Qualitative risk assessment in animal health: past principles and future directions

PhD Thesis

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October 2025

Declaration

This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination which has led to the award of a degree.

Abstract

Risk assessment (RA) is concerned with the systematic compilation of data/evidence related to an unwanted risk, with the objective of providing an evidence base for risk management decisions. This thesis set out to evaluate how the use of qualitative RA has developed in the animal health sphere since the 1990s for purposes such as assessing the probability of disease introduction via global trade and veterinary RAs which can form part of a national exotic disease outbreak response. Compared to quantitative RA the field of qualitative is less well developed and this thesis aimed to expand the area by reviewing how qualitative RA has been used in the past including what the general difficulties were with its application. Specific issues were then addressed in assessments developed to expand existing literature and a method was proposed to address one of these issues, namely, uncertainty.

Qualitative RAs use non-numerical terms to describe and communicate levels of risk and uncertainty, such as, high, medium and low. Therefore, to avoid concluding different estimates of risk from the same evidence it is important to standardise qualitative RA methodology for consistency by utilising a common set of methods and technologies. Demonstration of how the results were obtained using these methods, is additionally as valuable as the results themselves to ensure that misinterpretation by the risk manager is avoided.

This thesis has contributed to the field of qualitative RA by identifying areas within a RA that can be standardised to ensure transparency of results. It has also pinpointed some topics that can be further developed and proposed a method for addressing uncertainty within qualitative RA. The conclusions from this thesis emphasise that qualitative RA plays an important role in animal health and that efforts to develop methodology should not detract from its usefulness in transparently communicating results.

Publications associated with this research

List of additional papers co-authored by the author throughout duration of thesis and relating to the application of risk assessment to animal health (2018 to 2025):

- Marques ARP, Gonzalez Villeta L, Simons R, **Horigan V**, de Vos C and Conrady B (2025) Quantitative risk assessment for infectious disease introduction in animal populations: a comprehensive review. Front. Vet. Sci. 12:1648695. doi: 10.3389/fvets.2025.1648695

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Acknowledgements

I would like to thank Dr Robin Simons, Dr Louise Kelly and Dr Kim Kavanagh for their supervision and support. Additionally, I would like to acknowledge Dr Emma Snary for her constructive comments on the literature review presented in Chapter 2 and all the co-authors of the work contributing to this thesis for their collaboration and expertise.

Thank you also to the University of Strathclyde for funding this PhD, the Animal and Plant Health Agency for funding the projects presented in Chapters 3 and 5 and for the publication costs for the literature review paper presented in Chapter 2, and lastly the Poultry Health and Welfare group for funding the work reported in Chapter 4.

Finally, I would like to thank my family and friends for being there throughout the duration.

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Chapter 1: Introduction

1.1 Background and aims

Risk is defined as the probability that a particular adverse event occurs during a stated period of time, or results from a particular challenge, and the impact of the event occurring (Adams 1995). Assessing risk is a subconscious process that we undertake in everyday living in response to a risk question we might ask ourselves e.g. is it safe to cross the road now? Should I eat the ham that's one day past its use by date? Our responses to these questions are based on intuitive risk assessments (RA) and provide a rough, but useful, estimate of risk based on our available knowledge at the time. We progressively refine our risk-taking skills in everyday life by coping with the uncertainty of events either through prior experience or by trial-and-error processes. In this way 'everyone is a true risk expert in the original sense of the word' (Adams 1995).

The formal application of RAs as a systematic process of evaluating risks in a projected activity, originally arose out of a quest to understand the risk of equipment failure in the aerospace industry and subsequently became commonly used in other fields such as financial management, engineering and insurance (Osborne *et al.,* 1995). These RAs work in the same was as our subconscious everyday assessments, in that the outcome of something which is currently unknown is assessed using available information that is relevant to the risk question. The primary objective is also similar to our subconscious everyday RAs, that is, to identify critical control points and to support decision making processes.

Since the 1990s, RA has become a powerful tool in animal and public health, for example, import RAs which assess the probability of disease introduction via global trade of livestock or animal products (e.g. Faverjon *et al*., 2015; Herrera-Ibatá *et al.,* 2017), microbial risk assessments, and/or farm-to-consumption RAs, which explore human exposure to a defined hazard under a food safety scenario (e.g. Nauta *et al*., 2005; Snary *et al*., 2016), and rapid veterinary RAs which can form part of a national

disease outbreak response. The latter are often commissioned by the Government of an individual country to provide evidence that enables policy makers to offer guidance on control strategies during an animal disease outbreak. Risk assessments, therefore, perform the role of decision-making tools to assist risk managers or decision makers in the selection and application of the most efficient risk mitigation measures (Corbellini *et al.,* 2010).

Risk assessment for animal health is one element of the risk analysis process along with risk management and risk communication. It is concerned with the systematic compilation of data/evidence related to an unwanted event, with the objective of providing an evidence base for risk management decisions (Stark *et al.,* 2002). The main stages of an animal health RA include: 1) identification of the hazard, 2) defining the risk question, 3) outlining the steps of the risk pathway, 4) gathering data and information, 5) identifying uncertainty and variability, 6) combining the information in a logical manner, and ensuring the assessment is transparent and easy to understand with sound and reproducible methodology. This enables the decision maker to comprehend the basis of the assessment and its strengths and limitations allowing them to question or provide additional knowledge to improve the assessment if necessary.

Animal health RAs are frequently conducted to address a risk question which is formulated as a result of the requirement for animal health policy. The World Organisation for Animal Health (WOAH) has a recognised framework for RA based on a model that distinguishes between release (now referred to as entry), exposure and consequence assessment (WOAH 2024). This framework estimates the probability of a hazard being introduced through to the consequences of exposure of a susceptible population to the hazard in terms of health, welfare, economy etc. (WOAH 2024). For each of these, a detailed risk pathway outlining the steps leading to the unwanted event is developed which allows the risk manager to follow the conclusions of the risk assessors and to identify where the main risks and/or uncertainties lie (Wieland *et*

al., 2011). Consistency in RA methods is encouraged by WOAH, particularly when considering those used for government decision making which may impact global trade (WOAH 2024). Trade deals between individual countries are fluid and subject to continual change/re-evaluation with regards to types and volumes of products over time. As such, RA can be an important factor in determining acceptance of risk levels of such imports. However, despite the WOAH recommendation for consistency in methods, a comparison of veterinary import RAs found that methods used were heterogeneous in terms of methodology and completeness with RAs that were classified as adhering to the WOAH guidelines being no more rigorous than those that did not (de Vos *et al*., 2011).

Risk Assessments can be carried out using two general approaches, termed qualitative and quantitative. Qualitative RAs use non-numerical terms to communicate or describe levels of risk, such as, high, medium, low or negligible whilst quantitative assessments use mathematical and statistical models to express risks numerically e.g. number of cases in one year, number of years before an event occurs. Using the previously mentioned example of the risk question of 'when is it safe to cross the road', we would assess the risk qualitatively by roughly assessing the likelihood of a car reaching us and knocking us over, using estimates of how far away the car is and how fast it appears to be travelling. If we had more time or information, then we might be able to conduct a quantitative RA and calculate 'I know that x% of people travel at 10mph over the speed limit, the car is 100m away from me and it will take me 10 seconds to cross the road therefore it gives me a 1: xxx chance that I might get knocked over'. Qualitative RAs are therefore often used as an initial screening method to give a rapid result in situations when rapid decisions are required or in cases where resources or data of sufficient quantity or quality are limited (Dufour *et al.*,2011).

An example of how a qualitative RA can inform risk management decisions, even with incomplete information, is the geographical Bovine Spongiform Encephalopathy

(BSE) RA (Salman *et al.,* 2012). In 1986 the first case of BSE occurred in the United Kingdom (UK), before later being detected in many other European Union (EU) countries. The geographical BSE RA formed the basis of the EU's risk management decisions and trade-related measures to prevent the (re-)introduction of the BSE agent and protect animal and human health. When first applied to countries, that at that time had not reported any BSE cases, the RA results sometimes predicted the presence of BSE cases and were strongly contested by these countries. As a result, active surveillance was undertaken that led to the detection of a BSE positive animal in some of these countries, confirming the RA's estimations. The critical element was that the RA provided a consistent and pre-defined framework into which all available information could be integrated and be complemented by assumptions and estimates where necessary (Salman *et al.,* 2012).

Qualitative RAs have become an integral part of animal health trade agreements and are frequently used in disease outbreak situations providing evidence for urgent policy decisions. Conducting a short qualitative RA can also provide useful insights into the feasibility of a conducting larger scale quantitative RA, e.g. clarifying the risk pathway and assessing the availability of data. Important criteria for a successful qualitative RA include transparency and objectivity and for the RA to be well documented. In instances where a qualitative RA may contain subjective judgement it is essential to clearly define when such a judgement has been used. A description of uncertainties and assumptions made, and the effect of these on the final risk estimate should also be recognised (de Vos *et al*., 2011).

Compared to a quantitative RA model the lack of mathematical rigour in a qualitative RA can, to some extent, weaken the robustness of the outcomes. One of the main challenges when conducting qualitative RAs is adhering to the rule of probabilities when probabilities are nonnumerical and undertaking what would be a mathematical operation in a quantitative RA using words instead (Crotta *et al.,* 2024). Several semi-quantitative tools have been created which have applied a mathematical context to

the qualitative RA framework. This does not make them quantitative RAs *per se*, as data are not being used to give a numerical outcome, rather the mathematical theory is applied to substantiate the results which are expressed in qualitative terms (Kyyrö *et al.*, 2017; de Vos *et al.,* 2021). Other developments in which quantitative methods have been applied to qualitative RAs include a contour plot for calculating the aggregated probability based on the likelihood of risk associated with one product and the number of products considered (Kelly *et al.,* 2018). A recently published pairwise summation as a method for the additive combination of probabilities in qualitative RAs has also been proposed as a method for situations where the probability of an event occurring can increase as the result of different and independent pathways contributing to one risk outcome (Crotta *et al.,* 2024).

Qualitative RAs therefore need to be as reproducible and standardised as possible so they can provide a reliable evidence base upon which the risk manager can base appropriate decisions. This thesis sets out to evaluate how the use of qualitative RA has developed in the animal health sphere since the 1990s and explores the evolution of the application of qualitative RA to animal health including problems which have been addressed throughout the years and those that may still persist to be dealt with in the future.

1.2 Thesis structure

The work in this thesis is presented as a series of papers which have been published (or been prepared for submission) in peer reviewed journals and which explore the use of qualitative RAs in a range of scenarios in the animal health field to address the research question:

"*To what extent has qualitative risk assessment methodology developed in the sphere of animal health policy and how can it further advance in the future?* "

The thesis set out to evaluate how the use of qualitative RA has progressed in the animal health domain since the 1990s, starting with a review of relevant literature with the aim of identifying how methods have developed, including any standardization of methodologies and highlighting those areas which still require development to increase the value of qualitative RA (Chapter 2). Whilst the overall methodology used in Chapters 3, 4 and 5 is based on the WOAH risk analysis framework (WOAH 2024), all three Chapters demonstrate different applications of the methodological approaches for specific parts of the qualitative RA process, specifically the risk matrix approach, incorporation of dose response and aggregated probability, respectively. These three Chapters demonstrate how these components of qualitative RA can be used in the setting of animal health control policy and contribute to the standardised approach of methodology in this field. Chapters 4 and 5 also assess specific issues and expand the application of incorporating consideration of the level of pathogen at each step of the risk pathway and accounting for the volume of units being assessed which can enhance a qualitative RA by removing potential under-estimation of the risk.

Chapter 3 considers the entry and exposure of an exotic disease into the United Kingdom (UK) using risk pathways and the risk matrix approach of combining pathway steps to conclude an overall risk of both entry, exposure and combining the two for an overall risk estimate. Chapter 4 further develops the WOAH qualitative RA approach by applying it to cleansing and disinfection of individual items of equipment

after an avian influenza outbreak and considers how the viral load differs throughout the risk pathway in addition to the likelihood of virus being present.

Prior to the work in Chapter 5 being carried out, a paper describing the use of aggregated probability (Kelly *et al.,* 2018) was published and Chapter 5 demonstrates the use of this methodology in an import RA where the risk of entry of a pathogen for an individual unit (for example, animal or product) is assessed in combination with the volume of units entering to give an aggregated probability. The work in this Chapter therefore uses up to date RA methodology in a real-world situation to emphasise the importance of considering the effect of the volume of any product/ live animals entering a country on the conclusions of a risk pathway.

The final Chapter (Chapter 6) critically highlights the key area of communicating the effect of uncertainty on the risk estimate in a qualitative animal health RA and compares different approaches used to illustrate this in addition to proposing a novel method of assessing uncertainty. The value of the different methods used is described and explored, highlighting how consideration of the effect of uncertainty on the risk estimate of each pathway step could persuade a risk manager to explore different options in their decision making for animal health policy. This final Chapter uses examples of risk pathways from Chapters 3 and 5 to contribute to the discussion on how uncertainty is communicated to the risk manager to ensure that the most risk appropriate decisions are made.

Whilst the original versions of the published papers are detailed in the following Chapters, further discussion during the PhD viva has resulted in a few amendments which have been added to the thesis, and which will therefore differ to the published versions. These amendments are considered to have improved the clarity of terminology and/or understanding of concepts described in the papers.

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Chapter 2: A review of qualitative risk assessment in animal health: suggestions for best practice

2.1 Authorship and funding statement

The development of the methodology and the analysis of the evidence and review of literature was my own work. Dr Robin Simons, Dr Kim Kavanagh and Dr Louise Kelly contributed to this work by reviewing and providing expert knowledge. Dr Emma Snary also provided constructive comments on the Chapter. The publication cost of the manuscript was funded by the Animal and Plant Health Agency.

2.2 Summary of the published paper

The published paper in this chapter reviews the application of qualitative RA in animal health and was published in Frontiers in Veterinary Science journal February 2023 https://www.frontiersin.org/articles/10.3389/fvets.2023.1102131/full. Conducting a literature review on the application of qualitative RA in animal health was the first step in addressing the research question: "*To what extent has qualitative risk assessment methodology developed in the sphere of animal health policy and how can it further advance in the future?*" as it explored which elements of qualitative RA had been previously utilised and published with relevance to animal health. The search terms "*Qualitative* and *risk* and *assessment* and *animal* and *health*" in the "title, keyword or abstract" were used to search both the Scopus and PubMed databases, returning 56 papers for review after all the specified criteria had been met. The work identified, and described, how the authors of the reviewed manuscripts had addressed five themes of qualitative RA: the description of risk levels; uncertainty; combining probabilities; dose response and accounting for trade volume and time period (aggregated probability). Methodology to standardise some of these elements had been proposed although this varied between authors.

Additionally, several semi-quantitative tools were described which had been developed to improve the objectivity of the qualitative RA framework. They also allowed for an overall risk level that can be lower than any individual step within a risk pathway reducing the likelihood of over-estimation which can occur if using some of the risk matrix methods described in the paper. Some of these tools operate by the risk assessor

inputting qualitative descriptive terms for the risk estimates into the model for each step of the risk pathway. These terms are then converted to numerical values within the model for the model parameters resulting in a numerical output which is finally converted back to a qualitative term for use by the risk assessor (Kyyrö *et al.,* 2017; de Vos *et al.,* 2021). Several of the tools also incorporate uncertainty at each step of the risk pathway by using probability distributions deemed appropriate for representing the input parameters (Biosecurity 2001; de Vos *et al.,* 2021).

The papers selected for review included both reviews of qualitative RA and case studies with several of the early reviews noting that for qualitative RA to fulfil its purpose it is necessary to have a common set of methods and technologies to avoid concluding different estimates of risk from the same evidence (Peeler *et al.,* 2007). Of note, this work did highlight that qualitative RAs which are used by governments for rapid policy decisions may be less likely to be published in peer reviewed journals and therefore not captured on the PubMed and Scopus search engines.

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2.3 Full text of the published paper

A review of qualitative risk assessment in animal health: suggestions for best practice

Verity Horigan, Robin Simons, Kim Kavanagh, Louise Kelly

Abstract

Qualitative risk assessment (QRA) can provide decision support in line with the requirement for an objective, unbiased assessment of disease according to the Agreement on the Application of Sanitary and Phytosanitary Measures of the World Trade Organisation. However, in order for a QRA to be objective and consistently applied it is necessary to standardise the approach as much as possible. This review considers how QRAs have historically been used for the benefit of animal health, what problems have been encountered during their progression, and considers best practice for their future use.

Four main elements were identified as having been the subject of some proposed standard methodology: (i) the description of risk levels, (ii) combining probabilities, (iii) accounting for trade volume and time period and (iv) uncertainty. These elements were addressed in different ways but were highlighted as being fundamental to improving the robustness in estimating the risk and conveying the results to the risk manager with minimal ambiguity. In line with this, several tools have been developed which attempt to use mathematical reasoning to incorporate uncertainty and improve the objectivity of the qualitative framework. This represents an important advance in animal health QRA.

Overall, animal health QRAs have established their usefulness by providing a tool for rapid risk estimation which can be used to identify important chains of events and critical control points along risk pathways and inform risk management programmes as to whether or not the risk exceeds a decision-making threshold above which action should be taken. Ensuring a robust objective methodology is used and that the reasons for differences in results, such as assumptions and uncertainty are clearly described to the customer with minimal ambiguity is essential to maintain confidence in the QRA process. However, further work needs to be done to determine if one objective uniform

methodology should be developed and considered best practice. To this end, a set of best practice guidelines presenting the optimal way to conduct a QRA and regulated by bodies such as the World Organisation for Animal Health or the European Food Safety Authority would be beneficial.

Introduction

Risk assessment (RA) is one of the fundamental elements of the risk analysis process alongside hazard identification, risk management and risk communication. It is concerned with the systematic compilation of data/evidence related to an unwanted event, with the objective of providing an evidence base for risk management decisions on how to best mitigate against such an event (Stark *et al.,* 2002). Since the 1990s, RA has become a useful tool in animal health, for example, import RAs which assess the likelihood of disease introduction via international trade of livestock or animal products (e.g. Faverjon *et al.,* 2015; Herrera-Ibatá *et al.,* 2017). The development of such RAs was driven by the need for an objective, unbiased assessment of disease risk in line with the Agreement on the Application of Sanitary and Phytosanitary (SPS) Measures of the World Trade Organisation (WTO). Under this agreement all WTO members were required to ensure that their SPS measures were based on an assessment of the risks to human, animal or plant health taking into account available scientific evidence and using RA methods developed by the World Organisation for Animal Health (WOAH, previously OIE). The agreement could thus facilitate trade whilst recognising that trade cannot be risk free and enable common judgements about the level of risk mitigating measures required. Other uses include microbial risk assessments (MRAs) and/or farm-to-consumption RAs, (e.g. Nauta *et al.,* 2005; Snary *et al.,* 2016), and rapid veterinary RAs (VRAs), which can form part of a national disease outbreak response. Risk assessments can also perform the role of decision support tools to assist decision makers in the selection and application of the most efficient control and risk mitigation measures during an animal disease outbreak (Corbellini *et al.,* 2012; Squarzoni-Diaw *et al.,* 2020).

The WOAH RA framework is based on a model that distinguishes between entry, exposure and consequence assessments (WOAH 2013). For each assessment the main stages typically include: 1) defining the risk question, 2) outlining the steps of the risk

pathway, 3) gathering data and information, 4) identifying uncertainty and variability, 5) combining the information in a logical manner and 6) ensuring the assessment is fully referenced and transparent with reproducible methodology (WOAH 2013). Structuring a RA in this way enables the decision maker to understand the basis of the assessment, its strengths and limitations and allows them to question or provide additional knowledge to improve the assessment (Wieland *et al.,* 2011). Consistency in methods is encouraged by the WOAH, in order to allow for comparison, especially when considering those used for Government decision making (WOAH 2013).

Risk Assessments can be carried out using two general approaches, termed qualitative and quantitative. Qualitative RAs use non-numerical terms to communicate or describe levels of risk, such as, high, medium, low or negligible, whilst quantitative assessments use mathematical calculations to express risks numerically e.g. a risk will occur once every 500 years. Qualitative RAs are often used as an initial screening method to determine the feasibility, needs and data requirements for quantitative RAs. They may also be used in cases where data of sufficient quantity or quality are limited, as they are less demanding in terms of resources and data (Dufour *et al.,* 2011). In situations when rapid decisions are required, such as in an outbreak situation, the speed of conducting a qualitative RA compared to a quantitative counterpart can also be advantageous (Cabral *et al*.,2019).

This literature review was conducted to evaluate how the use of qualitative RA has progressed in the animal health sphere since the 1990s, by assessing relevant literature, including both reviews and specific case studies. The aim was to identify how methods employed by risk assessors have developed, recognise any standardisation of methodologies which have occurred and highlight those areas which still require development to increase the value of qualitative RA.

Methods

A literature search was conducted in September 2022 in both Scopus (www.scopus.com) and PubMed (www.ncbi.nlm.nih.gov/pubmed) using the search terms “Qualitative and risk and assessment and animal and health” in the “title, keyword or abstract”. No date

range was specified to capture as many articles as possible acknowledging that the field is relatively new. Articles were screened and selected using the exclusion criteria as shown in Fig 1. Initially, any duplicate articles were removed; articles were subsequently included if they were: in English, described qualitative RA and pertained to animal health.

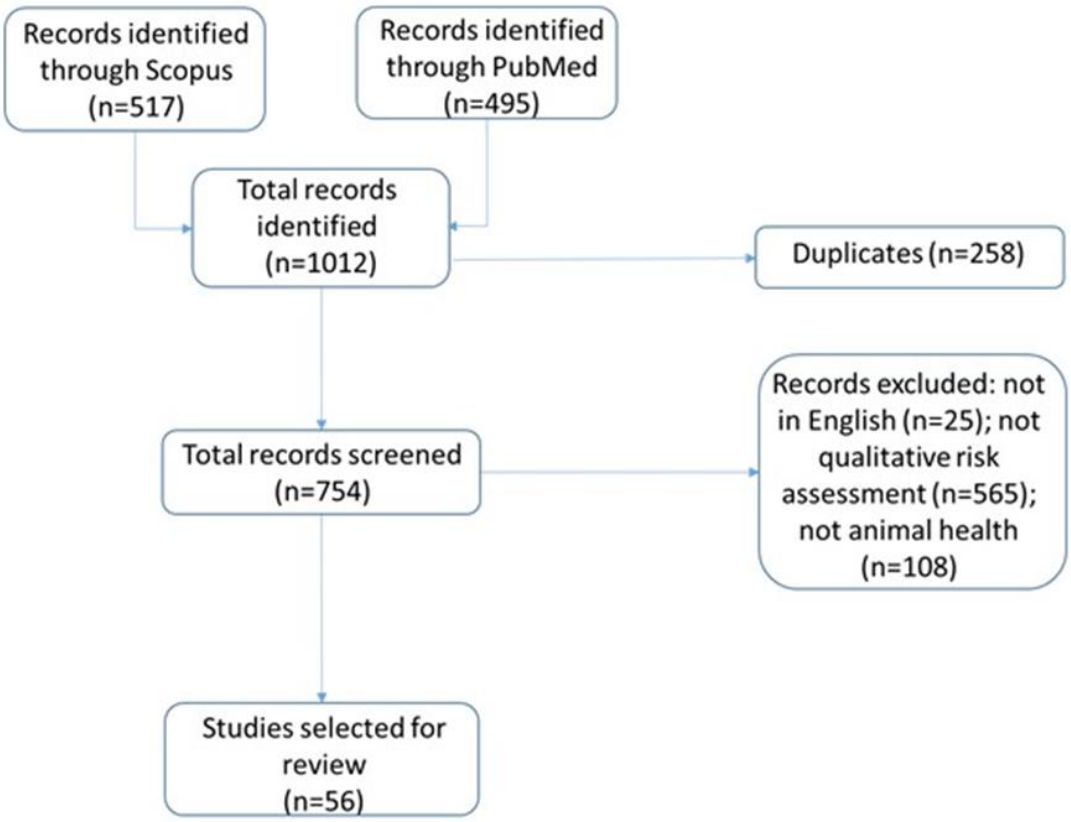

Fig 1. Flow diagram of the decision process and exclusion criteria

It is acknowledged that no set of search terms will be able to capture all RA articles and that there will inevitably be some that would not have been captured here. Nevertheless, the search terms used were considered optimal as they were found to give the most comprehensive results. It is also acknowledged that the focus on published QRAs is a limiting factor as they are often used by governments for policy decisions and may therefore be less likely to result in publications. Articles concerning risk factors, used to define an 'at risk' population, risk management, risk prioritisation or risk ranking

were excluded. Similarly, animal health was taken as meaning "a pathogen affecting animal health which may result in the importation or transmission of disease via either livestock (including fish) or animal/fish products". Articles referring to food safety risk assessments from a public health perspective were therefore excluded.

Results

After reviewing the titles and abstracts, 56 articles meeting the inclusion criteria were selected; both reviews (n=15) and case studies (n=41) were included (see Appendix for full details). The earliest article selected was from 1993, prior to that year the search results were mostly regarding the application of animal experiment results to human cancer RAs, i.e., they were not concerning animal health *per se*.

Out of all the papers reviewed, 25% (n=14) dealt with entry only, i.e. the probability of introduction of a hazard, 7.1% (n=4) covered both entry and exposure and 41.1% (n=23) covered entry, exposure and consequence. A further 26.8% (n=15) were reviews or described a RA tool. The number and scope of the selected articles over time can be seen in Fig 2.

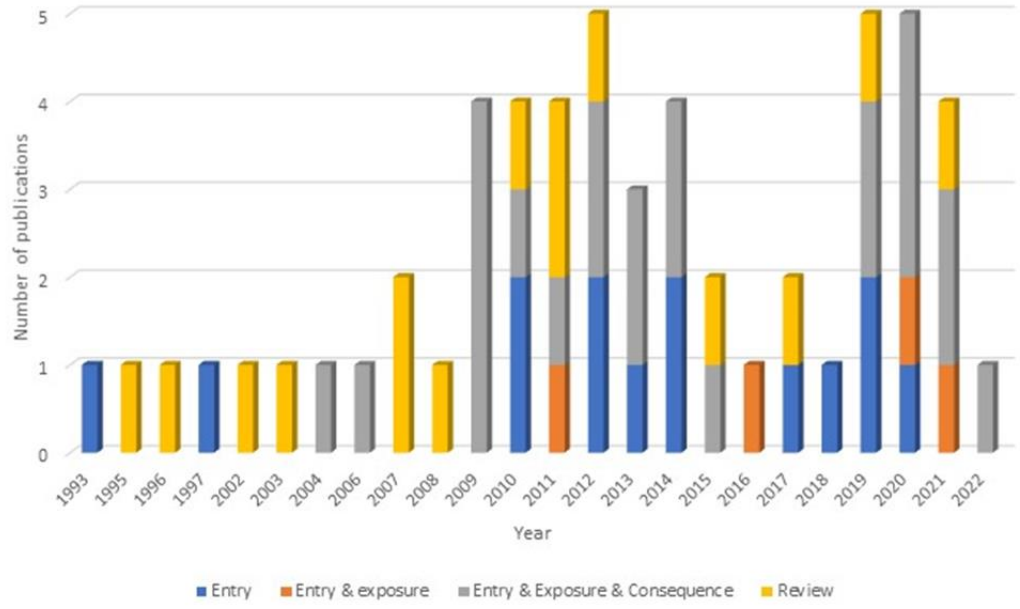

Fig 2. The number and scope of qualitative risk assessments resulting from the search criteria by year

Several of the earliest articles selected were reviews describing the evolution of the qualitative RA process, or elements of it with fundamentals such as defined terminology still under discussion (Osborne *et al.,* 1995; Ahl 1996). It was noted even in its infancy, however, that for qualitative RA to fulfil its purpose it is necessary to have a common set of methods and technologies. If different methods are used it is possible that disparate risk estimates may be concluded from the same evidence (Osborne *et al.*, 1995).

There were six themes identified from this review as being fundamental to the operation of a robust qualitative RA that are described in detail in the following sections. The first theme was how to communicate the meaning of the terms describing the probability of occurrence at each step of the risk pathway in a standard manner. Secondly, was how to combine these probability terms to give an overall estimate of risk. Another topic highlighted was how to address the uncertainty associated with the probability estimates of the risk pathway steps. In particular, how to derive an overall uncertainty level, and how to make the influence uncertainty can have on the overall risk estimate clear to the decision maker. The topics of dose response and accounting for multiple products/animals (aggregated probability) were discussed by only a limited number of articles (n=11) but are important aspects of risk and are highlighted here as topics for future consideration. Finally, four articles discussed the use of semi-quantitative tools which have been developed to convert the descriptive terms in qualitative RA pathways into numerical values.

Description of terms – definition of risk levels

In a qualitative RA the level of risk is communicated to the decision maker, or risk manager, by assigning a certain number of descriptive risk levels with associated definitions. The terms need to be well defined, and it is important to interpret individual qualitative RA results in light of whatever specific categorical definitions are used (Peeler *et al.,* 2007; Heller *et al.,* 2010). For example, an overall risk estimate of “low” can be meaningless to a risk manager without some sort of indication of what this definition constitutes in the eyes of the author of the risk assessment (EFSA 2012).

The definitions of the different risk levels varied in the articles reviewed here (Table 1); the most commonly used were those defined by the European Food Safety Authority (EFSA) (EFSA 2006). The number of levels used ranged from 4 to 7 with all articles using the levels “negligible”, “low”, “medium” and “high” and only some using “extremely low”, “very low” and “very high”. Whilst the EFSA (2006) definitions were predominantly used, it was noted that some of the examples relate to the frequency of repeated events or outcomes (e.g. often, regularly) and some to the likelihood of a single event or outcome (EFSA 2012). Additionally, although the term ‘negligible’ is commonly used in the risk assessment terminology, it can be perceived as having a risk management connotation in everyday language. Clarification may therefore be needed avoid the impression that risk assessors are making risk management judgments (EFSA 2012).

Table 1. Summary of the definitions of qualitative risk/probability levels used/defined in the papers selected through the literature review.

Original Definitions first published	(Kahn *et al*., 1999)	(Zepeda 1998)	(Moutou *et al*., 2001)	(WOAH 2004)	(Wieland *et al.*, 2011)	(EFSA 2006)	(WOAH 1999)	(Roche *et al.,* 2015)	(Biosecurity 2009)
Subsequently used in these risk assessments	(Peeler *et al*., 2007; 2009; Pearce *et al*., 2014; Crotta *et al.,* 2016)	(Jori *et al.,* 2009; Chazya *et al.,* 2014)	(Heller *et al*., 2010; Babayani *et al.*, 2022)	(Paton *et al*., 2010)	(Wieland *et al.*, 2011)	(Auty et al., 2019; Common et al., 2021; Snary et al., 2012; Alemayehu et al., 2012; Hill et al., 2013; Hill et al., 2014; Gale et al., 2014; Wieland et al., 2015; Coultous et al., 2022; Friker et al., 2021)	(Corbellini *et al.,* 2012)	(Rinchen *et al*., 2020)	(Peeler *et al.,* 2015)
Very high	Almost **certain** to occur					Event occurs almost at **certainly**			
High	Expected to occur	Occurrence of the event is clearly a possibility (probable)	When exposure or transmission is likely to occur	Extending above the normal of average level	Occurrence of event is clearly a possibility	Occurs (very) often	An event is almost certain to occur	Likelihood of an event occurring is very often	The event would be very likely to occur
Moderate	Less than 50:50 probability	Occurrence of the event is a possibility (in the majority of cases)	When exposure or transmission may occur in all cases	The usual amount, extent, rate	Occurrence of event is a possibility	Occurs regularly	An event is likely to occur with a high probability	Likelihood of an event occurring is regular	The event would occur with an even probability
Low	Unlikely to occur	Occurrence of an event is a possibility in some (a minority of) cases	When exposure or transmission may occur in some cases	Less than average, coming below the normal level	Occurrence of event is a possibility in some cases	Rare but could occur	An event is unlikely to occur	Likelihood of an event occurring is occasional	The event would be unlikely to occur
Very low	Rarely occur					(very) Rare but cannot be excluded	An event is very unlikely to occur	Likelihood of an event occurring is rare but does occur	The event would be very unlikely to occur

Extremely low	Very rarely occur							Likelihood of an event occurring is extremely rare but cannot be excluded	The event would be extremely unlikely to occur
Negligible	Chance of occurrence so small it can be ignored	Probability of occurrence of the event is possible only in exceptional circumstances (or sufficiently low to be ignored)	When the probability of exposure or transmission is sufficiently low to be ignored, or if the event is possible only in exceptional circumstances	Not worth considering; insignificant	Probability of event sufficiently low to be ignored or event only possible in exceptional circumstances	So rare that it does not merit consideration	An event virtually would not occur	Likelihood of an event occurring is so rare that it does not merit consideration	The event would almost certainly not occur

Several articles drew attention to the clustering of risk at the lower end of the descriptive scale and the potential benefit of the inclusion of additional levels to extend the range of adjectives used for the lower probabilities in order to provide greater detail (Dufour *et al.,* 2011; Heller *et al.,* 2010). One article suggested the use of a ten-point ordinal scale with corresponding adjectives such as 'null', 'nearly null', 'minute', 'extremely low' etc. However, because of the difficulty of gaining universal agreement on specific definitions of the words, it proved challenging to define each word precisely (Dufour *et al.,* 2011). Another complication highlighted was that differentiating between 'low', 'very low' and 'extremely low' in these circumstances may be considered arbitrary and as such, add a further level of uncertainty to the RA (Heller *et al.,* 2010).

Analysis of 219 EFSA Opinions revealed that RA terminology is not fully harmonised within EFSA. An Opinion is structured in accordance with 'EFSA's guidance for the drafting of scientific opinions' and consists of a risk assessment or an evaluation of a risk assessment conducted by a Scientific Panel comprised of an independent group of experts. The lack of harmonisation was caused, in part, by sectoral legislation defining specific terminology and international standards for specific fields of RA and thus for specific Opinions (EFSA 2012). In order to reduce ambiguity, EFSA recommended that Scientific Panels should, wherever possible, work towards quantitative expression of the probability of the adverse effect and of any quantitative descriptors of that effect (e.g. duration). For example, in a United Kingdom (UK) Non-native Organism RA, likelihood levels for entry and establishment were defined for events over a 5 year period using the following quantitative terms (Table 2).

Table 2. UK Non-native Organism Risk Assessment scheme likelihood descriptors for entry and establishment (Peel *et al.,* 2012).

Likelihood levels	Chance of occurrence over a 5 year period
Very unlikely	<10% chance of occurring
Unlikely	10-33% chance of occurring
Moderately likely	33-66% chance of occurring
Likely	66-90% chance of occurring
Very likely	>90% chance of occurring

Suggested best practice: Harmonised and consistent use of one set of definitions e.g. EFSA (EFSA 2006). The clustering of risk at the lower end of the scale requires further development.

Combining Probabilities

The majority of the risk pathways described in the articles reviewed, were designed as a series of multiplicative conditional probabilities i.e. each step in the pathway has to occur in order for the next step to be possible. As such, the likelihood level for each step of the pathway is independent of the previous step and combining these levels cannot lead to an increase in risk. However, there was not always transparency on how the probabilities of the events were combined.

There is not a universally recognised standard methodology to combine the probabilities of each step of a risk pathway, or across the risk assessments steps (entry, exposure and consequence), to produce and communicate an overall estimate. As such, it was not surprising to find that the articles reviewed used different methods. One way of visually demonstrating how to combine risk levels is by using risk matrices, which have previously been used in RA to combine the probability and impact of an event occurring to give the overall risk level (see (Cox 2008) for an overview). Matrices provide a transparent methodology for combining risk levels and help decision-makers to focus on the highest priority risks. However, the approach doesn't always account for all considerations in more complex assessments, such as the volume of a product being imported or issues around combining a large number of probabilities using the same matrix. As such, it has been suggested that they should only be used to illustrate results rather than as calculators of likelihood or risk (Peeler *et al.,* 2015).

Published matrices using a multiplicative risk framework varied in the RAs reviewed here. One of the most commonly used adheres to the principle that the product of two probabilities is always equal to the lowest probability (Table 3) (Corbellini *et al.,* 2012; Wieland *et al.,* 2011; Babayani *et al.,* 2022; Coultous *et al.,* 2022; Rinchen *et al.,* 2020; Peeler *et al.,* 2004). This matrix defines a likelihood estimate for any binary combination

of conditional events but does not allow for the product of multiple conditional probabilities to be lower than the lowest value of the individual probabilities.

Table 3. When combining two probabilities, the resulting probability is not greater than the lower probability scale of the two (Rinchen *et al.,* 2020) (from (Dufour *et al.,* 2011))

Probability	**Negligible**	**Extremely low**	**Very low**	**Low**	**Medium**	**High**
Negligible	Negligible	Negligible	Negligible	Negligible	Negligible	Negligible
Extremely low	Negligible	Extremely low	Extremely low	Extremely low	Extremely low	Extremely low
Very Low	Negligible	Extremely low	Very low	Very low	Very low	Very Low
Low	Negligible	Extremely low	Very low	Low	Low	Low
Medium	Negligible	Extremely low	Very low	Low	Medium	Medium
High	Negligible	Extremely low	Very low	Low	Medium	High

This matrix has been further developed to allow for an improved estimation of risk when multiplying more than two conditional probabilities and takes into account that the product of probabilities that are assessed to be “low” or “very low” will likely be lower than the lowest individual probability (Table 4) (Gale *et al.,* 2014) but could underestimate the risk for a small number of probabilities.

Table 4. Expanded risk matrix to account for the product of two “low” probabilities being less than the lowest probability (Gale *et al.,* 2014).

Probability	**Negligible**	**Very low**	**Low**	**Medium**	**High**	**Very high**
Negligible	Negligible	Negligible	Negligible	Negligible	Negligible	Negligible
Very low	Negligible	Negligible	Negligible	Very low	Very low	Very low
Low	Negligible	Negligible	Very low	Low	Low	Low
Medium	Negligible	Very low	Low	Medium	Medium	Medium
High	Negligible	Very low	Low	Medium	High	High
Very high	Negligible	Very low	Low	Medium	High	Very high

Further expansion of this idea shows the product of two probabilities to be usually less than the lowest probability (and sometimes given as a range) (Table 5).

Table 5. Expanded risk matrix to account for the product of two probabilities being less than the lowest probability (Crotta *et al.,* 2016).

Probability step *'n+1'*	**Conditional probability step '*n*'**					
	Negligible	**Extremely low**	**Very low**	**Low**	**Moderate**	**High**
Negligible	Negligible	Negligible	Negligible	Negligible	Negligible	Negligible
Extremely low	Negligible	Negligible	Negligible-Extremely Low	Extremely low	Extremely low	Extremely low
Very low	Negligible	Negligible-Very Low	Extremely low	Extremely low	Very low	Very low
low	Negligible	Extremely low	Extremely low	Very low	Very low	Low
Moderate	Negligible	Extremely low	Very low	Very low	Low	Moderate
High	Negligible	Extremely low	Very low	Low	Moderate	Moderate

In the event that two or more independent factors contribute to the probability estimation for a single pathway step, the probability for each factor can be estimated by considering them as being additive rather than conditional probabilities that should be multiplied. Risk Matrices for such combinations can also be developed to show the overall probability for that step (Crotta *et al.,* 2016). Alternatively, the factor with the "worst" estimate for a specific step can be selected (Wieland *et al.,* 2011). This method, however, does not acknowledge that in some cases the assessment of one factor may dominate and determine the overall assessment in which case it may be necessary to combine the overall risk in a more complicated fashion, for example, using weightings etc. (Leighton 2002).

Wieland et al., (2011) takes this one step further and provides a matrix for combining probabilities of independent steps where an increase of the overall risk is possible between steps, for example spread of disease leads to an increased number of infected animals and therefore to an increased overall risk. The matrix averaged the risk

estimates of independent steps and was based on one developed by Zepeda (1998) (Table 6).

Table 6. Combination matrix, used to combine two risk estimates that are independent of each other and/or where an increase of risk is possible. This matrix's principle transfers the average of independent probabilities to combinations of qualitative risk levels (based on (Zepeda 1998)).

	Results of the assessment of Parameter 2			
Results of the assessment of Parameter 1	**Negligible**	**Low**	**Moderate**	**High**
Negligible	Negligible	Low	Low	Moderate
Low	Low	Low	Moderate	Moderate
Moderate	Low	Moderate	Moderate	High
High	Moderate	Moderate	High	High

Overall, the choice of an appropriate risk matrix varied between qualitative RAs, with some authors arguing that a limited number of risk categories can result in a general over-estimation of the risk and a low resolution overall. Whilst an increased number of risk categories can increase the resolution of the RA, introducing more risk levels can reduce the accuracy/confidence about the final estimate if there is limited data or high uncertainty. As tables 4, 5 and 6 demonstrate, it is not inherently incorrect for a risk assessor to develop a bespoke risk matrix for a given RA, it is much more important that the matrix is applied consistently, transparently and is appropriate for the risk pathway.

Some authors deliberately chose not to use a risk matrix approach for combining probabilities concluding that they can give a false impression of scientific robustness, whilst actually relying on subjective risk level estimates which may be influenced by a range of other considerations such as personal knowledge and beliefs (Heller *et al.,* 2010; Auty *et al.,* 2019). They also highlighted the issue of the inability to account for marked variation in estimates within categories, and loss of information with successive levels of multiplication. As a result, they preferred to use a qualitative descriptive approach that allowed them to conclude an overall risk level and highlight areas of particular uncertainty and variability.

Suggested best practice: Transparent use of a specified matrix for conditional probabilities. Further development is required to take into account that the product of probabilities that are assessed to be "low" or "very low" will likely be lower than the lowest individual probability. For independent pathways, an additive approach should be taken with the use of weightings to identify the contribution of these pathways to the overall risk level.

Consideration of trade volume and time period

For the qualitative RAs reviewed here, risk levels were often assessed on a per product/animal basis, with no consideration being made of the impact if multiple products/animals were assessed. Such an impact can be significant if the number of products/animals is very high. WOAH guidance (WOAH 2013) indicates that the volume should be taken into account but offers no detailed methodology on how to do this. A RA that does not specify the volume of products/animals, constrains its use to determine mitigation measures to reduce risk to an acceptable level (Peeler *et al*., 2015). Thus, the transparency and defensibility of a qualitative RA are enhanced by defining both the unit and volume of products/animals.

Consideration of the volume of trade was mentioned descriptively in some articles. For example, one article on the risk of introducing peste des petits ruminants into Tanzania used a questionnaire to estimate the amount of trade along the border area between Zambia and Tanzania. Responses led them to conclude that 'the probability of entry as determined by trade volume was rated low' (Chazya *et al.,* 2014). Peel et al., (Peel *et al.,* 2012) found that the imprecise monitoring of live amphibians into the UK meant that on further investigation the undeclared volume of amphibian trade into the UK, was sufficiently large to make the introduction of batrachochytrium dendrobatidis into the UK natural environment very likely under current systems.

Similarly, the probability of Henipavirus entering the UK was assessed by combining the number of products imported annually (*N*) with the results from the probability pathway (P) which assesses the probability per animal, human or tonne of foodstuff using a non-matrix approach, i.e. assessing each combination of *N* and *P* on a case-by-case basis. It

was assumed that if the number of imports (*N*) was negligible, then the probability of entry was also negligible (Snary *et al.,* 2012).

A qualitative RA for entry of highly pathogenic avian influenza (HPAI) strain H5N1 into the UK accounted for increased risk due to number of birds migrating from different regions of the world with different pathogen prevalence (Gale *et al.,* 2014). Although the predicted probabilities of entry of H5N1 per individual bird per year were low, very low or negligible, the overall risk was high for a few species reflecting the high numbers of birds migrating from some regions. The number of birds was addressed qualitatively but with comparable numerical values i.e. >1 000 000 very high; 100 001–1 000 000 high; 10 001–100 000 medium; 1001–10 000 low; 1–1000 very low; 0 negligible (Gale *et al.,* 2014).

A key paper addressing the aggregated probability for qualitative RA communicating the risk per year or per unit of product concluded that it was essential to phrase the risk question to account for aggregated risk, whether due to volume of trade or length of time period (Kelly *et al.,* 2018). The assumption in many RAs is that units are independent and have the same probability of being infected. For the higher levels of probability (very high, high, medium) this is logical because if an individual unit is likely to be infected/contaminated then a group of units will also have a high chance of being infected/contaminated. However, for the lower levels of probability, if the volume is high enough, the aggregated risk could be under-estimated, that is, assessed as being of a lower qualitative category of risk than is probably realistic.

Given an individual risk level and volume of product the estimated values of aggregated probability can be derived from a contour plot (see (Kelly *et al.,* 2018)) and then be used to give guidance on the likely level of qualitative risk. Even though this application relies on making assumptions concerning the individual probability it can give an idea of the possible magnitude of the aggregated probability and provide a range of uncertainty around it. The contour plot relies on quantitative bounds used for the qualitative levels and results are therefore dependent on the choice of these bounds with different results likely being derived for different values.

The aggregated probability method described by Kelly et al., (Kelly *et al.,* 2018) has been applied to two RAs (Snary *et al.,* 2012; Horigan *et al*., 2020) with the assumption that the aggregated probability calculations used the same quantitative bounds as used in the tool by Kelly *et al*., (Kelly *et al.,* 2018) acknowledging that this probability could change if these bounds were to be altered. For the RA previously described on the risk of introduction of henipavirus into the UK (Snary *et al.,* 2012), it was found that for the lower categories of individual probability, the number of imports was important in determining whether or not the aggregated probability is of a higher qualitative level than the individual probability. Overall, the results were consistent between the two methods, identifying the imported commodity with the highest associated risk. However, whilst the methodology adopted by Snary *et al*., (Snary *et al*., 2012) provided results that clearly highlight the routes of highest risk, the evaluation of the aggregated risk was not as transparent as the method described by Kelly et al., (Kelly *et al.,* 2018).

*Suggested best practice: The risk question should be phrased to account for the number of units or time period, not on a per product basis. The use of a specified metric such as the contour plot developed by Kelly et al., (*Kelly *et al.,* 2018*), should be used. This metric should also be further explored with regard to the effect of using different quantitative bounds.*

Uncertainty

The concept of risk involves uncertainty in both the likelihood of occurrence and the magnitude of the consequences. Uncertainty in risk estimates can stem from lack of data, biological variation (reflecting true ranges and variability in biological systems) and measurement error (Suedel *et al*., 2007). Reducing the amount of uncertainty does not necessarily change the actual risk but gives a more precise evaluation of it, thereby giving more confidence in the risk assessment outputs (Osborne *et al.,* 1995). This is particularly important where, within the range of uncertainty, the risk estimate could potentially surpass a key decision-making threshold (EFSA 2018).

For qualitative RA the dilemma is how to deal with uncertainty so that it is clear to the decision maker where it exists and how it may influence the overall risk estimate. If done

well, characterisation of uncertainty is a beneficial aspect of qualitative RA, as it emphasises the importance of uncertainty and can include guidance on its management (Suedel *et al.,* 2007). Such assessments are also beneficial in identifying data gaps as a result of recognising where areas of uncertainty exist. Some of the review papers assessed here stated that more comprehensive guidance is needed, firstly on the assessment and reporting of uncertainty and secondly on the use of uncertainty estimates when judging assessments against acceptable levels of risk (Peeler *et al*., 2015).

Providing the uncertainty level of all estimates can make a RA more transparent and accessible for risk managers. Several articles provided descriptive levels of uncertainty in a similar manner to that of the likelihood definitions as shown in Table 2. Risk managers are then able to identify which steps drive the risk in the model and what results need to be interpreted with care due to high uncertainty (Wieland *et al.,* 2011). However, few articles mentioned, or dealt with, how to estimate an overall level of uncertainty associated with the overall risk estimate. In one example, the highest uncertainty estimate was selected along the steps of the pathways so a high uncertainty in any one level led to a high uncertainty in the overall outcome. An exception was made if the occurrence of an event was Negligible with Low uncertainty (Crotta *et al.,* 2016).

The use of expert opinion was described by some authors to reduce the uncertainty surrounding parameters where data were scarce (Squarzoni-Diaw *et al*., 2020; , Babayani et al., 2022; Wieland *et al.,* 2015; Friker *et al.,* 2021; Rinchen *et al.,* 2020; Islam *et al.,* 2020). Some studies used workshops involving experts from a range of relevant backgrounds to confirm risk parameters, risk pathways and numerical weightings for risk factors reaching a final consensus of agreement (Squarzoni-Diaw *et al*., 2020; Islam *et al.,* 2020). Additional studies employed the Delphi technique (Wieland *et al.,* 2015; Rinchen *et al.,* 2020) to reach consensus. One study used the level of disagreement between different experts as an indicator of the level of uncertainty (Wieland *et al.,* 2015). Qualitative risk estimates were transformed into quantitative scores (negligible = 1; very high = 6) and then the average of the absolute difference of individual risk estimates to the mode was calculated. The resulting averages were ranked and

subjective cut-offs for three uncertainty levels were defined. The purpose of these categories was mainly for communication reasons.

Finally, one article used numerical terms to describe uncertainty as confidence levels by using associated levels of the chance of being correct (Table 7).

Table 7. UK Non-native Organism Risk Assessment (NNRA) scheme: confidence descriptors for uncertainty levels (Peel *et al*., 2012).

Confidence descriptor	Associated level of chance
Low	~35% chance or less of being correct
Medium	~50% chance of being correct
High	~80% chance of being correct
Very high	~90% chance or better of being correct

Suggested best practice: The definitions of uncertainty levels and method of calculation should be clearly described and explained. Risk assessors should be transparent in their decision to either identify at which stages the highest uncertainty exists or whether to give an overall uncertainty level. Further development of how to calculate an overall uncertainty level is required e.g. whether the assessor uses the highest uncertainty level along the risk pathway or the uncertainty level associated with the pathway step that decides the overall risk level.

Dose-response

Risk is often viewed as a binary outcome of entry and exposure in qualitative RAs and does not take into account the amount of pathogen released which may not always be sufficient for infection to occur (Peeler *et al.,* 2015). As such, any qualitative RA that considers infection should assess not only the likelihood of exposure to a pathogen, but also the level of pathogen exposure (Paton *et al.,* 2010; Peeler *et al.,* 2015). The behaviour of any pathogen throughout the risk pathway will vary according to the type of pathogen being assessed and whether it is in the live animal or on an animal product. Whether or not infection occurs will subsequently depend on the animal which is exposed to the pathogen and whether it has prior immunity for example (Peeler *et al.,* 2007).

Articles that used qualitative methods for addressing the level of pathogen were limited. Those that did had varying approaches, for example, purely descriptive (Paton *et al.,* 2010; Peeler *et al.,* 2004), qualitatively evaluating the risk pathways whilst using quantitative evaluations of the level of pathogens (Yamamoto *et al.,* 2006) and considering the reduction in viral load using a matrix approach (Horigan *et al.,* 2019). The latter paper estimated the probability of avian influenza virus survival on different types of equipment before and after preliminary and secondary cleansing and disinfection (C&D) procedures after an outbreak. A risk matrix spreadsheet tool identified those areas of the house which may still contain sufficient virus post-preliminary C&D for infection to occur and on which attention should be focussed during secondary C&D (Horigan *et al.,* 2019).

Suggested best practice: A RA should assess both the likelihood of exposure to a pathogen and the level of pathogen exposure. This area needs to be fully explored before specific best practice methodology can be advised.

Tools of the trade

Some articles described tools, or models, which have been developed to convert descriptive levels used in qualitative RAs into numerical values and so able to use mathematical probabilities to calculate the risk in quantitative terms (Dalziel *et al.,* 2017; Biosecurity 2001; Kyyrö *et al.,* 2017; de Vos *et al.,* 2020). The process is then reversed to conclude with an overall risk estimate in qualitative descriptive terms. These tools are often termed semi-quantitative with respect to their use of numerical values.

De Vos et al., (de Vos *et al.,* 2020) compared generic risk models that can be applied to assess the incursion risk for multiple animal diseases. Of the 7 tools assessed, 4 were semi-quantitative (RRAT (de Vos *et al.,* 2018), MINTRISK (de Vos *et al.,* 2021), IDM (Roberts *et al.,* 2011), NORA (Kyyrö *et al.,* 2017)) and one was qualitative (SVARRA (EFSA 2017)). All the tools were primarily based on the WOAH import RA framework (WOAH 2013). The tools varied in their approaches to uncertainty, MINTRISK and SVARRA explicitly asked the risk assessor for their assessment of uncertainty in estimating the

input parameter values, but MINTRISK additionally used stochastic simulation to assess uncertainty.

The main algorithms used in MINTRISK were sampling from triangular distributions on a linear scale between 0 and 1, these were then translated into qualitative risk scores for each step in the model and for the overall risk estimate. The method developed by Australian Biosecurity (Biosecurity 2001) is similar to that of MINTRISK but a uniform distribution was used. With NORA, the combination of values within a pathway were calculated by applying the basic probability calculation rules of serial (multiplying) and parallel (summing) processes. As an output the final numerical value of probability was then converted into a 'verbal score' (descriptive risk level). This conversion was for the purpose of inclusivity acknowledging that "some people merely like to see numbers, while others need to have a verbal score to feel comfortable with the answers." As mentioned in the description of terms section, the same verbal score can actually mean a different risk level for different people and so definitions of the verbal scores for probability and impact are included in the NORA guidebook. The tool developers also caveat that the location of the qualitative definitions within the numerical class should be taken into account as the estimated risk might be close to a limit between two classes and is therefore relatively sensitive to small changes in input values (Kyyrö *et al.,* 2017).

These semi-quantitative tools are still qualitative RAs but have introduced the concept of mathematical principles, such as the use of probability distributions and stochastic simulation, to standardise their approach. No automated tools were captured in this literature review which addressed the aggregated probability in an entry assessment or the level of pathogen in an exposure assessment.

Suggested best practice: These should be explored further, specifically the use of probability distributions to take uncertainty into account and the incorporation of the volume of trade to give an overall risk level.

Discussion

This review set out to investigate the progression of qualitative RA in animal health and to identify the main themes that have been explored and addressed as the method has

evolved. The qualitative RA methodology was chosen in several case studies reviewed here because it was perceived as being simple to conduct, easy to communicate and helped to provide credibility to the work due to being an accepted methodology for customers and policy makers. Furthermore, a qualitative RA is ideal for identifying important chains of events and critical control points along risk pathways which can then be used to construct robust and informed risk management programs.

It should be acknowledged that this review did not cover grey literature and only those articles which had undergone a peer review process and were available via the search engines PubMed and Scopus were included. This may underreport the general "usefulness" of qualitative RAs which are very often used by governments for rapid policy decisions and may be less likely to result in published articles. As a general estimate the authors consider that between 70% and 80% of qualitative RAs commissioned by governments may go unpublished. However, as these RAs are not published on grey literature search sites and may not be publicly available on government websites it is not possible to verify this estimate.

The four main elements of qualitative RA that were identified in this review as having been the subject of some proposed standard methodology were (i) the description of risk levels, (ii) combining probabilities, (iii) treatment of aggregated probabilities and (iv) uncertainty. These elements were addressed in different ways by the articles reviewed but were highlighted as being fundamental to improving the accuracy in estimating the risk and conveying the results of the RA to the risk manager with minimal ambiguity. The development of standardisation of methodology thus represents an important advance in qualitative animal health RA.

Despite these developments a few key challenges remain. Further work needs to be done regarding an objective uniform methodology for deriving an overall uncertainty and risk estimate. More thought also needs to be given to improve the perceived robustness of qualitative RAs. Ensuring a robust objective methodology is used and that the reasons for differences in results, such as assumptions and uncertainty are clearly described to the customer is essential to maintain confidence in the qualitative RA process. One way of doing this is by adopting some of the characteristics of a

quantitative analysis (Dufour *et al*., 2011), as has been shown by the development of semi-quantitative tools such as NORA and MINTRISK.

Guidelines for RA in international trade have been published by the WOAH (2013), but little detail is provided about how to use qualitative methods in practice and several solutions were proposed to address this across the papers reviewed. This is in line with the need for RA to remain flexible to deal with real life scenarios, recognising that no single approach may be applicable in all cases. Despite this, it can be concluded that some level of standardisation is important to help prevent discrepancies in results due to the broad approaches used. A set of best practice guidelines set out by a body such as WOAH or EFSA would be beneficial to establishing a standard methodology for conducting qualitative RAs. Preliminary suggestions for current best practice based on the findings from this review and areas where best practice is yet to be substantiated have been identified for all of the themes discussed here.

In summary, the robustness of conclusions from qualitative RAs has improved since the 1990s with the introduction of consistent definitions of probability terms, risk pathways, tabulated matrices illustrating the combination of conditional probabilities, methods to assess the aggregated probability and consideration as to how uncertainty can be addressed. Several tools have been created which apply mathematical reasoning by allowing for uncertainty to be accounted for and for the probabilities of the risk pathway steps to be combined. Overall animal health qualitative RAs have established their usefulness by providing a tool for rapid risk estimation which can be used to identify whether or not risk exceeds a decision-making threshold above which action should be taken. Based on this review, future directions should include further development of a uniform methodology for deriving an overall uncertainty estimate and further improvement to the standardised methodologies employed to maintain confidence in the qualitative RA process.

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2.4 Conclusion to Chapter 2

This Chapter presents a literature review of qualitative RA in animal health, detailing the main elements that were identified as having advanced in the field of qualitative risk assessment: (i) the description of risk levels, (ii) combining probabilities, (iii) accounting for trade volume and time period (iv) dose response (v) uncertainty and (vi) semi-quantitative tools. A set of suggested best practice guidelines were also presented for each element whilst acknowledging that these would be best controlled, or regulated, by bodies such as the World Organisation for Animal Health (WOAH) or the European Food Safety Authority (EFSA).

The following chapters demonstrate how some of the identified elements have been applied in different animal health scenarios as illustrative examples of using standardised methodologies. Chapter 3 follows the WOAH risk assessment framework for entry and exposure (WOAH 2024) and the definitions of likelihood from EFSA (EFSA 2006). The overall likelihood for individual risk pathways for both entry and exposure was estimated using a risk matrix approach derived from Gale *et al*., 2010. This illustrates the influence the pathway step with the lowest likelihood can have on the overall likelihood and the importance of being transparent about how this has been estimated.

Chapter 3: Assessing the probability of introduction and transmission of Lumpy skin disease virus within the United Kingdom

3.1 Authorship and funding statement

The application of the methodology and the analysis of the evidence and review of literature was my own work. Dr Helen Roberts contributed by providing expertise on import risks and policy regulations and reviewing the work. Dr Pip Beard and Dr Carrie Batten provided disease expertise, and Dr Amie Adkin and Dr Paul Gale reviewed the work. Dr Louise Kelly supervised the project. This work was funded by the Department for Environment, Food and Rural Affairs (Defra) and the Scottish and Welsh Governments.

3.2 Summary of the published paper

The paper presented in this chapter describes a risk assessment carried out to assess the risk of introduction of Lumpy skin disease (LSD) virus into the United Kingdom (UK) and the risk of spread within the UK should it be introduced. The paper was published in the Microbial Risk Analysis journal in 2018 https://www.sciencedirect.com/science/article/abs/pii/S2352352218300082. Lumpy skin disease is an economically important viral disease of cattle that has never been reported in the UK but had been spreading from the Middle east to south-eastern Europe since 2012 and was first reported in Greece in 2015. Outbreaks were reported in several European countries including Bulgaria, Serbia and Albania but the disease was contained in Europe by 2017 mainly as a result of a large-scale vaccination campaign which achieved high vaccination coverage among cattle herds (Tuppurainen *et al.,* 2020). Since the paper was published outbreaks have additionally been reported in Italy (Sardinia and mainland) France and Spain in 2025. Whilst the source of the initial outbreak in Sardinia is still inconclusive it was likely as a result of the entry of infected insects and the infection then spread to mainland Italy as a result of the movement of an infected animal (WOAH 2025).

The paper in this chapter reports the results of a project carried out to assess whether LSD should be elevated to the UK Disease Emergency Response Committee (DERC) list,

given the situation in Europe at the time (2017/2018). The results of the project were used to make an evidence-based policy recommendation not to add LSD to the DERC list. A qualitative RA was deemed appropriate for the project due to the tight timeline and the low expectations of sufficient good quality data to populate a quantitative RA. This lack of data was confirmed by the RA and resulted in high uncertainty levels for many of the risk pathway steps.

The approach used followed the WOAH RA framework for entry and exposure (WOAH 2025) and the definitions of likelihood were taken from EFSA (EFSA 2006). As the likelihoods assessed in the risk pathways were conditional, i.e. each step assessed the likelihood of occurrence given the knowledge that the previous step has already occurred, a risk matrix method was used to combine likelihoods for each step of the risk pathways giving an overall estimate of risk. The structure of the matrix selected accounted for the fact that probabilities are always between 0 and 1. Therefore, when 'multiplying' two probabilities together the resulting probability must be, at the absolute maximum, equal to the lower probability (Gale *et al.,* 2010). The overall uncertainty estimate for any given risk pathway was selected as the uncertainty estimate associated with the pathway step with the lowest likelihood i.e. the likelihood that influenced the overall pathway risk estimate.

This RA highlighted that for the risk pathway regarding the legal entry of livestock the likelihood that an animal infected with LSD virus would not be detected if entering from a 'non-risk' country would be Medium as no testing was required. Thus, the traceability for any livestock entering the UK from the European mainland was highlighted as being important as if an animal had originally travelled from an 'at risk 'to a 'non-risk' country it is possible that the latter could then be declared as the country of origin. This opens up the potential for an infected animal originally from an 'at risk' country not undergoing any testing on entry to the UK.

The RA was updated in 2022 using the same framework and methodology but populated using an updated literature search. This demonstrates that a standardised and robust qualitative RA framework can be regularly updated showing comparable results.

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WOAH 2025 Statement on recent lumpy skin disease outbreaks in Europe Statement on recent lumpy skin disease outbreaks in Europe - WOAH - World Organisation for Animal Health

3.3 Full text of the published paper

Assessing the probability of introduction and transmission of Lumpy skin disease virus within the United Kingdom

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Abstract

Several emerging exotic diseases are currently oscillating on the eastern borders of the European Union (EU) including the bovine pathogen Lumpy skin disease virus (LSDV). Given the recent transboundary spread of LSDV into the EU, assessing the probability of further expansion is an important part of EU surveillance and can inform policy regarding risk mitigation priorities. This qualitative assessment focuses on the probability of introduction and onward transmission of LSDV into the United Kingdom (UK) for the time period June 2017 to June 2018.

Overall the probability of introduction was considered, at most, to be very low. The probability of onward transmission was considered highest for vector mediated routes either via contact of an infected vector with susceptible cattle or contact of a competent native vector with an infected cattle. Factors with high uncertainty were identified to emphasise their impact on the assessment conclusions and for future research requirements. Medium to high uncertainty surrounds the probability of introduction to the UK via several of the routes assessed, in particular, the species of vectors involved and the illegal/legal import of meat and milk products; all estimates made consequential to these probabilities are therefore underpinned by high uncertainty.

Whilst the assessment was UK centric the knowledge gaps are relevant to the probability of introduction and spread of LSDV in any geographical region. The value of estimating uncertainty lies in the identification of research required to make conclusions more robust.

Introduction

The geographical expansion of animal diseases traditionally thought of as exotic to the European continent, for example, African swine fever (ASF), and lumpy skin disease (LSD), are causing increasing concern to European Union (EU) member states (MS). The steady movement of these diseases across European boundaries has required the EU to put surveillance activities and mitigation programmes in place to prevent further spread. Despite these preventive controls which significantly reduce the likelihood of spread, rare geographical random jumps of pathogens can, and do, occur with the consequence that introduction of an emerging disease into an EU MS may go undetected for a certain period of time during which silent spread could occur. This has been demonstrated with the 2006 Bluetongue virus (BTV) serotype 8 appearance in the Netherlands (EFSA 2007) and the 2016 diagnosis of besnoitiosis in Ireland (Ryan *et al.,* 2016; Alvarez-Garcia *et al*., 2016).

For the United Kingdom (UK), situated on the north western perimeter of Europe, national surveillance of emerging exotic diseases has been assisted by the predominantly east to west/south to north direction of spread allowing the progressive reporting of outbreaks in individual MSs to be monitored and continually reassessed. The data generated by these outbreaks can be used in risk assessments with particular emphasis on the probability of introduction from continental Europe to the UK (Burgin *et al.,* 2013). The island status of the UK needs to be accounted for when assessing the probability of disease incursion with the surrounding water boundary likely to affect pathogen incursion via routes such as vector movements (Burgin *et al.,* 2013) and wild animals (Barun *et al.,* 2010).

Lumpy skin disease came to particular prominence in 2016 as an exotic disease that emerged as a major threat to European cattle populations. It is a viral disease of cattle (*Bos indicus* and *B. taurus*) and water buffalo (*Bubalus bubalis*) and is categorised as a notifiable disease by the World Organisation for Animal health (WOAH) (Tuppurainen 2015). The disease is present in most, if not all, African countries and is now considered endemic in Turkey (EFSA 2017). Since 2012, LSD has spread from the Middle East to south east Europe, affecting EU MSs (Greece and Bulgaria) and several other countries

in the Balkans. This spread has been rapid, possibly aided by civil unrest and the breakdown of veterinary services in countries such as Iraq and Syria (Beard 2016). Since 2015 in south east Europe there have been over 7,600 outbreaks with 12,800 affected animals (EFSA 2017). Indirect production losses are incurred by control and eradication measures and restrictions/total ban of international trade of live cattle and their products.

Lumpy skin disease has never been reported in the UK but, given the current situation within the EU, assessing the probability of incursion is important to inform surveillance activities and national policy regarding risk mitigation. This qualitative assessment focuses on the probability of LSD virus (LSDV) introduction into the UK within the time period June 2017 to June 2018. The probability of onward transmission, were disease incursion to occur within the UK, was also assessed. Factors with high uncertainty were identified to emphasise their impact on the assessment conclusions and future research requirements. Such research would assist risk assessors in making more robust conclusions for national preparedness and mitigation strategy prioritisation.

Material and Methods

Risk Questions:

The risk questions to be addressed were:

- *What is the probability of introduction of LSDV into the UK within the next year*?*
- *What is the probability of onward transmission of LSDV within the UK, should it be introduced within the next year*?*

**'within the next year' is here on in interpreted as being from 1st June 2017 to 1st June 2018*

Risk framework:

The approach used was based on the framework set out by WOAH (WOAH 2004). The variables (i.e. probabilities and their associated uncertainties) are expressed qualitatively as negligible, very low, low, medium, high and very high (EFSA 2006; FAO 2009) and defined as: *negligible*, so rare that it does not merit to be considered; *very*

low, very rare but cannot be excluded; *low*, event is rare but does occur; *medium*, event occurs regularly; *high*, event occurs very often; and *very high*, event occurs almost certainly.

Risk Pathway:

The risk pathway highlighting the potential routes of introduction of LSDV into the UK within the next year is shown in Figure 1.

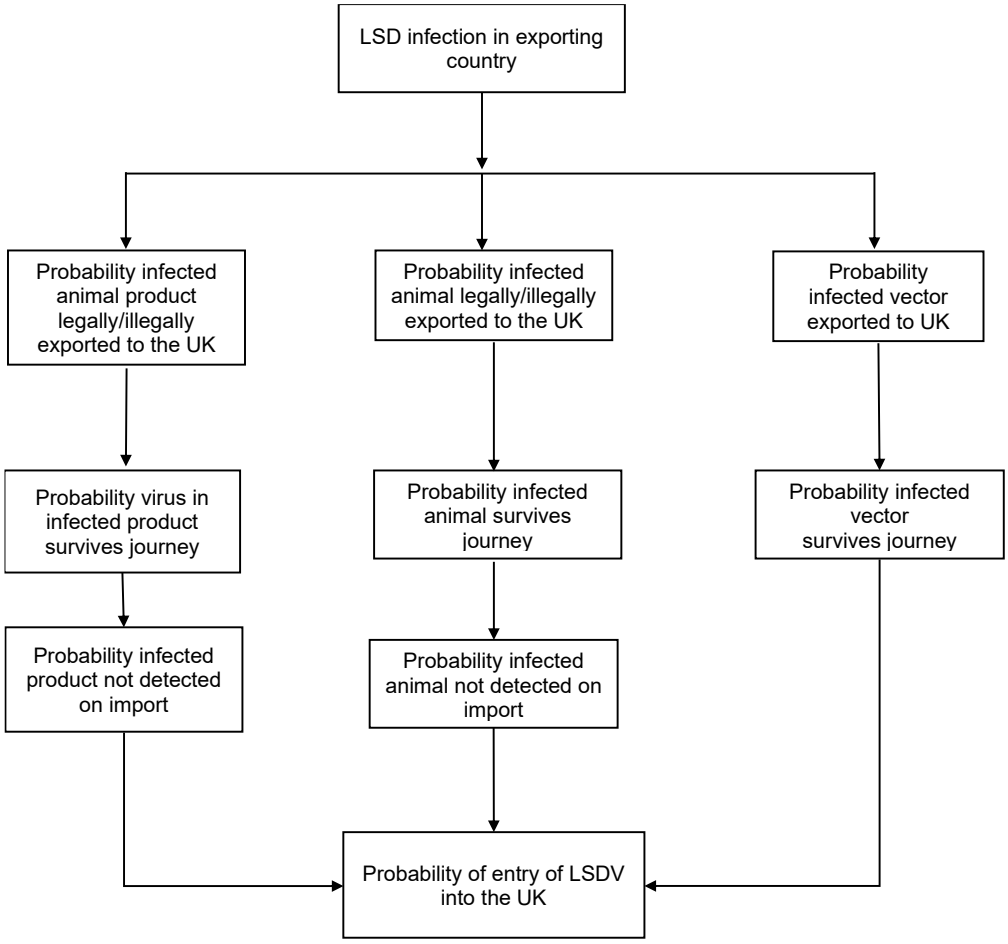

Figure 1: Risk pathway for the probability of introduction of Lumpy skin disease virus into the United Kingdom within the next year. Exporting country here refers to both European Union and third countries.

Disease introduction was defined as the presence of an LSDV positive vector or animal/animal product in the UK and included the probability of detection at post-import testing. Onward transmission to UK cattle, given introduction has occurred, is

described in the second pathway (Figure 2) using the outputs from Figure 1 (infected live animals, contaminated animal products and infected vectors) as sources of LSDV. The primary routes of introduction and onward transmission considered were based on literature reviews and expert opinion.

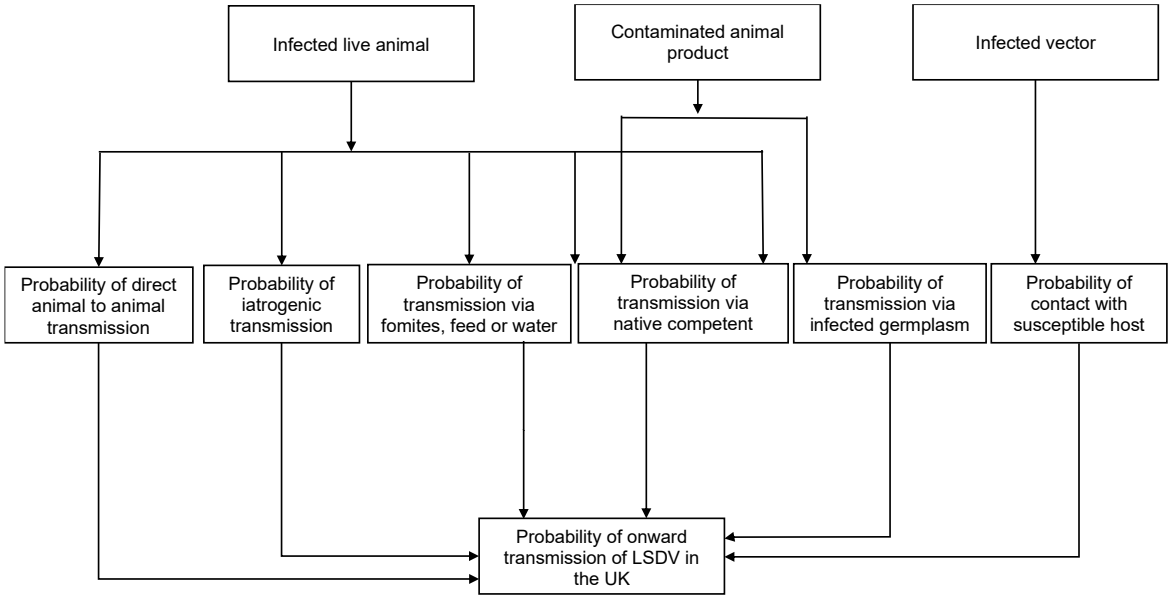

Figure 2: Risk pathway for the onward transmission of Lumpy skin disease virus should the disease enter the United Kingdom within the next year

The qualitative estimates for the combined probability of introduction and onward transmission for individual routes i.e. live animals, animal products and vectors were derived using a matrix approach as described previously (Gale *et al.,* 2010).

Parameterisation

Data used to estimate the pathway probabilities are summarised in Table 1. Data used for these estimates can be found in the Appendix. An overview of the data required for each route is presented.

Table 1: Summary of data used to estimate probabilities of Lumpy skin disease virus introduction and onward transmission

Data requirement	**Estimate**	**Source**
'At risk' countries (countries with an OIE reported LSD outbreak 2015 – 2016)	African continent countries, Albania, Armenia, Bahrain, Bulgaria, Former Republic of Macedonia, Georgia, Greece, Iran, Iraq, Kazakhstan, Kuwait, Montenegro, Oman, Russian Federation, Saudi Arabia, Samoa, Serbia, Turkey	WAHIS (WOAH)
Countries consigning cattle to UK	Austria, Belgium, Denmark, Finland, France, Germany, Italy, Luxembourg, Netherlands, Norway, Poland, Republic of Ireland, Spain, Switzerland	Traces*
EU MSs which consign cattle from LSD affected countries	Austria, Belgium, Czech republic, Germany, Italy, Netherlands, Poland, Portugal, Spain	Eurostat**
Livestock animals considered	Cattle; water buffalo	
Seroprevalence of LSDV in cattle	23% - 31% by virus neutralisation test	(Gari *et al.*, 2012)
'At risk' countries: UK post-import testing required	Bulgaria, Croatia, Greece, Hungary, Romania, Slovakia, Slovenia	Animal and Plant Health Agency Operations manual
Import test used	Real time PCR	(Stubs *et al.*, 2012)
Import test sensitivity/specificity	63 DNA copies/100%	(Stubs *et al.*, 2012)
Mortality rate	0.4% - 10%	(WOAh 2016; EFSA 2015)
Morbidity rate (intraherd)	10% - 50%	(EFSA 2017)
Incubation period	28 days	(WOAh 2016)
Duration of viraemia	1-12 days	(FAO 2016)
Presence of clinical signs	50%	(Weiss 1968)
Seroprevalence of LSDV in exotic animals	0.69% by virus neutralisation test	(Fagbo *et al.*, 2014; Hamblin *et al.,* 1990; Hedger *et al.,* 1983)
Survival time of virus in semen	42 days (viral DNA 159 days) (longer if frozen)	(Irons *et al.*, 2005)
Third countries which export germplasm to the UK	Australia; United States of America	Traces*
Viral levels in skin lesions	8.1 – 8.3 $\log_{10}$ PFU/g	(Babiuk *et al.*, 2008)
Survival time of virus in skins/hides	>18 days	(Weiss 1968)
Third countries which export hides/skins to the UK	Australia; China; USA	Traces*

Data requirement	Estimate	Source
Survival time of virus in meat/milk products	Unknown	-
Vector species involved	Unknown	
Vector spread rate of LSDV	<10–15 km/week	(Mercier *et al*., 2017)
Virus survival time in vector	2-6 days	(Chihota *et al.,* 2001; 2003)
R_0 of direct animal to animal transmission	0.36	(Magori-Cohen *et al.,* 2012)
Environmental survival	6 months at ambient temperature	(EFSA 2015)
Virus susceptibility	No significant reduction at pH 6.6 - 8.6 for 5 days @ 37°C	(EFSA 2015)
R_0 of indirect transmission (vector?)	15.7	(Magori-Cohen *et al.*, 2012)

*TRACES: Trade Control and Expert System is the European Commission's platform for sanitary and phytosanitary certification, tracking the import, export, and intra-EU trade of animals, food, feed, and plants

**Eurostat: is the statistical office of the European Union (EU), responsible for publishing official, harmonized, and comparable statistics on the EU and the euro area

Live animals

This route considers animals in which LSDV infection has been documented i.e. domestic cattle and water buffalo. For completeness exotic wildlife such as African buffalo, wildebeest and impala are also assessed acknowledging the very limited detection of LSDV seropositive results in documented studies (Fagbo *et al.*, 2014; Hamblin *et al.,* 1990; Hedger *et al.,* 1983). The probability that an infected live animal is consigned (i.e. intra-community trade) or exported (i.e. from outside the EU) to the UK was estimated from the number of animals arriving from each country of origin and the presence of LSDV infection in those countries. These data were then combined with the probability of the infected animal being infected and surviving the journey from its country of origin and the probability of it being detected at destination, depending on the incubation period, clinical infection and post-import test sensitivity. Data on animal level seroprevalence were limited to one study in Ethiopia and ranged from 31% (CI: 24-40) to 23% (95% CI: 18-29) (Gari *et al.,* 2012). This seroprevalence value was therefore assumed for animals in countries where LSD was endemic. These countries are referred

to as 'at risk' countries hereon in and are those for which post-import testing within the UK is required for compliance checks and in which an LSD outbreak has been reported to WOAH for the years 2015 – 2016. Both illegal and legal trade were assessed. The final estimate is the probability that an infected animal enters the UK from any other country of origin.

The estimate of the probability that onward transmission of LSDV could occur within the UK from the introduction of an infected animal considers transmission via local competent vectors, directly via animal to animal or indirectly via fomites, iatrogenic, germplasm, feed or water (Figure 2). Onward transmission from an infected animal depends upon the animal remaining sub-clinically infected or differentially diagnosed whilst still being viraemic for a sufficient time period for transmission to occur. Duration of viraemia, percentage of sub-clinically infected animals and virus survival in the environment were, therefore, all considered.

In general, there are very few non-EU countries which are approved for the export of cattle to the European Union. The list of countries is in Regulation (EU) 206/2010 and includes Canada, Chile, Switzerland, Greenland, Iceland and New Zealand for bovidae. Otherwise, exotic ungulates may be moved between approved bodies (e.g. zoos and collections) only if they are risk assessed and suitable testing and quarantine procedures are in place.

Animal products

The probability that an LSDV infected product enters the UK from any affected country was estimated by combining the probabilities of an infected product being consigned or exported to the UK, survival time of the virus within the product and whether or not it would be detected at destination. The animal products considered were germplasm; hides and skins; meat and milk products. The assessment considers the presence of contamination in the product at source and any reduction in viral load which may occur during the time taken for travel to the UK including any processing effects. Both illegal and legal trade/ imports were assessed.

Onward transmission of LSDV from animal products was considered to be either via a native competent vector or using infected germplasm as the source. Data on UK vector competency and survival and transmissibility of LSDV in germplasm were used to estimate the probability.

Vectors

Whether or not an infected vector could be introduced to the UK would depend upon the type of vector and the environmental conditions. It is currently unknown which vectors are involved in transmission of LSDV and whether transmission is mechanical, biological or both. Because of this knowledge gap, high uncertainty surrounds how far vectors can travel e.g. different modes of transport could potentially be involved (Tatem *et al*., 2006; Barre *et al*., 2010; Sedda *et al.,* 2012), and for how long virus can survive in/on the vector. It was assumed that only vectors in countries where infected cattle were reported, or in their bordering countries, were infected.

Onward transmission via a vector could be possible either through an incoming infected vector contacting susceptible UK cattle or a native competent vector contacting an infected animal or contaminated animal product. The probability was estimated using data on UK vector competence and UK cattle density.

Results

Probability of introduction

The probability of introduction of LSDV into the UK via each route considered was calculated by combining the relevant steps in the risk pathway (Figure 1) as described previously (Gale *et al.*, 2010). The probability was estimated to be very low for vectors and both illegal and legal trade of livestock, skins/hides and meat/milk products. All other routes were considered to have a negligible probability of introduction (Table 2).

Table 2: Probability of introduction of Lumpy skin disease virus into the United Kingdom within the next year (1st June 2017 to 1st June 2018) via animals /animal products and vectors

Probability				**Qualitative scores**		
Legal	**Livestock**	**Exotic animals**	**Germplasm**	**Hides/skins**	**Meat and milk products**	**Vector**
Probability consigned to the UK	Very low	Negligible	Negligible	Very Low	Very low	Very low
Probability infected animal/virus survives journey	High	High	High	High	Very low	Very low
Probability not detected on arrival	At risk country: Very low Non-risk country: Medium	Very low	High	Low	High	N/A
Probability of introduction of animal/animal product/vector infected with LSDV	Very low	Negligible	Negligible	Very Low	Very low	Very low
Illegal	**Livestock**	**Exotic animals**	**Germplasm**	**Hides/skins**	**Meat and milk products**	**Vector**
Probability consigned to the UK	Very low	Negligible (Low)	Negligible	Very Low	Very low	N/A
Probability infected animal/virus survives journey	High	High	High	High	Very low	N/A
Probability infected animal/product reaches UK undetected	Low	Low	High	Medium	High	N/A
Probability of introduction of animal/animal product infected with LSDV	Very low	Negligible	Negligible	Very Low	Very low	N/A

No animals were consigned from 'at risk' countries (see Table 1) to the UK in the last 12 months. In order for the UK to legally trade an infected animal, the disease would need to have spread undetected into one of the UK's trading partners and would, therefore, in all likelihood, be at a very low prevalence. The numbers of animals traded by the UK from the MSs concerned, were also relatively low (See Appendix). It is likely that the highest risk would be from breeding or production stock rather than slaughter animals as they would have a longer period of time to make further contacts with other live animals or vectors. Based on these considerations, the probability that an infected animal is legally consigned to the UK within the next year was considered to be very low. Although LSD has been endemic in Africa for decades no actual cases have been reported in wildlife and prevalence by antibody detection has been reported to be very low (Fagbo *et al.*, 2014; Hamblin *et al.,* 1990; Hedger *et al.,* 1983) suggesting that exotic animals (i.e. non-livestock) are unlikely to be important in the epidemiology of LSD. The import from third countries of such animals is covered by strict regulations under EU

rules and the risk of introduction via the exotic animal route was thus estimated as negligible.

The probability that an infected animal survives the journey from the country of origin to the UK was considered to be high given the relatively low mortality rate but the probability that an infected animal is not detected on arrival was considered to be very low for 'at risk' countries due to the post-import testing regime in place. For animals consigned from non-risk countries the probability was assessed as medium assuming that only 50% of infected animals show clinical symptoms (Weiss 1968) and that no testing on arrival would occur.

No bovine germplasm (semen or embryos) were traded from 'at risk' countries during the year 2016. It is likely that once an LSD outbreak has been confirmed in a herd all animal products, including semen, would be destroyed. The probability of LSDV infected germplasm being legally consigned to the UK was therefore considered to be negligible. The probability of any virus surviving in semen was, however, estimated to be high as it was assumed that semen will be transported as frozen straws thereby preserving any virus within it (Tuppurainen 2016).

For the year 2016 the number of intra EU imports of hides into the UK is not known as they are not recorded in TRACES, but instead rely on commercial documentation. Imports from third countries (i.e. those outside of the EU) were from Australia, China and the USA. The probability of untreated LSD infected animal hides or skins being legally exported to the UK from a third country was therefore considered to be very low. Untreated products consigned from within the EU must only originate from a country which is approved for the import of fresh or frozen meat or products for human consumption (EU 2011) and be destined for an approved processing plant within the EU. Otherwise, skins and hides must be processed in an EU approved establishment in the country of origin. Skin/hides are likely to be transported to the UK via trucks and ships with temperatures below 37^{o}C and in the dark; hence it is likely that little or no inactivation of the virus would occur during transport (Gale *et al*., 2015) particularly in those products which do not undergo specific inactivating treatment (Weiss 1968). The probability of virus surviving in infected hides/skins was therefore assessed to be high

but the probability of not being detected on import was considered to be low due to the identifiable nodules and scabs on the products.

Concerning milk and milk products, while there is some experimental evidence that conditions equivalent to the low temperature / long time pasteurisation method inactivate capripoxvirus (62^{o}C for 30 minutes) (Ferreira 1973; Datta *et al.,* 1991) there is no available data on pasteurisation at 72^{o}C; furthermore, the presence of fat, protein and other solids in milk may protect the virus thereby decreasing the inactivation rate compared to that of virus in a laboratory buffer. There is therefore insufficient evidence on both the presence of virus in milk and whether pasteurisation inactivates LSD virus to a negligible level. However, the WAOH code (WOAH 2016) recommends that pasteurisation of milk or any combination of control measures with equivalent performance as described in the Codex Alimentarius Code of Hygienic Practice for Milk and Milk Products (FAO 2009) is a suitable prerequisite to import of these products. There is no public health risk of LSD from meat products and therefore the trade in meat is not subject to risk management procedures. The probability of meat/milk products infected with LSDV being consigned to the UK was therefore considered to be very low with the probability of LSDV surviving in these products also assessed as very low assuming that all dairy products would be pasteurised for human consumption in accordance with WOAH recommendations. The probability of infected germplasm or meat and milk products not being detected on arrival was considered to be high as no physical signs of contamination will be evident and no post-import tests are currently carried out.

In order to estimate the probability of introduction of LSDV into the EU via the illegal movement of animals, the number of animals that need to be moved to have a probability of introduction of LSDV into Europe of greater than 0.95 was calculated to be above 1,300 (for country seroprevalence equal to 30%), or above 7,800 (for country seroprevalence equal to 5 %) i.e. a large and likely improbable number of animals (EFSA 2015). The logistics and costs involved of illegally transporting cattle from mainland Europe to the UK is another mitigating factor against this event occurring. Contradicting this is the high chance of virus survival and the fact that no post-import testing would

be carried out on illegally transported animals. As such the probability that an LSDV infected livestock animal is illegally transported to the UK was considered to be very low. The probability is reduced to negligible for exotic animals due to the assumption that non-livestock animals are not important in terms of LSDV transmission and do not act as a reservoir of disease.

For illegal products, the probability of infected germplasm being consigned to the UK was considered to be negligible due to the availability of cheap and health tested products legally available in the UK. The probability for meat and milk products was assessed as very low although it is unknown whether large scale consignments might occur or whether illegal trade or imports may only be occurring as goods for personal consumption. The probability of illegally importing untreated hides/skins was also estimated as very low. Although these products can be of high value, thereby increasing the likelihood of them being imported as a commodity for onward sale, it was assumed that hides spoiled by skin lesions would not be selected for export. The probability that animal products illegally consigned from the EU into the UK are not detected was assessed as high for germplasm and meat/milk products and medium for hides/skins. The latter has a slightly higher likelihood of being detected due to the size of the product and the probability that they will be shipped as bulk imports rather than personal imports. There are no checks carried out on passengers and trade products for intra EU trade.

The possibility of long term virus survival in vector populations cannot be excluded with certainty (FAO 2016). Vectors have been previously implicated in transboundary cases of LSD e.g. the first cases in Greece were suspected of coming from Turkey via vector movement (DEFRA 2015). However, these are neighbouring countries unlike the UK and mainland Europe which are separated by a ~ 33 km stretch of water. Modelling of LSDV transmission suggests that vector borne transmission is responsible for short distance transmission only (Magori-Cohen et al., 2012). For this reason the probability that an infected vector will reach the UK successfully within the next year was assessed as being very low.

Uncertainty associated with the probability of introduction of LSD virus into the UK

Qualitative uncertainty scores for the routes of introduction are shown in Table 3. The highest levels of uncertainty were associated with the introduction of LSDV via legal and illegal meat and milk products and via vectors. High uncertainty surrounds all of these estimates due to the lack of robust scientific evidence and lack of data on the numbers involved. The uncertainty associated with the vector route is high due to the unknown vector species involved (and therefore its associated mode of entry to the UK) and whether biological transmission or only mechanical transmission is involved which will influence virus survival on or within the vector.

Table 3: Uncertainty surrounding the estimates for probability of introduction of Lumpy skin disease virus into the United Kingdom within the next year

Probability	**Uncertainty scores**					
Legal	**Livestock**	**Exotic animals**	**Germplasm**	**Hides/skins**	**Meat and milk products**	**Vector**
Probability consigned to the UK	Medium	Very low	Low	Medium	High	High
Probability infected animal/virus survives journey	Low	High	Medium	Medium	High	High
Probability not detected on arrival	At risk country: Very low Non-risk country: High	Very low	Low	Low	Low	N/A
Illegal	**Livestock**	**Exotic animals**	**Germplasm**	**Hides/skins**	**Meat and milk products**	**Vector**
Probability consigned to the UK	Low	Low	Very low	Medium	High	N/A
Probability infected animal/virus survives journey	Low	Medium	Medium	Medium	High	N/A
Probability infected animal/product reaches UK undetected	Medium	Medium	High	High	High	N/A

A level of medium uncertainty was derived for the trade of infected livestock to the UK as the complete movement history of the animals is unknown and the time between disease incursion within a country and disease detection, which is dependent on the clinical signs and the methods of surveillance and post-import test sensitivity, was unknown and likely to be variable. During this window movement of potentially infected animals could occur. The uncertainty score for exotic animals, however, was considered to be very low due to the robust scientific data available on the very low levels of natural infection in this population.

The lack of data on the number of hides traded around the EU and undergoing different preservation treatments and the effect of those treatments on LSDV makes it difficult to estimate virus survival. An assessment of medium uncertainty for the virus surviving the journey on these products was therefore assumed. However, there was low uncertainty concerning the probability of not being detected on arrival as nodules and scabs are likely to be evident on the product thereby identifying infected items.

Uncertainty surrounding the probability that an LSDV infected livestock animal or exotic animal is illegally imported to the UK was considered to be low. Conversely, a high level of uncertainty was associated with the probability of animal products being illegally imported into the UK due to the unknown number of illegal consignments.

Probability of onward transmission

The probability of onward transmission of LSDV, assuming introduction to the UK, and the associated uncertainty for all of the assessed routes is shown in Table 4.

Table 4: Probability of onward transmission of Lumpy skin disease virus within the United Kingdom during the next year (June 2017 to June 2018) via animals /animal products and vectors

Probability	**Qualitative score**	**Uncertainty**
Live animal		
Direct animal to animal transmission	Very low	High
Iatrogenic transmission	Very low	Low
Transmission via fomites, feed or water	Low	High
Transmission via germplasm	Very low	High
Transmission via native competent vector biting infected animal	High	Medium
Animal product		
Transmission via competent vector biting animal product	Negligible	Very low
Transmission via germplasm	Very low	High
Vector		

Probability	**Qualitative score**	**Uncertainty**
Transmission via contact with susceptible host	High	High

The probability of direct animal to animal transmission was considered to be very low as the basic reproduction number (R_0) of this mode of transmission has been calculated to be 0.36 (Magori-Cohen *et al*., 2012), i.e. infection is unlikely to be able to spread in a population. Studies have demonstrated direct transmission from infected animals to be inefficient with lack of spread from infected animals to naïve animals housed together (Carn *et al*., 1995). Transmission of this type would also be dependent on a situation when high densities of cattle are in close contact e.g. communal grazing or cattle markets which have been associated with the occurrence of LSD. For exotic animals, there are very low numbers of seropositive animals reported in the literature (Fagbo *et al.*, 2014; Hamblin *et al.,* 1990; Hedger *et al.,* 1983) and serological positivity does not necessarily imply that the virus replicates in the animals and is excreted; thus, they may not be able to transmit the virus and represent an end-point for disease (EFSA 2015). The probability of onward transmission of LSDV from exotic animals was therefore assessed as being negligible.

If infected cattle remain undetected, further iatrogenic spread may occur if unhygienic practices (e.g. use of contaminated hypodermic needles and surgical equipment) takes place (Darpel *et al.,* 2016). It is assumed that in the UK good veterinary practice is undertaken for both herd wide testing and vaccination campaigns requiring the use of needles; the probability of iatrogenic transmission was therefore assumed to be very low.

For other live animal routes, only transmission of LSDV via semen has been demonstrated; disease itself was not transmitted (Annandale *et al.,* 2014). The probability of onward transmission via germplasm was therefore assumed to be very low. The probability of onward transmission via fomites, food or water was assumed to be low due to the lack of evidence of this transmission occurring but acknowledging the

potential of the virus to survive for long periods at ambient temperatures (for up to 6 months if protected from sunlight), and the fact it survives well at cold temperatures.

The probability of a competent vector contacting an LSDV infected skin/hide or meat product was considered to be negligible. Lumpy skin disease virus is considered to be transmitted mainly through haematophagus vectors which do not bite bloodless hides or skins; therefore, even if the virus on or in insufficiently treated hides was imported, further transmission would not take place (EFSA 2015). Meat is not considered to be a significant risk for transmission for LSDV (FAO 2016) and untreated hides/skins go straight to a designated processing plant for treatment; the transmission route between an infected meat product or hide/skin and a susceptible animal was considered unlikely (Tuppurainen 2015).

The probability that a native vector would contact an LSDV infected animal was considered to be high depending on the competence of native vectors in the UK for transmitting the virus and the co-occurrence of such a vector and infected host. Whilst the competency of vectors in the UK is currently unknown the fact that the disease has moved steadily up from southern Africa through many different climatic zones involving potentially many different vectors suggests that it is also likely to be transmitted by vectors present in the UK. The probability of an infected vector contacting a susceptible host and initiating onward transmission was also assessed as high. Proximity to livestock, warm temperatures and vector abundance are among the main risk factors for LSD spread. The R_0 value induced by indirect transmission has been estimated at 15.7. Sensitivity analysis showed that this result was robust to a wide range of assumptions regarding mean and standard deviation of incubation period and regarding the existence of sub-clinically infected cattle (Magori-Cohen *et al.,* 2012). This indirect transmission was assumed to be vector mediated and the efficiency of transmission of an infected vector to a naïve animal was therefore assumed to be high.

Uncertainty associated with the probability of onward transmission of LSD virus within the UK

Very little is known about the probability of transmission of LSDV via fomites, feed or water and, as such, uncertainty associated with this route of transmission is high. Transmission via these routes could occur under any situation when high densities of cattle come in close contact but in the natural setting it is difficult to differentiate this type of indirect transmission from vector mediated transmission within a herd. Similar high uncertainty was associated with onward transmission via direct animal to animal contact and germplasm due to lack of robust scientific evidence of natural transmission in the field and the need for more extensive experimental studies.

Regarding vector mediated routes, there is high uncertainty surrounding the ability of an incoming infected vector to initiate onward transmission due to lack of robust evidence on which vector species are involved in transmission and, therefore, what effect temperature and other environmental conditions would have upon efficiency of transmission. There was considered to be slightly less uncertainty (medium) about whether or not vectors native to the UK would be competent to transmit LSDV due to the speed with which LSD has moved geographically suggesting many different vectors are competent transmitters.

When the probabilities of introduction and onward transmission were combined (Gale *et al.,* 2010), exotic animals, germplasm, hides/skins and meat/milk products were considered to have an overall negligible probability with regards to disease incursion (Table 5).

Table 5: Overall risks for main routes of potential introduction and further onward transmission of Lumpy skin disease virus within the United Kingdom

Route	Probability of LSDV introduction	Probability of LSDV onward transmission	Overall probability
Livestock	Very low	High	Very low
Exotic animals	Negligible	Negligible	Negligible
Germplasm	Negligible	Very low	Negligible
Hides/skins	Very low	Negligible	Negligible
Meat and milk products	Very low	Negligible	Negligible
Vectors	Very low	High	Very low

For livestock and vectors the overall probability was considered to be very low as dictated by the very low probability of introduction into the UK despite the high probability of onward transmission should an introduction event occur. As stated previously, these probabilities are associated with often high uncertainty due to lack of robust scientific evidence.

Discussion

This risk assessment has estimated the probability of incursion into, and onward transmission of LSDV within, the UK. In doing so it has highlighted those knowledge gaps with significant impact on the uncertainty associated with the overall conclusions. Whilst the assessment was UK centric the knowledge gaps are generic and relevant to the uncertainty surrounding the probability of introduction and spread in any geographical region. Overall the probability of LSDV being introduced to the UK was considered, at most, to be very low for all routes with the exception of exotic animals and germplasm (negligible). The probability of onward transmission was considered highest for vector mediated routes either via contact of an infected vector with a susceptible cattle or contact of a competent native vector with infected cattle. The probability of onward transmission is, however, likely to be reduced once the first case of LSD has been detected if vaccination is undertaken. Risk-based vaccination, to avert the spread of the disease, may even be carried out in the UK if LSD is detected in mainland northern Europe as has recently been recommended with regard to countries that have not yet been affected by LSD but are considered at risk (FAO 2017).

For the live animal import or trade route, it was considered that entry of disease would require infected animals entering the UK from a country which was currently not classed as ‘at risk’ and where no UK post-import testing for LSDV is required. Such countries would be those which had previously imported or consigned animals from an ‘at risk’ country or those that were in close enough proximity to infected countries whereby virus could have entered their cattle populations as a result of transboundary vector and/or cattle movements. Infection and exportation of an animal to the UK would rely on a series of events whereby infection goes undetected and the animal selected for export comes from the same herd (or neighbouring herd to allow for short distance

vector transmission) which had previously imported an animal from an 'at risk' country. This very low risk is, however, likely to be mitigated by the regulated vaccination of cattle carried out by countries currently affected by LSDV and their neighbouring countries.

In the unlikely event that the disease spreads undetected into western continental Europe (to Germany or the Netherlands for example), the likelihood of consigning an infected animal into the UK from a country that is erroneously believed to be uninfected, could increase due to subclinical or incubation period infection. Using the European Food Safety Authority (EFSA) model, if seroprevalence of LSDV in the country of origin was 5%, but currently undetected, the import of 140 or 7,809 animals from that country would give a probability of introduction of 5% or 95% respectively. The highest number of cattle imported into the UK during 2016 was 4,074 from the Republic of Ireland (ROI). According to the same EFSA model, if seroprevalence of LSDV was 5% and undetected in the ROI then the probability of introduction into the UK would be ~ 75% using 2016 trade data (EFSA 2015); this scenario is, however, extremely unlikely due to the control and prevention measures put in place by EU MSs.

Within the UK, preliminary outbreak assessments are undertaken by the Government on notification of a disease outbreak from the EU or WOAH. These assessments indicate the threat of the disease incident at present and in the future and are used to inform the Governments' advice and consideration of preventative controls. For LSD, however, medium to high uncertainty surrounds the probability of introduction to the UK via several of the routes assessed here. These are the initial stages of the risk pathway and therefore all assessments made consequential to these probabilities are underpinned by high uncertainty. Previous risk assessments have so far assumed 2 routes of spread, that is, direct and indirect but they can only assume that the more rapid local spread is vector borne and longer distance transmission is direct spread due to cattle movements (Magori-Cohen *et al.,* 2012; Mercier *et al.,* 2017). The accuracy of the calculation of R_0 for LSDV, i.e. the number of cases one infected case can generate over the course of its infectious period, could be greatly improved if the vectors involved in transmission were definitively identified. This would allow for vector abundance to be taken into account (Hartemink *et al.,* 2009), the influence of the extrinsic incubation period (if any) (Brand

et al., 2016) and the ratio of host to vector species when calculating R_0 (Turner *et al.,* 2013).

This risk assessment acknowledges that the current understanding of the epidemiology of LSD and the potential pathways for the introduction and further dissemination has a number of limitations. Therefore, any inferences made have varying degrees of uncertainty which needs to be acknowledged. The key uncertainties associated with the transmission of LSDV have been summarised elsewhere (EFSA 2015), but how they impinge on risk assessment is highlighted here. The highest uncertainty was found to be associated with the current data available on vector species, transmission rates via all routes and illegal trade of animal products. The matrix method used here to calculate the probabilities of introduction and onward transmission dictates that the product of two probabilities is, at most, the minimum of the two values (Gale *et al.,* 2010). If, therefore, the lowest probability within a pathway has high uncertainty associated with it the overall probability calculated may be artificially skewed towards underestimation.

The results here show that for the period June 2017 to June 2018 the overall probability of introduction and onward transmission of LSDV to the UK is very low. However, perhaps of more value are the uncertainty estimates surrounding the probabilities of the pathway stages and on which research should be targeted to make conclusions more robust.

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3.4 Conclusions to Chapter 3

The work presented in this chapter describes a RA carried out to assess the risk of introduction of LSD virus into the UK and the potential risk of onward spread. The RA makes use of the matrix method for combining conditional probabilities for the individual pathways for entry and onward transmission of the virus and of the overall risk for both entry and onward transmission combined.

Several issues have been identified with using a risk matrix for combining likelihoods. For example, the overall risk estimate may be over-estimated if the matrix does not allow for the product of multiple conditional probabilities to be lower than the lowest value of the individual probabilities. Using a quantitative example, if 10^{-3} represents low for a release estimate and 10^{-5} represents very low for exposure then numerically $10^{-3} \times 10^{-5} = 10^{-8}$ i.e. the result would be lower than the lowest of the two original probabilities. Thus, multiplying two probabilities may, in some cases, result in a level that is lower than the lowest of the two initial levels and this issue can be compounded when combining more than two probabilities together within a risk pathway (Dufour *et al*., 2011).

Conversely, underestimation of the risk could occur if a matrix is used which does take into account that the product of probabilities that are assessed to be “low” or “very low” can be lower than the lowest individual probability (Gale *et al.,* 2014). Despite these draw backs, however, this RA demonstrated how the use of a risk matrix has the advantage of being an objective and reproducible method for combining estimates, visually demonstrating to the risk manager how the conditional probabilities within a risk pathway have been combined.

The next Chapter presents a qualitative RA that considers the risk of infection to sentinel birds at each stage of the risk pathway, considering both the level of pathogen and the minimum infectious dose, and concludes when the risk becomes negligible.

Chapter 4: A qualitative risk assessment of cleansing and disinfection requirements after an avian influenza outbreak in commercial poultry

4.1 Authorship and funding statement

The development and implementation of the methodology and the analysis of the evidence and review of literature was my own work. Prof. Ian Brown provided disease expertise. Dr Paul Gale and Dr Amie Adkin provided review and Dr Jane Clark provided policy advice. Dr Louise Kelly supervised the project. The following poultry experts provided valuable information to estimate model parameters: Rob Davies, Mark Williams, Paul McMullin, Stephen Lister, Maire Burnett, Daniel Parker and Dan Pearson. This worked was funded by the UK Poultry Health and Welfare Group.

4.2 Summary of the published paper

The published paper in this chapter assesses the cleansing and disinfection (C&D) requirements after an avian influenza (AI) outbreak in commercial poultry and was published online in September 2019 in the British Poultry Science journal https://www.tandfonline.com/doi/full/10.1080/00071668.2019.1655707. The paper was based on a commercially funded (by the Poultry Health and Welfare Group) project to assess whether it was necessary to dismantle all complex equipment in a poultry house prior to secondary C&D after an AI outbreak. This was following the AI outbreaks in 2014 and 2015 during which the dismantling and reassembling of equipment led to high costs to individual farmers. For example, the cost of secondary C&D including the dismantling of the complex equipment in one HPAI outbreak in 2015 was in the order of £300-400k in labour and washing and took 3-4 months to complete.

The work presented in this paper was used to make an evidence based risk management decision to change UK policy from interpreting the European Commission Directive (2005/94/EC) (EU 2006) as necessitating all complex equipment or installations to be dismantled prior to secondary C&D to permitting the latter to be undertaken without dismantling equipment that could otherwise be appropriately cleansed and disinfected.

The work was presented as a tool whereby for each piece of equipment the likelihood of AI virus surviving, and the level of virus surviving, was assessed after preliminary C&D

only, for secondary C&D without dismantling and for secondary C&D with dismantling using evidence from literature and opinions from disease experts. In quantitative risk assessment the probability of survival and pathogen load can be modelled at different steps of the risk pathway. For example, a quantitative RA looking at the risk of human exposure to ESBL-producing *Escherichia coli* via milk and unpasteurised cheese addressed both the probability of an animal contaminating the bulk tank milk as well as the amount of faeces contaminating the milk from the animal. Similarly, both the probability of a pasteurisation failure and the number of ESBL *E. coli* present after a failed pasteurisation were both assessed (Berriman *et al.,* 2015).

In qualitative RA the dose response is not usually accounted for until the end stage of the risk pathway after the probability of pathogen survival has been assessed for each preceding step and up to the point of exposure of a susceptible host to the pathogen. At this stage, the likelihood of infection is subjectively considered assuming the amount of pathogen present at the point of exposure and the dose response within the host. In this tool, however, as the level of virus remaining was estimated at each step of the risk pathway for individual pieces of equipment, it was possible to estimate the probability of infection under each scenario for each step. As a virus is incapable of multiplying outside of a living host but is subject to decay depending on the environmental conditions only the reduction in level of virus considering natural decay over time and the effects of preliminary and secondary C&D needed to be accounted for. Qualitative risks of infection in a sentinel flock were, therefore, derived for different possible combinations of farm-type, items of equipment and matrix in which the organism may be present by following the fate of the organism throughout the full C&D procedure.

The project concluded that, provided secondary C&D is carried out with due diligence (i.e. to a defined code of practice as agreed by both industry and government), the risk of re-infection of AI viruses from equipment was considered negligible and it was, therefore, not necessary to dismantle complex equipment in every case.

In the event of the increased number of AI cases in poultry in Great Britain since this work was carried out (Figure 1) the burden on the farmers regarding the requirements of secondary C&D has been reduced as a result of this policy change. This RA was

updated in 2024 to further amend policy with regards to reducing the time scale between secondary C&D and restocking of birds.

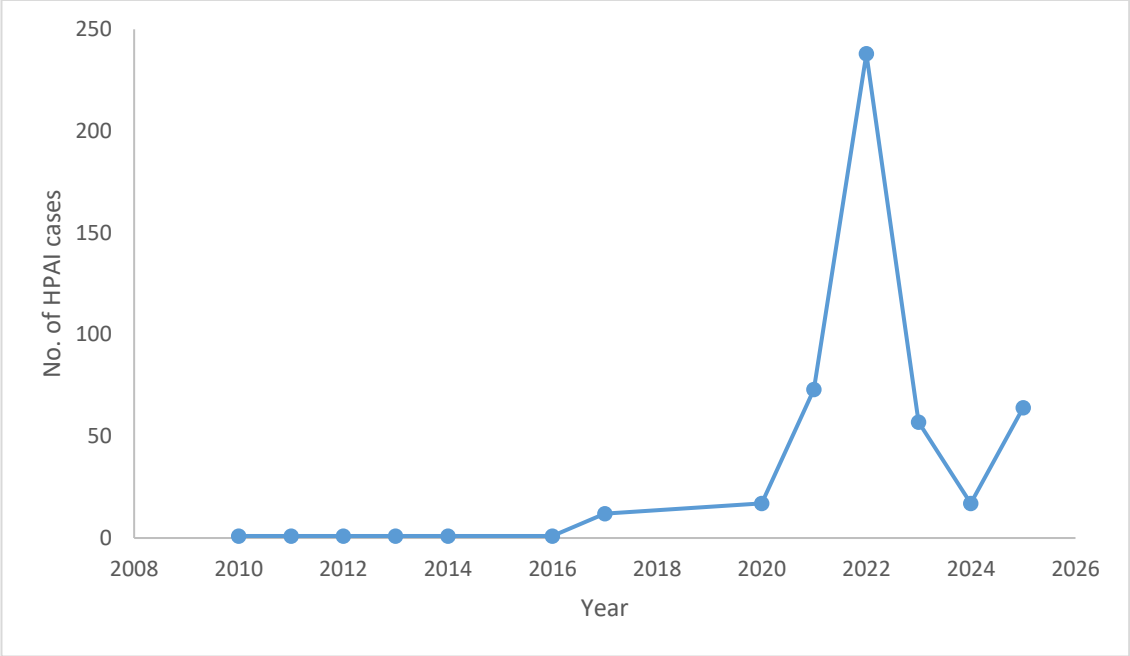

Figure 1: Number of highly pathogenic avian influenza cases in Great Britain poultry from 2010 to 2025 (as of October 24th 2025)

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4.3 Full text of the published paper

A qualitative risk assessment of cleansing and disinfection requirements after an avian influenza outbreak in commercial poultry

Verity Horigan, Paul Gale, Amie Adkin, Ian Brown, Jane Clark, Louise Kelly

Abstract

1. During an Avian influenza (AI) outbreak in the United Kingdom the joint aim of the poultry industry and the Government is to eliminate and prevent the spread of infection, through control measures based on the current European Union (EU) Council Directive (2005/94/EC). An essential part of these measures is the cleansing and disinfection (C&D) of infected premises.

2. This risk assessment assessed the differences in risk of re-infection in a repopulated flock if the EU Directive is interpreted to permit secondary C&D to be undertaken either with or without dismantling complex equipment. The assessment estimated the probability of virus survival on different types of equipment in a depopulated contaminated poultry house before and after preliminary and secondary C&D procedures. A risk matrix spreadsheet tool was used to carry out the assessment and concluded that provided secondary C&D is carried out with due diligence (i.e. carried out to a defined code of practice as agreed by both industry and policy makers), the risk of re-infection from equipment is negligible both with and without dismantling complex equipment in all farm types considered.

3. By considering the equipment types individually, the assessment identified those areas of the house which may still contain viable virus post preliminary C&D and, therefore, on which attention should be focussed during secondary C&D. The generic risk pathway and risk matrix spreadsheet tool have the potential to be used for other pathogens and species given appropriate data.

Introduction

Poultry can be affected by a variety of diseases and parasites but Avian Influenza (AI) viruses and Newcastle disease (ND) viruses are the only avian diseases that must be notified to the competent authority by law if suspected in the United Kingdom (UK). Their notifiable status is due to the high mortality and morbidity experienced within an infected poultry population and the economic impacts from trading restrictions and embargoes placed on infected areas or countries (Aldous *et al.,* 2010). During a notifiable avian disease (NAD) outbreak the Government's aim is to prevent the spread of infection through proportionate and evidence-based control measures based on the current European Union (EU) Council Avian Influenza Directive (2005/94/EC) (EU 2006). An essential part of these control measures is the cleansing and disinfection (C&D) of infected premises (IP) to remove virus from the IP before restocking can occur and movement/trade restrictions can be lifted. The efficiency and speed with which C&D is completed directly impacts the wider industry with economic implications. In the UK, following government funded preliminary C&D, a notice will be served on the owner/occupier of the IP requiring them to carry out secondary C&D at their own expense and to the satisfaction of a Government veterinary officer. Preliminary C&D essentially involves spraying all surfaces with disinfectant to 'damp down' any virus in the environment whilst secondary C&D involves cleansing to remove organic debris, degreasing and disinfecting and then repeating the process to provide a high level of confidence that any virus on the premises is eliminated.

The EU Directive states that during secondary C&D "washing and cleansing by careful brushing and scrubbing of the ground, floors, ramps and walls following the removal or dismantling, where possible, of equipment or installations otherwise impairing the effective cleansing and disinfection procedures" is required. The directive may be interpreted and implemented by necessitating all complex equipment or installations e.g. cages, egg belts etc., to be dismantled prior to secondary C&D. Dismantling and then reassembling the complex equipment is, however, time and labour intensive, leading to high costs to the individual producer and may result in an extended period before trade can re-commence for the wider industry.

This risk assessment assesses the differences in risk to a sentinel flock of poultry if the EC Directive was interpreted to permit secondary C&D to be undertaken either with or without dismantling all complex equipment that could otherwise be appropriately cleansed and disinfected. The results are presented as a qualitative assessment risk matrix tool based on a generic risk pathway with the potential to be used for other pathogens and species, given appropriate data. Worst case assumptions were made when no other data were available. The assessment estimated the probability of virus survival on different types of equipment in a depopulated contaminated poultry house before and after preliminary and secondary C&D procedures before deriving a probability of re-infection in a sentinel poultry flock.

Methods

Risk question

The following risk question was used as a basis for this assessment:

"What is the risk of re-infection with Avian Influenza in a layer breeder, broiler breeder, layer or broiler flock from complex equipment/installations, given the different interpretations and implementations of the EU directive with regards to C&D?"*

** detailed in the following sections*

Throughout this report, poultry is taken to refer to the sectors being considered as outlined in the risk question for chickens *Gallus gallus* only.

Risk Pathway

The pathway, as shown in Figure 1, is generic for all poultry groups and premises type being considered in this assessment. Each step on the pathway considers a key stage of the process, in relation to either virus levels or risk mitigation. The pathway divides according to whether or not secondary C&D is carried out and, if it is carried out, whether or not dismantling of complex equipment occurs.

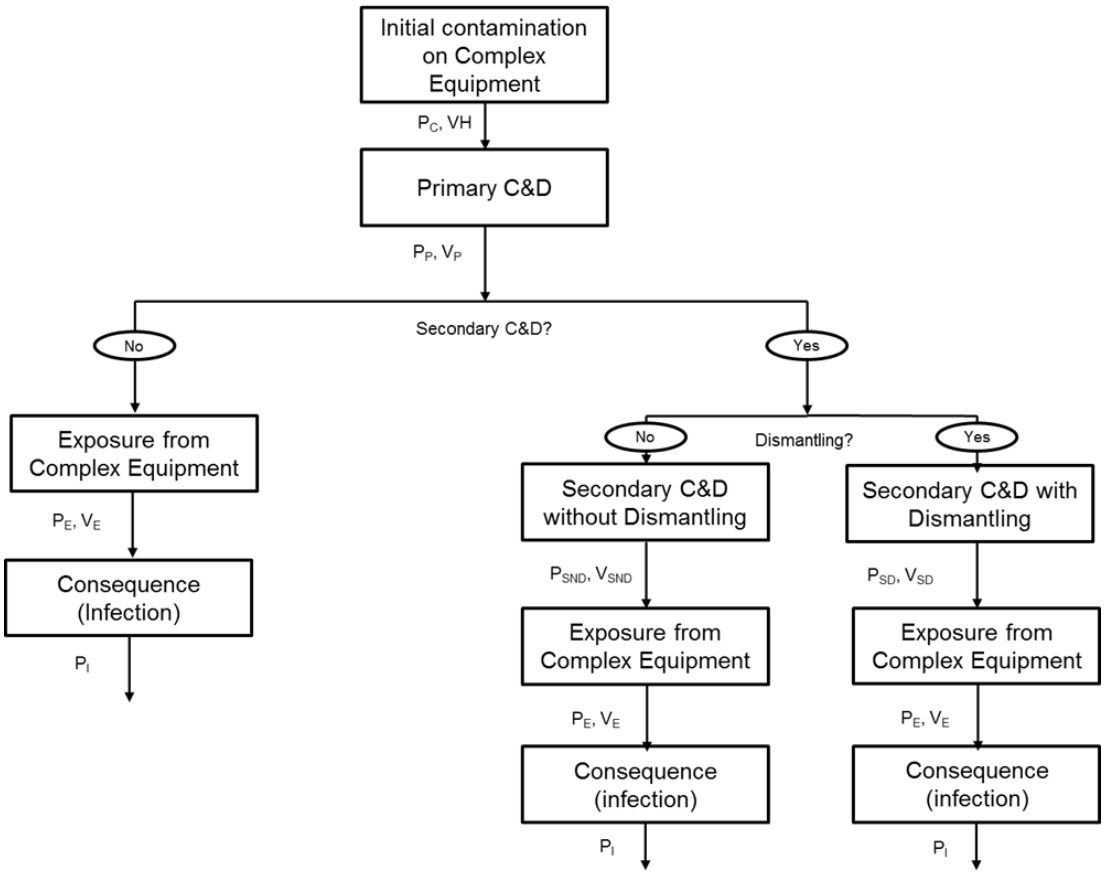

Figure 1: Generic risk pathway considering key stages of the C&D process and illustrating the three scenarios for which the risk of re-infection is assessed. The different stages of the pathway will incorporate more detail including, for example how the virus survives over time. The variables are defined in table 1.

Risk assessment

There are three scenarios for which the risk was assessed:

1. Infection from complex equipment with preliminary C & D and no secondary C&D

2. Infection from complex equipment with preliminary C&D and secondary C&D without dismantling

3. Infection from complex equipment with preliminary C&D and secondary C&D with dismantling

For each step, the key outputs are probabilities of contamination and virus levels and are defined as in Table 1.

Table 1: Probability definitions for the generic risk pathway derived for individual types of equipment

Scenario	Steps and Outputs
No Secondary C&D	Initial contamination on Complex Equipment P_C: Probability virus present on complex equipment at time of preliminary C&D V_H: Viral load on complex equipment at time of preliminary C&D Preliminary C&D P_P: Probability virus present on complex equipment after preliminary C&D V_P: Viral load on complex equipment after preliminary C&D Exposure P_E: Probability birds exposed to virus on complex equipment V_E: Viral load on complex equipment to which birds are exposed Consequence (Infection) P_I: Probability of infection, given exposure and viral load to which birds are exposed (dose-response)
Secondary C&D without Dismantling	Initial contamination on Complex Equipment P_C: Probability virus present on complex equipment at time of preliminary C&D V_H: Viral load on complex equipment at time of preliminary C&D Preliminary C&D P_P: Probability virus present on complex equipment after preliminary C&D V_P: Viral load on complex equipment after preliminary C&D Secondary C&D without Dismantling P_{SND}: Probability virus present on complex equipment after secondary C&D without dismantling V_{SND}: Viral load on complex equipment after secondary C&D without dismantling Exposure P_E: Probability birds exposed to virus on complex equipment V_E: Viral load on complex equipment to which birds are exposed Consequence (Infection) P_I: Probability of infection, given exposure and viral load to which birds are exposed (dose-response)
Secondary C&D with Dismantling	Initial contamination on Complex Equipment P_C: Probability virus present on complex equipment at time of preliminary C&D V_C: Viral load on complex equipment at time of preliminary C&D Preliminary C&D P_P: Probability virus present on complex equipment after preliminary C&D V_P: Viral load on complex equipment after preliminary C&D Secondary C&D with Dismantling P_{SD}: Probability virus present on complex equipment after secondary C&D with dismantling V_{SD}: Viral load on complex equipment after secondary C&D with dismantling Exposure from Complex Equipment P_E: Probability birds exposed to virus on complex equipment V_E: Viral load on complex equipment to which birds are exposed Consequence (Infection) P_I: Probability of infection, given exposure and viral load to which birds are exposed (dose-response)

The risk assessment follows the guidelines and risk terminology as amended from the European Food Safety Authority (EFSA) (EFSA 2006) and the World Organisation for Animal Health (WOAH) (WOAH 2004). Briefly, the probabilities are expressed qualitatively as *negligible, very low, low, medium, high* and *very high* and defined as: *negligible*, so rare that it does not merit to be considered; *very low*, very rare but cannot be excluded; *low*, event is rare but does occur; *medium*, event occurs regularly; *high,* event occurs very often; and *very high*, event occurs almost certainly.

An uncertainty level was not included for the likelihoods in this risk assessment as the results were described relative to each other for the 3 different scenarios (Table 1) making use of the same data to populate the same likelihoods for each scenario e.g. level of pathogen in matrix, rate of contact between equipment and matrix, accumulation of matrix on equipment, P_c, V_H, P_p, V_p. However, as characterization of uncertainty is also beneficial in identifying data gaps and their possible effect on the assessment results, these were considered in detail in the discussion with two of the main uncertainties being the infection dynamics and survival of AI viruses and the virus strain variability.

The following assumptions were made:

- Low temperature environmental conditions mirroring historical winter AI outbreaks in Europe. Barns will normally reduce to external ambient temperature during C&D and downtime; the speed at which this happens will depend on time of year and the particular system (and internal temperatures prior to depletion).

- Heating to high temperatures for a number of days to kill the virus is not carried out (although this technique has sometimes been used to kill red mites and may be approved as an option for notifiable disease control in the future)

- No water based products would be used in below freezing temperatures

- Viral load and survival within different organic matrices were based on values from the literature. When data were not available worst case assumptions were adopted using expert opinion (See the Supplementary material for details). For example, in some cases proxy data, in particular, Salmonella studies, were used to assess

probabilities. Data on the number of bacteria pre and post C&D can help to indicate those areas where organic material is concentrated and those that are difficult to clean thoroughly whilst acknowledging that there will be differences between viral and bacterial environmental survival characteristics and susceptibility to C&D. Approved dilution rates for statutory use of Virkon S for 'diseases of poultry order and the avian influenza and influenza of avian origin order' which uses ND virus as the target organism is 2.8 X greater than that for general orders which uses Salmonella Enteritidis as the target organism. AI is less robust than ND so could therefore be considered very susceptible to disinfectants. It is also possible for bacteria to multiply in suitable conditions after C&D has been carried out whereas viruses will continue to be subject to natural decay over time depending on the environmental conditions.

- Highly pathogenic avian influenza (HPAI) and low pathogenic avian influenza (LPAI) are treated as one generic virus with the same parameters e.g. titres in organic matrices, survival times (due to variability among strains within these groupings and insufficient data to assess the viruses independently)

- Time periods between C&D stages and repopulation (based on expert opinion and timescales from previous AI outbreaks (see Supplementary material)) with the exception of the post preliminary C&D which is an unrealistic scenario.

- Secondary C&D carried out with due diligence (i.e. according to a defined code of practice as agreed by both industry and policy makers)

- No risk mitigation strategies for outdoor paddocks in free range poultry houses

In terms of approach, for each poultry species and premises type combination (referred to hereafter as farm-type), there are different types of equipment and matrices in which the virus may be present. The four organic matrices considered were dust, feathers, faecal material (cloacal) and oropharyngeal deposits. Each matrix can vary in relation to the extent to which it contributes to the risk of infection for the different poultry houses and different items of equipment. For example, whilst oropharyngeal deposits can contain high levels of virus, there is very little organic material protecting the virus which makes it exposed to the effects of disinfectants unless it is in a hard to access area. Avian

influenza virus is known to survive for up to 120 days in feathers (Yamamoto *et al.,* 2010), however, direct environmental contamination from these contaminated feathers may be limited to a local area because of the nature of the material (Yamamoto *et al.,* 2010).

For the assessment, each combination of equipment and matrices has its own set of probabilities along the pathway and therefore its own overall estimate of probability of infection (see Supplementary material). Due to the fact that these overall probabilities are a product of the conditional probabilities, each is therefore determined by the lowest of the pathway estimates (Gale *et al.,* 2010). Thus, for a particular piece of equipment and matrix, if there is a negligible or very low probability present in the pathway, the risk from that equipment will be negligible or very low (at most). Clear definitions were allocated to each qualitative rating and agreed by the project board. Risk assessors then used these ratings with evidence from peer reviewed literature. Initial ratings were subsequently presented and discussed with disease experts and the poultry industry (see acknowledgements) and revised where necessary.

The risk assessment process maps all of the individual probabilities and pathways to identify any types of equipment which have a non-negligible risk using a risk matrix approach. Exposure via contamination of a particular piece of equipment is determined after a period of time before restocking and includes natural virus decay. The risk matrix assessment, including exposure, is presented as a spreadsheet tool to assist in the visualisation of the relative risks for the equipment types, matrices, farm types and C&D scenarios.

Results

In the spreadsheet based risk matrix tool, qualitative estimates of risk are provided for possible combinations of, farm-type, equipment and organic matrix in which the organism may be present. Figure 2 illustrates the assessment tool with the pathway flowing from left to right. It begins with the level of pathogen in each matrix, accumulation of the matrices on individual items of equipment and through the different C&D scenarios. It assesses the probability of virus survival, viral load and

probability of exposure to virus for a sentinel flock for each scenario. The use of different equipment, farm types and matrices can be examined in the spreadsheet by using the filter facility in the column header row. For example, Figure 3 illustrates the use of the tool filtered to show only results for enriched colony caged layers. This demonstrates how the estimates for probability of infection and viral loads differ between the scenarios as described in Table 1. It is estimated until the point where the probability of virus survival and any remaining viral load is not considered to be at a significant enough level to cause infection in a sentinel flock of birds.

Equipment	Farm Type	Matrix with which equipment can come in contact with	Level of pathogen in matrix	Rate of contact between equipment and matrix	Accumulation of matrix on equipment	Probability virus present in matrix on equipment after depopulation and before primary C&D (assume 2 days) (P_C)	Viral load in matrix on equipment at time of preliminary C&D (V_H)	Probability of virus survival in matrix on equipment after primary C&D (P_P)	Viral load in matrix on equipment after primary C&D and at time of restocking (V_P)	Probability birds exposed to virus in matrix on or from equipment (P_E)
scratching mat	Enriched Colony cages layers	Dust	Medium	High	Medium	Medium	Medium	Low	Low	Low
	Enriched Colony cages layers	Oropharyngeal	High	High	Medium	Medium	High	Low	Low	Low
	Enriched Colony cages layers	feathers	High	Low	Low	High	Low	high	Low	Very low
	Enriched Colony cages layers	Faecal (cloacal)	Medium	High	High	High	High	medium	Medium	Medium
Colony cages	Enriched Colony cages layers	Dust	Medium	High	Low	Medium	low	Low	Very Low	Very Low
	Enriched Colony cages layers	Oropharyngeal	High	High	Low	Medium	low	Low	Very Low	Very Low
	Enriched Colony cages layers	feathers	High	Low	Low	High	low	high	Low	Very low
	Enriched Colony cages layers	Faecal (cloacal)	Medium	High	Medium	High	Medium	medium	Medium	Low
Slatted area	Barn layers	Dust	Medium	High	Medium	Medium	Medium	Low	Low	Low
	Barn layers	Oropharyngeal	High	High	High	Medium	High	Low	Low	Low
	Barn layers	feathers	High	Medium	Low	High	low	high	Low	Very low
	Barn layers	Faecal (cloacal)	Medium	High	High	High	High	medium	Medium	Medium
	Free range layers	Dust	Medium	High	Medium	Medium	Medium	Low	Low	Low
	Free range layers	Oropharyngeal	High	High	High	Medium	High	Low	Low	Low
	Free range layers	feathers	High	Medium	low	High	low	high	Low	Very low
	Free range layers	Faecal (cloacal)	Medium	High	High	High	High	medium	Medium	Medium
	Broiler-rearer	Dust	Medium	High	Medium	Medium	Medium	Low	Low	Low
	Broiler-rearer	Oropharyngeal	High	High	High	Medium	High	Low	Low	Low
	Broiler-rearer	feathers	High	Medium	low	High	low	high	Low	Very low
	Broiler-rearer	Faecal (cloacal)	Medium	High	High	High	High	medium	Medium	Medium

Figure 2: Risk Matrix qualitative assessment tool: example output

Equipment	Rate of contact between equipment and matrix	Accumulation of matrix on equipment	Probability virus present before primary C&D (P_C)	Viral load at time of preliminary C&D (V_H)	Probability of virus survival after primary C&D (P_P)	Viral load after primary C&D (V_P)	Probability birds exposed to virus (P_E)	Viral load to which birds are exposed (V_E)	Probability of infection in sentinel flock after preliminary C&D (P_I)	Probability of virus survival after secondary C&D (no dismantling) (P_{SND})
Metal trough	High	Medium	High	High	High	Very Low	Low	Very Low	Very Low	Negligible
Moving hopper	Medium	Low	High	Low	High	Very Low	Low	Very Low	Very Low	Negligible
Moving chain	Medium	Low	High	Low	High	Very Low	Negligible	Very Low	Negligible	Negligible
Bulk bins and augers	Low	Low	Medium	Very Low	Very Low	Negligible	Negligible	Negligible	Negligible	Negligible
Nipples	High	High	Medium	High	Medium	Medium	High	Medium	Medium	Negligible
Drinkers	High	High	Medium	High	Low	Low	Medium	Low	Low	Negligible
Nest box	Low	Low	High	Low	High	Low	Very Low	Very Low	Very Low	Negligible
Nest box liner	Medium	Medium	High	Medium	High	Medium	Medium	Medium	Medium	Very Low
Perches	High	High	High	High	High	Medium	Medium	Medium	Medium	Negligible
Scratching mat	High	High	High	High	High	Medium	Medium	Medium	Medium	Very Low
Colony cages	High	Medium	High	Medium	High	Medium	Low	Low	Low	Negligible
Ventilation	High	High	Medium	Medium	Medium	Medium	Very Low	Low	Very Low	Negligible
Egg belt	Medium	Low	High	Low	Low	Very Low	Very Low	Negligible	Negligible	Negligible
Cross conveyor (eggs)	Medium	Low	High	Low	Low	Very Low	Very Low	Negligible	Negligible	Negligible
Packing area	Low	Low	High	Low	Low	Very Low	Negligible	Negligible	Negligible	Negligible
Manure belt	High	High	High	High	High	Medium	Low	Medium	Low	Very Low
Cross conveyor (manure)	High	High	High	High	Medium	Medium	Negligible	Negligible	Negligible	Negligible
Manure air drying equipment	High	High	High	High	High	Medium	Negligible	Negligible	Negligible	Negligible
Manure store	High	High	High	High	Medium	Medium	Negligible	Negligible	Negligible	Negligible
Floors	Low	Low	High	Low	High	Very Low	Very Low	Very Low	Very Low	Negligible
Walls	Low	Low	Medium	Low	Low	Very Low	Very Low	Negligible	Negligible	Negligible

Figure 3: Risk matrix qualitative assessment tool for enriched colony caged layers showing results for Scenario 1 (P_1) and the 'Negligible' probability of virus survival on most bits of equipment after secondary C&D without any dismantling

Based on evidence in the literature dust and faecal deposits were considered to contain a medium level of AI virus while oropharyngeal deposits and feathers were considered to contain high levels of virus (Yamamoto *et al.* 2008b, Yamamoto *et al.,* 2008a, Pepin *et al.,* 2014, Spekreijse 2013, Reis *et al.,* 2012). Table 2 shows those items of equipment which give the highest predicted probability of infection for each of the three C&D scenarios for individual farm production types. The risk assessment predicts that, within any farm-type other than free range layers, the probability of infection in a sentinel flock from any equipment is negligible after secondary C&D, irrespective of whether or not dismantling occurs (Table 2). The 'Medium' probability results for preliminary C&D are assuming a sentinel flock is introduced directly after C&D has occurred. Whilst this is an unrealistic scenario, it demonstrates the probability of where residual virus may still be present within the poultry house at this time.

Table 2: Probability of infection in a sentinel flock for the three scenarios included in the risk pathway (equipment in brackets are those items with the highest risk at that stage)

Farm Type	**Preliminary C&D only (R_P)**	**Secondary C&D without dismantling (R_{SND})**	**Secondary C&D with Dismantling (R_{SD})**
Enriched Colony Caged	Medium (nipples; nest box liner; perches, scratching mat)	Negligible (All equipment)	Negligible (All equipment)
Free range layer	Medium (nipples; floor; outdoor areas; nest box liner; perches; slatted areas; enrichments)	Low (outdoor areas)	Low (outdoor areas)
Barn layer	Medium (nipples; floor; nest box liner; perches; slatted areas; enrichments)	Negligible (All equipment)	Negligible (All equipment)
Broiler breeder	Medium (nipples; floor; nest box liner; autonest; slatted areas; enrichments)	Negligible (All equipment)	Negligible (All equipment)
Broiler rearer	Medium (nipples; floor; slatted areas; enrichments)	Negligible (All equipment)	Negligible (All equipment)

For free range layers, the probability of infection from outdoor areas (which would not be affected by dismantling) was assessed as low (assuming no risk mitigation strategies

have been applied to these areas), with the risk from all types of equipment being negligible; this is assuming a time period of ~37 days between culling and restocking and low temperature conditions. By considering the equipment types individually, the assessment identifies those areas of the house which may still contain viable virus post preliminary C&D to which sentinel birds may have access and where attention should be focussed during secondary C&D. Considering all poultry production types, these areas are drinking nipples, floor, outdoor areas, nest box liner and autonests, perches, slatted areas and enrichments.

Figure 4 shows the relative risk of infection across the different types of equipment, within a particular farm-type, for the preliminary C&D scenario, demonstrating the areas of highest risk. The two secondary C&D scenarios are not shown graphically because the risk from all equipment types was predicted to be negligible with the exception of the outdoor areas (risk was considered 'Low') for both scenarios. It is stressed that the ordinal scales used to produce Figure 4 are not quantitative values and are used only to illustrate qualitative relative risk.

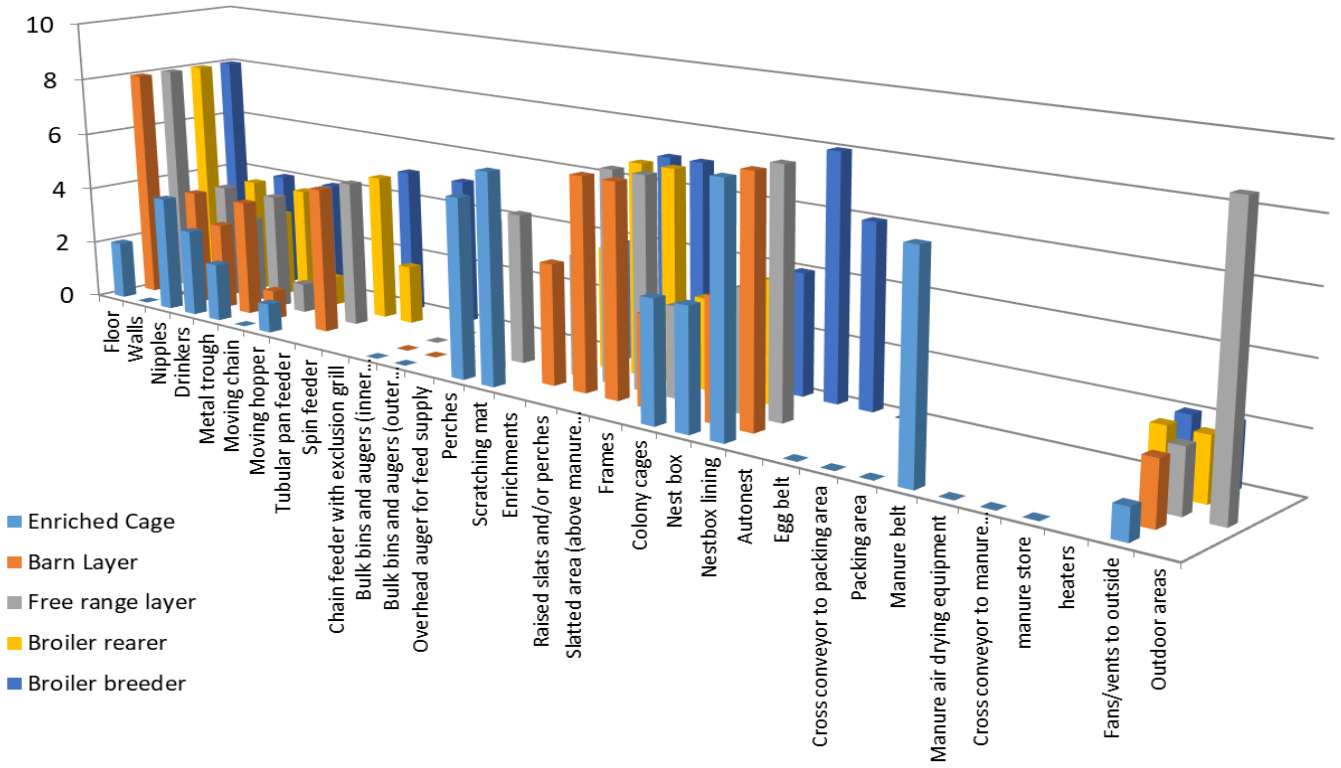

Figure 4: Comparison of the combined risk for items of equipment from all four organic matrices in the different poultry sectors immediately after preliminary C&D. The ordinal scales are not quantitative values and are used only to illustrate qualitative relative risk. The results for preliminary C&D are assuming a sentinel flock is introduced directly after C&D has occurred. Whilst this is an unrealistic scenario, it demonstrates the probability of where virus may still be residual within the poultry house at this time.

The risk assessment found a negligible risk of re-infection in sentinel chickens resulting from contact with any equipment in enriched colony caged systems for both the secondary C&D scenarios. This is the poultry sector with the most complex equipment involving numerous cages and hard to access areas such as manure belts and nest boxes. A very low probability of virus survival was associated with faecal deposits on the nest box liners and scratching mats. At this stage of the C&D procedure, however, taking into account natural virus decay, the viral load was considered to be negligible as was the probability of a bird being exposed to a high enough level of virus to constitute an infectious dose. This is based on experimental minimum infectious dose data (Aldous *et al.,* 2010) and the assumption that the birds would not come into direct contact with virus within the nest boxes. Nest box liners can be perforated to allow all the dust and muck to fall away, however, they can still become soiled by faeces and have been found to be more heavily soiled than wired areas due to droppings stuck in the mats (Guinebretiere *et al.,* 2012). It is considered that a thorough C&D procedure would eliminate the majority of the organic matter and that the blades on the artificial turf mats, which prevent eggs from coming into direct contact with the droppings trapped within the blades, would also reduce the risk of the bird accessing any remaining virus.

A very low probability of virus survival and estimate of viral load was also found for dust and faecal deposits on the manure belts of colony caged systems. Due to the slow movement of these belts resulting in negligible dispersal of residual dried organic matter it was assumed that there would be negligible probability of the birds being exposed to an infectious dose of virus present on the belt.

For those poultry sectors with less complex equipment such as barn and free range layers and broiler breeders and rearers, the floor was found to have a very low probability of viral survival for both secondary C&D scenarios. The viral load at the time of restocking, however, was considered to be negligible as was the probability of infection in a sentinel flock. A very low probability of virus survival in faecal deposits on the nest box lining was also found after secondary C&D for barn and free range layers and broiler breeders but the risk of infection was reduced to negligible for the same reasons as colony caged birds.

For barn and free range layers, broiler breeder and the broiler rearer sector a medium risk of infection immediately after preliminary C&D was predicted for nipples, drinkers, the floor area, nest box liners, perches, enrichments, and slatted areas. Again these are the items of equipment that are most difficult to access during the spraying of disinfectant during preliminary C&D and which the chickens have close access to. The majority of the risk, for those items other than nipples and drinkers, arises from faecal deposits whereby the organic matter of the deposits could protect the virus from the full effect of the disinfectant applied during preliminary C&D thereby reducing its efficacy.

Discussion

This risk assessment concluded that provided secondary C&D is carried out with due diligence (i.e. carried out to a defined code of practice as agreed by both industry and policy makers) the risk of recrudescence of infection of AI viruses is negligible both with and without dismantling complex equipment in all farm types considered. The correct application of secondary C&D combined with the period of time between depletion and restocking allowing for viral decay are key components in the negligible risk rating for both scenarios. The few items of equipment which still had a very low probability of contamination were generally not in contact with the birds thereby reducing the risk of re-infection.

A low risk after secondary C&D was predicted for the outside paddocks of free range poultry houses but this is assuming that no risk mitigation activities take place. The outdoor areas or paddocks are unique to free range poultry sectors whereby C&D will have very little effect on any virus present. Virus here, however, will be subject to UV effect, in addition to natural decay as a result of temperature and other environmental factors. Outdoor survival of virus in wet, puddled cold paddocks, could be longer than in the poultry house but by the time the house has been cleaned and disinfected, restocked and the birds trained to use nest boxes before release to range, the natural decay of virus should result in a negligible risk at restocking. Additional interventions for outdoor areas include: scraping off heavy faecal load close to pop-holes, cutting pasture short to allow drying and exposure to the sun, use of products to ‘dress’ pasture, absorbing

moisture and containing an anti-viral disinfectant or a heavy lime application to reduce pathogen growth.

By considering the equipment types individually, the assessment identifies those areas of the house which may still contain viable virus immediately post preliminary C&D and therefore on which attention should be focussed during secondary C&D e.g. those areas where feathers accumulate or there is a build-up of faecal material. It was assumed that in some areas of the house there will still be viable virus after preliminary C&D has taken place as it was assumed that organic matter will still be present when the disinfectant is applied. It should be stressed that the results are assuming a sentinel flock is introduced directly after preliminary C&D has occurred. Whilst this is an unrealistic scenario, it demonstrates the probability of where virus may still be residual within the poultry house at this time, and so helps prioritise areas for secondary C&D. For the colony caged layer sector a medium risk was found for nipples, nest box liners, perches and scratching mats. These areas of equipment could still potentially harbour significant viral loads after preliminary C&D and also be accessible to the birds so that they are exposed to a sufficient viral load to cause infection (Aldous *et al.,* 2010).

In answering the risk question it was important to consider where the virus is likely to be present in the house, how it is affected by C&D and what access the birds have to those areas predicted to contain high enough levels of virus to constitute an infectious dose. Each poultry system has its own specific design and therefore the critical points for each housing system will differ. Some systems are easier to clean than others and when something is difficult to clean, the risk of it not being cleaned properly will be higher. This will be reflected in the efficacy of the disinfection because heavy organic soiling will influence the performance of the disinfection procedure negatively. In a study on C&D of different layer systems the necessity to pull the laying mats out of the nests and the extra attention spent on cleaning the dust and manure stuck between the tiered flooring were the two main reasons why the colony systems were more labour intensive in terms of cleaning. When this is done properly, however, the disinfection results should not be influenced by equipment type (Bossuyt 2012).

The length of time AI virus can remain infective in the environment, the specific conditions of the environment that increase persistence, and the infective dose required for primary transmission, have all been the subject of many experimental investigations. The majority of the data available for this assessment were based on laboratory conditions without factoring in 'environmental realism' (Dalziel *et al.,* 2016). Persistence of AI viruses is dependent on many parameters such as time, temperature, pH, salinity, light (UV), desiccation and relative humidity (RH) (Stallknecht *et al.,* 2009) and the tenacity of AI viruses to physical and chemical factors also increases in the presence of organic material (Lu *et al*., 2003). In experimental conditions, multiple variables may be held constant (e.g., strain/isolate, pH, salinity, UV, and RH), while others are then varied (e.g., time and temperature). Although this helps isolate the effect of treatments, the interactions of treatments (Stallknecht *et al.,* 2009) may be missed and the results may therefore apply less well to field conditions. Considering the need for environmental realism to be applied to experimental data for survival of AI viruses within the poultry house environment, studies are currently underway to assess the survival of AI virus in a barn setting after C&D has been carried out and whether recrudescence of the virus in a sentinel flock occurs.

The infectivity of AI viruses at different temperatures is also variable from strain to strain (Paek *et al.,* 2010). The lack of data of AI virus survival at low temperatures is particularly relevant, for example, nine out of the fourteen NAD outbreaks since 2006 in the UK occurred between November and February. Variation between viruses was most evident under cold water (4°C) conditions, with little variation observed at temperatures >28°C (Stallknecht and Brown 2009). Studies have also demonstrated that significant variability exists in the infection dynamics observed between individual virus strain, challenge dose and the specific host it infects (Aldous *et al.,* 2010; Swayne *et al.,* 2008a). It should therefore be acknowledged that extrapolation of data from a single virus strain across other avian species or for different strains should be viewed with caution. The application of a 'worst case scenario' for this assessment will have ensured that the risks have not been underestimated but, as such, there remains a medium level of uncertainty associated with the data used for these parameters.

Within this assessment LPAI and HPAI were treated as one virus. While there are likely to be differences between them in terms of persistence, infectious doses and shedding levels in the various matrices, it was considered that there was insufficient data available to assess the viruses independently, although where possible, virus specific data are presented. HPAI viruses are typically found in both the faeces and respiratory secretions of experimentally infected chickens (Spickler *et al.,* 2008). LPAI viruses have also been detected in both these secretions of experimentally infected chickens but the findings are less consistent than with HPAI (Spickler *et al.,* 2008). Naïve wild bird mediated introduction of LPAI viruses are often more likely shed via the cloaca but once the virus moves through a Galliforme host, shedding via the respiratory tract becomes more common. There have been no published studies on shedding of LPAI virus in feathers although the mechanism for virus presence in the follicle is unclear. Data also suggests that LPAI viruses require higher infectious doses to cause infection but that the broad variation in susceptibility of poultry species makes the probability of infection occurring unpredictable (Swayne *et al.,* 2008a; Jones *et al.,* 2004; Pantin-Jackwood *et al.,* 2017; Van der Goot *et al.,* 2003). HPAI virus has been found to be more persistent than LPAI virus in faeces and bedding material (Hauck *et al.,* 2017), although this persistence may be related to the initial higher viral load deposition and degree of contamination with HPAI viruses. Thus, a lower infectious dose and high virus shedding (Aldous *et al.,* 2010), along with greater environmental persistence, likely increase the risk of infection for HPAI compared to LPAI when there is an exposure event. The results are therefore presented for one generic virus acknowledging that this is likely to be a worst cases scenario for LPAI The generic nature does, however, mean that should more data become available, the assessment can be re-parameterised and rerun to obtain pathogen specific results.

C&D is a costly and laborious task and its success in eliminating virus from the houses depends not only on the choice and correct application of disinfectants but specifically upon attention to detail to remove organic matter from those areas identified as still capable of causing infection directly after preliminary C&D. In the UK, reference should be made to the Defra approved disinfectant list which provides a list of products that

can be used in case of an AI outbreak and the concentration they must be used at. Consideration should be given to the efficacy of disinfection at different temperatures and in the presence of organic matter whilst minimising corrosion of metal surfaces, the pitted nature of which could harbour virus and protect it from the disinfectant. Laying houses are difficult to clean thoroughly because of their intrinsically complicated structures, which are even more complex in the case of cage laying houses (Wales *et al.,* 2006). Access to cage interiors, feeders and muck belts is very difficult unless effort and time is invested. It would appear that in these circumstances a large amount of residual organic matter is expected after a standard disinfection procedure (Carrique-Mas *et al.,* 2009). Removal of equipment in on-floor houses which were cleaned separately resulted in a high standard of cleaning. However, this was during routine C&D between flocks so does not allow for the natural decay of the virus over the time taken between culling and re-population that is accounted for in this assessment. Whilst minimal virus decay is likely take place in light of the assumption of low temperature environmental conditions, the time period of 37 days used in this assessment falls within the bounds of viral decay in faeces reported in some studies (Webster *et al.,* 1978; Beard 1984; Lu *et al.,* 2003).

Two of the main uncertainties within this assessment are the infection dynamics and survival of AI viruses and the virus strain variability which may influence these data. There is a need to fully understand the complexity of the large number of potential interacting variables that can affect virus survival within the poultry house environment. Survival of virus on fomites constructed from different materials is important at the interface of the equipment with the deposit containing the virus (Wood *et al.,* 2010; Greatorex *et al.,* 2011; Tiwari *et al.,* 2006; Noyce *et al.,* 2007; Sakaguchi 2010; Bean *et al.,* 1982; McDevitt *et al.,* 2010) but more studies are required to determine viral decay within the organic matrix itself.

Based on these conclusions, recommendations for improving the efficacy of secondary C&D could include the improvement in equipment design to allow better access to those items of equipment with which a higher risk was associated e.g. muck belts and nest boxes. Specific C&D guidelines for higher risk equipment such as this could be outlined

in the C&D procedure (Huneau-Salaun *et al.,* 2010). Design of new poultry sheds could include the requirement to eliminate horizontal surfaces that collect dust, with smooth surface finishes and level concrete floors to facilitate cleaning. The height of new sheds should be tall enough to allow the use of a vehicle fitted with an enclosed, ventilated cab with filtered air intakes to clean the whole of the floor (HSE 2012).

Overall, the risk pathway and matrix tool used for this assessment are generic in nature and can be applied to other pathogens and species to compare scenarios where appropriate data exists. The risk assessment matrix 'tool' complements the pathway and is a novel application which allows the probability of infection from individual items of equipment to be compared taking into consideration probability of virus survival, viral load and probability of exposure throughout the pathway. In this assessment, the pathway and tool provide a framework for effective application of C&D in a way which can lead to reduction of costs to industry and mitigating some delays in recovering country freedom.

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4.4 Conclusion to Chapter 4

The work carried out in this chapter assessed whether it was necessary to dismantle all complex equipment in a poultry house prior to secondary C&D after an AI outbreak. The work was presented as a tool whereby for each piece of equipment the likelihood of AI virus surviving and the level of virus surviving was assessed after various C&D scenarios. In qualitative RA the dose response is not usually accounted for until the end stage of the risk pathway. In this tool, however, as the level of virus remaining was estimated at each step for individual pieces of equipment, it allowed the probability of infection under each scenario and for each item of equipment to be estimated at each step of the risk pathway.

The risk assessment followed the WOAH risk assessment guidelines (WOAH 2025) and risk terminology as amended from EFSA (EFSA 2006). Addressing the dose response is often difficult as data to determine the probability that a given ingested dose will cause infection are often limited, depending on whether the relevant pathogen has been studied experimentally (where an artificially high dose is usually used sometimes using a transmission route that is unlikely to naturally occur), and rarely take into account variation due to factors such as pathogen strain, individual susceptibility and immunity. This is in line with Peeler *et al.,* (2007) who found that susceptibility, or dose response, was one of the weakest elements of any qualitative RA.

This risk assessment underpinned a change in Government policy which impacted both individual farmers and the wider UK poultry industry. The dismantling and reassembling of equipment, as a requirement for secondary C&D, had previously led to high costs to individual farmers also causing impact on their health and wellbeing through the stress and anxiety of the financial pressure and potential loss of livelihood. The conclusions from this risk assessment, which resulted in the policy change, meant there was a reduced financial burden on the farmers regarding the requirements of secondary C&D. The interpretation of the EU directive necessitating all complex equipment to be dismantled prior to secondary C&D also had practical impacts for the UK poultry industry as a whole, such as a potentially extended period before trade could re-commence.

Chapter 4: A qualitative risk assessment of cleansing and disinfection requirements after an avian influenza outbreak in commercial poultry

The next Chapter (Chapter 5) presents a publication which assesses the aggregated probability of the entry of a pathogen into the UK. The paper utilised a published aggregated probability tool and applied it to a case study demonstrating a practical application of the tool. This work has helped expand the literature on the consideration of aggregated probability in qualitative animal health risk assessment.

Chapter 5: Assessing the aggregated probability of entry of a novel prion disease agent into the United Kingdom

5.1 Authorship and funding statement

The application of the methodology and the analysis of the evidence and review of literature was my own work. Dr Timm Konold, Dr Claire Cassar and Dr John Spiropoulos provided disease expertise and Dr Paul Gale and Dr Amie Adkin reviewed the work. Dr Louise Kelly supervised the project. This work was funded by Defra, Scottish Government and Welsh Government.

5.2 Summary of the published paper

The published paper in this chapter assesses the probability of entry of the camel prion disease agent into the UK and was published in the Microbial Risk Analysis journal in December 2020 https://www.sciencedirect.com/science/article/pii/S2352352220300402. The paper was based on a request for an entry assessment by the Department for Environment and Rural Affairs (DEFRA) in response to the first detection of prion disease in dromedary camels (CPD) in Algeria and Tunisia. The pathogen was identified as the animals presented with clinical signs compatible with those in other species suffering from prion disease. Considering the threat that prion diseases pose to both animal and human health, the scope of the assessment was expanded to assess the entry of a novel prion disease agent into the UK via livestock and livestock products using CPD as an example.

The work in this Chapter made use of a recently published aggregated probability tool devised by colleagues at the Animal and Plant health Agency (APHA) (Kelly *et al.,* 2018). The tool was developed to try and account for assessing the risk from more than one product in a qualitative RA, for example, using the number of imports per year, to avoid potential under-estimation as can occur when the volume of imports is not considered. The tool presents the calculated values of aggregated probability as a contour plot, which can be used to give guidance on the likely level of qualitative risk, given an individual risk level and volume of product. Even though this application relies on making assumptions concerning the individual probability it can give an idea of the possible

magnitude of the aggregated probability and provide a range of uncertainty around it. The contour plot also relies on quantitative bounds used for the qualitative levels and results are therefore dependent on the choice of these bounds with different results potentially being derived for different values.

The plot is based on the premise that probabilities can only take a value of between 0 and 1. This forms the X axis of the plot with the descriptive values from 'negligible' to 'very high' being divided along the axis according to the quantitative bounds assigned to them. This axis represents the individual probability of one unit. The Y-axis is the number of products expressed as Log10n where n is the number of products. Logarithms are used because they allow negligible probabilities and large numbers of units to be shown together in a clear way. The contour plot is constructed such that as the number of units increases the aggregated probability for each individual probability increases until it enters the next descriptive category. Thus, a very low individual risk plus many opportunities gives a higher overall risk whereas high individual risk plus few opportunities still has a potentially high risk. Equal overall risk shows up as straight diagonal lines on logarithmic axes with each diagonal band representing different combinations that lead to the same overall likelihood.

The risk question in the prion agent paper specified the probability of entry within the next year considering all the products which are currently imported from the regions of interest. Whilst the paper refers only to the aggregated probability, the original project report compared results using both the aggregated probability method and a more traditional qualitative assessment of the probability of export based on the number of products imported, for example, if the trade volume was low then the probability of entry was also assumed to be low. The steps of the risk pathways for the two methods therefore differed slightly as shown in Figure 1.

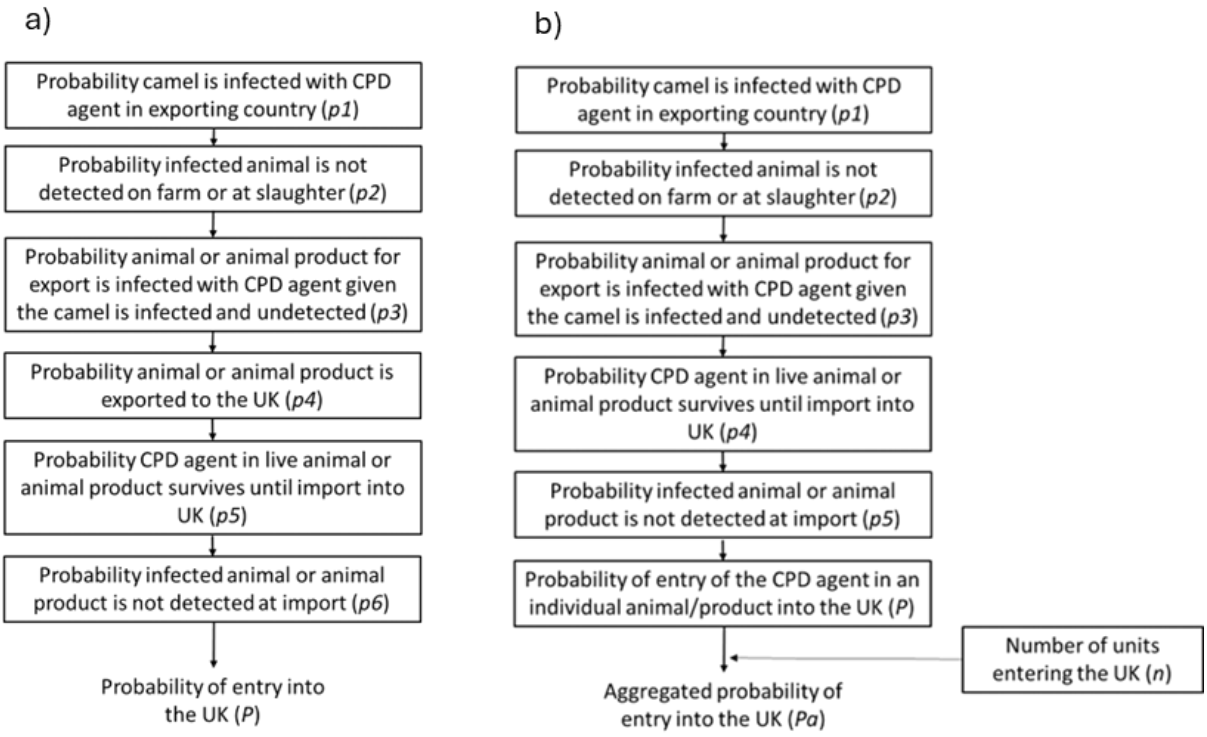

Figure 1: Comparison between the two methods of addressing the risk pathways for the probability of entry of camel prion disease agent within the next year considering the products which are currently imported from the regions of interest; a) probability of entry was qualitatively estimated for each commodity based on the trade volume b) aggregated probability method

Overall, the qualitative estimates for annual probability using the graphical tool were of a higher order than those derived using the method based on assessing the probability using the trade volume only. In general, the aggregated probabilities were assessed as being equal to the individual probability. The pathway combinations for which there was agreement between the two methods used were mostly associated with 'Negligible' individual probabilities and very small numbers of imports (of order 10).

The original paper by Kelly *et al.,* (2018) set out to consider whether or not it was feasible to develop a generic method that considered the aggregated probability of introduction in qualitative RA. They concluded that that it would be difficult to specify a generic method because, as has previously been mentioned, any such approach would rely on specifying numerical bounds for qualitative categories of probability as well as an idea

of the number of imports and would thus be case-specific (Kelly *et al.,* 2018). However, this method represents one of the most robust methodologies to deal with aggregated probability for an entry assessment and the CPD agent work demonstrates the application of this method as a case study.

5.3 Full text of the published paper

Assessing the aggregated probability of entry of a novel prion disease agent into the United Kingdom

Verity Horigan, Paul Gale, Amie Adkin, Timm Konold, Claire Cassar, John Spiropoulos, and Louise Kelly

Abstract

In 2018 prion disease was detected in camels at an abattoir in Algeria for the first time. The emergence of prion disease in this species made it prudent to assess the probability of entry of the pathogen into the United Kingdom (UK) from this region. Potentially contaminated products were identified as evidenced by other prion diseases. The aggregated probability of entry of the pathogen was estimated as very high and high for legal milk and cheese imports respectively and very high, high and high for illegal meat, milk and cheese products respectively. This aggregated probability represents a qualitative assessment of the probability of one or more entry events per year into the UK; it gives no indication of the number of entry events per year. The uncertainty associated with these estimates was high due to the unknown variation in prevalence of infection in camels and an uncertain number and type of illegal products entering the UK. Potential public health implications of this pathogen are unknown although there is currently no evidence of zoonotic transmission of prion diseases other than bovine spongiform encephalopathy to humans.

Introduction

Prion diseases, or transmissible spongiform encephalopathies (TSEs), are progressive neurodegenerative disorders that affect both humans and animals and are characterised by long incubation periods frequently of many years. Such disorders are biochemically characterised by conversion of a normal cellular form of the prion protein (PrP^{c}) into a misfolded disease associated form (PrP^{Sc}) that accumulates into amyloid protein aggregates in the brain (Norrby 2011).

Scrapie in sheep was the first animal TSE to be described in the 18th century in Great Britain but TSEs have since been detected in a number of species, including scrapie in goats, chronic wasting disease (CWD) in deer and bovine spongiform encephalopathy

(BSE) in cattle. The BSE crisis led to the slaughter of 3.3 million cattle and an estimated economic loss of £3.7 billion in the United Kingdom (UK) (Beck *et al*., 2007). It is believed that BSE crossed the species barrier to humans through the consumption of contaminated beef and bovine products during the 1990s (ECDC, 2017) and that this zoonotic transmission of BSE has since led to the death of 178 people with variant Creutzfeldt-Jakob disease (NCJDRSU, 2019). Prion diseases can therefore pose serious risks to both animal and human health and the first detection of a TSE in deer in Europe in 2016 demonstrates the continued need for a global awareness of these diseases (Benestad *et al.,* 2016).

Within the European Union there is a statutory requirement to test for TSEs where disease is suspected and active surveillance systems to test for disease in healthy slaughter animals or fallen stock. However, in countries that do not have active surveillance systems, detection of cases relies on the reporting of clinical suspects where, if the animal keeper or veterinary surgeon are not familiar with the clinical signs, TSEs may not be considered in the differential diagnosis of neurological diseases or other conditions that present with similar signs (Konold *et al.,* 2014). Prion disease has recently been confirmed in three dromedary camels (*Camelus dromedarius*) from an Algerian slaughterhouse (Babelhadj *et al*., 2018) after clinical signs compatible with those of TSEs in other species were observed ante mortem. Disease associated pathological changes or prion protein were found in brain by Western blotting, histology, immunohistochemistry (IHC) and paraffin-embedded tissue blot; PrP^{Sc} was also detected in the lymph nodes of the one camel tested by IHC.

Information gathered from breeders and slaughterhouse personnel suggests that similar clinical signs had been observed since the 1980s (Babelhadj *et al*., 2018). Subsequently, the disease has also been reported in a single case of a 12-year-old dromedary camel from the region of Tataouine, Tunisia (Agrimi 2019; WOAH 2019).

There are many knowledge gaps about the biological characteristics of this new TSE, termed camel prion disease (CPD). Detection of infection in lymph nodes of one animal suggests extra-neural pathogenesis and, therefore, potential transmission of CPD between animals similar to that of classical scrapie and CWD. Such transmission of CPD

could be facilitated over long distances by the traditional nomadic herding practices of dromedaries and the trade patterns between Algeria and other countries in North Africa and the Middle East (Bouslikhane 2015). In light of the devastation caused by BSE, and its subsequent zoonotic transmission, CPD was used here to assess the probability of entry of a novel prion disease agent into the UK via livestock and livestock products. The approach used was to assess the aggregated probability, using the number of imports per year to avoid potential under-estimation as has previously been described (Kelly, 2018). Of note, the zoonotic potential of the disease is unknown and this assessment is of the probability of introduction of the CPD agent into the UK only, not of any onward transmission to humans or animals.

Methods

Risk Question and Pathway

The risk question to be addressed was:

'What is the aggregated probability of entry of the CPD agent into the United Kingdom from North Africa or the Middle East in one year?'

The risk pathway highlighting the probabilities to be considered for potential entry of the CPD agent into the UK is shown in Figure 1.

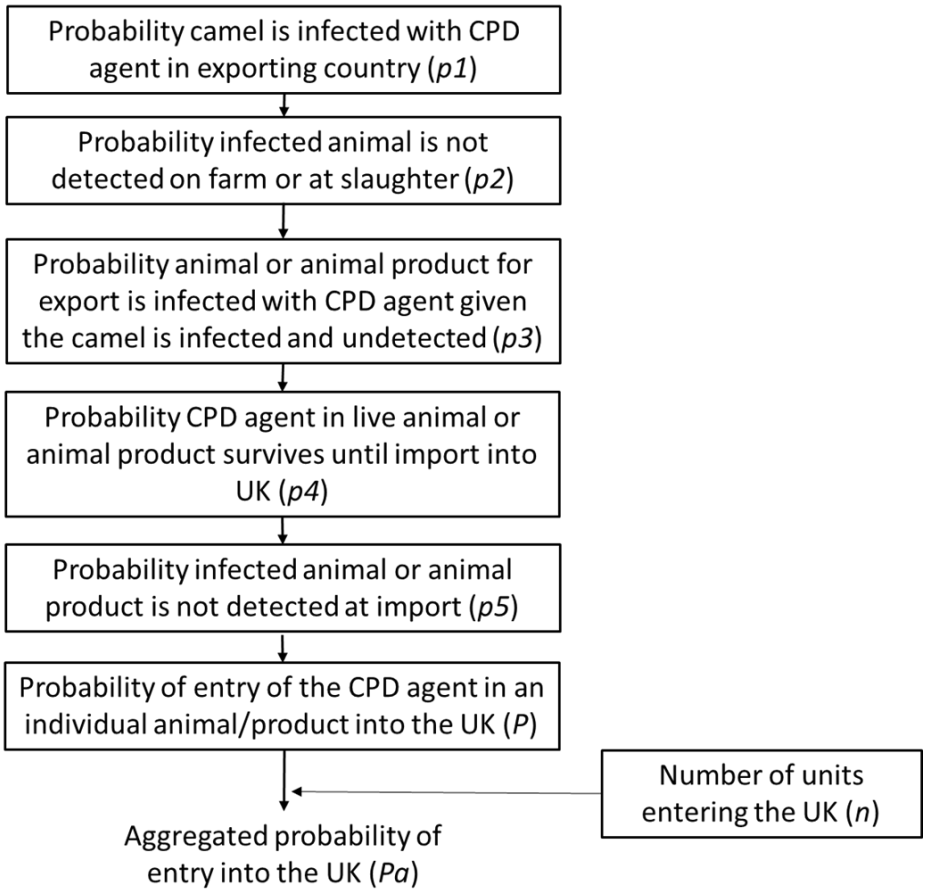

Figure 1: Risk pathway for the aggregated probability of entry of the CPD agent into the UK in one year

The approach used was qualitative and based on the framework set out by the OIE (World Organization for Animal Health) (WOAH 2004). The probabilities in Figure 1 are conditional and were expressed qualitatively as *negligible*, *very low*, *low*, *medium*, *high* and *very high* (EFSA 2006; FAO 2009). The qualitative probabilities for each stage of the risk pathway up to, and including, the probability that an infected animal/animal product is not detected at import (*p1, p2, p3, p4, p5*) were combined as described previously (Gale *et al.,* 2010) to give the probability of entry of an individual infected animal/product (*P*). Entry was defined as the probability of entry of a CPD positive animal or contaminated animal product into the UK within one year taking into account the current products which are imported from the regions of interest. For comparison, an aggregated probability of entry (*Pa*) of all categories of live animals/products was also assessed to provide an annual probability of entry using a graphical reference tool

proposed by Kelly *et al.* (Kelly *et al.,* 2018). This tool removes some of the subjectivity that is often associated with deriving the annual qualitative probability of entry for animal import risk assessments as it enables the number of units imported to be combined with this individual qualitative event probability. In this way, the reference tool 'considers various qualitative categories of individual probability and determines the relationship between these probabilities, the number of imports and the annual probability of entry' (Kelly *et al.,* 2018).

The quantitative bounds for the individual probability correspond to previously published example definitions (FAO 2009) (Table 1). The X axis represents the individual probability of one unit, and the Y-axis is the number of products expressed as Log10n where n is the number of products. As the number of units increases the aggregated probability for each individual probability increases until it enters the next descriptive category.

Table 1: Definitions of the quantitative bounds used to correspond to the qualitative probability (taken from FAO 2009)

Qualitative level	**Quantitative bounds**	**Quantitative bounds (%)**
Negligible (N)	Indistinguishable from 0	Indistinguishable from 0%
Very Low (VL)	$<^{10-4}$, except 0	<0.01%, except 0%
Low (L)	10^{-3} to 10^{-4}	0.1% to 0.01%
Medium (M)	10^{-2} to 10^{-3}	1% to 0.1%
High (H)	10^{-1} to 10^{-2}	10% to 1%
Very High (VH)	$>10^{-1}$, not 1	>10%, not 100%
Certain	1	100%

Uncertainty associated with the estimates for the probabilities were categorised according to Spiegelhalter *et al.* (Spiegelhalter *et al.,* 2011) depending on availability, completeness and quality of evidence.

Relevant data for use in the risk assessment were scarce. Briefly, the number of camel products imported into the UK from the area of interest was obtained from the EU Trade Control and Expert System (TRACES) where available. Otherwise, the following assumptions were made:

- The prevalence of CPD in camels in the region of interest - 3.1% (based on Bablehadj (Babelhadj *et al.,* 2018))
- The incidence and prevalence of CPD in camel products, derived from:
    - Disease progression in camels – similar to scrapie (based on Bablehadj (Babelhadj *et al.,* 2018))
    - Relative resistance of CPD associated PrP^{Sc} to heat and chemicals – similar to other TSEs (see Results section for references)
    - Correlation of disease presence and PrP^{Sc} deposition – similar to other TSEs (see Results section for references)
    - Systemic distribution of disease – similar to scrapie (based on Bablehadj (Babelhadj *et al.,* 2018))
- The number of illegally imported products – based on data on illegal seizures and FAOSTAT production data
- The number of processed camel products both legally and illegally imported – assumed by the author

A further assumption made was that the aggregated probability calculations used the same quantitative bounds (FAO 2009) as used in the tool by Kelly *et al*. (Kelly *et al.,* 2018). It is acknowledged that this probability could therefore change if these bounds were to be altered.

Results

Risk Assessment

Probability camel is infected with camel prion disease in exporting country (p1)

Detection of abnormal neurological signs since the 1980s within a restricted geographical area of Algeria suggests that the expansion of CPD to other areas (and countries) may be restricted or that the disease can remain largely undiagnosed. According to a recent presentation of the Mediterranean Animal Health Network, the disease was also reported in Tunisia and the incidence in the initial region of Algeria was described as 'rapidly and progressively increasing' (Agrimi 2019). It is, therefore, possible that movement of camels has allowed infected animals to enter other countries. Asides from the legal trade of camels, approximately 268 million people in Africa practice some form of pastoralism (Luizza 2017). For example, over 95% of cross-border trade within the Horn of Africa is unofficial and carried out by nomadic pastoralists trading livestock. Given that disease was first noticed in the 1980s and the nomadic way of life in this area, exporting countries were therefore considered as those making up the regions of North Africa and the Middle East for the purpose of this assessment.

Twenty of 937 camels in 2015 and 51 of 1,322 in 2016 showed neurologic signs at slaughter giving an overall estimated apparent prevalence of 3.1% in dromedaries brought for slaughter (Babelhadj *et al.,* 2018). In the absence of further information including confirmatory testing, an assumption was made that the prevalence of CPD in live camels in the regions of interest was *high* with *high* uncertainty because of the lack of testing data from countries other than Algeria and in only 3 camels in Algeria itself.

Probability infected animal is not detected on farm or at slaughter (p2)

Although anecdotal evidence suggests that herdsmen have noticed neurological signs in camels on the farm and at slaughter (Babelhadj *et al.,* 2018) it was assumed that these animals were still being sent for slaughter and entering the food and feed chains. It was also assumed that as the other countries in the regions of interest have not been aware of the presence of this disease that they would not be surveying their animals for clinical

signs and therefore animals will still be sent to slaughter. The probability of a camel with CPD not being detected on farm or at slaughter was therefore assumed to be *high* with *low* uncertainty.

Probability animal or animal product for export contains the CPD agent given the camel is infected and undetected (p3)

Camel products that can be legally exported to the UK, those for which databases exist to monitor the levels of exports and the probability of containing the CPD agent (given the source camel is infected) of these products are shown in Table 2.

Table 2: Probability of containing the CPD agent for individual commodities originating from camels including primary and processed products.

Commodity	Primary product used	Import to the UK allowed from regions of interest	Traceable (source)	Probability of containing the CPD agent (uncertainty in brackets)
Live animals				
Live camels	-	No	-	Certain
Primary products				
Meat	-	No	-	High (high)
Milk	-	Yes	Yes (Traces)	High* (high)
Hair	-	Yes	Yes (Traces)	Negligible (high)
Urine	-	No	-	High (high)
Semen	-	No	-	Low (high)
Treated Hides and skins	-	Yes	Yes (Traces)	High (high)
Processed products				
Soap	Milk	Yes	No	Negligible (high)
Lip balm	Milk	Yes	No	Negligible (high)
Chocolate	Milk	Yes	No	Negligible (high)
Leather products	Skin	Yes	No	Very low (high)
Cheese	Milk	Yes	Yes (Traces)	High (high)
Bone ornaments	Bone	Yes	No	Very low (high)

*milk is likely to be a composite from multiple animals, and potentially also farms, which will result in a high dilution effect of prions from individual camels and affect the relationship between prevalence in individual camels and the proportion of "servings" potentially containing prions.

The probability of a commodity containing the CPD agent depends on the presence of infectivity in the live animal and processes the commodity has undergone which may

destroy it. As such, the uncertainty associated with this probability for all products was high as a result of knowledge gaps concerning these two factors.

The prion protein, PrP^{Sc}, has been shown to accumulate with infectivity and is therefore considered a reliable biochemical marker for infection (Thomzig *et al*., 2007). PrP^{Sc} has been isolated from the muscle tissue, skin, milk and urine of TSE affected animals (Thomzig *et al*., 2007; Andréoletti *et al.,* 2004; 2011; Chianini *et al.,* 2015; Buschmann *et al.,* 2005; Konold *et al.,* 2013; Rubenstein *et al.,* 2011; Henderson *et al*., 2015) and the pessimistic assumption here is that CPD distribution in a camel is similar to classical scrapie and CWD based on the detection of PrP^{Sc} in the lymphatic system (Bablehadj *et al*., 2018; Haley *et al.,* 2014). It was, therefore, estimated that the probability that a camel meat/milk/urine product contains the CPD agent, given it comes from an infected, undetected animal was *high*.

The only milk imported from the region of interest to the UK is Ultra-High temperature treated (UHT). This processing involves heating to ~135-145ºC for 1-10 seconds (Deeth 2004) which is not sufficient to fully destroy prion activity (Yoshioka *et al.,* 2013; Franscini *et al.*, 2006). Similarly for hides/skins, if they are not treated with a transformation process with a proven capacity to reduce TSE infectivity (SSC 2000), then it is considered unlikely that the CPD agent would be destroyed. The probability of UHT milk and hides/skins containing the CPD agent, was therefore estimated as *high*.

The European Food Safety Authority (EFSA) considered the risk of TSE transmission associated with semen and embryos collected from classical scrapie incubating sheep and goats to range from negligible to low (EFSA 2010). PrP^{Sc} in semen from a scrapie affected ram has been reported (Rubenstein *et al.,* 2012) so the probability of semen from infected undetected camels containing the CPD agent was estimated to be *low* (worst case assumption based on the EFSA opinion). For hair PrP^{Sc} has been detected in the fibres of the follicular neural network and in the hair follicle isthmus in hamsters but not in the outer root sheet cells or the bulb region (Thomzig *et al.,* 2007). The probability of camel hair being infected with the CPD agent was therefore assumed to be *negligible* given the lack of evidence for PrP^{Sc} in the cells of the hair.

Soap products are described as containing ~ 25% raw camel milk and use a saponifying agent which starts the process of turning the raw ingredients into soap. This agent is usually 100% sodium hydroxide which is known to inactivate PrP^{Sc} at a concentration of 0.1M (Käsermann *et al*., 2003). The probability of soap products and lip balm retaining the CPD agent was therefore estimated to be *negligible*. Chocolate products manufactured using camel milk can contain ~ 21% pure camel milk powder. Milk powder production involves spray drying milk in a flow of hot air between 180°C to 220°C (CWD 2019), sufficient to destroy prion activity (Somerville *et al.,* 2011). The probability of chocolate being infected with the CPD agent was thus estimated to be *negligible*. Camel milk does not curdle readily so camel cheese is traditionally consumed in fresh or fermented form. Fermentation is not expected to reduce the levels of infectivity so the probability of cheese from infected undetected animals being infected with the CPD agent was estimated to be *high*.

Products made from treated skins/hides from infected animals are assumed to have undergone a tanning process whereby the use of strong alkali and acid solutions will reduce the level of TSE infectivity (Käsermann *et al.,* 2003; Appel *et al.,* 2006; Hughson *et al.,* 2016). The probability of infection was therefore assumed to be *very low*. Similarly, although experimental evidence has demonstrated TSE infectivity in bone marrow (Huor *et al*., 2017; Seelig *et al.,* 2010), during the process of cleaning bones for use in processed products such as jewellery it is assumed that the bone marrow is removed. The probability of camel bones being infected with the CPD agent, given an animal is infected, was therefore assumed to be *very low*.

Probability prion in live animal or animal product survives journey to the UK (p4) and is not detected at import (p5)

The probability of prions remaining infectious throughout the journey to the UK was assumed to be *high* with *low* uncertainty for all products for both legal and illegal routes due to the characteristic resistance of PrP^{Sc} to both chemical and physical degradation (Taylor 1999) and evidence of its long term survival (Brown *et al.,* 1991; Georgsson *et al.,* 2006). There are no gross lesions suggestive of TSE infection in animal products. There are also no post import tests for TSEs in either legal milk imports or illegal seizures.

The probability of CPD infectivity not being detected on import to the UK was therefore assumed to be *high* with *low* uncertainty for all products for both legal and illegal routes. Additionally, the annual proportion of searched luggage among the total number of passengers entering a European country (Switzerland) has been estimated at between 0.06% and 0.24% (Jansen *et al.,* 2016). If this is applied to the UK, then it suggests that the probability of an illegally imported infected animal product not being detected at import is *high*.

The probability of CPD not being detected in a live animal was considered to be *medium* as detection will depend on several factors including the animal showing clinical signs of TSE infection and the signs being correctly diagnosed as TSE by the veterinary inspector. The age of the animal and the progression of clinical disease will also be relevant. The uncertainty associated with this estimate was *low*.

Probability of entry of the CPD agent in an individual animal/product into the UK (P)

The probability of entry of the CPD agent in an individual animal/product into the UK was calculated by combining the probabilities in the risk pathway as described previously (Gale *et al.,* 2010). Results are summarised in Table 3 for both legal and illegal routes of entry for live animals and products

Table 3: Probability of entry (P) of an infected camel or camel product for both legal and illegal pathways (uncertainty in brackets)

Probability	Livestock	Camel meat	UHT Milk products	Treated hides/skins	Urine	Semen	Hair	Soap and lip balm/Chocolate	Cheese	Bone/skin products
Camel Infected	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)
Not detected	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)	High (High)
Animal or animal product (per unit) for export contains CPD agent	Certain (High)	High (High)	High (High)	High (High)	High (High)	Low (High)	Negligible (High)	Negligible (High)	High (High)	Very low (High)
Prion survives journey to UK	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)
Not detected on import	Medium (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)	High (Low)
Entry for individual infected product	Medium (Low)	High (High)	High (High)	High (High)	High (High)	Low (High)	Negligible (High)	Negligible (High)	High (High)	Very low (High)

Number of units imported into the UK per year (n)

Legal exports of live camels, camel meat (including untreated hides), urine and semen from the regions of interest to the UK are prohibited (Table 2). There were no imports of treated hides from camels from the region of interest recorded for the period 2010 to 2016 but, as such imports are permitted, the number of treated hides being exported to the UK was estimated to be within the range of 0 - 1. Since 2010 there has only been one possible consignment of 'hair' of species 'other' so may not have been of camel origin but an estimate of 1 unit was used here.

The Traces database has details of the volumes of milk and milk products imported into the UK. Approximately 10,830 kg of UHT milk products (it is assumed that the average product is 1 litre in size or 1 kg in weight giving a total of 10,830 units) and 11 Kg (equivalent to 22 units based on a 500g product) of cheese were exported to the UK in one year. For processed products, soap, lip balm and milk chocolate made from camel milk are available in the UK via the internet or instore. Camel bone jewellery and ornaments and leather goods are also available for sale via the internet. It is assumed that these are all niche products with a limited market and the number of units of each product imported into the UK was estimated to be 1,000.

For illegal imports, data on illegal seizures were used to estimate the number of camel meat and dairy products illegally entering the UK. Illegal imports of red meat and dairy products are not categorised by species so, as a proxy for this, data (FAOSTAT) on the production of animals in the regions of interest were used to predict what percentage of each category would be a camel product. For 2016, camel meat contributed 4.7% to production of all red meat species and camel milk represented 0.47% of whole milk production (FAOSTAT) in the regions of interest. It is unknown whether the illegal milk/milk products seized would have undergone any heat treatment, but as stated above, UHT would not destroy infection. Using the illegal seizure data and FAOSTAT production data it was estimated that 242 units (200g products) of camel meat, 19 units (1Kg product) of milk and 20 units (500g product) of cheese illegally enter the UK in one year.

The number of illegal imports of treated skins/hides and hair was estimated to be between 0 -100 due to the size of the commodity and the low value placed on camel skins in the region of interest. The same figure was used for camel urine which has been used as a traditional medicine since ancient times (Abdel Gader *et al.,* 2016) so it is possible that passengers entering the UK could illegally import camel urine for medicinal purposes.

For semen, there are difficulties associated with the application of artificial insemination in camelids in particular the collection and handling of semen due to the viscous nature of the seminal plasma (Skidmore 2018). Therefore, the estimate for the number of illegal camel semen straws imported to the UK was between 1-10. The illegal import of batches of camel hair was also estimated to be between 1 - 10 due to the low value placed on camel hair in the region of interest. The number of illegal imports of all processed products was estimated to be between 0 - 1000 assuming these are luxury products aimed at a niche export market.

Aggregated probability of entry of the CPD agent into the UK from North Africa or the Middle East per year (Pa)

The aggregated annual probability of entry of the CPD agent was estimated using the number of units of animals/products imported per year where known (or estimated by the authors where unknown) and the qualitatively assessed probability of entry for an individual infected product (Table 3) using the graphical framework described by Kelly *et al*. (Kelly *et al.,* 2018).

Here, the individual probabilities lie on the X axis taking a value of between 0 and 1, with the value 'High' being between the quantitative bounds of 10^{-1} to 10^{-2}. The Y-axis is the number of products expressed on a log scale. For milk and cheese where the number of products imported is known the aggregation of individual probabilities (per product) increases to Very High when the number of products is 10^{2}.

For legal imports, the aggregated probability of entry was negligible for livestock, camel meat, urine and semen as these products are prohibited (Table 4). The probability was also negligible for hair, soap, lip balm and chocolate based on the assumed lack of

infectivity in these products and the number of products imported. For cheese and UHT milk the probability of at least one infected unit entering the UK per year was high and very high respectively. The individual probability per unit for UHT milk increased from high to an aggregated probability of very high as a result of the number of units imported ($>10^4$) in one year.

Table 4: Aggregated probability of entry (*Pa*) of CPD infected animals/animal products via legal import with associated uncertainty in brackets using the method of Kelly *et al.* 2018 *estimated by the authors

Legal	Livestock	Camel meat	UHT Milk products	Treated hides/skins	Urine	Semen	Hair	Soap and lip balm/Chocolate	Cheese	Bone/skin products
Entry for individual infected product	Medium (Low)	High (High)	High (High)	High (High)	High (High)	Low (High)	Negligible (High)	Negligible (High)	High (High)	Very low (High)
Number of units imported	0 (animals)	0 (200g product)	10830 (1 kg product)	0 – 1 (skins)	0 (500g product)	0 (straw)	1 (1 batch)	1,000* (item)	22 (500g product)	1,000* (items)
Aggregated probability of entry into the UK	Negligible (High)	Negligible (High)	Very high (High)	Negligible - High (High)	Negligible (High)	Negligible (High)	Negligible (High)	Negligible (High)	High (High)	Very low (High)

The number of units per product illegally imported to the UK was estimated by the authors due to lack of data. This resulted in a range of probabilities for some products, from negligible if no items were imported to very high if 100 products were imported (treated hides/skins, urine) (Table 5). Milk products and cheese both had a high probability of entry and camel meat had a very high probability based on the estimated number of products imported.

Table 5: Aggregated probability of entry (*Pa*) of CPD infected animals/animal products via illegal import with associated uncertainty in brackets using the method of Kelly *et al.* 2018 *estimated by the authors

Illegal	Livestock	Camel meat	Milk products	Treated hides/skins	Urine	Semen	Hair	Soap and lip balm/Chocolate	Cheese	Bone/skin products
Entry for individual infected product	Medium (Low)	High (High)	High (High)	High (High)	High (High)	Low (High)	Negligible (High)	Negligible (High)	High (High)	Very low (High)
Number of units imported	0-10* (animals)	242* (200g product)	19* (1 kg product)	0 – 100* (skins)	0 – 100* (500g product)	0 – 10* (straw)	0 – 10* (1 batch)	0 - 1,000* (item)	20* (500g product)	0 - 1,000* (items)
Aggregated probability of entry into the UK	Negligible - Medium (High)	Very high (High)	High (High)	Negligible – Very high (High)	Negligible - very high (High)	Negligible - Low (High)	Negligible (High)	Negligible (High)	High (High)	Negligible - Very low (High)

Discussion

This assessment used the example of CPD to address the probability of entry of a novel prion agent into the UK. The estimated probability per unit was aggregated to take into account the number of units of each product imported per year. Thus, the predicted probability is the probability of entry of one or more (i.e. at least one) infected unit per year into the UK. The predicted aggregated probability for legal imports was highest for UHT milk products and cheese whilst for treated hides and skins it was estimated to range from negligible to high depending on whether any units were imported in one year. For illegally imported meat, milk and cheese products the aggregated probability of at least one entry event per year was estimated as very high, high and high respectively. If testing were to be carried out to negate the presence of CPD in the camel population used to produce milk legally exported to the UK then the annual probability of entry would be reduced to negligible. Similarly, as the aggregated probability is based on an example of assumed quantitative bounds (FAO 2009), were these bounds to be changed then the aggregated probability could also change.

The estimates of probability are associated with high uncertainty throughout the risk pathway hinging, in particular, on the application of a blanket prevalence of CPD within the camel population. The Middle East Respiratory syndrome coronavirus (MERS-CoV) provides an example of an undetected pathogen in camels which, once identified, has since been detected throughout much of the regions of interest suggesting that movement of camels has provided a route of incursion of the virus to different countries (Reusken *et al.,* 2013; 2014; Haagmans *et al.,* 2014; Meyer *et al.,* 2014). It is possible that transmission of CPD between animals could have similarly been facilitated by movement of infected live animals although the disease has currently only been described in a restricted geographical area of Algeria and Tunisia. The involvement of lymphoid tissue, observed in both the Algeria and Tunisia cases, is suggestive of a peripheral pathogenesis, similar to scrapie and CWD in which horizontal transmission occurs efficiently under natural conditions (WOAH 2019). The uncertainty is compounded by lack of data on the epidemiology of CPD. As of June 2020, there is no publically available up-to-date information with regards to the prevalence of CPD in the area of interest or

whether additional cases have been detected. The WOAH Scientific Commission has called for the collection of further scientific evidence in countries with dromedary camel populations to measure the impact of the disease (WOAH 2019). This could influence the results of the risk assessment should an increase in the incidence of CPD have occurred.

The import of animal products in travellers' personal consignments presents a considerable risk of introducing infectious agents (Simons *et al.,* 2016; Hartnett *et al.,* 2007; Falk *et al.,* 2013). Analysis from a study on illegal seizures of airline passengers in Germany, found that seizures are typically local foodstuffs reflecting culturally enrooted consumption patterns. Camel milk and meat are esteemed in the regions of interest for their medicinal properties; camel meat is also frequently eaten on special occasions or for ritual celebrations (Jansen *et al.,* 2014). It is, therefore, not unreasonable to assume that a proportion of illegal seizures of milk products and red meat originate from camels.

Significant knowledge gaps exist about prion disease in camels. Although PrP^{Sc} is believed to be the most useful marker of TSE disease identified to date, it has also been shown that its presence does not always directly correlate with infectious titres and that bioassay is still required for verification of infection (Chianini *et al.,* 2015). So far, this has not been reported for CPD. The relative heat resistance of camel prions is also unknown, a factor which could affect the risk pathway if it were proven to show a greater susceptibility to heat than BSE or scrapie prions. Disease progression in CPD could also affect the risk pathway, specifically the prevalence of infection in camel products, if the slaughter age of most camels is young and disease is only detected in older animals. Likewise, products from animals with CPD but not yet showing clinical signs could also contribute to the probability of entry; this is particularly important regarding the long incubation period of the prion diseases. Further research to gain a better understanding into the CPD agent behaviour and improvement of the market traceability of camel products may alter the probability estimates stated here and should be considered in future risk assessments.

In conclusion, this paper assesses the annual probability of at least one entry event of camel products containing the CPD agent into the UK. The probability of entry from the

Middle East or North Africa was considered to be highest from legal import of milk and cheese and the illegal import of camel meat, milk and cheese. These estimates are associated with high uncertainty due to the number of assumptions made throughout the risk pathway in particular the prevalence of CPD in camels, and of the CPD agent in camel products, and the number of products illegally entering the UK. However, this assessment does not consider the consequence of the exposure of uninfected animal populations to these products, only the probability of entry of the agent. Therefore, whilst a high probability of entry of the CPD agent has been estimated for some products, whether there is a subsequent probability of onward transmission is unknown (Fryer *et al.,* 2011). The zoonotic potential of CPD is unknown but there is currently no evidence of zoonotic transmission of TSEs other than BSE to humans. Further research to look at the zoonotic potential and risks to public health would be beneficial.

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5.4 Conclusion to Chapter 5

The work in this Chapter uses an aggregated probability tool proposed by Kelly *et al.,* (2018). This tool removes some of the subjectivity that is often associated with deriving the annual probability of disease entry for qualitative animal import RAs as it enables the number of units imported to be combined with the individual qualitative event probability. In this way, the tool 'considers various qualitative categories of individual probability and determines the relationship between these probabilities, the number of imports and the annual probability of entry' (Kelly *et al.,* 2018).

This Chapter demonstrated the application of the aggregated probability tool using the Camel prion agent as a case study. The estimated probability of entry of the agent per unit was aggregated to take into account the number of units of each product imported per year. Thus, the predicted probability was the probability of entry of at least one infected unit per year. The tool is based on an example of assumed quantitative bounds so were these bounds to be changed then the aggregated probability could also change and this is an area that could be further explored in the future.

In the following Chapter (Chapter 6) the final element of qualitative RA identified in the initial literature review is considered. Uncertainty, associated with estimates for likelihoods, is often categorised depending on availability and completeness of evidence to support the likelihood level. In a quantitative RA uncertainty can be incorporated into a model using probability distributions but in qualitative RAs, addressing uncertainty is complicated by the use of descriptive terms which may be interpreted differently by individual risk managers. Few published articles have dealt with how to convey a final uncertainty estimate for qualitative RAs so Chapter 6 contributes to this conversation by proposing a novel method of how to demonstrate uncertainty to the risk manager and also how to estimate an overall estimate of uncertainty.

Chapter 6: Addressing uncertainty in qualitative risk assessment for animal health

6.1 Authorship and funding statement

The application of the methodology and the analysis of the evidence and review of literature was my own work. One of the methodologies used in this paper was based on the European Union Pratique (Enhancements of Pest Risk Analysis Techniques) project using confidence bounds for likelihoods that had been previously described by the Intergovernmental Panel on Climate Change (IPCC). Dr Robin Simons, Dr Rachel Taylor, Dr Emma Snary and Dr Louise Kelly contributed by reviewing the work and providing risk assessment expertise.

6.2 Summary of the paper for submission

This paper is currently under revision and is intended to be submitted to the Microbial Risk Analysis journal. The concept for this last topic in the thesis was to address how uncertainty was dealt with in qualitative RAs for animal health. A study on how to improve risk communication between risk assessors and risk managers found that there was a lack of clarity regarding the estimation of uncertainty amongst both groups, specifically for qualitative RAs (Taylor *et al.,* in preparation). Science is inherently uncertain, yet, decisions need to be made, despite the uncertainty (Schneider *et al.,* 2022) and studies suggest that people prefer to be openly informed about uncertainty associated with scientific findings (EFSA 2019).

Uncertainty is an issue for any RA and thus presents as a key challenge when communicating results even in quantitative RAs (Wiedemann *et al.,* 2021). For example, an incorrect choice of a probability distribution for the parameterisation of any particular step within the risk pathway by the assessor would likely not be obvious to the risk manager (Clough *et al.,* 2025). Presenting a range of risk estimates has been found to increase risk perception compared to point estimates in some studies (Johnson *et al.,* 1995; Han *et al.,* 2009). Clough *et al.,* (2025) states that “exclusive focus on point estimates neglects uncertainty in its entirety, and this has impacts for the decision maker. On the other hand, a poorly represented measure of uncertainty can be as damaging as no measure at all”. A review of the effects of communicating scientific uncertainty on decision making in a public health also found that the way in which direct

uncertainty (e.g., probabilistic predictions) around a number is communicated, such as verbally or numerically can lead to different interpretations of the information (Schneider *et al.,* 2022).

The literature review in Chapter 2 found that there have been several semi-quantitative tools developed to incorporate uncertainty into qualitative RAs. The MINTRISK model assesses the likelihood for each step by choosing from qualitative categories associated with three options for the uncertainty about this estimate (low, moderate and high). Monte Carlo simulation is then used to determine the overall probability by sampling a value from triangular distributions with different ranges around the likelihood according to the chosen uncertainty level (de Vos *et al.,* 2020). Similarly, Australian Biosecurity divided the 0 to 1 interval in to mutually exclusive probability intervals correlating with qualitative descriptors ranging from negligible to very high. These intervals were then converted into individual uniform probability distributions using the interval range values as distribution bounds and the model samples from the uniform distributions using @Risk©. The statistics obtained from running the semi-quantitative model can give an indication of the 5^{th}, 50^{th} and 95^{th} percentile with the median value (50^{th} percentile) being selected as the value to be returned as the output distribution when interpreted back into qualitative terms (Biosecurity 2001).

When it comes to sharing/communicating results to risk managers it is important that the latter understand how the results have been obtained using these tools. The use of semi-quantitative tools may therefore not be as transparent on how uncertainty has been addressed because of the conversion between numerical values and descriptive terms. Crotta *et al.,* (2024) states that the descriptive terms for uncertainty that are used in qualitative RAs are not qualitative representations of numbers or numerical ranges, and mathematical operations are therefore not justified on qualitative uncertainty terms. Whilst acknowledging that it would be desirable for the overall risk estimate to have an associated uncertainty level Crotta *et al.,* (2024) was doubtful that a general rule for combination of qualitative uncertainty terms could be established. Rather, it could be preferable to have individual consideration of the probabilities and uncertainties of the events and how those affect the outcome.

The work in this chapter adheres to the original principles of qualitative RA and emphasises the transparency of the assessment in communicating the results of uncertainty on the risk scores to the risk manager. The concept is based on a visual method of demonstrating levels of uncertainty previously developed for pest risk assessments using uncertainty definitions based around IPCC (2005) guidelines on climate change. In the pest risk assessment, an uncertainty "Visualizer" was developed to aid in summarising the rating and uncertainty for each section of the risk to view rating scores and uncertainties in a pictorial manner. The "Visualizer" presents a summary bubble graph where the size of the bubble correlates to the level of uncertainty the experts associated with that rating (Holt *et al.,* 2012).

The choice of using a graphical representation of confidence levels for each step of the risk pathway rather than a descriptive term in this Chapter was, therefore, based on the premise that this would give the risk manager a better understanding of the impact of uncertainty on estimates of likelihood. This would allow the risk manager to observe how other likelihood levels could also be possible depending on the uncertainty, or level of confidence in the likelihood score, given the evidence available at the time of the assessment as "poor understanding of uncertainty can impact upon the ability to make good decisions" and "an incorrect representation of uncertainty can either make the decision maker overly and artificially confident, or unnecessarily cautious" (Clough *et al.,* 2025).

As mentioned in EFSA (2018) it is likely that people may perform poorly at judging how multiple uncertainties in an assessment combine so it may be more reliable to divide the uncertainty analysis into parts and quantify uncertainty separately (EFSA 2018). However, the work described in this Chapter also proposes a novel method and describes how a simple probability distribution of uncertainty at each pathway step can be combined in a Microsoft Excel tool to derive an overall uncertainty score using the risk matrix approach.

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6.3 Full text of the paper for submission

Addressing uncertainty in qualitative risk assessment for animal health

V. Horigan, L. Kelly, R. Taylor, E. Snary, R. Simons

Abstract*:*

In addition to providing an estimate of the likelihood of an event occurring, a qualitative risk assessment should also identify areas of uncertainty around the evidence, and the possible effect of this uncertainty, on the assessment results. This is important as it can affect a risk managers decision making when considering the risk estimate, particularly if the uncertainty could influence any key decision-making threshold. This paper focuses on developing a method to demonstrate the effect of uncertainty on the risk estimates to the risk manager to enable appropriate decision making. It also describes how a probability distribution of uncertainty at each pathway step can be combined using a risk matrix approach to derive an overall uncertainty score for a risk pathway.

The methods illustrated here empowers risk managers to make a decision at each step of the pathway as to whether they consider the risk is at an acceptable level. This allows the risk manager to see where further research could increase the confidence in the risk scores, and where mitigations could be put in place either to reduce the risk or reduce the uncertainty around that score. Communicating uncertainty at each step of the pathway using the method described here will increase the transparency of the scientific risk assessment process and provide risk managers with a more informed evidence base on which to make decisions.

Introduction

Risk assessments (RAs) are important tools that can be used to inform Government policy decisions to help prevent potential threats to animal health, for example, imposing trade restrictions from an area where an exotic disease outbreak has been declared. In addition to providing an estimate of the likelihood and impact of the threat occurring, a comprehensive RA should also identify areas of uncertainty, and the possible effect of this uncertainty, on the assessment results. How uncertainty is addressed is, therefore, inherently important as it can affect a risk managers decision making when considering the risk estimate, particularly if this will influence any key decision-making threshold (Pratique 2011; EFSA 2018). Characterization of uncertainty is also beneficial as it can help identify data gaps in the evidence whilst making the RA more transparent for risk managers by recognising which steps within a risk pathway need to be interpreted with care (Horigan et al., 2023). Thus, effective communication of uncertainty by the risk assessor can help the risk manager to understand the range and likelihood of possible events occurring (EFSA 2018).

The European Food Safety Authority (EFSA) defines 'uncertainty' as all types of limitations in available knowledge that affect the scale and probability of possible answers to an assessment question (EFSA 2018). Different types of uncertainty include epistemic uncertainty when there is a lack of precise knowledge due to insufficient data, (Briggs *et al.,* 2009); aleatory uncertainty caused by natural variation, which can be better understood, but not reduced, by collecting additional data (Martin *et al.,* 2012); linguistic uncertainty when the vocabulary used is undefined or ambiguous resulting in differences in interpretation or effectiveness of communication. As a result of any of these types of uncertainty, decision-makers may misinterpret the assessment of uncertainty, which may result in suboptimal decisions (EFSA 2018).

A requirement for the expression of uncertainty in any RA can be summarised as: what is the range of possible answers, and how likely are they (EFSA 2018). Most qualitative RAs provide two metrics for communicating the degree of certainty in key findings. The first is a qualitative metric of confidence, for example, low, medium or high, based on assessments of the underlying evidence and degree of agreement. The second metric is

likelihood, and is conveyed through pre-defined terms e.g., the Intergovernmental Panel on Climate Change (IPCC) defines unlikely as 0–33% probability and very unlikely as 0–10% probability (IPCC 2007). Thus, confidence can be raised by widening the probability interval; conversely, a likelihood assignment can be narrowed by accepting lower confidence (Helgeson *et al.,* 2018). The IPCC metrics have been further developed into a ”visualizer” by the European Union Pratique (Enhancements of Pest Risk Analysis Techniques) project providing a visual summary of the risk ratings and uncertainty scores, and as a rule-based matrix model providing an integrated summary of risk ratings and uncertainty and an overall assessment of risk (Holt *et al.,* 2013).

Uncertainty can be interpreted as referring either to a source of uncertainty in a RA or to its impact on the conclusion of the assessment (EFSA 2018; 2019). Uncertainty associated with estimates for probabilities is often categorised depending on availability, completeness and quality of evidence (Spiegelhalter *et al.,* 2011), however, its effect on the estimates needs to be recognized, accommodated, and accurately reported (Clough *et al.,* 2025). In a quantitative RA uncertainty can be incorporated into a model using probability distributions with any one iteration of the model randomly selecting a value from a distribution defined by a range of values describing the uncertainty for that particular parameter. The overall uncertainty is then accounted for in the final risk estimate, usually by confidence/credibility intervals.

In qualitative RAs, addressing uncertainty is further complicated by the use of descriptive terms such as ‘low’, ‘high’, etc. which may be interpreted differently by individual risk managers (Horigan *et al.,* 2023). Few published articles have dealt with how to convey a final uncertainty estimate for qualitative RAs because it is challenging to develop a methodology that is transparent without numerical probabilities (Hartley 2018). Narrative explanations for the reasons for uncertainty at each stage in the risk pathway have previously been advocated as aiding transparency and enabling risk managers to make decisions at different steps where the level of acceptable risks may be different (Briggs *et al.,* 2009). Semi-quantitative models have also been developed which incorporate uncertainty through probability distributions, as with a quantitative

RA, but convey the results using qualitative descriptive terms (Biosecurity Australia 2001; Kyyrö *et al.,* 2017; de Vos *et al.,* 2021).

This paper focuses on developing a method to integrate uncertainty and likelihood estimates within qualitative risk assessment for animal health visually demonstrating the effect of uncertainty on the risk estimates to the risk manager to enable appropriate decision making.

Methods

Overview

An adaptation of the method developed for plant pest RAs (Pratique 2011; Holt *et al.,* 2013) was applied to three examples of animal health RAs which used risk pathways with conditional probabilities i.e. each step assesses the probability that an event will occur given the knowledge that the event from the previous step has already occurred. The results were then compared to a recognised methodology for combining risk levels of each pathway step using a risk matrix (Rinchen *et al.,* 2020) where the product of two probabilities is always equal to the lowest probability. The methodology used for both methods and the RA examples are outlined in further detail below.

For all of the examples the terminology used for risk levels and uncertainty levels were as shown in Tables 1 and 2.

Table 1: Definitions for qualitative risk terms, adapted from EFSA (2006)

Risk level	**Definition**
Negligible	Event is so rare, does not merit consideration
Very low	Event is very rare, but cannot be excluded
Low	Event is rare, but does occur
Medium	Event occurs regularly
High	Event occurs very often
Very High	Event occurs almost certainly

Table 2: Terminology used to describe the level of uncertainty (EFSA 2006; Spiegelhalter *et al.,* 2011)

Uncertainty category and definition	**Type of information/evidence to support uncertainty category**
Low	• Solid and complete data available • Complementary evidence provided in multiple references • Numerous consistent field observations • Authors report similar conclusions
Medium	• Some but no complete data available • Limited field observational studies • Evidence provided in a small number of references • Authors report conclusions that vary from one another
High	• Scarce or no data available • No published scientific studies available • Evidence is provided in grey literature (unpublished reports, few observations, personal communication) • Authors report conclusions that vary considerably between them

Risk matrix method

Risk matrices have frequently been used in many applications of RA to combine the probability and impact of an event occurring to give the overall risk level having the advantage of visually demonstrating how the probabilities have been combined. One of the most commonly used matrix adheres to the principle that the product of two probabilities is always equal to the lowest probability (Table 3) (Corbellini *et al.,* 2012; Wieland *et al.,* 2011; Rinchen *et al*., 2020) but can tend towards overestimation of risk, as it does not allow for the product to be lower than the lowest value of the individual probabilities.

Table 3: Example of a risk matrix for combining probabilities (adapted from Rinchen *et al.,* 2020)

Probability	Negligible	Very low	Low	Medium	High	Very High
Negligible	Negligible	Negligible	Negligible	Negligible	Negligible	Negligible
Very Low	Negligible	Very low	Very low	Very low	Very Low	Very Low
Low	Negligible	Very low	Low	Low	Low	Low
Medium	Negligible	Very low	Low	Medium	Medium	Medium
High	Negligible	Very low	Low	Medium	High	High
Very High	Negligible	Very low	Low	Medium	High	Very High

There is, however, no recognised methodology for estimating an overall level of uncertainty for a qualitative RA. Examples of different methods include selecting the highest uncertainty estimate along the steps of the pathways (Crotta *et al*., 2012) or selecting the uncertainty level for the step which dictates the overall risk level, according to the matrix approach. The difficulty can be illustrated by using the example of the probability of an infected animal entering a country which can be defined as:

- Step 1: High probability that an animal is infected on import with high uncertainty
- Step 2: Very low probability that an import test does not detect the infected animal with low uncertainty

Using the risk matrix method, the overall probability will be High (Step 1) x Very Low (Step 2) = Very Low but the uncertainty could be cited as either high (the highest level of uncertainty associated with any of the pathway steps) or low as this is the uncertainty associated with the lowest probability which dictates the final risk estimate. As using the uncertainty level for a step that does not influence the overall risk estimate appears counter intuitive, the uncertainty estimate associated with the lowest probability was used for the overall uncertainty estimate in this paper.

Adapted Pratique method

The Pratique method is based on the IPPC premise of linking uncertainty scores of low, medium, and high, to frequency distributions of likelihood levels. The selected likelihood level for any risk pathway step has a higher frequency than the others and the distribution becomes progressively wider as the uncertainty increases (Pratique 2011, IPCC 2007). The adapted method provides an uncertainty distribution for the qualitative

likelihoods associated with each step of a risk pathway using the confidence levels shown in Figure 1. Negligible and very High were omitted as it was assumed that these likelihoods would be associated with Low uncertainty.

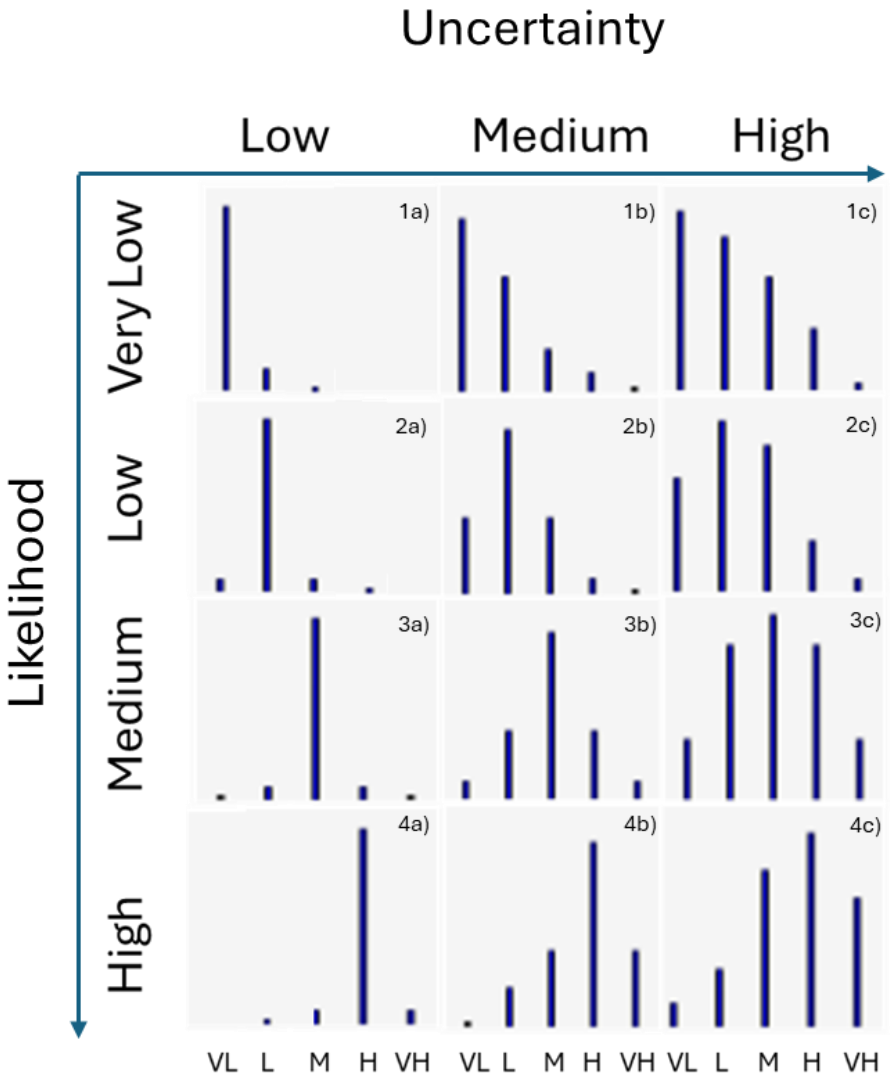


Figure 1: Uncertainty distributions for qualitative likelihoods of Very Low, Low, Medium and High (y-axis) with Low, Medium and High uncertainty (x-axis) (VL=Very Low; L=Low; M=Medium; H=High; VH=Very High)

For this paper, the overall risk estimate using the confidence levels from Figure 1 was also determined stochastically. Here, the likelihoods were treated as categorical variables with sample space and for each step of the risk pathway, the confidence level

of each likelihood occurring was used as inputs for a discrete probability distribution. Thus, for step *s* of the pathway the distribution, R_s, is given by Equation 1:

$$R_s = (\{1,2,3,4,5\}, \{p_1, p_2, p_3, p_4, p_5\}),$$

where *p1:p5* are the confidence levels (see Figure 1) that the score for step *s* is very low (1), low (2), medium (3), high (4) and very high (5) respectively. This returns a value between 1 and 5, which corresponds to the qualitative likelihood score scale. Stochastic simulation from these categorical distributions was used to derive an overall risk estimate from the uncertainty distributions for each step. On each iteration the scores for each step were combined using the risk matrix method, i.e. the lowest value was selected, to determine the overall risk estimate. The final result is shown as an uncertainty distribution for the overall qualitative likelihood.

Example 1 – typical teaching example for assessing 'probability of introduction'

This example demonstrates a risk pathway of the likelihood of a pathogen X entering Country B via infected beef products imported from Country A (Figure 2). This follows a commonly used pathway for assessing the probability of pathogen introduction in both quantitative and qualitative entry assessments.

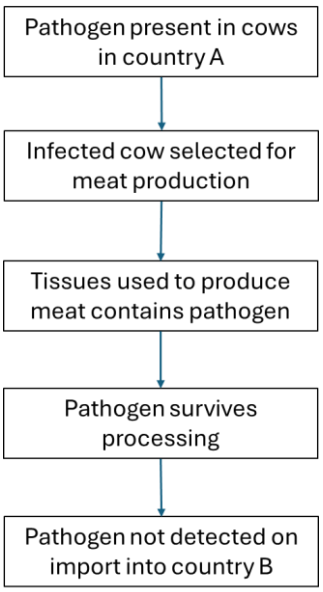


Figure 2: Risk pathway for the likelihood of pathogen X entering Country B via infected beef products imported from Country A

Hypothetical likelihood/uncertainty estimates were assigned for each step of the pathway and the overall likelihood and uncertainty were estimated using the risk matrix and the adapted Pratique method.

Example 2 – Lumpy skin disease

The results of a published RA answering the question "what is the risk of introduction of Lumpy skin disease (LSD) into the United Kingdom (UK) within the next year?" previously assessed using a risk matrix method (Horigan *et al.,* 2018), were compared with the results using the adapted Pratique method. The risk pathway selected from this RA was the entry of the virus via legal import of livestock (cattle; water buffalo) from a non-risk country i.e. a country in which an LSD outbreak had not been reported to the World Organisation for Animal health (WOAH) and, therefore, for which post-import testing within the UK was not required for compliance checks.

Example 3 – Camel prion disease

The final example compared results using the risk matrix method and the adapted Pratique method for the probability of entry of the Camel prion disease (CPD) agent into the UK from North Africa or the Middle East via the import of camel semen (Horigan *et al.,* 2020). Whilst import of this commodity is currently not allowed from the regions of interest this risk pathway was selected here as it provides an example of how high uncertainty in the lowest risk step can potentially influence the overall result.

Results

Example 1 – Probability of introduction pathway

Using the risk matrix approach the likelihood of pathogen X entering Country B was estimated to be Low (Table 4) as this is the estimate for Step 4 'Pathogen survives processing' which has the lowest likelihood of occurring and is therefore the defining estimate according to this approach. This estimate of Low has High uncertainty associated with it so this is the overall uncertainty level for the pathway as outlined in the methods section.

Table 4: Hypothetical likelihood and uncertainty estimates for the 5 steps of the risk pathway for probability of introduction of Pathogen X.

S	**Step (S)**	**Likelihood**	**Uncertainty**	**Fig 1 distb.**
1	Pathogen present in cows in Country A	Medium	Medium	3b
2	Infected cow selected for slaughter	Medium	High	3c
3	Tissues used to produce meat contains pathogen	High	Low	4a
4	**Pathogen survives processing**	**Low**	**High**	**2c**
5	Pathogen not detected on import into Country B	High	Low	4a
	Overall risk estimate using risk matrix method	**Low**	**High**	**2c**

When using the adapted Pratique method (Figure 3) the effect of the uncertainty on the likelihood estimates for each step can be visualised,

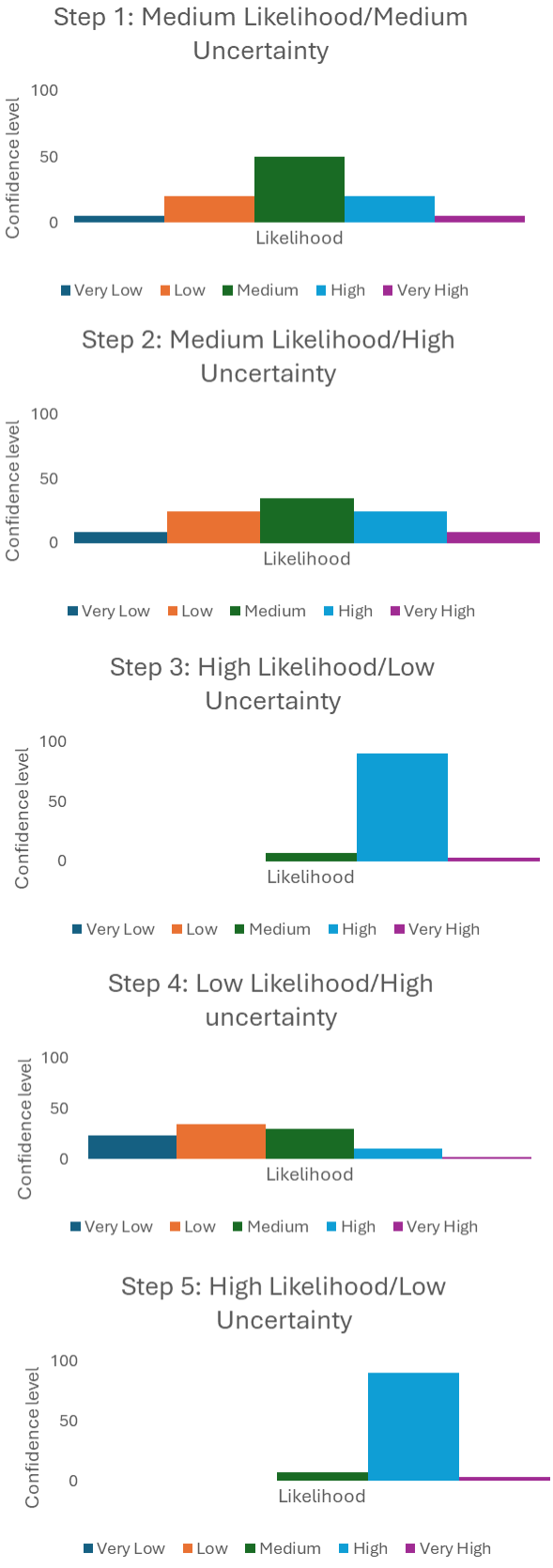
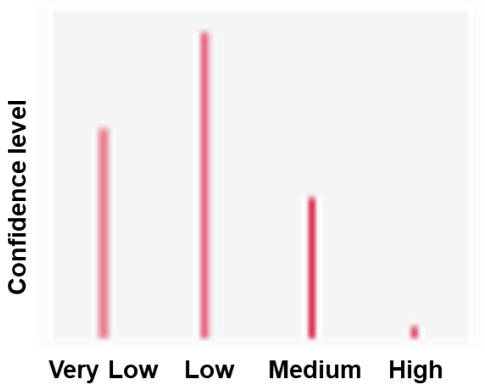


Figure 3: Visual representation of uncertainty associated with the likelihood estimates for each step of the risk pathway shown in Figure 2 and Table 4.

The effect of high uncertainty can be seen in step 2 and 4 (Figure 3) in that the confidence level of the likelihood estimates of these steps is only slightly higher than the adjoining estimates. Step 4 'Pathogen survives processing' is the mitigating step of the pathway as it is estimated that there is only a low likelihood of the pathogen surviving processing. However, the high uncertainty suggests that whilst there is 35% confidence that this estimate is Low there is also a 30% likelihood that it could be Medium. Visualising these results in this way highlights areas where the risk manager could request further research to reduce the uncertainty and therefore increase the confidence in the estimate. Using EFSA definitions of risk (EFSA 2006), this would mean the difference between this step being "rare but does occur" and "occurring regularly". Of note, this likelihood is for one product only. If the number of products imported is known then, using an aggregated likelihood method (Kelly *et al.,* 2018), the likelihood could actually increase to Medium or High respectively.

The distribution for the overall risk estimate, using stochastic simulations from a discrete probability distribution, is shown in Figure 4a, along with the summary statistics (Figure 4b). There is alignment with the risk matrix method which gave an overall estimate of Low with High uncertainty. This method more explicitly highlights this, showing that the most likely estimate is also assessed to be Low, but that the confidence level in scores of Very Low and Medium was also relatively high and that a score of High was also possible (Figure 4a). Compared to Step 4 (Figure 4c), whilst the highest confidence level is still for a likelihood of Low, the stochastic results shows a higher confidence level in a likelihood of Very Low rather than Medium. This is likely because, on each iteration the lowest value is selected, to determine the overall risk estimate.

a)



b)

Minimum	1.0000
Maximum	4.0000
Mean	1.9126
Mode	2.0000
Std. Deviation	0.7469

c)

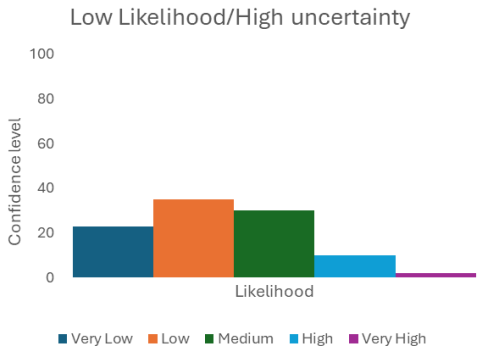


Figure 4: a) Graph showing distribution for the overall risk estimate, using stochastic simulations b) summary statistics of the overall risk estimate using simulations of the adapted Pratique method outcomes for probability of introduction of Pathogen X. c) Step 4: Pathogen survives processing, (low likelihood with high uncertainty) from Figure 3 which is the most influential step for example 1

Example 2 – Lumpy skin disease

The LSD pathway has 3 steps with Medium, Low and High uncertainty associated with their likelihoods, respectively. Using the risk matrix approach the most influential step is Step 1: Infected animal is legally exported to the UK which is estimated to be Very Low with associated Medium uncertainty (Horigan *et al.,* 2018).

Table 5: Likelihood and uncertainty estimates for the 3 steps of the risk pathway.

S	Step (S)	Likelihood	Uncertainty	Fig 1 distb
1	**Infected animal is legally exported to the UK**	**Very Low**	**Medium**	**1b**
2	Infected animal and/or virus survives journey	High	Low	4a
3	Infected animal/product is not detected on import	Medium	High	3c
	Overall risk estimate using risk matrix method	**Very Low**	**Medium**	**1b**

The visualisation of the steps is shown in Figure 5. For the risk manager the relatively high confidence in a likelihood of Low compared to the highest confidence value for Very Low for Step 1 might flag this step as a cause for concern and one worthy of investigating to see if further data could be obtained which could increase the confidence in the estimate of Very Low likelihood.

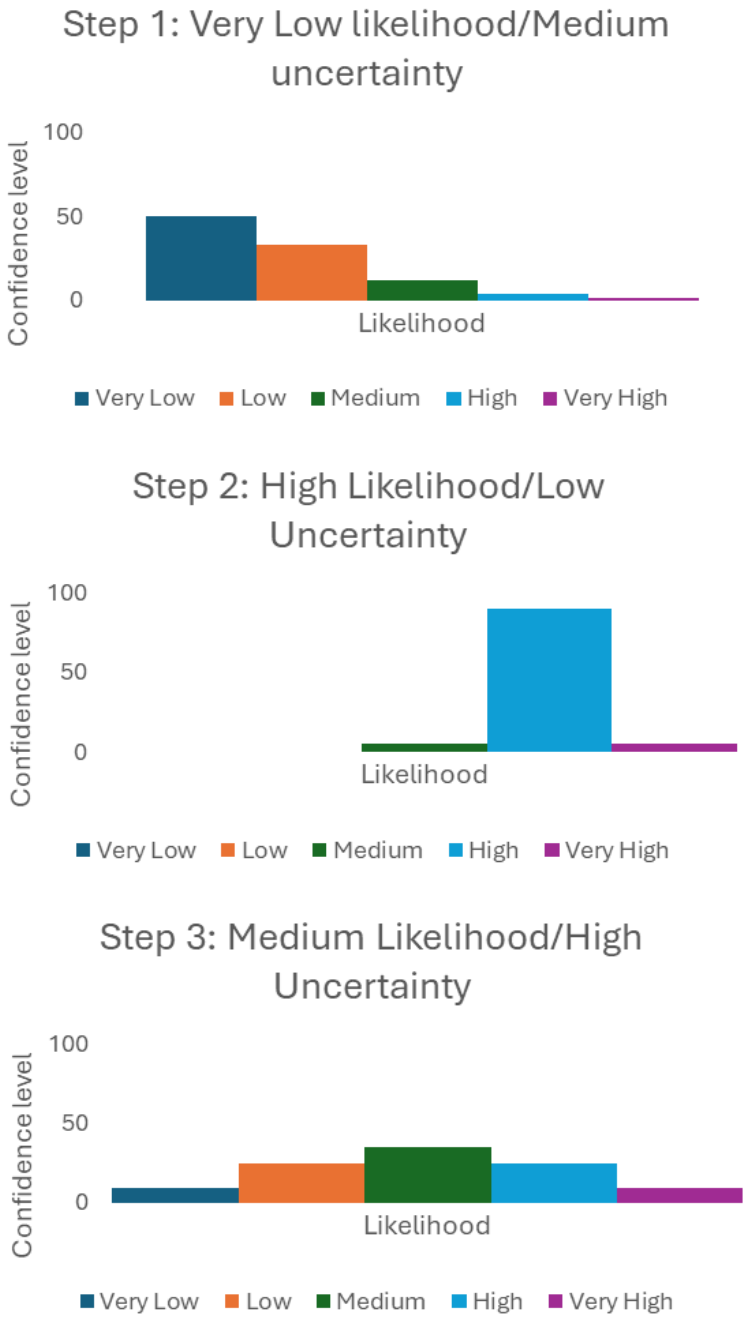
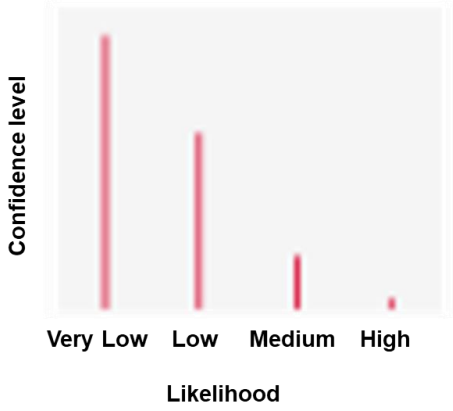


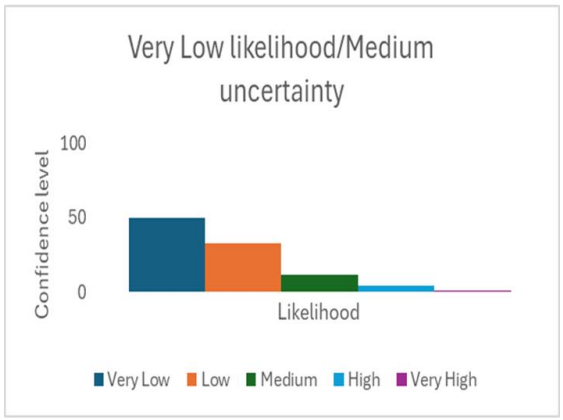
Figure 5: Visual representation of uncertainty associated with the likelihood estimates for each step of the risk pathway shown in Table 5.

The distribution for the overall risk estimate is shown in Figure 6a, along with the summary statistics (Fig 6b). There is alignment with the risk matrix method which gave an overall estimate of Very Low with Medium uncertainty. This method more explicitly highlights this, showing that the most likely estimate is Very Low, but that scores of Low are also likely and that a score of Medium or High was also possible.

a)



c)



b)

Minimum	1.0000
Maximum	4.0000
Mean	1.9679
Mode	2.0000
Std. Deviation	0.8053

Figure 6: a) Graph showing distribution for the overall risk estimate, using stochastic simulations and b) summary statistics of the overall risk estimate using simulations of the adapted Pratique method outcomes for the risk of introduction of Lumpy skin disease (LSD) into the United Kingdom (UK) within the next year; c) Step 1: Infected animal is legally exported to the UK (Very Low likelihood, Medium uncertainty) from Figure 5 which is the most influential step for example 2

Example 3 – Camel prion disease

For the CPD example, 4 steps had a High likelihood of occurring but the most influential step using the risk matrix approach was Step 3: likelihood that semen for export contains the CPD agent which was estimated to have a Low likelihood with High uncertainty.

Table 6: Likelihood and uncertainty estimates for the 5 steps of the risk pathway.

S	**Step (S)**	**Likelihood**	**Uncertainty**	**Fig 1 distb.**
1	Camel Infected	High	High	4c
2	Infected camel not detected	High	High	4c
3	**Semen (per straw) for export contains CPD agent**	**Low**	**High**	**2c**
4	Prion survives journey to UK	High	Low	4a
5	Pathogen in semen not detected on import	High	Low	4a
	Overall risk estimate using risk matrix approach	**Low**	**High**	**2c**

This example helps to demonstrate the effect of High uncertainty for the step which defines the overall risk estimate if using the risk matrix approach. The confidence in the estimate of Step 3 having a Low (35%) or Medium (30%) likelihood is very similar so it would be up to the risk manager to request further data to increase the confidence in the likelihood level. Alternatively, additional mitigating factors could be proposed at another step in the pathway which could reduce the likelihood of that step occurring and so lower the overall likelihood estimate.

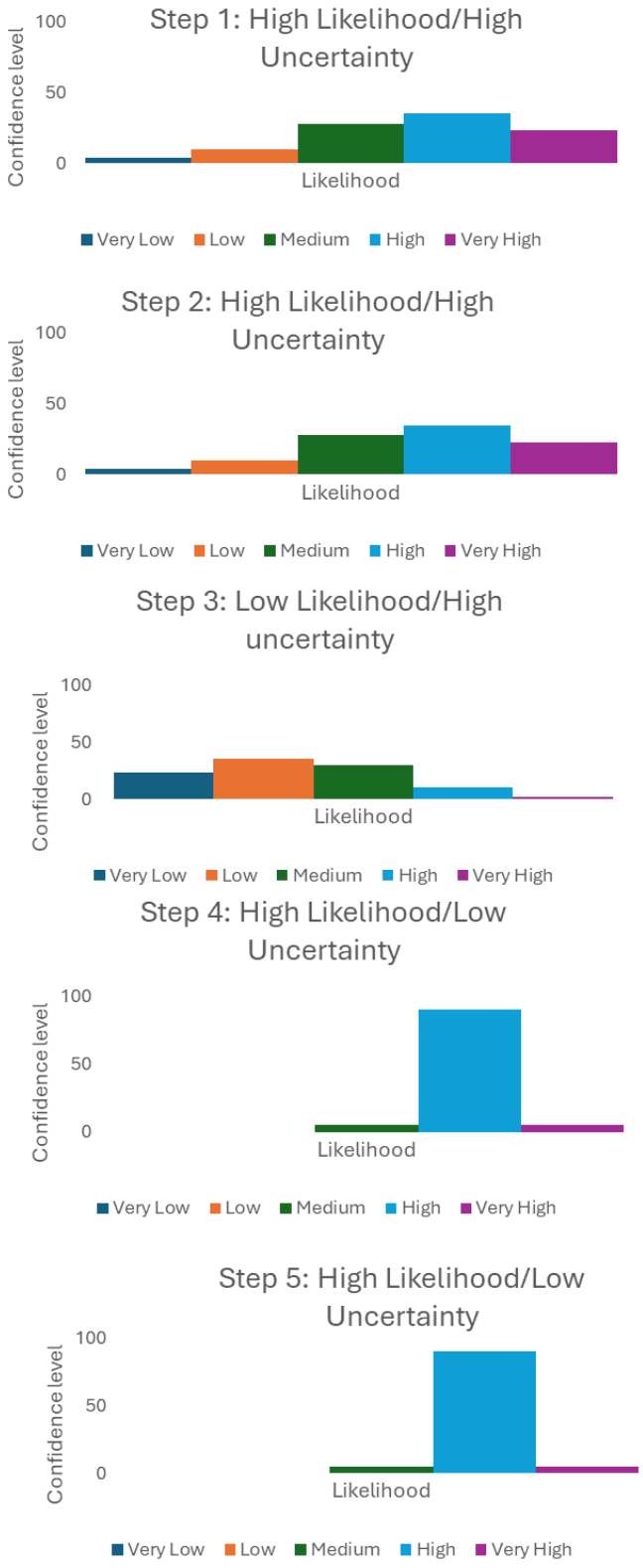
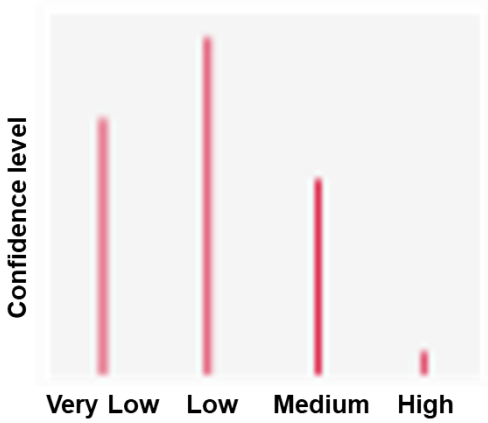


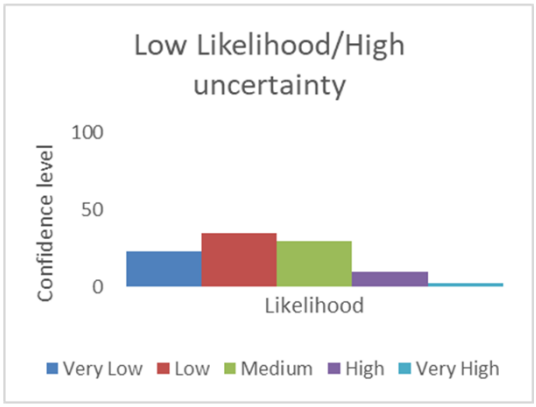
Figure 7: Visual representation of uncertainty associated with the likelihood estimates for each step of the risk pathway shown in Table 4.

The distribution for the overall risk estimate, using stochastic simulations, is shown in Figure 8a, along with the summary statistics (Figure 8b). There is alignment with the risk matrix method which gave an overall estimate of Low with High uncertainty. However, this method also highlights that whilst the most likely estimate was Low, there was relatively high confidence in estimates of Very Low and Medium and a score of High was also possible.

a)



c)



b)

Minimum	1.0000
Maximum	4.0000
Mean	1.5932
Mode	1.0000
Std. Deviation	0.7273

Figure 8: a) Graph and b) summary statistics of the overall risk estimate using stochastic simulations of the adapted Pratique method outcomes for probability of entry of the Camel prion disease agent into the UK from North Africa or the Middle East via the import of camel semen; c) Step 3: Semen (per straw) for export contains CPD agent (Low likelihood, High uncertainty)

Discussion

Conducting a qualitative, rather than a quantitative, RA is often preferred due to the perception that this type of RA will be more accessible and easier for the risk manager or policymaker to understand (FAO 2009). The validity of this perception will, however, depend on how the results are communicated between the risk assessor and the risk manager. Development of the qualitative RA process in animal health has seen the

application of risk matrices to combine probabilities and the development of semi-quantitative tools. Whilst these apply some standardisation when carrying out the RA, an alternative view is that some transparency throughout the RA process could be lost and results mis-interpreted by the risk manager. This is particularly true when it comes to communicating the effect of uncertainty on the RA outcomes. This paper set out to investigate whether a simple visualisation of the risk assessment steps could be more effective in communicating results to the risk manager.

Probability is the preferred measure for expressing uncertainty, as it quantifies the relative likelihood of alternative outcomes, which is what decision-makers need to know (EFSA 2018a). The Pratique method uses graphs to illustrate the confidence in each likelihood rating occurring for each step of the risk pathway. Whether a high uncertainty estimate is interpreted as meaning that the score could be higher or lower than estimated or whether its taken to be based on quality of evidence, further information is very likely to have an important impact on our confidence in the probability estimate. Thus, reducing the amount of uncertainty will not necessarily change the risk level but can give more confidence in the risk assessment outputs (Suedel *et al.,* 2007).

The examples used here illustrate results whereby the risk manager has information to make more informed decisions using a visualisation of the confidence in the likelihood of each step occurring, and in the overall risk, rather than an overall uncertainty estimate. Some risk assessors have highlighted the issue of the inability of risk matrices to account for marked variation in estimates within categories, and the loss of this information with successive levels of multiplication (Heller *et al.,* 2010; Auty *et al.,* 2019). Using the adapted Pratique method highlights not only which steps have the lowest likelihood of occurring and therefore where the risk can be mitigated against but also the confidence in these likelihoods so the risk manager can make more informed decisions.

For qualitative RA the dilemma is how to deal with uncertainty so that it is clear to the decision maker both where it exists and how it may influence the overall risk estimate. This is particularly important where, within the range of uncertainty, the risk estimate could potentially surpass a key decision-making threshold (EFSA 2018).

Illustrating the effect of the uncertainty level on the likelihood estimates for each pathway step can make a RA more transparent and accessible for risk managers who are then able to identify which steps drive the risk and what results need to be interpreted with care due to high uncertainty (Wieland *et al.,* 2011).

The method described here empowers risk managers to make a decision at each step of the pathway as to whether they consider the risk is at an acceptable level. The value of new research can be assessed by weighing up how much the research would cost against how much it is expected to reduce the overall uncertainty in the risk estimate and, consequently, how the reduction in uncertainty might lead to different decision options. This allows the risk manager to see where, further research could increase the confidence in the risk scores, and where mitigations could be put in place either to reduce the risk or reduce the uncertainty around that score.

In a recent study, Clough *et al.,* (2025) states that "An incorrect representation of uncertainty can either make the decision maker overly and artificially confident, or unnecessarily cautious. When uncertainty is described well the decision-maker has a full range of scenarios at their disposal." Communicating uncertainty at each step of the pathway using the method described here will increase the transparency of the scientific RA process and provide risk managers with a more informed evidence base on which to make decisions.

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6.4 Conclusion to Chapter 6

The work carried out in this chapter addressed the final element of qualitative RA identified from the literature review in Chapter 2, namely, uncertainty. It focussed on developing a visual method to demonstrate the effect of uncertainty on the likelihood levels in a qualitative RA. It also described a probability distribution of uncertainty which, when combined, can derive an overall uncertainty score for any risk pathway. Communicating uncertainty at each step of the pathway using the method described here increases the transparency of the scientific risk assessment process and can provide risk managers with a more informed evidence base on which to make decisions.

The next Chapter discusses how the research question investigated in this thesis has been addressed by the work carried out specifically assessing how certain aspects of animal health qualitative RA methodology have developed and proposing new concepts of how some elements can be further advanced in the future.

Chapter 7: Discussion

7.1 Introduction

This thesis set out to address the research question "*To what extent has qualitative risk assessment methodology developed in the sphere of animal health policy and how can it further advance in the future?* ". The thesis is presented as a series of papers aligned to the development of approaches and the application of the approaches in different animal health scenarios. A literature review was initially carried out on the use of qualitative RA in animal health to gauge which elements of the methodology proved problematic and what had been done by way of developing techniques to standardise or evolve the methodology. This review identified four main elements as having been the subject of some development but where some issues still existed (i) the description of risk levels - how to communicate the meaning of the terms describing the probability of occurrence at each step of the risk pathway in a standard manner, (ii) combining probabilities - how to combine these probability terms to give an overall estimate of risk, (iii) accounting for trade volume and time period - how to account for the risk presented by multiple products/animals (aggregated probability), (iv) uncertainty - how to address the uncertainty associated with the probability estimates of the risk pathway steps and derive an overall uncertainty level.

In Chapters 3, 4 and 5 qualitative RA methodology was applied to different scenarios in the animal health sphere including how RAs can influence policy decisions. The WOAH RA framework is an accepted model for qualitative RA and the work presented in these chapters demonstrates the application of this framework and the consistent use of descriptive terms for risk levels. The same qualitative terms of risk levels were used in all Chapters and were based on the EFSA (2006) definitions in line with the most commonly used in the literature reviewed in Chapter 2. The description of risk levels is an essential component of improving consistency of results as without this, descriptive terms such as 'Low' or 'High' are open to differences in interpretation by individual risk managers and could lead to confusion when considering an acceptable level of risk. The literature review identified that problems still exist with the description of terms for the definition of risk levels such as the use of frequencies of events occurring. Going forward, a table highlighting these descriptions and emphasising and reiterating them throughout the RA so that the risk manager does not lose sight of the definitions would

be beneficial. Attaching a description of the likelihood terms in an appendix may often not be sufficient if the risk manager does not refer to them.

A conclusion from the literature review was that suggested best practice for combining likelihoods was the transparent use of a specified matrix for conditional probabilities to provide consistency of results. Different matrices have been developed, as described in Chapter 2 and, despite their drawbacks, they still remain a simple method for demonstrating how likelihoods have been combined throughout a risk pathway. Further development of risk matrices is required to take into account that the product of probabilities that are assessed to be “low” or “very low” will likely be lower than the lowest individual probability.

Chapter 5 illustrates the use of a tool which was developed to account for aggregated probability. The use of the tool is not yet accepted methodology, in that, it is not advocated by, for example, WOAH but it can provide consistency of results albeit if the quantitative bounds used are appropriate. Using this tool provides a standardised methodology to estimate the probability of entry of at least one infected/contaminated unit per year. Future developments could include conducting various scenarios with different quantitative bounds which may be more applicable to different case studies.

Like the descriptive terms for risk levels, qualitative expressions of uncertainty are ambiguous as the same word or phrase (low, medium, high) can mean different things to different people. As a result, decision-makers may misinterpret the assessment of uncertainty, which may result in suboptimal decisions (EFSA 2019). This theme was approached in Chapter 6 employing the use of a distribution of the relative confidence levels in each likelihood estimate for all steps within a risk pathway. Decision-making by the risk manager can depend on whether a risk exceeds an acceptable level so visualising uncertainty as demonstrated in Chapter 6 is preferable to using a single qualitative expression as risk assessors and risk managers may agree on a single descriptive term but interpret it differently. Expressing uncertainties in terms of their impact on the assessment steps, as demonstrated in Chapter 6, enables enhanced transparency of results. Graphs have been shown to be an asset to risk communication practice as they tend to present information in a way that demands relatively little cognitive effort and result in better comprehension (Smerecnik *et al.,* 2010).

Two of the papers in this collection described RAs that were used to inform policy decisions, (i) whether to elevate LSD to the UK's DERC (Chapter 3; Horigan *et al.,* 2018) and (ii) as evidence to change current policy of requiring the dismantling of equipment for secondary C&D after an AI outbreak (Chapter 4; Horigan *et al.,* 2019). The uncertainty surrounding the likelihood estimates was communicated in qualitative terms with a single descriptive term and the interpretation of these terms provided in an appendix. An alternative method of visualising the uncertainty levels as confidence intervals was demonstrated in Chapter 6 as a comparison to the original methods (Chapter 3 and 5). For the risk manager those steps with relatively low confidence in the likelihood estimates could be identified as a cause for concern and worthy of further investigation.

Relatively few papers were identified in the literature review (Chapter 2) which addressed the topic of dose response in animal health qualitative RAs. Chapter 4 described a spreadsheet tool which considered the reduction in avian influenza viral load using a risk matrix approach. Ideally, a qualitative RA that considers onward infection should assess not only the likelihood of exposure to a pathogen, but also the level of pathogen exposure. This could be considered using a risk matrix approach as demonstrated in Chapter 4 and could assist in identifying at which step of a risk pathway the risk becomes negligible or where risk mitigations are best placed.

Quantitative (or semi-quantitative) methods have been developed using the qualitative RA framework. A pairwise summation method for the additive combination of probabilities in qualitative RAs has been formulated so that it satisfied key conditions including that "the method should be applicable to qualitative risk assessments without the need to assume any numerical reference or quantitative probability estimates" (Crotta *et al*., 2024). Other methods such as some of the semi-quantitative tools have adapted the qualitative RA framework by using probability distributions and numerical bounds for the probability intervals assigned to qualitative terms of probability (Biosecurity 2001; de Vos *et al.,* 2020). Similarly, the aggregated probability tool also assigns numerical bounds for the probability intervals assigned to qualitative terms within the graphical tool (Kelly *et al.,* 2018).

Qualitative RAs will always have an element of subjectivity as likelihood and uncertainty estimates will be assigned by the risk assessor based on the available evidence/data at the time of the assessment. This thesis has identified core elements of the qualitative

RA process from a literature review and developed assessments using specific elements of the process to expand the literature further. The thesis has also proposed a method to address uncertainty in qualitative RA. This is particularly important where, within the range of uncertainty, the risk estimate could potentially surpass a key decision-making threshold.

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Chapter 8: Conclusion

Qualitative RAs are frequently used to address animal health issues when data are scarce and/or rapid decisions are required. They can provide risk managers with evidence-based risk estimates on which to formulate their decisions. But, for a qualitative RA to be objective and consistently applied, it is optimal to standardise the approach as much as possible ensuring confidence in the RA results especially when contributing to Government policy decisions. This thesis presents case studies as Chapters which are stand-alone with regards to their application of qualitative RA to animal health, but they also contribute to wider research into the development of qualitative RA in the animal health sphere.

A qualitative RA is ideal for identifying important chains of events and critical control points along risk pathways. This can then be used to construct robust and informed risk management programs when there is insufficient data to conduct a meaningful quantitative assessment. Each risk assessment presented in Chapters 3, 4 and 5 uses the same format of risk pathway and definitions of risk and uncertainty to ensure standardisation. This allows the assessments to be comparable, updatable and enhances transparency for the risk manager by ensuring there are clear and comprehensive descriptions of likelihood avoiding misinterpretation. Chapter 5 demonstrates how it is important to consider the volume of products/animals concerned that are being imported when assessing the risks of entry into an area/country as this could potentially increase the risk estimate and so, influence the bounds of decision-making thresholds.

This thesis has contributed to the field of qualitative RA by demonstrating the usefulness of these RAs in different scenarios using standardised and transparent methodology such as definitions of risk levels, combination of probability and accounting for trade volume and time period (aggregated probability). It has also helped identify elements which could be further developed in the future. An example of this is the subject of uncertainty which forms the method paper presented in Chapter 6. How to deal with uncertainty is a continual problem with all risk assessments, but especially with qualitative risk assessment where it is difficult to convey the effect of uncertainty on risk levels using single words and to communicate the overall effect of uncertainty on the risk as a whole. The visual representation of uncertainty at each step of a risk pathway as outlined in Chapter 6 is a potential solution to the quandary of effective

communication and should be further investigated by applying it to different real-life situations.

In conclusion, the evidence presented in this thesis contributes to a more comprehensive understanding of how standardised methodologies can be applied in the use of animal health qualitative RA. Whilst it is important to develop qualitative RA methodology for consistency it is equally important for results to be transparently communicated to the risk manager. The Chapters presented here, which describe case studies, also demonstrate in detail how the results of the qualitative RA were obtained as this is equally as important as the results themselves so that misinterpretation is avoided. Areas for future research arising from the findings presented in this thesis include further development of the novel methodology approach to the consideration of uncertainty presented in Chapter 6, including scenario analyses using different confidence levels for each uncertainty score as a potential method of improving accuracy in communication.