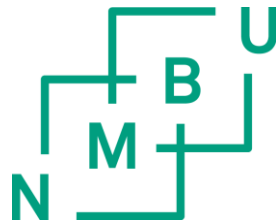


Epidemiological investigations of footrot in the Norwegian sheep population

Thesis for the degree of *Philosophiae Doctor (PhD)*

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2. SUMMARY

Footrot is a contagious disease where *Dichelobacter nodosus*, a Gram negative bacterium, is the necessary transmitting agent. The disease mainly affects small ruminants. The clinical signs range from mild inflammation in the interdigital space to under-running of the claw horn which causes welfare problems and economic losses.

Footrot was detected in Norway in 2008 for the first time since 1948. A surveillance programme was initiated in 2008 which was followed by an elimination programme in 2009. From 2008 to 2012, severe footrot was only diagnosed in the county of Rogaland, but in 2013 the disease was also diagnosed in the county of Aust-Agder. Epidemiological and bacteriological investigations have indicated that the disease was introduced to Norway in 2005 through import of sheep from Denmark.

The spread of *D. nodosus* and the development of footrot are dependent on management and climatic factors. Some of these factors are specific for Norway and are not found in other countries. Therefore, the aim of this study was to perform epidemiological investigations to gain knowledge of footrot under Norwegian conditions. The results produced would be used to inform and help decision making for managing footrot for the Government and the sheep industry.

A retrospective longitudinal study was conducted to investigate the risk factors for introduction of severe footrot into sheep flocks in the south west of Norway. A questionnaire was used as the main data source, and the questions were mainly about direct and indirect contact between sheep flocks. All sheep farms in the municipality of Rennesøy in the county of Rogaland were selected as the study population since the prevalence of footrot was high in this region. Two risk factors were significant: 1) contact with sheep infected with severe footrot through trespassing of fences, and 2) distance (less than 1 km) to the main building of a sheep farm with severe footrot. This shows that proper fences and good maintenance are important for reducing the risk of introduction of footrot into a flock. In addition, reduction of direct and indirect contact between sheep

farms geographically close to each other is recommended. Although no other risk factors were found in this study, purchase of sheep is thought to be the route of introduction to Norway in 2005 and to the county of Aust-Agder and the municipality of Rennesøy in the county of Rogaland in 2006. Therefore, we cannot exclude that other factors are important risk factors in other areas of Norway.

The potential spread of severe footrot in Norway without an elimination programme was estimated with a stochastic compartment model. The model was based on introduction of the disease in Rogaland in 2005, and thereafter a possible spread within and between counties in the whole of Norway. A uniform spread throughout the whole of Norway was not expected since few sheep are transported between the counties of Norway. This is mostly because of the maedi and scrapie legislations prohibiting transport of sheep between counties without derogation. The spread of disease was estimated for each of the 19 counties separately based on climatic factors and the density of sheep flocks within the counties. The possible between-county spread in the model was transport of sheep and cattle and common pasture cooperation. The model was run with sheep flocks as the study unit and year as a time step. If no elimination programme had been initiated in Norway, footrot would have spread to 16 counties and 64% of the sheep flocks would have been infected with footrot by 2035. This would have resulted in welfare problems and large economic losses for the sheep industry. By 2014, footrot would have been introduced in six counties and 19% of the sheep flocks would have been infected. This, compared to the observed total number of flocks with severe footrot in Norway in 2014 (<1%), shows the importance of an early initiation of an elimination programme to reduce the magnitude of the spread.

Surveillance systems are important for control and elimination of animal diseases. Two simulation models were used to estimate the most sensitive of two possible surveillance systems for virulent footrot in Norway. The first system was On-farm surveillance which is targeted surveillance where farms expected to have a higher probability of contracting footrot were examined. The other surveillance system was Abattoir surveillance where the sheep arriving at the abattoir were examined. This was not targeted surveillance, as the examination was performed at randomly selected abattoirs in Rogaland and on randomly

selected days. The surveillance systems were compared based on an equal amount of resources invested. Abattoir surveillance was found to be the most sensitive under Norwegian conditions.

The studies in this thesis have increased the knowledge of footrot under Norwegian conditions. Such knowledge is important for the decision making in the industry and Government.

3. SAMMENDRAG (summary in Norwegian)

Fotråte er en smittsom infeksjonssykdom der *Dichelobacter nodosus*, en Gram negativ bakterie, blir betegnet som det viktigste agenset for infeksjonen. Sykdommen berører hovedsakelig småfe. De kliniske tegnene varierer fra mild betennelsesreaksjon i klauvspalten til underminering av klauvkapselen. Dette gir velferdsproblemer og økonomiske tap.

Fotråte ble oppdaget i Norge i 2008 for første gang siden 1948. Et overvåkningsprogram ble initiert i 2008 og ble etterfulgt av et bekjempelsesprogram i 2009. Fra 2008 til 2012 ble alvorlig fotråte kun funnet i Rogaland fylke, men i 2013 ble sykdommen også oppdaget i Aust-Agder fylke. Epidemiologiske og bakteriologiske undersøkelser tyder på at sykdommen ble introdusert til Norge i 2005 via import av sau fra Danmark.

Spredning av *D. nodosus* og utvikling av fotråte er avhengig av driftsforhold og klimatiske faktorer. Noen av disse faktorene er spesifikke for Norge og finnes ikke i andre land. Derfor var hovedmålet for denne studien å utføre epidemiologiske undersøkelser for å øke kunnskapen om fotråte under norske forhold. Resultatene vil bli brukt til å informere og hjelpe til i beslutningsprosesser vedrørende håndtering av fotråte for myndigheter og næringen.

En retrospektiv longitudinell studie ble gjennomført for å undersøke risikofaktorer for introduksjon av alvorlig fotråte til saueflokker på sør-vest landet i Norge. Et spørreskjema ble brukt som primær datakilde hvor spørsmålene hovedsakelig dreide seg om direkte og indirekte kontakt mellom saueflokker. Alle saueflokkene i Rennesøy kommune i Rogaland fylke ble valgt som studiepopulasjon siden prevalensen av fotråte var høy i dette området. To risikofaktorer var signifikante; 1) kontakt med sau som har alvorlig fotråte gjennom forsering av gjerder og 2) distanse (mindre enn 1km) til hovedbygningen til en sauegård som har alvorlig fotråte. Dette viser at riktige gjerder og godt vedlikehold er viktig for å redusere risikoen for introduksjon av fotråte i en besetning. I tillegg anbefaler vi en reduksjon i direkte og indirekte kontakt mellom sauebesetninger som har kort geografisk

avstand mellom hverandre. Selv om det ikke ble funnet andre signifikante risikofaktorer i denne studien, er kjøp av sau antatt å være introduksjonsveien til Norge i 2005 og til Aust-Agder fylke og Rennesøy kommune i Rogaland fylke i 2006. Derfor kan vi ikke utelukke at det kan være viktige risikofaktorer i andre deler av Norge.

Den potensielle spredningen av alvorlig fotråte i Norge uten et bekjempelsesprogram ble estimert med en stokastisk modell. Modellen var basert på introduksjon av sykdommen til Rogaland i 2005 og deretter spredning innad og mellom alle fylker i hele Norge. Man forventet ikke at fotråte ville spre seg med like stor hastighet gjennom hele Norge da få sauer blir transportert over fylkesgrensene. Dette skyldes først og fremst mædi og scrapie forskriftene som forbyr transport av sau mellom fylkene uten dispensasjon. Derfor ble spredningen av sykdommen estimert for hvert av de 19 fylkene separat basert på klimatiske faktorer og tetthet av saueflokker i de respektive fylkene. Mulige spredningsveier mellom fylkene i modellen er transport av sau og storfe og fellesbeite. Modellen hadde saueflokker som studieenhet og år som tidsenhet. Dersom et bekjempelsesprogram ikke hadde blitt initiert i Norge, ville fotråte ha spredd seg til 16 fylker og 64 % av besetningene ville vært infisert med fotråte innen 2035. Dette ville resultert i velferdsproblemer og store økonomiske tap for saueindustrien. Innen 2014 ville fotråte ha blitt introdusert til seks fylker og 19 % av sauebesetningene ville vært infisert. Når man sammenlikner dette med det totale antallet flokker som er diagnostisert med alvorlig fotråte i Norge i 2014 (<1 %), viser det viktigheten av å initiere et bekjempelsesprogram på et tidlig stadium for å redusere omfanget av spredningen.

Overvåkningsprogram er viktige for å kontrollere og eliminere dyresykdommer. To simuleringsmodeller ble brukt til å estimere den mest sensitive og effektive av to mulige overvåkningsprogram for virulent fotråte i Norge. På-gård overvåkning var en målrettet overvåkning der gårder som er forventet å ha høyere sannsynlighet for å bli smittet av fotråte ble undersøkt. Det andre overvåkningsprogrammet var Slakteriovervåkning der sauer som ankom slakteriet ble undersøkt. Dette var ikke-målrettet overvåkning da undersøkelsene ble gjennomført på tilfeldig valgte slakteri i Rogaland på tilfeldig valgte dager. Overvåkningsprogrammene ble sammenliknet basert på likt økonomisk grunnlag. Slakteriovervåkingen var den mest sensitive og effektive under Norske forhold.

Studiene i denne doktorgraden har økt kunnskapen om fotråte under Norske forhold. Slik kunnskap er viktig for å ta beslutninger om fotråte for næringen og myndigheter.

4. ABBREVIATIONS

AprB2	acidic protease isoenzymes 2 from benign strains
AprB5	acidic protease isoenzymes 5 from benign strains
AprV2	acidic protease isoenzyme 2 from virulent strains
AprV5	acidic protease isoenzyme 5 from virulent strains
BprB	basic protease from virulent strains
BprV	basic protease from virulent strains
CODD	Contagious ovine digital dermatitis
<i>D. nodosus</i>	<i>Dichelobacter nodosus</i>
<i>F. necrophorum</i>	<i>Fusobacterium necrophorum</i>
GG-test	Gelatin Gel test
ID	Interdigital dermatitis
PCR	Polymerase Chain Reaction
RNA	Ribonucleic acid
RPS	The Register of Production Subsidies

5. LIST OF PAPERS

Paper 1

A longitudinal study of the risks for introduction of severe footrot into sheep flocks in the south west of Norway.

Gry M Grøneng, Laura E Green, Jasmeet Kaler, Synnøve Vatn, Petter Hopp, 2014.
Prev. Vet. Med. 113: 241-248.

Paper 2

The potential spread of severe footrot in Norway if no elimination programme had been initiated: a simulation model.

Gry M Grøneng, Synnøve Vatn, Anja Bråthen Kristoffersen, Ola Nafstad, Petter Hopp, 2015.
Vet. Res. 46: 10.

Paper 3

Comparing sensitivity of two surveillance strategies for footrot in Norway by using simulation models.

Gry M Grøneng, Gertraud Schuepbach-Regula, Synnøve Vatn, Petter Hopp
(Submitted Prev. Vet. Med. 23. February 2015).

6. INTRODUCTION

6.1 Background

Footrot in sheep is a contagious disease which can cause major welfare problems and economic losses (Ley et al., 1994; Nieuwhof and Bishop, 2005).

Footrot was reported as early as in the 18th century in England, and in the early 19th century in Australia, France, Germany, Italy and the United States (Beveridge, 1941). Footrot is present in most countries farming sheep throughout the world, and it is endemic in many of these countries (Beveridge, 1941; Graham and Egerton, 1968; Skerman et al., 1982; Stewart, 1989; Ghimire and Egerton, 1996; Hurtado et al., 1998; Younan et al., 1999; Cagatay and Hickford, 2005; Gurung et al., 2006; Green et al., 2007; Aguiar et al., 2011; Rather et al., 2011; Friedrich et al., 2012).

Footrot has been reported in Norway in conjunction with the import of sheep on several occasions in the late 19th century and in 1947, but the disease was eliminated on all occasions. After 1948, footrot was not diagnosed in Norway for many decades (Klevar, 1943; Øverås, 1994). In 2008, footrot was detected in a sheep flock with lameness problems (Meling and Ulvund, 2009). Shortly after the detection of footrot in Norway, a surveillance programme was initiated which was followed by an elimination programme in 2009. Information from other countries showed that management and climatic factors are important factors for the development and spread of the infection. These factors vary from country to country. Therefore, epidemiological investigations under Norwegian conditions were needed, and the research project “Ovine footrot and related contagious bovine claw diseases in Norway” was initiated in which this thesis is included.

In the literature, footrot has been described using different terms. The terms have developed because of the advances in the research on footrot and differences between countries. The terms used are briefly described in this paragraph with reference to more detailed descriptions in other chapters of this thesis. In this thesis footrot is used for describing the disease for which *D. nodosus* is the necessary transmitting agent, regardless

of which species is diseased (Chapter 6.2 "*Dichelobacter nodosus*"). *D. nodosus* can be divided in two groups: benign and virulent *D. nodosus* which can be distinguished by laboratory tests (Chapter 6.2 "*Dichelobacter nodosus*"). Ovine footrot is footrot in sheep (Chapter 6.3 "Pathogenesis"). A division into benign and virulent footrot is also used in the literature; this is based on the severity of the clinical signs in sheep, and in some countries it is also based on laboratory tests that examine the virulence of *D. nodosus* (Chapter 6.4 "Clinical signs"). In some countries, intermediate footrot has also been used and is based on clinical signs in sheep and in some cases laboratory examination (Chapter 6.4 "Clinical signs"). In Norway, severe footrot has been used both for sheep with severe clinical signs of footrot and for sheep diagnosed with virulent *D. nodosus* by the laboratory, regardless of clinical signs (Chapter 6.11 "Footrot in Norway").

6.2 *Dichelobacter nodosus*

Dichelobacter nodosus (*D. nodosus*) is the necessary transmitting agent of footrot (Beveridge, 1941; Roberts and Egerton, 1969). It is a Gram negative, rod shaped anaerobic bacterium. Based on the type IV fimbrial antigens, *D. nodosus* has been classified into 10 serogroups (A-I and M) and at least 21 serotypes (Claxton, 1989; Ghimire et al., 1998; Bhat et al., 2012). The bacterium can be categorised as virulent or benign. Virulent *D. nodosus* usually produce more severe clinical signs in sheep than the benign. Extracellular protease produced by the bacterium is assumed to be important for the severity of the clinical signs as some of the proteases are proposed to be responsible for the tissue damage. The virulent strains of *D. nodosus* produce acidic protease isoenzymes 2 and 5 from virulent strains (AprV2 and AprV5) and basic protease from virulent strains (BprV), while the benign strains produce acidic protease isoenzymes 2 and 5 from benign strains (AprB2 and AprB5) and basic protease from benign strains (BprB). The AprV2 is the major thermostabile protease and is responsible for elastase activity, hence more likely to be virulent than the more thermolabile proteases which is produced by benign strains (Depiazzi et al., 1991; Kennan et al., 2001; Kennan et al., 2010). The thermostability of proteases can be measured by a Gelatin Gel test (GG-test) (Palmer, 1993) and the elastase activity of proteases can be measured by the elastase test (Egerton and Parsonson, 1969).

6.3 Pathogenesis

D. nodosus is the necessary transmitting agent of footrot in sheep (ovine footrot) (Beveridge, 1941; Roberts and Egerton, 1969). Although, there seems to be agreement that presence of the bacteria on intact, dry and healthy skin is usually not alone sufficient to develop footrot. The mechanism behind the reduced defence of the interdigital skin for development of footrot is widely discussed. Environmental conditions such as wet pastures, physical damage of the skin by for instance coarse grass and/or the involvement of one bacterium or a mixture of several bacteria to facilitate the invasion of *D. nodosus* have been discussed (Graham and Egerton, 1968; Egerton, 2014; Witcomb, 2014; Witcomb et al., 2014). In several studies *Fusobacterium necrophorum* (*F. necrophorum*) has been proposed to be the bacterium necessary for the initiation of footrot alone or in synergy with *D. nodosus* (Egerton et al., 1969; Roberts and Egerton, 1969; Bennett et al., 2009). But the possibility that this bacterium rather is a secondary invader in footrot lesions has also been proposed (Witcomb, 2014; Witcomb et al., 2014).

6.4 Clinical signs

The clinical signs of affected sheep range from mild inflammation of the interdigital skin to under-running and separation of the hoof horn from the sensitive tissues (Beveridge, 1941). The severity of clinical signs depends on bacterial virulence, environmental factors and breed of sheep (Stewart, 1989).

To standardize the description of clinical footrot, several scoring systems have been introduced to categorise the severity of the clinical lesions with scores for each foot. Egerton and Roberts (1971) were some of the first to develop such a system, with scores ranging from 0 (healthy) to 4 (worst clinical signs). Most countries use this scoring system or a modification (Whittington and Nicholls, 1995; Foddai et al., 2012). In Norway, we have used a modification of the Egerton and Roberts (1971) scoring system that includes score 5 (separation of the sole and the wall of the hoof from underlying tissue) as described by Whittington and Nicholls (1995) and Woolaston (1993). The Norwegian scoring system also includes a subdivision of score 2 into 2A, 2B and 2C, where 2A is the least affected, and 2C is the worst affected.

Mild redness and inflammation of the skin in the interdigital space is usually the first clinical sign of footrot (score 1). This can be followed by loosening of hair in the interdigital space and a production of odorous pus can sometimes be seen and smelled (score 2A). A separation of the horn from the underlying epithelium in the interdigital space (score 2B), and under-running of the horn along the interdigital space, often the axial aspect (score 2C) can then develop. Separation of the horn on the sole in a half-moon shape (score 3), and further separation of the whole sole to the wall (score 4) is the subsequent development. Under-running of the whole sole and the outer wall of the claw capsule is given the highest score of footrot, a score 5 (The Norwegian Food Safety Authority, 2011; Fig. 1-4).



Fig.1. Sheep foot with clinical signs of footrot score 2B/C (photograph by Gry M Grøneng).



Fig.2. Sheep foot with clinical signs of footrot score 3 (photograph by Gry M Grøneng).



Fig.3. Sheep foot with clinical signs of footrot score 4 (photograph by Gry M Grøneng).



Fig.4. Sheep foot with clinical signs of footrot score 5 (photograph by Gry M Grøneng).

At flock level, a division into benign and virulent footrot has been made based on the severity of clinical signs and, in some countries, the results of the laboratory examination of the involved bacteria (Stewart, 1989; Raadsma and Egerton, 2013). Virulent footrot usually gives the most severe clinical signs and a high within flock prevalence of sheep with clinical signs. The flocks with benign footrot usually have a few sheep with mild clinical signs where the lesions are confined to the interdigital space, and under-running of the hoof horn is seldom seen (Stewart, 1989). Some countries also describe flocks as having intermediate footrot. In these flocks, a low percentage of sheep show severe clinical signs; and a differentiation of an intermediate *D. nodosus* in the laboratory has been proposed to be possible, but inconsistency in the results has been a problem (Stewart, 1989; Abbott and Egerton, 2003; Raadsma and Egerton, 2013). Sheep with footrot may feel pain which may cause additional clinical signs such as lameness and weight loss (further described in Chapter 6.9 “Welfare”). Footrot does usually not cause death, unless the flock is neglected (Beveridge, 1941).

Some breeds are found to be more prone to develop clinical signs of footrot than others. In several studies Merino sheep have shown to be less resistant to initial infection of footrot than British breed sheep (Beveridge, 1941; Skerman et al., 1982; Emery et al., 1984).

Adult sheep have been found to be more susceptible and have more severe lesions than lambs (Beveridge, 1941, 1983; Grogrono-Thomas and Johnston, 1997). However, in Norway, clinical signs of severe footrot have been more frequently seen in lambs than adult sheep (Klevar, 1943; Synnøve Vatn, personal communication).

In addition to sheep, other species can also be infected by *D. nodosus*. Goats can be infected both with the benign and virulent *D. nodosus* (Egerton et al., 1989; Ghimire et al., 1999). Isolation of benign *D. nodosus* from cattle is well known (Egerton et al., 1989; Knappe-Poindecker et al., 2013), and recently virulent *D. nodosus* has also been isolated from cattle co-grazing with sheep (Knappe-Poindecker et al., 2014). No clinical signs or only mild clinical signs are usually reported when cattle and goats are infected with *D. nodosus*. *D. nodosus* has also been isolated from deer (Egerton, 1989), pigs (Piriz et al., 1996), ibex (Belloy et al., 2007) and mouflon (Belloy et al., 2007).

6.5 Differential diagnoses

There are several differential diagnoses for lameness in sheep such as systemic diseases like foot and mouth disease, bluetongue, tetanus, scabby mouth (orf) and muscle diseases. Joint diseases, traumatic injuries and foot lesions can also cause lameness. Footrot is a disease characterised by clinical signs with foot lesions, hence this chapter only includes the differential diagnosis of foot lesions.

It is of great importance that both farmers and veterinarians are informed about the clinical signs of footrot and the possible differential diagnoses. Thereby, early detection of clinical signs, correct diagnosis and treatment is possible. A study by Kaler and Green (2008) showed that 85% of farmers and 98% of specialists correctly identified footrot based on a picture and a written description of different foot lesions. In Norway, when a flock has clinical signs compatible with footrot, samples should be submitted to the

laboratory and the presence of *D. nodosus* is necessary for confirmation of a footrot diagnosis.

Interdigital dermatitis (scald, strip)

The clinical sign of interdigital dermatitis is redness in the skin of the interdigital space. Grey or white paste might also be present. Interdigital dermatitis only affects the interdigital space. The causative agent is *F. necrophorum*. Interdigital dermatitis, footrot caused by benign *D. nodosus*, and early stages of virulent footrot are very similar in appearance and hard to distinguish only by visual examination (Stewart, 1989; Winter, 2004).

Interdigital hyperplasia (fibroma)

The clinical signs of interdigital hyperplasia are overgrowth of skin in the interdigital space. These overgrowths may become infected, often by *F. necrophorum*. The cause is not known, but sheep might be genetically disposed (Winter, 2004).

Contagious ovine digital dermatitis

The clinical signs of contagious ovine digital dermatitis (CODD) are loss of hair and lesions at the coronary band. The lesion can then progress down the claw, under-running the wall of the claw capsule, and in severe cases, complete detachment of the wall can be seen. There are usually no lesions in the interdigital space associated with CODD. The cause of CODD is partly unknown, but bacteria including *Treponemes* phylogenetically identical to those associated with digital dermatitis in cattle have frequently been isolated from the lesions, hence these are thought to be involved in the pathogenesis (Winter, 2004; Duncan et al., 2014).

Shelly hoof (white line degeneration)

The clinical signs of shelly hoof are presence of a half-moon shaped pocket which in some cases is filled with soil or debris. The claw wall has been separated from the laminae at the white line, and pus might be present. The cause is unknown, but might be associated with nutrition or walking on hard surfaces (Stewart, 1989; Winter, 2004).

White line abscess (toe abscess)

The clinical signs of these abscesses are a normal claw horn, but with one or more black marks in the white line. The claw is hot and painful, and the sheep are usually very lame. If not treated, swelling of the skin and pus at the coronary band can be seen. The cause is usually injury or a thorn in the interdigital space (Winter, 2004).

Horizontal and vertical cracks (sand cracks)

White line abscesses with an outburst of pus at the coronary band and laminitis can develop into horizontal cracks. The crack moves downward when the horn grows, and then eventually disappears. When the horn producing tissue at the coronary band becomes damaged, vertical cracks can develop. Infection and pus formation may develop in these cracks and lead to lameness (Winter, 2004).

Pedal joint abscess

The clinical signs of pedal joint abscess are pus and often red granulation tissue at several places of the coronary band. A large swelling is seen, and the sheep usually do not want to bear any weight on the foot. Infection can arrive at the pedal joint from local injury through the skin or from other local infectious lesions. In lambs, the infection may arrive via the bloodstream (Winter, 2004).

Toe granuloma

The clinical sign of toe granuloma is a growth at the toe that looks like a strawberry. The cause might be injury, excessive trimming of the toe resulting in bleeding, or chronic footrot (Winter, 2004).

Laminitis (toxic laminitis, founder)

The clinical sign of acute laminitis is lameness of all four feet, and the claws are warm when palpated. After several weeks one or more deep horizontal lines or grooves can be seen which move down the claw wall with the growth of the horn. Laminitis is inflammation in the corium caused by toxin-producing bacteria. The cause can be over eating of grain or other starchy food, metritis, acute mastitis, difficulties lambing or other generalised diseases (Winter, 2004).

Strawberry footrot

The clinical signs of strawberry footrot are multiple scabs or granulomatous outgrowths which can be accompanied by pus or blood. These lesions are found between the coronary band and the hock or knee. Strawberry footrot is due to small injuries which are often caused by thistles or stubble grass which is infected with orf virus and the bacterium *Dermatophilus congolensis*. Although the name could indicate a relation to footrot, this disease does not look like footrot and is not caused by *D. nodosus* (Stewart, 1989; Winter, 2004).

6.6 Transmission

Sheep with footrot shed *D. nodosus* on mud, pasture and soil. When susceptible sheep are situated in the same area at the same time, the bacteria can be transmitted to their feet (via contamination of the ground) and infection can develop (Beveridge, 1941; Stewart, 1989). In the literature, this is often called direct transmission of *D. nodosus* between sheep, even though the bacterium is not directly transmitted through physical contact between sheep. In this thesis, I will also use direct transmission between sheep referring to this meaning.

The infectious and susceptible sheep do not have to be on the same pasture at the same time for transmission of *D. nodosus* to occur (indirect transmission between sheep). Under favourable environment and weather conditions, the bacteria can survive on pasture up to one week and still be able to infect susceptible sheep (Beveridge, 1938, 1941; Whittington, 1995). The bacteria has also been found to survive up to 24 days on pasture when hoof powder is added to the soil (Cederlöf et al., 2013) and in claw horn trimmings for up to six weeks (Winter, 2009), but the ability to infect susceptible sheep after one week is unknown.

Favourable conditions for the survival of *D. nodosus* outside the host and for the development of clinical signs of footrot are generally warm weather and wet environment (Beveridge, 1941), but differences have been reported between countries. In Australia, a mean temperature above 10°C and long exposure of the feet to wet environments favoured the spread of disease. In dry environments, or when the temperature fell below

10°C, footrot did not spread (Graham and Egerton, 1968). However, in the UK, transmission and expression of footrot are found to occur throughout the year, irrespective of temperature (Ridler et al., 2009; Smith et al., 2014), but the prevalence is lower in areas with colder temperatures and less precipitation (Wassink et al., 2003; Kaler and Green, 2009).

Transmission of *D. nodosus* between flocks can occur through direct and indirect transmission between sheep, as described above, for instance by trade of sheep, shared pastures and travelling stock (Beveridge, 1941; Whittington, 1995; Wassink et al., 2003). Cattle and goats can also act as a reservoir of infection for sheep (Wilkinson et al., 1970; Laing and Egerton, 1978; Ghimire and Egerton, 1996; Ghimire et al., 1999; Knappe-Poindecker et al., 2014). In addition, mechanical transmission through equipment like instruments for paring claws, contaminated boots, vehicles or other species of animals is also possible, but is assumed to have low transmission efficiency (Beveridge, 1983; Stewart, 1989; Wassink et al., 2003).

6.7 Treatment and prevention

There are several ways to treat sheep with footrot, and most of these are also used for prevention. When footrot is detected in a flock, isolation of the affected animals and treatment or culling should be performed as soon as possible to reduce the spread (Beveridge, 1941). To prevent re-infection, all animals which have been treated should be placed in areas where there have not been sheep the last two weeks (Beveridge, 1941). The main methods of treatment and prevention of footrot are listed below.

Trimming of hoof horn (paring)

Trimming of hoof horn removes the excessive claw horn, making the bacteria easier to reach when using a footbath or topical treatment (Fig. 5) (Beveridge, 1941). Recently there have been discussions of whether paring is beneficial in the context of eliminating footrot (Wassink et al., 2003; Kaler and Green, 2009; Kaler et al., 2010). Trimming of diseased and healthy feet could increase transmission through increased environmental load of *D. nodosus* when gathering sheep in small areas for performing paring and through contaminated equipment. In addition, paring can increase the susceptibility to infection by

D. nodosus due to damage caused by excessive trimming (Wassink et al., 2003; Green et al., 2007).

Footbathing

Footbathing can be used both for treatment and prevention of footrot (Beveridge, 1941; Pryor, 1954; Stewart, 1989)(Fig. 6). Footbathing reduces surface bacteria, and thereby prevents *D. nodosus* from invading the interdigital skin of healthy sheep. In addition, footbathing reduces the environmental contamination of *D. nodosus* from infected sheep. Kaler and Green (2009) and Wassink et al. (2003) reported no beneficial effect of footbathing, except in one group in the study by Wassink et al. (2003), where the facilities for footbathing were excellent. This is because when gathering sheep for treatment, the increased stocking density can increase the transmission of *D. nodosus* (Wassink et al., 2003). This shows the importance of good facilities when performing footbathing; otherwise footbathing might promote the spread of *D. nodosus*. Zinc sulphate, copper sulphate and formalin are the most commonly used solvents, but organic acids have also been used in several countries (Stewart, 1989; Wassink and Green, 2001; Winter, 2004; Kaler et al., 2010). Most of the solutions are toxic, hence, care should be taken when using footbaths to reduce the health risk for sheep and farmers and to protect the environment.

Topical foot treatment

Topical foot sprays reduce surface bacteria on the hoof the same way as footbathing, and are used when few sheep are to be treated. Topical antibiotic spray, zinc sulphate or copper sulphate sprays have successfully been used (Stewart, 1989; Wassink et al., 2003). Topical foot sprays have often been used together with parenteral antibiotics (Wassink et al., 2003; Wassink et al., 2010) (see description of parenteral antibiotics below). When a large number of sheep are to be treated, footbathing is more convenient than topical treatment (Pryor, 1954).

Parenteral antibiotics

Parenteral antibiotics are effective in killing bacteria in the deep layers of the hoof and skin and have been used successfully to treat individual sheep for footrot (Egerton et al., 1968; Green et al., 2007). When parenteral antibiotics have been combined with footbathing or

topical foot sprays, the effect has been better than parenteral antibiotic treatment alone (Egerton et al., 1968; Stewart, 1989; Wassink et al., 2003). Because of the risk of antibiotic resistance with widespread use, parenteral and topical antibiotics should only be used for treatment, not as prevention. In addition, correct use of antibiotics is essential for proper treatment and for reducing the probability of resistance. Hence, guidance from a veterinarian is of great importance.

Vaccination

Vaccines are used to prevent infection but have also been reported to accelerate the recovery of infected sheep (Egerton and Roberts, 1971; Beveridge, 1983). *D. nodosus* has 10 serogroups which are related to surface antigenicity and hence have relevance for the protection obtained by vaccination. Many flocks have a multi-serogroup infection (Claxton, 1989; Zhou and Hickford, 2000), and since there is little or no cross-protection between the serogroups, a multi component vaccine is often needed. Multi component footrot vaccines have been found to be less efficient, most probably because of antigenic competition in the host immune system. The vaccines have also been shown to give a short immunity, hence they have to be administered just prior to the transmission period every year (Beveridge, 1983; Stewart, 1989; Wassink et al., 2003).



Fig. 5. Examination and trimming of the claw of a sheep infected with *D. nodosus* (photograph by Gry M Grøneng).



Fig. 6. Footbathing of a sheep in a flock infected with *D. nodosus* (photograph by Gry M Grøneng).

6.8 Control and elimination

Although footrot has been recognized for decades, and considerable research has been performed in the field, the control and elimination of the disease is still a challenge in many countries. Control may be achieved by reducing the environmental load of *D. nodosus* and/or reducing the probability of spread between individuals and flocks. The bacterial strain, climate, season, management system and husbandry practices are factors that have to be taken into consideration to find the best way of controlling and eliminating the disease. Elimination also requires a high sensitivity of diagnosis, low prevalence of disease and a source of non-infected sheep for restocking (Stewart, 1989). In countries where there are potential non-transmission periods, elimination should take place during these periods to reduce the risk of transmission of *D. nodosus* between sheep. In Western Australia the summer is hot and dry and the implementation of an elimination programme in this region has reduced the prevalence of footrot (Mitchell, 2003; Seaman, 2006). In the

UK, there is no period of hot dry weather and footrot has been reported in over 90% of the flocks (Wassink et al., 2003). An elimination programme in this country would therefore be challenging, and a control programme has been implemented instead (Green and George, 2008).

The main ways of controlling and eliminating footrot in sheep flocks are listed below. In addition, to prevent re-introduction of disease, the flock should be kept closed, or new animals should be quarantined (Beveridge, 1941). Goats and cattle can be carriers of *D. nodosus*, hence, these animals also need to be treated or kept separate from the sheep (Beveridge, 1983; Knappe-Poindecker et al., 2014). Under dry weather conditions, the recovery rate of sheep can be high, but since the bacteria can hide in pockets of the claw-wall, some sheep usually remain infected. However, the possibility of some flocks becoming free from footrot without human intervention cannot be excluded in cases of dry conditions for a year or more (Abbott and Lewis, 2005).

Culling affected animals

Culling of affected animals is an effective way of controlling footrot in a flock because it reduces the environmental load of *D. nodosus*, and hence, the spread of disease is reduced. To eliminate footrot from the flock by this method, the sheep that are not culled should be footbathed and re-examined after a few weeks (Beveridge, 1941; Stewart, 1989).

Treatment of affected animals

Treatment of affected animals as described in chapter 6.7 “Treatment and prevention” is another possibility to control footrot. But as *D. nodosus* can survive in small pockets in the claw horn, treatment does not always render the animal free from footrot and hence in a flock, there might be chronic carriers which shed the bacterium. To eliminate footrot from the flock, the affected sheep should not be included in the flock until they are cured. This method requires more labour than the culling of affected animals, because treating affected animals is time-consuming compared to culling (Stewart, 1989).

Complete depopulation

Complete depopulation by slaughtering the whole flock is an efficient way of eliminating footrot. The farm should be empty for at least two weeks before replacements are bought from disease free flocks. This type of elimination is often a very drastic approach for the farmer, and might be inappropriate for genetically valuable flocks (Stewart, 1989).

Selective breeding for resistance

A novel way of controlling footrot is by selective breeding. The aim is to reduce the impact of infection or improve the responsiveness to vaccination (Nieuwhof et al., 2008; Nieuwhof et al., 2009; Raadsma and Dhungyel, 2013; Russell et al., 2013). The results of the studies show the potential of selective breeding for increasing resistance to footrot, but several factors for performing successful selective breeding still require further study.

6.9 Welfare

Footrot causes lesions in the foot of the sheep. This can cause pain, especially when the lesions extend into the corium which is a layer of the foot that contains blood vessels and nerves. When the nerves are affected, the animals feel pain which may be expressed as lameness (Winter, 2004). Decreased food intake can also be observed, possibly because of reduced mobility, less ability to compete for food and general pain (Marshall et al., 1991; Winter, 2004). Lameness are also found to have significantly higher plasma cortisol concentrations (Ley et al., 1994). This parameter shows stress and it is increased in lame sheep most probably because of pain (Ley et al., 1994). Pain in sheep is often not easy to assess as they are prey animals which tend to mask the signs of suffering and distress. Different ways to assess welfare in sheep include thoroughly observing and examining the animals, studying databases of health and performance and by measuring various physiological parameters.

In 1965, one of the first definitions of animal welfare was stated in the Brambell Report. The Farm Animal Welfare Council later refined the contents of the Brambell Report to describe welfare as the Five Freedoms (Farm Animal Welfare council, 2009). The freedoms are: 1) Freedom from thirst and hunger, 2) Freedom from discomfort, 3) Freedom from pain, injury and disease, 4) Freedom to express normal behaviour and 5) Freedom from

fear and distress (Farm Animal Welfare council, 2009). Lamé sheep are affected by at least three out of the five freedoms (3, 4 and 5). This shows the importance of controlling and eliminating footrot to reduce welfare concerns for the affected sheep.

6.10 Economic consequences

Economic consequences of footrot can be due to loss of performance, reduced value of stock for sale, cost of preventive measures, treatment and elimination of the disease (Stewart, 1989; Nieuwhof and Bishop, 2005). Lost performance includes reduced slaughter weight and reduced wool growth (Marshall et al., 1991). In addition, weakened body condition can result in fewer lambs and a higher probability of barren ewes, ewes not producing healthy lambs and having problems with colostrum production and rearing, which in turn can lead to increased lamb mortality (Winter, 2004). Lower sperm count in rams has also been found as a result of lameness (Winter, 2004). The costs of footrot in Norway have not been calculated. In Great Britain, there were approximately 16.4 million breeding ewes in 2003 (Nieuwhof and Bishop, 2005) and footrot was found to be present in 90% of the flocks (Kaler and Green, 2008). In 2005, footrot was estimated to cost the industry in Great Britain £24 million annually (Nieuwhof and Bishop, 2005) which corresponds to approximately €35 million.

6.11 Footrot in Norway

6.11.1 Introduction and spread

Footrot was detected in Norway in 2008, for the first time since 1948 (Meling and Ulvund, 2009). The first cases of severe footrot were detected in the county of Rogaland, and further investigations showed that the disease was present in 1.5% of the sheep flocks in this county in 2008. In particular, the disease had a high prevalence in the municipality of Rennesøy where 11.2% of the sheep flocks were infected with severe footrot (Fig. 7). For five years the disease was only found in the county of Rogaland, but in autumn 2013, 14 flocks were diagnosed with severe footrot in the county of Aust-Agder in the southern part of Norway. By January 2015, a total of 121 flocks had been diagnosed with severe footrot in Norway (Fig. 7 and 8).

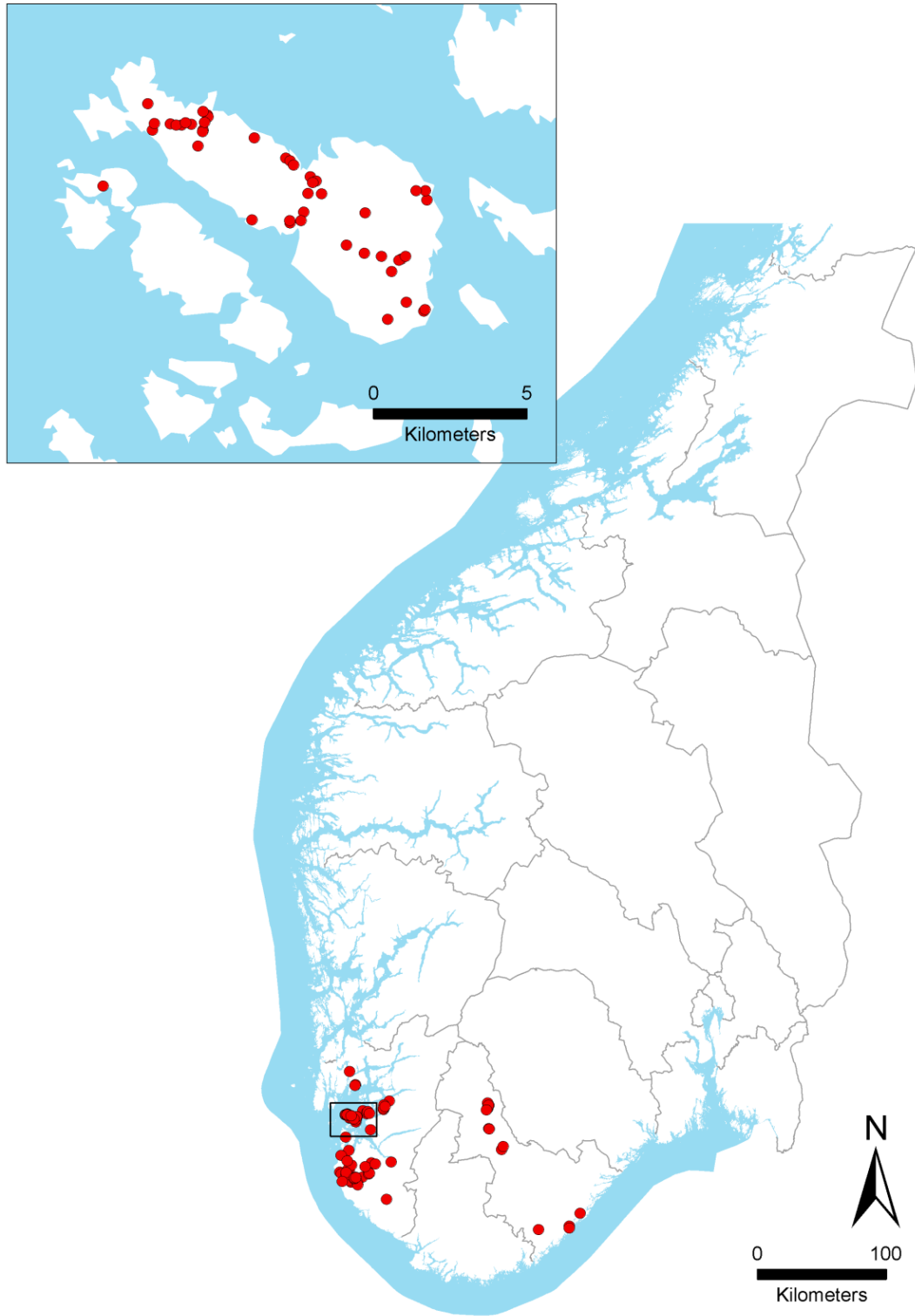


Fig. 7. Map showing the geographical distribution of flocks diagnosed with severe footrot from 2008 to 2014 in Norway and Rennesøy (map detail). The map is based on data from the Healthy Feet Project (made by Attila Tarpai, The Norwegian Veterinary Institute).

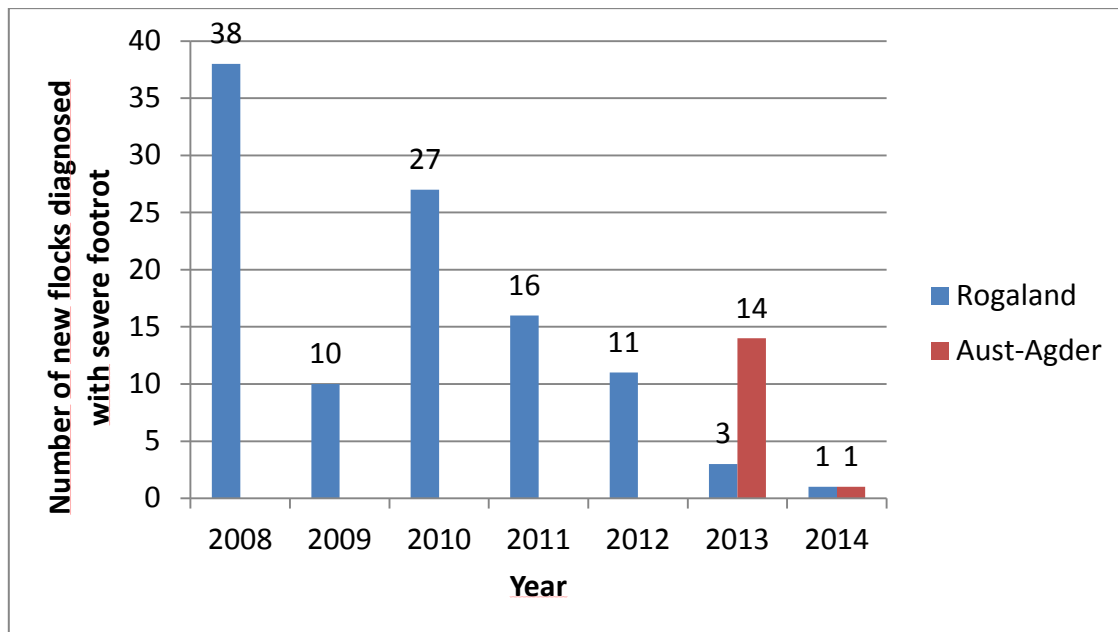


Fig. 8. The number of new flocks diagnosed with severe footrot from 2008 to 2014 in Norway. Footrot was only detected in the county of Rogaland from 2008 to 2012. In 2013 it was also detected in the county of Aust-Agder. The figure is based on data from the Healthy Feet Project (made by Gry M Grøneng).

The term severe footrot has been used in Norway to include both flocks with diagnosed virulent strains of *D. nodosus* and flocks with severe clinical signs of footrot together with a positive PCR result for detection of *D. nodosus* (Vatn et al., 2012). This is because a method for differentiation between virulent and benign *D. nodosus* was not available in Norway until 2009. Hence, in 2008 and 2009 flocks were defined as having severe footrot solely based on severe clinical signs and a PCR test for 16 S RNA of *D. nodosus*. The PCR test could only detect the presence of *D. nodosus* and did not differentiate between virulent and benign strains. Epidemiological and laboratory investigations performed in recent years indicate that most of the flocks defined as having severe footrot in 2008 and 2009 also were infected by virulent *D. nodosus*. From 2010 and onwards, testing for differentiation of benign and virulent *D. nodosus* by a GG-test has been routinely performed.

The possibility of differentiating between virulent and benign *D. nodosus* in the laboratory in Norway was also important for footrot legislation. Footrot infection in small ruminants with both the virulent and benign *D. nodosus* was notifiable in Norway until 2011. From 2011, only infection with virulent *D. nodosus* has been notifiable in Norway.

Bacteriological investigations have shown that more than 95% of the virulent *D. nodosus* strains in Norway belong to serogroup A, while the benign strains include several different serogroups (Gilhuus et al., 2013). Based on this, and epidemiological investigations, it is believed that virulent *D. nodosus* has been introduced from abroad to the county of Rogaland prior to 2008 and thereafter spread locally (Gilhuus et al., 2013; Gilhuus et al., 2014). An import from Denmark to a single flock in Rogaland in 2005 is the probable route of introduction (Gilhuus et al., 2014; Synnøve Vatn, personal communication). The introduction of footrot to the municipality of Rennesøy in the county of Rogaland and to the county of Aust-Agder is believed to have occurred by purchase of sheep from Rogaland in 2006 (Synnøve Vatn, personal communication).

6.11.2 Surveillance and control

A regional surveillance programme was initiated by the sheep industry in Rogaland in 2008, followed by a co-operative national elimination programme named the Healthy Feet Project (Healthy Feet project, 2009; Vatn et al., 2009). This was a collaboration between the Norwegian Food Safety Authority, The Norwegian Veterinary Institute and the sheep industry. Clinical examination of more than 5000 sheep flocks was performed during the years 2008-2014. This is approximately 35% of the whole Norwegian sheep population and includes close to 100% of the flocks in Rogaland. In addition, more than 4000 PCR samples and 2500 bacteriological samples were submitted for examination and differentiation of *D. nodosus* in the laboratory of the Norwegian Veterinary Institute (Healthy Feet project, 2009, 2010, 2011, 2012, 2013, 2014). Most flocks were examined at the farms, but examination of sheep arriving at abattoirs was performed as a pilot study during 2012 and 2013 and included as a part of the surveillance and control programme in 2014. Clinical signs of severe footrot have been reported the whole year round, but 80% of the flocks have been diagnosed from August to November (Synnøve Vatn, personal communication). These months are therefore believed to be the main period for transmission and development of footrot in Norway.

The Healthy Feet Project aims to eliminate severe footrot in Norway (Healthy Feet project, 2014). Flocks that are diagnosed with severe footrot are isolated and elimination is

initiated. Complete depopulation has been recommended in areas with a high incidence of footrot, such as in the municipality of Rennesøy, but culling and treatment of affected animals in a flock has also been used in the elimination programme. To limit the spread of severe footrot, flocks that have been in contact with diagnosed flocks and flocks where there is a suspicion of severe footrot have also been isolated and restricted from all movement and contact with other sheep flocks until examined and declared free from the disease.

6.12 Sheep demography and husbandry in Norway

In 2012 there were approximately 14,315 sheep flocks and 1,107,775 sheep in Norway. The mean flock size is 62.5 breeding ewes (Statistics Norway, 2012). The density of sheep flocks differs substantially between the 19 counties in Norway. The county of Rogaland, situated in the south-western part of Norway, is the county with the highest percentage of sheep flocks (18%) and is also the area with the highest density of sheep flocks in Norway (Fig. 9). The two northernmost counties, Finnmark and Troms, have 0.9% and 3.6% of the sheep flocks, respectively, and thus a low density of sheep flocks (Fig. 9).

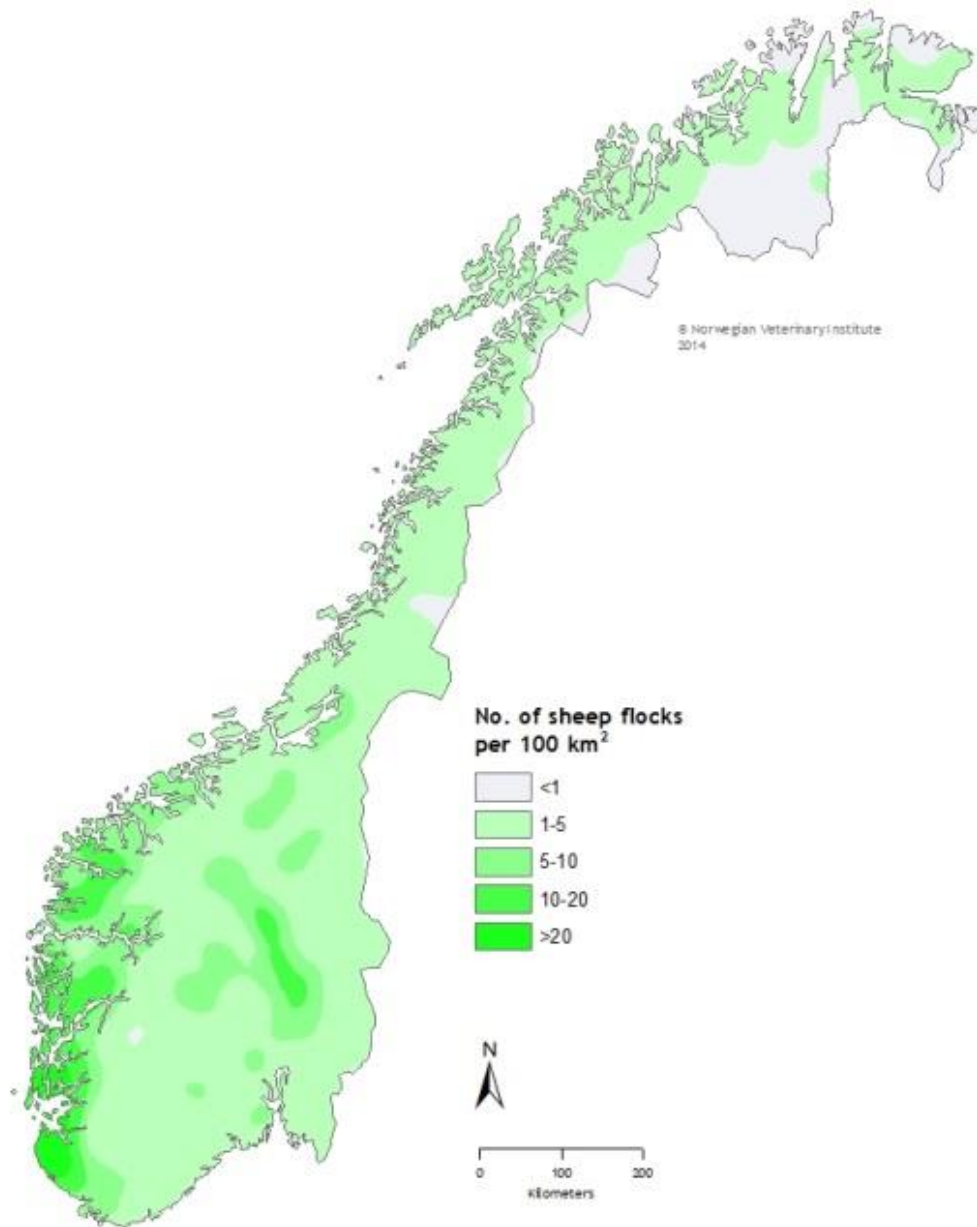


Fig. 9. The density of sheep flocks per 100km² in Norway in 2013 (the map is made by Madelaine Norström, the Norwegian Veterinary Institute).

Norwegian white sheep is the most common breed in Norway, comprising 79% of all the ewes in the Sheep Recording System in 2013 (Jensen, 2013). It is a long-tailed synthetic crossbreed between Dala, Steigar, Rygja and Sjeviot, and is mainly bred for meat production. In addition, there are some other breeds for meat production such as Texel and Old Norwegian Short Tail Landrace, and a few breeds for milk and wool production (The Norwegian Association of Sheep and Goat Farmers).

There is a strong seasonality in the sheep industry in Norway. Most sheep flocks are housed during winter. The type of building and the flooring are variable, but in most farms the humidity and temperature during the winter season would be favourable for developing clinical signs of footrot. The spread of *D. nodosus*, on the other hand, is dependent on the flooring material, which may differ considerably. Slatted floor is usually considered to be the flooring which causes the least spread of footrot, while other flooring types often create a more humid environment and thereby, a higher rate of spread is possible.

Lambs are born by the end of the housing season from March to May and put on pasture shortly after they are born. Common pastures are often used for the whole or parts of the sheep flock during summer (Fig.10). This is an old tradition, and is important both to decrease the feed expenses for the farmer, and for maintaining cultural landscapes and biodiversity (Blumentrath et al., 2014). There are nearly 1000 common pasture groups in Norway, each having several members and designated area for their sheep to graze (Norwegian Forest and Landscape Institute, Ås). The common pastures are mostly situated in the mountain areas. Lower temperatures and less precipitation compared to lowland areas, together with low density of sheep, reduces the rate of spread of *D. nodosus* and development of clinical signs of footrot on common pastures. However, there is a possibility of spreading footrot on these pastures both to flocks within a county and between counties. The spread of footrot between counties is possible since some sheep farmers have common pastures in other counties. In addition, many of the common grazing areas share borders with neighbouring counties common grazing areas, and because there are no fences or other barriers, the sheep from different counties may mix and footrot infection can spread to flocks from another county.

Sheep that are not transported to mountain pastures may co-graze with cattle. This is a common management practice in Norway, since all cattle need to be on pasture for at least eight weeks during summer (The Norwegian Ministry of Agriculture and Food, 2004).



Fig.10. Sheep on mountain pasture in Norway (photograph by Gry M Grøneng).

Sheep and lambs are selected for slaughter when they return from common pastures. The main slaughter season for sheep in Norway is August to November, when 44% of the sheep are slaughtered; of these, 91% are lambs and 9% are adult sheep (The Register of Delivery of Carcasses, Norwegian Agricultural Authority). The ewes that are not slaughtered are mated during November and December. There is a tradition of using ram circles in Norway. These are breeding cooperatives where rams are shared between a group of farmers in order to enhance production performance (Eikje, 1995). There are approximately 170 ram circles in Norway, and 25 are situated in the county of Rogaland (The Norwegian Association of Sheep and Goat Farmers).

Movement of sheep is highly regulated in Norway. Due to maedi-visna legislation implemented in 1975 and subsequent scrapie legislation, there is a general movement ban on small ruminants between counties without derogation (Norsk Lovtidend, 1975). From 1997, there has also been a ban on selling ewes (Thorud et al., 2006). Farmers need to

apply for permission from the Food Safety Authority every time they move sheep between counties, except when transporting sheep to and from common pastures. When a farmer uses common pasture in another county, the farmer only needs to apply for permission to transport the sheep the first year; if accepted, the permission is valid until the farmer changes to another pasture cooperation.

Import of sheep is strictly regulated by the Government (The Norwegian Ministry of Agriculture and Food, 1999, 2005). In addition, The Norwegian Livestock Industry's Biosecurity Unit (KOORIMP) (2014) advises farmers who import sheep to carry out footbathing and isolation for at least two weeks before imported animals are introduced into their flocks. In the period 2005–2013, a total of 249 sheep were imported into Norway (The Norwegian Livestock Industry's Biosecurity Unit (KOORIMP), 2014).

6.13 Climate in Norway

Climate, expressed through temperature and precipitation, is an important factor for the development and spread of footrot (Beveridge, 1941; Graham and Egerton, 1968; Wassink et al., 2003; Kaler and Green, 2009; Ridler et al., 2009). The climate in Norway shows great variation due to the rugged topography and the geographical distance from north to south which has a span of 13 degrees in latitude. The south-western part of Norway, where footrot was first detected, is the area in Norway with the highest annual precipitation and highest mean temperature (Fig. 11). The more northern and inland areas have less precipitation and lower temperatures (Fig. 11).

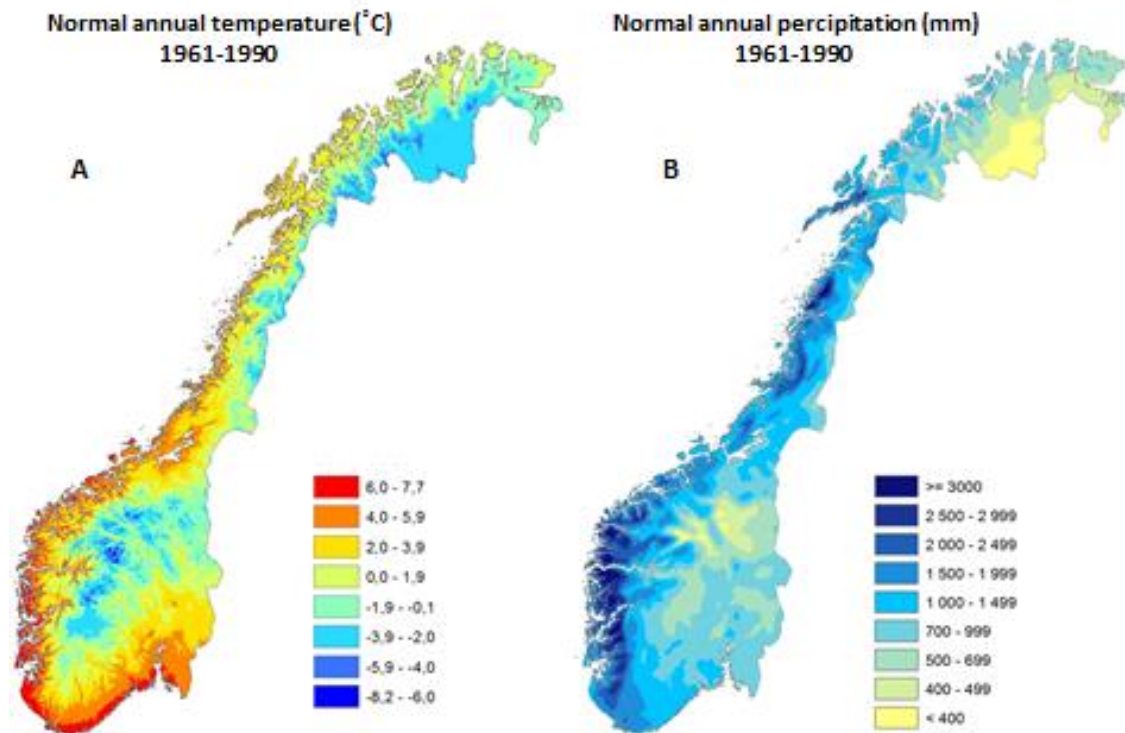


Fig. 11. The average annual temperature and precipitation in Norway from 1961 to 1990. A: Normal annual temperature. B: Normal annual precipitation (maps are made by the Norwegian Meteorological Institute and modified by Gry M Grøneng).

6.14 The need for epidemiological investigations of footrot in Norway

The sheep industry and the government aim to eliminate severe footrot from Norway. Footrot is a complex disease, and management and climate are important factors in its development and spread. Therefore, epidemiological investigations are needed to efficiently control and eliminate the disease. Prohibition of moving sheep between counties and selling ewes, and management such as ram circles and common pastures are practices specific to the Norwegian sheep industry. In addition, the climate and density of sheep flocks are different from many other sheep-producing countries, and show great variation between counties in Norway. These factors may influence the spread of *D. nodosus* and the development of footrot. Therefore, the disease may progress differently in Norway than in other countries. Investigations under Norwegian climatic conditions and management practices are therefore important for developing the most suitable and most efficient system for surveillance, control and elimination of the disease.

7. AIMS

The overall aim of this study was to increase the epidemiological knowledge of severe footrot under Norwegian climate conditions and management. Such knowledge can be used by the Government and the sheep industry to support decisions to implement a more effective and targeted surveillance programme for control and elimination of the disease in Norway.

To meet the overall aim, the specific objectives were to:

1. Identify risk factors for introduction of severe footrot in sheep flocks (**Paper 1**).
2. Estimate the potential spread of severe footrot without an elimination programme (**Paper 2**).
3. Estimate the sensitivity of two possible surveillance strategies for severe footrot (**Paper 3**)
4. Identify possible measures for controlling severe footrot under Norwegian conditions and management (**Paper 1, 2 and 3**)

8. MATERIALS AND METHODS

8.1 Study design

The study design of the research should be chosen based on the objectives, the available material and the knowledge of the advantages and the limitations of the different study designs to reduce the sources of error. The reason for choosing the different study designs in each of the studies is described in the following sections.

8.1.1. Risk factor study (Paper 1)

The objective for this study was to estimate the risks for introduction of severe footrot into sheep flocks in the south west of Norway. Dohoo et al. (2010) outline two main categories of research studies: descriptive and exploratory. In descriptive studies, no measure of association between exposure factors and the disease are made. We wanted to measure the associations, hence we chose an exploratory study. There are two main groups of exploratory studies: experimental and observational (Dohoo et al., 2010). In experimental studies, the conditions can be manipulated and the exposure factors are chosen by the researcher, but they can be difficult to perform, expensive and may have ethical implications. We wanted to explore a wide range of exposure factors in a natural environment, hence the observational study design was found suitable for our study in addition to being cheaper and having fewer ethical implications. Case-control studies and cohort studies are the main types of observational studies (Rothman, 1986). A case-control study is often used when the prevalence of disease is low such as severe footrot in Norway. But since the prevalence of footrot in the municipality of Rennesøy was high, a cohort study of this area was chosen, namely a retrospective longitudinal study with flock as the study unit and year as the time interval. By this approach, we could include all flocks in the municipality and distinguish the outcome and the exposure factors for each flock and time period. The further advantages and limitations of cohort studies are discussed in chapter 10.2 “Methodological considerations”.

8.1.2 Potential spread study (**Paper 2**)

The objective of this study was to estimate the potential spread of severe footrot in Norway without an elimination programme. An experimental study involving the national sheep population would not be possible. In addition, such an experiment would have caused unnecessary pain and lameness to hundreds of sheep. Hence a theoretical model simulating the spread was chosen. Model building is a way to estimate the spread of a disease, and with the right assumptions and model inputs it can give important insight into the population dynamics of infective agents (de Jong, 1995). In a mathematical model the population parameters are described by symbols and linked by the use of mathematical formulae to simulate real-world events (Vynnycky and White, 2010). There are two main categories of mathematical models: deterministic and stochastic. In a deterministic model, development always takes the same course and thereby gives the same outcome because the input parameters are described with one specific value. In a stochastic model, however, development has many possible courses and therefore provides different outcomes due to simulation of a range of values for the input parameters (Vynnycky and White, 2010). We used a stochastic compartment model to ensure that the input parameters could have a range of values. To simulate the spread of severe footrot with no elimination programme we needed a model where we could allocate the different states of the sheep flocks in a simulated epidemic. Several compartmental models have been developed by different researchers. We chose to base our model on the SIR (susceptible, infectious, removed) model by de Jong (1995), but with modifications as described further in **Paper 2**. We used sheep flocks as the study unit and year as the time step. A Pert distribution was chosen for estimating the infection rate within the county of Rogaland. This was based on the knowledge that the rate of spread in the municipality of Rennesøy was much higher than in the rest of the county of Rogaland. By using a Pert distribution where the minimum was Rogaland without Rennesøy, mode was the whole of Rogaland and the maximum was Rennesøy, the difference could be accounted for. The input parameters and the validity of the model are further discussed in chapter 10.1 “Epidemiology of ovine footrot in Norway” and chapter 10.2 “Methodological considerations”.

8.1.3 Surveillance system study (*Paper 3*)

Surveillance may be performed to estimate the prevalence of a disease in a population, to control a disease by detecting infected flocks, for early detection of a disease or to document freedom from a disease. In 2014, only two flocks were detected with severe footrot in Norway. The purpose of a surveillance programme for footrot in Norway in the coming years would be to detect infected flocks and hopefully, within a few years, document freedom from disease.

The objective of this study was to compare two surveillance systems for detecting severe footrot in Norway with regard to their sensitivity. The two surveillance systems were On-farm and Abattoir surveillance. An experimental study was not possible; it would have had ethical implications and been expensive and time consuming. Instead, two different simulation models were developed: 1) a stochastic scenario tree model and 2) a simulation of the surveillance systems to estimate the number of flocks detected with virulent footrot.

1) A stochastic scenario tree model (Martin et al., 2007a; Martin et al., 2007b) was chosen since this is a widely used method to estimate the sensitivity of surveillance systems. The method is based on the probability of detecting at least one positive flock at a given design prevalence. The design prevalence (Cannon, 2002) is the hypothetical proportion of flocks infected in the population. The scenario tree model is applicable for both surveillance systems in this study, although the risk of contracting disease is higher in the population examined in the targeted (On-farm) surveillance than in the non-targeted (Abattoir) surveillance. When using this model to compare the sensitivity of two surveillance systems, we need to have a population with low design prevalence. The reason for this is that we can only estimate the probability of detecting at least one infected flock with this method. This means that a surveillance system where, for instance, ten flocks were detected with footrot could not be differentiated from a surveillance system where, for instance, 30 flocks were detected with the same disease. This is because the probability of detecting one infected flock would be high in both cases and possibly be of equal value. The scenario tree model is also widely used for documenting freedom from disease in an area or country.

2) A simulation of the surveillance systems to estimate the number of flocks detected with virulent footrot complements the scenario tree model by enabling a comparison of two surveillance systems when a high design prevalence is present in an area or country. The method is not the best for comparing two surveillance systems when the design prevalence is very low or for documenting freedom from disease. This is because in these cases, the number of detected flocks would be zero in both surveillance systems, hence the differences are not detected.

The input parameters and the validity of the models are further discussed in chapter 10.1 “Epidemiology of ovine footrot in Norway” and chapter 10.2 “Methodological considerations”.

8.2 Study populations

The main aim of the studies was to generate epidemiological knowledge of footrot in the Norwegian sheep population. In Norway, the whole flock is considered as infected with severe footrot with regard to surveillance and control measures. Hence, the sheep flock was the study unit in all the studies in this thesis. The Register of Production Subsidies (RPS) was the most comprehensive of the available registers of the Norwegian sheep population and therefore used to retrieve the study populations in the various studies (The register is further described in chapter 8.3 “Data sources”).

To estimate the value of the risk factors for spread between sheep flocks in Norway (**Paper 1**) we needed to select an area where severe footrot was present. To obtain a reliable study result, inclusion of the highest possible number of infected flocks was desired. The prevalence of severe footrot was high in the municipality of Rennesøy compared to other parts of Rogaland hence, this was selected as the study area. All sheep flocks registered in the RPS from this area was selected as the source population and thereby received a questionnaire. The study population was all the sheep farms where the farmer answered the questionnaire.

To compare the two surveillance systems (**Paper 3**), data from the Healthy Feet Project were used to estimate reliable input parameters. Rogaland was selected as the study area as this was the county where most of the flocks with severe footrot were situated. All sheep flocks registered in RPS from the county of Rogaland were selected as the study population for the On-farm surveillance and all the sheep flocks registered in the Register of Delivery of Carcasses from the abattoirs in Rogaland were selected for the Abattoir surveillance. (The Register of Delivery of Carcasses is further described in chapter 8.3 “Data sources”).

In the study of the spread of severe footrot without an elimination programme (**Paper 2**), we wanted to estimate the spread from the county of Rogaland to the whole of Norway. All the sheep flocks registered in the RPS from all the counties in Norway were included as the study population.

8.3 Data sources

Several data sources were used in this study. Data can be retrieved from primary and secondary data sources, where data from primary data sources have been collected for the specific purpose in question and data from secondary data sources have been collected for other purposes (Sørensen et al., 1996). All the data sources used in these studies were secondary data sources, except the questionnaire used in **Paper 1**. The secondary data sources were owned by the government or industry as shown in Table 1.

The unique identification number for all the farmers in Norway (holding ID) is registered in most of the registers used in this study. This ID is composed of sets of two digits each with reference to county, municipality, locality, farm and farmer, altogether 10 digits. The holding ID was used when data from different sources were merged.

Questionnaire

A questionnaire was used as the main data source in the risk factor study (**Paper 1**). Questionnaires can be administered through interview or by self-administration. Interviews can be conducted via telephone or face-to-face. Self-administered questionnaires can be delivered by post or internet. For reasons of convenience and

economy, a self-administered questionnaire was chosen for this study. The questionnaire was sent by e-mail to all farmers for whom an e-mail address was known; the remaining farmers received the questionnaire by post. The questionnaire contained 32 binary and multiple choice questions. The information obtained was mainly on direct and indirect contact between sheep in different sheep flocks between 2007 and 2011. The questionnaire was voluntary to fill in.

Register of Production Subsidies (RPS)

The register gives one of the most comprehensive coverage of the Norwegian sheep population and includes >92% of the total number of sheep holdings in Norway; most of the holdings missing are farms with very few sheep. The species, number, sex and age of the animals on each unique holding ID are registered twice a year. The study population in **Papers 1 and 2**, and the study population in the On-farm surveillance in **Paper 3** were selected from the Register of Production Subsidies.

Register of Delivery of Carcasses

For all animals slaughtered at abattoirs in Norway, the species, animal category, holding ID and date and place of slaughter are registered in the Register of Delivery of Carcasses. The study population of the Abattoir surveillance in **Paper 3** was selected from the Register of Delivery of Carcasses.

Register of Pastures

The register includes approximately 80% of all the sheep using common pastures in Norway. Information about geographical location, size, and number of flocks using the different pastures is registered in the Register of Pastures. The register was used in **Paper 2** to select pastures where sheep from different counties could mix and transfer infection between counties.

Agricultural Property Register

The Agricultural Property Register contains the geo-referenced locations of the main building of almost all farms in Norway (approximately 97%). The register was used in **Papers 1 and 2** for calculating the geographical distance between sheep farms. The register

was also used in **Paper 2** for linking the geographical locations to the climatic parameters for the area.

Meteorological database

Meteorological stations are distributed throughout the whole of Norway. Records of precipitation, temperature and wind for all the meteorological stations are provided by the Norwegian Meteorological Institute. The institute also provides statistical data and geographical grids in regards to weather and climate registrations. In **Paper 2**, a grid with a cell size of 1x1 km for the whole of Norway with the mean yearly precipitation and temperature was used to estimate the difference in climate between counties.

Norwegian Sheep Recording System

The Norwegian Sheep Recording System includes all the sheep of all member farms with date of birth, ancestry, lambing, purchase and date and reason for culling. All flocks which are part of a ram circle need to be members of the Norwegian Sheep Recording System; membership is voluntary for other flocks. Approximately 25% of Norwegian sheep farmers are found in this register. Animalia (Norwegian Meat and Poultry Research Centre, Oslo) is responsible for the register. The register was used in **Paper 1** to retrieve information concerning ram circles and purchase of sheep.

Registers of the Healthy Feet Project

The Healthy Feet Project is the national surveillance and control programme for footrot, and their register includes information collected during the latest footrot epidemic in Norway. The number and localisation of flocks diagnosed with severe footrot were obtained from the project and used in **Papers 1, 2 and 3**. In **Paper 1** this information was used as the response variable. In **Paper 2** the number of flocks positive for severe footrot in 2008 was used to calculate the rate of spread within Rogaland. In **Paper 3** the number of infected flocks in 2014 was used to estimate the design prevalence in the scenario tree model. The register has also been used as basis for several other parameters in all the papers.

Table 1. Overview of the secondary data sources used in this thesis.

Data source	Ownership	Responsible institution	Primary use
Register of Production Subsidies	Governmental	Norwegian Agricultural Authority	Payment of production subsidies in agriculture
Register of Delivery of Carcasses	Governmental	Norwegian Agricultural Authority	Payment of carcass subsidies
Register of Pastures	Governmental	Norwegian Forest and Landscape Institute	Payment of pasture cooperation subsidies
Agricultural Property Register	Governmental	Norwegian Agricultural Authority	Basic information on agricultural properties (ownership, geo-coordinates, etc.)
Meteorological database	Governmental	Norwegian Meteorological Institute	Weather forecast
Norwegian Sheep Recording System	Industry	Norwegian Association of Sheep and Goat Farmers	Calculating breeding indexes of sheep
Data from the Healthy Feet Project	Industry	Animalia -Norwegian Meat and Poultry Research Centre	Information on the national elimination programme of ovine footrot

8.4 Ethical concerns

There were no animal interventions done in any of the studies. The questionnaire was voluntary, and was reported to the Norwegian Data Protection Authority. There is no other requirement for doing a questionnaire study in Norway when it does not include sensitive personal information. No other ethical concerns were identified and needed to be addressed for this thesis.

9. MAIN RESULTS

The main results are presented paper by paper.

Paper 1

A longitudinal study of the risks for introduction of severe footrot into sheep flocks in the south west of Norway.

The aim of this study was to identify risk factors for introduction of severe footrot in sheep flocks in the south west of Norway.

A retrospective longitudinal study was performed with a questionnaire as the main data source and footrot status of flocks as the response variable. There were two main risk factors: 1) sheep from negative flocks directly or indirectly in contact with sheep in positive flocks by trespassing fences, and 2) geographical proximity of 0–1 km between the main buildings of a positive and negative flock. Trespassing of sheep could be decreased by farmers upgrading and maintaining boundary fences. Since we do not know precisely why farm proximity is an important risk factor, it is difficult to make specific recommendations. But as a general preventive measure, we would encourage farmers to avoid direct and indirect contact between nearby flocks. Furthermore, proximity to a positive flock could be used to select flocks in a targeted surveillance programme. Although movement of sheep by purchase, ram circles or shared pasture did not come out as risk factors for introduction of footrot to sheep flocks in this study, we cannot exclude that they might be important risk factors in other areas of Norway.

Paper 2

The potential spread of severe footrot in Norway if no elimination programme had been initiated: a simulation model.

The aim of this study was to estimate the potential spread of severe footrot in Norway if no elimination programme was implemented and estimate the importance of the different spreading routes of virulent *D. nodosus*.

The stochastic compartmental model was based on the infection rate of the first diagnosed cases and the management and climatic factors specific to Norway. The model showed that by 2013, severe footrot would have spread to six counties and infected 16% of the sheep flocks if no elimination programme had been initiated. If this is compared with the 1% of flocks that were diagnosed in Norway by 2013, it seems that the implemented footrot elimination programme had a large effect. By 2035, it was estimated that severe footrot would have spread to 16 counties and 64% of the sheep flocks. Such an extensive spread would probably have a large negative impact on the sheep industry and the welfare of the sheep. The most effective way to curb the spread of severe footrot was by decreasing the within county infection rate. This could be achieved by decreasing the contact between flocks or by decreasing the environmental load of *D. nodosus*, for example by footbathing sheep, culling diseased sheep or eliminating severe footrot in the flock.

Paper 3

Comparing sensitivity of two surveillance strategies for footrot in Norway by using simulation models

The aim of this study was to assess which of two potential surveillance systems for detecting virulent footrot in Norwegian sheep flocks was most sensitive.

The two surveillance systems are On-farm surveillance and Abattoir surveillance. A stochastic scenario tree model was used to estimate the surveillance system sensitivity for demonstrating freedom from infection at a design prevalence of 0.2% infected flocks. In addition, the number of flocks diagnosed with virulent *D. nodosus* was estimated by simulating both surveillance systems. The comparison was based on an equal amount of resources invested. Abattoir surveillance was estimated to be the most sensitive of the two surveillance systems for detecting virulent footrot in Norway. On-farm examination was found useful when high flock level sensitivity was particularly important, for example for certifying single flocks free from footrot and follow-up on flocks diagnosed with virulent *D. nodosus* and their contacts.

10. DISCUSSION

10.1 Epidemiology of ovine footrot in Norway

10.1.1 Risk factor study (Paper 1)

Two risk factors were significant for the introduction of severe footrot into sheep flocks in Norway: 1) sheep trespassing through fences and coming into contact with animals positive for severe footrot, and 2) at least one sheep farm with severe footrot within 0–1 km.

Previous studies have found that the most important route of transmission of *D. nodosus* is through direct transmission between sheep, for instance, by common pastures or purchase of infected sheep (Beveridge, 1941; Whittington, 1995). Indirect transmission between sheep, for instance by subsequent use of grazing areas, is also possible since the bacteria can survive for at least one week on pasture, in mud and faeces (Beveridge, 1941; Whittington, 1995; Wassink et al., 2003). Transmission through contaminated fomites such as vehicles and boots has also been reported, although the probability of contracting footrot through this route is considered to be low (Beveridge, 1983; Stewart, 1989).

In our study, only factors indicating local spread between farms were significant. Sheep trespassing through fences was an important risk factor. This is in agreement with the knowledge that pasture contamination is an important transmission route for *D. nodosus*. Geographical distance of 0–1 km between an infected and a susceptible farm was the other significant risk factor in this study. The exact factors for transmission were not identified, but it could be due to a general pasture contamination from several routes or through contaminated fomites. This shows that both the risk factors identified in our study are in agreement with mechanisms for spread reported in other countries.

Transmission routes where *D. nodosus* could be spread over larger geographical distances like trade of sheep, transhumance, and sharing rams were not significant risk factors in this study. In the study area (the municipality of Rennesøy) the density of sheep farms is high

compared to other areas in Rogaland and Norway. This might be the reason why transmission routes for local spread were the only significant risk factors in our study. In addition, a very low number of flocks use common pasture in the municipality of Rennesøy, which can explain why this factor was insignificant in the study. Moreover, trade of sheep was minimal in the study period. This is because trade of female sheep is prohibited in Norway, and is only permitted after application to the authorities based on special needs (Thorud et al., 2006). In addition, trade of rams was reduced in this area because of government restrictions on movement of sheep from flocks diagnosed with severe footrot. However, epidemiological investigations of case flocks have revealed that trade of sheep is the most probable explanation for the introduction of footrot to Norway in 2005 (Gilhuus et al., 2014; Synnøve Vatn, personal communication) and for the spread of footrot to the county of Aust-Agder and to the municipality of Rennesøy in 2006 (Synnøve Vatn, personal communication). In addition, one flock is believed to have been infected by *D. nodosus* through common pastures in 2012 (Synnøve Vatn, personal communication). Therefore, although not detected as a risk factor in the study, there are examples showing that long distance spread can also be important in Norway.

The results in our study indicate that local spread may be important once a disease has been introduced to an area with a high density of sheep farms. The results do not exclude movement of animals and common pasture as important mechanisms of spread in less densely populated areas or over larger geographic distances.

10.1.2 Potential spread study (Paper 2)

In this study a stochastic compartment model was used to estimate the possible spread of footrot in Norway without an elimination programme. When designing a model, proper model assumptions and input variables are important for a reliable result, and the validity of the model should be examined.

The model assumptions and input parameters were based on the observed spread of footrot, management factors and demography specific to Norway. Models based on real data are expected to have a higher reliability than models based on assumptions and input parameters from other sources such as expert opinions.

Each of the 19 counties in Norway was assigned as a subpopulation. This was decided based on real data showing little sheep transport between counties in Norway, hence the rate of spread of footrot between counties was expected to be lower than within counties. The reason for the limited transport in Norway is maedi and scrapie legislations stating a general ban of movement of small ruminants between counties without derogations (Thorud et al., 2006). Without legislations, more sheep would probably have been moved across county borders and the spread of sheep diseases between counties in Norway would have been faster. Classical scrapie (Hagen et al., 2000; Sviland et al., 2013) and maedi (Kampen et al., 2013) are examples of diseases whose spread has been limited, most probably because of these legislations. The sheep industry in Norway supports the legislations limiting movement of sheep across county borders, so an increased movement of sheep is not expected. Three routes of transmission of infection between counties were modelled: 1) Movement of sheep 2) Movement of cattle and 3) Transmission through common pasture. There are approximately 1000 goat flocks in Norway, and the flock size is, in general, small. This gives a low probability of spread by this route, hence movement of goats was not included in this study.

Spread of footrot within the counties of Norway was estimated based on the infection rate observed in the county of Rogaland from the assumed introduction in 2005 to the initiation of an elimination programme in 2009. This value was then adjusted to the other counties in Norway based on climate and sheep density in the respective counties and thereafter fitted to the spread observed in the county of Aust-Agder. This gave a rate of spread which was different for each county, and where the counties with a high density of sheep flocks and with wet and warm climates had the highest rate of spread. This is in accordance with the studies by Kaler and Green (2009) and Wassink et al. (2003) which showed that areas of England where the temperature and precipitation were low also had a lower prevalence of footrot.

The validity of the model outputs can be examined by comparing them with data from other geographical areas. In Norway, footrot is only found in two counties, and information about its spread in both these counties has been used for calculating input

parameters for our model. Hence, no national data is available for examining the validity of the output. The climate in the county of Rogaland in Norway is similar to the climate in the UK (Green and George, 2008). Hence, we used the real prevalence of footrot from the UK and compared it with the model outputs for the county of Rogaland. Footrot is endemic in the UK, therefore we compared the data from the UK with the model outputs when the number of infected flocks had stabilised in the county of Rogaland. The estimated prevalence of infected flocks in the county of Rogaland was then 88%, which is similar to the prevalence of between 86% and 96% reported in the UK (Wassink et al., 2003). That the model output for Rogaland was in the same magnitude as seen for the UK increases the trust in the model. For the other counties in Norway, the prevalence of infected flocks was lower than reported in the UK. This was expected since these counties have a lower average temperature, less precipitation and a lower density of sheep flocks than both Rogaland and the UK.

Sensitivity analysis can also be used to increase the validity of the model by determining how variation in individual parameter values affects the outputs of the model. If a parameter is expected to be important for the outcome based on prior knowledge of the disease, the sensitivity analysis should bear out these expectations. The sensitivity analysis showed that climate (temperature and precipitation) and density of sheep flocks were important parameters. When the values of these parameters were increased, the infection rate increased, and thereby a higher number of infected flocks were seen in the model outputs. Also, lower parameter values resulted in a lower number of infected flocks. This is consistent with the knowledge that favourable conditions for the spread of *D. nodosus* and development of footrot are warm climates and humid environments (Beveridge, 1941; Wassink et al., 2003; Kaler and Green, 2009). In addition, this is consistent with the knowledge from **Paper 1** where sheep flocks with less than 1km to an infected flock were at risk of being infected with severe footrot, while a larger geographical distance was not a significant risk factor. These results contribute to an increased reliability of the model.

In the sensitivity analysis, the values of the parameters that caused major changes in the model outcome should be further examined. The climatic value and the density of sheep flocks were two of the parameters that caused major changes in the model outcome. The

modelled time unit was a year, hence changes in the climate during the year are not included, only changes in the yearly median value. With the expected global warming, temperatures and precipitation are not expected to increase with more than 20% within the modelled period (2035), and with this value, the number of infected flocks in 2035 increased with 9% compared to the basic scenario. Similarly, the probability of increase or decrease with more than a 20% in the density of sheep flocks in Norway is not expected, and with a 20% change, no major changes in the model outcome were seen. This shows that the climate and density parameters we have used have a low range of uncertainty. Nevertheless, the climate and density parameters used have been based on available data and have not been calculated based on a generally accepted standard, hence the values used might not be the most appropriate. Therefore we cannot exclude the possibility of other model outcomes.

The rate of flocks with low susceptibility (flocks with natural barriers towards other sheep flocks and flocks that have recovered from the disease) becoming infected was another parameter which changed considerably in the sensitivity analysis. This was one of the few parameters in the model which was not based on real data. Therefore, there was uncertainty about the proper value for this parameter. We cannot exclude the possibility of other model outcomes because of this parameter; hence, further research on this parameter is desirable.

In the case of no elimination programme and no control, virulent footrot is expected to have spread to 16 counties and approximately 64% of the sheep flocks in Norway would be infected by 2035. This shows the possible large impact for the sheep industry, both with regards to animal welfare and economy. This is expected to be a worst case scenario, since no measures of control or elimination are included to reduce the infection rate. In the case of an extensive outbreak of severe footrot, although an elimination programme is not initiated, many farmers would most probably treat or cull severely affected sheep because of welfare issues in addition to increasing their biosecurity. We believe that such measures would reduce the within county infection rate up to 20%, which would reduce the spread of footrot by 11% compared to the scenario described above. This gives 57% infected

flocks by 2035, but still the impact on welfare and economy would be extensive. This model shows the benefits of implementing a national elimination programme in Norway.

The elimination programme in Norway was initiated a year after footrot was diagnosed, and in 2014, the total number of infected flocks was less than 1% and only two counties were affected. In our worst case scenario, six counties and 19% of the sheep flocks were estimated to be infected by 2014. This shows that initiating an elimination programme early in a disease development has benefits with regards to reduced spread.

The most effective way of curbing the spread of footrot in the model was by reducing the within county infection rate. This can be achieved by reducing the environmental load of *D. nodosus* or reducing the contact between flocks, which is further discussed in chapter 10.1.4 "Implications for control". For the spread of *D. nodosus* between counties, common pastures were estimated to be the most important of the transmission routes. However, a total exclusion of this route of spread did not cause a major reduction in the number of infected flocks. The reason for this is that in the model, a successful transmission of disease to a neighbor county is occurring in a more or less similar way and at the same time by all the between county transmission routes. Transmission is dependent on the number of infected flocks, and the higher the number of infected flocks in a county, the higher the probability of transmission to a neighbour county, regardless of transmission route. Hence, when excluding one of the between county transmission routes, the model output indicates that spread will occur by one of the other transmission routes instead. Another important consideration is that between county transmission is most important for the first introduction of disease into a county. But once the infection is introduced, the further increase in the number of infected flocks within the county is dependent on the within county infection rate. This is why the number of infected flocks was not significantly reduced when excluding one of the between county transmission routes.

The results in this study show the importance of early initiation of the elimination programme for the reduced spread of footrot in Norway. If no elimination programme had been initiated, the spread would have been extensive which would have caused welfare issues and large economic losses. The developed model can be used for other areas or

countries when the assumptions and input parameters special for the area in question are implemented.

10.1.3 Surveillance system study (Paper 3)

In this study we have compared two possible surveillance systems for detection of severe footrot in Norway using two different simulation models. Surveillance systems are important for control and elimination of animal diseases. However, there are often limitations with regards to human and financial resources for the surveillance (Stärk et al., 2006), hence a high sensitivity and efficiency of the systems is requested. A surveillance system should be designed based on the purpose of the surveillance, knowledge of the disease and factors important for the disease's development and spread.

By comparing two surveillance systems, their relative strengths and limitations are examined and areas of improvement can be detected. The comparison of the surveillance systems in our study was based on an equal amount of resources invested. The design of the surveillance systems and the input parameters were mainly based on data from the Healthy Feet Project.

The two surveillance systems compared in this study were On-farm surveillance and Abattoir surveillance.

In On-farm surveillance, specially trained foot inspectors performed a clinical examination of all the adult sheep and 20% of the lambs at selected farms. The number of examined adult sheep and lambs was based on experience from the Healthy Feet Project where this was found to be the most convenient. The farms selected in the On-farm surveillance were expected to have a higher probability of being infected with severe footrot because of close geographical distance to other farms or management indicating high contact rate with other sheep farms. This is in accordance with the findings in **Papers 1** and **2** where close proximity to farms infected with severe footrot gives a higher risk of contracting the disease. This type of surveillance is called targeted surveillance (Doherr et al., 2001). Surveillance systems based on sampling from a strata of the population having higher

probability of being infected may increase the probability of disease detection (Martin et al., 2007b).

In the Abattoir surveillance, trained foot inspectors performed clinical examination of 75% of the sheep arriving at the abattoir on randomly selected days. This type of surveillance was not targeted to high risk flocks, but the foot inspectors used less time travelling and assembling the sheep. Hence this surveillance would include examination of a higher number of sheep and sheep flocks at the same unit of time and resources invested compared to the On-farm surveillance. Other surveillance strategies than the two outlined are possible, but we developed the strategies in collaboration with the Healthy Feet Project which used both the surveillance systems in the surveillance of footrot in 2014. Hence, we believe this is very close to what will be used for future footrot surveillance in Norway.

Abattoir surveillance was found to be most sensitive surveillance strategy and the one with which most sheep flocks were detected at a design prevalence of 0.2%. With a higher and lower prevalence and higher and lower amount of resources invested, Abattoir surveillance was still the most sensitive. This shows that Abattoir surveillance is the most sensitive of the two surveillance systems for detecting virulent footrot under Norwegian conditions. This may not seem to be consistent with the knowledge that targeted surveillance usually yields a higher probability of detecting disease (Martin et al., 2007b). This is because in this study, a higher number of animals and flocks could be examined using the Abattoir surveillance compared to On-farm surveillance when an equal amount of resources were invested. In addition, the difference in prevalence of infected flocks when flocks are randomly selected from the population (as in the Abattoir surveillance) and when flocks are exclusively selected among the high risk flocks (as in the On-farm surveillance) was low. Consequently, the high number of flocks examined in the Abattoir surveillance results in a higher sensitivity even if this is non-targeted surveillance. If the surveillance systems were compared based on equal number of flocks examined, the On-farm surveillance would have had the highest sensitivity because of the higher probability of detecting disease in targeted surveillance. But comparing surveillance systems based on equal number of flocks examined would not be proper since financial resources are the

limiting factor in surveillance, and this would be highly different for the Abattoir and the On-farm surveillance. Another factor important for targeted surveillance is how precisely the high risk flocks are defined. A high precision in selecting the high risk flocks in a population would reduce the number of high risk flocks in the population which, in turn would increase the prevalence of infected flocks in the high risk flock group. This would increase the probability of detecting the disease when selecting flocks from the high risk group. If the high risk flocks are not precisely defined, there will be a large group of high risk flocks in the population which reduces the prevalence of infected flocks in the high risk flocks, and thereby reduces the probability of selecting a flock with infection even within the group of high risk flock. Therefore, precise criteria for selecting high risk flocks are important. Nevertheless, optimizing the criteria for high risk flocks is difficult for a disease like footrot because of the complexity of the disease.

Sensitivity analysis can be used to examine if the parameters of the model are performing as expected. Both surveillance systems were sensitive to changes in the within flock prevalence and the prevalence of animals showing clinical signs. This was expected since only the animals that are infected and are showing clinical signs can be detected in the surveillance.

Passive surveillance (examination of flocks because of disease suspicion) and flocks which have been in contact with a flock diagnosed with footrot was not included in the surveillance systems in this study as this would be expected to be similar for both surveillance systems, and hence not yield any additional information when comparing the two surveillance systems. Nevertheless, examination of animals on the basis of disease suspicion is very important for detecting emerging diseases or when the prevalence of disease is low. An On-farm examination would be the best option for excluding false positives and contact flocks by its thorough examination of the flock.

This study showed that Abattoir surveillance is the most sensitive system for detecting virulent footrot under Norwegian conditions and management. On-farm examination can be used for passive surveillance for exclusion of disease in single flocks for instance when a flock is notified because of lameness.

10.1.4 Implications for control

To control and eliminate a disease, an efficient surveillance method, proper treatment and measures for limiting the spread to other flocks are important.

In **Papers 1** and **2** important aspects of the spread of footrot have been studied. In the potential spread study (**Paper 2**), the most effective way to reduce the spread of severe footrot was by decreasing the within county infection rate. This could be achieved by reducing the environmental load of virulent *D. nodosus* or reducing the contact between flocks. Reducing the environmental load of virulent *D. nodosus* can be achieved by the measures described in chapter 6.7 “Treatment and prevention” and 6.8 “Control and elimination”, for instance footbathing and culling diseased sheep. The most important contact routes for local transmission of *D. nodosus* in Norway are the ones found as significant risk factors in **Paper 1**. Sheep trespassing through fences and thereby coming in contact with infected flocks and short geographical distance to an infected sheep farm were factors increasing the risk of contracting severe footrot. Hence, upgrading and good maintenance of fences and encouraging farmers to reduce local contact between flocks are important. However, since the study was performed in a small area of Norway, we cannot exclude the possibility that other risk factors such as purchase of sheep, common pastures and sharing rams are important for spread of the disease in other areas.

Without a good surveillance system, infected flocks will not be detected and the infection can spread. In **Paper 3** the most sensitive of two surveillance strategies for detecting virulent footrot was estimated. Abattoir surveillance was found to be the most sensitive and the best method to detect flocks with virulent footrot in the sheep population of Rogaland. But On-farm examination was estimated to be the most sensitive method to detect footrot infection within a single flock shown by the higher flock sensitivity. On-farm examination is therefore recommended when single flocks need to be examined because of disease suspicion based on clinical signs (passive surveillance) or known contact with infected flocks. In addition, based on the results from **Paper 1**, the flocks in close vicinity to positive flocks should be examined in a surveillance since they are shown to have a high risk of contracting footrot.

The importance of maedi and scrapie legislations for reducing the spread of footrot and other sheep diseases is highlighted in all the studies in this thesis. This, in addition to the prompt initiation of the surveillance and elimination programme in 2008, is probably the reason for the limited geographical spread of severe footrot in Norway.

10.1.5 Climate changes in relation to the spread of footrot

Because of global warming, the annual precipitation might increase by 5–30% and the mean annual temperature may rise by 2.4–4.3 degrees in Norway by 2100 (Nordic Council of Ministers, 2014). The consequence of climate changes with regard to infectious diseases is not known, but a further northern shift of vectors similar to what we have seen in Europe with the spread of Bluetongue (Purse et al., 2005) and tick borne diseases (Lindgren and Gustafson, 2001; Jore et al., 2011) is expected. Also an increased occurrence and rate of spread of microorganisms such as *Vibrio cholerae* and *Campylobacter* species are expected (Nordisk Ministerråd, 2008; Nordic Council of Ministers, 2014).

A wet and warm climate enhances the spread of *D. nodosus* and the development of clinical signs of footrot (Beveridge, 1941; Graham and Egerton, 1968; Wassink et al., 2003; Kaler and Green, 2009). Therefore, global warming would most probably result in an increased rate of spread of footrot in Norway and give a higher within flock prevalence of clinical signs. The rate of spread is potentially already relatively high in the counties in the south-western part of Norway, while further north and in inland areas there are lower average temperatures and less precipitation, hence a lower rate of spread. Therefore, Norway will probably have an increased rate of spread of footrot in the future because of global warming, especially the northern and inland counties. This shows the importance of eliminating footrot and prevent new introduction of the disease in Norway.

10.2 Methodological considerations

10.2.1 Study design

Risk factor study (Paper 1)

A retrospective longitudinal study was conducted to estimate the risk factors for severe footrot. A longitudinal study is a type of cohort study where the exposure status is not known beforehand, but a group of subjects has been selected for which there is thought to be a range of exposures of interest (Dohoo et al., 2010). A case-control study is an alternative study which is often used when the incidence or prevalence of disease is low (Rothman, 1986). We chose a cohort study of the municipality of Rennesøy since the cumulative number of infected flocks was high (38%) in this area. A cohort study in a limited geographical area where the spread has been extensive reduces possible unmeasured confounding and background noise because the study units have numerous characteristics in common (Dohoo et al., 2010). An example of this is the minimal differences in climate between the farms in the small geographical area of Rennesøy. This is an advantage, as climate is of importance for the spread of footrot and differences in climate could have obscured other important risk factors. A prospective study could not be conducted because an elimination program was implemented in Norway in 2009, hence spread was expected to be minimal in the future. A retrospective study was therefore performed. Bias can be a problem in retrospective studies and is further discussed in chapter 10.2.3 "Systematic error". A discrete time survival analysis was used as we wanted to analyse the association between the outcome (infected with severe footrot or not) and several different potential risk factors.

Potential spread study (Paper 2)

A stochastic compartment model was used to simulate the potential spread of severe footrot in Norway. The model was based on the widely used susceptible-infectious-removed (SIR) model (de Jong, 1995) hence the concepts are well known and accepted. We used a stochastic model as this is a closer reflection of the random nature of events in real life as different outcomes can be produced for each iteration (Vynnycky and White, 2010). We used year as the time step in this model. This means that all the units of the

input parameters including the rates at which the susceptible flocks are infected, the infected flocks recover and the recovered flocks are again infected are based on year as the time unit. This is because of the seasonality in the sheep industry in Norway (described in chapter 6.12 “Sheep demography and husbandry in Norway”) where the probability of transmission, developing clinical signs and detection of footrot varies depending on the time of year. By using year as a time step, the spread of footrot through all of the transmission routes could be managed by one time step, even though some of them could occur throughout the year while others are only possible during certain times of the year.

Surveillance system study (Paper 3)

Two simulation models were used to estimate the most sensitive surveillance strategy of On-farm surveillance and Abattoir surveillance. The two simulation models were the scenario tree model and a model simulating the number of infected flocks. A stochastic scenario tree model is a well known concept which has been used to state freedom from several diseases both when using targeted and non-targeted surveillance (Martin et al., 2007b). This is important as On-farm surveillance is targeted and Abattoir surveillance is non-targeted. Also the simulation of the surveillance for estimating the number of infected flocks was used for both surveillance systems. By using a random sampling of the real population of sheep flocks in Rogaland, the differences in number of animals and the percentage of lambs and adults in each flock were included. This reflects the variability that would be seen in a surveillance system.

10.2.2 Random error

Random error arises from fluctuations between an observed or measured value and the true value. The fluctuation could be due to precision limitations in the measurement device or a study population which is not representative for the target population. Where repeated measurements or large sample sizes are used, random errors usually cancel each other out and their sum approaches zero.

All the sheep flocks in the municipality of Rennesøy were selected to receive a questionnaire in the risk factor study (**Paper 1**), and 76% (n=81) answered the questionnaire. Therefore, random error is expected to be small in relation to the source

population of the municipality of Rennesøy. There is a probability of a larger random error when extrapolating to the target population (sheep flocks in the south west of Norway). This could probably have been reduced by conducting a case-control study with random sampling of the sheep flocks in Rogaland. However, as described in chapter 10.2 “Methodological considerations”, a cohort study was determined to be the suitable method in this study.

The potential spread study (**Paper 2**) and the surveillance system study (**Paper 3**) were performed by simulation models. In these kinds of studies, the random error is dependent on the number of iterations performed. For each simulation of a scenario, 2000 iterations were made of the surveillance system study, and 10,000 iterations were made for the potential spread study. These are both large numbers of iterations, hence random error is not expected to be a major problem.

10.2.3 Systematic error (bias)

Systematic errors are reproducible inaccuracies which often persist throughout the entire study. They occur in the same direction and hence do not cancel each other out.

Selection bias

Ideally, when performing research, the study population should be representative of the source population, which again should reflect the target population (Dohoo et al., 2010). When these groups differ and the relation between exposure and disease is different for the responders and non-responders it is called selection bias (Rothman, 1986).

In all the studies in this thesis, the flocks were selected from the RPS. As described in chapter 8.3 “Data sources”, the register does not include flocks with a low number of sheep. These flocks are mostly kept as non-commercial flocks and therefore have little contact with other flocks. Hence, the probability of both introduction of footrot and spread to other flocks is small. The exclusion of these flocks is therefore expected to be of minor concern in relation to the spread of footrot. On the other hand, the flocks can be of importance when dealing with diseases where direct or indirect contact is not necessary for the spread of the disease. An example is foot-and-mouth disease where the contagion

can be spread by wind, and therefore flocks with no contact with other flocks can also be important for disease spread.

The risk factor study (**Paper 1**) is a cohort study of the municipality of Rennesøy. All the sheep flocks in the RPS from Rennesøy were selected for receiving a questionnaire, and therefore selection bias is not a major concern. By using a self-administered questionnaire, more valid responses to sensitive questions are expected than would be obtained by interviews. However, there might be a lower response rate to a self-administered questionnaire (Martin, 1987) which gives a probability of non-response bias. This can be reduced by reducing the number of non-responders (Dohoo et al., 2010). In our study, the farmers who had not replied within approximately two months were contacted by telephone or e-mail. The final response rate was 76%. When examining the two groups of the outcome separately, the response rate was 71% for farmers with flocks diagnosed with severe footrot and 79% for farmers with flocks which had not been diagnosed with severe footrot. This is a good response rate, hence the non-response bias is expected to be low in this study. The study population (sheep flocks in the municipality of Rennesøy) might not completely reflect the target population (sheep flocks in the south west of Rogaland) as Rennesøy is a small geographical area densely populated with sheep farms. Hence we cannot exclude the possibility of other risk factors in other parts of the south west of Norway. This was discussed in chapter 10.1 “Epidemiology of ovine footrot in Norway”.

For the surveillance system study (**Paper 3**), a random selection of the flocks in Rogaland was made from the RPS in the On-farm surveillance and from the Register of Delivery of Carcasses in the Abattoir surveillance. A new random selection was made for each surveillance system, scenario and iteration. A different combination of sheep flocks would be produced for each iteration. Therefore, when a large number of iterations are conducted, all the flocks in Rogaland would probably be included in one or more of the selections. Hence selection bias is not expected to be a major concern in this study.

For the potential spread study (**Paper 2**), all the flocks in the RPS from the whole of Norway were included. A selection bias, other than for the RPS (see discussion above), is therefore not expected in this study.

Detection bias (The certainty of the footrot status)

Detection bias results when animals or flocks infected with an agent are not detected as infected or when animals or flocks which are not infected with an agent are detected as infected. To reduce the possible detection bias, the controls can undergo the same examination as the cases or in retrospective studies, the outcomes may be blinded (Dohoo et al., 2010).

Close to 100% of the sheep flocks in the county of Rogaland have been clinically examined for severe footrot. Many of these flocks have even been examined twice or three times in the active surveillance. In addition, passive surveillance has been considered to be good because both farmers and veterinarians have a large focus on noticing and reporting lame sheep in this area. Hence, the probability of not detecting infected flocks is expected to be minor.

Some flocks infected with benign strains of *D. nodosus* may have been misclassified as having severe footrot. This is because in some instances benign strains can cause more than 5% of sheep to have a footrot score two and even single animals to have a score above two (Glynn, 1993). When clinical signs of footrot have been detected in a flock, samples for laboratory examination have been used to confirm the presence of *D. nodosus* by a PCR test. In addition, a GG-test can be used to distinguish benign and virulent *D. nodosus*, but this test was not developed and used in Norway in 2008 and 2009. Therefore, some Norwegian sheep flocks have been defined as having severe footrot based on clinical signs and PCR test only. There is a probability that some of these flocks have been misclassified. After implementing the GG-test, misclassification is not expected to be a major problem as the test is expected to have a high specificity.

Information bias

Information bias can either be misclassification or measurement bias. Misclassification bias occurs when there are errors in the classification of categorical variables, while measurement bias occurs when there are errors in the classification of continuous

variables (Dohoo et al., 2010). Both primary and secondary data sources were used in this study as described in chapter 8.3 “Data sources”.

A questionnaire was the main data source for the risk factor study (**Paper 1**). A questionnaire can be disadvantageous because of the possibility of misclassification and measurement errors. To reduce possible information bias, the questionnaire was pilot-tested on four sheep farmers in areas outside Rennesøy and was also sent to the local sheep association for discussion. The feedback from the test panel was used to develop the final version of the questionnaire. In addition, when all the questionnaires from Rennesøy were collected, possible links between the respondents were compared. For instance, when one farmer had reported contact with a second sheep flock, the information was compared with information from the second farmer. If inconsistencies were found, the most precise information was assumed to be correct for both farmers involved, and if a contact was only reported from one farmer, the contact was considered valid for both. Also, the information from the respondents concerning purchases and ram circles was cross-checked with other data sources. This way, the probability of information bias is expected to be reduced. In addition, all the sheep farmers in the municipality of Rennesøy received the same questionnaire, therefore we believe that they would have the same misclassification bias. When both groups of the response variable (footrot diagnosis: yes/no) have the same errors of misclassification, it is considered as non-differential. However, we cannot exclude the possibility that sheep farmers who have experienced footrot in their flocks have an opinion of the causative factor for the disease and therefore might answer differently than the farmers whose flocks do not have the disease.

Recall bias might be a problem in the risk factor study since the questions covered five years. However, some of the factors such as pasture sharing, sharing of weighing scales and ram circles does not vary considerably from year to year and records of purchase and selling of sheep must be kept for ten years, therefore recall bias is less likely to be a problem for these factors. For the remaining factors, the questionnaires were compared and cross checked (as described above). In addition, sheep farmers in the south west of Norway have been interested in learning about footrot and possible risk factors for its introduction and spread. This increases the probability of recalling incidences where

contact with other flocks has occurred. Taking all these factors into consideration, recall bias is not expected to be major problem in this study, but cannot be excluded.

The input parameters in the potential spread study (**Paper 2**) and the surveillance system study (**Paper 3**) could have been based on real world data or expert opinions. Using real world data is the best way to mimic the way in which the disease behaves in a population, while expert opinions provide a good way of estimating input data when real data is not available. Almost all the factors in the models in **Papers 2** and **3** were based on existing data extracted from different secondary data sources which have mainly been collected for economic purposes and have therefore been validated by the government or the sheep industry. This reduces the probability of information bias. Some of the input parameters are based on data from complex sources where several calculations have been performed, which may render the models complicated to understand. Although this might be a disadvantage compared to the use of expert opinion, we believe using real data is the best choice. This is also based on the knowledge that collecting expert opinions is time consuming and thorough consideration must be taken when selecting experts and proper phrasing of the questions to reduce possible bias.

Confounding

A confounder is associated with the exposure factor and the outcome at the same time, and might influence the strength of association between the risk factors and the disease (Rothman, 1986). When possible confounding factors are known, they can be controlled by sampling from strata in the population or matching. Age and gender are possible confounding factors for animal diseases, but because we use flock as the study unit in our studies, these are not expected as confounding factors. Other possible confounding factors are flock size and geographical region. If conducting a case-control study in a large area, matching based on region and flock size might have been proper. The risk factor study (**Paper 1**) was a cohort of the municipality of Rennesøy, hence the study population was all the flocks from this region. Therefore geographical region was not a concern.

Approximately 60% of the flocks in this study consisted of 50–150 sheep, and only three of the sheep flocks consisted of more than 400 sheep. Therefore we do not expect flock size to be a major confounding factor in this study. However, to reveal possible confounding

factors, the final model in the risk factor study was tested by including the non-significant factors one by one. A large change of the model estimates would indicate a possible confounding factor. We did not detect any confounding factors by this process; however, we cannot exclude the possibility of confounders that were not adjusted for in the analysis.

10.2.4 Statistical methods

For the risk factor study (**Paper 1**), all the variables with p-value ≤ 0.05 were included in the final model. Another cut off value could have been chosen, but this is the most widely used, and the same two risk factors would have been significant if increasing the cut off value, as the other variables had much higher p-values. Odds ratios and the 95% confidence interval (CI) were estimated. An odds ratio (OR) is a relative measure of effect, and if it deviates significantly from 1 there is a significant association. The OR was 11.4 (3.9,33.2) (95%CI) and 8.6 (2.2,32.9) for the two factors in the final model, hence we interpret the factors to have a significant association with the outcome. The confidence interval indicates the level of uncertainty of the effect estimate, or in other words the sampling error. When the sample size increases, the sampling error decreases and the confidence interval get narrower. The 95% CI means that the true value of the parameter is included in the CI with 95% probability. The study was based on a few flocks (n=81), and the relatively low number is most probably the reason for the wide confidence interval. A larger number of study objects would have been desirable, but sample size was limited by the small number of infected flocks in Norway.

For the potential spread study (**Paper 2**), the outcome was estimated with the median value and 2.5, 25, 75 and 97.5 percentiles. These percentiles were chosen to show the range of possible outcomes when using a stochastic model.

For the surveillance system study (**Paper 3**), the results were shown with the median and the 95% credibility intervals. This has been used to get an impression of the range of the results in the simulation models.

10.3 External validity

External validity relates to how generalizable the results in the studies are to other settings and populations. The representativeness of the study population for the target population in the studies is discussed in 10.2.3 “Systematic error”. For readers in other countries, the validity of the results to other countries might be of interest.

Management, climate and density of sheep flocks are factors important for the spread of *D. nodosus* and development of footrot. Specific factors for Norway include restriction of movement of sheep flocks across county borders and relatively cold climate and low density of sheep flocks. Epidemiological investigations in Norway based on these specific factors were performed in this study. Hence, the results of the studies are not expected to be valid for other countries. However, areas with similar density of sheep farms as Rennesøy might have risk factors similar to those we estimated in **Paper 1**. Also, the within county spread of footrot as seen in **Paper 2** might be similar to areas in other countries with similar climatic factors and density of sheep flocks. In addition, abattoir surveillance may also be the most sensitive surveillance system for detecting footrot in other countries (**Paper 3**).

11. FURTHER RESEARCH

The risk factor study (**Paper 1**) showed two significant risk factors for transmission of severe footrot to sheep flocks. Both these factors were important for local spread. This study only covered a small geographical area, hence a study of a larger area, for instance the whole county of Rogaland, would be useful. Such a study might identify other risk factors including purchase of sheep and use of common pastures which have been shown to be important risk factors in other countries (Beveridge, 1941; Whittington, 1995; Wassink et al., 2003) and the route of spread for some of the cases in Norway (see chapter 10.1.1. "Risk factor study").

Clinical signs of severe footrot have been detected throughout the year in Norway (Synnøve Vatn, personal communication). A spatio-temporal analysis including climatic factors such as temperature and precipitation for a period of time prior to clinical diagnosis of footrot could be conducted. This would be of importance for examining the specific climatic factors for development of clinical signs of footrot in Norway.

The study examining the spread of severe footrot without an elimination programme (**Paper 2**) estimates an extensive spread of severe footrot in Norway. A cost-benefit analysis as an extension of this article would be useful to examine the cost effects of the early initiation of the elimination programme.

12. CONCLUSION

The aim of this thesis was to use epidemiological investigations to increase the knowledge of severe footrot under Norwegian management and climate conditions. The studies were performed to provide information for decision support for the sheep industry and the government for the surveillance, control and elimination of footrot in Norway.

The risk factor study (**Paper 1**) generated knowledge of two important risk factors for introduction of severe footrot in sheep flocks; 1) sheep trespassing through fences and coming into contact with sheep infected with severe footrot and 2) an infected sheep farm less than 1 km from another farm. This knowledge has contributed to the implementation of examination of farms in close vicinity to farms diagnosed with severe footrot in the surveillance and elimination strategy for footrot in Norway. In addition, the knowledge from this study has caused increased awareness of the importance of keeping sheep fences intact for reducing the spread of footrot.

An extensive spread of severe footrot in Norway was estimated if no elimination programme had been implemented (**Paper 2**). This shows the importance of implementing an elimination programme for footrot, and the advantages of early initiation for reducing the spread. The study also showed the importance of the maedi and scrapie legislations (prohibiting transport of sheep across county borders without derogations) for reducing the spread of footrot. The results of this study increased the confidence that virulent footrot was not spread to counties other than Rogaland and Aust-Agder in the years from the assumed introduction (2005) to the first detected case (2008). This was based on the knowledge that the estimated number of infected flocks in these counties would have been large, and therefore probably would have been noticed. The experience gained from the Healthy Feet Project and the results of these studies can be used to motivate the Government and the industry to implement elimination programmes for emerging diseases in Norway in the future.

In the surveillance system study (**Paper 3**), Abattoir surveillance was estimated to be the more sensitive of two possible surveillance systems in Norway. This result increased the confidence of the industry and the government in using Abattoir surveillance for the surveillance of footrot in 2015 and in the coming years.

The results from this thesis increased the knowledge of the spread of severe footrot under Norwegian management and climatic factors. This contributes to a more targeted and efficient surveillance, control and elimination of the disease. This causes fewer sheep to be infected with footrot, which is of high value for the health and welfare of Norwegian sheep.

The results from this thesis may be valid for other countries or regions if the density of sheep flocks and climate is similar to Norway. The models in the studies can be used for diseases in other regions or countries when the assumptions and the input parameters specific for the disease, demography, management and climate in the area or country in question are used.

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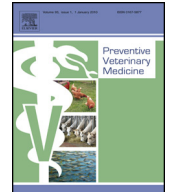
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14. ENCLOSED PAPERS (1-3)



A longitudinal study of the risks for introduction of severe footrot into sheep flocks in the south west of Norway



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ABSTRACT

In 2008, ovine footrot was detected in Norway for the first time since 1948. By December 2012 it had spread to 99 flocks, all in the county of Rogaland in the south west of Norway, and 42% of which were located in the municipality of Rennesøy in Rogaland. The aim of this study was to investigate risk factors for contracting severe footrot in flocks of sheep. A flock was considered positive for severe footrot based on positive virulence test or by clinical signs in addition to a positive PCR test.

A retrospective longitudinal study was performed with a questionnaire as the main data source. All sheep farmers (107) in the municipality of Rennesøy were selected for inclusion in the study. The questions focused on direct and indirect contacts between sheep in different sheep flocks and general information about the farm. The questions covered the years 2007–2011. Data were analysed using discrete time survival modelling.

A total of 81 (76%) farmers responded to the questionnaire including 29 of 41 (71%) farmers with flocks positive for severe footrot. Factors that increased the risk of a flock becoming positive for severe footrot in the final multivariable survival model were sheep that trespassed boundary fences and came into contact with a flock positive for severe footrot (odds ratio 11.5, 95% confidence interval 4.1–32.2) and at least one flock with severe footrot within 0–1 km radius of a farm (odds ratio 8.6, 95% confidence interval 2.3–32.6). This study highlights the importance of upgrading and maintaining boundary fences and encouraging farmers to avoid direct and indirect contact between nearby flocks.

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1. Introduction

In 2008, ovine footrot was detected in Norway for the first time since 1948 (Melting and Ulvund, 2009). Footrot is present in most countries farming sheep throughout the world (Beveridge, 1941; Graham and Egerton, 1968; Gurung et al., 2006; Kaler and Green, 2008). Footrot is painful, and causes lameness and poor welfare (Ley et al.,

1994) and also affects ewe and lamb productivity (Wassink et al., 2010). *Dichelobacter nodosus*, a Gram negative anaerobic bacterium, is the causative agent of footrot in small ruminants (Beveridge, 1941). Sheep are the most affected species and the clinical signs range from mild inflammation of the interdigital skin to under running and separation of the hoof horn from the sensitive tissues (Beveridge, 1941). Footrot is typically categorised by the severity of the clinical foot lesions with scores for each foot ranging from 0 (healthy), 1 to 2 (interdigital inflammation) and 3 to 4 (under running of the sole) (Egerton and Roberts, 1971). Most countries use this scoring system or a modification

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(Whittington and Nicholls, 1995; Foddai et al., 2012). In some countries, scores 3 and 4 have been associated with virulent strains of *D. nodosus* which secrete a heat stable protease that is detected by a gelatin gel test (Palmer, 1993; Gilhuus et al., 2013).

Footrot can spread between sheep flocks by direct and indirect contact between sheep. Direct contact is the most important route of transmission (Whittington, 1995); some potential risk factors are animal trade and shared pastures (Beveridge, 1941; Wassink et al., 2003). *D. nodosus* may survive for up to seven days outside the host (Beveridge, 1941; Whittington, 1995) and pastures contaminated with *D. nodosus* can be a source of infection for 1–24 h after diseased sheep have been removed (Beveridge, 1941). Transmission of footrot through indirect contact in sheep yards (Whittington, 1995) and sharing a road to pasture and sheep transport vehicles (Whittington, 1995) may also be potential sources for spreading footrot. In addition, it is possible that the infection can be spread through contaminated boots or other species of animals (Chimire et al., 1999; Mitchell, 2003). Cattle, in particular, can be infected with both virulent and benign strains of *D. nodosus* and can act as a reservoir of infection for sheep, although this is rare in virulent strains (Wilkinson et al., 1970; Laing and Egerton, 1978) (Maren Knappe-Poindecker, Norwegian School of Veterinary Science, personal communication).

Climate plays a role in the initiation and development of ovine footrot (Beveridge, 1941; Graham and Egerton, 1968). Wet, warm environments favour the expression and spread of footrot (Beveridge, 1941). In Australia, a mean temperature above 10 °C and evenly distributed rainfall sufficient to saturate the soil for considerable periods of time favoured spread of disease, however, when the temperature fell below 10 °C, or when pastures were dry, footrot did not spread (Graham and Egerton, 1968). In the UK, Ridler et al. (2009) demonstrated that transmission and expression of footrot could occur throughout the year, irrespective of temperature and Green and George (2008) highlighted the challenge of understanding elimination and control of footrot in different climates.

Because of varying climates and methods for farming sheep, the risks for development and transmission of footrot vary from country to country, and the design of control and elimination programmes differ. In Western Australia there are periods of hot and dry weather during summer where there is thought to be no transmission of footrot, this makes an elimination programme possible (Mitchell, 2003). In the UK, there is no period of hot dry weather and with a high seasonal and annual rainfall and little variation in temperature and footrot in over 95% of flocks (Wassink et al., 2003), an elimination programme would be challenging (Green and George, 2008).

Footrot is a notifiable disease in Norway (Norwegian Food Safety Authority). When an outbreak with several cases of severe footrot was detected in Rogaland, a county in south west Norway, in 2008, a regional surveillance programme was initiated by the sheep industry, and was followed by a co-operative national elimination programme named the Healthy Feet project.

Clinical inspection of sheep in >4500 sheep flocks was performed between 2008 and 2011, this includes close to

100% of the flocks in Rogaland. In addition, many of these flocks were inspected twice and some three times. In the municipality of Rennesøy in the county of Rogaland, all the sheep flocks were examined in 2008, and the ones not diagnosed with severe footrot were examined again in 2010 and 2011.

Virulent strains of *D. nodosus* have only been isolated from sheep in Rogaland (Vatn et al., 2012), and the majority belonged to the same serogroup (A) (Gilhuus et al., 2013). Benign strains of many serogroups have been found in most parts of Norway. This could indicate recent introduction and local spread of virulent *D. nodosus* (Gilhuus et al., 2013). The term severe footrot has been used in Norway to include both flocks with diagnosed virulent strains of *D. nodosus* and flocks with severe clinical signs of footrot together with a positive PCR result. Virulence testing of isolates of *D. nodosus* was first established in Norway in 2009, and was only done routinely from 2010. Before that, the presence of virulent and benign strains were not elucidated and emphasised, hence, in 2008 and 2009 flocks were defined as having severe footrot solely on severe clinical signs and a PCR-positive test result. From 2010 all flocks examined for footrot were sampled for cultivation and PCR-test, irrespective of clinical signs, and if the PCR-test was positive and culture was successful, virulence testing was performed using the gelatine gel test (Figs. S1 and S2 in Supplementary data 1: Flow diagram for diagnosis of severe footrot). Because of the widespread distribution of benign strains of footrot and the recent outbreak of disease associate with severe footrot the current study focuses on risks for spread of severe footrot. By December 2012, 99 flocks had been diagnosed with severe footrot (Synnøve Vatn, Animalia, personal communication). Of these, 38, 10, 27, 16 and 8 flocks were detected in 2008, 2009, 2010, 2011 and 2012, respectively. A total of 41 flocks were located in the municipality of Rennesøy.

In Norway, outbreaks of disease have occurred throughout the whole year, including winter, but the majority have been during late summer (Synnøve Vatn, Animalia, personal communication). In south west Norway, where all flocks with detected virulent isolates are situated, the rainfall is typically up to 362 mm/month (Norwegian Meteorological Institute, Oslo). In winter there can be periods of cold weather, with sub-zero temperatures, when sheep are typically housed in a barn and the disease might spread. There are no prolonged periods with warm dry weather in the summer. This indicates that there is no non-transmission period in this part of Norway and hence knowledge of risk factors for contracting severe footrot is important when designing an elimination programme.

In 2012, there were 14,315 sheep flocks in Norway, and 2597 of them were situated in the county of Rogaland (Register of Production Subsidies 2012, Norwegian Agricultural Authority, Oslo). The mean flock size was 62.5 breeding ewes (Statistics Norway) and with a flock density varying from 0 to 130 per 10 km² in the county of Rogaland (Register of Production Subsidies 2012, Norwegian Agricultural Authority, Oslo). Norwegian white sheep are the most common breed in Norway, comprising of 69% of all the ewes in the Sheep Recording System in 2006 (The Norwegian Association of Sheep and Goat Farmers). It is a long-tailed

synthetic crossbreed mainly bred for meat production. In addition there are some wool producers but very few sheep milk producers in Norway. There is a tradition of using ram circles in Norway, these are breeding cooperatives where rams are shared between a group of farms (Eikje, 1995). There are approximately 170 ram circles in Norway, and 25 are situated in Rogaland (The Norwegian Association of Sheep and Goat Farmers).

The aim of this study was to investigate risk factors for introduction of severe footrot into sheep flocks in the south west of Norway.

2. Materials and methods

2.1. Study design

The study design was a retrospective longitudinal study using a self-administered questionnaire as the main data source. The sheep flock was the study unit, and data were analysed using discrete time survival modelling (Singer and Willett, 1993; Goldstein et al., 2004).

2.2. Study population

The population consisted of all sheep flocks in the municipality of Rennesøy in the county of Rogaland between 2006 and 2011, a total of 107 sheep flocks (Fig. 1) (Register of Production Subsidies, Norwegian Agricultural Authority, Oslo and Healthy Feet project). Rennesøy is comprised of several islands, sheep flocks are only present on six of them, with 93 (87%) flocks on the two largest islands. All of these, except one island, are connected by bridges or tunnels (Fig. 1).

When flocks were inspected a modification of the Egerton and Roberts (1971) scoring system was used that also included a score 5, separation of the sole and wall of the hoof from underlying tissue (Whittington and Nicholls, 1995). A flock was defined as positive for severe footrot using the criteria explained in the introduction. Thus before 2010 flocks with severe clinical signs (defined as $\geq 5\%$ sheep had footrot score 2 or ≥ 1 sheep had footrot score of 3–5) and a positive PCR test were defined as positive for severe footrot. From 2010 diagnosis of severe footrot was mainly based on a positive virulence test by the gelatinase gel test. If severe clinical signs were present, but no virulent strains were detected, the flock could be considered negative for severe footrot when at least five benign isolates had been cultivated (Figs. S1 and S2 in Supplementary data 1: Flow diagram for diagnosis of severe footrot; Vatn et al., 2012).

2.3. Collection of data

The questionnaire was pilot tested on four sheep farmers in areas outside Rennesøy and was also sent to the local sheep association for discussion. The comments were used to develop the final version of the questionnaire (available in Norwegian on request). The farmers were informed that completing the questionnaire was voluntary. The questionnaire was reported to the Norwegian Data Protection Authority, there were no other requirements for

ethical approval in Norway, because the questionnaire did not include personal or sensitive information. In January 2012, the questionnaire was sent by e-mail to all farmers for whom an was known (67%); the remaining farmers received the questionnaire by post. Farmers who had not replied by the end of February 2012 (71%) were contacted by telephone or e-mail to remind them to return the questionnaire. In addition, information about purchase of sheep was obtained from the Sheep Recording System (Animalia – Norwegian Meat and Poultry Research Centre, Oslo), and information about ram circles (Eikje, 1995) and a list of farms diagnosed with severe footrot was obtained from the Healthy Feet project (Animalia – Norwegian Meat and Poultry Research Centre, Oslo). Georeferenced locations of the sheep farms were obtained from the Agricultural Property Register (Norwegian Agricultural Authority, Oslo).

2.4. Description of variables

The questionnaire included data from 2007 to 2011 and had 32 binary and multiple choice questions on potential risk factors for introduction and transmission of footrot. The questions covered three main subjects; general information on the sheep flock including breed and number of sheep on the farm, direct contacts between flocks including purchase of sheep, ram circles and sharing pasture with other sheep flocks, and indirect contacts between flocks, including sharing weighing scales or roads to pasture (Table 1). For each type of direct and indirect contact, the farmers were asked to give the exact year of the contact and the identity of the other sheep flocks involved. When relevant, the number of sheep that had been in contact, the duration of the contact, and if it was a lamb or adult and which sex were also asked. The data were entered into a spread sheet (Microsoft Excel 2007).

A binary response variable was used to indicate whether or not severe footrot occurred in each year of each flock. Of the 41 sheep flocks diagnosed with severe footrot in Rennesøy municipality (Fig. 1), 12 were diagnosed in 2008, 20 in 2010 and 9 in 2011. Based on this, each flock was subdivided into 3 discrete-time periods, the years 2008, 2009/2010 and 2011. As no mass screening for footrot was performed in the municipality of Rennesøy in 2009, the probability of detecting footrot in 2009 was very low. Therefore, the years 2009 and 2010 were analysed together. The robustness of the model was tested by analysing the data with the years 2009 and 2010 kept separately, by excluding 2009 data, or excluding 2010 data. The first diagnosed case of severe footrot in Norway was in 2008, hence information on the response variable was only available from 2008 and onwards and could not be used for previous years.

For each flock, time period and type of contact, the number of other flocks and other positive flocks that had been in contact was calculated. Binary predictor variables were then calculated based on zero or more contacts with other positive flocks that could potentially have transmitted the infection. A flock was considered as a potential transmitter of infection the year it was diagnosed, the year

before it was diagnosed and the year after it was diagnosed with severe footrot. So, for example, the variable Sheep trespassed fences and were in contact with a positive flock was coded positive for the year before, the actual year and the year following positive diagnosis of severe footrot. Similarly, it was considered that a flock could have received the infection the same year it was diagnosed or the year before it was diagnosed with severe footrot (see time varying and non-time varying covariates in Table S1 in the supplementary data 2: Dataset prepared for discrete time survival analysis).

When one farmer had reported contact with a second sheep flock, the information was compared with information from the second farmer. If inconsistencies were found, the most precise information was assumed to be correct for both farmers involved, and if a contact was only reported from one farmer, the contact was considered valid for both.

The geographical distances between sheep farms were calculated by computing the geodetic distance in R (R Development Core Team, 2011). For sheep farms located on different islands, the distance between the farms was considered to be infinite as the likelihood of a sheep crossing the water was regarded as negligible. For each flock, the presence of at least one positive flock was calculated each year within areas 0–1 km zone, >1–2 km zone, >2–3 km zone and >3–5 km zone of the flock.

A variable consisting of all the islands with sheep flocks in the municipality of Rennesøy was included in the analysis. This comprised the 6 islands Rennesøy, Vestre Åmøy, Bru, Brimse, Sokn and Møsterøy.

Statistical analysis, model building and model fit were performed using R (R Development Core Team, 2011). The dataset was ordered so that each flock (j) had one row of data per year of observation for the years 2008, 2009/2010 and 2011 (i). To distinguish these multiple records within a flock, categorical time indicators (T) were created for each discrete time period 2008, 2009/2010 and 2011. The response variable (π_{ij}) indicated whether severe footrot was diagnosed in flock j in time period i . If severe footrot was not diagnosed, its value was 0 and if it was diagnosed its value was 1. Flocks were censored (excluded from all subsequent time periods) once they had become positive with severe footrot. The values of the covariates were recoded so that they were appropriate to each flock and time period. There were two types of covariates, time dependent characteristics of a flock such as purchase data noted X_{ij} and non-time dependent such as breed noted X_j (Singer and Willett, 1993; Goldstein et al., 2004; Table S1 in Supplementary data 2: Dataset prepared for discrete time survival analysis).

Univariable discrete time survival analysis was performed with severe footrot as the response variable. All

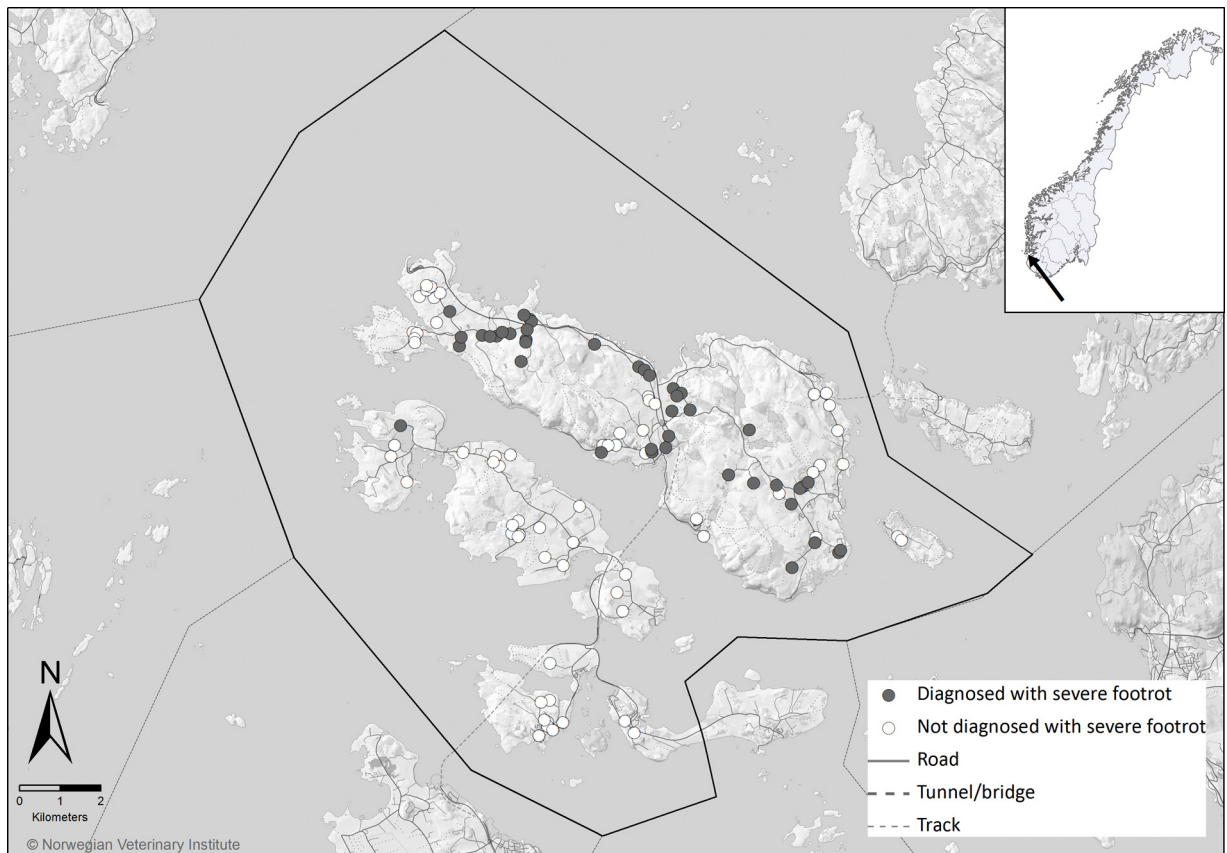


Fig. 1. Sheep flocks in the municipality of Rennesøy in Norway, divided into positive for severe footrot (dark grey dots) and negative for severe footrot (white dots) in 2008–2012.

the variables with p -value ≤ 0.2 were considered as candidates for the multivariable analysis. Correlations of pairs of variables were tested with Spearman rank correlation, and if ≥ 0.7 , the variable considered most biologically plausible was selected for inclusion in the multivariable analysis. Forward selection was done, and all the variables with p -value ≤ 0.05 were included in the final model. All the remaining variables were then tested against the model for any confounding effects. Odds ratios and the 95% confidence interval were estimated.

The equation for the discrete time survival model was as follows:

$$\text{Logit}(\pi_{ij}) = \alpha + \beta_1 X_{ij} + \beta_2 X_j + T_{ij} + u_j + e_{ij}$$

$$u_j \sim N(0, \sigma_u^2)$$

where π_{ij} is the conditional probability of getting diagnosed severe footrot in the i th year/discrete time interval of the j th flock respectively, α is the regression intercept, X_{ij} is the vector of covariates associated with each observation, β_1 is the coefficients for covariates X_{ij} , X_j is the vector of covariates associated with each flock, β_2 is the coefficients for covariates X_j , T_{ij} is the categorical time indicator variable; u_j is a random effect to reflect residual variation between flocks which were assumed to follow an unordered correlation structure and a normal distribution with mean zero and variance σ_u^2 and e_{ij} is a random effect which reflects residual variation between years that followed a binomial distribution.

Table 1

Results from the univariable discrete time survival analysis on potential risk factors for severe footrot in sheep flocks in the south west of Norway (2008–2011).

Variable	Positive flocks (No.)	Negative flocks (No.)	OR	95% CI	p -Value
General information					
Breed: Rygja sheep in flock					
Yes	1	30	0.2	0.02, 1.4	0.10
No	28	151	1		
Breed: Norwegian pelt sheep in flock					
Yes	4	6	4.7	1.2, 17.7	0.02
No	25	175	1		
Direct contact					
Purchase of sheep from a positive flock					
Yes	13	24	5.3	2.3, 12.4	<0.001
No	16	157	1		
Contact with sheep from a positive flock that had trespassed fences					
Yes	20	14	9.8	4.7, 20.5	<0.001
No	9	164	1		
Sheep trespassed fences and were in contact with a positive flock					
Yes	20	14	26.5	10.2, 69.0	<0.001
No	9	167	1		
Borrowed ram from a positive flock					
Yes	1	1	6.4	0.4, 106	0.19
No	28	180	1		
Shared pasture with another flock					
Yes	5	8	4.7	1.4, 15.4	0.01
No	23	171	1		
Indirect contact					
Shared weighing scales with a positive flock					
Yes	3	4	5.1	1.1, 24.1	0.04
No	26	177	1		
Shared a road to pasture with a positive flock					
Yes	6	4	11.5	3.0, 44.0	<0.001
No	23	177	1		
Neighbouring flocks with severe footrot					
At least one positive flock within 0–1 km zone					
Yes	26	53	20.9	6.1, 72.1	<0.001
No	3	128	1		
At least one positive flock within >1–2 km zone					
Yes	27	74	19.5	4.5, 84.6	<0.001
No	2	107	1		
At least one positive flock within >2–3 km zone					
Yes	24	81	5.9	2.2, 16.2	<0.001
No	5	100	1		
Island					
Rennesøy	28	94	15.2	2.0, 115	<0.001
Vestre Amøy	0	12	0		0, ∞
Bru	0	15	0		0, ∞
Brimse	0	6	0		0, ∞
Sokn	0	3	0		0, ∞
Mosterøy	1	51	1		

OR, odds ratio; CI, confidence interval.

3. Results

3.1. Response proportion

A total of 81 of 107 (76%) of the sheep farmers in the municipality of Rennesøy responded to the questionnaire including 29 of 41 (71%) sheep farmers that had flocks with severe footrot.

3.2. Univariable analysis

A total of fourteen predictor variables had a p -value ≤ 0.2 (Table 1). Of these, two variables were excluded due to correlation ≥ 0.7 (Table 2), giving twelve variables for testing in the multivariable analysis. The two variables “Sheep trespassed fences and were in contact with a positive flock” and “Contact with sheep from a positive flock that had trespassed fences” were correlated (Table 2). The former was selected to be in the multivariable analysis. The remaining factors had a p -value > 0.2 and were not included in the multivariable analysis. Among these were the farmer’s perception of the general condition of his own fences, flocks in a ram circle that had exchanged rams with a positive flock, and flock size grouped as more or fewer than 100 adult sheep.

3.3. Multivariable analysis

The final model included the variables: “Sheep trespassed fences and were in contact with a positive flock” and “At least one flock with severe footrot within 0–1 km” (Table 3). The same two variables were significant in all combinations of models. Time period was forced in as an explanatory variable in the final model, when excluding this variable the other variables did not change significantly.

4. Discussion

Both factors that were associated with an increased risk of occurrence of severe footrot in the final model indicated that local spread was important for transmission of footrot in Norway in this recent introduction of footrot. Consequently, sheep holdings positive for footrot constitute a threat to the footrot status of other nearby flocks.

The fact that sheep trespassing into the pasture of a positive flock was a risk factor suggests that sheep in contact with a positive flock were able to transfer *D. nodosus* to the other flock. This is in agreement with other papers which have reported that pasture contamination is a risk factor for transmission of footrot between flocks (Beveridge, 1941; Whittington, 1995). Sheep trespassing fences into a positive flock and vice versa were highly correlated (Table 2) and so we do not know which of these two variables was the true risk for spread of *D. nodosus*, most likely it is a combination of both sheep trespassing into positive flocks and sheep from positive flocks trespassing into negative flocks. What is clear is that there were sheep moving between flocks via insecure fences.

The fact that most of the farmers reported that their sheep fences were more than 80% secure indicates that

fences needed to be more secure than this to be of use to prevent the spread of footrot. It may also indicate that the farmers’ perception of the condition of their fences was greater than reality. Nevertheless, the results of this study suggest that improving fence security and maintaining them regularly to prevent spread of footrot between flocks is very important.

Previous reports have shown that direct contact between sheep is an important way of spreading footrot (Whittington, 1995). In this study, we did not identify any other factor than trespassing, such as purchase of sheep or sharing rams between flocks, as risk factors. This study was performed in a small geographical area, with intensive sheep farming where many flocks have close contact and cooperation. Common pastures in the mountains are rarely used by farmers in this area; hence, the density of sheep at pasture is very high during the grazing season. Therefore, once footrot had been introduced into the area, local spread may have been the most important factor for spread between flocks. Furthermore, trade of female sheep is illegal in Norway, and is only permitted after application to the authorities based on special needs (Thorud et al., 2006) and so there is little movement of adult sheep between flocks. In addition, the spread by trade of rams was reduced in this area because of government restrictions on movement of sheep from flocks diagnosed with severe footrot and, to some extent, from contact flocks. A contact flock was a flock that had been in direct or indirect contact with a flock positive for severe footrot, and therefore banned until it was cleared from suspicion by clinical examination and sampling. The results from the current study do not exclude movement of animals as an important risk in general; however, the results of this study show that local spread may be important once the diseases have been introduced to an area.

The fact that at least one flock with severe footrot within 0–1 km of the farm increased the risk of a flock contracting severe footrot suggests that there were mechanisms for local spread in addition to trespassing of sheep via broken fences. This study was not able to identify these factors specifically, but factors including unrecorded trespassing, local trade and sharing breeding rams could be included in this risk. Furthermore, we cannot exclude factors such as spread of infection by veterinarian, milk collecting trucks, wild deer or other risks that could be included in this factor, although we are unaware of scientific reports about these as risks. Nevertheless, this indicates that additional control measures reducing local contact between flocks in addition to upgrading and good maintenance of fences may be necessary to prevent spread of footrot between neighbouring farms. In addition, it highlights that in an elimination programme, flocks in close vicinity to positive flocks have a higher risk of footrot and should be targeted for examination.

Rennesøy consists of several islands, and spread of footrot would be thought to be of less significance between islands than within islands. But two farmers from different islands might, for instance, share a sheep weighing device or rams. The different islands within the municipality of Rennesøy were added as a categorical variable, and this was significant in the univariable analysis (Table 1), but not in

Table 2Pairs of variables with Spearman rank correlation ≥ 0.70 in a study on risk factors for severe footrot in sheep flocks in the south west of Norway (2008–2011).

Variable 1	Variable 2	Spearman rank correlation	p-Value
Sheep trespassed fences and were in contact with a positive flock ^a	Contact with sheep from a positive flock that had trespassed fences	0.7	<0.001
At least one positive flock within 0–1 km zone ^a	At least one positive flock within >1–2 km zone	0.7	<0.001
At least one positive flock within >2–3 km zone ^a	At least one positive flock within >1–2 km zone	0.8	<0.001

^a The variables selected for inclusion in the multivariable analysis.

the multivariable analysis. The variable “at least one flock with severe footrot within 0–1 km of the farm” became less significant in the multivariable analysis when the categorical variable of the islands was forced into the model, but it still had a *p*-value below 0.05 and an odds ratio of 10.5. This indicates that the two variables both measure the importance of geographical proximity for transmission of footrot.

The study was done in the municipality of Rennesøy which was a focus area for the Healthy Feet project, and hence all the flocks were thoroughly examined by the project in 2008, and those not positive for severe footrot at that time were re-examined at least once more in subsequent years. The geographical area is small with sheep grazing close to people. Hence, we consider it likely that lame sheep would be observed, both by farmers and people working in the Healthy Feet project. Therefore we consider the certainty of the footrot status in our study to be good, but there is a risk of misclassifying a flock infected with benign strains of *D. nodosus* as having severe footrot, as these strains might cause more than 5% animals with score 2 and even single animals with score above 2 (Glynn, 1993). Seven out of the 41 flocks in our study were defined as severe based only on clinical signs, if a few of these were truly misclassified it would reduce the chance of detecting true risk factors, that did not prove significant in our study. Finally farmers were aware of the project and most of them were keen to ensure footrot did not spread and so they also notified the project if they thought they, or their neighbour, had sheep with footrot.

Previous studies have shown that breed and flock size may be risk factors for acquiring footrot (Beveridge, 1941; Emery et al., 1984; Wassink et al., 2003). Within Rennesøy the flocks have a mean of 129 sheep (Register of Production Subsidies of 1.1.2011, Norwegian Agricultural Authority, Oslo) and 68 out of the 81 flocks (84%) that answered the

questionnaire had some Norwegian white sheep in their flock. The flock size in Rennesøy is relatively large compared with the rest of the country, but on an international scale this is a median flock size. Based on these facts, and the ubiquity of Norwegian white sheep in this area, we did not expect these factors to be significant risks.

Most of the data used in the study were collected by questionnaire. The response proportion was high in both footrot positive and negative flocks. The questionnaire would have taken longer to complete if the farmer had many contacts and we cannot exclude the fact that that farmers with many contacts might have been less likely to complete the questionnaire, or report all contacts. Recall bias could be dependent on variable and year in question. The questions covered the time period from 2007 to 2011, and therefore it might have been difficult for the farmers to recall all the information, in particular events from 2007. However, footrot is a new disease in Norway, and the farmers have been interested in learning about the disease and possible risk factors for contracting and spreading it. In addition, we consider that use of pastures and roads to pastures, pasture sharing, sharing of weighing scales and sharing of rams including within ram circles is information that does not vary considerably between years and so recall bias is less likely to be a problem for these factors. When considering trade, all sheep farmers are obliged to keep records on purchase and selling of sheep for ten years and movement data can be retrieved from these records. In addition, the data on purchases and ram circles from the questionnaire were cross checked with data from other sources. By cross checking trade information with sources not dependent on the farmers' responses we believe we have minimised information bias. The number of sheep in contact, and duration of contact are less likely to be accurate when there is such a long time span. Therefore, these variables were transformed into categorical variables with

Table 3Results from the multivariable discrete time survival analysis in a study on risk factors for severe footrot in sheep flocks in the south west of Norway (2008–2011) *n* = 81.

Variable	Estimate	SE	OR	95% CI	p-Value
Sheep trespassed fences and were in contact with a positive flock					
Yes	2.44	0.54	11.4	3.9, 33.2	<0.001
No	1				
At least one positive flock within 0–1 km					
Yes	2.15	0.69	8.6	2.2, 32.9	0.002
No	1				
Time indicators					0.89
Year 2008	0.34	0.71	1.4	0.3, 5.7	
Year 2009 and 2010	0.16	0.68	1.2	0.3, 4.5	
Year 2011	1				

Null deviance 169 on 209 degrees of freedom and AIC 171. Residual deviance 105 on 205 degrees of freedom and AIC 115. SE, standard error; OR, odds ratio; CI, confidence interval.

yes/no. Nevertheless, information bias cannot be excluded and it is difficult to give the direction of any bias if it exists.

5. Conclusions

Risk factors for contracting severe footrot have been investigated for the first time in Norway. There were two key risks, sheep from positive flocks directly or indirectly in contact with sheep in negative flocks by trespassing fences and geographical proximity of 0–1 km between a positive and negative flock. Trespassing of sheep could be decreased by farmers upgrading and maintaining boundary fences. Since we do not know precisely why farm proximity is an important risk factor, it is difficult to make specific recommendations, but we would encourage farmers to avoid direct and indirect contact between nearby flocks. Furthermore, proximity to a positive flock could be used to select flocks in a targeted surveillance programme.

Although movement of sheep by purchase, ram circles or shared pasture did not come out as risk factors for spread of footrot in this study, we cannot exclude that they might be important risks in other areas of Norway.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.prevetmed.2013.11.007>.

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Supplementary data 1: Flow diagram for diagnosis of severe footrot

A longitudinal study of the risks for introduction of severe footrot into sheep flocks in the south west of Norway

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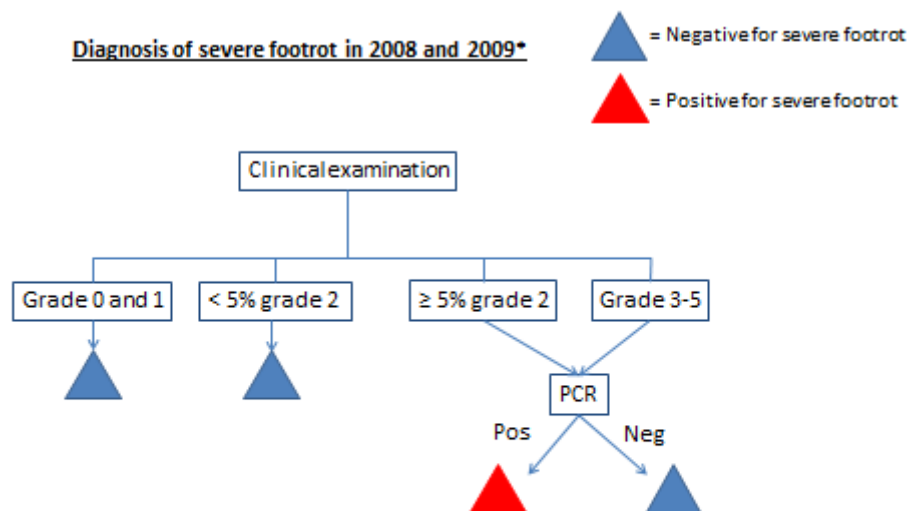
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* In 2009, some of the flocks were virulence tested with gelatinase gel test, but the diagnosis was based on the clinical signs and PCR result.

Fig. S1. Flow diagram for diagnosis of severe footrot in sheep flocks in Norway in 2008 and 2009. The diagnosis is based on clinical signs in the flock and PCR samples as there was no routinely virulence testing.

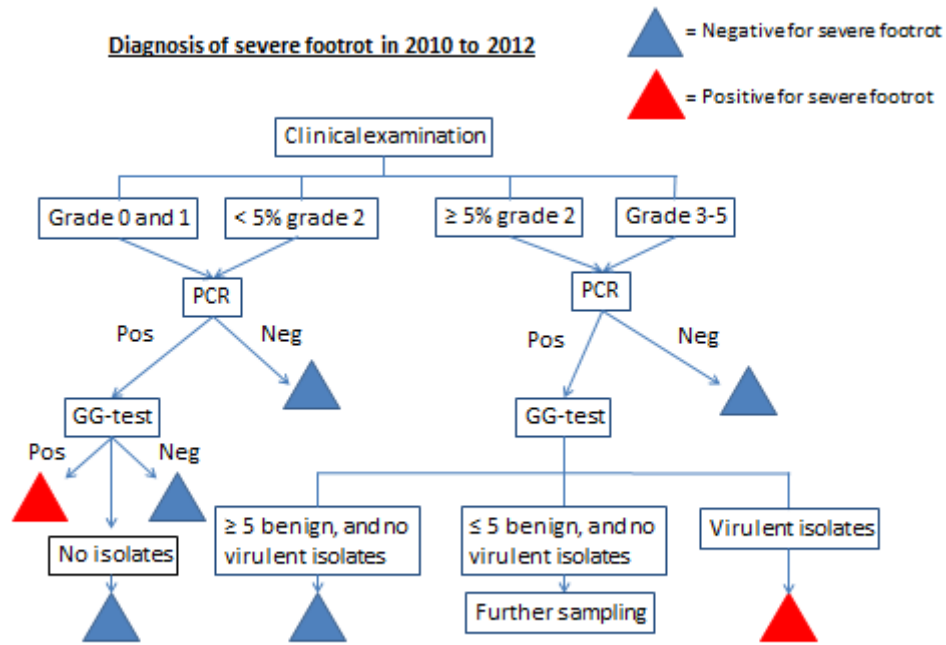


Fig. S2. Flow diagram for diagnosis of severe footrot in sheep flocks in Norway in 2010 to 2012. The diagnosis is based on clinical signs in the flock, PCR and bacteriology samples. The bacteriology samples are cultured to be able to perform a Gelatinase Gel test (GG-test). Culture of the bacteria is not shown in the figure, as this is a preparing step for the GG-test, and is not used for the final diagnosis.

Supplementary data 2: Dataset prepared for discrete time survival analysis

A longitudinal study of the risks for introduction of severe footrot into sheep flocks in the south west of Norway

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Table S1. Example of a simple data set that has been prepared for discrete time survival analysis.

Flock ID	Time indicators (T)*	Severe footrot Y/N (π_{ij})	Breed: Rygja sheep in flock (X_j)	Sheep trespassed fences and were in contact with a positive flock (X_{ij})
1	1	0	0	0
1	2	1	0	1
2	1	0	1	0
2	2	0	1	1
2	3	0	1	1

*Time indicators (T): 1 = year 2008, 2 = 2009/2010, 3 = 2011.

The flock is identified by the flock ID. For each flock (j) had one row of data per year of observation for the years 2008, 2009/2010 and 2011(i). To distinguish these multiple records within a flock, categorical time indicators (T) were created for each discrete time period 2008, 2009/2010 and 2011. The response variable (π_{ij}) indicated whether severe footrot was diagnosed in flock j in time period i . If severe footrot was not diagnosed, its value was 0 and if it was diagnosed its value was 1. Flocks were censored (excluded from all subsequent time periods) once they had become positive with severe footrot as exemplified by flock ID 1 in Table S1.

Non-time dependent variables (X_j) are stable for all time periods as exemplified by the variable "Breed: Rygja sheep in flock" in table S1. The variable was given the value 1 if the flock had Rygja sheep, and 0 if the flock did not have Rygja sheep.

The values of the time dependent covariates (X_{ij}) were coded so that they were appropriate to each flock and time period. Binary predictor variables were calculated based on zero or more contacts with other flocks that could potentially have transmitted the infection (potential transmitter flock). A positive flock was considered as a potential transmitter of infection the year it was diagnosed, the year before it was diagnosed and the year after it was diagnosed with severe footrot. Similarly, it was considered that a flock could have received the infection the same year it was diagnosed or the year before it was diagnosed with severe footrot (delayed diagnosis).

This is shown in Table S1 exemplified by the variable "Sheep trespassed fences and were in contact with a positive flock". The value 1 indicates that the flock had been in contact with a potential transmitter and 0 if it was not in contact with a potential transmitter.

For example, the flock with ID 1 had been in contact with a potential transmitter flock in the year 2009 and/or 2010 (Table S1). The flock with ID 2 had been in contact with a potential transmitter flock in the year 2010. Therefore, the value for 2009/2010 is 1. In addition, the value was lagged one down because of the possibility of receiving the infection one year before the disease is diagnosed (delayed diagnosis).

RESEARCH

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The potential spread of severe footrot in Norway if no elimination programme had been initiated: a simulation model

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Abstract

When severe footrot was detected in Norway in 2008, a surveillance programme was initiated and followed by an elimination programme. By 2013 the disease had spread to two of 19 counties and a total of 119 (1%) sheep flocks had been diagnosed with severe footrot. A simulation model was developed to estimate the potential spread of severe footrot in Norway and to estimate the relative importance of the different spreading routes. The model parameters were based on the rate of spread of the first 38 diagnosed cases and the management and climatic factors particular for Norway. The model showed that by 2013, severe footrot would have spread to six counties and infected 16% of the sheep flocks if no elimination programme had been initiated. If this is compared with the 1% of flocks that were diagnosed in Norway by 2013, there seems to be a large effect of the implemented footrot elimination programme. By 2035, it was estimated that severe footrot would have spread to 16 counties and 64% of the sheep flocks. Such an extensive spread would probably impose a large negative impact on the sheep industry and welfare of the sheep. The most effective way to curb the spread of severe footrot was by decreasing the within county infection rate. This could be achieved by decreasing the contact between flocks or by decreasing the environmental load of *D. nodosus*, for example by footbathing sheep, culling diseased sheep or eliminating severe footrot in the flock.

Introduction

Footrot is well known in sheep-producing countries worldwide. The clinical signs range from mild inflammation of the interdigital skin to under-running and separation of the hoof horn from the sensitive tissues [1]. Footrot is a painful disease and causes lameness, poor welfare and affects ewe and lamb productivity [2,3]. *Dichelobacter nodosus* (*D. nodosus*), a Gram negative anaerobic bacterium, is the causative agent of footrot in small ruminants [1]. *D. nodosus* is divided into benign and virulent strains that can be differentiated in the laboratory by a gelatin gel test [4]. Clinical signs are often more severe when sheep are infected with the virulent *D. nodosus* strain than with the benign strain.

Severe footrot is a notifiable disease in Norway, and in 2008 the disease was diagnosed in the county of Rogaland in the south west of Norway [5]. This was the first

detection of the disease in Norway since 1948 [6]. The term severe footrot has been used in Norway to include both flocks with diagnosed virulent strains of *D. nodosus* and flocks with severe clinical signs of footrot together with a positive PCR result but no bacterial isolates. A regional surveillance programme was initiated by the sheep industry in 2008, and in 2009, this was followed by a co-operative national elimination programme called the Healthy Feet Project (Animalia - Norwegian Meat and Poultry Research Centre). Between 2008 and 2011, clinical inspections were made of sheep in > 4500 sheep flocks. This includes close to 100% of the flocks in Rogaland. In addition, many of these flocks were inspected twice and some three or four times. By 2008, the disease had been detected in 1.5% of the flocks in Rogaland. The disease spread particularly rapidly in the municipality of Rennesøy, where 11.2% of the flocks were diagnosed with severe footrot in 2008 (Table 1). By 2012, severe footrot had only been detected in the county of Rogaland [7], but in 2013, virulent *D. nodosus* was diagnosed in 14 flocks in

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Table 1 Data used for estimating minimum, mode and maximum infection rate of severe footrot in Rogaland

	Rogaland excluding Rennesøy (minimum)		Whole of Rogaland (mode)		Rennesøy (maximum)	
Number of sheep flocks	2490		2597		107	
Year	Assumed infected	Predicted infected	Assumed infected	Predicted infected	Assumed infected	Predicted infected
2005	1	1	1	1	0	0
2006	ND	3	ND	3	1	1
2007	ND	9	ND	14	ND	4
2008	26	26	38	48	12	13
Regional percentage of infected flocks in 2008	1.0%		1.5%		11.2%	
Estimated infection rate (β)	1.13		1.31		1.36	

ND = No data.

The estimates was based on data on the total number of sheep flocks and number of flocks assumed to be infected with severe footrot in the regions, from the introduction of the disease (2005 in Rogaland and 2006 in Rennesøy) until the initiation of the elimination programme in 2009. The predicted number of infected flocks in each region was the median value, of 2000 replicates of the model based on Equations 1–3. The infection rate is calculated using a constant yearly recovery rate of 5.3% and reversion rate of 1/3 of the infection rate.

the county of Aust-Agder, also situated in the southern part of Norway. By the end of 2013, 119 flocks in Norway had been diagnosed with severe footrot. Of these, 118 are now declared to be free from footrot, and measures have been implemented to eliminate severe footrot from the remainder [8]. Epidemiological and bacteriological investigations have indicated that virulent *D. nodosus* was introduced into a single flock in the county of Rogaland in 2005 through the purchase of sheep from abroad and thereafter spread locally [9,10].

The aim of this study was to estimate the potential spread of severe footrot in Norway if no elimination programme was implemented and estimate the importance of the different spreading routes of virulent *D. nodosus*. The developed model was based on the infection rate of the first diagnosed cases and the management and climatic factors specific to Norway.

Material and methods

A stochastic compartmental model can be used to simulate spread of disease within a population [11]. In a SILLI-compartmental model, the susceptible(*S*), infected(*I*) and low susceptible(*L*) compartments and the transmission of flocks between these compartments describe the infection dynamics of the population. The susceptible flocks are not, and have not been, infected with the agent causing the disease. The infected flocks have at least one sheep infected with the agent causing disease and could infect susceptible or low susceptible flocks. The low susceptible flocks do not have any animals carrying the infection, and have a smaller contact network than the susceptible flocks, hence are less at risk of acquiring a disease than the susceptible flocks. The low susceptible flocks comprise of flocks with natural barriers towards other sheep flocks (called isolated flocks) and flocks that have recovered from

the disease and by this increased their biosecurity measures (called recovered flocks). The latent period is assumed to be zero, and the immunity period for a flock is negligible.

In the model, flocks are transferred from one compartment to another at different rates. The infection rate (β) is the rate at which susceptible flocks become infected. This is dependent on the number of contacts, and the risk of transmission of disease per contact. The recovery rate (σ) is the rate of recovery of infected flocks, and which are accordingly assigned to the low susceptible compartment. The reversion rate (γ) is the rate at which low susceptible flocks become infected, and by this transferred to the infected compartment.

Spread within subpopulations

Subpopulations can be defined if the spread of disease is not uniform in the population [12], but highly reduced from one geographical area to another. Each subpopulation is then modelled with their own SILLI-compartmental model with their own infection, recovery and reversion rate. These rates are based on specific values for each subpopulation that influence the spread of the disease in question.

Spread between subpopulations

Spread of disease is expected to be faster within the subpopulations than between two subpopulations as flocks within each subpopulation are expected to have more contact than flocks from two different subpopulations. Different types of contact between flocks in separate subpopulations may occur, leading to different transmission routes. Each transmission route between subpopulations are specified and quantified separately. Only susceptible flocks in the subpopulations are expected to be infected by other subpopulations as most of the low risk flocks

have increased biosecurity and thereby will not be infected through the between subpopulation transmission route.

Model

Equations 1–3 and Figure 1 show the differential equations of the SILI-compartmental model for one subpopulation with the possible introduction of infection from other subpopulations. The equations give the number of flocks in the susceptible (1), infected (2), and low susceptible (3) compartments in a subpopulation for each year.

$$S_{i,y+1} = S_{i,y} - \min \left[\left(\beta_i \cdot S_{i,y} \cdot I_{i,y} + \sum_{j \neq i} \theta_{j,i,y} + \sum_{j \neq i} \tau_{j,i,y} + \sum_{j \neq i} \delta_{j,i,y} \right), S_{i,y} \right] \quad (1)$$

$$I_{i,y+1} = I_{i,y} - \sigma \cdot I_{i,y} + \min \left[\left(\beta_i \cdot S_{i,y} \cdot I_{i,y} + \sum_{j \neq i} \theta_{j,i,y} + \sum_{j \neq i} \tau_{j,i,y} + \sum_{j \neq i} \delta_{j,i,y} \right), S_{i,y} \right] + \gamma_i \cdot L_{i,y} \quad (2)$$

$$L_{i,y+1} = L_{i,y} + \sigma \cdot I_{i,y} - \gamma_i \cdot L_{i,y} \quad (3)$$

where *i* is the subpopulation receiving the infection, *j* is the subpopulation transmitting the infection and *y* is the time interval in years, *S* is the number of susceptible flocks, *I* is the number of infected flocks, *L* is the number of low susceptible flocks, β is the rate at which susceptible flocks become infected, σ is the rate at which infected flocks recover and hence become low susceptible flocks, γ is the rate at which low susceptible flocks

become infected, θ , δ and τ is three possible ways of introduction of infection between subpopulations.

As the starting point for the simulations, the flocks infected with the disease was assigned to the infected compartment, the isolated flocks were assigned to the low susceptible compartment, and the remaining flocks were assigned to the susceptible compartment. Year was the time step and the model was run for the number of years desired.

Adaptation of the model to footrot in Norwegian sheep flocks

A SILI-compartmental model was developed for estimating the spread of severe footrot in Norwegian sheep flocks without an elimination program. The isolated flocks in the low susceptible compartment were defined as sheep farms more than 3 km away from any other sheep farm. This was based on a study by Grøneng et al. [13] which showed that a geographic distance of more than 3 km between the main buildings of different sheep farms was not a significant risk factor in the univariable analysis. We interpret this as sheep farms with more than 3 km distance to the nearest sheep farm have a lower risk of contracting footrot.

The infection rate of footrot was calculated based on the rate of spread from the introduction of footrot in Norway in 2005 until the initiation of the elimination programme in 2009. At this time, severe footrot had only been detected in the county of Rogaland, but since different regions within the county possessed highly different rate of spread, the infection rate was expressed by a Pert distribution. Rogaland County excluding Rennesøy, Rogaland County with Rennesøy and the municipality of Rennesøy was the regions used to calculate the minimum (min), mode (mod) and maximum (max) infection rate respectively. The rates were then used in the Pert distribution.

To estimate the infection rate of the regions, the total number of sheep flocks and the number of flocks assumed to be infected with severe footrot in the region, from the introduction of the disease (2005 in Rogaland and 2006 in Rennesøy) until the initiation of the elimination programme in 2009 was used (Table 1). The infection rate was simulated based on Equations 1–3, with a constant annual recovery rate (σ) of 5.3% and a reversion rate (γ) of 1/3 of the infection rate (see below for descriptions of recovery and reversion rate). The assumed number of infected flocks was the number detected in the footrot outbreak in Norway, and the predicted median number of infected flocks was as close to this number as possible. The appurtenant infection rate was used in the model. The min, mod and max predicted median number of infected flocks and the appurtenant infection rates in parentheses were 26 (1.13), 48 (1.31) and 13

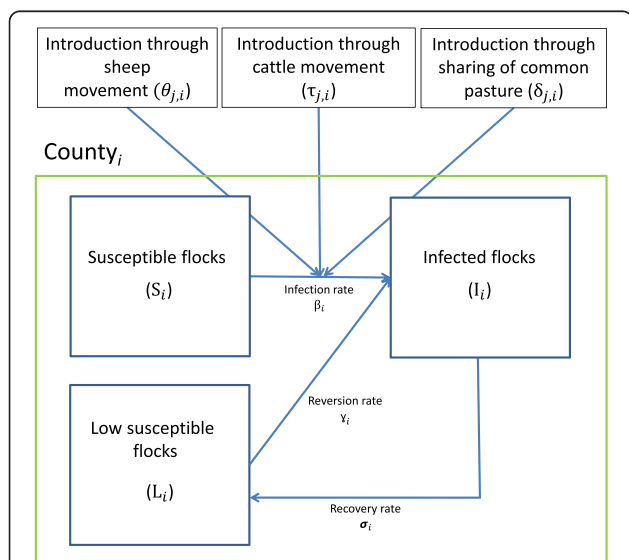


Figure 1 Susceptible - Infected – Low susceptible - Infected (SILI) model of severe footrot among sheep flocks. The simulation model was developed to estimate the potential spread of severe footrot in Norway if no elimination programme was initiated and to estimate the relative importance of the different spreading routes. The figure shows the transmission dynamics of severe footrot within one county (*i*) for one time step with possible introduction from other counties (*j*) through sheep movement, cattle movement and sharing of common pastures. The model was used to calculate all the 19 counties separately.

(1.36), respectively (Table 1). The Pert distribution for the infection rate for Rogaland was then ($\beta_{\text{Rog}} \sim \text{Pert}(1.13, 1.31, 1.36)$).

The recovery rate was based on spread of severe footrot without an elimination programme and hence no compensation for sanitation or other measures to eliminate the disease. The recovered flocks have therefore either undergone sanitation procedure at their own cost or recovered from the disease spontaneously. Two of 38 flocks completed a successful sanitation procedure at the farmers own expense in 2008 (Vatn S, Healthy Feet project, personal communication), corresponding to a recovery rate of 5.3% per year. Some of the flocks might also recover from the disease with no intervention. Since it takes a long time for sheep in a flock to recover without human intervention [14], the percentage of these flocks is thought to be small and was not included. The recovery rate was assumed to be constant for all years.

Since none of the flocks which completed a successful sanitation procedure at the farmers own expense in 2008 was re-infected, the reversion rate could not be calculated based on data. The reversion rate was therefore set based on knowledge of the infection dynamics. The susceptible flocks were assumed to have a three times higher infection rate than the low susceptible flocks, hence a reversion rate of ($\gamma = \beta/3$) was used.

Spread within subpopulations in Norway

Because of national maedi and scrapie legislation, sheep and goats are not allowed to be moved from one county to another without derogation. This gives a reduced spread from one county to another hence each of the 19 counties in Norway was assigned as a subpopulation. A SILLI-compartmental model was constructed for each county. The number of sheep flocks, cattle herds and combined sheep and cattle flocks was allocated to each county from the Register of Production Subsidies of 31.07.2012 (Table 2). The register contains all holdings receiving production subsidies in Norway, hence includes >92% of the total number of sheep flocks; the ones missing are farms with very few sheep. The number was kept constant for all years.

The infection rate calculated earlier was only based on the rate of spread within the county of Rogaland. To calculate the rate of spread within each of the other counties, values which would interfere with the spread of footrot are quantified and used to adjust the minimum, mode and maximum within county infection rate for Rogaland.

One of the values expected to interfere with the infection rate of footrot was the climate within each county as this is

an important factor for the survival of *D. nodosus* and for the initiation and development of ovine footrot [1,15]. In particular the precipitation and temperature are considered important for the spread of footrot [15,16]. The geo-coordinates of all sheep farm buildings in Norway (f) (the Agricultural Property Register, 2011) were linked to a mean value of precipitation ($\bar{p}_{f,i}$) and temperature ($\bar{t}_{f,i}$) from May until October (Norwegian Meteorological Institute, data from 1971 till 2000). By summarising the mean daily precipitation in mm and mean daily temperature in degrees Celsius of the individual sheep farms in a county, and dividing by the number of sheep farms in that county ($N_{f,i}$), a climatic value (called Cl_i) was calculated for each of the 19 counties (Equation 4).

$$Cl_i = \frac{\sum_f \bar{p}_{f,i} + \sum_f \bar{t}_{f,i}}{N_{f,i}} \quad (4)$$

The fraction between the climatic factors in county i and the climatic factor in Rogaland was incorporated in Equation 5 to adjust the infection rate within each county.

Another value expected to interfere with the infection rate of footrot was the density of sheep farms within each county. Grøneng et al. [13] showed that a risk factor for contracting the disease is a sheep farm located less than 1 km from a sheep farm positive for severe footrot. The distances between farms were calculated based on the locations of the main building on each farm. Hence, for each sheep farm, the number of other sheep farms within 1 km (neighbour farms) was obtained. Based on this, the mean number of neighbour farms to the sheep farms within each county ($\bar{n}_{1km,i}$) was calculated (Table 2). The fraction between the mean number of sheep farms within 1 km in county i and the county Rogaland was used to adjust the infection rate in county i (Equation 5). By using the knowledge of the spread of disease in the county of Aust-Agder, the effect of the fraction between counties was adjusted. In 2013, 14 flocks in the county of Aust-Agder were diagnosed with severe footrot, and epidemiological investigations indicate that sheep moved from the county of Rogaland in 2006 were the source. The spread from the introduction in 2006 to 2013 was simulated based on Equations 1–3, and a value k , adjusting the effect of the density factor between Aust-Agder and Rogaland, was chosen so that the median value of 2000 replicates matched the number of infected flocks in Aust-Agder in 2013. A median of 14 (range 1–26) infected flocks was predicted for $k = 2.3$ (Equation 5).

For all counties except Rogaland, a county specific min, mod and max infection rate was estimated by

Table 2 Overview of demographic data, climatic rate and infection rate for modelling spread of severe footrot

County	N° of sheep flocks (nSh)	N° of cattle herds (nCa)	N° of combined flocks (nShCa)	N° of isolated flocks	Mean number of neighbouring flocks ($\bar{n}_{1km,i}$)	Climatic rate (CI_i/CI_{Rog})	Infection rate (β) (minimum, mode, maximum)
Østfold	160	360	43	49	0.2	0.61	0.04, 0.05, 0.05
Akershus	226	359	45	43	0.8	0.61	0.17, 0.19, 0.20
Oslo	8	5	4	6	0.0001*	0.67	0.01, 0.01, 0.01
Hedmark	669	1108	200	99	1.4	0.51	0.24, 0.28, 0.29
Oppland	1323	2224	324	60	1.6	0.51	0.28, 0.32, 0.34
Buskerud	552	593	111	53	1.5	0.56	0.29, 0.33, 0.35
Vestfold	129	225	29	25	0.3	0.69	0.07, 0.08, 0.09
Telemark	372	360	72	54	1.3	0.67	0.30, 0.35, 0.36
Aust-Agder	220	250	47	60	0.8	0.76	0.21, 0.24, 0.25
Vest-Agder	450	583	150	45	1.2	0.93	0.38, 0.44, 0.46
Rogaland	2597	2735	1297	20	3.3	1	1.13, 1.31, 1.36
Hordaland	1997	1457	603	37	2.3	1	0.79, 0.91, 0.95
Sogn og Fjordane	1617	1756	625	59	2.5	0.97	0.83, 0.96, 1.00
Møre og Romsdal	1053	1880	358	94	1.2	0.89	0.37, 0.42, 0.44
Sør-Trøndelag	728	1729	187	99	1.1	0.62	0.23, 0.27, 0.28
Nord-Trøndelag	524	1737	178	98	0.6	0.67	0.14, 0.16, 0.17
Nordland	1045	1366	272	169	0.8	0.73	0.20, 0.23, 0.24
Troms	522	442	92	92	0.8	0.5	0.14, 0.16, 0.16
Finnmark	123	192	26	42	0.5	0.38	0.07, 0.08, 0.08

*In the county of Oslo no flocks had any neighbouring flocks within 1 km, hence the value was set at 0.0001.

The data are displayed for all the 19 counties in Norway. The number of sheep and cattle flocks includes the number of combined flocks. The number of isolated flocks (no other flocks within 3 km), the mean number of neighbouring flocks (sheep farms within a distance of 1 km), and the climatic rate (CI_i/CI_{Rog}) was calculated on the basis of the geographical co-ordinates of the building of the sheep farms. The infection rate (β) was the rate of susceptible flocks becoming infected due to within county transmission.

adjusting the min, mod and max infection rate for Rogaland with the constant k , the mean number of sheep farms within 1 km and climatic value for the respective counties. These values were then used in a Pert distribution, where a new value was estimated for each county and each replicate (Equation 5).

$$\begin{aligned} \beta_i &\sim \text{Pert} \left(\beta_{\text{Min.Rog}} \cdot \sqrt[2.3]{\frac{\bar{n}_{1\text{km},i}}{\bar{n}_{1\text{km,Rog}}} \cdot \frac{Cl_i}{Cl_{\text{Rog}}}}, \right. \\ &\quad \beta_{\text{Mod.Rog}} \cdot \sqrt[2.3]{\frac{\bar{n}_{1\text{km},i}}{\bar{n}_{1\text{km,Rog}}} \cdot \frac{Cl_i}{Cl_{\text{Rog}}}}, \\ &\quad \left. \beta_{\text{Max.Rog}} \cdot \sqrt[2.3]{\frac{\bar{n}_{1\text{km},i}}{\bar{n}_{1\text{km,Rog}}} \cdot \frac{Cl_i}{Cl_{\text{Rog}}}} \right) \end{aligned} \quad (5)$$

where i is the county, and *Rog* is Rogaland County.

The recovery rate was not expected to differ between counties and was expected to be constant for every year. The reversion rate for each county was defined as one third of the infection rate ($\gamma_i = \beta_i/3$).

Spread between subpopulations in Norway

The spread of footrot between counties in Norway was modelled taking three potential transmission routes into consideration: 1) movement of sheep between counties, 2) movement of cattle between counties, and 3) introduction by sharing of common pastures (Figure 1).

Introduction from other counties through sheep movement (θ)

Although there is a general ban on movement of sheep from one county to another because of maedi and scrapie, derogations from the legislation can be authorised by the Norwegian Food Safety Authority. Two movements of sheep between counties were recorded in 2013 (MATS, the supervision system of the Norwegian Food Safety Authority). There may have been movements of sheep that have not been reported to the central Food Safety Authority, but these are believed to be minimal. We therefore assumed that some of the sheep in 0.05% of the flocks in a county would be moved to each of the neighbouring counties each year. In addition, some of the sheep in 0.025% of the flocks in a county would move sheep to each of the counties bordering on neighbouring counties each year. Thus the number of movements from county j to county i was estimated ($MSh_{j,i}$), and used to calculate the introduction of severe footrot to other counties (Equation 7). For Norway as a whole, this is equivalent to approximately 44 between county movements of sheep each year. As this is more than reported to the Norwegian Food Safety Authority, we believe the effect of moving sheep across county borders has been overestimated rather than underestimated.

Only movement of sheep that is infected with footrot can transmit the disease to other sheep flocks. This depends on the probability that sheep from an infected flock are moved ($\frac{I_j}{nSh_j} \cdot MSh_{j,i}$), and also on the probability that at least one of the sheep moved is infected (*ProbMove*). The *ProbMove* is based on the number of sheep moved and the prevalence of infected sheep within the flock. The minimum *ProbMove* value was based on movement of one sheep from a flock with an infection prevalence of 0.01. The maximum *ProbMove* value was based on movement of five sheep from a flock with a prevalence of 0.65. The values were calculated to be 0.01 and 0.995 as shown in Equation 6. Consequently, a uniform distribution with a minimum and maximum value of the *ProbMove* was used ($\text{ProbMove} \sim \text{Unif}(0.01, 0.995)$) in Equation 7.

$$\text{MaxProbMove} = 1 - (1 - \text{Prevalence})^{\text{NumberMoveSheep}} \quad (6)$$

The number of sheep moved was based on the knowledge that mostly rams are purchased, and since the sheep flocks are small, rarely more than two rams are acquired at the same time. The lowest prevalence was based on one infected sheep in a flock of 100 sheep. The highest prevalence was based on PCR examination of all sheep in three flocks infected with severe footrot, and the median of these values was used. This was chosen since only sheep from flocks with a veterinary health certificate may be moved across county borders. We therefore believe that flocks with a prevalence above 0.65 would not be allowed to move sheep because they would show pronounced clinical signs of footrot.

The introduction of severe footrot from other counties by sheep movement is shown in Equation 7, where the percentage of susceptible sheep flocks in county i ($\frac{S_i}{nSh_i}$) was included in order to calculate the probability of an infected sheep arriving at a susceptible sheep flock. We expect that a sheep which is infected with footrot would infect a flock of susceptible animals.

$$\theta_{j,i} = \frac{I_j}{nSh_j} \cdot MSh_{j,i} \cdot \text{ProbMove} \cdot \frac{S_i}{nSh_i} \quad (7)$$

where i is the county receiving infectn, and j is the county transmitting the infection, I is the number of infected sheep flocks, nSh is the total number of sheep flocks, MSh is the number of flocks that have moved sheep, and S is the number of susceptible sheep flocks.

Introduction from other counties through cattle movement (τ)

Cattle that have been in contact with infected sheep may be carriers of virulent *D. nodosus* and transmit the

infection to sheep [17,18]. Hence, virulent *D. nodosus* might be introduced to a new county by movement of cattle. The number of moved cattle aged >1 year (*M_{Ca}*) in 2007 was retrieved from the Norwegian National Cattle Register (Norwegian Food Safety Authority) (Table 2). Cattle aged <1 year were not included as calves are usually not in contact with sheep, and the probability of a calf being infected by its mother and remain infected until moved to another flock was expected to be minimal. Only information from 2007 was available. In cases where there was no registered movement between neighbouring counties in 2007, movement of one head of cattle was imputed. The register also included records of movement of cattle without information about which county they were moved from. These were included by giving the unknown county the mean number of cattle flocks, the mean number of combined flocks and the mean number infected for all the counties. The number of infected sheep flocks in a county that transmit the disease (*I_j*), the number of sheep flocks in the county *j* (*nSh_j*), the number of cattle flocks in counties *i* and *j* (*nCa_i*, *nCa_j*), and the number of combined cattle and sheep flocks in counties *i* and *j* (*nShCa_j*, *nShCa_i*) (Table 2) are used to calculate the probability of severe footrot being introduced from other counties by movement of cattle. The probability of a sheep infecting cattle (Sh2Ca) and vice versa (Ca2Sh) was also needed for the calculation. On the basis of a study by Knappe-Poindecker et al. [18], the value was found to be 0.1 (gelatin gel test showed five of fifty cattle to be positive after co-grazing with sheep), while a study by Rogdo et al. [19] found this probability to be 0.3 (18 of 58 cattle were PCR-positive for footrot with serogroup A). The probability of sheep infecting cattle and vice versa was given by a uniform distribution (Ca2Sh ~ *Unif* (0.1, 0.3), Sh2Ca ~ *Unif* (0.1, 0.3)), a new value was generated for each movement. The percentage of susceptible sheep flocks in county *i* ($\frac{S_i}{nSh_i}$) was included to enable calculation of the probability of infected cattle entering a susceptible sheep flock. Equation 8 expresses the introduction of severe footrot from other counties through movement of cattle:

$$\tau_{j,i} = I_j \cdot \frac{nShCa_j}{nSh_j} \cdot Sh2Ca \cdot \frac{MCA_{j,i}}{nCa_j} \cdot \frac{nShCa_i}{nCa_i} \cdot Ca2Sh \cdot \frac{S_i}{nSh_i} \quad (8)$$

where *i* is the county receiving infection, and *j* is the county transmitting the infection.

Introduction from other counties through sharing of common pasture (δ)

In Norway, many sheep flocks are transported to common pastures during the summer. This is mainly pastures situated in mountain areas. This is an old tradition, and it is important both for reducing the farmer's feed expenses and for conserving the countryside. There are

nearly 1000 common pasture groups in Norway, each with several members and a designated area for their sheep to graze (Norwegian Forest And Landscape Institute). The organisation of the pasture groups is quite complex, with some common pasture areas crossing county borders. Some pasture groups also have members from several counties. Information about common pastures that share borders with common pastures in other counties and common pastures that have members from different counties are included in the estimation of cross-county transmission on pasture. In these pastures there are no fences or other barriers, with the result that sheep from different counties can mix and transfer infection. The spread of severe footrot on common pasture was calculated in a same way as the within county infection rates (Equation 5) by adjusting the infection rate for Rogaland for differences in sheep flock density and climate. Since sheep flocks are free ranging on common pasture, it is difficult to estimate the mean number of flocks within 1 km, as was done when calculating the within county infection rates. But sheep flocks are often put on common pasture at different times and in different areas, and 1–2 ewes with their lambs tend to keep together within a small area and rarely be in contact with other sheep. Assuming maximum dispersion of flocks on common pasture, we calculated the mean number of flocks per 1 km² for each of the common pastures and used this as a proxy for the number for flocks within 1 km of each other. The higher the density of sheep flocks on common pasture, the higher the infection rate then will be. The mean number of flocks within 1 km² on the common pastures where flocks from county *j* and *i* can be in contact with each other ($\bar{N}_{1km^2,past,j,i}$) was calculated as shown in Equation 9 by adding the density of common pastures in county *j* and *i* which have a common border (*B_{past}*) to the density of common pasture which have members from both counties *j* and *i* (*M_{past}*). This was used in Equation 10 to calculate the common pasture infection rates.

$$\bar{N}_{1km^2,past,j,i} = \frac{\sum_{B_{past}} \left(\frac{(N_{f(j)/A_{past(j)}} + N_{f(i)/A_{past(i)}})}{2} \right) + \sum_{M_{past}} (N_{f,j,i}/A_{past(j,i)})}{n_{B_{past}} + n_{M_{past}}} \quad (9)$$

where *N_f* is the number of sheep flocks on pasture, *A_{past}* is the geographic area of the pasture in km² and *n* is the number of pastures.

The climate of the common pastures (*Cl_{past}*) could not be calculated in the same way as the within county climate because we did not have specific geographical points, but rather large areas across which the sheep flocks were spread. The common pastures are often situated at a higher altitude than the general location of sheep farms, and the climate is often colder and dryer. Given this knowledge, we believe that the climate on common pasture has a lower value than the climate in any of the counties, so the climatic rate of

common pasture (CI_{past}/CI_{Rog}) was assumed to be 0.3, lower than the lowest climate rate (Table 2). The climatic rate was constant for all years, and was used in the calculation of the common pasture infection rates as shown in Equation 10.

The common pasture infection rate was calculated in the same way as the within county infection rates (Equation 5) with a Pert distribution for each county and each iteration (Equation 10).

$$\beta_{past,j,i} \sim \text{Pert} \left(\beta_{Min,Rog} \cdot \sqrt[2.3]{\frac{\bar{N}_{1km^2,past,j,i}}{\bar{n}_{1km,Rog}}} \cdot 0.3, \right. \\ \left. \beta_{Mod,Rog} \cdot \sqrt[2.3]{\frac{\bar{N}_{1km^2,past,j,i}}{\bar{n}_{1km,Rog}}} \cdot 0.3, \right. \\ \left. \beta_{Max,Rog} \cdot \sqrt[2.3]{\frac{\bar{N}_{1km^2,past,j,i}}{\bar{n}_{1km,Rog}}} \cdot 0.3 \right) \quad (10)$$

The introduction of severe footrot from other counties through sharing of common pasture was calculated on the basis of the common pasture infection rate ($\beta_{past,j,i}$), the percentage of infected flocks in county j ($\frac{I_j}{nSH_j}$), and the percentage of susceptible flocks in county i ($\frac{S_i}{nSH_i}$). The number of flocks from county i ($n_{past,i}$) and county j ($n_{past,j}$) on common pasture was also included to calculate the number of flocks in county i that were newly infected by sharing common pasture with county j (Equation 11).

$$\delta_{j,i} = \beta_{past,j,i} \cdot \frac{I_j}{nSH_j} \cdot n_{past,j} \cdot \frac{n_{past,i}}{(n_{past,j} + n_{past,i})} \cdot \frac{S_i}{nSH_i} \quad (11)$$

where i is the county receiving infection, and j is the county transmitting the infection.

Model for Norway

As the starting point for the simulations, one flock in the county of Rogaland was assigned to the infected compartment, the isolated flocks in each county were assigned to the low susceptible compartment in the respective counties, and the remaining flocks in each county were assigned to the susceptible compartments. When the probability of transferring flocks between compartments resulted in decimal number of flocks, the decimal number was converted to an integer by performing a Bernoulli trial with the decimal fraction as the probability. The county results were aggregated to give the results for Norway.

Scenarios

Basic scenario

The basic scenario was simulation of the spread of severe footrot without any elimination or control with input values as presented in Tables 1 and 2. For all the scenarios where input parameters were changed, the basic scenario was used as the reference.

Scenarios with different control measures

The disease can be controlled by reducing the within county or between county transmissions compared to the basic scenario. Scenarios with a 20%, 40%, 60% and 80% lower infection rate within the counties were modelled. Scenarios with 20%, 40%, 60%, 80% and 100% less movement of sheep between counties were modelled. Scenarios with 20%, 40%, 60%, 80% and 100% less movement of cattle between counties were modelled. Scenarios with 20%, 40%, 60%, 80% and 100% fewer flocks sharing common pasture were modelled.

Scenarios with increased between county transmission

Increased between county movement of both sheep and cattle, and an increased number of flocks on common pastures are scenarios that we might see in the future. Hence the importance of this factor is highlighted. A five-fold and ten-fold increase was modelled.

Sensitivity analyses

By increasing and decreasing the basic scenario parameters one by one, an indication of the robustness of the model and the sensitivity of the model parameters is found. The sensitivity analysis was performed by stepwise increasing and decreasing of the parameters, starting with 80%, then 60%, 40% and 20%. The analysis was continued until the number of infected flocks did not deviate by more than 5% compared to the basic model. Thus, only the 80% increase and decrease was performed for the parameters which showed little variance in the results compared to the basic scenario. The parameters included in the sensitivity analysis were the infection rate, recovery rate, reversion rate, climatic value, climatic rate on common pasture, number of farms within 1 km (neighbouring flocks) and number of farms within 3 km (isolated flocks).

Model simulations

The model was run from 2005 and 30 years onward. In addition, the basic scenario where the time interval was extended to the year 2100 was made. The intention was to capture the percentage of flocks in each of the compartments when the equilibrium state was reached. The model was run using R v2.15.1 [20] and the additional package deSolve [21]. For each simulation of a scenario, 2000 replicates were made.

Results

Basic scenario

In the basic scenario, severe footrot was estimated to have spread to six of the 19 counties and 16% of the sheep flocks in Norway by 2013, and 16 counties and 64% of the flocks were infected by 2035 (Figure 2). In 2100, severe footrot was estimated to be spread to all counties except Oslo, and to 76% of the sheep flocks.

The counties in the south-west of Norway were infected during the early years; after that, the remaining counties in southern Norway were infected, except Oslo, where none of the eight flocks were infected by 2035. Nor did the two northernmost counties, i.e. Troms and Finnmark, experience an introduction of severe footrot during the simulated period (Figures 3 and 4).

After the initial introduction of infection into a county, the model estimates that it takes four to twenty years before approximately 5% of the sheep flocks in the county are infected. Thereafter, one to nineteen years elapses before more than 30% of the sheep flocks in the county are infected. The steepest increase in the number of infected sheep flocks is observed in the five counties Rogaland, Hordaland, Vest-Agder, Sogn og Fjordane and Møre og Romsdal. Infected flocks in these counties increase from 5% to 60% within two to five years, while in the other counties it takes from eight to more than twenty years to reach this percentage (Figure 3). The counties of Rogaland and Finnmark have the highest and lowest percentages of infected flocks in 2100, at 88% and 7%, respectively, when the county of Oslo is excluded (0%). A state of equilibrium between the compartments are reached in the year 2068, when the number of infected flocks and low susceptible flocks stabilises at 76% and 24%, respectively.

Scenarios with different control measures

A 20% and 40% reduction in the infection rate results in 57% and 46% infected flocks respectively in 2035 (Figure 5). The exclusion of one of the between counties transmission routes at a time, while keeping the other two routes, reduces the number of infected flocks (Figure 5). The prohibition of common pasture reduces the number of infected

flocks in 2035 by 9% compared to the basic scenario. The prohibition of movement of cattle reduces the number of infected flocks by 2%, and delays the introduction of severe footrot to one more county compared to the basic scenario, i.e. the county of Østfold is not infected by 2035 in this scenario. By concurrent exclusion of two between county transmission routes, the number of infected flocks is further reduced compared to the basic scenario. Excluding both the movement of cattle and common pasture results in a 20% decrease in the number of infected flocks in 2035 compared with the basic scenario.

Scenarios with increased between county transmission

A ten-fold increase in the movement of sheep, the movement of cattle, and the use of common pasture increase the number of infected flocks in 2035 by 3%, 9% and 17%, respectively. The spread of severe footrot is further extended (compared to the basic scenario) to the county of Troms in the scenarios with increased movement of cattle and increased use of common pasture, and also to the county of Oslo in the scenario with increased movement of cattle.

Sensitivity analysis

In the sensitivity analysis, the variables with a more than 5% decrease or increase in the number of infected flocks compared to the basic scenario in 2035 are listed underneath. When reducing the climatic value with 80, 60, 40 and 20%, the number of infected flocks was reduced to 3%, 30%, 44% and 55%, respectively. When increasing the climatic value with 80, 60, 40 and 20%, the number of infected flocks was increased to 81%, 78%, 73% and 70%, respectively. When reducing the number of neighbouring flocks with 80, 60 and 40%, the number of

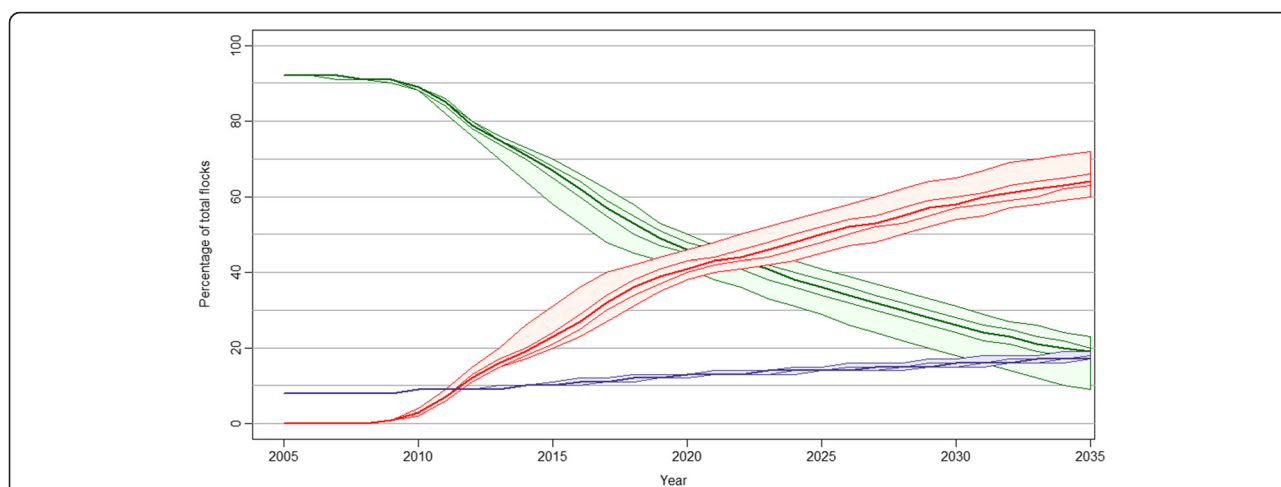


Figure 2 Simulated development of severe footrot in Norwegian sheep flocks without an elimination programme. The percentage of susceptible (green), infected (red) and low susceptible (purple) flocks are shown for each of the years 2005 – 2035 with the median value and 2.5, 25, 75 and 97.5 percentiles.

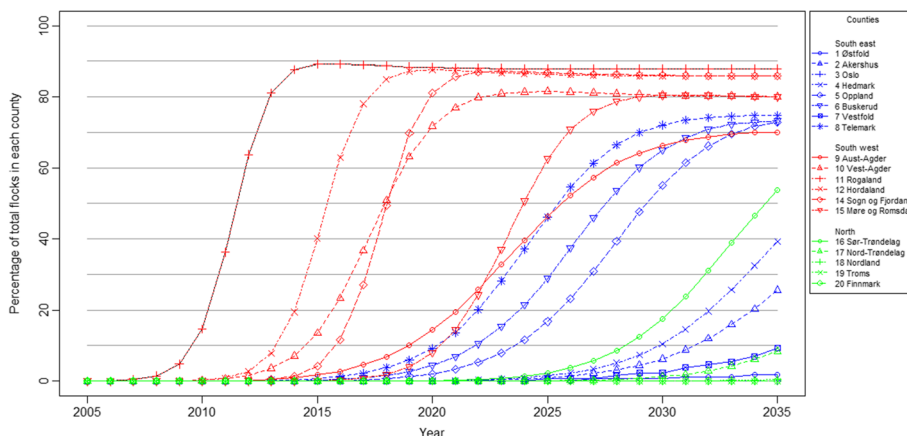


Figure 3 Simulated spread of severe footrot without an elimination programme in the 19 Norwegian counties. The median percentage of infected flocks within each county for each year in the period 2005 – 2035.

infected flocks was reduced to 38%, 48% and 55%, respectively. When increasing the number of neighbouring flocks with 80, 60 and 40%, the number of infected flocks was increased to 72%, 70% and 69%, respectively. When reducing the reversion rate by 80, 60 and 40%, the number of infected flocks was reduced to 44%, 53% and 58%, respectively. When increasing the reversion rate with 80, 60, 40 and 20%, the number of infected flocks was increased to 70%, 69% and 68%, respectively. When reducing the recovery rate by 80, 60 and 40%, the number of infected flocks was increased to 77%, 74% and

70%, respectively. When increasing the recovery rate by 80, 60 and 40%, the number of infected flocks was reduced to 53%, 56% and 59%, respectively. The variables which with an 80% increase or decrease deviated 5% or less from the basic scenario were; increased and decreased 3 km distance and increased and decreased climate on common pasture (Figure 6).

Discussion

A simulation model is a useful tool to predict the spread of disease in a population. But spread of an infectious

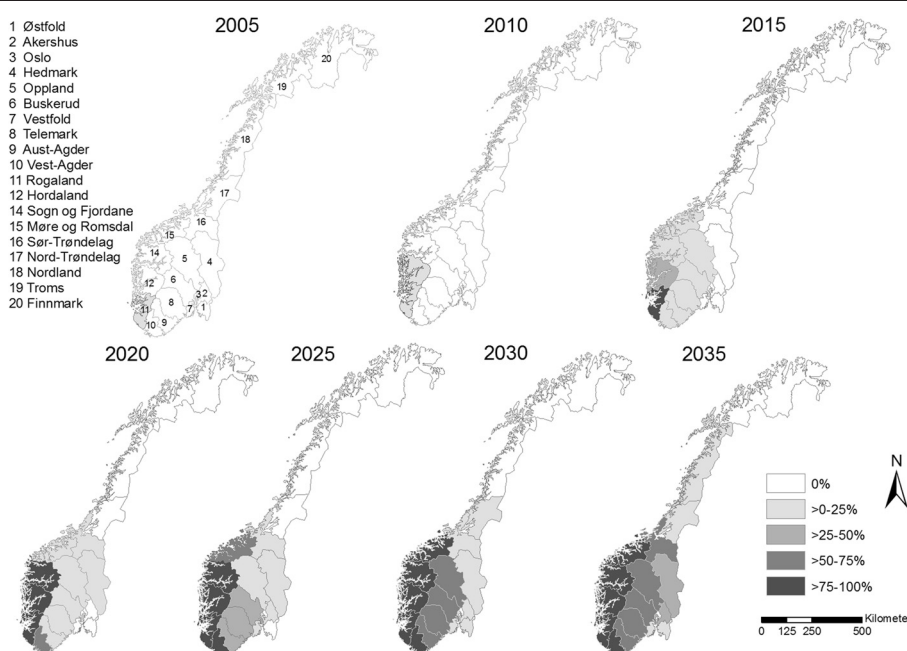


Figure 4 Simulated geographical spread of severe footrot in Norwegian sheep flocks without an elimination programme. The maps show the spread of severe footrot in the 19 counties of Norway at five-year intervals. The intensity of the grey shading shows the percentage of infected flocks in each of the counties.

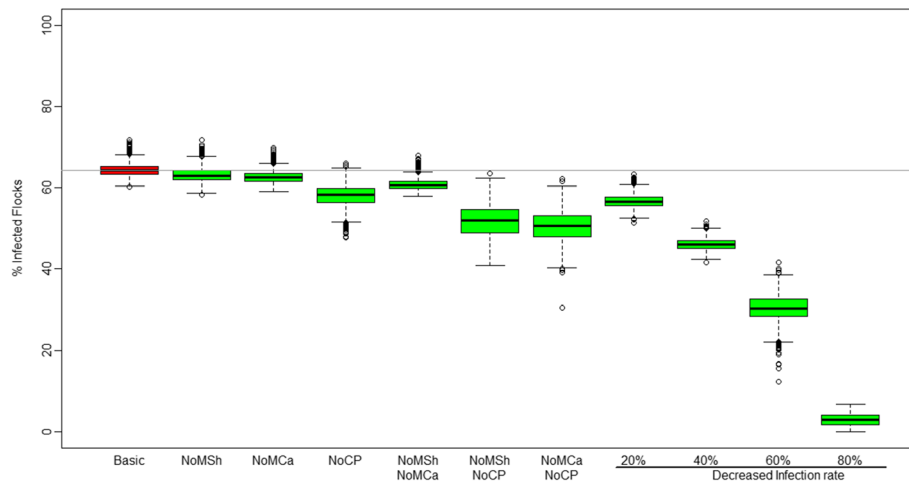


Figure 5 Estimated percentage of infected flocks in 2035 using different strategies for reducing severe footrot. The box-and-whiskers plot shows the distribution of the percentage of total flocks infected in Norway in 2035 based on 2000 replicates. The basic scenario is shown in red and various reduction strategies of the infection in green. The box represents the 25 and 75 percentiles and the black line inside the box represents the median value. Circles outside the whiskers are outliers. BasicS = Basic Scenario, NoMSh = exclusion of sheep movement, NoMCa = exclusion of cattle movement, NoCP = exclusion of common pasture, 20%, 40%, 60% and 80%: decrease in infection rate by 20%, 40%, 60% and 80%, respectively.

disease is a complex phenomenon with many interacting factors. Hence the development of a model must be based on knowledge of the specific disease in question and the routes of spread within the population as the model assumptions and the input variables used are important for obtaining a reliable result.

Most of the assumptions and input variables in this study have been based on observed parameters of the population, management and climate in Norway. In

addition, the infection rate was based on observed values of the spread of footrot in Rogaland from introduction in 2005 until implementing the elimination program in 2009, and then adjusted to the other counties in Norway by using the observed spread in Aust-Agder. Data on spread for more than four years and more than two counties would have been desirable, but since an elimination program was implemented in Norway, such data was not available.

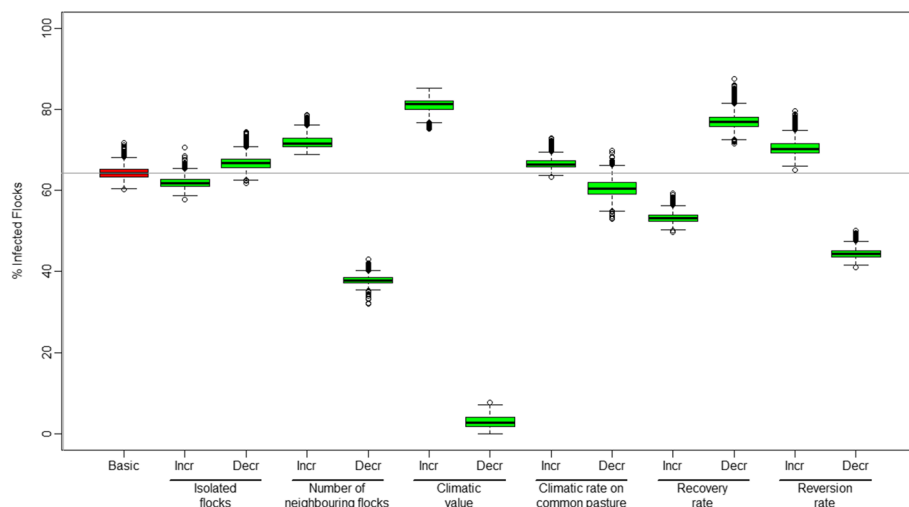


Figure 6 Sensitivity analysis of parameters used in a model for the spread of severe footrot. The box-and-whiskers plot shows the distribution of the estimated percentage of flocks infected with severe footrot in Norway in 2035 based on 2000 replicates. The basic scenario is shown in red and the 80% increase and decrease in the variables in the model is shown in green. The box represents the 25 and 75 percentiles and the black line inside the box represents the median value. Circles outside the whiskers are outliers. BasicS = Basic scenario, Incr = 80% increase in the variable and Decr = 80% decrease in the variable.

The sensitivity of the input parameters has also been examined. The variables found important in the sensitivity analysis were changes in the climatic value, the number of neighbouring flocks, the recovery, and the reversion rate. As expected, the climatic value is an important parameter for the spread of footrot. The values used in the model were based on observed mean precipitation and temperature for a 30 year period. More than a 20% increase or reduction of the observed value is not expected. Hence up to 14% decrease or 9% increase in the number of infected flocks compared to the basic scenario might be possible. The number of neighbouring flocks is also an important parameter. This value was based on the geographical coordinates of sheep farms. A higher or lower density of sheep farms might be possible, but we do not expect more than 20% change in this factor during the modelled 30 years. This would result in less than 5% deviation compared to the basic model. The recovery rate was based on data from the Healthy Feet project, and an increase or decrease in this value of more than 20% is not expected. With an increase/decrease of 20% the deviation from the basic scenario was less than 5%. The reversion rate is an important model parameter, and data on this value would have been desirable, but this is one of the few parameters in the model for which no data is available. A 40% change in this variable gives a more than 5% deviation in the result compared to the basic scenario. We cannot exclude the possibility that the reversion rate can have other values than the ones modelled. Low reversion rate is an advantage, and this can be achieved by good biosecurity measures. The rest of the variables did not change the outcome in the sensitivity analysis.

The reliability of the model can be assessed by comparing the infection dynamics in the model with what is expected based on knowledge of the disease and the spread in other populations.

Severe footrot was not introduced into the two northernmost counties in Norway in the period covered by the simulation. These counties are situated far from the county of Rogaland and to reach them the infection would have to cross several county borders that act as barriers for the transmission of the infection. In addition, the average temperature decreases going north in the country, resulting in a climate that is less favourable to the spread of footrot. A delayed introduction and spread to these counties, as predicted by the model, would accordingly be expected.

Another of the factors which increase the reliability of the model is the fact that the steepest increase in number of infected sheep flocks was seen in five counties that are all characterized by having a wet, warm climate and a relatively high density of sheep flocks compared to the other counties in Norway. These factors are known to enhance the development and spread of *D. nodosus*,

resulting in a high within county infection rate, hence a steep increase is expected.

We also compared the modeled results with parameters from the UK, where footrot is endemic. In a study, 86% of the sheep farmers in the UK reported to have footrot within a twelve-month period, and more than 95% had experienced footrot at some time [22]. This is similar to the situation in Rogaland county which stabilised at 88%. The overall prevalence of infected flocks in Norway stabilised at a lower level, but this was as expected since the other counties with the exception of Hordaland, have a climate less favourable for footrot (Table 2).

Even though this model was based on the factors specific for Norway, a similar approach can be used to predict the spread of disease in other populations by estimating the input variables specific to the disease and the country or region in question.

Basic scenario

Extensive spread of severe footrot, in terms of both the number of infected flocks and the number of counties affected is predicted within 30 years (Figures 2, 3 and 4). This results in a large proportion of the Norwegian sheep population being affected by pain, lameness and welfare problems which would have a high economic cost for the sheep industry [23]. A comparison of the predicted number of infected flocks with the cumulative number of flocks diagnosed with severe footrot in 2013 appears to show that the footrot elimination programme initiated in 2009 was highly effective. This shows the importance of early implementation of an elimination programme for a newly introduced disease like severe footrot.

Scenarios with different control measures

The most effective way to reduce the spread of severe footrot was by decreasing the within county infection rate (Figure 5). This could be achieved by reducing contact between flocks or by reducing the environmental load of virulent *D. nodosus*, for example by footbathing, culling diseased sheep or eliminating severe footrot from the flock. In the event of an extensive outbreak of severe footrot, we believe that some farmers would implement control measures to reduce the welfare problem in their flock. A 20% or possibly a 40% decrease in the infection rate might be realistic, which would decrease the number of infected flocks in 2035 by 11% and 28%, respectively, compared with the basic scenario where no control measures are included.

The exclusion of one of the between counties transmission routes at a time, keeping the other two routes in the model, resulted in only a small decrease in the number of infected flocks in 2035. When two of the three transmission routes were excluded, a larger reduction in the number of infected flocks in 2035 was seen. When sheep

movement was the only between county transmission route, the number of infected flocks decreased by 20%. Of the between county transmissions, this was the scenario with the largest deviation from the basic scenario. The low number of sheep moved across county borders is the main reason why the spread of disease is slowest for this route. National maedi and scrapie legislation prohibits the movement of sheep across county borders without derogation. This shows that keeping this transmission route only in the model at the current level limits the spread. This reflects the importance of the legislation in decreasing the spread of disease across county borders. With no such legislations, more sheep would be moved across the county borders and the spread of sheep diseases to other counties would be faster. The sheep industry in Norway supports the derogations for moving sheep across county borders, hence an increase is not expected.

Scenarios with increased between county transmission

Increased use of common pasture and movement of cattle gave the highest increase in the number of infected flocks of the between county transmissions. This shows the importance of the risk of spreading severe footrot by these means. But an extensive increase in these routes of transmissions is not expected as they are not restricted with legislations, and therefore not a major concern for the control of footrot in Norway.

The county-specific infection rates were based on the spread of severe footrot in Rogaland and adjusted to other counties by taking account of differences in climate and sheep density. The adjustment factors were fitted to the spread in Aust-Agder. We cannot exclude the possibility that other ways of generating the correction factors would be better. In view of the importance of the model results, data to validate the adjustment factors would have been beneficial, but such data does not exist for Norway.

In conclusion, a simulation model is a useful tool to estimate the spread of an infectious disease, but care must be taken so that model assumptions and values used are reasonable as the results are highly dependent on these. By using sensitivity analysis and assessing the consistency with spread in other populations, the reliability of the model can be assessed.

The spread of severe footrot in Norway without an elimination programme would have been extensive. Control measures decreasing the within county infection rate would delay the spread, but a ban on a single of the between county infection routes would not reduce the spread substantially. This shows the large effect, and the importance of initiating an elimination programme to prevent a large proportion of the Norwegian sheep population from being faced with pain, lameness and welfare

problems. We cannot exclude the possibility of disease being introduced and spread by other means than those modelled, but we do believe that the model predicts a possible scenario for how the disease would develop in Norway without an elimination programme.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

GMG was main responsible for the design of the study, programming the simulation model, performing the statistical analysis and writing the manuscript. SV participated in the design of the study and contributed to writing the manuscript. ABK supervised the programming of the simulation model and the statistical analysis and contributed to writing the manuscript. ON participated in the design of the study and contributed to writing the manuscript. PH supervised the design of the study and contributed to writing the manuscript. All authors read and approved the final manuscript.

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Comparing sensitivity of two surveillance strategies for footrot in Norway by using simulation models

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Abstract

The aim of this study was to assess which of two potential surveillance systems for detecting virulent footrot in Norwegian sheep flocks was the most sensitive. The two surveillance systems are On-farm surveillance and Abattoir surveillance. A stochastic scenario tree model was used to estimate the surveillance system sensitivity for demonstrating freedom from infection at a design prevalence of 0.2% infected flocks. In addition, the number of flocks diagnosed with virulent *D. nodosus* was estimated by simulating both surveillance systems. The comparison was based on an equal amount of resources invested. Abattoir surveillance was estimated to be the most sensitive of the two surveillance systems for detecting virulent footrot in Norway. On-farm examination was found useful when high flock level sensitivity was particularly important, for example for certifying single flocks free from footrot and follow-up on flocks diagnosed with virulent *D. nodosus* and their contacts.

Keywords: *Dichelobacter nodosus*; Footrot; Norway; Scenario tree; Sheep; Surveillance

1 Introduction

Footrot is a disease present in most sheep farming countries throughout the world (Beveridge, 1941; Graham and Egerton, 1968; Skerman et al., 1982; Egerton et al., 1989; Ghimire and Egerton, 1996; Gurung et al., 2006; Kaler and Green, 2008; König et al., 2011; Rather et al., 2011). *Dichelobacter nodosus*, a Gram negative anaerobic bacterium, is the essential transmitting agent of footrot in sheep (Beveridge, 1941). The first clinical sign of footrot is mild inflammation of the interdigital skin. Thereafter, under-running and separation of the hoof horn from the sensitive tissues may occur (Beveridge, 1941). The severity of the clinical foot lesions can be categorised with scores for each foot ranging from 0 (healthy), through 1 - 2 (interdigital inflammation) to 3 - 4 (under-running of the sole) (Egerton and Roberts, 1971). In Norway, we have used a scoring system where score 5 is included (separation of the sole and the wall of the hoof from underlying tissue) as described in Whittington and Nicholls (1995) and Woolaston (1993). In addition to scoring of clinical signs, *D. nodosus* isolates can be categorised as benign or virulent. The virulent strains usually cause more severe clinical signs than the benign strains. A Gelatin Gel test (GG-test) (Palmer, 1993) was implemented in Norway in 2009 to distinguish between the virulent and benign strains of *D. nodosus* (Gilhuus et al., 2013). In addition to the feet lesions, lameness and reduced productivity can be seen in affected sheep (Winter, 2004). Footrot is a major welfare problem for sheep (Ley et al., 1994) in addition to being a cause of large economic losses to the sheep industry (Nieuwhof and Bishop, 2005). The expression and spread of footrot is increased in wet and warm environments (Beveridge, 1941). Because of variation in climate and sheep management, the risks for development and transmission of footrot vary from country to country.

In 2008, *D. nodosus* was diagnosed in Norway. This was the first reported case of the disease in Norway since 1948 (Meling and Ulvund, 2009). Since 2008, a regional surveillance programme, and later, a national elimination programme named the Healthy Feet Project have been running the surveillance and elimination of footrot. Surveillance has primarily been based on examining sheep flocks at the farm. Foot inspectors, who are specially trained for the purpose, performed the clinical examination of sheep feet and scoring of footrot lesions. More than 4,500 different sheep flocks comprising approximately 25% of the national sheep population were clinically examined during the years 2008-2014. In addition, more than 4,000 samples were examined for presence of *D. nodosus*. Surveillance performed at abattoirs was also pilot tested during 2012, run on a larger scale in 2013 and was thereafter used as a part of the official surveillance program in 2014. During these years, approximately 165,000 sheep were clinically examined for footrot by foot inspectors at abattoirs in Rogaland.

Virulent *D. nodosus* has been diagnosed in 77 flocks. In addition 44 flocks are assumed to be infected with virulent *D. nodosus* based on severe clinical signs but as the GG-test was not yet implemented in Norway, the strain type has not been determined by laboratory methods. Per February 2015, all except one of the 121 flocks are declared to be free from the disease. The first cases of footrot in Norway in 2008 were diagnosed in the county of Rogaland situated in the south-western part of the country. In subsequent years the disease was only found in this county, but in autumn 2013, 14 flocks were diagnosed with virulent footrot in the county of Aust-Agder, bordering Rogaland. Clinical signs of footrot have been detected the whole year around in Norway, but 80% of the flocks have been diagnosed between August and November when humidity usually is at the highest levels and temperatures usually being above 0°C. Therefore, these months are believed to be the main period for development and transmission of footrot in Norway.

The aim of this study was to assess which of two potential surveillance systems for virulent footrot in Norwegian sheep flocks was the most sensitive. The evaluated surveillance strategies were On-farm surveillance and Abattoir surveillance. Follow-up on flocks diagnosed with virulent *D. nodosus* and their contacts was not included in the surveillance systems evaluated.

2 Materials and methods

2.1 Study design

The surveillance system for virulent footrot in Norway has two main objectives: 1) detecting and eliminating virulent *D. nodosus* in individual infected flocks until disease elimination is complete and 2) demonstrating freedom from infection after successful eradication of the disease on a national basis. We compared the two possible surveillance systems for detecting virulent footrot in Norway by measures for surveillance sensitivity. The surveillance systems were compared using two different simulation methods: 1) A stochastic scenario tree model (Fig. 1) was used to estimate the sensitivity of the surveillance programs for the objective of demonstrating freedom from infection (Martin et al., 2007b). 2) A simulation of the surveillance (Fig.2) was used to estimate the number of flocks detected with virulent footrot in the surveillance programs. The comparison of the two surveillance systems was based on equal design prevalence of disease in the population and an equal amount of resources invested in both of the two surveillance systems.

2.2 Population

All sheep in the county of Rogaland were included in the study because until autumn 2013 virulent *D. nodosus* was found in this county only. The county of Rogaland has 2,597 sheep flocks which represent 18% of the total number of sheep flocks in Norway. A total of 277,133 lambs and 181,638

adults were situated in the county of Rogaland per 31 July 2012 (Register of Production Subsidies, Norwegian Agricultural Authority, Oslo). The main slaughter season for sheep is from August to November, when approximately 44% of the sheep in Norway are slaughtered. Of these, approximately 91% are lambs and the remaining are adult sheep. There were five abattoirs slaughtering sheep in the county of Rogaland, and a total of 202,567 sheep from Rogaland were slaughtered at these abattoirs from August to November in 2012 (The Register of Delivery of Carcasses, Norwegian Agricultural Authority, Oslo).

2.3 Surveillance programs

Experience from the surveillance and elimination program of footrot administered by the Healthy Feet Project has been used to design two different outlines for future surveillance systems for footrot.

In On-farm surveillance, sheep flocks are examined at the farm. This is designed as risk based surveillance, which targets sheep flocks with a potential higher risk of contracting virulent footrot. Sheep flocks, that for different reasons have a high frequency of contact with other flocks are categorized as high risk flocks. In addition, farmers with management and/or geographical location which creates a humid environment for sheep over a long period of time are also expected to be high risk flocks. Trained foot inspectors travel to selected farms and examine sheep at the farm by visual inspection of all four feet. In addition, if clinical signs of footrot score ≥ 2 are present in the flock, five sheep with clinical signs are sampled for laboratory analysis.

In Abattoir surveillance, trained foot inspectors are placed at the abattoirs on randomly selected days. The sheep arriving at the abattoir on these days are examined by visual inspection of all four feet. All sheep with clinical signs of footrot score ≥ 2 are sampled for laboratory analysis, regardless of flock affiliation. The number of samples submitted for diagnosis each day is dependent on the prevalence of infected flocks, the within flock prevalence of clinical signs and the number of sheep arriving at the abattoir as shown in Appendix 2.

We restricted the surveillance to the period from August to November as this is the main period for development of clinical signs of footrot due to the favourable climatic conditions. This increases the probability of detecting footrot in the surveillance systems during this time of year compared to the rest of the year. In addition, most sheep are slaughtered in autumn; hence, this is the best time of year for Abattoir surveillance.

2.4 Scenario tree model

A stochastic scenario tree model as described by (Martin et al., 2007b) was designed (Fig.1). The model estimates the total surveillance system sensitivity ($SSSe$) measured as the probability of detecting at least one infected flock if the population was infected at the design prevalence of 0.2% (hypothetical proportion of flocks infected in the population; Cannon, 2002). The $SSSe$ was calculated by three main steps: 1) The individual flocks and the number of animals to be examined in the surveillance systems were selected by random procedures. 2) The probability of detecting an infected flock (SeF) was calculated for each single examined flock (Eq. 1). This was based on the flock size (N), the number of lambs and adults examined in each individual flock (n), the effective probability of infection for lambs and adult ($EPI_{Lamb/Adult}$) and the sensitivity of the testing regime (Use) for each examined animal. 3) The probability of detecting at least one infected flock in the whole surveillance system ($SSSe$) was estimated based on the SeF of each flock and the effective probability of infection in each flock ($EPI_{HR/LR}$) (Eq. 2).

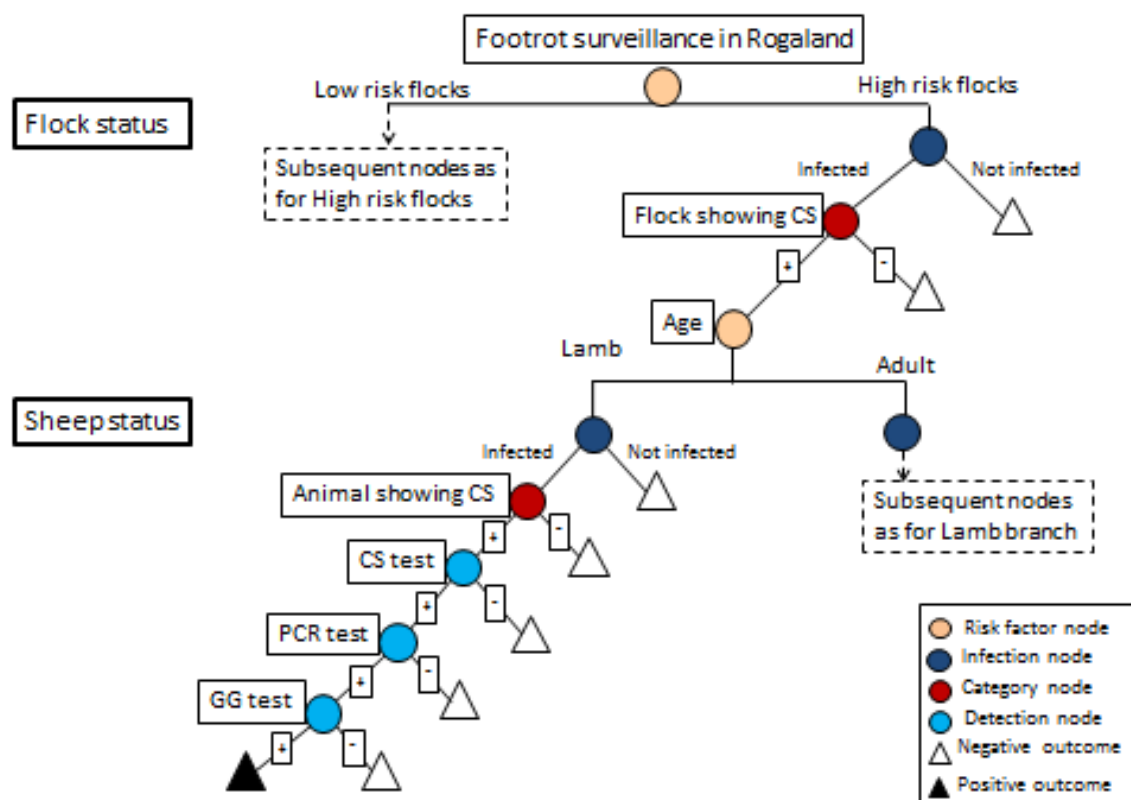


Fig. 1. Stochastic scenario tree model of a surveillance system of footrot in Norway. The scenario tree was used for simulating both On-farm and Abattoir surveillance. Only one branch is completed at the level of flock status and sheep status; assume the other branches to be comparable. CS test is visual examination for clinical signs, GG test is Gelatin Gel test and PCR test is polymerase chain reaction test.

The sensitivity of each examined flock (SeF_i) was calculated using an approximation to the hypergeometric distribution (MacDiarmid, 1987), as shown in Eq. 1. A new variable was generated for each flock and for each iteration.

$$SeF_i = 1 - \left(1 - Use_i * \frac{n_{Lamb,i}}{N_{Lamb,i}}\right)^{EPI_{Lamb,i} * N_{Lamb,i}} * \left(1 - Use_i * \frac{n_{Adult,i}}{N_{Adult,i}}\right)^{EPI_{Adult,i} * N_{Adult,i}} \quad (1)$$

where i is the flock, Use is the unit sensitivity, N_{Lamb} and N_{Adult} is the total number of lamb and adult, respectively. The n_{Lamb} and n_{Adult} is the total number of lamb and adult examined, respectively. The EPI_{Lamb} and EPI_{Adult} is the effective probability of infection in lamb and adult, respectively.

A new surveillance system sensitivity ($SSSe$) was generated for each iteration and surveillance system (Martin et al., 2007b).

$$SSSe = 1 - \prod(1 - SeF_i * EPI_i) \quad (2)$$

Model input

The nodes and branches of the scenario tree are shown in Fig 1. The estimated input parameters for the two surveillance systems are shown in Table 1.

Examined flocks and animals

The number of examined flocks and animals was calculated for each of the surveillance systems based on the amount of resources invested and the expenditures needed for the surveillance per flock and per animal, respectively.

In the On-farm surveillance, the number of examined flocks was calculated by dividing the amount of resources invested for each of the cost scenarios by the total expenditures of examining one sheep flock. The total expenditures of examining one sheep flock were calculated by including the mean expenses for the foot inspectors for examining one flock (NOK 2,763) and the mean expenses of five laboratory samples for flocks with clinical signs of footrot (NOK 920 for each sample) as shown in Appendix 1. The high risk flocks to be examined were randomly selected from the Register of Production Subsidies (31.07.2012, Norwegian Agricultural Authority, Oslo) which contains a unique

identification of all sheep flocks in the county of Rogaland, and the total number of adult (N_{Adult}) and lambs (N_{Lamb}) in each flock. All adult (n_{Adult}) and 20% of the lambs (n_{Lamb}) in the selected flocks were expected to be examined. For each scenario and iteration, a new random selection of flocks was generated.

In the Abattoir surveillance, the number of inspection days at the abattoirs was calculated by dividing the amount of resources invested by the total expenditures for one day of footrot examination at the abattoirs. The total expenditures for one day of footrot examination at the abattoirs were calculated by including the mean expenses for the foot inspectors for one day (NOK 5,250) and the expenses of laboratory analysis of footrot samples for one day (NOK 920 for each sample) as shown in Appendix 2. The number of days was distributed between the five abattoirs in Rogaland in accordance with the proportion of sheep from the county of Rogaland that were slaughtered at each of the abattoirs during 2012. The dates of the days with footrot examination at the abattoirs were randomly selected from the actual days with sheep slaughter in 2012 in accord with the Register of Delivery of Carcasses (Norwegian Agricultural Authority, Oslo). This register contains a unique identification of all flocks slaughtered in Rogaland with the number of lambs and adults delivered at each abattoir, and the dates for each delivery. Days where less than five flocks from the county of Rogaland were slaughtered were excluded as these days would not be efficient in a surveillance system and therefore should be avoided. Examination of 75% of the adult sheep (n_{Adult}) and lambs (n_{Lamb}) arriving at the selected abattoirs on the selected days was expected. When the number of days or number of sheep resulted in a decimal number, the decimal number was converted to an integer by performing a Bernoulli trial with the decimal fraction as the probability.

Design prevalence

The design prevalence of flocks (P^*F) is the hypothetical proportion of flocks infected in the population (Cannon, 2002) and was set to 0.2%. This corresponds to approximately five sheep flocks infected with virulent *D. nodosus* in the county of Rogaland. This prevalence was chosen because early detection of footrot is an advantage for controlling disease spread (Grøneng et al., 2015).

High and low risk flocks

The flocks in the surveillance system were divided into high ($PopPr_{HR}$) and low risk ($PopPr_{LR}$) flocks, where the high risk flocks were expected to have a higher risk of contracting footrot compared to the low risk flocks. For the purpose of this model, we assumed that 10% of the flocks in Rogaland were high risk flocks.

The relative risk (RR) is the risk of contracting footrot in the high risk flocks compared to the risk of contracting footrot in the low risk flocks. The relative risk of high risk flocks was set to two ($RR_{HR}=2$) when the relative risk of the low risk flocks was one ($RR_{LR}=1$).

On-farm surveillance is risk based surveillance where the aim is to exclusively select high risk flocks, hence the proportion of high risk flocks sampled in the On-farm surveillance system was set to 100% ($Pr_{HR}=1$). In the Abattoir surveillance, all flocks were examined on randomly selected days; hence, the proportion of high risk flocks sampled was expected to be the same as in the overall population ($Pr_{HR}=0.1$).

The adjusted risk was calculated for the high risk (AR_{HR}) and low risk flocks (AR_{LR}) based on the relative risk (RR) and the population proportion ($PopPr$) as given by Martin et al. (2007a).

The effective probability of a unit being infected (EPI), given that the population is infected at the design prevalence is calculated based on the adjusted risk of high risk flocks and low risk flocks (AR_{HR} and AR_{LR} respectively), and the design prevalence (P^*F) as given by Martin et al. (2007b). The effective probability of a unit being infected was calculated for the high risk flocks (EPI_{HR}) and the low risk flocks (EPI_{LR}) separately as shown in Equation 3.

$$EPI_x = AR_x * P^*F \quad (3)$$

where $x \in (HR,LR)$

Probability of infected flocks not showing clinical signs of footrot score ≥ 2

Some infected flocks do not have any animals showing clinical signs of footrot with a score of ≥ 2 (PrF_{NCS} ; Vatn et al., 2013). In both the surveillance systems, these flocks would not be detected since only animals with a footrot score of ≥ 2 would be sampled. In the Healthy Feet Project, the prevalence of infected flocks without clinical signs was 37%, 25% and 9% in 2010, 2011 and 2012, respectively. Based on this, we estimated the probability of an infected flock not showing clinical signs of footrot score ≥ 2 by a uniform random selection with a minimum value of 0.09 and a maximum value of 0.37 $PrF_{NCS} \sim Unif(0.09,0.37)$. A new random value for each flock was generated in each iteration.

Within flock prevalence

The within flock prevalence ($Prev$) of infection with *D. nodosus* regardless of clinical signs was estimated based on PCR examination of three Norwegian sheep flocks diagnosed with virulent

footrot from August to November 2010 (Gry Grøneng, personal communication). The right foreleg of all the sheep in the three flocks was sampled. A within flock prevalence between 56% and 74% was found. Based on this, the within flock prevalence of each flock was simulated with a uniform random selection $Prev \sim Unif(0.56, 0.74)$. A new random value for each flock was generated in each iteration.

Risk of footrot in lambs and adult sheep

The relative risk for contracting footrot in lambs and adult sheep was calculated based on data from nine Norwegian sheep flocks with clinical outbreak of virulent footrot from August to November (registers of the Healthy Feet Project). Lambs were found to have 1.9 times higher risk of being infected with *D. nodosus* ($RR_{Lamb} = 1.9$) than adults ($RR_{Adult} = 1$).

The population proportions for lambs ($PopPr_{Lamb}$) and adults ($PopPr_{Adult}$) were calculated based on the total sheep population in Rogaland to be 0.6 and 0.4 respectively (Register of Production Subsidies of 31.07.2012, Norwegian Agricultural Authority, Oslo).

The adjusted risk (AR) was calculated in accordance with Martin et al. (2007a) with lambs as high risk (AR_{Lamb}) and adult sheep as low risk (AR_{Adult}) animals.

The effective probability of an animal being infected (EPI) was calculated as described in accordance with Martin et al. (2007b), with lambs as high risk (EPI_{Lamb}) and adult sheep as low risk (EPI_{Adult}) and within flock prevalence instead of P^*F (Equation 3).

Proportion of sheep showing clinical signs of footrot

In the Abattoir surveillance, the proportion of sheep showing clinical signs of footrot (Pr_{CS}) was based on the observed proportion in thirteen Norwegian sheep flocks diagnosed with virulent footrot from August to November (registers of the Healthy Feet Project). Between 1% and 60% showed clinical signs of footrot score ≥ 2 . Based on this, the proportion of sheep showing clinical signs was simulated with a uniform random selection $Pr_{CS} \sim Unif(0.01, 0.60)$. A new random value for each flock was generated in each iteration. Since the within flock prevalence was the proportion of infection of *D. nodosus* in a flock, the Pr_{CS} was restricted to be less than $Prev$.

In the flocks with clinical signs in the On-farm surveillance, five samples were submitted for laboratory examination, regardless of the total number of animals with clinical signs in the flock. The samples were exclusively taken from animals with clinical signs, hence the Pr_{CS} in On-farm surveillance was set to 1. The Pr_{CS} was used in the calculation of the unit sensitivity described in Eq. 4.

Sensitivity of diagnostic tests

Three diagnostic tests were used in both the On-farm and Abattoir surveillance systems. The tests were clinical sign examination, PCR test and bacteriology including virulence test (GG-test). Clinical sign examination is a visual inspection of all four feet of selected sheep for clinical signs of footrot. Clinical signs of footrot score ≥ 2 were interpreted as a positive clinical sign test. Foot inspectors especially trained for the purpose were used for the clinical examinations. The test sensitivity of diagnosing clinical signs (Se_{CS}) was estimated to vary between 90% and 95% (Synnøve Vatn, personal communication). Each flock was designated a Se_{CS} by a uniform random selection $Se_{CS} \sim Unif(0.90, 0.95)$. A new random value was generated for each flock and each iteration. The PCR test was a *D. nodosus* specific 16S real-time PCR with a test sensitivity estimated to be 95% (Se_{PCR}) (Hannah Jørgensen, personal communication). The bacteriology and subsequent GG-test was only performed on PCR positive samples. The combined sensitivity of the bacteriology and GG-test was estimated to be 60% (Hannah Jørgensen, personal communication).

In both surveillance systems, a clinical sign examination was performed first. Then, sheep positive in the Se_{CS} in the Abattoir surveillance was sampled for laboratory examination, regardless of flock affiliation. While in the On-farm surveillance, five sheep positive in the Se_{CS} were sampled from the flocks where animals showed clinical signs. Only samples positive on the GG-test resulted in a flock status as positive for virulent footrot. A serial interpretation (Eq. 4) was used to calculate the combined test sensitivity (CSe). A new value was generated for each flock and each iteration. The combined test specificity was set to 100%.

$$CSe_i = Se_{CS,i} * Se_{PCR} * Se_{GG} \quad (4)$$

where i is the flock, Se_{CS} is the sensitivity of visual examination of clinical signs, Se_{PCR} is the sensitivity of PCR, Se_{GG} is the sensitivity of the bacteriological examination and the subsequent GG-test.

Unit sensitivity (USE) was calculated for each branch in the surveillance systems. The unit sensitivity is based on the proportion of sheep showing clinical signs of footrot score ≥ 2 (Pr_{CS}) and the CSe . The USE was calculated in series assuming independence between tests as shown in equation 5. A new value was generated for each flock and each iteration.

$$USE_i = Pr_{CS,i} * CSe_i \quad (5)$$

where i is the flock, Pr_{CS} is the proportion of sheep showing clinical signs score ≥ 2 , CSe is the combined test sensitivity.

2.5 Simulation of surveillance systems

Simulation of the surveillance systems was performed to estimate the number of flocks diagnosed with virulent footrot ($NDiagF$) at the design prevalence of 0.2% (Fig. 2). The $NDiagF$ was calculated by four main steps: 1) The flocks and animals to be examined in the surveillance systems were selected. 2) For each farm selected to be examined, the status as infected or non-infected was estimated by the effective probability of infection (EPI) of each individual flock. 3) For the flocks estimated to be infected, their status as correctly diagnosed or not was estimated by the farm-level sensitivity (SeF) of each individual flock. 4) The flocks designated as detected were summarised ($NDiagF$). A new value for $NDiagF$ was calculated for each surveillance system and each iteration.

Model input

Examined flocks and animals

The selection of flocks and animals to be examined was performed as described in section 2.4 Scenario tree model. The selection of examined flocks produced in each iteration was identical for the scenario tree model and the simulation of surveillance model.

Design prevalence

The design prevalence was set to 0.2% as described in chapter 2.4 Scenario tree model, subsection Design prevalence.

Infected flocks

The status of the flocks as infected or non-infected was estimated by performing a Bernoulli trial with the effective probability of infection (EPI) as the probability of the flock being infected. The EPI was calculated for each single flock as described in chapter 2.4 Scenario tree model, subsection High and low risk flocks.

Detected flocks

The status of the flocks as detected or not detected was estimated by performing a Bernoulli trial with the sensitivity of flock (SeF) as the probability of the flock being detected. The SeF was calculated for each single flock as described in chapter 2.4 Scenario tree model (Eq. 1).

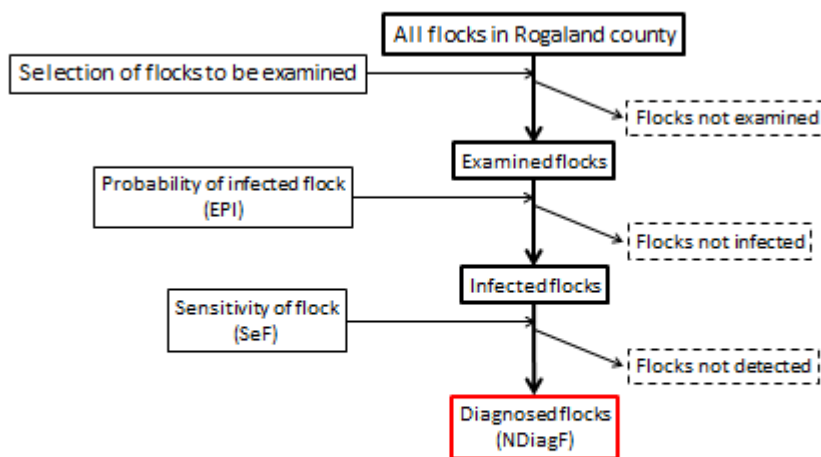


Fig. 2. A simulation of the surveillance systems of footrot in Norway to estimate the number of flocks diagnosed with virulent footrot. Simulation of both On-farm and Abattoir surveillance was performed using the same model and surveillance specific input values.

2.6 Scenarios

The Basic scenario (*BS*) was modelled as described in section 2.4 and 2.5 with input values as presented in Table 1. The amount of resources invested in the Basic scenario was NOK 500,000 (approximately €61,500) which was the approximate amount of money used in the surveillance of footrot in Rogaland in 2013.

Since we do not know the exact amount of resources that would be invested in a surveillance of virulent footrot in Norway, scenarios with higher and lower amounts of resources invested were also modelled. In the Low scenario (*LS*), NOK 250,000 (approximately €31,000) was invested, in the High scenario (*HS*), NOK 750,000 (approximately €92,000) was invested and in the Very High scenario (*VHS*), NOK 1 million (approximately €123,000) was invested (Table 2).

The design prevalence of flocks (P^*F) is a central value in this study since the models are based on finding one or several infected flock(s) when the disease is present at the design prevalence. We therefore modelled four sensitivity analysis using the input parameters from the *BS* and a design prevalence of 0.1%, 0.5%, 1% and 2% in both the surveillance systems (Table 1). The number of flocks

examined in the On-farm surveillance and the number of days with examination in the Abattoir surveillance were kept constant with the values in *BS* (179 flocks and 84 days respectively).

2.7 Sensitivity analyses

A sensitivity analysis determines how variation in individual parameter values affects the outputs of the model. This is important to estimate the sensitivity of the input parameters and further examine the trust of the model. This analysis was performed by using the *BS* and increasing or decreasing one by one the parameters shown in Table 1. Parameters which gave more than 5% deviation in the *SSSe* and the *NDiagF* from the *BS* were interpreted as important for the model outcome. The number of flocks examined in the On-farm surveillance and the number of days with examination in the Abattoir surveillance was kept constant at the values used in *BS* (179 flocks and 84 days respectively).

2.9 Running simulations

The model was run using R v2.15.1 (R Development Core Team, 2012). For each simulation of a scenario, 10 000 iterations were run.

There were no ethical considerations on animal welfare in this study since no interventions were done on animals.

Table 1

Input parameters in the Basic scenario for On-farm and Abattoir surveillance for virulent footrot in Norway. The values are used both for the stochastic scenario tree model and the model simulating the number of detected flocks.

Parameter	Notation	Input values		Sensitivity analysis	
		On-farm	Abattoir	On-farm	Abattoir
<u>Flock level</u>					
Design prevalence at flock level	$P*F$	0.002	0.002	0.001, 0.005, 0.01, 0.02	0.001, 0.005, 0.01, 0.02
Proportion of infected flocks with no clinical sign score ≥ 2	PrF_{NCS}	Uniform (0.09 – 0.37)	Uniform (0.09 – 0.37)		
Population proportion of high risk flocks	PPr_{HR}	0.1	0.1	0.2 - 0.5 in steps of 0.1	0.2 - 0.5 in steps of 0.1
Population proportion of low risk flocks	PPr_{LR}	$1 - PPr_{HR}$	$1 - PPr_{HR}$	$1 - PPr_{HR}$	$1 - PPr_{HR}$
Proportion of high risk flocks examined	Pr_{HR}	1	0.1	0.5 - 0.9 in steps of 0.1	0.5 - 0.9 in steps of 0.1
Proportion of low risk flocks examined	Pr_{LR}	$1 - Pr_{HR}$	$1 - Pr_{HR}$	$1 - Pr_{HR}$	$1 - Pr_{HR}$
Relative Risk for high risk flocks	RR_{HR}	2	2	1, 3	1, 3
Relative Risk for low risk flocks	RR_{LR}	1	1	1	1
<u>Animal level</u>					
Within flock prevalence	$Prev$	1 (of the tested animals)	$Unif(0.56,0.74)$	0.2, 0.4, 0.5, 0.8	0.2, 0.4, 0.5, 0.8
Proportion of sheep showing clinical signs score ≥ 2	Pr_{CS}	1 (of the tested animals)	$Unif(0.01,0.60)$	0.1 - 0.7 in steps of 0.1	0.1 - 0.7 in steps of 0.1
Total number of lambs	N_{Lamb}	Data for each flock	Data for each flock		
Total number of adult sheep	N_{Adult}	Data for each flock	Data for each flock		
Population proportion of lamb	PPr_{Lamb}	0.6	0.6		
Population proportion of adult sheep	PPr_{Adult}	$1 - PPr_{Lamb}$	$1 - PPr_{Lamb}$		
Proportion of lambs examined	Pr_{Lamb}	20% of lambs in the flock	75% of the lambs arriving at the abattoir	All sheep in the flock	All sheep arriving at the abattoir
Proportion of adult sheep examined	Pr_{Adult}	100% of adult sheep in the flock	75% of the adult sheep arriving at the abattoir		
Total number of lambs examined	n_{Lamb}	Data for each flock based	Data for each flock based	See Pr_{Lamb}	See Pr_{Lamb}

		on N and Pr _{Lamb}	on Pr _{Lamb}		
Total number of adult sheep examined	n_{Adult}	Calculated for each flock based on N and Pr _{Adult}	Calculated for each flock based on Pr _{Adult}	See Pr _{Adult}	See Pr _{Adult}
Relative Risk for lamb	RR_{Lamb}	1.9	1.9	0.33, 0.5, 1, 3	0.33, 0.5, 1, 3
Relative Risk for adult	RR_{Adult}	1	1	1	1
<u>Diagnostic tests</u>					
Test sensitivity of clinical sign examination	Se_{CS}	Uniform (0.90-0.95)	Uniform (0.90-0.95)	See CSe	See CSe
Test sensitivity of PCR test	Se_{PCR}	0.95	0.95	See CSe	See CSe
Test sensitivity of bacteriology and subsequent Gelatin Gel test	Se_{GG}	0.60	0.60	See CSe	See CSe
Combined test sensitivity	CSe	Range(0.51-0.54)	Range(0.51-0.54)	0.3, 0.4, 0.6, 0.7	0.3, 0.4, 0.6, 0.7
Unit sensitivity	USe	Range(0.01-0.32)	Range(0.01-0.32)		

3 Results

In the Basic scenario, the Abattoir surveillance showed the highest median value of *SSSe* and *NDiagF* compared to the On-farm surveillance (Table 2, Fig. 3). The median *SeF* for detecting an infected flock with clinical signs was 0.77 for the Abattoir surveillance and 0.91 for the On-farm surveillance. The *SeF* for flocks without clinical signs was zero. For both surveillance systems, a higher median *SSSe* and median *NDiagF* were observed when more resources were invested (Table 2 and Fig. 3).

Furthermore, a higher median *SSSe* and median *NDiagF* were observed with increased design prevalence in both surveillance systems (Fig. 4). When the design prevalence was decreased to 0.1%, the median *SSSe* of the Abattoir and On-farm surveillance was 0.59 and 0.2, respectively. When the design prevalence was set to 2%, the median *SSSe* of the Abattoir and On-farm surveillance was 1 and 0.99, respectively. The median *NDiagF* of the Abattoir and On-farm surveillance was 1 (50% of infected flocks) and 0 (0% of infected flocks), respectively at 0.1% design prevalence. When the design prevalence was increased to 2%, the median *NDiagF* of the Abattoir and On-farm surveillance was 18 (35% of infected flocks) and 2 (4% of infected flocks), respectively.

In the sensitivity analysis, the median *SSSe* of the On-farm surveillance was never above the median *SSSe* of the Basic scenario of the Abattoir surveillance for any of the combination of input values (Table 3). The *SSSe* of the On-farm surveillance was sensitive to changes in the parameters of the high and low risk flocks, the within flock prevalence and when reducing the proportion of examined sheep showing clinical signs score ≥ 2 . The *SSSe* of the Abattoir surveillance was sensitive to changes in the parameters of lambs and adult sheep, within flock prevalence and proportion of sheep showing clinical signs score ≥ 2 . The median *NDiagF* of the Abattoir surveillance was reduced by 50% compared to the BS when the within flock prevalence was decreased to 0.2 and 0.4, when the proportion of examined sheep showing clinical signs score ≥ 2 was set to 0.1, the RR of lambs was set to 0.33 and the combined test sensitivity was decreased to 0.3 and 0.4. The median *NDiagF* was not changed in any of the sensitivity analyses of the On-farm surveillance. Further results of the sensitivity analyses are described in Table 3 and Fig. 5.

Table 2

The surveillance system sensitivity (*SSSe*) and the number of diagnosed flocks (*NDiagF*) in the On-farm and the Abattoir surveillance of virulent *D. nodosus* in Norway. The scenarios are based on the input values given in Table 1, and four different amounts of resources invested. Results are shown with the median and the 95% credibility intervals in brackets.

	Basic scenario (500,000*)	Low scenario (250,000*)	High scenario (750,000*)	Very High scenario (1 million*)
On-farm surveillance				
<u>Input</u>				
Number of flocks examined	179	89	269	359
<u>Results</u>				
Number of adult sheep examined	12,409 (11,047, 13,898)	6,155 (5,201, 7,216)	18,651 (16,959, 20,432)	24,931 (23,021, 26,869)
Number of lambs examined	3,720 (3,262, 4,228)	1,848 (1,523, 2,212)	5,593 (5,031, 6,199)	7,475 (6,832, 8,143)
Surveillance system sensitivity (<i>SSSe</i>)	0.37 (0.34, 0.39)	0.20 (0.18, 0.22)	0.49 (0.47, 0.51)	0.55 (0.52, 0.57)
Number of diagnosed sheep flocks (<i>NDiagF</i>)	0 (0, 2)	0 (0, 1)	0 (0, 3)	1 (0, 3)
Abattoir surveillance				
<u>Input</u>				
Number of days at abattoirs	84	42	126	168
<u>Results</u>				
Number of flocks examined	1,619 (1,413, 1,814)	1,032 (782, 1,267)	2,054 (1,883, 2,211)	2,358 (2,226, 2,476)
Number of adult sheep examined	4,631 (3,553, 5,753)	2,368 (1,505, 3,371)	7,082 (6,076, 8,013)	9,170 (8,539, 9,808)
Number of lambs examined	46,821 (37,585, 55,979)	24,004 (16,519, 32,231)	71,582 (63,149, 79,694)	92,787 (87,292, 98,464)
Surveillance system sensitivity (<i>SSSe</i>)	0.83 (0.75, 0.89)	0.66 (0.53, 0.77)	0.90 (0.84, 0.93)	0.93 (0.88, 0.96)

Number of diagnosed sheep flocks (<i>NDiagF</i>)	2 (0, 5)	1 (0, 4)	2 (0, 6)	2 (0, 6)
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*Amount of resources invested given in Norwegian kroner (NOK). 1 NOK is €0.123.

Table 3

Sensitivity analysis of the On-farm and the Abattoir surveillance of footrot in Norway.

The table shows the deviation in the surveillance system sensitivity from the Basic scenario when the input parameters are changed one by one. The *SSSe* of the Basic scenario is shown with an underline and in bold. The *SSSe* deviating more than 5% from the Basic scenario are shown in bold.

Input parameter	On-farm surveillance			Abattoir surveillance		
	Basic scenario	Sensitivity analysis	Median <i>SSSe</i>	Basic scenario	Sensitivity analysis	Median <i>SSSe</i>
<u>Basic scenario</u>			<u>0.37</u>			<u>0.83</u>
Population proportion of high risk flocks (PPr_{HR})	0.1	0.2	-7%	0.1	0.2	<5%
		0.3	-13%		0.3	<5%
		0.4	-18%		0.4	<5%
		0.5	-22%		0.5	<5%
Proportion of high risk flocks examined (Pr_{HR})	1	0.9	<5%	0.1	0.9	<5%
		0.8	-6%		0.8	<5%
		0.7	-11%		0.7	<5%
		0.6	-15%		0.6	<5%
		0.5	-19%		0.5	<5%
Relative risk of high risk flocks and low risk flocks ($RR_{HR} \cdot RR_{LR}$)	2:1	1:1	-39%	2:1	1:1	<5%
		3:1	27%		3:1	<5%
Within flock prevalence ($Prev$) in infected flocks	1 [#]	0.2 [#]	-51%	0.65*	0.2	-16%
		0.4 [#]	-26%		0.4	<5%
		0.5 [#]	-18%		0.5	<5%
		0.8 [#]	<5%		0.8	<5%
Proportion of sheep showing clinical signs score ≥ 2 (Pr_{CS})	1 [#]	0.1 [#]	-72%	0.295*	0.1	-10%
		0.2 [#]	-52%		0.2	<5%
		0.3 [#]	-37%		0.3	<5%
		0.4 [#]	-27%		0.4	<5%
		0.5 [#]	-18%		0.5	<5%
		0.6 [#]	-13%		0.6	6%
		0.7 [#]	-8%		0.7	6%
Proportion of lambs and adults examined ($Pr_{Lamb} \cdot Pr_{Adult}$)	20% lambs 100% adults	100% lambs 100% adults	<5%	75% lambs 75% adults	100% lambs 100% adults	<5%
Relative risk of lambs and adult sheep ($RR_{Lamb} \cdot RR_{Adult}$)	1.9:1	0.33:1	<5%	1.9:1	0.33:1	-7%
		0.5:1	<5%		0.5:1	<5%
		1:1	<5%		1:1	<5%
		3:1	<5%		3:1	<5%
Combined test sensitivity (CSe)	0.525*	0.3	-12%	0.525*	0.3	<5%

0.4	<5%	0.4	<5%
0.6	<5%	0.6	<5%
0.7	<5%	0.7	<5%

*To facilitate interpretation, only the median value is shown for the parameters which are modelled with a distribution. # The parameters of within flock prevalence and the proportion of sheep showing clinical signs in the On-farm surveillance is valid for the group of tested sheep in each flock, not the whole flock.

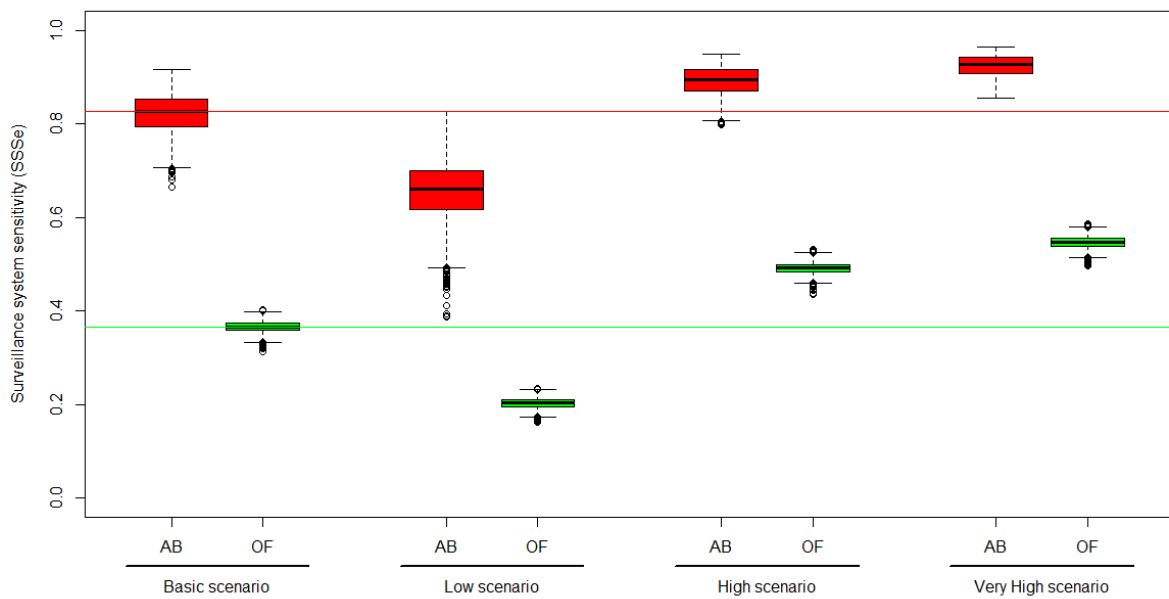


Fig. 3. The box-and-whiskers plot shows the surveillance system sensitivity (SSSe) of the Abattoir surveillance (red) and the On-Farm surveillance (green) with four different amounts of resources invested. The box represents the 25th and 75th percentiles and circles outside the whiskers are outliers. The red boxes are the results of the Abattoir surveillance and the green boxes are the results of the On-farm surveillance. The red and green lines represent the median SSSe of the Basic scenario in the Abattoir (red) and the On-farm (green) surveillance. AB=Abattoir surveillance (red), OF=On-farm surveillance (green), Basic scenario=The amount of money invested is NOK 500,000, Low scenario =The amount of money invested is NOK 250,000, High scenario =The amount of money invested is NOK 750,000, Very High scenario =The amount of money invested is NOK 1 million. 1 NOK is €0.123.

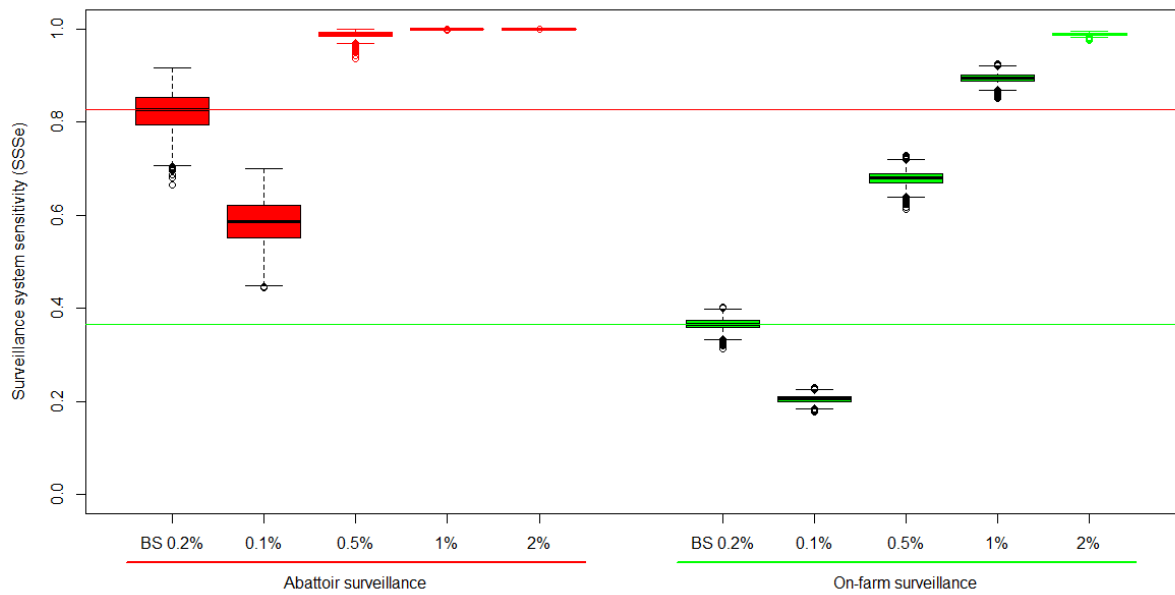


Fig. 4. The box-and-whiskers plot shows the surveillance system sensitivity (*SSSe*) of the Abattoir surveillance (red) and the On-Farm surveillance (green) with different design prevalence. The box represents the 25th and 75th percentiles and circles outside the whiskers are outliers. The red and green lines represent the median *SSSe* of the Basic scenario in the Abattoir (red) and the On-farm (green) surveillance. BS=Basic scenario. The percentages on the x-axis show the design prevalence of the flocks.

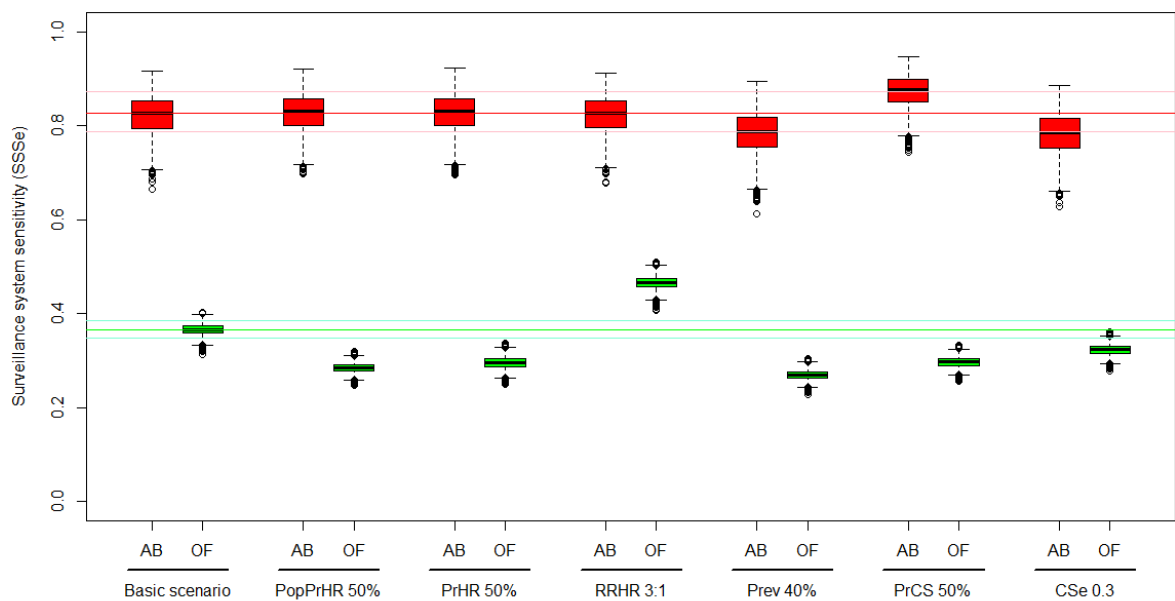


Fig. 5. The box-and-whiskers plot shows the surveillance system sensitivity (*SSSe*) of the Abattoir surveillance (red) and the On-Farm surveillance (green) for selected parameters from the sensitivity

analysis. The sensitivity analysis was based on the Basic scenario, where parameters were changed one by one. The box-and-whiskers plot shows the SSSe where the box represents the 25th and 75th percentiles and circles outside the whiskers are outliers. The red and green lines represent the median SSSe and the 5% deviation from the median of the Basic scenario in the Abattoir surveillance (red) and the On-farm surveillance (green). AB=Abattoir surveillance (red); OF=On-farm surveillance (green); Basic scenario=The scenario as described in Table 1; PopPrHR 50%=population proportion of high risk flocks is 50%; PrHR 50%=proportion of high risk flocks is 50%; RRHR 3:1=relative risk of high risk flocks is 3 and low risk flocks is 1; Prev 40%=within flock prevalence is 40%; PropCS 50%=Proportion of animals showing clinical signs is 50%; CSe 0.3=Combined test sensitivity is 0.3.

4 Discussion

Abattoir surveillance was estimated to be the more sensitive of the two surveillance systems to detect virulent footrot under Norwegian conditions. Abattoir surveillance had the highest SSSe in all the scenarios and had the highest median number of flocks detected with virulent footrot (*NDiagF*) as shown in Table 2, Fig. 3 and 4. In the sensitivity analysis, the median SSSe of On-farm surveillance never increased above the median SSSe of the Basic scenario of the Abattoir surveillance. These results further strengthen the use of Abattoir surveillance as the best alternative under Norwegian conditions.

Both simulation methods used were valuable when comparing the surveillance systems in this study. A stochastic scenario tree model has been widely used to document freedom from several diseases (Wahlstrom et al., 2010; Blickenstorfer et al., 2011; Norström et al., 2014). With this method the sensitivity of detecting at least one infected flock at a given design prevalence can be estimated, and the SSSe of two surveillance systems can be compared. This method is especially useful in cases where the probability of detecting a positive flock is low. The other method (simulation of a surveillance system) is better at estimating the difference between the surveillance programs when the probability of detecting positive flocks is higher.

The reliability of a model is based on the assumptions and the input variables used. A model based on real data is expected to give a higher reliability than models based on expert opinions or other presumed values and assumptions. All the assumptions in the models were based on information from the surveillance performed by the Healthy Feet Project during 2009–2014, and the input variables were retrieved from real data. However, for some of the parameters the number of flocks from which trustworthy data could be obtained was small and more data would have been

beneficial. Nevertheless, a conservative approach has been followed when estimating the parameters; hence, we do not think we have overestimated the effect of the surveillance systems.

The input parameters and the trust of the model can also be examined by sensitivity analysis. The parameters sensitive for changes in both surveillance systems were the within flock prevalence and the proportion of sheep showing clinical signs score ≥ 2 (Table 3). This was expected since the sensitivity of detecting virulent footrot in a flock is dependent on these factors.

The surveillance system sensitivity (*SSSe*) is calculated based on the number of flocks examined and their respective sensitivity of flock (*SeF*) and effective probability of infection (*EPI*) of high and low risk flocks (Eq. 2). When the *SeF*, *EPI* or number of examined flocks increases, the *SSSe* increases. In the Abattoir surveillance, the *SeF* is lower than in the On-farm surveillance because the number of animals examined in each flock is lower in the Abattoir surveillance. This alone would lead to a reduction in the *SSSe* in the Abattoir surveillance compared to the On-farm surveillance, but since a large number of flocks are examined in the Abattoir surveillance the overall effect is that the *SSSe* of the Abattoir surveillance is higher than the *SSSe* of the On-farm surveillance.

The parameters of high and low risk flocks were important for the outcome of the On-farm surveillance, but not in the Abattoir surveillance. This was expected since On-farm surveillance targets high risk flocks. A reduction in the relative risk of high risk flocks and an increase in the proportion of high risk flocks in the population reduced the *SSSe*. This shows the importance of the proper selection of high risk farms in the On-farm surveillance of footrot. But optimizing the selection is not easy in this study since footrot is a complex disease with many risk factors which complicate the selection of the at risk flocks.

The *SSSe* of the Abattoir surveillance was sensitive to changes in the parameters describing the risk of footrot in lambs and adult sheep. The *SSSe* was reduced when reducing the RR of lambs. The RR of lambs in the Basic scenario was set higher than that of adults which also is in accordance with another report from Norway (Klevar, 1943). Other countries have reported a higher proportion of adults having clinical signs of footrot (Beveridge, 1941, 1983; Grogrono-Thomas and Johnston, 1997). The RR of adults and lambs is an important parameter, and further investigations should be performed for estimating the RR of lambs and adults.

There was no major increase in the sensitivity of the surveillance systems when all the animals in the flock or all the animals arriving at the abattoir on the selected days were examined. This shows

that for instance having one more person at work on the days of examination is not beneficial for increasing the sensitivity of the surveillance system.

The aim of a surveillance and control programme for virulent footrot in Norway is to eliminate the disease and eventually document freedom from the disease. In 2014, only one flock was detected with virulent *D. nodosus* in Rogaland (Synnøve Vatn, personal communication), which corresponds to a prevalence of 0.04% in this county. In the Basic scenario, the design prevalence was 0.2% corresponding to five infected flocks in the county of Rogaland. When using one million Norwegian kroner to perform Abattoir surveillance in Rogaland, the probability of detecting at least one flock infected with virulent *D. nodosus* was 93% and a median of two flocks were detected. This suggests that we may need to increase the amount of resources to detect and eliminate the last flocks infected with footrot in Norway.

Another aspect of the elimination of footrot is that farmers are allowed to transport sheep to abattoirs in other counties for slaughter. In 2012, very few farmers from Rogaland were sending sheep to abattoirs in other counties (n=39). Even so, this shows that there is a possibility for farms to escape the Abattoir surveillance of footrot, and by this be infected without being detected. To perform a complete coverage of all flocks within a county with Abattoir surveillance, economic resources must also be used to examine sheep on abattoirs outside the county. Alternatively, On-farm examination of the farms sending flocks to abattoirs in other counties can be performed.

The surveillance strategies evaluated in this study do not include examination of flocks which are notified because of disease suspicion. Nor have we included flocks which had contact with a flock diagnosed with virulent footrot, and thereby are considered as possibly infected by *D. nodosus*. When considering the total surveillance activities for footrot in Norway, these flocks would be examined in addition to the flocks examined within the designed surveillance systems. Therefore, the total number of flocks diagnosed with footrot would most probably be higher than the results that this study suggests. Examination of notified flocks and contact flocks might be important for detecting the last infected flocks. An On-farm examination and sampling would be the best option for this purpose since a thorough examination of the whole flock is necessary for having a high probability of detecting disease.

The farmers should not send lame animals to the abattoir because of welfare issues, and farmers who do so, may be penalized. Experience shows that sheep with footrot score ≥ 2 have been recorded in Norwegian abattoir surveillance (Synnøve vatn, personal communication) as well as in

a Swedish study on abattoir surveillance (König et al., 2011). This might be explained by the sheep not being lame despite a score ≥ 2 or that lameness in sheep may be difficult to detect. Therefore, we believe that the Abattoir surveillance still will be better than On-farm surveillance despite that some lame sheep may not be sent for slaughter. In addition, abattoir surveillance at the end of the slaughter season is also important, since it can take longer time for sheep affected with footrot to reach optimal slaughter weight.

In conclusion, Abattoir surveillance is estimated to be the most sensitive way of detecting virulent footrot in Norway. However, On-farm examination is important for certifying single flocks free from footrot, as well as for examining flocks which have been in contact with flocks diagnosed with virulent *D. nodosus*.

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Appendix 1:

The cost of examining one flock in the On-farm surveillance was calculated by including the cost of two feet inspectors examining one flock and the cost of the laboratory examination of one flock.

Information from the surveillance and elimination program of footrot performed by the Healthy Feet Project has been used.

Table A1

Calculation of average cost of examining one flock in the On-farm surveillance and calculation of the number of flocks examined in the Basic scenario1-4.

		Total
Personnel		
<u>Mean cost for personnel for examining one flock</u>		<u>2,763</u>
Samples		
Cost of one laboratory sample	920	
Number of samples from each flock with clinical signs	5	
Mean cost of samples for each flock with clinical signs	$920 \cdot 5$	4,600
Design prevalence	0.002	
Adjusted Risk of High risk flocks	1.82	
Proportion of high risk flocks examined	1	
Minimum probability of infected flock without clinical signs	0.09	
Maximum probability of infected flock showing clinical signs	$1-0.09$	0.91
Probability of flock with clinical signs	$0.002 \cdot 1.82 \cdot 1 \cdot 0.91$	0.0033
Mean cost of samples for each flock	$4,600 \cdot 0.0033$	<u>15.18</u>
<u>Total cost of examining one flock on the farm</u>	$2,763 + 15.18$	<u>2,778</u>
Number of flocks examined in different scenarios		
<u>Number of flocks examined in the Basic scenario</u>	$500,000/2,778$	<u>179*</u>
<u>Number of flocks examined in the Low scenario</u>	$250,000/2,778$	<u>89*</u>
<u>Number of flocks examined in the High scenario</u>	$750,000/2,778$	<u>269*</u>
<u>Number of flocks examined in the Very High scenario</u>	$1 \text{ million}/2,778$	<u>359*</u>

*rounded down to an integer.

Appendix 2:

The cost of examining sheep for one day of Abattoir surveillance was calculated by including the cost of two foot inspectors examining sheep for one day and the cost of the laboratory examination of samples taken on one day in an abattoir. Information from the surveillance and elimination program of footrot performed by the Healthy Feet Project has been used.

Table A2

Calculation of average cost for one day and calculation of the number of days with Abattoir surveillance in the Basic scenario 1-4.

		Total
Personnel		
Cost of one foot inspector/day	2,625	
Number of foot inspectors needed	2	
<u>Calculation of cost of personnel/day</u>	<u>2,625·2</u>	<u>5,250</u>
Samples		
Cost of one laboratory sample	920	
Mean number of flocks from the county of Rogaland entering the abattoir per day	22.24	
Design prevalence	0.002	
<u>Mean number of positive flocks per day</u>	<u>22.24 · 0.002</u>	<u>0.044</u>
Mean number of lamb slaughtered/flock/day	24.40	
Mean number of adult slaughtered/flock/day	2.4	
Relative Risk of lamb	1.9	
Relative Risk of adult	1	
Proportion of sheep arriving at the abattoir that is examined	0.75	
Median proportion of animals with clinical signs (mean:0.22)	0.15	
Number of examined lamb showing clinical signs in each positive flock	$24.40 \cdot 0.75 \cdot 1.9 \cdot 0.15$	5.21
Number of examined adult sheep showing clinical signs in each positive flock	$2.4 \cdot 0.75 \cdot 1 \cdot 0.15$	0.27
Mean total number of sheep showing clinical signs in each positive flock	$5.21 + 0.27$	5.48
Sensitivity of diagnosing clinical signs	0.95	
<u>Mean number of samples from each positive flock</u>	<u>$5.48 \cdot 0.95$</u>	<u>5.21</u>
<u>Number of samples submitted for laboratory</u>	<u>$0.044 \cdot 5.21$</u>	<u>0.23</u>

<u>examination/day</u>		
The cost per day for sampling positive animals	$0.23 \cdot 920$	212
Number of false positive samples/day	0.5	
The cost per day for sampling false positive animals	$0.5 \cdot 920$	460
<u>Total cost of one inspection day at the Abattoir</u>	$5,250 + 212 + 460$	<u>5,922</u>
<u>Number of inspection days in the Basic scenario</u>	$500,000/5,903$	<u>84*</u>
<u>Number of inspection days in the Low scenario</u>	$250,000/5,820$	<u>42*</u>
<u>Number of inspection days in the High scenario</u>	$750,000/5,820$	<u>126*</u>
<u>Number of inspection days in the Very High scenario</u>	$1 \text{ million}/5,820$	<u>168*</u>

*Rounded down to an integer.