SCIENTIFIC OPINION

Scientific Opinion on lumpy skin disease[1]

EFSA Panel on Animal Health and Welfare (AHAW)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Lumpy skin disease (LSD) is a viral disease of cattle characterised by severe losses, especially in naive animals. LSD is endemic in many African and Asian countries, and it is rapidly spreading throughout the Middle East, including Turkey. LSD is transmitted by mechanical vectors, but direct/indirect transmission may occur. The disease would mainly be transferred to infection-free areas by transport of infected animals and vectors. In the EU, it could only happen through illegal transport of animals. The risk for that depends on the prevalence in the country of origin and the number of animals illegally moved. Based on a model to simulate LSD spread between farms, culling animals with generalised clinical signs seems to be sufficient to contain 90 % of epidemics around the initial site of incursion, but the remaining 10 % of simulated epidemics can spread up to 400 km from the site of introduction by six months after incursion. Whole-herd culling of infected farms substantially reduces the spread of LSD virus, and the more rapidly farms are detected and culled, the greater the magnitude of the reduction is. Only live attenuated vaccines against LSD are available. Homologous vaccines are more effective than sheep pox strain vaccines. The safety of the vaccines should be improved and the development of vaccines for differentiating between infected and vaccinated animals is recommended. Epidemics are not self-limiting when effective vaccination or culling are not applied. Active surveillance, rapid detection and prompt culling of infected herds are effective measures for LSD control. The role of vectors for LSD transmission should be further investigated in both controlled environments and the field. Awareness-raising campaigns for farmers and veterinary staff to promote recognition of LSD should be considered. The cooperation of the EU with neighbouring countries should be encouraged to prevent transboundary disease spread.

KEY WORDS

Lumpy skin disease, spread, prevention, control and surveillance, vaccines

[1] On request from European Commission, Question No EFSA-Q-2013-00917, adopted on 3 December 2014.

[2] Panel members: Charlotte Berg, Anette Bøtner, Howard Browman, Aline De Koeijer, Klaus Depner, Mariano Domingo, Christian Ducrot, Sandra Edwards, Christine Fourichon, Frank Koenen, Simon More, Mohan Raj, Liisa Sihvonen, Hans Spoolder, Jan Arend Stegeman, Hans-Hermann Thulke, Ivar Vågsholm, Antonio Velarde, Preben Willeberg and Stéphan Zientara. Correspondence: alpha@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on lumpy skin disease: Aline De Koeijer, Mariano Domingo, Yuval Gottlieb, Simon Gubbins, Eyal Klement, Arjan Stegeman, Hans-Hermann Thulke and Eeva Tuppurainen for the preparatory work on this scientific opinion and EFSA staff: Alessandro Broglia, Mattia Calzolari, Josè Cortinhas, Andrey Gogin, Justyna Jaskiewicz and Anna Zuliani for the support provided to this scientific opinion.

Suggested citation: EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), 2015. Scientific Opinion on lumpy skin disease. EFSA Journal 2015;13(1):3986, 73 pp. doi:10.2903/j.efsa.2015.3986

Available online: www.efsa.europa.eu/efsajournal

SUMMARY

Following a request from the European Commission, the EFSA Panel on Animal Health and Welfare (AHAW Panel) was asked to deliver a scientific opinion on lumpy skin disease (LSD), in order to provide an update on the characterisation of the disease; to assess the risk of introduction into the European Union (EU) and the speed of spread, the risk of becoming endemic and its impact; and to determine if further measures are justified. This request is linked to the recent and important spread of LSD throughout the Middle East, including Turkey, where it is now considered endemic.

In particular, EFSA was asked to (i) characterise the disease and provide an update on the global occurrence of LSD and changes in the distribution during the last 10 years; (ii) map the region of concern and other countries of the Mediterranean Basin and Black Sea, displaying identified, or likely, major live animal trade routes; (iii) evaluate all possible pathways of introduction of LSD into the EU, ranking them on the basis of their level of risk, with a view to enhancing preparedness and prevention; (iv) assess the risk and speed of propagation of LSD into the EU and neighbouring countries; (v) assess the risk of LSD becoming endemic in animal populations in the EU and neighbouring countries; (vi) assess the impact of LSD if it were to enter the EU, considering different scenarios as regards the effectiveness of surveillance and control measures; and (vii) review the feasibility, availability and effectiveness of the main disease prevention and control measures (diagnostic tools, biosecurity measures, restrictions on movement, culling).

Regarding disease characterisation, the AHAW Panel reported that LSD is characterised by significant losses, especially in naive and young animals, due to chronic debility, reduced milk production and weight, infertility, abortion and death, but it is not a zoonosis. There is evidence that only around half of infected animals develop generalised skin lesions, but these animals can be viraemic and can transmit the virus. African wild ruminant species may have a role in the epidemiology of LSD. Although certain wildlife species can be experimentally infected by LSD virus (LSDV), information on the susceptibility of wildlife to LSD is scarce and further limited by the inability to distinguish antibodies evoked by LSDV from those evoked by sheep pox and goat pox viruses. LSDV can be detected in animal secretions (e.g. ocular, nasal discharge) up to 15 days post infection. If protected from sunlight, the virus can survive in scabs, and therefore also in the environment, for up to six months, and in dried hides of infected animals for up to 18 days.

LSD is endemic in most African countries. Since 2012, LSD has been spreading on an unusually large scale throughout Middle Eastern countries, including Israel and Turkey, and in the latter it is now considered endemic. The outbreaks that have occurred in Turkey most likely originated by the introduction of LSD from Syria, thus suggesting that political unrest may facilitate the disease spreading. The extensive outbreak investigation conducted in Israel provided useful insights into the epidemiology of LSD.

Field evidence strongly suggests the involvement of haematophagus arthropod vectors in LSDV transmission among cattle by the mechanical route. However, the spread of the virus in situations with very low abundances of vectors may occur, thus suggesting direct and/or indirect transmission (e.g. through fomites contaminated with secretions from infected animals) as possible routes of LSD transmission. The fast spread of LSD as recorded in some areas indicates a minor role of ticks in the transmission of the virus under field conditions. Nevertheless, laboratory experiments suggest that ticks may play a role in the transmission as well as maintenance of LSDV. The importance of different mechanical vectors in the transmission of LSDV is likely to vary in different geographical regions, depending on the environment, temperature, humidity and abundance of the vectors.

Considering the identified or probable animal movements in the regions of concern, the movement of live animals from third countries in the Mediterranean Basin and Black Sea areas into the EU is currently forbidden, according to EU animal health legislation on the import of live animals from countries where LSD is endemic. However, illegal movements of animals cannot be quantified. In Turkey, there are a large number of within-country movements of live cattle from provinces that have

been affected by LSD in 2013–2014. There is significant trade in cattle skin, wool and hides into the EU from countries where LSD is present. In order to complete an import risk assessment, detailed information is needed to clarify if each commodity has undergone appropriate treatment to inactivate LSDV. Skins and hides processed by drying treatments only may pose a risk of the introduction of LSDV into the EU if imported from affected areas, although further spread through this route is unlikely.

The main possible pathways for LSD introduction into free areas are considered to be the movement of infected animals and vectors. The introduction of infected animals is the most efficient way to introduce LSDV into a country, in particular for long-distance spread. The spread of LSD is usually limited in distance when sick animals are not moved to non-affected areas. The active movement of flying vectors can be a pathway for LSD introduction into a naive country from a short distance, e.g. from infected areas close to the borders. Circumstantial evidence indicates that windborne transmission of vectors carrying the virus (after a blood meal on an infected animal) could be a potential route of LSDV introduction into a country.

In order to estimate the risk of introduction of LSD into the EU via the illegal movement of animals, a model was used to assess the probability of an individual being infectious in a given shipment size. For different levels of seroprevalence in the country of origin, the number of animals that need to be moved to have a probability of introduction of LSD into Europe greater than 0.95 or lower than 0.05 would be above 1 300 and below 25, respectively (seroprevalence equal to 30 %), or above 7 800 and below 140, respectively (seroprevalence equal to 5 %).

Based on the transmission patterns of LSD as investigated in Israel, a mathematical model was developed to simulate LSD spread between farms over space after an incursion in Greece. When the control measures entail the removal of animals showing generalised clinical signs, approximately 90 % of epidemics remain confined to the region around the initial site of incursion. However, the remaining 10 % of simulated epidemics are more extensive, with the virus spreading up to approximately 300 to 400 km from the site of introduction by six months after the incursion. Under the assumptions made when developing the model for the transmission of LSDV between farms, there is the potential for outbreaks to spread in Bulgaria and Greece. Applying whole-herd culling to infected farms substantially reduces the spread of LSDV and, the more rapidly farms are detected and culled, the greater the magnitude of the reduction is.

Regarding the risk of LSD becoming endemic in animal populations in the EU, owing to a lack of data regarding the ability of potential European vectors of disease transmission, the international data cannot be extrapolated directly to the European situation. Nevertheless, under the current EU policy and according to the scenarios produced using the spread model, if the situation and ability of vectors was the same as in Israel, LSD would most likely not become endemic in the EU.

When assessing the impact and consequences of LSD entering the EU, according to the model developed to simulate LSD spread over space, under a scenario of an incursion of LSD in Greece, by applying the measures of vaccination and culling of generalised cases, as applied in Israel, 100 days after the onset of the epidemics, the median number of infected farms would be 16 (upper and lower bounds: 690 and 6, respectively) and the median number of animals in the infected farms would be 951 (upper and lower bounds: 67 908 and 476, respectively). In the worst-case scenario, the number of infected farms would increase and the outbreak would not stop, even after 200 days. If culling the whole herds took place 7 or 15 days after infection, the median numbers of infected farms would be 5 and 7, respectively, and the number of animals in the infected farms to be culled would be limited, with median numbers of 467 (407; 780) and 558 (419; 1 454), if culling was done 7 or 15 days after infection, respectively. The outbreak would be controlled in the worst case after 12 or 43 days, respectively, thus indicating the significant impact of this measure in controlling the outbreaks.

The main prevention and control measures for LSD have been assessed. In general, the AHAW Panel concluded that rapid laboratory confirmation of suspected LSD field cases is essential for successful eradication of the disease.

Regarding diagnostic methods, validated general real-time polymerase chain reaction (PCR) is the method of choice for the detection of LSDV. Several national reference laboratories within the EU have the molecular diagnostic capacity required for LSDV detection already in place.

As far as LSD vaccines are concerned, only live attenuated vaccines against LSD are currently commercially available. RM-65 attenuated sheep pox vaccine at the recommended dose for sheep has limited effectiveness in protecting animals from LSD. There is field evidence that 10 times the dose of RM-65 is more effective in terms of protection, although is less effective than vaccination with a homologous strain. The Neethling attenuated lumpy skin disease virus vaccine is highly effective in the prevention of morbidity, thus confirming the need to use homologous vaccines for the control of *Capripoxvirus* infections. Nevertheless, some safety issues have been reported that are linked to generalised clinical reactions due to vaccination with LSD strains that can be observed.

Concerning the effectiveness of control measures, according to Israeli experience, while using the attenuated RM-65 vaccine at the recommended dose for sheep, epidemics of limited extent have been controlled by culling only those animals with generalised skin lesions. Large epidemics can be controlled by the use of effective vaccination. Epidemics are not self-limiting when effective vaccination or culling are not applied. Although insecticides are frequently used to control LSD outbreaks, there is no evidence to date to prove their effectiveness in controlling LSD spread.

The AHAW Panel recommends further investigation into the potential relevant vector species for LSD transmission in controlled environments and the mode of transmission, besides the ecology of different blood-feeding and biting arthropod species in the cattle farming setting. In relation to this, the effectiveness of insecticides for LSD control should also be investigated.

Owing to the risk of LSD spreading from the Middle East to the rest of Asia or to Europe, the development of safe, efficient and non-replicating 'differentiating infected from vaccinated animals' (DIVA) vaccines against LSDV is required, as well as an associated diagnostic test. Furthermore, the efficacy of currently available live vaccines in cattle against LSDV should be evaluated using challenge experiments in controlled environments.

In term of preparedness, the AHAW Panel suggests that a quantitative import risk assessment of skins and hides coming from affected regions should be performed. This will allow specific measures to be identified to reduce the risk posed by this commodity. Inter-laboratory ring-trials for *Capripoxvirus* diagnostics should be organised. Adequate veterinary care and improved surveillance should be in place, in particular for transhumant flocks along migratory routes in risk areas, especially for long-distance migrations. Moreover, awareness-raising campaigns and training for farmers and veterinary staff in recognising the disease under field conditions should be considered, especially for regions at a higher risk of introduction of LSD (i.e. those bordering affected regions). Finally, if non-biological drivers of the transmission of LSD and other transboundary animal diseases change (e.g. breakdown of veterinary infrastructures, human migration, political unrest), the risk of LSD introduction should be accordingly reassessed. Under this perspective, the cooperation of the EU with neighbouring countries should be encouraged for the prevention of transboundary animal diseases and enhancing preparedness.

In terms of the control of LSD, the AHAW Panel recommends that, if LSD entered the EU, rapid detection and prompt culling of infected herds should be considered as effective measures in limiting the spread and impact of the outbreaks. Furthermore, clinical surveillance conducted in protection and surveillance zones should be designed to detect animals showing characteristic LSD signs (clinical inspection by veterinary authorities and awareness campaigns for farmers and other stake holders and

viraemic animals with silent infection (blood samples tested with real-time PCR method). Clinical surveillance should be combined with serosurveillance.

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Lumpy skin disease (LSD) is a pox disease of cattle caused by capripoxvirus, of the genus Capripoxvirus, in the family Poxviridae. It is characterised by fever, nodules on the skin, mucous membranes and internal organs, emaciation, enlarged lymph nodes, oedema of the skin, and sometimes death.

Various strains of capripoxvirus are responsible for the disease yet they are not the same strains causing sheep and goat pox. Transmission of LSD virus appears to occur predominantly by insects (possibly through mechanical vectors like mosquitoes, flies and ticks), natural contact transmission in the absence of insect vectors being a minor source of infection, while feed and water contaminated with infected saliva may also be transmission routes.

LSD is exotic to the EU. It has been reported in the African continent as well as in the Middle East and in Asia. Turkey reported the first occurrence of LSD in 2013. If the virus were to enter the EU it could have severe direct losses related to temporary reduction in milk production, temporary or permanent sterility in bulls, damage to hides and death due to secondary bacterial infections. The consequential losses related to trade restrictions could be even more important.

LSD is a disease included within the category of cattle diseases on the OIE list of diseases in Article 1.2.3 of the Terrestrial Animal Health Code (the Code) of the World Organisation for Animal Health (OIE). This consequently entails notification obligations to the OIE for the EU Member States and its trading partners. Specific international trade standards for LSD are provided for in Chapter 11.12 of the Code as well as in Chapter 2.4.14 of the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.

There are several legislative acts in the EU that pertain to LSD, of which the most relevant ones are:

- Council Directive 82/894/EEC of 21 December 1982 on the notification of animal diseases within the Community. It sets an obligation for Member States to notify the Commission of the confirmation of any outbreak of LSD.

- Council Directive 90/425/EEC of 26 June 1990 concerning veterinary and zootechnical checks applicable in intra- Community trade in certain live animals and products with a view to the completion of the internal market. It recognises LSD as a disease subject to mandatory emergency action, including territorial restrictions.

- Council Directive 92/65/EEC of 13 July 1992 laying down animal health requirements governing trade in and imports into the Community of animals, semen, ova and embryos. It identifies LSD as a notifiable disease and requires that trade of Bovidae and Giraffidae and their products be subject to specific health requirements.

- Council Directive 92/119/EEC of 17 December 1992 introducing general Community measures for the control of certain animal diseases. Disease control measures are foreseen for a series of diseases exotic to the EU, including LSD, with the intent to control and eradicate them.

The risk manager is in need of updated scientific advice in order to assess the risk of introduction of LSD and to determine if further measures are justified. This is linked to the absence of the disease from the EU while it appears to spread in some EU neighbouring countries. Another important aspect is related to the characterisation of the disease for facilitating any further categorisation exercise by the risk manager in the framework of the prioritisation of actions. Therefore, the Commission is in need of scientific advice on the assessment of the significance of the risk posed by LSD considering the current control measures.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In view of the above, and in accordance with Article 29 of Regulation (EC) No 178/2002, the Commission asks EFSA for a scientific opinion on the following aspects of LSD:

1. Characterise the disease and provide an update on the global occurrence of LSD and changes in the distribution during the last 10 years.

2. Provide a mapping of the region of concern and other countries of the Mediterranean Basin and Black sea, displaying identified, or likely, major live animal trade routes.

3. Evaluate all possible pathways of introduction of LSD into the EU, ranking them on the basis of their level of risk, with a view to enhance preparedness and prevention.

4. Assess the risk and speed of propagation of LSD into the EU and neighbouring countries.

5. Assess the risk of LSD becoming endemic in animal population in the EU and neighbouring countries.

6. Assess the impact of LSD if it were to enter the EU considering different scenarios as regards the effectiveness of surveillance and control measures.

7. Briefly review the feasibility, availability and effectiveness of the main disease prevention and control measures (diagnostic tools, biosecurity measures, restrictions on the movement, culling).

ASSESSMENT

INTRODUCTION

Lumpy skin disease (LSD) is an economically important *Capripoxvirus*-induced disease of cattle, of great concern for animal health and welfare. LSD is currently exotic to the European Union (EU), but incursions of LSD have occurred in EU neighbouring areas. Recent outbreaks of LSD in Israel and Turkey have stressed the need to update the disease profile, specifically focusing on surveillance and control measures, as well as to assess the risk of spread to the EU and of become endemic in affected Member States (MSs).

APPROACH TAKEN TO ANSWER TERMS OR REFERENCE

This scientific opinion was prepared by an ad hoc working group, and reviewed and adopted by the Animal Health and Welfare (AHAW) Panel of EFSA, to answer the terms of reference (ToRs) as provided by the European Commission (EC). The following approach was followed to answer risk questions:

- In order to update the disease profile and the global occurrence of LSD (**ToR 1**), a literature review was conducted to retrieve recent scientific information on aetiology, pathogenesis, clinical signs and lesions, and epidemiology. This information is contained in section 1. The global occurrence of LSD and changes in its distribution during the last 15 years were analysed through data reported to the World Organisation for Animal Health (OIE) and the EU. For EU neighbouring regions, maps were produced showing the occurrence of infection in different years (2005, 2010 and 2013, see section 1.2) and the number of years of presence.
- The identification and display of probable major live animal trade routes (**ToR 2**) was done in accordance with trade and animal movement data from TRACES, COMTRADE and Eurostat, providing information of trade routes from third countries of the Mediterranean Basin and Black Sea to the EU.
- To identify possible pathways of introduction of LSD into the EU (**ToR 3**), information from the literature and about recent outbreaks occurring in Israel and Turkey was reviewed with the aim of understanding the complex events leading to transboundary transmission into the EU (section 4). This information was gathered from experts from veterinary services of the countries directly affected by LSD and involved in the study of the outbreaks. The identified pathways were ranked by importance (section 4.5).
- The risk and speed of propagation of LSD into the EU and neighbouring countries (**ToR 4**) was assessed by using a model fed with epidemiological data from Israel outbreaks. The model was developed in collaboration with the Mathematical Biology Group of Institute of Animal Health, Pirbright, UK, and the EFSA Unit for Assessment and Methodologies (AMU). A detailed description of the spread model is given in section 6 and Appendix A.
- The risk of LSD becoming endemic in animal populations in the EU and neighbouring countries (**ToR 5**) was assessed qualitatively by a review of data about viral physicochemical and biological properties, stability in the environment, the capacity of transmission by vectors, the existence of potential reservoirs of the virus and the ability of the virus to persist in animals and herds.
- The impact and the consequences of LSD entering the EU considering different scenarios as regards the effectiveness of surveillance and control measures (**ToR 6**) were assessed based on the spread model (section 8).
- The feasibility, availability and effectiveness of the main disease prevention and control measures (**ToR 7**) were reviewed using available information from the scientific literature and expert opinion (see section 9).

1. Disease characterisation

1.1. Agent characteristics

LSD virus (LSDV) belongs to the family *Poxviridae* which is divided into two subfamilies—poxviruses affecting insects (*Entomopoxvirinae*) and vertebrates (*Chordopoxvirinae*)—and several genera. The genus *Capripoxvirus* comprises LSDV, sheep pox virus (SPPV) and goat pox virus (GTPV). The prototype of LSDV, Neethling strain, was isolated in South Africa (Alexander et al., 1957). Poxviruses are large (320–260 nm), enveloped or non-enveloped, brick- or oval-shaped viruses (Fenner et al., 1987) with similar morphology (except parapoxviruses).

All capripoxviruses grow slowly on cell cultures and may require several passages. They can be propagated on a variety of cells of bovine and ovine origin, causing easily recognisable cytopathic effects (CPE) (Alexander et al., 1957; Prydie and Coackley, 1959; Munz and Owen, 1966). In addition, the virus can be propagated in the chorioallantoic membranes of embryonated chicken eggs, causing macroscopic pock lesions (Alexander et al., 1957; van Rooyen et al., 1969). Generalised skin lesions can be detected in LSDV-infected rabbits.

The replication of LSDV occurs in the cytoplasm of the host cell in intracytoplasmic eosinophilic inclusion bodies (Weiss, 1968; Prozesky and Barnard, 1982), which can be detected using microscopic examination of a haematoxylin- and eosin-stained LSDV-infected monolayer of cells.

1.1.1. Phylogenetics

LSDV is a double-stranded DNA virus (Weiss, 1968). The size of the LSDV genome is 151 kbp and it consists of a central coding region with identical 2.4-kbp inverted terminal repeats and 156 putative genes. The genes encoding host range, virulence and immune evasions are located at the terminal parts of the genome (Tulman et al., 2001). DNA analysis using restriction endonucleases on field samples and vaccine strains showed 80 % homology between strains of capripoxviruses (CaPV) (Black et al., 1986). The genomes of SPPV and GTPV are very similar to that of LSDV, sharing 96 % nucleotide identity within the genus (Tulman et al., 2002). It is not possible to distinguish between different strains of CaPV using serological assays (Kitching, 2003). Molecular studies have demonstrated that LSDV, SPPV and GTPV are phylogenetically distinct (Tulman et al., 2001; Tulman et al., 2002) and, recently, by sequencing the host-specific G-protein-coupled chemokine receptor (GPCR), or RNA polymerase (RPO30) genes, species-specific molecular assays have been developed for differentiation of CaPVs, enabling the phylogenetic grouping of CaPVs (Le Goff et al., 2009; Lamien et al., 2011a; Lamien et al., 2011b).

1.1.2. Virulence

According to the current information available, there is no evidence about differences in virulence of the different LSDV strains. The severity of the disease depends mainly on the host immune status, breed, production stage and age.

1.1.3. Resistance and survival of the virus

The resistance of LSDV to physical and chemical action is reported below (OIE, 2014b).

- Temperature: susceptible to 55 °C/two hours, 65 °C/30 minutes. Can be recovered from skin nodules kept at −80 °C for 10 years and infected tissue culture fluid stored at 4 °C for six months.
- pH: susceptible to alkaline or acid pH. No significant reduction in titre when held at pH 6.6–8.6 for five days at 37 °C.
- Chemicals/disinfectants: susceptible to ether (20 %), chloroform, formalin (1 %) and some detergents, e.g. sodium dodecyl sulphate. Susceptible to phenol (2 % for 15 minutes), sodium

hypochlorite (2–3 %), iodine compounds (1:33 dilution), Virkon® (2 %) and quaternary ammonium compounds (0.5 %).

The virus is susceptible to sunlight and detergents containing lipid solvents, but in dark environmental conditions, such as contaminated animal sheds, it can persist for many months (OIE, 2014a).

Table 1 summarises information from the literature about survival times of LSDV in different matrices.

Table 1: Period of detection of LSD in different matrices

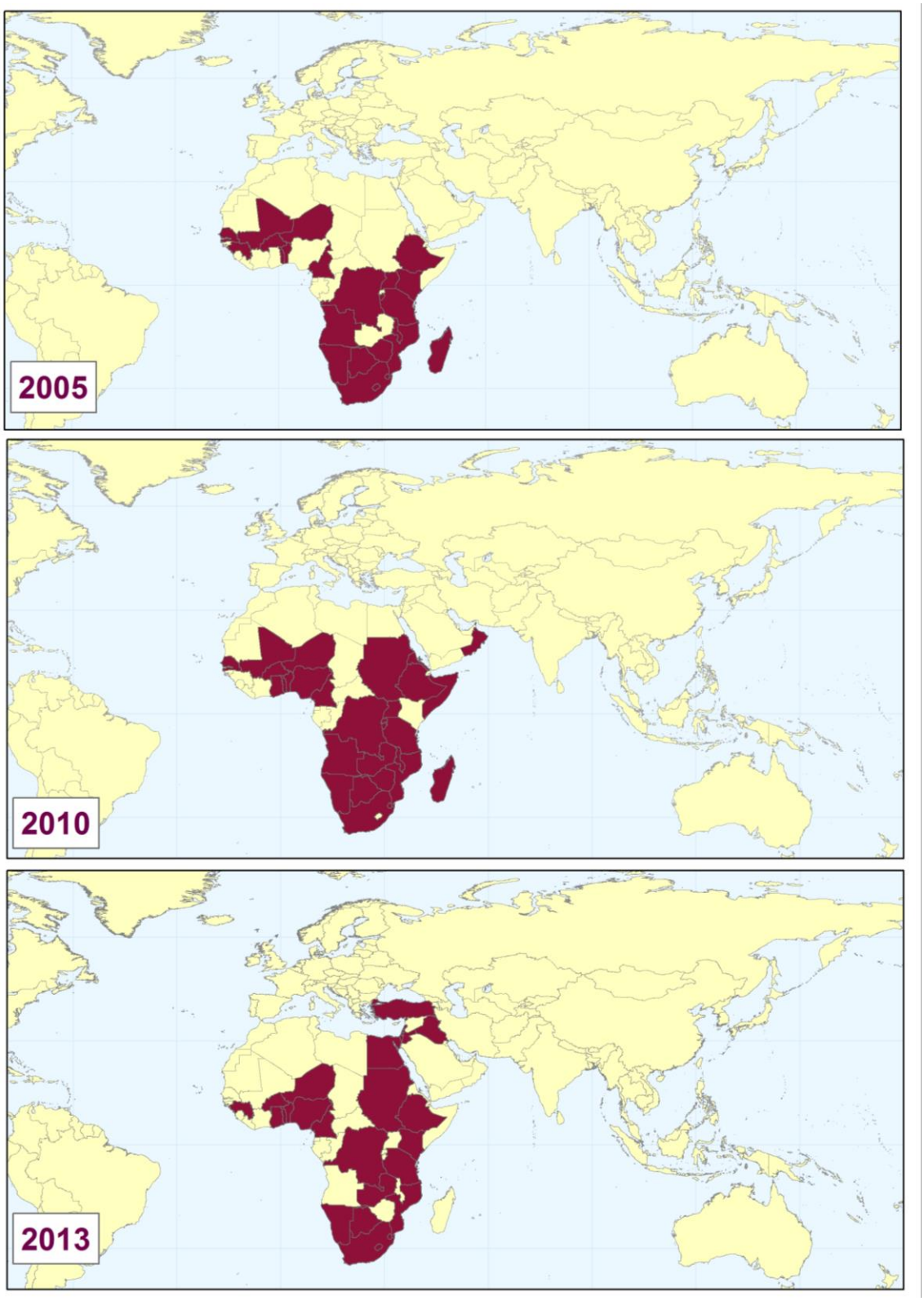
Matrix		Period of LSD virus detection (days post infection, dpi) [(a)]	Reference	Notes
Live animals and products	Blood	4–21 (5–16)	Tuppurainen et al. (2010, 2005)	
	Saliva	11 days post onset of fever	Weiss (1968)	Viable virus has also been recovered from saliva of animals with asymptomatic infection (Weiss, 1968)
		12–18 (15–18)	(Babiuk et al., 2008)	
	Nasal discharge	12–21 (12–18)	Babiuk et al. (2008)	
	Ocular discharge	15		
	Scabs	Several years when kept at –20 °C	Tuppurainen, personal communication	
	Skin lesions	92 (39)	(Tuppurainen et al., 2005)	Live virus also in apparently normal looking skin
	Urine	Not known		
	Faeces	Not known		
	Semen	159 (42)	(Irons et al., 2005)	
	Meat	Known to persist	Weiss (1968)	
	Milk	Not known		
	Hides	18 days in air-dried hides	Weiss (1968)	
Feed		Not known		
Fodder		Not known		
Shaded pens, bedding		6 months in shaded premises		
Environment, pastures		Not known		
Fomites	Vehicles, clothing equipment	Not known		
Insects	*Stomoxys calcitrans*	2 days post feeding	(Chihota et al., 2003)	
	Aedes aegypti	6 days post feeding	(Chihota et al., 2001)	

(a): dpi expressed if tested by polymerase chain reaction or, in brackets, by virus isolation.

1.2. Geographical distribution

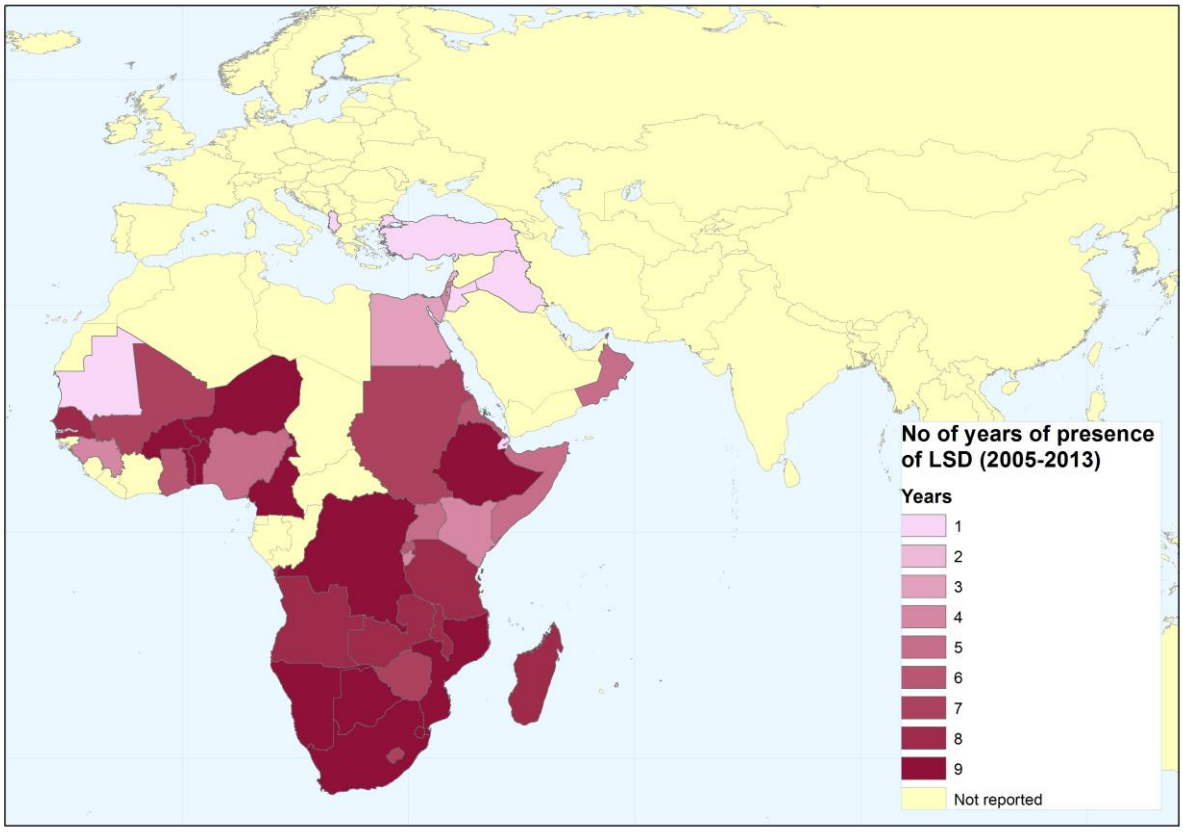
LSD is endemic in most African countries, and outbreaks outside the African continent mainland occurred in the Middle East in 2006 and 2007 and in Mauritius in 2008 (OIE, 2014b). The American continent and Australia are free of CaPV infections. LSD was first reported in Zambia in 1929, then 15 years later was observed in Botswana and then in South Africa, where eight million cattle were

affected. Until the 1970s, LSD had spread northwards to Kenya and Sudan, westwards to Nigeria and was then reported from Mauritania, Mali, Ghana and Liberia (OIE, 2014b). The global occurrence of LSD from 2005 to 2013 and the number of years of presence is reported in the maps below (Figures 1 and 2).



Data source: OIE

Figure 1: Global occurrence of LSD as reported to OIE in 2005, 2010 and 2013

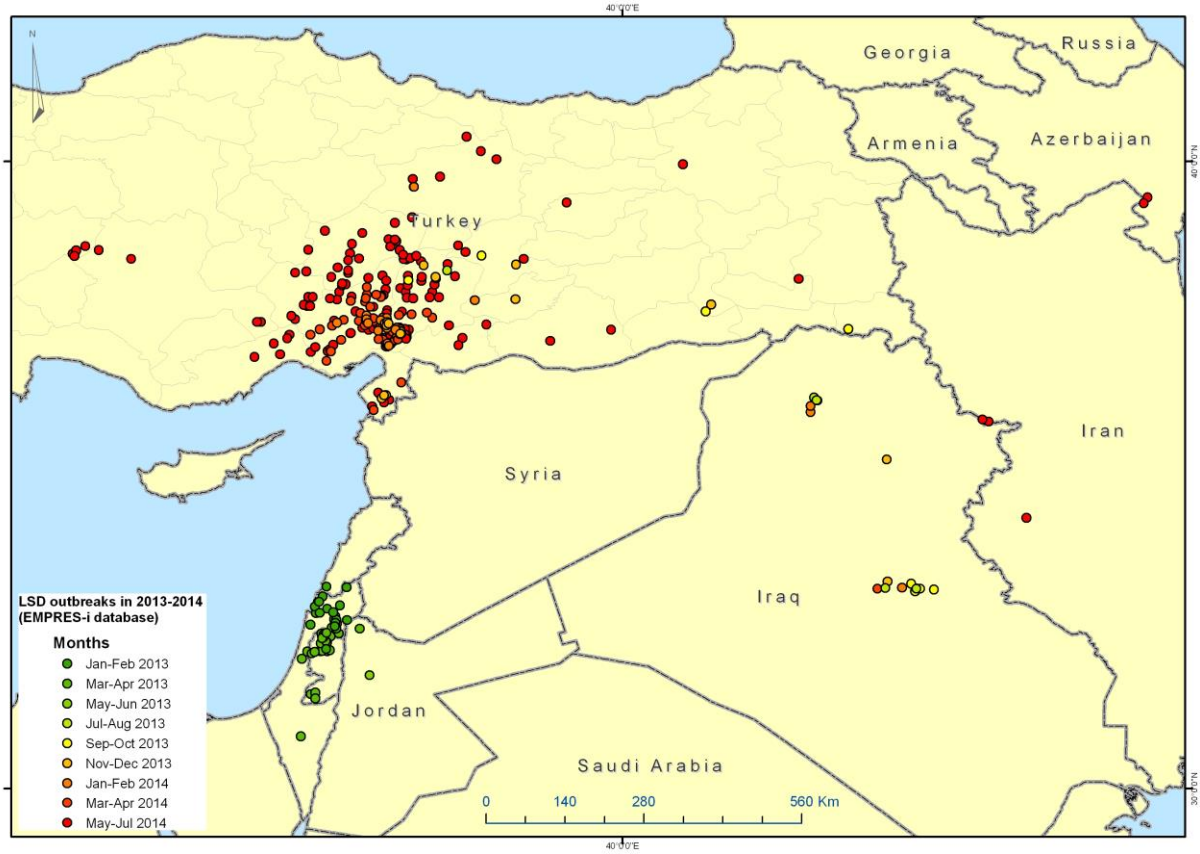


Data source: OIE

Figure 2: Number of years of presence of LSD in different countries as reported to OIE for the period 2005–2013

Until 1989, LSD occurrence was restricted to sub-Saharan Africa, but Egypt reported its first LSD outbreak in 1988 (House et al., 1990) and Israel in 1989 (Yeruham et al., 1995).

In subsequent years, Bahrain, Kuwait, Oman, Yemen, Israel and the West Bank also reported LSD incursion. From July 2012 to August 2013, 293 outbreaks were reported in Israel; in 2012, 34 outbreaks were reported to OIE in Lebanon; in May 2013, two outbreaks were reported in Jordan; in September 2013, 28 outbreaks were reported in Iraq (still on-going); since August 2013, 236 outbreaks have been reported in Turkey; in May 2014, four outbreaks were reported in Iran; and, in July 2014, two outbreaks were reported in Azerbaijan. LSD may have now become endemic in Turkey. Although LSD has not been reported in the Syrian Arab Republic—most likely owing to the current armed conflict—the disease is present (FAO, 2013b). LSD probably spread from Syria and Iraq to Turkey, as most outbreaks in Turkey occurred along the eastern part of the southern border with Syria and Iraq (Figure 3).



Data source: OIE

Figure 3: Outbreaks of LSD in Middle Eastern countries reported bimonthly in 2013 and 2014

1.3. Host range

1.3.1. Livestock

In addition to cattle, natural infections have been reported in Asian water buffalo (*Bubalus bubalis*) in Egypt, but with significantly lower prevalence rate (1.6 %) than in cattle (30.8 %) (Ali et al., 1990; El-Nahas et al., 2011). Lumpy skin disease virus replicates in cell cultures of sheep and goat origin and the in experimentally infected sheep and goats there is local reaction at the inoculation site but no reports on clinical disease in small ruminants caused by LSDV.

Thin-skinned, high-producing dairy *Bos taurus* breeds are highly susceptible against LSDV, whereas indigenous (*Bos indicus*) breeds such as zebu and zebu hybrids are likely to have some natural resistance against the virus (Davies, 1991; Gari et al., 2011).

It is not known what genetic factors influence the disease severity (Babiuk et al. 2008). High ambient temperatures, coupled with farming practices to produce high milk yields, could be deemed to stress the animals and contribute to the severity of the disease in Holstein–Friesian cattle (Tageldin et al., 2014).

1.3.2. Wildlife

In general, CaPVs are highly host specific, with only a few known exceptions. Very few data are available on the susceptibility of wild ruminants to LSD. Clinical signs of LSD have been demonstrated in impala (*Aepyceros melampus*) and giraffe (*Giraffa camelopardalis*) after experimental inoculation with LSDV (Young et al., 1970). LSD was reported in an Arabian oryx (*Oryx leucoryx*) in Saudi Arabia (Greth et al., 1992). In this case, the virus was detected using electron microscopy in skin nodules of the oryx and raised antibody levels against CaPV were detected in

paired serum samples tested using a neutralisation test. However, whether the disease was actually caused by LSDV or SPPV was never confirmed. Recently, the persistence of LSDV nucleic acid was reported in skin samples collected from springbok (*Antidorcas marsupialis*) in South Africa (Le Goff et al., 2009; Lamien et al., 2011b).

Antibodies against SPPV, GTPV and LSDV cannot be differentiated from each other by serological tests, and this is an important limitation. The presence of antibodies in an animal species indicates its susceptibility to the virus and its potential involvement in the epidemiology of the disease (Barnard, 1997).

However, 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. Antibodies against CaPV have been detected in blue wildebeest (*Connochaetes taurinus*), black wildebeest (*Connochaetes gnu*), springbok, eland (*Taurotragus oryx*) and impala (Barnard, 1997). The seroprevalence varied from 10 to 27 %, averaging 17 % in a grassland and 33 % in a forest transition environment (Barnard, 1997). Antibodies were also detected in serum samples collected from African buffalo (*Syncerus caffer*) in Kenya (Davies, 1982). In another study, low levels of antibodies were detected in kudu (*Tragelaphus strepsiceros*), two waterbuck species (*Kobus ellipsiprymnus* and *Kobus defassa*), reedbuck (*Redunca arundinum*), impala, springbok and giraffe, leading to the conclusion that the samples may have contained non-specific virus inhibitors (Hedger and Hamblin, 1983). However, the antibody titres in the giraffe and reedbuck samples were as high as in convalescent cattle that were assumed to be indicative of past infection (Hedger and Hamblin, 1983).

Animals with mild or asymptomatic infection with LSDV do not always develop antibody levels detectable with a neutralisation assay. Therefore, it is possible that the actual number of LSDV-infected wild ruminants may be considerably higher than revealed by this test. Wild animals showing clinical signs of LSD are likely to be more susceptible to predators, which could explain the lack of reports of clinical disease in wildlife species. In addition, the presence of clinical signs of LSD in wildlife is easily missed, as the monitoring of skin lesions is difficult or impossible, especially in mild cases (Barnard, 1997).

In conclusion, there is evidence that African wild ruminant species may have a role in the epidemiology of LSD. Although certain wildlife species can be experimentally infected by LSDV, information on the susceptibility of wildlife to LSD is scarce and further limited by the inability to distinguish antibodies evoked by LSDV from those evoked by sheep pox and goat pox.

1.4. Pathogenesis and clinical signs

The clinical signs of natural and experimentally produced LSD have been well described (Thomas and Marè, 1945; Haig, 1957; Capstick and Coackley, 1961; Weiss, 1968; Prozesky and Barnard, 1982; Davies, 1991; Barnard et al., 1994). The course of the disease may be acute, subacute or chronic. Only 40 to 50 % of experimentally infected animals develop generalised skin lesions; many cases are subclinical but can be viraemic and can transmit the virus (Weiss, 1968). The incubation period of LSD under field conditions is two to four weeks (Haig, 1957), while, in the experimentally induced disease, it is between 4 and 14 days (Prozesky and Barnard, 1982; Carn and Kitching, 1995a).

The disease affects cattle and tends to be more severe in milking cows in the peak of lactation and in young animals (Gari et al., 2011). In animals that develop clinical disease, there is a biphasic febrile reaction that may exceed 41 °C. They remain febrile for 4 to 14 days. This is accompanied by depression, disinclination to move, inappetence, salivation, lachrymation and a nasal discharge, which may be mucoid or mucopurulent. Lachrymation may be followed by conjunctivitis and, in some cases, by corneal opacity and blindness. The superficial lymph nodes, especially prescapular, precrural and subparotid, are usually markedly enlarged (Thomas and Marè, 1945; Haig, 1957; Weiss, 1968; Prozesky and Barnard, 1982; Barnard et al., 1994; Carn and Kitching, 1995a).

The eruption of nodular skin lesions usually occurs within 48 hours of onset of the febrile reaction. They may be very numerous and cover the entire body or there may be only a few of them. Predilection sites are the skin of the head, neck, perineum, genitalia, udder and limbs. Nodules are 5 to 50 mm in diameter, circumscribed, firm, round and raised, and involve the skin, subcutaneous tissue and sometimes even the underlying muscles. Ulcerative lesions may appear on the conjunctiva, muzzle, nostrils, mucous membrane of the mouth, larynx, trachea, oesophagus and abomasum. Small nodules may resolve spontaneously without any consequences or may become ulcerated and sequestered. Secondary bacterial infection or infestation by fly larvae may occur. Large nodules may become fibrotic and persist for several months; these are referred to as "sit fasts" (Thomas and Marè, 1945; Alexander et al., 1957; Haig, 1957; Capstick and Coackley, 1961; Weiss, 1968; Prozesky and Barnard, 1982; Davies, 1991; Carn and Kitching, 1995b). The scars may remain indefinitely, thus rendering the hide worthless (Green, 1959).

Some acutely affected animals may develop severe subcutaneous oedema of the ventral parts of the body such as the dewlap, brisket, limbs, udder, scrotum and vulva. The skin of the oedematous limbs may become necrotic and slough off, leaving deep ulcers, which may become secondarily infected with bacteria. Oedematous and necrotic lesions in the udder may result in mastitis. In some animals, necrotic lesions in the trachea and lungs may lead to pneumonia. Contraction of connective tissue in healed tracheal lesions may result in a localised collapse of the trachea and subsequent suffocation. Bulls usually become temporarily infertile, but sometimes because of severe orchitis they may become permanently sterile. Pregnant cows may abort and be in anoestrus for several months (Thomas and Marè, 1945; Alexander et al., 1957; Haig, 1957; Capstick and Coackley, 1961; Weiss, 1968; Prozesky and Barnard, 1982; Davies, 1991; Carn and Kitching, 1995b).

1.5. Immune response

Immunity to CaPV infections is predominantly cell mediated and requires a replicating agent to be effectively stimulated (Carn, 1993). Most progeny viruses remain inside infected cells with the exception of enveloped viruses, which are released into the blood (Boulter and Appleyard, 1972). By spreading from cell to cell, the virus is out of reach of circulating antibodies. Circulating antibodies against capripox virus are able to limit the spread of the virus in experimental animals, but do not prevent replication of the virus at the site of infection (Kitching and Smale, 1986). The immune status of a previously infected or vaccinated animal cannot be related to serum levels of neutralising antibodies (Kitching et al., 1986).

All the viruses in the CaPV genus share a common major antigen for neutralising antibodies; animals recovered from infection by one virus are believed to be at least partially protected from infection with the other. It is not possible to distinguish CaPVs with the serum neutralisation test (SNT), fluorescent antibody test (FAT), indirect fluorescent antibody test (IFAT) or agar gel immunodiffusion (AGID) (Davies and Otema, 1981; Kitching et al., 1986). Serological evidence (Davies and Otema, 1981), cross-infection and cross protection experiments (Kitching and Taylor, 1985) indicate that the viruses of the genus capripox cross-react immunologically.

Animals that have recovered from apparent or inapparent natural infection with LSD develop antibodies capable of neutralising up to 3 logs of the virus and are also resistant to reinfection (Weiss, 1968). Animals that have been vaccinated or showed mild disease develop low levels of neutralising antibodies (Kitching and Hammond, 1992).

For experimentally produced LSD, only 40–50 % of the infected cattle developed generalised skin lesions. The remaining animals either developed localised and circumscribed painful swelling at the inoculation site of LSDV or showed no clinical signs apart from a fever reaction (Weiss, 1968).

1.6. Routes of transmission

1.6.1. Direct transmission

Experimental and field evidence indicates that LSDV is inefficiently transmitted between animals through direct contact (Weiss, 1968; Carn and Kitching, 1995b), although further experimental studies are needed using a sufficient number of animals and modern investigation methods (e.g. real-time PCR) to demonstrate direct transmission.

Transmission of LSDV through semen (natural mating or artificial insemination) has been experimentally demonstrated (Annandale et al., 2013), and LSDV has been isolated in the semen of experimentally infected bulls for 22 days post infection (dpi) (Weiss, 1968). A more recent study demonstrated the persistence of the live virus in bovine semen for up to 42 dpi and viral DNA was detected until 159 dpi (Irons et al., 2005). In both studies, the virus was isolated from the semen of bulls with unapparent disease. Using both PCR and virus isolation, the epididymis and testis were identified as the sites of persistence of LSDV, and viral DNA was detected in all fractions of semen (Annandale et al., 2010). Vaccination of the bulls with the South African live attenuated Neethling strain prevented shedding of LSDV in the semen in animals challenged with LSDV after vaccination, and vaccinated animals did not shed vaccine virus in the semen (Osuagwuh et al., 2007). During the natural outbreak of LSD in Egypt in 2006–2007, the ovarian activity in 640 cows was examined on a regular basis by transrectal examination and ultrasonography. Of these cows, 25 % were infected with LSDV and a high percentage of the infected cows (93 %) suffered from ovarian inactivity and showed no signs of oestrus. In the infected cows, the ovaries were smaller than average and no activity was detected on the ovarian surface. In addition, lower progesterone and decreased albumin, copper and iron levels were detected in their blood (Ahmed and Zaher, 2008).

1.6.2. Role of vectors

Circumstantial evidence suggests that LSDV can be mechanically transmitted by a variety of blood-feeding vectors. Circulation of LSDV is often, but not necessarily, associated with warm and humid weather conditions and with a high density of biting insects (Ali et al., 2012; Tuppurainen and Oura, 2012). The disease is more prevalent in low-lying areas and along water courses (Weiss, 1968). Intravenous administration of the virus has been demonstrated to be the most efficient way to infect experimental cattle with LSDV when compared with intradermal infection, via conjunctival sac or direct contact between naive and infected animals (Carn and Kitching, 1995b). The long range of transmission between distant herds and the ineffectiveness of quarantine measures suggests that the transmission may have occurred by vectors (Weiss, 1968). In addition, mathematical models of the LSD outbreak dynamic in an Israeli dairy herd in 2006 supports the assumption that transmission of the virus occurred by insect vectors (Magori-Cohen et al., 2012).

Little is known about the importance of different arthropod vectors for LSDV in the field. It has been suggested that a large population of insects has a better chance to acquire, preserve and transmit the virus (Reisen, 2009). So far, there is no evidence of biological arthropod vectors for LSDV. In the mechanical mode of transmission, the virus is transmitted via contaminated mouth parts of vectors without actual replication of the virus in arthropod cells or tissues. Mechanical transmission of LSDV has been experimentally demonstrated to occur by the *Aedes aegypti* mosquito (Chihota et al., 2001) and *Rhipicephalus appendiculatus* male ticks (Tuppurainen et al., 2013a).

The importance of different arthropod vectors for LSDV is likely to vary in different areas depending on the abundance and feeding behaviour of the vector, but may also require specific interactions, such as dissemination in a specific organ (e.g. diverticulum) between the arthropod and the virus (not necessarily with biological duplication), as was shown for plant viruses (Ng and Falk, 2006). Therefore, cattle-oriented interrupted feeders found in high abundance all year long are good candidates for transmitting LSDV. Depending on different environmental and ecological conditions in LSDV-affected countries, any blood-feeding arthropod species may play an important role in the mechanical transmission of the virus.

In Israel, the stable fly (*Stomoxys calcitrans*) is considered as the most important vector candidate owing to its characteristic behaviour, bionomics and abundance in the country (Muller et al., 2011). During the LSDV outbreak in 1993 and 2006, infected *Stomoxys* flies were suspected to be transported by wind from Egypt to Israel (Yeruham et al., 1995; Brenner et al., 2006). Previously, *S. calcitrans* has been demonstrated to be able to mechanically transmit sheep and GTPV under laboratory conditions (Kitching and Mellor, 1986; Mellor et al., 1987) . In addition, LSDV has been isolated from *S. calcitrans* and *Musca confiscata* flies immediately after feeding on infected animals (Weiss, 1968), but an experimental attempt to transmit the virus between cattle by *Stomoxys* flies failed (Chihota et al., 2003). In this experiment, LSDV could be detected by PCR only on the feeding day and the day after, with a virus titre of 2.1 $TCID_{50}$ (the 50 % tissue culture infectious dose)/ml on feeding day, but no detectable titre on the first day after feeding. However, the infected flies were tested only on days 1, 2 and 3 post feeding, and therefore it is possible that the flies had already lost the effective dose for efficient transmission. In southern Africa, *Biomyia fasciata* flies have been associated with the spread of LSDV (Weiss, 1968).

The role of the horn fly (*Haematobia irritans*), which was highly abundant on beef cattle during the 2012–2013 outbreaks in northern Israel, needs to be investigated.

Non-biting flies *Musca domestica* and *M. autumnalis*, which have been demonstrated to be mechanical vectors for bacteria and nematodes (Rosef and Kapperud, 1983; Levine and Levine, 1991; Förster et al., 2007; Förster et al., 2009) and which are found in close contact with eye and nasal secretions of infected cattle, may also be relevant vectors; however, the vector capacity of these flies has not been experimentally tested.

The occurrence of LSD outbreaks has also been linked with high densities of mosquitoes, such as *Culex mirificus* and *Aedimorphus* (*Aedes*) *natronius* (Burdin, 1959). Moreover, in an experimental work, LSDV was isolated six days after blood-feeding on infected animals in *Aedes aegypti* that was also able to transmit the virus between infected and naive animals, which showed a mild disease (Chihota et al., 2001). It should be noted that the role of *Aedes aegypti* in LSD transmission may not be relevant in the farm environment because of its anthropophilic host preference (Schaffner et al., 2013); therefore, the study of vectors should consider the local conditions. Experimental attempts to infect animals with two other mosquitoes, *Culex quinquefasciatus* and *Anopheles stephensi*, were unsuccessful, even if the virus was isolated from insects four days after the infected blood meal (Chihota et al., 2001). Another relevant nematoceran tested for LSDV transmission was *Culicoides nubeculosus*, with unsuccessful results (Chihota et al., 2003).

The role of the tabanids in the transmission of LSDV was only speculated, as these insects are able to mechanically transmit a wide range of disease agents (such as *Trypanosoma evansi*, *Besnoitia besnoiti*, *Loa loa* and equine infectious anaemia virus) and are found around cattle (Baldacchino et al., 2014). Direct evidence is lacking to date.

The vector capacity of hard ticks has recently been under intense investigation. Mechanical transmission of LSDV by male *Rhipicephalus appendiculatus* ticks was demonstrated. After feeding on experimentally infected cattle, semi-engorged male ticks were transferred onto naive animals, which became viraemic and seroconverted (Tuppurainen et al., 2013a). In another study, evidence of mechanical transmission was obtained for *Amblyomma hebraeum* males, although no seroconversion was detected and the level of viraemia was very low (Lubinga et al., 2013a). The presence of viral nucleic acid was demonstrated at the feeding sites of *A. hebraeum* and *R. appendiculatus* males in the recipient animals (Tuppurainen et al., 2010). Owing to their large mouthparts and interrupted feeding patterns, it is most likely that *Amblyomma* males are equally important as mechanical vectors of LSDV as *Rhipicephalus* males.

Using PCR and virus isolation, the presence of the virus has been detected in experimentally induced saliva samples collected from *A. hebraeum* and *R. appendiculatus* males after feeding on LSDV-infected cattle. In the same study, it was demonstrated that, in both tick species, the virus survived the

process of moulting to adults, following feeding of nymphs on LSDV-infected cattle. Before the salivation was induced, newly moulted adults were allowed to harden for approximately one month and saliva samples then tested positive using real-time PCR and virus isolation (Lubinga et al., 2013b).

LSDV has been detected in eggs (Tuppurainen et al., 2010) and larvae (Lubinga et al., 2014c) originating from *R. decoloratus* females fed on LSDV-infected hosts. When these larvae were allowed to feed on two naive cattle, they became viraemic and developed skin lesions which tested positive for LSDV using real-time PCR (Tuppurainen et al., 2013b). Larvae hatched from eggs laid by *A. hebraeum* females previously fed on infected cattle also tested positive by real-time PCR and virus isolation (Lubinga et al., 2014b), although the recipient animal used for feeding these larvae did not show clinical signs or seroconversion. Evidence of vertical transmission of the virus by *R. appendiculatus* has been published (Lubinga et al., 2014b). In transstadially and intrastadially infected adult *R. appendiculatus* and *A. hebraeum* ticks, the presence of the virus was also demonstrated using immunohistochemical staining in various tick organs including the midgut, salivary glands, ovaries, testes and body fat, demonstrating that the virus was able to pass from the midgut into the haemocoel. Interestingly, the presence of the virus was demonstrated in tick tissues that do not undergo histolysis, such as synganglia and haemocytes, and in tissues which develop during the moulting process, such as reproductive organs (Lubinga et al., 2014a). The attempts to propagate LSDV in tick cell lines were not successful (Tuppurainen et al., 2014b). In addition, a high proportion (two-thirds) of ticks collected from LSD naturally infected cattle during outbreaks was found to harbour LSDV when investigated by real time-PCR (Tuppurainen et al., 2014b).

These findings indicate a possible role of ticks in the transmission and maintenance of LSDV in the environment. However, despite the interrupted feeding pattern of *Amblyomma hebraeum* and *Rhipicephalus appendiculatus* males, which would allow mechanical transmission, the life cycle, host seeking and feeding behaviour of these arthropods do not fit with fast spread patterns of LSD as recorded in epidemiological investigations performed in Israel.

On the other hand, vertical transmission of LSDV in ticks could have greater epidemiological relevance, because ticks could be a maintenance reservoir of LSDV in the environment, thus helping to understand the over-wintering capacity of the virus. Clearly, further studies are required to investigate the importance of tick vectors for the spread, and especially for the maintenance, of LSDV in the field in endemic regions. The potential vector capacity of the European tick species should also be investigated.

In conclusion, there is field evidence that strongly suggests the involvement of haematophagus arthropod vectors in LSDV transmission among cattle by the mechanical route, including some tick species, although the competence of each species is not fully documented and there is no evidence for European vector species. However, the spread of the virus in situations with very low abundance of vectors may occur, thus suggesting direct and/or indirect transmission (e.g. through fomites contaminated with secretions from infected animals) as possible routes of LSD transmission.

1.6.3. Indirect transmission

Deliberate attempts to transmit LSDV via the manual handling of infected animals immediately prior to contact with susceptible cattle, or keeping naive and infected animals in the same pen, failed. Therefore, it was concluded that direct or indirect contact between infected and susceptible animals is an inefficient method of transmission (Weiss, 1968; Carn and Kitching, 1995b). Transmission studies are further complicated by recent experimental observations that only 50 % of infected animals are likely to show clinical signs, while the majority of experimentally infected animals become viraemic (Tuppurainen et al., 2005; Osuagwuh et al., 2007; Annandale et al., 2010). Molecular diagnostic tools such as PCR methods were not developed when these earlier transmission experiments were conducted and thus further studies using current diagnostic techniques are required to fully understand the complexity of the transmission mechanisms of LSDV.

2. Case studies of recent LSD outbreaks in the Middle and Near East

In order to provide possible insights into the LSD dynamics and its possible control, some examples of recent epidemics of LSD in the Middle East countries of Israel, Turkey and Jordan are reported in the following sections. Middle Eastern countries have often been characterised by unstable animal health situations and recurrent epidemics. This is caused by several factors such as (i) the geographical position at the crossroads of international transportation between three continents—Europe, Asia and Africa; (ii) an unstable political situation (see section 3.6), which is reflected in inadequate regional cooperation and little or no exchange of epidemiological information; (iii) the need to restructure and consolidate national veterinary services; (iv) the climatic conditions common to the various ecological subregions; (v) the diversity of livestock production systems, including predominantly extensive, traditional animal husbandry, characterised by communal grazing, as well as uncontrolled animal movements and nomadism; (vi) the fact that most countries in the region are consistent importers of livestock and animal products; (vii) the fact that the major routes of migratory birds are between Europe and Africa; (vii) different market trends in animals and animal products; and (viii) demographic changes, characterised by a growing human population, desertification and increasingly limited water resources (Shimshony and Economides, 2006).

2.1. LSD occurrence in Israel

The outbreaks in Israel have been extensively investigated and could provide further insights about the epidemiology of LSD.

In Israel, four LSD epidemics have occurred, in 1989, 2006, 2007 and 2012 (Yeruham et al., 1995; Herziger, 2009; Magori-Cohen et al., 2012). All but the last epidemic occurred in southern Israel and during the summer. The first two epidemics were confined to a single area. In 1989, it was the village of Peduim and, in 2006, it took place in the kibbutz Ein-Tzurim, with limited outbreaks in two neighbouring villages, Shafir and Kfar Warburg. In contrast to the first two epidemics, the third epidemic, in 2007, involved seven villages adjacent to the Gaza Strip, where an outbreak occurred in fattening calves a few weeks before the epidemic in Israel started (Bellaiche, 2007; Herziger, 2009).

In late July 2012, suspected outbreaks of LSD were reported to the veterinary services of Israel (IVSAH) from several beef (cow-calf) herds located in the north-eastern part of Israel, next to the borders with Syria and Lebanon. As some of the infected cattle showed old lesions, it was estimated that the disease was circulating in the Druze herds for at least one month before the identification and reporting of these outbreaks. In contrast to the outbreaks which occurred during 1989, 2006 and 2007, almost no culling of sick cattle was applied in the beef herds. However, severely sick or moribund animals were culled to prevent suffering. The veterinary services applied movement restrictions to the zone, including infected herds and, along with that, initiated an emergency vaccination campaign, using subcutaneous injections of 1 ml of an attenuated sheep pox vaccine of the RM-65 strain ($10^{2.5}$ $TCID_{50}$/ml). Despite this, the epidemic kept moving southwards, mainly among free ranging beef cattle in the Golan Heights and among several feedlots. However, in October, first outbreaks began to appear among intensive zero-grazing high-producing Holstein dairy cattle herds. The veterinary services implemented a differential culling strategy: beef cattle were culled only as a measure for preventing animal suffering, while any moderately and severely affected dairy cattle were culled in order to prevent the spread. This was similar to the culling policy practised during the Israeli epidemics of 2006 and 2007. Since November, the number of dairy herds infected increased gradually, while the epidemic spread south-westwards to Galilee and leaped westwards to the northern coastal plain. Unexpectedly, new outbreaks appeared throughout winter in both dairy and beef herds. The epidemic reached its peak in the spring of 2013. During April alone, 70 new herds were affected, including more than 40 new dairy herds. At this stage, the disease was spread among the herds in the entire northern part of Israel, with one isolated focus in the centre of Israel more than 100 km south, probably due to the unauthorised movement of sick cattle. In March, a decision was taken by the IVSAH to vaccinate all cattle in Israel against LSD, using either the attenuated RM-65 sheep pox vaccine in a 10 times concentrated dose of RM-65 sheep pox strain (X10POX) or the attenuated Neethling LSD vaccine developed in Onderstepoort (South Africa). Roughly almost all dairy herds

were vaccinated within three months with the Neethling vaccine, while most of the feedlots and beef cattle herds were vaccinated with the X10POX vaccine. In May, a sharp reduction in the number of newly affected herds was noticed and, since August 2013, the number of newly affected herds was reduced to only a few. The last outbreak in 2013 was reported on 29 August. Since then, no new confirmed outbreaks have been reported in Israel.

Table 2: Summary table about LSD epidemics in Israel since 1989

	1989	2006	2007	2012
Outbreaks	14 herds in one farm and two outbreaks in two farms	Three farms	10 herds in seven locations and an unofficial report of an outbreak of feedlot cattle in the Gaza Strip	293 herds
Epidemiological parameters	Herd attack rate ranged from 0.5 to 65 %. All cattle in the farm were culled including all cattle in three unaffected herds. Five cows were affected in the two other farms	One big outbreak (206 generalised cases and 39 localised, out of 605) and two single cases in two adjacent farms. All generalised cases culled	508 generalised cases, all culled. Incidence ranged from 0.3 to 44 %. No details on the Gaza Strip outbreak	Incidence ranged between less than 1 and 95 %. 632 deaths and 451 culled animals
Duration of epidemic (onset resolution)	Detected on 17 August. Probably began several weeks before	7 June until 2 August (about two months)	9 June until 1 November (about five months)	Detection on 26 July 2012, but it is estimated that the epidemic was ongoing for at least one month before this date. Last confirmed case 29 August 2013
Control measures applied	Culling of all cattle in the affected farm (affected and non-affected). In other farms, affected cattle culled. Vaccination with RM-65 attenuated vaccine was applied later for all surrounding farms	Culling of all generalised cases. Vaccination with RM-65 attenuated sheep pox vaccine Insecticides	Culling of all generalised cases. All herds were vaccinated at least once with the RM-65 attenuated sheep pox vaccine prior to the outbreaks Insecticides	Culling of generalised cases in dairy cattle. No culling in beef cattle Vaccination with RM-65 attenuated sheep pox vaccine. From March 2013, vaccination of dairy farms with Neethling attenuated LSD vaccine and beef cattle with attenuated RM-65 attenuated sheep pox vaccine (X10 dose) Insecticides
References	Yeruham et al. (1995)	(Magori-Cohen et al., 2012) Pro-Med mail—Archive Number: 20060812.2265	Israeli veterinary services annual report (2007)	Information provided by Dr Nadav Galon (Israeli CVO)

From the experience in Israel, it could be concluded that early culling of generalised LSD cases could reduce morbidity, as the RM-65 sheep pox strain vaccine was ineffective in controlling the outbreak, whereas the Neethling vaccine was more effective, and even more effective than the POX10. Efficient surveillance is considered of high importance for early detection and for the control of LSD spread.

2.2. LSD occurrence in Turkey

The first clinically suspected cases of LSD in cattle were seen in September 2013 in the Kahramanmaras and Batman provinces on the border with Syria. Samples including skin lesions, blood samples and nasal discharge were sent to an LSD reference laboratory, Pendik Veterinary Control Institute, where they were found positive by PCR testing, in accordance with the OIE manual (OIE, 2014b). Following the initial report in late summer 2013, a total of 236 LSD outbreaks occurred in Turkey, with around 90 % of those in southern provinces on the border with Syria, with a cluster in the provinces of Kahraman Maras, Adana, Osmaniye, Gaziantep and Hatay, and some on the border with Iraq. However, the spread of the virus was also reported in the Sivas province in January 2014, which is more than 400 km north of the previous outbreak that occurred a few days before, is at 1 300 m above sea level and, in the middle of winter, the average temperature is −5 °C; thus, this outbreak occurred in a situation without or with a very low abundance of arthropod vectors (Işidan et al., 2014). This was likely to be associated with the illegal movement of clinically sick or asymptomatic infected animals. A similar example is the isolated outbreaks observed in the province of Konya, which is 500 km north-west of the main outbreak cluster. In addition, according to OIE reports, the possible source of the LSD outbreaks in Turkey could be due to the illegal movement of animals and vectors.

In response to the outbreak, vaccination with Bakirkoy sheep pox strain has been applied with the coverage as reported in Figure 4. The vaccination coverage has been calculated, comparing the number of vaccinated animals per province (OIE report) with the demographic data of cattle at the province level.

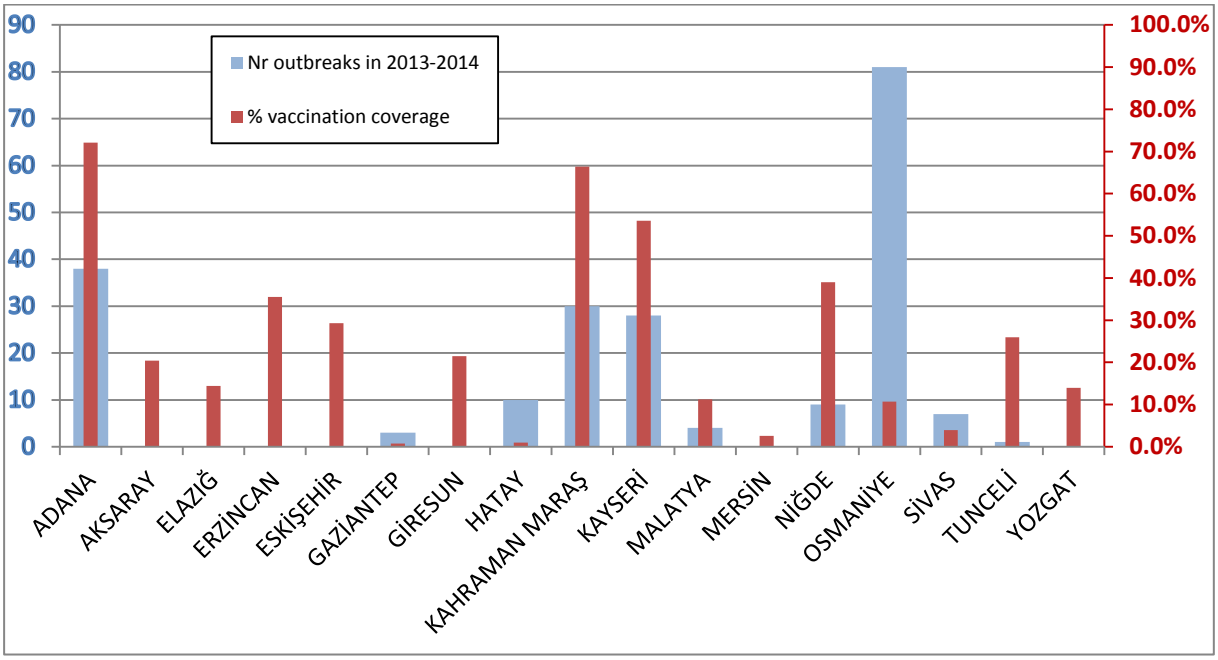


Figure 4: Number of outbreaks in 2013–2014 and vaccination coverage (RM-65 sheep pox strain) in Turkish provinces

The average vaccination coverage was about 25 % and in only two provinces was it above 50 %, which is still considered too low to provide sufficient protection if compared with the level that can be estimated from the R_0 value from the study done in Israel in 2006 (Magori-Cohen et al., 2012), which is around 93 % of the coverage needed. Moreover, the RM-65 strain is a sheep pox strain (heterologous vaccine) which is known to confer insufficient protection. For this reason, if movement restriction and biosecurity measures are not strictly applied, and if they are sufficient, LSD in Turkey will be endemic and spread throughout the country.

2.3. LSD occurrence in Jordan

LSD is also emerging in other countries neighbouring Israel such as Jordan, where it has never been reported before (Abutarbush et al., 2013). In April 2013, two adult dairy cows developed clinical signs suggestive of LSD and were confirmed as positive by PCR. The first outbreak was located in the north of Jordan, bordering Israel and Syria, and the second one was located in the Amman district. The disease spread rapidly to all the districts of the governorate, with a total of 65 cases. During the month following the detection of the disease, data were collected related to the epidemiology of the disease and the numbers of affected cattle on the premises. In total, 41 dairy cattle holdings were surveyed; the overall morbidity rate was 26 % and mortality rate was 1.9 %. Affected cattle were initially treated with broad-spectrum antibiotics and anti-inflammatory drugs.

Farmers outside the outbreak area were recommended to vaccinate their cattle using the SPPV RM-65 vaccine at 10 times the dose used to vaccinate sheep against sheep pox. In a number of cases, another type of vaccine was used that was not labelled and was of unknown origin, which was later identified as an LSD strain and which caused severe adverse clinical reactions (Abutarbush et al., 2014).

The efficacy of the vaccination campaign was assessed by collecting epidemiological data from 101 vaccinated and unvaccinated farms (Abutarbush, 2014). The overall morbidity rate was almost 10 times higher in the unvaccinated cattle group than the vaccinated cattle group, although this was not tested for statistical significance. Clinical signs were observed in animals one day after vaccination; therefore, those animals were incubating the disease when vaccinated.

The mortality rate in the vaccinated group in this study was 4.7 %. The results of this study indicate that vaccination against LSD with RM-65 sheep pox strain does not provide complete protection, although the fact that some farmers used the unlabelled LSD strain may have confounded the assessment.

There is a risk of LSD becoming endemic in the country, owing to different reasons (Abutarbush et al., 2013). At the initial stage, the possibility of disease eradication was not explored. The vaccination started in the affected district only a few weeks after the emergence of the disease, and provided only partial protection; moreover, there was a lack of control of vaccines used by farmers, since unlabelled vaccines were available (Abutarbush, 2014). In addition, no emergency vaccination at the time of the initial outbreak with sufficient vaccination coverage was implemented. Neither animal movement restrictions nor a contingency plan were enforced in a timely manner, and there was an initial lack of awareness about the disease in field veterinarians (Abutarbush et al., 2013).

2.4. OIE-reported information on LSD outbreaks that occurred in 2014

The OIE reports of the immediate notifications and follow-up contain some epidemiological information about outbreaks, including their possible source. In Table 3, this information is summarised for the Middle Eastern countries that reported LSD outbreaks in 2014.

Table 3: LSD reports from affected countries in 2014 including origin of the outbreaks and measures applied (Source: OIE)

Country	Origin of infection	Epidemiological comments	Control measure applied
Azerbaijan	• Illegal movement of animals • Vectors	The diagnosis is based on only clinical signs. Laboratory confirmation will occur after diagnostic kits are obtained	• Control of arthropods • Quarantine • Movement control inside the country • Disinfection of infected premises/establishment(s) • No vaccination • No treatment of affected animals
Egypt	• Unknown or inconclusive • Illegal movement of animals • Vectors	• Biosafety measures in the infected farms • Epidemiological and clinical surveillance around the infected farms • Post-vaccination serosurveillance programme to estimate the immune level of the vaccinated animals in order to evaluate the efficacy of the vaccine • Awareness campaigns in different areas	• Quarantine • Movement control inside the country • Vaccination in response to the outbreak(s) • Disinfection of infected premises/establishment(s) • Dipping/spraying • Treatment of affected animals (symptomatic treatment with antibiotics, anti-inflammatories and antipyretics)
Iran	• Illegal movement of animals • Vectors	The affected cow was detected during routine foot-and-mouth disease vaccination. The vaccination team reported abnormal skin problems in a native dairy cow. Following this report, the affected epidemiological unit was visited by state veterinarians, and skin tissue samples were collected and submitted to the OIE Reference Laboratory for sheep pox and goat pox and tested by restriction fragment length polymorphism PCR. Following laboratory confirmation, all affected animals were destroyed. This was the first time that LSD had been identified in Iran; the notification as first occurrence applies to the country but the event is in fact circumscribed to a zone	• Control of arthropods • Quarantine • Movement control inside the country • Screening • Zoning • Vaccination in response to the outbreak(s) • Disinfection of infected premises/establishment(s) • Dipping/spraying • Modified stamping out • No treatment of affected animals
Iraq	• Unknown or inconclusive	Vaccination started on 27 October 2013	• Control of arthropods • Movement control inside the country • Vaccination in response to the outbreak(s) • Disinfection of infected premises/establishment(s) • No treatment of affected animals

Country	Origin of infection	Epidemiological comments	Control measure applied
Lebanon	• Unknown or inconclusive • Illegal movement of animals • Vectors		• Control of arthropods • Quarantine • Movement control inside the country • Screening • Zoning • Disinfection of infected premises/establishment(s) • Dipping/spraying • No vaccination No treatment of affected animals
Palestine	• Unknown or inconclusive • Legal movement of animals • Illegal movement of animals	• Control of arthropods • Screening Vaccination in response to the outbreak(s)	• Quarantine • Movement control inside the country • No vaccination No treatment of affected animals

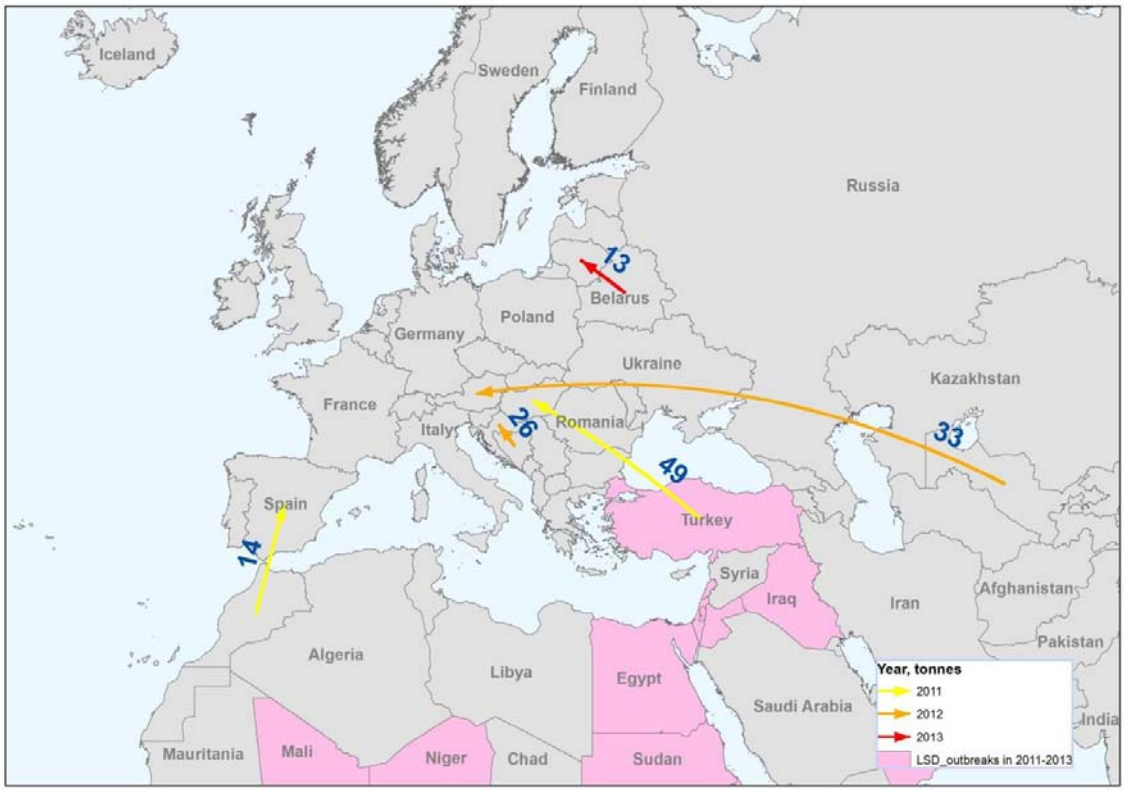
3. Mapping of animal movements in the regions of concern and other countries of the Mediterranean Basin and Black Sea

3.1. Data and methodologies

Movements of live bovines and raw hides and skins from third countries in the Mediterranean Basin and Black Sea area to MSs and inside the affected MSs and Turkey are presented in the following sections with the use of flow maps. The data underlying the maps originates from trade records from Eurostat and the UN COMTRADE database, from records from border inspection posts (checks from the TRACES system) and from data from national authorities of Turkey, as an example of a neighbouring country affected by LSD. Furthermore, the risk of LSD spread associated with political unrest and the related movements of people and refugees, especially in Middle Eastern countries, has been considered.

3.2. Import/export of live bovines

According to animal health EU legislation (EC Regulation No 206/2010[4]) the import of live cattle from third countries such as northern African and Middle Eastern countries to MSs is forbidden; therefore, there should be no movement of live cattle across the border. Nevertheless, some discrepancies were noted when commercial data (Eurostat) were compared with veterinary border checks (TRACES system). For example, some movements of live cattle were registered in Eurostat in 2011–2013 and these are displayed on the map below (Figure 5).



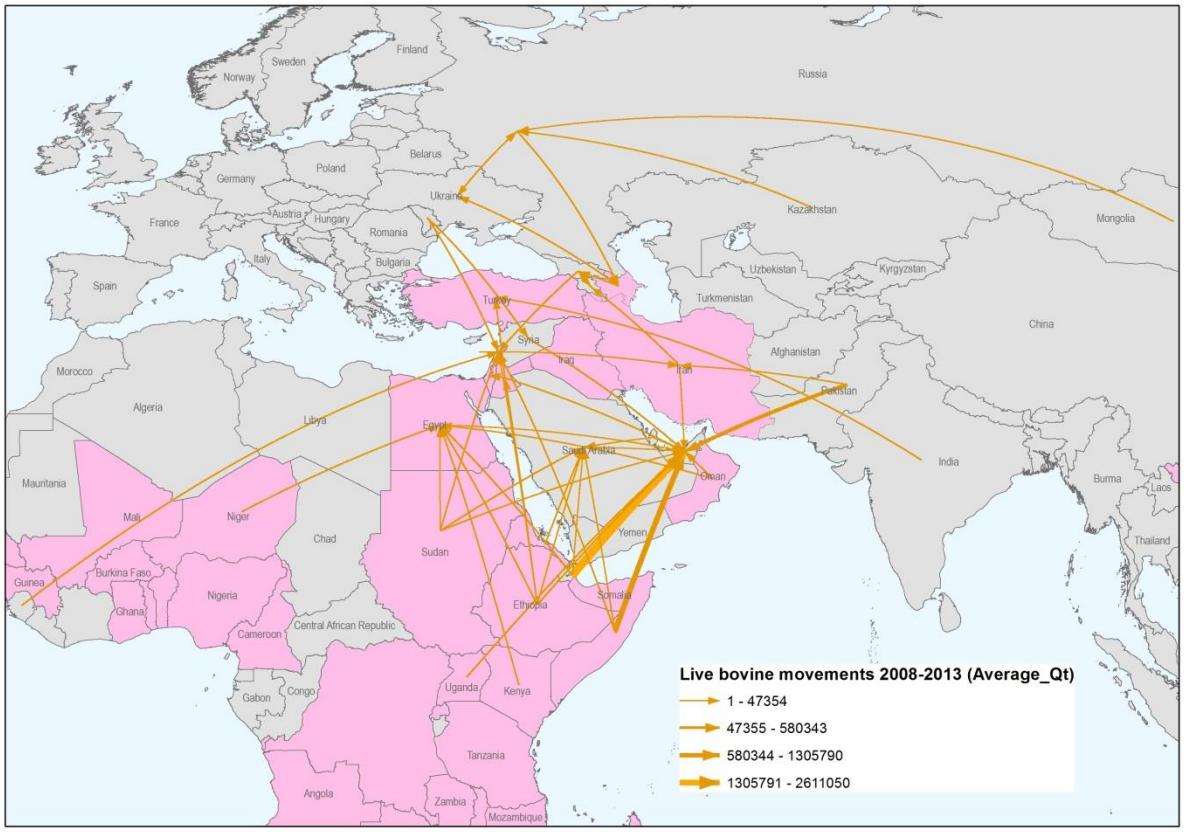
Data source: Eurostat

Figure 5: Trade movements of live cattle from some northern African and Middle Eastern countries towards MSs in 2011–2013 and related amounts LSD-affected countries in 2011–2013 are highlighted

[4] Commission Regulation (EU) No 206/2010 of 12 March 2010 laying down lists of third countries, territories or parts thereof authorised for the introduction into the European Union of certain animals and fresh meat and the veterinary certification requirements.

These discrepancies in the records could be explained by the different data collection systems in place at Eurostat (data collection through MS Ministry of Finances) and TRACES (data collection according to veterinary checks taken place at EU borders as defined by EU public or animal health legislation). In the case of live animal import, TRACES data could be considered as more accurate; nevertheless, proper validity cross-checking should be carried out.

In order to provide insights into cattle movements in areas where LSD is endemic and from where there is a possible risk of introduction into Europe or neighbouring countries, the trade movements of live cattle between some African and Middle Eastern countries as registered in the UN COMTRADE database are displayed in Figure 6.



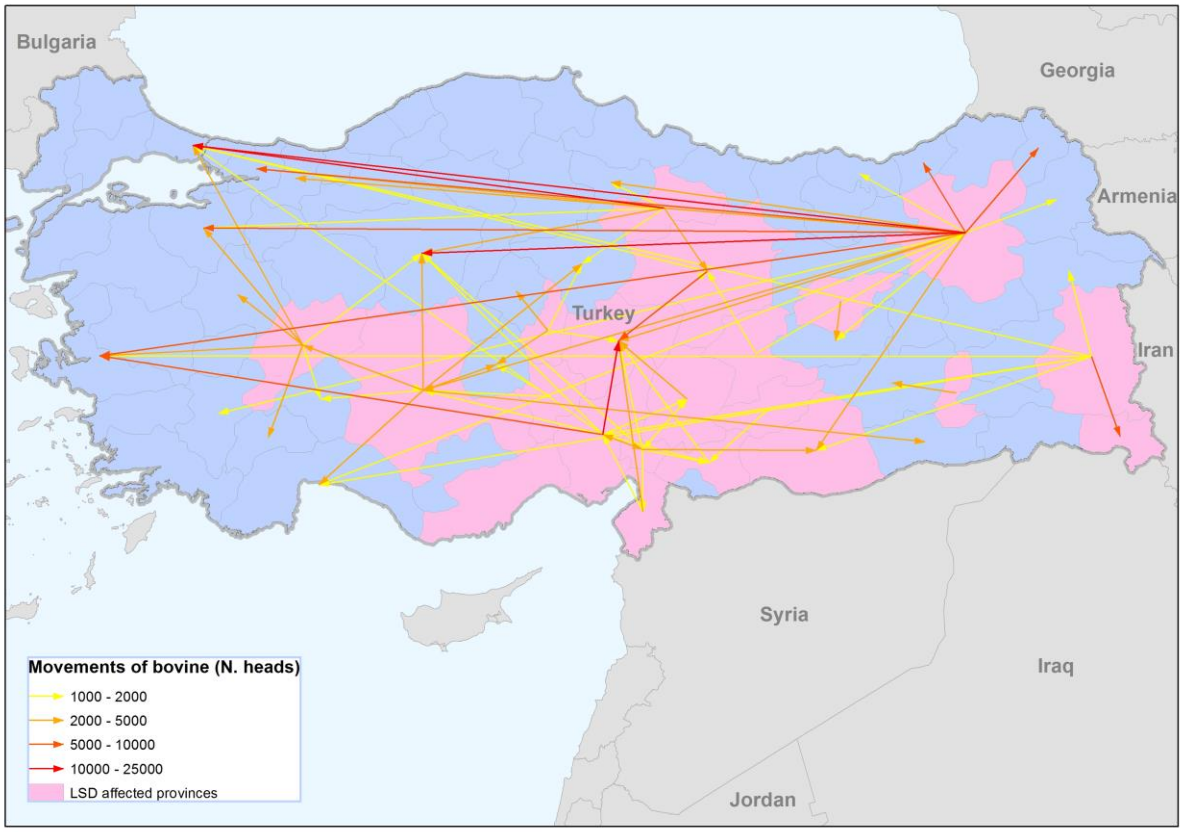
Data source: COMTRADE. Countries reporting LSD in 2011–2014 according to OIE are displayed

Figure 6: Movements of live cattle among African and Middle Eastern countries displayed as yearly average amounts in the period 2008–2013.

It is evident from the map that the biggest movements of live cattle are from East Africa towards the Arabian Peninsula and Middle Eastern countries such as Lebanon and Jordan. The consumption and importance of these products in Muslim countries reaches its peak during religious festivities, which encourage trade and commerce of the animals in the region. Such movements of high numbers of animals in short periods of time, with peaks before festivities, may often be poorly regulated, thus representing a risk of introduction of transboundary diseases.

3.3. Animal movements inside Turkey

In Figure 7, the movements of live cattle inside Turkey as an affected neighbouring country are presented. The data were obtained by the Ministries of Agriculture of Turkey. The LSD-affected provinces are also displayed.



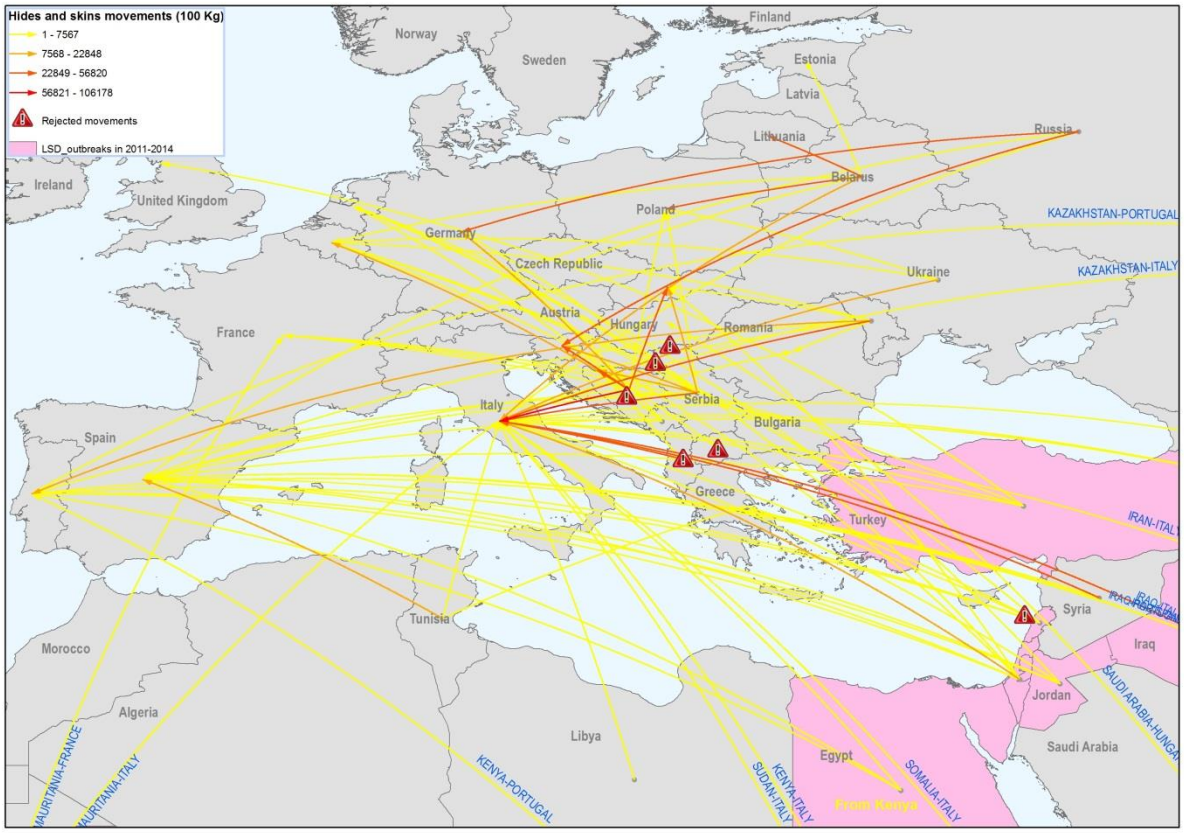
Data source: Turkish Ministry of Food, Agriculture and Livestock and OIE

Figure 7: Movements of cattle in Turkey in 2012 from LSD-affected provinces (2012–2014)

In Figure 7, it is evident that several thousands of cattle, up to 25 000 heads a year, are usually shipped within Turkey, including from provinces in southern and eastern Turkey at the border with Syria, Armenia and Iran, which have been affected by LSD, over long distances to provinces in western Turkey including to big urban centres such as Istanbul. This highlights the importance of promptly setting movement restrictions when LSD cases were detected, in order to limit the spread of the disease.

3.4. Movement of cattle hides and skins from third countries to Member States

CaPVs could be associated with sheep and goat skins if the animals were infected at the time of death. As reported in section 1.1.3 and in a previous qualitative risk assessment (DEFRA, 2014), it is likely that LSD survives being transported in wool/hide/skin if the skin does not undergo specific inactivating treatment, as the virus can survive for up to 18 days in dried hides. Data on the shipment of cattle hides or skin from northern African countries, Middle Eastern countries facing the Mediterranean Sea and extra-EU countries around the Black Sea to MSs are available from Eurostat (Figure 8).



Data source: Eurostat. LSD-affected countries in 2011–2014 according to OIE are displayed

Figure 8: Movements related to the trade of cattle hides to MSs in 2011–2013 and rejected shipments according to the TRACES system

It has to be noted that the category of commodity is defined, according to Eurostat, as "raw hides and skins of bovine fresh, or salted, dried, limed, pickled or otherwise preserved, whether or not dehaired or split". Therefore, this category includes both raw and treated hides, which may have different levels of risk related to virus survival, depending on the treatment applied. Moreover, another mitigation factor is that hides spoiled by skin lesions, e.g. of CaPVs, would probably be condemned for commercial reasons.

The conditions for the import of hides and skins into the EU laid down in the Regulation (EU) No 142/2011[5] are summarised in a recent EFSA opinion on sheep and goat pox (EFSA Panel on Animal Health and Welfare, 2014), which states that untreated hides and skins should come from third countries from those listed in Part 1 of Annex II of Regulation (EU) No 206/2010, from which MSs authorise imports of fresh meat from the same species. These hides must be obtained from animals that have passed the ante-mortem health inspection at the slaughterhouse during the 24 hours before slaughter, and, if this inspection is correctly carried out, the typical skin lesions of LSD could be detected and the hide condemned. The same regulation defines "treated hides and skins" as products derived from untreated hides and skins, other than dog chews, that have been (i) dried; (ii) dry-salted or wet-salted for a period of at least 14 days prior to dispatch; (iii) salted for a period of at least seven days in sea salt with the addition of 2 % sodium carbonate; (iv) dried for a period of at least 42 days at a temperature of at least 20 °C; or (v) subject to a preservation process other than tanning. In particular, hides can be imported from any third country if they have been subjected to treatments referred to in points (i), (ii) and (iii) above, and if, after treatment, they have been kept separate for 21 days or if they will undergo transport for 21 uninterrupted days before importation. It was reported

[5] Annex XIV, Chapter II, Section 4, point 2, of Regulation (EU) No 142/2011 and Annex XIII, Chapter V, point C.2 of Regulation (EU) No 142/2011.

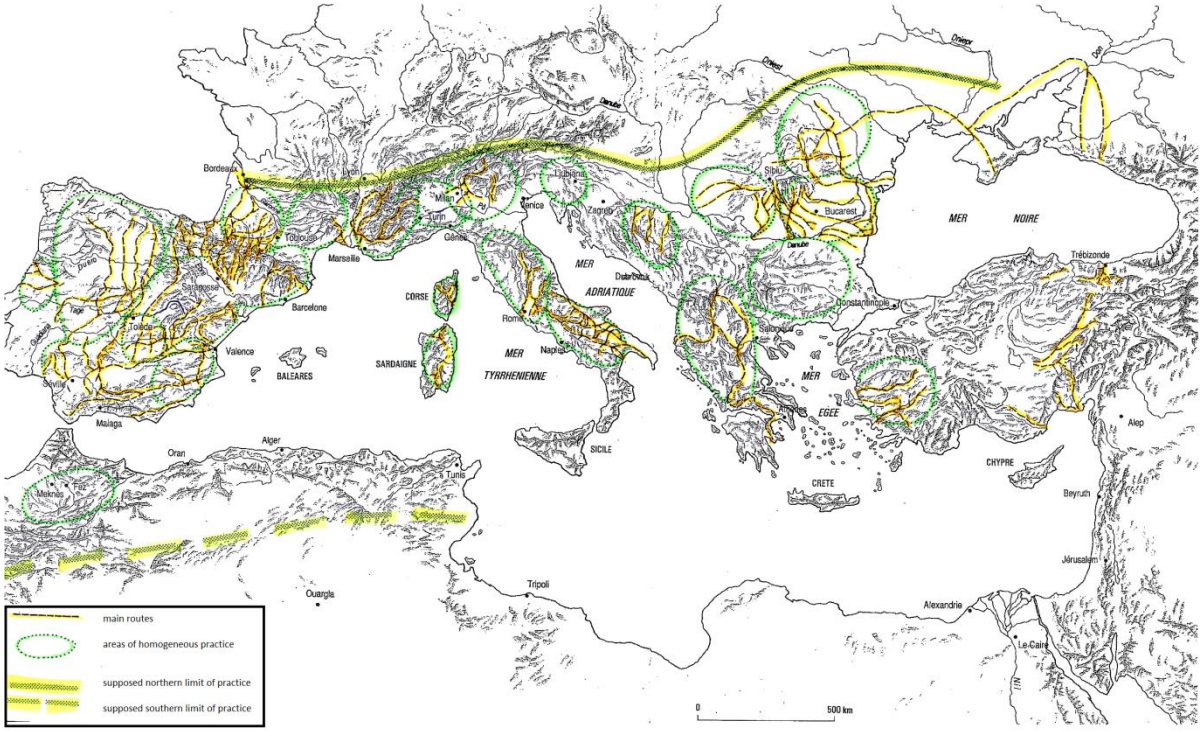
that LSDV can survive for up to 18 days in air-dried hides (see section 1.1.3); therefore, further investigation is needed about the time needed for complete inactivation of LSDV using a drying treatment of hides.

If further data are needed for a proper assessment of the risk of LSD introduction through the import of hides, the risk of LSD spread into naive areas through the import of cattle hides could be considered negligible, as LSD 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 is imported, further transmission would not take place.

3.5. Animal movements related to transhumance of cattle herds

An understanding of nomadic movement patterns at the regional level can be considered a necessary element for providing insights into the potential spread of animal disease.

In many countries, including in Europe, transhumance (a traditional livestock practice based on the movement of livestock between winter and summer pastures) and pastoralism (a practice of mobile livestock raising using extensive grazing on rangelands) are husbandry practices used to take advantage of the characteristic instability of rangeland environments, characterised by economic rationality and ecological sustainability (Krätli et al., 2013). In mountain areas of many European countries, although they have shown a declining trend in the last decade, transhumance is still largely practised (Figure 9), and its advantages in playing a significant role in conserving biodiversity and in sustainably using marginal areas are broadly described (Halstead, 1987; Ruiz, 2001; Olea and Mateo-Tomás, 2009).



Modified from Duclos and Pitte (1994)

Figure 9: The main transhumance routes in the Mediterranean area

Through strategic mobility, pastoralism finds an asset in the existence of dynamic variability in the drylands, where sedentary agriculture or mixed farming are not suitable practices. When this balance is disrupted by external factors, and the mobility of pastoralists is impeded by, for example, unstable political situations, wars, etc., the resulting decreased and constrained access to pasture and water

resources, impeded livestock movements and limited access to veterinary services are identified as key contributing factors to the increasing prevalence and persistence of livestock diseases in the nomadic system (Bett et al., 2009).

Moreover, considering the lessons learnt in the Saharan–Sahelian context, pastoralism has been internationally recognised as one of the best stabilisation strategies for remote and unstable areas (Plateforme Regional Tchadienne, 2013); thus, it could be seen as a practice to be promoted, especially in critical situations such as those currently prevailing in the Middle East (see section 3.6). Furthermore, the support of pastoralism may lead to socio-economic advantages, as it can keep or open employment opportunities and reduce land abandoning and urbanisation of rural communities, with their potential related social problems.

It is possible that long-distance movements may have repercussions in spreading disease throughout countries and across borders. Therefore, while these farming systems should be supported for the economic, environmental and political reasons explained above, proper veterinary care and improved surveillance should be in place for nomadic and semi-nomadic farmers along the migratory routes.

3.6. Socio-political drivers

Times of political unrest could increase the potential risk of transboundary livestock diseases spreading into other countries, especially into those bordering the affected countries. This is mainly driven by the disruption of veterinary and public health services and of trade and movement routes; insecurity; massive displacement of refugees across borders and/or internally displaced people; and impeded access to pasture, water and feeds. The situation in the Middle East, with the current civil war in Syria and the recent crisis in Iraq, and the instability in Ukraine are relevant examples of crises that may contribute to the potential spread of livestock disease across EU borders.

A mission report by the Food and Agriculture Organization (FAO) (FAO, 2013a) provides useful insights about the impact of the Syrian crisis on the livestock sector.

The Syrian crisis has compounded the already difficult economic situation in the majority of Syria's neighbouring countries (i.e. Egypt, Iraq, Jordan, Lebanon and Turkey). Exports, tourism and transportation have all been negatively affected by the interruption of trade routes and the deterioration of regional and national security. The Syrian crisis is affecting all sectors in neighbouring countries, but its impact on the agriculture and food sectors is particularly important, as these sectors are the main source of income for a significant proportion of the population, particularly for the poorest and most vulnerable communities in rural areas.

The Syrian veterinary services collapsed in 2012. Uncontrolled livestock movements have increased significantly, with Turkey the only country having a relatively strict border control system in the slaughtering of all non-registered animals. Nevertheless, this remains a challenge owing to the 900-km long border shared with Syria, with cases of PPR, bovine tuberculosis and brucellosis reportedly confirmed in captured animals. In Gaziantep province alone, 13 cases of rabies have been reported at the border with Syria, which has never been observed before. In other neighbouring countries, foot-and-mouth disease, peste des petits ruminants, bluetongue, brucellosis and LSD in animals and cutaneous leishmaniasis and tuberculosis in refugee camps have all been unofficially reported in the Syrian border areas of Iraq, Jordan and Lebanon. Syrian livestock enter Turkey because of different factors. Animals are brought along the Syrian border into the southern Turkish provinces by Syrian refugees fleeing their country, or are brought to be sold at a cheaper price by Syrian traders and smugglers profiting from the fact that Syrian shepherds trade their livestock for money, fearing they will lose them from bombardments.[6,7,8]

[6] http://www.latimes.com/world/middleeast/la-fg-turkey-syria-sheep-20141006-story.html
[7] http://www.aljazeera.com/indepth/features/2013/04/201342893919660254.html
[8] http://www.worldbulletin.net/news/144979/turkey-pledges-to-save-syrian-refugees-livestock

Unvaccinated live animals are being legally imported or are illegally transported into Iraq, Jordan and Lebanon, sometimes without quarantine, for sale on the open market and slaughterhouses throughout those countries (e.g. FAO reported that 300 000 goats were illegally imported from Syria to Jordan in 2012).

Moreover, nomadic Bedouins and agro-pastoralists from the Syrian border areas of Iraq, Jordan and Lebanon can no longer access free or subsidised Syrian vaccines and animal feeds, and the disruption of traditional transhumance routes has led to overgrazing, land degradation and animal suffering and concentration, thus increasing the risk of disease transmission.

The UNHCR estimated 6.5 million people had been displaced in Syria, while more than 3 million refugees had fled to countries such as Lebanon (1.14 million), Jordan (608 000) and Turkey (815 000) since the start of the Syria crisis (UNHCR communication, 29th August 2014). This massive immigration of refugees, both legal and illegal, may represent a risk of both human and animal disease transmission, by refugees being potentially active or passive carriers of pathogens.

A further impact of the Syrian crisis on animal and human health is the safety and quality of animal feeds and animal source foods. The illegal trade of unsafe foods and animal feeds is being practised owing to the disruption of regulatory systems, border inspection posts and law enforcements in Syria and is possibly the case in neighbouring countries owing to insecurity in border areas.

4. Possible pathways of introduction of LSD into the EU and ranking on the basis of their level of risk, with a view to enhancing preparedness and prevention

4.1. Data and methodologies

The main potential pathways of introduction of LSD from endemic countries into the EU are identified on the basis of the possible transmission routes and virus survival in various matrices (see section 1.1.3), literature evidence, epidemiological information reported to OIE and the Animal Disease Notification System (ADNS) and expert knowledge.

4.2. Introduction of LSD into free areas

The main pathway of introduction of an arthropod-transmitted disease into a previously non-affected area is the introduction of infected hosts or infectious vectors. As described previously (section 1.6.1 of this opinion), as the main transmission route of LSD is through mechanical vectors, a short persistence time of the virus in the vector is assumed (one day in stable flies, but with experimental evidence from only one study), and this would suggest that vector-borne transmission of LSD is efficient only if it occurs in the short interval between the feeding event on the infected animal and the feeding event on the next susceptible host. For transmission over longer times and distances, besides the possible movement of vectors through wind currents, the movement of infected/asymptomatic animals appears to be the most plausible cause.

The situation of LSD for ticks could be different, as there is evidence of transovarial and transstadial transmission and longer times of persistence in infected specimens.

LSD outbreaks tend to depend upon animal movements, immune status, and wind and rainfall patterns affecting vector populations. For example, the recurrence of outbreaks in Egypt and Israel after an absence of 17 years could be attributed to a combination of these factors (Brenner et al., 2006).

4.3. Possible introduction of LSD by live animal movements

The countries in the Middle East region have become more vulnerable to foreign animal diseases due to the increasing demand for food from their growing populations. To meet this demand, Middle Eastern countries have increased rates of importation of live cattle from different continents such as Europe, Asia and Africa (see section 3.2).

In the OIE reports of the immediate notifications and follow-up of the LSD outbreaks that occurred in 2014 in Azerbaijan, Iran, Lebanon, Egypt and Palestine, epidemiological information shows that the legal or illegal movement of animals is a possible LSD introduction pathway.

Concerning the outbreaks in Jordan, if the disease was introduced to Jordan from Israel, it is possible that this occurred through vector transmission, because there is no legal live animal movement or smuggling that occurs across the Jordanian/Israeli border and because the first outbreak was very close to the border, thus making it possible that the introduction occurred through active movement of flying vectors. The other possible disease incursion to Jordan is from Syria, which is politically unstable, and it is possible that live animal movements and smuggling occur across the Jordanian/Syrian border (Abutarbush et al., 2013).

The same happens at the border between Syria and Turkey, where uncontrolled movement of live cattle occurs, and this is most likely the origin of the incursion and spread of LSD in Turkey in 2013 (see sections 1.2.2 and 2.5).

The same could be described from outbreak investigations. In Oman, it is reported that the disease may be introduced by infected cattle imported from the African Horn countries including Somalia and Djibouti (see section 2.2) (Tageldin et al., 2014).

From outbreak notifications to the ADNS system by Turkey, information was reported about the origin of some of the LSD outbreaks that occurred in 2014. In Figure 10, the location of the outbreaks according to their presumed source is displayed.

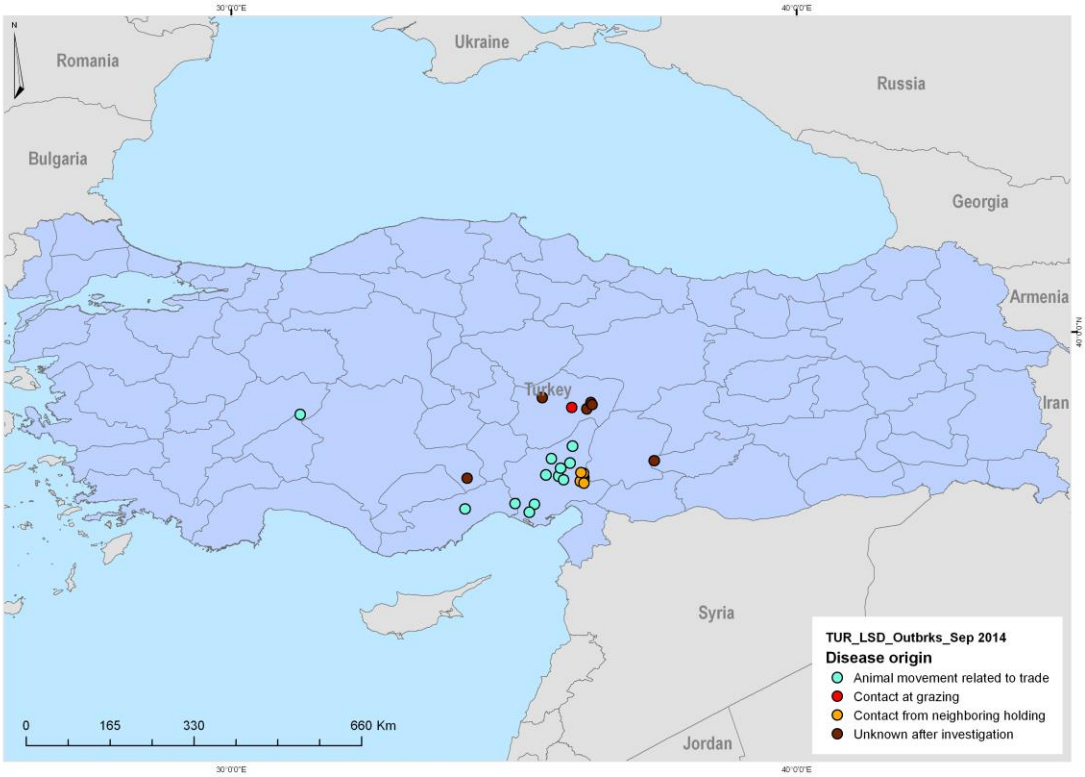


Figure 10: Presumed origin of LSD outbreaks that occurred in Turkey in 2014 as reported to ADNS (modified)

The information reported to ADNS is reported by central veterinary structures at the national level, which collect the information from veterinarians who work at the provincial and district levels.

From the map in Figure 10, the most frequent source of outbreaks appears to be the movement of infected animals. In most cases, animal dealers or the purchase of infected animals were considered to be the source of the infection. In Turkey, there are animal dealers who collect and transport animals from farm to farm, sometimes during the incubation period of the disease. This happens in particular before the period of Eid al-Adha, when live animals are moved from the areas of cattle rearing, e.g. central and eastern Turkey, towards the big urban centres.

Finally, LSD spread over very long distances, as demonstrated by the latest LSD outbreak in Azerbaijan in July 2014 from Iraq, Iran and/or Turkey, is more likely to occur via animal movements than through arthropod vectors (Tuppurainen and Oura, 2014).

4.4. Possible introduction of LSD by the movement of vectors

In the OIE reports of the immediate notifications and follow-up of the LSD outbreaks that occurred in 2014 in Azerbaijan, Iran, Lebanon, Egypt and Palestine, epidemiological information shows that vectors are a possible LSD introduction pathway.

Apart from the active movements of vectors, especially of flying vectors, whose action radius is related to the biology of each species, vectors may translocate by movements of animals including wildlife (e.g. birds) or by wind currents. For example, stable flies were suspected of being transported by wind, so importing LSDV into Israel from Egypt (Yeruham et al., 1995; Brenner et al., 2006).

The role of wind currents in spreading vector-borne diseases has been suggested and reviewed for the spread of viruses carried by either *Culicoides* or mosquitoes (Sellers, 1980; Sellers and Pedgley, 1985; Reynolds et al., 2006; Finlaison et al., 2010; Aziz-Boaron et al., 2012; García-Lastra et al., 2012). It was even suggested that, in some vector species, windborne transmission is not accidental but is rather the result of deliberate migration initiated by the ascent of blood-engorged females to high altitudes (Reynolds et al., 2006). There are several examples of the possibility of transmission of such virus-carrying vectors by winds. Examples include the spread of bovine ephemeral fever and its incursion into Japan and Korea, which was associated with wind direction in a low-level jet stream from China (Shirakawa et al., 1994); the spread of bluetongue virus of serotype 8 (BTV-8) in Europe (Hendrickx et al., 2008); and the dissemination of BTV among herds in Turkey, Greece and Bulgaria (Ducheyne et al., 2011; Eagles et al., 2014; Roberts et al., 2014) and its introduction into the Balearic Islands in 2000 (Alba et al., 2004). Several studies demonstrated that this route of transmission can occur in Eastern Mediterranean areas as well. It was previously suggested that BTV was introduced into Israel by winds (Braverman and Chechik, 1996). There is evidence of the role of winds in the dispersion of epizootic haemorrhagic disease virus within Israel during 2006 (Kedmi et al., 2010), as well as strong evidence for windborne transmission of bovine ephemeral fever from Turkey to Israel in 2008 (Aziz-Boaron et al., 2012). Biting midges are small enough (950–1 000 μm) to be considered as particulate matter if compared with, for example, desert grains in Israel (30–70 μm) (Kalderon-Asael et al., 2009); thus, they are similar to dust and can be modelled as an atmospheric tracer, neglecting their limited autonomous flight ability (Morag et al., 2013).

Bigger insects have more mass and a stronger flight ability. It was shown in laboratory experiments that mosquitos can sometimes fly upwind for short distances (Pile et al., 1991). In the context of *S. calcitrans*, it is interesting to mention the work of Chapman et al., who conducted a sampling campaign in the UK at a height of 200 m using a net supported by a tethered balloon (Chapman et al., 2004). A specimen of the Muscidae family was caught, to which *S. calcitrans* also belongs. Additionally, wind-aided movement of *S. calcitrans* up to a distance of 225 km was recorded in Florida, in a mark–capture experiment (Hogsette and Ruff, 1985).

There is also mineralogical evidence for the capability of the synoptic systems in this region to collect particulate matter (and thus also insects) from sources along their path and to transport them within the Eastern Mediterranean areas. A sampling campaign was held in Israel, in which aerosols were collected during episodes of these systems. The analysis showed differences in the mineralogical and chemical compositions of the inorganic fraction of the aerosols transported by the different synoptic systems. These differences in the composition of the aerosols provided the evidence that each of the systems carries aerosols which originate from different regions (Kalderon-Asael et al., 2009).

Taken together, all this evidence suggests that it is likely that windborne transmission of vectors infected with LSDV can occur both within Eastern Mediterranean regions and from these regions into Europe. The probability of such an occurrence is higher if large-scale outbreaks of LSD are taking place in adjacent countries. During the first two epidemics in Israel, in 1989 and 2006, Egypt suffered from severe outbreaks of LSD. The 1989 epidemic was exceptionally severe in scale, spreading to 22 of the 26 governorates of Egypt (Davies, 1991). In a recent study (Klausner et al. – in press), the relevant synoptic systems during the three months preceding each outbreak were examined and backwards Lagrangian trajectories (BLTs) were calculated from the receptor sites in Israel for each occurrence of such relevant synoptic systems. The analysis revealed several events in which atmospheric connection routes between the affected locations in Egypt and Israel were established. An total of 28 relevant BLTs from Egypt to Israel, scattered among nine events, were found during the three months preceding the outbreak that occurred in 1989, and 84 BLTs scattered among 13 events were found in the three months preceding the epidemics that occurred in 2006. Specifically, in 1989, Damietta and Port Said stand out as the likely sources for the epidemics in Israel. These were found to be possible sources of an outbreak which occurred at that time in Saudi Arabia. In 2006, different locations acted simultaneously as potential sources of the epidemics in Israel. These locations were situated in the Nile Delta, the Suez Canal and northern Sinai.

Altogether, the accumulation of these studies indicates that long-distance dissemination of infected vectors by winds is a plausible route of transboundary transmission of vector-borne viruses in the Middle East and should be taken into account when analysing the risk of emergence of new pathogens, including LSD, into new geographic regions such as Europe. This is of primary importance because of the location of the Middle East: it is an area which connects Europe, Africa and Asia.

The role of birds in introducing novel tick species over long distances into new areas has not been demonstrated, but the evidence strongly suggests that it can happen (Hasle, 2013). Birds alone cannot, however, spread ticks if environmental temperature, humidity and other factors at the destination do not meet the requirements specific for the tick species. Under these circumstances, they would not be able to establish permanent populations, although they could be introduced into new areas by birds (Hasle, 2013). To date, there is no documented evidence for the dissemination of the virus by birds carrying LSDV-positive ticks.

Regarding the tick species for which there is already evidence about their LSD transmission capability, more data are needed on if they actually feed on migratory birds inhabiting Europe and/or if other tick species feeding on relevant birds are able to transmit LSDV.

A survey on the tick species collected from migratory birds and their microbial content is currently being performed in Israel (unpublished data). Preliminary results showed 0.38 % infestation of birds by ticks, which is similar to the values found in a study performed in Turkey (Leblebicioglu et al., 2014), but lower than the values found in a study performed in Morocco (3.85 %) (Palomar et al., 2013). Nevertheless, when ticks were tested for specific pathogens, positive results were found for the Crimean Congo haemorrhagic fever virus and bacterial pathogens such as Rickettsia (Toma et al., 2014).

Currently, more research data should be obtained on the transmission of the virus by tick vectors to be able make relevant conclusions about the potential involvement of birds in transmission. This option is theoretically possible for LSD, but not very likely and difficult to demonstrate.

4.5. Pathway ranking

From what has been explained above, the different pathways of LSD introduction can be ranked in the following order:

1. The introduction of infected animals is the most efficient pathway to introduce LSDV into a country, in particular for long-distance spread.
2. The active movement of flying vectors can be a pathway for LSD introduction into a naive country from a short distance, e.g. from infected areas close to the borders.
3. Circumstantial evidence indicates that windborne transmission of vectors carrying the virus (after a blood meal on an infected animal) is a potential route of LSDV introduction into a country.

5. Risk of introduction of LSD into the EU

A quantitative approach to estimate the likelihood of introduction of an infectious disease agent into a disease-free country through the movement of animals is essential to assess the risk of introduction of such a disease agent. The movement of animals has been considered to be the main risk factor for the introduction of several infectious diseases into disease-free areas.

The European legislation identifies LSD as a notifiable disease and requires that trade of Bovidae and their products be subject to specific health requirements. Moreover, EU legislation set a series of animal health rules governing the production, processing, distribution and introduction of products of animal origin for human consumption and addresses all stages of the production, processing and distribution within the Union and the introduction from third countries of products of animal origin intended for human consumption. Therefore, an introduction of LSD by live animals into the EU would be possible only through illegal import.

The approach followed here is that used to establish the likelihood of introduction of LSD into Europe, and is based on probability theory as reported in a previous EFSA scientific report (EFSA, 2012). The objective of the assessment is to propose an approach to assess the risk of introduction of LSD into a free area via import. In particular, this approach should help in the evaluation of the likelihood of introduction of LSD. The approach should focus on the relevant animal species that could potentially be introduced into Europe.

5.1. Methodology and implementation

The output of this assessment is an estimate of the numbers of animals needed to be imported to introduce LSD into Europe with a level of probability higher than 95 % or lower than 5 % based on single shipments and according to different scenarios of seroprevalence in the country of origin.

In order to estimate the probability of introduction into the EU via the illegal movement of animals, it was considered that no testing is applied to the animal moved; thus, using the binomial distribution, the probability that all animals are free of LSD in a shipment of size N, where ρ is the probability of being infectious, will be:

$$P(x = 0) = \binom{n}{0}\rho^0(1-\rho)^{N-0} = (1-\rho)^N \quad (1)$$

The intention here is to know if at least one animal is LSD infectious, rather than to know the probability that all moved animals are LSD free; thus, it is of interest to calculate the following probability:

$$P(x > 0) = P(x \geq 1) = 1 - P(x = 0) = 1 - (1-\rho)^N \quad (2)$$

On the other hand, it is of interest to estimate the prevalence of infectious animals in a population with a reported seroprevalence. Considering a Susceptible-Infected-Removed (SIR) model to describe disease transmission, it is possible to establish a relationship between infectious prevalence and seroprevalence at equilibrium. The relationship is derived from the following differential equation:

$$\frac{dR}{dt} = \text{RecoveryRate} \times I - \text{InverseDurationImmunity} * R \quad (3)$$

where R and I refer to the recovered and infectious cases, respectively, and

$$\text{RecoveryRate} = \frac{1}{\text{Mean Infectious Period}}$$

The mean infectious period was considered to be 14 days and

$$\text{InverseDurationImmunity} = \frac{1}{\text{Mean Duration of Immunity}}$$

which in this case is considered to be the lifespan of the host (five years), but shorter or longer periods might be considered if needed. Hence, at equilibrium:

$$\text{I} = \frac{\text{Mean Infectious Period} \times \text{Seroprevalence}}{\text{Mean Duration of Immunity}} \quad (4)$$

In order to estimate the probability of introduction, equation (4) should be inserted into equation (2) as follows:

$$\text{P}(x > 0) = 1 - \left(1 - \frac{\text{Mean Infectious Period} \times \text{Seroprevalence}}{\text{Mean Duration of Immunity}}\right)^{N} \quad (5)$$

The probability of the introduction of LSD into the EU could be then calculated using equation (5) for different levels of seroprevalence (0.05, 0.15 and 0.30), including different numbers of illegal animals moved into the EU (1 to 10 000). The maximum level of seroprevalence (30 %) as a worst-case scenario has been selected from the study conducted in Ethiopia, where LSD is supposed to be endemic (Gari et al., 2012).

The results are shown in Figure 11, considering the infectious period to be 14 days and the lifespan of the host (cattle) to be five years.

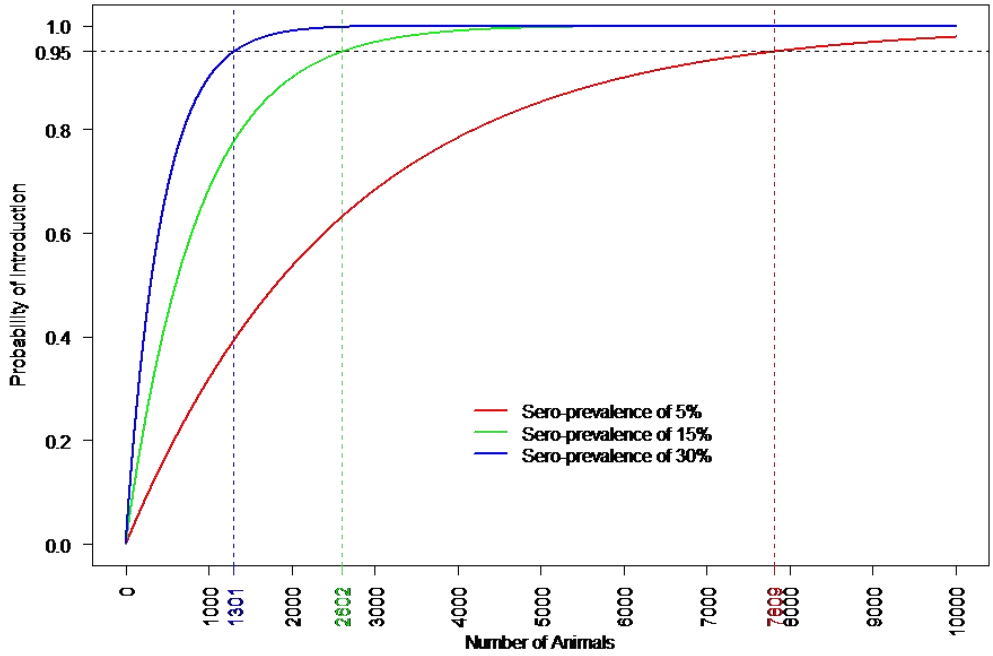


Figure 11: Probability of introduction for different seroprevalence levels as well as the number of animals moved

If seroprevalence was 30 %, the number of animals that would need to be moved to have a probability of introducing LSD into Europe of greater than 0.95 or lower than 0.05 would be 1 301 and 25, respectively. On the other hand, if seroprevalence was 5 %, the number of animals that would need to be moved would be 7 809 and 140 for probability levels of 95 % and 5 %, respectively.

6. Spread simulation of LSD into the EU

A stochastic, farm-level model was developed to describe the transmission of LSDV between farms. The model assumes that:

- the force of infection is proportional to the farm size, depends on the distance between farms (described by a transmission kernel) and varies seasonally;
- if a farm becomes infected, the duration of the outbreak is proportional to log farm size.

The model was parameterised using data from the epidemic in Israel during 2012–2013 (section 2.1). Consequently, the baseline parameter estimates implicitly assume similar control measures will be implemented (i.e. removal of animals showing generalised clinical signs of LSD; and vaccination with a single sheep dose of RM-65 sheep pox vaccine, thought to be ineffective in controlling the spread of LSDV). The model was validated by comparing its predictions with the observed spread of LSDV in Turkey during 2013–2014. Finally, the model was used to explore four scenarios of the spread and control of LSDV in Bulgaria and Greece. Because farm-level data are not available for Bulgaria, Greece or Turkey, synthetic locations and sizes (i.e. number of cattle) for farms in these countries were generated from regional-level data. A full description of the approach is provided in Appendix A.

In each scenario for the spread and control of LSDV in Bulgaria and Greece, the initial incursion was assumed to result in the infection of the same three farms in the Evros region of Greece, which borders Turkey. The four control strategies explored using the model were: (i) the culling of animals showing generalised clinical signs of LSD; (ii) the culling of whole herds on farms seven days after infection; (iii) the culling of whole herds on farms 15 days after infection; and (iv) the culling of whole herds on farms 28 days after infection.

When control measures entail the removal of animals showing generalised clinical signs (as was applied in Israel during the 2012–2013 epidemic), approximately 90 % of epidemics remain confined to the region around the initial site of incursion (Figure 12A). However, the remaining 10 % of simulated epidemics are more extensive, with the virus spreading up to approximately 300 to 400 km from the site of introduction by six months after the incursion (Figure 12A). Applying whole-herd culling to infected farms substantially reduces the spread of LSDV (Figure 12B–D). Moreover, the more rapidly farms are detected and culled, the greater the magnitude of the reduction is; for example, compare culling 28 days after infection (Figure 12B) with culling 15 days after infection (Figure 12C) and with culling seven days after infection (Figure 12D).

Under the assumptions made when developing the model for the transmission of LSDV between farms, there is the potential for outbreaks to spread in Bulgaria and Greece. However, rapid detection and culling of infected farms is able to substantially reduce the size and extent of an epidemic.

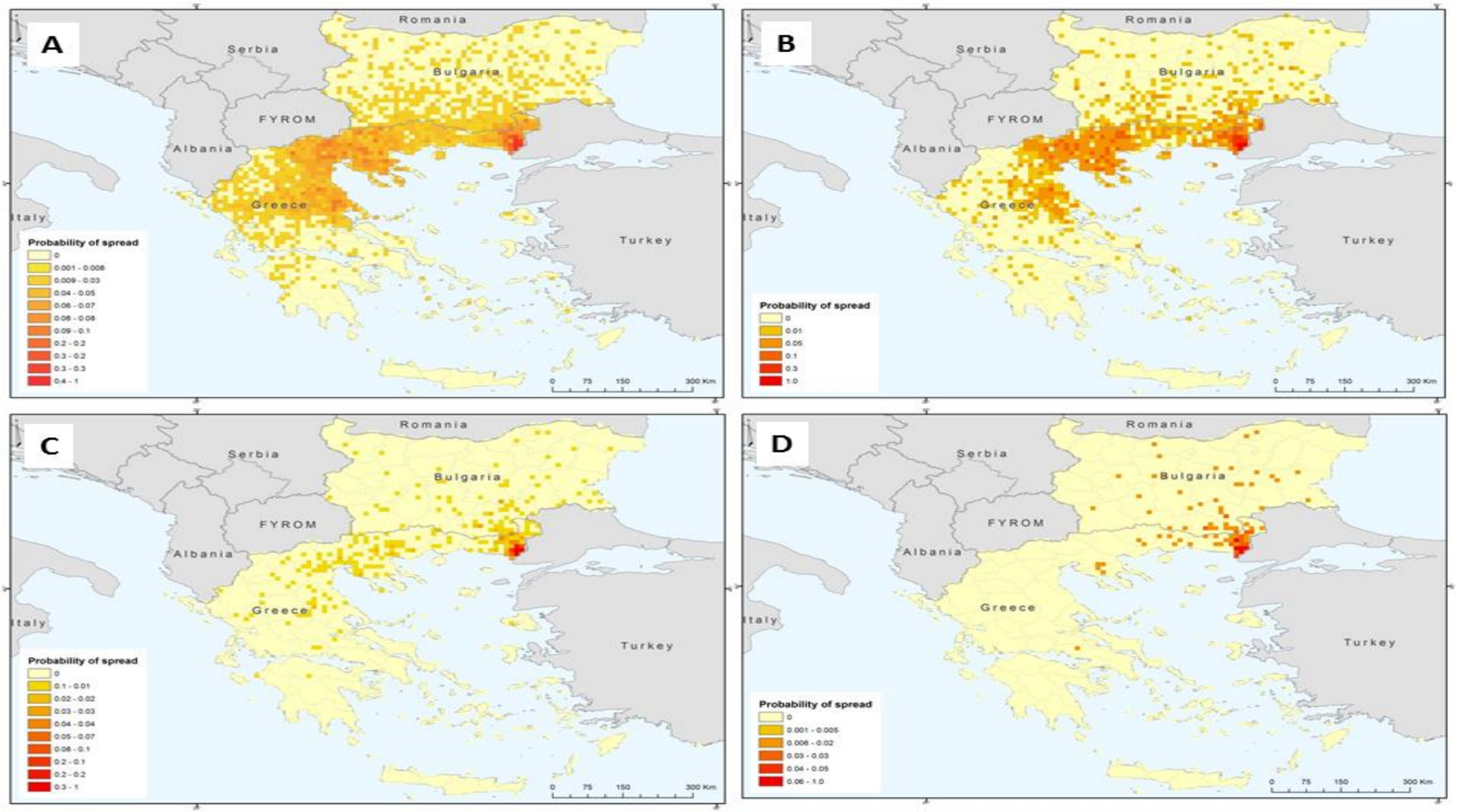


Figure 12: Simulated spread of LSD in Bulgaria and Greece when control is by (A) the removal of animals showing generalised clinical signs; (B) the culling of whole herds on farms 28 days after infection; (C) the culling of whole herds on farms 15 days after infection; (D) the culling of whole herds on farms seven days after infection. The map shows the proportion of simulations (indicated by the scale bar) for which at least one farm in a 0.1 ° by 0.1 ° grid square became infected. The model was run from the time of incursion (assumed to be 30 May) until 31 December.

7. Risk of LSD becoming endemic in animal populations in the EU and neighbouring countries

Endemicity of LSD is defined as the long-term persistence of the infection in an area (i.e. several years). Long-term presence of an infection in an (already) affected area can occur if new susceptible animals arise prior to the infection fade-out in that area. Long-term persistence therefore requires maintaining infectiousness for a sufficiently long time along the infection chain of multiple hosts or delayed/intermittent infectiousness of individual infected hosts or external reservoirs.

Thus, endemicity can be enhanced by (i) a very long latent or long infectious period (i.e. carriers, reactivation), (ii) persistence of the infection in a reservoir population other than the one at risk (often wildlife and often with mild clinical disease) or (iii) persistence of the infectious agent itself in the environment (including biological vectors).

None of these three mechanisms of persistence appears to apply to LSD, although persistence in vectors cannot be excluded. Data from Israel show that, in Israel at least, this risk was not very high and the disease faded out once effective control measures at the herd level (e.g. culling generalised cases, vaccination with homologous vaccines) were implemented.

The nearest neighbouring country to the EU with an endemic situation, Turkey, has experienced persistence of the infection, which is probably due to low vaccination coverage and use of a sub-optimal vaccine, leading to persistence of the infection in the vaccinated livestock herds, rather than in the vectors.

There are no data on the potential of European vectors and their role in persistence of the infection; therefore, the international data cannot be extrapolated directly to the European situation. Nevertheless, under the current EU policy and according to the scenarios produced using the spread model (section 8.7), if the situation and ability of vectors was the same as in Israel, LSD would most likely not become endemic in the EU.

If they occur, epidemics within the EU should be properly investigated and data should be collected to enable evaluation of the probabilities of these potential risks of persistence of the infection. This information can subsequently be used to evaluate the need for additional control measures.

8. Assess the impact and consequences of LSD when entering the EU, considering different scenarios as regards the effectiveness of surveillance and control measures

The impact of animal disease can broadly be divided into direct losses, i.e. the direct impact on animal health and productivity, and indirect losses, which include mitigation or control efforts, lost export opportunities for EU MSs and impacts on human health.

Direct losses include visible losses such as animal death and illness or stunting that result from disease or subsequent control methods. Invisible losses, on the other hand, include less immediate impacts of animal disease, such as reduced productivity or changes in herd fertility, which result in the need to have a higher proportion of animals in a breeding group rather than in production (IFAH, 2012). This kind of loss primarily affects the stakeholders of the agriculture sector, for example farmers.

Among indirect losses, forgone revenues should be considered, namely the indirect economic impact of animal diseases resulting from curtailed market access, losses in consumer confidence and negative effects on other sectors of the economy. Estimates of indirect losses can be obtained by a value chain analysis (FAO, 2011). The dynamics of supply and demand of animals and animal products can be disturbed by large outbreaks and their impact can be much larger than combining the impacts observed on single farms.

Furthermore, the mitigation and control costs should be also considered, i.e. the costs of the drugs, vaccines, surveillance and labour needed to carry out control measures. These costs may also have an impact on tax payers because of the supplementary resource that may be needed for the implementation of control programmes. If the animal diseases affect human populations, the human health impact should be also considered, such as treatment costs and losses in life quality because of illness or death.

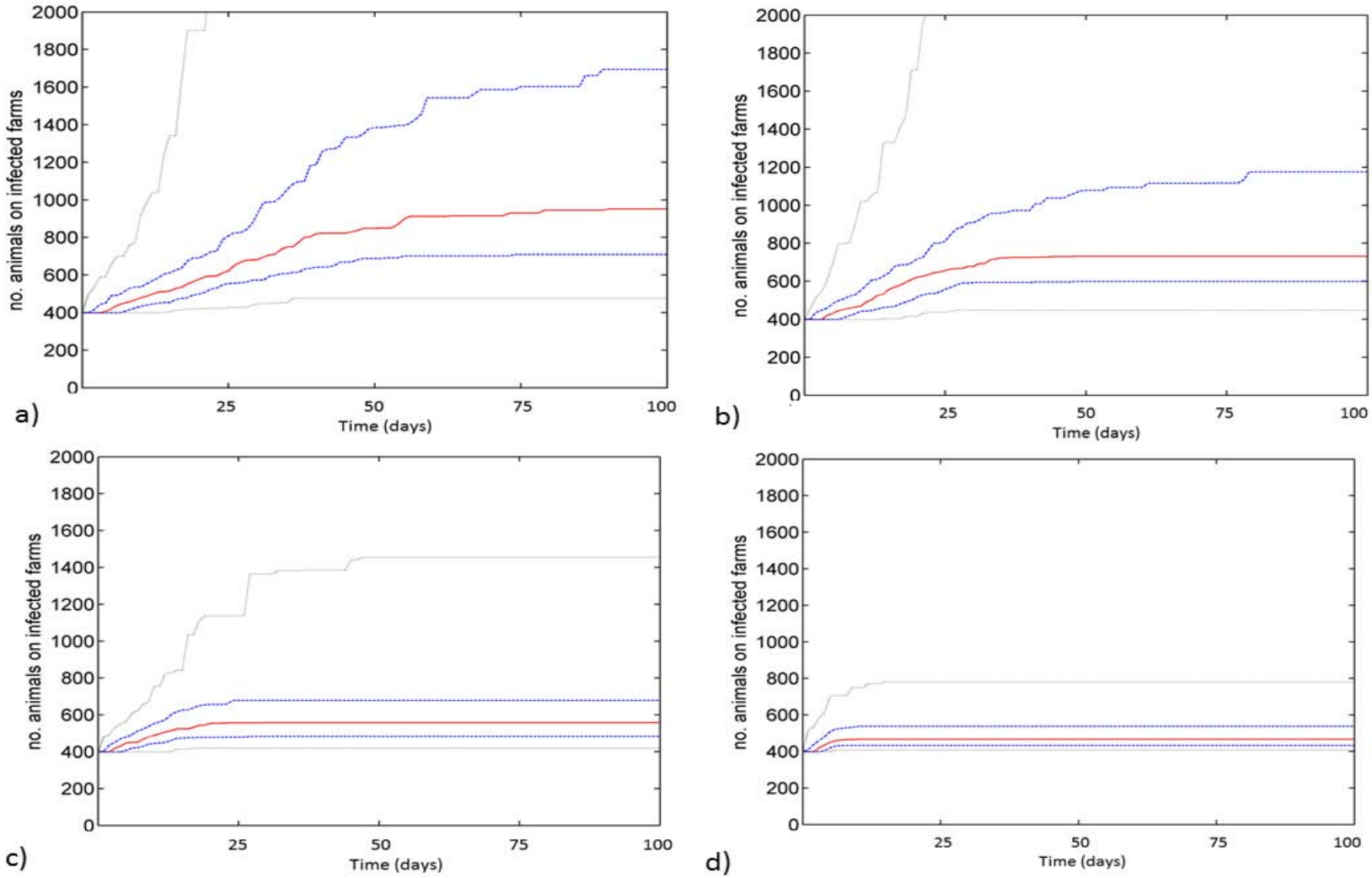
For LSD, there are examples of impact assessment conducted in areas where LSD is endemic, such as in Ethiopia (Gari et al., 2012). In that context, with an annual mortality of 7.43 % in cross-bred cattle and 1.25 % in zebu cattle, the annual financial cost was calculated as the sum of the production losses due to morbidity and mortality arising from milk loss, beef loss, traction power loss, and treatment and vaccination costs at the herd level, and this was estimated to be USD 6.43 (range 5.12–8) per head for local zebu and USD 58 (range 42–73) per head for cross-bred cattle.

In areas where LSD was not considered endemic, in the recent epidemics in Israel, 293 herds were infected causing the death of 632 animals and leading to the culling of 451 animals. The compensation paid was around EUR 1 million and the losses in terms of culling and milk loss were estimated to be EUR 2–3 million (information provided by the Israeli CVO).

In the hypothetical scenario of LSD entering the EU, the impact assessment presented in this section will provide an estimation of direct losses as the number of infected farms according to different control measures applied.

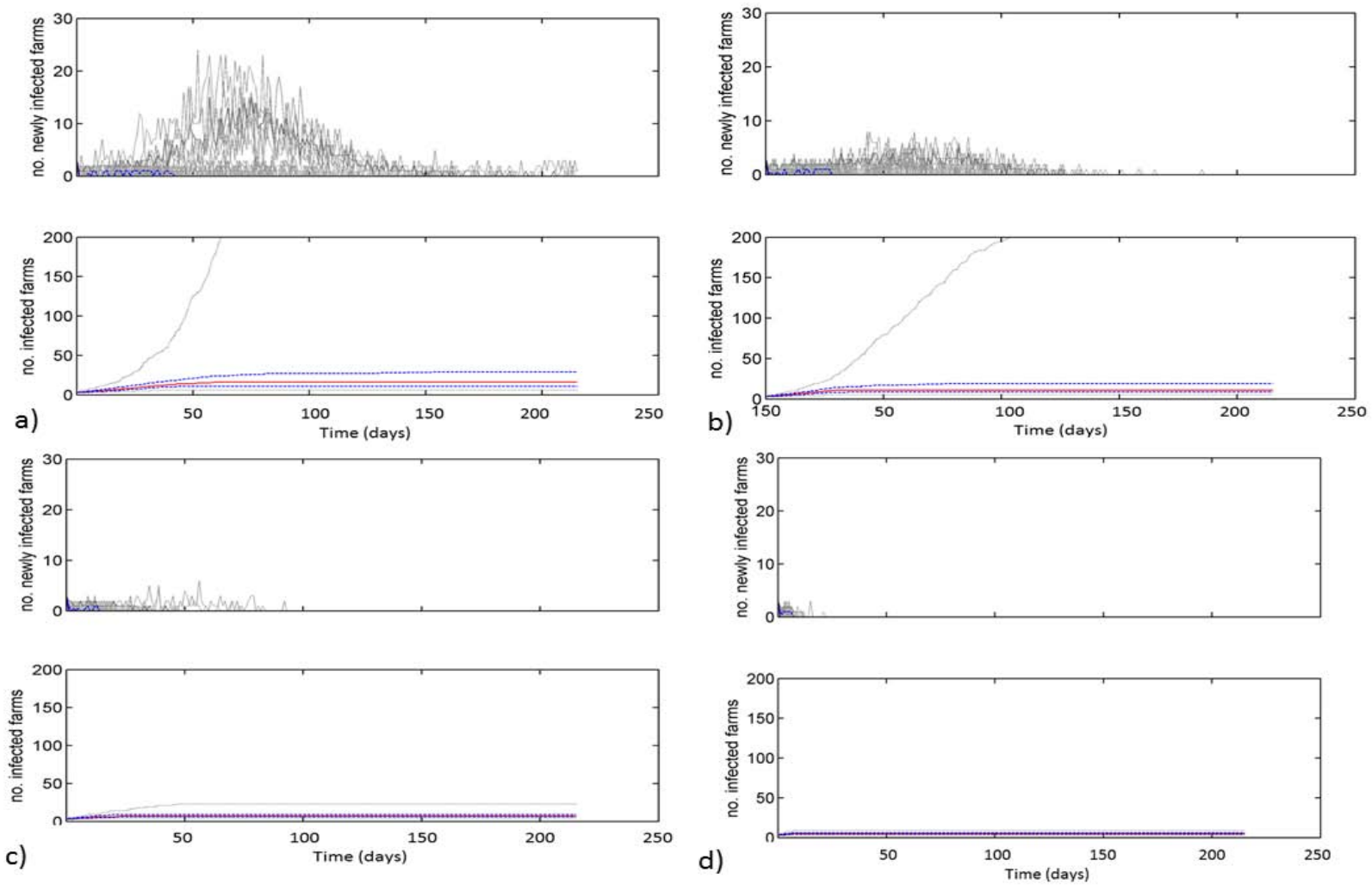
8.1. Impact assessment: scenario analysis of LSD incursion in the EU

The number of affected livestock at different time intervals after the occurrence of an outbreak in eastern Greece, as an estimate of the impact of LSD in the EU, is simulated and presented in this section. The scenario of an incursion in Greece has been chosen because of the dynamics of the recent epidemics of sheep pox in Greece, probably introduced from Turkey (EFSA Panel on Animal Health and Welfare, 2014). This is based on the farm-level spread model presented in section 6, which uses the data from Israel. In particular, the number of farms, the number of animals in infected farms and the duration of the outbreaks are presented in the simulated scenarios of application of the same control measures as applied in Israel (vaccination and culling of only generalised cases), and in the situation of culling the whole herd 7, 15 or 28 days after the infection, as it would occur according to the current EU legislation if there was an LSD outbreak in the EU.



Solid red line: median; dotted blue lines: 25th and 75th percentiles; grey lines: 2.5th and 97.5th percentiles

Figure 13: Estimation of the number of animals in infected farms in the scenario of an incursion in Greece when (a) only generalised cases are culled, (b) whole herds are culled 28 days after infection, (c) whole herds are culled 15 days after infection and (d) whole herds are culled 7 days after infection



Solid red line: median; dotted blue lines: 25th and 75th percentiles; grey lines: 2.5th and 97.5th percentiles

Figure 14: Estimation of the duration of outbreaks and the number of infected farms in the scenario of an incursion of LSD in Greece when (a) only generalised cases are culled, (b) whole herds are culled 28 days after infection, (c) whole herds are culled 15 days after infection and (d) whole herds are culled 7 days after infection

Figures 13 and 14 show the spread of LSD after incursion in Greece in terms of infected farms, the number of animals in infected farms to be culled and the duration in days of the outbreaks under different control measures applied, namely by culling of only generalised cases (as it was applied in Israel) and by culling of whole infected herds 28, 15 and 7 days after infection. The last three scenarios would occur under the conditions described by the EU policy, but this would still depend on the time lapse between the onset of infection and the implementation of culling of the infected herd. As reported in section 1.4, the incubation period of LSD under field conditions is reported to be two to four weeks (Haig, 1957), while, in the experimentally induced disease, it is between 4 and 14 days (Prozesky and Barnard, 1982; Carn and Kitching, 1995a). Four weeks could be considered a worst-case scenario for the late detection of LSD, as this mainly reflects the experience of early studies in South Africa in different farming situations from the ones in the EU. If culling is applied almost simultaneously after detection, as occurred in Greece during the sheep pox epidemics (EFSA Panel on Animal Health and Welfare, 2014), the detection of the disease up to two weeks from infection could be considered realistic.

In the case of culling only generalised cases, 100 days after the onset of the outbreak, the number of animals in the infected farms would be 951 (upper and lower bounds: 67 908 and 476, respectively; Figure 13a), and the median of infected farms would be 16 (upper and lower bounds: 690 and 6, respectively; Figure 14a). Interestingly, with a worst-case scenario, there is a continuous increase in the number of infected farms (see the increasing 97.5th percentile). In this case, the outbreak would not stop, even after 200 days (Figure 14a).

In contrast, in the scenarios of culling the whole herd 7 and 15 days after infection (Figures 13 and 14b, c and d), the numbers of infected farms are significantly lower, with median numbers of 5 (lower and upper bounds: 4; 9) and 7 (lower and upper bounds: 4; 23), respectively. In addition, the number of animals in the infected farms to be culled would be limited, with median numbers of 467 (lower and upper bounds: 407; 780) and 558 (lower and upper bounds: 419; 1 454) if culling took place 7 or 15 days after infection, respectively. Finally, the outbreak would fade out in the worst case (upper bound) after 12 or 43 days when culling after 7 or 15 days, respectively, thus indicating the significant impact of prompt culling in the control of outbreaks.

9. Availability, effectiveness and feasibility of the main disease prevention and control measures

9.1. Data and methodologies

The information used in this section derives from a literature search, field evidence and expert knowledge.

Several studies for validating diagnostic tests for CaPV infections have been conducted and published. Experimental, retrospective and observational studies performed worldwide were identified for domestic small ruminants through mapping the collected evidence and the extracted information on development and validation criteria for diagnostic assay. These studies, including a test of performance in terms of sensitivity and specificity, were summarised in a previously adopted opinion by EFSA about sheep and goat pox (EFSA Panel on Animal Health and Welfare, 2014), which is also valid for LSDV. Most of the studies were found to show the same results for both CaPVs, which show high similarity. Here, a description of the currently used diagnostic tests for LSD and the differentiation from other CaPVs is provided.

9.2. Diagnostic tools

9.2.1. Clinical diagnosis

9.2.1.1. Effectiveness and feasibility

A presumptive diagnosis of the disease can be made based on highly characteristic clinical signs of LSD. However, mild and asymptomatic disease may be difficult to diagnose and rapid laboratory methods are needed to confirm the diagnosis.

9.2.1.2. Differential diagnosis

The skin lesions of pseudo LSD (bovine herpesvirus-2, BHV-2), insect bites, *Demodex* infection, onchocerciasis, besnoitiosis and dermatophilosis can be confused with LSD (Barnard et al., 1994). Generally, BHV-2 infection causes more superficial skin lesions, has a shorter course and is a milder disease than LSD. In addition, the presence of histopathologically demonstrable intranuclear inclusion bodies in BHV-2 infection, as opposed to intracytoplasmic inclusions in LSD, is characteristic. In contrast to the rapid molecular diagnostic tools available for LSD, the detection of BHV-2 in negatively stained biopsy specimens by electron microscopy or the isolation of the virus is only possible approximately one week after the development of skin lesions (African Veterinary Information Portal (AfriVIP)[9]).

In some cases, diseases causing mucosal lesions, can be confused with LSD, such as bovine viral diarrhoea/mucosal disease and bovine malignant catarrhal fever (Barnard et al., 1994).

9.2.2. Laboratory techniques

Rapid diagnostic confirmation of the tentative field diagnosis is fundamental for the successful control and eradication of LSD in endemic and particularly in non-endemic countries. Different molecular tests are the preferred diagnostic tools and are currently replacing other less sensitive and slower diagnostic methods. Serological assays are suitable for retrospective serosurveys at the herd level, but these assays are not sufficiently fast or reliable at the individual level to be used as a primary test.

9.2.3. Detection of antigens (live virus or viral nucleic acid)

The general CaPV real-time PCR method is more sensitive than other diagnostic assays for the detection of the virus. The test detects CaPV viral DNA, but does not differentiate between the different members of the genus, which may be required if characteristic clinical signs for LSD are

[9] http://www.afrivip.org/

detected in wild ruminants in regions where all three CaPVs are endemic. Validation of the real-time PCR assay has been published in several publications (see Appendix A in (EFSA Panel on Animal Health and Welfare, 2014)). The real-time PCR method for CaPV displays greater sensitivity than conventional gel-based PCR assays, with values of 100 % in five out of seven studies screened from the literature compared with one study out of two for gel-based PCR (EFSA Panel on Animal Health and Welfare, 2014). The detection level of the assay is less than 10 genome copies per reaction. During the validation process, no cross-reaction with related pox viruses and no false-positive results were detected when tested against a panel of other poxviruses or negative samples. Real-time PCR is quantitative, simple, sensitive and specific, thus enabling rapid, high-throughput testing for CaPV. Currently, the real-time PCR method is commonly used in diagnostic laboratories within the EU. If combined with robotic extraction, it can be used for large-scale testing.

Species-specific real-time PCR methods for differentiation between SPPV, GTPV and LSDV have been published (Lamien et al., 2011b). The species-specific PCR assay detects differences in the melting point temperatures for SPPV, GTPV and LSDV, obtained after fluorescence melting curve analysis. It targets a 200-bp region within the capripox host-range GPCR gene and this method is currently under validation. The species-specific method would be required within EU MSs in order to a select homologous vaccine in situations where all three CaPVs are present in a country or if clinical signs resembling those caused by LSDV are observed in wild ruminants. In some cases, real-time PCR equipment and reagents may still be relatively expensive for laboratories with limited resources, and trained staff are needed. Suitable sample material is blood in ethylenediamine tetraacetic acid (EDTA), skin and other tissues such as scabs. Ocular, nasal and saliva swabs as well as semen samples may be used.

The general CaPV gel-based PCR method has been validated and published in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals for LSD and is revised in Appendix A. As mentioned above, this method is not as fast or as sensitive as real-time PCR. However, the gel-based method is a good choice if real-time PCR is not available in laboratories with limited resources or as a back-up PCR method for real-time PCR. The conventional PCR method is cheaper to perform than real-time PCR and is less vulnerable to technical problems, but it is not quantitative. However, both sensitivity and specificity are still superior to those of other methods available (EFSA Panel on Animal Health and Welfare, 2014). Gel-based PCR for differentiation between SPPV and GTPV has been described (Lamien et al., 2011a), as well as a novel method based on snapback primers (Gelaye et al., 2013). PCR equipment, reagents and trained staff are needed, and suitable sample material is blood in EDTA, skin and other tissues such as scabs, ocular, nasal and saliva swabs, and semen samples.

Portable pen-side PCR was recently developed, and it has promising preliminary results, is easy to use in field conditions and results are obtained within one hour (unpublished data). Owing to the freeze-dried reagents, no cold-chain is needed in the field setting, sample collection is easy and convenient—blood in EDTA, skin lesions or scabs from skin lesions, and saliva, eye and nasal discharge swabs can be used as sample material—and no separate DNA extraction is required. The PCR assay set up in the portable PCR machine is the above-mentioned general capripox PCR assay, routinely used for CaPV at the OIE reference laboratory in Pirbright (Bowden et al., 2008; Stubbs et al., 2012). A pen-side test will provide rapid confirmation for the tentative field diagnosis allowing a swift implementation of stamping-out and movement restrictions and therefore enhancing the efficacy of the eradication and control measures.

Loop-mediated isothermal amplification assays (LAMP) have been published but are not yet ready for pen-side use (Das et al., 2012; Murray et al., 2013; Zhao et al., 2014). LAMP assay test results are based on colour changes and therefore the interpretation of the results may be a source of misdiagnosis. The performance of the test in the above-mentioned studies ranges from 70 to 100 % for the sensitivity and from 92.3 to 100 % for specificity (EFSA Panel on Animal Health and Welfare, 2014). A suitable pen-side extraction method for the LAMP assay still needs to be developed.

Sequencing of host range genes GPCR and RPO30 can be used to detect the virus strain. However, sequencing is expensive and requires expensive equipment, as well as competent and highly trained staff.

Electron microscopy: CaPV is morphologically indistinguishable from *Orthopoxvirus*, but, apart from vaccinia virus, no *Orthopoxvirus* causes lesions in sheep and goats. However, CaPV is distinguishable from *Parapoxvirus*, which causes bovine popular stomatitis, and this is one of the differential diagnoses for LSD. In addition, electron microscopy lacks sensitivity and could mainly be considered as a confirmative method; it requires expensive equipment and specialised and trained laboratory staff, but results are obtained within a day.

Virus isolation is not suitable for primary diagnostics but is needed to confirm the infectivity of the virus. If tissue culture systems are available, then the virus can be isolated on a variety of cells, such as primary lamb kidney or testis cell cultures. However, CaPVs grow slowly on cell cultures and several passages may be required to grow the virus. Bacterial and fungal contaminations are frequently encountered when the virus is isolated from skin samples or scabs. Some cell lines such as Vero or BHK21 C 13 may also be used, but they are less sensitive. A commercially available lamb testis cell line (OA3.Ts) has been evaluated for the propagation of CaPV isolates (Babiuk et al., 2007). Quantitative measure of sensitivity and specificity are not available from the literature.

9.2.4. Detection of antibodies against LSDV

Serum/virus neutralisation tests: these are gold standard tests for serology. They are very specific but not sufficiently sensitive for the detection of low antibody titres in animals with mild clinical disease and vaccinated animals; they are too labour-intensive and time-consuming; and they are not suitable for primary assay or testing large number of samples. The sensitivity of neutralisation assays varies between 70 and 96 % and specificity can reach 100 % (Sadri et al., 2002; Gari et al., 2008; Babiuk et al., 2009). However, as a cell-based test, standardisation of the assay is difficult and the sensitivity of the assay may vary in different laboratories. The test requires the use of a live virus and can be performed only in laboratories operating on biocontainment level 3. Facilities suitable for cell culture work are needed, including appropriate primary cells or cell lines and reference sera. The sample material is the serum from infected animals.

Indirect fluorescent antibody test (IFAT) performance for the detection of antibodies against LSDV was recently evaluated by Ethiopian researchers (Gari et al., 2008) as a diagnostic tool and in serosurveillance. The capacity of the assay (45 samples per plate) allows testing of larger numbers of samples than with the neutralisation test. Tests may cross-react with other poxviruses. The interpretation of IFAT results is, however, subjective, owing to background fluorescence and non-specific staining of the cytoplasm of the cells, and needs careful standardisation before the results of the test can be interpreted. IFAT has previously successfully been used for the diagnosis of sheep and goat pox (Davies, 1976) and in epidemiological studies to assess the immune status of cattle and sheep (Kulshreshtha et al., 1991).

The agar gel immune diffusion test is a very simple test requiring the bare minimum laboratory facilities. However, it lacks sensitivity (EFSA Panel on Animal Health and Welfare, 2014) and can cross-react with *Parapoxvirus* (Mangana-Vougiouka et al., 2000), which is one of the differential diagnoses. Positive test results must be confirmed with another test.

The performance of **enzyme-linked immunosorbent assays (ELISA)** for sheep pox/goat pox screened from the literature ranges from 70 to 100 % for sensitivity and from 84 to 100 % for specificity (EFSA Panel on Animal Health and Welfare, 2014). The performance of the P32 ELISA described in the OIE Manual of Diagnostic Tests and Vaccines (Bhanot et al., 2009) has not met the requirements for use in serosurveillance. A novel recombinant ELISA has recently been developed by researchers at CSIRO/Australian Animal Health Laboratory (unpublished). The evaluation of the performance of this assay using experimental and field serum is in its final stage and, based on these

results, the test seems to be showing promising results for detecting antibodies in a wide range of samples collected from experimentally and naturally infected and vaccinated cattle, sheep and goats.

Western blotting is difficult to perform and requires purified antigens, and it cannot be used as a primary assay but can be used if inconclusive or positive SNT/ELISA results need to be confirmed.

9.3. Vaccines

Only live attenuated vaccines against LSD are currently commercially available. The attenuated Neethling strain (LSDV) vaccine is used to vaccinate cattle in Africa. It is possible to use the sheep pox/goat pox vaccine for cattle (Capstick and Coackley, 1961) but the cross-protection is not satisfactory and the use of this vaccine has been restricted to those countries where sheep and goat pox are endemic. Neutralising antibodies to LSDV persist for at least two to three years after vaccination. In some animals, the antibody levels are too low to demonstrate, but they are, nevertheless, still resistant to challenge (Weiss, 1968). Antibodies appear 10 days after vaccination and reach the highest level 30 days post inoculation. Calves born to immunised cows will have passive immunity that persists for about six months (Weiss, 1968).

A granulomatous local skin reaction at the site of inoculation, as well as fever and reduction in milk yield, may follow vaccination with live, attenuated CaPV. Severe, generalised reactions, typical of LSD, occurred in dairy cattle in Israel vaccinated with live attenuated virus (Kenya sheep and goat pox strain 0240) (Yeruham et al., 1994). A decrease in milk production of 3.5 % over a period of 12 days was observed. Some of the animals which had calved for the first time (3.5 %) and some older cows (0.5 %) had to be slaughtered because of the severity of the reaction. Positive virus isolations and positive electronic microscopy findings were found for the skin lesions of the animals. On the other hand, the same vaccine strain of CaPV has been used effectively without any severe adverse vaccine reactions in sheep and goats in Kenya (Kitching, 1986). The reduction in milk yield, the granulomatous local reaction at the vaccination site and the possibility of generalised reaction in the vaccinated animals have made some farmers unwilling to vaccinate their cattle, except if an actual threat of the disease is evident.

A retrospective study carried out by Brenner et al. (2009a) involving 4 607 vaccinated cattle showed that the number of clinical LSD cases was five times greater in unvaccinated than in vaccinated herds, which demonstrated that increased levels of protection were indeed achieved in the vaccinated animals compared with those not vaccinated. However, 11.1 % of the vaccinated animals developed cutaneous lesions after exposure to the virus in the field. Skin nodules collected from these animals tested LSDV positive using a PCR test which enabled differentiation between SPPV and LSDV (Stram et al., 2008). Therefore, the authors were able to exclude the possibility that the vaccine virus was responsible for inducing the skin lesions (Tuppurainen and Oura, 2012).

CaPV is an excellent vector for the recombinant vaccines because of its narrow host range (Ngichabe et al., 1997) and the relatively large size of its genome (Carn, 1993). CaPV has been combined, for example, with rinderpest or rabies virus (Aspden et al., 2002; Ngichabe et al., 2002).

9.4. Vaccination in endemic areas

It is widely agreed that vaccination using a homologous vaccine is the only effective way to control the spread of LSDV in endemic countries. In previously disease-free countries, the slaughter of infected and in-contact animals and movement restrictions have been effective, as long as the disease is detected at a very early stage and control measures are implemented without delay. However, if the disease has accidentally gone unnoticed, allowing time for vectors to become infected, it is difficult if not impossible, to eradicate LSDV without vaccination.

It is known during vaccination campaigns that not all animals develop absolute protective immunity against LSDV (Carn, 1993; Kitching, 2003). This may be due to several factors such as cattle incubating the disease when vaccinated or some animals being “missed” during a vaccination

campaign. If proper needle hygiene is not practised, needles or diluents contaminated with virulent LSDV during the actual vaccination procedure may transmit the virus. Inappropriate storage of vaccines or a failure in one or more steps of the cold-chain may occur, or the vaccine may be inactivated owing to exposure to direct sunlight or high environmental temperatures during the vaccination process. In some cases, vaccine may be poorly administrated or an incorrect dosage may be used. In addition, maternally derived antibodies are known to cause interference in the development of active immunity in calves up to six months of age, so calves vaccinated before six months of age that were born to naturally infected or vaccinated dams may not be protected.

In resource-limited countries, the slaughter of infected and in-contact animals is usually seen as a waste of a valuable source of food and is not usually feasible. In addition, in these regions, it is often impossible to effectively implement movement restrictions for small and large ruminants (Kitching, 1986). Owing to the cross-immunity between the members of the CaPV (Kitching, 1983) SPPV and GTPV can be used as a vaccine against LSDV. Because sheep pox and goat pox do not occur in southern Africa, only attenuated LSDV vaccines are used in the region.

However, in central and northern Africa and in the Middle East, where the distribution of sheep pox, goat pox and LSD overlap, attenuated SPPV vaccines, such as KSGP O-240, Yugoslavian RM-65 and Romanian SPPV strains, have been used against LSDV (Davies, 1991; Brenner et al., 2009b; Kumar, 2011). However, incomplete protection against LSD has been reported in cattle vaccinated with all sheep pox vaccines (Ali et al., 1990; Khalafalla et al., 1993; Ayelet et al., 2013). In addition, the KSGP O-240 strain has been identified as an LSDV strain. The low level of attenuation for safe use is insufficient for cattle and, in some cases, the vaccine has been observed to still be virulent (Tuppurainen et al., 2014a).

From the recent epidemics in some Middle Eastern countries, some conclusions can be drawn. In Israel, the RM-65 attenuated sheep pox vaccine had very limited effectiveness in preventing LSD morbidity, whereas the Neethling attenuated LSDV vaccine was effective in the prevention of morbidity around four times more than the 10-fold dose of RM-65 sheep pox vaccine, although some adverse reaction can be observed. In addition, in Jordan, the SPPV RM-65 vaccine used at 10 times the dose used to vaccinate sheep against sheep pox seemed not to provide complete protection, although the fact that some farmers used the unlabelled LSD strain may have confounded the assessment.

9.4.1. Vaccination as control option in free areas

All the commercially available vaccines for LSDV are live attenuated vaccines, prepared with a limited number of strains. General requirements set up for LSDV vaccines are described in the European Pharmacopoeia and in the OIE Manual of Diagnostic Tests and Vaccines (OIE, 2014b).

None of the existing live LSDV vaccines are licensed within the EU and the use of these vaccines would inflict immediate restrictions for the international trade of live cattle and their products. Currently, there are no inactivated or DIVA vaccines of any kind (or associated tests) commercially available.

In non-endemic areas, the use of live attenuated vaccines would be highly questionable on the grounds of safety. In addition, the use of genetically modified recombinant live vaccines may not be permitted. The use of inactivated vaccines could be considered as a short-term solution in an emergency; however, the protection provided by inactivated vaccines is not solid and is only short lived (Kitching, 1983). Because of the limited commercial market for LSDV vaccines, suppliers may not be able to provide a sufficient amount of vaccine at short notice to non-endemic countries. It is not possible to differentiate between infected and vaccinated animals using the currently available tests (Tuppurainen and Oura, 2012).

9.5. Lessons learnt about movement restrictions, culling and biosecurity as applied in Israel

9.5.1. Culling and zoning

In the three series of outbreaks that occurred in Israel, three different policies were implemented in order to mitigate the spread of LSD.

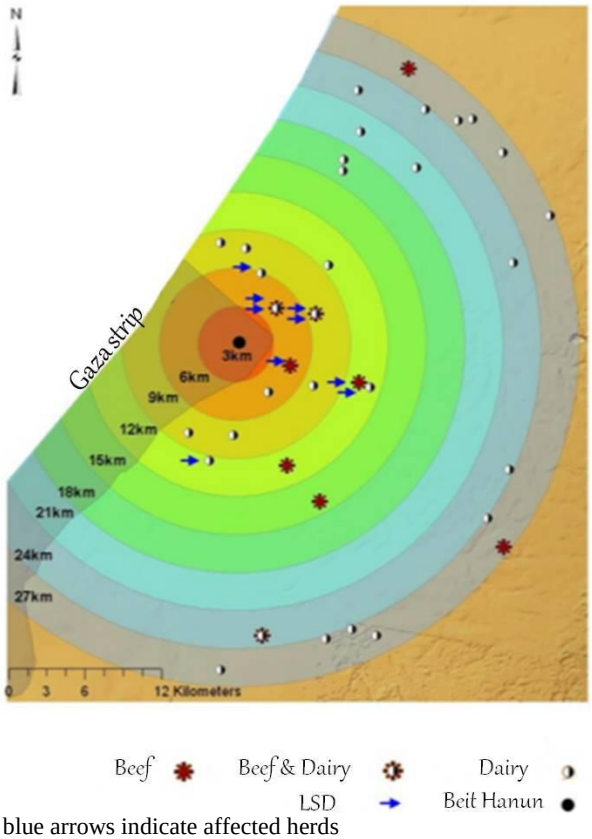
In the outbreak of 1989, all sick and healthy cattle in the affected herds and in non-affected herds from the same farm were culled. This was followed by vaccinating a wide area surrounding the affected farm with the attenuated RM-65 sheep pox vaccine.

In 2006 and 2007, only generalised cases were culled. The outbreaks in 2007 occurred in farms which were previously vaccinated with the RM-65 sheep pox vaccine. This fact confirmed the ineffectiveness of this vaccine for preventing LSD spread. During the outbreak of 2007, there was a probable continuing source of LSD in Beit Hanoun in the Gaza Strip, which is located a few kilometres from where the affected herds were in Israel.

During 2012, only a few affected beef cattle were culled (there were only rare cases of culling to prevent animal suffering), while every generalised case in dairy cattle was culled in order to control outbreak spread. Vaccination was initially performed with the RM-65 vaccine. Nine months later, the vaccine was replaced and all dairy cattle herds were vaccinated with the LSD strain Neethling vaccine and the beef cattle herds with a 10-fold dose of RM-65 sheep pox vaccine. Both vaccines appeared to be more effective than the vaccine used earlier, especially the Neethling vaccine, which was shown to be four times more effective than the 10-fold dose of RM-65 sheep pox vaccine.

Some conclusions can be drawn from the investigation of this series of three outbreaks.

The outbreaks which occurred during 1989 and 2006 did not spread from the initially affected herds, apart of few sporadic cases in herds up to 3 km away. This is despite a high incidence of disease in the initially affected herds. In these cases, the outbreaks were controlled, despite the use of an ineffective vaccine (Figure 15).



Source: Herziger (2009). The blue arrows indicate affected herds

Figure 15: Proportion of clinically affected herds as a function of distance from Beit Hanun (north of the Gaza Strip)

During 2007, LSD spread did not occur beyond a distance of 12 km from the Gaza Strip, which was considered the continuous source of the disease. The extent of outbreaks in each herd was correlated with the time elapsed from outbreak onset until culling initiation.

In the outbreak of 2012–2013, no culling was implemented and the outbreak continued to spread for nine months among the beef cattle herds and spread to dairy cattle herds as well.

From the Israeli experience, it can be concluded that culling of generalised cases is a necessary step to take when no vaccine or ineffective vaccines (e.g. sheep pox strain vaccine) are used. However, there seems to be no need for pre-emptive culling of healthy animals suspected to be in contact with the generalised cases. Culling of only generalised cases seems to be a "good enough" policy in order to enable fast control of an LSD epidemic.

Continuing with this rationale, zoning is an important prerequisite for the prevention of LSD spread. This is supported by several observations from the outbreaks which occurred in Israel. As mentioned earlier, the outbreak in 2007 did not spread beyond a distance of 12 km from a continuous source of the disease, showing that spread of LSD is usually limited in distance when sick animals are not moved to non-affected areas. During 2013, two cases were documented in which the disease leaped to distant cases. In one case, the disease leaped 100 km southwards from its initial occurrence in the north of Israel. This caused limited spread of the disease in the south of Israel. In this event, the investigation revealed that un-authorised delivery of potentially sick cattle took place from affected herds in the north to a herd in the south, which was later affected by LSD. In another case, the disease leaped from the Golan Heights to the northern coastal plain, about 40 km westwards. As the affected herds in the coastal plain are situated near the Israel central facility for carcass disposal, it was suspected that transfer of affected carcasses was the possible cause for the transmission of the disease to this area.

9.5.2. Insecticides

As opposed to the data available on vaccines and also on culling and zoning, there are no experimental quantitative data showing that the use of insecticides was effective. A case–control study performed showed no reduction in morbidity in herds for which insecticides were used. These data are always very difficult to document retrospectively and there are so many covariate factors that determine morbidity that accurate and valuable data regarding this are very rare. Despite this, as stated in the OIE reports about LSD outbreaks that occurred in 2014 in Azerbaijan, Iran, Lebanon, Egypt and Palestine, in all these countries, the control of vectors through spraying or dipping was implemented.

However, it is very likely that the use of effective insecticides which will reduce the rate of bites will have an effect on the probability of infection. One important preventative measure is to heavily use insecticides on corpses delivered to facilities for corpse disposal. As described earlier, one of the long-distance jumps observed during the 2012–2013 outbreaks might have occurred because of the delivery of corpses to such a facility. This is, however, just circumstantial evidence. Therefore, it should be interpreted very carefully. In addition, investigations could be conducted on if flies bite corpses. Strictly haematophagus insects do not usually bite dead animals. Some biting flies, however, including *Stomoxys*, do not feed on blood exclusively. Thus, they may be attracted to other body exudates, and continue to feed on live animals. Corpses, as well as wounds, are highly attractive to other filth flies, flesh flies and bottle flies, but these flies do not bite. They may transmit the virus by contamination, but this has never been tested.

Regarding insecticides, if they contain repellents, they may reduce the attraction to corpses on site, and they may affect some of the flies, but they will not prevent initial contact. The best option would be to cover the animal corpse with repellent-containing insecticides.

It would also be necessary to distinguish between the use of insecticides on animal, using ones that also have an anti-feeding effect, and the use of insecticides to control vectors in the environment, using ones that could be a preventative measure. Regarding vector control, it is also important to mention that the LSD vector is not known exactly, and pest control methods may change in relation to vector species, especially if effective control including anti-larval strategies is foreseen.

9.6. Movement restrictions, culling and biosecurity in other Middle Eastern countries

The poor animal health situation in the Middle East has been repeatedly demonstrated by the presence of major epizootic livestock diseases in the region (Shimshony and Economides, 2006).

During LSD outbreaks in Oman, the usual quarantine methods, including animal isolation and vaccination, were ineffective control measures in preventing the spread of LSD within the herd at the Sohar farm. This could have been due to the animals already incubating the virus, thus meaning it was too late for the vaccine to afford protection (Hunter and Wallace, 2001). Moreover, as observed in Israeli dairy herds (Brenner et al., 2006), the possibility exists that the Kenya sheep and goat pox vaccine is under attenuated, causing clinical disease in a significant proportion of vaccinated animals (Tageldin et al., 2014).

In many countries in the Middle East, there are no strict testing/quarantine measures in place to prevent these foreign infectious diseases from entering the region. In addition, there is a lack of transparency between these countries and the international organisations that aim to control and eradicate veterinary infectious diseases (Shimshony and Economides, 2006). The under-reporting of notifiable diseases by these countries is likely to be largely due to fears of affecting international trade, although most of these countries are principally consumers rather than producers. In addition, most of the veterinary authorities in these countries are inefficient, and there is a lack of laboratory capacity that hinders early detection of diseases, a lack of notifiable disease control and prevention strategies and no disease eradication policies (Abutarbush et al., 2013).

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

ToR 1. Characterise the disease and provide an update on the global occurrence of LSD and changes in the distribution during the last 10 years

- LSD is a disease of domestic cattle caused by viruses of the genus *Capripoxvirus*. It can be characterised by significant losses, especially in naive and young animals, due to chronic debility, reduced milk production and weight, infertility, abortion and death.
- There is evidence that only around half of infected animals develop generalised skin lesions; however, all infected animals can transmit the virus.
- There is evidence that African wild ruminant species may have a role in the epidemiology of LSD. Although certain wildlife species can be experimentally infected by LSDV, information on the susceptibility of wildlife to LSD is scarce and further limited by the inability to distinguish antibodies evoked by LSDV from those evoked by sheep pox and goat pox.
- CaPVs are not considered to be zoonotic agents.
- LSDV can be detected in animal secretions (e.g. ocular, nasal discharge) up to at least 15 days post infection. If protected from sunlight, the virus can survive in scabs, and therefore also in the environment, for up to six months, and in dried hides of infected animals for up to 18 days.
- LSD is endemic in most African countries. Since 2012–2013, LSD has been spreading on a unusually large scale throughout Middle and Near Eastern countries including Turkey, where it is now considered endemic.
- Field evidence strongly suggests the involvement of haematophagus arthropod vectors in LSDV transmission among cattle by the mechanical route, although the role of each species is not well documented. However, the spread of the virus in situations with very low abundances of vectors may occur, thus suggesting direct and/or indirect transmission (e.g. through fomites contaminated with secretions from infected animals) as possible routes of LSD transmission.
- The fast spread of LSD as recorded in some areas indicates a minor role of ticks in the transmission of the virus under field conditions. Nevertheless, laboratory experiments suggest that ticks may play a role in the transmission as well as maintenance of LSDV.
- The importance of different mechanical vectors in the transmission of LSDV is likely to vary in different geographical regions, depending on the environment, temperature, humidity and abundance of the vectors.

ToR 2. Map the region of concern and other countries of the Mediterranean Basin and Black Sea, displaying identified, or likely, major live animal trade routes

- The movement of live animals from third countries in the Mediterranean Basin and Black Sea areas into the EU is currently forbidden, according to EU animal health legislation on the import of live animals from countries where LSD is endemic. However, currently, illegal movements of animals cannot be quantified accurately.
- In Turkey, there are a large number of within-country movements of live cattle from provinces that have been affected by LSD in 2013–2014.
- There is substantial trade in cattle skin, wool and hides into the EU from countries where LSD is present. In order to complete an import risk assessment, detailed information is needed to clarify if each commodity has undergone appropriate treatment to inactivate LSDV. Skins and hides processed only by drying treatments may pose a risk of introduction of LSDV into the EU if imported from affected areas, although further spread through this route is unlikely.

- The several outbreaks that occurred in southern Turkey most likely originated from the introduction of LSD from Syria, thus suggesting that political unrest may facilitate disease spreading.

ToR 3. Evaluate all possible pathways of introduction of LSD into the EU, ranking them on the basis of their level of risk, with a view to enhancing preparedness and prevention

- The movement of infected animals and vectors are the main possible pathways for LSD introduction.
- The introduction of infected animals is the most efficient way to introduce LSDV into a country, in particular for long-distance spread.
- The spread of LSD is usually limited in distance when sick animals are not moved to non-affected areas.
- The active movement of flying vectors can be a pathway for LSD introduction into a naive country from a short distance, e.g. from infected areas close to the borders.
- Circumstantial evidence indicates that windborne transmission of vectors carrying the virus (after a blood meal on an infected animal) could be a potential route of LSDV introduction into a country.

ToR 4. Assess the risk of introduction and speed of propagation of LSD into the EU and neighbouring countries

- In order to estimate the risk of introduction into the EU via the illegal movement of animals, a model was used to assess the probability of an individual being infectious in a given shipment size. For different levels of seroprevalence in the country of origin, the number of animals that would need to be moved to have a probability of introduction of LSD into Europe greater than 0.95 or lower than 0.05 would be above 1 300 and below 25, respectively (with seroprevalence equal to 30 %), or above 7 800 and below 140, respectively (with seroprevalence equal to 5 %).
- According to a model developed to simulate the LSD spread between farms over space after an incursion in Greece, when the control measures only entail the removal of animals showing generalised clinical signs, approximately 90 % of the simulated epidemics remain confined to the region around the initial site of incursion. However, the remaining 10 % of simulated epidemics spread further to approximately 300 to 400 km from the site of introduction by six months after the incursion.
- Under the assumptions made when developing the model for the transmission of LSDV between farms, there is the potential for outbreaks to spread in Bulgaria and Greece. Applying whole-herd culling to infected farms substantially reduces the spread of LSDV and, the more rapidly farms are detected and culled, the greater the magnitude of the reduction is.

ToR 5. Assess the risk of LSD becoming endemic in animal populations in the EU and neighbouring countries

- LSD is considered to be endemic in Turkey, probably owing to low vaccination coverage and the use of a sub-optimal vaccines.
- Owing to a lack of data regarding the ability of potential European vectors of disease transmission, the international data cannot be extrapolated directly to the European situation.
- Under the current EU policy, according to the scenarios produced using the spread model, if the situation and ability of vectors was the same as in Israel, LSD would most likely not become endemic in the EU.

ToR 6. Assess the impact of LSD if it were to enter the EU, considering different scenarios as regards the effectiveness of surveillance and control measures

- According to the model developed to simulate LSD spread over space, under a scenario of an incursion of LSD in Greece, by applying the measures of vaccination and culling of generalised cases, as applied in Israel, after 100 days from the onset of the epidemics, the median number of infected farms would be 16 (range: 6 to 690) and the median number of animals in these farms would be 951 (range: 476 to 67 908). In the worst-case scenario, the outbreak did not stop even after 200 days.
- If culling whole herds took place 7 or 15 days after infection, the median number of infected farms would be reduced by about 80 and 70 %, respectively. Using these measures, the outbreak would be controlled in the worst case after 12 days and 43 days, respectively, indicating the efficacy of the measures in controlling the outbreaks.

ToR 7. Briefly review the feasibility, availability and effectiveness of the main disease prevention and control measures (diagnostic tools, biosecurity measures, restrictions on the movement, culling)

- Rapid laboratory confirmation of suspected LSD field cases is essential for the successful eradication of the disease.
- In non-endemic countries, handling LSDV-infected samples requires high containment facilities.
- The validated general real-time PCR method is the method of choice for the detection of LSDV.
- Host-specific genes for CaPVs are known and several species-specific PCR assays have been published. Alternatively, sequencing of the GPCR or RPO30 genes can be used for the differentiation of CaPVs.
- Several national reference laboratories within the EU have the molecular diagnostic capacity already in place for LSDV detection.
- Only live attenuated vaccines against LSD are currently commercially available. No LSDV vaccines are licensed in the EU.
- According to the Israeli experience, epidemics of limited extent could not be effectively controlled by using only the sheep pox vaccine at the recommended doses for sheep. Only when animals with generalised skin lesions were also culled were the epidemics controlled.
- Large-scale epidemics can be controlled by the use of effective vaccination (homologous vaccine) together with culling of animals with generalised symptoms.
- RM-65 attenuated sheep pox vaccine at the recommended dose for sheep has limited effectiveness in preventing LSD morbidity. There is field evidence which suggests that 10 times the dose of RM-65 is more effective in terms of protection, although is less effective than vaccination with the homologous strain.
- The Neethling attenuated LSDV vaccine is highly effective in protecting animals from the disease, thus confirming the need to use homologous vaccines for the control of CaPV infections. Nevertheless, some safety issues have been reported that are linked to generalised clinical reactions due to vaccination with LSD strain.
- Although insecticides are frequently used to control LSD outbreaks, there is no evidence to date to prove their effectiveness in controlling LSD morbidity.

RECOMMENDATIONS

Preparedness

- A better knowledge of legal and illegal livestock and animal product movements should be sought, especially in areas at risk of or affected by LSD.
- A quantitative import risk assessment of skins and hides coming from affected regions should be performed. This will allow specific measures to be identified to reduce the risk posed by this commodity.
- Inter-laboratory ring-trials for CaPV diagnostics should be organised.
- Adequate veterinary care and improved surveillance should be in place, in particular for transhumant flocks along migratory routes in risk areas, especially for long-distance migrations.
- Awareness-raising campaigns and training for farmers and veterinary staff in recognising the disease under field conditions should be considered, especially for regions at a higher risk of introduction of LSD (i.e. those bordering affected regions).
- If non-biological drivers of the transmission of transboundary animal diseases change (e.g. breakdown of veterinary infrastructures, human migration, political unrest), the risk of LSD introduction should be accordingly reassessed. Under this perspective, the cooperation of the EU with neighbouring countries should be encouraged for the prevention of transboundary animal diseases and enhancing preparedness.

Control

- If LSD entered the EU, rapid detection and prompt culling of infected herds should be considered as effective measures in limiting the spread and impact of the outbreaks.
- Clinical surveillance conducted in protection and surveillance zones should be designed to detect animals showing characteristic LSD signs (clinical inspection by veterinary authorities and awareness campaigns for farmers and other stake holders and viraemic animals with silent infection (blood samples tested with real-time PCR method)). Clinical surveillance should be combined with serosurveillance.

Research needs

- In order to effectively control LSDV in affected countries, a comprehensive understanding of the ecology of different blood-feeding and biting arthropod species in the cattle farming setting is required.
- Potential relevant vector species should be identified, including the species present in Europe, and their capability to transmit the virus from infected to naive animals should be investigated in a controlled environment, using a sufficient number of experimental animals.
- The infection rate within each suspected vector species should be evaluated and the mode of transmission (mechanical/biological) should be investigated in detail.
- A pen-side test for CaPVs needs to be developed.
- The risk of LSD spreading from the Middle East to the rest of Asia or to Europe underlines the need for the development of safe, efficient and non-replicating DIVA vaccines against LSDV, as well as an associated diagnostic test.
- The efficacy of currently available live vaccines in cattle against LSDV should be evaluated using challenge experiments in controlled environments.
- The effectiveness of insecticides for LSD control should be investigated.

REFERENCES

Abutarbush S, 2014. Efficacy of vaccination against lumpy skin disease in Jordanian cattle. Veterinary Record, 175, 302-302.

Abutarbush SM, Ababneh MM, Al Zoubi IG, Al Sheyab OM, Al Zoubi MG, Alekish MO and Al Gharabat RJ, 2013. Lumpy Skin Disease in Jordan: Disease Emergence, Clinical Signs, Complications and Preliminary-associated Economic Losses. Transboundary and emerging diseases. doi: 10.1111/tbed.12177.

Abutarbush SM, Hananeh WM, Ramadan W, Al Sheyab OM, Alnajjar AR, Al Zoubi IG, Knowles NJ, Bachanek-Bankowska K and Tuppurainen ES, 2014. Adverse Reactions to Field Vaccination Against Lumpy Skin Disease in Jordan. Transboundary and emerging diseases. doi: 10.1111/tbed.12257.

Ahmed W and Zaher KS, 2008. Observations on lumpy skin disease in local Egyptian cows with emphasis on its impact on ovarian function. African Journal of Microbiology Research, 2, 252-257.

Alba A, Casal J and Domingo M, 2004. Possible introduction of bluetongue into the Balearic Islands, Spain, in 2000, via air streams. Veterinary Record, 155, 460-461.

Alexander RA, Plowright W and Haig DA, 1957. Cytopathic agents associated with LSD of cattle. Bulletin of epizootic diseases of Africa, 5, 489–492.

Ali AA, Esmat M, Attia H, Selim A and Abdel-Hamid YM, 1990. Clinical and pathological studies on lumpy skin disease in Egypt. Veterinary Record, 127, 549-550.

Ali H, Ali AA, Atta MS and Cepica A, 2012. Common, emerging, vector-borne and infrequent abortogenic virus infections of cattle. Transboundary and Emerging Diseases, 59, 11-25.

Andrieu C and Thoms J, 2008. A tutorial on adaptive MCMC. Statistics and Computing, 18, 343-373.

Annandale CH, Holm DE, Ebersohn K and Venter EH, 2013. Seminal Transmission of Lumpy Skin Disease Virus in Heifers. Transboundary and emerging diseases, 61, 443-8. doi: 10.1111/tbed.12045.

Annandale CH, Irons PC, Bagla VP, Osuagwuh UI and Venter EH, 2010. Sites of persistence of lumpy skin disease virus in the genital tract of experimentally infected bulls. Reproduction in domestic animals, 45, 250-255.

Aspden K, van Dijk AA, Bingham J, Cox D, Passmore JA and Williamson AL, 2002. Immunogenicity of a recombinant lumpy skin disease virus (neethling vaccine strain) expressing the rabies virus glycoprotein in cattle. Vaccine, 20, 2693-2701.

Ayelet G, Abate Y, Sisay T, Nigussie H, Gelaye E, Jemberie S and Asmare K, 2013. Lumpy skin disease: preliminary vaccine efficacy assessment and overview on outbreak impact in dairy cattle at Debre Zeit, central Ethiopia. Antiviral research, 98, 261-265.

Aziz-Boaron O, Klausner Z, Hasoksuz M, Shenkar J, Gafni O, Gelman B, David D and Klement E, 2012. Circulation of bovine ephemeral fever in the Middle East--strong evidence for transmission by winds and animal transport. Veterinary Microbiology, 158, 300-307.

Babiuk S, Bowden TR, Boyle DB, Wallace DB and Kitching RP, 2008. Capripoxviruses: an emerging worldwide threat to sheep, goats and cattle. Transboundary and Emerging Diseases, 55, 263-272.

Babiuk S, Parkyn G, Copps J, Larence JE, Sabara MI, Bowden TR, Boyle DB and Kitching RP, 2007. Evaluation of an ovine testis cell line (OA3.Ts) for propagation of capripoxvirus isolates and development of an immunostaining technique for viral plaque visualization. Journal of Veterinary Diagnostic Investigation, 19, 486-491.

Babiuk S, Wallace DB, Smith SJ, Bowden TR, Dalman B, Parkyn G, Copps J and Boyle DB, 2009. Detection of antibodies against capripoxviruses using an inactivated sheeppox virus ELISA. Transboundary and Emerging Diseases, 56, 132-141.

Baddeley A and Turner R, 2005. Spatstat: an R package for analyzing spatial point patterns. Journal of statistical software, 12, 1-42.

Baldacchino F, Desquesnes M, Mihok S, Foil LD, Duvallet G and Jittapalapong S, 2014. Tabanids: Neglected subjects of research, but important vectors of disease agents! Infection Genetics and Evolution, 28, 596-615.

Barnard B, Munz E, Dumbell K and Prozesky L, 1994. Lumpy skin disease. Infectious diseases of livestock with special reference to Southern Africa, 1, 604-612.

Barnard BJ, 1997. Antibodies against some viruses of domestic animals in southern African wild animals. Onderstepoort Journal of Veterinary Research, 64, 95-110.

Bellaiche M, 2007. Report of lumpy skin disease in Israel 2007. Health (San Francisco).

Bett B, Jost C, Allport R and Mariner J, 2009. Using participatory epidemiological techniques to estimate the relative incidence and impact on livelihoods of livestock diseases amongst nomadic pastoralists in Turkana South District, Kenya. Preventive Veterinary Medicine, 90, 194-203.

Bhanot V, Balamurugan V, Bhanuprakash V, Venkatesan G, Sen A, Yadav V, Yogisharadhya R and Singh RK, 2009. Expression of P32 protein of goatpox virus in Pichia pastoris and its potential use as a diagnostic antigen in ELISA. Journal of Virological Methods, 162, 251-257.

Bivand R and Lewin-Koh N, maptools: Tools for reading and handling spatial objects, 2014. R package version 0.8-29.

Black DN, Hammond JM and Kitching RP, 1986. Genomic relationship between capripoxviruses. Virus Research, 5, 277-292.

Boulter E and Appleyard G, 1972. Differences between extracellular and intracellular forms of poxvirus and their implications. Progress in medical virology. Fortschritte der medizinischen Virusforschung. Progres en virologie medicale, 16, 86-108.

Bowden TR, Babiuk SL, Parkyn GR, Copps JS and Boyle DB, 2008. Capripoxvirus tissue tropism and shedding: A quantitative study in experimentally infected sheep and goats. Virology, 371, 380-393.

Braverman Y and Chechik F, 1996. Air streams and the introduction of animal diseases borne on Culicoides (Diptera, Ceratopogonidae) into Israel. Revue scientifique et technique (International Office of Epizootics), 15, 1037-1052.

Brenner J, Bellaiche M, Gross E, Elad D, Oved Z, Haimovitz M, Wasserman A, Friedgut O, Stram Y, Bumbarov V and Yadin H, 2009a. Appearance of skin lesions in cattle populations vaccinated against lumpy skin disease: statutory challenge. Vaccine, 27, 1500-1503.

Brenner J, Haimovitz M, Oron E, Stram Y and Fridgut O. BV, Kuznetzova L., Oved Z., Waserman A., Garazzi S., Perl S., Lahav D., Edery N., Yadin H., 2006. Lumpy Skin Disease (LSD) in a large dairy herd in Israel. Israel Journal of Veterinary Medicine, 61, 3-4.

Brenner J, Sharir B, Yadin H, Perl S and Stram Y, 2009b. Herpesvirus type 2 in biopsy of a cow with possible pseudo-lumpy-skin disease. Veterinary Record, 165, 539-540.

Burdin ML, 1959. The use of histopathological examination of skin material for the diagnosis of lumpy skin disease in Kenya. Bulletin of epizootic diseases of Africa, 7, 21-26.

Capstick P and Coackley W, 1961. Protection of cattle against lumpy skin disease. Research in Veterinary Science, 2, 362-375.

Carn V, 1993. Control of capripoxvirus infections. Vaccine, 11, 1275-1279.

Carn VM and Kitching RP, 1995a. The clinical response of cattle experimentally infected with lumpy skin disease (Neethling) virus. Archives of virology, 140, 503-513.

Carn VM and Kitching RP, 1995b. An investigation of possible routes of transmission of lumpy skin disease virus (Neethling). Epidemiology and infection, 114, 219-226.

Chapman J, Reynolds D, Smith A, Smith E and Woiwod I, 2004. An aerial netting study of insects migrating at high altitude over England. Bulletin of entomological research, 94, 123-136.

Chihota CM, Rennie LF, Kitching RP and Mellor PS, 2001. Mechanical transmission of lumpy skin disease virus by Aedes aegypti (Diptera: Culicidae). Epidemiology and infection, 126, 317-321.

Chihota CM, Rennie LF, Kitching RP and Mellor PS, 2003. Attempted mechanical transmission of lumpy skin disease virus by biting insects. Medical and Veterinary Entomology, 17, 294-300.

Das A, Babiuk S and McIntosh MT, 2012. Development of a loop-mediated isothermal amplification assay for rapid detection of capripoxviruses. Journal of Clinical Microbiology, 50, 1613-1620.

Davies FG, 1976. Characteristics of a virus causing a pox disease in sheep and goats in Kenya, with observation on the epidemiology and control. The Journal of hygiene, 76, 163-171.

Davies FG, 1982. Observations on the epidemiology of lumpy skin disease in Kenya. The Journal of hygiene, 88, 95-102.

Davies FG, 1991. Lumpy skin disease, an African capripox virus disease of cattle. The British veterinary journal, 147, 489-503.

Davies FG and Otema C, 1981. Relationships of capripox viruses found in Kenya with two Middle Eastern strains and some orthopox viruses. Research in Veterinary Science, 31, 253-255.

DEFRA, 2014. Qualitative assessment for the release of sheep pox virus and lumpy skin disease virus into Great Britain from the European Union. ED1043, Department for Environment Food & Rural Affairs, UK 1-11.

Ducheyne E, Lange M, Van der Stede Y, Meroc E, Durand B and Hendrickx G, 2011. A stochastic predictive model for the natural spread of bluetongue. Preventive Veterinary Medicine, 99, 48-59.

Duclos J-C and Pitte A, 1994. L'homme et le mouton dans l'espace de la transhumance. Glénat, Grenoble, 312 pp.

Eagles D, Melville L, Weir R, Davis S, Bellis G, Zalucki M, Walker P and Durr P, 2014. Long-distance aerial dispersal modelling of Culicoides biting midges: case studies of incursions into Australia. BMC veterinary research, 10, 135.

EFSA (European Food Safety Authority), 2012. Assessing Risk of Introduction via Import. EFSA Journal 2012; 10(4):2657, 20 pp. doi:10.2903/j.efsa.2012.2657.

EFSA Panel on Animal Health and Welfare (AHAW), 2014. Scientific Opinion on sheep and goat pox. EFSA Journal 12(11): 3885. , 122 pp. doi:110.2903/j.efsa.2014.3885

El-Nahas E, El-Habbaa A, El-bagoury G and Radwan ME, 2011. Isolation and Identification of Lumpy Skin Disease Virus from Naturally Infected Buffaloes at Kaluobia, Egypt. Global Veterinaria 7, 234-237.

FAO (Food and Agriculture Organiszation of the United Nations), 2011. A value chain approach to animal diseases risk management – Technical foundations and practical framework for field application. Animal Production and Health Guidelines, No. 4. Rome.

FAO (Food and Agriculture Organization of the United Nations), 2013a. Agricultural Livelihoods and Food Security Impact Assessment and Response Plan for the Syria Crisis in the Neighbouring Countries of Egypt, Iraq, Jordan, Lebanon and Turkey. Mission assessment report, 2013.

FAO (Food and Agriculture Organiszation of the United Nations), 2013b. Emergence of lumpy skin disease in the Eastern Mediterranean Basin countries. EMPRES WATCH, Vol. 29, November 2013, Rome.

Fenner F, Bachmann P, Gibbs EPJ, Murphy FA, MJ S and DO W, 1987. Veterinary Virology. Academic Press, Inc. London.

Finlaison D, Read A and Kirkland P, 2010. An epizootic of bovine ephemeral fever in New South Wales in 2008 associated with long-distance dispersal of vectors. Australian veterinary journal, 88, 301-306.

Förster M, Klimpel S, Mehlhorn H, Sievert K, Messler S and Pfeffer K, 2007. Pilot study on synanthropic flies (eg Musca, Sarcophaga, Calliphora, Fannia, Lucilia, Stomoxys) as vectors of pathogenic microorganisms. Parasitology research, 101, 243-246.

Förster M, Klimpel S and Sievert K, 2009. The house fly (*Musca domestica*) as a potential vector of metazoan parasites caught in a pig-pen in Germany. Veterinary parasitology, 160, 163-167.

García-Lastra R, Leginagoikoa I, Plazaola JM, Ocabo B, Aduriz G, Nunes T and Juste RA, 2012. Bluetongue virus serotype 1 outbreak in the Basque Country (northern Spain) 2007–2008. Data support a primary vector windborne transport. PLoS One, 7, e34421.

Gari G, Biteau-Coroller F, LeGoff C, Caufour P and Roger F, 2008. Evaluation of indirect fluorescent antibody test (IFAT) for the diagnosis and screening of lumpy skin disease using Bayesian method. Veterinary Microbiology, 129, 269-280.

Gari G, Bonnet P, Roger F and Waret-Szkuta A, 2011. Epidemiological aspects and financial impact of lumpy skin disease in Ethiopia. Preventive Veterinary Medicine, 102, 274-283.

Gari G, Grosbois V, Waret-Szkuta A, Babiuk S, Jacquiet P and Roger F, 2012. Lumpy skin disease in Ethiopia: seroprevalence study across different agro-climate zones. Acta tropica, 123, 101-106.

Gelaye E, Lamien CE, Silber R, Tuppurainen ES, Grabherr R and Diallo A, 2013. Development of a cost-effective method for capripoxvirus genotyping using snapback primer and dsDNA intercalating dye. PLoS One, 8, e75971.

Green HF, 1959. .Lumpy skin disease: its effect on hides and leather and a comparison on this respect with some other skin diseases. Bulletin of epizootic diseases of Africa, 7, 63.

Greth A, Gourreau JM, Vassart M, Nguyen Ba V, Wyers M and Lefevre PC, 1992. Capripoxvirus disease in an Arabian oryx (Oryx leucoryx) from Saudi Arabia. Journal of Wildlife Diseases, 28, 295-300.

Gubbins S, Richardson J, Baylis M, Wilson AJ and Abrahantes JC, 2014. Modelling the continental-scale spread of Schmallenberg virus in Europe: Approaches and challenges. Preventive Veterinary Medicine.

Haig DA, 1957. Lumpy skin disease. Bulletin of epizootic diseases of Africa, 5, 421-430

Halstead P, 1987. Traditional and ancient rural economy in Mediterranean Europe: plus ça change? The Journal of Hellenic Studies, 107, 77-87.

Hasle G, 2013. Transport of ixodid ticks and tick-borne pathogens by migratory birds. Front Cell Infect Microbiol, 3, 48.

Hedger RS and Hamblin C, 1983. Neutralising antibodies to lumpy skin disease virus in African wildlife. Comp Immunol Microbiol Infect Dis, 6, 209-213.

Hendrickx G, Gilbert M, Staubach C, Elbers A, Mintiens K, Gerbier G and Ducheyne E, 2008. A wind density model to quantify the airborne spread of Culicoides species during north-western Europe bluetongue epidemic, 2006. Preventive Veterinary Medicine, 87, 162-181.

Herziger Y, 2009. Epidemiological and entomological aspects of lumpy skin disease in Israel. MSc Thesis. Hebrew university of Jerusalem.

Hogsette J and Ruff J, 1985. Stable fly (Diptera: Muscidae) migration in northwest Florida. Environmental entomology, 14, 170-175.

House JA, Wilson TM, el Nakashly S, Karim IA, Ismail I, el Danaf N, Moussa AM and Ayoub NN, 1990. The isolation of lumpy skin disease virus and bovine herpesvirus-4 from cattle in Egypt. Journal of Veterinary Diagnostic Investigation, 2, 111-115.

Hunter P and Wallace D, 2001. Lumpy skin disease in southern Africa: a review of the disease and aspects of control. Journal of the South African Veterinary Association, 72, 68-71.

IFAH (International Federation for Animal Health), 2012. The costs of animal disease Oxford Analytica.

Irons PC, Tuppurainen ES and Venter EH, 2005. Excretion of lumpy skin disease virus in bull semen. Theriogenology, 63, 1290-1297.

Işidan H, Sözdutmaz I and Turan T, 2014. Spreading Lumpy Skin disease to the North. Proceedings of the Epizone 2014, Copenhagen.

Kalderon-Asael B, Erel Y, Sandler A and Dayan U, 2009. Mineralogical and chemical characterization of suspended atmospheric particles over the east Mediterranean based on synoptic-scale circulation patterns. Atmospheric Environment, 43, 3963–3970.

Kedmi M, Herziger Y, Galon N, Cohen RM, Perel M, Batten C, Braverman Y, Gottlieb Y, Shpigel N and Klement E, 2010. The association of winds with the spread of EHDV in dairy cattle in Israel during an outbreak in 2006. Preventive Veterinary Medicine, 96, 152-160.

Khalafalla AI, Gaffar Elamin MA and Abbas Z, 1993. Lumpy skin disease: observations on the recent outbreaks of the disease in the Sudan. Revue d'elevage et de medecine veterinaire des pays tropicaux, 46, 548-550.

Kitching P, 1983. Progress towards sheep and goat pox vaccines. Vaccine, 1, 4-9.

Kitching RP, 1986. Passive protection of sheep against capripoxvirus. Research in Veterinary Science, 41, 247-250.

Kitching RP, 2003. Vaccines for lumpy skin disease, sheep pox and goat pox. Developments in Biologicals (IABS Symposia Series), 114, 161-167.

Kitching RP and Hammond JM, 1992. Poxvirus, infection and immunity. In: Encyclopaedia of immunology, Eds Roitt, I. M. and Delves, 1261- 1264. Academic press, London. .

Kitching RP, Hammond JM and Black DN, 1986. Studies on the major common precipitating antigen of capripoxvirus. The Journal of general virology, 67, 139-148. doi: 110.1111/tbed.12102.

Kitching RP and Mellor PS, 1986. Insect transmission of capripoxvirus. Research in Veterinary Science, 40, 255-258.

Kitching RP and Smale C, 1986. Comparison of the external dimensions of capripoxvirus isolates. Research in Veterinary Science, 41, 425-427.

Kitching RP and Taylor WP, 1985. Clinical and antigenic relationship between isolates of sheep and goat pox viruses. Tropical Animal Health and Production, 17, 64-74.

Krätli S, Huelsebusch C, Brooks S and Kaufmann B, 2013. Pastoralism: A critical asset for food security under global climate change. Animal Frontiers, 3, 42-50.

Kulshreshtha AK, Pathak PN, Moghe MN and Tanwani SK, 1991. Studies on comparative efficacy of different sheep pox viruses as vaccines. Indian Veterinary Journal, 68, 506-509.

Kumar SM, 2011. An outbreak of lumpy skin disease in a Holstein dairy herd in Oman: a clinical report. Asian Journal of Animal and Veterinary Advances, 6, 851-859.

Lamien CE, Le Goff C, Silber R, Wallace DB, Gulyaz V, Tuppurainen E, Madani H, Caufour P, Adam T, El Harrak M, Luckins AG, Albina E and Diallo A, 2011a. Use of the Capripoxvirus homologue of Vaccinia virus 30 kDa RNA polymerase subunit (RPO30) gene as a novel diagnostic and genotyping target: development of a classical PCR method to differentiate Goat poxvirus from Sheep poxvirus. Veterinary Microbiology, 149, 30-39.

Lamien CE, Lelenta M, Goger W, Silber R, Tuppurainen E, Matijevic M, Luckins AG and Diallo A, 2011b. Real time PCR method for simultaneous detection, quantitation and differentiation of capripoxviruses. Journal of Virological Methods, 171, 134-140.

Le Goff C, Lamien CE, Fakhfakh E, Chadeyras A, Aba-Adulugba E, Libeau G, Tuppurainen E, Wallace DB, Adam T, Silber R, Gulyaz V, Madani H, Caufour P, Hammami S, Diallo A and Albina E, 2009. Capripoxvirus G-protein-coupled chemokine receptor: a host-range gene suitable for virus animal origin discrimination. The Journal of general virology, 90, 1967-1977.

Leblebicioglu H, Eroglu C, Erciyas-Yavuz K, Hokelek M, Acici M and Yilmaz H, 2014. Role of migratory birds in spreading Crimean-Congo hemorrhagic fever, Turkey. Emerging infectious diseases, 20, 1331-1334.

Levine OS and Levine MM, 1991. Houseflies (Musca domestica) as mechanical vectors of shigellosis. Review of Infectious Diseases, 13, 688-696.

Lubinga JC, Clift SJ, Tuppurainen ES, Stoltsz WH, Babiuk S, Coetzer JA and Venter EH, 2014a. Demonstration of lumpy skin disease virus infection in Amblyomma hebraeum and Rhipicephalus appendiculatus ticks using immunohistochemistry. Ticks and tick borne diseases, 5, 113-120.

Lubinga JC, Tuppurainen ES, Coetzer JA, Stoltsz WH and Venter EH, 2014b. Transovarial passage and transmission of LSDV by Amblyomma hebraeum, Rhipicephalus appendiculatus and Rhipicephalus decoloratus. Experimental & applied acarology, 62, 67-75.

Lubinga JC, Tuppurainen ES, Mahlare R, Coetzer JA, Stoltsz WH and Venter EH, 2013a. Evidence of transstadial and mechanical transmission of Lumpy Skin Disease Virus by *Amblyomma hebraeum* ticks. Transboundary and Emerging Diseases.

Lubinga JC, Tuppurainen ES, Stoltsz WH, Ebersohn K, Coetzer JA and Venter EH, 2013b. Detection of lumpy skin disease virus in saliva of ticks fed on lumpy skin disease virus-infected cattle. Experimental & applied acarology, 61, 129-138.

Lubinga JC, Tuppurainen ESM, Coetzer JAW, Stoltsz WH and Venter EH, 2014c. Transovarial passage and transmission of LSDV by *Amblyomma hebraeum*, *Rhipicephalus appendiculatus* and *Rhipicephalus decoloratus*. Experimental and Applied Acarology, 62, 67-75.

Magori-Cohen R, Louzoun Y, Herziger Y, Oron E, Arazi A, Tuppurainen E, Shpigel NY and Klement E, 2012. Mathematical modelling and evaluation of the different routes of transmission of lumpy skin disease virus. Veterinary Research, 43, 1.

Mangana-Vougiouka O, Markoulatos P, Koptopoulos G, Nomikou K, Bakandritsos N and Papadopoulos P, 2000. Sheep poxvirus identification from clinical specimens by PCR, cell culture, immunofluorescence and agar gel immunoprecipitation assay. Molecular and Cellular Probes, 14, 305-310.

Mellor PS, Kitching RP and Wilkinson PJ, 1987. Mechanical transmission of capripox virus and African swine fever virus by Stomoxys calcitrans. Research in Veterinary Science, 43, 109-112.

Morag N, Mullens BA and Gottlieb Y, 2013. Assessment of survival and body size variation of Culicoides imicola (Diptera: Ceratopogonidae) as functions of "Candidatus Cardinium" (Bacteroidetes) infection status. Applied and environmental microbiology, 79, 6260-6263.

Muller GC, Hogsette JA, Kravchenko VD, Revay EE and Schlein Y, 2011. New records and ecological remarks regarding the tribe Stomoxyini (Diptera: Muscidae) from Israel. Journal of Vector Ecology, 36, 468-470.

Munz EK and Owen NC, 1966. Electron microscopic studies on lumpy skin disease virus type Neethling. Onderstepoort Journal of Veterinary Research, 33, 3-8.

Murray L, Edwards L, Tuppurainen ES, Bachanek-Bankowska K, Oura CA, Mioulet V and King DP, 2013. Detection of capripoxvirus DNA using a novel loop-mediated isothermal amplification assay. BMC veterinary research, 9, 90.

Ng JC and Falk BW, 2006. Virus-vector interactions mediating nonpersistent and semipersistent transmission of plant viruses. Annual review of phytopathology, 44, 183-212.

Ngichabe CK, Wamwayi HM, Barrett T, Ndungu EK, Black DN and Bostock CJ, 1997. Trial of a capripoxvirus-rinderpest recombinant vaccine in African cattle. Epidemiology and infection, 118, 63-70.

Ngichabe CK, Wamwayi HM, Ndungu EK, Mirangi PK, Bostock CJ, Black DN and Barrett T, 2002. Long term immunity in African cattle vaccinated with a recombinant capripox-rinderpest virus vaccine. Epidemiology and infection, 128, 343-349.

OIE (Office International des Epizooties), 2014a. Lumpy skin disease - Technical disease card. Available online at: http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/LUMPY_SKIN_DISEASE_FINAL.pdf.

OIE (Office International des Epizooties), 2014b. Lumpy Skin Disease. Manual of Diagnostic Tests and Vaccines for Terrestrial Animals. 7th Edition. Available online, http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/.

Olea PP and Mateo-Tomás P, 2009. The role of traditional farming practices in ecosystem conservation: The case of transhumance and vultures. Biological Conservation, 142, 1844-1853.

Osuagwuh UI, Bagla V, Venter EH, Annandale CH and Irons PC, 2007. Absence of lumpy skin disease virus in semen of vaccinated bulls following vaccination and subsequent experimental infection. Vaccine, 25, 2238-2243.

Palomar AM, Portillo A, Santibanez P, Mazuelas D, Arizaga J, Crespo A, Gutierrez O, Cuadrado JF and Oteo JA, 2013. Crimean-Congo hemorrhagic fever virus in ticks from migratory birds, Morocco. Emerging infectious diseases, 19, 260-263.

Pile M, Simmonds M and Blaney W, 1991. Odour-mediated upwind flight of Culex quinquefasciatus mosquitoes elicited by a synthetic attractant. Physiological entomology, 16, 77-85.

Plateforme Regional Tchadienne 2013. Declaration de N'Djamena sur la contribution de l'elevage pastoral a la securite et au developpement des espaces Saharo-Saheliens. Available online: http://www.oecd.org/fr/csao/evenements/Livre_elevage-pastoral_light.pdf.

Plummer M, Best N, Cowles K and Vines K, 2006. CODA: Convergence diagnosis and output analysis for MCMC. R news, 6, 7-11.

Prozesky L and Barnard BJ, 1982. A study of the pathology of lumpy skin disease in cattle. Onderstepoort Journal of Veterinary Research, 49, 167-175.

Prydie J and Coackley W, 1959. Lumpy skin disease: tissue culture studies. Bulletin of epizootic diseases of Africa, 7, 37-50.

R Core Team, 2012. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available online: http://www.R-project.org.

Reeves A, 2012. Construction and evaluation of epidemiologic simulation models for the within-and among-unit spread and control of infectious diseases of livestock and poultry. Colorado State University, Fort Collins, Colorado.

Reisen W, 2009. Epidemiology of vector-borne diseases. In: Medical and Veterinary Entomology. Eds Mullen GR and Durden LA, Elsevier, New York

Reynolds DR, Chapman JW and Harrington R, 2006. The migration of insect vectors of plant and animal viruses. Advances in virus research, 67, 453-517.

Roberts HC, Elbers AR, Conraths FJ, Holsteg M, Hoereth-Boentgen D, Gethmann J and van Schaik G, 2014. Response to an emerging vector-borne disease: surveillance and preparedness for Schmallenberg virus. Preventive Veterinary Medicine, 116, 341-349.

Rosef O and Kapperud G, 1983. House flies (Musca domestica) as possible vectors of Campylobacter fetus subsp. jejuni. Applied and environmental microbiology, 45, 381-383.

Ruiz M, 2001. The ecological and economic rationale for transhumance practices in Spain'. Examples of European Agri-Environment Schemes and Livestock Systems and Their Influence on Spanish Cultural Landscapes'. Alterra Rapport, 309, 97-100.

Sadri R, Masoudi S, Kargar R, Khedmati K, Varshovi H and Haghighi S, 2002. A single radial haemolysis technique for rapid diagnosis of goat pox diseases. Archives of Razi Institute, 93-99.

Schaffner F, Medlock JM and Van Bortel W, 2013. Public health significance of invasive mosquitoes in Europe. Clinical microbiology and infection, 19, 685-692.

Sellers RF, 1980. Weather, host and vector--their interplay in the spread of insect-borne animal virus diseases. The Journal of hygiene, 85, 65-102.

Sellers RF and Pedgley DE, 1985. Possible windborne spread to western Turkey of bluetongue virus in 1977 and of Akabane virus in 1979. The Journal of hygiene, 95, 149-158.

Shimshony A and Economides P, 2006. Disease prevention and preparedness for animal health emergencies in the Middle East. Revue scientifique et technique (International Office of Epizootics), 25, 253-269.

Shirakawa H, Ishibashi K and Ogawa T, 1994. A comparison of the epidemiology of bovine ephemeral fever in South Korea and south-western Japan. Australian veterinary journal, 71, 50-52.

Spiegelhalter DJ, Best NG, Carlin BP and Van Der Linde A, 2002. Bayesian measures of model complexity and fit. Journal of the Royal Statistical Society: Series B (Statistical Methodology), 64, 583-639.

Stram Y, Kuznetzova L, Friedgut O, Gelman B, Yadin H and Rubinstein-Guini M, 2008. The use of lumpy skin disease virus genome termini for detection and phylogenetic analysis. Journal of Virological Methods, 151, 225-229.

Stubbs S, Oura CA, Henstock M, Bowden TR, King DP and Tuppurainen ES, 2012. Validation of a high-throughput real-time polymerase chain reaction assay for the detection of capripoxviral DNA. Journal of Virological Methods, 179, 419-422.

Szmaragd C, Wilson AJ, Carpenter S, Wood JL, Mellor PS and Gubbins S, 2009. A modeling framework to describe the transmission of bluetongue virus within and between farms in Great Britain. PLoS One, 4, e7741.

Tageldin MH, Wallace DB, Gerdes GH, Putterill JF, Greyling RR, Phosiwa MN, Al Busaidy RM and Al Ismaaily SI, 2014. Lumpy skin disease of cattle: an emerging problem in the Sultanate of Oman. Tropical Animal Health and Production, 46, 241-246.

Thomas A and Marè C, 1945. Knopvelsiekte. Journal of the South African Veterinary Association, 16, 36–43.

Tildesley MJ, House TA, Bruhn MC, Curry RJ, O'Neil M, Allpress JLE, Smith G and Keeling MJ, 2010. Impact of spatial clustering on disease transmission and optimal control. Proceedings of the National Academy of Sciences, 107, 1041-1046.

Tildesley MJ and Ryan SJ, 2012. Disease prevention versus data privacy: using landcover maps to inform spatial epidemic models. PLoS computational biology, 8, e1002723.

Toma L, Mancini F, Di Luca M, Cecere JG, Bianchi R, Khoury C, Quarchioni E, Manzia F, Rezza G and Ciervo A, 2014. Detection of microbial agents in ticks collected from migratory birds in central Italy. Vector Borne Zoonotic Dis, 14, 199-205.

Truscott J, Garske T, Chis-Ster I, Guitian J, Pfeiffer D, Snow L, Wilesmith J, Ferguson NM and Ghani AC, 2007. Control of a highly pathogenic H5N1 avian influenza outbreak in the GB poultry flock. Proceedings of the Royal Society B: Biological Sciences, 274, 2287-2295.

Tulman ER, Afonso CL, Lu Z, Zsak L, Kutish GF and Rock DL, 2001. Genome of lumpy skin disease virus. Journal of Virology, 75, 7122-7130.

Tulman ER, Afonso CL, Lu Z, Zsak L, Sur JH, Sandybaev NT, Kerembekova UZ, Zaitsev VL, Kutish GF and Rock DL, 2002. The genomes of sheeppox and goatpox viruses. Journal of Virology, 76, 6054-6061.

Tuppurainen E and Oura C, 2014. Lumpy skin disease: an African cattle disease getting closer to the EU. Veterinary Record, 175, 300-301.

Tuppurainen ES, Lubinga JC, Stoltsz WH, Troskie M, Carpenter ST, Coetzer JA, Venter EH and Oura CA, 2013a. Mechanical transmission of lumpy skin disease virus by *Rhipicephalus appendiculatus* male ticks. Epidemiology and infection, 141, 425-430.

Tuppurainen ES and Oura CA, 2012. Review: lumpy skin disease: an emerging threat to Europe, the Middle East and Asia. Transboundary and Emerging Diseases, 59, 40-48.

Tuppurainen ES, Pearson CR, Bachanek-Bankowska K, Knowles NJ, Amareen S, Frost L, Henstock MR, Lamien CE, Diallo A and Mertens PP, 2014a. Characterization of sheep pox virus vaccine for cattle against lumpy skin disease virus. Antiviral research, 109, 1-6.

Tuppurainen ES, Stoltsz WH, Troskie M, Wallace DB, Oura CA, Mellor PS, Coetzer JA and Venter EH, 2010. A potential role for ixodid (hard) tick vectors in the transmission of Lumpy Skin Disease virus in cattle. Transboundary and emerging diseases. doi: 10.1111/j.1865-1682.2010.01184.

Tuppurainen ES, Venter EH and Coetzer JA, 2005. The detection of lumpy skin disease virus in samples of experimentally infected cattle using different diagnostic techniques. Onderstepoort Journal of Veterinary Research, 72, 153-164.

Tuppurainen ES, Venter EH, Coetzer JA and Bell-Sakyi L, 2014b. Lumpy skin disease: Attempted propagation in tick cell lines and presence of viral DNA in field ticks collected from naturally-infected cattle. Ticks and Tick Borne Disease. doi:10.1016/j.ttbdis.2014.11.002.

Tuppurainen ESM, Lubinga JC, Stoltsz WH, Troskie M, Carpenter ST, Coetzer JAW, Venter EH and Oura CAL, 2013b. Evidence of vertical transmission of lumpy skin disease virus in *Rhipicephalus decoloratus* ticks. Ticks and tick borne diseases, 4, 329-333.

van Rooyen PJ, Munz EK and Weiss KE, 1969. The optimal conditions for the multiplication of Neethling-type lumpy skin disease virus in embryonated eggs. Onderstepoort Journal of Veterinary Research, 36, 165-174.

Weiss KE, 1968. Lumpy skin disease. In: Virology Monographs. Vienna-New York, Springer Verlag, 111-131.

Yeruham I, Nir O, Braverman Y, Davidson M, Grinstein H, Haymovitch M and Zamir O, 1995. Spread of lumpy skin disease in Israeli dairy herds. Veterinary Record, 137, 91-93.

Yeruham I, Perl S, Nyska A, Abraham A, Davidson M, Haymovitch M, Zamir O and Grinstein H, 1994. Adverse reactions in cattle to a capripox vaccine. Veterinary Record, 135, 330-332.

Young E, Basson PA and Weiss KE, 1970. Experimental infection of game animals with lumpy skin disease virus (prototype strain Neethling). Onderstepoort Journal of Veterinary Research, 37, 79-87.

Zhao Z, Fan B, Wu G, Yan X, Li Y, Zhou X, Yue H, Dai X, Zhu H, Tian B, Li J and Zhang Q, 2014. Development of loop-mediated isothermal amplification assay for specific and rapid detection of differential goat Pox virus and Sheep Pox virus. BMC Microbiology, 14, 10.

APPENDIX

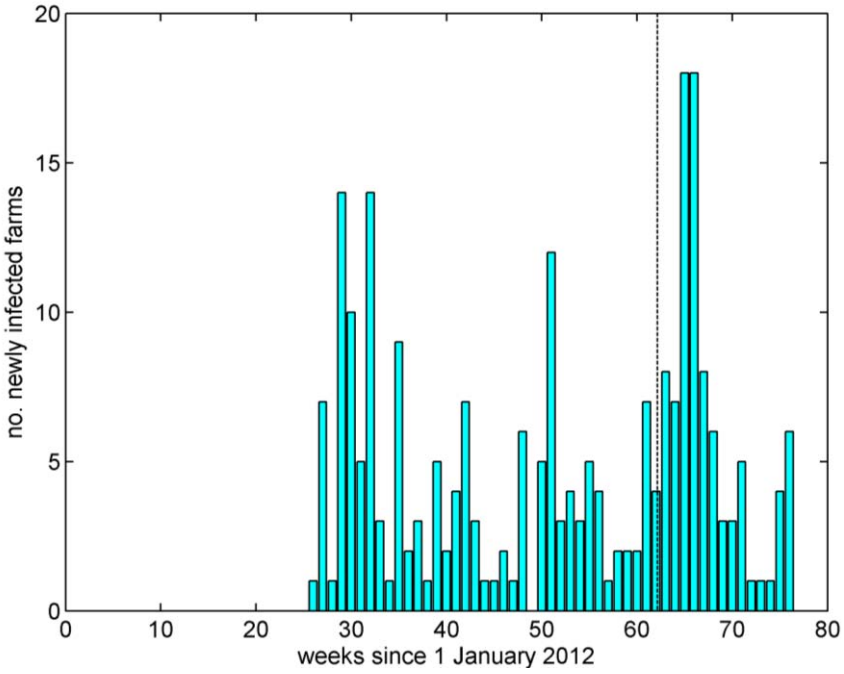
Appendix A. Geographical spread of lumpy skin disease virus

This appendix presents full details of the modelling approach used to describe the geographical spread of lumpy skin disease virus (LSDV). The approach taken was to estimate model parameters using data from the LSDV epidemic in Israel during 2012–2013 (see section 2.1 in the main body of the Opinion). The model using these parameter estimates was then validated against data on reported cases in Turkey. Finally, it was used to explore scenarios for the spread and control of LSDV in Bulgaria and Greece.

MATERIALS AND METHODS

Epidemiological data

The location and time of infection for reported cases of LSDV from the epidemic in Israel during 2012 and 2013 (Figure 16) were used to estimate parameters for the spread of LSDV. Only cases reported between 1 July 2012 (the first case) and 10 March 2013 (after which the more effective vaccines were used) were included in the analysis. In addition, we assumed there was very limited under-ascertainment of cases given the surveillance efforts applied during the epidemic.



The bars show the number of newly infected farms each week, while the black dashed line indicates the date at which the vaccine being used was changed (10 March 2013)

Figure 16: Time course of infected farms for an epidemic of lumpy skin disease virus (LSDV) in Israel, 2012–2013

Demographic data

Demographic data (number of holdings with cattle, number of cattle) for each NUTS (Nomenclature of Units for Territorial Statistics) level 2 (NUTS2) region in Europe for 2010 were extracted from Eurostat. In addition, demographic data (number of holdings with cattle, number of cattle) for each NUTS3 region in Turkey for 2012 were extracted from data provided by the Ministry of Food, Agriculture and Livestock of Turkey.

The epidemiological data from Israel and, hence, the model used to analyse them are at the farm-level. Actual farm-level data could not be obtained for the EU or Turkey and, accordingly, the regional-level data were used to generate synthetic farm-level data-sets for each country of interest (i.e. Bulgaria, Greece and Turkey). This was done by generating a location for each farm in a region by sampling a point uniformly at random from within the boundary of that region and then generating a farm size by sampling from an exponential distribution with mean equal to the mean holding size for the region (European Food Safety Authority 2012). The synthetic data sets were generated using the *maptools* (Bivand and Lewin-Koh) and *spatstat* (Baddeley and Turner, 2005) packages in R (R Core Team, 2012).

Modelling approach

The geographical spread of LSDV was modelled at the farm level. Transmission between farms was modelled using a kernel-based approach. In this case, the force of infection, $\lambda_i(t)$, for farm i on day t is given by,

$$\lambda_i(t) = hN_i \sum_{j \neq i} K(d_{ij}) N_j I_j(t), \quad (1)$$

where h is the transmission parameter, N_i is the number of cattle on farm i, $K(d_{ij})$ is the distance kernel (see below), d_{ij} is the distance between farms i and j and $I_j(t)$ is a variable indicating whether farm j is uninfected (0) or infected (1) on day t.

Both density-dependent and density-independent formulations of the distance kernel, $K(d_{ij})$, were considered (Truscott et al., 2007; Gubbins et al., 2014). For the density-dependent formulation, the kernel is given by,

$$K(d_{ij}) = k(d_{ij}),$$

while for the density-independent formulation it is given by,

$$K(d_{ij}) = \frac{k(d_{ij})}{\sum_{j \neq i} k(d_{ij})}.$$

Three different functional forms for $k(d)$ were explored, reflecting different assumptions about how rapidly the kernel decays with distance. These were,

$$\text{Fat-tailed kernel:} \quad k(d) = \left(1 + \left(\frac{d}{d_0}\right)^{\alpha}\right)^{-1},$$

$$\text{Gaussian kernel:} \quad k(d) = \exp\left(-\alpha d^2\right), \quad (2)$$

$$\text{Exponential kernel:} \quad k(d) = \exp\left(-\alpha d\right).$$

Here α and d_0 are parameters which control the shape of the kernel.

Seasonality in transmission was explored by allowing the transmission parameter, h, to vary over time as follows,

$$h = h(t) = h_0\left(1+\varepsilon\cos\left(\frac{2\pi(t-\phi)}{365}\right)\right), \qquad (3)$$

where h_0 is the mean transmission parameter, $0 \leq \varepsilon \leq 1$ is the seasonal amplitude and ϕ is the seasonal phase.

Once a farm became infected, the duration of the outbreak, T_E, was assumed to be proportional to the log number of cattle (Swinton 1998), that is,

$$T_E = \mu_D \log N, \qquad (4)$$

where μ_D is the constant of proportionality and N is the number of cattle.

Parameter estimation

Parameters in the model were estimated in a Bayesian framework. Because we only have locations for affected farms for Israel, we used a conditional likelihood for the data (Szmaragd et al., 2009). In this case, the likelihood is given by,

$$L = \prod_j \left\{ \frac{\exp\left(-\sum_{t=t_0}^{t_{\text{inf}}^{(j)}-1}\lambda_j(t)\right)\times\left(1-\exp\left(-\lambda_j(t_{\text{inf}}^{(j)})\right)\right)}{\sum_{t_I=t_0}^{t_{\text{end}}}\exp\left(-\sum_{t=t_0}^{t_I-1}\lambda_j(t)\right)\times\left(1-\exp\left(-\lambda_j(t_I)\right)\right)} \right\}, \qquad (5)$$

where $\lambda_j(t)$ is the force of infection defined by equation (1), t_{inf} is the time at which the farm became infected, t_0 is the time at the start of the epidemic and t_{end} is the time at the end of the epidemic.

Non-informative priors (diffuse exponential) were used for the kernel parameters (h_0, ε, ϕ, α and d_0). Three priors were considered for the outbreak duration parameter (μ_D): (i) a non-informative (diffuse exponential) prior; (ii) an informative gamma prior with mean 7.95 and shape parameter 100; and (iii) a Dirac delta function prior, $\delta(\mu_D\text{-}7.95)$ (i.e. fixing the value of μ_D). The value of 7.95 was derived from the farm size (610 cattle) and reported duration (51 days) for an outbreak of LSDV on a dairy farm in Israel in 2006 (Magori-Cohen et al. 2012).

Samples from the joint posterior distribution for the parameters were generated using an adaptive Metropolis scheme (Haario et al. 2001) in which the scaling factor was tuned during burn-in to ensure an acceptance rate of between 20 % and 40 % for more efficient sampling of the target distribution (Andrieu and Thoms, 2008). Two chains of 200,000 iterations were run, with the preceding 200,000 iterations discarded to allow for burn-in of the chain. The chains were then thinned (taking every twentieth sample) to reduce autocorrelation amongst the samples. Convergence of the scheme was assessed visually and by examining the Gelman-Rubin statistic in the coda package (Plummer et al., 2006) in R (R Core Team 2014). The fit of models using the different kernels was compared using the deviance information criterion (DIC) (Spiegelhalter et al., 2002).

Spread of LSDV in Turkey

To simulate the spread of LSDV in Turkey, four large farms in Kahraman Maras province close to the location of the first report case in Turkey were assumed to become infected on 1 August 2013. A total of 1600 replicates of the model were simulated, with parameters for each replicate drawn from the joint posterior distribution obtained from analysis of the Israeli data.

Spread of LSDV in Bulgaria and Greece

When exploring scenarios for spread in the EU, we considered an incursion to Greece and Bulgaria from Turkey on 30 May. More precisely, three large farms (in the 95th percentile of farm sizes) in the Evros region of Greece close to the border with Turkey were seeded with infection; the same three farms were used for all replicates. Two control strategies were investigated: (i) the removal of clinical cases (cf. the epidemic in Israel, 2012–2013); and (ii) whole-herd culling following detection of clinical signs. In the latter case, we assumed an infected farm would be culled either 7 or 15 days after infection. For each scenario 100 replicates of the model were simulated, with parameters for each replicate drawn from the joint posterior distribution obtained from analysis of the Israeli data.

RESULTS

Parameter estimation

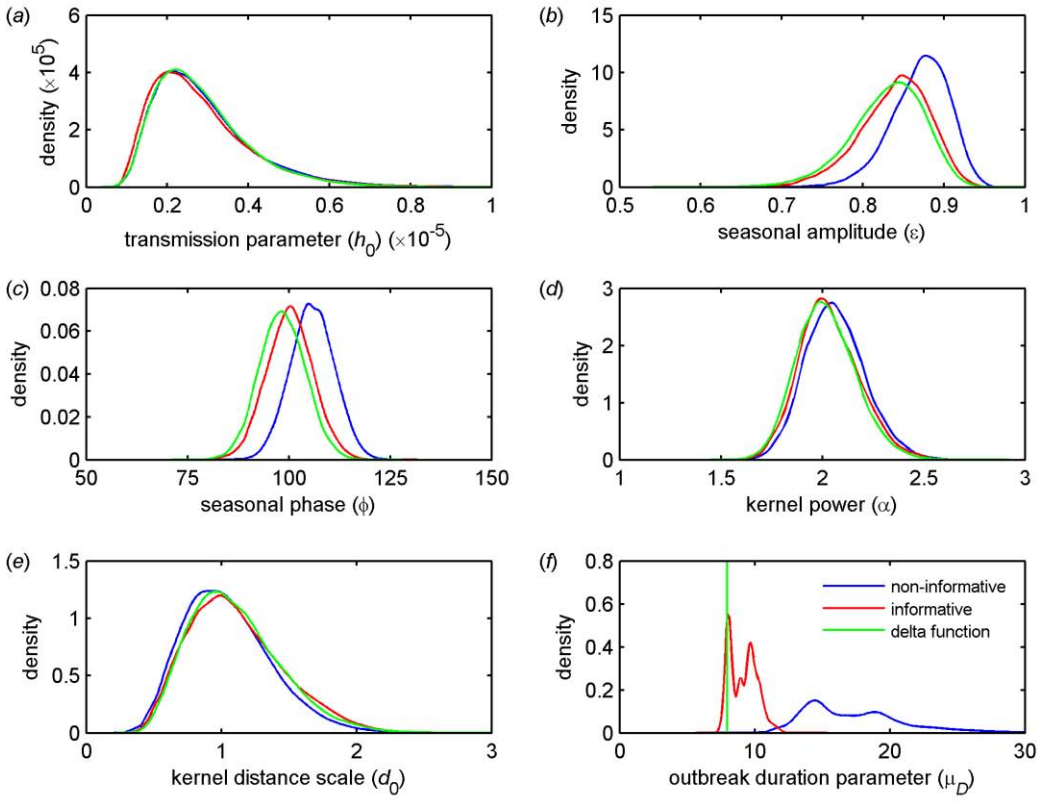
For all kernels, a model including seasonality yielded a better fit than a model without it (Table 4).

Table 4: Comparison of different models for the transmission of lumpy skin disease between farms in Israel based on the deviance information criterion (DIC).

kernel	seasonality	
	no	yes
fat-tailed		
density-dependent	1825.6	1747.3
density-independent	1906.9	1863.6
Gaussian		
density-dependent	1957.6	1896.8
density-independent	1928.7	1882.0
exponential		
density-dependent	1886.1	1824.8
density-independent	1910.8	1846.9

Similarly, density-dependent kernels resulted in a better fit than density-independent ones (Table 4). Overall, the best-fit was for the density-dependent fat-tailed kernel with seasonality, and this form was used in the subsequent simulations.

The prior distribution used for the outbreak duration parameter, μ_D, had limited impact on the estimates for the remaining model parameters (Figure 17).



(*a*) Transmission parameter, h_0. (*b*) Seasonal amplitude, ε. (*c*) Seasonal phase, ϕ. (*d*) Kernel power, α. (*e*) Kernel distance scale, d_0. (*f*) Outbreak duration parameter, μ_D. Results are shown for different prior distributions for the outbreak duration parameter, μ_D: non-informative (blue), informative (red) or delta function (green)

Figure 17: Marginal posterior densities for parameters in a model for the spread of LSDV between farms assuming a density-dependent fat-tailed kernel with seasonality

In particular, the marginal posterior distributions for the transmission parameter (h_0), kernel power (α) and kernel distance scale (d_0) were all similar regardless of the prior for μ_D. However, the seasonal amplitude (ε) and seasonal phase (ϕ) were both higher for the non-informative prior compared with both the informative and delta function prior for μ_D. In the subsequent simulations the joint posterior distribution for the delta function prior was used (i.e. μ_D was fixed at 7.95) (Table 5).

Table 5: Estimates for parameters in the model for the spread of lumpy skin disease assuming a density-dependent fat-tailed kernel with seasonality†.

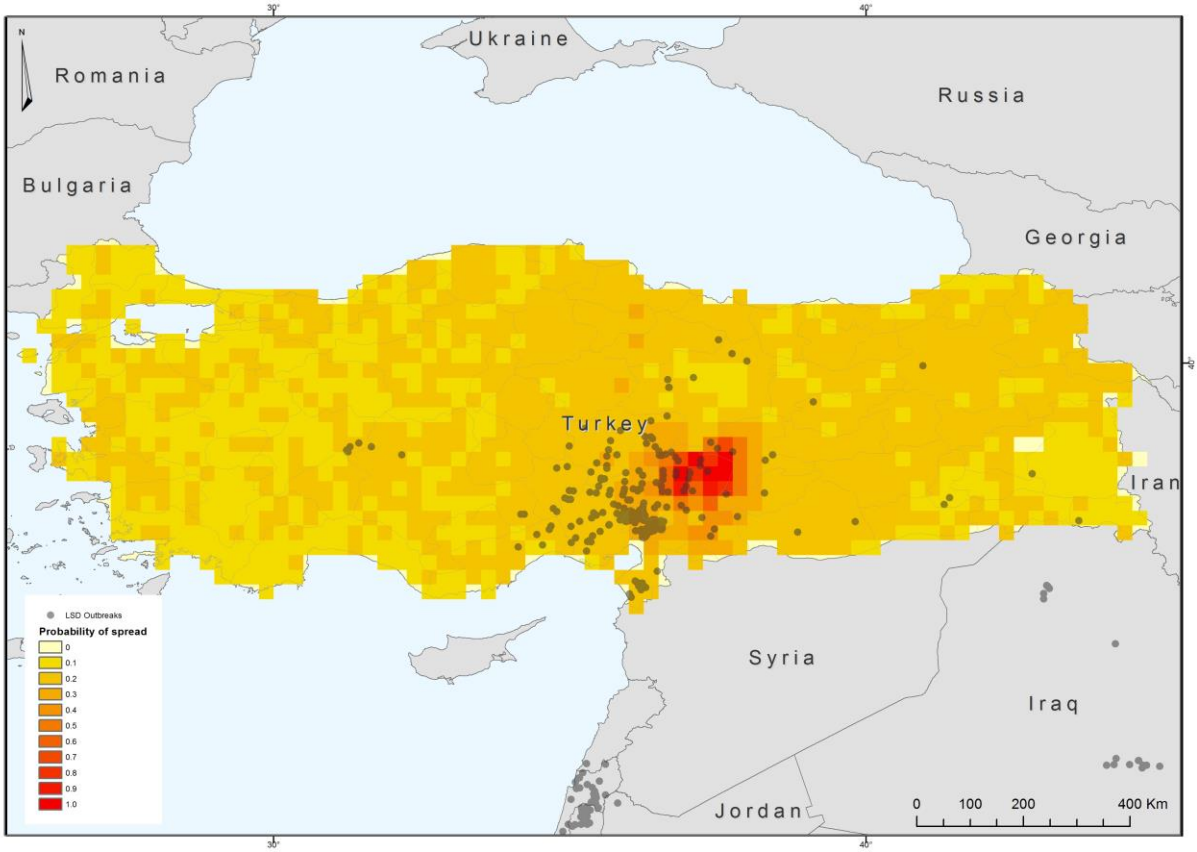
parameter	median	95 % credible limits	
		lower	upper
transmission parameter (h_0)	2.64×10^{-6}	1.25×10^{-6}	5.69×10^{-6}
seasonal amplitude (ε)	0.83	0.73	0.91
seasonal phase (ϕ)	98.34	87.37	109.66
kernel power (α)	2.01	1.76	2.33
kernel distance scale (d_0)	1.05	0.57	1.87
outbreak duration parameter (μ_D)	7.95	-†	-†

† estimates are shown only for the analysis using a delta function prior for μ_D

This choice was made because the estimates for the outbreak duration parameter obtained using either the informative or non-informative priors (Figure 17f) resulted in unrealistically long outbreaks in farms. In particular, the estimated outbreak duration (posterior mean and 95 % credible interval) for a farm of 610 cattle was 115 (77–180) days (non-informative prior) or 58 (49–72) days (informative prior) compared with the reported duration of 51 days (Magori-Cohen et al. 2012).

Model validation: spread of LSDV in Turkey

The model parameterised using Israeli data were applied to synthetic farm location data to predict spread in Turkey (Figure 18).



The map shows the proportion of simulations (indicated by the scale bar) for which at least one farm in a 0.25 ° by 0.25 ° grid square became infected and the location of observed outbreaks (grey circles). Results are based on the model assuming a density-dependent fat-tailed kernel with seasonality using estimates derived using a delta function prior for μ_D (Table 5). The model was run from 1 August 2013 (five days before the first report case) until 14 July 2014 (date of the last report case).

Figure 18: Comparison of the simulated spread of lumpy skin disease (LSD) in Turkey and observed outbreaks (i.e. reported to the OIE)

Most outbreaks predicted by the model were confined to the regions around the initial report cases (assumed to be site of incursion). However, there were outbreaks resulting in substantial geographic spread in Turkey, potentially across the entire country. Comparing the simulated epidemics with the location of report cases indicated that the model does predict a risk of spread to all observed infected locations. However, potential under-ascertainment of infected farms precludes a more formal comparison of model predictions with observed cases.

Discussion

The kernel that yielded the best fit to the Israeli data (fat-tailed, density-dependent) and the corresponding parameter estimates are consistent with lumpy skin disease being transmitted by

vectors. Spread of a vector-borne disease between farms would be expected to be more rapid in a region of high farm density compared with one where farms are at a low density (as reflected in a density-dependent kernel). Moreover, the shape parameters of the fitted kernel (Table 5) indicate a disease in which most spread occurs over a relatively small distance (of the order of a kilometre; $d_0 \approx 1$ km), as would be expected for vector dispersal, but with some transmission over much longer distances (reflected by a relatively low value of $\alpha \approx 2$), as would be expected for less frequent long-distance movement of infected cattle.

In this study, the data on the location and size of individual farms required for the model were not available. According, synthetic farm locations and sizes were generated from regional-level data for Turkey and for Bulgaria and Greece. The impact of using data simulated from regional-level data rather than actual farm locations is, however, difficult to assess. One study reported that, provided the model was carefully parameterised to match epidemic behaviour, it was possible to use random farm locations to identify optimal control measures (Tildesley et al., 2010). Another study determined that, although simulations using empirical and simulated farm locations agree qualitatively, quantitative differences could be substantial (Reeves, 2012). One possibility would be to use land use data (e.g. on location of pasture) to refine the simulated farm locations, which may improve the robustness of model predictions (Tildesley and Ryan, 2012).