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Developing the pillars for a canine disease surveillance and outbreak response framework in the UK

Developing the pillars for a canine disease surveillance and outbreak response framework in the UK

By

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Abstract

Currently, no coordinated strategies exist for surveillance and control of canine diseases worldwide. Thus, our ability to detect and respond to outbreaks is limited, leaving canine populations unprotected. This thesis addresses this problem by focusing on four objectives:

Prioritisation of canine diseases for surveillance and control in the United Kingdom: Using a stakeholder opinion-led approach, criteria for evaluating diseases were established through a multicriteria decision analysis, and a consensus among 19 participants on the disease ranking was achieved through a Delphi technique. Leptospirosis, babesiosis, and respiratory disease were the top-priority endemic diseases, exotic diseases, and syndromes, respectively.

Developing a text mining tool to harness electronic health records for early disease detection: Canine parvovirus was used to illustrate this methodology. A dataset with cases was established for key term extraction from clinical annotations. Key terms were grouped into regular expressions, that were used to define the criteria for a rule-based classifier to estimate a parvovirus likelihood score for each dog. The tool performed successfully in a new dataset.

Exploring clinically relevant thresholds for outbreak notification: Seven veterinarians were interviewed to elicit their preferred levels of case incidence and predictive certainty of the alerts. Interview data were transcribed and coded for relevant elements through a thematic analysis. Notification thresholds were defined for six top-priority canine diseases.

Developing an outbreak response framework for canine diseases in the UK: A response framework was designed and tested in its application to a real-life outbreak through a formative process evaluation. Nine veterinarians were interviewed to improve the design and implementation process of a future response framework, and a Strengths, Weaknesses, Opportunities and Threats analysis identified strategies for its nation-wide implementation.

Together these studies create the opportunity to improve the detection and response to canine disease outbreaks and can be used to inform a surveillance and control system for the UK.

Acknowledgements

I would like to acknowledge all my family, friends, and colleagues, who have supported me throughout this PhD.

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To all my colleagues at Bristol Veterinary School, with a special thank you to Erika, Alessandro, and Sharyn, for welcoming me into Langford and making this PhD so enjoyable, and to my friend, colleague, and roommate Rocío, for your immeasurable loyalty and kindness.

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Dedicated to my father,

Dr Manuel Tamayo Sáez.

Covid-19 statement

The COVID-19 pandemic significantly impacted the research conducted in this thesis. A full summary of the impacts that the pandemic has had on the chapters of this thesis can be found below:

Chapter Two: prior to the COVID-19 pandemic, the data collection for this chapter consisted in a qualitative group interview, namely, a Nominal Group Technique, which involved an in-person meeting with participants. Through this approach, the data collection for this Chapter would have been completed in one day. However, due to the pandemic, an alternative methodology, consisting of a Delphi panel technique, was developed, so that the data collection could be asynchronous and conducted online. While this new approach allowed me to obtain satisfactory results, it was significantly slower than the initially developed methodology (several weeks vs one day). Further, since the development of the remaining chapters of this thesis was based on the results of the prioritisation exercise, the disruption in this chapter resulted in a subsequent delay of the overall development of the thesis.

Chapter Four: before COVID-19, this chapter's data collection consisted in a series of focus group meetings with veterinary practitioners. However, as a result of the pandemic, veterinary practice services in the UK were overwhelmed, with many shutting down to offer only emergency services. This meant that the workload for veterinary clinicians was significantly increased, and therefore many potential participants, although expressing their interest, refused the invitation to participate. As a result, this chapter's methodology was changed to one-to-one interviews, to accommodate for the schedule of participants. Further, the sample size in this chapter was smaller than anticipated. This limitation was also experienced in Chapter Five.

Details on changes due to the pandemic are described throughout the dissertation.

Author's declaration

I declare that the work in this dissertation was carried out in accordance with the requirements of the University's Regulations and Code of Practice for Research Degree Programmes and that it has not been submitted for any other academic award. Except where indicated by specific reference in the text, the work is the candidate's own work. Work done in collaboration with, or with the assistance of, others, is indicated as such. Any views expressed in the dissertation are those of the author.

SIGNED: Carmen Tamayo Cuartero DATE: 30.10.2023

Abbreviations

AI: Artificial intelligence

AMR: Antimicrobial resistance

APHA: Animal and Plant Health Agency

BSAVA: British Small Animal Veterinary Association

DEFRA: Department for Environment Food and Rural Affairs

EHR: Electronic Health Records

MCDA: Multicriteria Decision Analysis

PCR: Polymerase Chain Reaction

RCVS: Royal College of Veterinary Surgeons

SAVSNET: Small Animal Veterinary Surveillance Network

SWOT: Strengths, Weaknesses, Opportunities and Threats

UKHSA: United Kingdom Health Security Agency

VMD: Veterinary Medicines Directorate

WHO: World Health Organisation

WOAH: World Organisation for Animal Health

WSAVA: World Small Animal Veterinary Association

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Chapter One. Introduction and literature review

1.1. Introduction

1.1.1. Background

Infectious diseases have constituted a threat for the health and wellbeing of humans and animals since ancient times (Barberis et al., 2017). Epidemics have plagued us throughout history (Sakai & Morimoto, 2022), costing many lives and having a significant impact in the economy, hindering societal progress. This has become more apparent than ever in recent times due to the COVID-19 pandemic (Pak et al., 2020). To address this issue, disease surveillance and response systems have been established globally to prevent and mitigate the impacts of infectious diseases, at national (*APHA Vet Gateway - Surveillance and Diagnostics*, 2022) and international levels (FAO, 2023; WOAH, 2023c).

Over the last decade, the interest in companion animal infectious diseases has grown. Research initiatives have been established that acknowledge the importance of these diseases, mainly in the UK (*SAVSNET, University of Liverpool*, 2023; *VetCompass, Royal Veterinary College*, 2023), United States (Glickman et al., 2006a; Kass et al., 2016a), Canada (Anholt et al., 2015), Australia (McGreevy et al., 2017), and New Zealand (Muellner et al., 2016). While these initiatives constitute great improvements in this field, their extent and real-world impact is limited in nature, since they are research projects with limited funding and limited ability to influence decision making. To this date, no nation-wide, coordinated strategies for the timely surveillance and control of companion animal diseases exist, neither in the UK nor in other countries. This leaves canine populations unprotected, as we currently do not have access to standardised data on the national prevalence of canine diseases, or a way to promptly detect and respond to potential outbreaks.

There are several potential reasons for the current lack of disease surveillance systems for dogs, or companion animals in general. Resources are limited, and other animal species have historically been prioritised when developing these programmes, namely, farm animals. This is because of the economic significance that infectious diseases have on livestock, for instance, the 2001 Foot and Mouth (FMD) disease outbreak in the UK is estimated to have caused economic losses in excess of £8 billion (Thompson et al., 2002). Another potential factor is the focus on farm animals and their products because of the risk they pose to public health, given the emergence of threats of world-wide impact, such as avian influenza (ECDC, 2023b).

Furthermore, the role of livestock in the emergence of antimicrobial resistance has also been a prominent topic of discussion in recent years (Woolhouse et al., 2015). In essence, companion animal diseases have not constituted a priority for governments and epidemiological research in the past as these have historically not been perceived as a public health threat.

However, it appears like institutions are beginning to acknowledge the importance of companion animal diseases and the role that they play in the wider public health sector. For instance, recent UK government reports on antimicrobial usage and resistance explicitly recommend the development of national indicators to compare human and companion animal antimicrobial usage and joint horizon scanning to monitor resistance bacteria in both humans and companion animal species (GOV.UK, 2017a). Studies have also reported the high prevalence of resistant genes in pet bacterial isolates (Haulisah et al., 2022), and investigated the potential transmission of resistant bacteria between pets and their owners (Bhat et al., 2015; JPIAMR, 2020; Y. Li et al., 2021). Regarding the zoonotic transmission of diseases, there are notorious risks that emerge from dogs, such as rabies, for which dogs remain as the main reservoir worldwide (WHO, 2023), or leptospirosis (Schuller et al., 2015). Beyond these well-known diseases, many other canine pathogens and parasites pose a risk to humans (Francois Watkins et al., 2021; Ghasemzadeh & Namazi, 2015a), either via direct contact (Álvarez-Fernández et al., 2018; Robb et al., 2017; Walther et al., 2012), animal bites (Oehler et al., 2009), contact with excretions (CDC, 2021a; Santos et al., 2021), or by dogs acting as intermediary/accidental disease hosts (Dyachenko et al., 2008; Rojas et al., 2021; Tse et al., 2019).

On top of these public health considerations, canine infectious diseases are relevant, since they pose a threat for dogs' wellbeing, either acutely or as chronic, debilitating illnesses. Over recent decades, the human-canine bond has continued to grow across societies, and pets, particularly dogs, are now often considered as part of the family in many countries (Power, 2008). This is also evidenced by the steep increase in pet owning families, particularly since the COVID-19 pandemic (Ho et al., 2021; PDSA, 2022). As a society, we are increasingly caring for the health and wellness of pets and therefore perceive potential canine health risks as an important matter in its own right, regardless of whether these also pose a risk for humans.

Given the above-mentioned impacts of canine infectious diseases, both on dogs' health and on the wider public health, and society's interest in improving animal welfare (Sinclair et al., 2022), there is a strong need to develop a strategy to efficiently detect and respond to epidemic threats in canine populations. The present PhD project emerged in response to this need, as part of a wider initiative named SAVSNET-Agile (*SAVSNet-Agile, University of Liverpool*, 2019). This initiative builds on the previously established Small Animal Veterinary Surveillance Network (SAVSNET) (*SAVSNET, University of Liverpool*, 2023), that collects companion animal electronic health records from over 500 veterinary sites and most veterinary diagnostic laboratories in the UK to investigate disease trends across the country. These data have been utilised to study multiple aspects of companion animal disease, such as antimicrobial prescription and usage (Singleton et al., 2021), prevalence of infectious diseases (Jones et al., 2014a), pet owner demographics (Sánchez-Vizcaíno et al., 2017), risk factors of disease (Rigas et al., 2022), treatment of chronic conditions (Green et al., 2022), and factors that have an impact on animal welfare (Norris et al., 2023). SAVSNET-Agile was set up to develop state of the art tools in the fields of data science, epidemiology, microbiology, and text mining, to improve canine health in the UK. Within SAVSNET-Agile, the present PhD project aims to design a coordinated disease surveillance and response system for canine populations in the UK. This aim is achieved through the development of tools to improve the early detection of diseases, as well as a framework for the rapid and coordinated response to canine disease outbreaks. This framework will cover endemic diseases (present in the country and with an expected prevalence throughout the year), and exotic diseases (not normally found in the country, only sporadic cases, usually imported from other countries)

1.1.2. Structure of this thesis

The work described in this thesis aimed to develop tools to improve the surveillance of canine diseases and to design a framework of response to canine disease outbreaks. The present chapter constitutes an introduction to this work and sets the scene with an overview of the contents of this thesis (Figure 1.1), as well as a review of the most relevant literary findings in the field of disease surveillance and outbreak response with a focus on canine disease.

Chapter Two is entitled “A stakeholder opinion-led study to identify priority canine infectious diseases for surveillance and control in the UK”, where canine endemic diseases, exotic diseases, and syndromes, are prioritised for inclusion in a prospective system of surveillance and response.

Chapter Three, entitled "Development of a text mining tool to harness electronic health records for the early detection of canine diseases", explores the feasibility of using text mining tools to enable the early detection of specific canine pathogens using pre-diagnostic data.

Chapter Four's title is "Setting clinically relevant thresholds for notification of canine disease outbreaks to veterinary practitioners: an exploratory qualitative interview study", where a methodology is developed to establish outbreak notification thresholds that are informed by end-user opinion.

Chapter Five is entitled "Designing, evaluating, and exploring strategies for implementation of a framework of response to canine disease outbreaks in the UK", in which all the relevant elements of an outbreak response are integrated in a standardised framework.

Lastly, Chapter Six consists of a concluding discussion of the findings of the present thesis, as well as recommendations for future research initiatives.

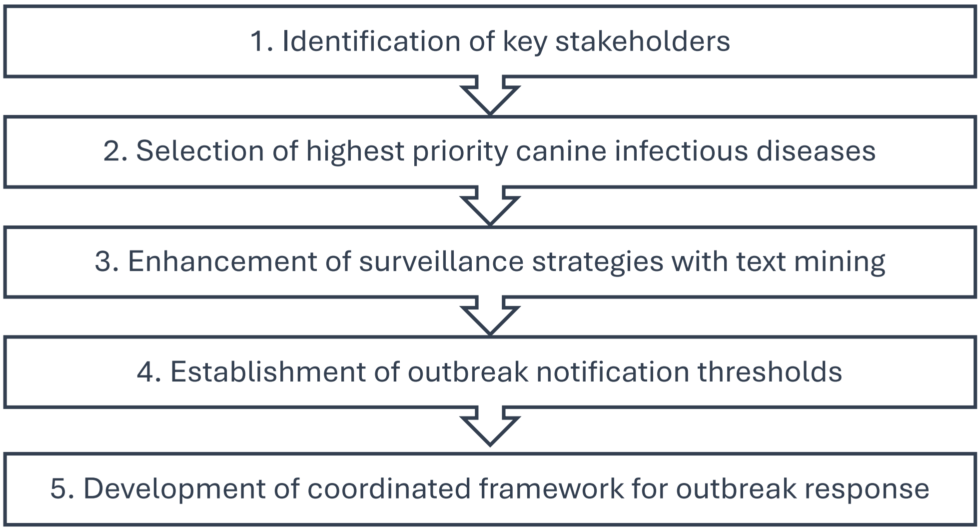

Figure 1.1. Outline of the work described in the present thesis.

1.1.3. Contribution to knowledge and research questions

The main gap in knowledge that this thesis' body of work contributes to is the existing lack of described preparedness plans for outbreak detection and response to canine infectious diseases. Having access to a robust, evidence-based epidemic preparedness plan is essential for the prevention of the spread of infectious diseases, as well as for the mitigation of the impacts that these have in the population (WHO, 2022b). The absence of such preparedness strategies lead to inefficiencies in outbreak detection and response efforts, which amplify the adverse impacts on public health and well-being, and the broader economy (Bochner et al., 2023). This thesis contributes to knowledge by proposing a framework of canine disease detection and response, that enables moving from ad-hoc, one-time interventions, to standardised outbreak responses that follow a unified approach, based on expert knowledge and research, and informed by the needs of relevant stakeholders. Each of the research questions included in this thesis addresses a specific gap in the knowledge, which all contribute to the overarching need for an improved canine disease surveillance system and a standardised outbreak detection and response framework. Overall, the present thesis aims to not only contribute to theoretical knowledge, but also to develop actionable resources with useful practical applications.

The first research question, addressed in Chapter Two, is to determine which canine diseases should be prioritised for surveillance and inclusion in a national surveillance and response system, as well as who are the actors that should be involved in the decision-making process when designing such framework. The latter is achieved through a stakeholder analysis, where the most relevant institutions for the companion animal health sector are identified, and representatives of these institutions are consulted in a consensus-building exercise to achieve the former. The results of this study provide a benchmark on which canine pathogens and syndromes to focus on for future research initiatives and policy decisions, that is informed by the opinion of relevant stakeholders for the companion animal health sector. Further, this work contributes to knowledge by providing a methodology to prioritise diseases for intervention that is suited to UK canine populations, which can be used as a blueprint for other countries.

The second research question, developed in Chapter Three, consists in assessing how the surveillance of canine infectious diseases can be streamlined to enable the early detection of disease anomalies using text mining tools to analyse pre-diagnostic surveillance data. This work contributes to the improvement of the surveillance of canine diseases in the UK, by developing a method for pathogen-specific surveillance, that complements existing methods, i.e., laboratory-based surveillance and syndromic surveillance based on veterinary practice data (A. Radford et al., 2010). This contribution aims to mitigate some of the current limitations of the existing systems for companion animal disease surveillance, namely the low specificity of detection of syndromic surveillance, and the difficulty to link veterinary clinical data with corresponding laboratory diagnostic results.

The third research question of this thesis (Chapter Four) focuses on when to notify end-users of a prospective system of surveillance and response about relevant outbreaks of canine disease. This is achieved by conducting qualitative interviews with a sample of small animal veterinary clinicians, to understand the impacts of canine outbreaks in practice, and establish appropriate threshold levels for outbreak notification. This work contributes to knowledge by providing a method to help establish outbreak notification thresholds that are clinically relevant to veterinary practitioners, which relies not only on statistically significant signals, but also on clinician's opinion. This method minimises the number of non-relevant outbreak alerts, thus saving end-users time and efforts that would otherwise be spent on these alerts. Further, notification thresholds developed in this study for selected canine diseases will be incorporated into SAVSNET's system of alert for veterinary practices, thus having a direct, real-world application to improve the detection of and response to actionable canine outbreaks.

This thesis' final research questions (Chapter Five) are concerned with how to design and evaluate a framework of canine outbreak response, and what are the best strategies for its improvement and future implementation at a national level. To achieve the first, a formative process evaluation is conducted, where a response framework is designed and evaluated in its application to a real-life outbreak of canine disease. The second aim is achieved through the conduction of qualitative interviews with veterinary clinicians on their needs and expectations from such framework, and a SWOT analysis to identify strategies for its implementation in the UK. This chapter contributes to the overarching gap in the knowledge addressed in this thesis, by providing an unified framework for outbreak response, and describing a method to monitor the performance of such framework, that can be used to document lessons learned and improve in future response interventions. Further, this study also contributes to knowledge by providing a series of evidence-based recommendations and strategies for implementation, which can be used to inform the development of future policies by government bodies that aim to establish a framework for canine outbreaks at a national level.

1.2. Literature review

This literature review focuses on retrieving relevant publications and documents, to critically assess previous efforts to detect and respond to canine disease outbreaks. Given the novelty of this study, the access to literature on this specific subject, i.e., rapid detection and response to canine outbreaks, with a focus on animal health, is limited. For this reason, it was necessary to draw knowledge from similar research conducted in humans and other animal species. Publications retrieved in this literature review were assessed according to the species primarily affected by the disease(s) in question, and according to the main focus of said publication, i.e., whether they intended to improve animal health and welfare, or focused on the protection of human and public health. For the present thesis, the most relevant publications were those that described systems of surveillance and response for canine diseases, with a focus on animal health and welfare. Conversely, less relevant publications were those that described these systems in humans or animal species other than dogs, e.g., livestock or exotic animals, with a focus on protecting human health. Those publications that described either systems of surveillance and response in animal species other than dogs, with a focus on animal welfare, or such systems for canine diseases, with a focus on human health, were considered of medium relevance. This is exemplified on Figure 1.2. Additionally, this literature review includes a section about disease surveillance and its different types, as well as the definition of outbreaks and epidemics in the context of this dissertation.

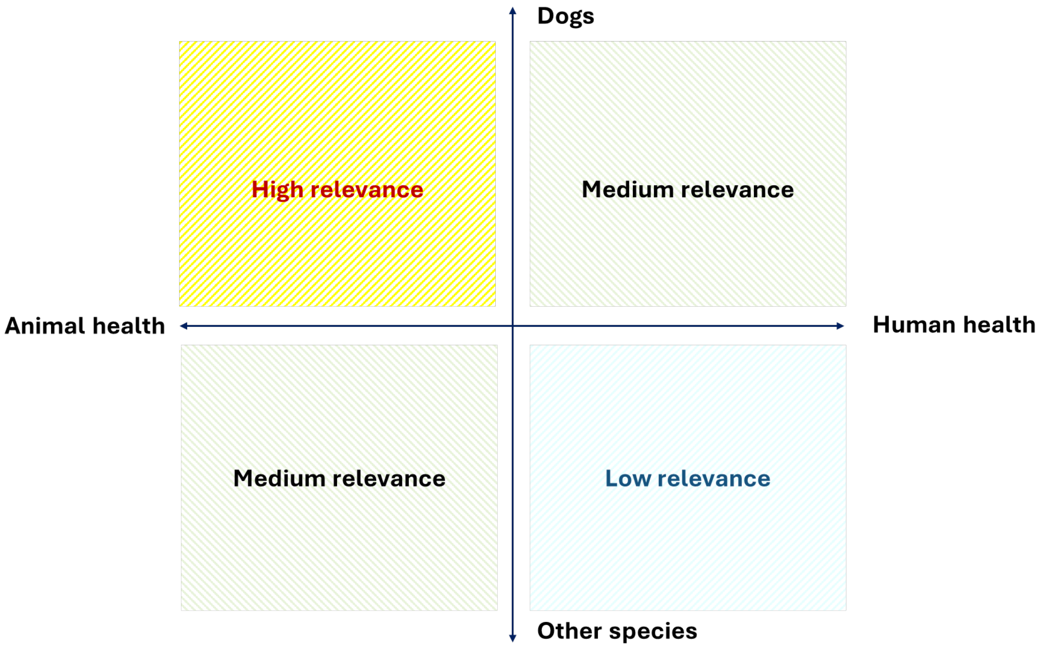

Figure 1.2. Diagram that represents the relevance of publications found in this chapter's literature. The y axis represents the species covered in the study, whether dogs, or another species including humans or animals. The x axis represents the focus of said studies, whether human or animal health. Studies that fit on the top left quadrant of this graph, i.e., studies on canine diseases with a focus on animal health and welfare, are the most relevant for the present thesis.

1.2.1. Structure of the literary review

The literature review for this thesis consisted of three elements: search strategy, search methodology and presentation of results.

1.2.1.1. Search strategy

Two different strategies were considered for the literary search. Backward planning consists in starting the search by using looser search terms, which would retrieve articles about systems of surveillance and response in both animal and human species, with a focus on either human or public health, and then narrowing down the search terms to extract the publications of highest relevance, i.e., first identifying publications that are in the periphery of the topic of interest, i.e., canine diseases with a focus on animal health. Conversely, forward planning involves first identifying the publications of higher relevance to the present thesis, and then broadening the search field to include other less relevant studies (Figure 1.3). In this case, the author hypothesised that the available publications of highest relevance for this thesis would be manageable, and therefore a forward planning approach was followed, to first retrieve said publications and gain an understanding of the state of the art, and then broaden the search if needed to include systems of surveillance and response in other species and humans. It is important to note that the latter studies are still valuable to learn lessons applicable for canine epidemic preparedness, even if they are not directly related to canine diseases, as the health of animals and humans are intertwined and cannot be compartmentalised.

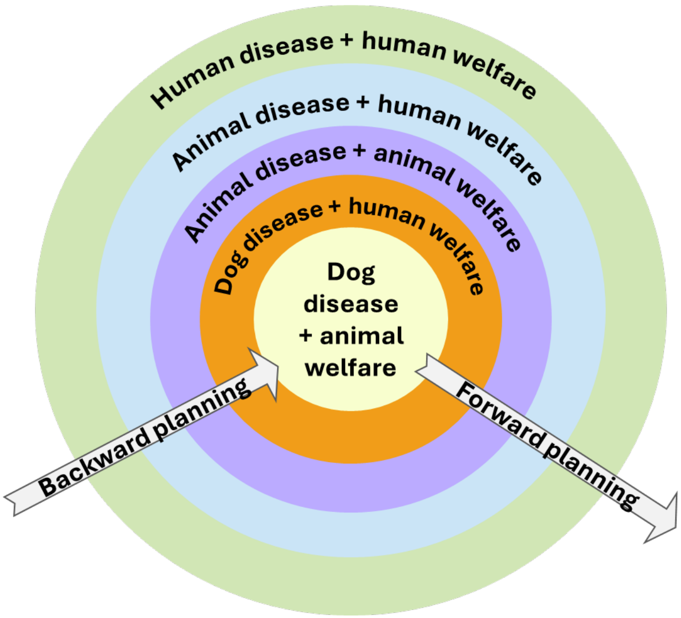

Figure 1.3. Graphic representation of the search field for this literature review. The research question is placed in the centre (outbreak response of canine diseases). The concentric circles represent other areas of knowledge, expressed in order of relevance for this project. The search strategies of forward and backward planning are also illustrated.

1.2.1.2. Search methodology

The search methodology consisted of the combination of search queries and literary sources used to retrieve publications. A schematic representation of the search methodology is detailed on Table 1.1. Keywords from the first column of this table defined the search field, i.e., publications about systems of outbreak detection and response. The combination of keywords from this first column and those on the second column in Table 1.1. intended to define the focus of the publication. The rationale was that the majority of published articles focus on human health, so by only searching keywords on Table 1.1., publications about human diseases would be retrieved by default. Therefore, to retrieve publications that were specific to canine diseases, and that focused on animal health, extra keywords were used.

Table 1.1. Summary of the search methodology used in this chapter's literature review, including the focus of the search and the keywords used to obtain the intended publications.

<table>
<tr><th>Keywords</th><th>Added keywords</th><th>Publication’s focus</th><th>Search engines</th></tr>
<tr><td rowspan="5">Outbreak/epidemic/ “infectious disease” + response/ investigation/ protocol/ “response planning”/ prevention/ control</td><td>+ dogs/ canine
+ “small animal”/ “companion animal”</td><td>Canine disease + Animal welfare</td><td rowspan="5">Web of science
Jstor
Google Scholar
PubMed</td></tr>
<tr><td>+ zoonosis</td><td>Canine disease + Human welfare</td></tr>
<tr><td>+ animal
+ veterinary</td><td>Animal disease + Animal welfare</td></tr>
<tr><td>+ zoonosis</td><td>Animal disease + Human welfare</td></tr>
<tr><td></td><td>Human disease + Human welfare</td></tr>
</table>

Keywords from Table 1.1. were combined through Boolean operators (AND, OR), by first searching for these in the title of the article and, where no publications were retrieved, by searching for them in the abstract and body of the publication. To assess the retrieved articles, the author first read the title and abstract and, where publications were relevant, the author proceeded to read the entirety of the publication's text. Retrieved publication's cited references were also analysed and included in the results of the process when relevant. Publications reviewed in this chapter included scientific publications, but not conference proceedings or reviews.

1.2.1.3. Presentation of results

When reviewing the literature, the author of this thesis identified a series of best practices in the described outbreak detection and response interventions, which constitute key elements for the detection and response framework developed in the present thesis. Results from this chapter's literature review are presented by using identified key elements, to assess whether the systems of detection and response described in the literature follow these best practices. These key elements are:

- **Nation-wide**: useful in any geographical area of the country. This involves designing communication strategies between local, regional, and national levels.
- **Rapid**: the capacity of a prevention and response plan to detect outbreaks of disease early and provide measures to control them before they reach catastrophic dimensions.
- **Generalisable**: this relates to the flexibility of the detection and response framework, so that it can be applied to a varied range of health threats. This includes establishing a structured chain of command, whilst providing adaptable intervention strategies. These intervention strategies will vary in two ways, in content (to fit different types of disease, e.g., different biosecurity measures depending on the transmission modality) and in intensity (to deliver a proportionate response that fits the magnitude of the epidemic).
- **Applicable**: this key element refers to the adequacy of the framework in terms of how well it translates to real-world situations. Even if the response methodology is well built from a theoretical perspective, it will not be successful unless proven appropriate for use when an outbreak is detected. Furthermore, in the long run, the aim is for this response framework to be translated into policy and become the standard course of action to handle companion animal epidemics. In order to achieve this, it will be

fundamental to work closely with those who would be affected by an outbreak of canine disease, as well as the primary actors who would execute the response.

- The response framework developed in this thesis includes zoonotic diseases, both those that are known to have a zoonotic potential, such as canine Leptospirosis, and emerging pathogens whose ability to infect humans is unknown. Because infectious diseases often affect multiple species and happen at the intersection of human and animal health, an essential element of the response framework is a **Public Health** approach. For this reason, it will be key to establish a multisectoral response methodology, that includes human and animal health experts and institutions, as well as the appropriate mechanisms of coordination between them.

1.2.2. Findings

Findings from the literature review were divided into two categories. On one hand, scientific publications that detail either one-time interventions for a particular outbreak, or that describe the development of systems of surveillance and control of infectious diseases. On the other hand, official protocols that are established as plans of action to prevent and mitigate epidemics, either from governments or international organisations, such as the World Health Organisation (WHO) or the World Organisation for Animal Health (WOAH) (Figure 1.4). When following the previously mentioned forward planning search strategy, a sufficient number of scientific publications about canine diseases were extracted to conduct a critical assessment and identify relevant gaps to address in the present thesis. However, no regional government or international protocols were identified for canine infectious diseases. Thus, the corresponding section of this chapter is dedicated to protocols developed for human diseases and livestock.

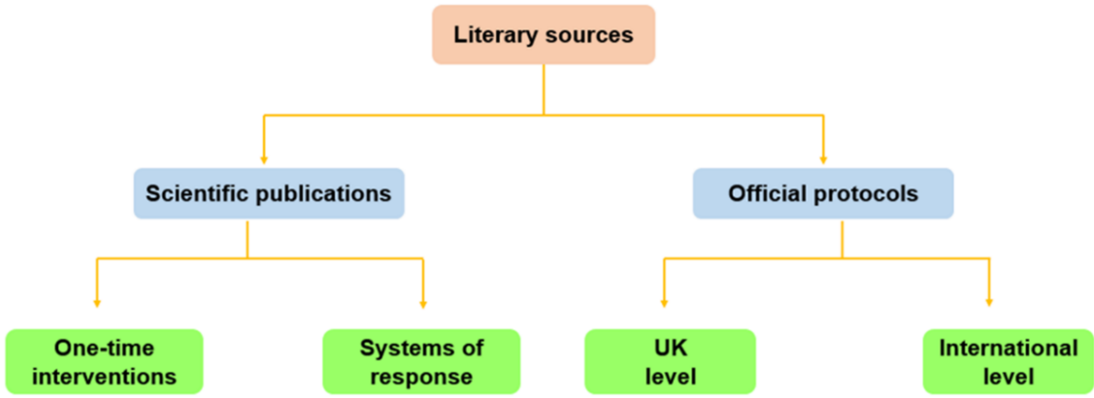

Figure 1.4. Classification of the relevant literary sources included in this chapter.

1.2.2.1. Literary findings: scientific publications on canine outbreak detection and response

Table 1.2 contains a summary of the most relevant scientific publications that focus on the detection and response to outbreaks of canine disease. Most of the retrieved publications describe one-off response investigations that take place once an epidemic has reached alarming dimensions in an ad-hoc, reactive manner. Out of all of the reviewed studies, none of those that focused on canine diseases without zoonotic implications described having access to a pre-existing coordinated plan of action in their epidemic responses, in contrast to those studies that described zoonotic outbreaks. Whether the response was a one-off intervention or part of an integrated framework of response is included in the column entitled "type" on Table 1.2.

1.2.2.1.1. Outbreak detection

The inherent problem for the control of canine epidemics is the lack of capacity for the detection of outbreaks in the first place, given the lack of adequate systems of surveillance. Without these systems, it is difficult to assess the true impact of canine infectious diseases, since there are no data on the incidence of cases or their distribution, and therefore not possible to understand their spread in the population. Therefore, there might be hundreds of canine disease outbreaks taking place across the globe that we are simply unaware of, which are only detected in specific circumstances, that are described in this section.

The epidemics described in scientific publications included in this chapter were detected through different means. Often outbreaks are investigated in canine populations because of previous zoonotic cases being detected in humans. Indeed, some of the most detailed canine epidemic responses found in this literary review only took place as a by-product of the detection of human cases, and it is likely that they would not have been investigated or detected otherwise (Montgomery et al., 2018).

Other studies describe outbreaks that take place in kennels or boarding facilities, where disease is spread more easily than in dogs kept in individual households, as large numbers of animals are housed in confined spaces. Outbreaks are therefore also more easily detected, given the fast progression of the disease and regular monitoring by keepers. For instance, a study in Belgium (Kaden et al., 2014) describes an outbreak of brucellosis that was detected and investigated in a kennel after two pregnant female dogs delivered stillborn litters within a short period of time. In other studies, outbreaks are suspected when observing abnormally high mortality rates (Decaro et al., 2004) or an unusually large number of kennelled dogs experiencing clinical signs (Payungporn et al., 2008; Willi et al., 2015). However, cases of disease detected in kennels and boarding facilities are not representative of the distribution of disease in the wider population. Therefore, systems of outbreak detection that are suitable for dogs kept as companion animals, which constitute most of the canine population, still need to be developed and implemented.

In other cases, potential canine epidemics are detected in large veterinary hospitals (Weese & Armstrong, 2003; Weese & Stull, 2013), as these have the capacity to conduct surveillance activities and to investigate potential outbreaks. A study in Finland (Grönthal et al., 2014) describes a nosocomial outbreak of methicillin resistant *Staphylococcus pseudintermedius* (MRSP) detected in a veterinary teaching hospital. This large hospital had the personnel and facilities to conduct a laboratory investigation to identify the pathogen, develop a tailored biosecurity protocol, and even evacuate the entire hospital for several days to clean and disinfect all the surfaces before re-opening the facilities to the public. However, most veterinary practices will not necessarily have the means to detect potential outbreaks, or the capacity and resources to carry out interventions that involve shutting their practice for extended periods of time.

Another important aspect that plays a role in the detection of outbreaks is whether the causative agent is classed as notifiable in the corresponding territory. An example of this are studies on responses to canine influenza outbreaks (H3N2 or H3N8) in the US and Canada (Voorhees et al., 2017; Weese et al., 2019), described and investigated only after these novel influenza strains were made reportable by veterinarians in 2018. In the UK, only two canine diseases, namely, echinococcosis and rabies, are notifiable to the authorities (see section 1.2.2.2.1), due to their public health impact. However, there are many other canine diseases that affect animal welfare, as well as diseases with a zoonotic potential, that are not included in this list, and for which there is no reliable system of rapid outbreak detection.

When outbreaks of disease are described in local canine populations, outside boarding or veterinary facilities, and not due to a previous detection of human cases, these are detected when the epidemic reaches extremely large proportions. For instance, a study in Mozambique (Zacarias et al., 2016) describes an outbreak of canine distemper where over 200 dogs died in less than a month, while another study in Dominican Republic (Maes et al., 2003) describes an outbreak of canine distemper where over 300 dogs died within three weeks. Therefore, systems for the early detection of outbreaks are needed, so that these can be addressed in a timely manner, before they reach the status of an epidemic. The work developed on the third chapter of this thesis aims to address this gap, by developing a text mining tool to analyse pre-diagnostic surveillance data in the form of veterinary clinical annotations. Since these annotations are routinely collected and constitute a readily available source of data, this tool provides a cost-effective surveillance strategy.

In conclusion, none of the outbreaks described in the reviewed literature were detected through a previously established system of surveillance for canine diseases, with the exception of some diseases that are notifiable. These findings highlight the existing gap in companion animal infectious disease surveillance, which exists not only in the UK, but in all countries and regions of the world. In this thesis, tools are developed to improve the surveillance of canine diseases and enable the early detection of potential outbreaks, as well as to notify veterinary clinicians of clinically relevant outbreaks in their area.

1.2.2.1.2. Data collection and analysis during an outbreak

Responses start after outbreaks are detected, by collecting and integrating data to gain situational awareness and inform the actions taken in the intervention. In the case of notifiable canine diseases, protocols for data collection and submission to the relevant authority do exist (see section 1.2.2.2.1). However, for non-notifiable canine diseases, protocols are not available, and data are collected and integrated reactively based on the characteristics of the outbreak, as investigators and stakeholders involved in the response see fit. This means that channels for data collection need to be established hastily, in a haphazard manner, so it is more likely that outbreak cases will be missed (Hedberg & Maher, 2018; Sigfrid et al., 2020). In the reviewed scientific publications, commonly used data sources are electronic health records (EHR), collected from surveyed veterinary practices (Garde et al., 2013a; Schumaker et al., 2012; Willi et al., 2015), epidemiological questionnaires, distributed to veterinary practitioners and/or to dog owners (Mandra et al., 2019; Woodward et al., 2018), serosurveys to estimate disease exposure or burden in canine populations (Johnson et al., 2018; Woodward et al., 2018), or collection of specific information, such as antimicrobial usage or details on animal movements and transportation between territories (Montgomery et al., 2018). In these publications, no pre-defined protocol was available for the integration of data sources used during the corresponding outbreaks. Not having a strategy for the integration of data sources results in inefficiencies, which consume time and effort that could otherwise be dedicated to controlling the spread of the outbreak (Pillai, 2021). This gap in the knowledge is addressed in the present thesis, by developing an outbreak response framework wherein a protocol to link laboratory and practice data is described.

When it comes to the analyses conducted during epidemics, some of the published studies focus heavily on the laboratory investigation of pathogens and provide great detail about the techniques used, such as Polymerase Chain Reaction (PCR) methods, pathogen culture, or immunofluorescence assays (Johnson et al., 2018). Regarding the statistical analyses conducted during epidemics, most studies provide only a brief overview of their analyses and lack in-depth information about data analytic pipelines. Among the most used methods are descriptive statistics to describe the demographic characteristics of the outbreak and multivariate logistic regressions to identify risk factors of disease (Dunn et al., 2018). None of the retrieved studies conducted further epidemiological analyses that arguably require more complex statistical methods, such as estimating the reproduction number or forecasting disease risk. It is likely that in most of these cases, conducting more complex analyses is not possible due to the lack of demographic and infectious disease prevalence data for canine populations.

1.2.2.1.3. Response interventions

Most of the studies found through this literary review only describe an outbreak's characteristics, whether clinical, epidemiological, or microbiological (Decaro et al., 2004; Johnson et al., 2018; Maes et al., 2003). While these studies sometimes provide advice to prevent further spread of disease, they do not implement any measures to control the outbreak. This is because investigations are carried out by research groups, with no capacity to effect change. Response interventions that implement measures, such as deployment of vaccinations or awareness campaigns, are usually only launched by the corresponding authorities when the disease in question is classed as notifiable or has a significant and measurable impact on public health. In those limited contexts where authorities are involved in the response, proactive measures are employed to detect new outbreak cases, such as active surveillance strategies (Mandra et al., 2019; Weese et al., 2019), or monitoring disease in wildlife (Arce et al., 2013; Woodward et al., 2018) and in free roaming dog populations (Mandra et al., 2019). The work developed in this thesis addresses some of the aspects that result in the lack of authority figures responsible for canine diseases, by providing a protocol for data collection and information dissemination, involving a range of relevant stakeholders in the prioritisation of diseases for a framework of surveillance and response, and engaging these stakeholders, to facilitate future collaborations to aid in the implementation of measures in future canine outbreaks.

Interventions to prevent the spread of canine outbreaks include the deployment of free vaccination campaigns in the affected area, either by the authorities if the disease is notifiable or has a zoonotic potential (Ravensberg et al., 2022), or by charitable organisations, such as Veterinarians Without Borders (Garde et al., 2013a). If the capacity is available, training materials or courses are provided for veterinary practitioners to improve their epidemic preparedness (Grönthal et al., 2014; Woodward et al., 2018), and sometimes also for dog owners and the wider public (Woodward et al., 2018). Information about the disease and its prevention is also sometimes disseminated through media channels (Ravensberg et al., 2022) or internally (Grönthal et al., 2014). However, these information exchanges do not rely in pre-established channels of communication, which are an essential component in an outbreak response intervention (Reddy & Gupta, 2020; Tumpey et al., 2018). The present thesis acknowledges this essential component by considering all relevant forms of information exchange during an outbreak, and including two-way communication strategy with veterinary clinicians as key component of an outbreak response framework.

In those outbreaks that take place in veterinary or breeding facilities, interventions consist of enhancing biosecurity measures, by setting up specific areas to isolate potential cases (Kaden et al., 2014), implementing the use of personal protective equipment (PPE) for veterinary professionals (Grönthal et al., 2014), barrier nursing potential cases, and conducting cleaning and disinfection activities. In severe outbreaks, facilities that do not meet basic biosecurity requirements can be closed down to quarantine animals (Schumaker et al., 2012). As mentioned on the previous section, outbreak detection and response practices conducted in facilities where dogs are collectively housed cannot be extraopolated to the majority of dogs, who live in private residences with their owners. While shelters or breeding facilities may have some form of infectious disease prevention or control plan, this does not apply to veterinary clinics or, of course, to individual households.

A significant consequence of the lack of a detection and response framework is the uncertainty experienced by veterinary practitioners, as they do not know who to contact to receive guidance on how to manage an outbreak in practice. This not only poses a risk for dogs, but also for the attending veterinary staff. For instance, those veterinarians working in practices without the appropriate biosecurity protocols are at an increased risk of contracting a zoonotic disease (Johnson et al., 2018).

1.2.2.1.4. Public Health component

Those studies that conduct canine outbreak responses that take into account the wider public health do so by collecting analogous data for human and animal populations in the same territory to compare incidence of disease (Arce et al., 2013). This might involve using animal and human electronic health records (Mandra et al., 2019) or comparing of laboratory test results from cases from both species (Ravensberg et al., 2022). Some studies also distribute questionnaires among households in the outbreak territory to identify potential zoonotic exposures (Lucero et al., 2010). Extraordinarily, in a study conducted to investigate the transmission of *Campylobacter* between dogs and residents of a nursing home (Moffatt et al., 2014), a multidisciplinary panel of veterinary and medical experts was convened to assess the zoonotic risk posed to the residents.

The lack of awareness of the clinical presentation of diseases of canine origin also poses a challenge during human epidemics, leading to the misdiagnosis of cases and therefore hindering timely disease detection and response interventions (Lucero et al., 2010).

1.2.2.1.5. Conclusions: scientific publications on outbreak detection and response

It is seldom to find scientific publications that describe the development or that use pre-established systems of surveillance and response to outbreaks of canine disease. Not having access to surveillance data in canine populations is one of the main issues discussed by the authors of the reviewed articles. The lack of established surveillance systems means that the early detection of potential outbreaks is often not possible, which limits the development of effective preparedness strategies for canine diseases (Colby et al., 2011). Further, because the prevalence and geographical distribution of disease in dogs is unknown in the majority of cases, it is difficult to estimate the extension of an outbreak or assess whether canine populations could act as a zoonotic reservoir for human disease (Arce et al., 2013). A consequence of this is the inability to link canine and human cases in similar geographical locations, thereby impeding a real-time analysis of cross-species disease transmission during an outbreak. The majority of the studies retrieved in this chapter's literary review describe one-time control interventions, rather than developing standardised protocols of response. This gap in epidemic preparedness means that responses are carried out in an ad-hoc manner, leading to inefficient collection and analysis of data, lack of communication between the involved actors, and delayed recommendation of measures to control the spread of the outbreak (Garde et al., 2013a, 2013b). The overarching aim of the body of work developed in this thesis is to address this gap, by developing tools to improve the surveillance of canine diseases, and a detection and response framework for canine outbreaks.

In most of the studies reviewed in this chapter, only one or two institutions from the same sector, e.g., academic research groups, participated on the response. Those studies where a multisectoral outbreak response is conducted highlight the importance of building multidisciplinary collaborations beforehand as the best way to conduct a robust intervention (Woodward et al., 2018). For this reason, the methods and tools developed in the present thesis are informed by users (e.g., the thresholds for outbreak notification informed by veterinary clinicians' opinion; Chapter Four) and stakeholders of multiple relevant backgrounds (e.g., the prioritisation of canine diseases for surveillance by reaching a consensus among stakeholders; Chapter Two).

A significant limitation reported in the reviewed studies was the financial needs related to canine epidemic responses. In most cases, unless diseases have zoonotic implications, there are normally not dedicated funds to investigate and respond to outbreaks of canine disease. This means that these costs are either passed on to pet owners or assumed by charitable organisations or research projects. These sources of funding are not sufficient to cover the costs of large-scale responses, or to investigate every potential disease anomaly detected in dog populations. Since the cost of testing is often assumed by dog owners, this can limit the detection of cases and therefore hinder the capacity to understand the spread of an epidemic (Grönthal et al., 2014). The financial barrier also has an impact on disease prevention since the costs of vaccination cannot be assumed by individuals in the lower income sectors of the population (Zacarias et al., 2016). Further, intervention costs also determine the possible measures that can be taken to control the spread of an outbreak. Establishing adequate isolation and quarantining facilities is costly and might not be possible for small veterinary clinics or for breeders and animal shelters with limited resources. For instance, during a canine distemper outbreak in a breeding centre in the US (Schumaker et al., 2012), over 1400 dogs were euthanised due to the lack of resources for testing and isolation facilities. This poses an ethical dilemma, especially as dogs (and other companion animals) are increasingly considered as members of the family and not as mere commodities, particularly in high income countries like the UK. Having access to early detection and response protocols maximises the chances of detecting potential disease anomalies early on and controlling the spread of the disease, thus decreasing the number of affected animals and the need for drastic measures, such as euthanisation.

Table 1.2. Summary of this chapter's literary findings, regarding scientific publications on canine infectious disease outbreaks, in alphabetical order.

Scientific publications							
Publication	**Type**	**Rapid**	**Nation-wide**	**Public Health**	**Multisectoral**	**Generalisable**	**Applicable**
1. APHA, 2022	Preliminary assessment	Yes	No	Yes	Yes	No	Yes
2. Arce, 2013	One-time intervention	Yes	No	Yes	Yes	Yes	Yes
3. Decaro, 2004	Descriptive study	No	No	No	No	No	No
4. Dunn, 2018	Descriptive study	Yes	No	No	No	No	No
5. Garde, 2013	One-time intervention	No	No	No	No	No	Yes
6. Gronthal, 2014	One-time intervention	Yes	No	No	No	Yes	Yes
7. Johnson, 2019	Retrospective investigation	No	Yes	Yes	Yes	No	No
8. Kaden, 2014	One-time intervention	Yes	No	Yes	Yes	No	Yes
9. Lucero, 2010	One-time intervention	Yes	No	Yes	Yes	No	Yes
10. Maes, 2003	Descriptive study	No	No	No	No	No	No
11. Mandra, 2019	One-time intervention	No	No	Yes	Yes	Yes	Yes
12. Moffat, 2014	One-time intervention	No	No	Yes	Yes	No	Yes
13. Montgomery, 2018	One-time intervention	Yes	Yes	Yes	Yes	Yes	Yes
14. Payungporn, 2008	Descriptive study	Yes	Yes	No	No	No	No

Publication	Type	Rapid	Nation-wide	Public Health	Multisectoral	Generalisable	Applicable
15. Ravensburg, 2022	Ongoing intervention	No	No	Yes	Yes	Yes	Yes
16. Schumaker, 2012	One-time intervention	Yes	No	No	Yes	No	Yes
17. Voorhees, 2017	Descriptive study	Yes	Yes	Yes	Yes	No	No
18. Weese, 2019	Multiple interventions	Yes	No	Yes	Yes	Yes	Yes
19. Willi, 2015	One-time intervention	Yes	No	No	No	No	No
20. Woodward, 2018	One-time intervention	Yes	No	Yes	Yes	Yes	Yes
21. Zacarias, 2016	One-time intervention	Yes	No	No	No	No	Yes

1.2.2.2. Literary findings: official protocols for outbreak detection and response

This section is dedicated to the official protocols, developed either by government departments in the UK, or international organisations, to respond to infectious disease threats. Specific protocols for canine diseases aimed at protecting canine welfare were not found in the reviewed literature. Therefore, available protocols for other animal diseases and humans have been included in this section.

1.2.2.2.1. UK level

Protocols of detection and response to animal diseases

In the UK, there is an established chain of disease notification, investigation, and response for those diseases in companion and food animals that fall under the Department for Environment, Food and Rural Affairs' (DEFRA) list of notifiable diseases (NDs) (GOV.UK, 2019c). For a disease to be classed as notifiable, it must be included in the Animal Health Act, consolidated in 1981 (GOV.UK, 1981). Diseases are made notifiable when the authorities determine that they pose a significant risk for international trade, public health, animal welfare, and the wider society. Both endemic and exotic animal diseases are included in the Notifiable Disease list. If a disease is notifiable, veterinary practitioners are legally obliged to report cases, or their suspicion, to the Animal and Plant Health Agency (APHA). When notified, APHA veterinary officials will carry out an investigation and, if a notifiable disease is confirmed in the premises, a full epidemiological investigation and control intervention will then be launched to control the spread of disease. Control measures included in such interventions mainly involve the restriction of animal movements, in and outside the affected premise(s), as well as their products, and the slaughter and carcass elimination of infected animals to prevent further cases. Currently, DEFRA provides specific guidance and legislation for the detection and management of forty-five notifiable diseases in animals, out of which only two are transmitted by canids, including domestic dogs, i.e., rabies and echinococcosis (for which foxes and dogs constitute the definitive host). These diseases are included in the Notifiable Diseases (NDs) list due to their zoonotic potential and high severity in human hosts, e.g., rabies is virtually fatal in humans (WHO, 2023), and estimated fatality risk for human alveolar echinococcosis can range between 50 and 75% (Prevention, 2019). However, there are many other canine infectious diseases that pose a severe threat to animal welfare, both zoonotic, e.g., canine leptospirosis, and non-zoonotic, e.g., canine parvovirus, that are not included in DEFRA's protocols, since they are not notifiable. This means that these diseases are currently not being monitored, and that local outbreaks will likely not be detected and, if these escalate to a larger epidemic, no strategy will be in place to control its spread.

Further, a specific contingency plan for exotic notifiable diseases (END) exists in the UK (GOV.UK, 2022d), see Table 1.3, which refers to the government guidelines to manage outbreaks for those animal diseases that are not normally present in the country, and for which the UK currently holds the "disease free" status. This status is awarded by the WOAH, on behalf of the Word Trading Organisation (WTO), to officially recognise disease-free areas for trade purposes (WOAH, 2023a). The compromise of this status has significant economic implications, as it would limit the UK's ability to trade animals and their products with other disease-free countries, and even lead to the imposition of a ban on trade by the European Union (EU). DEFRA's END contingency plan provides general guidelines for all exotic notifiable diseases, but also provides separate, specific guidelines for those diseases that are of most concern, namely, avian influenza, foot and mouth disease (FMD), bluetongue disease, African and classical swine fever, African horse sickness, and lastly, rabies, the only contingency plan that is relevant to companion animals. The Rabies control strategy for Great Britain (*Animal Disease Control Strategy*, 2019) defines the interventions that can legally be enforced during a rabies outbreak, such as requiring dogs to be muzzled and leashed in public places, compulsory vaccinations of dogs and other companion animals, implementation of movement restrictions within the infected area, as well as the forcible removal of pets from their owners and euthanasia of infected dogs.

The governmental control strategies for animal diseases developed in the UK described in this chapter present several core differences when compared to the outbreak response protocols developed in this thesis. The most notable is how their main aim is to stop the spread of disease for economic purposes, rather than to preserve the welfare of animals. Because they mostly regard farmed animals, their concept of welfare is to carry out actions such as "humanely destroy" individual animals if the premises of the farm become overcrowded when movement restrictions are imposed, or if they exhibit signs of the disease. Of course, this is something that cannot be proposed in the case of companion animals, with the exception of infectious diseases that severely compromise public health, such as rabies, where euthanasia of infected animals is regarded in the Rabies Control Order 1974 (GOV.UK, 1974). Another significant difference is how farmed animals are confined within a limited space, and therefore easily tracked and monitored. This facilitates the response intervention, since it is easy for health officials to have access to these animals, assess the status of the outbreak and follow the progression of the disease over time, as affected animals are located in a clearly defined space. Conversely, most dogs live at home with their owners, and are disseminated across the country, with no official registry of their location. This makes it difficult to determine the extension of an outbreak and the number of affected and exposed animals. Further, although these protocols include communication strategies and the implementation of measures for outbreak control (Table 1.3), these would not be directly applicable to the characteristics of the companion animal sector, and specific strategies still need to be developed for communication with veterinary practices and hospitals, as well as measures that can be implemented to protect canine welfare and that suit dog owner's needs and expectations. Future surveillance and response protocols for dogs also need to consider the existing sources of surveillance data, such as the information contained in electronic health records that are routinely collected by veterinary practices, and include strategies to integrate these sources for analysis during an outbreak.

Protocols of detection and response to human diseases

Similarly to the notifiable disease system for animals described above, the UK's Health Security Agency (UKHSA) also provides a list of notifiable infectious diseases, consolidated in the Public Health Disease Control Act 1984 (GOV.UK, 1984) and the Health Protection Notification regulations 2010 (GOV.UK, 2010). UKHSA's notifiable disease list is divided in two sections, notifiable diseases reportable by registered medical practitioners, e.g., acute encephalitis or cholera, and notifiable organisms (causative agents) reportable by diagnostic laboratories, such as *Bordetella pertussis*, or *Clostridium tetani* (GOV.UK, 2023a). In contrast with the UK's NDs system for animal diseases, UKHSA's has made notification forms available for medical practitioners to provide details about the observed communicable disease, so these can be effectively notified to the local health protection team (GOV.UK, 2016). Additionally, since the COVID-19 pandemic, SARS-CoV-2 has been added to the notifiable disease list, and diagnostic laboratories performing tests must notify the result (either positive or negative) to UKHSA, via a specific reporting feed (GOV.UK, 2020). This system of surveillance and reporting is more akin to the one developed by the present thesis, where medical records and diagnostic laboratory results are used as data sources for surveillance, and where the monitoring of diseases in the population is carried out for the main purpose of protecting the health and welfare of the subject, i.e., humans and dogs, in contrast to the aim of improving production, such as in the surveillance protocols for farm animals (section 1.2.2.2.1. *Protocols of detection and response to animal diseases*).

UKHSA's Communicable Disease Outbreak Management (*Communicable Disease Outbreak Management*, 2014) provides the framework to declare and respond to outbreaks of infectious diseases in the UK. This framework specifies the roles and responsibilities of the different government agencies that would be involved in such a response and provides a step-by-step description of the activities that must be conducted when a potential outbreak is suspected. It includes the initial assessment of the initial evidence; declaration of the outbreak, whether at a local, regional or national level; assembly of an outbreak control team (OCT) to assess the risk to public health and oversee the response; the investigation to ascertain the causative agent of the outbreak, including descriptive epidemiology, analytical studies, and microbiological investigations; the establishment of a communication strategy between members of the OCT, external partners, and the public through the media; the deployment of measures to control the outbreak; the declaration of the end of an outbreak and, lastly, the generation of an outbreak report for dissemination and to learn lessons that can be applied in future outbreaks. Again, this framework for outbreak response for human diseases shares similarities with the aim of the present thesis, of providing a comprehensive protocol on the steps to follow during the stages of an outbreak, as well as a system for documentation of the measures taken during the outbreak, so that the framework can be improved in future responses.

A specific Influenza pandemic preparedness strategy was published by the former Public Health England (PHE) in 2011 and updated in 2014 (GOV.UK, 2014), as a result of the 2009 H1N1 pandemic. The aim of this strategy was to consider lessons from the 2009 pandemic and develop an effective framework to prepare for future pandemic influenza instances, focusing on strengthening the collaborations between PHE (now UKHSA) and its partners. This response plan consists of five phases, with specific guidance for the different government bodies, known as DATER, which stands for "detection, assessment, treatment, escalation, and recovery".

Additionally, as a result of the COVID-19 pandemic, the UKHSA also published specific guidelines for health professionals to assess and manage of COVID cases (GOV.UK, 2022a). These guidelines provide information for clinicians on how to diagnose SARS-Cov-2 infections and reinfections, adequately use personal protective equipment (PPE) for aerosol generating and non-aerosol generating procedures, as well as indications on how to inform patients about quarantine periods and procedures. Further, the COVID-19 guidelines also provide indications for the adequate collection, packaging, and transportation of samples to be submitted to diagnostic laboratories (GOV.UK, 2021b). Similar guidelines are also needed by small animal veterinarians, who currently do not have access to such resources to guide how they should respond if an outbreak occurred in their practice. At present, these decisions are taken by individual practices. Therefore, standardised, evidence-based guidance needs to be established in small animal practice to promote best methods and a cohesive response framework, whose quality does not vary according to the individual practice or geographical area of the country.

Conclusions: UK level government protocols for outbreak detection and response

When reviewing UK government detection and response protocols infectious diseases, the first relevant conclusion for the present thesis is the limited, mostly non-existent coverage of canine diseases. Despite of the large number of canine diseases that can compromise dog's welfare and have implications for public health, only two canine diseases (rabies and echinococcosis) are included in the notifiable disease list. It is clear that if we want to protect these populations from the emergence of health threats, we must determine which other canine diseases should be prioritised for surveillance and inclusion in a national surveillance and response system, as well as who are the actors that should be involved in the decision-making process when designing such framework (Chapter Two). It is also of note, that current control plans for both canine notifiable diseases are based on single-case detection and containment, either via movement restrictions, or by culling potentially infected animals, with the purpose of maintaining the WTO's "disease free" status. These findings highlight the existing gap in knowledge and infrastructure for canine infectious disease surveillance and control, which is the main gap addressed in the present thesis.

Valuable lessons can still be learned from these protocols, despite not being directly applicable to canine diseases Table 1.3 provides a comparison between the framework of detection and response for canine outbreaks proposed in this thesis, and two UK government protocols for animal and human diseases, namely DEFRA's contingency plan for exotic notifiable diseases, and UKHSA's pandemic influenza response plan.

When it comes to the detection of outbreaks, the framework developed in the present thesis relies on laboratory and veterinary practice surveillance data, collected by SAVSNET and analysed by text mining tools (Chapter Three) and mathematical models. A similar system is described by UKHSA's Influenza Response Plan, by relying on surveillance data from multiple sources, including medical records and laboratory surveillance. In contrast, DEFRA's contingency plan relies on notifications by individuals, whether animal owners or veterinarians, who are legally obliged to report notifiable disease cases to the designated authority. This approach could not be considered for canine populations unless more canine diseases are included in DEFRA's notifiable list.

To confirm a potential outbreak and start the response, a specific methodology on how to consider a potential outbreak as clinically relevant for notification to companion animal practitioners is described on Chapter Four. This contrasts with the response protocols by DEFRA and UKHSA (Table 1.3), where a designated authority is tasked with confirming the outbreak by investigating the available evidence. Given the lack of accountable authorities for canine diseases, the notification system developed in this thesis focuses on notifying first-line respondents, i.e., veterinary clinicians, based on their opinion on what constitutes a significant outbreak. It will then be up to veterinarians receiving an alert whether to implement measures in response to the threat. However, when outbreaks affect a significant number of animals, or spread to multiple areas of the country, this framework takes inspiration from government protocols, by considering the possibility of an expert group being convened by SAVSNET members, to respond to the outbreak. This is limited by the availability and capacity of the researchers from SAVSNET, given that it is a research initiative and not a permanent governmental institution.

When analysing and integrating outbreak data, government protocols by UKHSA and DEFRA's (Table 1.3) main aim is to design and enforce the application of measures to control the spread of disease. Both UKHSA and DEFRA have a well-defined structure of command, where roles and responsibilities are defined at every stage of the response. This kind of infrastructure is not available for canine diseases at a government level and cannot be replicated through a research initiative. The strongpoint of research initiatives like SAVSNET is their analytical capacity, which is often greater than that of governmental institutions, that often consult on research teams to carry out outbreak analytic tasks. This thesis aims to capitalise on these strengths, by analysing the available data sources to determine the causative agent and describe the outbreak, but also by fostering the linkage with government groups to recommend measures and expert advice. In this manner, the present thesis' framework aims not only to generate research outputs, but to inform policy decision-making (see Chapter Five).

Regarding the communications during an outbreak, UKHSA's protocol (Table 1.3) mainly focuses on the planning of communication channels between institutions participating in the response, i.e., agencies within UKHSA. DEFRA's exotic notifiable diseases protocol offers a more comprehensive communication strategy that includes internal and external exchanges of information. The present thesis' framework for communication during an outbreak draws lessons from both of these protocols, by providing a comprehensive two-way communication strategy with veterinarians, dog owners, and other relevant stakeholders, and recommending the development of a centralised hub of information that acts as a go-to place for these actors to exchange relevant information (see Chapter Five).

Table 1.3. Essential steps for outbreak detection and response protocols, comparing the framework for canine diseases developed in the present thesis to DEFRA's Exotic Notifiable Diseases contingency plan and UKHSA's (formerly PHE) Influenza Response Plan

Epidemic response steps	**Detection and response framework developed in this thesis**	**DEFRA's Exotic Notifiable Diseases contingency plan** (GOV.UK, 2022d)	**UKHSA Pandemic Influenza Response Plan** (GOV.UK, 2014)
Threat detection	Laboratory and veterinary practice surveillance data from a network of UK diagnostic laboratories and veterinary first opinion practices analysed through text mining tools and mathematical models. Secondary: notifications from individual veterinarians.	Animal owner/ veterinarian raising the alert to the authorities.	Surveillance system combining consultation data, uptake in the number of deaths, uptake in the number of vaccinations, and laboratory results from sentinel schemes.
Risk assessment and Confirmation	When risk levels are beyond what has been established by our end-users as clinically relevant (above notification threshold). Additionally, when possible, panel of experts is established by	Assessment by a veterinary inspector, confirmation either on clinical grounds or after samples are sent to the laboratory. Official investigation by APHA to estimate the level of alert. Outbreak declared by Chief Veterinary Officer (CVO)	Higher-level organisation confirms the existence of an outbreak (WHO declares a PHEIC/ pandemic alert phase).

	SAVSNET to assess the situation and confirm the outbreak.	after an amber teleconference.	
Epidemic response steps	**Detection and response framework developed in this thesis**	**DEFRA's Exotic Notifiable Diseases contingency plan** (GOV.UK, 2022d)	**UKHSA Pandemic Influenza Response Plan** (GOV.UK, 2014)
Investigation *Data collection* *Data analysis*	Epidemiologic data collected via questionnaires. Samples collected from cases and controls are tested in partner laboratories. Electronic health records from participating veterinary practices. Modelling for the spatiotemporal distribution of the outbreak. Text mining tools for monitoring the outbreak.	Clear structure of response, divided into three levels of command, control and communication (C3): strategic, tactical, and operational. The strategic and tactical levels are responsible for the decision-making process during the outbreak, including the data collection and analysis process.	Response methodology divided into five specific phases: detection, assessment, treatment, escalation, and recovery. Collection and analysis of detailed clinical and epidemiological information of early cases using medical records, laboratory test results, and epidemiological questionnaires to assess the situation in the UK- FF100. Actively finding cases.
Interventions for mitigation	Recommendation of measures: guidelines of action targeting veterinary practitioners and dog owners. Provision of expert advice on disease	Measures can be imposed to control spread of disease. Movement restrictions on vehicles, animals and their products, fomites, etc. Banning on gathering activities.	Advise on treatment of disease and enhancement of public health measures to disrupt transmission: movement restrictions, targeted vaccinations,

	prevention to reduce the risk of future epidemics.	Deployment of vaccination campaigns. Sustained surveillance activities carried out by the Animal and Plant Health Agency (APHA).	and continued detailed surveillance activities.
Epidemic response steps	**Detection and response framework developed in this thesis**	**DEFRA's Exotic Notifiable Diseases contingency plan** (GOV.UK, 2022d)	**UKHSA Pandemic Influenza Response Plan** (GOV.UK, 2014)
Communications	Targeted communications to reach different stakeholders (practitioners, policy makers, dog owners, etc). Centralised online platform to act as data hub and gateway for communication.	Official structure of communications established. Tools to provide timely updates to: stakeholders, animal keepers, public, media. Mass messaging system for vets in collaboration with RCVS. Information available on DEFRA's website. Direct communications with ministers, and senior officials. Daily briefings for DEFRA departments held by the National Disease Control Centre (NDCC).	Led by specific directorate within Public Health England (UKHSA). Internal lines of communications formally established trough multiagency co-ordination structures.

1.2.2.2.2. International level

Protocols of detection and response to animal disease outbreaks

On an international level, the most relevant protocol is the WOAH's Terrestrial Animal Health Code (WOAH, 2023b), that provides the standards for the improvement of animal health, welfare and veterinary public health worldwide. The Terrestrial Code was originally published in 1968 as a result of the first Word Assembly of Delegates meeting, a now yearly event that brings WOAH 182 member states together to define and examine the international standards for animal health and trade (WOAH, 2023d). Since its first publication, the Terrestrial Code has been updated multiple times, and published in English, Spanish, and French.

The Terrestrial Code contains comprehensive guidelines on all aspects of animal disease surveillance, prevention, and control, the quality and evaluation of veterinary services, animal welfare, and the procedures for the importation and exportation of animals and their products. It also contains the procedures for countries to be recognised as 'disease-free' status for the 117 diseases and causative agents currently included in the WOAH's list under article 1.3.1 of the Terrestrial Code. Out of these 117 diseases, only three are diseases of dogs, namely, leishmaniosis, rabies, and echinococcosis by *Echinococcus granulosus* and *Echinococcus multilocularis*. As listed infections, these diseases have a dedicated chapter in the Terrestrial Code (WHO, 2023; WOAH, 2022b, 2022a), where guidelines are provided on how to recognise the disease, according to the clinical signs in animals, which diagnostic techniques to use to confirm the infection and how to adequately conduct them, and specific guidelines on disease prevention and control activities. A summary of the main prevention and control guidelines for canine diseases provided by the Terrestrial code can be found on Table 1.4.

Table 1.4. Summary of prevention and control guidelines for rabies, leishmaniosis, and echinococcosis provided by the WOAH's Terrestrial Code

Disease	Prevention guidelines	Control guidelines
Rabies	• Vaccination of dogs. • Vaccination campaigns in wildlife. • International protocols of importation/exportation of dogs, that include presenting an	• Humanely euthanising infected dogs and safely disposing of animal carcasses to minimise the risk of disease spread.

	international veterinary certificate that confirms the absence of clinical signs, and either the stay for 6 or more months in a rabies-free zone, or by following the quarantine guidelines provided in the Terrestrial Code.	
Disease	**Prevention guidelines**	**Control guidelines**
Leishmaniosis	• Vaccination of dogs. • Use of topical insecticide throughout the period of sandfly activity.	• Treatment of infected dogs to minimise risk of transmission. • Disinsectation programmes targeting the sandfly vector.
Echinococcosis	• Limiting access of dogs to livestock carcasses or waste from farms, abattoirs, or butchers. • Enhance detection of cysts at meat inspection. • Vaccination of livestock against larval parasite stage.	• Anthelmintic treatment in dogs to target the adult tapeworm. • Use of anthelmintic bait for wildlife, e.g., foxes.

Protocols of detection and response to human disease outbreaks

At an international level, the overarching global protocol for epidemic response to human diseases are the International Health Regulations (IHR) (WHO, 2022b), established in 2005 by those countries who are member states of WHO. The IHR are a legally binding instrument, currently implemented in 196 countries, that are required to report public health events to the WHO and maintain certain core capacities for surveillance and response. These requirements include the establishment of national public health emergency response plans that include multisectoral teams, the provision of training programmes to ensure that specialised staff can be deployed during an epidemic, or the establishment of systems of disease detection at international airports. Member states are also required to designate a Focal Point to establish communications with WHO; in the UK this role corresponds to UKHSA (GOV.UK, 2021c). The focus of IHR is to prevent and control the spread of diseases on an international scale, and mitigate their impacts on public health, traffic, and trade. Therefore, member states are not only required to strengthen their local capacities, but also to provide support to other countries, especially to those with developing economies. To further address this issue, the Global Outbreak Alert and Response Network (GOARN) (GOARN, 2023) was established by the WHO in 2000. GOARN consists of a network of 250 technical institutions located across the globe, that have the capacity to deploy public health experts to outbreak locations to minimise the spread and mitigate the impact of epidemics. The main GOARN partner in the UK is the Public Health Rapid Support Team (UK-PHRST) (UK-PHRST, 2022), that provides specialist support to respond to disease outbreaks in lower and middle income countries. At a European level, the European Centre for Disease Prevention and Control (ECDC) (ECDC, 2023a) is responsible for providing support to the European Economic Area (EEA) and EU Member States for public health preparedness, investigation and response. ECDC also provides a series of training opportunities for public health experts, as well as open-source tools for individuals and institutions to aid in their surveillance activities and decision-making (ECDC, 2023c).

The international institutions described int this section are not established for companion animals. However, lessons can be learned from these initiatives for the future development of companion animal surveillance and response strategies. Particularly, by establishing multisectoral partnerships that contribute to building capacity for canine outbreak detection and response, at a national and international levels, as well as providing training opportunities for veterinary practitioners and other stakeholders involved in response interventions.

Conclusions: international level protocols for outbreak detection and response

To conclude, not many canine infectious diseases are included in international protocols of surveillance and response. WOAH's Terrestrial Code focuses on diseases that can compromise international trade, and only three canine diseases are included in their list of reportable diseases. These three diseases are exotic to the UK, and their prevalence in the country is extremely low, therefore making these protocols not fully relevant for the protection of canine populations in the UK, since outbreaks are also caused by pathogens that are endemic in the country. Further, although WOAH's Terrestrial Code provides guidance for these three canine diseases, international protocols do not provide guidelines on how to establish systems of surveillance and coordinated response strategies for companion animals at national or local levels. The lack of diseases included in international protocols conveys a message to national and local governments that canine diseases are not of international concern, which does not encourage these governments to develop systems to monitor and control diseases in canine populations. The low number of notifiable canine diseases and coordinated strategies for disease surveillance also means that the circulation of canine disease across countries is not controlled, and therefore potential epidemics are not tracked. The international community should therefore emphasise the relevance of companion animal infectious diseases due to their impacts on animal welfare and public health. Similar efforts have been carried out by organisations such as the World Small Animal Veterinary Association (WSAVA), for other concerns like antimicrobial usage and resistance (WSAVA, 2021).

1.2.3. Disease surveillance

Disease surveillance, also often referred to as Public Health surveillance in the human context, is defined as the continuous and systematic collection, orderly consolidation and evaluation of pertinent data with prompt dissemination of results to those who need to know, particularly those who are in a position to take action (CDC, 2022; WHO, 2024a). Disease surveillance constitutes the basis for infectious disease prevention and control, and it is used in an array of animal and public health analyses and activities, such as detecting outbreaks, describing burden and distribution of disease in the population, identifying novel pathogens, informing response interventions, planning vaccination strategies, and allocating resources for health promotion (M’ikanatha, 2013).

1.2.3.1. Types of surveillance

Different surveillance strategies exist depending on the aim of the surveillance activities, the clinical presentation of the disease(s) of interest, and the resources that are available to carry out such activities (Murray, 2017). An overview of existing disease surveillance strategies that are relevant to the present thesis is provided in this section.

1.2.3.1.1. Active and passive surveillance

These methods differ in the coverage of disease cases, the level of resources employed for data collection, and the persons or institutions who lead the data collection process.

Active disease surveillance aims to identify all cases of the disease or pathogen of interest in a defined population (Gomes, 2022). The process of case detection and data collection is led by public health institutions, such as ministries of health or international health organisations, who actively engage in the process, by dedicating significant human and financial resources. Due to its resource-intensive nature, active surveillance is often carried out in specific circumstances, such as when implementing public health plans that aim to eradicate a disease, for instance, by the Global Polio Eradication Initiative (GPEI, 2024), and the active eradication programme of transmissible spongiform encephalopathies (TSEs) in UK livestock (GOV.UK, 2024); or restricted to sentinel sites to identify cases within a target population (WHO, 2019; CDC, 2023a). Further, and most relevant to the present thesis, active surveillance is also often carried out as part of outbreak investigations (Stehling-Ariza, 2016). Active disease surveillance, although costly and resource-intensive, is considered the gold-standard to robustly describe disease trends, especially when applied at a population-level, rather than in sentinel practices or hospitals (Van Beneden, 2013). However, active surveillance is rarely conducted for companion animal diseases; for instance, a systematic review of active surveillance systems in Europe (Bisdorff, 2017), found that out of the total of 644, only one of them included diseases that affect companion animals.

Passive disease surveillance (Nsubaga, 2006), also referred to as "scanning surveillance", relies on data that are provided by medical or veterinary professionals, either by routinely submitting patient clinical or laboratory records, or through individuals notifying the authorities of disease anomalies seen in clinical practice or, in the case of farm animals, detected in livestock facilities. Since data are directly submitted to public health institutions, and no active finding of cases is carried out, passive surveillance constitutes a more sustainable source of data, while also covering larger geographical areas. The main disadvantages of passive surveillance are the lack of data completeness and standardisation, and its dependence on individual's awareness of disease and willingness (unless legally enforced) to report disease cases (Gilbert, 2016). An example of passive disease surveillance in animals are notifiable diseases, whose detection and monitoring relies on notifications from veterinary officials (GOV.UK, 2019c). In the UK, the APHA conducts scanning surveillance for animal diseases and, since 2022, also covers companion animal diseases, through data provided by SAVSNET and VetCompass (*APHA Small Animal Surveillance*, 2022).

Although active and passive surveillance strategies have different aims and applications, in practice they are often used concurrently, as a complementary strategy. It is common for surveillance systems to rely mainly on passive surveillance, but carry out active case finding when an outbreak is detected, for instance (Murray, 2017).

1.2.3.1.2. Syndromic and laboratory-based surveillance

Another way to classify disease surveillance activities is according to the source of data that are used.

Syndromic surveillance tracks symptoms (or clinical signs, in animals) before a diagnosis is confirmed (CDC, 2023b). Since syndromic surveillance relies on pre-diagnostic data, this strategy enables the timely monitoring and interpretation of disease trends, and the early detection of disease anomalies in the population. Since a definitive diagnosis is not available at the time data are collected, this data source is not as specific as surveillance that involves a confirmatory diagnosis (Dórea, 2011). This means that causative agents cannot be identified, and a reliable estimate of the true burden of pathogens in the population cannot be obtained. However, due to the timeliness of syndromic surveillance, this data source is valuable for the early detection and follow-up investigation of potential outbreaks.

Laboratory-based surveillance relies on samples collected from clinical or diagnostic laboratories to monitor disease trends. This source of surveillance data offers great specificity of detection, as it is possible to establish the aetiology of disease, at the cost of timeliness of the surveillance. Due to the delay between the collection of samples and the obtention of diagnostic results, laboratory-based surveillance is often not adequate for early detection of potential outbreaks. However, this kind of surveillance is key during outbreak response investigations, to identify the causative agent(s) responsible for the observed increase in disease incidence, as well as to identify novel pathogens. Knowing the aetiology of disease deepens the understanding of disease progression, and enables the instution of appropriate control and prevention measures (Kay, 1996).

Both syndromic and laboratory-based surveillance are employed by systems of disease surveillance for companion animals in the UK, through initiatives like SAVSNET (SAVSNET-Lab, 2024; SAVSNET, 2024). These sources of surveillance data are explored for the detection of potential outbreaks of canine disease in the third chapter of the present thesis.

1.2.4. Definition of outbreak in the context of this thesis

According to WHO, an outbreak of disease is the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area, or season (WHO, 2024b). This definition is often expanded to include the implication that an outbreak is a sudden occurrence, which constitutes a public health emergency that must be tackled by the corresponding authority (Reintjes, 2009). The definition of outbreak is also commonly attributed to epidemics, i.e., an unexpected increase of the number of disease cases in a specific geographical area (CDC, 2015). However, the term “epidemic” is usually applied to unexpected increases of disease cases over a larger geographical area, and often with a larger number of cases. The present thesis adheres to this distinction, and uses the term “outbreak” to refer to smaller epidemics, that occur in restricted geographical areas, where more cases of disease than expected take place in a single or a few veterinary practices. Further, in the context of this thesis, a distinction is also made between statistically significant outbreaks, i.e., that correspond to increases in disease incidence with respect to their corresponding baseline, detectable by mathematical models; and clinically relevant outbreaks, i.e., that are not only relevant from a statistical stand point, but that constitute increases in case incidence that are actionable for companion animal veterinary practitioners. This is further explored and described on the fourth chapter of the present thesis.

Chapter Two. A stakeholder opinion-led study to identify priority canine infectious diseases for surveillance and control in the UK

2.1. Abstract

Many infectious pathogens cause disease in dogs. However, currently there are no implemented surveillance systems in small companion animals at a national level, and surveillance activities are constrained to research initiatives, with a limited coverage of the country's canine population. This means that meaningful surveillance is often possible only for those canine diseases that are the most impactful. This chapter describes the first stakeholder opinion-led approach to identify which canine infectious diseases should be prioritised for inclusion in surveillance and control strategies in the UK. Diseases prioritised in this chapter were divided into three categories: endemic diseases, exotic diseases, and syndromes. Study participants were identified through a stakeholder analysis. A multicriteria decision analysis was undertaken to establish and weight epidemiological criteria for evaluating diseases, and a Delphi technique was employed to achieve a consensus among participants on the top-priority canine diseases. Leptospirosis and parvovirus were identified as the top two endemic diseases of concern, whilst leishmaniasis and babesiosis were the top two exotic diseases. Respiratory and gastrointestinal diseases were identified as the top two syndromes of concern. Findings from this study were used to achieve the subsequent aims of the present thesis, such as enhancing the current surveillance system of canine infectious diseases and improving their detection and reporting tools for a network of veterinary practitioners in the UK. The list of priority diseases obtained in this chapter will need to be updated in the future as the epidemiological and sociodemographic characteristics of the country change. The methodology developed in this chapter could provide a blueprint for other countries.

2.2. Introduction

2.2.1. Background

Disease surveillance systems have been developed globally for the protection of animal and human health, facilitating the prevention and control of animal and human diseases, including zoonoses. The last decade has seen a growth in the field of disease surveillance in small companion animals, notably in the UK (*SAVSNET, University of Liverpool*, 2023; *VetCompass, Royal Veterinary College*, 2023) and in the USA (Glickman et al., 2006a; Kass et al., 2016a). However, despite the efforts made thus far, canine populations, still lack coordinated national and international strategies for the timely detection and control of infectious diseases (Hale et al., 2019). This leaves these populations susceptible to disease outbreaks and to the emergence of disease threats which can have direct implications for human health, given the existence of canine zoonoses (Baneth et al., 2016; Deplazes et al., 2011; Rijks et al., 2016) and the constant emergence of pathogens with unknown zoonotic potential (Chomel, 2014; Holm et al., 2015). Since an increasingly large number of dogs are kept as pets in some countries (J. K. Murray et al., 2015a), and living spaces are shared (Westgarth et al., 2008a), the risk of zoonotic disease transmission among dog and human populations is a growing concern (Chomel, 2014).

One of SAVSNET-Agile's (*SAVSNet-Agile, University of Liverpool*, 2019) main goals, which also constitutes the overall aim of this thesis, is the development of a nationwide disease surveillance and response framework to improve the timely detection and response to canine disease outbreaks in the UK. Many pathogens cause disease in dogs, but due to time constraints and limited financial resources, meaningful surveillance in small companion animals is often only possible on the most impactful diseases (OIE, 2010a). Thus, to develop such a surveillance and response system, the first step is to identify which diseases should be prioritized under the current epidemiological context of the UK.

The need to prioritise diseases to develop animal and human health protection plans due to the impossibility to cover every potential threat has been expressed multiple times in previous research publications and policy papers, independent from the size/type of authoring organisation. In fact, the number of publications that discuss this issue has steadily increased over recent years (V. Brookes et al., 2015). This is only natural, given the socioeconomic and climatic changes, which have created an environment which facilitates the emergence of disease threats (Semenza & Paz, 2021). This, coupled with an improving understanding of infectious diseases, means that the number of potential threats to look after are effectively multiplied. How will we manage to deal with so many potential threats, when we are limited by the amount of resources that can be destined for this purpose, in terms of finance, personnel and time?

This is where the need to prioritise becomes apparent. To prioritise means to make decisions based on what is considered most important. Of course, the definition of what is 'important' will vary depending on the discipline, the aim of the decision-making process and its specific settings. This chapter strives to decipher what *important* means in the context of canine infectious diseases in the UK.

2.2.2. History of the evolution of disease prioritisation studies

Disease prioritisation studies have evolved from ad-hoc techniques to standardised processes that incorporate a variety of factors and actors (Figure 2.1).

The first study about disease prioritisation was conducted in Ghana in 1981 (Ghana Health Assessment Project Team, 1981) and used an objective measure of disease impact ('healthy days of life lost'), without considering its utility to decision-makers. Since then, two paths were established in the evolution of disease prioritisation methods. One consisted in the development of quantitative methods and the other to account for the perceived impacts of disease to those directing the prioritisation, based on decision-science methodology (Bouwknegt et al., 2018). As an example of the former, in 1990 the WHO introduced the measure of Disability-adjusted Life Years (DALYs), as an objective measure to assess the amount of ill health incurred during one's lifetime due to a specific disease or injury (Murray, 1994). A Canadian study in 1987 (Carter, 1991) was the first to use a scoring system where participants are asked to assign scores to a set of criteria to evaluate diseases. In the 90s, disease prioritisation started to be seen as systematic process to direct resources through consultation between decision-makers (Rushdy & O'Mahony, 1998; Weinberg et al., 1999). The main criticism of these earlier studies was that they lacked transparency and reproducibility. To overcome this, newer studies proposed separating objective criteria measurements from subjective criteria weights, and using both to generate a linear weighted sum value to score each disease of interest. This approach improved transparency by separating the opinion of the decision makers involved from measurable impacts of disease, e.g., incidence or mortality.

Later, more importance was given to the validation of results obtained through prioritisation studies, with Del Rio Vilas, 2013 (Del Rio Vilas et al., 2013) being the first one to develop a tool to evaluate the trade-offs made by decision-makers during a prioritisation exercise. In this study, criteria were weighted directly by assessing the preferences of stakeholders using swing-voting, and these subjective weights were kept separate from disease measurements. Up until that point, all methods used linear weighted sum models, which assume that the preferences between criteria are independent (i.e., they do not account for the interactions between preferences), and this is not necessarily valid in the context of decision-making. Because of this, more recent studies have strived to improve this point by developing systems to indirectly weight criteria, using methods such as conjoint analysis (Ng & Sargeant, 2013) and probabilistic inversion (Kurowicka et al., 2010). These methods involve presenting decision-makers with disease scenarios, where they are forced to make trade-offs between criteria. Decisions are then evaluated to ensure they comply with normative rationality by checking that they are transitive and maximise utility. Given how these studies include realistic outbreak scenarios, explained in layman terms, they facilitate the participation of non-experts, as well as out-of-sample validation, which enables a wider range of decision makers to participate. The downside of these newer methods is that they are of higher complexity, as they use statistical

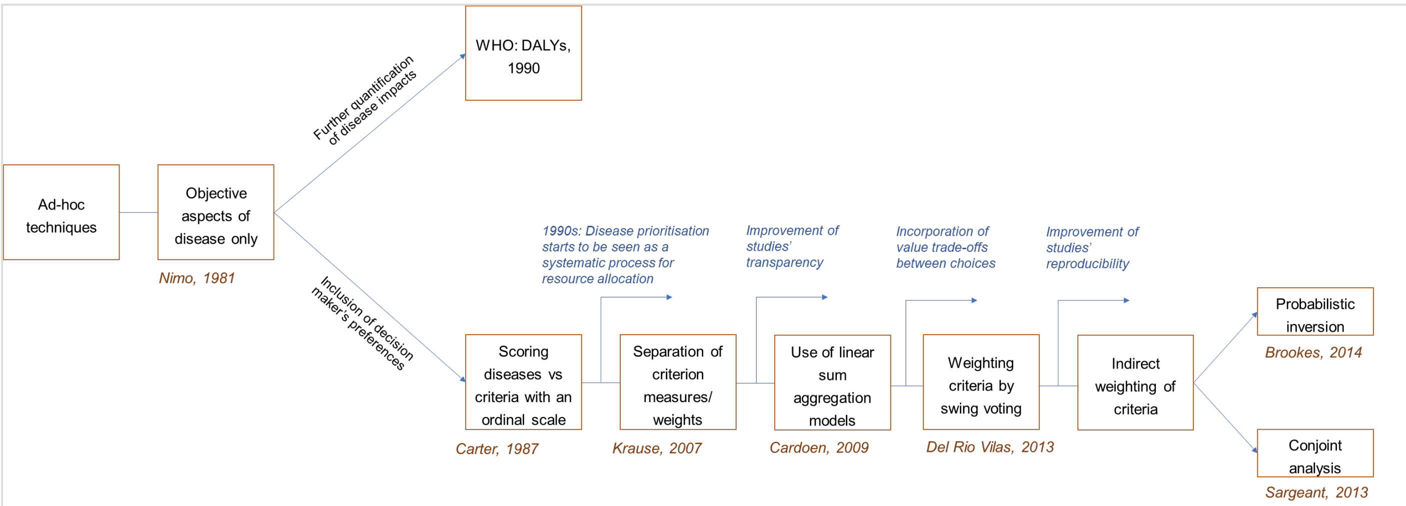

Figure 2.1. Diagram that summarises the evolution of disease prioritisation studies over time.

methods to assess the validity of results, and require large groups of participants, which is not suitable for studies with lesser resources and smaller groups of decision-makers.

2.2.3. Canine disease prioritisation

There is an extensive literature that describes methods to prioritise diseases in humans and animals, as well as strategies to identify criteria to use in prioritisation exercises (Appendix II.a). These methods, whether opinion-led (Buckland et al., 2014) or data-driven (Cassini et al., 2018), they all follow a similar underlying structure; first, an initial list of diseases is established and then ranked through the use of specific criteria relevant to the study's purpose, which are sometimes weighted to reflect participants' opinion (Balabanova et al., 2011a). Multicriteria decision analysis (MCDA) is a well-established approach to provide a sensible ordering of options, according to participant's opinion (Food Standards Agency, 2020), and is commonly used in disease prioritisation studies (Baltussen & Niessen, 2006; Norheim, 2018). Through MCDA, a range of relevant criteria is considered simultaneously and weighted according to their importance to stakeholders when setting priorities for policy development (O'Brien et al., 2016).

These disease prioritization methods have been applied to guide the allocation of resources in a variety of settings, such as zoonotic diseases (Salyer et al., 2017), food borne pathogens (Bouwknegt et al., 2018), and diseases that are specific to farm animals (Bessell et al., 2020a) and, very rarely, companion animals (Rioja-Lang et al., 2020). However, to the author's knowledge, the present study is the first that aims to identify canine infectious diseases that should be prioritised for surveillance in the UK. Given the novelty of the study, it was necessary to setup the prioritisation framework from the ground up. Published guidelines for disease prioritization recommend an evidence-based approach that uses available epidemiological data, related to the burden of diseases specific to the study's geographical location (WHO, 2006b). However, when such epidemiological information is lacking, as it often is for companion animal populations (Cito et al., 2016), a stakeholder opinion-led approach is the preferred method to inform the prioritization process (Bouwknegt et al., 2018). In this chapter, a variety of stakeholders that play a relevant role in the improvement of canine health in the UK were involved in every step of the prioritisation process. Stakeholder involvement was considered crucial in this study, since the overall aim of this thesis is to develop a framework to improve the surveillance and response to outbreaks of canine diseases that is relevant to the UK canine health sector.

2.2.4. Aims

The aim of this chapter is twofold; 1. to develop a qualitative methodology to prioritise canine infectious diseases that is informed by a wide range of stakeholders that play a role in safeguarding canine and public health, and 2. to use this methodology to identify canine infectious diseases that are of the highest relevance in the epidemiological context of the UK, and therefore, should be prioritised for surveillance and for the development of a nationwide outbreak response framework.

2.3. Materials and methods

The methodology steps followed in this study are summarized in Figure 2.2. Ethical approval for this work was granted by the University of Bristol Faculty of Health Sciences Ethics Committee (FREC, reference code: 98843).

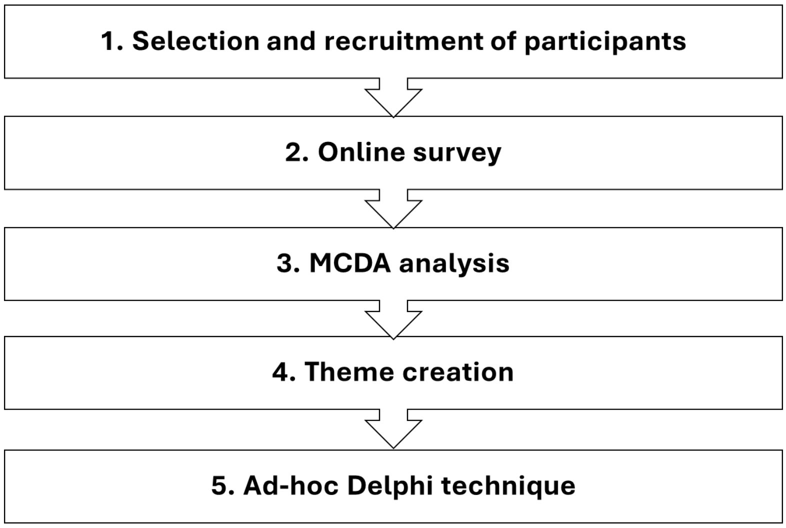

Figure 2.2. Flowchart that summarises the steps followed in this chapter's methodology (MCDA: Multicriteria decision analysis)

2.3.1. Selection and recruitment of participants

2.3.1.1. Identification of potential participants

Participants were selected through a stakeholder analysis process (Schmeer, 1999). First, institutions that play a relevant role in canine and public health in the UK were identified. Then the following criteria were used to shortlist potential participants:

i) Expertise in one or more of the following sectors:
   a. Small companion animal medicine.
   b. Veterinary public health.
   c. Public health.

ii) Seniority within their corresponding institution.

iii) Availability and willingness to take part in the study.

2.3.1.2. Participant recruitment

A purposive sampling approach was followed, and a wide range of key stakeholders was considered for inclusion in the study to maximize the generalisability of results. The following sectors were targeted in the recruitment process:

a) Government Department or Agencies: government bodies, that define policies to put into practice (departments) or are overseen by the departments to provide services (agencies) (GOV.UK, 2022b). In this case, bodies of interest were related to the protection of animal and public health, e.g., DEFRA.

b) Academic institutions: including those UK Universities that, at the time of the conduction of this study, did relevant research in the field of veterinary epidemiology and public health.

c) Veterinary associations: including relevant veterinary organisations in the UK that are representative of the veterinary profession, such as the British Veterinary Association (BVA) or the Royal College of Veterinary Surgeons (RCVS).

d) Animal charities: non-profit organisations dedicated to the health and welfare of dogs in the UK.

e) Veterinary corporate practice groups.

f) Independent veterinary practices.

g) Pharmaceutical industry: specifically, pharmaceutical companies that specialise in the development of drugs for veterinary usage in companion animals.

h) Veterinary diagnostic laboratories: that provide services to small animal veterinary practices in the UK.

Individual participants within these institutions were then selected and approached as follows; first, members of the SAVSNET-Agile team were asked to identify potential candidates. This was done to make use of their expertise and years of experience in the small animal sector. Team members were provided with a spreadsheet that contained the above-mentioned areas (a-h) and asked to suggest persons with whom they were acquainted. For those institutions without a previously known contact, relevant persons were identified through an internet search.

Amongst the identified candidates, potential participants were ranked in descending order of hierarchy, according to their position within the institution. Potential participants were first contacted via email by the member of the SAVSNET-Agile team that had put their name forward. In this manner, team members acted as gatekeepers, whose role is to act as an intermediary between the researcher and study participants, facilitating the access to research ('The SAGE Dictionary of Social Research Methods', 2006). In this first email, the gatekeeper provided a brief overview of the project and introduced the author of this thesis. This was done to increase the study's credence and maximise the engagement of potential participants. The initial email was immediately followed by a second email from the author of this thesis, which consisted of a formal invitation to participate in the study. A participant information sheet, which contained all the relevant details for study participants, as well as a consent form, were also included in this email. This was done in accordance with the University of Bristol's ethical regulations. Contacted candidates were given two weeks to respond to the invitation. After this, if no response was received, the next person in the hierarchy of candidates proposed by SAVSNET team members was contacted. If the initially contacted person responded but was not able to participate, snowballing sampling was used to identify an alternative candidate. In this case, the initially contacted individual acted as the gatekeeper and facilitated the communication with the newly proposed candidate. This process was repeated until either a satisfactory level of representation of the targeted institution was achieved or no suitable participant was found within the established timeframe for recruitment.

2.3.2. Elaboration of initial lists of canine diseases

Using an online survey, participants were asked to provide up to three relevant diseases to include in a future epidemic response framework. This process was repeated for endemic diseases, exotic diseases, and syndromes, and the following definitions were provided to participants:

- Endemic disease: known diseases that are normally present in the UK and have a certain level of constant prevalence over time (CDC, 2021b).
- Exotic disease: known diseases that are not present or not normally occurring in the UK (GOV.UK, 2019c).

- Syndrome: groups of conditions and clinical signs that appear concurrently and affect a particular organ system. The 11th International Classification of Diseases (ICD-11) (*ICD-11*, 2022) was given as a reference.

Proposed diseases on each of the endemic and exotic groups that had more than one vote were further evaluated throughout the disease prioritization process. A sufficient level of prioritisation was assumed in this first step for the syndromic category because only three syndromes had more than one vote.

2.3.3. Elaboration of disease fact sheets

Once the initial lists of canine endemic and exotic infectious diseases were established, an extensive literary review was done to obtain information about these diseases. The author was particularly interested in gathering information that would be relevant for the disease prioritisation process, i.e., that would potentially influence participant's views on the relative importance of the selected diseases. This information was then used to create fact sheets for each of the diseases from the initial lists (see Appendix II.b).

These fact sheets consisted of a summary of the most relevant epidemiological aspects of each disease and were loosely based on the guidelines for disease profiling proposed by WOAH (OIE, 2010a). The following information was included:

a) Epidemiological profile

b) Animal health profile

c) Public health profile

d) Control measures profile

e) Economic profile

The disease fact sheets were provided to participants, to aid them (if needed) in the subsequent steps of the prioritisation process. This was done to provide a well-rounded view of the potential impacts of an outbreak, and to ensure participants had a base-level knowledge of the diseases under scrutiny if these were outside their area of expertise.

When elaborating these fact sheets, the author refrained from adding any subjective judgements, and only objective information from highly trusted sources was used (see sources cited on Appendix II.b).

2.3.4. Selection and weight of epidemiological criteria to evaluate canine diseases

A qualitative multicriteria decision analysis (MCDA) (Norheim, 2018) was conducted to select and weight epidemiological criteria for prioritising canine diseases. MCDA provides a systematic framework for decision-makers to simultaneously consider various criteria when prioritising diseases, and allows researchers to assess how different aspects, such as disease severity, economic impact, or zoonotic potential, impact participant opinion. MCDA for disease prioritisation requires decision-makers to first identify which criteria are most relevant for evaluating the impact of diseases, and then assigning weights to such criteria, which reflect their importance, relative to each other. In this manner, participants are compelled to make trade-offs in their decision-making process, which allows them to discern which factors are of greatest significance in the context of disease prioritisation. The identified criteria are then used to assess the importance of diseases, by assigning a numerical score for each disease against each criterion, and multiplying said score by the previously assigned weights.

In thic chapter, a qualitative MCDA was conducted by first asking participants through an online survey to provide up to five epidemiological criteria that could be used to evaluate the relevance of canine infectious diseases in the context of the UK. Participants were given the option to either choose different or the same criteria to evaluate endemic and exotic diseases. Subsequently, participants were also requested to rank their answers in a scale from 1 to 5, 1 being the least and 5 the most important criterion. No further indications were given, so as not to influence participant's responses.

2.3.5. Grouping epidemiological criteria into themes and generating a score for each theme

Epidemiological criteria from every participant were pooled together for analysis to group them in overarching categories, or themes. The aim was to obtain the minimum number of criteria that were a) sufficient to evaluate the epidemiological relevance of canine infectious diseases; b) representative of participant's opinion; and c) manageable for participants to consider in the subsequent steps of the prioritisation process (Saaty & Ozdemir, 2003). Themes consisted of aggregations of criteria that represented similar ideas, e.g., responses that presented the same concepts but using different terminology. This exercise was conducted individually by the author of this thesis. Furthermore, the author of this thesis invited their main doctoral supervisor (FS-V) to perform this same procedure separately. The results obtained by both researchers were compared and the differences were discussed until an agreement was reached.

Whilst grouping criteria into themes, individual participant's scores given to each criterion were summed to generate an overall score for the corresponding theme, referred to as theme weight. Consequently, participant preferences were reflected qualitatively, by the themes that contained the criteria that they proposed, as well as quantitatively, through the weight associated to each theme, that reflected their relative importance based on participant's opinion. When a criterion provided by participants contained multiple elements that could be included in more than one of the themes, e.g., "morbidity and mortality", these elements were included, and their scores counted towards all the fitting themes, e.g., "morbidity and mortality" was included in the theme "prevalence of disease", as well as on the theme "mortality of disease". Themes defined by a single criterion that was only mentioned by a single participant and that scored under five points were included in the analysis only if they had been identified as relevant criteria for disease prioritisation in previous studies. These themes were otherwise included in a separate "miscellaneous" theme that was not used to evaluate diseases.

2.3.6. Scoring of canine diseases against identified themes and definitive lists of prioritised diseases

On the next stage of the prioritisation process, participants scored canine diseases from the initial lists of endemic and exotic diseases against the identified themes. This was done through a Delphi technique (Dalkey & Helmer, 1963). This is a well-established consensus-building method that consists in first collecting individual participant's opinion on the subject matter, collating individual responses, and then feedback the summary of the group results to participants. At this point, participants are given the opportunity to review their answers in light of the group's response. Following this technique, an online questionnaire was sent for participants to score diseases from the initial lists against previously identified themes, which included examples of the criteria relevant to each theme (Appendix II.c). A 25-point scale (0 no relevance; 25 maximum relevance of the disease for the theme) was used to provide sufficient discrimination between diseases (Gibbens et al., 2016).

An individual participant final score for each disease was derived from summing up the disease scores given to each theme. Participant's disease-level results were then added to obtain an overall score for each disease; see Equation 2.1, where O_i is the overall score for each disease i; k represents each participant, and D_{ij} calculates individual participant's score for each disease, by summing up the disease's score across themes.

$$O_i = \sum_k \left(\sum_j D_{ij}\right) \qquad \textit{(Equation 2. 1)}$$

To discern the impact of using weighted themes on the final lists of diseases, this process was repeated taken into account the overall theme score or weight as follows. For each disease, an individual participant final weighted score was derived from multiplying the disease score given to each theme by the corresponding theme's weight before being summed up. Participant's disease-level results were then added to obtain an overall weighted score for each disease; see Equation 2.2, where O_i^w represents the overall weighted score, w, for each disease, i; k represents each participant, and D_{ij} represents individual participant disease scores, by first multiplying their value by each theme's weight, W_j.

$$O_i^w = \sum_k \left(\sum_j D_{ij} \cdot W_j\right) \qquad \textit{(Equation 2. 2)}$$

Two separate disease rankings were ascertained according to their final overall unweighted scores and their final overall weighted scores. The resulting rankings of canine endemic and exotic diseases were shared with participants, who were then allowed to review and change their answers considering the group results, and any subsequent change was incorporated. All calculations conducted in the present chapter were done using the Microsoft Excel software (Microsoft Excel, 2024).

2.3.7. Pre-pandemic methodology

Before the COVID-19 pandemic, an in-person methodology to prioritise canine diseases was developed. This methodology is presented here as an alternative method for disease prioritisation to use when the number of participants is large (20 or more) and there are no restrictions for participants to attend an in-person event. This approach was based on the WHO's original guidelines for prioritisation of health threats (WHO, 2006b) and employs a Nominal Group Technique (NGT) (Ven & Andre L. Delbecq, 1971). NGT is a consensus-building method where group members are first consulted individually and then asked to share their ideas for discussion with the wider group (Harvey & Holmes, 2012). This approach means that every participant's ideas are considered, minimising the risk of groupthink, and preventing the domination of the discussion by a single/a few persons (Boddy, 2012). The following steps for this method were defined:

1. Introduction to the exercise: the research question is clearly stated, as well as a detailed description of the NGT procedure.
2. Silent generation of ideas: participants are provided with blank cards and asked to provide criteria for canine disease prioritisation. A sufficient amount of time is given so they can reflect on their answers.
3. Idea sharing: cards are collected and read aloud by the moderator of the group (in this case, the author of this thesis). Alternatively, participants can read their own answers out loud, round-robin style. As the content of the cards is shared with the group, the moderator writes down the answers/sticks down the cards on a whiteboard. The contents of the cards are discussed as they come up, and participants are given the opportunity to express their opinion.

4. Grouping criteria into themes: participants engage in a group discussion, moderated by the researcher. The aim of this discussion is to group the criteria into wider units of meaning, or themes. At this stage, criteria that cannot be grouped into any theme are included into a "miscellaneous" category. A discussion is held with the group to discern the importance of this miscellaneous theme, and whether it should be used or not in the subsequent steps of the prioritisation process.

5. Weighting themes: as the themes are created, a score that reflects their relative importance is generated. This is done quantitatively (by considering the number of participants that propose criteria grouped into a certain theme) and qualitatively (by gathering participant's opinion during the group discussion).

6. Scoring diseases against themes: participants are split into smaller groups (4-5 people) and asked to assign a score to each of the diseases from the initial lists for every theme identified and weighted on steps 4 and 5. The smaller groups facilitate the interaction between participants. Each of these groups are moderated by a researcher that is part of the research project.

7. Final lists of prioritised diseases: the results of the small groups are compared and discussed in a plenary session with all the participants. The main researcher facilitates the discussion, aimed at achieving a consensus among participants on the final ranking of diseases.

2.4. Results

2.4.1. Recruitment of participants

A total of 33 individuals from 29 relevant institutions were initially contacted and asked to take part in this study. Out of those initial targets, a final number of 19 individual persons from 16 institutions took part in this study. A full summary of the targeted institutions, and their corresponding number of recruited participants can be found on Table 2.1.

Although these 19 individuals agreed to take part in the study, due to the COVID-19 pandemic, not all of the participants were able to contribute to every step of the process. The specific number of participants on each section of the prioritisation exercise will be specified hereunder.

Table 2.1. Summary of sectors identified through a stakeholder analysis, with the corresponding targeted institutions and number of participants recruited to take part in the present study. A summary of the institutions contacted unsuccessfully within each sector is also provided.

Sectors identified through a stakeholder analysis	Targeted institutions	No. of recruited participants
Governmental Department or Agency	Department of Environmental, Food and Rural Affairs (DEFRA)	1
	Animal and Plant Health Agency (APHA)	1
	Other contacted government departments (2)	0
Veterinary Associations	British Small Animal Veterinary Association (BSAVA)	1
	European Scientific Counsel of Companion Animal Parasites (ESCCAP)	1
	Other contacted veterinary associations (2)	0
Animal Charities	Dogs Trust	2
	Kennel Club	1
	Other contacted animal charities (2)	0

Sectors identified through a stakeholder analysis	Targeted institutions	No. of recruited participants
Veterinary Corporate Practice Groups	CVS group	1
	IVC Evidensia	1
	Other contacted practice groups (3)	0
Small Veterinary Practice	Anderson Moores	1
	Vine Tree Vets	1
Academic Institutions	Royal Veterinary College	2
	University of Edinburgh	1
	University of Bristol	1
	University of Liverpool	1
	Other contacted Universities (1)	0
Pharmaceutical industry	MSD Animal Health	1
	NOAH (National Office of Animal Health)	2
	Other contacted pharmaceuticals (1)	0
Veterinary diagnostic laboratories	3 contacted	0
Total		19

2.4.2. Elaboration of initial lists of canine infectious diseases

Ten participants responded to the initial survey and provided their input on which canine diseases and syndromes they considered most relevant for inclusion in future surveillance and response protocols. The results from this initial survey are summarised on Table 2.2.

Table 2.2. Summary of participant responses to an online survey, aimed at establishing initial lists of most relevant canine endemic diseases, exotic diseases, and syndromes. The top five endemic and exotic diseases, as well as the top three syndromes are highlighted in bold.

Disease	***No. Of voting participants***
Canine endemic diseases	
Parvovirosis	**7**
Alabama Rot/ CRGV	**6**
Leptospirosis	**6**
Distemper	**5**
Lungworm	**2**
Kennel Cough	2
Campylobacter	1
Lyme disease	1
Coronavirus	1
Canine exotic diseases	
Leishmaniosis	**8**
Babesiosis	**7**
Canine Influenza	**4**
Ehrlichiosis	**2**
Dirofilariasis	**2**
Tickborne diseases	2
Brucella canis	1

Rabies	1
Disease	***No. Of voting participants***
Canine syndromes	
Respiratory disease	**8**
Gastrointestinal disease	**6**
Neurological disease	**3**
Circulatory system disease	1
Poisonings	1
Infectious and parasitic	1

As observed on Table 2.2, the initial list of endemic diseases included two votes for kennel cough, which tied in votes with lungworm. Since kennel cough can be caused by a variety of infectious agents, rather than a distinctive pathogen (Hurley & Miller, 2021), it was decided for these votes to contribute to its overarching syndrome, respiratory disease. Similarly, the initial list of exotic diseases included two votes given to "tick borne diseases". Given that both babesiosis and ehrlichiosis were already represented in this list, it was decided to allocate one of these votes to each, which did not alter the initial disease ranking.

Considering all of these amendments, the final list of diseases obtained through this survey and therefore used to perform the rest of the prioritisation exercise included:

a) Endemic diseases: parvovirosis, leptospirosis, cutaneous and renal glomerular vasculopathy (CRGV)/Alabama Rot, distemper, and lungworm.

b) Exotic diseases: leishmaniosis, babesiosis, ehrlichiosis, canine influenza and dirofilariasis.

c) Syndromes: respiratory disease, gastrointestinal disease, and neurological disease.

2.4.3. Selection and weight of epidemiological criteria to evaluate canine diseases and overarching themes

Sixteen individuals provided and weighed epidemiologic criteria (Table 2.3, and Table 2.4). All of the participants, except for one, provided five epidemiologic criteria to evaluate canine diseases, the maximum permitted. Four participants provided the same criteria and allocated the same weights for the purpose of evaluating both endemic and exotic diseases.

The remaining twelve participants either chose the same criteria but altered their weights (n=5) or picked different criteria altogether (n=7). Out of the five participants that altered the weights given to the same criteria for endemic and exotic diseases, two of them did so to rank the criterion "epidemic potential of disease", the highest in the case of exotic diseases, compared to "prevalence of disease", which ranked first in the endemic category. The remaining three chose different criteria rankings altogether for endemic and exotic diseases. Out of the seven participants that chose different criteria to weight endemic and exotic diseases, six of them did so to exchange a criterion that represented the prevalence of the endemic disease in the country for another criterion in the exotic category. The criteria used to replace disease prevalence in the exotic category were either related to the risk of the disease entering the country (3/6) or to the epidemic potential of the disease (3/6). The remaining participant removed the criterion "ease of monitoring, i.e., distinct clinical signs" from the criteria list for canine exotic diseases.

By grouping the criteria provided by individual participants, nine themes were generated to evaluate endemic diseases, and ten themes to evaluate exotic diseases (Table 2.3, and Table 2.4, respectively). The generated themes were the same, apart from the addition of the theme *risk of entry in the UK* for exotic diseases.

The themes with the highest scores were "amount of disease in the UK" for endemic diseases and "impact on public health" for exotic diseases; economic impact of disease was the lowest-rated theme.

Table 2.3. Summary of criteria selected and criterion score by each participant for the evaluation of endemic canine infectious diseases, grouped into their corresponding themes.

Theme	**Criteria included within each theme**	**Criterion score by each participant**	**Theme score**
Amount of disease in the UK	Prevalence	3	59
	Frequency in population	5	
	Current burden of disease	4	
	Disease incidence	5	
	Prevalence (high)	4	
	Severity/case fatality/burden of disease	4	
	Present burden of disease	1	
	Prevalence	1	
	Prevalence	5	
	Annual incidence of disease	5	
	Prevalence	5	
	Disease incidence	4	
	Number of animals affected	1	
	Morbidity and mortality	4	
	Morbidity (high severity)	5	
	Morbidity	3	

Theme	Criteria included within each theme	Criterion score by each participant	Theme score
Public Health impact of disease	Zoonosis	5	53
	Zoonotic threat	1	
	Does the disease have any zoonotic potential?	3	
	Is the disease zoonotic?	4	
	Zoonotic (yes)	3	
	Zoonotic potential	5	
	Zoonotic potential	3	
	Zoonotic potential	3	
	Risk of zoonotic transmission	4	
	Zoonotic potential	4	
	Zoonotic potential	5	
	Zoonotic potential	2	
	Zoonotic potential	2	
	Probability of spread and zoonotic potential	2	
	Consideration for CFR/severity in humans	5	
	Zoonotic potential	2	

Theme	Criteria included within each theme	Criterion score by each participant	Theme score
Impact of disease on dog welfare	pathogenicity	3	45
	Severity/case fatality/burden of disease	4	
	Severity / mortality	5	
	Severity	4	
	Severity of disease	5	
	Severity of disease (likely hospitalisation)	3	
	Quality of life impact	5	
	Degree of debilitation/severity	4	
	Length of time for the disease	3	
	Severity – effect on animal health and welfare	4	
	Duration / long term impact on quality of life	5	
Mortality of disease	Mortality	4	37
	Mortality	4	
	Morbidity and mortality	4	
	Case fatality rate	5	
	Mortality rate	3	
	Case fatality	3	
	Disease fatality rate	5	

	Severity/case fatality/burden of disease	4	
	Severity / mortality	5	
Theme	**Criteria included within each theme**	**Criterion score by each participant**	**Theme score**
Ability to prevent and control disease	Is tx available?	2	24
	Is there a preventative option? Ie vaccination	1	
	Effective preventative measures	3	
	Effective therapeutic measures	2	
	How easy is it to prevent or control the disease?	2	
	Preventable by vaccination (no)	1	
	Availability of effective preventative measures	2	
	Effectiveness of treatment	1	
	Availability of vaccine/treatability	2	
	Ability to respond (ie is anyone going to do anything with the knowledge)	4	
	Effective vaccine available / ability to prevent	4	
Transmission and risk of spread of disease	Likelihood/speed of transmission	4	22
	Transmissibility of infection	3	
	Infectivity	5	
	Route of transmission/control measures	1	

	Unclear epidemiology	5	
	Risk of spread – within and between species	2	
	Probability of spread and zoonotic potential	2	
Theme	**Criteria included within each theme**	**Criterion score by each participant**	**Theme score**
Changing trends of disease in morbidity and mortality	Potential for disease pattern to change	1	8
	Potential threat/emergence/changing pattern	3	
	Risk of increase (esp if in current circumstances preventive vaccination reduced)	3	
	Probability that risk increases in the next 5 years	1	
Ease of diagnosis of disease	Clinical manifestation	4	5
	Ease of monitoring (e.g. distinct signs)	1	
Economic impact	Cost of treatment	2	2

Table 2.4. Summary of criteria selected and criterion score by each participant for the evaluation of exotic canine infectious diseases, grouped into their corresponding themes.

Theme	Criteria included within each theme	Criterion score by each participant	Theme score
Public Health impact of disease	Zoonosis	5	62
	Zoonotic potential	5	
	Zoonotic threat	3	
	Does the disease have any zoonotic potential?	3	
	Is the disease zoonotic?	4	
	Zoonotic (yes)	5	
	Zoonotic potential	5	
	Zoonotic potential	4	
	Zoonotic potential	2	
	Risk of zoonotic transmission	4	
	Consideration for CFR/severity in humans	5	
	Risk for transmission to humans (+other spp)	2	
	Zoonotic potential	4	
	Zoonotic potential	2	

	Probability of introduction of pathogen and potential for spread, including to humans	5	
	Zoonotic potential	4	
Theme	**Criteria included within each theme**	**Criterion score by each participant**	**Theme score**
Impact of disease on dog welfare	Morbidity and mortality	4	47
	pathogenicity	3	
	Severity/case fatality/burden of disease	2	
	Severity	3	
	CFR/severity in canine population	3	
	Severity / mortality	5	
	Severity	5	
	Quality of life impact	5	
	Severity – effect on animal health and welfare	3	
	Degree of debilitation/severity	3	
	Length of time for the disease	2	
	Severity of disease (likely hospitalisation)	4	
	Duration / long term impact on quality of life	5	

Theme	Criteria included within each theme	Criterion score by each participant	Theme score
Amount of disease in the UK	Prevalence	3	39
	Morbidity	4	
	Disease incidence	5	
	Prevalence (high)	3	
	Severity/case fatality/burden of disease	2	
	Morbidity and Mortality	4	
	Annual incidence of disease	4	
	Disease incidence	4	
	Morbidity (high severity)	4	
	Number of animals affected	1	
	Prevalence	5	
Transmission and risk of spread of disease	Contagiousness	5	39
	Epidemic potential	4	
	Infectivity	3	
	Risk for transmission to other spp	2	
	Risk of spread – within and between species (e.g. are vectors present in UK)	4	
	Epidemiology- is it transmissible to other species, including wildlife	4	
	Risk of establishment and spread in the UK	5	

	Risk of transmission once in UK	3	
	Route of transmission/control measures	3	
	Source	1	
	Probability of introduction of pathogen and potential for spread, including to humans	5	
Theme	**Criteria included within each theme**	**Criterion score by each participant**	**Theme score**
Mortality of disease	Mortality	4	38
	Morbidity and Mortality	4	
	Case fatality rate	5	
	Case fatality	2	
	Disease fatality rate	5	
	Mortality	3	
	Mortality rate	3	
	Severity/case fatality/burden of disease	2	
	CFR in canine population	3	
	Severity / mortality	5	
Ability to prevent and control disease	Is tx available?	2	23
	Is there a preventative option? Ie vaccination	1	
	Available preventative measures	1	
	Available therapeutic measures	2	

	How easy is it to prevent or control the disease?	4	
	Preventable by vaccination (no)	1	
	Availability of effective preventative measures	2	
	Effectiveness of treatment	1	
	Availability of vaccine/treatability	1	
	Route of transmission/control measures	3	
	Ability to respond	1	
	Effective vaccine available / ability to prevent	4	
Theme	**Criteria included within each theme**	**Criterion score by each participant**	**Theme score**
Risk of disease entry in the UK	Risk of introduction	5	13
	Likelihood of incursion	4	
	Risk of entry	4	
Ease of diagnosis of disease	How easy/reliable is it to diagnose cases of disease?	1	4
	Clinical manifestation	3	
Changing pattern of disease	Probability that risk increases in the next 5 years	1	3
	Risk of increase (esp if in current circumstances preventive measures reduced)	2	

Theme	Criteria included within each theme	Criterion score by each participant	Theme score
Economic impact of disease	Cost of treatment	2	2

Five and four criteria were included in the miscellaneous theme for endemic and exotic diseases, respectively (see Table 2.5).

Table 2.5. Criteria to evaluate endemic and exotic canine diseases included in the "miscellaneous" theme.

Criteria included in the "miscellaneous" theme			
Endemic diseases		**Exotic diseases**	
Criteria	Criterion score by each participant	Criteria	Criterion score by each participant
Risk of AMR development	2	Risk of AMR development	2
Current neglectedness	2	Legislation	1
Health gain opportunity	2	Health gain opportunity	1
Legislation	1	Public perception	1
Public perception	1		

2.4.4. Scoring of canine diseases against identified themes and definitive lists of prioritised diseases

The three most voted canine syndromes were respiratory disease, gastrointestinal disease, and neurological disease, with eight, six and three votes, respectively (see Table 2.2).

The final lists of prioritised endemic and exotic diseases with their corresponding weighted and unweighted scores are shown in Table 2.6; the use of weighted criteria did not alter the disease rankings. The highest scored endemic and exotic canine diseases were leptospirosis and leishmaniasis, respectively.

Table 2.6. Final list of prioritised endemic and exotic canine diseases in descending order of their corresponding weighted and unweighted scores.

Disease	Total unweighted sum	Total weighted sum	Ranking
Endemic diseases			
Leptospirosis	1849	9275	1
Parvovirosis	1768	8198	2
Distemper	1580	7138	3
Lungworm	1538	7086	4
Cutaneous and Renal Glomerular Vasculopathy (CRGV, Alabama Rot)	1480	6727	5
Exotic diseases			
Leishmaniasis	1676	8815	1
Babesiosis	1586	8039	2
Ehrlichiosis	1431	7494	3

Disease	Total unweighted sum	Total weighted sum	Ranking
Exotic diseases			
Dirofilariasis	1430	7156	4
Canine Influenza	1214	6457	5

2.5. Discussion

This chapter presents a stakeholder opinion-led methodology to establish surveillance priorities for infectious diseases in canine populations. To the author's knowledge, this is the first study aimed to identify canine diseases and syndromes that are of the highest relevance in the UK, and therefore, should be prioritised for surveillance. Respiratory, gastrointestinal, and neurological diseases were identified as the top three syndromes of concern. In descending order of unweighted and weighted score, leptospirosis, parvovirus, distemper, lungworm, and CRGV (Alabama rot) were the top five endemic diseases of concern; and leishmaniasis, babesiosis, ehrlichiosis, dirofilariasis and canine influenza were the top five exotic diseases. These diseases will be the focus of the subsequent chapters of this thesis to inform the development of a national disease surveillance and response system aimed at improving the timely detection and response to canine disease outbreaks in the UK.

As mentioned throughout this thesis, the lack of population health surveillance for companion animal populations leaves them vulnerable to the emergence of health threats without means of early detection. This was the rationale for setting up SAVSNET-Agile, as well the present doctoral project. So far, surveillance and control activities for dog diseases have happened on an ad-hoc basis and are limited by the lack of available funding and epidemiologists dedicated to this purpose. For this reason, it is essential to develop strategies that allow the efficient allocation of resources. This is precisely what this chapter provides, a tailored methodology to identify canine diseases that are of the highest relevance in the epidemiological context of the UK. This section discusses the results obtained in this chapter and compares the developed prioritisation methodology to that described in previous publications.

2.5.1. Types of disease prioritisation studies

Disease prioritisation studies are often classified according to the source of data that are used to inform the prioritisation process, into quantitative, qualitative and semiquantitative (McKenzie et al., 2007). Qualitative studies base the disease rankings purely on participant opinion (Klamer, Van Goethem, Working group Disease and Criteria selection, et al., 2021). Participants are usually either stakeholders or experts in the subject matter. Conversely, quantitative studies rely on epidemiological data (e.g., case incidence levels) to establish disease priorities (Humblet et al., 2012a). Semiquantitative studies propose a mixed approach, that is based on participant opinion but uses numerical scales and statistical calculations to discern the relative importance of participant's choices (Rist et al., 2014). This chapter uses a group consensus approach (Delphi technique), which is sometimes classed as purely qualitative, and sometimes as a mixed-methods approach (Sekayi & Kennedy, 2017), as it entails several rounds of participant consultation and the use of numerical scales (e.g., intervals or Likert-type) (Clayton, 1997). The author of this thesis does not intend to participate in this ongoing debate but considers that the methodology presented in this chapter relies on stakeholder input and therefore could appropriately be classed as a qualitative approach.

Over recent years, research studies have increasingly placed importance on using quantitative methods for disease prioritisation, arguing for their objectivity and direct comparability of results (Havelaar et al., 2010) and criticising qualitative methodologies for their alleged lack of transparency and generalisability (McKenzie et al., 2007). In this chapter, these criticisms have been tackled by presenting a comprehensive, step-by-step account of its methodology to demonstrate the rigour of the study. The original responses obtained from participants to every step of the prioritisation process have been made available on Table 2.2, Table 2.3, and Table 2.4, as well as the principles followed to group criteria into themes. It is also worth mentioning the advantages that a qualitative approach can provide in a disease prioritisation setting. By consulting stakeholders and experts in the subject matter, it is possible to gain deeper insights into the impacts of disease and what they signify to those affected by them, compared to only using quantifiable indicators, such as prevalence data. Furthermore, from a policy-making perspective, it is arguable that individual's perceptions of risk are just as relevant as the risks themselves (Siegrist & Árvai, 2020). Therefore, to decide which diseases to include in a national surveillance and outbreak response framework, it is peremptory to understand stakeholder impressions of the risks posed by these diseases.

2.5.2. Stakeholder contribution

While the importance of stakeholder contribution to disease prioritisation is mentioned in previous publications (Cito et al., 2016), the methodology presented in this chapter is unique, in that it involved participating stakeholders in every step of the process. This includes the establishment of an initial list of diseases to work with and the definition of relevant criteria to evaluate diseases. In previous publications, initial diseases and criteria are usually pre-established by the authors of the study (Stebler et al., 2015). To use stakeholder opinion was deemed as the optimal approach to achieve the aims of this chapter, mainly for two reasons. First, given the novelty of the study, no previous guidelines were available for canine disease prioritisation in the UK. Hence, it was necessary to set up a methodology from the ground up and consult key actors on all the aspects of the process. By consulting a multidisciplinary stakeholder group, it is possible to set priorities for surveillance and control that accurately reflect the canine sector's needs. Second, although population health data are becoming available for some diseases from sentinel networks of practices and laboratories (Smith et al., 2021), significant gaps such as the lack of surveillance data from a number of veterinary practices that is representative of the canine population in the country, or lack of demographic data about this population mean they cannot yet inform quantitative approaches to prioritise canine diseases.

2.5.3. Assessing participant consensus

Previous disease prioritisation studies based on surveying either experts in the subject matter or stakeholders use different strategies to achieve a consensus among participants. These can consist of in-person interactions, such as workshops and face-to-face group discussions (Buckland et al., 2014), or remote methods, such as the Delphi technique (Balabanova et al., 2011a). This chapter presents two different approaches to use in circumstances where participants are able to travel to the same location (Nominal Group Technique), and for circumstance where this is not possible, e.g., due to schedule conflicts, participants being in faraway locations, or travel restrictions (modified Delphi technique). The latter was carried out, given the COVID-19 lockdown that was in place at the time of the conduction of this study. This methodology, even though it was not originally intended, brought about some advantages. For instance, it allowed for a large number of participants to be consulted over a period of time (vs a one-day event), which provided more opportunities for participation. Further, as participants answered the questions individually, there was no risk of influence by the wider group.

Ultimately, the methodology employed in this chapter proved adequate to obtain a consensus among participating stakeholders and offered enough differentiation to prioritise diseases. It is worth noting that participant responses were quite homogeneous at all the stages of the prioritisation process, e.g., in the low variability of diseases included on the initial lists, the criteria for prioritisation, and the final rankings of diseases. This indicates a high level of consensus among stakeholders on what the most relevant canine diseases are in the UK, as well as on the criteria that should be used to evaluate them. Indeed, final endemic and exotic disease rankings were not affected by using weighted criteria. Conversely, the use of weights only set the diseases further apart, offering an even more pronounced differentiation between them.

2.5.4. Disease classification

To the author's knowledge, this is also the first prioritisation study to use a classification that separates diseases caused by specific pathogens (endemic and exotic) and syndromes. This classification is proposed due to the purpose of the prioritisation, to inform the development of a disease surveillance and control system. Traditional surveillance can take place at a pathogen level in the case of endemic and exotic diseases that have a known causative agent, e.g., via laboratory-based surveillance (Paterson & Durrheim, 2013). However, this surveillance strategy cannot account for newly emerging diseases with an unknown causative agent. To tackle this issue, a syndromic category was included in the prioritisation process, that will be used to inform the development of syndromic surveillance strategies. The rationale is that epidemics caused by emerging pathogens with undetermined diagnoses and unspecific clinical presentations can be detected via syndromic surveillance, through increases in the reporting rate of the affected organ(s) system(s). This is widely regarded as one of the main advantages of syndromic surveillance (Dórea et al., 2011).

2.5.5. Rationale for weighting criteria and multicriteria decision analysis (MCDA)

Plenty of examples can be found in the literature where the criteria used to prioritise diseases were weighted to reflect relevant nuances (Cox, 2013; Krause et al 2008). Other relevant guidelines do not explicitly recommend using weighted criteria, although they mention how this practice is commonly used (WHO, 2006b). Some studies have even made the case that using weighted criteria might bias the results and lead to objectivity loss (McKenzie et al., 2007), while acknowledging the usefulness of this procedure to influence decision-making in public health policy. In this chapter, criteria were weighted to reflect participant's opinion and understand whether some epidemiological factors are more relevant to the stakeholders- and future end-users of the response methodology developed in this thesis. Thus, the weighting of criteria added a layer of complexity to the prioritisation process and provided further insights into participant's decision-making system.

Multicriteria decision methods (Zionts, 1979) are employed as a decision-making tool in circumstances where a range of criteria, that can be conflicting, are involved in evaluating decision alternatives (Frazão et al., 2018). MCDA has become increasingly popular in disease prioritisation studies, as it considers multiple impacts of health threats and incorporates participant opinion in the form of criteria weights (Montibeller et al., 2020). When using a MCDA framework, criteria can be weighted either directly or indirectly. When weighting criteria directly, participants are asked to assign a score to each criterion (Cardoen et al., 2009; R. Cox et al., 2013; Humblet et al., 2012a; Krause & Institute (RKI), 2008). However, when using indirect methods, participant’s preferences are elicited from the decisions that they make when presented with hypothetical outbreak scenarios. Their answers are then analysed using statistical methods and used to indirectly infer criteria weights (Ng & Sargeant, 2013). The advantage of using indirect methods is that they add context to the criteria weighting process, by framing it in a realistic decision-making scenario (Clayton, 1997; Havelaar et al., 2010; Semenza & Paz, 2021). This contributes to an accurate reflection of stakeholder values when weighting the criteria. However, these methods also entail greater difficulties and are more time consuming. Given the exploratory nature of this study and the time limitations, it was decided to ask participants to weight criteria directly.

2.5.6. Discussion of results

2.5.6.1. Canine syndromes

Respiratory and gastroenteric disease were the two top ranked syndromes of concern by participants. This opinion was almost unanimous, as six and eight out of the nine respondents included them on the initial list of priorities, respectively. The lower variability of participant responses in the syndromic category might be due to the also lower number of options to choose from, i.e., organ systems vs infectious agents. However, the overwhelmingly higher number of votes given to gastroenteric, and respiratory disease is indicative that these two syndromes are indeed the most concerning in the eyes of participants. For this reason, it was decided that a sufficient level of differentiation was reached at the first stage of the prioritisation process. The reason for this result may be related to the high prevalence of these two syndromes in small animal consultations in the UK (Collins et al., 2021), paired with the high severity and welfare impact of some of the infectious agents that can cause respiratory and gastroenteric signs in dogs (Day et al., 2020; Suchodolski, 2011).

2.5.6.2. Endemic and exotic pathogens

The highest ranked disease was a zoonosis in both the endemic and exotic categories. Leptospirosis is a bacterial disease of worldwide importance and is considered endemic to the UK. The disease is transmissible to humans mostly through water contaminated with infected animal urine (CDC, 2018). On the latest available yearly zoonoses reports by the UK government in 2017, 92 cases of leptospirosis were confirmed in the country (GOV.UK, 2017b). Leishmaniasis is a protozoal disease, transmissible to humans via its vector, the sandfly (Phlebotomus spp and Lutzomyia spp). The disease is generally considered exotic to the UK with an average number of 59 human leishmaniasis cases detected yearly in the country; all imported from endemic countries, with occasional autochthonous cases also in humans (HAIRS Group, 2022). The results of this study indicate that one of the participants' main concerns about canine epidemics is the protection of public health. Indeed, *impact of disease* *on public health* was the highest and the second highest-rated theme for exotic diseases and endemic diseases, respectively.

The relevance of canine diseases' impact on public health has been acknowledged on previous disease prioritisation studies in humans and animals. For instance, leptospirosis, leishmaniasis and dirofilariasis ranked among the top diseases in a WOAH study aimed at identifying the most relevant companion animal zoonoses in Europe (Cito et al., 2016). In the UK, DEFRA's disease prioritisation tool, D2R2, included rabies and echinococcosis among the highest ranked diseases in the animal welfare and public health profiles (HAIRS Group, 2022). Interestingly, these two diseases were not considered as relevant by the present study's participants. Perhaps this is due to the fact that rabies and echinococcosis are presently the only two canine diseases included in the UK government's animal notifiable disease list (GOV.UK, 2023a), for which there is a defined official, nation-wide control strategy (GOV.UK, 2019a). The fact that these two diseases are already covered by governmental plans is likely to have influenced participant's responses, that do not perceive them as a priority for the development of new control strategies.

2.5.6.3. Criteria and themes to evaluate canine diseases

Impact of disease on public health was the highest and second highest rated criteria to evaluate exotic and endemic diseases, respectively. As mentioned above, this had a significant impact on the final disease rankings, both led by zoonotic diseases. This reiterates the fact that participant's main concern is the protection of public health, an idea which coincides with other prioritisation studies (Cito et al., 2016; Ng & Sargeant, 2013).

The theme with the lowest weight for both the endemic and exotic categories was *economic impact of disease.* This means stakeholders do not consider costs of controlling an outbreak of canine disease as a determinant factor when establishing surveillance priorities. This finding supports the notion that companion animals, particularly dogs, are nowadays considered by many as a part of the family, and therefore their wellbeing overshadows economic considerations (Blouin, 2015). This juxtaposes with the results of prioritization studies of livestock diseases, where economic impacts were ranked among the most relevant criteria, in some cases even more so than zoonotic implications (V. J. Brookes et al., 2014). Comparing factors such as animal/human welfare to economic considerations can be controversial from an ethical perspective, that is why these criteria are regarded separately and are not directly comparable in some prioritisation studies (Vasileiou et al., 2018).

2.5.7. Limitations

The limitations of this study are mainly consequences of the COVID-19 pandemic. For instance, the number of participants was reduced from 30 (stakeholders that had agreed to take part in the in-person workshop) to 19 and not every participant could contribute to each step of the prioritisation process. This happened because of the restrictive measures introduced in March 2020, that had a significant impact on the schedules of many of the study participants. While this disruption will be mentioned in many doctoral theses, the author believes that the impact of the pandemic was even more pronounced in the present case, given how many of this chapter's stakeholders are precisely those who were involved in the COVID-19 response. Despite the disruption, the changes made to the original methodology, i.e., from an in-person workshop to a Delphi technique, provided enough leeway for enough participants of different backgrounds to contribute to this study (see Table 2.1).

It is pertinent to reiterate that looking at the number of participants is not particularly relevant, as a purposive sampling approach was followed in this study to ensure that relevant stakeholders contributed their opinion to achieve each step of the study (Vasileiou et al., 2018). Other prioritisation studies follow a quantitative paradigm, with large sample sizes of hundreds or even thousands of participants (Ng & Sargeant, 2013). However, as this thesis follows a codesign approach (Slattery et al., 2020), in which end-user contributions inform the development of the research process, it is relevant to look at the *quality* of the participants rather than their *quantity*. Thus, the validity of qualitative research methods should not be overlooked when conducting a disease prioritisation exercise, since they allow for a deeper understanding of participants' motivations and perspectives.

2.6. Conclusions and future work

In conclusion, this chapter describes the first stakeholder opinion-led approach to identify canine infectious diseases and syndromes that should be prioritised for inclusion in future surveillance and control strategies in the UK. The results of this chapter demonstrate the feasibility of the developed methodology to rank canine diseases in order of relevance and with sufficient differentiation for prioritisation purposes. This chapter's approach consisted in viewing the research question as a decision-making dilemma with multiple contributing factors through a MCDA framework. To answer to such dilemma, a consensus was reached among participating stakeholders using a Delphi technique. A face-to-face approach to achieve a consensus on the subject matter was also described for application wherever possible. The methodology developed in this chapter can easily be adapted to prioritise diseases in canine populations of different regions/countries.

The results of this study will inform the subsequent chapters of the present thesis, as well as to inform the development of other studies included under the SAVSNET-Agile umbrella. For instance, disease surveillance tools will be developed for the prioritised diseases, e.g., text mining tools for disease detection in pre-diagnostic clinical data (Chapter Three). Clinically relevant outbreak notification thresholds will also be established for the top priority diseases identified in this chapter, which will determine when veterinary practitioners are notified of disease anomalies in their area (Chapter Four). The lists of priority diseases obtained from this study will need to be periodically reassessed to ensure that they match the epidemiological and socioeconomic circumstances of the country. In the future, as the collection and processing of canine health and demographic data improve, the findings of this chapter could be complemented with a quantitative prioritisation approach. Furthermore, by contrasting the findings of canine disease prioritisation efforts to those in other animal species and in humans, it is possible to draw parallels between them and open the door for the development of policies with a one-health perspective.

Chapter Three: Development of a text mining tool to harness electronic health records for the early detection of canine diseases

3.1. Abstract

The current surveillance of canine infectious diseases mainly relies on syndromic and laboratory-based surveillance. Syndromic surveillance, which uses pre-diagnostic data to detect potential outbreaks, offers an improved timeliness of detection over laboratory-based surveillance, which is highly specific but time-consuming. However, syndromic surveillance is limited by its lack of specificity. This study aims to develop a text mining tool to detect canine disease signals using pre-diagnostic data from the free-text component of electronic health records. This tool is built based on the language used by veterinary practitioners to describe cases of disease in their clinical annotations and aims to capture disease cases in a timely manner while also enhancing the specificity of the detection of syndromic systems. Canine parvovirus and babesiosis were used to illustrate this study's methodology, as representative examples of endemic and exotic diseases in the UK, respectively. A training dataset of confirmed disease cases could only be established for canine parvovirus, as the available data for canine babesiosis were insufficient. Key terms were extracted from the training dataset and grouped into regular expressions (regex), that were weighted according to their specificity for disease detection. A rule-based classifier was built to categorise canine consultations according to regex matches. A method was also developed to estimate the likelihood of disease at an individual dog level, using regex weights to generate a cumulative score for each animal's follow-up consultations. The methodology developed in this study was tested in its application to the clinical annotations of 100 random dogs. This study demonstrates the feasibility of using text mining techniques to identify key signals for endemic canine disease detection in clinical narratives and presents an optimised source of surveillance data that can be used for the early detection of potential epidemic threats.

3.2. Introduction

3.2.1. Background

The last decade has seen a growth in the field of disease surveillance in companion animals, notably in the UK (Sánchez-Vizcaíno et al., 2015; *VetCompass, Royal Veterinary College*, 2023) and in the US (Kass et al., 2016a). Recently, electronic syndromic surveillance data from veterinary practices and electronic health data from diagnostic laboratories have become available in near real-time on a national scale in the UK through surveillance schemes such as the Small Animal Veterinary Surveillance Network (Sánchez-Vizcaíno et al., 2015). Syndromic surveillance uses pre-diagnostic data that is recorded before samples are taken and submitted for analysis to a diagnostic facility (Hughes et al., 2020). Syndromic-based surveillance is advantageous, as it allows for the early detection of potential epidemic threats, as it bypasses the time delays between disease suspicion, sample collection and submission, and the conduction of a diagnostic test, until results are available (Dórea et al., 2011). The main downside of syndromic infectious disease surveillance is the loss of specificity of results, since insights are drawn from data that precede an official diagnosis. Conversely, laboratory-based surveillance is highly specific, as it is based on laboratory test results, but the timeliness of detection is compromised. Previous studies in the UK and US have harnessed both syndromic and laboratory-based surveillance data to monitor disease trends in companion animal populations, and faced these limitations (Arsevska et al., 2017; Collins et al., 2021; Glickman et al., 2006a; Kass et al., 2016a). Given these limitations, it is necessary to develop optimised surveillance methods, that can harness the timeliness provided by syndromic data, whilst also improving the specificity of disease detection to enable a rapid identification of anomalies in disease incidence at a pathogen level.

Text mining is an area of computer science dedicated to the automated extraction of information from text (structured and unstructured) (R. Feldman & Sanger, 2007) which has increasingly been employed as a tool to aid in disease surveillance and outbreak detection (Corsi et al., 2021). It uses techniques derived from natural language processing (NLP), machine learning and information extraction to extract knowledge from large collections of data, that are usable for analysis (Chowdhary, 2020). These techniques are suitable to exploit electronic health data, especially to retrieve information from free-text clinical annotations (Cheerkoot-Jalim & Khedo, 2021) so that they can be harnessed for timely outbreak detection

(Jalal, 2015). Text mining has also been applied extensively in biomedical sciences (Cheerkoot-Jalim & Khedo, 2021) for various purposes, including disease classification (Govindarajan et al., 2020), disease status prediction (A. Ishaq et al., 2021), or analysis of antimicrobial use (Wind et al., 2021).

Studies that employ text mining and NLP to aid in early outbreak detection frequently use the web as a data source, e.g., by mining the content of online media reports (J. Feldman et al., 2019), social media (Amin et al., 2021), or web searches (Yang et al., 2013). Other sources of data have been mined to monitor epidemic responses, with many examples applied during the COVID-19 pandemic, such as contact-trace report forms (Caskey et al., 2022), social media publications (Osakwe et al., 2021; Xing et al., 2021), and research publications (Carracedo et al., 2021). In this chapter, a text mining tool is developed to harness veterinary clinical narratives to enhance the surveillance of canine infectious diseases. This tool is built based on the language that veterinary practitioners use in their clinical annotations. By utilising pre-diagnostic data and individual animal's clinical trajectory, disease cases can be detected in a timely manner. Moreover, by capturing veterinary professionals' opinion on disease suspicion and/or confirmation, the specificity of the detection is also enhanced.

3.2.2 Aims

This chapter aims to explore the feasibility of using a text mining tool to harness the information contained in electronic veterinary clinical annotations for the detection of potential cases of canine infectious disease in real time, before a definitive diagnosis is available, thus enhancing surveillance and timely outbreak detection. For this purpose, a text mining tool based on veterinary practitioner language is developed to estimate how likely it is that an animal has a specific disease at a consultation while considering its health trajectory. This approach is illustrated using parvovirus and babesiosis as representative examples of endemic and exotic canine infectious diseases in the UK.

3.3. Material and Methods

This chapter's methodology includes the following steps (Figure 3.1). First, training datasets of clinical narratives with a confirmed diagnosis of canine babesia and canine parvovirus were created using SAVSNET's veterinary practice database. Then, these training datasets were analysed to extract keywords and terms used by veterinary professionals to describe the diseases under study. Subsequently, a text mining tool was developed by grouping the extracted key terms into regular expressions, that were used to define the rules for a rule-based classifier algorithm to detect disease cases in the clinical annotations of canine consultations. Then, the risk of being a case of the disease under study, taking into account individual animal's clinical trajectory was estimated by looking at regular expressions matches across each animal's clinical history. Lastly, the performance of the text mining tool was assessed using a random sample of veterinary clinical narratives.

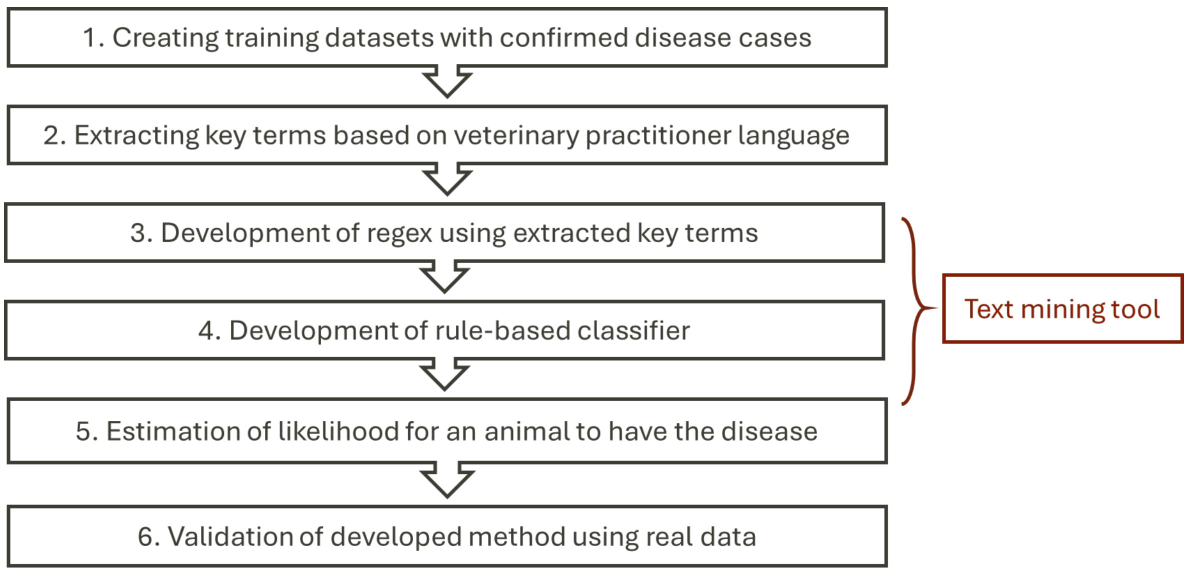

Figure 3.1. Summary of the methodology steps conducted in Chapter Three

3.3.1 Selection of diseases to illustrate the methodology

This chapter's methodology is applied to canine parvovirus and canine babesiosis, since this thesis focuses on both endemic and exotic diseases, and these two canine pathogens were among the top priority diseases identified on Chapter Two of this thesis. Further, it was necessary to work with diseases with a relatively high prevalence, as a large enough number of cases was needed to create and validate the text mining tool developed in this chapter. This is why parvovirus was chosen instead of leptospirosis, the top one endemic disease on the prioritisation list, as parvovirus is more commonly seen in UK veterinary practices (Godsall et al., 2010). Similarly, canine babesiosis was chosen instead of leishmaniosis since more cases of the former were found on SAVSNET's laboratory database.

3.3.2. Data collection

3.3.2.1. Electronic health record (EHR) data from veterinary practices

Canine health data were collected through SAVSNET in the form of EHR from booked consultations in collaborating veterinary practices. These data are routinely anonymised by SAVSNET so no identifiers were included. Data from 2017 to 2021 were used for canine parvovirus, while data from the start of the SAVSNET EHR collection (2014) until 2021 were used to retrieve data for canine babesiosis, to maximise the probability of finding confirmed cases, given the low prevalence of this disease. A full description of the data collection protocol has been previously provided elsewhere (Sánchez-Vizcaíno et al., 2015). A practice (n ≈ 200) was defined as a single business, whereas site(s) (n ≈ 500) included all branches that form a practice. Before submitting each consultation to SAVSNET, the attending veterinary surgeon or nurse was asked to categorise the main presenting complaint (MPC) into syndromes (currently gastrointestinal, respiratory, pruritus, tumour and renal) or other routine veterinary interventions (i.e., trauma, 'other sick', vaccination, 'other healthy' or postoperative check-up). The EHR further included animal signalment (i.e., species, breed, sex, neutering status, age, vaccination status), owner's full postcode, date of the consultation, and clinical narratives written by the attending veterinary practitioner or nurse in a free-text format.

3.3.2.2. Veterinary laboratory diagnostic data

SAVSNET collects health data from the majority of UK diagnostic laboratories. Laboratory test results from dogs tested for canine parvovirus and babesia were extracted from SAVSNET's veterinary diagnostic database. Data for each performed test included the postcode of the submitting veterinary practice (in some cases, in full, in others, only the area code), the type of diagnostic method, the date of sample reception, the test result, the date of the result and, in some cases, the animal's breed and sex. For canine parvovirus, laboratory results were extracted to match the dates of the clinical narratives (2017-2021). For canine babesiosis, all the available results were extracted from the database, which dated from 2010 until 2019.

3.3.3. Creation of training datasets with confirmed disease cases

To establish training datasets for keyword extraction, canine consultations with a confirmed diagnosis for canine parvovirus and babesiosis were identified through SAVSNET's veterinary practice and laboratory database using the approaches described in this section.

3.3.3.1. Using veterinary practice data

For both diseases under study, clinical narratives that recorded a confirmed diagnosis were retrieved in several steps. First, a broad search was performed to extract those EHR where an explicit mention of the disease of interest was made in their clinical narratives. For parvovirus, the search terms "parvo*" and "CPV" were used, and the term "babesia" was used for canine babesiosis. This search was conducted using SAVSNET's bespoke software *Datalab,* which enables the search of keywords in the veterinary clinical narratives stored within SAVSNET's practice database. For each dog identified through this initial search, its full recorded consultation history was also collected for analysis, and their annotations were manually read by the author of this thesis to identify consultations with an explicit mention of a parvovirus or babesia diagnosis. The training datasets consisted of the full clinical histories of those dogs with one or more consultations with an explicit mention of a parvovirus or babesia diagnosis.

3.3.3.2. Using diagnostic laboratory and veterinary practice data

Data manipulation in this section was carried out using the R software, version 4.2.1 (*R: The R Project for Statistical Computing*, 2022). This approach involved finding confirmed cases of canine parvovirus and babesia in SAVSNET's laboratory database, and then linking these cases to their corresponding clinical narratives in SAVSNET's veterinary practice database (Figure 3.2). This second approach was conducted to find further cases to include in the training datasets, given the low prevalence of these canine infectious diseases, and to account for the fact that veterinary practitioners do not always explicitly state whether cases are confirmed in their clinical annotations, which limits the number of cases that can be included in the training datasets if using only veterinary practice data. Because no common animal identifiers, e.g., canine patient id, are shared between the two evaluated databases, it was not possible to directly link positive laboratory test results to their corresponding canine cases in the veterinary practice data. The only identifier shared between these datasets was the full postcode of the veterinary practice that submitted the sample to a diagnostic laboratory. For this reason, it was decided to use the postcode information to manually match laboratory results with the canine consultations recorded in the veterinary practice database. The rationale for this is that samples tested at veterinary diagnostic laboratories are submitted by veterinary practices when an infectious disease is suspected during a consultation. By considering the postcode of the veterinary practice that submitted the sample, it is possible to contrast the dates of sample submission in the laboratory database and the date of consultation recorded in the veterinary practice database. Thus, if the postcode of the sample submitting veterinarian is found on both databases, and the sample submission date recoded in the laboratory database for a tested sample is reasonably close to a consultation date recorded in the veterinary practice database, e.g., the sample was submitted on the same day or a few days after the case was seen in veterinary practice, it may be possible to link canine consultations to their laboratory test results. Following this approach, clinical narratives of canine cases that were successfully linked to positive test results from SAVSNET's laboratory database were added to the training datasets.

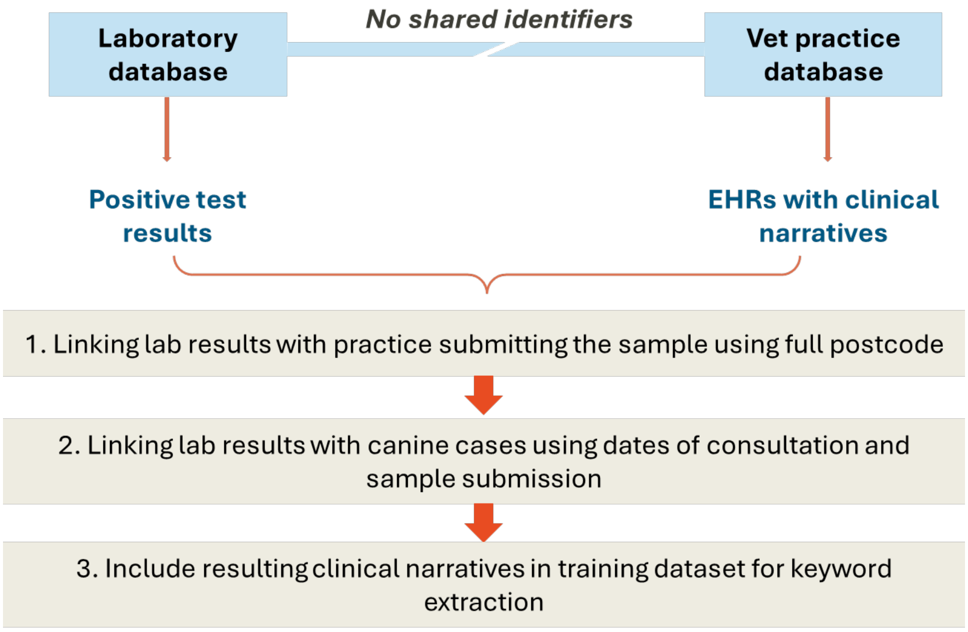

Figure 3.2. Diagram that represents the process of search for confirmed parvovirus and babesia cases using laboratory and veterinary practice data.

At this point of the methodology, it was discovered that the number of confirmed cases of canine babesiosis was not sufficient to create a training dataset to extract keywords, so the next sections of this chapter's methodology were only applied to canine parvovirus.

3.3.4. Extraction of key terms related to canine parvovirus based on veterinary practitioner language

Using the training dataset of clinical narratives for canine parvovirus developed in section 3.3.3 of this methodology, key terms related to the disease that are used by veterinary practitioners were identified. Two different but complementary methods were attempted for keyword extraction.

3.3.4.1. Using word frequencies

The tasks performed in this section were undertaken in the Python programming language, version 3.10.4 (*Python.Org*, 2022). The Graphical User Interface (GUI) *Anaconda Navigator* (Anaconda, 2022) and *Jupyter* (*Project Jupyter*, 2022) computational notebooks were used. Data were analysed using *Pandas*, a library that provides high performance data handling tools (version 1.4.0) (*Pandas - Python Data Analysis Library*, 2022). EHRs in the training dataset were imported into pandas in a .csv format, and word frequencies in the clinical annotations were calculated. To exclude commonly used words that would not add any relevant meaning from the estimation of word frequencies, Python's natural language toolkit's (NLTK) (*NLTK*, 2022) corpus of stop words was used. This corpus consists of a compilation of punctuation marks, connectors, and conjunctions, e.g., "and", "or", so that they can easily be removed from the text under analysis. All words were also converted to lower case, to avoid double counting when estimating word frequencies.

3.3.4.2. Manual annotation of clinical narrative data

Clinical narratives in the parvovirus training dataset were manually read by the author of this thesis. For each of the consultations included in the dataset, those words, expressions, and terms written by the attending veterinarian in relation to the disease were identified and extracted.

3.3.5. Development of a text mining tool to detect canine parvovirus cases at a consultation level

A text mining tool was developed to detect and extract consultations related to canine parvovirus. For this purpose, regular expressions were defined and used in conjunction with a rule-based data mining classifier.

Briefly, regular expressions, or regex, define search patterns to match characters, words, and phrases in a text string (Friedl, 2006). They include a combination of characters and special symbols to specify what type of information should be retrieved from the data (*Python Regex Cheatsheet*, 2022; *Rstudio Cheatsheets*, 2017).

Rule-based classifiers are a type of machine learning algorithm that utilise sets of rules, pre-defined by domain experts, to classify data into categories (Tung, 2009). Rules are computed as a series of "if-then" statements (Friedman, J.H., 1998), that can be nested to define multiple criteria for data (Rokach & Maimon, 2005).

In this chapter's methodology, regex were used to define the rules followed by the algorithm to classify canine consultations according to whether regex pattern matches are found in their free-text annotations.

3.3.5.1. Development of regular expressions using extracted key terms to detect canine parvovirus cases

Key terms extracted from the training dataset for canine parvovirus were used to build regular expressions. Since some of these key terms were more indicative of a parvovirus diagnosis than others, they were grouped into categories, depending on how strongly they represented a case of disease. Each of these categories was used to build separate regular expressions, with different levels of specificity for disease detection. The more indicative the key terms were of a parvovirus case, e.g., "parvovirus diagnosis" or "parvovirus positive", the highest the specificity of the regex. Using these regex as rules allowed the classification algorithm to determine the likelihood of the presence of parvovirus in the text data based on the specificity of the regex match.

Regex were built in Python through user-defined functions (UDF), as well as functions from the module *re* (*Re, Regex Operations*, 2022). UDF are customised functions created by the user to perform certain tasks in an optimised manner, as opposed to Python's built-in functions (McKinney, 2012).

The UDF function `build_regex` was defined (Figure 3.3), to specify the following regex elements:

- Feature words: set of key terms related to canine parvovirus extracted from the training dataset of confirmed cases.
- Negation prefixes: set of words that, when appearing before the feature words, negate the presence of the disease of interest, e.g., "no sign of", "does not have".

- Negation suffixes: set of words that, when appearing after the feature words, negate the presence of the disease of interest, e.g., “has resolved”, “stopped”.

```
def build_regex(feature_words: list,
                            negation_prefixes: list = None,
                            negation_suffixes: list = None)-> str:
    regex = r''
    if negation_prefixes is not None:
        for word in negation_prefixes:
            regex = regex+r'(?<!{})'.format(word)
    regex += r'\W*'
    feature_part = '|'.join(feature_words)
    regex += r'(?:{})'.format(feature_part)
    regex += r'\W+'
    if negation_suffixes is not None:
        for word in negation_suffixes:
            regex = regex+r'(?!{})'.format(word)
    return regex
```

Figure 3.3. Python UDF used to build regular expressions for detection of parvovirus cases in clinical narrative text.

<u>3.3.5.1.1. Weighting regular expressions according to their specificity</u>

As mentioned above, the developed regex had varying levels of specificity for disease detection. To account for this, a numerical weight, or score was assigned through expert elicitation, which was directly proportional to their level of specificity, i.e., to how indicative they were of the disease. If more than one regex had matches in a given consultation, the score for that consultation consisted of the sum of the scores or weights of the matching regexes. This consultation-level score ranged from 0 (minimum, i.e., none of the regex had matches in the consultation) to 100 (maximum, i.e., all the regex had matches in the consultation) and represented the likelihood of parvovirus disease in such consultation’s clinical annotations. This way, instead of just providing binary information on whether a match occurred on each consultation (Y/N), the classification algorithm assigned a score to each consultation, based on the weight of the matching regular expression(s). In other words, the weighted regex scores contributed to providing a best-informed estimate of the likelihood of parvovirus in a given canine consultation. Weights for the developed regex were assigned through expert elicitation, by reaching a consensus between the author of this thesis, their main supervisor, and a member of SAVSNET with extensive experience in clinical practice and text mining. Python UDFs were developed to assign regex weights and perform the sum of regex scores when more than one regex had matches in a consultation.

3.3.5.2. Development of a rule-based classifier to search for parvovirus regex matches in veterinary clinical narratives

The regular expressions containing key terms for the detection of canine parvovirus cases were used as the criteria for classification of the rule-based algorithm developed in this section.

3.3.5.2.1. Format of the data used in this section

Clinical narrative data are stored in a SQL database managed by SAVSNET. Narratives were extracted upon request on a Python Pickle (.pkl) format, a type of file created by the Python module *pickle* (*Pickle — Python Object Serialization*, 2022). This process is referred to as pickling and consists in the serialisation of objects into files so that they can be saved in a particular state and recreate it when needed. The main purpose of the pickling process is to save computing space and allow for fast transfers of data (*PKL File Extension*, 2022). Each .pkl file corresponded to an individual dog, whose unique id was used as the file name. These .pkl files consisted of a data frame where each consultation of the animal's history was recorded as a row, and where columns contained information on the unique id of each consultation, the consultation date, and the clinical annotations made by the veterinary professional. Figure 3.4 contains an example of such .pkl files' structure.

savsnet_consult_id	narrative	consult_date
8225661	Final vaccs. OR doing ok, currently on gastro...	2021-01-26 09:15:36+00:00
8314854	BIOP 15 weeks since was 7 weeks old. OR migh b...	2021-03-01 12:43:44+00:00
8426983	ITCHY EAR and SKIN. Last couple of days has be...	2021-04-09 16:25:41+00:00
8589196	Cytopoint + anxiety. Hx: cytopoint worked well...	2021-06-10 14:55:10+00:00
8889190	6 MONTHS HPC CHECK. OR seeing dermatologist. s...	2021-09-14 15:57:29+00:00

Figure 3.4. Example of the contents of the .pkl files used in the present section, each of which contains the consultation history of a unique dog.

3.3.5.2.2. Building the rule-based classifier for canine parvovirus

A Python UDF was designed to sequentially apply the regular expressions to canine clinical narrative data contained in .pkl files, and add columns to these files that indicated, for each consultation, the score for the matches of each individual regex, as well as a column to reflect the sum of the scores of all the matching regex to generate a consultation-level parvovirus score.

3.3.6. Estimation of the likelihood of canine parvovirus at an individual animal by analysing its clinical history with a text mining tool

In the previous sections of this methodology, a text mining tool was developed to detect potential cases of canine parvovirus by estimating the likelihood of disease at a consultation level. In this section, a method is developed to estimate how likely it is that an individual animal has parvovirus, by analysing each dog's clinical history and taking into account regex matches across all of their recorded consultations. This method offers an improved accuracy of ascertainment of parvovirus cases through the evaluation of clinical narratives for two reasons.

First, because it minimises a potential overestimation of the real number of parvovirus cases, which could result in a false outbreak alert. This is because parvovirus is an infectious disease where a dog's condition worsens over a period of time that, albeit short (Nandi & Kumar, 2010), can span over several consultations. Further, there may be a delay between the presentation of clinical signs and a diagnostic confirmation of the disease if samples are submitted for laboratory testing. In these cases, the attending veterinarian might log the test results in the dog's clinical history sometime after the initial consultation(s) where the dog exhibited clinical signs. Essentially, there can be multiple consultations in an individual dog's history with regex matches that are related to the same disease process, which should not be treated as individual potential parvovirus cases. Secondly, because it improves the sensitivity of disease detection by generating an animal-level score, through the aggregation of consultation-level scores for recorded follow-up consultations related to parvovirus. Since follow-up consultations are related to the same disease process, if their parvovirus scores were considered as independent, rather than aggregating them, this would result in an underestimation of the animal level likelihood of canine parvovirus. Lastly, this method can be used to estimate the level of parvovirus risk in real time, as the animal-level parvovirus scores are updated and recalculated as matches occur.

In this section, .pkl files containing consultation-level parvovirus scores were converted to .csv files. Analyses were conducted using R, specifically, functions from the packages *lubridate* (*Lubridate*, 2022) and Tidyverse's *dplyr* (dplyr, 2023). An R script was developed to generate, for each dog, an overall parvovirus likelihood score, by calculating a cumulative score, equal to the sum of each dog's parvovirus-related follow-up consultations. A follow-up consultation was defined as one that took place 30 days or less after an initial consultation with regex matches for parvovirus. After 30 days, the animal-level score was reset to 0, and subsequent regex matches were treated as corresponding to a potential new case of canine parvovirus. This generous margin of 30 days was established to account for the potential delays between the presentation of clinical signs and the laboratory confirmation of disease. Further, since the aim of this animal-level score was to capture new information about the risk of parvovirus provided by follow-up visits, consultation-level scores only counted towards the animal-level score if they contained regex matches that had not already been captured in previously recorded consultations for the same animal within 30 days prior. For instance, if a parvovirus-related clinical sign included in a regex was mentioned in two subsequent consultation less than 30 days apart, only the first match would be counted and contribute its score towards the animal-level parvovirus score. The purpose of this approach was to ensure that the cumulative score reflected new information about the dog's likelihood of having parvovirus over time, rather than simply repeating information that had already been captured.

As mentioned in section 3.3.5.1.1., consultation-level parvovirus scores ranged from 0-100. Since regex matches were only counted once within each set of follow-up consultations for each animal, the animal-level parvovirus score also ranged between a minimum of 0 and a maximum 100. This score was used to provide an estimation of how likely it is that an individual dog has parvovirus disease at each time point of their consultation history. A risk matrix was developed to categorise the animal-level parvovirus score into different risk categories that indicated the likelihood of disease. Cut off values for risk categories were established, according to the specificity of the regex matches. A traffic light system was used to present the results in the risk matrix, i.e., green for low risk, yellow for moderate risk, and red for high risk.

3.3.7. Validation of the developed methods by using real data

The methodology described in this chapter was applied to a random sample of clinical histories from 100 dogs, extracted from the SAVSNET veterinary practice database as .pkl files. To ensure the validity of the assessment, the author checked that these random sample of narratives did not include any dogs whose data were used in the training dataset.

3.3.7.1. Validation of the text mining tool developed to detect canine parvovirus cases at a consultation level

The developed text mining tool for parvovirus case detection, i.e., regex and rule-based classifier, was applied to the clinical histories of 100 random dogs. To evaluate the performance of the tool, the author also manually read and classified the same dataset of clinical narratives and then compared the results from both procedures (algorithm vs manual classification) (Figure 3.5). The following performance measures were calculated to establish the functionality of each of the regular expressions in their application to the randomly generated set of clinical narratives.

Accuracy: most often used statistic for assessing the performance of classification algorithms. It represents the overall proportion of correctly classified consultations by the rule-based classifier (J. P. Li et al., 2020). Accuracy of the text mining tool is defined by:

$$Accuracy = \frac{(TP+TN)}{(TP+FP+TN+FN)} \quad \textit{(Equation 3.1)}$$

Where TP and TN are true positives and true negatives, respectively, and FP and FN denote false positives and false negatives, respectively.

Precision/Positive predictive value (PPV): proportion of flagged consultations as a positive match that truly contain parvovirus-related terms that would be matched by the developed regular expressions. This measure is defined by:

$$Precision = \frac{TP}{TP+FP} \quad \textit{(Equation 3. 2)}$$

Recall/Sensitivity: true positive rate, or the proportion of true matches that were correctly classified by the text mining algorithm (Shemilt et al., 2022). This measure indicates how well the rule-based classifier is capable of categorising consultations that truly contain the key terms included in parvovirus-related regular expressions, and is defined by:

$$Recall = \frac{TP}{TP+FN} \quad \textit{(Equation 3. 3)}$$

Negative predictive value (NPV): proportion of non-flagged consultations by the rule-based classifiers that truly do not contain parvovirus-related terms that would be matched by the developed regular expressions. This measure is defined by:

$$NPV = \frac{TN}{TN+FN} \quad \textit{(Equation 3. 4)}$$

Specificity: true negative rate, or the proportion of true non-matches that were correctly classified by the text mining algorithm. It indicates the rule-based classifier's capacity to classify consultations that truly do not contain key terms included in parvovirus-related regular expressions. This measure is defined by:

$$Specificity = \frac{TN}{TN+FP} \quad \textit{(Equation 3. 5)}$$

F1 score: to calculate the mean between precision and recall, ranges from 0 (worst value) to 1 (best value). This measure provides an indication of the rule-based classifier's balance between these two performance measures, and is defined by:

$$F1\ score = 2\ x\ \frac{Precision\ x\ Recall}{Precision+Recall} \qquad \textit{(Equation 3. 6)}$$

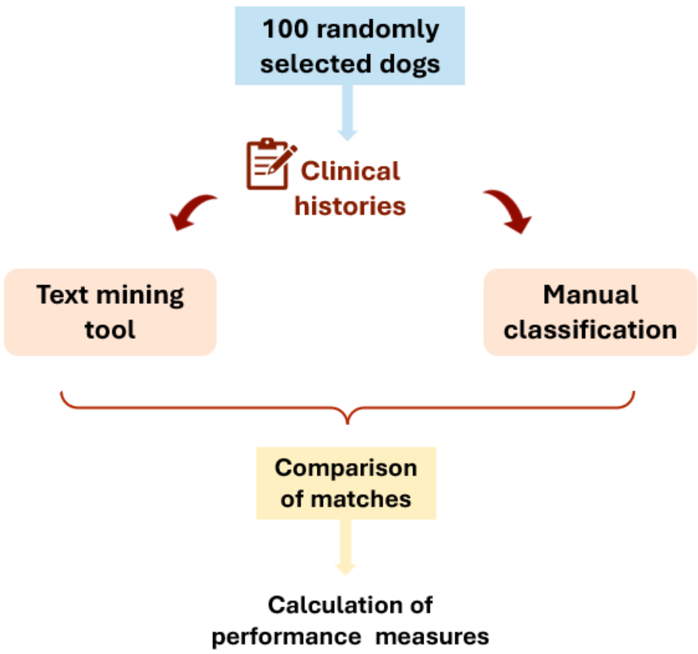

Figure 3. 5. Summary of steps for the validation of regex to detect canine parvovirus cases.

3.3.7.2. Validation of the method developed to estimate the likelihood that individual animals have canine parvovirus by analysing their clinical history

A parvovirus likelihood score was calculated for each of the 100 random dogs, by analysing each dog's clinical history and taking into account regex matches across all of their recorded consultations. The performance of the text mining algorithm was then manually contrasted by the author of this thesis, by checking that the generated scores matched the sum of the values of the matching regex's weights, and that scores were reset to 0 after the specified interval by the time decaying factor.

3.4. Results

3.4.1. Creation of training datasets with confirmed disease cases

3.4.1.1. Using veterinary practice data

<u>3.4.1.1.1. Canine babesiosis</u>

The full recorded clinical history from 51 dogs with a mention of "babesia" in their clinical narratives were analysed. It was found that the attending veterinary practitioner or nurse expressed a suspicion of disease in 38 of these animals, and a sample submission to a diagnostic laboratory to confirm the diagnosis was mentioned in 19 dogs. Out of those 19 animals, 10 dogs did not have any follow up about the test results in their subsequent recorded consultations, 5 received a negative test result for *Babesia* spp. and 3 dogs received an alternative diagnosis, i.e., tested positive for a parasitic infection other than babesiosis. Only one dog had an explicit laboratory confirmation of *Babesia* spp. diagnosis recorded in their clinical history. This was deemed as an insufficient number of cases to create a training data set for keyword extraction.

3.4.1.1.2. Canine parvovirosis

The full recorded clinical history from 3289 dogs with a mention of "parvovirus" or "CPV" in their clinical narratives were analysed. A total of 22 individual dogs were found to have recorded an explicit mention of a parvovirus diagnosis in their clinical histories, with a total of 35 consultations. These cases provided sufficient information to create a training data set for keyword extraction for canine parvovirus. Full animal histories from the training dataset for canine parvovirus can be found on Appendix III.a.

3.4.1.2. Using diagnostic laboratory and veterinary practice data

Even though it was possible to link a small proportion of the available laboratory results (2% for canine parvovirus and 2.1% for canine babesiosis) in SAVSNET laboratory database to their submitting veterinary clinic by searching in SAVSNET practice database, none of these results could be matched by date, as the sample submission and veterinary consultation had occurred in different months or, altogether, in different years.

3.4.1.2.1. Canine babesiosis

A total of 186 positive cases of *Babesia spp*., confirmed either by PCR (173) or serology (13), and that contained postcode information, were extracted from SAVSNET diagnostic laboratory database. A dataset of 489 consultations that mentioned the word babesia in their clinical narratives was extracted from SAVSNET's practice database. Out of those, 432 were canine consultations, which corresponded to the 51 unique dogs indicated in section 3.4.1.1.1. Each dog attended an average of ~8.5 consultations in relation to a potential diagnosis of canine babesiosis.

Using both datasets recorded practice full postcode, four of the laboratory submissions could be traced to a SAVSNET-collaborating practice. However, none of these four test results could be matched with the individual animals the samples were taken from based on a sample submission and a consultation date.

3.4.1.2.2. Canine parvovirosis

514 cases of canine parvovirus confirmed by PCR were found on SAVSNET laboratory database. By querying for the mention of the word "parvovirus" in the veterinary clinical narratives stored in SAVSNET's practice database, an initial dataset of 3692 consultations was extracted. Out of those, 3475 corresponded to canine consultations, with a total of 3289 unique animals (see section 3.4.1.1.2.*)*, i.e., an average of 1.05 parvovirus-related consultations per dog.

Following the same approach described for canine babesiosis, a total of 71 matching veterinary practice postcodes were found among both datasets. However, none of these sample submissions could be matched with the dogs whose samples were taken based on a submission and a consultation date.

3.4.2. Extraction of key terms related to canine parvovirus based on veterinary practitioner language

3.4.2.1. Using word frequencies

Table 3.1 contains a summary of the frequencies of words within the training dataset for canine parvovirus, in descending frequency order. Appendix III.b contains those words that were repeated two times or less. The most frequent word was "parvo", repeated 45 times, followed by the word "owner" (37 times). The word "puppy" was repeated 21 times among the 22 dogs (35 consultations) in the training dataset. Clinical signs typically associated with canine parvovirus were also mentioned, although less often, e.g., "diarrhoea", 13 times; or "vomiting", nine times.

This approach proved not to be adequate as the method for key term extraction, since it was unable to recover phrases that constitute relevant units of meaning, e.g., the word "positive" being separated from "parvovirus", and therefore failing to be useful to identify confirmed cases of disease. For these reasons, keywords were manually extracted to build regex in this chapter (see section 3.3.4.2).

Table 3.1. Summary of word frequencies found in the training dataset for canine parvovirus.

Frequency	Word in parvovirus training dataset
45	parvo
37	owner
27	o
22	today advise
21	puppy
18	well since
16	ok pink back home treatment
14	positive <<identifier>>
13	abdo diarrhoea time days
12	discussed weeks eating food test
11	vaccination diet next could yesterday

	palp
Frequency	**Word in parvovirus training dataset**
10	membranes d+ given heart chest
9	v+ check fine vomiting detected
8	t vac blood rate exam breeder vacc
7	ausc, pts, bright, bar, still, moist, pm, snap, appointment, morning, water, small
6	abnormal, give, dogs, bring, risk, kc, nad, needs, dog, faeces, try, bcs, hr, clear, need, drinking, fed, mucous
5	abdomen, long, temperature, vaccinated, skin, dhp, recheck, want, dehydrated, interested, eaten, sample, v, reports, <<location>>, seen, week, due, tacky, issues, second, injection, warned, happy, watery, good, possible, little
4	raw, obtained, lab, shedding, moment, abnormalities, opted, first, date, virus, guarded, inappetant, last, rhythm, times, vaccine, card, can, tent, <<name>>, fluids, cerenia, parvovirus, murmur, tomorrow, made, relaxed, insurance, came, often, started, colour, soft, better, strong, pulse, mm, adv, concerns, current, day, rectal

Frequency	Word in parvovirus training dataset
3	overnight, chip, bile, great, hydration, couple, flat, gastro, dull, weight, d, appetite, signed, worm, monday, worming, pup, faecal, biop, care, ph, prognosis, meds, fully, inj, v+d+, teeth, old, pale, self, stickers, recovered, shed, call, vet, aware, clinically, brought, vaccinate, discussed, pe, results, alert, generated, wormed, request, references, registered, slightly, bivac, gave, able, kg, neuro, pups, sounds, stool, bloods, wean, palpation, walk, fb, exposure, mild, asked

3.4.2.2. Manual annotation of clinical narrative data

Key terms that were manually extracted from the training dataset with confirmed parvovirus cases are included in Tables 3.2, 3.3, 3.4, 3.5, and 3.6.

3.4.3. Development of a text mining tool to detect canine parvovirus cases at an animal consultation level

3.4.3.1. Development of regular expressions using extracted key terms to detect canine parvovirus cases

Five regular expressions were developed to detect potential cases of canine parvovirus, based on their matching with key terms that were grouped in the following categories, in ascending order of specificity for disease detection: risk factors, general clinical signs, specific clinical signs, suspicion of parvovirus, and diagnostic words that confirm a parvovirus diagnosis. These regex are summarised in Tables 3.2, 3.3, 3.4, 3.5, and 3.6.

Table 3.2. Regular expression 1, developed to search for key terms that represent risk factors for canine parvovirus.

<table>
<tr><th>Regex 1: risk factors</th><th>Key terms included in regex 1</th></tr>
<tr><td>Puppy|puppy check|\d+\sweek\w* old|week\w*\sold|month\w*\sold|\blitter|\brunt|penmate died</td><td>"Puppy," "puppy check," "X weeks old," "X months old," "litter runt," "penmate died"</td></tr>
<tr><td>\bBIOP\W|been\s+in\s+owner\w*\s+pos*ession|new\s+pup\w*</td><td>"BIOP," "been in owner’s possession," "new pup," "new puppy"</td></tr>
<tr><td>No\w*(?:\s+\w*){1,2}(?:vacc\w*)|unknown\s+vacc\w*|vacc\w*(?:\s+\w*){1,3}(?:unknown)</td><td>"Not vaccinated," "unknown vaccination status," "vaccination unknown"</td></tr>
<tr><td>no\w*(?:\s*|\w*){1,3}(?:insur\w*)|uninsur\w*|no\w*\s+\bchip\w*|no\w*\s+\bmicrochip\w*|\bneed\w*\s+\bworm\w*|not\s+deworm\w*</td><td>"Not insured," "no insurance," "uninsured," "not chipped," "not microchipped," "needs worming," "not dewormed"</td></tr>
<tr><td>Puppy farm|puppy mill|obtained from travellers</td><td>"Puppy farm," "puppy mill," "obtained from travellers"</td></tr>
<tr><td>declined(?:\s+\w*){1,5}(?:\bcost\w*)|financial constraint\w*|financial restrictions</td><td>"Payment declined," "financial constraints," "financial restrictions"</td></tr>
<tr><td>RSPCA visit|has fleas|(?<!no)\W+fleas seen</td><td>"RSPCA visit," "has fleas," "fleas seen"</td></tr>
</table>

Table 3.3. Regular expression 2, developed to search for key terms that represent general signs of canine parvovirus.

<table>
<tr><th>Regex 2: general clinical signs</th><th>Key terms included in regex 2</th></tr>
<tr><td>\sdiarr\w+|\sd\+\s|\sd\+v|\sd\/v|has diah|motion on thermometers*|loose f.*?ces</td><td>"Diarrhoea," "has diarrhoea," "motion on thermometer," "loose faeces"</td></tr>
<tr><td>\svomit\w+|\sv\+|\sv\/|retching|\bbile\b</td><td>"Vomit," "vomiting," "retching," "bile"</td></tr>
<tr><td>Inappet.\w*',r'off food',r'appetite\W+(?:\w+\W+){0,2}(reduced)',r'not interested(.*?)food',r'Not\W*(?:\S*){1,3}(?:\beat\w*|drink\w*)</td><td>"Inappetent," "off food," "appetite reduced," "not interested in food," "not eating," "not drinking"</td></tr>
</table>

<table>
<tr><th>Regex 2: general clinical signs</th><th>Key terms included in regex 2</th></tr>
<tr><td>quiet\w*|letharg\w*|listless|\bdull\b|less playful</td><td>"Quiet," "lethargic," "listless," "dull," "less playful"</td></tr>
<tr><td>dehydrat\w*|tacky|skin tent</td><td>"Dehydrated," "skin tent," "tacky membranes"</td></tr>
</table>

Table 3.4. Regular expression 3, developed to search for key terms that represent specific signs of canine parvovirus.

<table>
<tr><th>Regex 3: specific clinical signs</th><th>Key terms included in regex 3</th></tr>
<tr><td>Acute gastro\w*|acute\w*(?:\s*|\w*){1,3}(?:diarr\w*)|sudden diarr\w*</td><td>"Acute gastroenteritis," "acute diarrhoea," "sudden diarrhoea"</td></tr>
<tr><td>Blood on motion|rectal blood|bloody dia\w*|bloody d\+|h.*?morrhagic dia\w*|diarr\w*(?:\s*|\w*){1,3}(?:blood\w*)|\bHGE\b</td><td>"Blood on motion," "rectal blood," "bloody diarrhoea," "haemorrhagic diarrhoea," "diarrhoea with blood," "haemorrhagic gastroenteritis"</td></tr>
<tr><td>Watery(.?)diarr\w*|diarr\w*(.?)watery|yellow(?:\s*|\w*){1,3}(?:f.*?ces|diarr\w*|motion)|white(?:\s*|\w*){1,3}(?:f.*?ces|diarr\w*|motion\w*|poo\w*)|diarr\w*(?:\s*|\w*){1,6}(?:bad smell|parvo smell)</td><td>"Watery diarrhoea," "yellow diarrhoea," "white faeces," "white motion," "diarrhoea with bad smell," "diarrhoea with parvo smell"</td></tr>
<tr><td>Bad prognosis|Guarded prognosis|intensive care|emergency|IVFT|IV fluids|advise\w* hosp\w*|DOA</td><td>"Bad prognosis," "guarded prognosis," "intensive care," "emergency," "intravenous fluid therapy," "hospitalisation advised," "dead on arrival"</td></tr>
<tr><td>\bPTS|euth\w*|put to sleep|parvovirus PTS</td><td>"Put to sleep," "euthanised," "parvovirus put to sleep"</td></tr>
</table>

Table 3.5. Regular expression 4, developed to search for key terms that represent suspicion of canine parvovirus.

<table>
<tr><th>Regex 4: suspicion of parvovirus</th><th>Key terms included in regex 4</th></tr>
<tr><td>Parvo\w*\s\bsnap|\bsnap\sparvo\w*|\bsnap\stest\sparvo\w*|parvo\w*\s\bsnap\stest|parvo\w*\s\bPCR|\bPCR\sparvo\w*|\bcheck\w*\sfor\sparvo\w*|\btest\w*\sfor\sparvo\w*</td><td>"Parvovirus snap test," "parvovirus PCR," "check for parvovirus," "test for parvovirus"</td></tr>
<tr><td>\bdd\w*\W+parvo\w*|differential\sdiag\w*\W+parvo\w*|\bcan\S*t\srule\sout\sparvo\w*|\bwouldn\S*t\srule\sout\sparvo\w*|\bsuspect\w*\sparvo\w*|\bpossibl\w*\s(?:was parvo\w*|parvo\w*)|\bcould\s(?:\bhave\b|\bbe\b|\bhave been\b)\sparvo\w*|\bconcern\w*\s(?:\bre\b|about)\sparvo\w*|(?<!not)(?<!nto)\W+\bsmell\slike\sparvo\w*</td><td>"Differential diagnosis includes parvovirus," "cannot rule out parvovirus," "would not rule out parvovirus," "suspected parvovirus case," "possible parvovirus case," "could have parvovirus," "concerned about parvovirus," "smells like parvovirus"</td></tr>
</table>

Table 3.6. Regular expression 5, developed to search for key terms that represent confirmation of canine parvovirus.

<table>
<tr><th>Regex 5: parvovirus diagnostic words</th><th>Key terms included in regex 5</th></tr>
<tr><td>Parvo\w*(?:\s+\w*){1,2}(?:positive|\+)|positive(?:\s+\w*){1,2}(?:parvo\w*)|(?:Parvo\w*\s\bsnap|\bsnap parvo\w*)(?:\s+\w*){1,3}(?:positive|\+)|diagnos\w*\s+with\sparvo\w*|confirmed\W+(?:to\shave\W+parvo\w*|parvo\w*)|recover\w*\s+from\s+parvo\w*|parvo\w*\son\ssnap|shedding\W+parvo\w*|parvo\w*\s\bcase\b</td><td>"Parvovirus positive," "positive parvovirus," "parvovirus snap test positive," "diagnosed with parvovirus," "parvovirus diagnosis," "confirmed to have parvovirus," "recovered from parvovirus," "parvovirus detected on snap test," "shedding parvovirus," "is a parvovirus case"</td></tr>
</table>

3.4.3.1.1. Weighting regular expressions according to their specificity

The following weights were assigned to each of the five regular expressions developed for the detection of canine parvovirus cases:

1. Regex 1: Risk factors: 2.5
2. Regex 2: General clinical signs: 7.5
3. Regex 3: Specific clinical signs: 10
4. Regex 4: Suspicion of disease: 25
5. Regex 5: Confirmation of disease: 55

Figure 3.6 and Figure 3.7 represent the Python UDF functions to assign these numerical scores to the matches of each regex, and to add their values when more than one regex matched the content of a canine consultation to generate a consultation-level score, respectively.

```python
def get_regex1_score_for(x:str)-> int:
	regex=re.compile(regex1, re.IGNORECASE)
	if re.search(regex, x):
		return '2.5'
	else:
		return '0'
def get_regex2_score_for(x:str)-> int:
	regex=re.compile(regex2, re.IGNORECASE)
	if re.search(regex, x):
		return '7.5'
	else:
		return '0'
def get_regex3_score_for(x:str)-> int:
	regex=re.compile(regex3, re.IGNORECASE)
	if re.search(regex, x):
		return '10'
	else:
		return '0'
def get_regex4_score_for(x:str)-> int:
	regex=re.compile(regex4, re.IGNORECASE)
	if re.search(regex, x):
		return '25'
	else:
		return '0'
def get_regex5_score_for(x:str)-> int:
	regex=re.compile(regex5, re.IGNORECASE)
	if re.search(regex, x):
		return '55'
	else:
		return '0'
```

Figure 3.6. Python UDF to assign numerical weights to each of the regex developed for the detection of canine parvovirus cases.

```python
def get_parvo_score_for(x:str)->int:
    score=0
    regex=re.compile(regex1, re.IGNORECASE)
    if re.search(regex, x):
        score=score+score_dictionary['regex_1']
    regex=re.compile(regex2, re.IGNORECASE)
    if re.search(regex, x):
        score=score+score_dictionary['regex_2']
    regex=re.compile(regex3, re.IGNORECASE)
    if re.search(regex, x):
        score=score+score_dictionary['regex_3']
        return score
    regex=re.compile(regex4, re.IGNORECASE)
    if re.search(regex, x):
        score=score+score_dictionary['regex_4']
        return score
    regex=re.compile(regex5, re.IGNORECASE)
    if re.search(regex, x):
        score=score+score_dictionary['regex_5']
        return score
    else:
        return 0
```

Figure 3.7. Python UDF to perform the sum of regex scores when more than one regex had matches in a consultation to generate a consultation-level parvovirus score.

3.4.3.2. Development of a rule-based classifier to search for regex matches detecting canine parvovirus cases in veterinary clinical narratives

Figure 3.8 contains the Python UDF used to detect regex matches in veterinary clinical narrative data contained in .pkl files and add columns that indicate the score for each regex on each consultation, as well as a column that represented the consultation-level parvovirus score.

```python
for filename in os.listdir():
    df =  pd.read_pickle(filename)
    if 'narrative' in df.columns:
        df['regex1_score']=df.narrative.apply(lambda x: get_regex1_score_for(x))
        df['regex2_score']=df.narrative.apply(lambda x: get_regex2_score_for(x))
        df['regex3_score']=df.narrative.apply(lambda x: get_regex3_score_for(x))
        df['regex4_score']=df.narrative.apply(lambda x: get_regex4_score_for(x))
        df['regex5_score']=df.narrative.apply(lambda x: get_regex4_score_for(x))
        df['parvo_score']=df.narrative.apply(lambda x: get_parvo_score_for(x))
        print (df)
        df.to_csv(f'{filename}.csv', index=False)
```

Figure 3.8. Rule-based classifier developed to categorise clinical narrative data according to the matches by each regex for parvovirus case detection.

3.4.4. Estimation of the likelihood that an individual animal has canine parvovirus by analysing its clinical history with a text mining tool

Table 3.7 contains the risk matrix created to indicate the likelihood of having parvovirus disease for a dog whose EHRs have been evaluated by using the developed text mining tool. The following risk tiers were established:

- Very low risk (score 0-9), generated if no matches or matches by:
  - Regex 1 only (risk factors), score = 2.5.
  - Regex 2 only (general clinical signs), score = 7.5.
- Low risk (score 10-24), generated if matches by:
  - Regex 1 and 2 (risk factors + general signs), score = 10.
  - Regex 3 only (specific clinical signs), score = 10.
  - Regex 1, 2, and 3 (risk factors + general + specific signs), score = 20.
- Medium risk (score 25-54), generated if matches by:
  - Regex 4 only (disease suspicion), score = 25.
  - Regex 4 and 1-3 (disease suspicion + risk factors/general signs/specific signs), max. score = 45.
- High risk (55-79), generated if matches by:
  - Regex 5 only (diagnostic words), score = 55.
  - Regex 5 and 1-3 (diagnostic words + risk factors/general signs/specific signs), max. score = 75.

- Very high risk (80-100), generated if matches by:
  - Regex 4 and 5 (suspicion of disease + diagnostic words), score = 80.
  - Regex 4 and 5 and 1-3 (suspicion of disease + diagnostic words + risk factors/general signs/specific signs), max. score = 100.

Table 3.7. Risk matrix generated using a traffic light system that represents the likelihood of canine parvovirus disease at an animal level, as well as the combination of regex that would have to match their clinical narrative data to generate the scores on each risk tier.

Parvovirus score	**Tier of parvovirus risk**	**Combination of regex matches needed to generate score**
0 - 9	**Very low**	Risk factors only or general clinical signs only
10 - 24	**Low**	Specific clinical signs only or combination with general signs and/or risk factors
25 - 54	**Medium**	Suspicion of disease only or combination with clinical signs and/or risk factors
55 - 79	**High**	Diagnostic words only or combination with clinical signs and/or risk factors
80 - 100	**Very high**	Combination of suspicion of disease and diagnostic words, or combination of all previous categories

3.4.5. Validation of the developed methods by using real data

3.4.5.1. Validation of the text mining tool developed to detect canine parvovirus cases at an animal consultation level

The dataset with EHR from 100 random dogs contained a total of 348 consultations. Out of these consultations, 51 had parvovirus-related regex matches, corresponding to 37 dogs. Table 3.8 contains a summary of the number of matching consultations for each of the five regex developed for parvovirus detection.

Table 3. 8. Summary of results of the parvovirus text mining tool when applied to the clinical histories of 100 randomly selected dogs.

Regular expression used	Number of matching consultations	Number of dogs
Regex 1: Risk factors	19	16
Regex 2: General signs	35	26
Regex 3: Specific signs	2	2
Regex 4: Parvovirus suspicion	0	0
Regex 5: Diagnostic words	0	0

A breakdown of the performance of each parvovirus-related regular expression can be found below.

3.4.5.1.1. Regex 1: Risk factors

All the canine consultations flagged by the rule-based classifier contained parvovirus-related risk factors, therefore regex 1 had a positive predictive value of 100%, Table 3.9. Further, all the consultations not flagged by the rule-based classifier did not contain parvovirus-related risk factors, hence the tool's specificity was 100%. However, five consultations that contained key terms representing parvovirus risk factors were incorrectly classified (FN), therefore impacting the tool's sensitivity (79%), and negative predictive value (98%). Overall, regex 1 had an accuracy of 98%, and a F1 score of 0.89.

Table 3.9. Summary of the performance measures for regex 1 (parvovirus risk factors).

Regex 1: risk factors		True class +	True class -	**Accuracy** 98%
Algorithm class	+	TP 19	FP 0	**PPV** 100%
	-	FN 5	TN 324	**NPV** 98%
		Recall/Se 79%	**Specificity** 100%	**F1 score** 0.89

Regex 1: analysis of false negatives

The five false negative consultations contained the following key terms, that were not captured by the text mining tool, since the vocabulary used to describe these terms was different from that of the training dataset:

1. "rescue **pup**"
2. "**pup**"
3. "o **does not treat for fleas/ticks**"
4. "**finances limited** so keep tx to minimum"
5. "**flea dirt and fleas** visible"

3.4.5.1.2. Regex 2: general clinical signs

Five consultations were wrongly flagged by the rule-based classifier (FP), as there were no key terms in their clinical annotations related to parvovirus general clinical signs, Table 3.10. This had an impact on the tool's precision (86%), and specificity (98%). Three consultations that contained parvovirus general clinical signs were not flagged by the algorithm (FN), having an impact on the text mining tool's negative predictive value (99%), sensitivity (90%). Overall, regex 2 had an accuracy of 98% and F1 score of 0.88.

Table 3.10. Summary of the performance measures for regex 2 (parvovirus general clinical signs).

<table>
<tr><th colspan="2" rowspan="2">Regex 2: general signs</th><th colspan="2">True class</th><th rowspan="2">Accuracy
98%</th></tr>
<tr><th>+</th><th>-</th></tr>
<tr><td rowspan="2">Algorithm class</td><td>+</td><td>TP
30</td><td>FP
5</td><td>Precision/PPV
86%</td></tr>
<tr><td>-</td><td>FN
3</td><td>TN
310</td><td>NPV
99%</td></tr>
<tr><td></td><td></td><td>Recall/Se
90%</td><td>Specificity
98%</td><td>F1 score
0.88</td></tr>
</table>

Regex 2: analysis of false positives

The five false positive consultations contained the following terms, incorrectly flagged by the text mining tool:

1. "**dehydrated** claw": the term "dehydrated" was included in the regular expression and was flagged in this consultation, however the usage of "dehydrated" in this context is unclear and it does not seem to refer to the state of the canine patient.
2. "no coughing/sneezing/**v+/d+**": in this case the term "v+/d+" was captured because the negative lookbehind argument used in the regex specified that there should be a non-word character between the word "no" and the term "v+/d+"

3. "did have **v+** a week ago, but resolved now": the term "v+" was correctly flagged, however the narrative refers to it in the past tense.
4. "5 mins of **quiet**": the term "quiet" here was flagged, although it is not relevant since it does not refer to the status of the canine patient.
5. "has had severe **d+** as reaction to meloxicam before": the term "d+" was correctly flagged, however the narrative refers to it as a past adverse reaction to a medication, rather than a clinical sign currently experienced by the canine patient.

Regex 2: analysis of false negatives

The three false negative consultations contained the following key terms, that were not captured by the text mining tool:

1. "has had slightly **looser stools**": this term was not included in the regular expression even though it was relevant for the disease of interest.
2. "**v** again…v food up": the term "v" was not included in the regular expression to represent "vomiting"; and would not be included in the future as this term is too unspecific and would likely result in many false positive matches.
3. "**Diarrhoea**.": this term was not captured by the regex as it was the only word included in the clinical narrative and no space character was located before it.

3.4.5.1.3. Regex 3: Specific clinical signs

When applying the regex containing parvovirus specific clinical signs, the algorithm correctly flagged 6 consultations, therefore having 100% precision and specificity, Table 3.11. However, one consultation was wrongly classified as not containing any parvovirus specific signs, which impacted the NPV (99.7%), and the sensitivity (86%). The overall accuracy and F1 of this regex were 99.7% and 0.92, respectively.

Table 3.11. Summary of the performance measures for regex 3 (specific parvovirus clinical signs).

Regex 3: specific signs		**True class**		**Accuracy**
		+	-	99.7%
Algorithm class	+	TP 6	FP 0	**Precision/PPV** 100%
	-	FN 1	TN 341	**NPV** 99.7%
		Recall/Se 86%	**Specificity** 100%	**F1 score** 0.92

Analysis of false negatives

In this case, the false negative occurred because of the distance between keywords in the clinical narrative: *"**Diarrhoea** since last Friday, gradually getting worse, O noticed small amount of **fresh blood** in it".* The regular expression used to detect haemorrhagic diarrhoea specified a 3-word maximum distance between these keywords, to increase the specificity of results: `diarr\w*(?:\s*|\w*){1,3}(?:blood\w*)`.

3.4.5.1.4. Regex 4 and 5: Suspicion of parvovirus and confirmation of parvovirus

There were no consultations that contained words that indicated a suspicion or a diagnosis of parvovirus in the randomly selected dataset. The text mining tool correctly classified all the consultations in this dataset as non-matches (Table 3.12). Given these results, both the specificity and NPV of detection were 100%, and no other performance measures could be calculated.

Table 3.12. Summary of the performance measures for regex 4 (suspicion of parvovirus) and regex 5 (diagnosis of parvovirus).

Regex 4 and 5: suspicion and diagnosis		True class		**Accuracy**
		+	-	NA
Algorithm class	+	TP 0	FP 0	**Precision/PPV** NA
	-	FN 0	TN 348	**NPV** 100%
		Recall/Se NA	**Specificity** 100%	**F1 score** NA

3.4.5.2. Validation of the method developed to estimate the likelihood that an individual animal has canine parvovirus by the analysis of its clinical history

Appendix III.b contains the R script developed to estimate the risk of canine parvovirus at an animal level for the 100 random dogs that were selected to validate this chapter's methods. Table 3.13 contains a list of the 37 dogs out of these 100 random dogs with regex matches in their histories, with their corresponding consultations and their animal-level parvovirus scores, as well as their corresponding risk tier, as described on Table 3.7. Seven of these dogs reached the "low" tier of parvovirus risk at some point in their clinical histories, while the remaining 30 dogs' parvovirus risk stayed in the "very low" tier.

Table 3.13 illustrates how the animal-level risk of parvovirus did not increase in follow-up consultations, i.e., less than 30 days apart, if the regex matching these follow-up consultations had already been counted in the initial consultation. For instance, the dog with ID 54476, whose animal-level parvovirus score is 17.5 (low) at consultation ID 98825 on 2/7/2014 and remained at the same level 23 days later on 25/7/2014 (consultation ID 128271), as these consultations' scores correspond to the same regular expression matches, namely regex 2 and 3.

Table 3.13 also shows how the animal-level parvovirus score resets 30 days after a consultation with regular expression matches. An example is dog ID 56221, whose clinical history contains four consultations with regex matches (IDs 138596, 244934, 1145801, 9043720). However, since over 30 days pass in between these consultations, as they take place on 4/8/2014, 7/11/2014, 3/2/2014, and 1/11/2021, respectively, this dog's parvovirus score is as high as its consultation-level scores at the above-mentioned time points.

Table 3.13. List of dogs with matching parvovirus regex in their histories with their corresponding animal-level parvovirus risk and their risk tier for parvovirus disease.

Animal ID	Consult ID	Date	Days since last consult	Matching regex	Animal risk	Risk level
1033662	7129826	2019-12-27	0	2	7.5	Very low
1088299	2899483	2017-03-13	0	1	2.5	Very low
1099695	2953477	2017-03-27	0	1	2.5	Very low
1280580	3765993	2017-10-19	0	1	2.5	Very low
1329731	3983069	2017-12-11	0	1	2.5	Very low
1486680	6103781	2019-05-14	0	2	7.5	Very low
1545556	4840959	2018-08-02	0	2	7.5	Very low
	5158708	2018-10-05	64	2	7.5	Very low
1566789	5095774	2018-09-24	0	2	7.5	Very low
1586601	8787739	2021-08-13	0	2 3	17.5	Low
1629930	6944364	2019-11-14	0	1	2.5	Very low
163334	296838	2014-12-31	0	1	2.5	Very low
1648601	5165845	2018-10-08	0	2	7.5	Very low
1799917	5709889	2019-02-08	0	1	2.5	Very low
1896647	6099271	2019-05-13	0	1 2 3	20	Low
1976931	8443329	2021-04-15	0	2	7.5	Very low
2130896	7036230	2019-12-05	0	2	7.5	Very low
2148173	7108229	2019-12-20	0	2	7.5	Very low
2264698	7595186	2020-06-15	0	1	2.5	Very low
2334143	7862939	2020-09-16	0	2	7.5	Very low
	8907692	2021-09-20	369	2	7.5	Very low
2393046	8101982	2020-12-07	0	1 2	10	Low
2423469	8225661	2021-01-26	0	1	2.5	Very low
	8314854	2021-03-01	34	1	2.5	Very low
	8426983	2021-04-09	39	1	2.5	Very low
	8589196	2021-06-10	62	1	2.5	Very low
2504133	8553791	2021-05-27	0	1	2.5	Very low
2532292	8662804	2021-07-05	0	1	2.5	Very low
2556078	8828146	2021-08-26	0	2	7.5	Very low
27214	114858	2014-07-15	0	2	7.5	Very low
288772	2121077	2016-09-05	0	2	7.5	Very low
388037	796199	2015-11-09	0	2	7.5	Very low
	806791	2015-11-11	2	2	7.5	Very low
436708	8533720	2021-05-20	0	2 3	17.5	Low
478942	1670672	2016-05-31	0	2	7.5	Very low
508875	3211190	2017-06-05	0	2	7.5	Very low
544723	1136569	2016-02-01	0	2	7.5	Very low

Animal ID	Consult ID	Date	Days since last consult	Matching regex	Animal risk	Risk level
54476	98825	2014-07-02	0	2 3	17.5	Low
	128271	2014-07-25	23	2 3	17.5	Low
56221	138596	2014-08-04	0	1	2.5	Very low
	244934	2014-11-07	95	2	7.5	Very low
	1145801	2016-02-03	453	2	7.5	Very low
	9043720	2021-11-01	2098	2 3	17.5	Low
596773	1260975	2016-02-29	0	2	7.5	Very low
7138	9950	2014-03-25	0	2	7.5	Very low
	13881	2014-04-01	7	1 2	10	Low
	200722	2014-09-25	177	2	7.5	Very low
	208277	2014-10-02	7	2	7.5	Very low
854468	6514519	2019-08-09	0	2	7.5	Very low
932031	2492553	2016-11-28	0	1	2.5	Very low
	2793432	2017-02-14	78	2	7.5	Very low

3.5. Discussion

This chapter aimed to develop a text mining tool to harness free text routinely collected in small animal health records for the early detection of potential cases of canine infectious disease. This tool relies on text mining and rule-based classification methods to identify key signals of disease in clinical narratives, such as mentions of clinical signs, disease risk factors, and expressions indicating suspicion or diagnosis of disease which are used to estimate the likelihood of disease. The developed tool was validated by evaluating its performance for the detection of canine parvovirus cases in the clinical histories of a sample of dogs randomly extracted from the SAVSNET database.

The aim of developing this text mining tool is to contribute to the design of a nationwide framework for the timely detection and response to canine disease outbreaks in the UK, by enhancing the surveillance of infectious diseases. Potential disease cases detected by the tool can be used as a source of data for surveillance, that complements the existing sources currently used by initiatives like SAVSNET, i.e., diagnostic laboratory data and syndromic data from the main presenting complaint (MPC) classification of EHR. The advantage of the tool developed in this chapter is that it relies on pre-diagnostic data, which offers an improved timeliness of disease detection when compared to diagnostic laboratory data, since potential cases are flagged before samples are collected, sent to the diagnostic laboratory, and a confirmation of results is received by the attending veterinarian. Further, it also offers an improved specificity of disease detection when compared to surveillance tools based on syndromic data, i.e., the MPC classification used by SAVSNET, since this text-mining tool targets specific pathogens. This is possible thanks to the usage of key terms that are representative of the vocabulary and expressions used by veterinary clinicians in practice to describe cases of the disease of interest in their clinical narratives. In summary, the tool developed in this chapter offers a timely and specific source for canine disease surveillance. Another advantage of this tool is that it provides user-friendly outputs, that could be easily interpreted by veterinary practitioners, by using a qualitative risk matrix that assigns an easily interpreted risk category to the numerical scores generated ty the tool.

One of the main aims of the framework of epidemic response developed in this thesis is the applicability to the specific circumstances of the UK's canine health sector. For this reason, the text mining strategy for canine disease detection developed in this chapter takes into account the vocabulary that is typically used by small animal veterinarians working in the UK when writing in a canine patient's clinical notes. To achieve this, the key terms used to build the text mining tool were extracted from training datasets that contained real-life examples of the vocabulary used in veterinary consultations that described the disease under study.

3.5.1. Use of text mining for disease surveillance in the literature

The use of text mining for disease surveillance and outbreak detection is a relatively new field, that is vastly unexplored (Chapman et al., 2011). The methods used in the literature can be divided into two main approaches. On one hand, statistical methods, that are based on the word frequencies in disease case and control datasets, to calculate the strength of association between a given term and the presence/absence of disease. On the other hand, machine learning (ML) methods, that can be supervised or unsupervised, and are used to make predictions or classifications on new, unseen data (Alfred & Obit, 2021). Supervised ML methods rely on previously labelled datasets, that are used to train disease detection algorithms (Muhammad et al., 2020). Conversely, unsupervised ML methods are used to extract hidden patterns from unlabelled datasets (Lim et al., 2017).

A study by Newman, 2018 (Newman, 2018), developed a text mining tool to detect cases of canine emerging disease in veterinary clinical annotations, and illustrated its functionality with cutaneous and renal glomerular vasculopathy (CRGV). The rationale for this study was that surveillance of newly emerging diseases is challenging, given their unknown causative agent, and the limited clinical data available for syndromic surveillance. This study faced this challenge by developing a tool to identify sentinel features in the text of the clinical records of dogs with a post-mortem diagnosis of CRGV, that could subsequently be used to identify future suspect cases of the disease. To do so, word frequencies were extracted from a sample of 33 clinical narratives of confirmed CRGV cases and compared to the word frequencies from a geographically matched control dataset, that contained the clinical histories of 3300 dogs, by calculating univariable odds ratios. Those words that were strongly associated with a CRGV diagnosis were then included in a multivariable logistic model to predict the likelihood of CRGV at a consultation level. The performance of the developed tool was assessed by applying it to a sample of 100 dogs' clinical narratives and comparing those obtained by manually classifying these narratives. The main difference between Newman's and the present study is that the former aimed to develop a text mining tool to identify the clinical features of a largely unknown emerging disease, so that this information could help veterinary practitioners to recognise disease cases in practice. This is why the study followed an exploratory statistical approach, to investigate the strength of association of different terms to the disease, with no interpretation of the extracted terms by the researcher. By contrast, the present study focuses on developing a tool to enhance the surveillance of well-known canine diseases by using key signals contained in veterinary clinical annotations. Since parvovirus is recognisable to UK practitioners, it was possible to obtain a training dataset of clinical narratives where the attending veterinarian suspected the disease, described parvovirus clinical signs and risk factors, and subsequently tested and confirmed the diagnosis. This allowed the extraction of veterinary language-based key terms to use for future detection of parvovirus cases. This process could not have been conducted for a newly emerging disease as our approach requires that a disease is well defined and their clinical signs, risk factors and diagnostic methods established before the text mining tool can be developed to detect such specific features.

A study by Arsevska, 2016 (Arsevska et al., 2016a), aimed to develop an automated method to identify key terms in online media reports that can be used as queries to mine the web for early signals of emerging disease outbreaks, which they illustrated with African swine fever (ASF). To automate the keyword extraction process, they first used a supervised machine learning algorithm that classified news report as relevant or not relevant. The ML algorithm was trained using a dataset of previously identified relevant reports, that had been manually labelled by a veterinary epidemiologist. Once relevant reports were identified by the ML algorithm, terms were first automatically extracted based on their frequencies, and then evaluated by a domain expert (veterinary epidemiologist) to keep only those terms that were relevant to the disease of interest. The validation of the method developed in this study was two-fold; the performance of the ML algorithm was assessed by calculating its accuracy, precision, recall, and F-score; and the relevance of the extracted terms was evaluated through a Delphi panel technique, where domain experts assessed the specificity of the terms. Both this study and the present chapter focus on developing a method to extract key terms that can be used for the detection of potential disease events (potential outbreaks of ASF and potential cases of parvovirus, respectively). The main difference is that this earlier study's source of data is so vast and so varied in content, i.e., web results, that it was necessary to develop a ML algorithm to generate a dataset of manageable size with relevant documents, so that key terms could be extracted. Conversely, the size of the present chapter's source of data is considerably smaller and its contents are more uniform, i.e., veterinary clinical annotations in canine consultations that take place in UK practices that collaborate with SAVSNET. Therefore, it was manageable to create a training dataset for key term extraction by querying for the name of the diseases of interest (parvovirus and babesia) in the SAVSNET database and manually reading through the resulting clinical narratives from 3289 dogs. Further, the study by Arsevska uses key terms to search in the title or main body of online media reports, that are usually directed to lay audiences, and that do not contain errors or misspellings. Therefore, these key terms consist of single words, such as "ASF", or the combination of words ", such as "pig haemorrhagic fever", "wild boar", or "fever outbreak". By contrast, in the present study it is necessary to account for the variations in the language used by veterinarians, as well misspellings, abbreviations, and specific jargon used in the veterinary clinical field. For this reason, regular expressions were used, since these can incorporate nuances, such as the distance between words, the type of characters present at the beginning and end of each word, e.g., a space or a special character, and whether to consider entire words or only parts of them in the search, e.g., "diarrh*" instead of "diarrhoea".

Teo, 2021 (Teo et al., 2021a), described a tool to monitor COVID-19 outbreaks in UK hospitals in real time by analysing EHR clinical annotations. In this study, the authors first searched the EHR database for consultations containing a series of pre-established key words, that represent COVID-19 symptoms, e.g., "anosmia", "dry cough". Then they performed a search for consultations that do not contain these symptoms, e.g., “no anosmia”, “no dry cough”, to use as a control dataset. Subsequently, they extracted the word counts from both datasets, to identify clusters of words that were positively associated with COVID-19 symptoms, to use as future search queries with improved accuracy to track the disease in real time. This method was validated by comparing the time series generated by the enhanced keyword search against that of positive PCR laboratory results, that was considered as the gold standard for disease detection. This study shares similarities with the present chapter, as both attempt to enhance the surveillance of infectious diseases by developing a text mining tool that enables the detection of potential cases in clinical annotations. The main difference is that in the study by Teo et al., keywords were extracted from a dataset of consultations where the patient presented with COVID-19 symptoms, but without a confirmation of disease. This method was appropriate to monitor the trends of a then-ongoing pandemic, with a very high incidence of disease and extensive data to compare these trends to, given the increased surveillance and testing. However, this method would not be adequate for canine diseases, with a low prevalence and limited availability of laboratory-based surveillance data. Instead, the present study prioritised the specificity of the text mining tool, by extracting key terms from a dataset of confirmed cases and doing so by manually reading and analysing the data for units of meaning, rather than relying only on word counts.

A recent study by Noble et al. (P.-J. M. Noble et al., 2021) used an unsupervised ML technique, namely, topic modelling, to monitor an outbreak of vomiting caused by an unidentified pathogen in the UK, using SAVSNET data. In this study, a sample of 200000 consultations with a gastroenteric main presenting complaint (MPC) was used as a training dataset for the automatic generation of topics, i.e., clusters of words and expressions. The obtained topics were applied to the EHR with a gastroenteric MPC collected during the timespan of the vomiting outbreak (December 2019-March 2020). Then, the performance of topics in the classification of consultations was compared to the MPC classification, to identify the word clusters that best described the outbreak. The main difference between this study’s method and the present chapter’s methodologies is that the former aimed to identify key terms to use for the surveillance of an unknown pathogen, while the present study aimed to identify key words to enhance the surveillance of an already well-known pathogen. The unsupervised ML approach was useful to generate clusters of words outside a pre-defined syndromic category, that could be used to describe the clinical features of a new/emerging disease. For this reason, the training dataset for the unsupervised model consisted of a large volume of consultations, whose criteria for inclusion was the gastroenteric MPC. However, this method is not feasible for the present study, since the training dataset consisted of confirmed parvovirus cases would not have been sufficiently large to train the unsupervised algorithm (35 consultations in the present study vs the 200000 in the study by Noble et al.). Further, it is unclear whether an unsupervised technique would offer the necessary specificity to detect cases of a particular known pathogen, especially compared to a classifier informed by expert opinion.

The text mining tool developed in this chapter consisted of a series of regular expressions, applied to canine consultation data through a rule-based classifier. This approach was chosen for several reasons. First, because it allows for the input of regex that are tailored to a specific disease or causative agent. This also offers an adaptable design, that can be applied to multiple pathogens by changing the key terms included in the regex. This flexibility also allows for the incorporation of new relevant key terms to the regex as these are identified. Further, the rules of the classifier are not mutually exclusive, i.e., multiple regular expressions can be applied to the same consultation. Thanks to this property, the rule-based classifier also has the functionality to combine regex matches in a consultation to generate a consultation-level disease score. The regular expressions developed in this chapter contain terms that are representative of different indicators, e.g., clinical signs or risk factors. What provides the specificity for disease detection is the combination of relevant regex through the text mining tool. In this way, it can be thought of as a modular tool, where each regex is a module that can be added or removed to improve the accuracy of detection.

3.5.2. Finding confirmed cases of disease to include in training datasets

Finding dogs with a confirmed diagnosis of parvovirus or babesiosis constituted the biggest obstacle for the development of the text mining tool. This is due to several reasons. Firstly, because canine infections constitute a small proportion of the cases attending veterinary practices, when compared to non-infectious conditions. For instance, when looking at SAVSNET's data dashboard (SAVSNET, 2022), only 116 cases of canine parvovirus, which is one of the canine infections most commonly seen in UK veterinary practice, were confirmed by collaborating diagnostic laboratories between February 2019 and November 2022. The prevalence of exotic diseases, such as canine babesiosis, is even lower, as they are only seen in the UK when imported from other countries. Further, disease cases will not be detected unless the owner is able/willing to take their dog to a veterinary clinic and, even if they do, the disease might not be detected, depending on its clinical presentation, the attending veterinarian's ability to suspect the presence of disease, and the owner's willingness for a diagnostic test to be conducted. Lastly, even if tests are performed and an official laboratory diagnosis is reached, it is currently not possible to link these results to their corresponding dogs' clinical histories using SAVSNET data, as there are no shared animal-level identifiers between both SAVSNET veterinary diagnostic laboratory and practice databases, and veterinarians might not record these results in follow-up consultation's clinical notes. In this chapter, two strategies were designed to overcome this obstacle and find confirmed cases of parvovirus and babesiosis to include in the training dataset for the text mining tool.

The triangulation of cases using laboratory and canine practice data was not successful for either of the diseases under study, as the laboratory results could not be matched to the EHR available in the SAVSNET practice database. This might be due to the relatively low number of veterinary practices that contribute data to SAVSNET (around 10% of the total number of UK veterinary clinics (Sánchez-Vizcaíno et al., 2017)), compared to the higher coverage of veterinary diagnostic laboratories (around 50% of the total number in the UK (A. D. Radford et al., 2021)).

The second strategy involved using only clinical narrative data. As expected, this approach was unsuccessful in the case of canine babesiosis, due to the lack of data available for this exotic pathogen. However, this approach could be applicable to exotic diseases if more data were available for case detection, e.g., by increasing the number of recruited veterinary practices that contribute data to SAVSNET, or by collaborating with other initiatives such as VetCompass (*VetCompass, Royal Veterinary College*, 2023), that also collect EHR data from a sample of UK veterinary practices. While this approach was not suitable for babesiosis, it proved sufficient to find consultations with an explicit mention of a parvovirus diagnosis, an endemic canine pathogen that is responsible for the majority of acute gastroenteric cases in the UK (Godsall et al., 2010). However, to find a sample of 22 cases of dogs with an explicit mention of a positive parvovirus diagnosis, it was necessary to manually read the clinical narratives of 3289 dogs, that had already been filtered by searching for the word "parvovirus" in their clinical histories. There are several reasons for this; firstly, in a big proportion of these dogs' consultations "parvovirus" was only mentioned to refer to the parvovirus vaccine, rather than the disease. Further, a large number of clinical narratives where the attending veterinarian expressed a high suspicion of parvovirus lacked follow-up consultations with a confirmation of the diagnosis. In some cases, simply because no further consultations were recorded for a particular dog. In other cases, this was due to the death of the animal, either as a result of the disease or because it was euthanised. Alarmingly, in many cases the veterinary practitioner stated that the owner's finances limited the diagnostic process, as they were not able to cover the costs of testing or treatment of disease. This does not only constitute a barrier to veterinary healthcare (Lem, 2019), but hinders disease surveillance and control efforts in companion animal populations. This issue has reportedly worsened due to the COVID-19 pandemic (Applebaum et al., 2020; PDSA, 2020) and the country's economic circumstances (BBC News, 2022; PFMA, 2022). Although organisms such as the People's Dispensary for Sick Animals (PDSA) or the Royal Society for the Prevention of Cruelty to Animals (RSPCA) offer subsidised treatment for lower income families, the relevance of infectious diseases and their potential impact on animal and public health may warrant further dedicated funding from government institutions for testing to ensure that epidemic risks are minimised.

Not having access to manually labelled datasets to use as training data for keyword extraction is a common issue in the field of text mining for clinical applications, and it is referred to as annotation bottleneck (Makki et al., 2019; Tan et al., 2016). Manually classifying data provides high quality, accurate results when done by domain experts. However, it can be a labour-intensive process, that is not always feasible when dealing with large amounts of text data. Different approaches have been proposed in the literature to overcome this challenge, for instance, crowdsourcing, so that datasets are annotated by a body of people, whether hired workers or volunteers, to speed up the process of data annotation (Munro et al., 2012). This approach could be used by SAVSNET, for instance, by inviting students to contribute to the annotation of clinical narrative data, who in turn would receive training in the field of text mining applications to canine disease surveillance. Another proposed approach consists in the routine annotation of data by researchers, so that a bank of readily available training data can be used in research studies (Newman, 2018). This approach has been used by SAVSNET in the past, where the bespoke software *Datalab* was routinely used by members to create a labelled dataset where the word "tick" is mentioned, with the aim of using these data for the surveillance of tick-borne diseases (Tulloch et al., 2017).

3.5.3. Extraction of key terms

Two methods were used to extract key terms from the parvovirus training dataset. The calculation of word frequencies was deemed as not an adequate approach to obtain key terms for the detection of canine parvovirus cases. This is mainly because this method only takes individual words into account, rather than word combinations or phrases, and therefore it cannot correctly identify relevant expressions. For instance, the words "skin" and "tent" separately do not have any meaning in the context of parvovirus disease, but the phrase "skin tent" is used by veterinarians to indicate that the animal is dehydrated, as the skin loses elasticity and stays up when being pinched. Further, this approach can also be misleading when word combinations that constitute units of meaning are separated, in expressions such as "blood in motions", "shedding parvovirus", or "positive parvovirus test". Also, even though stop words and connectors were removed before calculating word frequencies, other commonly repeated, non-relevant words, such as "owner", "visit", "days", or "advice", were still included. Additionally, words were inevitably not counted if they were misspelled, e.g., "diarrheoa", or if they lacked spaces between them, e.g., "vomitingdiarrheoa". Ultimately, it was determined that manually reading and selecting words and expressions was the best approach for key term extraction in this chapter.

3.5.4. Regular expression weights

The regular expressions developed in this chapter were weighted to reflect their different levels of specificity for the detection of potential parvovirus cases. For instance, the regex containing key terms that represented risk factors of disease received the lowest weight (2.5/100), while the regex containing parvovirus diagnostic words had the highest weight (55/100). However, the design of the regex in this chapter is flexible, so that the assigned weights can be adjusted over time as they are applied to real data and their performance for disease detection is evaluated. In future studies, the values of regex weights could be adjusted by surveying veterinary clinicians, so that regex weights are adapted to end-user preferences.

3.5.5. Validation of the text mining tool

There were two levels of validation when evaluating the performance of this chapter's text mining tool, i.e., the rule-based classifier and the regular expressions. The rule-based classifier succeeded in flagging consultations where regex matches occurred, and therefore proved its utility for detection of potential canine infectious disease cases. The regular expressions' performance was assessed by calculating their accuracy measures when applied to the clinical histories of randomly selected dogs. Since this dataset contained clinical narratives that mentioned parvovirus' risk factors and clinical signs (both general and specific), it was possible to calculate the sensitivity and specificity of regex 1, 2, and 3, whose accuracy scores were very promising, at 98%, 98%, and 99.7%, respectively. In the case of regex 4 and 5, only their specificity could be calculated, with a value of 100% for both of them, as the randomly selected dataset did not contain any consultations with suspicion or diagnosis of parvovirus. To test the sensitivity of these regexes, as well as the sensitivity of case detection for the overall text mining tool, it would be necessary to have access to a dataset of clinical narratives with confirmed parvovirus cases. However, the performance of the rule-based classifier and regex 1-3 were successful for the detection of consultations with a very low-low risk of canine parvovirus, which can be used to flag animals for follow up through SAVSNET's surveillance system. Further, as the text mining tool is applied to real data, it will be possible to test the sensitivity of regex 4 and 5, which will improve the proxy for case detection achieved through the combination of regex 1-3.

3.5.5.1 Discussion of FP/FN

When designing the regular expressions in this chapter, one challenge was to balance their sensitivity and specificity. For instance, the false negative consultations for regex 2 contained terms such as "v again". If the letter "v" had been included as a key term in this regex, these consultations would have been flagged, however, this would have potentially increased the number of false positives, as the letter v is often used by veterinarians as a short version of the word "very". This was similar in the case of the false negative consultation for regex 3, where the word “diarrhoea” was 13 words apart from the word “blood”. If the regex were modified to increase the distance between these words up to 13 or more, it is very likely that this would have incorrectly flagged a large number of consultations. In the case of one of the false positive consultations for regex 2, this happened because the regular expression specified that there should be a non-word character, e.g., a space or a symbol, between the negative prefix and the term “v+/d+” for the regex to exclude this term. In this case, the term “v+/d+” could be excluded from the regex to avoid this issue, however that would likely result in a high rate of FN, since vets often use the terms “d+/v+” or “v+/d+” to indicate that an animal is presenting both clinical signs. Alternatively, the term “coughing/sneezing” could be included in the list of negative prefixes, so that “v+/d+” would not be captured if preceded by these words. Another example is the word “diarrhoea”, that was included in the regex by specifying that a space should happen before the word for it to be captured (“\sdiarrhoea”), to avoid a false positive by capturing the expression “no vomiting/diarrhoea”. In turn, a consultation that included the word “Diarrhoea” as the first word in the narrative was not flagged by the text mining tool, as there was no space before this word. A potential solution would be to add a function to the rule-based classifier to add a space character to the first line of each consultation before searching for regex matches in their text.

3.5.6. Estimation of the likelihood that an individual animal has canine parvovirus by analysing its clinical history with a text mining tool

The animal-level parvovirus score was calculated by taking into account follow-up consultations and was reset to 0 after 30 days. In the field of text mining, this is known as a time decaying factor, which is used to prioritise recent data points over older data points, to account for changing trends over time (Tan et al., 2016). In the future, this could be addressed by assigning different weights to follow-up consultations, that are inversely proportional to the time that passes between them, until eventually after some predetermined time when the score is reset. This way, recent follow-up consultations would contribute their full score to the animal-level risk estimation and, as time went by, their score would be multiplied by increasingly smaller value, thus gradually having less impact on the overall risk estimation and eventually being reset to 0 to account for new parvovirus cases.

3.5.7. Limitations

The limitations faced in this chapter have been documented throughout the sections in this discussion. The main obstacle for the development and validation of a text mining tool for canine infectious diseases was the lack confirmed cases of disease, due to the reasons discussed in section 3.5.2 of this chapter. This limitation meant that it was not possible to develop a text mining tool for canine babesiosis. The lack of confirmed cases in the test dataset also limited the validation of the text mining tool developed for canine parvovirus, as it was not possible to assess the sensitivity of its performance.

3.6. Conclusions and future work

This chapter presents a state-of-the-art method to harness the information contained in EHR's free-text annotations for the detection of potential cases of canine disease. The text mining tool developed in this chapter consists of a rule-based classifier, whose criteria for the classification of canine consultations were defined through regular expressions that are representative of the vocabulary used by veterinary clinicians in practice. This tailored tool offers an increased specificity of disease case detection at a pathogen level when compared to syndromic surveillance systems, while also improving the timeliness of detection provided by laboratory-based systems because of its usage of pre-diagnostic surveillance data. Since this tool relies on data that are already routinely collected by SAVSNET, it could be easily implemented, and constitute a complementary source for canine disease surveillance, that does not require veterinary practitioners to submit extra information. The outputs generated by the text mining tool are user-friendly, as they provide risk scores easily interpretable by veterinary clinicians, that indicate the likelihood of parvovirus disease being present at a consultation and at an individual animal level. Future work includes the implementation of the text mining algorithm in SAVSNET's surveillance system, so that the disease-specific regular expressions can be routinely applied to the clinical narrative database. Outputs from this text mining tool could be used as a source of data for the early detection of canine disease outbreaks. To achieve this, cases flagged by the tool could be fed to statistical models for anomaly detection with appropriate outbreak notification thresholds (see Chapter Four). In conclusion, this chapter has demonstrated the feasibility of using a text mining tool to identify key signals for canine endemic disease detection in clinical narratives. The functionality of this tool has been validated using canine parvovirus as a case study, but it can be applied to other endemic diseases.

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

4.1. Abstract

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

An intensity sampling approach was followed to recruit participants from this study's target population of veterinary practitioners, according to their years of experience and the size of the practice where they were employed at the time of the conduction of the study. In depth semi-structured interviews were conducted to explore outbreak notification and outbreak response thresholds for six priority canine endemic diseases, exotic diseases and syndromes. These thresholds reflected participants' preferred balance between levels of excess case incidence and predictive certainty of the detection system. Interviews were transcribed and a thematic analysis was performed using NVIVO 12.

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

This chapter proposes an innovative methodology that uses veterinary practitioners' opinion 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 UK.

4.2. Introduction

4.2.1. Background

One of the main factors that determine the effectiveness of an epidemic response is the timeliness of detection and notification to those that are potentially affected (National Research Council (US) Committee on Climate, 2001). Even if a system of disease surveillance is effective at detecting health threats, this information will not aid in the prevention and control of epidemics if it is not harnessed correctly.

In the UK, a list of notifiable diseases in humans is available to health professionals, who are legally obliged to report observed cases to the corresponding authority (GOV.UK, 2023a). Similarly, in the farm animal sector, veterinarians have the duty to report notifiable diseases to the Animal and Plant Health Agency (APHA), the government agency responsible for investigating animal disease outbreaks (GOV.UK, 2019c). Further, in both of these sectors, health data are collected systematically at a national level, using a variety of sources, such as patient health records and diagnostic laboratory test results (GOV.UK, 2023b). These data are analysed to identify increasing disease trends and detect disease outbreaks in their early stage, facilitating the prevention and control of health threats nationally and regionally. The relevant information derived from these analyses is shared with the public via weekly reports (GOV.UK, 2022c) and online dashboards (*APHA Vet Gateway*, 2022). This way, the process of epidemic detection and notification in human and farm animal medicine is run centrally by government departments and agencies and implemented country wide.

These surveillance protocols however do not currently exist in small companion animals, for which there is no standardised system of disease reporting or routine collection of surveillance data at a national level (BVA, 2018). It was only recently, January 2022, that a dedicated species expert group (SEG) at APHA was setup for small animals (*APHA Small Animal Surveillance*, 2022). At the time of writing this thesis, this expert group is only actively doing surveillance on exotic worm-like parasites in imported and travelled dogs (APHA, 2022).

4.2.2. Outbreak alert thresholds

To begin to bridge this gap, the SAVSNet-Agile initiative (*SAVSNet-Agile, University of Liverpool*, 2019) is developing a nationwide system for the timely detection and response to canine disease outbreaks in the UK. However, before such a surveillance and control system can be set up and implemented, it is necessary to determine which notification thresholds of increased level 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 are 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 alert thresholds based on increases in case incidence, relative to the previously identified baseline (WHO, 2012). An example of this approach is the moving epidemic method (MEM), described by the WHO and used worldwide to establish alert thresholds for influenza (Rakocevic et al., 2019). Other commonly used methods to establish epidemic alert thresholds are multi-chart schemes, which combine the results of individual time series that enable the rapid detection of subtle changes in disease (Engmann & Han, 2020), or methods that involve setting a number of standard deviations above the baseline of expected cases (Brady et al., 2015). For exotic and rare diseases, with no historical levels of case incidence to rely on, there are fewer methods described in the literature to define alert thresholds, and it is often common to accept a single case as a threat that warrants generating an alert (Guagliardo et al., 2018). In the case of COVID-19, an initially exotic disease that became widespread in the UK population, the UKHSA has developed a system that categorises the levels of alert based on the incidence of disease, as well as other epidemiological factors (GOV.UK, 2023c).

The statistical models for early detection of disease outbreaks that this thesis response framework (see Chapter Five) will rely on are still under development. However, they will be similar to the models used by SAVSNET to investigate an outbreak of prolific vomiting in dogs in 2020 (Radford et al, 2021). These models detect increases in case incidence using a Bayesian paradigm, where credible intervals are set at values from 90 to 99%. An outbreak is declared when the disease levels increase beyond the model's predicted incidence and the predicted probability surpasses the credible interval. This is what from now on will be referred to as statistically significant threshold. Small animal veterinary clinicians will be on the receiving end of the alerts generated by these mathematical models. However, their perceptions of what constitutes an outbreak worthy of being notified might differ from the statistical threshold. For instance, veterinarians might not want to spend time dealing with an alert unless the incidence of a given disease reaches a certain level that they consider of practical importance, regardless of whether it is statistically significant. This is referred to as clinically relevant threshold. Whilst statistical methods have proven to be powerful for detecting disease anomalies, they often signal outbreaks that are not necessarily clinically relevant for veterinarians in practice, as they do not consider the clinical implications of said outbreaks, which are largely unknown in small animal medicine. Therefore, outbreak notification systems that rely on such statistical signals might overload practitioners with information that is not actionable. In the long term, this could lead to a lack of confidence and engagement with the surveillance and outbreak notification system.

4.2.3. Aim and objectives

To address the limitations of statistical models above described, the aim of this study was to explore what threshold values based on veterinary practitioners' opinion correspond to outbreaks that should be notified when detected by statistical methods because of their significant impact in veterinary practice for six priority canine diseases and syndromes in the UK (Chapter Two). To achieve this aim, the following two objectives had to be completed:

a) To understand which disease incidence levels are considered of practical importance by companion animal clinicians to be notified about for each disease under study.
b) To understand what levels of certainty associated with the prediction of an outbreak are required by veterinarians in practice when alerted of outbreaks of the diseases under study.

In addition, an understanding is gained of the reasons that drive veterinary practitioners in selecting such threshold values and of which disease incidence levels would change their in-practice behaviour and how. To achieve these aims, an innovative methodology was developed based on the combination of semi-structured and structured interviews with companion animal veterinarians.

4.3. Materials and methods

4.3.1. Study population

The population of interest were small animal veterinary clinicians working in the UK at the time of the conduction of the study. Study participants were selected from this population following an intensity sampling approach, a type of purposeful sampling which consists in selecting cases that are located at the ends of a population's distribution (Patton, 2014). The aim of this strategy was to maximise the efficiency of the recruitment process by selecting information-rich cases, that are able to provide valuable insights about the phenomenon under study (Benoot et al., 2016). To do so, relevant population characteristics, or descriptors, were defined. Descriptors for this study were chosen because they were believed to influence participant perspectives and behaviour regarding canine epidemics, and therefore influence their responses during the interviews. The following descriptors and levels of interest were used in the sampling process:

a) <u>Years of experience in small animal practice</u>: 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, and this could influence their opinions and decision-making. Cut-off points were established to differentiate newly graduated veterinarians from those with many years of in-practice experience.
    a. Recent graduates: with less than five years of experience.
    b. Senior veterinarians: with over ten years of experience.
a) <u>Practice size</u>: since smaller practices have fewer employed veterinarians and see a lower number of cases, compared to bigger veterinary centres, 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 practice, a summary of the existing veterinary practices by size in the UK was requested to the Royal College of Veterinary Surgeons (RCVS). This

database included the total number of registered practices in the UK, and a breakdown of the number of employed veterinarians per practice. The practice directory was analysed to understand what the average size of a practice is and inform the categorisation. A total of 4252 individual veterinary sites were listed on the database. Over half of these sites had four or fewer registered veterinary surgeons (2917 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: with fewer than four employed veterinarians.
b. Big veterinary practices: with more than ten employed veterinarians.

4.3.2. Participant recruitment

Potential study participants were contacted through different means of direct and indirect communication.

4.3.2.1 Direct communications

Veterinarians from the pre-established network of stakeholders for this project (See Chapter Two) were contacted directly via email by the author of this thesis. Furthermore, veterinary clinicians whose practice collaborated with SAVSNET at the time of the conduction of this study were notified directly through their practice management software (PMS); which contains a SAVSNET plugin window that can be used by the latter to relay messages to attending veterinarians (*Information for Veterinary Practices - SAVSNET*, 2023). Lastly, small animal clinicians acquainted with the author of this thesis and members of the SAVSNET team were personally contacted and asked to take part in this study.

4.3.2.2. Indirect communications

A participant recruitment advert was posted on the SAVSNET website (*Stories - SAVSNET*, 2021), and was shared on social media (Twitter and Facebook) by the funders of the

SAVSNET-Agile project, Dogs Trust. The author of this thesis also conducted an interview advertising the project with UK veterinary magazine, Vet Times (Silverwood, 2021). Lastly, participant recruitment for this study was advertised internally by the author of this thesis at a series of seminars at Bristol Veterinary School.

4.3.3. Data collection

Approval for this study was granted by the University of Bristol Faculty of Health Sciences Ethics Committee (FREC, reference code: 98843). All interviews were recorded with the permission of the participants. Interview recordings were transcribed for analysis, and the data were anonymised by using a code assigned to each of the participants. Once the analysis was completed, the recordings were destroyed, and the electronic transcripts were kept by the thesis author in a university protected folder.

Recruited veterinarians took part in an interview session, which was conducted online via Microsoft Teams (*Microsoft Teams*, 2022) or Zoom (*Zoom*, 2022). The overall aim of the interviews was to explore clinically relevant outbreak scenarios for notification, that corresponded to the top two canine endemic diseases, exotic disease and syndromes identified in the disease prioritisation study conducted on Chapter Two of this thesis:

- Endemic diseases: leptospirosis and parvovirosis.
- Exotic diseases: leishmaniosis and babesiosis.
- Syndromes: respiratory and gastrointestinal disease.

The interviews consisted of two components, with differentiated aims.

4.3.3.1. Semi-structured interview

The first part of the interview followed a semi-structured (Clifford et al., 2016), in-depth format and aimed to gain an understanding of the reasons that drive veterinary practitioners in defining what constitutes a clinically relevant outbreak and to understand how their in-practice behaviour 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, by providing information about the disease's severity, transmissibility, zoonotic potential, and prevalence in the UK (Appendix IV.a). The information used was obtained from the disease fact sheets elaborated in the second chapter of this thesis (see Appendix II.a).

The following topic guide was developed for the semi-structured interview:

- What is your experience with disease X? Do you see cases of it in your practice? If so, how many cases would you expect to see in a normal week/month/year? What is the severity of the cases like that you have observed in your practice?
- Are you aware of any exotic canine diseases that could potentially affect you practice? Do you believe there to be enough training or knowledge available to deal with exotic disease cases? What do you think about the risk of introduction of exotic canine pathogens into the UK?
- Have you ever experienced an outbreak of disease X? if so:
    - What did you/ your practice as an institution do to deal with this outbreak?
    - What was your strategy of communication with other veterinarians, the practice's clients and/or the public?
    - Did you receive any help from other institutions, such as government agencies, veterinary corporations, laboratories, or other?
    - Were there any protocols in place to deal with canine epidemics in your practice? If so, did you follow them at the time, and did you find that they were efficient for dealing with the outbreak?
    - Are there any lessons that you learned from that experience that you would implement in the future if you were faced with a similar situation?

During this initial part of the conversation, participants were given room to bring up and discuss any topic that they considered relevant to the subject matter. The interviewer intervened only to probe participants with follow-up questions, or to steer the conversation back to the topic guide's questions when it moved away from the study's subject matter. This was done to ensure that the main topics related to the subject matter were covered by every participant. If a new topic or idea was introduced, the interview protocol was updated to account for it, and subsequent participants were also asked about these new topics.

To obtain responses that were as realistic as possible, participants were asked to reflect upon the impacts that canine infectious diseases could have in their practice. Throughout the interview session, participants were continuously reminded of this notion, and asked to take their time to reflect on how they would answer the interview questions if they were faced by an outbreak whilst at their workplace in a veterinary clinic.

4.3.3.2. 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 in their practice, for each disease under consideration. In this chapter, outbreak scenarios were described using two parameters, which represented characteristics of an outbreak notification:

- Excess case incidence: increased incidence above the expected baseline of cases in a practice's catchment area, that would be of practical significance to a) warrant a notification about a potential outbreak, and b) drive practitioners to change their behaviour in practice in response to an outbreak. Where 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: level of confidence of the alerts generated by statistical outbreak detection models, defined by their credible interval, which normally takes values that range from 90 to 99% (Hale et al., 2019).

Questions included in the structured interview 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:

- Given what we have discussed so far, could you tell me how many cases of disease X you would need to see in your practice for you to become concerned? Please use a time frame that you are comfortable with, for example in a week, or a month.

- What number of cases in your area would be worrying for you so that you would want to be notified about a potential outbreak?
- How would your behaviour change in response to an outbreak alert of disease X?
- How do you think that a false alarm related to disease X would impact your practice?
- Could you think of an alert certainty level that you would be comfortable with for outbreaks of disease X?

The same structure was used to discuss every disease, but some flexibility was allowed during the interview to account for the differences between endemic diseases, exotic diseases, and syndromic health conditions.

4.3.3.3. Testing the methodology

The data collection process described in this section was tested through a series of mock interviews, to assess how difficult and how engaging the exercise was for participants, the time required to conduct the exercise, and to improve the interview's design. Mock interviews were conducted with three members of SAVSNET, as well as with two acquainted veterinary clinicians that were external to the project.

4.3.4. Data analysis

Interviews were audio recorded and transcribed verbatim. Interview data were analysed through a thematic analysis (TA), a qualitative method to search for themes within the data that aid in the description of the phenomenon under investigation (Daly et al., 1997). It consists in the identification and encoding of patterns of meaning, with the objective of organising primary research data for their subsequent interpretation (Braun & Clarke, 2006).

Figure 4.1 contains a summary of the steps followed in this chapter to analyse the data obtained by interviewing veterinary practitioners. Briefly, a coding framework was iteratively developed by the author of this thesis based on expected and emergent themes using deductive and inductive approaches, respectively. To enhance the consistency and reliability of the analysis, the author of this thesis and this thesis' main supervisor (FS-V) 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 (Fereday & Muir-Cochrane, 2006). To ensure reliability and transparency, themes were continuously compared to the interview transcripts, to ensure they were true to the original data (Sandelowski, 1993).

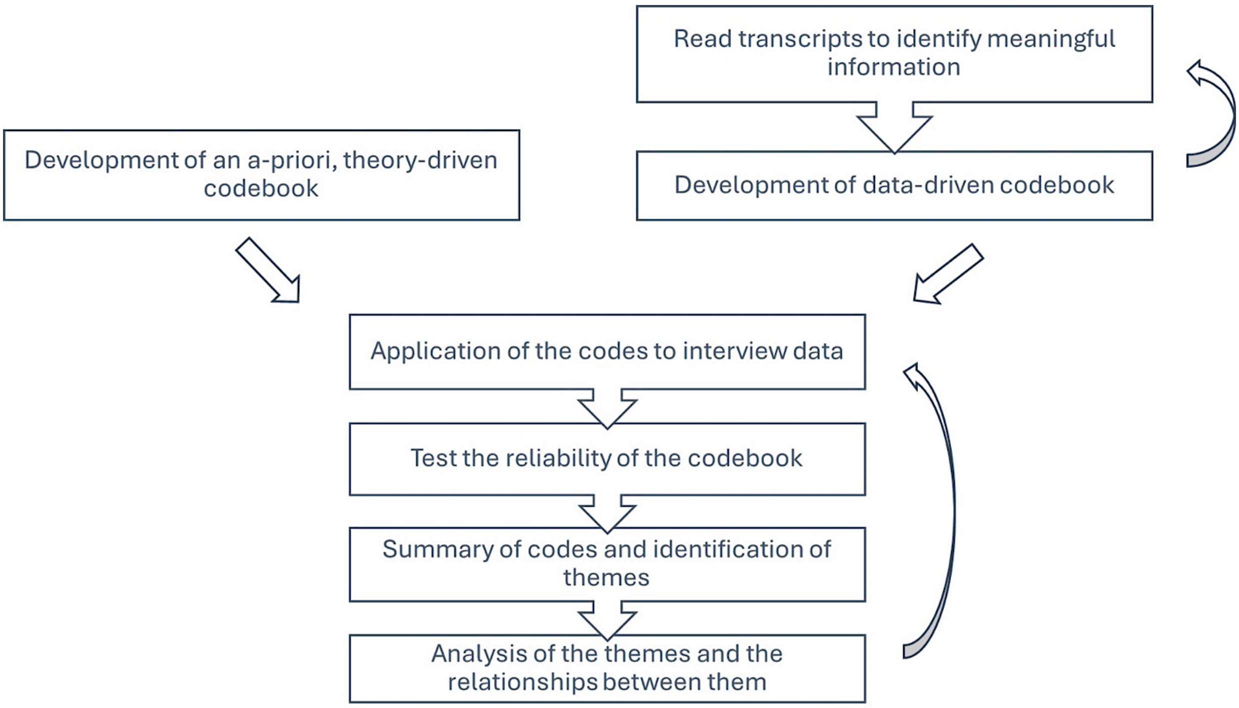

Figure 4.1. Summary of the data analysis process for veterinary clinician's interview transcripts.

All the analyses were conducted on NVivo 12 (NVivo 12, 2023) qualitative data analysis software. This program was chosen because it allows the researcher both a) to enter a pre-designed set of codes and use them to tag fragments of the text (deductive approach), and b) to simultaneously scan the transcribed text to identify units of meaning and log them as codes (inductive approach).

4.3.4.1. Deductive generation of codes

Prior to reading the interview transcripts, a set of theory-driven codes was developed, based on the research questions of the study. Table 4.1 contains a summary of the developed a-priori codes.

Table 4.1. Summary of deductive, a-priori codes, based on the study's research aims and questions.

Deductive code	Definition
Experience	Interviewee discusses their personal experience as a companion animal clinician with the canine infectious diseases included in this study.
Preventative action	Interviewee describes existing protocols used in their veterinary practice to prevent outbreaks of canine disease.
Behaviour change	Interviewee describes the actions they would take to respond to an outbreak of canine disease if it were to occur in their current veterinary practice.
Certainty	Interviewee discusses the levels of confidence of an outbreak alert that they would require for a specific canine disease.
Excess case incidence	Interviewee discusses the increases in case incidence that would a) warrant an outbreak notification, and b) result in a behaviour change to respond to an outbreak.

4.3.4.2. Inductive generation of codes

This approach consisted in carefully reading and re-reading transcript data, to identify relevant units of meaning, that were logged as codes in the qualitative analysis software. When a code was identified, it was logged in a codebook, a table of information that contained the code's assigned name and a brief description of it. The data were read systematically and iteratively, so whenever a new code was added to the codebook, the researcher read through all of the interview transcripts again, to ensure that all the relevant text excerpts were tagged within such code. After each round of reading and coding, the obtained results were analysed, and transcripts were re-read to see if any information was left uncoded. The process was repeated as many times as it was needed, until no new information emerged from the data. This was considered the point of data saturation. It is important to remark that the coding process was not linear, even though it is shown as a step-by-step process in this chapter's methodology, for ease of presentation.

4.3.4.3. Testing the reliability of the codebook

An important part of the thematic analysis is to check for the reliability of the study's coding framework (Belotto, 2018). For this purpose, the author of this thesis invited their main doctoral supervisors (FS-V) to participate in a process to review the developed codes. One full interview was selected at random and used in the validation process, which was two-fold.

To review the theory-driven codes, the second researcher (FS-V) was provided with the information contained on Table 4.1, and a discussion was held regarding whether these codes reflected the research questions of this chapter. They were also asked to read through the transcript and select those text excerpts that best fitted these a-priori codes, and their responses were compared to the author's.

To review the data-driven codes, I also asked my supervisor to read the interview text closely and code it for meaningful elements. In this case, they were blinded to the data-driven codebook elaborated by the author of this thesis. This is because in inductive TA the same piece of text can potentially yield different codes, depending on who is encoding the data. This will depend on how interpretive the coding framework is, but even when researchers attempt to refrain from making personal judgements, some degree of variation can be expected when comparing coding results, as the interpretation of data is inherently subjective (Kaptchuk, 2003). The strategy was to have a conversation among the two researchers about the interview data and the coding process, to detect potentially relevant information that could be overlooked and check for important sources of disagreement. Where differences in interpretations of the transcribed text were detected, a discussion was held to understand why and consider modifying the codebook. This was done to review the rigour of the author's coding strategy and enhance the reliability of the process and results (Bryman, 2016).

4.3.4.4. Grouping codes into themes

On the next step of the analysis, the codes obtained from all the transcripts were examined and grouped into wider units of meaning, or *themes*. This process can also be referred to as theming and allows the researcher to synthesise the concepts that arise from participant's opinion and establish associations between them (Sutton & Austin, 2015).

Codes that represented similar ideas/concepts were grouped together into overarching themes. The goal was to identify relevant ideas and patterns in the data that aid in the description of the phenomenon of interest, in this case, canine outbreaks and their impact in veterinary practice. These themes could either represent recurring topics found in the data, outliers/extreme opinions, surprising findings, controversial topics, or emotional responses. The initial themes and sub-themes were then refined in a data reduction process (Guest et al., 2012; Miles & Huberman, 1994), by checking for their internal homogeneity, i.e., that codes within a theme represented the same idea, and external heterogeneity, i.e., that each of the themes represented distinct ideas (Patton, 2003).

This stage of the analysis entailed a higher level of interpretation. However, under the principle of goodness in qualitative research (Emden & Sandelowski, 1998), the rigour of the study was enhanced by continuously referring back to the interview transcripts to make sure that the emerging themes were indeed grounded on the original data. The process consisted of comparing the themes to what the interviewee originally expressed by asking the question of *does this theme accurately reflect participant's opinion?*

4.4. Results

4.4.1. Characteristics of participants

Seven veterinary clinicians participated in this study. Table 4.2 contains a summary of the recruited participants, according to the study's population descriptors. Five out of the seven participants had more than ten years of experience in practice, and the remaining two had worked in small animal practice for less than five years. Four of the participants were employed by large veterinary centres, with more than ten veterinary surgeons, while the other three worked in small clinics, with fewer than five veterinary surgeons. In fact, in the latter case, two participants (number 2 and 6) worked in centres where a single veterinary surgeon was on duty at any given time.

Table 4.2. List of participating veterinary clinicians, with a breakdown of their characteristics according to the population descriptors of the study.

Participant	**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

4.4.2. Findings from interviews with veterinary clinicians

The codebook used to analyse interview transcript data can be found in Appendix IV.a. Interviews had a mean duration of 1h 10min, the longest one being 1h 34min and the shortest 50 minutes. Out of all of the diseases under study, canine leptospirosis took up the most time and had the largest number of associated coded elements (Figure 4.2). The results of this chapter are presented as follows; first, an overview of the excess case incidence and predictive certainty parameters. 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, outbreak response thresholds and predictive certainty.

Figure 4.2. Diagram that represents the canine diseases under study. The size of the inner ring is directly proportional to the number of coded elements associated to each disease, while the outer ring contains the most common themes discussed by participants for each of the diseases.

4.4.3. 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 to also change their in-practice behaviour. In other cases, especially if they had never personally dealt with the disease in question, participants felt more comfortable by discussing the excess incidence as a range of 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 of case incidence within a week or a month, whilst others found it extremely difficult to pinpoint a time unit with which they were comfortable and they simply provided an absolute number of disease cases. Further, 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, whilst others were unable to do so, and provided an absolute number of cases that would warrant a notification or that would trigger a behaviour change in their practice, e.g., two disease cases per week. Figure 4.3 contains an overview of the notification and outbreak response thresholds for each of the diseases and syndromes included in the present chapter.

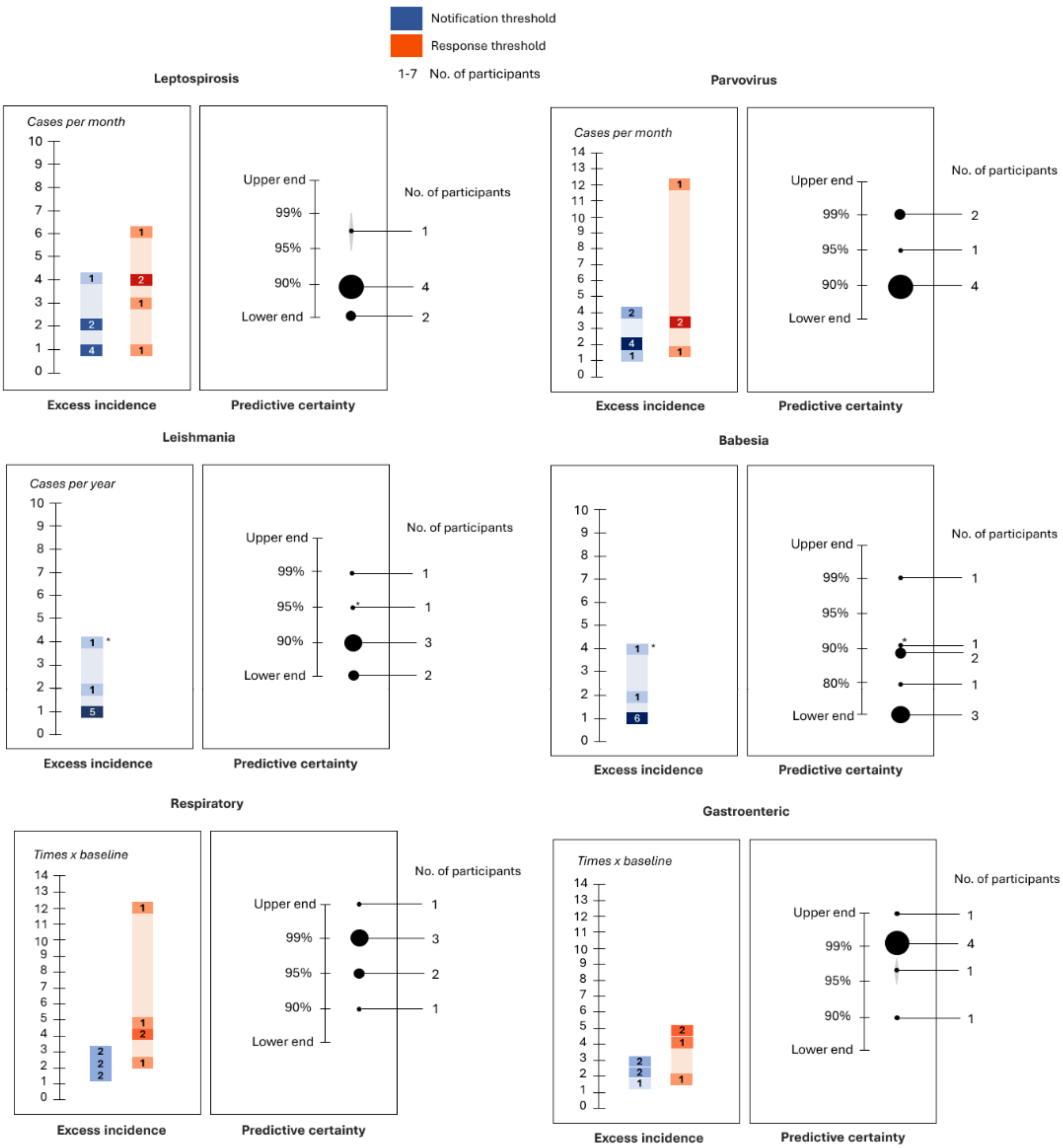

Figure 4.3. Summary of clinically relevant thresholds for the six canine diseases included in this study. The left graph included for each disease depicts the excess case incidence thresholds. The blue and orange bars represent the excess incidence values corresponding to the notification and outbreak response thresholds, respectively. Where the same participant provided more than one value of case incidence to define either the notification threshold or the outbreak response

threshold, 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 colours which serve as an indicator of the number of participants who provided a particular value, with darker colours 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 disease, the other responses refer to autochthonous cases.

4.4.4. Predictive certainty

The predictive certainty parameter was interpreted by participants in two distinct, opposite ways. On 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, they would only require a notification if the risk of receiving a false alert is minimised, to avoid either wasting time and resources in preparing for a non-existent epidemic or unnecessarily warning the practice's clients. This 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%), whilst others set this parameter value at 99%. Figure 4.3 contains an overview of the predictive certainty thresholds for each of the diseases and syndromes included in the present chapter.

4.4.5. Canine leptospirosis

Out of all the diseases included in this study, it transpired that canine leptospirosis was the one worried participating veterinarians the most, as they perceived this pathogen as the one that posed the highest epidemic risk to their practices. This was mainly due to the uncertainties surrounding this disease's diagnosis, prevention, and treatment.

4.4.5.1. Diagnostic challenges

Participants considered the diagnostic process for canine leptospirosis to be challenging, compared to that of the other diseases in this chapter. This was a source of concern, as they were unsure of how and when to use the different diagnostic test that are currently available for this disease:

"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.

Although participants seemed to have knowledge of the diagnostic tools available to them, they were concerned that they did not know which test to use (PCR or serology) to ensure the reliability of the results, depending on the stage of the infection. The factors that, according to participants, contributed the most to the uncertainties around *Leptospira* diagnosis were:

- Reliability of urine PCR, given the low survivability of the leptospires in urine, the intermittent excretion, and the inability to detect infection at the early stages of an infection.
- Reliability of blood PCR, due to the growing concern that it might pick up vaccinal serovars, and the drop in sensitivity as the infection progresses.
- Reliability of serology, because of the different cut-off values proposed by different guidelines and the concerns about the cross-reactivity of the serovars.

Another source of concern for interviewed veterinarians was the variety of clinical presentations of canine leptospirosis. Those participants that 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:

"We didn't see many cases with, um, hepatic and renal, so it wouldn't have been the case that would normally have sparked people to think about lepto, we would see a lot of cases with haemorrhagic gastroenteritis".

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

Another layer of difficulty around the diagnosis of leptospirosis were the asymptomatic cases, or carriers, that can shed the pathogen despite not showing any clinical signs. One of the interviewees mentioned how, during an outbreak of leptospirosis, many of the cases were found by accident when testing routinely for the disease:

"Back in three or four years ago when we had that outbreak, it seemed like a lot of dogs appeared to be carriers […] they presented asymptomatically and ended up having leptospires identified".

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

Lastly, given the rapid progression of the disease, participants reported that it was difficult to achieve a diagnosis since, once the dog shows clinical signs of infection, there is not enough time to take samples and perform the test of choice:

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

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

Due to these diagnostic barriers, only two of the interviewed veterinarians had ever reached a definitive diagnosis of canine leptospirosis throughout their careers. The other participants reported never having officially diagnosed a case but having had high suspicion levels based on the clinical signs and other risk indicators:

"[...] our diagnosis was empiric, it was a diagnosis just based on clinical signs, we didn't 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.

4.4.5.2. Prevention

The topic of vaccination came up very frequently during the conversations about canine leptospirosis. Participants perceived the issues regarding leptospirosis vaccines as big obstacle for the prevention of this disease. For instance, participants expressed a lot of doubts regarding the length of the immunity provided by the leptospirosis vaccines:

"I would love to know how long lepto immunity lasts in the system, the same way you can do a titer test for dhp".

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

Because of this, veterinarians are unsure of how frequently they should vaccinate and how they should convey to their clients the importance of administering this vaccine to their dogs, despite the uncertainty surrounding the immunity status of the animal against leptospirosis.

Overall, the leptospirosis vaccine seems to have the biggest controversies associated to it, out of all the infectious diseases included in this study. According to participants, the vaccine hesitancy is the highest amongst veterinary professionals and dog owners in the case of canine leptospirosis. Some of the interviewees argued that this is precisely because of the difficulties knowing how efficient and lasting the immunity they generate is:

"I'd like just to check the antibodies, and I know that it is a bit different because it's a bacteria, 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, because my clients are very antivax".

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

Another component of the leptospirosis vaccine controversy is linked to the L4 vaccine, which was newly introduced in the UK in 2014, with the aim to provide protection against four leptospirosis serovars, versus the two serovars covered by the pre-existing L2 vaccine (*Nobivac® Lepto 2*, 2018). The controversy stems from the potential side effects that the L4 can have, which are perceived as an unnecessary risk by the owners. This idea seems to be promoted by dog breeders, who offer vaccination advice to prospective owners:

"Very frequently actually I have new pet owners that tell us "Oh our breeder really advices against L4, he really said it was bad and can cause neurologic symptoms blah blah" so they're really resistant against L4 and want to use L2".

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

"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.

However, despite the controversies linked to the leptospirosis vaccine, interviewed practitioners believed vaccination to be effective. They stated that the cases of leptospirosis that they observed throughout their careers had either been unvaccinated dogs, or dogs that had been vaccinated with L2:

"Three or four years ago, we would see one or two leptospirosis cases a month […] and I don't know if it coincided with introduction of L4, but most of the leptospirosis we see now appears to be in unvaccinated dogs".

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

The two veterinarians that had been involved in outbreaks of leptospirosis in their practice recalled how the observed clinical signs were not indicative of the classic leptospirosis presentation, and believed this could be due to the introduction of a leptospirosis serovar in the country, not covered by the L2 vaccine:

"The investigations that we did at the time led us to believe that a portion of those dogs were having serovars that we haven't previously been concerned about in the UK, or that we haven't been vaccinated actively for".

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

4.4.5.3. Zoonotic risk

One of the main criteria why canine leptospirosis was included as a surveillance priority in this thesis (See Chapter Two) was the risk that this disease poses for public health, given its zoonotic potential. Interviewed participants perceived the zoonotic risk differently and, whilst they did acknowledge it as a possibility, they generally did not consider it as a big threat, at least initially, before being probed:

"I think there was a small amount of concern, but because people don't really appreciate that there is a significant zoonotic risk. And actually, I don't think we had a single person get affected with lepto during that outbreak.".

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

Only one veterinarian recalled 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.

4.4.5.4. Clinically relevant threshold

Most of the participants had either never seen a case of leptospirosis or had seen just a handful of them that were never diagnostically confirmed (n=5), but two had been involved in an outbreak of canine leptospirosis in their career (Table 4.3).

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 4.3 and Figure 4.3). Moreover, some participants enquired about the surveillance 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 4.3 and Figure 4.3). The only participant that did not agree with this approach was one of the two veterinarians that had been involved in a past leptospirosis outbreak. Their rationale was that, given the high levels of distress among employees and clients and the large amount of used resources during the outbreak, they would only want to be notified and mobilise the practice's staff if the predictive certainty of the alert was very high:

"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 that we didn't 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've done all of that and actually, it was just a false alarm".

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

Table 4.3. Summary of participant's preferred levels for the notification and outbreak response thresholds, and predictive certainty values for canine leptospirosis. The table includes participant's reported baseline of observed cases in their practices.

Canine leptospirosis				
Participant	**Baseline of cases in their practice**	**Notification threshold**	**Outbreak response threshold**	**Predictive certainty values**
1	0 / month Seen 3 times throughout 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	Lowest end of the possible range
7	0 cases/month Seen 2 cases (never confirmed)	>0 case/month	N/A	Lowest end of the possible range

Table 4.4 contains a breakdown of the clinically relevant thresholds for canine leptospirosis per type of participant. Those participants with less than five years of experience in practice (n=2) both chose the lowest possible values of predictive certainty of outbreak alerts. No differences were observed between participant types regarding the excess case incidence of the notification and outbreak response thresholds for this disease.

Table 4.4. Clinically relevant thresholds and predictive certainty values for canine leptospirosis, broken down according to participant characteristics.

Leptospirosis	Larger veterinary practice			Smaller veterinary practice		
Higher experience	>10 years of experience >10 veterinarians			>10 years of experience <5 veterinarians		
	Notification	Outbreak response	Predictive certainty	Notification	Outbreak response	Predictive certainty
	2/month 2/month 4/month	4/month 4/month 4/month	90% 90% 95-99%	1/month 1/month	NA 3/month	90% 90%
Lower experience	<5 years of experience >10 veterinarians			<5 years of experience <5 veterinarians		
	Notification	Outbreak response	Predictive certainty	Notification	Outbreak response	Predictive certainty
	1/month	N/A	Lowest possible end	2/month	4/month	Lowest possible end

4.4.6. Canine parvovirus

Parvovirus seemed to be the evaluated pathogen that was seen more often in clinical practice in the UK:

"We see tons of parvo, I mean, it's not something we see every week, but we do see parvovirus frequently, certainly more than leptospirosis, for sure".

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

4.4.6.1. Severity

Participants shared similar opinions about the severity of the parvovirus cases they had seen. Parvovirosis is perceived as a very severe disease, that appears as a per acute infection and is very intensive to treat. They also perceived this virus as more transmissible than canine leptospirosis among the dog population. For these reasons, 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 doesn't affect people doesn't 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.*

"My main concern is always animal welfare"

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

4.4.6.2. Transmissibility

A new topic that was introduced during the discussions about parvovirus was the possibility of infectious diseases being transmitted within the practice, i.e., by admitting an infected patient and allowing the pathogen to spread to other dogs. This was a big source of concern for participants, as they were afraid that it could negatively impact their practice:

"It would be a bit catastrophic for us to have a parvo outbreak within the practice where we were infecting otherwise healthy dogs when they come in the building with parvovirus".

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

Because of this risk of spread within the practice, participants spent a significant amount of interview time talking about the biosecurity measures they would put into place if an outbreak occurred. Notably, parvovirus was the only pathogen for which participating veterinarians 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're taking them and putting them straight in isolation or what we're doing with them".

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

4.4.6.3. Risk factors

All the interviewed veterinarians mentioned risk factors that they believed were associated with parvovirus. Most of them mentioned how it usually affects puppies and unvaccinated dogs, and others also mentioned other factors that they considered relevant, such as the socioeconomic background of the owners. This sparked some strong opinions during the interviews; 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 didn't 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:

"I think that would be a, a dangerous demographic to, to focus on these days. There is a wide range of beliefs in vaccination in the UK, in all walks of life. So, I don't think people should make an assumption based on what they think people are".

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

4.4.6.4. Clinically relevant thresholds

Study participants preferred higher notification and outbreak response thresholds for canine parvovirus, compared to canine leptospirosis (Table 4.5 and Figure 4.3).

The predictive certainty values chosen for parvovirus were the highest among all the specific pathogens included in this study for some participants (Table 4.5). They argued that, given the higher prevalence and ease of diagnosis of this disease, a lower predictive certainty would result in a high number of false alerts:

"Parvovirosis nowadays, it's so easy to be certain, you do a snap test, takes you 5 minutes to know, they're 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.

Table 4.5. Summary of participant's preferred levels for the notification and outbreak response thresholds, and predictive certainty values for canine parvovirus. The table includes participant's reported baseline of observed cases in their practices.

Canine parvovirosis				
Participant	**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 year	2 cases/month	3 cases/month	90%

Participant	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
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%

Table 4.6 contains a breakdown of the preferred clinically relevant threshold values for canine parvovirus per participant type. Those participants with less than five years of experience in practice chose the highest values of predictive certainty of outbreak alerts for canine parvovirus. No differences were observed between participant types regarding the excess case incidence of the notification and outbreak response thresholds for this disease.

Table 4.6. Clinically relevant thresholds and predictive certainty values for canine parvovirus, broken down according to participant characteristics.

<table>
<tr><th>Parvovirus</th><th colspan="3">Larger veterinary practice</th><th colspan="3">Smaller veterinary practice</th></tr>
<tr><td rowspan="3">Higher experience</td><td colspan="3">>10 years of experience
>10 veterinarians</td><td colspan="3">>10 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>2/month
2/month
4/month</td><td>4/month
12/month
N/A</td><td>95%
90%
90%</td><td>4/month
2/month</td><td>N/A
3/month</td><td>90%
90%</td></tr>
<tr><td rowspan="3">Lower experience</td><td colspan="3"><5 years of experience
>10 veterinarians</td><td colspan="3"><5 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>2/month</td><td>N/A</td><td>99%</td><td>2/month</td><td>4/month</td><td>99%</td></tr>
</table>

4.4.7. Canine leishmaniosis

4.4.7.1. Knowledge about the disease

When asked about their experience with canine leishmaniasis, most participants mentioned its vector (the sandfly) and were able to recall its transmission routes early in the conversation. However, some of them did not remember these details and needed to be reminded in order to continue the discussion. Further, some misconceptions about the transmission of leishmaniasis and its zoonotic potential were identified during the interviews:

“Well, I'd completely forgotten that it was zoonotic, so that's a good reminder”.

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

“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.*

4.4.7.2. Risk of entry in the UK

Some participants were greatly concerned about the possibility of leishmania entering the UK and infecting the local canine population. They believed this to be only a matter of time, and that factors such as climate change and globalisation will inevitably lead to the emergence of the disease in the country:

"I'm very concerned about it becoming endemic, to be honest [...] because global warming is going to get worse and temperatures are going to rise, and we will inevitably at some stage probably have sandfly vectors here."

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

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, such as leishmania:

"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 don't have. What we're doing really is creating a reservoir of a zoonotic disease that we didn't previously have".

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

Conversely, other participants did not share this concern and argued that leishmania does not pose a risk for the canine population or for public health in the UK. Since the vector is not present in the country, they did not believe that an outbreak could take place, and even challenged the decision to include leishmania in the surveillance and control protocols developed by SAVSNET-Agile:

"How do I respond to an outbreak of canine leishmaniasis? I don't believe canine Leishmania exists as an outbreak disease".

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

4.4.7.3. Clinically relevant thresholds

Most participants had seen chronic cases of leishmaniasis in their practice, although only two of them had ever diagnosed a case in the UK; participant no.3, who worked in a referral centre, and participant no. 5 (see Table 4.7). The notification threshold for leishmaniosis was over zero cases for all the participants (Figure 4.3), although some of them specified that they would only want to receive a notification if the cases were autochthonous (participants 3, 6 and 7), or if the disease vector became endemic in the country (participant 4) (Table 4.7). Participants did not provide an outbreak response threshold for this exotic disease, as they considered the notification threshold enough to change their in-practice behaviour.

Five participants (5/7) preferred to set the predictive certainty values for leishmania to relatively low levels, whereas the remaining two took the opposite approach and would only want a notification if the risk of receiving a false alarm was minimised (Table 4.7 and Figure 4.3).

Table 4. 7. Summary of participant's preferred levels for the notification and outbreak response thresholds, and predictive certainty values for canine leishmaniosis. The table includes participant's reported baseline of observed cases in their practices.

Canine leishmaniosis				
Participant	**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	Lowest end of the possible range

Participant	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
3	1-2/year referred	2 cases/year (if autochthonous) 4 cases/year (if not autochthonous)	N/A	95% travelled 90% untravelled
4	Seen cases but none personally diagnosed	No notification unless vector is present in the UK	N/A	No notification unless 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	Lowest end of the possible range

Table 4.8 contains a breakdown of the preferred clinically relevant threshold values for canine leishmaniosis per participant type.

Table 4. 8. Clinically relevant thresholds and predictive certainty values for canine leishmaniosis, broken down according to participant characteristics.

Leishmania	Larger veterinary practice			Smaller veterinary practice		
Higher experience	>10 years of experience >10 veterinarians			>10 years of experience <5 veterinarians		
	Notification	Outbreak response	Predictive certainty	Notification	Outbreak response	Predictive certainty
	2 or 4/year* N/A 1/year	N/A N/A N/A	90-95%* N/A 90%	1/year 1/year	N/A N/A	90% Lowest possible end
Lower experience	<5 years of experience >10 veterinarians			<5 years of experience <5 veterinarians		
	Notification	Outbreak response	Predictive certainty	Notification	Outbreak response	Predictive certainty
	1/year	N/A	90%	1/year	N/A	99%

4.4.8. Canine babesiosis

4.4.8.1. Knowledge about the disease

According to participant's experience, babesiosis was even rarer than leishmaniosis, as none of them had ever seen a case of it in first opinion practice, only in referral centres (participant 3). Two of the participants were even surprised to hear that babesiosis could affect companion animals, 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.

Overall, participants were doubtful about the disease's transmission and clinical presentation, and misconceptions were identified about its zoonotic potential, as some participants believed that it could be transmitted from dogs to humans.

When asked about the knowledge of canine babesiosis among the veterinary profession in the UK, participants did not believe it sufficient to adequately prevent the disease.

"Interviewer: would you say that the profession is aware of canine babesiosis and that vets would know what to do, or where to look for information on how to handle cases? // Interviewee: No, no, you might in large animal medicine. Because there's much more, we were taught most of our stuff about babesia as being related to cattle. Canine babesiosis was "oh, it can happen". Other than necessarily concentrating on it as the main disease".

—Participant 1: 32 years of experience, practice of 4 veterinarians.

4.4.8.2. Risk of endemisation

Those participants who knew that canine babesiosis can happen in dogs were aware that it is transmitted by ticks, and that the tick species that can carry canine babesiosis are present in the UK. For this reason, they were very concerned about the possibility of endemisation of babesia in the UK, and believed the risk to be much higher, compared to leishmania:

"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've 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.

4.4.8.3. Clinically relevant thresholds

Most participants considered a single case of canine babesiosis enough to receive a notification and chose to set the predictive certainty value at its lowest possible level (Table 4.9 and Figure

4.3). Participants did not provide an outbreak response threshold for this exotic disease, as they considered the notification threshold enough to trigger an outbreak response.

Table 4.9. Summary of participant's preferred levels for the notification and outbreak response thresholds, and predictive certainty values for canine babesiosis. The table includes participant's reported baseline of observed cases in their practices.

Canine babesiosis				
Participant	**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	Lowest end of the possible range
3	3 cases seen	2 cases/year (if autochthonous) 4 cases/year (if not autochthonous)	N/A	90% travelled 80% untravelled
4	Seen cases but none personally diagnosed	1 case/year	N/A	99%
5	0 seen	1 case/year	N/A	Lowest end of the possible range
6	0 seen	1 case/year	N/A	90%
7	0 seen	1 case/year	N/A	Lowest end of the possible range

Table 4.10 contains a breakdown of the preferred clinically relevant threshold values for canine babesiosis per participant type.

Table 4.10. Clinically relevant thresholds and predictive certainty values for canine babesiosis, broken down according to participant characteristics.

<table>
<tr><th>Babesia</th><th colspan="3">Larger veterinary practice</th><th colspan="3">Smaller veterinary practice</th></tr>
<tr><td rowspan="3">Higher experience</td><td colspan="3">>10 years of experience
>10 veterinarians</td><td colspan="3">>10 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>2 or 4/year*
1/year
1/year</td><td>N/A
N/A
N/A</td><td>80%-90%*
99%
Lowest possible end</td><td>1/year
1/year</td><td>N/A
N/A</td><td>90%
Lowest possible end</td></tr>
<tr><td rowspan="3">Lower experience</td><td colspan="3"><5 years of experience
>10 veterinarians</td><td colspan="3"><5 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>1/year</td><td>N/A</td><td>Lowest possible end</td><td>1/year</td><td>N/A</td><td>90%</td></tr>
</table>

4.4.9. Respiratory and gastroenteric disease

4.4.9.1. Prevalence

The reported prevalence of canine syndromes was much higher than that of specific pathogens. As seen on Table 4.13, the baseline of respiratory cases ranged from 3% to 7% of total consultations in first-opinion centres, and up to 15% in a referral centre (participant no. 3). The reported prevalence of gastroenteric disease ranged from 10%-15% in first-opinion practice and up to 40%-50% in referral centres (Table 4.11).

4.4.9.2. Severity

There was an agreement among participants that respiratory cases are usually not very severe, especially compared to gastrointestinal disease cases. They also reported that some cases are actually mislabelled by the owners as respiratory disease, when in fact the pathology comes from a different body system, e.g., a cardiovascular problem:

> *"Most respiratory consultations that I do in the UK at least, are kennel cough or elderly animals with heart disease that people bring thinking that it's a primary respiratory condition or allergy and it ends up being a heart condition".*
>
> —*Participant 7: 4 years of experience, practice of 11 veterinarians.*

They 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.*

4.4.9.3. Clinically relevant thresholds

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 two to twelve times over the baseline (see Table 4.11, Table 4.12, and Figure 4.3).

The predictive certainty value was also generally higher for canine syndromes than for canine pathogens and was set to values of 95% to 99% for both respiratory and gastrointestinal disease by most participants (see Table 4.11, Table 4.12, and Figure 4.3).

Tables 13 and 14 contain a breakdown of the preferred clinically relevant threshold values for canine respiratory and gastrointestinal disease per participant type, respectively.

Table 4.11. Summary of participant's preferred levels for the notification and outbreak response thresholds, and predictive certainty values for canine respiratory disease. The table includes participant's reported baseline of observed cases in their practices.

Respiratory disease				
Participant	**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	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%

Participant	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
7	3-5% of total consultations 2 cases/week	Very high increase over the baseline	N/A	Closer to 99%

Table 4.12. Summary of participant's preferred levels for the notification and outbreak response thresholds, and predictive certainty values for canine gastrointestinal disease. The table includes participant's reported baseline of observed cases in their practices.

Gastrointestinal				
Participant	**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 hospitalised/ week	6/cases week or 3 hospitalised/ 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 respiratory syndrome	+20% case increase	N/A	Upper end of the possible range
5	Up to 50% of total consultations	3x baseline	5x baseline	99%

Participant	Baseline of cases in their practice	Notification threshold	Outbreak response threshold	Predictive certainty values
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%

Table 4.13. Clinically relevant thresholds and predictive certainty values for respiratory disease, broken down according to participant characteristics.

<table>
<tr><th>Respiratory</th><th colspan="3">Larger veterinary practice</th><th colspan="3">Smaller veterinary practice</th></tr>
<tr><td rowspan="3">Higher experience</td><td colspan="3">>10 years of experience
>10 veterinarians</td><td colspan="3">>10 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>1.6x
1.2x
3x</td><td>2x
N/A
5x</td><td>95%
Upper possible end
95%</td><td>2x
2x</td><td>4x
12x</td><td>99%
90%</td></tr>
<tr><td rowspan="3">Lower experience</td><td colspan="3"><5 years of experience
>10 veterinarians</td><td colspan="3"><5 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>3x</td><td>4x</td><td>99%</td><td colspan="2">Very high increase over baseline</td><td>99%</td></tr>
</table>

Table 4.14. Clinically relevant thresholds and predictive certainty values for gastroenteric disease, broken down according to participant characteristics.

<table>
<tr><th>Gastroenteric</th><th colspan="3">Larger veterinary practice</th><th colspan="3">Smaller veterinary practice</th></tr>
<tr><td rowspan="3">Higher experience</td><td colspan="3">>10 years of experience
>10 veterinarians</td><td colspan="3">>10 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>3x
1.2x
3x</td><td>4x
N/A
5x</td><td>95-99%
Upper possible end
99%</td><td>2x
N/A</td><td>5x
1.4x</td><td>99%
90%</td></tr>
<tr><td rowspan="3">Lower experience</td><td colspan="3"><5 years of experience
>10 veterinarians</td><td colspan="3"><5 years of experience
<5 veterinarians</td></tr>
<tr><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td><td>Notification</td><td>Outbreak response</td><td>Predictive certainty</td></tr>
<tr><td>2x</td><td>N/A</td><td>99%</td><td colspan="2">Very high increase over baseline</td><td>99%</td></tr>
</table>

4.5. Discussion

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 veterinarian's opinion 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, this study 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 of a single case per month to trigger a notification and to change their behaviour in practice, as participants perceived that exotic disease outbreaks are likely to be potentially impactful to their practices. Participant's approaches differed when exploring the predictive certainty of canine endemic diseases, as some wanted the highest possible values to avoid false outbreak notifications, while others preferred to keep this parameter at relative low values to avoid missing out on potential clinically relevant outbreaks or in case of false alerts to be reminded of the risks that canine infectious diseases can pose to their practices. In addition, findings from the interviews with veterinary practitioners allowed us to gain an understanding of how the behaviour of veterinary clinicians is impacted by outbreaks of canine disease.

To achieve the study's aims we needed to explore individual perspectives and experiences of small animal veterinary clinicians. Therefore, a qualitative methodology, consisting of structured and semi-structured interviews was followed (SAGE, 2020b). Interview transcripts were analysed using a hybrid approach to thematic analysis (SAGE, 2018) which is a novel methodology to explore veterinarians' experiences with canine disease outbreaks. The methodology developed in this chapter was applied to four canine diseases and two canine syndromes, that had been previously identified as the top surveillance priorities in the UK (Chapter Two). 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 study aims. 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.

4.5.1. Structure of the interviews with veterinary companion animals

Interviews had a twofold aim, by first exploring veterinarian's experiences with canine infectious diseases before discussing outbreak scenarios in which they would want to receive an outbreak notification and respond to a potential outbreak. This strategy was followed since the subject matter had not been previously explored in UK veterinary practices, and it was necessary to first collect background information about participant's knowledge and perspectives. In the literature, this exploration has been carried out through Knowledge, Attitudes, and Practices (KAP) surveys (Crist et al., 2022; LaFerla Jenni et al., 2019; Lopes et al., 2022). These surveys, however, are usually made up of closed questions, administered to participants via email or as printed letters, that they then complete in their own time, without interacting with the researcher. While this is a viable option to reach a large sample of participants, it would not be an adequate method to meet the aims of this chapter, where the intention was to conduct an in-depth exploration of individual experiences and perceptions. Instead, one-to-one semi-structured interviews were conducted, as this method allows for fluidity in the conversation, so that questions can be tailored to the participant's experience, whilst also providing a framework for the interview (Flick et al., 2004). This flexibility was especially important in an exploratory study like the present chapter, where not much is known or there is no available literature on the subject of interest (DeJonckheere & Vaughn, 2019), since the necessary pillars of knowledge have not been established and there is no benchmark to determine what is relevant and what is not.

Once participants had reflected upon the subject matter, the interview changed to a structured format, where the interviewee was probed about the range of values of excess case incidence and certainty that they would choose to be notified about potential canine outbreaks. Obtaining a specific numerical value, or set of numerical values, was not the aim of the present study. However, it was part of the research to investigate whether veterinarians would be able to understand the concept of clinically relevant reporting threshold and predictive certainty and think about such parameters of an outbreak alert in relation to the expected baseline of cases that they observed in their practices and the balance between sensitivity and specificity of the outbreak detection they deemed appropriate.

4.5.2. Approach to thematic analysis

Thematic analysis (TA) is described in the literature as one of the most commonly used methods to analyse qualitative data (Wiltshire & Ronkainen, 2021) and has been widely used in studies that explored people's experiences with infectious disease outbreaks (Massaquoi et al., 2021; O'Kane & Boswell, 2018; Park & Lee, 2016), as well as in studies that explore companion animal veterinarians' experiences in practice (Phillips et al., 2017; Roshier &

McBride, 2013; Sutherland et al., 2022; White, 2018). In this chapter, a hybrid approach to thematic analysis was used to analyse interview transcripts. This method was chosen since the combination of inductive and deductive generation of codes and themes that emerge from interview data is an effective methodology to meet the aims of the present study, i.e., to answer the pre-defined research questions of the study, while also discovering new ideas and meanings that are relevant to the study's research subject (Swain, 2018). Although there is a lack of existing literature investigating the use of hybrid thematic analysis in exploring veterinarians' experiences with canine disease outbreaks, this analytical method has been previously employed in the fields of livestock health and human health for various objectives. For instance, in a study by Rojo-Gimeno et al (Rojo-Gimeno et al., 2018), interviews with veterinarians were conducted to gain an understanding of the complexities within the swine health system in Belgium, as part of their methodology to develop an integrative framework to describe the system. This study uses a combination of data-driven codes and deductive codes, that were generated by reviewing a previous study that also developed a systematic integrative framework in the agrifood sector. By contrast, since no previous studies have developed a methodology to explore clinically relevant outbreak reporting thresholds for veterinary clinicians, this chapter's deductive codes were generated according to the aims of this chapter by the author of this thesis, by considering characteristics of SAVSNET's surveillance system, e.g., how alerts are defined by their excess case incidence and predictive certainty, and the canine health sector in the UK, i.e., clinical experience and in-practice behaviour of companion animal veterinarians in the UK. Another study by Cox et al (M. Cox et al., 2022) employed hybrid TA to analyse data collected from emergency care doctors, to understand which lessons can be learned from the COVID-19 pandemic response. Similar to the present study, deductive codes were generated based on the researchers' prior knowledge on the subject matter and the study's research questions. However, in this earlier study, transcripts were coded individually by ten researchers, divided into five pairs, and results were checked twice: first by exchanging individual results between members of each pair, and then by sharing each pair's results among the five pairs during a workshop session. This is due to the large volumes of data that were collected in this study, corresponding to multiple one-to-one interviews, as well as group interviews. In contrast, transcripts from our study were only coded by the author of this thesis and checked by this thesis' main supervisor (FS-V). Reaching a consensus among both researchers was possible through this approach, given the smaller sample size of the present study. In some studies that use codes generated deductively, the consensus among researchers that have coded the same transcribed text is evaluated through the calculation of inter-coder reliability measures such as Krippendorff's alpha or Cronbach's alpha (SAGE, 2020a). However, this is only possible for coding frameworks that rely on deductive codes, since data-driven codes will inevitably differ among individuals, as their interpretation of the data will vary. Given the hybrid approach followed in this chapter, and the manageable sample size, an iterative discussion among coders was the best approach to reach an agreement about the coding framework to analyse interview data.

4.5.3. Discussion of results

For infectious diseases, most participants elicited low levels of predictive certainty at given notification thresholds to prioritise sensitivity over 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 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, improve their epidemic preparedness, and include infectious causes in their differential diagnosis list. These findings were based on participants response 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 outbreak detection systems that generate a high proportion of false alerts may result in information fatigue among end-users (Link et al., 2022) and can lead them to a loss of confidence and trust in the system (Cairns et al., 2013). Only by testing this study's clinically relevant thresholds for notification of outbreaks in real-world applications, we will 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 can represent an epidemic threat to their practices. This is not surprising, since such diseases correspond to the top priority canine diseases for surveillance in the UK, according to their impact on canine and public health, as found in Chapter Two of this thesis and previously published study (Tamayo Cuartero et al., 2023). Outbreak response threshold values were generally set to bigger increases in case incidence than those of the notification thresholds. However, for certain diseases, notification threshold values provided by some participants often overlapped with the values chosen for outbreak response thresholds by other participants. The reasons for this 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 4-5 times over the baseline, while this range was of 2-12 times over the baseline for respiratory disease. Whilst the specific reasons for this are unknown, they may relate to a higher consensus for certain diseases among participants about their potential epidemic threat and impact on practice.

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 response 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 behaviour in practice to respond to a potential outbreak. All of these factors indicate that participants perceive exotic disease outbreaks as potentially highly impactful to their practices. This might be because, as observed during the interviews, exotic diseases are perceived as very severe threats, whose epidemiological characteristics and treatment options are not well known amongst veterinary clinicians. According to decision theory, when making decisions that involve high risk and high uncertainty, people are more likely to take on a conservative approach and overestimate the risk rather than underestimating it (Pollutants, 1994). However, as these diseases are not perceived as an immediate threat, participants also reported to hardly ever think about them or carry 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 (Spence et al., 2022). In this study, participants reportedly presented a "firefighting approach" to veterinary medicine, where most of the time and effort are 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 to be sporadic, unrelated events, that would not result in an outbreak, as the vectors of disease are not currently present in the UK.

When comparing the clinically relevant outbreak scenarios for notification proposed by veterinarians according to their years of experience in practice, senior veterinarians took a more conservative approach with canine parvovirus, compared to recently graduated veterinarians, by choosing lower levels of alert certainty. The reasons for this are not clear, but it may be that more experienced veterinarians acknowledged the severity and transmissibility of parvovirus, as they had seen a wider range of clinical presentations of the disease. Interestingly, participant's perception of risk was similar across different years of experience when it came to exotic pathogens, probably since it was not likely for any of them to have encountered these diseases throughout their careers. Nevertheless, conclusions from the clinically relevant thresholds proposed by type of participating veterinarians should be interpreted with caution because of the low sample in each population descriptor. To understand the impact that this descriptor has in veterinary clinicians' preferences, further research would need to be undertaken, for instance, by interviewing a larger sample of participants in each descriptor.

4.5.4. Validity of the study

Currently, there is no agreed upon way to demonstrate the validity in qualitative research (H. Noble & Smith, 2015). However, guidelines have been described in the literature to ensure the rigour of a qualitative study. In this chapter, the author strived to follow the principles of goodness and trustworthiness of qualitative research, namely, credibility, dependability, and confirmability (Carminati, 2018; Mortari, 2015; Nowell et al., 2017). To ensure the credibility of the findings, i.e., the congruence between respondent's opinion and researchers' interpretation, the author continuously referred back to the interview transcripts and contrasted the generated codes and themes with the original responses provided by participants. This could have been further enhanced by using other techniques, such as member checking (Birt et al., 2016), where participants are consulted so that they can evaluate whether the codes emerging from the data resonate with their experiences. The confirmability of the study's results, or the extent to which these can be confirmed by other researchers as derived from the data, was promoted by comparing the developed codes and themes to those developed to this thesis' main supervisor (FS-V). Lastly, to ensure the consistency of study's methodology, or dependability, this chapter provided a thorough description of all the aspects of its design, data collection and analysis in a transparent manner, including the codebook used to analyse transcript data.

4.5.5. Strengths of the study and contributions to research

This study proposes an innovative methodology that uses veterinary practitioners' opinion to inform the selection of a notification threshold value in genuine applications of stochastic canine outbreak detection models, i.e., that predict possible outcomes by allowing for random variation in model parameters over time. An advantage of this chapter's approach is that it allows 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, outbreak notification thresholds determined by existing statistical methods (GOV.UK, 2023c; Rakocevic et al., 2019) often alert end-users about genuine statistical signals that are of no practical importance for health professionals. Another strength of the methodology developed in this study is that can be applied to any pathogen or disease of interest so 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 UK veterinary practitioners of potential outbreaks. This 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.

4.5.6. Limitations of the study

Since this is a doctoral study, data were analysed, and themes were developed by one person (the author of this thesis). The process was shared and contrasted by a supervisor, which contributed to the consistency of the methodology. However, future work could include several researchers involved in the coding and theme development process, to strengthen the confirmability of the study.

Another limitation was the number of participants in the study, 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 (The Sunday Times, 2021). Furthermore, the number of pet-owning homes in the UK has significantly increased over the last few years (PFMA, 2020), while the number of registered veterinarians in the UK has not increased at the same rate, partly because of Brexit (BVA, 2022). 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 that 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 UK.

Population descriptors used in this chapter, i.e., practice size and years of experience, were chosen because they were considered the most likely to influence veterinarian's perspectives about the prevention and control of canine outbreaks. Other relevant characteristic that could have been included in this study was the location of veterinary practices, since climatic and geographical factors (e.g., rural vs urban environment) are known to impact the distribution of infectious diseases (Polgreen & Polgreen, 2018). This would have also allowed to consider the influence of socioeconomic factors in the decision-making of veterinarians (e.g., by using indicators such as the index of deprivation) (GOV.UK, 2019b). However, given the difficulties that arose in the recruitment process, it was decided to only include the descriptors that the author of this thesis understood as the most relevant in the context of canine epidemics.

Lastly, personal experiences are subjective, and it is possible that participants incurred in memory bias when recalling past events. The author strived to compensate for these issues by immersing the participant 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.

4.6. Conclusions and future work

This study 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 in clinical practices. The methodology has been applied to six canine diseases and syndromes that currently represent the top-surveillance priorities among our stakeholders, as described in Chapter Two of this thesis. Clinically relevant thresholds included a notification threshold and an outbreak response threshold, that represented increases in case incidence that would warrant an outbreak alert or to activate an outbreak response, respectively, as well as the corresponding predictive values of these thresholds. 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. Future studies could include a larger sample of participants, to deepen the understanding of how veterinary clinician's preferences vary depending on their experience and background. 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 UK.

Chapter Five: Designing, evaluating, and exploring strategies for implementation of a framework of response to canine disease outbreaks in the UK

5.1. Abstract

Coordinated preparedness strategies are essential to effectively prevent and respond to epidemic threats. However, these strategies are currently lacking for canine populations, thus leaving them vulnerable to infectious disease outbreaks. In this study, an outbreak response framework is designed for canine diseases in the UK and evaluated in its application during an outbreak of prolific vomiting in the country through a formative process evaluation. The fidelity, dose, and reach of the interventions carried out in response to this real-life outbreak were assessed, and the lessons learned were documented. Some interventions adhered to the designed framework with high fidelity, such as the data analysis and external communications, and some areas of improvement were identified, such as the response activation and the documentation. In addition, the needs of the UK canine health sector were investigated through interviews with nine veterinary clinicians to improve the design of a future framework for canine disease outbreaks, and inform its implementation. The main identified needs for such a system to address were the lack of knowledge about the prevention of canine epidemics in the veterinary companion animal sector, the lack of availability of surveillance data, and the lack of communication channels across the actors involved in the prevention and control of canine diseases. Lastly, strategies for the implementation of a response framework at national level were identified through a strengths, weaknesses, opportunities, and threats (SWOT) analysis based on the results from the process evaluation and the veterinary interviews. These strategies included harnessing SAVSNET's expertise to satisfy the demand for specific training in canine infectious disease prevention and outbreak control practices among veterinary practitioners and strengthening the collaboration with other initiatives and relevant government groups, such as APHA's companion animal species expert group. Findings from this study will be used by SAVSNET to improve their preparedness and response activities. These findings can be used by other teams or institutions to develop their own response frameworks. In the future, these findings could also inform the development of policies to protect canine health at a UK-level.

5.2. Introduction

The previous chapters of this thesis have been dedicated to identifying the canine diseases of most relevance for surveillance in the UK and developing methods to improve detection and reporting of canine disease outbreaks. Another relevant component of epidemiological surveillance is the response to a health-related threat once an outbreak has been detected and confirmed. The present chapter is dedicated to this component, by designing and evaluating a framework of response to canine disease outbreaks, as well as investigating strategies to facilitate its implementation at a national level in the UK.

Coordinated preparedness strategies are essential to effectively prevent and respond to epidemic threats (Oppenheim et al., 2019). However, as mentioned throughout this thesis, such preparedness strategies have not been developed or implemented for companion animal diseases, neither at national nor at international levels. As a result, canine populations are vulnerable to potential epidemic threats that arise from endemic and exotic pathogens. The SAVSNET-Agile project was established in response to this pressing veterinary and public health need. Within this project, the present thesis' aim is to lay the foundation for a framework of disease surveillance and response to canine outbreaks in the UK context.

When planning an outbreak response framework, it is necessary to concurrently plan a strategy to test the adequacy of such framework before it is implemented (ECDC, 2020). This should be an iterative process, that is carried out throughout the planning of outbreak preparedness strategies (ECDC, 2017). The evaluation process should also be conducted in tandem with stakeholders that are involved in or are affected by outbreak response activities (*Framework for Program Evaluation - CDC*, 2022).

This chapter is dedicated to the three key elements of outbreak preparedness planning, namely the design, evaluation, and implementation of a canine outbreak response framework for the United Kingdom.

5.2.1. Aims

The aims of this chapter are:

a) To design a framework of response for canine infectious disease outbreaks and evaluate its application during a real-life outbreak of canine disease.
b) To investigate the needs and expectations of prospective users, i.e., veterinary practitioners, to inform the design of a future response framework for canine disease outbreaks and its implementation at a national level.
c) To identify strategies to facilitate the nation-wide implementation of the designed framework of response in the context of the UK.

5.3. Materials and methods

This section details the methods employed to achieve each of the aims of this chapter (Figure 5.1). First, a formative process evaluation (see section 5.3.1) was followed to design an outbreak response framework and evaluate its application to an outbreak intervention carried out by SAVSNET-Agile during the course of the present PhD project.

Second, individual qualitative interviews were conducted (see section 5.3.2) to elicit veterinary practitioner's opinions about the current gaps in the companion animal sector to effectively prevent and manage canine infectious diseases, as well as their suggestions on what to include in a prospective nation-wide outbreak response framework to be implemented in the UK.

Lastly, a strengths, weaknesses, opportunities, and threats (SWOT) (section 5.3.3) analysis was used to identify strategies to inform the future implementation of a nation-wide framework for response to canine disease outbreaks.

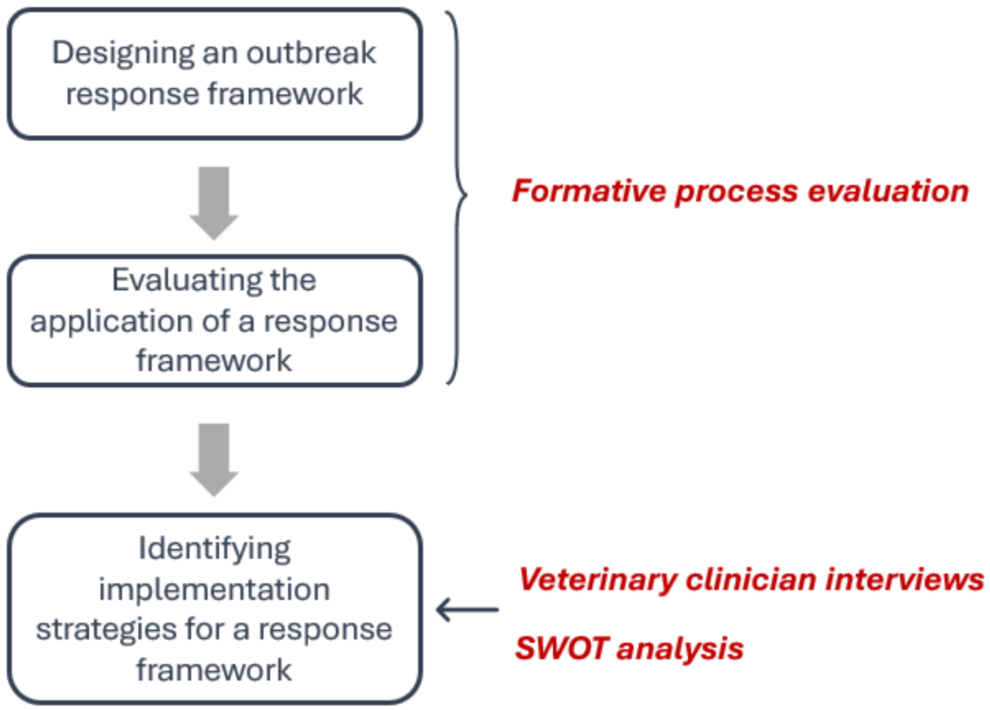

Figure 5.1. Summary of the aims of this chapter and, in red, the methods followed to address these key aims.

5.3.1. Formative process evaluation for the design and evaluation of a canine outbreak response framework

In this chapter's section, a canine outbreak response framework is designed and evaluated in its application to a real-life canine disease outbreak. For this purpose, a formative process evaluation is used. This type of evaluation focuses on ensuring the feasibility of a program during its development stages and before it is implemented (CDC, 2020; Saunders RP, 2005).

5.3.1.1. Steps of the response framework design and evaluation process

1. *Description of the response framework*: a response framework for canine infectious disease outbreaks was thoroughly described.

2. *Definition of the optimal/acceptable delivery of the response framework*: for each of the steps identified through the description of the response framework, the performance standards were established, by defining the ideal delivery of the response framework if an outbreak were to occur. These performance ideals were based on external frameworks of outbreak response, such as the WHO's communicable disease response strategy (WHO, 2006a).
3. *Definition of indicators:* the following indicators were used to assess the adequacy of the response framework for canine infectious diseases (Wilson et al., 2009):
    a. Fidelity: refers to the quality of the implementation, i.e., the delivery of the program compared to the optimal standard (defined on step 2 of this methodology).
    b. Dose: refers to the quantity of the program implementation, i.e., it is used to assess the completeness of the intervention, based on the pre-defined optimal standards (defined on step 2 of this methodology).
    c. Reach: refers to the extent to which the target audience came into contact with the intervention.
4. *Application of the response framework to a case study:* the response framework for canine disease outbreaks described in step 1 was applied during an outbreak of prolific vomiting that took place in the winter of 2020 across the UK. A complete description of the progression of the outbreak and the control intervention carried out by SAVSNET-Agile was published in a scientific article prior to the submission of the present thesis (A. D. Radford et al., 2021).
5. *Evaluation of response framework delivery during the case study:* the indicators developed on step 3 of this methodology were employed to assess the outbreak response intervention. To achieve this, two sources of information were utilised:
    a. The author of this thesis carried out a monitoring process, whereby information was logged on a daily basis about the activities carried out by the response team, their impact, and the progression of the outbreak, and how they were received by external stakeholders.
    b. Furthermore, a framework containing the steps of the response methodology was distributed among members of the response team, where they were asked to log events and describe their personal experiences during the epidemic, including the challenges and difficulties that they encountered. The response

team included epidemiologists, veterinary clinicians, microbiologists, and data scientists, so a wide variety of inputs and perceptions, resembling a real-world epidemic response team, were captured.

The evaluation consisted in assessing the activities conducted during the response intervention, by judging how closely the response steps resembled the pre-defined optimal standards. To represent the resemblance, the author of this thesis used a qualitative scale of low-medium-high values. To evaluate the dose, the author looked at the number of components for each of the response steps, and assigned a "high" value if all the components were delivered, a "medium" if not all but more than half of the components were delivered, and a "low" if less than half of the components were delivered. To assess the reach of the response steps, the author determined whether these had reached the intended audience in full ("high"), only partially ("medium"), or not at all ("low"). The fidelity criterion is subjective, as it indicates the quality of the delivered activities. High/medium/low values were assigned by the author of this thesis through a qualitative assessment. The reasoning behind the values assigned for the fidelity criteria on each of the response steps are provided in detail in section 5.4.1.3.

5.3.2. Interviews with veterinary clinicians

The process of participant recruitment in this chapter has been described in Chapter Four. Recruited veterinarians took part in an interview session that was held online via Microsoft Teams. Interview questions were semi-structured, although participants were given the freedom to discuss the ideas that they considered relevant in as much or little detail as they liked. The interview aimed to explore participant's opinion on two distinct topics:

a) Barriers for the prevention and control of canine infections: current gaps in the companion animal sector that compromise practicing veterinarian's ability to effectively prevent and manage canine disease outbreaks.
b) Resources to deal with canine outbreaks: characteristics/features that participants would like a prospective canine outbreak response system to include in order to better handle canine infectious diseases and epidemics.

Interviews were transcribed and a thematic analysis was carried out using NVIVO 12 qualitative software (*NVIVO12*, 2023), following the methods described in Chapter Four.

5.3.3. SWOT analysis to identify strategies for the implementation of a canine outbreak response framework

In this section, a strengths, weaknesses, opportunities, and threats (SWOT) analysis technique was employed to identify optimal strategies to help plan the future implementation of a response framework for canine outbreaks in the UK. Through this analysis, the current strengths and weaknesses of the institution involved in the outbreak response described in this chapter (SAVSNET) were identified, as well as the opportunities and threats present in the wider environment (the UK's canine health and public health sectors) that might positively or negatively impact the response activities. To carry out the SWOT analysis, data from the previous sections of this chapter were used; a) findings from the formative process evaluation and b) findings from the interviews with veterinary companion animals.

The SWOT analysis process consisted of four components. These components were divided into internal and externally related elements. The internally related elements are the "strengths" and the "weaknesses" of a system of response (Jasiulewicz-Kaczmarek, 2016). By contrast, the externally related elements are the "opportunities" and "threats" derived from the relationship of this system and the wider environment. Strengths were related to the inherent characteristics of the system that can be harnessed to achieve its objectives. Weaknesses referred to the limitations and/or faults of the system that may hinder the achievement of the project's intended goals. Opportunities consisted of the characteristics in the environment of the response system that are favourable for the consecution of its objectives. Lastly, threats referred to characteristics in the environment of the system that can potentially be detrimental and compromise its success. Through a SWOT analysis, the dynamics between these external and internal factors were evaluated to identify strategies that are optimal for the attainment of the intended objective, i.e., to implement a response system for canine outbreaks in the UK (Agarwal et al., 2012).

5.3.3.1. Steps of the SWOT analysis

1. *Strengths analysis:* identification of the current advantages and assets available within SAVSNET (that could be applicable to other similar nation-wide surveillance schemes) to respond to canine disease outbreaks.
2. *Weaknesses analysis:* identification of the vulnerabilities that exist within SAVSNET (and potentially in also in other similar nation-wide surveillance schemes) that compromise their capacity to respond to canine disease outbreaks.
3. *Opportunities analysis:* identification of external favourable conditions in the UK canine health sector, or in the wider public health sector, that can potentially be accessed to improve the responsible organisation's ability to manage canine outbreaks.
4. *Threats analysis:* identification of adverse external conditions that can negatively impact the responsible organisation's ability to manage canine outbreaks.
5. *Build SWOT matrix and identify priorities for intervention:* once the internal and external factors of the SWOT analysis were identified, they were entered in a 2x2 matrix, with the aim of visualising priorities to include in the intervention strategy.
6. *Generation of a strategy for intervention:* the identified factors (steps 1-5) were then used to formulate the response organisation's strategic planning, by combining the following elements (Weihrich, 1982):
    a. Strengths-opportunities: to optimise the use of the response organisation's resources in light of the available external opportunities for action (also referred to as *maxi-maxi* strategy).
    b. Strengths-threats: to minimise the potential negative impacts of external factors by utilising the response organisation's assets (or *maxi-mini* strategy).
    c. Weaknesses-opportunities: to plan effective measures to utilise external favourable circumstances to improve/compensate for the response organisation's internal shortcomings (or *mini-maxi* strategy).
    d. Weaknesses-threats: to evaluate the response organisation's gaps and develop a plan to prioritise improving on those that would result in a higher impact of the external threats (or *mini-mini* strategy).

5.4. Results

5.4.1. Formative process evaluation for the design and evaluation of a canine outbreak response framework

5.4.1.1. Description of the response framework

Figure 5.2 contains a summary of the response framework designed for the outbreak control interventions carried out by SAVSNET-Agile.

1. *Response activation:* the first step of the outbreak response framework consists in the decision to intervene and carry out an outbreak investigation. This decision is carried out by the response team of epidemiologists and other scientists working under the SAVSNET-Agile initiative.
2. *Case definition:* a working case definition is established for the disease under investigation. Case definitions include criteria to specify the affected population and clinical presentation of disease (CDC, 2021c).
3. *Data collection:* once the case definition has been established, epidemiologists involved in the response collect data from reported cases to investigate the outbreak. Three main sources of data are utilised to investigate canine outbreaks in the UK: veterinary practice data (in the form of electronic health records, associated to a particular main presenting complaint, or MPC); laboratory tests results (that provide data on the disease's causative agent); and clinical annotations made by veterinarians in practice during related consultations (exploited through text mining tools, see Chapter Three). Furthermore, epidemiological questionnaires are also developed and deployed to collect in-depth information about disease cases and controls.
4. *Data analysis:* collected data from the above-mentioned sources are integrated and analysed through descriptive and inferential statistics to monitor the progression of the outbreak and identify risk factors for the disease under investigation.
5. *Communications:* when the outbreak investigation starts, the response team develops and establishes a communication strategy, that has both internal and external components.

a. Internal communications: designed to keep the members of the response team updated on the progression of the outbreak and plan the response strategy accordingly.
b. External communications: which serve two main purposes: a) to disseminate information to those affected by the outbreak, either to recommend measures to prevent the spread of the outbreak or to request specific information, and b) to enable veterinary practitioners and dog owners (plus other stakeholders, when necessary) to communicate with the response team and report anomalies or ask for guidance to better respond to the ongoing outbreak.

6. *Recommendation of measures:* as the knowledge of the outbreak and the disease's risk factors increases, the response team develops tailored messages to inform those at risk/affected of the best practices to prevent the spread of the outbreak and/or to provide guidance on vaccination and disease treatment.
7. *Documentation and reporting:* as part of the intervention, the response team keeps records of the conducted activities, to draw lessons for future outbreak interventions. Lastly, once the end of the outbreak is officially declared, a final report is produced, that contains a summary of the overall response and its outcomes.

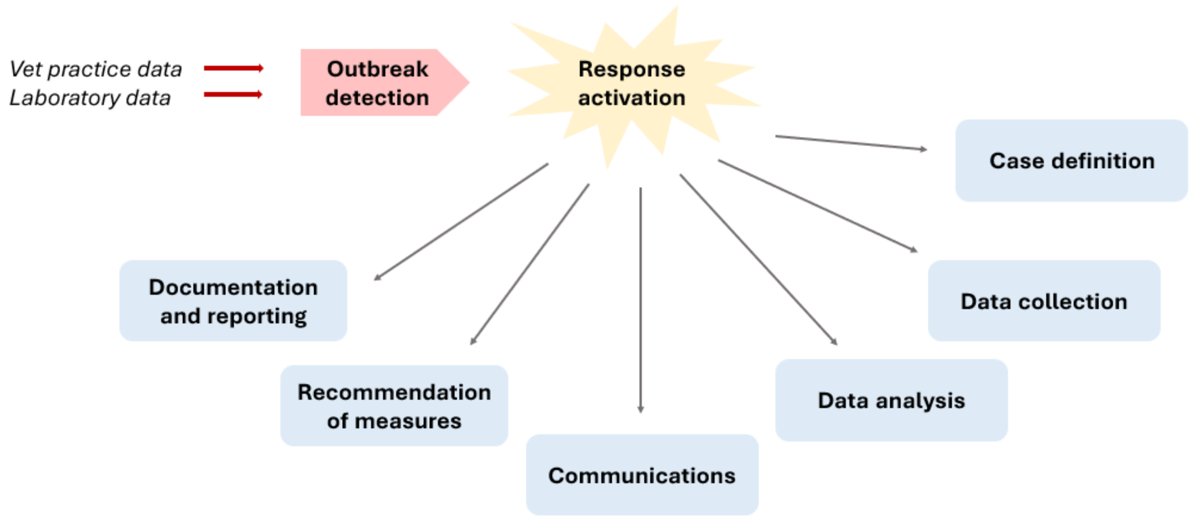

Figure 5.2. Diagram that represents the framework of response to canine outbreaks used by SAVSNET-Agile and evaluated in this chapter's section.

5.4.1.2. Definition of the optimal/acceptable delivery of the response framework

The following performance goals were established for each of the steps included in the framework of response developed for SAVSNET-Agile (Figure 5.2):

1. *Response activation:* must be rapid and coordinated, set up by gathering the response team and establishing a plan of action to manage the outbreak. This should include the definition of roles and responsibilities for the different members of the group, as well as an outline of the time dedicated to each of the activities included in the response.
2. *Case definition:* must be specific to the outbreak under investigation and allow the identification of cases while differentiating them from disease events that are linked to other causative agents. Case definitions must define outbreak cases by specifying the following characteristics: pathognomonic clinical signs of disease, duration of disease, if not country-wide, location of cases, and, if not widespread, characteristics of the canine population affected, e.g., certain breeds or age groups.
3. *Data collection:* must be conducted in a timely manner, ideally as soon as the outbreak is declared. A protocol for the collection of data must be defined to ensure that the case

information falls under the specifications of the outbreak's case definition. Different strategies for data collection must be planned according to the source of data.

4. *Data analysis:* different analysis techniques must be used to consider the different sources of data and draw relevant conclusions about the outbreak. The data analysis process should result in the identification of the causative agent behind the outbreak under investigation, as well as the identification of disease risk factors. Pertinent outputs obtained from the analysis process, such as tables, diagrams, and graphs, should be selected for distribution among team members and external stakeholders.
5. *Communications:*
    a. Internal communications: the response team should develop a communication strategy that facilitates the exchange of information within the team. This includes planning briefing meetings and their frequency at different stages of the outbreak and establishing an information-sharing platform to use within the team.
    b. External communications: a centralised data hub must be established, that serves the following functions: to post information about the progression of the outbreak and the response activities, to serve as an access point for the public to contact the response team with their enquiries, and to enable the access to the deployed epidemiological questionnaires. Further communications should be established by contacting relevant stakeholder institutions and, when pertinent, media outlets. If possible, a dedicated member of the response team should also engage with the public via social media sites, e.g., twitter or Facebook.
6. *Recommendation of measures:* using the channels of communications previously established, the response team should provide guidance for veterinarians, dog owners and the wider public during an outbreak. The recommended measures must be guided by scientific knowledge and updated as the data collection and analysis progresses.
7. *Documentation and reporting:* as the outbreak progresses, the response team must establish a system of documentation to log the activities that have been conducted and their impacts. Other information, such as the time dedicated to each activity, the manpower needed, and the difficulties faced during the intervention should also be documented. Once the outbreak has been controlled, a report that summarises the intervention must be produced, to make improvements to the response framework, and archived for future consultation.

5.4.1.3. Application of the response framework to a case study and evaluation of program delivery

Table 5.1 provides a summary of the levels of fidelity, dose, and reach of the different steps of the response carried out during the outbreak of canine prolific vomiting.

5.4.1.3.1. Response activation

Fidelity

a) Rapid

An unusual increase in the incidence of acute gastrointestinal disease in dogs was initially notified to the response team by a first opinion veterinarian on January 23rd, 2020. A week after the initial notification (January 31st), a Microsoft Teams channel was created to discuss the progression of the response. The first briefing meeting was held on February 3rd, eleven days after the initial notification of the potential outbreak. However, online reports via social media (The Liverpool Vets, Facebook, 2020) had been circulating weeks before this initial warning. Furthermore, an upward incidence trend was noticeable since December 2019, as presented in Figure 5.3. Considering the existing evidence, a delay of 1 to 1.5 months took place between the initial outbreak reports and the first response activities carried out by SAVSNET-Agile (Figure 5.4). Given this delay, the rapidity of the response activation was considered "medium" in the qualitative scale compared to an optimal standard. The "low" category was not chosen, given the timely organisation of a briefing meeting, despite the delay between the notification by a veterinary clinician and the earliest anomalies that could have been acknowledged by SAVSNET-Agile.

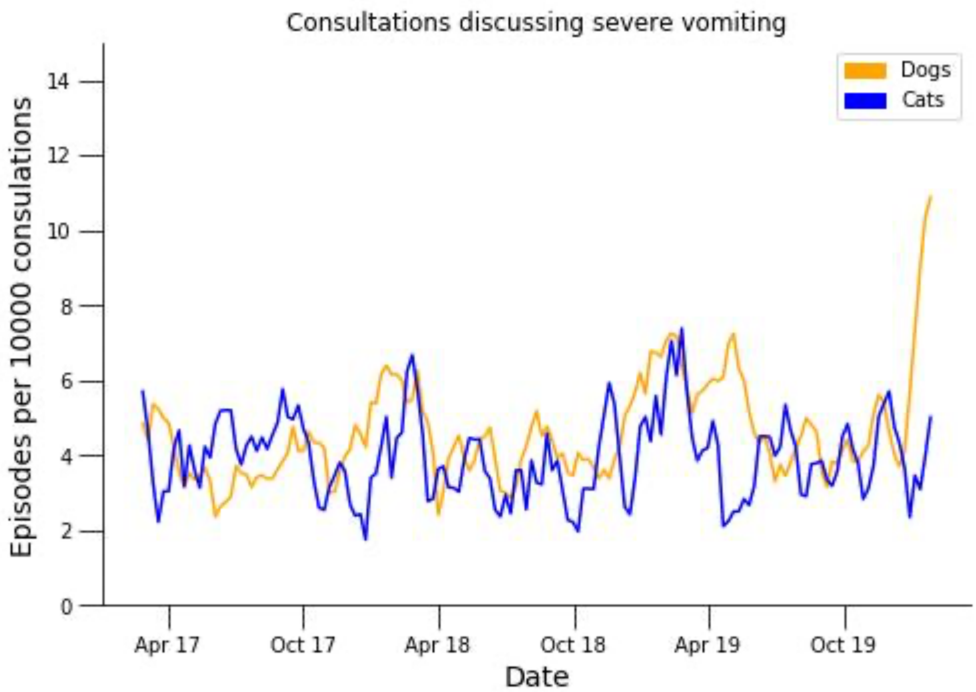

Figure 5.3. Graph displaying the number of canine and feline consultations where severe vomiting was discussed, per 1000 veterinary consults.

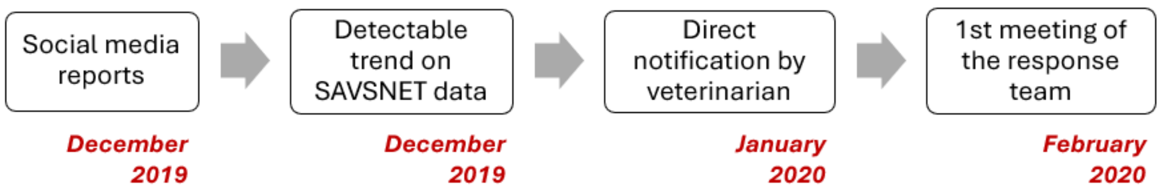

Figure 5.4. Diagram that represents the events leading up to the activation of the outbreak response carried out by SAVSNET-Agile in the beginning of 2020.

b) Coordinated, establishing plan of action, and defining roles and responsibilities.

In the first briefing held on February 3rd, it was agreed to host daily briefing meetings of up to 30 minutes for the duration of the outbreak. A structure for said meetings was also established, which included an update about the status of the outbreak investigation and the assignment of tasks to different members of the team. During this first briefing meeting (led by the author of this thesis), the response framework described on Figure 5.2 was built by the author of this thesis and agreed upon by the members of the team for use as a guide during the outbreak response.

Despite having a clear structure for the response intervention, the roles and responsibilities were vaguely defined, and jobs were assigned in a somewhat haphazard manner, according to who was available at the time. Furthermore, an outline of the time that would be dedicated to each of the activities included in the response intervention was not specified. For these reasons, the fidelity of this indicator was considered as "low".

Dose

Some of the elements of the optimal standard for a canine outbreak response activation were delivered; the response activation was coordinated and set up by gathering the response team, where a plan of action was established. However, some essential aspects of the response activation were not achieved, i.e., roles and responsibilities were not assigned, a timeline of the response activities was not established, and the activation of the response was not considered as rapid. For this reason, the dose of the response activation was categorised as "low".

Reach

After the initial outbreak alert, members of the SAVSNET-Agile team were notified and called to participate in the outbreak response. However, due to the rushed data collection process, not every member was properly notified and informed. Therefore, some of the members (3/14) did not attend the initial briefing meeting and were unaware of the decision made to proceed with an outbreak investigation. For this reason, the reach of the response activation was categorised as "medium".

5.4.1.3.2. Case definition

Fidelity

a) Specific

“Dogs that exhibit acute, prolific vomiting” was the initial case definition used to identify cases during the outbreak. A few days after the deployment of case questionnaires and the screening of veterinary clinical records, it became obvious that this definition was not specific enough, so it was updated to “Five or more vomiting episodes in a 12- hour period in dogs”. Later on, the case definition was updated again to include “where foreign body and pancreatitis are considered unlikely”. Though the initial versions of the case definition was not specific enough, the final version of the case definition that was used during most of the outbreak was specific for the clinical signs of disease and its duration. Hence, the fidelity of the case definition was considered “high”.

Dose

The optimal standards for the establishment of a case definition for canine epidemics were met during the prolific vomiting outbreak investigation, thus the dose of delivery was categorised as “high”.

Reach

Since the case definition used during this outbreak was adopted by members of the response team and used during the data collection process (both to collect physical samples and case/control questionnaires), and it was also used to describe the outbreak in external communications, e.g., published articles and media posts, the reach was considered “high” for this indicator.

5.4.1.3.3. Data collection

Fidelity

a) Timely

The data collection process began early in the outbreak investigation. After the initial notification on January 23rd, a research ethics application to collect data during the outbreak was submitted to the University of Liverpool on January 29th, highlighting the emergency of the circumstances. The ethical approval for epidemiologic questionnaires was obtained on

January 31st. These had been under development since the outbreak was first notified and were then deployed on the SAVSNET website on the same day that the ethical approval was obtained. The ethical approval for the collection of physical samples, i.e., saliva, vomitus, and faeces, was obtained on February 3rd. Veterinary practitioners were contacted as soon as the ethical approval was obtained, and the first samples were collected on February 28th. Despite the inevitable delay in the collection of physical samples, the process of data collection was initiated rapidly, as soon as the outbreak investigation started. For this reason, the timeliness of data collection was considered "high".

b) Protocol

The main downside of the speedy collection of data early on in the outbreak was the lack of time to design a data collection protocol. Arrangements to start the data collection process were made before the first team briefing meeting, so the agreed upon case definition was not initially used. Furthermore, the contributions of different members of the team in the data collection process were not specified, which meant that the burden of the job fell exclusively on certain team members. Thus, the fidelity of this indicator was set as "low".

c) Different strategies for different data sources

Multiple sources of data were used during the outbreak investigation, and these were considered early on by the response team. The SAVSNET database of laboratory test results and veterinary electronic health records was monitored for relevant cases, and ethical approval was sought for the collection of data from veterinarians and owners through questionnaires, as well as physical samples from affected dogs. The fidelity of this indicator was therefore set as "high".

Dose

The data collection process during the outbreak of prolific vomiting was complete, as all the elements specified in the optimal standards were delivered. Data from multiple sources were used to characterise cases and establish controls. Different strategies were planned for the data collection process according to the specific source, to enable the analysis and integration process. However, the data collection protocol was not adequately specified which led to inefficiencies in the process, such as duplication of work by members of the response team, and delays in the response given the discrepancies in the case definition. Therefore, the dose of delivery for the data collection step was considered "medium".

Reach

During the course of the investigation, a high number of dog owners engaged with the epidemiologic case questionnaires available on the SAVSNET website (n=1034). It was more difficult, however, to engage with veterinary practitioners, who had a relative lower participation rate (n=165). This number was even lower in the case of matched control questionnaires, that were distributed together with the case questionnaires to investigate disease risk factors, of which only 60 responses were obtained. The data collection process also proved difficult in the case of samples for laboratory testing. A recurrent problem during the outbreak investigation was receiving samples from small animal practices, especially for control samples. For these reasons, the reach of the data collection step was considered "low".

5.4.1.3.4. Data analysis and integration

Fidelity

a) Different analyses

Data from case-control epidemiological questionnaires were analysed through descriptive and inferential statistics to characterise the outbreak. Physical samples from cases and controls were examined in the laboratory through PCR phylogenetic analyses. Furthermore, data from SAVSNET electronic health records were used to identify cases that fitted the established case definition by reading veterinary clinical annotations. The fidelity of this indicator was therefore set as "high".

b) Identification of causative agent and risk factors

Laboratory findings indicated that the pathogen most likely to have caused the prolific vomiting canine epidemic was a canine enteric coronavirus (CeCoV). Univariable and multivariable mixed-effects logistic regression models were fitted to the data submitted by veterinarians and owners to identify risk factors. The results of this analysis indicated a higher risk of infection among male dogs, and dogs living in multi-dog households. Furthermore, a spatiotemporal analysis of cases through a logistic geostatistical model was used to identify disease clusters that were considered as "hotspots" of infection. For these reasons, the fidelity of this indicator was considered "high".

c) Outputs used.

Outputs of the above-mentioned analyses were shared internally with team members during briefing meetings and posted on the dedicated Teams channel for the outbreak investigation. Relevant graphs were also shared externally via social media (using SAVSNET's twitter account), as well as on the SAVSNET website. The fidelity of this indicator was considered "high".

Dose

All the elements specified for the data analysis optimal standards were delivered during the prolific vomiting outbreak investigation, hence, the dose of delivery of the data analysis was considered "high".

Reach

The outputs of the data analysis process were shared internally and externally, via different platforms, and published through research articles and opinion pieces, reaching the intended audiences. Therefore, the reach of the analytic outputs was considered "high".

5.4.1.3.5. Internal communications

Fidelity

a) Strategy of communications

The response team did set up a communication plan, which included daily briefing meetings and the creation of a Teams channel to exchange information between members. However, whilst the initial engagement from team members was high, it faded over time. Daily briefing meetings were attended by every team member early on in the outbreak investigation. The attendance dropped as the investigation progressed and, eventually, daily briefings became biweekly, and then weekly meetings, until they stopped. Similarly, team members engaged with the Teams channel by regularly posting updates and questions in the beginning of the outbreak, but these interactions dropped during the month of February and ceased in March 2020. Given the drop in attendance levels towards the end of the outbreak, the fidelity of this indicator during the response was classed as "medium".

Dose

All the elements specified for the internal communications optimal standards were delivered during the prolific vomiting outbreak investigation, therefore the dose of delivery of internal communications was considered "high".

Reach

Fragmented communications among team members remained an issue throughout the course of the outbreak investigation, however communications did involve most of the members of the response team. For this reason, the reach of internal communications was considered "medium".

5.4.1.3.6. External communications

Fidelity

a) Centralised data hub

A dedicated webpage was created and added to the SAVSNET site on January 29th (SAVSNET, 2020). This webpage contained relevant updates about the progression of the outbreak, as well as links to the epidemiological questionnaires for veterinarians and owners. The website also included SAVSNET's email address for general enquiries about the outbreak. The fidelity of this indicator was therefore categorised as "high".

b) Further communications

Multiple channels of communication were established during the outbreak investigation. A teleconference was held with the Animal and Plant Health Agency (APHA) and the Department for Environment, Food, and Rural Affairs (DEFRA) to update them on the situation. Meetings were also held with relevant stakeholder institutions, including the British Veterinary and Small Animal Veterinary Association (BVA and BSAVA), and Dogs Trust. Direct communications were established with veterinary practices collaborating with SAVSNET through their practice management software. Furthermore, articles were published in relevant UK veterinary magazines, namely Companion (Tamayo, 2021), and Vet Times (Woodmansey, 2020), as well as in peer-reviewed journals such as Vet Record (Singleton et al., 2020). Multiples posts were shared on social media, including Twitter and Facebook, that were shared by the above-mentioned institutional accounts. Given the established channels of communications, this indicator was considered "high".

Dose

All the elements specified for the external communications optimal standards were delivered during the prolific vomiting outbreak investigation. The dose of delivery was therefore considered "high".

Reach

Communications were held with veterinary practitioners across the country. Pertinent authorities were notified, as well as stakeholder institutions that could potentially contribute to the outbreak investigation. The intended target audiences were reached by using traditional and social media. Thus, the reach of external communications was classed as "high".

5.4.1.3.7. Recommendation of measures

Fidelity

Using the dedicated webpage, some advice for dog owners was posted, based on the findings of the risk factors analysis conducted as part of the outbreak investigation. No specific guidance was shared with veterinary practitioners on how to manage the outbreak. Furthermore, a disclaimer was included, to highlight that the response team would not be able to provide advice on a case-by-case basis, and instead suggested readers to seek their veterinarian's advice. Since the established channels of communications were used to provide scientifically accurate information, the fidelity was considered "high".

Dose

While general guidelines were provided for dog owners to prevent disease transmission, and general guidelines were shared on SAVSNET's website, no specific indications were given to veterinary practitioners. Since only part of the elements were delivered, the dose of the recommendation of measures was considered "medium".

Reach

No formal measures were put in place to analyse the uptake that the guidelines posted by SAVSNET had in the target audience. The outbreak investigation was publicised in multiple media outlets; however, these channels of communication are mostly intended for animal health professionals. Furthermore, veterinary practitioners were not specifically targeted and provided with tailored advice. As the reach of the recommendations was unclear for dog owners, and not complete for veterinary clinicians, the reach of the recommendation of measures was considered "low".

5.4.1.3.8. Documentation and reporting

Fidelity

a) System of documentation

After the response activation, efforts were made by the response team to document the progress of the intervention in parallel with the progress of the outbreak. This documentation consisted of a shared document, where team members logged the date and time, the activities that they conducted, and the challenges faced. This document also included a section to log the time dedicated to each of the tasks and the number of team members involved. The fidelity of this indicator was therefore classed as "high".

b) Improvements to the response framework

An internal report to summarise the response intervention was not produced. Although a specific framework of response was utilised to guide the outbreak investigation, the lessons learned were not incorporated into it after the epidemic ended. As a result, the fidelity was considered “low”.

Dose

One of the elements specified in the optimal standards for the documentation and reporting was delivered, i.e., the development of system of documentation. However, an internal report was not produced, and the response framework was not updated accordingly. Given that half of the elements of the documentation and reporting were delivered, the dose was classed as “medium”.

Reach

Although most members of the response team agreed to take part in the documentation process, only 3 people out of a team of 14 engaged with the progress monitoring document. The reach was therefore considered “low”.

Table 5.1. Summary of the results of the formative process evaluation for the response intervention to an outbreak of prolific vomiting in UK dogs.

Component of the response protocol	**Fidelity**		**Dose**	**Reach**
Response activation	Rapid	Medium	Low	Medium
	Coordinated	Low		
Case definition	Specificity	High	High	High
Data collection	Timely	High	Medium	Low
	Protocol	Low		
	Data sources	High		

Component of the response protocol	Fidelity	Dose	Reach	Component of the response protocol
Data analysis	Different analyses	High	High	High
	Causative agent & risk factors	High		
	Outputs used	High		
Internal communications	Strategy	Medium	High	Medium
External communications	Centralised hub	High	High	High
	Further communications	High		
Recommendation of measures	Using platform to provide guidance	High	Medium	Low
Documentation and reporting	System of documentation	High	Medium	Low
	Framework improvement	Low		

5.4.2. Interviews with veterinary companion animals

Nine veterinary practitioners took part in this study, seven of which were the same participants as those from Chapter Four. Characteristics from those seven participants have been described on Table 4.2, and the characteristics of the newly recruited veterinary practitioners are summarised on Table 5.2. The mean duration of these interviews was of 21 minutes, with the shortest one lasting for 15 minutes and the longest one for 30 minutes.

Table 5.2. Additional veterinary clinicians recruited into Chapter Five, with a breakdown of their characteristics according to the population descriptors described in Chapter Four.

Participant	Practice size (In no. of veterinarians)	Experience (In years)
8	58	21
9	58	17

Appendix V.a contains the codebook used to analyse interview transcripts in this chapter.

5.4.2.1. Barriers for the prevention and control of canine infections

The following themes were extracted from the analysis of the interviews' content:

5.4.2.1.1. Breeder's opinion

Participants often perceived the advice given to dog owners by their breeders as unhelpful, and even harmful, as it reportedly can contradict veterinarian's official position on matters related to canine infectious disease prevention, such as vaccination practices.

> *"I try to explain that there is no evidence for any of those things that the breeder has been telling them about, that they need to go for the advice of the vet and not the advice from the breeder, but in some cases if people insist, and I cannot make anyone vaccinate their pets with something they don't want."*
>
> *—Participant 7: 4 years of experience, practice of 11 veterinarians.*

5.4.2.1.2. Owner attitudes

Interviewees also mentioned how dog owners can sometimes question/resist veterinarians' indications, which they viewed as a barrier for the prevention and control of canine epidemics.

For instance, when owners refuse to vaccinate their pets or perform certain tests to diagnose canine infectious diseases, such as PCR tests.

"Some owners are quite difficult to discuss with because they're already on the backfoot that you're trying to sell them something dangerous and no matter how much you discuss it, and even if you refer them to the BVA's advice, they're kind of still like oh no I'm not doing it."

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

5.4.2.1.3. Staffing shortages

During the interviews, participants discussed how one of the main difficulties of working in small animal practice is the current lack of available personnel, which has resulted in an increased workload for practicing veterinarians. According to participants, this shortage of staff is the result of a combination of factors, that include the COVID-19 pandemic, Brexit, and the increase in pet-owning homes in the UK. Interviewees reported that this issue has compromised their capacity to adequately screen each individual patient, but also to absorb new patients in an emergency situation, such as an outbreak. The increasing workload has reportedly put a strain on small animal veterinarians, which is causing them to leave their jobs in practice.

"*With COVID quite a few international locums maybe have gone back home… um, plus Brexit […] and also because there's so many more pet owners, there's increasing demand for services. Um, vets are getting burnt out ant just not staying in practice for as long*".

—Participant 1: 32 years of experience, practice of 4 veterinarians.

"I do 15-minute appointments, and I have just one 30-minute break between all those appointments, so I end up seeing a lot, around 30 animals in one day, which is absolutely mental".

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

<u>5.4.2.1.4. Costs</u>

Participants agreed that cost was one of the main factors that complicate the early detection of canine infections, since dog owners are often either not able or not willing to afford the diagnostic tests that are required to confirm infectious disease cases.

"…the cost is around £250 I think to do a blood and a urine PCR. And that's something you would have… that that we charge the clients for. And that definitely is a bit of a barrier to, you know, to know what the disease incidence is, because if you're relying on clients to pick up the cost of that, some clients will do that willingly and some clients wouldn't do that".

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

Reportedly, this is often due to a negative cost-benefit decision making process, given the rapid progression of canine infections. This means that infectious diseases often progress too quickly to conduct any tests whose result would aid in the treatment of the animal.

"[canine infectious diseases] are very acute, I think owners to be fair are not very keen in spending a lot of money in investigating if the animals are so poorly and often end up dying. But yes, I think the main… possibly they would investigate if there was a better prognosis… Sometimes we do a necropsy for our own, umm, you know, because we want to know exactly what it was, but we don't, we don't even charge anything for it".

—Participant 9: 17 years of experience, practice of 58 veterinarians.

Cost was also reported as an obstacle for the management of canine outbreaks once they occur. This is because veterinary practices might not be able to absorb an increasingly large number of cases without hiring extra staff, which is usually not a possibility for most veterinary clinics. Further, interviewees mentioned the lack of funding available from public sources to cover the costs of conducting an outbreak investigation. As a result, some of the interviewees had a quite negative and pessimistic opinion about this issue:

"Government funding gets driven by economics, so unless there's an economic impact, then the funding doesn't tend to be there. Um, and unless it's gonna have a massive economic impact, there's not going to be a reporting system that the government puts in place would be my sort of view".

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

*"*referring to an outbreak of CRGV* There was no funding. There was no additional manpower. So obviously a lot of that we just took onto ourselves, we already had full time jobs and were already quite busy people, and obviously for all of us there was not sort of specific funding available to move things forward. There was quite a lot of feedback from general public at that time. Sort of this is not very satisfactory. You know, how can dogs be dying, and the government is doing nothing?".*

—Participant 8: 21 years of experience, practice of 58 veterinarians.

5.4.2.1.5. Lack of space

Participants mentioned that a concern they would have during an outbreak is the lack of suitable spaces in their practices to adequately treat and isolate dogs affected by a transmissible infectious disease. This compromises their capacity to admit patients, monitor the status of the outbreak, and prevent the transmission of disease within the practice to other unaffected dogs.

"If there was a local outbreak and the numbers were exponentially going up, I think we would struggle with kennel space and barrier nursing and all of that, yeah, that would quite quickly become an unsustainable situation, if it was truly infectious".

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

"During an outbreak, I will need to find more resources, because in my practice we've got four kennels, and if I have to have four dogs with us, during the day, hospitalised, I will need more people, more space and everything…".

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

5.4.2.1.6. Lack of information

A recurring theme that was brought up during the interviews was the lack of available information about the prevalence and distribution of canine infectious pathogens in the UK. Interviewees commented how this lack of knowledge makes it difficult to make effective recommendations to owners that protect dogs against infectious diseases, e.g., measures to prevent tick borne diseases in highly endemic areas.

"If we are all more aware and receive information about these diseases, I think they could be prevented. Because I think most of the vets in the UK have never had cases of some of these diseases, they're not even aware of them, they don't even put them in their differential diagnosis list".

—Participant 9: 17 years of experience, practice of 53 veterinarians.

5.4.2.1.7. Misinformation

Lastly, interviewed veterinarians discussed the repercussions of inaccurate information about canine diseases spread via traditional media and/or social media. These inaccurate media reports constitute an obstacle for the control of outbreaks, since they can provide misleading advice to the public and contribute to the distrust of dog owners towards veterinary authority figures and their recommendations.

5.4.2.2. Resources to deal with canine outbreaks

When asked about what resources they would like a prospective system of response for canine outbreaks to include in order to better deal with canine epidemics, participants provided numerous suggestions. These have been summarised into the themes detailed below.

5.4.2.2.1. System of surveillance for canine infectious diseases

The first theme was participant's need for a system of surveillance of canine infectious diseases that is widely available for use in veterinary practice. Specifically, they requested for the prospective system to have the following characteristics:

- Adjustable system: participants would like to have the option to choose which diseases are included in the system, so that they can monitor those diseases that are the most relevant in their corresponding area.

"[...] I think that it would be very helpful, to be able to adjust the system to what I think it's appropriate, then I think you would feel more part of it, and more in control, to understand what's going on".

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

- Centralised information hub: participants also mentioned that they would like to have access to a centralised point of information, that provides updated details about the ongoing epidemiological landscape of canine infectious diseases in the UK.

"A central system that was just solely responsible for monitoring infectious diseases and outbreaks and then putting that information back to GP vets would be really useful".

—Participant 9: 17 years of experience, practice of 58 veterinarians.

Participants also expressed their desire to have access to a system that allowed them to have access to other veterinary professional's experiences with canine infectious diseases.

5.4.2.2.2. Reporting system

Participants did not only want to receive notifications about potential canine disease outbreaks, but also stressed the importance of being able to report anomalies that they observed in practice, such as unusually high numbers of disease or rare clinical presentations that could indicate the presence of a new/exotic disease.

"I hope there will be something easy that you can do to report outbreaks, or even if they are just a suspicion. I think it will be very good for all of us to have a way to report potential outbreaks so someone can tell you if there is real danger or not".

—Participant 8: 17 years of experience, practice of 58 veterinarians.

However, they were also cautious about the potential implications of taking an active role in the reporting process, such as having to spend too much time of their already busy schedule.

For this reason, they would like for the reporting system to be as straight forward and easy to use as possible.

"I would like [the reporting system] to be easy to use, if you know what I mean. Instead of a lot of paperwork or filling a lot of forms or whatever, something that's like, yeah, like a chat almost that you can just chat to someone and let them know if something is going on… almost like a helpline".

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

5.4.2.2.3. Protocol of response to canine outbreaks

The second most prevalent theme among participants was the need for guidance on how to respond to an outbreak of canine disease. This need was expressed throughout the interviews in various ways, ranging from simple indications and advice on best practices to a demand of structured, step-by-step protocols of action that are standardised to the national level. Relevant characteristics of the protocol of response demanded by participants are detailed below.

- Evidence-based guidelines: that are informed by the research carried out by veterinary epidemiologists and infectious disease experts and updated to reflect new discoveries in the field.

"I would like to have good evidence-based guidelines on what really makes a difference, for example, whether you should try to essentially ring vaccinate the area, so trying to get people to come in, whether we should, for example, during a lepto outbreak, be saying: anything that's more than six months past its vaccination date, we recommend an early revaccination because we've got an outbreak".

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

- Readily available: as mentioned above, one of the main difficulties reported by participants was their increasingly busy schedules. For this reason, they stressed the importance of having easily accessible response protocols, that contain clear-cut information in the most succinct way possible.

"Ideally it would be a platform with the most important information only, that's very easy to see. You know what I mean, I imagine something like, if it's red, something is going on. If it's green, nothing to worry about, next. So, something that it's quick and easy to see, then people will use it, if it gets complicated, you know we are very busy so it might not work very well".

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

- Uniform biosecurity protocols: participants expressed their need for guidance on which biosecurity procedures to follow depending on the type of disease, to optimise the control of disease while minimising the impacts on the everyday activities of the veterinary practice.

"It is important that people know what to do, and that everyone is kind of doing the same […] to manage infectious disease cases, you know, for example, how to barrier nurse properly in practice, what you should barrier nurse, what you shouldn't. Um, those kinds of things".

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

- Adaptable: participants requested outbreak response protocols that are inclusive and take their individual circumstances into consideration, such as the type of practice or size of the clinic. They also highlighted the importance of having access to different options for those cases where the gold standard is not possible due to space or financial constraints.

"I envision the protocols as a nice sort of overview document that practices can access, that's adaptable to their mixed environments".

—Participant 9: 17 years of experience, practice of 58 veterinarians.

5.4.2.2.4. Knowledge of canine infectious diseases

Another relevant theme that emerged from the interviews with veterinary practitioners was their need for an improved knowledge of infectious diseases, their prevention and treatment.

This was especially true in the case of exotic and rare infectious canine diseases, that are not prevalent in the UK. Interviewees demanded standardised, easily accessible information about multiple aspects of canine infectious disease management, which included:

- Vaccination: although participating veterinarians were aware of the vaccination guidelines established by the Veterinary Medicines Directorate (VMD), they did not consider these indications sufficient to adequately prevent infectious diseases in veterinary practice.

"Another question is, when do we then vaccinate? So that would be useful information from the vaccine studies, you know, if a patient has just had lepto, do you let it fully recover, do you vaccinate it as soon as it's well? Same for parvo, you know, those sort of things I think would be useful information that vets will ask about, those are the kinds of recommendations that would help us who on the front line moving forward".

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

- Diagnosis: participants were concerned with the ability of the veterinary sector in the country to identify and correctly diagnose infectious canine diseases that are not usually present in the territory, as well as recognising uncommon disease presentations caused by well-known pathogens.

"I think it's necessary for vets to have a better awareness of common versus uncommon presentations for the different diseases, what are the best diagnostic tests to guide people".

—Participant 9: 17 years of experience, practice of 58 veterinarians.

- Treatment: participants also expressed how it would be useful for companion animal veterinarians to have access to evidence-based guidance on the treatment of infectious diseases that are unfamiliar to them, e.g., exotic diseases such as canine babesiosis or leishmaniosis.

"What are the evidence-based for the treatment recommendations? And I'm talking like bullet points here. It doesn't need to be an in-depth thing, it needs to be a, give people a very simple overview of what they should be doing, so the sort of the essential versus desirable kind of treatments".

—Participant 1: 32 years of experience, practice of 4 veterinarians.

"In a lot of cases, in small animal medicine, the simple questions haven't been answered".

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

5.4.2.2.5. Leadership

A recurring theme throughout the interviews was the notion that, in case of an outbreak, veterinary practitioners would not know who to contact for help and guidance.

"Who would you contact, that's the question, because I worked in mixed practice before so I was kind of familiar with the large animal notifiable side, but I don't know other than that, SAVSNET obviously now know about them, I don't know quite who you would contact or how you would go about doing that".

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

Participants also seemed to have a negative perspective on current authorities and showed their discontent and scepticism about their contribution to companion animal disease control. They expressed their feelings of helplessness, derived from the current lack of a government department or agency that is accountable for supporting veterinary professionals in the management of canine disease outbreaks.

"I think that as part of a central organizations process, they need to consider in an emergency situation if we suddenly get a disease outbreak and we need manpower like who will provide the manpower, how will they be freed up from their normal role, how will they be trained to be able to provide the help that's needed?".

—Participant 9: 17 years of experience, practice of 58 veterinarians.

"But I've always found it a little bit petty and difficult to know who am I supposed contact? Do I contact public health England directly, or do I just contact the APHA and that gets done for me?".

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

Participants who had handled an outbreak in their practice in the past commented on the lack of accountable persons to lead the response and provide guidance to first line veterinarians and requested policy changes to improve this issue.

**During an outbreak of CRGV* "Truly somebody did need to take charge and try and move things forward because you know you have veterinary professionals who are absolutely desperate and don't know what to do or who to ask for help".*

—Participant 8: 21 years of experience, practice of 58 veterinarians.

5.4.2.2.6. Material resources

As well as intangible resources, such as information and advice, participants also mentioned their need for concrete measures to help them prevent and control canine disease outbreaks.

- Funding: as mentioned above, cost was considered by participants as one of the biggest barriers for the control of canine infectious diseases. Interviewees mentioned that it was necessary for the authorities in charge to set up specific funds to cover the costs of testing.

  "Definitely I think we miss a lot of stuff because clients just hit this cost barrier, and this leads to diseases being severely underreported. The financial support would definitely help, if there was some level of financial support there for specific disease testing where you had a really high suspicion".

  —Participant 1: 32 years of experience, practice of 4 veterinarians.

- Training: another resource that participants would like to have access to are training programmes to teach veterinarians practical skills to manage canine outbreaks in practice. Either as part of the curriculum taught as part of the medical veterinary degree or through complementary courses offered to practicing veterinarians. This also included media training, to help practitioners handle emergency situations where the press might get involved, e.g., in an outbreak of CRGV.

**Discussing their needs during an outbreak of canine disease* "[...] we quickly realised that people need to have a certain skill set or they need to be trained very quickly".*

—Participant 8: 21 years of experience, practice of 58 veterinarians.

5.4.3. SWOT analysis to identify strategies for the implementation of a canine outbreak response framework.

5.4.3.1. Strengths analysis

- Existing framework of response: a strength for the control of canine outbreaks in the UK is the availability of a response framework, that has been developed and tested in a scientifically rigorous manner.
- Dedicated team of experts: another relevant strength is the existence of a highly skilled multidisciplinary group of academics and veterinary professionals that are motivated to improve canine health in the UK, in many cases, even without a financial incentive to do so.
- Established institutional presence: SAVSNET is a well-known initiative amongst stakeholders, with over 10 years of development and experience in the field. Furthermore, through SAVSNET-Agile, they have gained further recognition from a wider range of stakeholders, including government agencies and pet owners. They have effectively taken the lead responding to canine and feline outbreaks and established themselves as the go-to institution for companion animal epidemics.
- Network of collaborators: one of SAVSNET's biggest assets is their existing network of collaborators, that has been built over the years, i.e., the hundreds of veterinary practices and diagnostic laboratories that routinely contribute data to SAVSNET, as well as other partners from different academic institutions and animal charities.
- Communication channels: another one of SAVSNET's assets that is crucial for canine disease outbreak responses is their already established channels for direct communication with veterinary practitioners, via their PMS.
- Highly efficient: despite the scarce resources and limited funding (compared to similar health emergencies in human medicine or farm animals), the SAVSNET initiative has

been able to maximise the available resources to conduct multiple outbreak investigations, which are now classified as Rapid Disease Investigations or "RDIs" (*Rapid Disease Investigation, SAVSNET*, 2022).

5.4.3.2. Weaknesses analysis

- Funding: this remains one of the biggest obstacles for SAVSNET, and for any other organisation that focuses on companion animal health. The SAVSNET project has managed to survive by applying for different sources of funding, including BSAVA, BBSRC and Dogs Trust. However, funding sources are intermittent and depend on the success of the grant applications, as there is no stable/continuous source of income to maintain this initiative.
- Manpower: related to the previous weakness is the lack of professionals available to contribute during a canine outbreak response intervention. Most of SAVSNET team members that participate in outbreak investigations do so voluntarily, while working full time in academic positions.
- Inability to implement change: whilst able to provide advice and guidance, SAVSNET is a research initiative, and is therefore unable to establish policies or implement measures to prevent and control canine epidemics.
- Internal miscommunications: as demonstrated in this chapter's process evaluation case study (Table 5.1), fragmented communications between SAVSNET-Agile team members were an important source of inefficiencies and delays during an outbreak response intervention.

5.4.3.3. Opportunities analysis

- Demand from end-users: the main opportunity that SAVSNET, or future initiatives, can seize to establish a nation-wide response framework for canine outbreaks is the demand for such a system from end-users, i.e., veterinary practitioners. As evidenced from the interviews, veterinarians explicitly state their need for a canine surveillance system, that enables disease reporting and provides tailored advice for managing outbreaks in veterinary practice. There is also a demand to receive further training on infectious disease epidemiology, prevention, and treatment.

- Development and improvement of canine health surveillance in the UK: despite the current gap in accountable organisations in the companion animal health sector, interest in the subject has been growing over the last few years. The emergence of threats such as CRGV received high levels of attention from the public, that even petitioned the UK government to fund research to investigate the disease's causative agent (DEFRA, 2018). Since the start of the present PhD, a new APHA Species Expert Group has been established, exclusively focused on companion animal disease surveillance (*APHA Vet Gateway*, 2022). Furthermore, other research initiatives with similar aims as SAVSNET have also developed (*VetCompass, Royal Veterinary College*, 2023).

5.4.3.4. Threats analysis

- Misinformation: a threat for the implementation of scientific-based disease prevention and control guidelines are sources that divulge misleading information. Examples of this issue were brought up by participating veterinarians during the interviews conducted in this chapter, such as advice given by dog breeders, or information read by dog owners in social media platforms.
- Resource scarcity: this refers both to the current shortages in the UK's veterinary sector, as well as to the low availability of public funds to cover the costs of companion animal healthcare.
- Accountable organisations: companion animal diseases are not currently regarded by governmental institutions in the same way that human or production animal diseases are. This has resulted in a vacuum of accountability during canine outbreaks and a lack of leadership for control interventions.

5.4.3.5. SWOT analysis matrix

Table 5.3. Summary of SWOT analysis results, that highlights SAVSNET's strengths and weaknesses, as well as the threats and opportunities emerging from the veterinary public health sector.

Internal / External	**Strengths** Framework of response Team of experts Institutional presence Collaborator network Comms. Channels High efficiency	**Weaknesses** Funding Manpower Change implementation Internal miscommunications
Opportunities Demand among end-users Improvement of canine surveillance	Maxi-maxi strategy	Mini-maxi strategy
Threats Misinformation Scarce resources Lack of leadership	Maxi-mini strategy	Mini-mini strategy

5.4.3.6. Generation of a strategy for intervention

5.4.3.6.1. Maxi-maxi strategy (Strengths-Opportunities analysis)

- Expertise ↔ demand for training and knowledge: the demand shown by end-users for specific training in canine infectious disease management and prevention can be harnessed by SAVSNET. Their knowledge and expertise in the field could be used to provide training materials, delivered in an accessible format, e.g., Massive Open Online Courses (MOOCs), tailored to the needs of veterinarians in practice.
- Framework of response ↔ existing organisations: another strategy for improvement of interventions to control canine outbreaks emerges from the potential collaborations

between SAVSNET and the newly established SEG for companion animals. The existing framework of response developed and tested in this thesis could inform the policies and interventions by the SEG, thus avoiding the duplication of efforts and building a symbiotic relationship.

5.4.3.6.2. Mini-maxi strategy (Weaknesses-Opportunities analysis)

- Lack of funding ↔ improvement of canine surveillance: the recent growing interest and investment of resources in companion animal health constitutes an opportunity that SAVSNET, and other potential initiatives, could seize to compensate the existing lack of funding for projects that focus on canine disease surveillance.
- Inability to implement change ↔ newly developed companion animal institutions: by liaising with the newly developed companion animal SEG, an opportunity opens up to put the research-based recommendations and guidelines developed by SAVSNET into practice.

5.4.3.6.3. Maxi-mini strategy (Strengths-Threats)

- Established communication channels ↔ misinformation: the existing channels of communication established by SAVSNET are an asset to consider spread research-based, scientifically sound information and fight the mis/disinformation emerging from less reliable sources.
- High efficiency ↔ scarce resources: another asset is SAVSNET's efficient and timely system of response, considering the low budget available and the lack of dedicated manpower. This is a relevant asset, especially taking into account the relatively low priority of veterinary companion animal initiatives in funding schemes. In other words, a research initiative like SAVSNET would be able to leverage their resources to maximise the results of their interventions.

5.4.3.6.4. Mini-mini strategy (Weaknesses-Threats)

- Lack of funding ↔ lack of resources: despite the increase in attention given to companion animal health, as demonstrated with the establishment of a dedicated SEG, the material resources available are scarce, especially during times of financial hardship, such as post-COVID-19 pandemic. To minimise this threat, SAVSNET, or any other initiative that takes on the role of implementing a prospective framework to deal with canine disease outbreaks, should focus on optimising the utilisation of resources and finding new/alternative sources of funding, e.g., from government sources.
- Inability to implement change ↔ lack of leadership: SAVSNET is a research initiative, without authority to implement change, and limited power to influence policy development. This, coupled with the current lack of accountable organisations for companion animal epidemics, means that there is a very limited window of action to put a system of response into practice.

5.5. Discussion

This chapter aimed to design a framework of response for canine disease outbreaks in the UK and evaluate its application to a real-life outbreak of canine profuse vomiting through a formative process evaluation. A sample of veterinary practitioners were interviewed about their needs and expectations from a future system of canine disease surveillance and response. In addition, strategies for a nation-wide implementation of such system of response were identified by conducting a SWOT analysis based on the results from the process evaluation and the veterinary interviews.

5.5.1. Formative process evaluation

A process evaluation was chosen to design and assess the outbreak response framework developed in this thesis for SAVSNET-Agile. Process evaluation is a well-established method to examine how complex interventions are delivered to the intended target audience (Thomas et al., 2015). An outbreak response is, by definition, a complex intervention, since it involves a large number of interacting components, delivered to a range of stakeholder groups at different organisational levels, and that need to be tailored to specific circumstances, making it difficult to fully standardise the process (Petticrew, 2011).

Within the process evaluation umbrella, there are different types that can be applied depending on the objective of the evaluation. In this chapter, a formative process evaluation (FPE) was used, as this is indicated in cases when new programs or interventions are being proposed and it is therefore necessary to assess the needs and gaps that the project should address (CDC, 2016). The structure of this chapter's FPE was inspired by Saunder's Implementation Monitoring and Process Evaluation guidelines (SAGE, 2023). These guidelines propose a systematic approach to evaluation, that consist in defining the acceptable and optimal delivery of the program, and then establishing indicators to how well the actions adhere to the initially developed plan.

Even though the available literature on evaluation guidelines for outbreak response interventions are useful to provide an indication of how these should look like, these do not offer in depth, step by step indications on how to conduct this process, in a way so that they can be easily adapted to any given infectious disease. Given the scarcity of available frameworks for response evaluation, and the inexistence of any dedicated to canine or companion animal diseases, it was necessary to develop a framework from scratch in this chapter. In the literature, it is recommended that the application of FPE is a shared effort between experts with a multidisciplinary perspective (Saunders RP, 2005). In this chapter, although the work was carried out by the author of this thesis, members of the SAVSNET-Agile team provided their input through a progress monitoring document. This was particularly useful to understand the within group dynamics and internal weaknesses of an outbreak response team.

5.5.2. Monitoring and evaluation of outbreak response interventions

To establish and maintain an outbreak response framework it is essential to parallelly develop a monitoring and evaluation plan. These plans are used to assess the performance of a response framework when applied to a real-life outbreak, versus the planned/intended outcomes of such frameworks. In reality, this process is not often carried out, and response frameworks vary greatly in quality and quantity of delivery (Warsame et al., 2020). The literature dedicated to the evaluation of outbreak response activities is scarce. This issue is frequently highlighted in studies that strive to develop their own monitoring and evaluation plans for their specific circumstances, i.e., for particular infectious diseases in certain regions of the world (Harrington et al., 2013).

The first available monitoring and evaluation guidelines for infectious disease control and prevention activities were developed for assessing the implementation of activities within the International Health Regulations (IHR), established in 2005 (WHO, 2018). These guidelines provide indications for WHO member states on how to collect data based on monitoring indicators, to assess the country's health security capacity and identify areas for improvement. In 2006, the WHO published their guidelines for monitoring and evaluating communicable disease surveillance and response systems (WHO, 2006a). These guidelines provide their definition of standard core activities that must be included in any surveillance system, and specific indicators to monitor to assess the system's performance. They also provide a step-by-step outline on how to conduct the monitoring process and how to measure the performance of the surveillance system against the previously identified indicators. One of the consequences of the COVID-19 crisis has been the increasing interest not only in having access to pandemic preparedness and response strategies, but in plans on how to assess the efficacy of the implemented response measures, so that they can be optimised (WHO, 2022a). Perhaps this experience will be the catalyst for the acknowledgement of the importance of these practices and their development and implementation for other infectious diseases, both in humans and animals.

To the author's knowledge, there are currently no published evidence-based guidelines for the evaluation of outbreak control strategies in companion animals. Therefore, this chapter constitutes the first study where a formal evaluation of a canine outbreak response framework was conducted. The response evaluation methodology described in this chapter was developed from scratch to suit the characteristics of canine populations and can be used as a blueprint for future studies in companion animals.

5.5.3. Interviews with veterinary companion animals

The main issue that transpired through the interviews with veterinary practitioners is the overall lack of resources that the profession currently faces for dealing with all aspects of infectious diseases in dogs. These needs can be divided into three areas: first, the lack of knowledge in the profession in relation to the prevention of canine outbreaks. Second, the lack of availability of information, including surveillance data for companion animal diseases and tailored notifications about potential epidemic threats in their area. This thesis addresses some of these issues, by identifying top-priority diseases for surveillance (Chapter Two) and developing text mining tools to enhance their early detection (Chapter Three), as well as defining clinically relevant thresholds for outbreak notification in Chapter Four. Lastly, the insufficient routes of communication between the different actors that are involved in the canine and public health sector in the UK, i.e., veterinarians in practice, academics, policy and decision makers, and members of other relevant institutions, such as animal charities and pharmaceutical industry. This issue also encompasses the deficient communication routes between these stakeholders, pet owners, as well as dog breeders.

An underlying issue that has an impact on all the areas mentioned above is the current insufficiency of funds to cover the costs of a sustainable, nation-wide system of disease surveillance and response for UK dogs. As reported by participants, this is an obstacle for the detection of canine infectious cases, given the costs of testing and the lack of incentivisation for owners and veterinarians to diagnose disease. Specific funding is also needed to provide further training to veterinarians about canine infectious diseases and their prevention in practice.

According to participating veterinarians, misinformation/disinformation is as detrimental to the prevention of outbreaks as the lack thereof. They related this issue to inaccurate reports spread via social media, but they mainly discussed the role played by pet breeders, as they are often the first, and even main, point of contact and source information for prospective dog owners. For instance, participants believed the recent surge in vaccine hesitancy among pet owners, e.g., with the L4 vaccine, to be linked to the inaccurate advice provided by dog breeders. Better communication channels are therefore needed between these two professional bodies to ensure that reliable, evidence-based information is distributed to pet owners. A recent study found that pet owners view their veterinarians as the most relevant source of information on vaccination

(Schwedinger et al., 2021). Vaccination efforts should therefore harness this power to tackle misinformation. Another key challenge related to the availability of reliable information was the need for access to standardised data about canine infectious diseases and their status in the country, not only during an outbreak, but also during non-epidemic periods. Participants felt the need for this information to be incorporated into the sector's knowledge, especially in the case of exotic or rare diseases that they might not frequently encounter in veterinary practice in the UK. Efforts have been developed to address the lack of knowledge in the veterinary companion animal sector, by initiatives like SAVSNET, that publishes dashboards where trends in the patterns of relevant small animal diseases are shared in real-time with the public via a dedicated website page (*Real Time Data, SAVSNET*, 2023).

5.5.4. SWOT analysis

Strengths, weaknesses, opportunities, and threats analysis (SWOT) is a technique originally developed in business management to assess companies' performance, investigate their position with respect to their competitors, and contribute to strategic project planning (Leigh, 2009). Since its creation, SWOT analysis has been applied in multiple fields of knowledge to plan strategies for development, such as marketing, education, and healthcare (Benzaghta et al., 2021).

Many studies published during COVID-19 use SWOT analysis to assess their respective countries' response to the pandemic (Lokossou V, 2022). However, most of these only include the first part of the analysis, by focusing on enumerating the strengths, weaknesses, opportunities and threats, but without using these insights to draw strategies for future intervention. By contrast, in this chapter, a complete analysis was conducted, given this thesis' intention to describe actionable and practical ideas to facilitate the implementation of a response framework for canine disease outbreaks. When comparing the current chapter to other studies that do carry out the full SWOT analysis of an outbreak intervention (Wang & Wang, 2020), there are similarities between some of the identified strategies, such as mitigating the lack of available manpower by harnessing the innovations developed at academic institutions. However, since these studies are based on human diseases, it is difficult to draw comparisons, as systems of epidemic surveillance are already in place and managed by governmental institutions. Therefore, the weaknesses and threats identified in such studies are related to issues such as the public's opinion, inefficient collaboration between government departments, or supporting different industries' activities when an epidemic has a strong impact in the economy. Conversely, in this chapter, since there is no established system of canine surveillance and response, the identified weaknesses and threats constituted obstacles for the implementation of the response system in itself. In the future, if such a system is implemented, further evaluation will be needed to re-assess its strengths and weaknesses once the system is functioning in the UK.

5.5.5. Limitations

One of the limitations of this study was that external stakeholders were not recruited for inclusion in the process evaluation exercise, as this is beyond the means of a doctoral study. According to the literature, this exercise would ideally include a range of stakeholders with a multidisciplinary background to take part iteratively during the process evaluation planning (Fernandez et al., 2019). Nevertheless, members of SAVSNET-Agile, a multidisciplinary team of epidemiologists, microbiologists, and data scientists, were involved in the process evaluation conducted in the present chapter. The results therefore reflect the perspectives of experts from different backgrounds and provide scientifically rigorous insights about the current status and potential for implementation of the response framework for outbreaks in dogs developed throughout this thesis.

When conducting interviews with veterinary practitioners, as with the fourth chapter of this thesis, another limitation was the difficulty in the participant recruitment process (see Chapter Four's Discussion), due to the added pressure of the COVID-19 crisis and the staffing shortages in veterinary practices. However, nine veterinary practitioners took part in the in-depth interviews conducted in this chapter, which provided the necessary, rich information to gain a well-rounded understanding of the current needs and challenges of the veterinary sector in the UK regarding the prevention and control of canine outbreaks.

5.6. Conclusions and future work

This chapter explores the design, evaluation, and strategies for implementation of a framework of response for canine disease outbreaks in the UK. A formative process evaluation (FPE) was used to design the response framework and evaluate it in its application to a real-life outbreak of canine disease. Through this evaluation, areas of improvement were identified for future applications of this framework, such as the need for coordinated strategies of internal communication and data collection during the outbreak. Veterinary practitioners were interviewed to understand their needs and expectations from a prospective nation-wide framework of canine outbreak response. Some of the obstacles described by participants for the prevention and control of infectious diseases were the lack of information and/or disinformation about these diseases, and the lack of personnel and resources to handle excess cases during an outbreak. The findings from the FPE and veterinary interviews were used in a SWOT analysis to identify best strategies for the implementation of an outbreak response framework at a national level. Some of the strategies outlined in this chapter are achievable in the short-medium term and will be used by SAVSNET to improve their surveillance and response capacities, e.g., liaising with government expert groups and developing training courses for interested veterinary practitioners. Other strategies would require further involvement of institutions with capacity to enact change, such as government bodies and external organisations. In the future, the strategies for implementation described in this chapter could be used by decision makers to scale the proposed framework of response and implement it at a national level.

Chapter Six: Concluding discussion

6.1. Pillars of canine disease surveillance and outbreak response systems

Companion animals constitute key species in today's society, given the role that they play as part of the family unit, particularly in the case of dogs (Laurent-Simpson, 2021; McClaskey, 2019). Because of this, the size of the pet population continues to increase in the UK (J. K. Murray et al., 2015b; *Pet Populations*, 2023). Canine infectious diseases not only pose a risk to companion animal health and welfare, but also to public health, given the existence of canine pathogens with zoonotic potential (Ghasemzadeh & Namazi, 2015b). Further, given the bond between humans and their pets, living spaces are often shared in the household (Westgarth et al., 2008b), thus increasing the risk of zoonotic transmission. To protect dog welfare and public health, it is therefore necessary to prevent and control the spread of canine infectious diseases.

Disease surveillance and response frameworks are an essential component of any infectious disease control programme (J. Murray & Cohen, 2017; Noah, 2021). The last decade has seen a growth in companion animal disease surveillance initiatives, in countries like the US (Glickman et al., 2006b; Kass et al., 2016b), Australia (Ward & Kelman, 2011), and other European countries (Martini et al., 2017). In the UK, pioneering initiatives such as VetCompass (*VetCompass, Royal Veterinary College*, 2023) and SAVSNET (*SAVSNET, University of Liverpool*, 2023) have been established to conduct surveillance activities in companion animals. As part of SAVSNET, the Agile research project was established in September 2018, to build on previous efforts and develop tools to streamline the surveillance and control of infectious canine diseases (*SAVSNet-Agile, University of Liverpool*, 2019).

Despite the progress made thus far, significant efforts still need to be made to establish the key pillars of canine disease surveillance and outbreak response globally. The present thesis contributes to the development of such pillars in the context of the United Kingdom. Thus, given the lack of established institutions and funding for surveillance in companion animals, this thesis aimed to develop a system which can be realistically attained through a research initiative or a governmental institution and be sustained over time for the detection and response to canine infectious disease outbreaks (Figure 6.1). To achieve this, the first step was to identify which diseases should be prioritized for inclusion in surveillance and control strategies under the current epidemiological context of the UK (Chapter Two). Another key pillar of such system is its ability to harness electronic health records for the early disease detection. Previous initiatives have harness both syndromic and laboratory-based surveillance data to monitor disease trends (Small Animal Disease Surveillance 2019; Jones et al. 2014). However, the implementation of text mining techniques to aid in early outbreak detection by exploiting information contained in free-text clinical annotations is still in its infancy (Chapter Three). The next necessary pillar is the detection of outbreaks through mathematical models, and their notification to those that will be in the first line of response. There are, however, no validated methods available to establish the clinical relevance of these genuine outbreaks before their formal investigation is conducted. To address this, in Chapter Four an innovative methodology that uses veterinary practitioners' opinion was developed to inform the selection of a notification threshold value in real world applications of stochastic canine outbreak detection models. The last key pillar is a coordinated strategy to respond to canine disease outbreaks. Such strategies have been developed for human diseases, as well as for farm animals, but are lacking for companion animals. To address this shortcoming, in Chapter Five an outbreak response framework for canine diseases in the UK was designed and the strategies for its nation-wide implementation were identified.

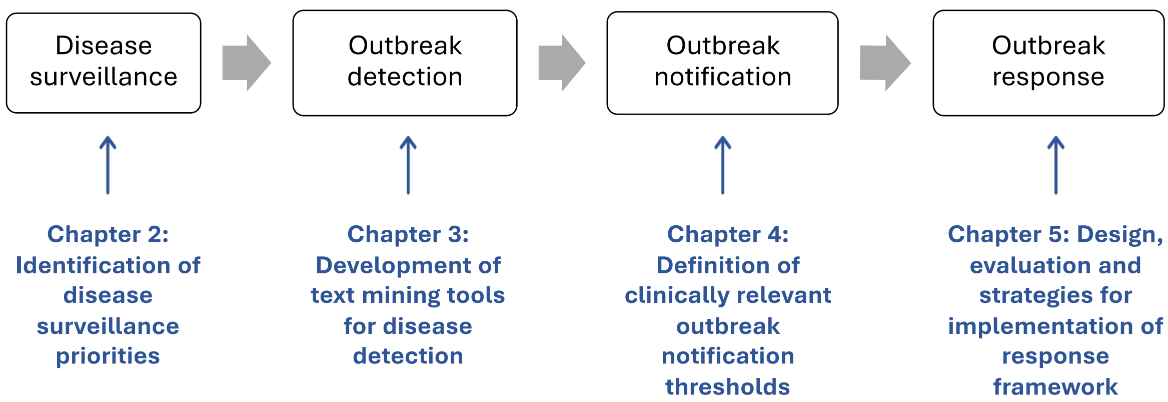

Figure 6.1. Summary of the components of a canine disease surveillance and response system, with the chapters of this thesis dedicated to each of these components.

The following sections of this chapter provide an overview of these key pillars, and how they were addressed in the different analytical chapters of this thesis.

6.1.1. Priority diseases for the optimization of canine disease surveillance and outbreak response systems

Currently, there are no coordinated surveillance systems implemented in small companion animals at a national level. The lack of dedicated funding and accountable institutions for surveillance in companion animals means that the capacity to develop and sustain surveillance systems over time is limited. Therefore, the first necessary step to efficiently allocate the limited resources available for surveillance and to establish such systems is to identify those diseases that constitute the most pressing threats, and that therefore should be prioritised for inclusion in surveillance and response plans. Disease prioritisation frameworks have been previously developed for humans (Balabanova et al., 2011b; Food Standards Agency, 2020; Klamer, Van Goethem, Muyldermans, et al., 2021), and for certain species of animals, including livestock (Bessell et al., 2020b; Humblet et al., 2012b). However, no prioritisation framework specific to canine diseases has been described in the literature. The prioritisation methodology described in Chapter Two consists of a qualitative, stakeholder opinion-led process, which was developed based on the WHO guidance for prioritisation of infectious diseases for policy intervention (Mehand et al., 2018), and the WOAH (former OIE) methodological manual for the listing and categorisation of priority animal diseases (OIE, 2010b). In this chapter, key stakeholders that should be involved in the process of developing a surveillance and response framework for canine infectious diseases were identified through a stakeholder analysis. A sample of these stakeholders were consulted to determine which diseases to prioritise for inclusion in such framework through a Delphi panel technique. The prioritisation process also involved establishing key criteria to evaluate canine diseases through a multicriteria decision analysis. These criteria included "amount of disease in population" as the most relevant for endemic diseases, and "impact of disease on public health" for exotic diseases. Through the prioritisation process, a total of ten canine endemic diseases and exotic diseases, and three syndromes were identified. From this list, the top six diseases of concern (i.e., leptospirosis and parvovirosis for endemic diseases; leishmaniosis and babesiosis for exotic diseases; and syndromes of respiratory and gastroenteric disease) constituted the focus of the tools and framework developed in the subsequent studies included in this thesis. Prioritising diseases by consulting relevant stakeholders in the companion animal sector contributes to the strategic allocation of resources for surveillance activities that the canine sector needs. The prioritisation method described in this chapter constitutes a blueprint for future studies that aim at efficiently allocating resources for disease surveillance and control in companion animals and can be used by future research initiatives or governmental institutions in other countries.

6.1.2. Harness electronic health records for disease outbreak detection

Research initiatives like SAVSNET in the UK harness electronic syndromic surveillance data from veterinary practices and electronic health data from diagnostic laboratories for rapid and actionable surveillance of diseases in small animal populations. These surveillance sources have complementary strengths and limitations. Pre-diagnostic syndromic veterinary practice data provide a source of surveillance in near-real time, at the cost of low specificity, while laboratory-based surveillance provides highly specific results, albeit with a significant delay between the collection of samples and the obtention of these results. To effectively detect clinically relevant patterns (anomalies) in canine health data, the text mining tool developed in Chapter Three relies on pre-diagnostic veterinary clinical narrative data and tackles the main limitations from these two data sources for surveillance, by offering an improved timeliness of anomaly detection when compared to systems based on diagnostic laboratory data, and by increasing the specificity of detection of canine pathogens when compared to surveillance tools based on syndromic data. Previously described text mining tools for disease surveillance and outbreak detection commonly rely on statistical techniques, to find combinations of keywords that are strongly associated with certain diseases or syndromes (Arsevska et al., 2016b; Teo et al., 2021b). However, these methods are not applicable to infectious diseases in dogs because initiatives that use electronic health data for disease surveillance in canine populations, very often cannot link laboratory and practice data for this purpose, and commonly can only identify a low number of confirmed cases of disease in their practice database for model training. To tackle this limitation, a method that relies on the manual identification of disease cases and key term extraction from clinical annotations was followed in Chapter Three. The text mining tool described in this chapter was applied to canine parvovirus as a prototype. A training dataset of 22 confirmed parvovirus cases was established, using SAVSNET's veterinary clinical narrative database. Relevant key terms for disease identification were extracted from the training dataset, which were used to build five regular expressions, divided into the following themes: risk factors of disease, general clinical signs, specific clinical signs, suspicion of disease, and diagnosis of disease. To search for regular expression matches in veterinary clinical notes, a rule-based classifier was designed through user-defined functions, using the R programming language. The accuracy of the text mining tool was tested on the clinical histories of 100 randomly selected dogs and offered promising results regarding the specificity of the matching clinical narratives. Since the dataset used to validate the tool did not contain confirmed cases of canine partovirus, future work should include the identification of confirmed cases so that the sensitivity of the developed tool can be also adequately assessed. The tool presented in this chapter contributes to enhancing the surveillance of infectious diseases by complementing available methods to harness electronic health data for canine outbreak detection, with an increased timeliness and specificity of case detection when compared to systems based on diagnostic laboratory data and syndromic data, respectively. This methodology can be expanded to other canine and companion animal diseases.

6.1.3 Notification of clinically relevant canine disease outbreaks

The ability to detect disease anomalies and communicate them to relevant actors involved in an outbreak response is an essential component of a disease surveillance and response framework. Systems of outbreak reporting and communication to relevant stakeholders are centrally established in the UK in humans and farm animal medicine and implemented at a national level (GOV.UK, 2019c, 2023a). However, no such systems are available for companion animals. Methods described in the literature to establish outbreak notification thresholds are adapted to the type of disease and available surveillance data, including for endemic and exotic diseases (Guagliardo et al., 2018; Rakocevic et al., 2019). Mathematical models for anomaly detection that are specific to SAVSNET's data for canine diseases are under development by SAVSNET-Agile. Whilst statistical methods have proven to be powerful for detecting disease anomalies, they do not consider the implications that these potential outbreaks have in clinical practice. In Chapter Four of this thesis, a method that uses veterinary practitioners' opinion was developed to inform the selection of threshold values that correspond to outbreaks that should be notified when detected by statistical methods because of their significant impact in veterinary practice. This qualitative methodology involved a combination of structured and semi-structured interviews, aimed at investigating which levels of excess case incidence and predictive certainty of an outbreak notification system were preferred by veterinary clinicians to define reporting thresholds for six priority canine diseases in the UK (Chapter Two). Seven veterinarians were interviewed and two different threshold levels were defined, a "notification threshold", for veterinary practices to be made aware of potential disease anomalies, and an "outbreak response threshold", to inform veterinarians of more pressing outbreak threats that would warrant triggering a response. In the case of exotic diseases, participants chose not to make a distinction between these two thresholds, since alerts with the lowest levels of excess case incidence and predictive certainty were deemed actionable. Overall, excess case incidence levels were considered clinically relevant when they increased around two to four times, and up to twelve times over the baseline for endemic diseases and canine syndromes, respectively, while a single case of an exotic disease was considered as a threat by most participants. Further, participants preferred higher levels of predictive certainty for endemic diseases and syndromes than for exotic diseases, to prioritise sensitivity over specificity of an outbreak detection system for the latter type of health threat. The clinically relevant thresholds for notification derived from the needs of veterinary practitioners participating in this study are currently being incorporated into SAVSNET's system of surveillance. In the future, these thresholds will be used as a guide to determine when to alert veterinary practices of potential outbreak threats in their areas in order to reduce the proportion of outbreak alerts that are not actionable in clinical settings. The methodology developed in this study allows to choose notification thresholds adapted to the epidemiological characteristics of any given region so it can inform policy development when establishing outbreak notification thresholds that are clinically relevant in a future, nation-wide framework of canine disease surveillance and response.

6.1.4 Framework of response to canine disease outbreaks

Once the strategies and tools have been developed for the improvement of surveillance and detection of disease anomalies, the final pillar of a system of prevention and control for canine diseases is a framework of response to outbreaks. Such a framework must include a comprehensive list of steps that need to be taken in order to efficiently respond to an outbreak, as well as communication strategies to exchange information among all the relevant actors involved in the response. While research initiatives aiming to harness electronic health data for disease surveillance have been previously described for companion animals in the UK, such as

SAVSNET and Vet Compass, no outbreak response strategies have previously been described or implemented. Thus, even if disease anomalies are detected, no centralised response will be carried out and, if any response is locally conducted by the affected veterinary practices or by involved research initiatives, actions will be carried out in a reactive, ad-hoc manner. This means that canine populations are vulnerable to outbreak threats, which also poses a risk for the wider public health. The work carried out in Chapter Five of this thesis describes the first outbreak response framework for canine populations. To build such framework, a formative process evaluation was followed for its design and evaluation. There is available literature on evaluation guidelines for outbreak response interventions (Klaucke et al., 2001; WHO, 2006a, 2022a). However, these do not provide an indication on how to build such an outbreak response framework. For this reason, and due to the inexistence of any dedicated to canine or companion animal diseases, it was necessary to develop a framework from scratch in this chapter. The designed framework included elements to conduct an outbreak investigation relevant to the UK companion animal sector, including the detection of the outbreak, establishing a case definition, data collection and analysis, communication strategies, recommendation of measures, and documentation and reporting. This framework was applied to a real-life outbreak of prolific vomiting that took place in 2020 in UK dogs, and gaps and lessons learned were identified and documented so that they can be improved upon when responding to future outbreaks. For instance, the need to improve the data collection process by following a standardised protocol, and the need to optimise the response activation process to intervene in a timelier manner. To gain further insights that could be used to improve this framework and help plan its future implementation at a national level, nine veterinary clinicians were interviewed. Participants expressed a series of needs and expectations from a prospective surveillance and response framework, which were mainly related to the existing lack of resources, whether financial, personnel, or reliable sources of information, and the lack of communication channels across the actors involved in the prevention and control of canine diseases. Lastly, a SWOT analysis was also conducted in this chapter to identify best strategies for implementation of an outbreak response framework at a national level. The data used to conduct the SWOT analysis in this chapter were collected from the formative process evaluation and the interviews with veterinary clinicians. SWOT techniques have been employed to evaluate outbreak response interventions (Torri et al., 2020; Wang & Wang, 2020), however they often only conduct the first component of this analysis, i.e., describing the strengths, weaknesses, opportunities, and threats, but do not plan subsequent implementation strategies. In contrast, in this thesis, specific strategies for implementation of the response framework are described, to maximise the advantages of the internal strengths of the response organisation (in this case, SAVSNET), e.g., by harnessing internal expertise to meet the demand for knowledge about infectious diseases in the veterinary sector; and minimise the impact of the external threats, e.g., by liaising with newly established APHA companion animal species expert group (SEG). The framework described in Chapter Five can be used to respond to future canine epidemic threats more effectively, and it can also be used as a template for other companion animals, e.g., to respond to outbreaks of feline disease. The strategies for improvement and implementation of this framework are designed to be used by government bodies and other relevant stakeholders to establish a national framework for canine diseases in the UK.

6.2. Recommendations for future work

The work developed in this thesis constitutes the beginning of the response to a pressing animal and public health need, which is a coordinated system for the surveillance and control of canine infectious diseases. While this work has laid the pillars for a national canine outbreak detection and response framework, many challenges still need to be overcome. Some of these key challenges have been identified in the present thesis, and are summarised in this section, together with corresponding informed recommendations for future work on how these may be addressed.

6.2.1. Infectious disease surveillance and outbreak detection

A key challenge identified in this thesis is the loss of potential disease surveillance information due to the lack of dedicated centralised funding for disease monitoring, including for diagnostic testing of potential infectious diseases that are observed in clinical practice. Costs of diagnostic testing are assumed exclusively by pet owners; therefore, tests are usually only conducted to inform a subsequent therapeutic plan, but not for disease surveillance purposes. This means that, if the owners lack the necessary financial means, or if the disease progression is too acute or severe to warrant such therapy, it is likely that no investigation will be carried out to identify the specific pathogen that is the causative agent. Consequently, although a large number of laboratory test results is currently routinely collected from collaborating diagnostic laboratories by surveillance schemes like SAVSNET, many infectious disease cases observed in clinical practice are not investigated by diagnostic testing and can only be accounted for via syndromic surveillance through veterinary practice clinical data. This issue would be tackled by providing dedicated funding to facilitate sample collection and testing, in cases where this could not be covered by the owners or the veterinary practice. Further, as described on Chapter Three, a big obstacle for canine disease surveillance is the lack of connection between existing data sources, namely EHRs from veterinary practices that include the signalment and clinical history of the animal, and diagnostic test results from laboratory records. Future research initiatives could work to integrate these surveillance data sources into canine electronic health records as a standard procedure in the practice management software (PMS) of veterinary practices across the UK so these data can be electronically retrieved in a standardised format. Test results are currently included in many PMS as pdf files into each animal's clinical history, so software tools could be used to extract the information contained in such pdfs, e.g., using pdf scraping tools (Ariga, 2022; *Tabulizer*, 2016), and adding the obtained raw data to EHR files that contain the corresponding animal's history. In addition, text mining tools like the one described in Chapter Three should be developed to tackle both the above-mentioned challenges, as this tool can improve the specificity of syndromic surveillance by using pre-diagnostic data, and the timeliness of laboratory-based surveillance, while taking into account the health trajectory of the animal. To build on the described text mining tool, future studies should also be conducted to estimate the overall sensitivity of such tool, by establishing a larger validation dataset with confirmed disease cases. Further, the performance of the developed tool could also be evaluated against the performance of artificial intelligence (AI) technology, to compare their accuracy and understand whether the process of key-term extraction could be automated, which would significantly reduce the necessary time and efforts invested in detecting cases of disease in clinical narrative data.

As described in Chapter Four, we currently do not fully understand the impacts that outbreaks of canine disease have in veterinary practice. Therefore, a relevant challenge when developing a system of outbreak notification is to strike the adequate balance between overlooking genuine outbreaks of practical importance whilst not overloading veterinarians with surveillance information. To build on the findings from this chapter, future research should be conducted, through the consultation of a larger sample of small animal clinicians across the country, so that a wider range of perspectives can be considered, and to increase the number of interviewees per segment of the population, so that it is possible to observe meaningful differences between their viewpoints. Clinically relevant outbreak notification thresholds have been described for top-priority canine diseases in this thesis. Findings from this chapter will be utilised by research initiatives like SAVSNET to inform the outbreak alerts generated to notify participating veterinary practices. This practical implementation is a requirement if we are to test the validity of clinically relevant thresholds under empirical conditions. In the future, the methodology described in this chapter could also be used to explore the development of outbreak notification thresholds for other canine diseases.

6.2.2. Leadership and accountability

One of the main challenges identified through this thesis is the current lack of appointed authorities to be responsible for the surveillance of canine diseases, as well as for the response to epidemic outbreaks, with the exception of three canine pathogens, which are included in official response plans due to their zoonotic potential (GOV.UK, 2019a, 2021a).

In the UK, a species expert group (SEG) for small animals was established by APHA in January 2022 (*APHA Small Animal Surveillance*, 2022). As of now, this SEG primarily offers guidance to dog owners on how to prevent the transmission of canine salmonellosis and canine brucellosis. They also provide a comprehensive list of infectious canine diseases that could potentially be introduced into the country. Additionally, the SEG offers free of charge identification services for worm-like parasites that veterinarians may encounter in their practice. While the creation of the SEG represents a positive step forward, a notable gap still exists in the accountability of the institutions for companion animal diseases. This lack of accountable figures and institutions spans across the different levels of intervention, from the lack of legislation and dedicated funding streams to manage and prevent canine infectious disease threats, to the lack of official veterinarians (OV) (*APHA Vet Gateway: Official Veterinarians*, 2023) for small animal veterinary practitioners to report potential disease anomalies.

Research initiatives such as SAVSNET can offer valuable domain expertise and act as consultants when making decisions about a future framework for canine infectious diseases. However, it is important to recognise that these initiatives often do not possess the resources or capabilities required to establish the essential infrastructure for a comprehensive nationwide surveillance and response framework. Research or policy initiatives that aim to improve the surveillance and response to canine infectious diseases would need to effectively allocate their limited available resources. To this aim, they can start by focusing on those diseases that pose the biggest threat to the country, either by selecting those identified on Chapter Two, or, in the future, by following the described methodology to update the list of priorities.

At the time of writing, APHA's SEG for companion animals collects data from research initiatives, namely SAVSNET and Vet Compass, to monitor the status of companion animal diseases in the country. However, there exists a degree of ambiguity regarding the precise utilisation of these data and whether this collaborative effort will culminate in the development of actionable plans or strategies. Future initiatives that aim to implement a framework for canine disease prevention and management should further leverage the existence of the newly established SEG. Collaboratively planning this implementation could foster a symbiotic relationship, in which the participating academic institution(s) would provide their scientific knowledge and expertise, and the government body would contribute towards the funding structure and necessary manpower to effectively carry out outbreak investigations. Government-academic partnerships have been successfully developed in the UK to address outbreak preparedness and response, such as the UK Public Health Rapid Support Team (UK-PHRST), a collaborative of the UK Health Security Agency and the London School of Hygiene and Tropical Medicine (Raftery et al., 2021). This example showcases the success of these type of partnerships in harnessing the complementary strengths of the participating institutions to develop organisational models, or frameworks, for outbreak preparedness and response. Further, this type of collaboration also promotes the sustainability of such frameworks in the long term since the workforce and funding source are secured by an established government institution. This is in contrast to the exclusive reliance on time-limited grants that are typically awarded through academic funding schemes, which compromise the continuity of research and response efforts. These cross-sectoral collaborative principles that have proven effective for human public health could also be applied to animal health, to implement a framework for outbreak prevention and response in companion animals. In the short term, this collaboration could consist of an academic veterinary expert group linked to the SEG, dedicated to the analysis of surveillance data to confirm the existence of potential outbreaks, and prioritise outbreak threats to respond to, as well as provide guidance on best practices during the response. This collaboration could build on the work developed on Chapter Five, as it constitutes the first outbreak detection and response framework for canine populations in the UK.

6.2.3. Knowledge and awareness

The lack of knowledge about different aspects related to canine infectious diseases and their management was also identified in this thesis as one of the main challenges to address through future initiatives. Several key obstacles are included in this section.

The first issue arises from the existing lack of awareness among veterinarians about the epidemiological aspects of canine infectious diseases in the UK. Companion animal veterinarians currently do not possess up-to-date insights into the distribution of canine diseases, their prevalence, and transmission dynamics in the context of this country. This lack of availability of epidemiological canine disease data results in a disconnect between veterinary practice's local context and the broader regional or national disease landscape, thus hindering practitioner's ability to stay informed and respond proactively to emerging threats. In the long term, this issue could be addressed by establishing an information hub for veterinary practitioners with regularly updated information on the epidemiological landscape of canine infectious diseases in the UK. This would require widening the current data collection systems offered by SAVSNET and Vet Compass to provide a larger coverage of UK veterinary practices, as well as the development of an online dashboard to display this information in a user-friendly manner.

Another key challenge is the lack of knowledge among small animal veterinarians about which steps to take, if an outbreak of canine disease were to be detected in their practice. This encompasses the uncertainties surrounding how to determine which disease anomalies constitute significant outbreak threats to respond to, how to establish effective communication strategies with other veterinary practices and dog owners, which biosecurity measures to implement, or whether to plan vaccination campaigns for dogs in their catchment area. To tackle this challenge, it is essential to implement official protocols that provide clear and standardised guidelines that outline the specific steps that veterinarians should take in response to canine outbreaks in their practices.

Additionally, another key challenge identified in this thesis is the current lack of knowledge and experience among veterinary practitioners about the prevention, diagnosis, and treatment of rarely encountered canine diseases, especially in the case of pathogens that are exotic to the UK. To address this challenge, it is necessary to strengthen the education of veterinary practitioners on canine infectious diseases, by expanding the curriculum provided by veterinary schools to include relevant information and practical training on the epidemiology and prevention of exotic and newly emerging canine diseases. Further, ongoing professional development and training opportunities should be offered to practicing small animal clinicians to ensure that they remain up to date with best practices and scientific findings in the field of infectious disease control and prevention.

Overall, a comprehensive solution to address the key challenges for the prevention and control of canine infectious diseases that arise from gaps within the veterinary sector would involve establishing a centralised information hub. This hub could consist of an online platform, integrating crucial elements, such as real-time updates on active outbreaks and a summary of canine disease incidence nationwide, a repository of evidence-based biosecurity protocols tailored for canine infectious diseases, guidance on outbreak response, as well as a compilation of available training resources for practicing veterinarians.

6.2.4. Information and communications

Another key limitation for the efficient prevention of canine epidemics in the UK are the issues related to the communication and exchange of information among the relevant stakeholders involved in outbreak prevention and response.

Among these limitations is the current lack of reliable and robust channels for veterinary clinicians to disseminate information during an outbreak to other veterinary professionals, to infectious disease experts, or to authority figures. In case of an outbreak, these communications would either not take place, or do so in an ad-hoc manner, leading to fragmented communications and delays in the response, thus hindering the containment of disease spread.

This lack of communication pathways also means that there is no effective means for veterinarians to convey information to dog owners about potential disease threats in their area. Future steps to address this limitation could consist in the addition of a section to the centralised online platform mentioned above for veterinary practitioners to exchange information about the status of canine infectious diseases in their corresponding areas. This platform could act as a forum of discussion, for practitioners to become aware of potential outbreak threats in neighbouring areas, so that they can carry out disease preventative actions, which would also foster a sense of community and knowledge sharing among veterinary professionals in the country. To improve the communication with dog owners, particularly with those that are not clients of a specific practice where an outbreak is detected, this platform could include a dedicated section to post relevant information for members of the public. This resource could also take the form of software application, for owners to visualise relevant canine infectious disease data. Examples of such apps can be found in other countries, for instance, the online app "ParvoAlert" was developed in Australia to track and display cases of canine and feline parvovirus in the country, or the mobile app "Tekenscanner" (Jongejan et al., 2019), developed in the Netherlands to perform surveillance on tick-borne diseases and provide information on potential hotspots. In the UK, an initiative named PetHack (PetHack, 2020) has been established to plan hackathons for the development of software tools to improve companion animal health in the country, in which future endeavours could be dedicated to canine infectious diseases.

6.3. Conclusion

To conclude, this thesis has investigated the current gaps in the canine health sector for infectious disease outbreak prevention and management and it has developed surveillance tools and a response framework to improve the surveillance and response to such outbreaks in the UK. Both quantitative and qualitative methods have been developed and employed to identify disease surveillance priorities to focus on throughout this thesis, improve the surveillance and detection of potential disease anomalies using pre-diagnostic clinical narrative data, establish clinically relevant outbreak notification thresholds for veterinary practitioners, and develop a robust framework of response to conduct an outbreak investigation and recommend measures to control the spread of disease. The surveillance tools and response framework developed in this thesis will be used by disease surveillance initiatives like SAVSNET and could also be used by decision makers when designing future policies to improve canine and public health in the UK. In this way, this project's legacy has the potential to bridge the divide between academic research and practical policy implementation, and ultimately enhance the overall preparedness and resilience of the canine health sector against infectious disease threats.

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Appendix Chapter Two

Appendix II.a. Table summary of the main disease prioritisation studies found through a literature review and used to inform the methodology of the second chapter of this thesis.

Study	Aim of the prioritisation	Actors involved	Initial list of diseases	Criteria selection	Criteria weighting	Disease scoring	Final disease ranking
1. WHO, 2006	Setting priorities in communicable disease surveillance	Group of various experts	By study authors through a literature review and expert advice	By study authors 5-8 criteria	Unweighted criteria	By study participants Delphi technique	By collating the results of the prioritisation workshop
2. Phylum, OIE, 2010	Prioritisation of animal diseases to facilitate policy decision making at a local/regional/global level	Group of various experts	Based on stakeholder input	Uses a disease profiling approach at global and local levels	By study authors Weights assigned to criteria and specific values	By study participants Using epidemiologic data	Different rankings for each disease profile

					for criterion levels		
3. CALLISTO Cito et al, 2014	Prioritisation of companion animal zoonoses in Europe	Group of various experts	By study authors through a literature review	Uses OIE's disease profiling approach	By study authors Weights assigned to criteria and specific values for criterion levels	By study participants Delphi technique	2 rankings for public health impact and economic impact
4. D2R2 Gibbens, 2016	DEFRA prioritisation tool of animal health issues for government intervention	Stakeholder group	Pre-established by the study authors	By study participants 5 criteria	By study participants during a workshop	By study participants during a workshop	10 disease priorities identified

5. Stebler, 2016	Prioritisation of diseases in Switzerland	Stakeholder group	Pre-established by the study authors 16 zoonotic and emerging diseases	By study authors 28 initial criteria Reviewed by study participants 8 final criteria	By study participants MCDA Direct weighting	By study participants Delphi technique	2 rankings for lay and expert opinion
6. Stebler, 2015	Prioritisation of diseases in Switzerland (test of criteria weighting method)	Group of 7 veterinarians	Pre-established by the study authors 16 zoonotic and emerging diseases	By study authors 28 criteria under 5 domains	By study participants MCDA Direct weighting	By authors of the study Delphi technique	By collating the results of the Delphi panel
7. Rist, 2014	Prioritisation of zoonoses in the US	Group of representative stakeholders 6-12 participants	Pre-established by the authors 15-30 diseases	By study participants 5-9 criteria	By study participants Analytical hierarchy process	By study participants Decision tree	By collating the results of the decision tree

8. Krause, 2008	Prioritisation of diseases in Germany	Group of expert epidemiologists 11 participants	Pre-established by the study authors 85 diseases	By study authors 12 criteria included in 5 themes	By study participants MCDA Direct weighting	By study participants Using epidemiologic data	Comparison of weighted and unweighted rankings
9. Balabanova, 2011	Communicable Diseases for Surveillance and Epidemiological Research	Group of experts 86 participants	Pre-established by the study authors and reviewed by participants 127 pathogens	By study authors 12 criteria	By study participants MCDA Direct weighting	By study participants Delphi technique	By collating the results of the Delphi panel and normalised to 0-100 scale
10. Buckland, 2014	Prioritisation of threats to canine welfare	Group of experts 7 participants	By study authors through a literature review 37 welfare issues	By study authors 8 criteria	Unweighted criteria	By study participants during a workshop	Final ranked list of 25 welfare issues
11. Ng et al, 2012	Prioritisation of zoonoses in North America and Canada	General public Over 1500 participants	Pre-established by the study authors 62 zoonoses	By study authors 21 criteria	By study participants MCDA Indirect weighting	By study authors Using epidemiologic data	Final ranked list of 62 zoonoses

12. McKenzie, 2007	Prioritisation of wildlife pathogens in New Zealand	Group of experts	By study authors through a literature review 82 pathogens	From OIE's risk assessment tool 3 criteria	Unweighted criteria	By study authors Using epidemiologic data	By collating the results of the study and consulting wildlife experts
13. Renault, 2018	Prioritisation of cattle diseases in Belgium	200 rural veterinary practitioners	By study authors through a literature review 74 diseases	By study authors 3 criteria	Unweighted criteria	Using multiple data sources: survey, laboratory data and literature	48 diseases classified as important, with 6 priorities
14. Bouwknegt, 2016	Prioritisation of foodborne parasitic infections in Europe	Group of experts 35 participants	From WHO/FAO 2012 disease priority list 93 diseases	From WHO/FAO 2012 disease prioritisation study	By study participants MCDA Direct weighting	By study participants during a workshop	Comparison of weighted and unweighted rankings
15. Havelaar, 2010	Prioritisation of emerging zoonoses in the Netherlands	Group of experts with a background in infectious diseases	By study authors through a literature review	By study authors	By study participants MCDA Indirect weighting	By study participants through outbreak scenarios	List of 86 pathogens

16. Klamer, 2021	Prioritisation of communicable diseases in Belgium	Group of various experts	By study authors through a literature review 98 diseases	By study participants 18 criteria in 5 themes	By study participants MCDA Direct weighting	By study participants Delphi technique	Comparison of weighted and unweighted rankings
17. Brookes, 2014	Prioritisation of diseases relevant to the pig industry in Australia	Stakeholder group of Australian pig producers	N/A Only includes criteria weighting	By study authors	By study participants MCDA Indirect weighting	N/A Only includes criteria weighting	N/A Only includes criteria weighting
18. Humblet, 2012	Prioritisation of livestock and zoonotic diseases in Europe	Group of experts 40 participants	From OIE and ISID priority list 100 diseases	From DEFRA's prioritisation guidelines 57 criteria in 5 themes	By study participants MCDA Direct weighting	By authors of the study using epidemiologic data	Ranking of the 100 diseases
19. Kurowicka, 2010	Prioritisation of emerging zoonoses	Group of experts 11 participants	N/A Only includes criteria weighting	By study authors 9 criteria	By study participants MCDA	N/A Only includes criteria weighting	N/A Only includes criteria weighting

					Indirect weighting		

Appendix II.b. Disease fact sheets provided to study participants during the prioritisation exercise

ENDEMIC DISEASES **CANINE PARVOVIRUS (CPV-2)** SAVSNet-Agile

General info	Single stranded DNA virus with high mutation rates. First emerged in 1978, causative agent of severe enteritis in dogs. Different antigenic variants: CPV 2, 2a, 2b, 2c. No association between virus type and clinical signs. Targets actively dividing cells: intestinal crypt epithelial cells, bone marrow and lymphoid tissue in dogs.
Epidemiological profile	Worldwide spread, endemic in the UK. Up to 100% morbidity.
Susceptible species	Dogs, cats, other Canidae such as coyotes, foxes and wolves.
Zoonotic potential	Non-zoonotic. However, co-infections with zoonotic GI agents can occur.
Persistence	Can survive for long periods (over 1 year) in the environment. Extremely resistant to disinfectants. Wildlife reservoirs (canids).
Transmission modalities	Faecal-oral (contact with vomitus/ faeces/contaminated fomites). Shedding for days before the onset of clinical signs. Other: Vertical (in utero infection), insects and rodents may serve as mechanical vectors.
Animal health profile (Dogs)	
Clinical signs	Acute haemorrhagic diarrhoea, vomiting, lethargy, dehydration. Myocarditis (very rare).
Severity of the disease	Very severe in puppies (9% of survival if untreated). Up to 10% mortality in adults.
Profile of control measures	
Diagnostic means	Number of tests for prompt, specific and accurate diagnosis: - Faecal ELISA antigen detection kits: reasonable sensitivity and specificity. - Conventional/ RT PCR: more sensitive than other methods. - False negatives can occur if testing is delayed (period of virus shedding is quite short: 5-7 days)
Vaccination in dogs	Targeted in UK core vaccinations. Licensed vaccines: highly effective and induce cross protection against all 3 types.
Medical treatment in dogs	Focused on active management of shock: fluid therapy, medication to control vomiting and diarrhoea, secondary bacterial infections and intensive nursing care. One commercially produced antiviral interferon is licensed for the reduction of mortality and clinical signs of parvovirosis (enteric form) in dogs from one month of age.
Economic profile	
Affects commercially farmed animals	No
Direct costs	Vaccination costs, Expensive due to the necessary intensive care.

Sources

- Canine and feline infectious diseases, J.E. Sykes, 2014.
- VMD position paper on authorised vaccination schedules for dogs https://www.gov.uk/government/publications/vaccination-of-dogs.
- Molecular Epidemiology and Phylogeny Reveal Complex Spatial Dynamics in Areas Where Canine Parvovirus Is Endemic, Clegg et al, 2011.

General info	10 different serovars have been associated with disease in dogs worldwide. The two most common are *L canicola* and *L icterohaemorrhagica*. All vaccines in the UK incorporate these serogroups.
Epidemiological profile	Worldwide spread. Largely unknown in UK dogs. Uncommon, more present in tropical areas.
Susceptible species	Dogs, rarely cats, more than 150 other mammalian species, including cattle, pigs, rats, foxes.
Zoonotic potential	Zoonotic disease.
Persistence	Environment: Inactivated when exposed to: heat, UV irradiation, a variety of disinfectants and freezing conditions. It can survive in water and wet soils from weeks to months. Symptomless carriers and maintenance hosts can excrete the bacteria in their urine for months or throughout life. Rodents are important reservoirs in urban environments.
Transmission modalities	Oronasal/ contact with wounds through: o Wildlife/ farmed animals: exposure to their urine, ingestion of infected tissues. o Environmental water sources. Bite wound inoculation (such as from infected rodents). Venereal and placental transfer.
Public Health Profile	Indigenous cases in the UK: linked to occupational and recreational activities. Transmission from pet dogs to humans: unclear evidence, uncommon.
Severity of disease in humans	No signs, mild influenza-like illness, or severe illness with multiorgan failure (Weil's disease) have the potential to occur.
Interhuman transmission	Rare.
Control of disease in humans	Lab tests not done unless patients present "textbook manifestation" of Weil's disease- jaundice + fever + renal failure + pulmonary haemorrhage. Treatment with AM therapy.
Animal health profile (Dogs)	
Clinical signs	Acute kidney injury, hepatic injury, stillbirth/abortion/neonatal death. Fever, lethargy, reluctance to move, anorexia, polyuria and polydipsia, vomiting, diarrhoea, icterus, respiratory difficulty.
Severity of the disease	In the UK- in 2014, more than 60% of cases resulted in fatality (Ball et al). With aggressive and treatment: survival rates usually exceed 50%. In centres where haemodialysis is available- over 89%.
Profile of control measures	

Diagnostic means	Clinical detection: difficult due to non-specific signs. Lab testing: different options, variable in sensitivity and specificity- MAT, ELISA, PCR, Cell culture. Cell culture is the only method that permits accurate serovar identification.
Vaccination in dogs	Targeted in UK core vaccinations. Effective- in 2013, all but one case of Lepto in the UK were non-vaccinated animals.
Medical treatment in dogs	AM therapy (doxycycline), renal replacement therapy (haemodyalisis), aggressive supportive care: IV fluids.
Economic profile	
Affects commercially farmed animals	Yes
Notifiable disease	Yes.
Direct costs	Expensive due to the necessary intensive care, referrals, access dialysis, continuous monitoring.

Sources

- Canine and feline infectious diseases, J.E. Sykes, 2014.
- VMD position paper on authorised vaccination schedules for dogs https://www.gov.uk/government/publications/vaccination-of-dogs
- NHS- Weil's disease https://www.nhs.uk/conditions/leptospirosis/
- WHO- Leptospirosis https://www.who.int/zoonoses/diseases/leptospirosis/en/
- Despite high-risk exposures, no evidence of zoonotic transmission during a canine outbreak of leptospirosis, Guagliardo et al, Zoonoses Public Health, 2019.
- Leptospira cases and vaccination habits within UK vet-visiting dogs, Ball et al, Veterinary Record, 2014.
- Leptospirosis Diagnosis: Competancy of Various Laboratory Tests, Budihal et al, Journal of Clinical and Diagnostic Research, 2013.

General info	Enveloped RNA virus. Closely related to human measles and rinderpest virus. Occurs mostly in younger dogs.
Epidemiological profile	Worldwide spread. Highly infectious. Now rare in dogs in the UK due to widespread uptake of vaccines. Recently reported cases in unvaccinated puppies. Considerable concern has been raised about the disease risk of importing dogs into the UK.
Susceptible species	Dogs and other Canidae such as coyotes, foxes, and wolves; Procyonidae (raccoons, pandas); Mustelidae (ferrets, mink, skunks, otters). Large wild Felidae can also be affected.
Zoonotic potential	Non-zoonotic. Some evidence relates CDV and Paget's disease in humans.
0Persistence	Susceptible in the environment, readily inactivated by heat, drying, and disinfectants. Dogs: some continue to shed the virus for several months if they survive initial infection. Wildlife: in the UK, foxes act as a wildlife reservoir.
Transmission modalities	Oronasal contact with virus in secretions or excretions. Airborne: droplet nuclei, large particle aerosol transmission.
Animal health profile (Dogs)	
Clinical signs	Multisystemic disease that primarily affects the gastrointestinal, respiratory, and neurologic systems. Up to 30% of dogs develop CNS signs that do not resolve and have residual neurologic deficits.
Severity of the disease	Severe disease, prognosis highly dependent on virus strain, animal age and immune status and concurrent infections.
Profile of control measures	
Diagnostic means	Clinically: most easily accomplished in dogs that have the full spectrum of clinical abnormalities, and especially when myoclonus is present. Challenging in dogs with isolated respiratory/ GI/ neurologic signs. Lab testing: can be insensitive, and the presence of attenuated live vaccine virus can lead to false-positive results.
Vaccination in dogs	Targeted in UK core vaccinations. Effective- routine vaccination has successfully controlled the disease.
Medical treatment in dogs	No specific drug available, focus on supportive care. Dogs with severe disease: IV fluids, AM therapy for secondary infections, oxygen supplementation, among others. Euthanasia for dogs with progressive neurologic signs that are not compatible with a good quality of life.
Economic profile	
Affects commercially farmed animals	No
Notifiable disease	No
Direct costs	Vaccines, supportive care, impact on wildlife.

Sources
- Canine and feline infectious diseases, J.E. Sykes, 2014.
- VMD position paper on authorised vaccination schedules for dogs https://www.gov.uk/government/publications/vaccination-of-dogs
- Cross-species transmission of canine distemper virus, Beineke et al, One Health, 2015.
- Diagnoses of canine distemper virus in puppies, Adamantos and Warman, Veterinary Record, 2014.
- Canine distemper imported into the UK, D Walker, Veterinary Record, 2014.

General info	Unknown causative agent. Emerged recently in the UK (2012).
Epidemiological profile	Mostly unknown. Annual outbreaks of cutaneous and renal glomerular vasculopathy (CRGV) reported in UK dogs display a distinct seasonal pattern (November to May) suggesting possible climatic drivers of the disease. Clusters identified in the areas of New Forest and Manchester. Cases were generally associated with woodlands, increasing mean maximum temperatures in winter, spring and autumn, increasing mean rainfall in winter and spring and decreasing cattle and sheep density.
Susceptible species	Dogs (???)
Zoonotic potential	No evidence.
Persistence	Unknown.
Transmission modalities	Unknown.
Animal health profile (Dogs)	
Clinical signs	Ulcerated skin lesions, followed by acute kidney injury (in most cases) after 1-10 days.
Severity of the disease	Reports indicate a fatality rate of 9/10 dogs.
Profile of control measures	
Diagnostic means	Presence of compatible clinical signs (including skin lesions), laboratory diagnostics (including AKI ± oligoanuria, progression to azotaemia, hyperbilirubinemia, anaemia and thrombocytopenia) and renal histopathology findings compatible with thrombotic microangiopathy (TMA).
Vaccination in dogs	None
Medical treatment in dogs	No specific drug available, focus on supportive care.
Economic profile	
Affects commercially farmed animals	Unknown
Notifiable disease	No
Direct costs	Intense supportive care

Sources

- Spatiotemporal patterns and agroecological risk factors for cutaneous and renal glomerular vasculopathy (Alabama Rot) in dogs in the UK, Stevens et al, Veterinary Record, 2018.
- CRGV updates, D Walker and L Holm, BSAVA news, 2018 and 2019.

General info	Caused by round worm (Nematode) *Angiostrongylus vasorum*, up to 2.5cm in length, living in the pulmonary arteries and less often in the right cardiac ventricle. Other: *Crenosoma vulpis, Oslerus osleri.*
Epidemiological profile	Endemic in the UK. Affects mostly young dogs.
Susceptible species	Dogs, foxes, other canids.
Zoonotic potential	No evidence.
Persistence	Dogs: without deworming, dogs can secrete Angiostrongylus larvae to the environment for the rest of their lives. Wildlife: foxes as reservoirs in the UK (estimation of 20% infected). Intermediate host: gastropods (slugs, snails). Paratenic hosts: frogs, lizards, rodents.
Transmission modalities	Oral transmission: from eating the intermediate/ paratenic host. Not transmissible from dog to dog through direct contact.
Animal health profile (Dogs)	
Clinical signs	Cardio-respiratory signs, pulmonary haemorrhage. Chronic cough, dyspnoea, tachypnoea, coagulopathies: haematomas and prolonged bleeding, neurological damage: ataxia, loss of vision, paresis, behavioural changes and seizures (due to CNS haemorrhages). Sudden death.
Severity of the disease	Mortality rates high among severe cases, deaths occur in dogs with severe coagulopathies. The prognosis for respiratory cases in primary care are excellent.
Profile of control measures	
Diagnostic means	Long incubation period where dogs are asymptomatic. Lab testing: detection of larvae in faecal sample. Low sensitivity as parasites are shed intermittently. Other: PCR, lung radiography.
Prevention in dogs	Prophylactic use of macrocyclic lactones. To reduce risk of exposure: limit access to areas where slugs and snails may be present, regular removal of faecal matter.
Medical treatment in dogs	Licensed in the UK: Milbemycin oxime (reduces burden by 85%), Moxidectin (prevents establishment of adult parasites). Off label use of Fenbendazole. Supportive treatment: steroids, whole blood/ fresh frozen plasma may be required, transfusion products and heparin.
Economic profile	
Affects commercially farmed animals	No
Notifiable disease	No
Direct costs	Preventive medication, treatment, supportive care.

- Canine Parasites and Parasitic diseases, Saari et al, 2019.
- Canine Lungworm in the UK- Angiostrongylus vasorum and beyond, Ian Wright, Vetcpd, 2017.
- Angiostrongylus vasorum infection in dogs: continuing spread and developments in diagnosis and treatment, Journal of SA practice, E. Morgan and S. Shaw, 2010.

General info	Protozoal agent *Leishmania infantum*. Vector borne disease transmitted by female sandflies (*Phlebotomus spp*). Three presentations of the disease: cutaneous, visceral and mucosal.
Epidemiological profile	Geographical distribution: Primarily southern Europe and the Middle East, central and South America. In Europe: *Leishmania infantum*. In the UK: travel-related cases. Some anecdotal cases of non-travelled dogs. Vector is NOT present in the UK. Evidence of spread of sand flies towards the north of Europe.
Susceptible species	Dogs and less commonly cats; also humans, rodents, wild canids, and marsupial species.
Zoonotic potential	Zoonotic disease.
Persistence	Dogs: some remain sub clinically infected, with the possibility of reactivation later in life with immunosuppression. Vector: sandflies breed in cracks in the walls and feed primarily at night. They fly a max of 2.5km from their breeding site.
Transmission modalities	Through sandfly (*Phlebotomus spp*) bites. Vertical/ venereal transmission. Blood transfusion. Not normally transmissible from dog to dog (anecdotal evidence in the UK)- dog bitten or wounded by infected dog.
Public health profile	Indigenous cases in the UK: no. Only reports in people who travel to endemic areas. Dogs are considered the main human reservoir for L. infantum.
Severity of disease in humans	For all 3 forms: ranges from asymptomatic to severe. Visceral leishmaniasis fatal if untreated (CFR 95%). Mucosal and cutaneous: cause substantial morbidity and followed by life threatening secondary bacterial infections.
Interhuman transmission	Through vector, shared syringes, blood transfusions, vertical transmission.
Control of disease in humans	No vaccines or drugs to prevent infection are available. Treatment with Pentavalent antimonials.
Animal health profile (Dogs)	
Clinical signs	Cutaneous lesions: alopecia, scaling, ulceration. Systemic signs: fever, weight loss, muscle atrophy, inappetence, and lethargy; oral ulceration; progressive splenomegaly and lymphadenomegaly; mucosal pallor due to anaemia; and rarely, hepatomegaly. Visceral lesions: Almost any organ can be affected. Nephrotic syndrome and/or failure of tubular function for many dogs, with polyuria and polydipsia, vomiting, diarrhoea, and dehydration. Immune-mediated thrombocytopenia, epistaxis, melena, lameness, polyarthritis, myositis, uveitis, vasculitis.
Severity of the disease	Fatal if untreated. Prolonged disease course.

Profile of control measures	
Diagnostic means	Challenging sometimes due to the long incubation period and co-infections with other vector-borne pathogens. PCR assays, cytologic examination, culture, antibody serology (IFAT, ELISA), histopathology- with variable sensitivity and specificity.
Prevention in dogs	Ectoparasiticides (deltamethrin): collars, spot on. Vaccine licensed in Europe (CaniLeish)- rarely used in the UK. Dopamine-based oral suspension available for prevention in dogs that travel to endemic regions.
Medical treatment in dogs	Antiprotozoal therapy. Regardless of treatment, complete parasitological cure is rare, and relapses frequent. Glucantime + allopurinol- treatment of choice.
Economic profile	
Affects commercially farmed animals	No
Notifiable disease	No
Direct costs	Prolonged course of disease, preventive medication and treatment.

Sources

- Canine and feline infectious diseases, J.E. Sykes, 2014.
- First reported UK case of likely dog to dog transmission of leishmaniosis, BMJ news, 2018.
- A summary of the evidence for the change in European distribution of phlebotomine sand flies (Diptera: Psychodidae) of public health importance, Medlock et al, Journal of Vector Ecology, 2014.
- ECDC- Leishmaniasis https://www.ecdc.europa.eu/en/leishmaniasis/facts

General info	Protozoal agent that parasite red blood cells. There are large (*B canis, B vogeli*) and small (*B gibsoni, B microti*) forms. Their geographical distribution, transmission, clinical signs, treatment, and prognosis vary widely for each species.
Epidemiological profile	Geographical distribution: Both the large and small forms are present in Europe and infect dogs. In the UK: B gibsoni and B canis- in the last few years, endogenous cases have been reported. Tick activity was continuous throughout the year- no vector-free periods. Vector is present in the UK: YES- *Dermacentor reticulatus, Rhiphicephalus sanguineus, Ixodes Ricinus.*
Susceptible species	Domestic dogs and cats.
Zoonotic potential	None of the Babesia species that affect dogs and/or cats are considered to be of zoonotic importance.
Persistence	Dogs: many carriers, with chronic infections but no clinical signs unless health deteriorates. Wildlife: deer and rodents as reservoirs. Vector: transovarial transmission.
Transmission modalities	Tickborne. Blood transfusion (merozoites). Vertical transmission (*B canis, B gibsoni*). Direct contact through wounds, saliva, blood ingestion (*B. gibsoni*).
Animal health profile (Dogs)	
Clinical signs	Frequent clinical signs are apathy, weakness, anorexia, pale mucous membranes and a poor general condition. All species can cause fever, enlarged lymph nodes and spleen, anaemia, thrombocytopenia, jaundice and pigmenturia.
Severity of the disease	Moderate to severe. Prognosis for *B canis* and *B gibsoni* is "guarded to poor".
Profile of control measures	
Diagnostic means	Blood smear- easy and accessible. Full diagnosis with PCR or quantitative serology (IFAT/ ELISA).
Prevention in dogs	Focus on tick control. Difficult by their endophilic nature. Vaccine available in EU (B canis), that blocks the initiation of many of the pathological processes- lowers parasitemia.
Medical treatment in dogs	Little robust scientific evidence for effectiveness of treatment. Licensed in the UK: Imidocarb (large species), Azithromycin (small species). Doxycycline has been described as lessening the severity of clinical signs. Supportive treatment: Fluid therapy (dehydrated/ hypovolemic dogs), packed red blood cell and plasma transfusions.
Economic profile	
Affects commercially farmed animals	No
Notifiable disease	No
Direct costs	Preventive medication, treatment, supportive care.

Sources

- Canine and feline infectious diseases, J.E. Sykes, 2014.
- A review of canine babesiosis: the European perspective, Solano-Gallego et al, Parasites and Vectors, 2016.
- Bristol University Tick Id http://www.bristoluniversitytickid.uk/
- Canine babesiosis and tick activity monitored using companion animal electronic health records in the UK, Sanchez-Vizcaino et al, Veterinary Record, 2016.

General info	Emerging disease, novel influenza A virus, derived from a strain of equine influenza virus (H3N8). Highly contagious.
Epidemiological profile	Geographical distribution: Emerged in the US in 2004, now endemic in this country. Prevalence in neighbouring countries unknown. In the UK: Outbreak among foxhounds in 2002, second outbreak reported in 2007 by the AHT.
Susceptible species	Dogs, horses.
Zoonotic potential	Confirmed cases of canine influenza caused by the porcine H1N1 presumably transmitted from infected pet owners.
Persistence	Can remain in the Environment for 48h. Horses as a reservoir: close contact/ ingestion of tissues have been proposed
Transmission modalities	Dog to dog transmission occurs, through aerosols and contaminated surfaces.
Animal health profile (Dogs)	
Clinical signs	Pulmonary lesions are generally mild and transient, but infected dogs are susceptible to secondary bacterial bronchopneumonia. Sudden death caused by pleural and pulmonary haemorrhages.
Severity of the disease	High morbidity (close to 100%) but relatively low mortality (around 8% or less).
Profile of control measures	
Diagnostic means	Clinical detection: challenging, as signs resemble those seen in dogs with kennel cough or secondary bacterial pneumonia. Non pathognomonic. Lab testing: limited published info- PCR (75% specificity), Immunohistochemistry.
Prevention in dogs	Vaccine licensed in the US, although influenza vaccines are not the most effective- the emergence of H3N8 virus has resulted in outbreaks worldwide due to vaccine failure.
Medical treatment in dogs	No specific treatment. Cough suppressants, AM therapy for secondary bacterial pneumonia.
Economic profile	
Affects commercially farmed animals	No
Notifiable disease	No
Direct costs	Preventive medication, treatment, supportive care.

Sources

- Canine and feline infectious diseases, J.E. Sykes, 2014.
- Pathologic Basis of Veterinary Disease (Sixth Edition), Lopez and Martinson, 2017.
- Transmission of equine influenza virus to dogs, Crawford et al, Science, 2005.
- Canine influenza virus: cross-species transmission from horses, Newton et al, Veterinary Record, 2007.
- Transmission of canine influenza virus (H3N8) among susceptible dogs, Farris et al, Veterinary Microbiology, 2010.
- Canine Influenza, Dubrovi et al, Veterinary Clinics of North America- SA practice, 2008.

General info	Group of tick transmitted bacterial diseases. Parasites of Two species affect dogs: *E. canis* (monocytic ehrlichiosis) and *E. ewingii* (granulocytic ehrlichiosis).
Epidemiological profile	Geographical distribution: *E canis* is present worldwide, especially in tropical regions. Presence in neighbouring countries: endemic in Mediterranean regions but appears to be moving northward in Europe. In the UK: reported endogenous cases in dogs over the past few years. Vector present in the UK: Yes (*Rhiphicephalus sanguineus*).
Susceptible species	Dogs, cats, humans.
Zoonotic potential	Zoonotic disease. Cases in humans linked to *E canis*.
Persistence	Dogs with subclinical infection. Vector: transstadial transmission.
Transmission modalities	Tickborne.
Public health profile	
Severity of human disease	Estimated fatality rate of 1%.
Interhuman transmission	No.
Control of disease in humans	AM therapy with Doxycycline.
Animal health profile (Dogs)	
Clinical signs	Three stages: acute, subclinical and chronic. Fever, lethargy, inappetence, weight loss, mucosal hemorrhages, uveitis, pallor, edema, and sometimes neurologic signs.
Severity of the disease	Most severe form: chronic ehrlichiosis. Bad prognosis for dogs with severe leukopenia and anaemia.
Profile of control measures	
Diagnostic means	Cytology findings are strongly supportive. Complementary methods: PCR, serology.
Prevention in dogs	No vaccination available. Focus on tick control.
Medical treatment in dogs	Antimicrobial treatment (doxycycline) min 28 days. Supportive care for dogs that are anaemic and dehydrated, additional therapy with immunosuppressive doses of glucocorticoids.
Economic profile	
Affects commercially farmed animals	No
Notifiable disease	No
Direct costs	Preventive medication, treatment, supportive care.

Sources

- Canine and feline infectious diseases, J.E. Sykes, 2014.
- Pathologic Basis of Veterinary Disease (Sixth Edition), Lopez and Martinson, 2017.
- CDC https://www.cdc.gov/ehrlichiosis/symptoms/index.html
- Human Infection with Ehrlichia Canis Accompanied by Clinical Signs in Venezuela, Perez et al, Annals of the NY Academy of Sciences, 2006.
- Emerging infectious diseases in the UK, L Bird, Vetcpd, 2016.

Appendix II.c. Questionnaire provided to participants to score endemic and exotic canine diseases against the previously identified themes

Endemic canine diseases

	Diseases				
	Parvovirus	Leptospira	Distemper	CRGV	Lungworm
Criteria	Score (0-25)	Score (0-25)	Score (0-25)	Score (0-25)	Score (0-25)
Ability to prevent and control e.g. availability/ effectiveness of treatment including prophylaxis and preventive measures					
Amount of disease in the UK e.g. Incidence, prevalence.					
Changing trends in morbidity and mortality e.g. probability of risk increase.					
Ease of diagnosis e.g. distinct clinical signs.					
Economic impact of disease e.g. treatment costs.					
Impact on dog welfare e.g. Severity, chronicity.					
Impact on public health e.g. zoonotic potential, severity in humans.					
Mortality of disease e.g. Mortality, fatality rate.					
Transmission and risk of spread e.g. routes of infection, methods of transmission, epidemic potential, types of hosts and vectors.					

	Diseases				
	Leishmania	Babesia	Canine influenza	Ehrlichia	Dirofilaria
Criteria	Score (0-25)	Score (0-25)	Score (0-25)	Score (0-25)	Score (0-25)
Ability to prevent and control e.g. availability/ effectiveness of treatment including prophylaxis and preventive measures					
Amount of disease in the UK e.g. Incidence, prevalence.					
Changing trends in morbidity and mortality e.g. probability of risk increase.					
Ease of diagnosis e.g. distinct clinical signs.					
Economic impact of disease e.g. treatment costs.					
Impact on dog welfare e.g. Severity, chronicity.					
Impact on public health e.g. zoonotic potential, severity in humans.					
Mortality of disease e.g. Mortality, fatality rate.					
Risk of entry in the UK e.g. probability of introduction of the pathogen.					
Transmission and risk of spread e.g. routes of infection, methods of transmission, epidemic potential, types of hosts and vectors.					

Appendix Chapter Three

Appendix III.a. Complete clinical histories of the 22 dogs included in the training dataset with confirmed canine parvovirus cases.

Animal ID	Consult ID	Date	Narrative
109864	180038	08/09/2014	*in contact with parvo pups. had had diarrhoea yesterday none today b+a off food no vomit yet t 102 trace blood on motion rectal blood prostate normal chest heart normal not dehydrated colour and refill normal so far starve 24 white meat diet injection emeprid home on zitac. has another dog as well. snap test parvo positive. warn can go well or can go very suddenly badly he is aware consequences and will vaccinate when both ok. relaxed abdomen owner will syring small amounts water little and often. Next appointment in 3 days.*
201615	395705	23/04/2015	*Other dog died y/day after having bloody D+ and V+ (no blood) was v v dehydrated. T 38.9 abdopalp unreamarkable tacky chest ok. O reports is vaccinated so would be odd if parvo, just serious HGE with dehyd? no known access to poisons and no petechiations/ echymoses etc. Best chance is IV fluids and abx, doing bare minimum is going to cost £200 which may not be an option. Parvo snap POSITIVE, dsicuss Pts sounds like had all vacs at right time, O to bring vac card in so I can alert ref vaccine breakdown. Only had £40.00 cash doent have a bank card, is coming back to bring vacc card we also have Blondies collar it is in the big reezer in the shed*

267344	2133915	07/09/2016 18:10	*Re-check. Doing well at home, gaining more strength daily, eating well, no V/D (hasn't passed any faeces since at home). On PE, mm pink and moist, crt 1-2s, smln wnl, T 38.5, HR 120, RR 20 with clear lung sounds, abdo palp maybe slightly painful but much less than before. Re-check on Friday. Next appointment in 2 days. POC2*
267344	2142238	09/09/2016 11:52	*Final check. Doing really well at home bright and playful eating well, no faeces yet but no straining no constpation on exam and quite wriggly today! Informed results very weak positive PCR possible did have parvo but could also have had at some point contacted virus and intermittently shedding without being clinically infected. O happy to continue as though parvo from biosecurity point, see in 3w or so for vaccs.*
301919	620218	18/09/2015 11:31	*wt-2kg. Puppy purchased from same place as puppy diagnosed with parvo this am. This puppy has vomitted once todaya nd has diah, hes not eaten this morning. Clinically looks well, m.m-pink, crt-ok, chest no abnormality detected, abdom palpation no abnormality detected, t-38.5, very thin. Parvo test negative but didnt get much from anus for sample do advise owner to bring a fecal sample in nxt time he goes to recheck. This could be a mild case as within an outbreak can see some puppies severly affected and others mildly. I certainly wouldnt rule out parvo at this stage and will advise symptomatic treatment. Well hydrated at moment and hospitalising in isolation here with positive puppy may be putting him at risk so advise owner to monitor at home but if he becomes unwel in self or stops drinking or continues to vomit/diah bring straight back in. Inj synulox/cerinia/po metronidazole. S/a <<identifier>> or sooner if deteriorates.*
301919	623424	19/09/2015 10:16	*Revisit to check for parvo. OR no defecation at all since consult so was unable to get faecal sample, no further V+ but was inappetant all yest, struggled to try feed <<identifier>>, OR today, more BAR than yesterday. O to try get faecal sample to us before 1pm today, weight is decreased since yest but not eaten, given OOH number and advise tempting w/ any food to encourage appetite, BCS 1.5-2/5, advise if continuing to improve, worm on*

			monday. Adv would wait at least 2 wks before vaccinating considering history of origin (w/ other parvo pups) and v. low BCS.
301919	720972	19/10/2015 16:43	*2nd vacc DHP + KC. BAR, owner no concerns since last seen. 2 weeks L4. Discussed parvovirus positive, shedding of virus, advised owner care with other unvaccinated dogs, potentially leave public spaces until after the 2nd injection to be safe, advised play dates with other fully vaccinated dogs.*
545142	1157941	05/02/2016 15:56	*in for chk up as diarrhoea - very watery today, vomited couple of times overnight and once this morning, quieter than normal, not eating today, owner noticed worms in faeces. bright, alert and responsive,mucous membranes pink, crt<2secs,mucous membranes nto tacky, no skin tent, teet good, no oral lesions. eyes/ears/skin ok. lns normal. heart rate 200 rhythm noraml no murmur. femoral pulse strong good qualtiy no deficits. respiratory rate 40 effort noraml no abnoram lung sounds. nothing abnormal detected on abodalp. temperature 39. watery yellow faeces on digital rectal exam. acute gastroenteritis. bland diet little and often, pro bind, injection cerenia, given <<identifier>> info if any deterioration overnight, recommedn ring tomorrow with update.*
545142	1198799	15/02/2016 16:27	*Next appointment in 10 days. 2nd vaccination. in for chk up post <<identifier>>, diagnosed with parvo virus, was kept in for 7 days, came home over weekend, fine since, on abx at moment and gastro food, owner mixing normal food in with gastro, faeces solid, no vomitng, bright and active. bright, alert and responsive,mucous membranes pink, crt<2secs,mucous membranes nto tacky, no skn tent, teeth good, no oral lesions. eyes/ears/skin ok. lns normal. heart rate and rhythm noraml no murmur. nothing abnormal detected on ab dpalp. femoral pulses strong good qualtiy no defictis. temperature 38.4. finish off meds, delay 2nd vaccination until happy been home and weaned back onto nroaml diet without any recurrence ofsymptoms.*
602788	1275588	03/03/2016 12:45	*BIOP 2days. D+ since and V+ up pebble this morning. Retching since and inappetant. Temp 39.3. Abdo comfy. Chest clear. Pink mms. Lethargic in consult. Came from a breeder with lots of dogs? 8 weeks old and not vaccinated yet, breeder said would need vaccination ASAP. Needs worming also. Adv parvo snap test initially*

			and await results. parvo faint positive. Long discussion with owner. guarded prognosis. Estimate created by <<identifier>> for first 24hrs (roughly £400). Opted for PTS. Adv need to advise breeder of outcome and warn that breeder if not necessarily at fault.
798507	1819621	01/07/2016 10:34	*BIOP since yesterday. Today V+/D+ described as watery. Appetite reduced, is drinking ok. Quiet but is interested in stuff at home, wagging tail etc. Not been vaccinated or chipped yet. O reports one other puppy from litter has had parvo. Exam fairly unremarkable. No abdo pain, no obvious abnormalities felt. Lns WNLs. T=37.9. Chest fine. MM pink + moist. Hydration appears fine. O keen to run bloods to check for parvo, did disc there is no specific treatment for parvo and will be giving same symptomatic treatment anyway. Ddx include stress, other infectious agent/parasites, dietary indescretion. Warned owner she could go downhill quickly particularly if not eating much, so needs careful monitoring at home. O will call again if concerned.*
798507	1896193	18/07/2016 10:04	*recovered after parvo, still has occasional mild D+, but generally v well. gained weight. PE all ok, no abnormalities found. See 4wks for 2nd Inj. ID chipped.*
798507	2036206	17/08/2016 10:36	*2nd vac. BAR, mucous membranes pink, teeth fine, eyes and ears fine, NAD on ausc, NAD on abdo palp, no D+- compeltely recovered from parvo. Given 2nd vac and KC vac today- warned about transient side effects of vac.*
941086	2280592	10/10/2016 12:35	*BIOP 2 days - breeder reports all other pups V+ and had anti nausea drug and abs. Off food since this am. Came with raw diet and O been introducing kibble. V+ 3-4x this morning. had eaten over weekend. Colour good, hydration Ok. Abdo relaxed and nothing abnormal detected. T39.6C. Inj cerenia / betamox. advise starve today water only and start gastro diet tomorrow. rex if no improvement / continued V. otherwise can grad reintroduce N diet.*
941086	2361374	27/10/2016 12:22	*OR much better since last seen. Day after seen by us O reports to <<identifier>> that puppy has been back to breeder and seen their vet - and O reports didnt give treatment as puppy was well. Did not receieve any*

			treatment and hasnt been back to us. When asked again today O says didnt actually go to vets, went to breeder and they said didnt need treatment. OR has been fine since, mild episode of diarrhoea the other day but changing diet at the moment - trying to wean off raw diet and put onto puppy kibble and diarrhoea started. Normal poos since. Puppy eating and drinking. No vomiting. Advised cannot say that he's completely recovered, could still become ill. Can vaccinate today, will protect when 1 week after second vaccination for future exposure but won't treat previous exposure. Clinical exam - BAR, pink and moist mucous membranes, NAD chest ausc, NAD abdominal palp no hernia palpable, both testes descended. Rectal temperature 38.8 (puppy). Microchipped - note made of number. Asked O to check registered in their details. Puppy pack given. Advised needs to be wormed. O will try and get from elsewhere. Advised we can provide them but would need a current weight. To be weighed at home and not here as previously parvo positive. Advise try and slowly wean onto puppy biscuits, better than raw as right proportions of nutrients. If wishes to change back onto raw can do when fully grown. Second vaccination in 2-4 weeks. Any worries in the meantime - if he becomes unwell then bring back.
987553	2460486	19/11/2016 11:02	*After walk two days ago being unwell not interested on her food but interested in treats. not sure if she could have eaten anything during walk. yesterday vomiting a couple of times and after that retching but not bringing anything up. and today diarrhoea watery and very bad smell but owner didn't see blood on it. Not eating or dinking since yesterday morning. Lethargic in consult room, mucous membranes pink, a bit tacky CRT 1-2", heart rate 132, normal rhythm, periferal pulse a bit weak. respiratory rate 20, clear chest auscultation, on abdominal palaption a bit unconfortable but not able to feel any FB. temperature 38.8. diarrhoea staining on bacl end. LN ok. Dehydrated. Discussed DD with owner: FB, intoxication, parvovirus as main concerns, and secondary dehydration and electrolyte unbalance. Will need fluids to recover possible for longer than the time we can offer here in a Saturday. Gave estimate for parvo test and fluids for a few hours.*

			Parvovirosis test Positive. As requiring intensive care advised to go to emergency service Owner not sure about if able to afford PM so he decided to try with RSPCA. gave adress.
1000302	2511787	02/12/2016 10:31	*D+. wt= 1.86kg. O has financial constraints. not eligible for PDSA. new puppy. acquired from breeder. 9 weeks old. no vaccines. picked up sunday. being fed <<identifier>> complete. Fed caesar sunday, O then got morrisons complete, D+ started weds, blood in faces but resolved, vomited yesterday 4-5 times bile left over, and then inappetant. Every time he drinks water he is vomiting. Not eaten for more than 24 hours. on exam dull, heart rate 180, chest clear, pale pink mucous membranes, skin tent, T 38.8 blood on thermometer. warned regarding parvo risk. this could be fatal. abdo palp comfortable. has had a lot of diet changes. discussed differential diagnosis with owner: infection, parvo, FB, intessusception. advised admit, intravenous fluid therapy, parvo test and treatment as needed. O declined on grounds of cost. owner has no insurance. owner not eligible for pdsa. advised other option- not ideal and warned may deteriorate is cerenia, ranitidine, synuclav injection. tempt to eat chicken bland at home, small meals often. Advised if vomits at all today with cerenia this could be surgical, need to see back as soon as possible. If eating feed small amount often and can tempt with rehydration sachet dissolve, care regarding aspiration risks. If eating see back tomorrow. ensure bright. if any cocnerns at all must see back as soon as possible. Next appointment in 1 day. recheck*
1000302	2569242	16/12/2016 12:22	*1.82kg Primary vaccination DHP/L4. Well at home since discharge from PH on 8 Dec. At PH was confirmed to have parvovirus - owner aware been a very lucky pup to survive. O had owned for 4d at time of diagnosis and thinks was from a puppy farm. Advise owner I have rung MSD and confirmed can have DHP vaccination if <<identifier>> is clinically well, no V+/D+ and not on ANY medication for 7 days. O confirms last meds were given 8d ago. PE: ausc within normal limits. Abdo palp within normal limits. BCS 4.5/9 a little underweight but likely to be expected given recent ordeal. Very BAR. MM pink CRT<2s teeth great. Long discussion many topics covered. Advise IVC - owner does want to insure having been through recent*

			£700 bill at PH. Advise difference btwn 12mo/lifetime policies. Advise PetPlan. Advise there are certain insurers we cannot do direct claims with. Any questions do ask us. Advise will give KC next time knowing what he has been through would like to avoid overloading immune system. O asks if can catch parvo again - advise yes, may have some level of immunity but unsure how long would last and also there are different strains. Even vacc'd dogs can get parvo but may get a lesser version of it. Later in the consultation owner asks if can take out for walk. Advise I cannot advise this - should be clear now as >8d since discharged so shouldn't shed parvo into environment, but risk could get parvo again (WILL NOT be covered on IVC or future insurance explain why), risk could get lepto and this has even lower survival chances than parvo. O has a back garden but this is shared and another dog "rules" it and is aggressive to other dogs so not an option altho I advise owner ANY outdoor space is a risk as lepto is carried by rats. Have made my advice clear to owner he will consider, advise if he takes <<identifier>> out this is at his own risk!. O was very unhappy w/ prev visit, felt parvo wasn't even mentioned?? (see notes!!!) but returned to us for HPC. As stated in notes 8 Dec owner does not want to be booked in w/ TS again but o been made aware leaving at end of month. O seems happy today. Next appointment in 4 weeks. 2nd vaccination + KC
1000302	2668889	13/01/2017 12:29	2nd Vac DHP/L4 &KC: Wt- 1.95kg. bcs- 4/9. hr-88. DUDE all fine past 4 weeks, has vomitted twice but well in self, has continued access to water. Kept in large crate overnight with h20, food and bedding, RSPCA visited this week due to anonymous complaint. BAR in consult, a little underweight. Is being fed Wagg TID at 12pm, 5pm and 10pm, advised too long a gap between evening and morning feeds, needs to be fed around 6-8am, and maybe increase to 4 meals a day, and needs better quality diet, needs a puppy, small dog, hypoallergenic diet. Wagg of no nutritional value. Does not have insurance yet, advised as soon as possible because breed known for ear and skin issues. Ears today quite waxy but not smelly. Advised to clean regularly and discussed how to using cotton wool (not buds!!) and warm water. Checked with NS, advised although just

			over 10 weeks at first vac, to give DHP and L4 today along with KC. All given with no issues, advised can go for small walks in 1 week but to be vigialant. Endectrid given to apply at home in a few days as was bathed this am, shown where and how to apply. Advised resee in 4 weeks for weigh and worm, sooner if concerned. All nails clipped with no issues. Next appointment in 4 weeks. Weigh and Worm
1024696	2613993	29/12/2016 19:17	*brought in collapsed, bloody D+ and V+. parvo POSITIVE, unable to catheterise, hypothermic. 60ml s/c fluid. Extremely guarded prog - owner opted for PTS. 15ml pentoject intracardiac. O will ring tomorrow to decide on crem.*
1069704	2812726	18/02/2017 12:45	*Gb-parvovirus PTS. Second opinion from <<location>>. Dog obtained from travellers, no chip. v+, haemorrhagic d+, anorexia lethargy 3 days. V4P diagnoses parvo on snap and recommended PTS as poor chance of survival but owner wanted second opinion. On pres, cold, pale muscle, flat Hr200. Improved a little on warming but still flat and passing d+, foaming at the mouth. Discussed intestive treatment and gave rought est of costs but prognosis still guarded. After long discussion elected to PTS. Cath placed R cephalic and 5mls pentojuect intravenous. No cardiac output, corneal reflex etc. Taken home for burial.*
1096421	3486301	12/08/2017 12:42	*started vomiting and acute watery diarrhoea durign a walkin <<location>> woods, quick <<name>> went cold nothing abnormal detected listless, other dog starts as well but not as bad, DOA. parvo snap test was positive on a pooled sample. spoke to MSD will pay for PM and cremation, trying to arrange a courier for monday*
1105890	2982694	04/04/2017 10:25	*Email sent to owner: Hello. I am emailing to advise you that they have all got a strong positive for Hepatitis, Parvovirus and Distemper. We would recommend you retest next year and want to remind you that this does not check for Leptospirosis to which the vaccine does have a shorter duration of activity than the others. Any questions give us a call or email. Best wishes. <<name>> SVN. Lab Request References Generated: Interpretation time is 014153.*

1222170	3518546	21/08/2017 15:11	*EUTH. Parvo +, very flat and dehydrated on presentation, warned guarded prognosis, o elect PTS. Do not want ashes back.*
1292906	3817366	31/10/2017 12:01	*Puppy check - touch of diarrhoea only picked up yesterday suspect due to stress - motions formed on thermometer 38.3, bright in self. pink moist mucous membranes. heart all ok, no abnormalities detected abdo palp. eating ok etc. had nobivac injection yesterday. due 2nd in 2 wks. uptodate with worming due at 2nd vac. keen for ppins, disucssed php. Give out puppy pack at 2,d vacc.*
1292906	3854840	08/11/2017 17:08	*Much brighter. Put on 600g since saturday. Eating well. O's supplementing with water as not drinking a great deal. No vomiting. Normal stool today followed later by soft stool. T 38.7. HR 140, synch pulse. MM pink, moist. Abdo palp - relaxed, soft. Cant palpate diarrhoea today but also cant palpate normal stool. Wean back onto puppy food. Repeated PAB today to check WBC count. Booked in for second vacc on Monday. Consider changing if still leucopaenia. Parvo results attached*
1292906	3894100	17/11/2017 18:44	*O called 5.30pm - upset that nobody had called her to let her know if <<identifier>> could have vaccination, was expecting a call. I reassured O and she was happy to be seen tonight to check <<identifier>> with view to give 2nd vacc. CE: Looking great, different pup. BCS 4/9, gained wt. NAD cardiac ausc, NAD abdomen palp. Has slightly lopsided face, also small raised pink area within whisker follicles LHS - has been like this since acquired - monitor. T38.9C today. Ok for 2nd vacc. Prev had nobivac DHP and L2. Recom top up to L4 so rv in 4wks for this. Advise can be socialised with fully vacc dogs from 7 days time. Discussed <<name>> be shedding parvo virus intermittently but would required rpt pooled faecal samples for PCR to assess this and may not shed when sampled. Rv 4wks for nobivac L4 amnesty.*
1292906	4180053	05/02/2018 09:45	*Had diarrhoea for 3 consecutive days. Now cleared up. Ran out of food at parents house, fed scrambled egg one mornign and then back to normal food (was mixing 2 diets, fed one of those diets). Now back to mix again. Appetite has been reduced since. T 38. Heart and chest ausc n. Dental - all adult dentition. Abdo palp n, soft*

			relaxed. Lns n. NEURO: slight tremor and abnormal gait. Not deteriorated - has remained like this. Query did <<identifier>> have in utero exposure of parvo that has affected cerebellum? No change or deterioration so don think neospora or toxo at this moment in time. No stiff limbs etc. Keep an eye on her locomotion etc. If any dterioration re-see.
1292906	4402026	13/04/2018 11:08	*Ongoing issues assoc with gait tremors etc etc, as prev discussed cerebella/vestibular (occasional head tilt and nystagmus when over excited) disucssed further investigations MRI neuro specialist etc. Also behavioural issues - training associated. Heart chest ok, no abnormalities detected abdo palp eating drinking well. disucssed season and neutering adv after first season preferable.*
1363289	4137409	23/01/2018 20:45	*Presented by O with concerns re: inappetance and vomiting. 14 weeks old, reported as vaccinated. brought down to back for triage, verbal consent to start stabilisation. cardio - no murmur on ausc, pulses moderate, HR 200, mmems pale pink. resp - normal effort, pattern, ausc. neuro - qar. abdo - soft on palpation, no palpable masses/FBs. haemorrhagic diarrhoea on rectal exam. integ - no gross lesions on assessment, fleas. hydration - mmems tacky, skin tent prolonged. haematology - neutropaenia. parvo test - POSITIVE. discuss above with Os, during consult after discussing estimates and payment terms Os advised severe financial restrictions, not able to cover consultation fee, no means of payment brought to clinic. asked Os if could contact family etc for help, not an option. discussed on that basis would be emergency first aid treatment, and given potential severity of condition advised this is likely to be euthanasia. Os given time to discuss. discussed with staff members on duty, offer made to take on ownership of patient and to cover ongoing treatment for this. offered this as an option to the owners, after discussion accepted. paperwork signed to transfer ownership, Os <<location>> liable for all treatment so far and that they will not have any information about patient going forward. Lab Request References Generated: Lab in-hse Parvovirus/Giardia Snap Test is 020163. Lab Request References Generated: Haematology (4 Part) is 020163*

1444933	4515185	17/05/2018 19:38	*been in owners possession 3 days. v+ and d+ started today, no blood or mucus. v+ bile like. exam dehydrated T39.5 very Q, minimally alert/responsive. tachycardia. coat purple when obtained puppy, O attempted to wash out. parvo test +ve. euthanasia opted for. obtained from <<identifier>> S who claimed to live near <<identifier>> top. previous owner supplied current with 'vaccine card' that is not official. 'vaccine' stickers are not recognised by any member of team. the vet who has signed the card is not registered on the RCVS website. the date of vaccination is after the expiry date on one of the vaccine stickers. the date next vaccine due is the expiry date of the other sticker not in 1 years time. the microchip stickers provided match the chip in the dogs neck (<<microchip>>) but were not registed to the breeder/previous owner. the only details found are those the current owner has registered. the flea treatment written is not flea treatment. photos taken of the body to confirm puppy is not a shih-tzu as stated and purple colour. screenshot of advert from where current owner obtained puppy from.*
1496476	4704004	06/07/2018 10:13	*1.42kg-vomiting++. no better, actually worst, not interested in food, not had any probiotic. from yesterday night vomiting, yesterday couple of times, this morning 4 time, bile, no keep down water either. no interested in food. diarrhoea still, now with some bloods, owner report like clots?, nothing in consult. vacc ok. worming status ok. clinical examination- still quite brighte, less playful, pink, rct<2sc, pulse strong, T38.8, HR 100, abdomen uncomfortable at palpation. no blood on termomether. dd- gastroenteritis/colitis VS else. owner very stressed by the whole situation, no coping well with her sick. options-. - conservative treatment home again- not think owner can do it, and owner agrees. - adivse hosp at least 24h, fluids, bloods, and treatment in hospital. owner agrees. consent for signed, owner to transport <<name>>. handover to ips vet.*
1496476	4746046	14/07/2018 10:29	*recheck. bright, happy, playing, eating, drinking, passing normal faeces (occasionally) no vomiting, Heart rate and resp fine, abdomen comfortable, colour fine, plan vaccinate late next week and research how to check when she stops shedding parvo/.*

1574695	4928437	20/08/2018 15:33	*temperature 102.2, no vomiting/diarrohea but inappetant and penmate died suddenly of suspected parvo, gums moist and capillary refill time normal, abdomen slightly tender, was wormed about 4 weeks ago, rc. POSITIVE parvo test, discussed options with owner, opted to try and treat at home, advise if any vomiting/diarrohea then no option but to bring them in for IVFT and meds, rc*
1659376	5201719	15/10/2018 17:11	*got pup from pet fbi in <<location>> 1 week ago. yesterday vomiting and dull and today white/yellow diarrhoea. one litter mate diod die and was very small and other littter mate currently being treated for parvo in another clinic. on exam parameters all normal but very thin and dull. yellow coloured motion on thermometers. has been wormed. did snap parvo test and is parvo positive. owner spoke to charity that she came from and they want her to return to their own vets- st <<location>> for treatment*

Appendix III.b. Summary of words that appeared two or less times in the training dataset for canine parvovirus

Frequency	Word in parvovirus training dataset
2	taken, palpable, treat, mixing, mmems, previous, dd, abdominal, clinical, pulses, end, consent, future, resp, called, body, bland, up, cardiac, thing, sure, after, yellow, unwell, cant, acute, discuss, haematology, details, palpate, meals, change, wishes, deteriorating, ring, tempt, kept, weekend, pack, fluid, think, normal, reduced, gained, occasional, estimate, respiratory, regarding, concerned, thermometer, &#, diets, financial, again, email, eligible, rspca, pdsa, stress, acquired, gait, picked, chipped, sunday, litter, keep, complete, felt, keen, found, comfortable, put, seas, trying, changing, went, vets, actually, will, intravenous, retching, pooled, lethargic, top, rv, continued, ears, offer, diagnosis, start, saturday, tc, said, kibble, hours, as, now, spoke, emergency, effort, contact, payment, weigh, intermittently, point, pcr, weak, different, playful, resee, flea, later, consultation, take, less, maybe, lung, ml, asks, s, haemorrhagic, covered, symptomatic, ivc, others, affected, opinion, quality, thin, expiry, abnormality, questions, vomited, diagnosed, apply, crt, stops, warn, bloody, stated, died, booked, mate, suddenly, wt, es, starve, far, refill, motion, wagging, h, rc, known, on, right, all, lepto, survival, doing, options, agrees, Â£, access, cost, consider, abx, chance, best, vomitingdiarrohea, becomes, bad, purple, owners, cover, vomited, yest, msd, check, feed, passing, neutering, least, endectrid, clinic, cold, hernia, crt&lts, patient, ownership, confirmed, dec, euthanasia, dhpl, primary, dude, unable, number, likely, sore, al, eyesearsskin, nto, responsive, femoral, underweight, recent, limits, deal.

1	walkin, waxy, warm, o's, motions, buds, costs, complaint, burial, suspect, ashes, is, cotton, smelly, durign, touch, elected, clean, regularly, wool, using, formed, g, tid, cath, around, cephalic, php, increase, ppins, quality, uptodate, mls, cneal, output, feeds, r, hypoallergenic, checked, nutritional, reflex, value, does, evening, placed, gap, breed, pentojuect, brighter, ear, do, walks, elect, improved, remind, prog, pentoject, year, intracardiac, decide, pay, retest, crem, cremation, muscle, gbparvovirus, travellers, recommend, anorexia, we, distemper, lethargy, vp, hepatitis, diagnoses, arrange, pres, emailing, recommended, hello, po, sent, courier, sc, warming, presentation, hypothermic, euth, ns, although, alg, est, interpretation, woods, wanted, quick, rought, vigialant, bathed, intestive, shown, listless, supplementing, starts, doa, svn, activity, duration, nails, clipped, mouth, shter, foaming, leptospirosis, collapsed, catheterise, extremely, verbal, followed, supplied, card', official, 'vaccine', recognised, member, team, rcvs, website, sticker, years, microchip, provided, match, neck, <<microchip>>, registered, breederprevious, written, photos, confirm, shihtzu, screenshot, advert, 'vaccine, near, staff, live, duty, offered, accepted, paperwork, transfer, liable, information, forward, inhse, parvovirusgiardia, part, possession, mucus, q, minimally, alertresponsive, tachycardia, coat, attempted, wash, #NAME?, f, claimed, from, kgvomiting++, wst, probiotic, occasionally, plan, late, research, penmate, suspected, gums, capillary, tender, ivft, pet, fbi, whiteyellow, diod, die, littter, currently, treated, parameters, coloured, thermometers, charity, return, playing, ips, handover, gastroenteritiscolitis, night, either, rept, clots?, status, examination, brighter, rct<sc, uncomfortable, termomether, vs, transpt, else, stressed, whole, situation, coping, sick, conservative, adivse, hosp, hospital, members, cdition, synch, required, samples, assess, sampled, amnesty, had, consecutive, cleared, ran, parents, house, scrambled, egg, mornign, was, mix, dental, adult, dentition, slight, tremor, deteriorated, remained, query,

	rpt, socialised, severity, recom, repeated, pab, wbc, count, leucopaenia, attached, upset, let, kw, expecting, reassured, tight, view, ce, looking, has, lopsided, face, raised, area, whisker, follicles, lhs, utero, cerebellum?, neospora, toxo, cardio, moderate, pattern, qar, massesfbs, integ, gross, assessment, fleas, prolonged, neutropaenia, discussing, estimates, terms, severe, restrictions.

Appendix III.c. R script used to estimate the risk of parvovirus disease present at an animal level.

```
library(tidyverse)
library(lubridate)


#First loading .pkl files and merging them into a single csv file where the
#file_name is equal to each animal's unique id

list_of_files <- list.files(path = "path_to_folder",
                            recursive = TRUE,
                            pattern = "\\.csv$",
                            full.names = F)


#Formatting files to add column names and check for duplicated columns

merged_dogs <- readr::read_csv(list_of_files, id = "file_name")
colnames(merged_dogs) <- c("animal_id","savsnet_consult_id","narrative",
                           "consult_date", "regex1_score", "regex2_score",
                           "regex3_score","regex4_score","regex5_score",
                           "consult_score")
merged_dogs$animal_id <- gsub("\\..*","", merged_dogs$animal_id)
merged_dogs <- merged_dogs %>%
  group_by(animal_id) %>%
  filter(!duplicated(savsnet_consult_id))


#Keeping only consultations with parvo risk

parvo_risk_only <- merged_dogs %>% filter(!consult_score == 0)
```

```
#Adding column with the number of days since the previous recorded consultation.
#If it is the first one for a given animal, this column = 0.

parvo_risk_only$consult_date <- sub(" .*", "", parvo_risk_only$consult_date)
parvo_risk_only$consult_date <- ymd(parvo_risk_only$consult_date)
parvo_risk_only <-   parvo_risk_only %>% group_by(animal_id) %>%
  mutate(days_since_last = as.numeric(difftime(consult_date, lag(consult_date),
                                               units = "days")))
parvo_risk_only$days_since_last <-
  ifelse(is.na(parvo_risk_only$days_since_last)==T,as.numeric(0),
         parvo_risk_only$days_since_last )
parvo_risk_only <- parvo_risk_only[,c(1,2,4,11,5,6,7,8,9,10)]


#Now creating a data framw containing only consults with their follow-up, to
#re-calculate their parvovirus risk by removing same regex matches
#that take place in follow ups within the time specified by the time-decaying
#factors

parvo_risk_followup <- parvo_risk_only %>% group_by(animal_id) %>%
  filter(days_since_last <= 30)

parvo_risk_followup <- parvo_risk_followup %>%
  mutate_at(vars(5:9), ~ifelse(. == 0, NA, .))

parvo_risk_followup <- parvo_risk_followup %>%
  group_by(animal_id) %>%
  mutate(across(c(regex1_score,regex2_score, regex3_score, regex4_score,
                  regex5_score), ~ ifelse(is.na(.), NA,
                                          ifelse(
                                            row_number() == which.max(
                                              !is.na(.)), ., NA))))

parvo_risk_followup <- parvo_risk_followup %>%
  mutate_at(vars(5:9), ~ifelse(is.na(.), 0, .))


#Recalculating consult scores with new values after removing regex matches

parvo_risk_followup <- parvo_risk_followup %>% ungroup()
parvo_risk_followup <- parvo_risk_followup %>% mutate_at(vars(5:9), as.numeric)

followup_cons_scores <- parvo_risk_followup %>%
  mutate(consult_score_b = rowSums(parvo_risk_followup[5:9]))


#Merging both datasets

parvo_risk_recalc <- left_join(parvo_risk_only,followup_cons_scores)
parvo_risk_recalc$consult_score_b <-
  ifelse(is.na(parvo_risk_recalc$consult_score_b)==T, 0,
         parvo_risk_recalc$consult_score_b)

animal_risk <- parvo_risk_recalc %>%
  group_by(animal_id) %>% summarise(animal_risk= sum(consult_score_b))
```

```
parvo_risk_total <- merge(parvo_risk_recalc, animal_risk, by = "animal_id")
parvo_risk_total$animal_risk <-
  ifelse(parvo_risk_total$days_since_last > 30,
         parvo_risk_total$consult_score, parvo_risk_total$animal_risk)


#Presentation of results

parvo_risk_total$matching_regex <-
  ifelse(parvo_risk_total$regex1_score > 0 &
           parvo_risk_total$regex2_score > 0 &
           parvo_risk_total$regex3_score > 0, "1 2 3",
           ifelse(parvo_risk_total$regex1_score > 0 &
                    parvo_risk_total$regex2_score > 0,"1 2",
           ifelse(parvo_risk_total$regex1_score > 0 &
                    parvo_risk_total$regex3_score > 0, "1 3",
           ifelse(parvo_risk_total$regex1_score > 0 &
                    parvo_risk_total$regex2_score == 0 &
                    parvo_risk_total$regex3_score == 0, "1",
           ifelse(parvo_risk_total$regex1_score == 0 &
                    parvo_risk_total$regex2_score > 0 &
                    parvo_risk_total$regex3_score > 0, "2 3",
           ifelse(parvo_risk_total$regex1_score == 0 &
                    parvo_risk_total$regex3_score == 0 &
                    parvo_risk_total$regex2_score > 0, "2", NA))))))

results_animal_level <- parvo_risk_total %>%
  group_by(animal_id) %>% |
  summarise(savsnet_consult_id,consult_date,days_since_last,
            matching_regex, animal_risk)

results_animal_level$risk_level <-
  ifelse(results_animal_level$animal_risk <= 9, "Very low",
  ifelse(results_animal_level$animal_risk <= 24 &
           results_animal_level$animal_risk >= 10, "Low", NA))


#Write it as a table

write.table(results_animal_level, sep = ",", quote = F, row.names = F)
```

Appendix Chapter Four

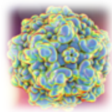
Appendix IV.a. Overview of information provided to participating veterinarians to facilitate the discussions during the interviews aimed at exploring clinically relevant outbreak scenarios, for the six canine diseases included in Chapter Four.

Potential outbreak of **canine leptospirosis**

Key aspects of disease

- **Severity**: 40% of cases end in fatality in the UK. With aggressive treatment, over 50% survive, 90% if access to haemodialysis.
- **Transmissibility**: through environmental sources, vectors (rodents), direct contact with infected tissues (farm animals, wildlife).
- **Zoonotic potential**: yes (around 50 cases/year).
- **Prevalence in the UK**: endemic disease, distribution is largely unknown.

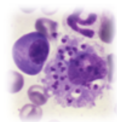
Potential outbreak of **canine parvovirus**



Key aspects of disease

Severity: Very severe in puppies (91% fatality if untreated). Up to 10% mortality in adults.
Transmissibility: Direct contact and fomites. Virus shedding for days before the onset of clinical signs.
Zoonotic potential: none known.
Prevalence in the UK: endemic disease, primary causative agent of haemorrhagic diarrhoea.

Potential outbreak of **canine leishmaniosis**



Key aspects of disease

- **Severity**: fatal if untreated, no vaccine available.
- **Transmissibility**: Vector borne (sandfly, *Phlebotomus*),
- **Zoonotic potential**: yes, dogs as main reservoir of *L. infantum*.
- **Prevalence in the UK**: exotic disease, vector not yet present in the country.

Potential outbreak of **canine babesiosis**

Key aspects of disease

- **Severity**: Moderate to severe prognosis.
- **Transmissibility**: Vector borne (ticks, *Ixodes/Dermacentor/Rhipicephalus*).
- **Zoonotic potential**: no (not the same species that colonise humans).
- **Prevalence in the UK**: exotic disease, vector is present in the country.

SAVSNet AGILE

Potential outbreak of **respiratory disease**

Key aspects of disease

- Detected via syndromic surveillance
- Multiple potential causes (infectious AND non infectious)
- E.g.: bacterial pneumonia, kennel cough, distemper, allergies, asthma, parasites…
- Prevalence in the UK: around 3-5% of total canine consultations.

SAVSNet AGILE

Potential outbreak of **gastrointestinal disease**

Key aspects of disease

- Detected via syndromic surveillance
- Multiple potential causes (infectious AND non infectious)
- E.g.: coronavirus, parvovirus, foreign bodies, indigestion, poisoning…
- Prevalence in the UK: around 2-4% of total canine consultations.

SAVSNet AGILE

Appendix IV.b. Codebook with deductive and inductively generated codes used to analyse Chapter Four interview transcripts.

Code	Description	Files	References
Babesia	The interviewee talks about any topic that is related to canine babesiosis	7	7
Behaviour change	Interviewee describes the actions they would take to respond to an outbreak of canine disease if it were to occur in their current veterinary practice	3	3
Change advice about importation of dogs into the UK	Would change the legislation about the importation of pet dogs into the UK to include more strict measures of testing and quarantining to avoid the introduction of exotic diseases into the country	3	4

Code	Description	Files	References
Communication with the public	Would attempt to launch a communication strategy with the wider public to share information about the prevention of canine babesiosis	3	4
Contact authorities	Would contact the authorities to notify them of autochthonous/imported cases of canine babesiosis	2	2
Contact diagnostic laboratories and specialists	Would contact diagnostic laboratories and/or veterinary specialists to aid in the diagnosis and/or treatment of canine babesiosis	2	3
Increase testing	Would increase te sting in their practice to detect further cases of canine babesiosis	2	4
Information seeking	Would research the clinical presentation/diagnosis/treatment of canine babesiosis to better prepare for potential cases in their practice	3	4

Code	Description	Files	References
Proactive recommending tick prevention and treatment	Would recommend owners to actively search for ticks in their dogs, as well as preventative actions, such as topical tick prevention, avoiding walks in grassland areas, and using tick repelling collars	3	5
Would not consider contacting authorities	Interviewee explicitly states that they would not try to alert the corresponding authorities of a potential outbreak of canine babesiosis	1	1
Certainty	Interviewee discusses the levels of confidence of an outbreak alert that they would require for a specific canine disease	7	10
Has enough info about the disease	Interviewee believes that the knowledge available in their practice is enough to handle potential cases of canine babesiosis	1	1
Impacts of a false alarm	Interviewee discusses the potential impacts that a false alarm of the disease under discussion would have on their practice	5	5

Code	Description	Files	References
Costs	Economic impact of the outbreak in their practice	2	2
Information fatigue	Receiving an unnecessarily high number of outbreak alerts, which would result in them becoming desensitised with potential future outbreaks	2	2
No impact	They would not experience any impacts at all from a false outbreak alert	1	1
Positive impact	They would experience a positive effect from false outbreak alerts	1	2
Treatment side effects	They would provide dogs with unnecessary prophylactic treatment, which could result in harmful side effects for the animal	1	1
Imported dogs only	Interviewee discusses only having seen cases of canine babesiosis when imported from other countries into the UK	4	5

Code	Description	Files	References
Increasing endemic risk	Interviewee perceives the risk of canine babesiosis as increasing as an endemic threat in the UK, for whichever factor(s)	2	2
Lyme disease	Interviewee talks about Lyme disease, in the context of it being a zoonotic disease caused by *Babesia spp,* whether mentioning or not that this is not the same species that causes disease in dogs	1	1
Most worrying disease	Interviewee talks about how canine babesiosis is the disease that worries them the most out of all of the diseases included in Chapter Four	2	4
No clue about babesia	Interviewee mentions how they have never heard about babesiosis as a disease that affects dogs	1	3
Prevalence	Interviewee talks about the prevalence of canine babesiosis in the UK	7	11

Code	Description	Files	References
Never had a case	Has never seen a case of canine babesiosis in their veterinary practice	4	8
Not more common than Leishmania	Does not consider canine babesiosis as more prevalent than canine leishmaniasis	3	3
Excess incidence	Interviewee discusses the levels of disease/increases in case incidence that would result in a behaviour change or that would warrant a notification	7	7
Imported vs non travelled	Makes the distinction between excess incidence values chosen for autochthonous and imported cases of canine babesiosis	3	3
Severity of disease	Interviewee discusses the severity of the cases of canine babesiosis	2	2

Code	Description	Files	References
Suspicion of disease	Interviewee discusses the clinical signs and other risk factors that would make them suspect a potential case of canine babesiosis in veterinary practice	3	5
Ticks	Interviewee talks about ticks as the vector for canine babesiosis	5	6
Veterinarian's knowledge about Babesia	Interviewee provides their opinion about the knowledge of the veterinary profession in the UK about canine babesiosis	3	4
Wonders about zoonotic potential	Interviewee is not sure about whether canine babesiosis is a zoonotic disease	2	2
Gastroenteric	The interviewee talks about any topic that is related to canine gastroenteric disease	7	7

Code	Description	Files	References
Behaviour change	Interviewee describes the actions they would take to respond to an outbreak of canine disease if it were to occur in their current veterinary practice	7	7
Increased testing	Would consider increasing the frequency of testing for gastroenteric infectious agents	3	3
Causative agents	Interviewee talks about potential causative agents of an outbreak of gastrointestinal disease	4	5
Certainty	Interviewee discusses the levels of confidence of an outbreak alert that they would require for a specific canine disease	7	7
High cost to manage (time, money, effort)	Interviewee talks about the impacts that an outbreak of gastroenteric disease would have in their practice	2	3

Code	Description	Files	References
Impacts of a false alarm	Interviewee discusses the potential impacts that a false alarm of the disease under discussion would have on their practice	7	7
Prevalence	Interviewee talks about the prevalence of canine gastroenteric disease in the UK	7	9
More common than respiratory	Considers that the prevalence of gastrointestinal disease is higher than that of respiratory disease among UK dogs	7	8
Rarely infectious	Has the opinion that the cases of gastrointestinal disease cases observed in their practice are rarely caused by infectious pathogens	2	3
Excess incidence	Interviewee discusses the levels of disease/increases in case incidence that would result in a behaviour change or that would warrant a notification	7	8

Code	Description	Files	References
Severity of cases	Interviewee discusses the severity of the cases of canine gastroenteric disease that they have seen in their practice	2	2
Leishmania	The interviewee talks about any topic that is related to canine leishmaniasis	7	7
Behaviour change	Interviewee describes the actions they would take to respond to an outbreak of canine disease if it were to occur in their current veterinary practice	7	7
Client communication	Would modify their frequency/channel of communication with dog owners	4	5
Information seeking	Would seek information about the potential outbreak and/or study the clinical characteristics of the disease to recognise potential cases in their practice	3	3

Code	Description	Files	References
Investigation of cases	Would conduct an investigation of the potential cases seen in their practice, e.g., by testing, contact tracing, etc.	3	3
Certainty	Interviewee discusses the levels of confidence of an outbreak alert that they would require for a specific canine disease	7	8
Clinical signs	Interviewee discusses clinical signs that they have either observed or that they believe are indicative of the disease	5	6
Difficulties	Interviewee talks about the difficulties that they believe surround the diagnosis, treatment, or prevention of the disease	3	4
Accurately knowing dogs' travel and vaccination history	Not knowing the history of the animal is considered as a difficulty for the detection of leishmaniosis cases	1	1

Code	Description	Files	References
Impacts of a false alarm	Interviewee discusses the potential impacts that a false alarm of the disease under discussion would have on their practice	2	3
Costs	Economic impact of epidemic preparedness in their practice	1	1
No impact	False outbreak alerts would not have an impact in their practice	1	2
Not bothered by frequent alerts	False outbreak alerts would not be an inconvenience	2	2
Increasing awareness	Interviewee believes there is an increasing awareness of canine leishmaniosis by the veterinary profession	1	1
Low prevalence	Interviewee believes that the prevalence of canine leishmaniosis is very low in the UK	4	6
Never diagnosed a case	Has never diagnosed a case	2	2

Code	Description	Files	References
Only seen imported cases	Has only seen cases that were imported from other countries	5	7
Aware of non-travelled cases	Is aware that autochthonous cases of canine leishmaniosis have been reported in the UK	1	1
Misconceptions	Participant's misconceptions regarding the transmission and characteristics of canine leishmaniosis	3	5
Preventative action	Interviewee describes existing protocols used in their veterinary practice to prevent outbreaks of canine disease	1	1
Excess incidence	Interviewee discusses the levels of disease/increases in case incidence that would result in a behaviour change or that would warrant a notification	7	10

Code	Description	Files	References
Imported vs non travelled dogs	Interviewee makes a distinction in the excess incidence levels chosen for the notification and outbreak response thresholds for canine leishmaniosis	3	3
Sandfly	Interviewee mentions the vector for canine leishmaniosis	4	6
Screening and import refusal	Interviewee discusses screening protocols for canine leishmaniosis	1	1
Severity of disease	Interviewee talks about the severity of canine leishmaniosis	1	1
Uncertainty about treatment, diagnosis, monitoring	Interviewee discusses the uncertainties surrounding the diagnosis, treatment, or prevention of the disease	4	7
Unlikely to be transmissible	Interviewee does not think that leishmaniosis is a highly transmissible disease	3	4

Code	Description	Files	References
Not concerned about epidemic potential	Is not concerned about leishmaniosis as an outbreak-causing pathogen	1	5
Vaccination	Interviewee talks about the vaccination of canine leishmaniosis	3	4
Very concerned about it becoming endemic	Interviewee expresses concern about the potential endemisation of canine leishmaniosis in the UK	2	3
Climate change	Impact of climate change in the likelihood of endemisation of canine leishmaniosis in the UK	2	2
Zoonotic potential	Interviewee talks about the zoonotic potential of canine leishmaniosis	5	7
Leptospirosis	The interviewee talks about any topic that is related to canine leptospirosis	7	8

Code	Description	Files	References
Behaviour change	Interviewee describes the actions they would take to respond to an outbreak of canine disease if it were to occur in their current veterinary practice	4	4
Active investigation	Would investigate of the leptospirosis cases seen in practice, e.g., through contact tracing	3	3
Costs covered by practice	The costs of responding to the outbreak would be covered by their practice	1	1
Biosecurity measures	What biosecurity measures they would put in place to prevent the spread of the outbreak	3	7
Communication strategy	Talks about whether or not they would start a communication campaign during an outbreak of canine leptospirosis	2	3

Code	Description	Files	References
Advice to clients	Would provide advice to clients on how to prevent the disease	3	6
Didn't contact anyone	Did not contact anyone during a past outbreak of canine leptospirosis	1	1
Don't know who I would contact	Does not know who they would contact during an outbreak of canine leptospirosis	3	4
Social media	Would use social media to post about the outbreak	2	2
Vaccination companies	Would get in touch with vaccination companies	1	1
With other vets	Would attempt to contact other veterinarians in the area	2	2
Increase testing	Would increase testing to detect further cases of leptospirosis	3	4

Code	Description	Files	References
Information seeking	Would seek information about the status of the outbreak or about the characteristics of the disease	3	3
Knowledge within own practice	Would check the available knowledge within their own practice	1	2
MSD	Would use the resources provided by MSD	1	1
Vet voices	Would seek information using the Facebook group “vet voices”	1	1
Isolation and movement control	Would recommend isolation of and movement restrictions of cases	1	1
Not much can be done	Interviewee believes that not many actions could be taken to respond to an outbreak of canine leptospirosis	1	1
Recommend vaccination	Would recommend dog owners to vaccinate their animals	3	4

Code	Description	Files	References
Unlikely to do financial preparedness		1	1
Unsure what to do	Would not know what to do	1	1
Certainty	Interviewee discusses the levels of confidence of an outbreak alert that they would require for a specific canine disease	7	16
Diagnosis	Interviewee talks about the diagnosis of canine leptospirosis	3	3
Difficulties	Difficulties surrounding the diagnosis of the disease	4	7
Necropsy	Necropsies to confirm the diagnosis of leptospirosis	1	2
Not confirmed	Suspected cases of canine leptospirosis were not diagnostically confirmed	3	8

Code	Description	Files	References
Serology vs PCR testing	Compares different diagnostic methods for canine leptospirosis	2	3
Experience with outbreak	Interviewees who were involved in outbreaks of canine leptospirosis discuss their experiences	3	3
Case load	Case incidence of canine leptospirosis during the outbreak	3	4
Clinical presentation	Clinical presentation the observed cases during the outbreak	2	5
Concerns about zoonotic potential	Concerns about the zoonotic potential of leptospirosis during the outbreak	2	3
Lessons learned	Lessons learned during the outbreak of canine leptospirosis that participants would apply in future outbreaks	2	16
Duration	Duration of the outbreak of leptospirosis	2	2

Code	Description	Files	References
Emotions	Emotions expressed by the participant in relation to how they felt during the outbreak of canine leptospirosis	2	6
Impacts of an outbreak	Interviewee discusses the impacts that the outbreak of leptospirosis had in their practice	1	2
Economic impact	Financial impacts of the outbreak	2	8
Higher workload	Increased workload for the veterinarians employed at their practice	2	4
Mental health	Impact on staff's wellbeing and mental health	2	3
Training	Need to invest in staff training to handle the leptospirosis cases during the outbreak	1	1

Code	Description	Files	References
Information sources	Information sources that participants used during the outbreak of leptospirosis	2	2
Response	Actions that were taken by participants during the outbreak of leptospirosis to handle the outbreak	1	2
Biosecurity	Increased biosecurity measures	2	5
Communications	Communications that participants carried out during the outbreak of leptospirosis	2	12
Media	Interactions with the media	2	3
Owners	Interactions with dog owners	1	1

Code	Description	Files	References
Participating institutions	Contact with institutions that provided advice/resources during the outbreak	2	5
Public perception	Opinions that members of the public shared with participants during the outbreak	2	4
Success of communications	Whether communications were successful during the outbreak	2	2
With referring vets	Communications with veterinarians that referred the cases of leptospirosis to participant’s practice during the outbreak	1	1
Within practice	Internal communications during the leptospirosis outbreak	1	1
Proactive treatment	Proactively treating highly suspicious cases of leptospirosis	2	3

Code	Description	Files	References
Testing	Actively testing for the disease when recognising clinical signs	2	7
Vaccination	Started a vaccination campaign during the outbreak to prevent further cases	2	2
Well-coordinated	Interviewee believes that the outbreak response was well-coordinated at the time	2	2
Lack of help	Interviewee talks about how they did not receive any help during the outbreak from external institutions	2	8
Lessons learned	Interviewee discusses the lessons that they learned during their experience with an outbreak with canine leptospirosis	2	3

Code	Description	Files	References
Negative opinion about the authorities	Interviewee expresses a negative perspective about the authorities, regarding the lack of help provided during the outbreak of leptospirosis	2	4
Outbreak detection	Interviewee talks about how the leptospirosis outbreak was detected	3	10
Outcome	Interviewee talks about the outcome of the cases of canine leptospirosis that they experienced during the outbreak	4	9
Severity of cases	Interviewee talks about the severity of the cases of leptospirosis that they saw during the outbreak	1	2
Sources of funding	Interviewee talks about the sources of funding that they received when responding to the leptospirosis outbreak	1	1

Code	Description	Files	References
I would certainly want it on the notification system	Direct quote from participant	1	1
Impacts of a false alarm	Interviewee discusses the potential impacts that a false alarm of the disease under discussion would have on their practice	5	7
Explaining to owners	Having to discuss the potential outbreak and its implications with dog owners	3	4
Inappropriate use of antibiotics	Using antibiotics prematurely when suspecting that there is an outbreak	1	1
Increased testing	Covering the costs of testing	1	1
Information fatigue	Receiving too many alerts that are not relevant and becoming disengaged with the alert notification system	1	1

Code	Description	Files	References
No extra cost	Does not believe that there would be any costs associated to a false outbreak alert	2	3
No impact	Does not believe that there would be any impacts associated to a false outbreak alert	3	4
Positive impact	Participant believes that the impacts of a false alert would be positive for their practice	2	2
Resource investment	Investment in resources for epidemic preparedness	2	2
In dairy farms	Interviewee talks about the cases of canine leptospirosis that they have seen in dairy farms	1	2
Prevalence	Interviewee talks about the prevalence of canine leptospirosis in the UK	7	9

Code	Description	Files	References
Decreased	Has decreased over recent years	4	7
Very rare	Considers canine leptospirosis as a very rare occurrence in the UK	6	11
Mostly in unvaccinated dogs	Most cases occur in unvaccinated animals	4	6
L4 controversy	Interviewee talks about the controversies associated with the leptospirosis L4 vaccine	4	4
Most important disease	Interviewee considers canine leptospirosis as the most important disease for their practice	1	1
Excess incidence	Interviewee discusses the levels of disease/increases in case incidence that would result in a behaviour change or that would warrant a notification	7	20

Code	Description	Files	References
Risk factors	Interviewee talks about the risk factors for canine leptospirosis	6	11
Severity of disease	Interviewee discusses the severity of the cases of canine leptospirosis	1	2
Suspicion of disease	Interviewee talks about the clinical signs that would make them suspect a case of canine leptospirosis	5	13
Uncommon clinical presentation	Has seen cases with an unusual clinical presentation	1	3
Talked about every day	Participant says that they talk about the risk of canine leptospirosis every day in their practice	1	1
Treatment	Participant talks about the treatment for canine leptospirosis	3	4

Code	Description	Files	References
Underdiagnosed	Participant believes that the disease is underdiagnosed in the country and that the real prevalence is higher than what we currently estimate	2	4
Vaccination	Participant talks about the vaccination of canine leptospirosis	5	8
Core vaccine	Mentions how leptospirosis is included in the core vaccinations list in the UK	2	2
L4	Participant mentions the L4 vaccine	3	5
Shortage	Participant talks about the current shortage of leptospirosis vaccines	1	1
Zoonotic risk	Interviewee talks about their perception of the zoonotic risk of canine leptospirosis	5	9
Misconceptions	Misconceptions about canine leptospirosis	2	4

Code	Description	Files	References
Parvovirus	The interviewee talks about any topic that is related to canine parvovirus	7	7
Behaviour change	Interviewee describes the actions they would take to respond to an outbreak of canine disease if it were to occur in their current veterinary practice	1	1
Biosecurity measures	Would implement biosecurity measures	4	8
Communications	Would start a communication campaign	5	8
Increase testing	Would increase testing to detect parvovirus cases	2	3
Proactive treatment	Would proactively treat potential cases of disease to mitigate their severity	2	2

Code	Description	Files	References
Promote vaccination	Would recommend vaccination to dog owners	2	2
Specific parvo protocol	Participant talks about a specific protocol for canine parvovirus in their practice	1	2
Certainty	Interviewee discusses the levels of confidence of an outbreak alert that they would require for a specific canine disease	7	12
Client concerns	Interviewee talks about their practice's clients concerns about canine parvovirus	2	3
Difficulties and lessons learned	Interviewee talks about the lessons learned from previous cases of canine parvovirus	3	6
Expensive to treat	Considers parvovirus as an expensive disease to treat	2	2

Code	Description	Files	References
Fatal outcome due to funds running out	Participant discusses how the disease often results in fatalities due to the lack of funds from dog owners	2	2
Impacts of a false alarm	Interviewee discusses the potential impacts that a false alarm of the disease under discussion would have on their practice	6	7
Costs	Financial impacts of a false alarm	2	2
Low impact	Would not have a very big impact in their practice	3	5
Owner's concern	Would create unnecessary concerns for dog owners who are clients of the practice	1	1
Positive impact	Would have a positive impact in their practice	1	1
Waste of resources	Would result in resources being wasted	1	1

Code	Description	Files	References
Prevalence	Interviewee talks about the prevalence of canine parvovirus in the UK	7	12
Hearing of outbreaks	Participant reports how it is common to sporadically hear about outbreaks of canine parvovirus in the country	5	7
Not seen over a period of time	Has not seen any cases of the disease in recent times	3	6
Upsurge due to new variants	Has observed an increase in the prevalence of disease, presumably due to newly emerging variants	1	1
Portrayal in the media	Interviewee talks about the media's portrayal of canine parvovirus	1	1
Excess incidence	Interviewee discusses the levels of disease/increases in case incidence that would result in a behaviour change or that would warrant a notification	7	19

Code	Description	Files	References
Relevance despite non zoonotic	Interviewee stresses how canine parvovirus is an important disease despite it not having a known zoonotic potential	7	7
Risk factors	Interviewee talks about the risk factors for canine parvovirus	4	6
Puppies	Higher prevalence in puppies	5	5
Socioeconomic status	Families' socioeconomic status	4	5
Urban areas	Dogs living in urban areas	2	2
Vaccination history	Not vaccinated, unclear history, wrong vaccination times, etc	5	8
Severity of disease	Interviewee talks about the severity of canine parvovirus	2	4

Code	Description	Files	References
Suspicion of disease	Interviewee discusses the clinical signs of canine parvovirus that would make them suspect the disease in practice	3	4
Clinical signs observed	Interviewee talks about the clinical signs of parvovirus that they have observed previously in clinical practice	4	4
Testing and vaccination	Participant discusses the testing and vaccination practices for canine parvovirus in their practice	4	7
Respiratory	The interviewee talks about any topic that is related to canine respiratory disease	7	7
Behaviour change	Interviewee describes the actions they would take to respond to an outbreak of canine disease if it were to occur in their current veterinary practice	2	2

Code	Description	Files	References
Increase awareness only	Would only consider speaking with dog owners to increase their awareness about potential signs of disease	1	1
No extra cost	Does not believe that their practice would incur in extra costs during an outbreak of respiratory disease	1	1
Not much can be done	Does not believe that many actions could be taken to respond to an outbreak of canine parvovirus	1	2
Refer cases	Would refer cases to a veterinary hospital	1	1
Wouldn't consider hiring someone extra	Does not believe that extra staff would be hired to manage the extra workload during an outbreak	1	2
Causative agents	Interviewee talks about the infectious pathogens that cause respiratory disease in dogs	5	6

Code	Description	Files	References
Usually unknown	Participant discusses how the causative agent of respiratory disease is not normally known, as no tests are performed	2	4
Certainty	Interviewee discusses the levels of confidence of an outbreak alert that they would require for a specific canine disease	6	7
Impacts of a false alarm	Interviewee discusses the potential impacts that a false alarm of the disease under discussion would have on their practice	4	5
Costs	Financial impacts of a false alarm	1	1
No impact	Does not think that a false alarm would have any impacts in their practice	2	3
Low severity	Participant believes that the severity of respiratory disease cases is low	2	2

Code	Description	Files	References
Overwhelming	Participant discusses how an outbreak of respiratory disease would overwhelm their practice	3	3
Prevalence	Interviewee talks about the prevalence of canine respiratory disease in the UK	7	10
Rarely infectious	Interviewee talks about how the causes are rarely infectious	2	2
Low prevalence (compared to GI)	Interviewee believes that the prevalence of respiratory canine disease is low, especially compared to gastrointestinal disease	2	3
Excess incidence	Interviewee discusses the levels of disease/increases in case incidence that would result in a behaviour change or that would warrant a notification	7	12

Appendix Chapter Five

Appendix V.a. Codebook with deductive and inductively generated codes used to analyse Chapter Five interview transcripts

Code	Description	Files	References
Barriers	Interviewee discusses any topic related to what they perceive as barriers for the prevention and control of canine disease outbreaks	9	9
Breeders' opinion	Opinions of dog breeders that are perceived as wrongful advice that hinders the prevention and control of canine infectious diseases	2	3
Brexit	Interviewee talks about the negative impacts that Brexit has had in their practices, which has limited their ability to handle canine infectious diseases	2	2
Costs	Economic costs of conducting preventative practices	5	7

Disease progression	Infectious diseases progress too quickly to be deemed worthy for the owners to spend money on testing and diagnosis just for the sake of the investigation	2	4
Lack of equipment	Veterinary practices lack the necessary equipment to conduct outbreak prevention practices	4	5
Lack of personnel	Veterinary practices lack the necessary available staff to conduct outbreak prevention practices	3	3
Lack of information	Veterinary practices lack the necessary information about the prevalence of canine infectious diseases to adequately conduct outbreak prevention practices	3	4
Lack of space	Veterinary practices lack the necessary facilities to conduct outbreak prevention practices	3	6
Lack of time	Veterinarians are too busy to conduct disease prevention activities	4	4
Misinformation	Wrongful information about the prevention and control of canine outbreaks that hinders veterinarian's ability to do so	3	4

Not enough or wrong testing		1	1
Owners' attitudes	Dog owners' opinions and behaviours that hinder veterinarian's ability to prevent and control outbreaks of canine disease	4	8
Antivax	Anti-vaxxer opinions and behaviours	2	2
Client communication	Issues with the communication from veterinarians to their clients	1	2
Control protocols in their practice	Participants discuss prevention/response protocols that exist in their current practices	2	2
No protocols	Interviewees mention that there are not protocols that exist in their current practices	2	3
COVID	Interviewee talks about the negative impacts that the COVID-19 pandemic has had in their practices, which has limited their ability to handle canine infectious diseases	2	3
Authorities	Interviewee discusses their negative perceptions of the existing authorities	2	3

Positive factors	Interviewee talks about factors that help during an outbreak	4	4
Referral team	Having access to a referral team of veterinarians with knowledge about infectious diseases	2	2
Network	Being part of a network of veterinary practitioners, so that they are able to exchange useful information	2	4
Large practice	Being part of a veterinary hospital, or a large practice, with access to helpful resources	1	2
Working conditions in the UK	Interviewee talks about the working conditions as a veterinary practitioner in the United Kingdom	6	7
Shortages	Existing staffing shortages	2	3
Burn out	Veterinarians being overwhelmed and suffering from burnout	4	4
Maternity leave	Employees going on maternity leave and not being substituted, thus causing more pressure on the employees of the practice	1	1

Increase in pet owners	More pet owning homes, which has resulted in more pressure on the veterinary sector	1	1
In small animal medicine, um, the simple questions haven't been answered	Direct quote	1	1
Needs	Interviewee talks about any topic related to their needs and expectations from a prospective system of surveillance and response for canine disease outbreaks	9	9
Adjustable system	That the system can be tailored to the specific needs of end-users	4	5
Advice on when and how to vaccinate	That provides advice about the vaccination of canine infectious diseases	2	3
Client communication	Requesting clients submit samples not only for the sake of their pets, but in the interest of wider surveillance	2	5
Easily accessible information	That provides information that is summarised and available at a glance	3	6

Evidence-based guidelines	That the information provided is based in scientific studies or expert opinion	2	9
Expanding system to cats	That the system of surveillance and response is expanded to include feline diseases	1	2
Expanding system to other diseases	That the system of surveillance and response is expanded to include multiple canine diseases	1	2
Funds for testing	That the responsible authorities provide specific funding dedicated for testing, so that the cost of testing is not an obstacle for disease surveillance	5	6
Info about leptospirosis	That provides information specifically related to canine leptospirosis, and its immunity, vaccination, treatment etc.	2	6
Information about origin of exotic diseases	That provides information specifically related to exotic diseases, and where the observed cases during an outbreak originated from, e.g., imported from another country	3	6
Information about emerging diseases	That provides information specifically related to emerging diseases of unknown causative agent	3	5

Investigation of syndromic outbreaks	The response system should include the investigation of the causative agent(s) behind an anomaly detected through syndromic surveillance	3	8
Knowing who to contact	The system should provide information on who to contact, should veterinary practitioners suspect that there is an outbreak of canine disease	5	5
Not a lot can be done to help	Interviewee believes that a prospective system of surveillance and response would not be able to contribute much to the prevention and control of canine infectious diseases	1	1
Online platform	The system of surveillance and response should include an online platform that is available to end-users	8	9
Centralised information hub	With clear-cut information, not too much detail, that considers the characteristics of different practices and gives options for those cases where the gold standard is not possible due to space or financial constraints	4	6

To compare experiences	That the online platform provides a space, e.g., a forum, so that veterinary practitioners can communicate and exchange information about canine outbreaks	2	2
Reporting system	The system should also incorporate a system of reporting, so that veterinarians can report anomalies that they observe in practice	5	11
Stricter guidelines for importation	Participant believes that a future system of surveillance and response should also include policy changes so that the rules for the importation of dogs are more strict, to prevent the importation of exotic diseases	2	3
To include also high suspicion of diseases	Especially for those that are difficult to reach a definitive diagnosis for and that are suspected to be underdiagnosed (e.g., leptospirosis)	1	1
Uniform biosecurity protocols	The system should promote biosecurity protocols that offer uniform standards of application across the country	3	3
Information sources for veterinarians	Interviewee talks about the current sources of data that are available for veterinary practitioners about canine infectious diseases	3	4

Experience with SAVSNET data collection	Participant whose practice contributed data to SAVSNET talks about their experience	1	1

Appendix: List of publications and presentations

Publications in peer reviewed journals

Publications included in this thesis

Chapter Two

Tamayo Cuartero C, Radford AD, Szilassy E, Newton JR, Sánchez-Vizcaíno F (2023). Stakeholder opinion-led study to identify canine priority diseases for surveillance and control in the UK. *Veterinary Record,* e3167. doi: 10.1002/vetr.3167. Epub ahead of print. PMID: 37415378. https://pubmed.ncbi.nlm.nih.gov/37415378/

Chapter Four

Tamayo Cuartero C, Radford AD, Szilassy E, Newton JR, Sánchez-Vizcaíno F. Setting clinically relevant thresholds for notification of canine disease outbreaks to veterinary practitioners: an exploratory qualitative interview study. Submitted to *Frontiers in Veterinary Science* on July 14th 2023. *Status: under review (minor comments from reviewer 1 received on October 27th 2023).* Preprint available at https://doi.org/10.22541/au.169843066.69018962/v1

Publications related to this thesis

Chapter Five

Radford AD, Singleton DA, Jewell C, Appleton C, Rowlingson B, Hale AC, Cuartero CT, Newton R, Sánchez-Vizcaíno F, Greenberg D, Brant B, Bentley EG, Stewart JP, Smith S, Haldenby S, Noble PM, Pinchbeck GL (2021). Outbreak of Severe Vomiting in Dogs Associated with a Canine Enteric Coronavirus, United Kingdom. *Emerging Infectious Diseases*, 27(2), 517–528. doi: 10.3201/eid2702.202452. PMID: 33496240; PMCID: PMC7853541. https://pubmed.ncbi.nlm.nih.gov/33496240/

Other publications

Tamayo Cuartero C. (2021) Prolific vomiting outbreak in UK dogs. *BSAVA Companion*, 17–19.

Presentations given at international conferences

Tamayo Cuartero C. (August 2022) Establishing clinically relevant threshold of outbreak notification to veterinary clinicians. Oral presentation at the 16th International Symposium of Veterinary Epidemiology and Economics.

Tamayo Cuartero C. (March 2022) Establishing clinically relevant threshold of outbreak notification to veterinary clinicians. Poster presentation at the 40th Symposium of Veterinary Epidemiology and Preventive Medicine.

Tamayo Cuartero C. (August 2022) Prioritisation of canine infectious diseases for surveillance and control. Poster presentation at the 16th International Symposium of Veterinary Epidemiology and Economics.

Tamayo Cuartero C. (March 2021) Prioritisation of canine infectious diseases for surveillance and control. Poster presentation at the 39th Symposium of Veterinary Epidemiology and Preventive Medicine.