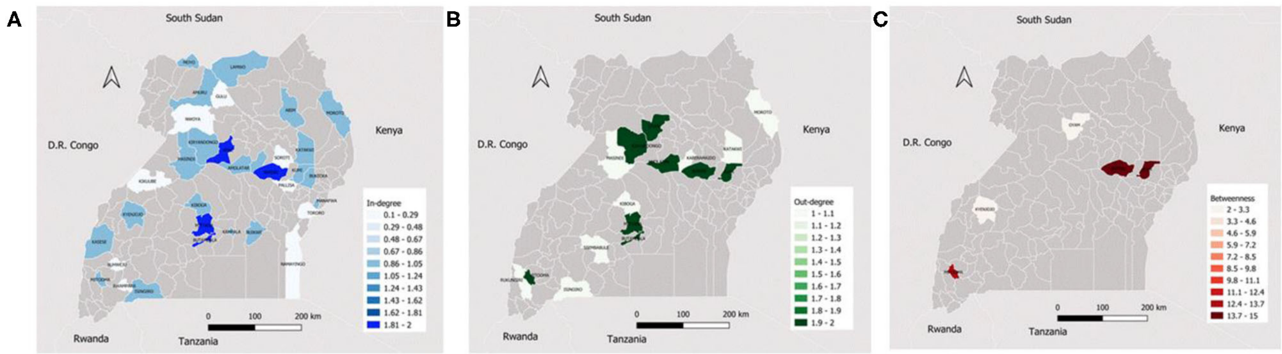

FIGURE 5
Maps showing the median monthly in-degree **(A)**, out-degree **(B)** and betweenness centrality **(C)** in the pig inter-district movement networks in the Cattle Corridor of Uganda between 2019 and 2021.

that the APL and diameter of the seasonal networks of cattle, small ruminants and pigs were slightly larger in size than their respective monthly networks. Whereas, the small APL and diameter can aid the quick spread of an infectious animal disease to different nodes, the larger APL found in the seasonal networks as compared to the monthly ones could be due to the longer temporal coverage giving rise to chances of exhibiting longer shipments (24).

The small ruminant and cattle networks across the monthly and seasonal timescales had small-world topology. Such networks are prone to facilitating the quick spread of an infectious disease (24, 36). Any infectious agent, once introduced into a small-world network, spreads quickly because of shorter APL between the nodes and higher connectivity among them (34).

Similarly, this study also found that the monthly and seasonal networks for cattle and small ruminant had degree distributions typical of scale-free networks, highlighting heterogeneity in the degree distributions of the districts studied. Such scale-free networks are well-known to facilitate the quick spread of infectious diseases given that they possess hubs with many connections, which once infected can transmit the disease to many nodes quickly (39).

The existence of heterogeneity associated with scale-free networks promotes epidemic spread, not only by surpassing the epidemic threshold, but also by accelerating the propagation of the pathogens within the population (40). For disease preparedness, early warning is paramount in such networks. Strategic nodes (districts) with high in-degree and out-degree could be targeted for surveillance and application of intervention and control measures (24, 34).

Our findings also highlighted the fact that although the geographical adjacency matters in the spread of an infectious disease, even geographically distant nodes can still be connected within a few path lengths which puts them at risk of infectious disease outbreak despite the fact that they are spatially distant (24). This may explain the sporadic outbreaks of FMD in districts which are very distant from the index outbreak districts in Uganda (11). Additionally, when the direction of movements was ignored in the monthly networks, on average, more than 83, 61, and 47.3% of the districts were part of the largest GWCC for cattle, small ruminant, and pig networks, respectively, while a mean of 7.6, 13.2, and 14.9% of the districts were involved in the GSCC for cattle, small ruminant and pig networks. Previous studies have suggested that the GSCC and the GWCC can be taken as indicators of the lower and upper limit of the projected epidemic size, respectively, if there is an outbreak of an infectious disease in a population. Therefore, infectious disease incursions during the months with the highest GSCC and GWCC by species networks would translate into wide transmission (19, 34, 41, 42). Keen interest must be paid to such periods as far as infectious disease surveillance is concerned.

The present study found the border districts of Kasese, Bunyangabu, Bundibugyo, Nebbi, and Arua (which neighbor the Democratic Republic of Congo); Moyo, Kaabong, and Koboko (neighboring South Sudan); Isingiro (touching Tanzania); and Manafwa and Kaabong (bordering Kenya) to have a high in-degree centrality for cattle and small ruminant networks. Whether or not the high number of animal shipments to the border districts could be headed for neighboring countries in undocumented cross-border trade is a detail which this study could not conclude about, but such activity was observed by Lichoti et al. (26) and Mugezi et al. (43) in Uganda. Interestingly, the districts (Lira, Isingiro, Sembabule, Oyam, and Kaberamaido) with highest out-degree have the highest cattle and small ruminant populations in the country (5, 44).

Recent studies showed that higher betweenness nodes were often super-spreaders during the early stages of an outbreak (45–47). Therefore, districts with high betweenness in the cattle (Lira, Insingiro, and Serere), small ruminant (Oyam, Sembabule, and Kiruhura) and pig (Butambala, Kumi, and Serere) networks should be the first targets of intervention during an outbreak to minizine the spread of an infectious disease.

It was noteworthy that the networks based on district-to-district movement of farm animals in the cattle corridor presented very similar structural properties to most other published animal movement networks, even though farming systems were different between countries and production types (15, 21, 34, 48, 49). Although the results did not include all districts in Uganda, they showed the value of such data for epidemiological studies in the country, given that most ruminants are farmed in the cattle corridor. Descriptions of network characteristics as well as network and node-level parameters for different network types obtained from this study can be useful for infectious disease transmission models and for effective management of infectious diseases outbreaks in animals (50).

The biggest limitation of this study was the undocumented inter-district movement of livestock; however, this did not affect the quality of data utilized because these are rare due to the strict policing and could constitute to <4% of livestock movements in the cattle corridor. Another limitation could have been the COVID 19 restrictions which may have affected financially many buyers of cattle.

5. Conclusion

Our findings, in the context of low resources, underscored the usefulness of control measures targeting a few "at risk" districts to prevent and contain the spread of infectious diseases effectively. Targeted strategies in the key-player districts identified in this study could mean the following: (i) enhanced bio-security measures, (ii) prioritized active surveillance of selected infectious diseases because of the high risk of infection and spread, and (iii) movement control as an emergency disease control response. We further suggest that a more robust database of intra- and inter-district livestock movements be maintained at all administrative levels, including markets, slaughterhouses, and other gathering points. This could call for the issuance of digital movement permits to ease future network studies and further utilization of the data in preventing the spread of infectious diseases.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation upon permission from the Ministry of Agriculture, Animal Industry and Fisheries (MAAIF) of Uganda.

Ethics statement

Ethical review and approval was not required for the animal study because it is the animal movement data.

Author contributions

Study conception and design: EH, KT, HL, and MD. Data validation: EH, SK, and IM. Data analysis: EH, KT, and HL. Manuscript writing: EH. Manuscript review: EH, KT, HL, MD, and SK. All authors contributed to the article and approved the submitted version.

Funding

This study was funded by the CGIAR initiative on Sustainable Animal Productivity for Livelihoods, Nutrition and Gender Inclusion (SAPLING).

Acknowledgments

This research was conducted under the CRP Livestock and continued under the CGIAR Sustainable Animal Productivity for Livelihoods, Nutrition and Gender Inclusion (SAPLING) Initiative. CGIAR research is supported by contributions from the CGIAR Trust Fund. CGIAR is a global research partnership for a food-secure future dedicated to transforming food, land, and water systems in a climate crisis. Special gratitude is directed toward the personnel that helped in the retrieval and clerking of data from the AMPs, Dr. Anna Rose Ademun (Chief Veterinary Officer, Uganda), who authorized the use of the secondary data in this study and finally Terry Mwenda for the English editing for this manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2023.1095293/full#supplementary-material

SUPPLEMENTARY FIGURE 1
Network visualization showing out-degree for **(A)** the most connected seasonal network (April–June 2019) and **(B)** the most connected monthly network (January 2019) in the cattle inter-district movement networks in the Cattle Corridor of Uganda between 2019 and 2021.

SUPPLEMENTARY FIGURE 2
Network visualization showing out-degree for **(A)** the most connected seasonal network (April–June 2019) and **(B)** the most connected monthly network (June 2019) in the small ruminant inter-district movement networks in the Cattle Corridor of Uganda between 2019 and 2021.

SUPPLEMENTARY FIGURE 3
Network visualization showing out-degree for **(A)** the most connected seasonal network (April–June 2021) and **(B)** the connected monthly network (May 2021) in the pigs inter-district movement networks in the Cattle Corridor of Uganda between 2019 and 2021.

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TYPE Original Research
PUBLISHED 02 February 2023
DOI 10.3389/fvets.2023.1012978

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OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Veterinary Humanities and Social Sciences, a section of the journal Frontiers in Veterinary Science

RECEIVED 06 August 2022
ACCEPTED 16 January 2023
PUBLISHED 02 February 2023

CITATION
Murato Y, Hayama Y, Kondo S, Sawai K, Yamaguchi E and Yamamoto T (2023) Region-wise analysis of beef cow movements in Japan. *Front. Vet. Sci.* 10:1012978. doi: 10.3389/fvets.2023.1012978

Region-wise analysis of beef cow movements in Japan

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Animal movement is an important factor in the transmission of animal infectious diseases. A better understanding of movement patterns is therefore necessary for developing effective control measures against disease spread. In Japan, a cattle tracing system was established in 2003, following a bovine spongiform encephalopathy epidemic, and the information on all cattle movements has been stored in a national database maintained by the National Livestock Breeding Center. Using these data, we previously analyzed the movement of dairy cows, concluding that heterogeneities in cattle movement are associated with regional and seasonal factors. In the present study, we aimed to identify specific factors affecting the regional and seasonal movement patterns of beef cows in Japan. From April 2012 to March 2017, 797,553 farm-to-farm movement events were recorded. We analyzed movements by month and by cattle age and looked at the frequency of movement within and between seven regions spanning the national territory. Our results show that calf movement peaked at 9–10 months old; these movements were considered to be *via* the market and were frequent within and between regions. For inter-regional movements, Kyushu region was the top producer of calves for calf trading markets throughout Japan. With regard to intra-regional movements, round-trip movements for summer grazing were observed in May and October for cattle of various ages in the northern regions, especially Hokkaido and Tohoku. Moreover, the movements of Japanese Shorthorn breeds in Tohoku region exhibited consistent annual peaks in May and October/November, in accordance with their seasonal breeding practice. In the areas with high relative densities of dairy cows, such as Hokkaido, the shipping of newborn beef calves produced *via* embryo transfer to dairy cows was also observed. Overall, understanding the patterns of beef cow movement will help develop effective disease surveillance measures, such as pre-movement inspections focused on specific regions and types of movement.

KEYWORDS
animal infectious diseases, cattle movement, beef cow, Japan, tracing system

1. Introduction

Animal movement represents a major means for the transmission of animal infectious diseases. Several important diseases, such as foot-and-mouth disease and tuberculosis, can spread through the movement of animals (1–4). A better understanding of animal movement is therefore essential for developing effective control measures against the spread of infections. Movement patterns are affected by factors such as species, breeds, and regions. Studies on animal movement have been conducted in some countries, including the United Kingdom and Australia, where regional and seasonal heterogeneities in the movement patterns of cattle were reported (5–8).

In Japan, all cattle numbers and their movements are to be reported into a cattle tracing system, which was established following the outbreak of bovine spongiform encephalopathy (BSE) in 2001. This system ensures that all cattle in Japan are registered with a unique number, and all movements from birth to death are recorded and stored in the database (9). In a previous study, we analyzed the movement of 1.36 million dairy cows, accounting for approximately one-third of the total cattle population in Japan, based on data from the cattle tracing system; we revealed heterogeneities in dairy cow movement, which were associated with regional and seasonal factors (10). However, the nationwide movement of beef cattle in Japan has not yet been studied.

In Japan, the primary breeds of beef and dairy cattle are Japanese Black and Holstein, respectively. The suitable environments for rearing these two breeds differ. Japanese Black cattle, which are relatively tolerant to high temperatures, are commonly raised in Kyusyu, which is located in the southern part of Japan, while Holsteins are commonly raised in Hokkaido, located in the northern part. Such differences in biological and geographical factors are expected to result in different movement patterns between beef and dairy cattle. In this study, we focused on breeding beef cattle, as they are expected to have more varied movement patterns because their rearing period is longer than that of feedlot cattle. Female beef cattle for breeding account for 35% of all beef cattle, including feeding cattle, whereas male breeding beef cattle account for <0.1%. Therefore, male breeding beef cattle were removed from this study because their movement patterns do not represent general trends (11, 12). Herein, we tried to determine specific factors which affect beef cow movement patterns regionally and seasonally.

2. Materials and methods

2.1. The national database of cattle information and movement record

Following the outbreak of BSE in September 2001, a cattle tracing system based on "the law for special measures concerning the management and relay of information for individual identification of cattle" was introduced throughout Japan in December 2003. As a result, all cattle are required to wear an ear tag with a unique individual identification number within 7 days of birth, and all movements from birth to death, including movements to slaughtering plants, are recorded and stored in a national database called the "Individual Cattle Identification Register (ICIR)," maintained by the National Livestock Breeding Center (NLBC). As required by law, all facilities involved in cattle movements, such as cattle farms, livestock markets, and slaughterhouses, must report all cattle movements to the NLBC with the following details: movement date, movement type (birth, transfer, and slaughter), and facility identification number. In this study we evaluated cattle movement data for 16 years from FY2005 (FY is the Japanese fiscal year, from April 1 to March 31) to FY2020 accumulated in the ICIR, along with cattle individual and facility information related to each movement. All data were obtained directly from the NLBC to the National Institute of Animal Health under the condition of "the Regulation for the Second Use of Individual Cattle Identification Register of National Livestock Breeding Center" and were anonymized by replacing farm- and cattle-identifiable data with randomized identification numbers before the analysis.

2.2. Preparation of data for analysis

Cattle movement data were connected to individual information and facility information *via* the individual identification number and facility number, respectively. Records of cattle with inaccurate movement histories, such as movement after death or before birth, were removed. Two movements connected by a stay of <1 day at any facility were converted to a single movement, considering that the movement was between farms, occurring *via* markets or traders. Individual information included individual identification number, date of birth, sex, breed, and the individual identification number of the mother. Cattle that appeared as mothers in the individual information for cattle involving whole movement data for 16 years were considered to have a history of calving at the birth date of the calf. Among female beef breed cattle, such as Japanese Black, those with at least one calving history as of March 31, 2021 (the last date of the study period) were considered beef cows. However, lifetime calving history was used as a criterion to identify a mother cow, because the feeders were excluded in this study; cattle younger than the expected age of their first delivery at the end of the study period could not be correctly classified. Since the 95th percentile of the age at first delivery was 36 months, movement records in the last 3 years (FY2018 to FY2020) were excluded. Additionally, in Japan, several major events influencing cattle movement have occurred in recent years, including the outbreak of foot-and-mouth disease in 2010 and the Great East Japan Earthquake in 2011. As this study aimed to reveal general characteristics of cattle movement, we focused on the period after FY2012, that is, a period without any major accidental events influencing livestock movements. Consequently, beef cow movement records within the 6 years from FY2012 to FY2017 were included in the analysis.

2.3. Regional-level movement

In this study, "between-farm movement" records were extracted by removing "births (including imports)" and "deaths (including slaughter)" from the dataset. For between-farm movement, departure and arrival farms were classified into the following seven regions: Hokkaido (HKD), Tohoku (THK), Kanto (KTO), Chubu (CHU), Kinki (KNK), Chugoku/Shikoku (C_S), and Kyushu/Okinawa (K_O), as shown in Figure 1, according to their locations. The number of between-farm movements of beef cows was tabulated by the departure and arrival regions.

2.4. Month at the time of movement

The number of monthly inter-regional and intra-regional movements of beef cows was counted. When the number of monthly movements suggested possible seasonality, time series analysis was conducted by plotting seasonal subseries. In the seasonal subseries plotting, the length of the seasonal pattern was defined as a year and the subseries data for each month are plotted side by side

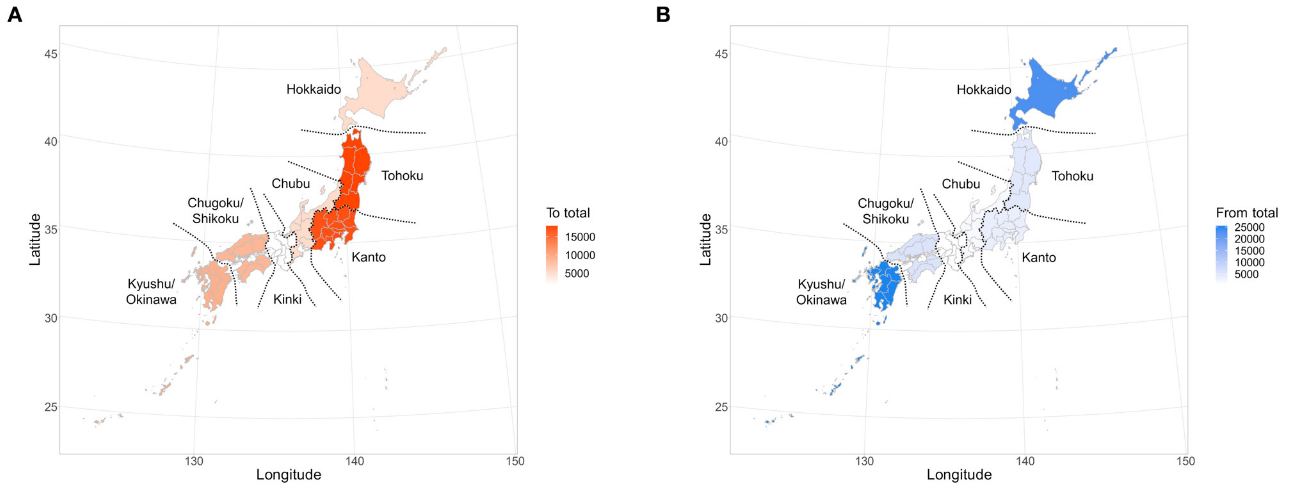

FIGURE 1
Classification of Japanese regions in this study and total number of movements of beef cows toward each region **(A)** and from each region **(B)**.

TABLE 1 The number of beef cow births by region and breed of mother cow in Japan in FY2017.

Region	Number of cattle (Proportion for each region)						Total number of cattle (Proportion for grand total)	
	Breed type of mother cow							
	Beef breed		Dairy breed		Crossbreed			
Hokkaido	7,902	(80.8%)	1,260	(12.9%)	622	(6.4%)	9,784	(13.6%)
Tohoku	8,876	(93.0%)	529	(5.5%)	137	(1.4%)	9,542	(13.2%)
Kanto	3,141	(76.1%)	885	(21.4%)	100	(2.4%)	4,126	(5.7%)
Chubu	1,158	(74.6%)	344	(22.2%)	51	(3.3%)	1,553	(2.2%)
Kinki	1,695	(93.9%)	39	(2.2%)	71	(3.9%)	1,805	(2.5%)
Chugoku/Shikoku	3,502	(87.7%)	419	(10.5%)	74	(1.9%)	3,995	(5.5%)
Kyushu/Okinawa	39,910	(96.5%)	957	(2.3%)	470	(1.1%)	41,337	(57.3%)
Total	66,184	(91.7%)	4,433	(6.1%)	1,525	(2.1%)	72,142	(100%)

Crossbred, or F1 cattle, are calves derived from dairy cows with beef breed semen.

horizontally. Regarding intra-regional movements, the number of movements per month was also counted by region.

2.5. Age in months at the time of movement

The number of movements by age in months was counted for inter-regional and intra-regional beef cow movements, respectively. When the number of movements by age was particularly skewed toward specific ages, further analysis, such as tabulating by the departure and arrival regions, was conducted focusing on the ages of interest. Additionally, the number of movements by age of month was counted by the calendar month. Regarding the intra-regional movements, the number of movements by age in months was also counted by region. When the number of movements by age showed a unique pattern for a specific region, further analysis, such as counting by the calendar month and breed, was conducted focusing on the regions of interest. All analyses were conducted using R version 4.0.5. with the forecast package for time series analysis.

3. Results

3.1. Overview of the beef cow population in Japan

A total of 700,000 beef cows of all ages were raised in Japan, of which 380,000 (55%) were kept in Kyushu/Okinawa (Supplementary Figure 1). The demographics of beef cows born in FY2017 are described in Table 1, in terms of region and breed of the mother cow. A total of 72,000 beef cows were born in Japan, of which 41,000 (57%) were born in Kyushu/Okinawa.

3.2. Overview of between-farm movement

A total of 797,553 between-farm movements were recorded for beef cows in the period from FY2012 to FY2017. The number of movements per year remained relatively constant across the study period, ranging from 124,610 to 138,676, with an average of 133,000. The numbers of regional-level movements are shown in Table 2

TABLE 2 The number of inter-regional movements of beef cows.

Departure region (from)	Arrival region (to)							From total
	Hokkaido	Tohoku	Kanto	Chubu	Kinki	Chugoku/ Shikoku	Kyushu/ Okinawa	
Hokkaido	-	8,356	9,848	1,545	124	522	2,689	**23,084**
	-	(12.7%)	(15.0%)	(2.4%)	(0.2%)	(0.8%)	(4.1%)	**(35.1%)**
Tohoku	688	-	2,277	441	83	250	1,193	**4,932**
	(1.0%)	-	(3.5%)	(0.7%)	(0.1%)	(0.4%)	(1.8%)	**(7.5%)**
Kanto	849	1,419	-	978	111	105	274	**3,736**
	(1.3%)	(2.2%)	-	(1.5%)	(0.2%)	(0.2%)	(0.4%)	**(5.7%)**
Chubu	294	281	680	-	187	157	324	**1,923**
	(0.4%)	(0.4%)	(1.0%)	-	(0.3%)	(0.2%)	(0.5%)	**(2.9%)**
Kinki	19	70	35	85	-	172	192	**573**
	(0.0%)	(0.1%)	(0.1%)	(0.1%)	-	(0.3%)	(0.3%)	**(0.9%)**
Chugoku/Shikoku	270	236	254	172	254	-	4,703	**5,889**
	(0.4%)	(0.4%)	(0.4%)	(0.3%)	(0.4%)	-	(7.2%)	**(9.0%)**
Kyushu/Okinawa	3,127	7,642	4,114	2,025	1,159	7,478	-	**25,545**
	(4.8%)	(11.6%)	(6.3%)	(3.1%)	(1.8%)	(11.4%)	-	**(38.9%)**
To total	**5,247**	**18,004**	**17,208**	**5,246**	**1,918**	**8,684**	**9,375**	**65,682**
	(8.0%)	**(27.4%)**	**(26.2%)**	**(8.0%)**	**(2.9%)**	**(13.2%)**	**(14.3%)**	**(100.0%)**

The number of movements by beef cows between each departure and arrival region in Japan from FY2012 to FY2017 are shown. The bold values indicate the number (or %) for the total.

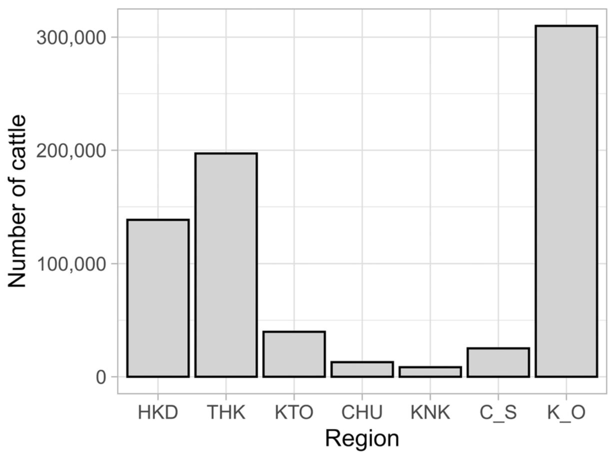

FIGURE 2
Number of intra-regional movements of beef cows by region in Japan from FY2012 to FY2017. HKD, Hokkaido; THK, Tohoku; KTO, Kanto; CHU, Chubu; KNK, Kinki; C_S, Chugoku/Shikoku; K_O, Kyushu/Okinawa.

and Figure 2 for inter- and intra-regional movements, respectively. Ninety-two percent (731,871) of all farm-to-farm movements were intra-regional, and 8% (65,682) were inter-regional.

3.3. Inter-regional movement

The number of inter-regional movements per month was lower in August-September (7–8%) and January-March (6–7%) than in other months (9–10%; Figure 3a). This seasonality was observed throughout the study period (Supplementary Figure 2A). The age distribution of inter-regional movements peaked at 9–10 months of age, and this peak was observed for all seasons (Supplementary Figure 3). Movements at 8–11 months of age accounted for 30% of all inter-regional movements (Figure 4a), with 69% of these movements originating in Kyusyu/Okinawa (Table 3).

3.4. Intra-regional movement

The number of monthly intra-regional movements was higher in May (14%) and October (12%) than in other months (6–10%; Figure 3a), and this seasonality was observed throughout the study period (Supplementary Figure 2B). Comparing the number of movements per month by region, peaks were clearly observed in May and October in all regions other than Kinki and Kyushu/Okinawa, especially in Hokkaido and Tohoku, which are located in the northern part of Japan (Figure 5). To examine the characteristics of movements in May and October, we analyzed these at the individual level using FY2017 data. Consequently, 38% of cows in Hokkaido that moved in May also moved in October, accounting for 34% of those that moved in October. In Tohoku, 39% of the cows that moved in May also moved in October, accounting for 49% of those moving in October. Comparing the age distribution at intra-regional movement by region, a peak at 8–10 months was observed in all regions (Figure 4b, Supplementary Figure 3), and another peak at <1 month was observed in Hokkaido, Kanto, Chubu, and Chugoku/Shikoku (Figure 6). Additionally, the age distribution for movement within Tohoku showed several small

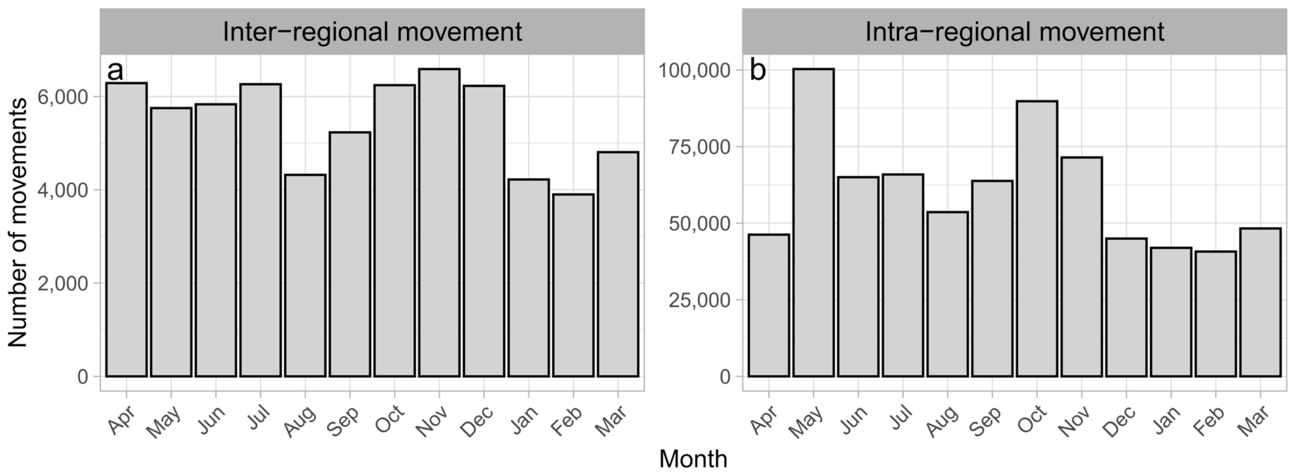

FIGURE 3
Number of monthly movements of beef cows. Inter-regional **(a)** and intra-regional movements **(b)** of beef cows in Japan from FY2012 to FY2017.

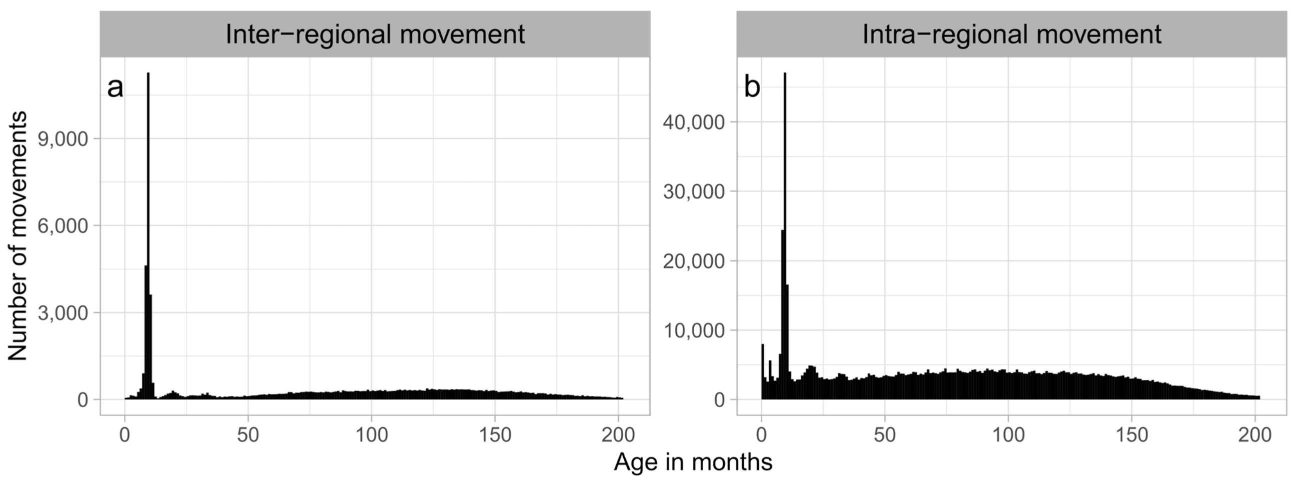

FIGURE 4
Age distribution of beef cows that moved within regions **(a)** and between regions **(b)** in Japan from FY2012 to FY2017.

peaks, with intervals of 5–7 months over almost 150 months of age (Figure 6). When the distribution of age at movement within Tohoku was broken down by month, peaks with 12-month intervals were observed in May, October, and November, and the difference between peaks of the age at the movement in May and October/November was about 5 months (Supplementary Figure 4). To examine the reason for these peaks with 12-month intervals, we compared the age distribution at movement by breed. The peaks with 12-month intervals were only observed for Japanese Shorthorn cattle (Supplementary Figure 5).

4. Discussion

The analysis of beef cow movements revealed that the frequency of movement varied depending on the season, age, rearing area, and breed. Further, these characteristics differed from the ones observed for dairy cows.

Regarding the distribution of age at the time of movement, a peak of high frequency of movements was observed for calves around 9–10 months of age, visible in every month of the year, irrespective of movement type (inter- or intra-regional). The beef-calf markets in Japan generally deal with calves aged about 8–10 months, be it for breeding or fattening (13, 14). This suggests that these movements mainly represent the movement of calves through markets. With regard to inter-regional movements, two-thirds or more of these were of calves departing from Kyushu/Okinawa, which accounted for more than half of both the number of beef cows raised in Japan and newborn beef cows, highlighting Kyushu/Okinawa as the major supplier of replacement beef cows to other regions. Meanwhile, Hokkaido, which holds the largest share of dairy cows kept and born in Japan, exported the largest number of replacement dairy cows to other regions (93%), highlighting its significance as a source of replacement dairy cows (10).

Peaks of high frequency of movements for calves at <1 month of age were observed in the age distribution for intra-regional

TABLE 3 The number of inter-regional movements of beef cows from 8 to 11 months old.

Departure region (from)	Arrival region (to)							From total
	Hokkaido	Tohoku	Kanto	Chubu	Kinki	Chugoku/ Shikoku	Kyushu/ Okinawa	
Hokkaido	-	1,228	236	221	13	148	203	**2,049**
	-	(6.3%)	(1.2%)	(1.1%)	(0.1%)	(0.8%)	(1.0%)	**(10.5%)**
Tohoku	129	-	371	207	50	104	160	**1,021**
	(0.7%)	-	(1.9%)	(1.1%)	(0.3%)	(0.5%)	(0.8%)	**(5.2%)**
Kanto	119	856	-	218	7	19	170	**1,389**
	(0.6%)	(4.4%)	-	(1.1%)	(0.0%)	(0.1%)	(0.9%)	**(7.1%)**
Chubu	74	135	77	-	63	49	106	**504**
	(0.4%)	(0.7%)	(0.4%)	-	(0.3%)	(0.3%)	(0.5%)	**(2.6%)**
Kinki	1	45	8	10	-	15	101	**180**
	(0.0%)	(0.2%)	(0.0%)	(0.1%)	-	(0.1%)	(0.5%)	**(0.9%)**
Chugoku/Shikoku	175	131	132	111	74	-	333	**956**
	(0.9%)	(0.7%)	(0.7%)	(0.6%)	(0.4%)	-	(1.7%)	**(4.9%)**
Kyushu/Okinawa	2,497	6,179	1,407	1,301	875	1,172	-	**13,431**
	(12.8%)	(31.6%)	(7.2%)	(6.7%)	(4.5%)	(6.0%)	-	**(68.8%)**
To total	**2,995**	**8,574**	**2,231**	**2,068**	**1,082**	**1,507**	**1,073**	19,530
	(15.3%)	**(43.9%)**	**(11.4%)**	**(10.6%)**	**(5.5%)**	**(7.7%)**	**(5.5%)**	(100.0%)

The number of movements by beef cows between each departure and arrival region in Japan from FY2012 to FY2017 are shown. The bold values indicate the number (or %) for the total.

movements in Hokkaido, Kanto, Chubu, and Chugoku/Shikoku. The proportion of beef calves delivered from dairy cows among all beef calves was relatively high in these regions. In Japanese dairy farms, it is common practice to transfer beef cattle embryos, usually Japanese Black embryos, into dairy cows in order to produce beef calves while inducing the lactation of delivered dairy cows (13, 15). Although a similar practice can be performed *via* the artificial insemination of dairy cows with beef breed semen, the produced beef cow calves are crossbred (also called F1 cattle), and this study is targeting the movements of beef breeding cows. Thus, these are considered movements of newborn beef calves produced *via* embryo transfer to dairy cows.

As for the number of monthly movements, lower inter- and intra-regional movement numbers were commonly observed in the summer and winter months. Shipping animals potentially causes physical and mental stress, which could in turn reduce productivity. This may explain the seasonality of the movement, as movement is avoided during the hot summer months and cold winter months to minimize such shipping stress. The number of intra-regional movements was much higher in May and October than in any other month. Moreover, in Hokkaido and Tohoku, where such seasonality was clearly observed, over one-third of intra-regional movements in May and October were conducted by the same cattle. Thus, these movements were likely round-trip movements. In Japanese cattle farming, summer grazing is commonly practiced, as cattle are transferred to the pasture in May, when the grassland becomes available, and leave the pasture around October, before the snowfall (16, 17). This indicates that the seasonality observed is due to summer grazing and is represented by movements between the source farms and common pastures. However, in Kyushu/Okinawa, which is located in the southern part of Japan with a relatively high average temperature, this seasonality was not clearly observed, presumably because year-round grazing is possible (17). In Kinki, which hosts only 0.1% of the total pastureland area in Japan, the smallest share compared to other regions (0.6–84%) (18), it is possible that summer grazing is not actively practiced, and this may be a reason for the lack of a clear seasonality. Although the total number of monthly intra-regional movements was higher in May and October, the proportion of movements between 8 and 11 months of age was lower in these 2 months than in the other months. This indicates that the higher number of intra-regional movements in May and October was not mainly due to shipping calves to the market. In addition, the age distribution of beef cow that moved in both May and October 2017 indicated that these movements were not limited to heifers up to the average age of the first calving in beef cows (24.5 months old) in Japan (19), but was observed over a wide range of ages. Meanwhile, similar seasonality in cattle movements due to summer grazing was also observed in Japanese dairy cows (10). During the summer grazing of dairy cows, peaks in the age distribution at movement in May and October were observed at 13–14 and 19–20 months of age and thus were considered as the movement of growing heifers. This difference in the age of summer grazing movement between beef and dairy cows may result from the fact that the latter are rarely grazed after first calving because of milking, whereas beef cows do not need a milking period and can perform summer grazing regardless of age or calving number.

In the age distribution at movement within Tohoku, additional small peaks in small increments repeatedly appeared only in May, October, and November, and these peaks were 12 months of age apart, suggesting that cows forming these peaks may partake in summer grazing. Moreover, we found that Japanese Shorthorns

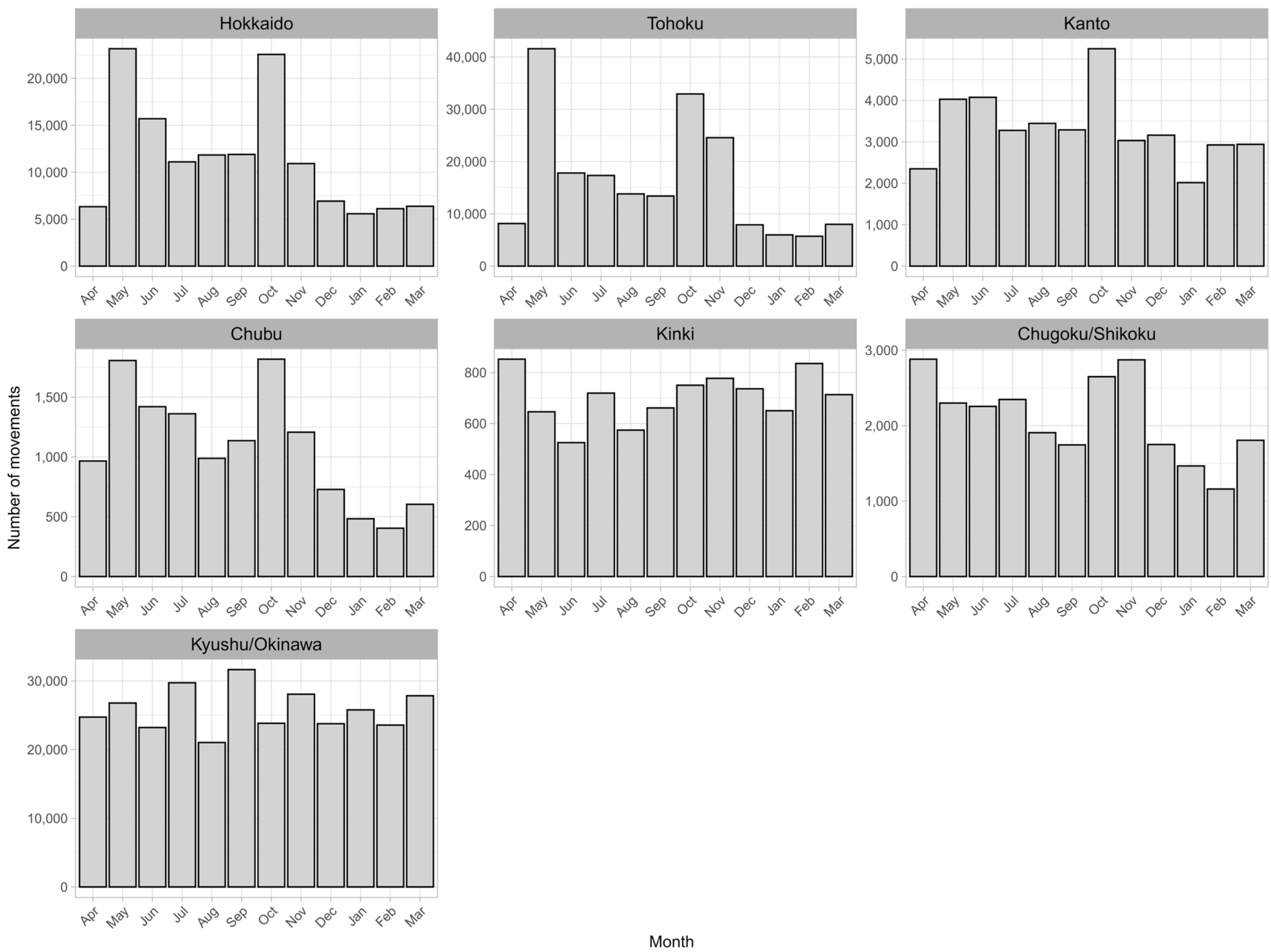

FIGURE 5
Number of intra-regional movements of beef cows by region and by month in Japan from FY2012 to FY2017 by region.

formed these peaks. The Japanese Shorthorn is a breed of Wagyu cattle that has been improved to be suitable for summer grazing by crossing the Nanbu cattle, a native breed raised in the highlands in Tohoku, with the imported Shorthorn breed (20–23). Japanese Shorthorn calves and their dam are usually extensively raised in Tohoku, with dam-calf summer grazing traditionally implemented to save labor. To allow mother-calf pairs to spend their suckling period in the summer pasture, Japanese Shorthorns have been subjected to seasonal breeding so that calves are born around March, prior to May when they are transferred to the pasture. Therefore, the clear peaks with annual intervals in Japanese Shorthorns can be explained by this seasonal breeding management followed by summer grazing every year throughout their lives.

In addition, as it provides insight into the movement heterogeneity of Japanese beef cattle, this study will also be useful for planning the surveillance of specific animal diseases. In Japan, chronic infectious diseases of cattle causing low productivity, such as enzootic bovine leukosis (EBL) and bovine viral diarrhea (BVD), endemically occur each year (24). Transmission of EBL and BVD is mainly caused by cohabitation with infected cattle, and thus the introduction of cattle from other farms has been reported as a risk factor for disease introduction (25, 26). For example, summer grazing has been reported to be an important risk factor for the transmission of BVD (26, 27). As this study revealed that summer grazing is more frequent in northern regions such as Hokkaido and Tohoku, inspections of cattle moving for summer grazing are encouraged in these regions. Similarly, regarding the inter-regional movements, the movement of 9–10-month-old calves was demonstrated to most frequently occur from Kyushu/Okinawa in this study. This suggested that the surveillance of calves shipped to the market in this region may effectively contribute to the suppression of trans-regional between-farm transmission. In addition, the expected number of samples and the human and budgetary resources required for these surveillances could be also driven by our results.

The results of this study revealed age-dependent movement, i.e., shipments of calves *via* markets, and season-dependent round-trip movement of the same cow, i.e., entering and returning into/from pasturelands during summer grazing. With regard to inter-regional calf shipment, Kyushu/Okinawa emerged as the most important supplier. Meanwhile, summer grazing was more commonly practiced in the northern regions, especially in Hokkaido and Tohoku. We also observed unique movement of Japanese Shorthorns in the Tohoku region and characteristic movement of newborn beef calves produced *via* embryo transfer to dairy cows. The findings regarding these heterogeneities in cattle movements depending on the season, age, or cattle breed, as identified in this study, will help develop effective

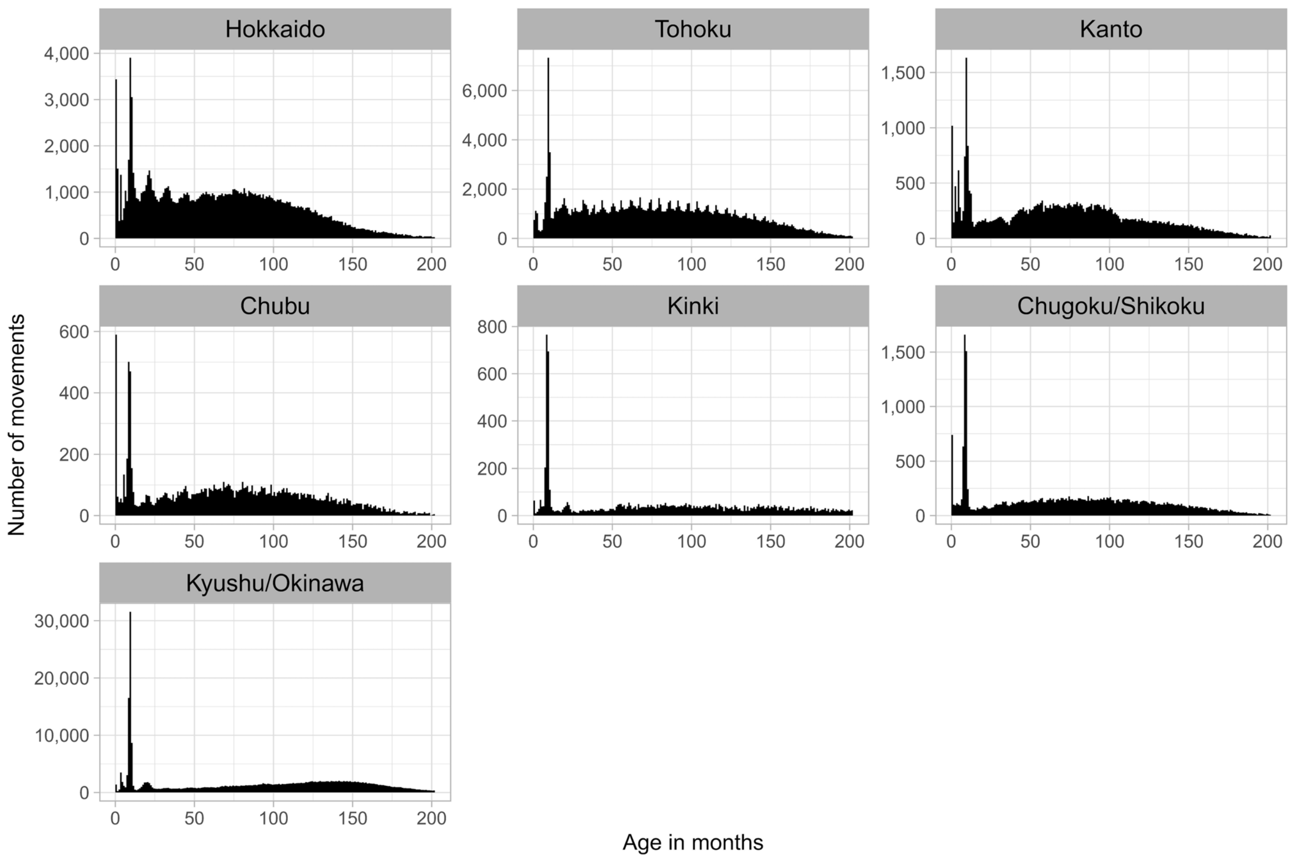

FIGURE 6
Age distribution of beef cows that moved within regions in Japan from FY2012 to FY2017 by region.

disease surveillance measures, such as pre-movement inspections focused on specific regions and movement types.

Data availability statement

The data that support the findings of this study are available from the National Livestock Breeding Center (https://www.nlbc.go.jp/); however, restrictions apply to the availability of these data, which were used under license for the current study, and are, therefore, not publicly available.

Author contributions

TY conceived and designed the study. YM and TY collected the data. YM, YH, and TY analyzed the data. SK, KS, and EY contributed to the interpretation of the results. YM drafted the manuscript. KS, YH, and TY revised the main manuscript text. All authors have read and approved the final manuscript.

Funding

This study was funded by the research project on Regulatory Research Projects for Food Safety, Animal Health, and Plant Protection (JPJ008617 and 18065101) funded by the Ministry of Agriculture, Forestry and Fisheries of Japan (FY2018–2022). The funder had no role in the study design, data analysis, and decision to publish or the preparation of the manuscript.

Acknowledgments

We appreciate the kind cooperation of the National Livestock Breeding Center in providing cattle movement records and relevant information.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2023.1012978/full#supplementary-material

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frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 13 March 2023
DOI 10.3389/fvets.2023.1074264

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OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to
Veterinary Epidemiology and Economics,
a section of the journal
Frontiers in Veterinary Science

RECEIVED 19 October 2022
ACCEPTED 22 February 2023
PUBLISHED 13 March 2023

CITATION
Ellis J, Brown E, Colenutt C and Gubbins S (2023) Assessing the effectiveness of environmental sampling for surveillance of foot-and-mouth disease virus in a cattle herd. *Front. Vet. Sci.* 10:1074264.
doi: 10.3389/fvets.2023.1074264

Assessing the effectiveness of environmental sampling for surveillance of foot-and-mouth disease virus in a cattle herd

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The survival of foot-and-mouth disease virus (FMDV) in the environment provides an opportunity for indirect transmission, both within and between farms. However it also presents the possibility of surveillance and detection *via* environmental sampling. This study assesses the effectiveness of environmental sampling strategies in the event of an outbreak, using a previous model for transmission of FMDV in a cattle herd that had been parameterized using data from transmission experiments and outbreaks. We show that environmental sampling can be an effective means of detecting FMDV in a herd, but it requires multiple samples to be taken on multiple occasions. In addition, environmental sampling can potentially detect FMDV in a herd more quickly than clinical inspection. For example, taking 10 samples every 3 days results in a mean time to detection of 6 days, which is lower than the mean time to detection estimated for the 2001 UK epidemic (8 days). We also show how environmental sampling could be used in a herd considered to be at risk as an alternative to pre-emptive culling. However, because of the time taken for virus to accumulate at the start of an outbreak, a reasonable level of confidence (> 99%) that an at-risk herd is indeed free from infection is unlikely to be achieved in less than 1 week.

KEYWORDS

environmental surveillance, foot-and-mouth disease, FMDV, mathematical model, cattle, epidemiology

1. Introduction

Foot-and-mouth disease (FMD) is a highly infectious disease, affecting cloven-hoofed animals such as cattle, sheep, goats, pigs and various wildlife species (1). The causative agent, foot-and-mouth disease virus (FMDV), is spread primarily through direct contact between infected and susceptible animals. Indirect transmission can occur *via* the environment and long distance transmission is facilitated through fomites or aerosols. In disease-free countries, FMDV can spread rapidly upon introduction, causing significant disruption and economic costs (2). The outbreak of FMD in the UK in 2001 resulted in the culling of 4.2 million animals for disease control purposes, another 2.3 million on welfare grounds, and costs of over £8 billion (3, 4). To reduce the spread between farms and bring the outbreak under control, the time between the first infection on a farm and the reporting of infection is vital.

FMDV is shed from infected animals into their environment through their excretions and secretions, potentially remaining infectious for a prolonged period of time (depending on environmental conditions, such as temperature and humidity) (5–7). The accumulation of FMDV in the environment also provides the opportunity for environmental sampling as a means of detecting virus circulation. This has been successfully demonstrated in countries where FMD is endemic in previous studies (7, 8). Furthermore, taking environmental swabs [see, e.g., (5, 7, 8)] is a non-invasive alternative to clinical examination, requires little prior knowledge of diseases or handling of animals and is low cost in terms of sample collection.

In the event of a future outbreak of FMD in the UK or other FMD-free country, environmental sampling could alleviate some of the burden of having experienced veterinarians examine large numbers of animals and reduce the detection time of suspected cases. It could also be used to monitor at-risk farms as an alternative to pre-emptive culling, thereby reducing the number of animals culled. Because of the ability to infer the disease status of a population without testing many individuals, environmental surveillance has also been utilized for other pathogens that cause animal diseases such as Johne's disease (9) and avian influenza (10), as well as human diseases including COVID-19 (11, 12) and polio (13–15).

Here, we assess environmental sampling as a means of FMDV surveillance for a single herd. We use an individual based model of FMDV transmission within a cattle herd where infection of a susceptible individual can occur through direct contact with an infected animal or through environmental contamination (16). The model estimates the amount of FMDV that accumulates in the environment where a herd is located as an outbreak develops. Using this, we estimate the probability of detecting FMDV in an environmental sample at any given moment during the outbreak. Different surveillance strategies, which vary in the number of samples taken and time intervals between sampling, are considered and the time from infection to detection is calculated. We also assess the utilization of environmental surveillance in a herd at risk of infection as an alternative to pre-emptive culling.

2. Methods

2.1. Transmission model

We have previously developed an individual based model for the within-herd transmission of FMDV that includes transmission *via* direct contact and *via* a contaminated environment (16).

2.1.1. Viral shedding

Following infection, the infectiousness of an animal is proportional to the level of viral shedding. The level of virus in an infected animal can be modeled as

$$V(\tau) = \frac{2V_p}{\exp(-\gamma_g(\tau - T_p)) + \exp(\gamma_d(\tau - T_p))}, \quad (1)$$

where V_p is the level of peak titre, T_p is the time of peak titre, γ_g and γ_d are the rates for the exponential viral growth and decay phases, respectively, and τ is the time since infection. The corresponding level of viral shedding is given by

$$S(\tau) = \log(V(\tau)) \quad (2)$$

where $V(\tau)$ is given by Equation (1) and $S(\tau)$ is restricted to be non-negative.

Variation amongst individuals in shedding is incorporated in the model by sampling the parameters from higher-order distributions. More specifically, γ_g, γ_d are drawn from gamma distributions with means μ_{γ_g}, μ_{γ_d} and shape parameters s_{γ_g}, s_{γ_d}, respectively. V_p is drawn from a log gamma distribution with parameters μ_V and s_V (the mean and shape parameter of the corresponding gamma distribution). Finally, the time of peak titre T_p and incubation period T_c are drawn from a bivariate log normal distribution with parameters μ_{T_p}, μ_{T_c}, σ_{T_p} and σ_{T_c} (the means and standard deviation of the corresponding normal distribution) and a correlation coefficient ρ_{pc}. This allows the within-host viral dynamics to be linked to the onset of clinical disease.

2.1.2. Environmental contamination

The rate of environmental contamination from each animal is assumed to depend on the amount of virus shed by an individual (given by Equation 2) and the natural decay rate of virus in the environment. The contamination and decay rates are assumed to vary between four areas: the floor, walls, trough, and feces. The level of virus in each location is given by

$$\frac{dE_i}{dt} = \frac{\alpha_i}{N} \sum_{j=1}^{N} S_j(t) - \delta_i E_i(t), \quad (3)$$

where E_i, $i = 1, ..., 4$ is the level of contamination found in the floor, walls, trough, and feces, respectively. α_i is the rate of contamination, δ_i is the rate of decay and N is the herd size.

2.1.3. Probability of transmission

Transmission of FMDV within the herd can occur through direct contact between animals or through environmental contamination. For direct transmission, the probability of an animal becoming infected through direct transmission over a time interval $[t, t + \Delta t]$ is given by

$$P_d(t) = 1 - \exp\left(-\beta_d \int_t^{t+\Delta t} \frac{\sum_{j=1}^{N} S_j(t)}{N} dt\right), \quad (4)$$

where β_d is the direct transmission rate. The probability of a susceptible animal becoming infected *via* environmental contamination in the interval $[t, t + \Delta t]$ is given by

$$P_e(t) = 1 - \exp\left(-\beta_e \int_t^{t+\Delta t} \sum_{i=1}^{4} E_i(t) dt\right), \quad (5)$$

where β_e is the environmental transmission rate which is assumed to be the same for all contaminated areas. The probability for a susceptible animal to become infected at each time interval is given by

$$P(t) = \left(1 - (1 - P_e(t))(1 - P_d(t))\right). \quad (6)$$

The dynamics of a within-herd outbreak described by this model are discussed in more detail in (16). An example of an outbreak in terms of the number of infected cattle and total environmental contamination over time is shown in Figure 1. The level of environmental contamination is used to estimate detection times.

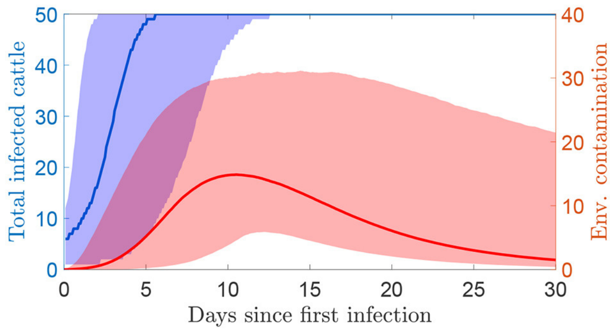

FIGURE 1
The simulated number of infected cattle and the total environmental contamination over time since the first infections using the transmission model (median and 95% prediction interval). Environmental contamination is taken as the sum of the measures at each of the four locations. The herd size is 50 cattle.

2.2. Detection of FMDV in environmental samples

We assume environmental samples will be tested by an rRT-PCR assay specific for FMDV (6, 7). The probability of detecting FMDV in an environmental sample depends on the amount of virus in the location (i.e., walls, floor, feed trough, or feces) being sampled. We assume the probability is given by

$$P(E_j) = 1 - \exp(-\xi_j E_j), \tag{7}$$

where ξ_j is a parameter relating the level of environmental contamination to the probability of detection and E_j, $j = 1, ..., 4$ is the level of environmental contamination on the walls, floor, trough, or feces, respectively. This probability incorporates the sensitivity of the test as well as the chances of finding virus in the location sampled. The test specificity is assumed to be equal to one.

2.3. Parameter estimation

Parameters in the transmission model were estimated previously using approximate Bayesian computation sequential Monte Carlo (ABC-SMC) (16). In the present study, a sample was drawn from the joint posterior distribution for the parameters and used in the simulation for each replicate.

The parameter ξ_j was estimated from data on the amount of virus and the proportion of positive samples from environmental samples collected during a series of transmission experiments (6). The likelihood for the data is given by,

$$L = \prod_{E_j} \binom{n_{E_j}}{k_{E_j}} P(E_j)^{k_{E_j}} (1 - P(E_j))^{n_{E_j} - k_{E_j}} \tag{8}$$

where n_{E_j} and k_{E_j} are the number of samples taken and the number of positive samples at each level of estimated environmental contamination E_j. The posterior distribution was generated using an adaptive Metropolis-Hastings algorithm with an non-informative uniform prior and a Gaussian proposal distribution, scaled to ensure an acceptance rate between 30 and 50%. For each replicate a value for ξ was drawn from its posterior distribution independently of the transmission parameters.

2.4. Environmental sampling strategies

Combining the transmission model, which simulates the level of environmental contamination over time, with the probability of detection, we can explore the effectiveness of different sampling strategies. For each strategy we assume that s samples are taken from the environment every d days, starting at a random day post-infection between 1 and d. The location of the samples is random, i.e., for each sample a number from one to four is randomly generated and the sample is taken at the corresponding area of the environment.

2.4.1. Sampling to detect an infected herd

The effectiveness of a strategy at detecting an infected herd was assessed in two ways. First, we estimated the time to detection, which is the number of days after the initial infection in the herd that an environmental sample tests positive under the sampling strategy. Second, we calculated the proportion of infectiousness that occurs before detection, which is indicative of how transmission could occur to other herds before detection.

As the transmission model includes two routes of transmission, the proportion of infectiousness can be estimated for each. The proportion of infectiousness from infected cattle is given by

$$\theta_S = \frac{\int_0^{t_d} \sum_{j=1}^{N} S_j(t)dt}{\int_0^{\infty} \sum_{j=1}^{N} S_j(t)dt}, \tag{9}$$

and the proportion of infectiousness from environmental contamination is given by

$$\theta_E = \frac{\int_0^{t_d} \sum_{i=1}^{4} E_i(t)dt}{\int_0^{\infty} \sum_{i=1}^{4} E_i(t)dt}, \tag{10}$$

where t_d is the time at which detection occurs.

For a strategy to be effective it needs to reduce the between-herd basic reproduction ratio R_h to below one. The upper confidence limit of R_h for farms during the initial phase of the 2001 UK FMD epidemic was estimated to be 3.2 (17, 18). We use this figure as a conservative estimate of the R_h with no surveillance to demonstrate the sampling effort required to reduce transmission so that $R_h < 1$, the point at which an epidemic can not sustain itself. This requires $\theta < 1/R_h \approx 0.31$.

2.4.2. Sampling in an at-risk herd

An alternative use of environmental sampling is in a herd deemed at risk of infection but in which no animals have shown clinical signs. This could be to detect infection, if it is present, as early as possible or as a means of showing the herd is free from infection as an alternative to pre-emptive culling. Sampling should begin as soon as FMDV is detected on the other farm and continue until either FMDV is detected on the at-risk farm or sufficient

TABLE 1 The median and 95% credible interval of ξ.

	Floor	Walls	Food trough	Feces
ξ	0.075 (0.060–0.091)	0.040 (0.026–0.057)	0.073 (0.051–0.098)	0.071 (0.060–0.083)

samples have been taken over a long enough time period to have confidence that FMDV is not present on the at-risk farm.

Given a time interval in which infection could have occurred, it is possible to show how many samples need to be taken for how many days consecutively before the probability that an infected herd would remain undetected is less than a given threshold. Detection occurs when any single sample returns a positive result. Therefore, we calculate the probability of a sampling strategy being negative as the product of negative results from all samples taken over the entire period of time when sampling is undertaken. We repeat 10,000 simulations and, starting on a random day within the given interval, test s samples for the next d days. The proportion of simulations that do not result in detection provides an estimate for the probability that all samples on an infected farm would be negative.

2.4.3. Comparison with clinical surveillance

Using the results given by the model, we can simulate the time taken from infection to detection using clinical surveillance. The onset of clinical signs is included in the transmission model and so this alternative detection method can be modeled in a similar manner to taking environmental samples. At each inspection interval, a given number of animals are randomly selected for inspection and the outbreak is detected if at least one of them is showing clinical signs.

We also consider the time taken from infection to reporting for farms during the 2001 UK outbreak, which was estimated to follow a gamma distribution with a mean of 8.07 days and a variance of 6.67 (19).

3. Results

3.1. Probability of detection

The posterior median and 95% credible interval for ξ is shown in Table 1, and the probability of detection at different levels of contamination is shown in Figure 2. The results are similar for each area of the environment except for the walls, which has a lower ξ and a shallower probability curve. Note that at each contamination level only a few samples were taken, which is why the proportion testing positive appears to take discrete values.

3.2. Sampling to detect an infected herd

Figures 3, 4 show contour plots for the time to detection, t_d, and proportion of infectiousness before detection, θ_S and θ_E, for different environmental sampling strategies, determined by the number of samples and the number of days between sampling, on a farm with 50 cattle. The two panels in Figure 3 shows the same results, overlaid with different dotted lines for comparison with clinical surveillance strategies. In Figure 3A, the dotted line corresponds to a time detection of 8.07 days, which is the mean estimated for the 2001 UK epidemic (19). This shows the combination of inspection interval and number of samples per inspection required to have the same mean detection time. In Figure 3B, the three dotted lines correspond to the detection time when inspecting cattle for clinical signs. At each inspection interval the dotted line is plotted on the corresponding point on the contour where the mean time of clinical detection is equal to the mean time of detection from environmental sampling.

In both cases, for environmental sampling to be more effective than the alternatives, the number of samples and inspection interval should be chosen to be to the right of or below the dotted lines. For example, a strategy of taking 20 environmental samples every 7 days would detect FMDV after an average of 7 days since infection, which is more effective than inspecting 20% of the herd for clinical signs every 7 days (and would also be more effective than clinical surveillance as implemented in the 2001 UK epidemic). A strategy of taking five samples every 3 days would also take an average of approximately 7 days from infection until detection, but would not be as effective as inspecting 5% of the herd every 3 days. The strategies that perform better than the estimate from the 2001 epidemic and inspections of 20% of the herd require several samples to be taken at a time; options include 12 samples every day, 15 samples every 2 days or 20 samples once a week.

We see from Figure 4 that the proportion of infectiousness before detection is higher for viral shedding than for environmental contamination. This is as expected as the sum of all viral shedding peaks earlier than the environmental contamination, which decays at a slower rate (16). Therefore, at the time of detection, in most scenarios, less than 40% of infectiousness from environmental contamination has occurred compared to up to 70% of that from viral shedding.

Assuming the between-herd reproduction ratio is $R_h = 3.2$ and infectiousness is measured by either viral shedding or environmental contamination alone to give R_S and R_E, respectively, then R_S and $R_E = 1$ when θ_S and $\theta_E = 0.31$, respectively. This is shown by the dotted lines in Figure 4. The area under or to the right of the lines show the required number of samples to be taken to achieve $R_h < 1$. As θ_S is higher than θ_E, a frequent sampling strategy is required for $R_S < 1$, whereas most strategies are below the threshold for $R_E < 1$. For example, 10 samples once a week would be sufficient to bring $\theta_E < 0.31$ but not θ_S, whereas 10 samples every 3 days would be sufficient to bring both below the threshold. Strategies of 5 samples every day or 15 every 4 days would also be sufficient for both measures.

The sensitivity of the results on sampling intervals and number of samples taken to changes in herd size was assessed (Supplementary Figures 1–3). This demonstrated that the size of the herd does not have a large impact on θ_E, though smaller herds have a slightly higher detection time and θ_S.

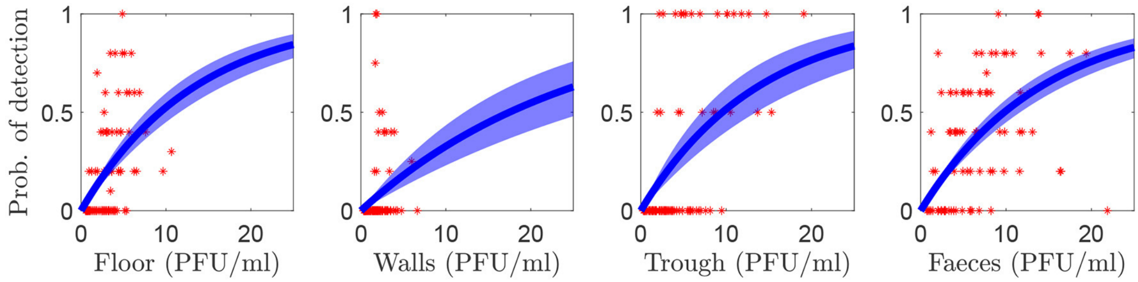

FIGURE 2
The probability of an environmental sample being positive for FMDV by rRT-PCR at different levels of environmental contamination. Red dots show the proportion of samples that were positive for FMDV when sampled at the same level of predicted environmental contamination. The blue line shows the posterior median and the shaded area shows the 95% credible interval.

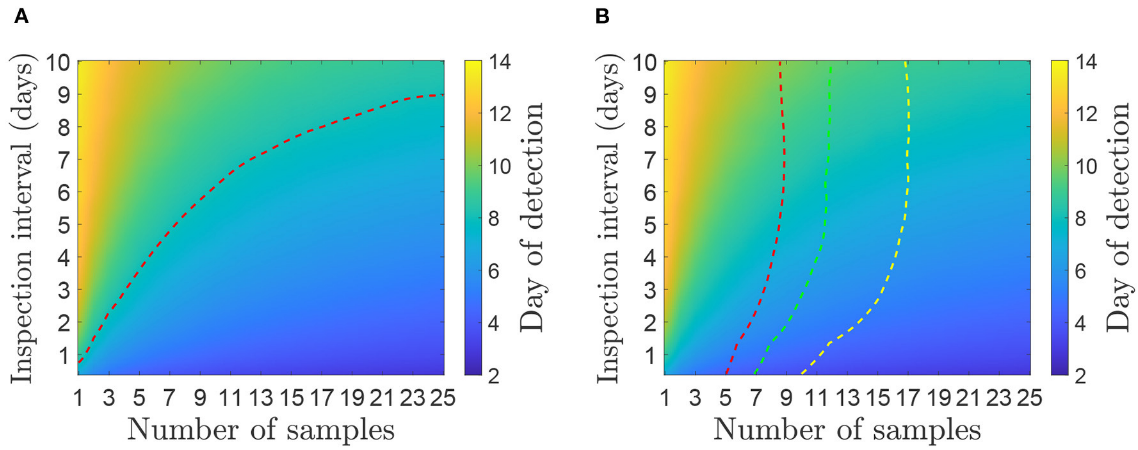

FIGURE 3
Mean day an outbreak would be first detected under different environmental sampling strategies for a herd size of 50 cattle. **(A)** Comparison with the mean time of detection (8.07 days) estimated for the 2001 UK epidemic (19). **(B)** Comparison with inspection for clinical signs assuming animals are inspected at the same frequency as environmental samples are taken (given on the y-axis). The red dotted line (left) shows day of detection when 5% of the herd are inspected, green line (middle) is 10% and yellow line (right) is 20%. A strategy below or to the right of the dotted line has a lower mean day of detection and therefore performs better than the corresponding level of clinical surveillance.

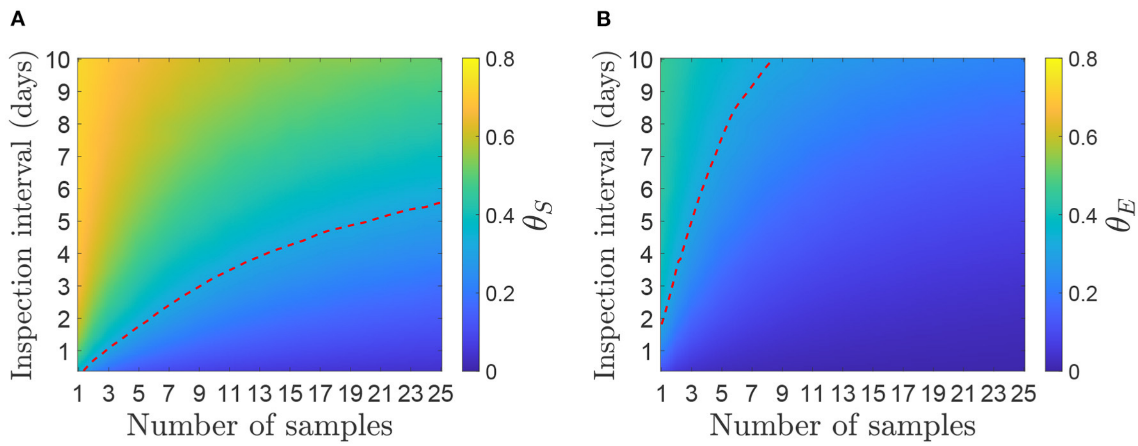

FIGURE 4
Mean proportion of infectiousness before detection for a herd size of 50 cattle. **(A)** Infectiousness is measured as the sum of viral shedding (θ_S). **(B)** Infectiousness is measured as the sum of environmental contamination (θ_E). The red dotted line represents the level of θ required for $R_h = 1$ if each measure of infectiousness was the only route of between-herd transmission.

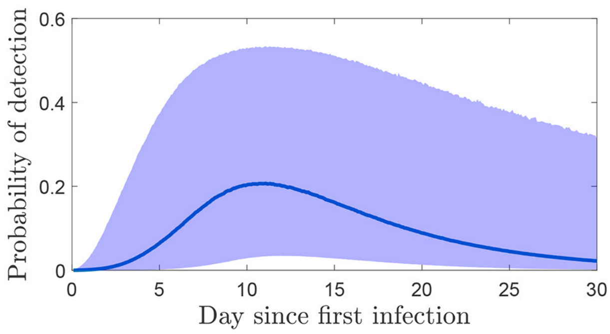

FIGURE 5
The probability (median and 95% credible interval) of detecting FMDV from a single sample on each day post infection.

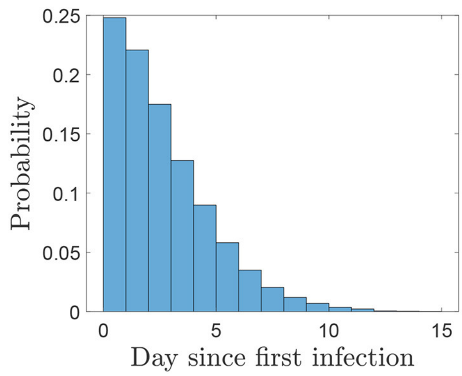

FIGURE 6
The probability of different time intervals between an infected herd infecting another premises and it being detected. This can be seen as the day that the other premises would be considered at risk and sampling would start. We exclude negative values as they indicate that infection occurs after detection. Estimates for herd generation time are made from viral shedding (T_{gd}) in (16) and detection times from (19).

3.3. Sampling in an at-risk herd

We now assess the value of environmental sampling in the scenario where a farm is deemed at risk, for example, due to FMDV being detected on a farm nearby or on a farm with close connections.

The probability of detecting FMDV on an infected farm after a number of days of taking samples is highly dependent on the length of time samples are taken and the time when the first infection occurred. This is shown in the probability of detection in Figure 5 where a single sample is taken from the environment on different days post infection of the herd. The highest probabilities occur at approximately 10 days, so this is when testing should happen to be most confident a premises is not infected.

Sampling in an at-risk herd would start at the time the nearby infected herd was detected. Although in most cases it is unknown for how long the premises could have been infected, we can use the herd generation time (16, 17) to estimate when spread to nearby farms would most likely have occurred. Assuming the detection time distribution follows that given estimated for the 2001 UK epidemic (19) (we could use detection times calculated above, but would have to choose a particular strategy), we can estimate the time since infection that sampling would start. For example, if the herd generation time is 6 days and the detection time is 8 days then sampling on nearby farms would start 2 days after they would most likely have been infected.

Using this distribution (Figure 6) the probabilities of different sampling strategies having produced at least one positive sample on, or before, each day of sampling is shown in Figure 7 and the number of days of surveillance required to reach different threshold probabilities of detection using a selection of strategies is given by Table 2. As we would expect, the more samples taken and the more frequently they are taken, the sooner each confidence threshold is reached. Note that when comparing strategies using the same number of samples overall, e.g., 5 samples daily and 10 samples every 2 days, there is little difference in the time to reach each confidence level.

Similar results are obtained when using environmental contamination instead of total viral shedding as an approximation of between herd infectiousness to calculate the herd generation time [T_{ge} in (16)]. This is shown in Supplementary Figures 4, 5 where the confidence thresholds are passed at a slightly later time compared to Figure 7.

4. Discussion

We have used a previously developed model for the transmission of FMDV through direct contact and environmental transmission (16) to assess the value of environmental sampling as a method of detecting FMDV-infected cattle herds. The probability of detecting FMDV in an environmental sample in the model was parameterized with results from transmission experiments (6).

Samples were taken from four areas of the environment that cattle were kept in: the walls, floor, trough, and feces. The probability of detecting FMDV from a sample was a combination of the probability of virus being present in the precise location sampled, and the sensitivity of the sampling method. We assume that this probability is homogeneous in each of the four locations, although in reality there will likely be areas where more virus accumulates depending on cattle behavior. We also assume a constant viral decay rate, parameterized from the indoor transmission experiments. However, viral decay are likely to be variable and will depend, for example, on environmental factors such as temperature and humidity and the surface material (5, 20, 21).

The probability of detecting FMDV in a single sample is low unless there is a high amount of virus in the environment (see Figure 2). Therefore, a strategy involving taking multiple samples over a period of time is necessary to have a high probability of obtaining a positive sample. In particular, early on in an outbreak there is less virus in the environment and, therefore, either a very large number of samples should be taken, sampling should be continued across several days or both.

The time for detection unsurprisingly increases if the interval between taking samples increases or the number of samples

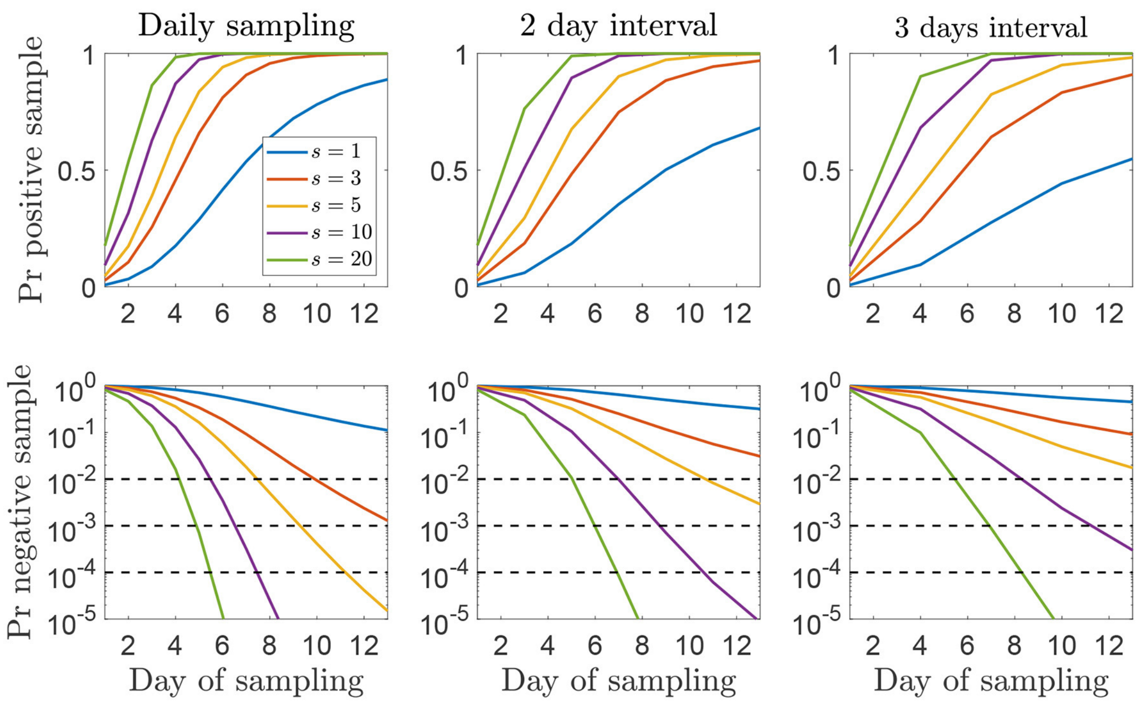

FIGURE 7
(Top) The cumulative probability of detecting FMDV at least once with different sampling strategies on an IP. **(Bottom)** The probability that all samples have tested negative up to and including the day of sampling if a premises is infected. The line color indicates the number of samples taken at each sampling interval, *s* (see legend). The three dotted lines are at 1, 0.1, and 0.01% which correspond to a 99, 99.9, and 99.99% confidence of a negative result. The first sampling day after infection is drawn from the distribution shown in Figure 6.

TABLE 2 Median number of days (and 95% credible interval) surveillance is required for to have different % probability of detection where sampling starts on a random day after first infection, given by Figure 6.

Strategy	99%	99.9%	99.99%
3 samples daily	10 (5–21)	13 (6–30)	16 (8–36)
5 samples daily	8 (3–15)	10 (4–19)	11 (5–24)
5 samples every 2 days	11 (5–25)	15 (7–33)	17 (9–39)
10 samples every 2 days	9 (3–15)	9 (3–19)	11 (5–25)
10 samples every 3 days	10 (4–19)	13 (4–28)	16 (7–34)
20 samples every 3 days	7 (1–13)	7 (4–16)	10 (4–19)

taken decreases. One criterion for judging the effectiveness of a surveillance strategy is if it improves on the mean detection time estimate from 2001 of 8.07 days (19) (see the dotted line in Figure 3A). Such effective strategies include 5 samples every 2 days, 10 samples every 5 days or 20 samples every 8 days. Which choice of strategy in the event of an outbreak will depend on multiple factors including the aims of the surveillance (early detection or proving absence) (22, 23), the cost and availability of sampling and laboratory testing (24, 25), the attitudes of farmers (26) and the wishes of the competent authority, and as such we do not suggest a single 'best' strategy.

Detection times using environmental surveillance can be compared with those for clinical inspection as the onset of clinical signs is included in the transmission model. This is illustrated by the dotted lines in Figure 3B, which shows the number of samples needed to improve upon clinical inspection when the inspection interval is the same for both surveillance measures. When the inspection interval is small, fewer samples are required to improve on clinical inspection compared to when the interval is large. For an inspection interval of 5 days or more, the number of samples does not change. This suggests that a good environmental surveillance strategy should prioritize a small inspection interval (i.e., $\leq$3 days). We note here that if clinical inspection requires the attendance of a dedicated team of veterinarians, this would be a large workload and anyone that attends an IP must isolate for a period of time. Conversely, the environmental sampling method is low-cost, low-technology and could be done by trained individuals or possibly the farmers themselves (7). An economic analysis of various surveillance strategies, such as those conducted in (27, 28), to determine the optimal combination of environmental sampling and clinical inspection would provide additional information for selecting an appropriate strategy, although this is beyond the scope of the present study.

The proportion of infectiousness before detection, θ, can be used to calculate the effective herd reproductive number, R_h, when control is applied. In particular, if transmission stops at the time of detection (e.g., because the herd is culled), it shows which strategies will reduce R_h to less than 1, meaning that number of infected herds will decline. This threshold is indicated by the red dotted line in Figure 4, which clearly shows that, for infectiousness from shedding, to achieve $R_h < 1$ a more demanding strategy is required than one that would match previous detection time estimates (c.f.

Figure 3). For infectiousness from environmental contamination, it is easier to achieve $R_h < 1$ because environmental contamination peaks later than shedding, at approximately 10 days after infection (16). We have treated infectiousness from animal shedding (θ_S) and the environment (θ_E) separately and consider the results as if each were the sole route of between-herd transmission. Although it may be possible to estimate a single θ that incorporates both routes, which would be somewhere between the two results we have shown, it is not clear what the relative contributions of each between-herd transmission route would be. Further investigation into transmission routes between herds would provide this information, but a detailed study of between-herd transmission is outside the scope of this study.

In the cases discussed above, sampling is an ongoing process and there is no particular reason to believe that a premises is infected. In the alternative situation where a herd is deemed at risk of being infected with FMDV, a different strategy will be necessary to either detect FMDV sooner or be confident that transmission did not occur after all (i.e., the herd is free from FMDV). In rare cases it may be possible to identify a particular day in which a herd could have been infected, however usually that is not possible and there is uncertainty in for how long the herd may have been infected. We modeled this uncertainty about the infection day using herd generation times and detection times from past outbreaks. Using this approach, it is far more likely that the infection would have occurred recently, 65% within the last 3 days and 86% within the last 5 days. This means that confidence that a series of negative results indicates a herd is free from infection takes longer to achieve as early in an outbreak there is less virus accumulated in the environment. If an infection occurred 10 days ago, there is a much higher probability of detecting it immediately than if it arrived 3 days ago (Figure 5). While it is clear that a single-sample strategy is never sufficient, the choice of the number of samples that should be taken and how frequently, depends on the required confidence level and how quickly it should be arrived at. However, because of the time taken for virus to accumulate at the start of an outbreak, a reasonable confidence level in less than 1 week is unlikely to be achieved.

Here we have compared detection from environmental surveillance with clinical inspection. However, FMDV can also be detected in blood, nasal fluid and saliva and surveillance based on these types of sample has previously been investigated by Nelson et al. (18). In particular, they determined the reduction in the between-herd reproduction ratio R_h through surveillance *via* different sampling strategies [see Table 2 in (18)], which can be compared to the proportion of infectiousness, θ_S and θ_E, shown in Figure 4. For example, they found that taking nasal or saliva swabs from 5 animals once a week would reduce R_h from 3.2 to 0.8 which is an equivalent of $\theta = 0.25$. The same would be achieved by 8 environmental samples every 2 days if we use θ_S to represent infectiousness, or 8 environmental samples once a week using θ_E. This suggests that animal sampling is the more efficient approach, although the low cost and ease of use of environmental samples may make environmental surveillance more efficient during an epidemic, where trained professionals required to take animal swabs will be in high demand. Also note that they used a different model which may affect the infectiousness profile and, hence, conclusions about the reduction in transmission for the different surveillance strategies.

Our results demonstrate that environmental sampling is a potentially useful tool to use during a FMD outbreak. Environmental sampling has previously been shown to successfully detect FMDV in countries where FMD is endemic (7, 8). Here we have shown that it could play a role in FMD-free countries too, where the aim is to eradicate the disease through early detection. If a suitable strategy is used, environmental sampling can produce detection times much lower than during the 2001 UK outbreak. It is also a low-cost and easy to use sampling method that can reduce the demand on trained veterinarians. Approximately 6.5 million animals were culled in the UK during the 2001 outbreak, in part due to a policy of culling at-risk farms (4). If careful surveillance strategies are applied, such as the ones described in this paper, it could reduce the need for culling and detect subsequent outbreaks quickly. Sampling to prove absence of FMDV could also be used as part of a wider surveillance strategy, such as discussed by (22), to regain an FMDV-free status.

The methodology behind this work and the previously developed model (16) is adaptable and could be used for other pathogens that are detectable in the environment as well as examining other locations, such as markets, or including other livestock. It could be useful to consider sheep in particular as it is often difficult to detect FMDV based on clinical signs in this species (1). Although the virus decay rate and the detection probability would be the same, data would need to be collected to parameterize the virus accumulation rate from sheep and develop an accurate transmission model.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: https://github.com/DrJREllis/FMDV_Sampling_Model.

Author contributions

SG conceived the study. SG and JE designed the study. CC and EB provided data. JE implemented the model and wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

Funding

This work was funded by the Department for Environment, Food and Rural Affairs (Defra) (Grant code: SE2722). The funder had no role in the study or in the decision to submit the manuscript for publication.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2023.1074264/full#supplementary-material

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frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 31 March 2023
DOI 10.3389/fvets.2023.1052349

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Veterinary Epidemiology and Economics, a section of the journal Frontiers in Veterinary Science

RECEIVED 23 September 2022
ACCEPTED 13 March 2023
PUBLISHED 31 March 2023

CITATION
Schrodt CA, Dilius P, Gibson AD, Crowdis K, Fénelon N, Ross Y, Bonaparte S, Gamble L, Lohr F, Joseph HC and Wallace RM (2023) Electronic application for rabies management improves surveillance, data quality, and investigator experience in Haiti. *Front. Vet. Sci.* 10:1052349.
doi: 10.3389/fvets.2023.1052349

Electronic application for rabies management improves surveillance, data quality, and investigator experience in Haiti

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Background: Integrated bite case management (IBCM) is a multi-sectoral response to animal-bites which reduces human and canine rabies mortality through animal quarantine, bite-victim counseling, and vaccination tracking. Haiti's national rabies surveillance program was established in 2013 using paper-based IBCM (pIBCM) with adoption of an electronic smartphone application (eIBCM) in 2018.

Methods: We evaluated the feasibility of implementing the electronic app in Haiti and compared pIBCM and eIBCM data quality collected January 2013–August 2019. Deaths prevented, cost-per-death averted, and cost-per-investigation during use of pIBCM and eIBCM were estimated using a previously validated rabies cost-effectiveness tool that accounted for bite-victim demographics; probability of acquiring rabies; post-exposure prophylaxis; and costs including training, supplies, and salaries. We compared pIBCM and eIBCM based on data comprehensiveness, completeness, and reporting efficiency. Surveys were administered to IBCM staff to evaluate the usefulness, simplicity, flexibility, and acceptability of eIBCM.

Results: Of 15,526 investigations, 79% were paper-based and 21% electronic. IBCM prevented 241 (estimated) human rabies deaths. Using pIBCM, cost-per-death averted was $2,692 and the cost-per-investigation was $21.02; up to 55 data variables were collected per investigation; data transmission took 26 days to reach national staff, and 180 days until analysis. Using eIBCM, the cost-per-death averted was $1,247 and the cost-per-investigation was $22.70; up to 174 data variables were collected per investigation; data transmission took 3 days to reach national staff, and 30 days until analysis. Among 12,194 pIBCM investigations, 55% were mappable by commune, compared to 100% of eIBCM investigations mappable by GPS. Animal case definitions were incorrectly ascribed by investigators in 5.5% of pIBCM investigations and zero for eIBCM; typically, errors were in determining probable vs. suspect case assignments. Overall, eIBCM was well-accepted by staff, who reported the app is easy-to-use, facilitates investigations, and compared to pIBCM hastens data reporting.

Discussion: In Haiti, eIBCM showed improved data completeness, data quality, and shorter notification times with minimal increase in operational cost. The electronic app is simple-to-use and facilitates IBCM investigations. Rabies endemic countries could refer to eIBCM in Haiti as a cost-effective means to reduce human rabies mortality and improve surveillance capacity.

KEYWORDS

rabies, Haiti, integrated bite case management, one health, surveillance, electronic application, tablet, smartphone

Introduction

Rabies is a highly lethal virus that is considered universally fatal among those who develop clinical signs and symptoms (1). Despite highly effective vaccines, 59,000 annual human deaths from rabies are estimated to occur world-wide, with 99% of deaths attributed to exposures from dog bites (2, 3). In countries with effective canine rabies vaccination and surveillance programs, coupled with ample availability of post-exposure prophylaxis (PEP), human rabies case fatality rates are drastically reduced (4). In the Western Hemisphere, Haiti is one of several countries that have not yet achieved effective canine rabies control and continue to report human deaths due to rabies (5–7). Whilst the true incidence of human rabies in Haiti remains unknown, a 2015 global rabies burden study estimated 130 human rabies deaths occur annually; an estimate which has likely been reduced by 50–65% since the implementation of a national Integrated Bite Case Management program (8–11).

Integrated Bite Case Management (IBCM) is recommended by the World Health Organization (WHO) for passive rabies surveillance (12). Typical IBCM programs rely on routine communication between healthcare providers who treat bite victims, and veterinary professionals who investigate animals suspected to have rabies. Under an ideal IBCM program, bites are immediately reported to veterinary professionals who initiate field investigations. Several publications have shown that the combined actions of risk assessments, patient counseling, dog quarantine, and sample collection and testing can greatly reduce the risk of human rabies deaths and can be implemented in manners that are highly cost-effective (8).

In 2011, the Haiti Animal Rabies Surveillance Program (HARSP) was created to improve rabies diagnostic laboratory testing capacity, train animal surveillance officers, and improve routine animal surveillance (13). In 2013, IBCM investigations began under HARSP, further building the framework for rabies management in Haiti through community animal bite and rabies investigations. Data during an IBCM investigation is collected by the investigators, reported to the treating healthcare provider and national animal health officials, and analyzed by the national program. In addition to collecting data for surveillance purposes, the bite case investigations identify sick animals and bite victims (human and animal) and facilitate testing or treatment as appropriate. In 2018, after realizing that paper-based surveillance forms were suffering from high data entry error rates and lacking variables necessary for programmatic monitoring and evaluation, the IBCM investigations converted from paper-based forms to a cell-phone or tablet-based application ("app") to facilitate case investigations and collect data simultaneously.

The REACT app is now used in eight countries, is available in five languages and has recorded over 40,000 notifications of suspect rabid animals; highlighting both the need for improved rabies surveillance capacity globally and the versatility of electronic tools to be adapted for use and implemented in a variety of low-resource rabies endemic settings (14). IBCM continues to provide a framework for bite case investigations and surveillance in Haiti, which is crucial for a One Health approach in combatting dog-mediated rabies.

Here, we describe the implementation of a national electronic IBCM (eIBCM) program in Haiti using a Rabies Exposure Assessment and Contract Tracing (REACT) app. We evaluated paper-based IBCM (pIBCM) and eIBCM to estimate the number of human deaths averted, costs, quality of data outputs, and user acceptability to determine the feasibility of introducing the electronic REACT app in low-resource settings.

Methods

The REACT app is developed and supported by the Worldwide Veterinary Service and is available on both Android and iOS operating systems (14). Investigators surveyed during this study used Android REACT versions 1.0–1.3 on handheld Samsung Galaxy Tab A T285 tablets. The REACT app interfaces with a secure cloud-based server and backend system which is accessed via password-protected logins by project managers. The REACT app is organized into five sections: (1) Event Notification, (2) Animal Health Investigation, (3) Rabies Exposure Investigation, (4) Animal Quarantine, and (5) Test Results. Each section has standardized data collection forms with limited open-text fields. REACT provides in-app guidance to investigators, such as the rabies risk status or case assignment of the animal, recommended quarantine schedules, and prompts to complete critical data fields. REACT is currently available in English, French, Creole, Spanish, and Vietnamese.

To evaluate the performance of IBCM in Haiti, we applied the U.S. Centers for Disease Control (CDC) Morbidity and Mortality Weekly Report (MMWR) Updated Guidelines for Evaluating Public Health Surveillance Systems (15). Quantitative and qualitative attributes (cost-effectiveness, timeliness, data quality, usefulness, simplicity, flexibility, acceptability, and stability) were evaluated by reviewing current methods/protocols as well as results derived from a survey administered to all IBCM investigators.

Data were evaluated from rabies IBCM data collected by the Haiti Ministry of Agriculture and Rural Development from January 2013–August 2019. We assessed the feasibility of HARSP to determine if the program is locally viable and pragmatic by estimating key economic indicators for program operation. The

$$\begin{aligned}
FR_{year} = \sum_{i=1\ldots n}\sum_{j} P(ER_{ij}) \\
&\times \Big(P(MC_{ij}) \times \big(P(R_{ij}|PEP) \times P(PEP_{ij}) + P(R_{ij}|NoPEP) \times \left(1 - P(PEP_{ij})\right)\big) \\
&+ \left(1 - P(MC_{ij})\right) \\
&\times \Big(P(MC_{ij}|BI) \\
&\times \big(P(R_{ij}|PEP) \times P(PEP_{ij}) + P(R_{i,j}|NoPEP) \times \left(1 - P(PEP_{ij})\right)\big) \\
&+ \left(1 - P(MC_{i,j}|BI)\right) \times P(R_{i,j}|NoPEP)\Big)\Big)
\end{aligned}$$

Where subscript *i* stands for a patient who was in contact with HARSP or local health clinics, i.e., is part of the study sample, *j* represents the type of exposure (i.e., confirmed, probably, suspected, negative).

FR_{year} = fatal rabies infections

ER_{ij} = patient *i* with type of bite exposure *j* was exposed to rabies, i.e., $P(ER_{ij})$ is the probability that a patient *i* with bite exposure type *j* was exposed to rabies (confirmed = 100%, probable = 75%, suspected = 6.3%, negative = 0%)

MC_{ij} = patient *i* with type of bite exposure *j* seeks medical care, i.e., $P(MC_{ij})$ is the probability that a patient *i* with bite exposure *j* seeks formal medical care

Rij = patient *i* with bite exposure *j* gets a rabies infection

PEP = Patient gets post-exposure prophylaxis

BI = bite investigation; the analyzed sample only includes bite victims who presented to a healthcare facility or were found through active community bite investigations.

FIGURE 1
Fatal rabies infections model excerpt from Undurraga et al., "Cost-Effectiveness Evaluation of a Novel Integrated Bite Case Management Program for the Control of Human Rabies, Haiti 2014–2015" Supplementary material.

number of human deaths prevented, cost per death averted, and cost per investigation were calculated separately for pIBCM and eIBCM and were estimated using a validated, evidence-based Rabies Cost-Effectiveness Tool developed by Undurraga et al. (11) in Microsoft Excel. Deaths averted were calculated compared to a non-IBCM (NBCM) rabies management program (Supplementary material; pIBCM & eIBCM Ecoomic Analyses). This tool applies a probabilistic model (Figure 1) to estimate deaths prevented utilizing IBCM-collected data on number of bite-victims, probability of acquiring rabies stratified by the case outcome of the animal, probability of initiating post-exposure prophylaxis, and the probability of dying from rabies in the absence of PEP. Cost factors included training, supplies, staff, and salaries (Supplementary material; pIBCM & eIBCM Economic Analyses). Differences among input parameters are highlighted in Table 1. We compared three aspects of surveillance data quality captured through pIBCM and eIBCM that correspond to the following MMWR evaluation categories: data comprehensiveness (total number of data fields available), data completeness (automatic variable, location, and animal case definition assignments), and reporting efficiency (time from data entry to reporting and data analysis ascertained from programmatic timelines).

Two survey versions were used, the first for staff who used both paper investigation forms and the REACT app (Survey 1.0), and the second for staff who only used the eIBCM app (Survey 2.0) (Supplementary material). Surveys were written in English and provided to Ministry of Agriculture, Natural Resources, and Rural Development (MARNDR) officials in Haiti, where they were adapted for local use by translating the surveys into local languages and reviewing them for comprehensibility. Each survey gathered data from the staff including demographics, years of experience working with HARSP, and perceptions regarding use of the REACT app and paper investigation forms for those who were employed by MARNDR from 2013 to 2019. The national program manager administered the survey in French or Haitian Creole during phone interviews with HARSP staff from April 6 to April 29, 2020. Survey 1.0 had 35 questions and Survey 2.0 had 34 questions. To evaluate qualitative attributes from the CDC MMWR Updated Guidelines for Evaluating Public Health Surveillance Systems, interviewees were read aloud a statement and asked to indicate the degree of agreement or disagreement using a typical five-point Likert scale (15) (Supplementary material). For the analysis, the answer "Strongly agree" received 5 points, "Agree" received 4 points, "Neither agree nor disagree" received 3 points, "Disagree" received 2 points, and "Strongly disagree" received 1 point. Average response values were calculated for the two groups and compared using a two-tailed independent *t*-test.

TABLE 1 Differences among input parameters for pIBCM and eIBCM.

Microsoft excel tab	Variable	Units	pIBCM	eIBCM
HARSP_data	Study population	N	12,194	3,332
	Time frame for analysis	Years	5.6	1.1
	Share of PEP treatment paid for by the government	%	50%	50%
	Human exposures to rabies			
	Confirmed	N	257	23
	Probable	N	892	794
	Suspected	N	2018	1099
	Negative	N	9362	1317
HARSP$Surv*	Tablet + Sim card	$/worker	0	145
HARSP$Train	Classroom days	N	5	3
	Field days	N	5	3
	Form training	N	1	2
	Number of participants	N	20	10
	Days in training destination	N	12	8
	Salary/wage	$/day	12	8
	Travel expenses (per diem, hotel)	$/day	12	8
Dog_invest	Dog-investigations	N	12,194	3,332
	Confirmed rabid	N	170	30
	Probable rabid	N	630	488
	Active surveillance	N	34	0
	Diagnosed	N	27	0
	Confirmed	N	3	0
	Passive surveillance (located & non-located)	N	12,160	3,332
	Non-located	N	2,100	1,153
	Probable	N	355	220
	Located	N	10,060	2,179
	Dogs investigated and found dead	N	517	110
	Confirmed rabid	N	95	27
	Probable rabid	N	129	61
	Dogs investigated and found alive	N	9,543	2,069
	Dogs immediately euthanized	N	121	3
	Confirmed rabid	N	35	2
	Probable rabid	N	5	0
	Dogs under observation	N	9,209	1,853
	Confirmed rabid	N	36	1
	Probable rabid	N	115	9
	Dogs quarantined	N	6	0
	Confirmed rabid	N	1	0
	Probable rabid	N	0	0
	Evaded capture	N	207	213
	Probable rabid	N	22	198

*Cost per vehicle for both pIBCM and eIBCM was $1200 which represents a $200 increase from the original model and reflects the increase in vehicle cost over time.

Results

From January 2013 to August 2019, there were 15,526 bite case investigations conducted in Haiti, of which 79% ($n = 12{,}194$) were paper-based and 21% ($n = 3{,}332$) were electronic (Figure 2). The REACT eIBCM app was introduced in January 2018 but was not fully recommended to be used by all staff until August 2018. From January to August 2018, an average of 12 eIBCM cases were recorded monthly. After August 2018, an average of 250 eIBCM cases were recorded monthly. From August 2018 until the end of the evaluation period (13 months), most cases were investigated by the eIBCM method (79%) compared to the pIBCM method (21%). The Rabies Cost Effectiveness Tool outputs estimate that, compared to a NBCM rabies management program, 170 human rabies deaths were prevented from January 2013 to August 2019 as a result of HARSP, or that one human life was saved for every 91 investigations. Investigations were performed in 100% (10/10) of departments, and 53% (76/144) of communes throughout the country (Figure 3). All communes are not represented because bite cases were not reported from all locations.

Evaluation of cost-effectiveness, timeliness, and data quality

During the 67 months in which pIBCM was the primary investigation method, an annual average of 30 cases were laboratory confirmed, 113 were clinically confirmed (probable), the cost per death averted was $2,692, and the cost per investigation was $21.02 (Supplementary material; pIBCM Economic Analysis). During the 13 months in which eIBCM was the primary investigation method, an annual average of 27 cases were laboratory confirmed, 444 were clinically confirmed (probable), the cost per death averted was $1,247, and the cost per investigation was $22.70 (Supplementary material; eIBCM Economic Analysis).

The number of days from investigation onset to notifying national animal health officials was up to 26 days when using pIBCM compared to only 3 days when using eIBCM *via* the REACT app. The number of days from investigation to analysis was up to 360 when using pIBCM and up to 45 days when using the REACT app (Figure 4). The pIBCM form had 55 data variables, whereas the REACT app had 174 data variables. Unlike pIBCM, eIBCM automatically assigns the user's name and animal ID, collects GPS coordinates, date of investigation, and assigns an animal case status, reducing entry errors and data cleaning requirements (Table 2). Among pIBCM case investigations, 55% (6,695) were mappable at the commune level without requiring extensive data cleaning of hand-written locality information, whereas 100% of eIBCM investigations collected GPS coordinates and were readily mappable (Figure 3). Among pIBCM case investigations, 94.5% (11,526) were determined to have correct animal case definition assignments (Table 3). Of the 5.5% (668) incorrectly assigned, the risk was under-stated for 29.2% (195) case investigations and over-stated for 70.8% (473) case investigations (Table A, Supplementary material).

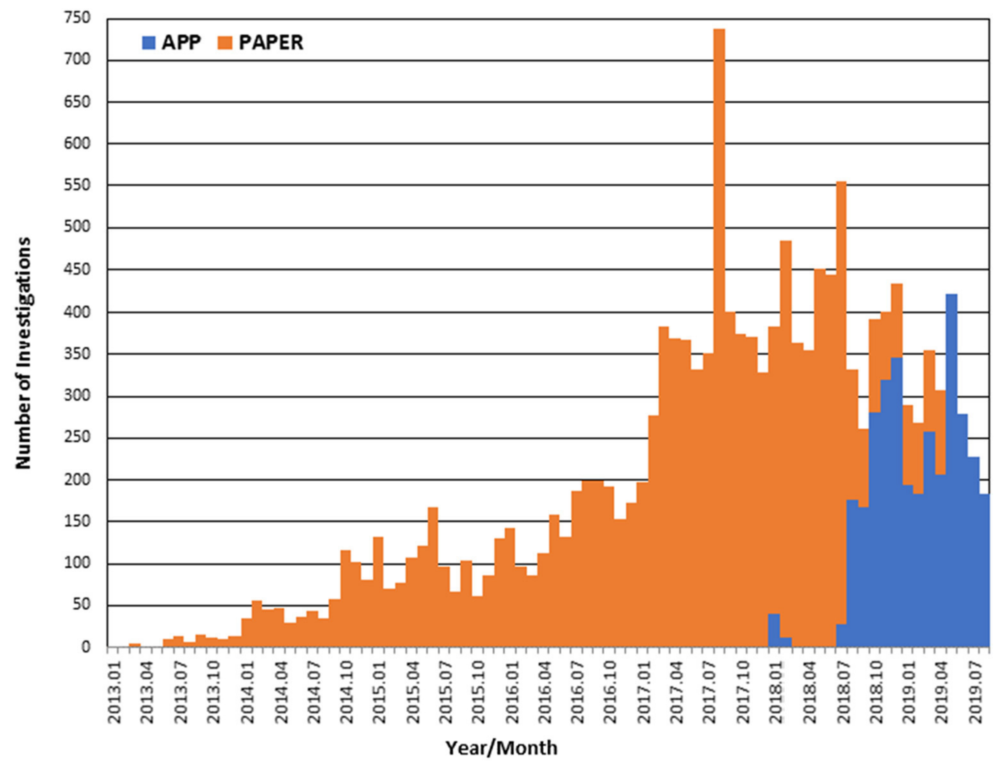

FIGURE 2
Transition from paper to app-based IBCM, 2013–2019.

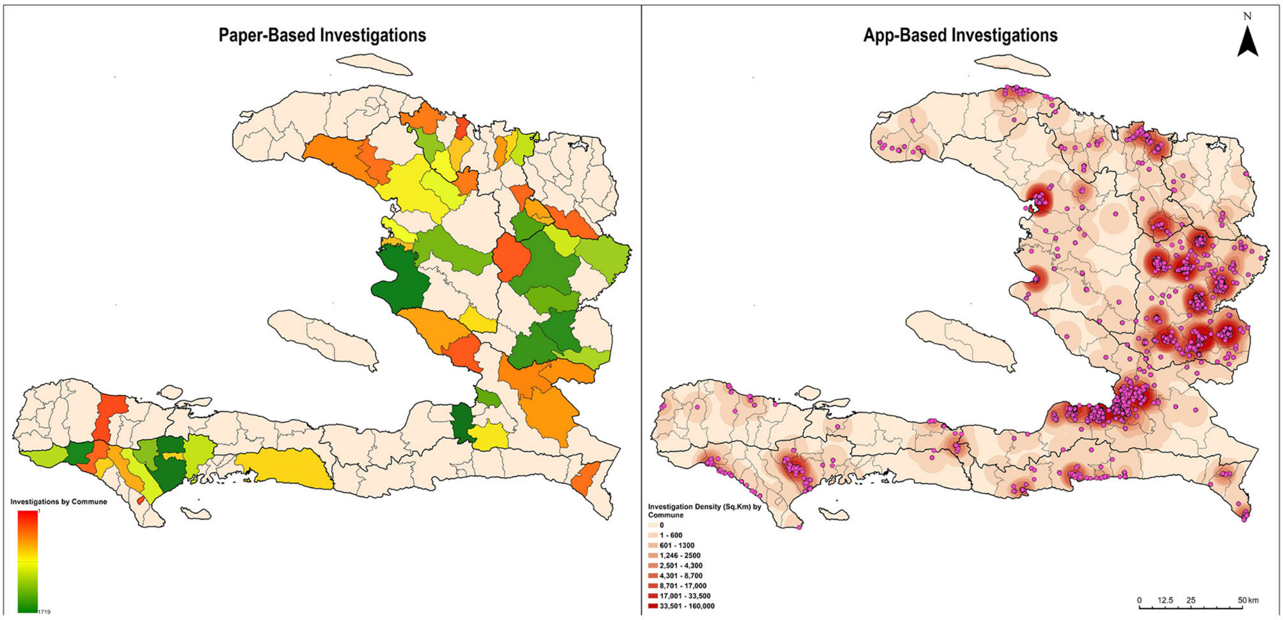

FIGURE 3
Location and Density of Rabies Case Investigations, Haiti, 2013–2019. Paper-Based Investigations: Total investigations: 12,194; Total mappable investigations: 6,695 (55%) Bite cases are mapped at the level of communes. *Spelling errors in handwritten paper-based investigations did not allow mapping of all investigations. App-Based Investigations: Total investigations, all mappable: 3,332 (100%). Bite cases are mapped using GPS coordinates.

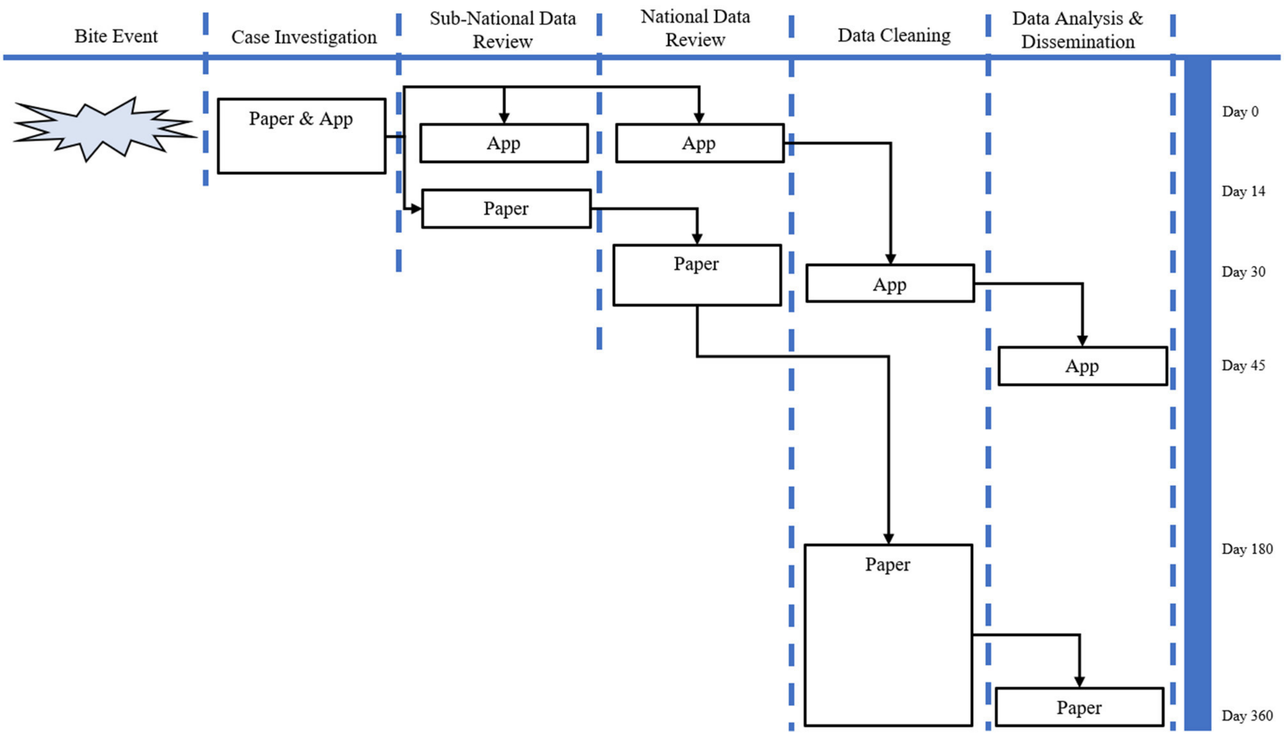

FIGURE 4
Programmatic flow chart of pIBCM vs. eIBCM.

TABLE 2 Surveillance system attributes.

Evaluation factor	Definition*	Assessment Criteria	pIBCM	eIBCM
Feasibility	*Feasibility standards ensure that the evaluation is viable and pragmatic. Differing political interests of those involved should be anticipated and acknowledged. The use of resources in conducting the program should be prudent and produce valuable findings.*	Human Deaths Prevented (Annual)**	20	55
		Program Operational Cost (Annual)	$45,772	$68,745
		Cost per Death/Disability-Adjusted Life Year Averted	$2,692	$1,247
		Cost per Investigation	$21.02	$22.70
Usefulness	*The program contributes to the prevention and control of adverse health-related events, including an improved understanding of the public health implications of such events. Surveillance data should be useful in contributing to performance measures, including health indicators.*	Frequency of Data Publications	1.4 per year	2.7 per year
		Frequency of Summary Reports Submitted to Relevant Stakeholders	Annually (1 per year), manually produced	Monthly (12 per year), automated in R
Timeliness	*The speed between steps in a public health surveillance system.*	Number of Programmatic Steps from Data Collection until Analysis	7	4
		Time to Complete Data Collection (per data field)	10 s	6 s
		Time from Collection Until Data Review	26 days	3 days
Data Quality	*The completeness and validity of the data recorded in the public health surveillance system*	Key Variables- User, Animal ID, GPS coordinates, Date of Investigation, Animal Case Status	Requires manual entry or retrospective cleaning	Automatically collects
		Investigations mappable without cleaning	55%	100%
		Case Outcomes Correctly Classified (%)	94.5%	100%
Flexibility	*Surveillance system can adapt to changing information needs with little additional time, personnel, or allocated funds. Flexible systems can accommodate new health-related events, changes in case definitions or technology, and variations in funding or reporting sources. In addition, systems that use standard data formats (e.g., in electronic data interchange) can be easily integrated with other systems.*	Number of Data Variables Collected	Up to 55	Up to 174
		Additional Cost per Investigation for eIBCM	Reference	+$1.68
		Data Format	Paper—manual entry required for integration	.csv file format merges with all major software
Acceptability	*The willingness of persons and organizations to participate in the surveillance system*	Average User Rating	Not assessed	97%
		User Preference	0%	100%
Stability	*The reliability (i.e., the ability to collect, manage, and provide data properly without failure) and availability (the ability to be operational when it is needed) of the public health surveillance system.*	Frequency of Lost Data Records	Unable to assess	8% of users reported losing app data at least one time
		Frequency of Inoperable Data Collection Tools	0%	26% of users reported a tablet malfunction at least one time
		Average Delay in Availability of Data to the National Animal Health System	26 days	3 days

*Adapted from: U.S. Centers for Disease Control (CDC) Morbidity and Mortality Weekly Report (MMWR) Updated Guidelines for Evaluating Public Health Surveillance Systems.
**Deaths prevented should not be directly compared, as this is often a function of changing epidemiology, rabies risks, and fluctuations in staff employed by the program. These numbers represent deaths prevented as compared to a non-IBCM (NBCM) rabies management program.

IBCM investigator assessment

Thirty-three past and current IBCM investigators and program managers completed the eIBCM satisfaction survey. Of these, 19 conducted pIBCM before transitioning to eIBCM and were administered Survey 1.0; the remaining 14 had only ever performed eIBCM and were administered Survey 2.0 (Supplementary material). Respondents consisted of 23 IBCM investigators, nine departmental managers, and the national manager. The mean number of years interviewees worked with HARSP was 2.2 years (26.7 months), ranging from 0.1 to 7.2 years (1 to 86 months).

Investigators self-reported that they were proficient with the REACT app after an average of 5 investigations (95% CI 4.2–5.7

TABLE 3 Comparison of interim and final animal case status assignments, pIBCM[§].

Investigator interim animal case assignment		Actual animal case assignment			
		Confirmed	Probable	Suspect	Non-case
Confirmed	185	**178**	3*	4*	0
Probable	629	0	**179**	442*	8*
Suspect	1.943	0	61†	**1,868**	14*
Non-case	9.362	0	14†	47†	**9,301**
Unassigned	75	0	22†	51†	2*
TOTALS	12.194	178	279	2,413	9,325
% Concordance		100%	64.2%	77.4%	99.7%

*Over-stated interim risk.
†Understated interim risk.
§There are no investigator-assigned animal case assignments when using eIBCM because the app automatically assigns the animal case status.
Bold text denotes concurrence between the interim animal case assignment by the investigator and the actual animal case assignment as determined by final data review.

TABLE 4 Frequency of problems experienced while using REACT smartphone application for investigation of suspected human rabies exposures, Haiti, 2020.

eIBCM Complications, $n = 33$				
Infrastructure-related	Never (%)	Rare (%)	Sometimes (%)	Often (%)
No internet	11	67	19	4
No electricity to charge	95	0	0	5
Battery died during data entry	38	52	5	5
Tablet is too difficult to use	100	0	0	0
Tablet is lost or stolen	100	0	0	0
Tablet is broken	61	29	11	0
App-related				
App is too difficult to use	95	5	0	0
App malfunction	63	30	4	4
Any problem	0	61	25	14

investigations) (range 2–10 investigations). On average, users reported that it took 17 min (95% CI 14–21 min) to complete a case investigation report in the REACT app, or 5.9 s per data field. Investigators who used paper investigation forms reported that it took an average of 5 min (95% CI 4–6 min) to complete the paper case investigation report, or 10 s per data field. Among 32 of the interviewees, 22 reported taking paper notes during the investigation and entering data into the REACT app at a later time, whereas the remaining 10 reported entering data directly into the REACT app at the time of the investigation.

Every user reported encountering at least one problem while using the REACT app, although this occurred rarely for the majority of users (61%) (Table 4). Issues encountered while using the REACT app were primarily due to infrastructural limitations including no internet access (11% "never," 67% "rare," 19% "sometimes," 4% "often"), tablet battery died during data entry (38% "never," 52% "rare," 5% "sometimes," 5% "often"), and no access to electricity to charge the tablet (95% "never," 5% "often"). App-related issues were also reported, including users indicating that the app was too difficult to use (95% "never," 5% "rare") and that the app malfunctioned during data entry (63% "never," 30% "rare," 4% "sometimes," 4% "often"). Survey respondents also expressed frustration due to incomplete translation from English to Creole for certain app modules (e.g., the Home Screen) (Figure 5).

On average, interviewees agreed or strongly agreed with statements assessing the REACT app in terms of ease of use [4.9 for Paper and App (P-A) Investigators; 4.7 for App-only (A) Investigators; $p < 0.01$], timeliness of report submission (4.9 P-A; 4.7 A), investigation thoroughness (4.8 P-A; 4.9 A), rabies risk assessment (4.8 P-A; 4.3 A; $p < 0.01$), case determination (4.8 P-A; 4.6 A), quarantine period determination (4.9 P-A, 5.0 A), communication with bite victims (4.9 P-A; 4.8 A), and timeliness of data analysis (4.7 P-A; 4.2 A; $p < 0.01$) (Table 5). All the interviewees agreed that the REACT app should be the primary method of data collection under the HARSP.

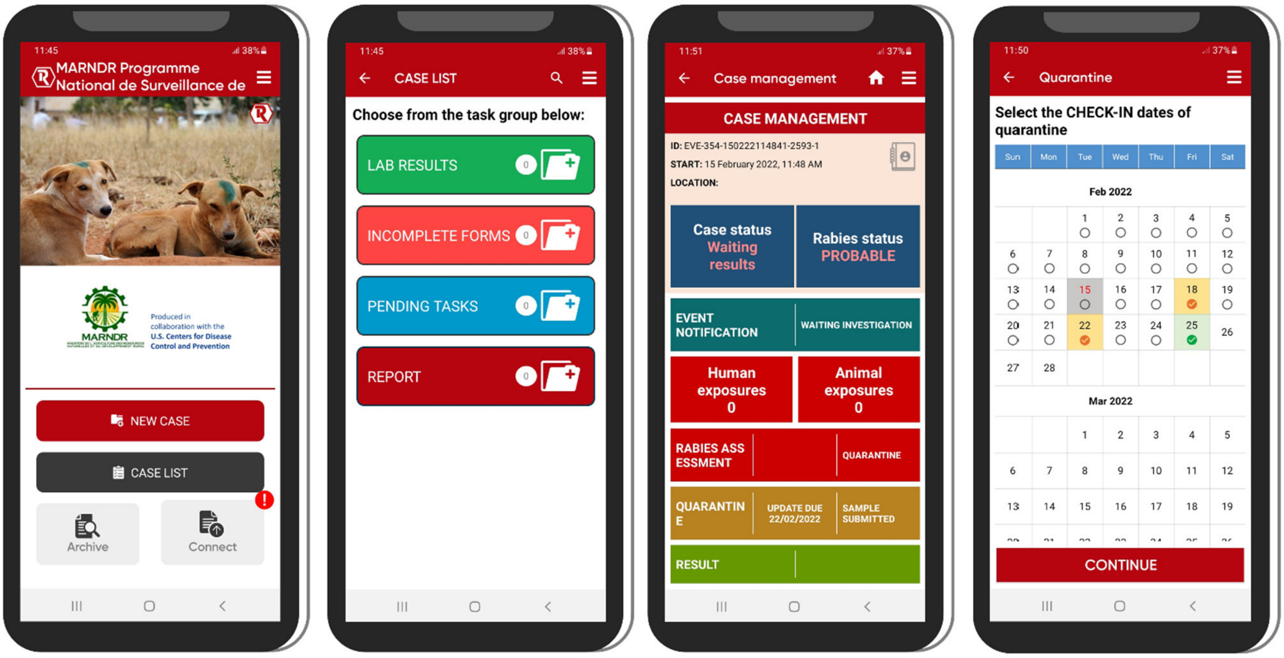

FIGURE 5
Examples of the user interface for the REACT app on Android devices. Left to right: Home screen with navigation buttons; Case list screen for navigating to pending cases; Case management screen for management of a specific case; Quarantine scheduling screen for scheduling follow-up actions during an animal's quarantine period.

TABLE 5 Comparison of investigator assessment of the REACT smartphone application for investigation of suspected human rabies exposures, Haiti, 2020.

Assessment criteria	P-A investigators[a]	A investigators[b]	*P*-value[c]
Easy to submit reports	4.9 (4.8–5.0)	4.7 (4.4 – 4.9)	<0.01
Fast to submit reports	4.9 (4.7–5.0)	4.7 (4.4–4.9)	0.11
Facilitates thorough investigations	4.8 (4.7–5.0)	4.9 (4.7–5.0)	0.75
Helps assess rabies risk	4.8 (4.6–5.0)	4.3 (4.1–4.6)	<0.01
Helps assess case determination	4.8 (4.6–5.0)	4.6 (4.3–4.9)	0.32
Helps determine quarantine periods	4.9 (4.7–5.0)	5.0 (5.0–5.0)	0.15
Helps communication to bite victims	4.9 (4.8–5.0)	4.8 (4.5–5.0)	0.36
Facilitates timely data analysis	4.7 (4.5–4.9)	4.2 (3.9–4.5)	<0.01
Total score (Maximum 40 points)	38.8 (37.9–39.6)	37.1 (35.9–38.4)	0.04

[a]Investigators who investigated rabid animals using the paper form, before transitioning to REACT app, $n = 18$.
[b]Investigators who have only ever used REACT app, $n = 15$.
[c]two-tailed *P*-value based on two-sample independent *t*-test.

Discussion

Rabies control in Haiti has been challenged by earthquakes, hurricanes, the COVID-19 pandemic, and political disruptions, yet the system has remained operational (16, 17). Neglected diseases are often ignored because of poor data quality that results in limited visibility to the true burden of disease (18). REACT offers a way to both increase case detection and improve data dissemination, offering a potential means of overcoming these systemic barriers in the control of neglected diseases. Compared to pIBCM, eIBCM is also cost-effective, has improved data quality, and facilitates more rapid data analysis and dissemination. As the REACT app has been used by all HARSP investigators with positive feedback, eIBCM in Haiti complies with the surveillance evaluation criteria as simple, flexible, and acceptable.

The increased cost per investigation associated with the REACT app is nominal compared to the paper-based system, and is clearly outweighed by the unique benefits offered by the app. The only costs required for eIBCM-specific investigations were for tablets, data, and training, which amounted to <\$300 per person-year. The cost per death-averted in both pIBCM and eIBCM were less than reported previously in Haiti by Underraga et al. in 2014 and 2015, who reported estimated ranges of \$2,891–\$4,735 and \$3,534–\$7,171 (11), and nearly three times lower than the cost effectiveness threshold set by the WHO (19). This difference can be attributed to changes in programmatic operations and a changing epidemiologic landscape; cost per death averted is heavily influenced by the proportion of high-risk cases that are investigated, which can change through both natural cycles as well as interventions (e.g., vaccination programs).

The differences noted in this evaluation between pIBCM and eIBCM cost per death averted likely reflect normal temporal variation in rabies risks and fluctuation in the number of investigators employed by HARSP. The economic model is sensitive to the proportion of investigation outcomes resulting in confirmed and probable rabid animals, which can change over time due to natural and surveillance operational factors. At the time of eIBCM implementation, HARSP underwent budget cuts resulting in the loss of half of investigators. A drop in operational costs resulted, as well as a noticeable decline in case investigations, as seen in Figure 2. Furthermore, the proportion of high-risk investigations increased from 9% during pIBCM to 24% during eIBCM, reflecting a combination of reduced staffing and an increase in rabies transmission across Haiti. These factors are difficult to control in low-and-middle income countries and highlight the difficulty of utilizing cost-effectiveness measures to compare programs operated in different time periods. Regardless of the operational and epidemiological changes over the 6 years of this program, pIBCM and eIBCM programs were both highly cost-effective per standards established by WHO.

In Haiti, eIBCM showed improved data completeness, data quality, and a shorter notification time compared to pIBCM. Improved data quality and shorter time to analysis allows program managers to identify trends and react more quickly to urgent events. Investigations using pIBCM are only readily mappable at the level of the commune, introducing bias in surveillance data. The automatic collection of GPS coordinates with eIBCM helps investigators accurately evaluate the program, monitor geographic trends, and focus control measures. Electronic IBCM expedites the availability of field rabies surveillance data to health officials and raises real-time awareness of outbreaks. For example, from July to December, 2018, a rabies outbreak was detected in a Dominican Republic city which borders Haiti. No data was available in the Haitian border-city to determine if the outbreak had spilled into Haiti. In January 2019, a bi-national dog vaccination program was conducted and the REACT app was deployed in this Haitian city to monitor rabies exposures (20). By June 2019, 26 rabies investigations were conducted and no dogs had signs consistent with rabies, affirming that the mass vaccination campaign had effectively halted rabies transmission in these two cities (20). Since July 2021, REACT has implemented monthly rabies reports to improve early outbreak detection, detailing location of cases, investigator activity, and laboratory results (Supplementary material). Timely reporting of surveillance data enables program managers to make informed public health decisions and allocate resources based on the changing epidemiology of the disease, allowing for better management of field staff and improving stakeholder engagement.

Following a bite event or reports of suspected rabid animals, timely IBCM investigations can result in a myriad of benefits (8, 13, 21). People exposed are identified more quickly and directed to appropriate medical care, resulting in improved patient outcomes (8). Rapid identification and removal of suspected animals prevents additional bite exposures to people or animals and interrupts the enzootic transmission cycle in dogs (13, 21). However, these benefits are dependent on a well-trained workforce that understands the risk assessment process, PEP recommendations, and quarantine guidance. Our evaluation found that risk assessment determinations from field investigators were prone to some degree of error, resulting in several hundred bite victims receiving incorrect risk counseling. Over-stating the risk in the biting animal can result in unnecessary PEP that can lead to unnecessary medical costs and can diminish oft-limited human vaccines. Conversely, understating the risk could lead to reduced compliance with the PEP regimen and put human lives at risk. The REACT app automatically applies the WHO case status definition for each animal under investigation (confirmed, probable, suspect) and assigns the appropriate quarantine recommendation based on data inputs. The automated algorithms prevent user misassignment of animals, ensuring the appropriate human rabies post-exposure prophylaxis recommendations are communicated. Automated case classification also improves timeliness of data analysis, as these case-by-case determinations do not need to be validated manually as was necessary under pIBCM. The ability of eIBCM to automatically interpret rabies case classifications, while incredibly important from an operational viewpoint, was also greatly appreciated by the investigators.

Mobile electronics are increasingly used for medical and public health purposes and, as of 2020, 93% of the world's population has access to mobile broadband networks (22, 23). However, few smartphone/tablet apps have been used in the surveillance, management, and prevention of rabies. Previous electronic apps used in Tanzania and Haiti, including a component of the app described in this paper, have been used for counting and geographic tracking during dog vaccination campaigns (24, 25). Additional data platforms and apps have been used in Sri Lanka, Tanzania, and Pakistan to monitor human rabies cases, notify and track persons receiving rabies post-exposure prophylaxis, and inform local animal control or public health officials of bite incidents (26–28). However, the programs in Sri Lanka and Pakistan were limited geographically and relied on bite victims to seek medical care (or a euthanized animal's lab report in the case of Sri Lanka) to trigger data input and case investigation (26, 28). This approach could be prone to under-detection of rabies cases (human and animal), as it is suspected that many dog bite victims do not seek medical care nor animal diagnosis after a potential rabies exposure (8). The REACT app is designed for programs that focus on community-based surveillance and risk-counseling with bite victims. This approach has been shown to increase rabies case detection and improve PEP adherence, both of which contribute to a reduction in human rabies cases and improved program cost-effectiveness (8, 17).

Implementation of REACT was not without difficulties, which primarily were attributed to infrastructural challenges that are common in low- and middle-income countries. Lack of access to electricity and internet were cited by most of the investigators. The REACT app was designed with these challenges in mind and is able to collect and store data locally (on the device) in the absence of internet. At a time when internet is available, data can be automatically or manually uploaded to a cloud-based server. Technology continues to evolve rapidly, including more reliable and low-cost tablets and longer battery life. Issues related to the performance of the app were rare, suggesting that general improvements in information and technology systems will only hasten the speed at which programs adopt app-based electronic health systems.

The evaluation and comparison presented here are subject to at least four limitations. First, this analysis did not evaluate year-to-year variation which would account for variations during the evolution of the program (e.g., improved efficiency, trainings, number of staff) and epidemiology over time. Second, responses to surveys were not anonymous and surveys were administered by the national program manager. While some respondents might not have felt comfortable answering, this is thought to be unlikely since use of the app, although encouraged, was optional. Third, when evaluating the length of time investigators reported to complete the paper investigation form (prior to the app's use) compared to entering data in the app, over half of interviewees reported taking notes on paper during an investigation and later entering the data into the app. While the survey asked how many minutes the paper form took to complete prior to existence of the app, respondents were not asked how many minutes were spent "taking notes" prior to app data entry. Therefore, the time required to complete the app may be under-reflected in this analysis. Correspondingly, respondents were not asked to explain why they took paper notes prior to entering data into the app. Finally, cost per death averted is subject to change based on epidemiologic factors that are difficult to control. As such cost per investigation is the more appropriate measure for comparing programs during different time frames.

Conclusion

IBCM in Haiti is an effective community-based surveillance system that provides a framework and guidance for bite case investigations and decreases human mortality from rabies. Adoption of the REACT app in Haiti has resulted in improved data quality and completeness, more efficient data reporting and analysis, and higher levels of user acceptability. Rabies endemic countries could refer to Haiti's eIBCM as a cost-effective means to reduce human rabies mortality and improve data consistency and transparency, even in the face of social, political, economic, and natural disruptions.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the CDC not to be research, as the purpose of these activities was to investigate and assess a condition of public health importance. CDC Institutional Review Board (IRB) review was not required under the following provision: Public health surveillance activities, 45 CFR 46.102(l)(2). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements. The animal study was reviewed and approved by CDC Institutional Animal Care and Use Committee (IACUC). Written informed consent for participation was not obtained from the owners because the purpose of this surveillance program is to monitor the occurrence of animal rabies cases in Haiti through the investigation of animal bites and through the testing of pathology samples from deceased animals. The surveillance program is a component of the national rabies control program, which includes vaccination programs, PEP guidelines, and animal quarantine and euthanasia policies. Surveillance will be used to inform ongoing practice within the national rabies control program. As an activity designed to monitor the occurrence of disease in a defined population, as well as to provide feedback to inform ongoing public health practice, this activity is consistent with the attributes of non-research public health practice, as described in current CDC policy.

Author contributions

RW and AG conceptualized the project. RW acquired funding and supervised the project. RW, CS, YR, and SB synthesized and analyzed study data. AG provided resources and software programming. PD, KC, NF, and HJ managed coordination/execution of activities. CS wrote original draft with review and editing by RW. All authors contributed to the article, reviewed, and approved the submitted version.

Funding

The Integrated Bite Case Management program in Haiti is supported by funding from the Global Health Security Agenda.

Acknowledgments

The authors would like to thank Matthew Toro, Multidor, Supreme Fritzner, and Eduardo Undurraga for their contributions.

Conflict of interest

AG was project lead for the development of the electronic application, with LG and FL supporting the development, as a part of their employment for Mission Rabies.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Author disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2023.1052349/full#supplementary-material

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frontiers | Frontiers in Veterinary Science

TYPE Correction
PUBLISHED 09 May 2023
DOI 10.3389/fvets.2023.1204839

Check for updates

OPEN ACCESS

APPROVED BY
Frontiers Editorial Office,
Frontiers Media SA, Switzerland

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RECEIVED 12 April 2023
ACCEPTED 13 April 2023
PUBLISHED 09 May 2023

CITATION
Schrodt CA, Dilius P, Gibson AD, Crowdis K, Fénelon N, Ross Y, Bonaparte S, Gamble L, Lohr F, Joseph HC and Wallace RM (2023) Corrigendum: Electronic application for rabies management improves surveillance, data quality, and investigator experience in Haiti. *Front. Vet. Sci.* 10:1204839.
doi: 10.3389/fvets.2023.1204839

Corrigendum: Electronic application for rabies management improves surveillance, data quality, and investigator experience in Haiti

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KEYWORDS

rabies, Haiti, integrated bite case management, one health, surveillance, electronic application, tablet, smartphone

A corrigendum on

Electronic application for rabies management improves surveillance, data quality, and investigator experience in Haiti

by Schrodt, C. A., Dilius, P., Gibson, A. D., Crowdis, K., Fénelon, N., Ross, Y., Bonaparte, S., Gamble, L., Lohr, F., Joseph, H. C., and Wallace, R. M. (2023). *Front. Vet. Sci.* 10:1052349. doi: 10.3389/fvets.2023.1052349

In the published article, there was an error regarding the affiliation for Haïm C. Joseph. Instead of having affiliation [2], they should have had [3].

In the published article, there was an error in the author list, and authors Luke Gamble, Frederic Lohr were erroneously excluded. The corrected author list and appears below.

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In the published article, there was an error. Luke Gamble and Frederic Lohr should have been included in the Conflict of interest and Author contributions sections.

A correction has been made to the Conflict of Interest section. This sentence previously stated:

"AG was project lead for the development of the electronic application as a part of employment for Mission Rabies.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest."

The corrected sentence appears below:

"AG was project lead for the development of the electronic application, with LG and FL supporting the development, as a part of their employment for Mission Rabies.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest."

A correction has been made to the Author Contributions section. This sentence previously stated:

"RW and AG conceptualized the project. RW acquired funding and supervised the project. RW, CS, YR, and SB synthesized and analyzed study data. AG provided resources and software programming. PD, KC, NF, and HJ managed coordination/execution of activities. CS wrote original draft with review and editing by RW. All authors contributed to the article, reviewed, and approved the submitted version."

The corrected sentence appears below:

"RW, AG, LG, and FL conceptualized the project. RW acquired funding and supervised the project. RW, CS, YR, and SB synthesized and analyzed study data. AG, LG and FL provided resources and software programming. PD, KC, NF, and HJ managed coordination/execution of activities. CS wrote original draft with review and editing by RW. All authors contributed to the article, reviewed, and approved the submitted version."

The authors apologize for this error and state that this does not change the scientific conclusions of the article in any way. The original article has been updated.

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frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 13 June 2023
DOI 10.3389/fvets.2023.1111057

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OPEN ACCESS

EDITED BY
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RECEIVED 23 December 2022
ACCEPTED 25 May 2023
PUBLISHED 13 June 2023

CITATION
Anagnostopoulos A, Griffiths BE, Siachos N, Neary J, Smith RF and Oikonomou G (2023) Initial validation of an intelligent video surveillance system for automatic detection of dairy cattle lameness.
Front. Vet. Sci. 10:1111057.
doi: 10.3389/fvets.2023.1111057

Initial validation of an intelligent video surveillance system for automatic detection of dairy cattle lameness

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Introduction: Lameness is a major welfare challenge facing the dairy industry worldwide. Monitoring herd lameness prevalence, and early detection and therapeutic intervention are important aspects of lameness control in dairy herds. The objective of this study was to evaluate the performance of a commercially available video surveillance system for automatic detection of dairy cattle lameness (CattleEye Ltd).

Methods: This was achieved by first measuring mobility score agreement between CattleEye and two veterinarians (Assessor 1 and Assessor 2), and second, by investigating the ability of the CattleEye system to detect cows with potentially painful foot lesions. We analysed 6,040 mobility scores collected from three dairy farms. Inter-rate agreement was estimated by calculating percentage agreement (PA), Cohen's kappa (κ) and Gwet's agreement coefficient (AC). Data regarding the presence of foot lesions were also available for a subset of this dataset. The ability of the system to predict the presence of potentially painful foot lesions was tested against that of Assessor 1 by calculating measures of accuracy, using lesion records during the foot trimming sessions as reference.

Results: In general, inter-rater agreement between CattleEye and either human assessor was strong and similar to that between the human assessors, with PA and AC being consistently above 80% and 0.80, respectively. Kappa agreement between CattleEye and the human scorers was in line with previous studies (investigating agreement between human assessors) and within the fair to moderate agreement range. The system was more sensitive than Assessor 1 in identifying cows with potentially painful lesions, with 0.52 sensitivity and 0.81 specificity compared to the Assessor's 0.29 and 0.89 respectively.

Discussion: This pilot study showed that the CattleEye system achieved scores comparable to that of two experienced veterinarians and was more sensitive than a trained veterinarian in detecting painful foot lesions.

KEYWORDS
cattle lameness, automated system, foot lesions, mobility scoring, artificial intelligence

1. Introduction

Lameness poses a major challenge to the dairy industry worldwide and has a well-documented negative impact on dairy cattle milk production, fertility and longevity (1–3). Apart from the financial implications of lameness its impact on animal welfare cannot be understated (4, 5). Early lameness detection has been shown to be an important aspect of lameness management in dairy herds (6) and yet for the most part relies on visual mobility/locomotion scoring by farm staff or trained scorers. This process, albeit useful, is time consuming, labour intensive and subjective even when agreement within the same experienced assessor is examined (7). Furthermore, farmers have been shown to significantly underestimate lameness prevalence in their herd (8). An automated system that could reliably identify lame cows would not only have the advantage of being objective and consistent but could also provide daily information about the lameness status of the herd.

CattleEye Ltd. (Belfast, United Kingdom) has recently developed and commercialised a system for automatic lameness detection. This system is the first to utilize inexpensive 2D surveillance cameras placed above the passageway exiting the milking parlour. Footage of cows exiting the milking parlour is sent directly to company servers where it is stored and processed. The footage analysis requires a minimum of 40 frames recorded over 2 s (20 fps setting). Initially, an object-tracking algorithm is used to identify the outline of the body and track it across frames. Based on information gathered during the enrolment of the herd, the algorithm identifies the individual animal (based on coat pattern and head shape) and assigns its identification number to the recording. Specific reference points are marked and their coordinates across frames are recorded on a matrix. This information is then processed by the convolutional neural network and the average pooling output is used during the linear activation stage to produce a mobility score. The final result of the analysis is a floating-point number between 0 and 100, indicating the degree of lameness in relation to changes observed between reference points in each frame and between frames. For example, a score of 0 indicates good mobility whilst a score of 100 would indicate a very poor level of mobility and therefore a very high likelihood of lameness.

The objective of this pilot study was to evaluate the performance of this video surveillance system for automatic detection of dairy cattle lameness. Our aim was to investigate the agreement between the mobility scores provided by the CattleEye system and the mobility scores recorded by two experienced veterinarians. Additionally, we examined the system's ability to detect cows with potentially painful foot lesions.

2. Materials and methods

2.1. Farms' characteristics and animals

From November 2020 to February 2021 three commercial dairy farms in Northwest England and North Wales participated in this validation study. All farms milked Holsteins cows that were housed during the study period and were already equipped with the CattleEye mobility scoring system. Farm 1 housed all year round a milking herd of *ca.* 180 cows. Farm 2 consisted of a milking herd of *ca.* 340 cows. Freshly calved and early lactation cows were housed year-round while late lactation cows were grazed during spring and summer. Farm 3 housed a milking herd of *ca.* 750 cows all year round. Farm staff were responsible for foot trimming in Farm 1. Farms 2 and 3 used the same professional foot trimmer who was performing routine and therapeutic foot trimming on each farm fortnightly.

2.2. CattleEye mobility scoring system

The CattleEye scoring system produces scores on a scale from 0 to 100, with each 25-increment representing one grade on the UK Agricultural and Horticultural Development Board (AHDB) mobility scoring system (9). More specifically, cows with a score <25 were graded as 0, those with a score ≥ 25 and <50 were graded as 1, those with a score ≥ 50 and <75 were graded as 2, and those with a score ≥ 75 were graded as 3. The four-grade mobility score variable that was produced by this transformation will be hereinafter referred to as the CattleEye mobility score (CE_MS).

2.3. Mobility scoring records

During the study, all three farms were visited approximately once a week by an experienced scorer (Assessor 1, AA) who was a veterinarian trained by an expert in dairy cattle lameness and had been working exclusively on cattle lameness research for a three-year period prior to the commencement of this study. During each visit, the entire milking herd was scored by Assessor 1 using the AHDB 0–3 four-grade scale scoring method (9). Reports containing CE_MS (weekly average for each cow) were also made available to the corresponding author (GO) of this study. Importantly, Assessor 1 did not have access to the CattleEye data and CattleEye Ltd. did not have access to the Assessor's scores. At the end of the validation period, the Assessor's records for each visit were merged with the corresponding CE_MS (for the week prior to the assessor's visit) using the cow identification numbers. Records from all visits were then combined to create Dataset A.

A second experienced assessor (Assessor 2, BG), a veterinarian accredited by the Register of Mobility Scorers (Register of Mobility Scorers Limited, Wimborne, United Kingdom) and trained by the same expert as Assessor 1, recorded mobility scores once on Farms 2 and 3. Assessor 2 evaluated cows on Farm 2 simultaneously with Assessor 1 and within 48 h from one of Assessor 1 scoring sessions on Farm 3. Assessors had no knowledge of each other's scores prior to or during the visit. Dataset B contained the individual mobility scores recorded by Assessor 1 and Assessor 2, and the corresponding CE_MS.

2.4. Foot lesion records

Assessor 1 was present during professional foot trimming sessions on Farm 2 and Farm 3 and soon after a mobility scoring session in order to consistently record presence of foot lesions. These included both routine and therapeutic trims and by the end of the study foot lesion data from 84 cows were recorded according to the ICAR claw health atlas (10). Lesions were graded for severity on a scale from 0 to 3 as described in Supplementary Table S1. Assessor 1 had no prior knowledge regarding which cows were sorted for routine trimming and which for therapeutic foot trimming. Lesion records were merged with Assessor 1 mobility scores and CE_MS obtained at the closest date prior to the foot trimming session to create Dataset C. An overall binary lesion score was generated (Lesion_BIN) with 1 representing cows that were found with at least one potentially painful lesion and 0 cows with milder or no lesions. Lesions described as potentially painful for the purposes of this classification were: sole ulcer lesions of grade >0, white line lesions of grade 3, toe ulcer lesions of grade >0, interdigital hyperplasia lesions of grade >1 and digital dermatitis lesions of grade 3.

2.5. Statistical analysis

Data were handled and analysed using R 3.6.

In all datasets, the four grade (0–3) mobility scores recorded by Assessor 1 (A1_MS), Assessor 2 (A2_MS) and CE_MS were also transformed into binary variables (0,1/2,3; non-lame/lame), namely A1_BIN, A2_BIN and CE_BIN, respectively.

Agreement between A1_MS and CE_MS (Dataset A) and between A1_MS, A2_MS and CE_MS (Dataset B; all pairwise combinations) was estimated by calculating the weighted Cohen's kappa (wκ) and the weighted Gwet's coefficient (AC_2) using quadratic weights.

Agreement between A1_BIN and CE_BIN (Dataset A) and between A1_BIN, A2_BIN and CE_BIN (Dataset B; all pairwise combinations) was estimated by calculating the percentage of agreement (PA), unweighted Cohen's kappa (κ), and the unweighted Gwet's coefficient (AC_1). Finally on dataset B, confusion matrixes (11) were created to calculate measures of accuracy (sensitivity (SE) and specificity (SP)) of A2_BIN and CE_BIN in predicting A1_BIN scores.

Interpretation of each agreement coefficient was according to the Landis and Koch (12) recommendations: values 0.00–0.20: slight agreement; values 0.21–0.40: fair agreement; values 0.41–0.60: moderate agreement; values 0.61–0.80: substantial agreement; values 0.81–1.00: almost perfect agreement. The benchmark of acceptable reliability used in this study was ≥0.60 for κ, wκ, AC_1, and AC_2 (13, 14).

Using dataset C, confusion matrixes were created to calculate measures of accuracy (SE; SP; positive predictive value (PPV), and negative predictive value (NPV)) of A1_BIN and CE_BIN in predicting the presence of potentially painful lesions, using Lesion_BIN as reference.

TABLE 1 Summary of four grade (0–3) mobility scores recorded by Assessor 1 and CattleEye for farms 1, 2, and 3 (Dataset A) and scores collected by both assessors and CattleEye for farms 2 and 3 (Dataset B).

Farm	1	2	3
Dataset A			
Observations	$n = 857$	$n = 1,387$	$n = 3,796$
Assessor 1 Mobility Score (A1_MS)			
0	141 (16%)	223 (16%)	1,007 (27%)
1	567 (66%)	971 (70%)	2,399 (63%)
2	131 (15%)	171 (12%)	342 (9.0%)
3	18 (2.1%)	22 (1.6%)	48 (1.3%)
CattleEye Mobility Scores (CE_MS)			
0	90 (11%)	285 (21%)	1,499 (39%)
1	573 (67%)	885 (64%)	1,846 (49%)
2	194 (23%)	215 (16%)	441 (12%)
3	0 (0%)	2 (0.1%)	10 (0.3%)
Dataset B			
Assessor 1 Mobility Score (A1_MS)			
0		27 (22%)	214 (37%)
1		73 (58%)	312 (54%)
2		25 (20%)	43 (7.5%)
3		0 (0%)	8 (1.4%)
CattleEye Mobility Scores (CE_MS)			
0		45 (17%)	230 (36%)
1		182 (67%)	310 (49%)
2		43 (16%)	89 (14%)
3		1 (0.4%)	3 (0.5%)
Assessor 2 Mobility Score (A2_MS)			
0		36 (29%)	332 (56%)
1		71 (57%)	190 (32%)
2		17 (14%)	61 (10%)
3		1 (0.8%)	5 (0.9%)

3. Results

The total number of records for each mobility score grade and farm according to all scorers for Dataset A and Dataset B are summarized in Table 1. Lameness prevalence for each farm and visit as recorded by Assessor 1 and by CattleEye is presented in Figure 1. Herd lameness prevalence ranged from 7 to 20% and from 8 to 25% between farm visits, according to Assessor 1 and CattleEye, respectively.

3.1. Inter-rater agreement

Dataset A consisted of a total of 6,040 paired mobility scoring records (Farm 1: 857; Farm 2: 1,387, and Farm 3: 3,796). Agreement between Assessor 1 and CattleEye mobility scores and binary scores is summarized in Table 2.

Cohen's wκ for agreement between A1_MS and CE_MS was >0.40 only on Farm 1. On the other hand, AC_2 was consistently >0.80 with an overall value of 0.835, indicating almost perfect agreement.

Percentage agreement between A1_BIN and CE_BIN was 87%; ranging from 82.6 to 88.9% between different farms. The overall agreement was fair using the Cohen's κ coefficient ($\kappa = 0.404$), while AC_1 was within the range of almost perfect agreement ($AC_1 = 0.832$).

Dataset B included observations from a total of 903 cows (Farm 2: 271, and Farm 3: 632). Agreement between A1_MS, A2_MS and CE_MS is shown in Table 3. Regarding Cohen's wκ, moderate agreement (w$\kappa > 0.40$) was only achieved between A1_MS and A2_MS. According to AC_2, agreement bellow the almost perfect range was only observed between A2_MS and CE_MS where AC_2 was 0.79 and 0.78 for Farms 2 and 3, respectively.

Percentage agreement between A1_BIN and CE_BIN and between A2_BIN and CE_BIN were the same (86.2%); a similar PA was also produced for the agreement between A1_BIN and A2_BIN (88.2%). According to Cohen's κ fair agreement was observed between

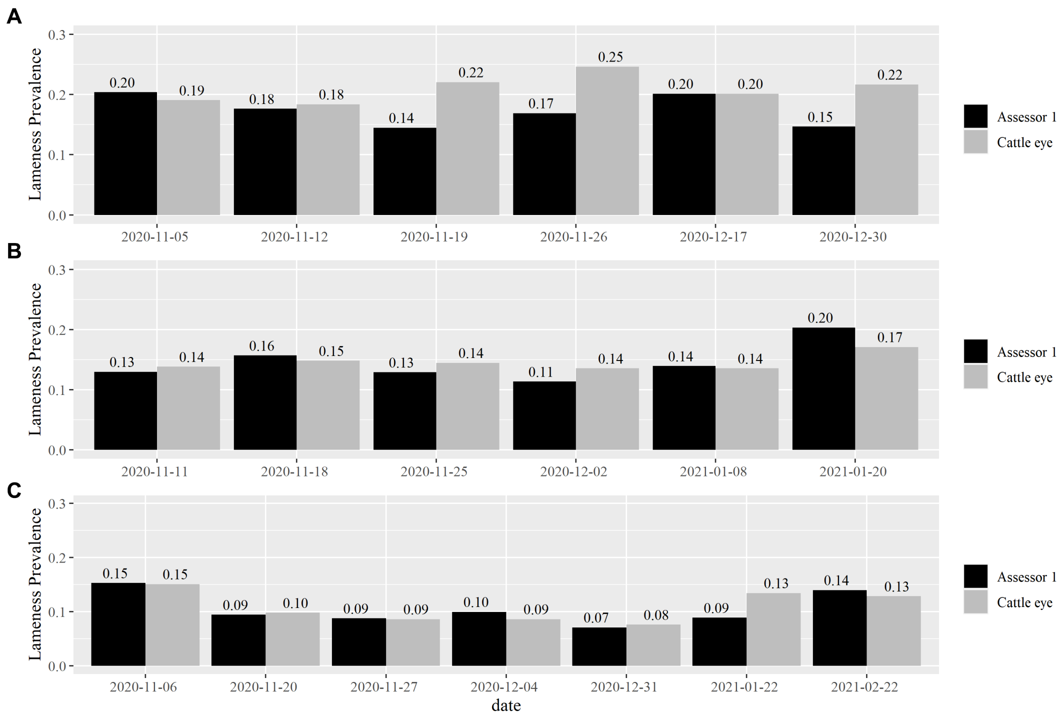

FIGURE 1
Lameness prevalence as recorded by Assessor 1 and the Cattle-eye system for each farm visit. Cows with mobility scores 2 and 3 were scored as lame. Data from each farm is presented separately (**A** for Farm 1, **B** for Farm 2 and **C** for Farm 3).

TABLE 2 Inter-rater agreement of mobility score between Assessor 1 and the CattleEye system, estimated with weighted Cohen's kappa (wκ) and weighted Gwet's agreement coefficient type 2 (AC_2) for the 4-grade scoring (0–3) and with percentage agreement (PA), unweighted Cohen's kappa (κ) and Gwet's agreement coefficient type 1 (AC_1) for the binary transformed 2-grade scoring (0,1/2,3).

Farm	*n*	PA	κ/wκ	AC_1/AC_2
1	857			
0–3			0.405	0.868
0,1/2,3		82.6%	0.441	0.747
2	1,387			
0–3			0.347	0.862
0,1/2,3		84.1%	0.342	0.789
3	3,796			
0–3			0.369	0.820
0,1/2,3		88.9%	0.411	0.863
All	6,040			
0–3			0.386	0.835
0,1/2,3		86.9%	0.404	0.832

n, number of observations.

all possible pairs across farms except for the pairs A1_BIN/A2_BIN and A1_BIN/CE_BIN where moderate agreement was achieved for Farm 3 (0.44 and 0.40 respectively). The overall AC_1 was ≥0.80 for all possible pairs, indicating almost perfect agreement.

According to the confusion matrixes produced, both A2_BIN and CE_BIN had almost the same ability to predict A1_BIN scores achieving combinations of 51% SE, 92% SP and 51% SE, 90% SP, respectively.

3.2. Detection of painful foot lesions

A summary of the lesions recorded throughout the study for Dataset C is presented on Table 4. Using Lesion_BIN as reference and CE_BIN as a predictor, the confusion matrix produced a combination of 52% SE and 81% SP in predicting the presence of potentially painful foot lesions with an accuracy of 73.81%. Positive and negative predictive values were 0.48 and 0.84, respectively.

TABLE 3 Inter-rater agreement of mobility score combinations between Assessor 1, Assessor 2, and the CattleEye system in Farms 2 and 3, estimated with weighted Cohen's kappa (wκ) and weighted Gwet's agreement coefficient type 2 (AC_2) for the 4-grade mobility score (0–3) and with percentage agreement (PA), unweighted Cohen's kappa (κ) and Gwet's agreement coefficient type 1 (AC_1) for the binary transformed 2-grade mobility score (0,1/2,3).

Farm	*n*	PA	κ/wκ	AC_1/AC_2	PA	κ/wκ	AC_1/AC_2	PA	κ/wκ	AC_1/AC_2
		Assessor 1 vs. Assessor 2			Assessor 1 vs. CattleEye			Assessor 2 vs. CattleEye		
2	271									
0–3			0.347	0.827		0.258	0.810		0.210	0.786
0,1/2,3		80.0%	0.382	0.720	77.6%	0.255	0.679	81.6%	0.302	0.750
3	632									
0–3			0.407	0.808		0.386	0.808		0.379	0.776
0,1/2,3		90.1%	0.442	0.879	88.0%	0.401	0.850	85.0%	0.325	0.806
All	903									
0–3			0.418	0.808		0.377	0.806		0.366	0.772
0,1/2,3		88.2%	0.408	0.853	86.2%	0.368	0.823	86.2%	0.321	0.797

n, number of observations.

Using A1_BIN as a predictor, the confusion matrix produced a combination of 29% SE and 89% SP with an accuracy of 73.81%. Positive and negative predictive values were 0.46 and 0.79, respectively.

4. Discussion

We have shown here that the CattleEye automatic lameness detection system performs similarly to two well trained veterinarians by calculating 3 different measures of inter-rater agreement (PA, Cohen's κ and Gwet's AC) for both the 4-grade (0–3) and the binary converted 2-grade (0,1/2,3) mobility scores. Overall, PAs were >80% and AC were constantly above the benchmarks of accepted reliability, while κ coefficients were low, indicating only fair to moderate agreement.

Kappa agreement between Assessor 1, Assessor 2, and CattleEye fell within the range described by Thomsen et al. (15) when inter-observer agreement was investigated (κ values ranged from 0.24 to 0.68). Linardopoulou et al. (16) recently reported very low to moderate κ coefficients (0.004 to 0.565) between multiple human assessors; results were affected by scoring method used and the farm visit. Higher κ values for inter-observer agreement have been reported by others (7, 17, 18), but those studies involved scoring cows using a relatively small number of video recordings trying to equally represent all mobility grades. Our study was conducted under commercial farm conditions and scorers had to record cow ID and evaluate mobility scores for 100 of cows exiting the milking parlour often having just a few seconds for each animal; this is how mobility scoring is performed in practice.

The discrepancy between AC and κ could be due to a statistical phenomenon called the kappa paradox. This phenomenon is defined by low κ values in the presence of high percent agreement, under the influence of raters' classification probabilities and low prevalence of the tested trait (19). Paradoxical situations, when using κ to test inter-observer agreement, have been reported across various medical fields (20, 21). As a result, the use of Gwet's AC (22) is becoming popular as it is considered a more stable coefficient, especially in low prevalence scenarios. To the best of the authors' knowledge, there are no published studies estimating inter-rater agreement in mobility scoring using Gwet's coefficients to compare to ours. Using AC_2, agreement between the two human assessors was almost perfect in Dataset B. Better results were obtained using AC_1 for the binary scores for Farm 3. Agreement of CattleEye with either human assessor was about the same and very similar to that between the two human assessors, and always above the benchmark of accepted reliability.

The impact of hoof pathologies on cows' gait is a proven concept (23) that has been recorded using kinematic techniques. Song et al. (24) described one of the first fully automated methods of recording trackway and gait characteristics. Utilizing kinematic techniques based on leg swing, Zhao et al. (25) developed an algorithm that achieved 90.18% accuracy on a tenfold cross validation using a total number of 621 video recordings of 98 cows. Both Viazzi et al. (26) and Poursaberi et al. (27) utilized the Body Movement Pattern that emphasizes on back curvature. They later automated this method and when tested on 1,200 video recordings of cows only 88 where misclassified by the algorithm (28). For the most part these systems involve video recordings of individual cows using as gold standard the mobility score provided by a scorer after evaluating the recording and not comparing human scorers against an automatic system in real time on commercial farm settings.

In our study, binary converted CattleEye scores achieved the same accuracy as Assessor 1 (when lesion detection was evaluated), being actually more sensitive in predicting the presence of potentially painful lesions. However, the SE produced by CattleEye was still relatively low, allowing for a high proportion of cows gone undetected (false negatives). On the other hand, SP was high, allowing only for a small percentage of false positives with the human assessor performing slightly better. Both human assessor and CattleEye produced low PPV and high NPV, with CattleEye performing slightly better. This suggests that, within the herd lameness prevalence observed in this study, a cow being assigned a "negative" score (0,1: non-lame) either by a human assessor or the

TABLE 4 Total number and percentage of foot lesions and severity (Dataset C).

	N	%
Farm		
2	42	50%
3	42	50%
Severity* SH	*n*	
0	21	25%
1	21	25%
2	29	35%
3	13	15%
SU		
0	72	86%
1	6	7.1%
2	5	6%
3	1	1.2%
WL		
0	48	57%
1	11	13%
2	20	24%
3	5	6%
TU		
0	83	99%
3	1	1.2%
IH		
0	78	93%
1	2	2.4%
2	4	4.8%
DD		
0	68	81%
1	9	11%
2	3	3.6%
3	4	4.8%

N, number of cows examined; *n*, number of lesions observed; SH, sole haemorrhage; SU, sole ulcer; WL, white line lesion; TU, toe ulcer; IH, interdigital dermatitis; DD, digital dermatitis. *: severity of the lesions recorded on a 0–3 scale with 0 representing absence and 3 representing the most sever stages of the lesion.

automated detection system has high odds of actually not baring potentially painful foot lesions.

The ability of CattleEye to outperform the human scorer in the detection of severe lesions when sensitivity is concerned might be due to the innate advantages of automatic systems and the frequency of scoring. Human assessor scoring is prone to errors and misclassifications due to various practical reasons, besides subjectivity. The human scorer only had a few seconds for each individual cow once a week. Circumstances when multiple cows exit the parlour at the same time disturbing the flow and scoring process are quite common in most farms. Difficult weather conditions and fatigue due to long hours of repeatedly scoring large herds may also add to the chance of human error. In contrast, an automated system is less prone to such errors. The system is able to assess each cow after each milking, every day, potentially reaching 14 to 21 scores for each individual cow per week. This ability guarantees that momentary disturbances to cow flow would not affect the average weekly score. Additionally, normal idiosyncrasies in an animal's gait are recognised by the algorithm. In other words, a slight change in movement pattern that would not justify a classification of a cow as lame by a human assessor might be highly irregular for a certain animal based on saved footage history and thus increasing the CE_MS algorithm above the lameness threshold.

Our study has several limitations. The intra-rater agreement of each human assessor and of the automated system was not considered. Therefore, we cannot acknowledge whether the lack of precision of each assessor influenced the observed inter-rater agreement. Ideally, multiple assessors of varying experience could have recorded mobility scores on all farms involved in this study. That way the deviation of each Assessor and the CattleEye system from the mean could have been calculated. Additionally, more lesions could have been recorded close to a mobility scoring visit to use as the gold standard of lameness detection. This should be the scope of future studies.

Based on the ability of CattleEye and Assessor 2 mobility scores to predict the binary scores recorded by Assessor 1, the agreement between all possible pairs, and the literature describing mobility score agreement between human assessors, it is not unreasonable to describe the system's performance as equivalent to that of a trained scorer. Granted there was slightly better agreement between the two human assessors but that is to be expected since they had the same training and working environment for more than 2 years. Future investigations should consider the addition of external professional mobility score assessors of various experience and background to put those differences in the calculated agreement into perspective. The system was more sensitive in identifying lameness causing lesions compared to Assessor 1. This further justifies the use of the CattleEye system not just as a herd lameness prevalence monitoring system, but rather as an early lameness detection aid for individual cows. Training CattleEye algorithms using large datasets containing foot lesion information could further improve its ability for early detection of foot pathology.

5. Conclusion

We showed that the CattleEye system is producing mobility scores comparable to those of two experienced scorers with similar training. When it came to lesion detection the system was more sensitive than the human scorer and achieved the same accuracy. Implementing a system that can produce reliable mobility scores for each animal multiple times per week (or even daily) regardless of herd size, could prove an invaluable tool in lameness management. Automatic lameness detection is not prone to subjectivity and fatigue in contrast to human scorers and the system's ability to detect lesions can aid in early treatment minimising production loss and improving animal welfare.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The animal study was reviewed and approved by University of Liverpool Veterinary Research Ethics Committee. Written informed consent was obtained from the owners for the participation of their animals in this study.

Author contributions

Data collection was undertaken by AA and BG. Statistical analysis was undertaken by AA and assisted by GO and NS. The manuscript draft was written by AA with significant contributions from GO and NS. GO (corresponding author) conceived and designed the study with significant contributions from RS and JN. All authors contributed to the article and approved the submitted version.

Funding

CattleEye Ltd. provided funding and approved the final version of this manuscript. The funder participated in the discussions leading to the study design but had no involvement in data collection and analysis.

Acknowledgments

The authors wish to thank the three farms which participated in the study. Preliminary results were presented as an Abstract at the Annual Congress of the British Cattle Veterinary Association, October 2021.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2023.1111057/full#supplementary-material

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frontiers | Frontiers in Veterinary Science

TYPE Brief Research Report
PUBLISHED 12 October 2023
DOI 10.3389/fvets.2023.1270532

OPEN ACCESS

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RECEIVED 31 July 2023
ACCEPTED 29 September 2023
PUBLISHED 12 October 2023

CITATION
Andriamandimby SF, Volasoa MH, Razafindraibe NP, Ranoaritiana DB, Razafindramparany MH, Rafisandratantsoa T, Nomenjanahary LA, Rakotondrabe N, Andriamananjara MA, Guis H, Lacoste V and Dreyfus A (2023) Rabies surveillance in Madagascar from 2011 to 2021: can we reach the target?
Front. Vet. Sci. 10:1270532.
doi: 10.3389/fvets.2023.1270532

Rabies surveillance in Madagascar from 2011 to 2021: can we reach the target?

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Rabies is endemic in Madagascar and a neglected disease. The aim of this study was to summarize human and animal rabies surveillance activities in Madagascar from 2011 to 2021. Samples from terrestrial mammals and humans were tested for rabies virus infection using direct fluorescent antibody, RT-PCR and virus isolation by the National Reference Laboratory (NRL) for rabies at the Institut Pasteur de Madagascar. Among 964 animal and 47 human samples tested, 66.7 and 70.2% were positive, respectively. The NRL received these suspect rabies samples from 48 of 114 districts of Madagascar. Most of them were submitted from the district of the capital city Antananarivo (26.3%) and mainly from its region Analamanga (68.9%). Animal samples were mainly from dogs (83%), cats (9.5%) and cattle (5.8%). Pigs, lemurs, goats accounted for less than 1%. During the 11 years of surveillance, 48 human skin and/or brain biopsy samples were received from 20 districts, mainly from Antananarivo and its surroundings (N = 13), Toamasina and its surroundings (N = 8) and Moramanga (N = 6). The high positivity rate for all species and the non-homogeneous spatial distribution of samples suggests substantial underreporting of rabies cases. There is a clear need to better understand the reasons for underreporting and prioritize rabies surveillance, prevention and control in Madagascar, with improvements in budget, education and infrastructure. A joint animal and human health rabies control program including vaccination of at least 70% of the dog population, is needed to achieve the goal of eliminating dog-transmitted human rabies by 2030 from Madagascar.

KEYWORDS

rabies, surveillance, Madagascar, direct fluorescent antigen test, dogs

1. Introduction

Animal and human rabies are preventable through vaccination and vaccine is available and safe (1). Nevertheless, the rabies virus remains endemic in many parts of the world and still represents an important threat to public health (1). For decades, over 99% of reported human cases worldwide are dog-transmitted. Despite the scientific literature reporting 59,000 annual deaths due to rabies, the perception of the importance of rabies control by policy makers, public health workers and even veterinarians may be different from country to country (2, 3). As a result, rabies mainly affects poor and vulnerable populations in rural areas due to ignorance and, in some cases, misinformation (1, 4). In this context, the World Health Organization (WHO), the World Organization for Animal Health (WOAH), the FAO and the Global Alliance for Rabies Control (GARC) adopted in 2015 a global initiative to eliminate human deaths from dog-mediated rabies by 2030 (5). Eliminating rabies in dogs is the optimal control method for preventing the spread of the disease (6–9). To reach this goal, accurate data on the incidence and true burden of rabies needs to be collected. It is therefore important to strengthen rabies surveillance and control at the local and national levels to provide robust estimates that will be used by policy makers (10).

In Madagascar, rabies remains a neglected disease. The first national vaccination campaign against rabies took place in 2019. It was organized by the Ministry of Agriculture and Animal Husbandry (MAAH), which had received 100,000 doses of animal vaccines from the Global Alliance for Rabies Control (GARC). However, the COVID-19 pandemic and other logistical issues hampered this momentum. As a result, no exact data on dog vaccination coverage is available to date. While very few dogs are vaccinated in Madagascar, post-exposure prophylaxis (PEP) for humans is in place. PEP is available in a network of 31 anti-rabies treatment centers (CTAR) distributed throughout the country. A CTAR is present in each district capital of each of the 22 administrative regions. A further nine CTARs are located in the most densely populated landlocked districts. All CTARs are supplied with rabies vaccine free of charge by the Institut Pasteur de Madagascar (IPM) in Antananarivo. It is the responsibility of the manager of each CTAR to obtain supplies from IPM, often at his/her own expense. As a result, while CTARs in major urban centers have large visitor numbers and provide PEP for free, patients in some remote rural areas can be asked to pay a financial contribution for PEP services in order to cover part of the transport costs (11). The fees charged are left to the discretion of each CTAR and no official information is available on their amount. Overall, in 2018 and 2019, about 15,000 patients per year required PEP nationwide, with 42% of patients visiting the major CTAR located at IPM in the capital city Antananarivo (11).

Rabies is a notifiable disease in Madagascar. Its surveillance is exclusively passive and involves three entities: the National Reference Laboratory (NRL) for rabies hosted by the Virology Unit at IPM, the MAAH and the Ministry of Public Health (MoPH). Animal and human rabies diagnosis is free of charge and financially supported by IPM. The MAAH manages the surveillance of animal diseases *via* the Madagascar Animal Disease Surveillance network while the MoPH is responsible for human disease surveillance. The NRL notifies both government bodies of all confirmed rabies cases. Upon receipt of a rabies notification by the NRL, the MoPH and MAAH work together to ensure that the bitten person receives PEP at one of the 31 CTARs. However, at all levels of the health system, any medical staff receiving patients who have been bitten or scratched should refer the patient to a CTAR to receive PEP even before the suspected animal is confirmed to have rabies, to be certain that they receive PEP during the incubation period. In theory, a dog suspected of having rabies or of having bitten a person is quarantined and remains under observation for 15 days by a veterinarian. If the animal develops rabies, the veterinarian euthanizes it and takes a sample for a confirmatory diagnosis at the NRL. However, animals are more often killed immediately or not handled at all.

This report summarizes rabies surveillance activities in Madagascar from 2011 to 2021. The aim is to provide an update of the rabies surveillance data since the publication of the previous report (2005–2010) (12), and to identify the specific factors associated with the poor performance of rabies surveillance.

2. Materials and methods

2.1. Diagnostic activities

Animal samples (entire head, brain samples or cadavers of terrestrial non-flying mammals) are received at the NRL at ambient temperature or ideally at +4°C. At the time of writing, there is no coordinated system for sending suspected rabies samples to the NRL. Samples are sent either by veterinarians or their assistants, animal health officers, or directly by animal owners or any person exposed at their own expense. In the case of group bites involving one or more stray dogs, a local administrative agent will submit the samples after catching the dog(s) (12). To limit the sending of large samples (brain sample vs. animal head) and reduce shipping costs, the NRL team has been organizing training courses on sampling techniques since 2019.Human samples (post-mortem skin biopsies, saliva, or brain biopsies taken from the nape of the neck) (13) are sent at ambient temperature or ideally at 4°C by the MoPH staff after the hospital team has notified a suspect case.

A sampling form has been issued by the NRL. In most cases, the laboratory technician receiving the sample fills in the information sheet based on the information provided by the remitter. The information is then recorded into a standardized database. The information collected includes the transmitter (veterinarian or other), the name and detailed address of the owner, if available, the animal's rabies vaccination status and related information, disease history, symptoms reported to assess clinical suspicion of furious or paralytic rabies, the aggressiveness of the animal, whether or not it has bitten, and the circumstances of the bite.

Direct fluorescent antigen test (DFAT) is the reference technique used at the NRL. All biopsy brain samples are first tested by DFAT. For any negative test result, a second test is performed: either an isolation attempt in cell culture (Neuro-2A) (14), or RT-PCR (13, 15, 16). A second negative result by one of these two other tests is definitive. Human skin biopsies are tested by RT-PCR.

2.2. Statistical analyses

We performed a descriptive analysis of the data, calculating absolute numbers and proportions using R version 4.3.1. software. The association between descriptive category variables and diagnostic test results was calculated using the chi square test with 95% confidence intervals.

3. Results

From 2011 to 2021, the NRL received a total of 987 samples from animals suspected of rabies and 48 samples from suspected human cases, of which 964 (97.7%) and 47 (97.9%) were eligible for testing, respectively. The remaining samples were not suitable for testing due to inadequate transport conditions. The annual number of samples submitted to the NRL varied from 55 to 151 between 2011 and 2021. Animal samples were mainly from dogs ($N = 819$, 83%), cats ($N = 94$, 9.5%) and cattle ($N = 58$, 5.8%). Other species (pig ($n = 3$), lemurs ($n = 2$), goat ($n = 1$)) accounted for less than 1% over the study period (Table 1). Among animal samples, 863 (87.4%) were from animals with owners.

3.1. Circumstances of sampling and sending samples to the NRL

Samples were taken after a bite or attack (768, 77.8%) or in the event of rabies symptoms (687, 69.6%) (p-value < 0.001). Only 350 (35.5%) samples were sent by a veterinarian or his/her collaborators. In most cases, it was the owners or the bitten victims who sent the samples to the NRL. The majority of samples sent by veterinarians (72%) were from livestock suspected of having rabies. When the samples arrived at the NRL, we had no information on the gender of the animal for 160 (16%) of them, on the species for 5 (0.5%), on the characteristics of the bite for 35 (3.5%), on the rabies vaccination status for 30 (3%) or on the circumstances of death for as many as 139 (14.1%) of them. When veterinarians submitted samples, more data on biting behavior was missing (19/350 (5.4%) vs. 16/637 (2.5%)) ($p = 0.01$). The proportion of animals showing rabies symptoms was higher in ownerless animals (84.3% vs. 70.2%, $p = 0.002$). Until 2020, most animal samples (70.5%) sent to the NRL were heads, whereas in 2021, only brain samples were sent to the NRL.

3.2. Geographical origin of samples

3.2.1. Animal samples

The NRL received suspect rabies samples from 51 of 114 districts of Madagascar. However, the majority of them were submitted from the district of the capital city Antananarivo (n = 259, 26.3%) and mainly from the region Analamanga, the region of the capital city (68.9%) (Figure 1). Rabies circulation was confirmed for 44 districts, where at least one received sample was confirmed to be rabies positive. For the remaining seven districts, the NRL only received one sample for each district, which tested negative.

3.2.2. Human samples

During the 11 years of surveillance, 48 human skin and/or brain biopsy samples were received from 20 districts (Figure 1). As in the case of animals, the majority of samples came from the capital and its surroundings ($N = 13$), the city of Toamasina (East Coast) and its surroundings ($N = 8$), Sainte-Marie ($N = 1$) and Moramanga ($N = 6$).

TABLE 1 Description of animal sample ($N = 987$) characteristics received at the National Reference Laboratory for rabies in Antananarivo, Madagascar from 2011 to 2021.

	Female	Male	Total
	N (%)	*N* (%)	*N* (%)
	342 (41.4)	485 (58.6)	987
Animal species			
Cat	39 (48.1)	42 (51.9)	94 (9.6%)
Cow	30 (57.7)	22 (42.3)	58 (5.9%)
Dog	269 (39.2)	418 (60.8)	819 (83.4%)
Goat	1 (100.0)	0 (0.0)	1 (0.1%)
Pig	2 (100.0)	0 (0.0)	3 (0.3%)
Lemur	0 (0.0)	0 (0.0)	2 (0.2%)
Rat	0 (0.0)	0 (0.0)	5 (0.5%)
Age category			
<1 year	112 (45.2)	136 (54.8)	356 (40.7%)
1–3 years	90 (38.8)	142 (61.2)	241 (27.6%)
3–6 years	80 (41.2)	114 (58.8)	199 (22.8%)
>6 years	32 (42.7)	43 (57.3)	78 (8.92%)
Biting animal			
No	79 (48.5)	84 (51.5)	184 (19.3%)
Yes	254 (39.5)	389 (60.5)	768 (80.7%)
History of rabies vaccination			
No	322 (42.5)	435 (57.5)	899 (93.9%)
Yes	14 (25.9)	40 (74.1)	58 (6.06%)
Death circumstances			
Euthanized	156 (41.5)	220 (58.5)	453 (53.4%)
Spontaneous	140 (41.3)	199 (58.7)	395 (46.6%)
Owned animal			
Yes	311 (41.0)	447 (59.0)	863 (87.4%)
No	31 (44.9)	38 (55.1)	124 (12.6%)
Symptoms of rabies			
No	95 (38.5)	152 (61.5)	269 (28.1%)
Yes	241 (42.4)	327 (57.6)	687 (71.9%)
Submitter			
Non-veterinarian	210 (39.4)	323 (60.6)	637 (64.5%)
Veterinarian	132 (44.9)	162 (55.1)	350 (35.5%)

Missing data: 160 (16%) on gender, 113 on age, 5 (0.5%) for animal species, 35 (3.5%) for biting information, 30 (3%) on anti-rabies vaccination, 31 (3.1%) on rabies symptoms and 139 (14.1%) on death circumstances.

3.3. Diagnostic results

3.3.1. Animal samples

Overall, of the 964 samples meeting the test criteria, 643 (66.7% (95% CI: 63.9–69.7) tested positive by DFAT, by cell culture (Neuro-2A) or by RT-PCR. The percentage of positivity ranged from 56.8%

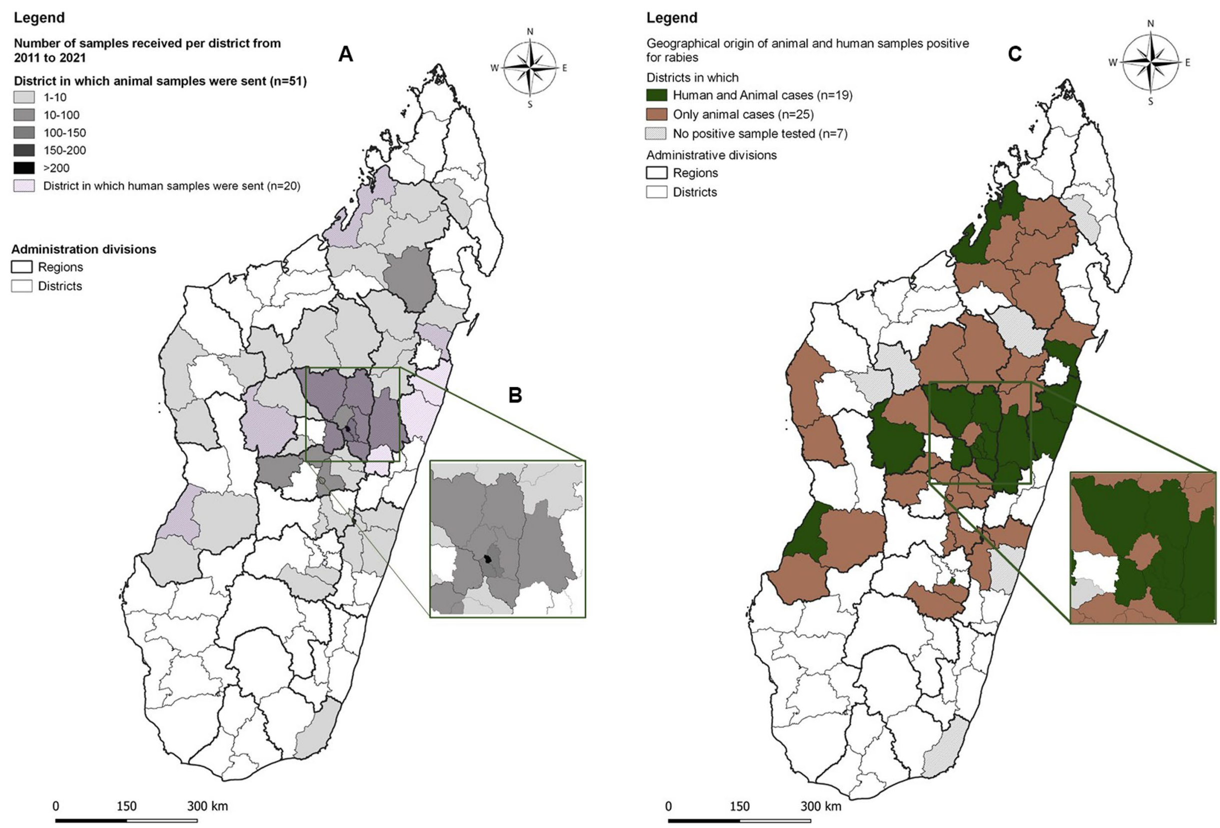

FIGURE 1
(A) Geographical origin and number of suspect rabies samples sent to the National Reference Laboratory for rabies, Antananarivo, Madagascar, received between 2011 and 2021. **(B)** Suspect samples for rabies received from the Analamanga region (Capital). **(C)** Origin of animal and human samples positive for rabies.

(95% CI: 45.8–67.2) in 2013 to 77.7% (95% CI: 69.9–89.9) in 2012 (Figure 2). Positivity was significantly higher in livestock ($p < 0.001$) (cattle (51/57, 89.5% (95% CI: 78.6–96.5), pigs (3/3, 100, 95% CI: 30.0–100), and goats (1/1, 100, 95% CI: 5.5–100), followed by dogs (564/798, 70.7, 95% CI: 67.4–73.0) and cats (22/93, 23.3, 95% CI: 15.7–33.8).

3.3.2. Human cases

Of the 48 human samples received, 47 were tested and rabies infection was confirmed in 33 individuals (70.2, 95% CI: 55.1–82.7) in 19 districts (Figure 1).

3.4. Association of sample characteristics and a positive diagnostic rabies result

Table 2 summarizes the association between descriptive category variables and diagnostic test results. We observed a statistically significant association ($p < 0.001$) between a positive test result and a sample originating from a biting animal, or an animal showing clinical symptoms. The proportion of positive test results was significantly higher in livestock than in pets ($p < 0.001$). Only 6.2% of tested animals had a history of vaccination, and of those vaccinated 22/56 (37.9%) were positive versus 598/878 (68.1%) among animals with no history of vaccination ($p < 0.001$). A higher number of positive cases were observed among samples submitted by veterinarians than among those submitted by bite victims and/or their relatives ($p < 0.001$).

4. Discussion

Over the 11 years of the study period, 66.7% of animal samples suitable for testing were positive for rabies. Overall, the positivity rate during this period increased in comparison to the previous report (48.9%; 220/450; 2005–2010) (12) and as compared to the period from 1959–1991 (57%;1416/2475) (p value < 0.001) (17). This high rate combined with the very limited number of districts submitting samples are indicative of underreporting and suggest that we are only measuring the "tip of the iceberg," both for animal and human data. In livestock, only 53 samples were submitted over 11 years, however we suspect that the rabies incidence in cattle is higher and very few samples are submitted, as the percentage of positivity indicates a potentially high incidence of rabies in these species and transmission most likely occurs through dog bites. In fact, requests for diagnosis mainly come from persons who had been exposed to cattle bites and underwent post-exposure treatment or in the event of a cluster of suspect cases in a cattle herd due to biting behavior or deaths, which is often the case for domestic livestock. Clustered cases of rabies are unlikely to be identified as only one sample of a suspect case is usually sent to the NRL and reported by

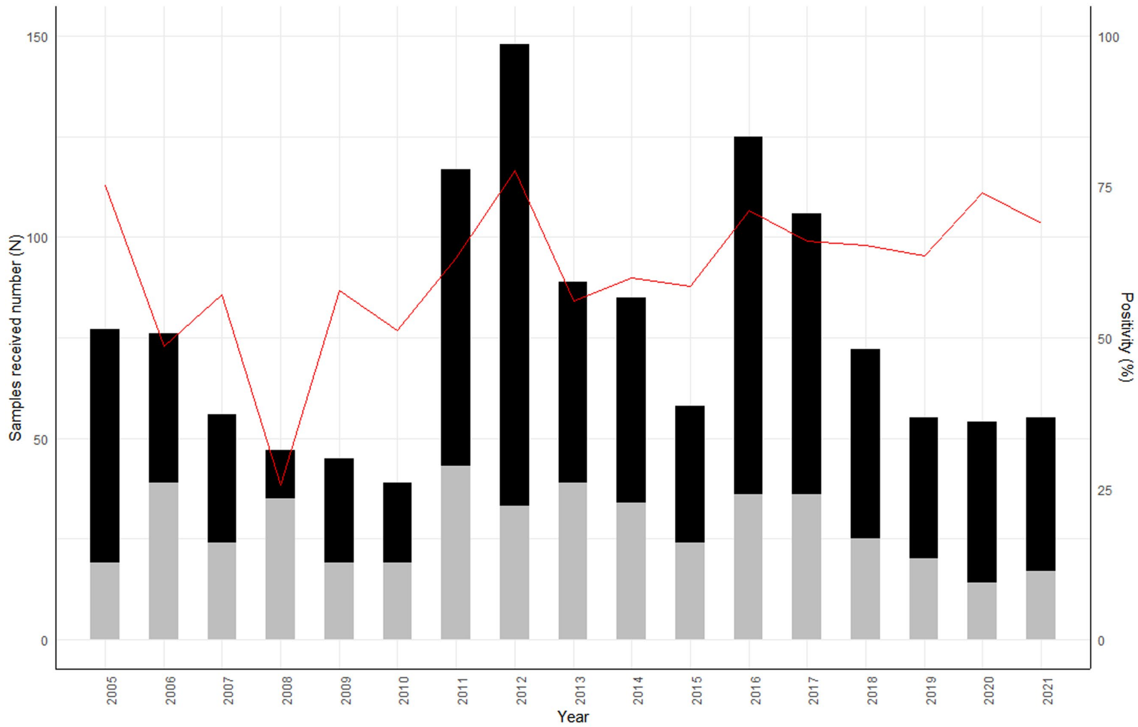

FIGURE 2
Number of animal samples received annually by the National Reference Laboratory for rabies from 2005 to 2021, Madagascar. The data from 2005–2010 were analyzed and published by Reynes et al. (12). Black: Positive samples, Grey: Negative samples, Red line: % of positivity.

laboratory rabies surveillance, which may also explain the low number of livestock samples in this report.

In 2011–2012, the NRL received an increasing number of samples with a higher positivity rate. This pattern was repeated in 2016. However, without data on population size, it is not possible to calculate the incidence or confirm the epidemic cycle with a 3 to 6-year period of rabies circulation in Madagascar, as previously suggested by Hampson et al. (18) (Figure 2).

For dogs, the majority of diagnostic requests were made following a bite event. Most veterinarians or citizens do not keep a biting dog for observation as required by law but kill it immediately with or without taking samples or ignore it (submitted). Despite the regulations for the observation of the biting animals, low access to veterinarians, the lack of adequate infrastructure for this purpose and the high uncovered costs of this intervention lead the population to kill or ignore the biting animal.

It is noteworthy that animal owners were more inclined to send an animal sample to the NRL than veterinarians, indicating a lack of implication of veterinarians in the passive surveillance system. This may be explained by the fact that veterinarians are primarily focused on livestock in Madagascar (submitted) and are therefore more involved in sending suspect samples when livestock are involved. If they request a rabies diagnosis, their aim is to confirm rabies infection for their own information and for their clients in an agricultural context, rather than for surveillance and public health purposes. The challenges veterinarians face with the current surveillance system needs to be better understood and addressed to improve their role in rabies control.

Out of 987 samples, 23 could not be tested due to their state of conservation. Although this number is limited, it indicates either a lack of information on the correct handling of samples or a lack of means to send these samples correctly. The cost of transport to the NRL is covered by the veterinarian or the animal's owner. This is certainly one of the main reasons for under-reporting. To avoid high transport costs, the NRL team has organized training courses on sampling techniques to limit the sending of large samples (brain sample vs. animal head). This led to a radical change in the type of samples sent to the NRL from 2021 onwards. However, even though all vets sent brain biopsies in 2021, surveillance coverage has not improved.

Information from rabies surveillance in Madagascar came mainly from the capital region where the NRL is located, and more than half of the districts remain "silent" about rabies. The lack of information on the occurrence/importance of rabies in these "data-less" areas leads to an erroneous perception of the absence of rabies in these regions.

The few control activities, such as dog culling and mass vaccinations conducted so far were in known "rabid" districts. Unfortunately, evaluation of these activities in terms of rabies incidence reduction is not available.

While Rajeev et al. (19, 20) estimated a human rabies incidence of 768 cases per year, the NRL only received an average of only four human samples per year (48 in total) over the 2011–2021 period. These samples were mainly sent by two medical services, indicating a lack of compliance with the surveillance system by other medical structures. However, when a case of rabies is suspected, the clinician's assignment is limited to the management of the patient and public health reporting is therefore not a priority for them. In this context, it is vital to clarify roles and communication paths in the legal text and to make clinicians aware of the importance of confirming the

TABLE 2 Test results of rabies diagnostics[a] on animal samples (N = 964) stratified by categorical variables[b], collected from 2011 to 2021 at the National Reference Laboratory for rabies in Antananarivo, Madagascar.

		Positive	Negative	Total	p-value
		N = 643 (%)	N = 321 (%)	N = 964 (%)	
Gender	Female	214 (64.5)	118 (35.5)	332 (41.0)	0.681
	Male	316 (66.1)	162 (33.9)	478 (59.0)	
Age category (in years)	<1	227 (66.4)	115 (33.6)	342 (40.1)	0.260
	1–3	169 (71.9)	66 (28.1)	235 (27.6)	
	3–6	130 (65.7)	68 (34.3)	198 (23.2)	
	>6	47 (61.0)	30 (39.0)	77 (9.04)	
Animal group	Pets	586 (65.1)	312 (34.9)	898 (93.6)	<0.001
	Livestock	55 (90.2)	6 (9.8)	61 (6.4)	
Clinical symptoms of rabies	No	94 (35.2)	173 (64.8)	267 (27.7)	<0.001
	Yes	534 (80.1)	133 (19.9)	667 (69.2)	
Biting animal	No	97 (53.0)	86 (47.0)	183 (19.7)	<0.001
	Yes	529 (70.7)	219 (29.3)	748 (80.3)	
History of rabies vaccination	No	598 (68.1)	280 (31.9)	878 (93.8)	<0.001
	Yes	22 (37.9)	36 (62.1)	58 (6.20)	
Circumstances of death	Euthanized	305 (69.3)	135 (30.7)	440 (53.0)	0.110
	Natural death	249 (63.8)	141 (36.2)	390 (47.0)	
Submitting person	Veterinarian	256 (74.9)	86 (25.1)	342 (35.5)	<0.001
	Other*	387 (62.2)	235 (37.8)	622 (64.5)	

*Usually the biting victim or owner of the animal.

[a]Direct fluorescent antigen test is the reference technique. For any negative test result, a second test is performed: either an isolation attempt in cell culture, or RT-PCR.

[b]Statistical significant difference calculated by chi square test.

diagnosis. In addition, one of the main causes of non-reporting could be the conflict over how to handle suspected human cases and their family (4). In the case of such a deadly disease, the family usually decides not to wait for the patient's death in the hospital for financial and administrative reasons, as transporting a corpse is more difficult. Moreover, although the risk of human-to-human transmission is null, family members potentially exposed to bodily fluid and healthcare workers are concerned about contracting rabies during care. Their concerns must be addressed not only to ensure the best possible care for patients suspected of having rabies, but also to maintain a solid relationship between different people involved in surveillance (21). Clinicians need to be informed about how to collect, package and transport appropriate specimens, and on the importance of explaining to the patient's family why specimen collection is necessary.

Eliminating rabies in dogs is the optimal control method for preventing the spread of the disease (2, 22). Actually, vaccination of dogs and control of stray dog populations are more efficient and cost effective than post-bite treatment in humans (2). However, most dogs in Madagascar are not vaccinated against rabies. While cultural factors (the dog is considered an unimportant or even "dirty" animal, not worthy of treatment) contribute to this situation, the fact that PEP is free certainly reduces the pressure to implement control measures in animals. Such phenomenon has also been observed in some communities in Chad (23). The "One Health" approach to rabies surveillance and control still needs to be implemented and awareness on this concept among stakeholders needs to be reinforced. It is still necessary to advocate among stakeholders for the absolute necessity of improving surveillance and control of rabies. Politicians have to understand the importance of funding to eliminate rabies in Madagascar. In 2023 a national strategic plan for rabies control was adapted and is a first step towards the goal of eliminating dog-transmitted human rabies by 2030.

In conclusion, rabies surveillance remains a challenge in Madagascar, mainly in terms of coverage and reporting. The activities carried out in response to a positive case of animal/human rabies focus on bitten victims or people potentially exposed to the rabid animal. There is a clear need to better understand the reasons for underreporting and to prioritize rabies surveillance, prevention and control in Madagascar, with improvements in budget, education and infrastructure. A more focused rabies control program, in the area of public health (information, awareness) and animal health, including vaccination of at least 70% of the dog population, is urgently needed to achieve the goal of eliminating dog-transmitted human rabies by 2030.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: Dataset will be provided on demand from the corresponding author. Requests to access these datasets should be directed to soafy@pasteur.mg.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements. Ethical approval was not required for the study involving animals in accordance with the local legislation and institutional requirements because we used anonymized laboratory surveillance data.

Author contributions

SA: Conceptualization, Methodology, Supervision, Writing – original draft, Writing – review & editing, Formal analysis, Project administration, Resources, Visualization. MV: Conceptualization, Formal analysis, Methodology, Writing – review & editing. NiR: Supervision, Writing – review & editing. DR: Supervision, Writing – review & editing. MR: Investigation, Writing – review & editing. TR: Investigation, Writing – review & editing. LN: Investigation, Writing – review & editing. NaR: Supervision, Writing – review & editing. MA: Supervision, Writing – review & editing. HG: Conceptualization, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. VL: Conceptualization, Methodology, Supervision, Writing – original draft, Writing – review & editing. AD: Conceptualization, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 07 February 2024
DOI 10.3389/fvets.2024.1270329

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RECEIVED 31 July 2023
ACCEPTED 19 January 2024
PUBLISHED 07 February 2024

CITATION
Eze JI, Correia-Gomes C, Gunn GJ and Tongue SC (2024) Bovine mortality: the utility of two data sources for the provision of population-level surveillance intelligence. *Front. Vet. Sci.* 11:1270329.
doi: 10.3389/fvets.2024.1270329

Bovine mortality: the utility of two data sources for the provision of population-level surveillance intelligence

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Introduction: The use of existing data to provide surveillance intelligence is widely advocated but often presents considerable challenges. Two data sources could be used as proxies for the mortality experienced by the Scottish cattle population: deaths recorded in the mandatory register [Cattle Tracing System (CTS)] and fallen stock collections by the National Fallen Stock Company (NSFCo) with a nationwide voluntary membership.

Methods: Data for the period 2011–2016 were described and compared to establish their strengths and limitations. Similarities and differences in their temporal, seasonal and spatial patterns were examined overall, at postcode area level and for different age groups. Temporal aberration detection algorithms (TADA) were fitted.

Results: Broadly, similar patterns were observed in the two datasets; however, there were some notable differences. The observed seasonal, annual and spatial patterns match expectations, given knowledge of Scottish cattle production systems. The registry data provide more comprehensive coverage of all areas of Scotland, while collections data provide a more comprehensive measure of the mortality experienced in 0–1-month-old calves.

Discussion: Consequently, estimates of early calf mortality and their impact on the livestock sector made using CTS, or successor registers, will be under-estimates. This may apply to other registry-based systems. Fitted TADA detected points of deviations from expected norms some of which coincided in the two datasets; one with a known external event that caused increased mortality. We have demonstrated that both data sources do have the potential to be utilized to provide measures of mortality in the Scottish cattle population that could inform surveillance activities. While neither is perfect, they are complementary. Each has strengths and weaknesses, so ideally, a system where they are analyzed and interpreted in parallel would optimize the information obtained for surveillance purposes for epidemiologists, risk managers, animal health policy-makers and the wider livestock industry sector. This study provides a foundation on which to build an operational system. Further development will require improvements in the timeliness of data availability and further investment of resources.

KEYWORDS

surveillance, cattle tracing scheme, bovine, mortality, fallen stock, aberration detection

1 Introduction

Most studies dealing with the mortality experienced by cattle populations have explored the potential use of statutory, or mandatory, registers in which deaths in the cattle population are recorded. Investigations have included use of these data for various purposes, including: as welfare indicators; to measure excess mortality in the presence of specific agents; to identify risk factors for and rates of mortality, and to develop systems to detect deviations from expected values (1–8). In Great Britain (GB), until recently, the British Cattle Movement Service (BCMS) had the statutory responsibility of recording all cattle deaths in England, Scotland and Wales. BCMS manages these data through the Cattle Tracing System (CTS) (9). While this data source may provide regular, comprehensive, temporal and spatially representative datasets, access to it in a timely fashion manner can be a challenge, especially for external parties. Consequently, the potential for use of such dataset to provide early warning systems for detecting aberrations in health events, while technically possible (10) may not be fully realized (3). Demonstration of this potential, through an examination of the utility of these data in retrospective analyses, may help to encourage the investment of both time and resources in the development necessary to move from applied research toward operational systems.

It is possible that there are alternative data sources that may be easier to access routinely. They may be complementary or may approach the challenge of measuring mortality from a different perspective, for example herd health records at farm level from benchmarking or herd health planning schemes. One data source that could provide a complementary indication of cattle mortality at a population level is fallen stock collections data. In two other countries, Spain and France, researchers have examined the utility of centralized fallen stock data for surveillance of health status of animal populations in different regions [(10, 11), respectively]. In Britain, the National Fallen Stock Company (NFSCo) collects such data as part of its business operations. A Community Interest Company (CIC), with voluntary membership, NFSCo provides access to competitive collection and disposal fallen stock services and prices to 44,000 farmers nationwide (12). NFSCo define fallen stock as "animals which were killed (euthanasia with or without definite diagnosis) or have died (including stillborn and unborn animals) on farm and which were not slaughtered for human consumption. This includes animals killed by routine culling as part of normal production arrangements" (13). It is therefore pertinent to also examine the utility of this alternative data source to determine if it too has the potential to contribute to surveillance intelligence.

The aim of this study was to evaluate these two sources of data, both related to deaths in cattle to determine their suitability and potential for use in an animal health surveillance system as a proxy for mortality experienced by the Scottish cattle population.

The objectives were to retrospectively (i) describe the mortality of Scottish cattle as provided by the two data sources- overall, by age-group and geographically; (ii) compare the temporal patterns and other characteristics of the fallen stock collections with that of the statutory death; (iii) investigate whether there is the potential for the use of aberration detection algorithms; (iv) compare the alarms generated by these algorithms in the two datasets and their subpopulations; and thus (v) identify any issues with the data that would present challenges in interpretation of any of the above objectives, or that may limit operational usage for surveillance activities.

2 Materials and methods

Cattle mortality data used in this study are for the period 2011–2016 inclusive, collected from two different sources: the Cattle Tracing System (CTS, hereafter mostly referred to as the registry data) and National Fallen Stock Company (NFSCo, hereafter mostly referred to as the fallen stock collections, or just collections data). The CTS database is managed by the British Cattle Management Services (BCMS) (9). It holds records of all births, on and off movements and deaths of cattle within the United Kingdom (UK). Cattle keepers are mandated to report the death of any cattle to BCMS (14). Data on all death events occurring in Scotland during the study period, excluding those at slaughterhouses, including animal unique identifiers, date of death, date of birth and farm/location of death were extracted from the collated and curated copy of the CTS database stored in the Scottish Government's Centre of Expertise on Animal Disease Outbreaks (EPIC) data repository.[1]

NFSCo was established in keeping with the European Union Animal By-Product regulations (15) and UK Government's guideline on fallen stock and dead animal safe disposal (16) which require that the disposal of dead farm animals is done through an approved, registered animal by-product premise. The NFSCo facilitates an efficient and competitive nationwide service for the collection and disposal of fallen farms animals and horses. This is accomplished by working with around 100 fallen stock collectors nationwide (12). Farmers can arrange for the collection of dead animals with any of the collectors in their postcode area. Farmers can also join as members of the company to facilitate collection and disposal. Membership is free and voluntary. The fallen stock collections data used was provided as aggregated data. They consisted of 217,255 records. Each contained information on the number of a stated livestock species (in this case bovines) of a specified age, that were collected in a given month/year, from a named Scottish postcode. They did not contain any record of production type.

The age at death recorded in the fallen stock data was provided in categories as follows: 0–1 month, 2–3 month, 4–6 month, 7–12 month, 13–23 month and 24+ month. For comparability, the calculated age at death in the registry data was categorized using the same age groups. These age categories are appropriate for investigating mortality at different time periods in a bovine lifetime. However, some data (28 out of 217,255 records) in the fallen stock collection dataset were not recorded as number of carcasses of a specified age group, but as "bags" with weight of the bags in units of 10 kgs. These were omitted from analysis as CTS data do not have contemporaneous data recorded in weight to compare with. Also, another 126 records were removed from

1 The EPIC data repository is a centrally curated collection of data resources established in 2011. The datasets are provided to the Scottish Government's Centre of Expertise on Animal Disease Outbreaks (EPIC) by individual agencies or institutions (the data-providers). Permissions for access and use for individual studies are granted, by arrangement with the data-providers, to support research within the Scottish Government's Strategic Research Programme.

the fallen stock data because their postcodes were in England. Consequently, 217,101 out of 217,255 (99.9%) records were used in the analyses. Each of the two datasets were aggregated to provide the number of deaths per month per year for the different age groups and postcode area.

Monthly time series plots of the number of deaths were used to compare the overall trend and seasonal patterns of the two datasets. The trends were captured by superimposing a smooth trend line on the monthly time series using locally weighted scatterplot smoothing (lowess) method. Differences in seasonal patterns and trends between age groups and geographic (postcode) areas of the two datasets were also examined. Seasonal patterns were represented as monthly boxplots, to show not only the seasonal pattern but also to reflect variations within year across months between the different age groups and the two datasets.

While the boxplots depict seasonal patterns, they do not give information on likely average contributions of each month (below or above the yearly average mortality) due to effects of production cycle, weather, and other factors. It is important to understand how the monthly effect differs between the registry and fallen stock collections data. To reflect this, we estimated monthly effects which indicate by how much the average number of deaths was influenced by a particular month. The effects were computed by first eliminating the trend by dividing each month's mortality by the mean number of deaths in the same year. The resulting quotients were then averaged for each month across all the 6 years. To express this mathematically, if we denote the mortality in month i and year j as $y_{ij},\ for\ i = 1,2,3,\ldots,12\ and\ j = 2011, 2012,..,2016$. The seasonal or monthly effect S_i is calculated as shown in Equation (1). These estimates were compared between the age groups in the two datasets. Note that the seasons are defined in this paper as winter (December, January, February), spring (March, April, May), summer (June, July, August) and autumn (September, October, November).

Correlation analyses between the monthly time series of the two datasets and by age groups were used to assess the strength of the linear relationship.

$$S_i = \frac{1}{6}\sum_{j=2011}^{2016}\frac{y_{ij}}{\bar{y}_j} \qquad (1)$$

In order to have a better understanding of the differences in spatial coverage of the two data sources, the percentage contribution of each postcode area to total mortality in each of the two datasets were represented on maps. Given that a greater proportion of the fallen stock data were calves aged 0–1 month old, it is of interest to see how the spatial distribution across the Scottish postcode areas differs from that of 0–1 month old category in the registry data. Consequently, the data were split into two: 0–1 month calves and the rest of the data. Differences in temporal patterns between these two groups were also examined.

The original Farrington algorithm (17) was used to explore the use of the two datasets for timely detection of aberrant counts of death. The choice of the algorithm is informed by its ease of use, can cope with smaller number of data in the reference and is commonly used in many established surveillance systems. It fits overdispersed Poisson generalized linear model with log link to the reference data and has the capacity to adjust for season and trend. Before fitting the algorithm, we validated the assumption of quasi-Poisson distribution by fitting a quasi-Poisson generalized linear model on the datasets as function of time and examined the behavior of the residuals.

If we denote y_i as the number of deaths in month t_i within a historical reference period and that y_i is independently distributed with mean μ_i and an overdispersed variance $\theta\mu_i$, then, the mean of the process can be modeled as a simple log-linear regression (Equation 2):

$$\log(\mu_i) = \alpha + \beta t_i \qquad (2)$$

Where α is the intercept and β is the slope of the trend line. Due to the assumption of overdispersion in the data, model estimates are obtained using quasi-likelihood approach. The algorithm implicitly adjusts for seasonal effect by estimating the current month's expected number of deaths based on corresponding month in the reference period. The model is trained by first fitting it on the reference data and residuals examined for outbreaks. Outbreaks in the reference data are down-weighted by assigning very small weights to mortality with large residuals. The model is refitted on the adjusted reference values and the weighting is repeated. This procedure is iterative and continues until each predicted reference value is within the range of the reference values. This reduces the effect of past outbreaks on the estimate of current mortality. The trained model is then used to predict current mortality in the monitored period (Equation 3).

The predicted mean number of deaths in any given month t_0 in the current period that is being monitored is estimated as

$$\hat{\mu}_0 = \exp\left(\hat{\alpha} + \hat{\beta} t_0\right) \qquad (3)$$

To correct for skewness in the mean number of deaths, the algorithm use $\frac{2}{3}$ power transformation resulting to approximate symmetric distribution that enables the computation of confidence interval. The upper bound of the confidence interval above which current monthly mortality is declared an aberrant is given as (Equation 4):

$$U = \hat{\mu}_0\left\{1 + \frac{2}{3} z_\alpha\, \hat{\mu}_0^{\,-1}\left(\theta\hat{\mu}_0 + \mathrm{var}\left(\hat{\mu}_0\right)\right)^{1/2}\right\}^{3/2} \qquad (4)$$

with a desired confidence level and z_α is the (1- α) percentile of the normal distribution [for more detailed account of this procedure, see (17)]. Given the short length of the monthly time series, the first 24 months (2011–2012) was used as the historic reference period. We show the results from the search of aberrations in the number of monthly deaths in year 2013 to 2016 using the original Farrington method. An upper bound U is calculated using the model predicted values, their variances and an alpha level of 0.01. An alarm is indicated when the observed number of deaths is higher than the predicted upper bound U. Aberrations detected in both datasets were compared to evaluate how close in time they occurred. We used similar set of parameters in the TADAs for ease of comparison of outputs from the two datasets. All data manipulation and analyses were conducted in R (18) and the TADAs were implemented using the surveillance package in R (19).

The outputs of the analyses were considered and interpreted in the light of expert knowledge of the underlying Scottish cattle population. This includes a diverse dairy industry and a beef industry, both with multiple production and management systems and a spatial distribution that is driven by geography, weather, land-use suitability and the human population distribution. A brief introduction is provided for the reader in Supplementary material.

3 Results

Within the period under study, a total of 450,903 deaths were registered in the registry (CTS) data for cattle in Scotland. Of these, 448,237 (99.4%) animals had information on date of birth. This compares with 445,676 individual animals collected as fallen stock in Scotland by NFSCo. The number in each age category varied between the datasets (Table 1). The fallen stock collections data provide a more comprehensive measure of the mortality experience in 0–1-month-old calves compared to the registrations in the registry data. About 55% of all fallen stock collections within the period of study were 0–1-month-old calves against 14% of the deaths registered in the registry data. Hence, the number of dead 0–1-month-old calves collected was 3.8 times the number recorded in the registry data. On average, 3,384 calves aged 0–1-month were collected each month from various farms compared to the 893 registered deaths in this age group each month. The picture is different for mortality in cattle aged more than 1 month. In the period of study, on average, about twice the number per age group were recorded in the registry data than were collected as fallen stock for the age groups over 1 month of age (Table 1).

3.1 Analyses of temporal patterns

The monthly number of cattle deaths in Scotland as represented by the registered deaths and the fallen stock collections has clear seasonal patterns and trends. Figure 1 shows the overall data series (first row) and the split of the data by calves aged 0–1 month (second row) versus others (third row). The first row shows the plot of the overall monthly time series and their seasonal patterns for the two datasets. The registry data are presented in black while the fallen stock collections data are in blue. The red lines are the smooth trends with that of the registry data shown as dotted red lines. Patterns are similar in the two datasets. Both time series show a decline until 2013 and a slow increase thereafter. The smooth trend is more pronounced in the fallen stock collections compared to the registry data. There are differences in the seasonal peaks across the years and these peaks seem to overlap in both datasets. The seasonal peak in April and May of 2013 are prominent. A better representation of the similarity in the seasonal patterns of the two monthly series is shown in the boxplots—the second graph in the first row. The boxplots suggest that peak mortality occurs in April and May (spring months), followed by the late autumn and early winter months, with the lowest number of deaths observed in the summer months. The estimates of monthly effect indicate an increased number of deaths of up to 1.4 times the yearly average number of deaths in spring (April) and about 20% reduction below the average yearly mortality in August (summer). A breakdown of the monthly effects by age groups suggest that effects differ depending on age (Supplementary Figure S2A).

In the age groups up to a year of age, trends and seasonal patterns are different for different age groups (Figures 2, 3) in both datasets. Trends are well defined among the fallen stock age groups while those of the registry data show little or no change over the years. The exception is that of the 4–6-month-old calves, in which there was an increase over time. There appears to be a demarcation of seasonal patterns by age groups. The shape of seasonal patterns is similar in the two youngest aged (0–1 and 2–3 months olds) and also similar among the older age groups (4–6 and 7–12 months old). The drastic change in the seasonal patterns after 3 months of age and the shift in the seasonal peaks with increasing age is noteworthy in Figure 1 (second row) and Figure 3. The seasonal peaks changed from April in the 0–1 month old to June in the 2–3 month old in fallen stock data and from May to June in the registry data. The shift in peak with older age is even more prominent when we compare the 0–1 month group with 4–6 and 7–12 month old groups where peaks are in the late autumn and winter months. For the two age-groups over 12 months of age (13–23 months and over 24 months old), there are spring peaks and a late autumn-winter peak in the 13–23 month group that is most obvious in the registry dataset. Peak mortality in the over 24 months old is in spring (Supplementary Figure S2B). For all the age groups, the minimum number of deaths were observed in the summer and early autumn in both datasets. The differences in seasonal patterns among the age groups match expectations, given knowledge of the age groups and production cycles in the Scottish cattle sector (Figure 3 and Supplementary Figure S2B). Overall, more variations were observed on monthly basis in the fallen stock collections data compared to the statutory registry data.

TABLE 1 Proportion of fallen stock collected and registered deaths by age category in the two datasets Fallen Stock Collections (NFSCo) and register of mortality (CTS) between January 2011 and December 2016.

Age group	NFSCo *N* = 445,676 %	CTS *N* = 448,237 %	Ratio: (CTS/NFSCo)
Bovine 0–1 month	54.67	14.35	0.26
Bovine 2–3 month	6.27	11.30	1.81
Bovine 4–6 month	4.50	8.63	1.93
Bovine 7–12 month	4.34	9.92	2.30
Bovine 13–23 month	3.56	8.45	2.39
Bovine 24 month+	26.66	47.36	1.79
Total	100	100	1.01

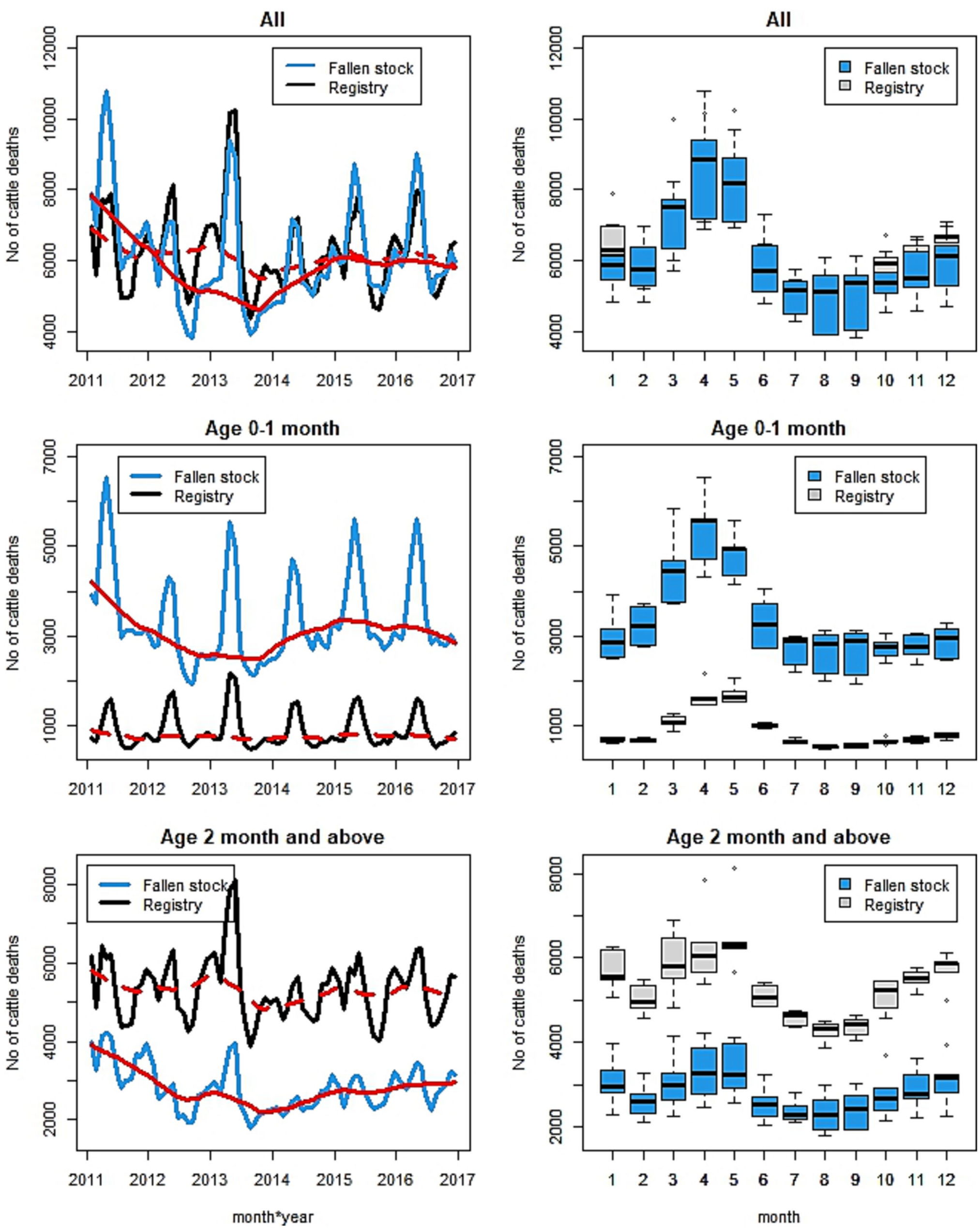

FIGURE 1
Plot of the monthly time series (first column) and seasonal patterns (second column) of number of fallen stock collected (in blue) and registered deaths (in black) for the overall (all-age) (1st row), calves aged 0–1 month only (2nd row), and the rest (excluding 0–1 month old) (3rd row). The red lines are the smooth trends—registry (dotted) and collections (solid).

3.2 Examining the extent of relationship between the two datasets

The estimate of Pearson correlation coefficient indicates a significant and strong positive (0.79, p <0.001) correlation between the monthly time series of the two sets of data (Supplementary Figure S3). This investigation was extended to the monthly time series of the age groups. There was a strong positive correlation between corresponding age groups in the two datasets. Estimated correlation coefficients for cattle aged up to 12 months old range from 0.67 in the 2–3 month old group to 0.85 in the 7–12 month old group (Figure 4). While the over 24 month group also has a strong positive correlation 0.84, that of the 13–23 month age group is lower at 0.6 (Supplementary Figure S4).

3.3 Temporal aberration detection algorithm

The potential utility of the two datasets for detection of population-level change was examined by fitting TADA to the monthly time series of each of the data series using the first 24 months as the historic reference period (Figure 5). The predicted

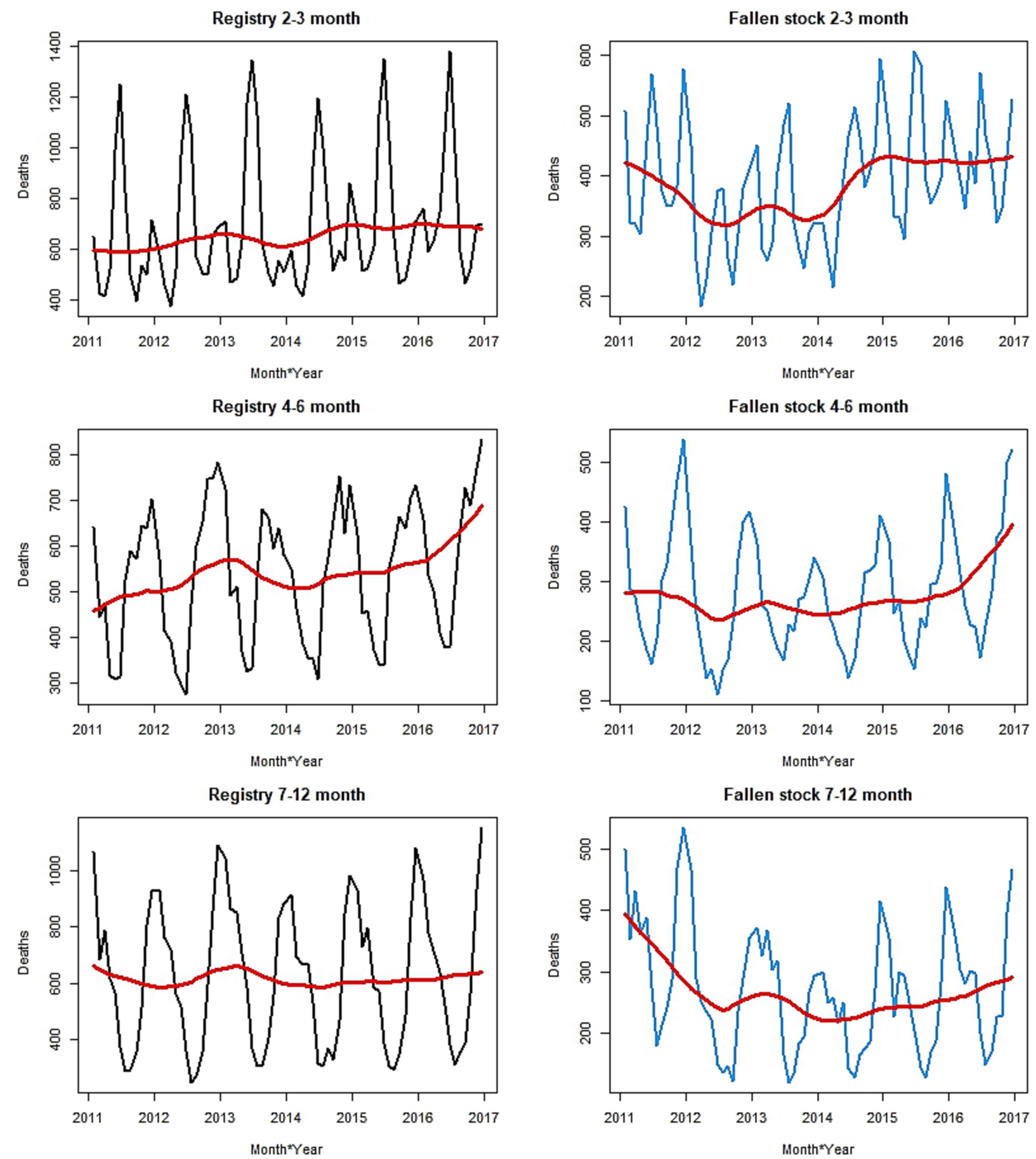

FIGURE 2
Monthly time series plots of mortality by age group, up to 12 months old, and by data sources. The smooth trend is shown in red.

upper bound of the fitted TADA is represented in Figure 5 by the blue dotted lines, the bars are the monthly observations. Aberrations (red triangles) are indicated whenever the observed (bars) are higher than the upper bound. Aberrations were detected in both dataset in April and May of 2013 as indicated by the alarms. Further alarms were highlighted in the fallen stock collections data from September to December of 2014.

Variations in the detected deviations from the expected norms are evident between the different age groups in the two datasets (Figure 6). On the whole, there seem to be more aberrations detected for each age group in the registry dataset compared to corresponding age groups in the collection dataset.

3.4 Spatial coverage

The maps of the split data (0–1 month calves and the rest) are displayed in Figures 7, 8. The first and the second map in Figure 7 show the percentage of dead cattle collected and registered deaths by postcode area for calves aged 0–1 month for the fallen stock and the registry data, respectively. The distribution appears similar in both maps, with the south of Scotland [Dumfries & Galloway (DG)] accounting for about 46 and 36% of the total fallen stock and registered deaths, respectively. Kilmarnock (KA) followed, contributing 20 and 13%, then Aberdeen, with 5 and 12%, respectively. The third map represents the numbers in the fallen stock divided by that of registry

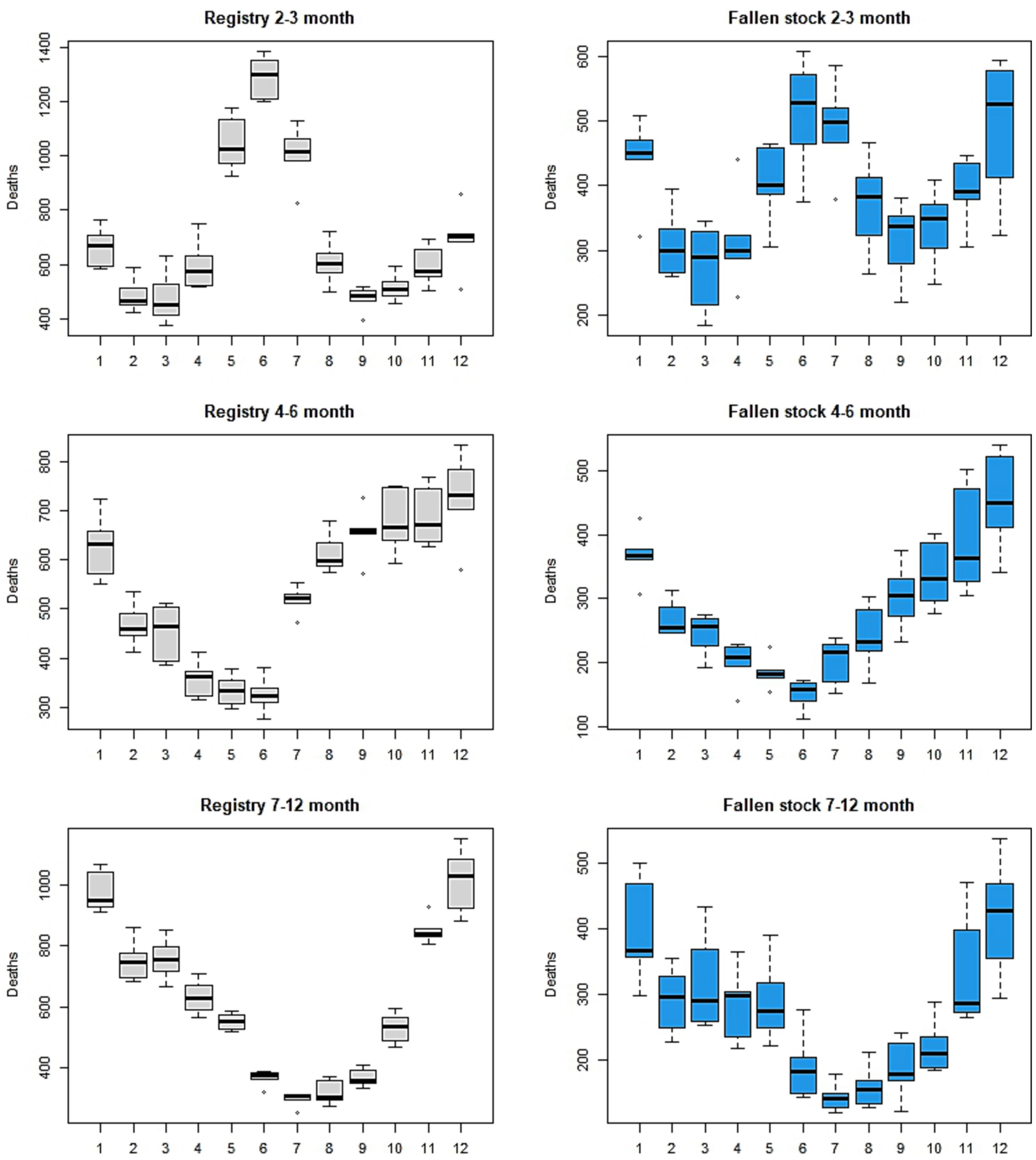

FIGURE 3
Seasonal patterns of mortality for each age group up to 12 months old, by the two data sources.

data for calves aged 0–1 months. It shows how large the fallen stock collection data is relative to the registry data in each postcode. The number of 0–1 month calves collected as fallen stock in Motherwell (ML) and Kilmarnock (KA) was six times the number of deaths recorded in the registry data for these two postcode areas. Also, fallen stock collections of calves aged 0–1 month are five times the number of registered deaths in this age group in Glasgow (G) and Dumfries & Galloway (DG). More fallen stock aged 0–1 month were collected than were recorded in the registry data in 12 out of the 14 postcode areas that have both datasets.

The first and the second map of Figure 8 present the percentage of animals collected, or registered deaths, by postcode area for all data excluding calves aged 0–1 month for the fallen stock and the registry data, respectively. About 42% of the total collected as fallen stock in this age group were from Dumfries and Galloway (DG); only 27% of the total registered deaths, for this age group, were recorded in the registry data in the same area. The third map in Figure 8 displays the magnitude by which the registry data are greater than fallen stock collections in each postcode. More deaths were recorded in the registry data than were collected as fallen stock

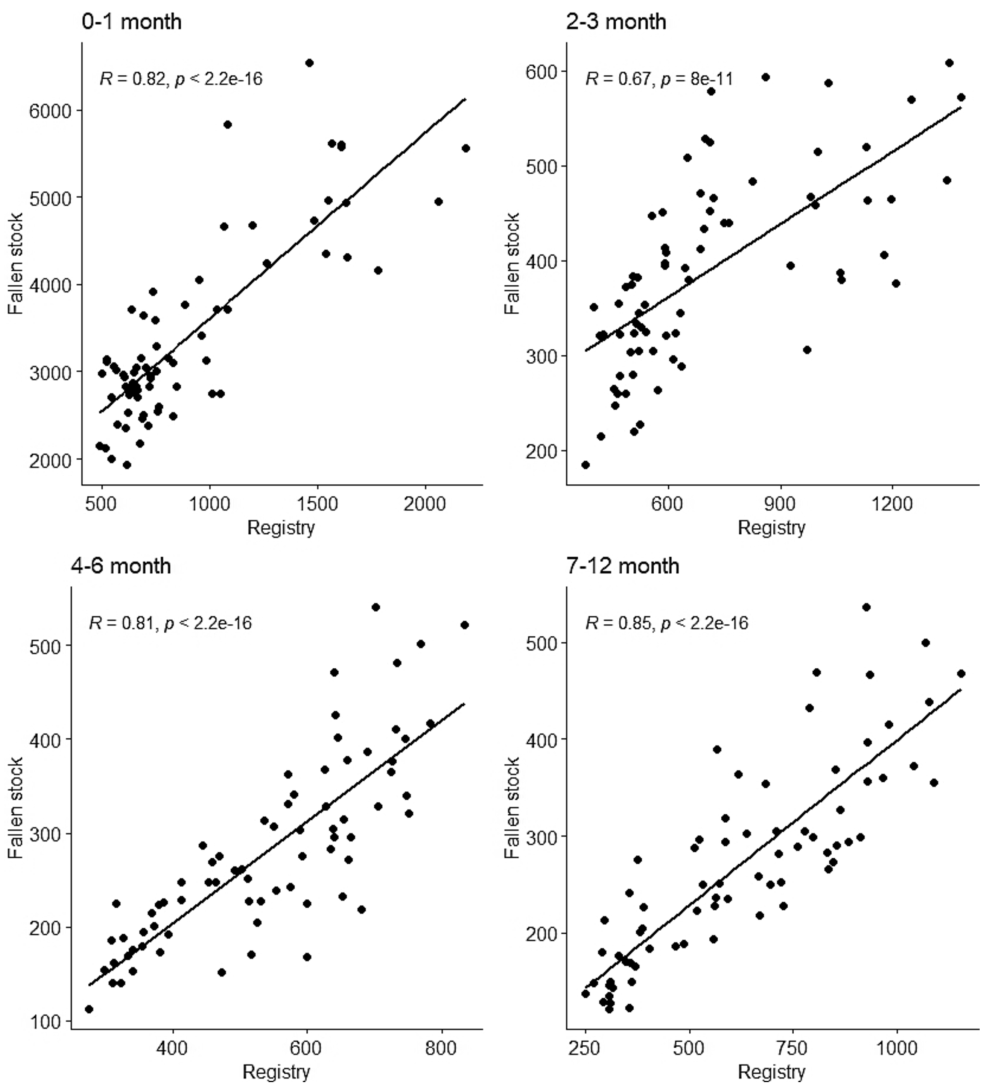

FIGURE 4
Scatter plots of the monthly time series of registry and fallen stock collections cattle data by age groups up to 1 year old. Moderate to strong positive correlation exist between the monthly time series of the age groups in two datasets.

in all the 14 postcode areas that have both data. The registry recorded more than twice the numbers of fallen stock collected in 10 postcode areas. In Kirkwall (KW), the registry recorded more than 10 times the number of deaths than the number of fallen stock collected.

Overall, the registry data provide more comprehensive coverage of all postcode areas of Scotland. There were no fallen stock data from Outer Hebrides (HS) and Shetland (ZE) over the 6 years of study. There seems to have been poor coverage of fallen stock collections in the north of Scotland but there was a strong presence in central Scotland.

The outputs of the temporal analyses of the deviations from expected mortality show differences in the timepoints indicated as alarm points, between the datasets in each Scottish postcode area (Figure 9). Overall, there are more aberrations in the registry data. However, aberrations were detected in 2013 in both datasets with some points coinciding in the two datasets.

4 Discussion

We have retrospectively analyzed the mortality experienced by the Scottish cattle population between 2011 and 2016 as provided by two different data sources namely, non-statutory collections by the National Fallen Stock Company cattle data and the mandatory death records, or registry, of the Cattle Tracing System managed by the British Cattle Management Services. Data from these two sources were compared with a view to establish their strengths and limitations in relation to their potential use in animal health surveillance as proxies for mortality for the Scottish cattle population. This was achieved by comparing the spatial and temporal patterns and other characteristics of fallen stock collections with that of the statutory dataset and their subpopulations. We have found that while there are some similarities in the information provided by each dataset, there are also some important differences. These findings have implications for their utility for the provision of surveillance intelligence.

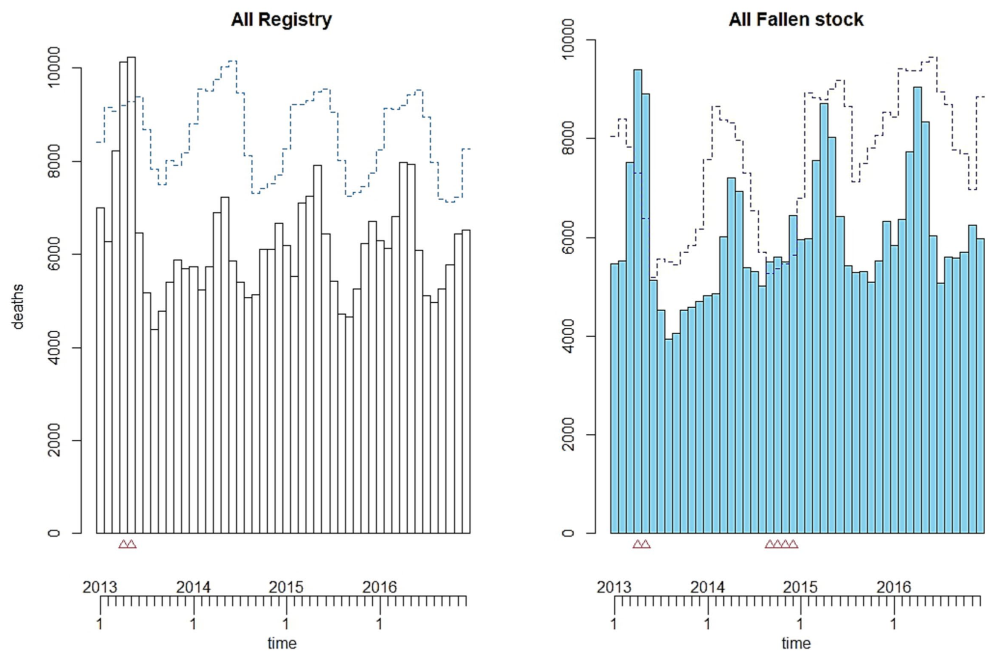

FIGURE 5
Monthly time series plots of number of all-age deaths (bar charts) and temporal aberration detection algorithm (TADA) (blue dotted lines) fitted to the two datasets. Alarms are indicated by the red triangles.

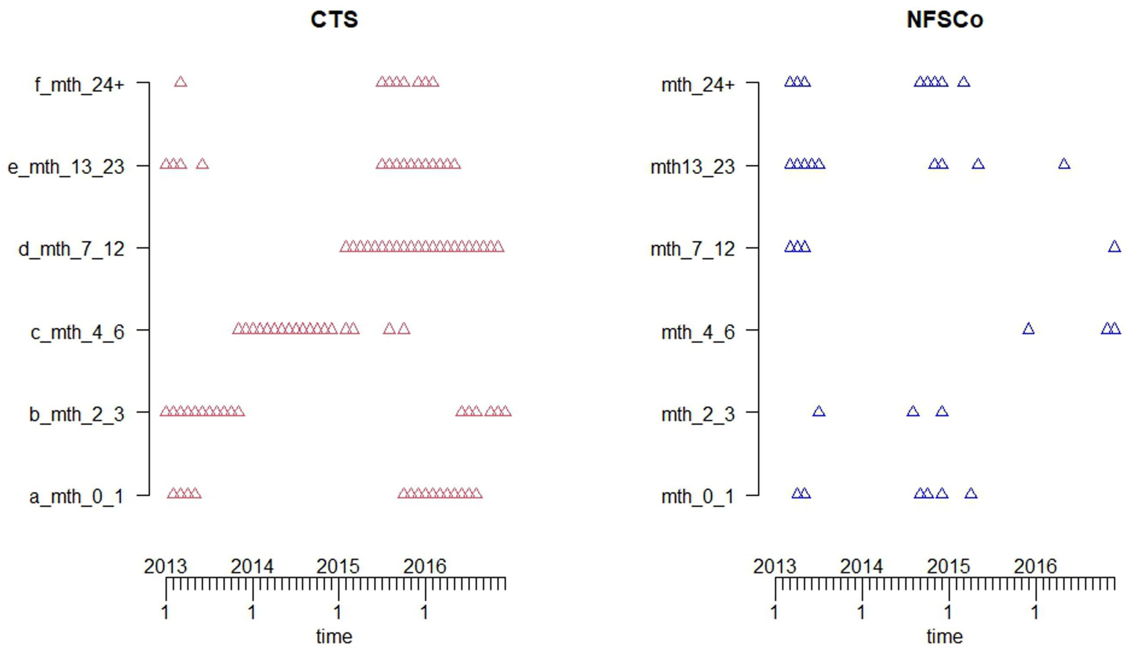

FIGURE 6
Alarms extracted from the temporal aberration detection algorithm (TADA) fitted to the monthly time series of each of the age groups in the two datasets. Alarms are indicated by the red triangles for the registry (CTS) data and blue triangles for the fallen stock collections (NFSCo) data.

As a statutory register, the registry data should provide the most comprehensive coverage of the mortality experienced by the cattle population, as all deaths should be notified to the central register within 7 days. This appears to be the case, with the aggregate number of deaths recorded over the period of study slightly (1.2%) higher compared to the aggregate fallen stock collections within the same period. However, the overall difference was smaller than expected given knowledge of NFSCo membership during this period (pers.comm. NFSCo).

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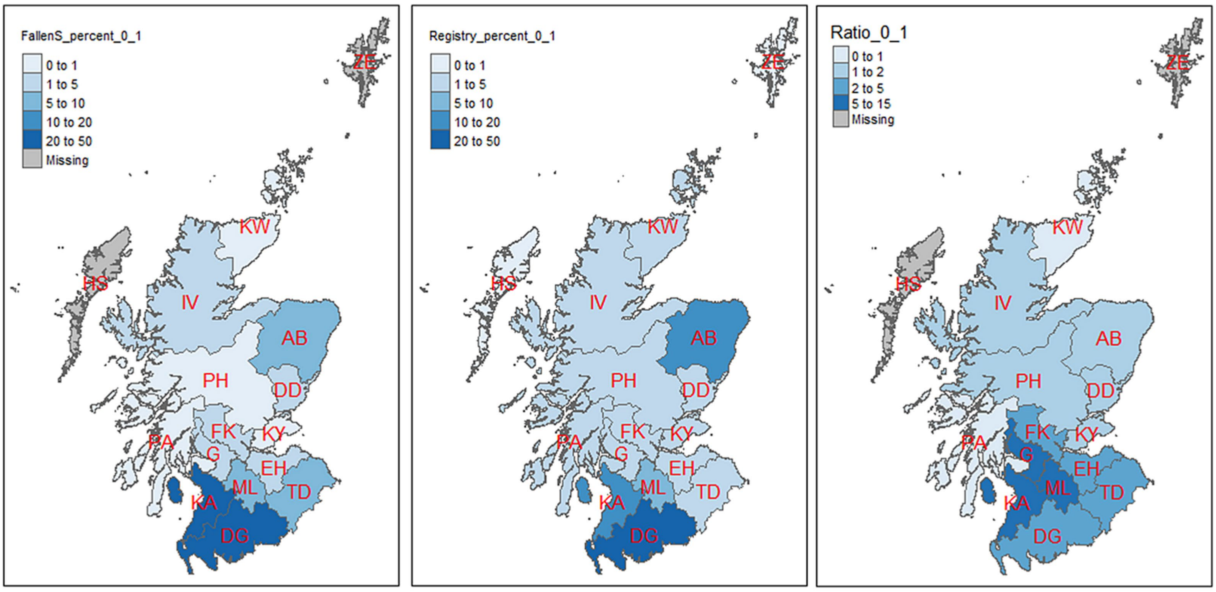

FIGURE 7
Percentage distribution of mortality in calves (age 0–1 month) by postcode area as represented by the two datasets (the first two maps). Third map is the ratio of 0–1 month old in the fallen stock collections (NFSCo) data to that of the registry (CTS) in each postcode area. There were no fallen stock collections (NFSCo) data from HS and ZE.

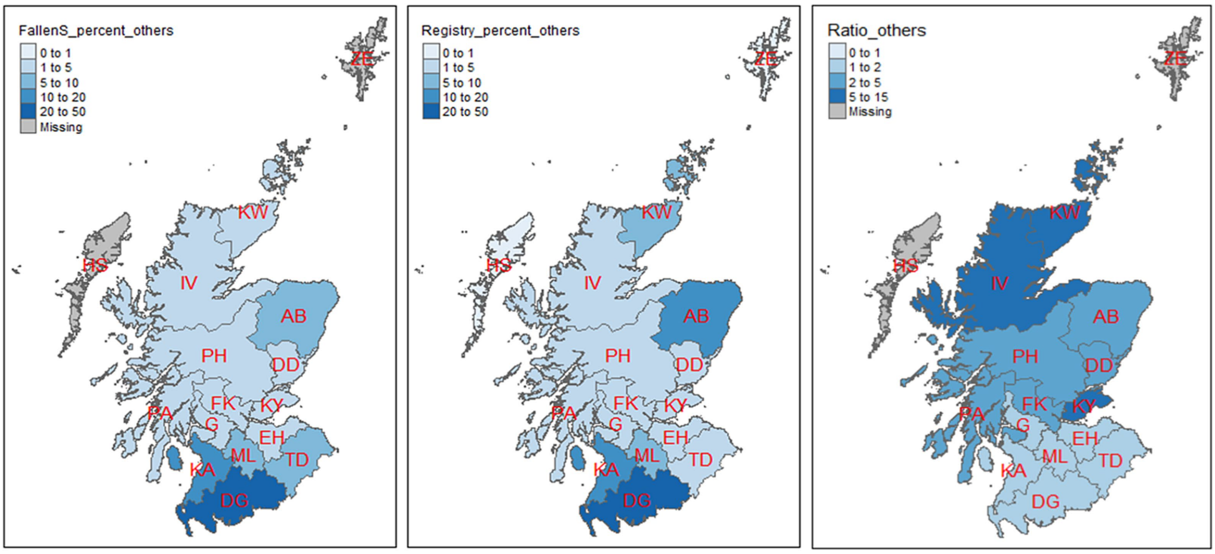

FIGURE 8
Percentage distribution of mortality in cattle aged 2 months and above by postcode area as represented by the two datasets (the first two maps). The third map is the ratio of cattle aged 2 months and above in the registry (CTS) data to that of fallen stock collections (NFSCo) in each postcode area. There were no fallen stock collections (NFSCo) data from HS and ZE.

4.1 Age effects

When the datasets were stratified by age groups, a different picture emerged. The analyses indicate that the fallen stock collections data provide a more comprehensive measure of the mortality experience in 0–1-month-old calves, with collections consistently about 3.8 times the number of deaths recorded in the registry data for this age group, in each month. The fallen stock collections data probably provides a more accurate representation of the mortality experienced on-farm by this age-group than the registry data does. This is most likely to be because farmers are not required to report a calf's death to BCMS if it dies prior to ear-tagging and registration. In Scotland, farmers must fit ear tags before a beef calf is 21 days old, or when it moves off the holding if that is earlier; dairy calves must have a primary ear-tag by 36 h after birth, and for both beef and dairy calves, they must be registered within 27 days after birth (20). If the calf dies before these

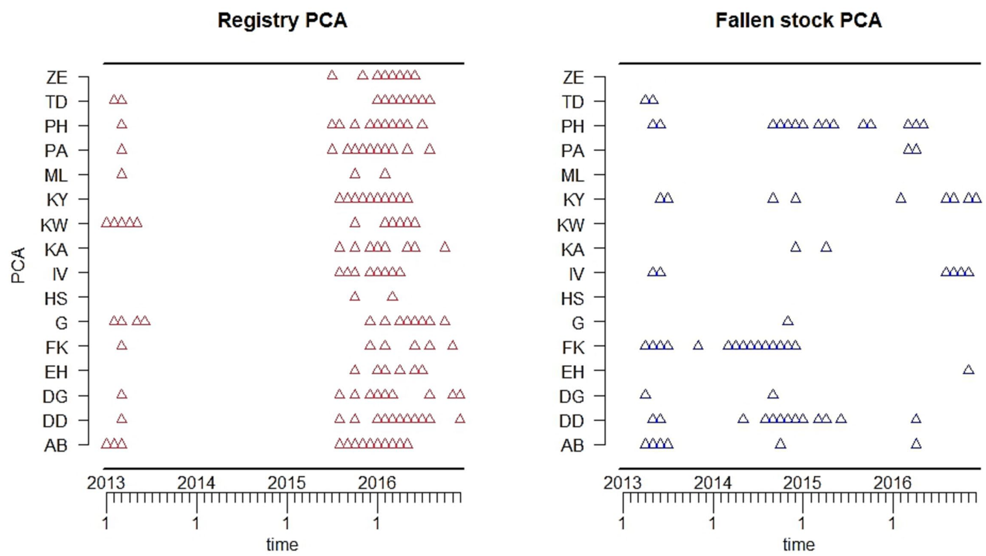

FIGURE 9
Alarms extracted from the temporal aberration detection algorithm (TADA) fitted to the monthly time series of each postcode area in the two datasets. Note: The were no fallen stock collections (NFSCo) data from HS and ZE.

deadlines, then they do not need to be registered centrally and electronically, only locally on-farm in the holding register. Consequently, all perinatal and most neonatal deaths will not be recorded in the registry data. By definition (see Introduction), these collections may also include still-born animals that would never be registered. However, the carcases will be collected for disposal by fallen stock services, such as NFSCo. This finding has implications for further interpretation of outputs from these data in this study and it also highlights the need to consider this data-gap carefully when conclusions are drawn, for this age-group, from other analyses of the registry data [e.g., (3, 5, 21)]. Whether this is a factor specific to the British datasets, or more widely relevant, requires further investigation. In a comparison of the utility of fallen stock and national cattle register data in France, Perrin et al. (7) noted that there was a potential difference between the number of cattle collected for disposal and deaths notified, which needed further investigation; in that study the former was higher than the latter. However, they did not publish age-specific details. It may well be possible that a contributory factor to their higher disposal figures is mortality in young calves, as identified in our study. The data-gap is also of relevance for population, livestock industry, or farm-level estimation of the impact of early calf mortality on green-house gas (GHG) emissions. With the move to achieve Net Zero and changes to agricultural policies, such calculations are being made for aspects of animal health such as liver fluke in cattle (22, 23). If the impact of early calf mortality is calculated using registry data, or successor registers (e.g., Scotmoves+ and the Livestock Information Service) they will be under-estimates.

Once cattle are registered, the registry data should provide comprehensive coverage of mortality experienced in the population. Hyde et al. (3) studied calf mortality between 2011 and 2018 in Great Britain and found that 25% of on-farm deaths happened within the first 3 months of age, with 54% occurring before 24 months of age. This is similar to our finding for Scotland only, which is as expected given no regional variations as we were using both a spatial and temporal subset of the same data source.

4.2 Coverage and spatial effects

There were twice as many deaths recorded in the registry data compared to fallen stock collected in each age group over 1 month of age in the study period. This is different to the aforementioned direction of the difference observed in preliminary analysis by Perrin et al. (7). In their French study, the fallen stock data were obtained from an interface where data from all the major collection services were centralized. In Britain, there is, as yet no similar centralized dataset. While there is a statutory requirement to arrange appropriate disposal of a bovine animal that dies on farm, there is no requirement to use the NFSCo service. NFSCo's coverage is determined by its membership and the geographical spread of the members. There are other collection services across Scotland, as well as Scottish cattle producers who are not NFSCo members; information about the numbers of carcasses collected by non-member providers, from non-member producers, are effectively lost for surveillance purposes.

This effect of NFSCo membership has to be considered when interpreting the geographic distribution of these fallen stock collections data. They suggest poor coverage in the north of Scotland, Anecdotally, the availability of alternative fallen stock collection services may be part of the reason behind the registry/ collected ratios that are more than 1 in some of these postcode areas. Another contributory factor in some postcode areas, especially those with lower livestock densities and in the crofting community areas is the 'remote area' derogation. This facilitates on-farm disposal and it applies in a number of areas in the north-west, Highlands and Islands (IV, KW, KY, HS, ZE). In conjunction with the exemption from TSE testing in the Scottish islands for animals over 48 months, it may lead to reduced availability of collection services and thus to less reported fatalities via fallen stock collections. There are, however, some postcode areas [Dumfries & Galloway (DG), Glasgow (G), Kilmarnock (KA), Motherwell (ML)] where fallen stock were collected than were recorded deaths in registry. Further examination of the data reveal that, as previously discussed, this was an age-related effect. In these postcode areas, far more collections of calves aged 0–1 month were made than in the other age groups. These areas have both high-density cattle population and are relatively easily accessible for collection and transportation. It is most likely that—as previously discussed—these calves died before they were registered, or even tagged, thereby not making it into the registry records. The early stages of life are known to be the most hazardous with higher levels of mortality noted in other studies (4, 24, 25). Findings from a systematic review highlight that approximately 80% of all mortalities, which occur in cattle within the first 12 months, had occurred by 6 months of age (26), with the majority of calves dying within the first month (27, 28).

4.3 Seasonal influences

Broadly, the overall all-age seasonal and trend patterns were similar in the two datasets, both depicting a seasonal peak in the spring, trough in the summer and increased mortality again in the late autumn and early winter. Several authors (3, 7, 29, 30) have reported similar seasonal variations in cattle mortality. The patterns were different for each of the age groups over 12 months of age and the size of seasonal effects was also age-dependent, varying between 1.4 and 2.0 times the yearly average. These variations in mortality reflect the seasonal patterns expected from knowledge of the British cattle production-year calendar and may reflect the association between mortality and the production cycle. For example, the aforementioned early age calf mortality, deaths due to calving injuries in heifers and cows combined with the predominance of Spring calving, and seasonally-associated disease influences such as spring turn-out, liver fluke, as well as environmental factors such as those described by Hyde et al. (3). Another contributory factor to this effect might be a result of looking at count data; the peaks of mortality in the 0–1 month age-group in April/May, bounded by March and June reflect the increased age-specific denominator population due to the predominance of the spring, rather than autumn, calving season in Scotland (21) and the larger Scottish National Beef Herd, rather than year-round or batch calving Dairy Herd. This age-specific denominator population effect then progresses through the age-groups with the peak in mortality for the 2–3 months age-group being May/June/July and so on. While it is possible to describe a denominator population and estimate risks and rates, as has been done before with the registry data (3, 27), this was not possible with the fallen stock collections data. This is because of the format in which the data was available. From experience with the equivalent sheep fallen stock collections data (31), even if this could be addressed, an appropriate denominator would be difficult to determine.

4.4 Count data, alerts, and other data limitations

To be able to make comparisons between the two datasets and to see whether they give us similar, or dissimilar surveillance information, we were, therefore, restricted to the application of statistical methods to detect deviations from the expected norms on mortality counts. Both datasets were amenable, with the position of alarms indicating points of deviation from expected deaths in the spring of 2013. These were similar in both all-age datasets. The spring of 2013 was particularly harsh with severe blizzards in many areas of Scotland during the latter part of March with consequent livestock fatalities (32).

Additional alert points were indicated in the fallen stock collections dataset in autumn of 2014, for which the cause is not clear. From the stratified analyses it would appear that these occurred mostly in post-code areas in the high cattle density south-west of Scotland, in calves up to 3 months of age and adults (over 13 months of age). This might suggest something associated with the autumn calving period. Similar alarms are not raised in the registry data, either overall (all-age), or in the spatially stratified analysis. There are alarms at that time in only the youngstock age-groups, which are not seen in the fallen stock collections analyses (4–12 months). This is just one example of differences in variation in detected deviations from expected norms in the two datasets, with more alarms indicated in the registry dataset compared to the corresponding age group in the fallen stock collections. The age-specific, geographic coverage, and membership effects discussed earlier are reflected in the distribution of detected TADA alarms across the postcode areas and have to be considered when attempting to interpret these alarms. In addition, this may be a reflection of the trend patterns seen in the fallen stock collections age groups. These seem to have higher mortality in the first 24 months of the study period, relative to 2013–2014. This period (2011–2012) was used as the historical reference period. This may be due to a decline in the number of members over time. Another explanation could be due to the fact that the registry dataset had better coverage of the older age groups. There is also the potential for a degree of age misclassification to be considered in the fallen stock collections data, as this is farmer reported, rather than calculated as in the registry data.

4.5 From applied research to operational information production

We have demonstrated that both the Scottish cattle registry and the fallen stock data can be analyzed retrospectively, and that while they tell similar stories, there are important differences, The most important difference is that the fallen stock collections data captures early calf more accurately than the registry data. If there are changes in the mortality experienced in the up to 1 month old group then they are less likely to be detected in the registry dataset. However, given the uneven geographical coverage of the collections, there is a potential for bias in the outputs from the fallen stock collections data, if the cause of the mortality experienced in the over 1 month age-group is spatially associated. Other important differences include the more complete coverage of cattle over 1 month of age through the registry data and the fact that the registry data have the advantage that they can be further stratified, for example, by type of production (dairy/beef) or breed, which may be of further interest. Finally, it is possible to identify both individual animals and their farms in the registry data, which is not possible in the fallen stock data. Therefore, the two datasets cannot be matched and there is the possibility to define a denominator and look at mortality rates with the registry data. Given that each data source has its strengths and weaknesses, parallel analysis of both would be complementary and ideal for operational purposes. Alternatively, advanced surveillance statistical approaches could be applied to jointly model both datasets and produce estimates that combine the strengths in both datasets.

To further develop animal health surveillance, periodic retrospective analysis could be automated and implemented providing data could be accessed in a timely manner and technological issues were not an obstruction. This has been achieved elsewhere (11). It would require further investment of resources as well as policy decisions about the time-scale of the surveillance and the purpose of the analysis. Within this study, the time-scale used was a month, as this was the level of aggregation that the fallen stock collections data are produced (for invoice and billing purposes) and provided in. The cattle registry data has the potential to be utilized at a finer scale; however, that brings with it various challenges such as timely access and determining the most appropriate surveillance scale as discussed by Perrin et al. (7). A change in legislation in Scotland, effective from October 2021, mandated that all Scottish cattle farmers in the country should report all cattle deaths to Scotmoves+. ScotMoves+ is managed by ScotEID, a multispecies database that also handles sheep, goat and pig movements in Scotland, and will act as the electronic holding register for all Scottish cattle keepers (20). At present the current Scottish cattle registry, Scotmoves+, data is available retrospectively on a more regular basis to the EPIC consortium. Its use for operational purposes is being further investigated. In addition, the provision of expertise, with industry knowledge, to not only interpret the outputs but also to investigate and follow-up alerts and alarms once they have been produced from the data, will need to be resourced. This may be achieved in Scotland through the proposed Veterinary Surveillance Intelligence Unit (VSIU).

The question raised by Perrin et al. (7) as to whether mortality monitoring provides any advantage over and above existing surveillance systems, remains a moot point. This, plus the discussions of whether, or not, monitoring mortality is a timely way to detect unexpected events and whether it is appropriate to call it syndromic surveillance, or not, probably contribute to the chasm that exists between investigations of the utility of data-sources as potential contributors to surveillance and advancement into operational systems. The steps that need be taken to build bridges and span this chasm are about more than basic data availability and appropriate technological requirements, although these are basic essentials. Often, the ability to advance animal health surveillance is hampered by the conundrum that until it can be demonstrated to be a worthwhile investment of resources, the resources required cannot be identified. Sometimes it requires a leap of faith; other times, a slow build of momentum and the perseverance to build sufficient evidence to progress is being made, able to make it to a tipping point. This study provides a foundation on which to build evidence contributing to further development of an operational system.

Further investigations using these data sources have occurred since this study was completed. They include: a pilot to see if the fallen stock collections data could be enhanced by collecting the "farmer-reported cause of death," in broadly defined categories, at the time of collection (pers. comm NFSCo); more detailed examination of the structure and efficiency of the Scottish Beef Cattle Herd (21); development of some of the algorithms developed for data-handling in Thomson et al. (21) into a potential farm-level benchmarking system and their application along with additional statistical aberration detection mechanisms to the registry data (ongoing within the EPIC consortium). Progress is being made; all be it slowly.

5 Conclusion

In Great Britain, there are two data sources routinely collected for primary purposes other than surveillance that contain data associated with mortality in cattle. These are the statutory registration of births, deaths and movements and fallen stock collections for disposal through voluntary membership scheme. We have produced the first retrospective analysis of the Scottish fallen stock collections dataset for cattle, in terms of frequency, space and time for 2011–2016. From these data, we can conclude that there is a data-gap in the mortality in calves up to 1 month of age recorded in the registry data. Therefore, early calf mortality estimates made using CTS data, or successor registers (such as Scotmoves+ and the Livestock Information Service) will be under-estimates. The retrospective analyses we conducted demonstrated that the two data sources can be utilized for monitoring the mortality experienced by the Scottish cattle herd. They are positively correlated and provide broadly similar information about seasonal and trend patterns, but some differences exist in their demographic and spatial coverage. However, they each have strengths and weaknesses, so ideally, a system where they are analyzed and interpreted in parallel or jointly would be the best way to optimize the information obtained for surveillance purposes for epidemiologists, risk managers, animal health policy-makers and the wider livestock industry sector.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: The data were obtained from third parties: the National Fallen Stock Company and British Cattle Management Services (BCMS). Request for access to any of these data should made directly to respective organization. Requests to access these datasets should be directed to https://nfsco.co.uk/; https://www.gov.uk/government/organisations/british-cattle-movement-service.

Author contributions

JE: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. CC-G: Funding acquisition, Validation, Supervision, Writing – review & editing. GG: Validation, Writing – review & editing. ST: Conceptualization, Data curation, Validation, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. ST, JE, CC-G, and GG were funded by the Scottish Government's Rural and Environmental Science and Analytical Services Division Strategic Research Portfolio 2011–2016 and 2016–2021 (extended to 2022). Within this portfolio, ST, CC-G, and JE were funded via the Strategic Research Programme (Food, Land and People) and GG was jointly funded by both this programme and the EPIC Centre of Expertise in Animal Disease Outbreaks. SRUC was part of the SEFARI consortium (https://sefari.scot/aboutus; Scottish Environment, Food and Agriculture Research Institutes).

Acknowledgments

We gratefully acknowledge the assistance of NFSCo, the EPIC data team, A. Reeves, J. Stirling, and S. Mohr, and BCMS for their collection, curation and provision of key datasets used in this study.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2024.1270329/full#supplementary-material

SUPPLEMENTARY FIGURE S2
Monthly time series plots of mortality for over 12 months old by data sources. The smooth trend is shown in red.

SUPPLEMENTARY FIGURE S2A
Average seasonal effects by age groups. Monthly effect is different depending on the age group. The green line represents average mortality each year.

SUPPLEMENTARY FIGURE S2B
Seasonal patterns of mortality for over 12 months old, by the two data sources. Fairly similar seasonal patterns per age group but monthly variation was higher in the fallen stock collections data.

SUPPLEMENTARY FIGURE S3
Scatter plot of the monthly time series of registry (CTS) and fallen stock collections (NFSCo) cattle mortality data for all-age groups. Strong positive correlation exists between the monthly time series of the two datasets.

SUPPLEMENTARY FIGURE S4
Scatter plots of the monthly time series of registry (CTS) and fallen stock collections (NFSCo) cattle mortality data by age groups over 12 months old. Positive correlation exists between the monthly time series of the age groups in two datasets.

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frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 28 February 2024
DOI 10.3389/fvets.2024.1270547

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OPEN ACCESS

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RECEIVED 31 July 2023
ACCEPTED 08 February 2024
PUBLISHED 28 February 2024

CITATION
Dreyfus A, Volasoa MH, Guis H, Razafindraibe NP, Razafindramparany MH, Arivony NL, Rakotondrabe N, Andriamananjara MA, Dussart P, Kassie D, Lacoste V and Andriamandimby SF (2024) Challenges of rabies surveillance in Madagascar based on a mixed method survey amongst veterinary health officers. *Front. Vet. Sci.* 11:1270547.
doi: 10.3389/fvets.2024.1270547

Challenges of rabies surveillance in Madagascar based on a mixed method survey amongst veterinary health officers

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Introduction: In Madagascar, rabies is endemic and a notifiable disease. The objective of this mixed study was to understand the challenges faced by the Veterinary Health Officers (VHOs) in the current rabies surveillance system in Madagascar.

Methods: A survey was conducted from mid-April to the end of July 2021 during which all officially-listed VHOs ($N = 150$) were contacted by phone at least twice. Participants, representative of the 22 regions of Madagascar, were interviewed by phone based on a semi-structured questionnaire on (1) their knowledge of rabies epidemiology in their area of activities, (2) the occurrence of human and animal rabies and the species affected in the region where they work, (3) the factors that might influence rabies surveillance depending on (a) their activities and area of operation, (b) the socio-cultural aspects of local communities, and (c) the general organization of animal rabies surveillance.

Results: The majority (80/90) of VHOs declared having been informed of at least one suspected or confirmed case of human and/or animal rabies in their area of activity during their work as VHOs: at least once a month for 11 of them, at least once a year for 40 and with undetermined frequency for 29. Several obstacles hinder the surveillance of rabies resulting in under-reporting. The lack of funds to access suspect animals, collect, pack and ship samples in compliance with biosecurity measures and the cold chain, was mentioned as a major obstacle to surveillance. The second barrier is socio-cultural: in many large coastal regions, dogs are taboo and VHOs fear rejection by the community if they treat dogs.

Discussion and conclusion: While the general population requires information on the rabies situation in Madagascar and on how to proceed in the event of a bite, veterinarians and decision-makers need to be fully aware of an evidence-based approach to rabies surveillance, prevention and control. Communication between the human and animal health sectors should be improved. Politicians need to be persuaded of the importance of funding to eliminate rabies in Madagascar. The adoption, in early 2023, of a national strategic plan for rabies control is a first step in this direction.

KEYWORDS

rabies, surveillance, survey, veterinary health officer, Madagascar, dog-mediated rabies, zoonosis, one health surveillance

1 Introduction

Rabies is a fatal viral zoonosis transmitted to humans by dogs in 99% of cases. It is responsible for approximately 60,000 human deaths per year, mainly in Asia and Africa (1). In Madagascar, rabies is endemic and a notifiable disease in humans and animals. Surveillance is based on a veterinary/medical (suspect cases) and laboratory (confirmed cases) reporting system (2). The National Reference Laboratory (NRL) for rabies hosted by the Virology Unit of the Institut Pasteur de Madagascar (IPM), carries out rabies diagnosis for free. Samples from suspected animal and human rabies cases are sent to the NRL, which then notifies all confirmed cases to both the Veterinary Services of the Ministry of Agriculture and Livestock, and to the Ministry of Public Health.

In Madagascar, most dogs, with or without owners, roam freely in the streets. Rabies vaccination coverage in dogs is very low as very few vaccination campaigns have been performed by the Ministry of Agriculture and Livestock or by private or non-governmental organizations (NGO) in recent years. In addition, most dogs are never seen by a veterinarian due to access difficulties, cultural issues (see below), education and costs. In this context, published data on vaccination coverage are scarce and usually limited to a given city or district (3–5). A study conducted in 2007–2008 in the capital city of Antananarivo on 2,180 owned dogs showed that the percentage of regularly vaccinated dogs with a valid vaccination certificate was 7.2% (95% CI 6.2–8.4%) (3). Ten years later, another study, conducted in the rural commune of Andasibe revealed that only 5% of dogs had a history of vaccination (4). However, in 2018, the vaccination coverage was high (62.5%) in Moramanga, a medium-sized city, due to a vaccination campaign carried out by an NGO called “Mad Dog Initiative” but was extremely low (2.4%) in surrounding rural communes (5).

Thirty-one anti-rabies treatment centers (ARTC) are spread over the 22 regions of Madagascar where an average of 15,000 bitten or scratched human patients receive post-exposure prophylaxis (PEP) each year (6). Rajeev et al. (7) estimated 960 (95% Prediction Intervals (PI): 790–1,120) human deaths from rabies annually, with PEP preventing an additional 800 (95% PI: 640–970) deaths. Given the paucity of data, rabies deaths were estimated as a function of the number of reported dog bites predicted by a Poisson regression model accounting for the distance to PEP health centers and estimates of the incidence of exposure to endemic rabies using an adapted decision tree framework. Exposure incidence data originated from the Moramanga district (42 exposures/100,000 persons) and assumed a 1% rabies incidence in dogs (8).

From 2011 to 2020, the annual number of animal samples sent to the NRL ranged from 55 (in 2019 and 2020) to 151 (in 2012). The proportion of rabies confirmed samples ranged from 56% (95% CI 45.2–66.7) in 2013 to 78% (95% CI 45.8–76.2) in 2012 (9). Given the low number of samples received, the high percentage of rabies confirmed cases and the limited number of districts sending samples ($n = 12$ to 23 out of 114 per year), it is very likely that we are only seeing “the tip of the iceberg” and that underreporting is frequent, as in most low-income countries where canine rabies is endemic (10). Furthermore, samples of rabies-suspect animals received by the NRL were geographically-clustered. Indeed, 74.8% ($n = 383/512$) of those of known origin, received between 2010 and 2015, were from the Analamanga region, which includes the capital Antananarivo (11). The NRL data are thus not representative of the entire country. At last, the NRL database indicates that, over the past 10 years, a larger number of samples (66.7%) were sent to the NRL by citizens (mostly dog owners) rather than by veterinary health officers (VHOs) (9), who are officially responsible for reporting and controlling suspected rabies cases in the animal population.

Madagascar has many different ethnic groups, mainly of African and Asian ancestry. Each group generally lives in a limited geographical area, covering one or a few districts. Some of these ethnic groups, located in the Western, Southern and Eastern coastal regions, consider dogs as “fady,” a Malagasy term meaning “taboo.” One example is the Antemoro (or Antaimoro) people who live on the southeastern coast, mostly between Manakara and Farafangana.[1] Consequently, for many people in these regions, touching and caring for dogs goes against their cultural beliefs, which represents a challenge for rabies surveillance and control (12, 13).

The objective of this mixed method study was therefore to understand the challenges faced by VHOs in the current rabies surveillance system in Madagascar. The survey’s objectives were to (1) evaluate their knowledge of rabies epidemiology, (2) describe the occurrence of human and animal rabies in their work area, (3) determine the factors that might influence rabies surveillance depending on (a) their activities/roles and area of operation, (b) socio-cultural aspects of local communities, and (c) the overall organization of animal rabies surveillance and (4) compare occurrence of rabies reported by VHOs to data from the NRL to map what is currently known on rabies circulation at the district level.

2 Methods

2.1 Study population

VHOs are private veterinarians mandated by the government to carry out various public health activities in accordance with their legal, technical and territorial competence. The veterinary mandate is issued by order of the Ministry of Agriculture and Livestock, which oversees animal health. Their activities consist of providing collective prophylaxis for animals in their area of jurisdiction (collective vaccination, deworming, testing for animal diseases, collective

1 https://en.wikipedia.org/wiki/Antemoro_people, accessed 11.01.2024.

treatment, issuing of vaccination or treatment certificates), as well as undertaking epidemiological surveillance of animal diseases, sanitary control and inspection related to veterinary public health (in particular meat hygiene).

2.2 Data collection

The survey was conducted from mid-April to the end of July 2021. A comprehensive list of VHOs was obtained from the Veterinary Services, Ministry of Agriculture and Livestock. All VHOs were contacted by phone. Those, who were not reached the first time were called back immediately and then after 2 months. The participating VHOs were interviewed by phone in Malagasy language based on a semi-structured questionnaire with open and closed questions (Supplementary Information). The KoboToolbox survey platform was used for data entry. Interviews were recorded and completed forms were exported to an online database at the end of each interview.

2.3 Data analysis

All responses to the closed questions were exported to an excel database and frequencies were calculated in R® and in Excel®. Responses to the open questions were transcribed and a thematic analysis of the textual data was carried out by developing a thematic analysis grid in which responses were grouped into subcategories for subsequent statistical analysis. All data were analyzed in R® version 4.0.4 and Excel®.

2.4 Ethical considerations

Oral consent to participate in this survey was obtained from the respondents at the beginning of the phone call. Study participants were informed at the beginning of the interview of the purpose of the study and that the interview was recorded but that the data would be used anonymously. They were also informed of their right to refrain from answering a question or to withdraw their participation at any time.

3 Results

3.1 Study population and region

Madagascar is geographically divided into districts ($N=114$) and regions ($N=22$) (Figure 1). We contacted 150 VHOs by phone of which 90 agreed to participate in the survey. Participating VHOs were from the 22 regions of Madagascar and 72 of the 114 districts. Of the 60 VHOs from 42 districts who did not take part in the survey, two declined to participate and 58 were unable to respond. The reasons for not responding were not having a network connection at the time of the calls (phone switched off or outside of connection signal) ($n=31$); not answering the calls, despite having been contacted twice ($n=26$); or having deceased ($n=1$). Interviewed VHOs had been working in their area for at least two years at the time of the survey (2 to 31 years, mean = 17.2 (95% CI 15.3–19.1)). Their offices are located along the main national roads, but they collaborate with veterinary assistants or communal animal health workers who provide veterinary assistance/service in very remote areas. Most VHOs (79%) reported having a work radius of more than 25 km. Their working area can cover several districts and some VHOs have overlapping working districts.

3.2 Types of clients

Most VHOs reported to work primarily with livestock (cattle, pigs) (95%; 86/90) and poultry (88%, 79/90), and to rarely treat "pets," such as dogs. Twenty-two VHOs (24.4%) reported not treating dogs at all for socio-cultural reasons, either because they were worried losing their clientele if they treated dogs ($n=9$), or even out of personal conviction ($n=4$). This is because some ethnic groups in several districts of Madagascar consider dogs to be a taboo animal, not to be touched or cared for. More detailed information can be found in section 3.5.

3.3 Knowledge of rabies epidemiology in their area of activities

During the interview, we assessed the VHOs knowledge of rabies epidemiology, transmission and vectors. While the role of dogs in rabies transmission was unanimously known, 80% (72/90) of the VHOs stated that the main vector of rabies in their locality was stray dogs and 15% (14/90) suspected that hungry feral dogs attacking livestock were the main vector.

3.4 Occurrence of rabies

The majority (80/90) of VHOs declared having encountered or been informed of at least one suspected or confirmed case of human and/or animal rabies in their area of activity during their work as VHOs. Overall, 89% (80/90) of VHOs reported human or animal rabies from 92% (66/72) of districts distributed among the 22 regions. Nine (10%) VHOs reported the occurrence of human cases in nine (12%) districts (numbers 101, 106, 113, 117, 203, 205, 207, 209, and 510 in Figure 1) (see Table 1 and Supplementary Figure 1 for the names of the regions). The ten (11%) VHOs that reported not having heard or observed any animal or human rabies circulation were from six districts illustrated in Figure 1 by numbers 417, 208, 516, 517, 211 and 310.

In terms of frequency, 11 (12%) VHOs from 11 (15%) districts said that they had heard of rabies cases in their area at least once a month, 40 (44%) from 38 (53%) districts at least once a year and 29 (32%) from 18 (25%) districts at an undetermined frequency (Figure 2). For those who had their mandate for more than 10 years (64 VHOs), 9 said that they had heard of rabies cases in their area at least once a month, 31 at least once a year and 18 at an undetermined frequency. Most of these suspected or confirmed cases concerned dogs (80 VHOs), bovines (18 VHOs) or humans (9 VHOs) and 9 VHOs mentioned cases linked to other species (small ruminants or pigs).

The reasons stated by the VHOs for the occurrence of human rabies cases were negligence/unawareness of the danger of dog bites ($N=18$). Sixteen VHOs stated that even in case of a dog bite, victims

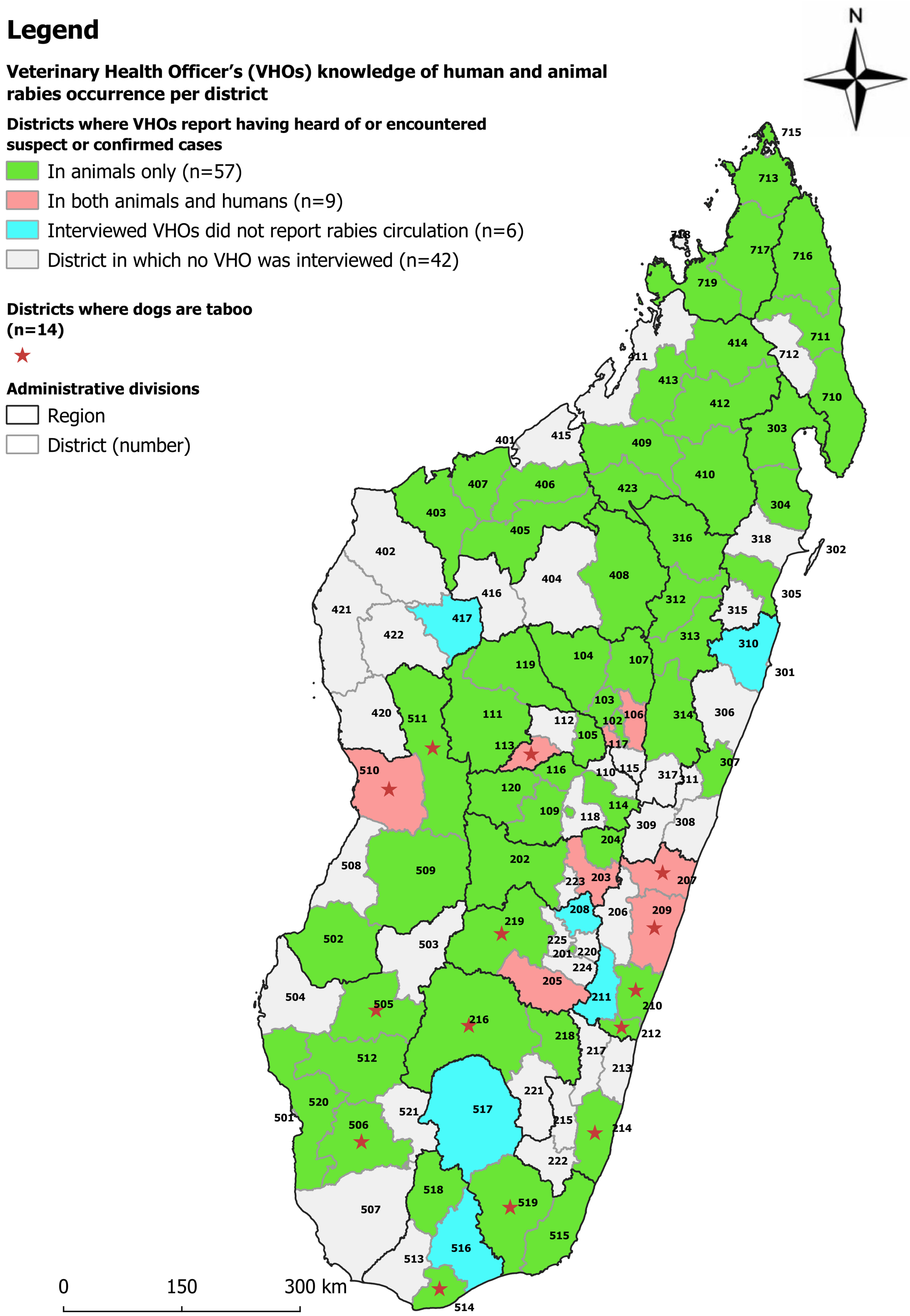

FIGURE 1
Map of Madagascar divided into regions and districts, illustrating the Veterinary Health Officers (VHOs) knowledge on occurrence of human and/or animal rabies cases. The name of the districts is listed by the number in Table 1 and Supplementary Figure 1.

TABLE 1 Districts of Madagascar per region, which can be located on the maps of Figures 1–3 by referring to the number.

Districts of Tananarivo Province		Districts of Fianarantsoa Province		Districts of Toamasina Province		Districts of Mahajanga Province		Districts of Toliary Province		Districts of Antsiranana Province	
Number	Name	Number	Name	Number	Name	Number	Name	Number	Name	Number	Name
Region ANALAMANGA		Region HAUTE MATSIATRA		Region ATSINANANA		Region BOENY		Region ATSIMO ANDREFANA		Region SAVA	
101	Antananarivo Renivohitra	201	Fianarantsoa I	301	Toamasina I	401	Mahajanga I	501	Toliary-I	710	Antalaha
102	Antananarivo Avaradrano	205	Ambalavao	306	Brickaville	403	Soalala	503	Beroroha	711	Sambava
103	Ambohidratrimo	208	Ambohimahasoa	307	Vatomandry	405	Ambato Boeni	504	Morombe	712	Andapa
104	Ankazobe	219	Ikalamavony	308	Mahanoro	406	Marovoay	505	Ankazoabo	716	Vohemar
106	Manjakandriana	220	Lalangina	309	Marolambo	407	Mitsinjo	506	Betioky Atsimo		
107	Anjozorobe	224	Vohibato	310	Toamasina II	415	Mahajanga II	507	Ampanihy Ouest	**Region DIANA**	
115	Andramasina	225	Isandra	311	Antanambao Manampontsy			512	Sakaraha	713	Antsiranana II
117	Antananarivo Atsimondrano					**Region MELAKY**		520	Toliary-II	715	Antsiranana I
		Region AMORON I MANIA		**Region ANALANJIROFO**		402	Besalampy	521	Benenitra	717	Ambilobe
Region ITASY		202	Ambatofinandrahana	302	Sainte Marie	417	Ambatomainty			718	Nosy-Be
105	Arivonimamo	203	Ambositra	303	Maroantsetra	420	Antsalova	**Region MENABE**		719	Ambanja
112	Miarinarivo	204	Fandriana	304	Mananara-Avaratra	421	Maintirano	502	Manja		
113	Soavinandriana	223	Manandriana	305	Fenerive Est	422	Morafenobe	508	Morondava		
				315	Vavatenina			509	Mahabo		
Region VAKINANKARATRA		**Region VATOVAVY FITOVINANY**		318	Soanierana Ivongo	**Region BETSIBOKA**		510	Belo Sur Tsiribihina		
108	Antsirabe I	206	Ifanadiana			404	Maevatanana	511	Miandrivazo		
109	Betafo	207	Nosy-Varika	**Region ALAOTRA MANGORO**		408	Tsaratanana				
110	Ambatolampy	209	Mananjary	312	Amparafaravola	416	Kandreho	**Region ANDROY**			
114	Antanifotsy	210	Manakara Atsimo	313	Ambatondrazaka			513	Beloha		
116	Faratsiho	211	Ikongo	314	Moramanga	**Region SOFIA**		514	Tsihombe		
118	Antsirabe II	212	Vohipeno	316	Andilamena	409	Port-Berge (Boriziny-Vaovao)	516	Ambovombe-Androy		
120	Mandoto			317	Anosibe-An'ala	410	Mandritsara	518	Bekily		
		Region IHOROMBE				411	Analalava				
Region BONGOLAVA		216	Ihosy			412	Befandriana Nord	**Region ANOSY**			
111	Tsiroanomandidy	218	Ivohibe			413	Antsohihy	515	Taolagnaro		
119	Fenoarivobe	221	Iakora			414	Bealanana	517	Betroka		
						423	Mampikony	519	Amboasary-Atsimo		
		Region ATSIMO ATSINANANA									
		213	Farafangana								
		214	Vangaindrano								
		215	Midongy-Atsimo								
		217	Vondrozo								
		222	Befotaka								

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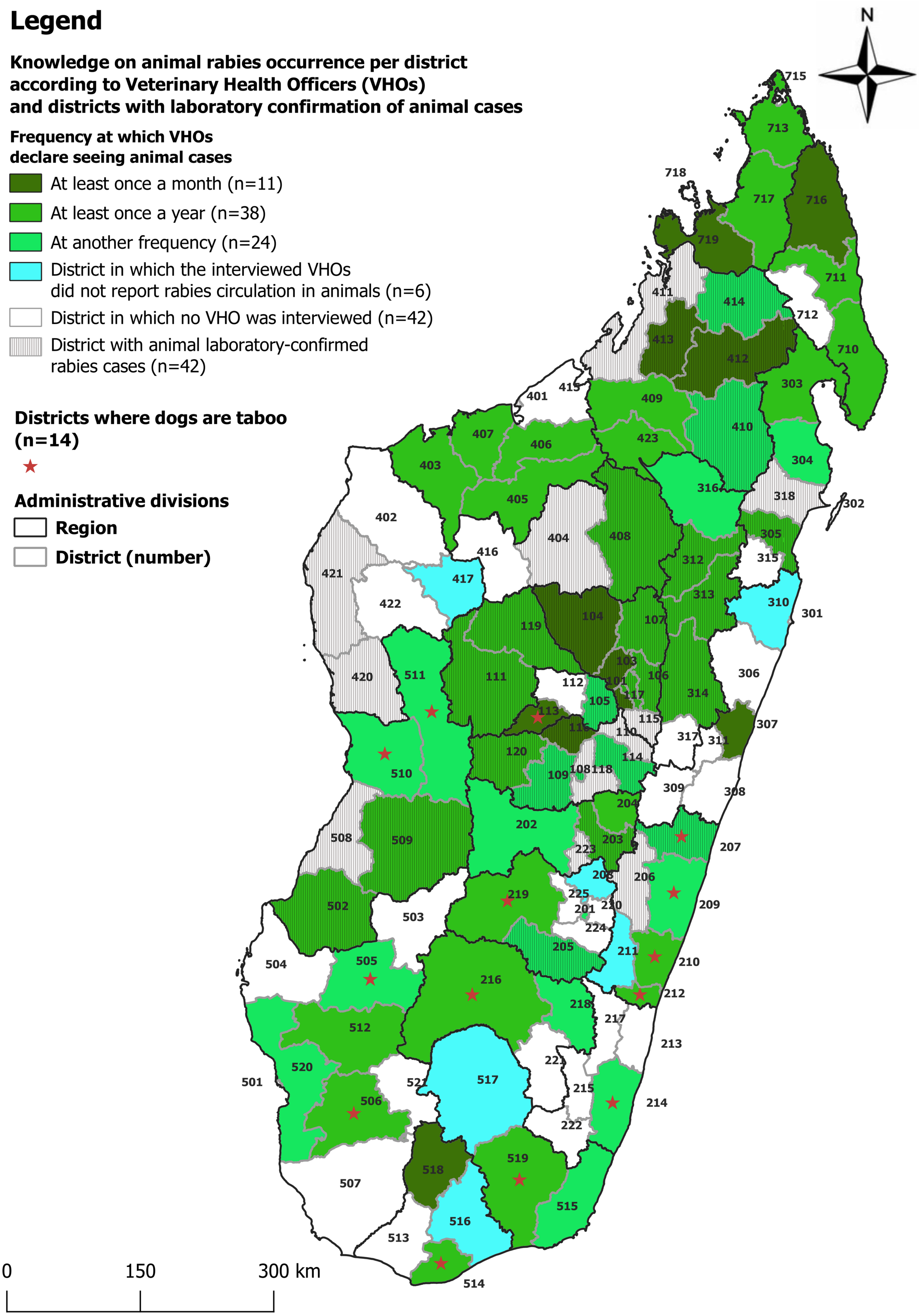

FIGURE 2
Map of Madagascar divided into regions and districts, illustrating the Veterinary Health Officers (VHOs) knowledge on the frequency of animal rabies occurrence and districts with confirmed animal cases by the National Reference Laboratory for Rabies at the Institut Pasteur de Madagascar. The name of the districts is listed by the number in Table 1 and Supplementary Figure 1.

and even medical doctors take no specific action. Another reason stated was the difficulty of accessing ARTCs, which offer PEP. These comments were made during the free discussion (and collected in the analysis grid) and not all VHOs were asked the question systematically. Absence of dog vaccination was not mentioned.

3.4.1 Comparison of VHOs knowledge on rabies occurrence and NRL confirmed rabies cases

Data on human or animal rabies cases confirmed by the NRL from 2011 to 2020 are presented in Figure 3. Confirmed human and animal cases were registered by the NRL in 18 (16%) and 42 (37%) districts, respectively (in 14 districts both confirmed human and animal cases were recorded). The areas without any confirmed cases (either because (i) no sample was received, (ii) sample was too deteriorated to be tested or (iii) no sample tested positive) are located in the five most southern regions of Madagascar (Atsimo Andrefana, Androy, Anosy, Ihorombe, Atsimo Atsinanana), the two most northern ones (Diana, Sava) and Boeny (north west) region. From 13 of the 14 districts where dogs are considered taboo by many persons (see Figure 1 and section 3.5 on this taboo), no confirmed cases were registered by the NRL.

NRL data was compared with the data collected through interviews of VHOs (Table 1; Figures 1–3; Supplementary Figures 2, 3). Overall, when combining the declarations made by the VHOs and the results of confirmed cases registered by the NRL from 2011 to 2020, animal and human rabies were reported to be circulating in 79 and 25 districts, respectively. Yet data from the NRL and suspected human and animal rabies cases as declared by the VHOs did not correlate well. The comparison of NRL and VHOs sources showed that in 37 districts VHOs had heard of or observed animal rabies cases although no sample had been sent to or confirmed by the NRL. Furthermore, in 7 districts, VHOs had heard of or observed human rabies cases although no sample had been sent to the NRL (Supplementary Figures 2, 3) (9).

3.5 Socio-cultural aspects of dog ownership in Madagascar

According to VHOs, almost everywhere in Madagascar, people keep a dog in/around their home for security reasons (89/90 VHOs). In addition, VHOs indicated that most Malagasy, especially in rural communities, are not inclined or cannot afford to spend money on treating or vaccinating their dogs. A VHO stated that many dog owners reject the idea of vaccinating dogs against rabies even if it is offered free of charge and 67/90 VHOs said that the local communities think that dogs are insignificant animals. As an example, one VHO said: "People keep dogs in their backyards but do not really care for them … they do not care about treating a dog … Even where there is a free vaccination campaign, there are still a lot of people who do not care and do not want to vaccinate their dogs." In addition, according to 20 VHOs working in the regions of Melaky, Menabe, Atsimo Andrefana, Atsimo Atsinanana, Vatovavy Fitovinany, Androy and certain areas of Fianarantsoa, the local communities consider dogs as taboo ("fady" in Malagasy) (Figures 1, 2) (12, 13). In these regions, even though dogs are present, they are rejected and touching or caring for them is insulting and goes against cultural beliefs. Even burying a dog would spoil the land (14).

3.6 Challenges in animal rabies surveillance

3.6.1 Notification of a suspected rabid dog to the VHOs by the population

The 80 VHOs who responded that they had heard/observed cases of rabies in their area said that once people have identified a biting dog or a suspected rabid dog, they kill it directly and dump the carcass into waterways (3 VHOs) or somewhere on the ground without notifying the VHO (80 VHOs). As a result, many suspected rabies cases go unreported and unidentified by the latter. However, the VHOs are sometimes contacted when a human is bitten in an area remote from an ARTC.

3.6.2 Sample collection by the VHOs

Three main problems were identified as potentially hindering animal rabies surveillance in terms of sample collection. Firstly, 35% of interviewed VHOs raised the problem of a lack of knowledge of procedures for collecting a sample for rabies diagnosis. Then, 19% of them mentioned a biosafety problem linked to the lack of personal protective equipment. Finally, 87% of VHOs reported a problem related to the lack of equipment for packing samples, in particular for maintaining the cold chain.

3.6.3 Sending samples to the NRL

Regarding sending a sample from a suspected rabid case to the NRL, some VHOs agreed that there was a huge problem of accessibility. Eighteen (20%) of them mentioned the lack of roads and bridges, with some remote areas accessible only by 4×4 vehicles, and/or the absence of an official postal or courier system, which all contribute to the fact that very few samples are taken and sent to the VHOs in first instance. Then, if a VHO receives a sample for rabies diagnosis, they mentioned that he/she will face the same problems.

3.6.4 Financial constraints

The 80 VHOs who reported the presence of rabies in their area described a major funding problem for rabies surveillance, including notification of rabies cases. The statement "who is going to pay the costs of rabies surveillance" was made by 66% (53/80) of VHOs during the interviews. In addition, 82% of them stated that owners were unwilling and 9% that they were unable to pay the costs of sampling, packaging and postage, and that they, the VHOs, needed to be subsidized given that they were paying the expenses out of their pocket.

4 Discussion

The main income generating activities of the VHOs, are livestock vaccination and meat hygiene. According to them, rabies is present in most regions of Madagascar. While it affects livestock, the disease remains marginal to their activities. However, canine rabies-related activities, such as identifying suspected cases, taking and sending samples for diagnosis and notification, represent an expense rather than an income-generating activity, due to a lack of funding. They are therefore not very keen to be part of the rabies surveillance system.

During interviews, VHOs reported having heard of a total of nine cases of human rabies during their VHO's activity (Figure 1). In comparison, laboratory surveillance reported 36 laboratory-confirmed

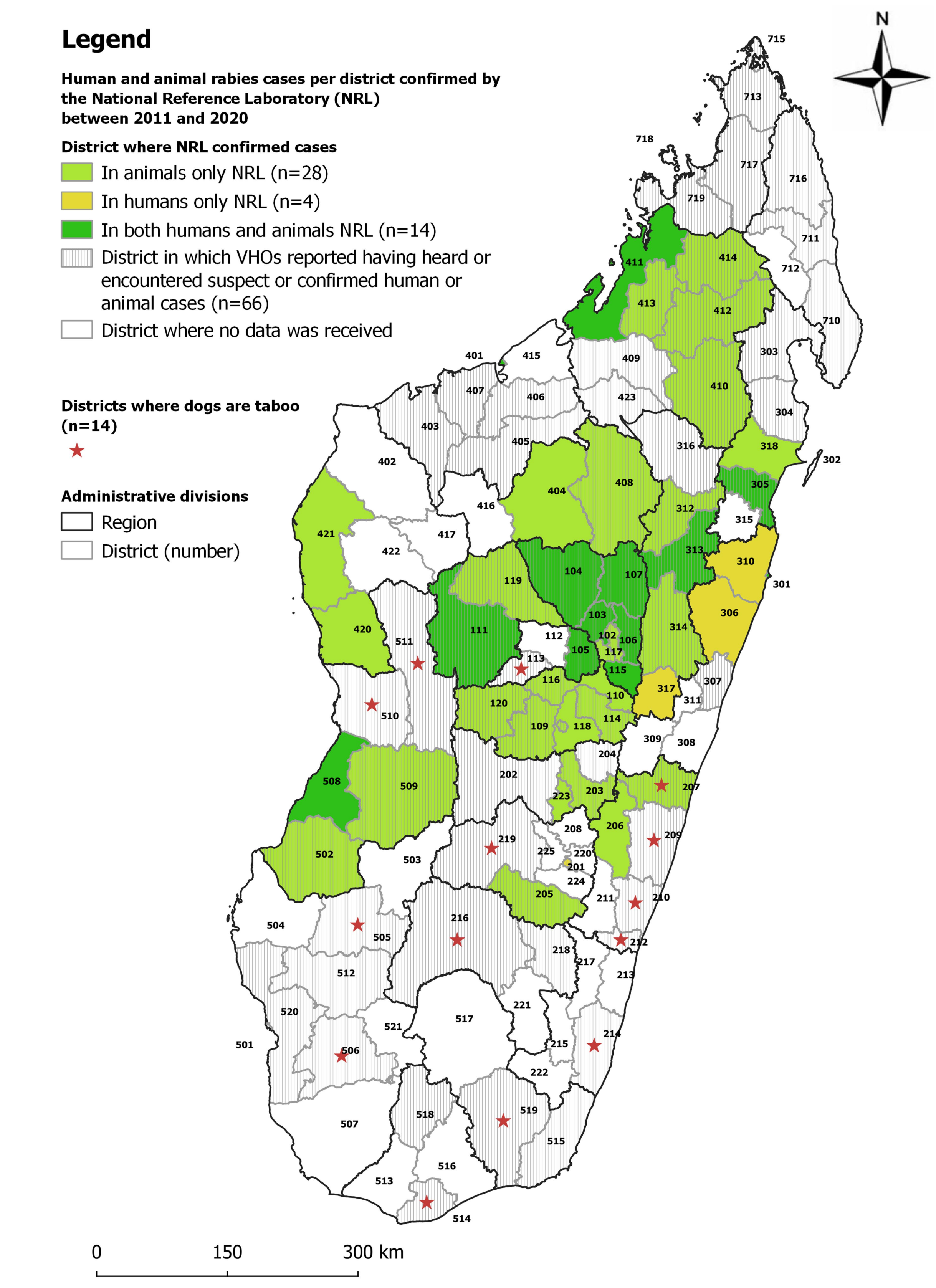

FIGURE 3
Map comparing districts with confirmed human or animal rabies cases from 2011 to 2020 by the National Reference Laboratory for Rabies at the Institut Pasteur de Madagascar and VHO-reported rabies occurrence. The name of the districts is listed by the number in Table 1 and Supplementary Figure 1.

human cases over the past 10 years in 18 districts (Figure 3). These 18 districts are closer to the capital and clinicians are likely better informed on their role in notification and collaborate more closely with the NRL. Comparing NRL and VHO sources showed that, VHOs had heard of or observed animal rabies cases in 37 districts and human rabies cases in 7 districts without any samples having been confirmed by the NRL. These are districts in the periphery, where the submission of samples to the NRL face more challenges. The contrary occurred in 9 districts, where VHOs were not aware of all NRL results. These figures demonstrate that VHOs are not systematically informed of human and animal rabies cases as required by the organizational scheme for rabies surveillance and that communication between the various actors involved in rabies surveillance clearly needs to be improved. It also suggests that the difference between the effective absence of disease and the absence of notification of a health event needs to be urgently assimilated by many actors in Madagascar, and that, for under-reported diseases such as rabies, several sources of information need to be completed, combined and crossed until concordant figures are obtained.

In Madagascar, rabies is very likely under-reported given that according to the VHOs (i) suspected rabies cases are seldom reported to the VHOs by the population, (ii) samples are rarely taken from suspected cases and (iii) if taken, their shipment to the NRL is very difficult due to logistical and financial issues. These are likely the main reasons why regions far from the capital Antananarivo, have only sent 0–2 samples of suspected rabies cases annually over the last 10 years (9). Underreporting for human cases is also reported by Rajeev et al., (7) who estimated 960 (95% Prediction Intervals (PI): 790–1,120) human deaths from rabies annually.

Dog owners are required to submit the biting animal for veterinary observation (Decree n°3483/99 – Ministry of Agriculture and Livestock). As there is no financially-supported surveillance program, owners are officially responsible for assuming the financial burden in the event of a dog bite. This is probably another reason why suspected rabies cases go unreported, as people might shy away from this responsibility for fear of having to pay for both the medical care of those bitten (PEP, transport, medication) and the laboratory diagnosis in case of suspected rabies (mainly transport costs) (this info had been communicated to one of the authors during stakeholder workshops on rabies prevention and control). Furthermore, even for wealthy families, bringing a dog to a veterinarian or getting a veterinarian to visit a biting dog can be extremely difficult, given the very limited number of veterinarians, especially in rural areas.

The stakeholders in charge of surveillance must improve the surveillance system and increase the budget to cover the costs of animal observation, sampling and shipping. Stakeholders at all levels of surveillance should be trained in basic surveillance concepts (including technical workshops on sampling and biosecurity), prevention and control of zoonotic infectious diseases, and the "One Health" approach. Especially human doctors need to be informed on their important role in the rabies notification system. It should be noted that most veterinarians are not vaccinated against rabies (authors personal comment).

Educational programs should target "responsible dog ownership," which could improve dog care and vaccination coverage. However, if people are suffering from poverty, as is the case in most parts of Madagascar, sheer survival is the main concern. Preventive measures concerning dogs will therefore have to be 100% subsidized. While many VHOs mentioned in the present study that dog vaccination was not tolerated by the population, Filla et al. (4) found in Moramanga in 2018 (where dogs are not taboo) that 60% of people agreed to vaccinate their dogs if the costs were covered.

During a Knowledge, Attitude and Practices (KAP) survey in Moramanga, 28 bitten people were interviewed. It was reported that only five dogs had been killed, of which four had bitten their owners (5). Rajeev et al. (8) showed that the percentage of biting dogs, which were killed was 1% in dogs classified as non-cases, 3.7% in dogs of unknown rabies status, 33.8% in probable rabies cases and 73% in confirmed rabies cases. Hence, the statement of the VHOs that most biting dogs are killed is not confirmed by the published data. The decision whether to kill a biting dog probably depends on several factors, such as the presence of someone who can kill the dog, the likelihood a dog is rabid or not (including whether the dog exhibited clinical signs of rabies), whether the bite was provoked or not, whether the dog had bitten other people or animals and whether it was vaccinated or not, whether the dog has an owner or not, and the social impact of the decision within the community.

The fear of feral dogs (feral dogs without owners) and their preponderant role in rabies transmission are repeatedly reported (5). However, firstly, often feral dogs are in reality free roaming dogs with unidentified owners, and secondly, when tracing biting dogs, most bites in Madagascar are not due to feral dogs [(5), CTAR data, personal communications].

Given that certain opinions held by the VHOs were not confirmed by field studies carried out in the country, such as the fact that most biting dogs are killed or the preponderant role of stray dogs compared to owned dogs in rabies transmission, it would be interesting to conduct studies on these topics and communicate these field study results to both veterinary and public health officers, VHOs and veterinary students.

Many low-income countries face problems of budget, infrastructure and a low coverage of veterinary services. In Madagascar, socio-cultural beliefs toward dogs in 14 districts, mainly in the Western, Southern and Eastern coastal regions, where they are "fady" (taboo), represent an additional challenge to rabies surveillance and control. Apparently, the compliance of the local communities to rabies surveillance and control might be difficult and handling dogs in any way creates tensions between the authorities and local communities. As a result, VHOs in these regions are not active in rabies prevention and control. Consequently, in the opinion of many VHOs, implementing a mass vaccination or sterilization campaign would be impossible in these areas, as traditional village authorities would adamantly be opposed to such measures. The following statement from a VHO illustrates the situation: "the society will reject you if you take care of a dog or touch it … even burying a dog is forbidden here, it is a taboo …, vaccination is impossible. It is a big problem here."

The fear of veterinarians of being rejected if they treat or vaccinate dogs in areas where dogs are taboo was confirmed by a KAP study conducted in Menabe 2020–2021 (12, 13). In this context, to carry out vaccination campaigns in regions where dogs are "fady," the temporary mobilization of veterinarians from outside these regions, with the prior agreement of local authorities, could be a solution. In any case, the first step is to ensure that the population will accept dog vaccination. Further, we recommend conducting studies on the "implementability," safety and efficacy of the use of controlled oral vaccination in food baits, which could be a way to avoid handling these dogs which are not used to being touched (15). However, these live vaccines hidden in an edible bait are likely to encounter resistance from a population many of whom suffer from hunger, and who might not understand why "dogs are fed" while children are malnourished. Whether this assumption is correct and which communication and participatory strategies would be needed to improve the acceptance of the population (if the "oral vaccine strategy" was a control option) warrant a qualitative research approach. An interesting One Health approach would be a collaboration of international and national organizations and NGOs involved in nutrition programs with those organizing a vaccination campaign or combining vaccination of children (Polio, Measles etc.) with a rabies vaccination campaign of dogs (16).

The KAP survey on rabies, conducted in the community of Moramanga, showed that while knowledge of the main hosts, transmission routes, symptoms and outcomes was high, knowledge of the existence of ARTCs, the usefulness and availability of PEP, and the need to confine and observe biting dogs was dramatically low (5). Therefore, it is important to inform communities about what to do after a dog bite (such as washing the wound with water and soap for at least 15 min, slow the bleeding, and look for PEP) and why dog vaccination is crucial to rabies elimination. The KAP study conducted in the Menabe Region demonstrated that an "awareness approach" can consequently improve the communities KAP regarding rabies (17).

Improving rabies surveillance is a real challenge, as most problems and challenges are poverty-related. Yet the path to rabies elimination has been thoroughly documented (18–20) and several authors have synthetized lessons learned to help countries willing to embark on this path (21–23). So far, in Madagascar, efforts have focused on eliminating human deaths due to rabies thanks to the privately-funded support of IPM, which offers PEP for free to the ARTC network (24). PEP is highly effective in preventing rabies deaths in humans, but it is well-known that only mass vaccination of dogs can lead to the elimination of dog-transmitted rabies. Although research has proven the ineffectiveness of dogs culling in rabies control (25), the current official recommendation in Madagascar is still based on dog culling (Decree 3482/99 – Ministry of Agriculture and Livestock).

Mass vaccination of dogs has been shown to be very cost-effective, particularly if carried out with a well-tailored One Health communication (26, 27). Madagascar has recently received dog vaccines and has begun mass vaccination in two regions. We therefore recommend pursuing these efforts and focusing on free mass vaccination of dogs in combination with awareness campaigns. To properly plan vaccination campaigns, it is recommended to estimate the turnover rate of the local dog population to adapt the frequency of dog vaccination. Further, to collect epidemiological data from active rabies surveillance (through sentinel sites?) to identify high-incidence areas in densely-populated zones to prioritize the locations for vaccination campaigns given limited funds. Most importantly, politicians and stakeholders need to be convinced of the importance of rabies prevention and control. This is a challenge in a country facing many poverty-related problems, with a wide range of communicable and non-communicable diseases. While the prevention and control of malaria, tuberculosis and plague has received much attention and funding, neglected diseases such as rabies require more attention, as the burden is high, especially in the underprivileged populations, who often remain forgotten (28).

4.1 Limitations

This mixed-methods study represents the opinions of 90 VHOs from different regions of Madagascar. By interviewing 60% (90/150) of all VHOs, a large variety of professional profiles was included, and all regions of Madagascar were represented. The opinions of the VHOs, which are based on personal experiences and convictions, may not represent the opinions of all. Nor do they represent the opinions of other stakeholders in the rabies surveillance system. Veterinarians who recently started working as VHOs (2 years) may have less knowledge on the rabies situation, in comparison to those who have been longer established in their working area (31 years). Nevertheless, the fact that all 22 regions of Madagascar were represented indicates a relatively good geographical coverage of the study. The second part of the interview was an open discussion. The opinions/answers of the VHOs were categorized in a thematic grid and presented in the results section. However, not all VHOs mentioned the same topics. For example, 18/80 VHOs mentioned the negligence/unawareness of the danger of dog bites as a reason for the occurrence of human rabies cases. These figures do not mean that the other 62 VHOs would not have made the same statement. They simply did not mention it during the open discussion. The advantage of the open discussion is that it allows to be informed of the opinion of the VHOs without influencing them, but the disadvantage of this non-systematic approach is the lack of representativeness.

4.2 Conclusion

This study shows that rabies cases are frequently observed by VHOs in the field, in all the 22 regions of the country, but that several obstacles hinder rabies surveillance, leading to under-reporting of cases. The main barrier to surveillance is financial, as noted by all the VHOs interviewed. Lack of funds to access suspected animals, collect and package samples, comply with biosecurity and cold chain measures, and ship samples are major obstacles to notification. The lack of funds has also a negative impact on dog owners' willingness to report a bite and follow procedures, as they are often reluctant -or unable- to cover the associated costs. The second obstacle identified by VHOs is socio-cultural. In many large coastal regions of the island dogs are taboo and VHOs fear rejection by the community if they take care of dogs. Moreover, the lack of community awareness of rabies and PEP was mentioned several times. Finally, the poor correlation between rabies cases confirmed by the NRL and rabies cases reported by the VHOs underlines the need to improve the information and communication within the surveillance network. In this context, while the general population needs to be informed about the rabies situation in Madagascar, that vaccination is crucial to control this disease and how to proceed in the event of a bite, veterinarians and decision-makers need to be fully aware of certain epidemiological concepts to understand the usefulness of an evidence-based approach to rabies surveillance, prevention and control. Stakeholder workshops to develop a program for the improvement of rabies surveillance in Madagascar using a participatory approach is highly recommended. For their part, politicians need to be persuaded of the importance and necessity of funding to eliminate rabies in Madagascar. The adoption, in early 2023, of a national strategic plan for rabies control is a first step in this direction.

Data availability statement

The data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the participants was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

AD: Conceptualization, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. MV: Conceptualization, Formal analysis, Methodology, Writing – original draft. HG: Conceptualization, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. NiR: Supervision, Writing – review & editing. MH: Investigation, Writing – review & editing. NA: Investigation, Writing – review & editing. NaR: Supervision, Writing – review & editing. MA: Supervision, Writing – review & editing. PD: Supervision, Writing – review & editing. DK: Conceptualization, Writing – review & editing. VL: Methodology, Writing – review & editing. SF: Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Visualization, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2024.1270547/full#supplementary-material

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frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 28 February 2024
DOI 10.3389/fvets.2024.1259021

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OPEN ACCESS

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RECEIVED 14 July 2023
ACCEPTED 31 January 2024
PUBLISHED 28 February 2024

CITATION
Tamayo Cuartero C, Szilassy E, Radford AD, Newton JR and Sánchez-Vizcaíno F (2024) Setting clinically relevant thresholds for the notification of canine disease outbreaks to veterinary practitioners: an exploratory qualitative interview study. *Front. Vet. Sci.* 11:1259021.
doi: 10.3389/fvets.2024.1259021

Setting clinically relevant thresholds for the notification of canine disease outbreaks to veterinary practitioners: an exploratory qualitative interview study

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Introduction: The Small Animal Veterinary Surveillance Network (SAVSNET) has developed mathematical models to analyse the veterinary practice and diagnostic laboratory data to detect genuine outbreaks of canine disease in the United Kingdom. There are, however, no validated methods available to establish the clinical relevance of these genuine statistical outbreaks before their formal investigation is conducted. This study aimed to gain an actionable understanding of a veterinary practitioner's preferences regarding which outbreak scenarios have a substantial impact on veterinary practice for six priority canine diseases in the United Kingdom.

Methodology: An intensity sampling approach was followed to recruit veterinary practitioners according to their years of experience and the size of their practice. In-depth semi-structured and structured interviews were conducted to describe an outbreak notification and outbreak response thresholds for six canine endemic diseases, exotic diseases, and syndromes. These thresholds reflected participants' preferred balance between the levels of excess case incidence and predictive certainty of the detection system. Interviews were transcribed, and a thematic analysis was performed using NVivo 12.

Results: Seven interviews were completed. The findings indicate higher preferred levels of predictive certainty for endemic diseases than for exotic diseases, ranging from 95 to 99% and 80 to 90%, respectively. The levels of excess case incidence were considered clinically relevant at values representing an increase of two to four times in the normal case incidence expectancy for endemic agents, such as parvovirus, and where they indicated a single case in the practice's catchment area for exotic diseases such as leishmaniosis and babesiosis.

Conclusion: This study's innovative methodology uses veterinary practitioners' opinions to inform the selection of a notification threshold value in real-world applications of stochastic canine outbreak detection models. The clinically relevant thresholds derived from participants' needs will be used by SAVSNET to inform its outbreak detection system and to improve its response to canine disease outbreaks in the United Kingdom.

KEYWORDS

disease surveillance, canine diseases, qualitative research, outbreak detection, outbreak reporting

1 Introduction

One of the main factors that determine the effectiveness of an epidemic response is the timely detection and notification to farm owners whose animals are potentially affected (1). In the United Kingdom, surveillance systems in farm animals and public health are run centrally by government departments and agencies to identify increasing disease trends and detect disease outbreaks in their early stage, facilitating the prevention and control of health threats nationally and regionally (2, 3). The relevant information derived from these surveillance activities is shared with the public via weekly reports (4) and online dashboards (5). However, these surveillance protocols do not currently exist in small companion animals, for which there is no standardized system of disease reporting or routine collection of surveillance data at a national level. This leaves canine populations in the United Kingdom vulnerable to epidemic threats.

To begin to bridge this gap, the Small Animal Veterinary Surveillance Network (SAVSNET)-Agile initiative (6) is developing a nationwide system for the timely detection and response to canine disease outbreaks in the United Kingdom. However, before such a surveillance and control system can be set up and implemented, it is necessary to determine which notification thresholds of increased levels in case incidence relative to a previously identified baseline of expected cases would warrant alerting relevant stakeholders of potential outbreak threats.

There are several methods that have been described to determine statistical outbreak notification thresholds. These methods vary depending on the disease type and the quality of the data that is available for surveillance purposes. For diseases that are endemic to the country, systems rely on historical data to establish a baseline level of disease and then use different mathematical methods to determine notification thresholds based on increases in case incidence, relative to the previously identified baseline (7, 8). Other commonly used methods to establish outbreak notification thresholds are multi-chart schemes, which combine the results of an individual time series that enable the rapid detection of subtle changes in the disease (8) or the methods that involve setting the number of standard deviations above the baseline of expected cases (9). For exotic and rare diseases, due to a lack of baseline data to draw patterns from, notification thresholds are defined *ad hoc*, and it is often common to accept a single case as a threat that warrants generating an alert (10).

While these statistical methods have proven to be powerful for detecting disease anomalies, they often signal outbreaks that are not clinically relevant for veterinarians in practice. Therefore, outbreak notification systems that rely on such statistical signals might overload practitioners with information that is not actionable. In the long term, this overloading could lead to a lack of confidence and engagement with the surveillance and outbreak notification system. To address these limitations, this study aimed to explore what threshold values based on veterinary practitioners' opinions correspond to outbreaks that should be notified when detected by the statistical methods because of their significant impact on veterinary practice for six priority canine diseases in the United Kingdom (11). In addition, we gained an understanding of the reasons that drive veterinary practitioners to select such threshold values and of how their in-practice behavior can be impacted by clinically relevant outbreaks. To achieve these aims, an innovative methodology was developed based on the combination of semi-structured and structured interviews with companion animal veterinarians.

2 Materials and methods

Ethical approval for this study was granted by the ethics committee of the University of Bristol Faculty of Health Sciences (FREC, reference code: 98843).

2.1 Study population

The population of interest for this study was small animal veterinary clinicians working in the United Kingdom at the time of its conduction. Study participants were selected from this population following an intensity sampling approach, which is a type of purposive sampling to select information-rich cases located at the end of a population's distribution (12). To select information-rich cases, relevant population characteristics, or descriptors, were defined. These descriptors were believed to influence participants' perspectives and behavior regarding canine epidemics and, therefore, their responses during the interviews. The following descriptors and levels of interest were used in the sampling process to categorize recruited participants:

(a) Years of experience in small animal practice: It was assumed that more senior veterinarians are more likely to have experienced canine outbreaks throughout their career and have spent more time in practice overall, which could influence their opinions and decision-making. The cutoff points were established to differentiate newly graduated veterinarians from those with many years of in-practice experience.

  (a) Recent graduates: Those with less than 5 years of experience.
  (b) Senior veterinarians: Those with over 10 years of experience.

(b) Practice size: Since smaller practices have fewer employed veterinarians and see a lower number of cases, compared to bigger veterinary centers, it was expected that an outbreak would affect them differently and could potentially overwhelm their ability to cope with the increase in case incidence. To accurately reflect the difference between small and big veterinary practices, a summary of the existing veterinary practices in the United Kingdom was requested from the Royal College of Veterinary Surgeons (RCVS). This database included the total number of registered practices in the United Kingdom and a breakdown of the number of employed veterinarians per practice. The practice directory was analyzed to understand what the average size of the practice is and inform the categorization. A total of 4,252 individual veterinary sites were listed on the database. Over half of these sites had four or fewer registered veterinary surgeons (2,917 or 68%). A total of 23% (984) of the sites had between five and nine employed veterinarians, and only a small number (348 or 8%) had 10 or more registered veterinary surgeons.

(a) Small veterinary practice: Those with fewer than four employed veterinarians.
(b) Large veterinary practices: Those with more than 10 employed veterinarians.

2.2 Participant recruitment

Participant recruitment was conducted from July 2021 to April 2022. Potential study participants were contacted through different means. Veterinary clinicians who were part of a pre-established network of collaborators for SAVSNET-Agile were emailed directly by the corresponding author (CTC). Furthermore, veterinary practices that contributed data to SAVSNET at the time of the conduction of the study were contacted via email and their practice management software (PMS); these practices contain a SAVSNET plugin window that can be used by the latter to relay messages to attending veterinarians (13). A participant recruitment advertisement was posted on the SAVSNET website (14) and shared on social media, including on Twitter and Facebook. Finally, an interview to advertise the study was conducted by the corresponding author (CTC) with the United Kingdom veterinary magazine, Vet Times (15).

2.3 Interviews with companion animal veterinarians

Recruited veterinarians took part in an interview session, which was conducted online via Microsoft Teams (16) or Zoom (17). Interviews were conducted between August 2021 and April 2022. The overall aim of the interviews was to explore clinically relevant outbreak scenarios for the notification of two canine endemic diseases (leptospirosis and parvovirus), two canine exotic diseases (leishmaniosis and babesiosis), and two canine syndromes (respiratory and gastrointestinal diseases). The interviews consisted of two components, with different aims.

2.3.1 Semi-structured interview

The first part of the interview followed a semi-structured (18), in-depth format and aimed to gain an understanding of the reasons that drive veterinary practitioners to define what constitutes a clinically relevant outbreak and to understand how their in-practice behavior can be impacted by such outbreaks. To facilitate the discussion, the interviewer first provided an overview of the epidemiological characteristics of the disease under consideration. The topic guide developed for the semi-structured interview can be found in Supplementary material S1. When participants did not know or had misconceptions about the characteristics of a particular disease, these doubts or misconceptions were clarified by the interviewer at the end of the interview session.

2.3.2 Structured interview

Once participants had reflected upon the subject matter, the interview changed to a structured format to understand which outbreak scenarios would be selected by participants to receive timely alerts due to their potential impact on their practice. Outbreak scenarios were described using two parameters, which represented the characteristics of an outbreak notification:

- Excess case incidence: An increased incidence above the expected baseline of cases in your practice's catchment area would be of practical significance to (a) warrant a notification about a potential outbreak and (b) drive you to change your behavior in practice in response to an outbreak. Thus, when selected levels of excess case incidence were different for (a) and (b), the selected value for the former was used to define a notification threshold, and the value for the latter was used to define an outbreak response threshold for canine diseases.
- Predictive certainty: The level of confidence of the alerts generated by the statistical outbreak detection models, defined by their credible interval, normally takes values that range from 90 to 99% (19).

The questions included in the structured interview (Supplementary material S2) aimed to introduce the concepts of excess case incidence and predictive certainty to study participants and use them to describe disease-specific outbreak scenarios in a way that resonated with participants and their experience in practice.

2.4 Data analysis

Interview data were audio-recorded and transcribed verbatim. All the analyses were conducted on NVivo (version 12) qualitative data analysis software (20). A coding framework was iteratively developed by the corresponding author (CTC) based on the expected and emergent themes using deductive and inductive approaches, respectively. To enhance the consistency and reliability of the analysis, two authors (CTC and FSV) independently coded the transcript data from one of the interviews. Codes generated deductively and inductively from interview transcripts were grouped together into themes by following a hybrid approach to thematic analysis (21, 22) (Figure 1). To ensure reliability and transparency, themes were continuously compared to the interview transcripts to ensure they were true to the original data (23).

3 Results

3.1 Characteristics of participants

Seven veterinary clinicians participated in this study. Out of these participants, four were part of SAVSNET's previously established network of collaborators, two had seen the recruitment advertisement on SAVSNET's PMS plugin window, and one reported having seen the

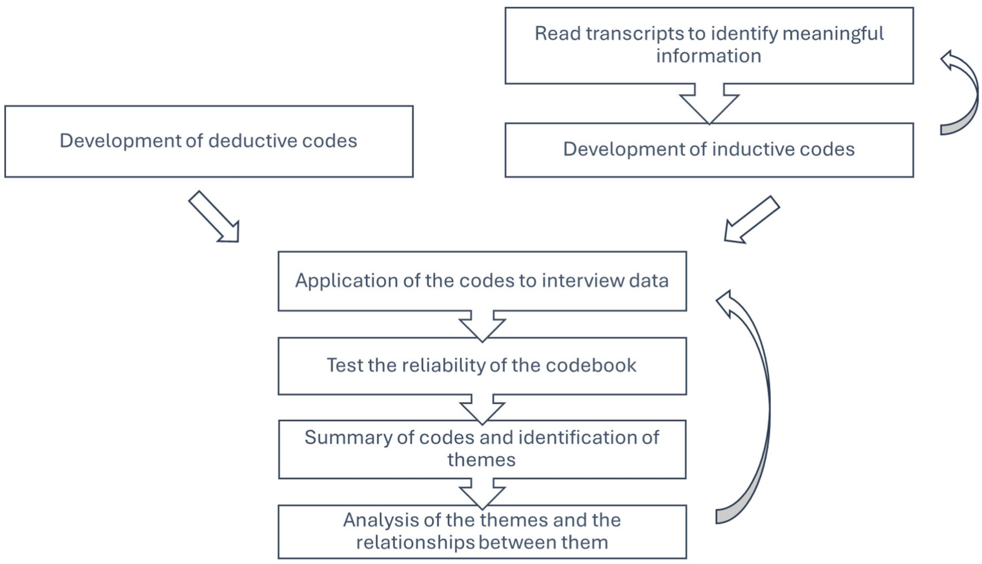

FIGURE 1
A summary of the data analysis process for veterinary clinicians' interview transcripts.

TABLE 1 The breakdown of participating veterinary clinicians, with a breakdown of their characteristics according to the population descriptors of the study.

Participants	Practice size (In no. of employees)	Experience (In years)
1	4	32
2	3	18
3	80	14
4	14	25
5	23	16
6	2	1.5
7	11	4

study in an online veterinary magazine. Table 1 presents a summary of the characteristics of the recruited participants, according to the study's population descriptors. Five out of the seven participants had more than 10 years of experience in practice, and the remaining two participants had worked in small animal practices for less than 5 years. Four of the participants were employed by large veterinary centers, with more than 10 veterinary surgeons, while the other three worked in small clinics, with fewer than five veterinary surgeons. In fact, in the latter case, two participants (numbers 2 and 6) worked in centers where a single veterinary surgeon was on duty at any given time.

3.2 Findings from interviews with veterinary clinicians

The codebook used to analyze interview transcript data can be found in Supplementary Table S3. Interviews had a mean duration of 1 h 10 min, the longest one being 1 h 34 min and the shortest being 50 min.

The results of this study are presented as follows: first, an overview of the excess case incidence and predictive certainty parameters was summarized, and second, for each of the diseases under study, themes that resulted from grouping inductive and deductively generated codes as well as the values chosen by participants for the outbreak notification and outbreak response thresholds were shown.

3.2.1 Excess case incidence

When discussing the levels of excess incidence to define notification and outbreak response thresholds, some participants preferred to discuss this parameter by providing a single value of disease case incidence that would make them want to either be notified about a potential outbreak in their area or—in addition to this notification—also change their in-practice behavior. In other cases, especially if they had never personally dealt with the disease in question, participants felt more comfortable discussing the excess incidence as a range of the values of case incidence. Participants also had different preferences for the time unit used to discuss the excess incidence, e.g., some participants referred to an increase in case incidence within a week or a month, while others simply provided an absolute number of disease cases. Furthermore, some participants discussed the excess incidence as an increase in the number of cases relative to the expected baseline, e.g., two or three times higher than expected, while others preferred to provide an absolute number of cases that would warrant a notification or that would trigger a behavior change in their practice.

3.2.2 Predictive certainty

The predictive certainty parameter was interpreted by participants in two distinct, opposite ways. On the one hand, some participants expressed that they would rather set the predictive certainty value at the lowest possible level when dealing with diseases that they considered as posing a high epidemic risk. They argued that they would rather be notified as soon as possible about severe potential threats to increase their practice's preparedness, despite the higher probability of receiving a false alert. Conversely, other participants preferred to set the predictive certainty value to the highest level when faced with the same situation. Their rationale was that, given the high severity of the disease threat, the participants would only require a notification if the risk of receiving a false alert is minimized in order to avoid either wasting time and resources in preparing for a non-existent epidemic or unnecessarily warning the practice's clients. This scenario was reflected, for example, in the case of canine leptospirosis, which was perceived as a very severe, life-threatening disease, for which some participants chose relatively low predictive certainty values (90%), while others set this parameter value at 99%.

3.2.3 Canine leptospirosis

Overall, participants perceived canine leptospirosis as the pathogen that posed the highest epidemic risk to their practices, mainly due to the uncertainties surrounding the disease's diagnosis, treatment, and prevention.

3.2.3.1 Diagnostic challenges

A recurring theme that emerged from the interviews was the challenges and uncertainties surrounding the diagnosis of canine leptospirosis. Although participants were aware of the different diagnostic tools that can be used to diagnose the disease, they were unsure of which tests to use to ensure the reliability of the results, depending on the stage of the infection.

> *"You're gonna end up with more questions than answers from me on this, because I still think there's an awful lot to be answered diagnostically, um, on lepto."*

— Participant 4: 25 years of experience, practice of 14 veterinarians.

Another source of diagnostic uncertainty was the variety of clinical presentations of leptospirosis. Those participants who had been involved in an outbreak in the past recalled how the cases of confirmed leptospirosis they had did not show the signs commonly associated with this disease. Furthermore, the rapid progression of the disease means that it is sometimes difficult to perform diagnostic tests or take samples to confirm the diagnosis.

> *"[leptospirosis] is very acute, the animal died in a couple of days…. So yeah, we did not even have time to perform more tests."*

— Participant 7: 4 years of experience, practice of 11 veterinarians.

Participants also discussed the difficulty posed by carriers that can spread the disease despite not showing any clinical signs. Due to these diagnostic barriers, only two participants had ever reached a definitive diagnosis of canine leptospirosis throughout their careers, while other participants had only seen highly suspicious, yet unconfirmed, potential cases.

> *"[…] our diagnosis was empiric, it was a diagnosis just based on clinical signs, we did not go any further diagnostic-wise […] and it was a dog living in a farm, so all of this made us suspicious."*

— Participant 7: 4 years of experience, practice of 11 veterinarians.

3.2.3.2 Vaccination

Study participants often discussed the vaccination practices for canine leptospirosis and highlighted key issues regarding leptospirosis vaccines. They perceived these issues as an important obstacle for the adequate prevention of this disease. For instance, participants were unsure of the length of the immunity provided by leptospirosis vaccines, the frequency of vaccinations that they should recommend to dog owners, and how to convey the importance of vaccination to their clients.

> *"I would love to know how long lepto immunity lasts in the system, the same way you can do a titre test for dhp […] but I'd like to have a way of knowing more accurately how long the immunity lasts in the dog's body… any kind of approach to know how protected the dog is against lepto."*

— Participant 6: 1.5 years of experience, practice of 2 veterinarians.

Furthermore, vaccine hesitancy was reported to be the highest among veterinary professionals and dog owners in the case of canine leptospirosis. The vaccine hesitancy was mainly related to the controversies associated with the relatively newly introduced L4 vaccine (a quadrivalent canine leptospirosis vaccine named Novibac L4® by Merck & Co., Inc.).

> *"Leptospirosis is one that is part of our core vaccines, and we use nobivac so it's the infamous leptospirosis 4, which obviously carries all the interesting discussions that go with it, probably similar to covid and 5G."*

— Participant 7: 4 years of experience, practice of 11 veterinarians.

3.2.3.3 Zoonotic risk

Study participants were either unaware of the zoonotic potential of leptospirosis or did not believe this pathogen to pose a relevant risk to humans. Only one participant recounted observing a potential dog-to-owner transmission of leptospirosis during their career:

> *"One dog, we had referred a Jack Russell a number of years ago, the owner died of leptospirosis. Um, the dog had leptospirosis, so we have seen that once."*

— Participant 3: 14 years of experience, practice of 80 veterinarians.

3.2.3.4 Clinically relevant threshold

Figure 2 shows an overview of the clinically relevant notification threshold values for canine leptospirosis, including the notification and outbreak response thresholds. When discussing the clinically relevant threshold for canine leptospirosis, most participants would like to be notified as soon as a single case was detected in their area (Table 2). Moreover, some participants enquired about the surveillance

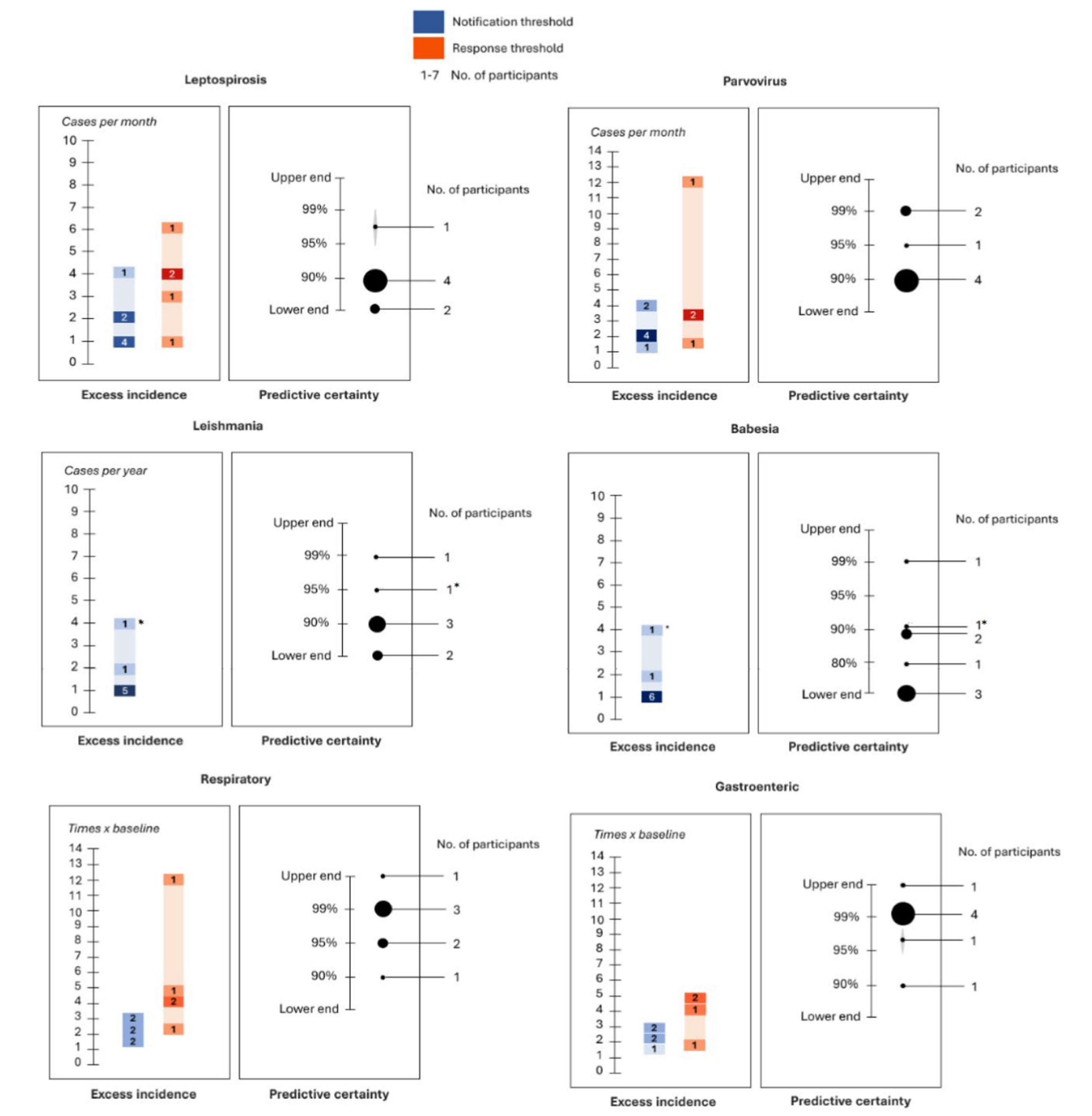

FIGURE 2
A summary of clinically relevant thresholds for the six canine diseases included in this study. The left graph included for each disease depicts the excess case incidence thresholds. The blue and orange bars represent the excess incidence values corresponding to the notification and outbreak response thresholds, respectively. If the same participant provided more than one value of case incidence to define either the notification threshold or the outbreak response threshold, then the lowest value was used to depict the former, while the highest value was used for the latter. These bars are rendered using a gradient of colors, which serve as an indicator of the number of participants who provided a particular value, with darker colors indicating a higher number of participants. For each disease, the right graph depicts the overall predictive certainty threshold as the range of values provided by participants. The size of the dots corresponds to the number of participants who provided that particular value, with larger dots indicating a higher number of participants. For exotic diseases, the asterisk denotes responses that were specific to non-autochthonous cases of the disease, and the other responses refer to autochthonous cases.

system's capacity to flag highly suspicious cases, even without an official diagnosis and account for "leptospirosis-like illness," given the existing diagnostic difficulties. For this reason, all but one of the participants preferred to set the predictive certainty of alerts to low levels (Table 3). The only participant who did not agree was one of the two veterinarians who had been involved in a past leptospirosis outbreak, who would rather be notified only if the certainty level was very high, given the high levels of distress among employees and clients and the investment in resources for preparedness:

> *"I think that a false alarm would be quite detrimental because of my experience of knowing how involved we got with this last time. I think you would want to have a relatively high level of certainty with this disease. We would have to be a bit careful*

TABLE 2 A summary of participants' preferred levels for the notification and outbreak response thresholds and predictive certainty values for canine leptospirosis.

Canine leptospirosis				
Participants	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
	0 / month Seen 3 times throughout the career	1 case/month	N/A	90%
2	0 cases/ month Seen 2 cases	1 case/month	3 cases/month	90%
3	2–3 cases/year Involved in outbreak	2–3 cases/month	4 cases/month	90%
4	1–3 cases/year Involved in outbreak	x2 baseline/ month	x3-4 baseline/ month	90%
5	0 cases/month Involved in outbreak	1 case/week	2–3 cases/fortnight	95–99%
6	0 cases/month Seen 1 case (never confirmed)	2 cases/month	4 cases/month	The lowest end of the possible range
7	0 cases/month Seen 2 cases (never confirmed)	>0 case/month	N/A	The lowest end of the possible range

The table includes participants' reported baseline of observed cases in their practices.

TABLE 3 A summary of participants' preferred levels for the notification and outbreak response thresholds and predictive certainty values for canine parvovirus.

Canine parvovirosis				
Participants	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
1	3–4 cases/year Expects certain prevalence	4 cases/month	N/A	90%
2	Expects certain prevalence throughout the year	2 cases/month	3 cases/month	90%
3	3–4 cases/year Common to hear about outbreaks	2x baseline	3–4x baseline	95%
4	Expects certain prevalence Common to hear about outbreaks	2 cases/month	12 cases/month	90%
5	Frequently seen	4 cases/month	N/A	90%
6	Expects certain prevalence Common to hear about outbreaks	2x baseline	3–4x baseline	99%
7	2–3 cases/year	2 cases/month	N/A	Closer to 99%

The table includes participants' reported baseline of observed cases in their practices.

> *that we did not create a massive scare around this and put all of this effort in, to then have clients be a bit angry and upset that we have done all of that and actually, it was just a false alarm."*

— Participant 4: 25 years of experience, practice of 14 veterinarians.

3.2.4 Canine parvovirus

3.2.4.1 Relevance of disease

Out of the evaluated diseases, canine parvovirus is a disease that is most often seen by participants in veterinary practice. Parvovirosis is perceived as a very severe disease that appears as a peracute infection and is very intensive to treat. The participants also perceived canine parvovirus as more transmissible than canine leptospirosis among the canine population. Consequently, participants agreed about the relevance of parvovirus and did not consider it as a lesser threat for its lack of zoonotic potential:

> *"Parvovirus is severe enough that I think it warrants an active response. Just because it does not affect people does not mean it's not important, you know, there's a significant proportion of affected dogs."*

— Participant 4: 25 years of experience, practice of 14 veterinarians.

3.2.4.2 Transmissibility

Participants mentioned how canine parvovirus was particularly concerning given the risk of transmission within a veterinary practice. It is notable that parvovirus was the only pathogen for which some participants reported having a pre-established protocol in their practice:

> *"Our practice protocol is extremely tight. Anything that arrives at the practice that even looks like it may be parvo, a staff member will go out and a sample in the car park and the client will wait in their car with their puppy until we know it's negative, so we know whether we are taking them and putting them straight in isolation or what we are doing with them."*

— Participant 5: 16 years of experience, practice of 23 veterinarians.

3.2.4.3 Risk factors

Participants discussed risk factors that they believed were associated with parvovirus. Most of them mentioned how it usually affects puppies and unvaccinated dogs, while the remaining participants also mentioned other factors that they considered relevant, such as the socioeconomic background of the owners. The factor of socioeconomic background sparked some strong opinions during the interviews, while some participants believed there to be a link between the owner's background and the disease:

> *"Where I used to work, it was a rougher area, so we tended to see little outbreaks then. I think there was a particular set of clientele… what's the right word? *long pause* sort of poorer families? They did not vaccinate and get dogs from not necessarily good areas so I think that's why it tended to sight through a bit more."*

— Participant 2: 18 years of experience, practice of 3 veterinarians.

However, other participants disagreed and even had a strongly negative reaction when probed about this idea.

3.2.4.4 Clinically relevant thresholds

Study participants preferred higher notification and outbreak response thresholds for canine parvovirus compared to canine leptospirosis (Table 3). The predictive certainty values chosen for parvovirus were the highest among all the specific pathogens included in this study for some participants (Table 3), given the higher prevalence of disease and the ease of diagnosis of canine parvovirus. Figure 2 shows an overview of the clinically relevant notification threshold values for canine parvovirus.

> *"Parvovirosis nowadays, it's so easy to be certain, you do a snap test, takes you 5 min to know, they are quite accurate those types of tests. So, I think, in this case, I'd prefer to know with more certainty."*

— Participant 7: 4 years of experience, practice of 11 veterinarians.

3.2.5 Canine leishmaniosis

3.2.5.1 Knowledge about the disease

Most study participants had knowledge about the transmission routes and transmission vector of canine leishmaniosis. However, some of them were not aware of the epidemiological characteristics of the disease, and some misconceptions were also identified.

> *"I'm worried because positive dogs can spread it to another dog just by skin contact […] and it's a zoonotic disease, it can be transmitted to people from their dogs through skin lesions."*

— Participant 6: 1.5 years of experience, practice of 2 veterinarians.

3.2.5.2 Risk of entry in the United Kingdom

Some participants were greatly concerned about this pathogen entering the United Kingdom and spreading in the local canine population, which they believed was inevitable due to factors such as climate change and globalization. Participants also shared some strong opinions about the current dog importation practices into the country and how they exacerbate their concerns about the entry of exotic pathogens.

> *"It makes me really uncomfortable, that people think it's a wonderful idea to import dogs from Romania and from elsewhere […] there seems to be this mass push for charities and organisations to bring them in. I personally think it's a really bad idea to be importing dogs that have or are at risk of having a disease that we do not have. What we are doing really is creating a reservoir of a zoonotic disease that we did not previously have."*

— Participant 5: 16 years of experience, practice of 23 veterinarians.

Conversely, other participants argued that leishmania does not pose a risk for the canine population in the United Kingdom, since the vector is not currently present in the country.

> *"How do I respond to an outbreak of canine leishmaniosis? I do not believe canine Leishmania exists as an outbreak disease."*

— Participant 4: 25 years of experience, practice of 14 veterinarians.

3.2.5.3 Clinically relevant threshold

Most participants had seen chronic cases of leishmaniosis in their practice, although only two of them, namely, participants 3 and 5, had ever diagnosed a case in the United Kingdom (see Table 4). The excess incidence notification threshold for leishmaniosis was over zero cases for all the participants, although some of them specified that they would only want to receive a notification if the cases were autochthonous or if the disease vector became endemic in the country (Table 4). Participants did not provide an outbreak response threshold for this exotic disease as the notification threshold would be enough for them to change their in-practice behavior. Five participants preferred to set the predictive certainty values for leishmania to the lowest possible level, whereas the remaining two participants took the opposite approach and preferred to only receive a notification if the risk of receiving a false alarm was minimized (Table 4). Figure 2 shows an overview of the clinically relevant notification threshold values for canine leishmaniosis.

3.2.6 Canine babesiosis

3.2.6.1 Knowledge about the disease

According to participants, canine babesiosis was even rarer than leishmaniosis as they had never seen these cases in first-opinion practice. Some participants were even surprised to hear that babesiosis could affect dogs as they had only heard about it in the context of large animals:

> *"No clue about babesia in dogs, I have only seen it or studied it in horses. I've never even heard about it in dogs, no one has ever mentioned babesia to me."*

— Participant 6: 1.5 years of experience, practice of 2 veterinarians.

Participants were doubtful about the disease's transmission and clinical presentation, and misconceptions were identified about its zoonotic potential. When asked, participants did not believe that the knowledge of canine babesiosis among the veterinary profession in the United Kingdom is currently sufficient to adequately prevent, treat, or control the disease if an outbreak occurred.

3.2.6.2 Risk of endemisation

Those participants with knowledge about canine babesiosis were greatly concerned about the possibility of endemisation of this disease in the United Kingdom, given that the tick

TABLE 4 A summary of participants' preferred levels for the notification and outbreak response thresholds and predictive certainty values for canine leishmaniosis.

Canine leishmaniosis				
Participants	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
1	0 seen or diagnosed	1 case/year	N/A	90%
2	Seen cases but none personally diagnosed	1 case/year	N/A	The lowest end of the possible range
3	1–2/year referred	2 cases/year (if autochthonous) 4 cases/year (if not autochthonous)	N/A	95% traveled 90% untravelled
4	Seen cases but none personally diagnosed	No notification unless the vector is present in the United Kingdom	N/A	No notification unless the vector is present
5	Seen and diagnosed cases	1 case/year	N/A	90%
6	Seen cases but none personally diagnosed	1 case/year (if autochthonous)	N/A	99%
7	Seen cases but none personally diagnosed	1 case/year (if autochthonous)	N/A	The lowest end of the possible range

The table includes participants' reported baseline of observed cases in their practices.

TABLE 5 A summary of participants' preferred levels for the notification and outbreak response thresholds and predictive certainty values for canine babesiosis.

Canine babesiosis				
Participants	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
1	0 seen	1 case/year	N/A	90%
2	0 seen	1 case/year	N/A	The lowest end of the possible range
3	3 cases seen	2 cases/year (if autochthonous) 4 cases/year (if not autochthonous)	N/A	90% traveled 80% untravelled
4	Seen cases but none personally diagnosed	1 case/year	N/A	99%
5	0 seen	1 case/year	N/A	The lowest end of the possible range
6	0 seen	1 case/year	N/A	90%
7	0 seen	1 case/year	N/A	The lowest end of the possible range

The table includes participants' reported baseline of observed cases in their practices.

species that can carry *Babesia* spp. are currently present in the country.

> *"Babesia in untraveled dogs, I think it would be the most alarming disease. I think it's probably only a matter of time as well, if we have already got the vector that once we introduce the pathogen it becomes established in the dog population and becomes established in those ticks."*

— Participant 5: 16 years of experience, practice of 23 veterinarians.

3.2.6.3 Clinically relevant threshold

Most participants considered a single case of canine babesiosis in their area enough to receive a notification and chose to set the predictive certainty value at its lowest possible level (Table 5). Participants did not provide an outbreak response threshold for this exotic disease as they considered the notification threshold enough for them to change their behavior in practice. Figure 2 shows an overview of the clinically relevant notification threshold values for canine babesiosis.

3.2.7 Respiratory and gastroenteric diseases

3.2.7.1 Prevalence

The reported prevalence of canine syndromes was much higher than that of specific pathogens. The baseline of respiratory cases ranged from 3 to 7% of total consultations in first-opinion centers and up to 15% in a referral center (Table 6). The reported prevalence of

TABLE 6 A summary of participants' preferred levels for the notification and outbreak response thresholds and predictive certainty values for canine respiratory disease.

Respiratory disease				
Participants	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
1	2 cases/day or 10–15 cases/week	2x baseline	4x baseline	99%
2	3–5% of total consultations (Total of 80 consults/week)	2x baseline (10 cases/week)	12x baseline (50 cases/week)	90%
3	10–15% of total consultations or (Total of 50 consults/week)	1.6x baseline (8/week)	2x baseline (10/week)	95%
4	Unable to provide a number, but lower than GI syndrome	+20% case increase	N/A	The upper end of the possible range
5	5–7% of total consultations 2 cases/week	3x baseline	5x baseline	95%
6	3–5% of total consultations	3x baseline	4x baseline	99%
7	3–5% of total consultations 2 cases/week	Very high increase over the baseline	N/A	Closer to 99%

TABLE 7 A summary of participants' preferred levels for the notification and outbreak response thresholds and predictive certainty values for canine gastrointestinal disease.

Gastrointestinal				
Participants	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
1	4 cases/day or 20 cases/week	2–3x baseline	4-5x baseline	99%
2	7 cases/week 1 hospitalized/week	6/cases week or 3 hospitalized/ week	1.4x baseline 10 cases/week	90%
3	40% of total consultations	3x baseline	4x baseline	95 to 99%
4	Unable to provide a number, but higher than the respiratory syndrome	+20% case increase	N/A	The upper end of the possible range
5	Up to 50% of total consultations	3x baseline	5x baseline	99%
6	15–20% of total consultations	2x baseline	N/A	99%
7	>10% cases/week	Very high increase over the baseline	N/A	Closer to 99%

The table includes participants' reported baseline of observed cases in their practices.

gastroenteric disease ranged from 10 to 15% in first-opinion practice and up to 40–50% in referral centers (Table 7).

3.2.7.2 Severity

Participants considered respiratory disease to be less severe than gastrointestinal disease. They also discussed how some dogs' illnesses are often mislabelled by owners as respiratory disease, e.g., cardiovascular disease. The participants also mentioned how gastroenteric conditions are usually more of a concern for the owners and more intensive and expensive to treat.

> *"*referring to gastrointestinal disease* this takes more time, it worries me more and it's more expensive for the owner as well. They're also more worried, I mean, a sick dog, with diarrhoea and vomiting, for the owner, it's a very big concern and they come to see us very quickly."*

— Participant 6: 1.5 years of experience, practice of 2 veterinarians.

3.2.7.3 Clinically relevant threshold

The excess incidence values were also much higher in the case of syndromes compared to canine pathogens. Most participants provided values for the notification and outbreak response thresholds that ranged between 2 and 12 times over the baseline (see Tables 6, 7). The predictive certainty value was also the highest among canine syndromes and was set to the values of 95 to 99% for both respiratory and gastrointestinal diseases by most participants (see Tables 6, 7). Figure 2 shows an overview of the clinically relevant notification threshold values for canine respiratory and gastrointestinal diseases.

4 Discussion

To our knowledge, this is the first study that explores clinically relevant thresholds of case incidence and predictive certainty at which veterinary practitioners would want to be notified about potential outbreaks of canine disease. These clinically relevant thresholds represent veterinarians' opinions on which outbreak events would be impactful in practice and therefore warrant either being notified about disease anomalies in their area (notification threshold) or triggering an outbreak response (outbreak response threshold). Overall, we found that canine syndromes had higher preferred values of excess case incidence and predictive certainty for the notification and outbreak response thresholds compared to specific canine diseases. Exotic diseases, such as leishmaniosis and babesiosis, had the lowest values of excess case incidence, often totalling to a single case per month to trigger a notification and to change their behavior in practice, as participants perceived that exotic disease outbreaks are likely to be potentially impactful to their practices. Participants' approaches differed when exploring the predictive certainty of canine endemic diseases, as some of them wanted the highest possible values to avoid false outbreak notifications, while others preferred to keep this parameter at relatively low values to avoid missing out on potential clinically relevant outbreaks or in the case of false alerts to be reminded of the risks that canine infectious diseases can pose to their practices. The findings from the interviews with veterinary practitioners also allowed us to gain an understanding of how the behavior of veterinary clinicians is impacted by outbreaks of canine disease, as included in the codes within the "behavior change" theme (Supplementary material S3). For instance, during an outbreak, participants would increase testing practices for infectious diseases, start vaccination campaigns to protect the local dog population, and increase the frequency of communications with their clients to provide advice on preventative measures.

To achieve the aims of this study, we needed to explore the individual perspectives and experiences of small animal veterinary clinicians. Therefore, a qualitative methodology, consisting of structured and semi-structured interviews, was followed (24). Interview transcripts were analyzed using a hybrid approach to thematic analysis (25). This qualitative methodology is a novel approach to exploring veterinarians' experiences with canine disease outbreaks, although it has been previously employed in the fields of livestock health (26) and human health (27). The methodology developed in this study was applied to six canine diseases and syndromes that had been identified in a previous study (11) as the top surveillance priorities in the United Kingdom. All participants satisfactorily completed the interviews, and positive feedback was received regarding the usefulness and levels of engagement of the exercise. The information gathered from participants through both types of interviews was rich and allowed us to successfully complete the aims of the study. Thus, this study demonstrates a workable methodology to gain an understanding of which canine outbreak scenarios are relevant to veterinary practitioners and to define their corresponding clinically relevant outbreak notification thresholds.

For infectious diseases, most participants elicited low levels of predictive certainty at given notification thresholds to prioritize sensitivity over the specificity of an outbreak detection system. This risk-averse attitude will ultimately increase the number of outbreak alerts and the proportion of false alerts generated by the system. Most participants argued that they would rather receive false alerts for potential outbreaks that they consider clinically relevant than missing out on relevant information. Some participants even argued that eventually receiving false alerts would be useful for them to be reminded of potential epidemic threats, to improve their epidemic preparedness, and to include infectious causes in their differential diagnosis list. These findings were based on participants' responses to hypothetical disease outbreak scenarios rather than on practical experience from dealing with actual outbreaks in settings where an alert system had previously been established. We are aware that the outbreak detection systems that generate a high proportion of false alerts could lead end users to a loss of confidence and trust in the system (28). Only by testing this study's clinically relevant threshold for notification of outbreaks in real-world applications will we be able to understand whether they strike the right balance between sensitivity and specificity.

Overall, notification thresholds for specific infectious pathogens were set at very low levels of excess case incidence, which means that they would like to be alerted of disease anomalies at very low levels of risk. Thus, participants perceived the diseases in this study could represent an epidemic threat to their practices, which is not surprising since such diseases correspond to the top-priority canine diseases for surveillance in the United Kingdom, according to their impact on canine and public health, as found in a previously conducted study (11). The outbreak response threshold values were generally set to greater increases in case incidence than those of the notification thresholds. However, for certain diseases, the notification threshold values provided by some participants often overlapped with the values chosen for outbreak response thresholds by other participants. The reasons for this overlapping may relate to the variation in participant's perceptions of risk and characteristics of their practice. The variation in participant responses resulted in different ranges of values for both the notification and the outbreak response thresholds, which were wider for some diseases than for others, e.g., the outbreak response threshold for gastroenteric disease ranged from 4 to 5 times over the baseline, while, for respiratory disease, this threshold ranged from 2 to 12 times over the baseline. Although the specific reasons for this variation are unknown, it might be due to the fact that the impacts in veterinary practice of certain diseases are similarly perceived by veterinarians, while other diseases' impacts are not easily measurable by participants, therefore resulting in a wider range of opinions.

When discussing exotic canine diseases, both the notification thresholds and the predictive certainty values were almost always set to the lowest possible values. Participants also opted to not provide an outbreak notification threshold for the exotic diseases included in this study as they considered that the excess incidence levels of the notification threshold would be enough for them to take action and change their behavior in practice to respond to a potential outbreak. All of these factors indicated that participants perceived exotic disease outbreaks as potentially highly impactful to their practices. This might be because, as observed during the interviews, exotic diseases were perceived as very severe threats despite their epidemiological characteristics and treatment being not well known among veterinary clinicians. According to the decision theory, when making decisions that involve both high risk and high uncertainty, people were more likely to take on a conservative approach and overestimate the risk rather than underestimate it (29). However, as these diseases were not perceived as an immediate threat, participants also reported hardly ever thinking about them or carrying out any preventative actions. Similar attitudes were observed in a previous study where first-line practitioners were interviewed about their experiences with exotic equine diseases (30). In this study, participants reportedly presented a "firefighting approach" to veterinary medicine, where most of the time and effort were spent on immediate threats rather than on preventive or preparedness activities. While not providing an outbreak response threshold for exotic diseases, some participants did make the distinction between autochthonous and imported cases. The threshold value for imported cases was set at higher levels, as participants considered these cases to be sporadic, unrelated events that would not result in an outbreak, as the vectors of the disease are not currently present in the United Kingdom.

We propose an innovative methodology that uses veterinary practitioners' opinions to inform the selection of a notification threshold value in genuine applications of the stochastic canine outbreak detection models. An advantage of our approach is that it allows us to choose notification thresholds tailored to meet the needs of end users of a surveillance system (i.e., veterinary surgeons in practice). Reducing the proportion of outbreak alerts that are not actionable in clinical settings helps to prevent overloading veterinarians with unnecessary surveillance information while keeping their confidence in such a system. In contrast, the outbreak notification thresholds determined by existing statistical methods (31, 32) often alert end users about genuine statistical signals that are of no practical importance to health professionals. Another strength of the methodology developed in this study is that it can be applied to any pathogen or disease of interest so that it can be adapted to the epidemiological characteristics of any given region.

The clinically relevant thresholds derived from participants' needs together with the contextual information gained from the qualitative interviews about participants' experiences with disease outbreaks are intended to be used by SAVSNET as a guide to determine when to notify United Kingdom veterinary practitioners of potential outbreaks. The notification step will be a crucial step for the addition of veterinary clinician input into canine outbreak detection and notification, thus bridging the gap between end users and statistical data.

This study was limited by the number of participating veterinarians, due to the difficulties faced in the recruitment process. The conduction of this study coincided with the peak of the COVID-19 pandemic, which had an overwhelming impact on small animal veterinary practices (33). Furthermore, the number of pet-owning homes in the United Kingdom has significantly increased over the last few years (34), while the number of registered veterinarians in the United Kingdom has not increased at the same rate, partly because of Brexit (35). All these factors have contributed to an increase in the workload of veterinary clinicians, which hindered the recruitment for the study. Indeed, many of the veterinarians who were contacted during the recruitment process reported being interested in the project but having no time to spare to participate. Despite the limited number of participants, their varied backgrounds offered a rich insight into the opinions of veterinary professionals in the United Kingdom. Furthermore, personal experiences are subjective, and it is possible that participants incurred memory bias when recounting past events. The authors strived to compensate for these issues by immersing the participants in outbreak scenarios and asking them repeatedly to reflect and consider the impacts that such outbreaks could have in their practice, given the increased workload, zoonotic risk, and client communications.

In conclusion, this study constitutes a proof of concept and describes a qualitative methodology to define clinically relevant notification thresholds for canine disease outbreaks that are informed by veterinary clinicians and correspond to outbreaks with a significant impact on clinical practice. The methodology has been applied to six top-priority canine diseases and syndromes. Clinically relevant thresholds included a notification threshold and an outbreak response threshold, which represented increases in case incidence that would warrant an outbreak alert or activate an outbreak response, respectively. To the authors' knowledge, this is the first study that consults end users of a disease surveillance and outbreak notification system (i.e., veterinary clinicians) about their preferences for notification's excess case incidence and predictive certainty levels. The findings from this study indicate that the developed methodology is adequate to elicit the end-user opinion to establish clinically relevant outbreak alert thresholds. Future studies that apply this methodology should include a larger sample of participants to deepen the understanding of how veterinary clinicians' preferences vary depending on their experience and background so that outbreak alert thresholds are representatives of the population of companion animal veterinarians in the United Kingdom. The clinically relevant thresholds derived from the needs of veterinary practitioners participating in this study will be used by SAVSNET to inform its outbreak detection system and increase its utility as a strategic informant on the clinical relevance of disease outbreaks in the canine population across the United Kingdom.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

CT: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Writing – original draft, Writing – review & editing. ES: Supervision, Writing – review & editing. AR: Funding acquisition, Project administration, Resources, Writing – review & editing. JN: Writing – review & editing. FS-V: Conceptualization, Funding acquisition, Methodology, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This work was funded by Dogs Trust as part of SAVSNET-Agile.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fvets.2024.1259021/full#supplementary-material

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frontiers | Frontiers in Veterinary Science

TYPE Community Case Study
PUBLISHED 21 August 2024
DOI 10.3389/fvets.2024.1249925

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OPEN ACCESS

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RECEIVED 29 June 2023
ACCEPTED 06 August 2024
PUBLISHED 21 August 2024

CITATION
Dupuy C, Locquet C, Brard C, Dommergues L, Faure E, Gache K, Lancelot R, Mailles A, Marchand J, Payne A, Touratier A, Valognes A and Carles S (2024) The French National Animal Health Surveillance Platform: an innovative, cross-sector collaboration to improve surveillance system efficiency in France and a tangible example of the One Health approach. *Front. Vet. Sci.* 11:1249925. doi: 10.3389/fvets.2024.1249925

The French National Animal Health Surveillance Platform: an innovative, cross-sector collaboration to improve surveillance system efficiency in France and a tangible example of the One Health approach

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The French National Animal Health Surveillance Platform (NAHSP) was created in 2011. This network of animal health stakeholders was set up to improve surveillance efficiency for all health risks that threaten animal health, as well as zoonoses affecting human health. The NAHSP steering committee decides on the strategies and program of activities. It is composed of 11 institutions from both public and private sectors (policy-makers, scientific institutions, and representatives of farmers, veterinarians, hunters, and laboratories). A coordination team guarantees the implementation of the program and facilitates the activities of different working groups (WGs). Each WG is composed of technical experts with scientific, legal, and field knowledge from the sectors of animal health (livestock, companion animals, and wildlife), human health, and environmental health. Some WGs focus on a specific disease or health indicator, such as African swine fever or cattle mortality, while others cover cross-cutting topics, such as epidemic intelligence (EI), or specialize in aiding epidemiological investigations, such as the Q fever WG. The NAHSP stands out for its innovative approach because it is based on the concepts of consensus-building among participants, fostering collaboration, and embracing interdisciplinarity. Each proposal designed to improve surveillance is jointly developed by all the stakeholders involved, thereby ensuring its sustainability and acceptability among stakeholders. This process also has added value for decision-makers. As a pioneer platform, the NAHSP inspired the creation of two additional national surveillance platforms in 2018, one for plant health and the other for food chain safety. Both are organized in the same way as the NAHSP, which created a framework to place the emphasis on a One Health approach. For instance, four WGs are common to the three national surveillance platforms. This article aims to present this innovative approach to improve surveillance efficiency that could be of interest to other European countries or that could be rolled out at the European level.

KEYWORDS

animal health, surveillance, epidemiology, One Health, collaboration, consensus

1 Needs and challenges in animal health surveillance

The needs and challenges presented in this section are relevant for France but may also find relevance in other countries. Historically, most animal disease surveillance systems were designed as separate and stand-alone entities, with, for example, one system for a single species, sector, or notifiable disease. The interface between livestock and wildlife (e.g., organic farming, extensive farming, and urban farming), alongside the interaction between livestock/pets and humans (e.g., backyards), has increased over the past 20 years. This has led to increased disease transmission between these compartments, such as avian influenza and bovine tuberculosis (BT), highlighting the need to implement effective and integrated surveillance (1, 2). For instance, in France, certain diseases are monitored through various surveillance components involving different stakeholders. Influenza is monitored based on the assessment of the influenza virus in poultry, wild birds, swine, and humans. Bovine tuberculosis involves monitoring in cattle farms, at slaughterhouses, and in wildlife. Aujeszky's disease is monitored in swine farms, wild boars, and dogs. Integrating these components into a unified surveillance system for all diseases is challenging. This integrative thinking has been encouraged since the beginning of the 21st century through the One Health approach, but the main difficulty still lies in making the approach effective, sustainable, and efficient (3). Increasing the effectiveness of animal disease surveillance through an integrative approach helps identify and tailor more suitable prevention measures. It also helps prepare strategies for disease management or eradication.

Laboratory diagnostic methods are continuously improving, but the benefits are sometimes associated with more complex interpretations for epidemiologists. For instance, the interpretation of interferon-gamma (IFN-gamma) for bovine tuberculosis or polymerase chain reaction cycle threshold (PCR Ct) values for blue tongue requires laboratory expertise in addition to epidemiological knowledge. Improving a surveillance strategy involves having laboratory experts identify the most relevant methods to be used while considering their limitations to avoid misinterpretation. For instance, a positive bluetongue PCR result with high Ct values needs to be interpreted in light of the epidemiological context to discriminate between the active circulation of the virus and traces of earlier infection. The increasing complexity of the livestock sector, related to the international movement of animals, and the food and feed markets, means that more data are to be considered when working on animal disease surveillance. This also involves carrying out constant epidemic intelligence (EI) to help in assessing the risk of a disease being introduced into a country. Another aspect to consider is the diversity of stakeholders involved in surveillance, which include farmers, hunters, veterinarians, competent authorities, laboratories, among others. Their expectations and constraints are different and need to be taken into account when changes in the surveillance strategy are being considered, especially in the current context of financial limitations. Neglecting these considerations could lead to surveillance stakeholders finding the new strategy unacceptable and not implementing it as a result. These various aspects highlight the need to consider a variety of skills, such as field and laboratory expertise, risk assessment abilities, and knowledge of epidemiology, when working to improve surveillance effectiveness. All surveillance stakeholders should be involved in discussing topics of interest, understanding different perspectives, and reaching an agreement that maintains both scientific rigor and field pragmatism.

The rise in digitalization is helpful for gathering surveillance information and centralizing data. While financial support has been provided to develop new databases, it is far more difficult to obtain long-term human resources to analyze these data. For instance, in France, cattle mortality data have been used for syndromic surveillance (SyS) since 2013, but the sustainability of this approach is still challenging due to a lack of available and long-term human resources. The lack, or inappropriate timing, of data exploitation and feedback to surveillance stakeholders is one of the main issues in maintaining a high level of surveillance acceptability and stakeholder motivation. As an example, this has been demonstrated for bovine tuberculosis surveillance in wildlife in France (4). Finding new approaches to automatically and robustly produce relevant surveillance indicators with secure access is crucial; however, the indicators still need human interpretation.

Since the early 2010s, emerging animal diseases have been identified as a new challenge for disease surveillance (5). The outbreak of the Schmallenberg virus (SBV) in 2011, the COVID-19 pandemic in 2020, and the introduction of epizootic hemorrhagic disease into Europe in 2022 have highlighted the necessity to improve disease preparedness and response. Traditional surveillance approaches may not be sufficient in these cases. It is important to consider new methodologies, such as syndromic surveillance, and the research sector plays an essential role in identifying new methodologies to meet these needs. Implementing novel tools in practice remains challenging nonetheless. In addition, adopting a One Health approach is vital given the complexity of disease transmission, the ever-increasing movement of people, animals, and goods, and the increasing role of wildlife.

In light of these needs and challenges, a new approach was considered necessary. In 2010, stakeholders in France initiated a national brainstorming round table to suggest methods for achieving a paradigm shift. The subsequent action plan included the creation of a country-wide platform that became the National Animal Health Surveillance Platform, or NAHSP. This innovative approach is presented along with how it can provide a solution to meet these needs and challenges.

2 Development of the NAHSP

In 2011, the NAHSP was created to improve the efficiency of surveillance for all health risks that threaten animal health, as well as zoonoses that affect human health in France. The platform is a network of animal health stakeholders who work together to improve collaboration and increase efficiency. It is based on an agreement signed by the members of the NAHSP steering committee. Importantly, it is neither a legal entity nor a data-sharing platform.

The emergence of the Schmallenberg virus (SBV) in northern Europe in late 2011 provided the NAHSP with an opportunity to demonstrate its utility. A working group (WG) was rapidly established to propose a surveillance protocol to detect the potential introduction of SBV into France. This protocol was implemented by the French Ministry of Agriculture (MoA) at the beginning of 2012 and enabled the first cases to be detected at the end of January of the same year (6). A surveillance protocol was maintained until 2018, with the drafting of a surveillance report to support the competent authority's decisions in terms of surveillance and management of the disease (7). After this first successful proof-of-concept work, and after a few years of relevant activities with positive feedback from all stakeholders, the French MoA decided to extend the platform concept to plant health and food chain surveillance. The National Plant Health Surveillance Platform and the National Food Chain Surveillance Platform were thus created in 2018.

The governance of the NAHSP is overseen by a steering committee that is responsible for deciding on its strategies and program of activities. In 2023, the committee members represented 11 institutions from both public and private sectors: policy-makers, scientific institutions, representatives of farmers, veterinarians, hunters, and laboratories. These institutions are, in alphabetic order, mentioned in the following: ADILVA, an association of directors and managers of public veterinary analysis laboratories; ANSES, the French Agency for Food, Environmental, and Occupational Health & Safety; CIRAD, the French Agricultural Research Center for International Development; the French MoA; INRAE, the National Research Institute for Agriculture, Food, and the Environment; LCA, a federation of agricultural cooperatives; FNC, the national hunters' federation; GDS France, an animal health protection group; OFB, the French Biodiversity Office; SNGTV, a collective of veterinarians; and Santé Publique France, the National Public Health Agency (Figure 1). The NAHSP aims to support surveillance systems to meet their needs but does not make decisions regarding these systems. This decision process is attributed to surveillance system managers.

Several types of actions can be performed by dedicated working groups (WGs) to implement the NAHSP action plan, as mentioned in the following: (i) assist in the development and improvement of surveillance systems that the NAHSP supports; (ii) support the collection, analysis, and interpretation of surveillance data; (iii) facilitate communication of surveillance results, mainly through the NAHSP website or online restricted-access tools, to allow feedback to surveillance stakeholders and ensure suitable mainstream communication; (iv) support epidemiological investigations when cases are detected; and (v) perform national and international epidemic intelligence activities with both official and non-official data sources. Epidemic intelligence involves the collection, analysis, and interpretation of different sources of data to produce reports that are able to support decision-makers for further investigation and the prevention of potential health risks.

Currently, a total of 33 WGs have carried out activities concerning 31 topics of interest in several different sectors of animal health: bees, cattle, horses, pets, poultry, small ruminants, swine, and wildlife (Figures 1, 2). Some WGs focus on a specific disease or health indicator, while others are cross-cutting or are dedicated to supporting epidemiological investigations (Figure 2). Each WG includes relevant technical experts with field expertise as well as scientific and legal knowledge from various animal health (livestock, wildlife, and pets), human health, and environmental health sectors (Figure 1). In 2023, 396 experts from 86 institutions were part of at least one of the NAHSP WGs. Their work is supported by a technical support team of 10 full-time equivalent staff members, eight of whom are long-term staff members with skills in epidemiology, statistics, information technology, or communication. An NAHSP coordination team of two full-time equivalent staff members ensures the implementation of the program, coordinates different WG activities, and manages the technical support team (Figure 1).

The platform is funded mainly by the French MoA, which covers the salaries of the technical support and coordination teams. An audit was carried out in 2021 and found an estimate of €3 million in annual funding for the three epidemiological surveillance platforms combined (8). Experts participate in WGs on a voluntary basis, constituting indirect financial support for the NAHSP from their employers. It was estimated in 2022 that this support amounted to six full-time equivalent staff members for 345 experts from 75 organizations. Importantly, actions are prioritized to match the human and financial resources available. The impact of any conflict of interest is limited by the diversity of experts within each group and the consensus approach, which enables unanimous agreement to be reached.

Three core values underlie the activity of all components of the NAHSP: consensus, collaboration, and a 2-fold multi-sectoral

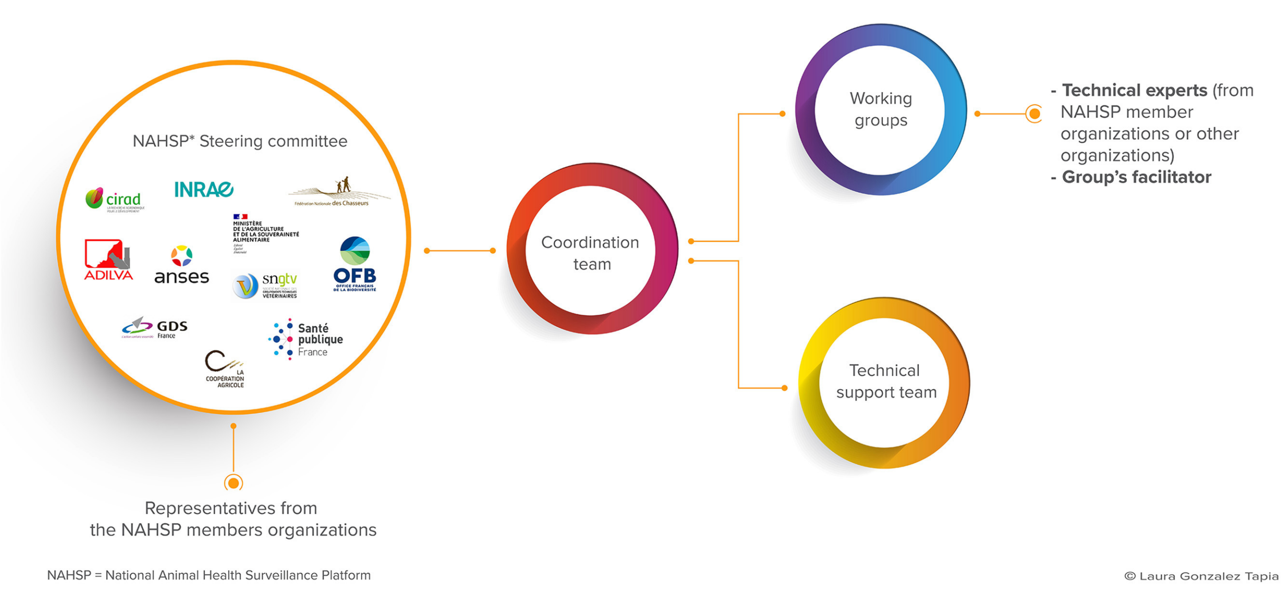

FIGURE 1
The NAHSP's organizational framework with its steering committee representing both the public and private sectors and its coordination team making the link between the steering committee, working groups, and the technical support team.

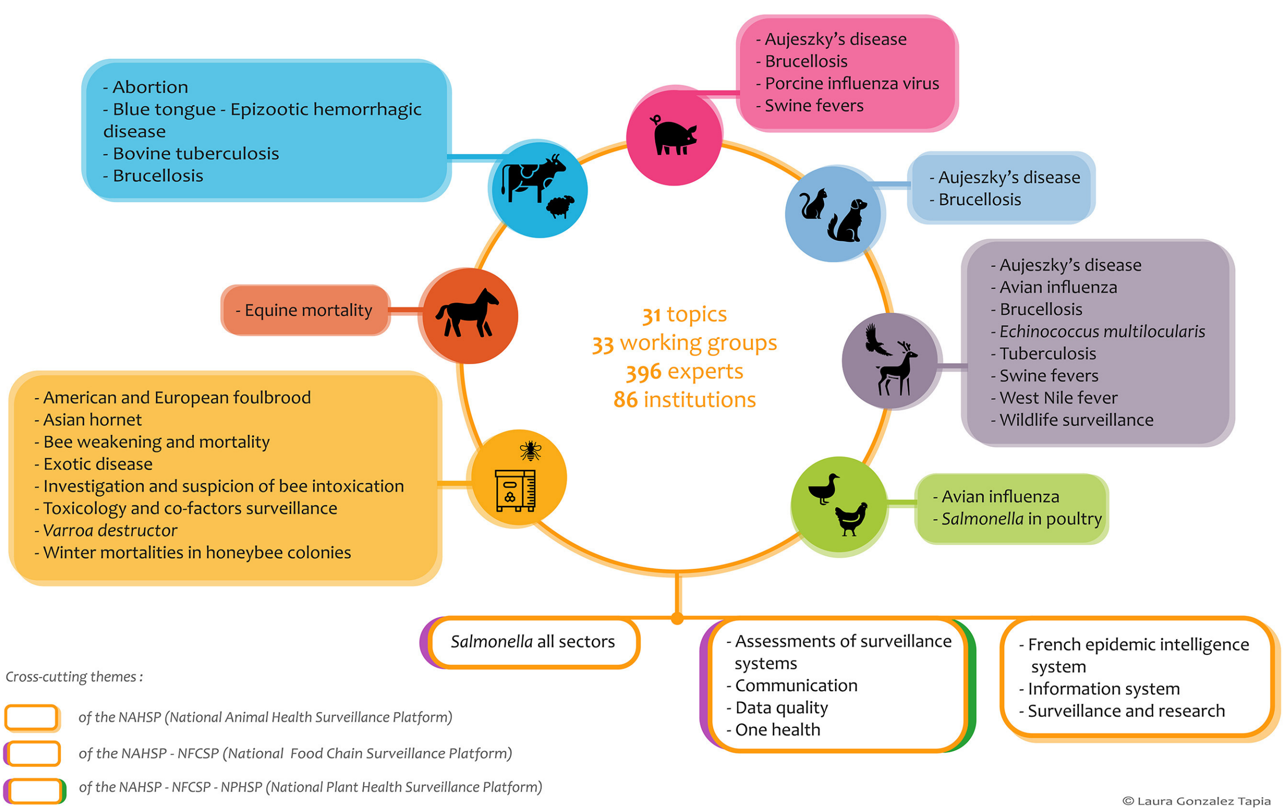

FIGURE 2
Topics of NAHSP working groups, which are composed of experts from animal health, human health, and environmental health sectors, depending on the scope of each WG.

and multi-partnership approach. Suggestions for improving surveillance efficiency are put forward by WGs through a co-construction process and validated by consensus. This involves allowing sufficient time to listen to each stakeholder, to understand the expectations and constraints of the stakeholders, and to take scientific innovations into account. This process decreases the risk of rejection by any of the surveillance stakeholders and increases the robustness of a WG's suggested solution because all stakeholders are part of the proposal process.

The platform's organizational structure and the type of actions carried out were designed to address some of the challenges presented in the introduction of this article. The tangible examples developed in the following section demonstrate the platform's added value.

3 Added value and One Health approach

Detecting emerging diseases is challenging in many ways. The scientific community (9) posits that syndromic surveillance (SyS) appears to be increasingly relevant to such a program. Based on French cattle mortality data, Perrin et al. demonstrated the relevance of SyS both for the early detection of unexpected health events causing cattle mortality and for assessing health events with an impact on cattle mortality (10). In 2013, the French MoA asked the NAHSP to implement an operational SyS system based on the cattle mortality data. A dedicated WG was created to co-construct the future SyS system with data providers, competent authorities, field experts, including farmers and veterinarians, researchers, and data managers. A pilot phase of this SyS system, known as the syndromic bovine mortality surveillance sytem (OMAR) alert tool, was launched in 2018 in various local administrative regions to calibrate the thresholds to use based on the best trade-off between sensitivity and specificity for surveillance needs (11). These thresholds were revised twice before 2022, when they were accepted as final values in these local regions. This tool is used on an ongoing basis and has demonstrated its ability to detect signals not otherwise found by field actors. It enables early detection of events on farms and results in the early implementation of solutions to animal health and welfare issues that might otherwise lead to increased mortality. Moreover, the WG used the same data to develop additional tools that complement the SyS system. These tools are reports or dashboards that are automatically updated with indicators at the national, regional, and farm levels. They were designed to meet other needs identified by the WG experts for both animal health surveillance and animal welfare. For instance, dashboards were implemented to support the following: (i) competent authorities when performing risk-based inspections; (ii) farmers and veterinary associations to enable them to set up prevention actions for fellow farmers and veterinary associations; and (iii) rendering plants to facilitate monitoring activities. These complementary tools integrated the OMAR tool and are clearly considered positive collateral effects of the implementation of the SyS system. Interestingly, the same mortality data can be used for purposes other than the detection of emerging diseases, such as the detection of animal welfare issues. It is particularly challenging to maintain stakeholder motivation to interpret weekly alert reports that will probably not detect any emerging disease for a long period of time because such emergences are, by definition, unusual events. Finding complementary objectives for the SyS tool was, therefore, beneficial. A second positive effect of the OMAR project was to foster constant improvement in the quality of the mortality data in terms of completeness, robustness, and timeliness. This improvement is useful for any other project that exploits these data, regardless of the project's purpose. The next step will be to interpret alerts from the OMAR tool and the human health mortality SyS system to anticipate zoonotic diseases or factors influencing both animal and human health, such as climate phenomena.

The surveillance of bovine tuberculosis (BT) is based on several complementary surveillance systems: (i) active surveillance on the farm; (ii) systematic surveillance at the slaughterhouse; (iii) active surveillance when animals are moved; (iv) active surveillance in wildlife; and (v) passive surveillance in wildlife. Links between animal health and environmental sectors (wildlife) are thus essential to provide effective surveillance, taking into account this type of multi-host pathogen. These systems involve several stakeholders, some of whom are common to several of the systems, while others are only part of one system. Data from these surveillance systems were not initially centralized in the same database and were analyzed separately when used. Stakeholders from the livestock, wildlife, or slaughterhouse sectors did not usually process, analyze, or discuss their data together. Since its creation in 2011, the NAHSP has addressed the topic of BT to increase the efficiency of surveillance.

Two separate WGs were created in 2011, one dedicated to on-farm BT surveillance, named the BT WG, and the other dedicated to BT surveillance in wildlife, named the Sylvatub WG. These two WGs were linked together from the start through the participation of the coordinator of one group as an expert in the other group and vice versa. A single group would have been very large, potentially leading to difficulties in working efficiently. Over several years, each group took the time needed to learn how to work collectively, considering the diversity of expertise within each group, and conducted its work plan in its own area, i.e., to improve its surveillance effectiveness via indirect information gathering through each WG coordination team. Strong working relationships were developed over time, with co-constructed surveillance zoning taking into account both the farm and wildlife surveillance indicators. The NAHSP technical support team helped these WGs to centralize, clean, and analyze their data. A restricted-access dashboard dedicated to Sylvatub was implemented to share the surveillance indicators and their representation in a secure yet user-friendly way with local and national surveillance coordination teams. Since 2019, an annual publication common to both BT and Sylvatub WGs has been published in a national epidemiological journal (12, 13). The publication is co-constructed with experts from both groups. Since 2022, common data analysis reports have been produced by the NAHSP technical support team as input for these WGs, stimulating ideas on how to improve surveillance effectiveness and as support material for the competent authority (MoA), which is required to forward official indicators to the European Food Safety Authority. The automation of the data analysis process has saved time and increased data quality. This automation process is carried out as soon as it has been identified as relevant and efficient for any of the NAHSP topics.

Although data related to outbreaks detected through slaughterhouse surveillance were taken into account by the

BT WG, there was no expert from the slaughterhouse sector in this WG. Consequently, actions to improve BT surveillance in slaughterhouses were not taken into consideration by this WG. In 2020, a third WG dedicated to BT was created to focus on BT slaughterhouse surveillance. The coordinator of the BT WG is part of the coordination team of this BT slaughterhouse WG. Slaughterhouse data analysis was automated, and a user-friendly dashboard was created, with the support of the NAHSP technical support team. A step-by-step approach was chosen to gradually increase the integrative approach to bovine BT surveillance. These WGs are also a place where experts can regularly discuss ideas and feel free to exchange their points of view on the situation of BT surveillance, even when there are no outbreaks. These discussions help facilitate communication in times of crisis, as the same stakeholders are involved and have already been working together for a long time. This is a highly valuable positive collateral effect of all NAHSP WGs.

Animal health surveillance cannot be considered a stand-alone unit due to globalization, which leads to an international movement of animals, food, feed, and people. Importantly, globalization is associated with an ever-increasing risk of new diseases or health threats being introduced into a country, an aspect that must be considered by both competent authorities and all surveillance stakeholders. In this regard, the NAHSP was tasked with developing a national and international epidemic intelligence (EI) project. Since the creation of the NAHSP in 2011, a dedicated epidemic intelligence WG has been set up. This WG includes representatives of epidemic intelligence end users (competent authorities and representatives of farmers, veterinarians, hunters, and laboratories), researchers of EI methodology, and epidemiologists (14). Official and non-official data are analyzed by the NAHSP technical support team (1.5 full-time equivalent staff members). An EI editorial board, comprised of the competent authority and epidemiologists, meets weekly as it is responsible for producing EI publications. This editorial board relies on its national and international network of experts to complement its interpretation. Weekly, seasonal, and "breaking news" reports are generated and made public through the NAHSP website (15). The EI WG has confirmed the value of EI publications in increasing the awareness of surveillance stakeholders and helping prevent diseases from entering France. The NAHSP EI process has gradually evolved in several ways. An increasing number of data sources are considered for EI production through the support of researchers, with, for instance, the implementation of a tool known as "Padiweb" for media data analyses (16). This tool has been in routine use since 2022. More epidemiologists have joined the editorial team for its weekly meetings (from three people in 2011 to 14 people in 2023). This increases the robustness of interpretation through multiple viewpoints and helps identify additional experts to contact as needed to investigate certain signals in more depth.

For zoonotic diseases, such as West Nile (WN) fever, both animal health data and human health data have been considered for the creation of the EI team. Before 2020, only animal health experts were involved in the interpretation. Since 2020, human health experts have also been involved in the development of the WN seasonal report, and since 2022, for WN weekly reports. During the SARS-CoV-2 period, the EI teams monitored animal cases through a dedicated report updated 13 times from April 2020 to February 2022. Similarly, for WN, the SARS-CoV-2 report was also produced initially with a team of animal health experts and then extended to include human health experts. Data analyses within the EI team were also improved over time, from manual analysis based on Excel files to automated data analyses using R. This has made it possible to save time while increasing quality. These examples demonstrate the NAHSP's ongoing improvement process and step-by-step approach when implementing improvements.

Concerning the measurement of success, there are no formalized indicators on the usefulness or success of the work of the NAHSP but there are several examples of successful projects. Each year, several national regulations are issued or amended by the MoA based on work produced by the platform's WGs. Examples include surveillance of bovine tuberculosis, avian influenza, and blue tongue. Dashboards are used by surveillance stakeholders both during peacetime between outbreaks and during emergencies, receiving positive feedback (tuberculosis, avian flu, epidemic intelligence, etc.). The data analyses performed are used by the national competent authority to submit official indicators to the European Food Safety Authority or European Commission (tuberculosis, blue tongue, salmonella, etc.). The time required to analyze surveillance data has been greatly optimized by both the automation of data analysis and the improvement of the data collection process. For instance, while 1,600 h were needed to analyze bovine tuberculosis data in 2019, only 300 h/year have been required since 2022.

4 Constraints and challenges

Since 2011, stakeholders involved in the NAHSP, from steering committee members to WG experts, have been satisfied with what was considered an innovative approach with shared governance between the public and private sector and a co-construction method based on the principle of consensus. However, managing this organization presents challenges in several aspects.

First, sustainable financial resources are difficult to find. Since its creation in 2011, the main source of funding has been the public sector, i.e., the French MoA, which has funded the human resources needed for coordination and technical support teams. Since 2011, the NAHSP has demonstrated its usefulness and has been receiving an increasing number of requests to address issues within the scope of surveillance, even as public funding has been decreased. There is, thus, a discrepancy between its objectives and the means available to achieve them, considering the challenge of ensuring sustainable financial support. Exploring other sources of funding that comply with keeping a not-for-profit approach while remaining independent from potential private financial support will be necessary. This constraint also highlights the need to prioritize actions, which is one of the tasks of the steering committee.

Second, the benefits of developing long-term WGs have already been described, but it has proven difficult to maintain WG organization and facilitation over time. Without a dynamic and committed team of experts in the appropriate field to lead the WG, it cannot operate correctly. In this regard, staff turnover can affect WG coordination. To limit this risk, it is preferable to set up an internal WG coordination team when possible. Another challenge with long-term WGs is to maintain experts' motivation to contribute as these contributions are made on an individual and voluntary basis and depend on the parent institution's willingness to grant experts sufficient time. Therefore, it is essential that experts benefit from their participation in WGs, for example, through network-building and information exchange. They also need to be aware that their contribution to the improvement of surveillance efficiency in practical ways is of great value.

Finally, although the NAHSP has improved its One Health approach over time, much work remains to be done. New environmental and climate concerns need to be better integrated and addressed. This is particularly important for topics related to bee health and vectorial disease surveillance, but these concerns should be considered for many topics in animal health. Looking to the future, new methodological approaches should be investigated to address this challenge effectively, which will, in practice, lead to a broadening of the scope of expertise represented in existing WGs.

5 Lessons learned

Over 10 years of operation, the NAHSP has demonstrated its value in supporting managers in the surveillance of animal health and disease to improve surveillance efficiency. Several examples of this are described in Section 3. The NAHSP has adopted the One Health philosophy over time through different approaches. Based on the platform's decade of experience, it appears that an incremental approach with a commitment to continuous improvement is a good strategy for building a solid and consistent One Health approach. The membership of the steering committee has also evolved over the years. The environmental sector was included via the French Hunters' Federation and the French Biodiversity Office in 2013, and then the human health sector was included via the National Public Health Agency in 2022. Experts from these institutions were already participating in some of the WGs before they became members of the steering committee, but this was a step toward closer cooperation. Similarly, the same approach was applied to the WGs. Since 2011, a swine flu WG has focused on supporting the RESAVIP network, a surveillance system that monitors the swine influenza A virus. Its goal is to describe the virological and epidemiological patterns of the virus and to detect the occurrence of new patterns that could have an impact on animal or human health (17). Until 2021, this WG included only animal health experts. However, it was decided that a human health expert would be invited occasionally, when information related to the impact of the virus on human health was discussed. After a year, initial feedback revealed that this was not an appropriate way of operating, primarily due to a large number of gaps in meeting invitations. In 2022, it was therefore decided to systematically invite the human health expert. The following year, it was further decided to include this expert in the WG. The same step-by-step approach was implemented for the WG investigating Q fever. Naturally, a certain amount of time was needed for animal health stakeholders to learn how to work together (2019–2021), after which the group added two experts from the human health sector, who have been part of the WG since 2022.

To build a One Health approach in the same incremental manner, interactions between WGs on the same topic can gradually increase to allow each WG to take shape and then develop new cooperative relations between existing WGs. The BT WGs illustrate this approach effectively (see Section 3).

In 2018, a new step in improving the One Health approach was achieved when two more surveillance platforms were set up, one on plant health and the other on the food chain. A coordination group common to both platforms was created simultaneously and was composed of each platform's coordination team. This group provided a suitable framework for exchanges and for identifying joint work. Since 2018, five WGs common to two or three platforms have been created (Figure 2). One WG is dedicated to a zoonotic disease (*Salmonella*), while the others are dedicated to methodological topics.

These examples show that there was no magic recipe for the NAHSP's implementation of a successful One Health approach. Each situation needed a tailored strategy. For WGs, the best way was found to be through co-construction with WG experts, keeping in mind the need for flexibility, because one set-up may meet the requirements at one point but a different set-up may be best when other experts are involved. The key is to enable constant reevaluation. It has, however, become clear that it is easier to develop a One Health approach between crises or outbreaks than during crises because experts need to be given time to develop working relationships and mutual understanding. The NAHSP aims to implement a sustainable One Health approach, and as such, WGs are designed to be long-term groups. Unsurprisingly, short-term WGs have rarely been created.

The "platform concept" based on consensus, collaboration, and a multisectoral and multi-partnership approach can be applied to other fields. The extension of the concept in France from animal health to plant health and food chain safety demonstrates this principle. Although our examples relate to France, this concept could be applicable in other countries, provided there are similar needs identified.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

CD wrote the first draft of the article and took into account the co-authors' remarks. All authors critically reviewed the content of the article and gave the final approval for the version to be published.

Funding

This work was supported by the The National Animal Health Surveillance Platform benefits from the French Ministry of Agriculture funding.

Acknowledgments

The authors would like to warmly thank all those who contributed to the NAHSP, especially the experts participating in the NAHSP WGs, the steering committee, the technical support team, and all the surveillance stakeholders. We would also like to thank those who are no longer directly involved in the NAHSP but worked on its creation before 2011 and together built what the NAHSP has become. Finally, our thanks go to Delphine Libby-Claybrough, professional translator, and Craig Stevens, MA, DESS, ELS, medical writer, and life sciences editor, for English language editing. Our thanks also go to Laura Gonzalez Tapia for the figure design.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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