

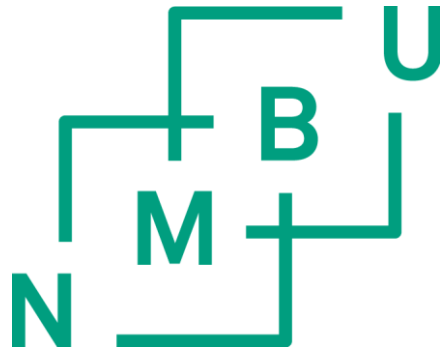
Healthier Goats disease eradication programme
- a healthy initiative

Philosophiae Doctor (PhD) Thesis

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Preface

Based upon promising results in the Healthier Goats disease eradication programme, the Norwegian dairy goat farmer organisations wanted to establish an optimal national health programme for all the dairy goat herds in Norway, also after the ending of the Healthier Goats programme. With this in mind, an application for financial support for a project called “Optimal health, welfare and food safety for quality products from Norwegian goats” was sent to the Research Council of Norway in 2005. This project was a cooperation between the Norwegian Goat Health Services (TINE Norwegian Dairies SA, Norwegian Sheep and Goat Association, Norwegian School of Veterinary Science and National Veterinary Institute) and the Norwegian Agricultural Economics Research Institute and the present PhD project and this thesis was developed from that project.

The PhD research work presented in this thesis was carried out at the Norwegian School of Veterinary Science (Norwegian University of Life Sciences), Department of Production Animal Clinical Sciences, from September 2006 to September 2014.

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Summary

The Norwegian Goat Health Services (NGHS) initiated the Healthier goats disease eradication programme – Healthier Goats (HG) in 2002. The objectives of HG was to eradicate and control the three contagious diseases caseous lymphadenitis (CLA), caprine arthritis-encephalitis (CAE) and caprine paratuberculosis, all present at a high prevalence and believed to cause severe production losses and impair animal welfare in affected herds and thus to be detrimental for the goat industry in Norway.

HG is reported to show positive results with regard to health status, animal welfare and production results for the animals and herds participating in the programme. A very low number of herds (1.2%) have been re-infected with the abovementioned diseases, after eradication. At present time, all dairy goat herds have undertaken disease eradication through HG and the total volume of goat milk distributed by TINE Dairies SA now comes solely from farms that have completed disease eradication.

The main objectives of the present PhD-study was to provide documentation for the effect of the HG on health and production in Norwegian milk goat herds, to evaluate the potential effect of HG on direct economical outcome for the farmer, and to evaluate the diagnostic tools used in the HG. The final objective was to investigate the risk of spreading CLA between sheep and goats by contact on pasture by prevalence testing of sheep flocks in close contact with goat herds. The four different studies constituting the basis for this thesis were established and conducted between 2007 and 2011. Three of the studies (Paper II-IV) are published in international peer reviewed journals, and the fourth (Paper I) has recently been submitted for publication.

Different methods were applied for the individual studies. The study of the financial effect of HG for the farmers was conducted as a cost-benefit analysis (CBA) using stochastic simulation to account for uncertainty and variation in the parameters. The modelling of lactation curves was conducted applying a data-driven approach using mixed-effects regression models and implementing spline functions due to the non-linear nature of lactation. The evaluation of the two Enzyme-Linked

Immunosorbent Assay (ELISA) tests for the detection of CAE and CLA was conducted comparing individual animal tests with herd level testing, i.e. bulk tank milk (BTM) testing. The use of BTM in the surveillance of the dairy goat population after disease eradication was assessed. Finally, the investigation of pasture areas and contact between sheep and goats considering the possible spread of CLA infection was conducted using a questionnaire. This included the recording of pasture information on maps and the subsequent analysis with a Geographic Information System (GIS; ArcGIS©9.1).

The material for the four studies comes from different sources, including the Goat Milk Recording System (GMRS), the Efficiency Control Database for Goats (ECDG), serological and BTM test results and serological samples from sheep, questionnaires and map recordings, among others.

The present project revealed that HG as conducted with governmental support has a beneficial financial effect for the farmers in that the net present value (NPV) of investments becomes positive over less than a 10 years investment-horizon. Furthermore, the study of lactation curves revealed that the total milk yield in a lactation increased with over 20% from before to after enrolling in HG, controlling for the general development of milk yield over time, independent of HG. The evaluation of the BTM ELISA tests showed that both tests were suitable for application as a first-step surveillance tool with further follow-up testing at individual level within the herd, when deemed necessary.

It can be further concluded that without the substantial financial support from the government HG would have been much less beneficial and would have faced greater challenges in recruiting farmers/herds than what has been the case with governmental support. When that is said, the monetary support is not the sole success factor in this programme. The initiative and will to succeed characterise the dairy goat farmers enrolled in HG. Other success criteria are believed to include good cooperation between field veterinarians, the project management, the TINE Dairies advisors and the farmers themselves.

HG has proven that it is possible to eradicate three major infections from a national dairy goat population. It is reasonable to believe that experience from this programme should have implications when establishing other disease eradication strategies in Norway, but can also be of relevance in other parts of the world and for other species.

Samandrag

Helsetjenesten for Geit starta i 2002 saneringsprogrammet Friskare Geiter (FG). Hovudmålet for FG var å sanere den norske melkegeitpopulasjonen for dei tre kronisk smittsame sjukdommane byllesjuke, caprin artritt-encefalitt og paratuberkulose. Desse tre sjukdommane har hatt stor førekomst i den norske geitepopulasjonen og det har vore antatt at sjukdommane har ført til alvorlege produksjonstap i tillegg til å generelt påverke dyrehelse og dyrevelferd særst negativt.

FG kan vise til gode resultat kva angår helsestatus, dyrevelferd og produksjonsresultat for dyr og besetningar som har delteke i FG. Svært få besetningar har opplevd re-smitte av sjukdommane etter sanering. Pr januar 2015 er alle melkegeitbesetningar sanerte og TINE SA foredlar berre melk frå sanerte flokkar. Hovudmålet for doktorgradsprosjektet presentert i denne avhandlinga, var å beskrive og dokumentere effekten av FG på helse og produksjon i norske melkegeitbesetningar. Konkret ville ein evaluere den potensielle økonomiske gevinsten for bøndene av å delta i FG. Det var også vurdert som viktig å studere det diagnostiske verktøyet brukt i FG for om mogleg å forbetre dette og tilpasse det til framtidig overvaking av dei tre sjukdommane. Førekomst av byllesjuke hos sau og smitteoverføring av byllesjuke mellom sau og geit var tema i ein av dei fire studiane som utgjer denne avhandlinga.

Dei fire studiane som utgjer denne avhandlinga vart gjennomført i perioden 2007-2011. Tre av desse arbeida er publisert i internasjonale tidsskrift mens den fjerde nyleg er sendt inn til vurdering for publisering.

Ulike metodar vart anvende i dei individuelle studiane. For å studere den økonomiske effekten av FG for bøndene, blei det utført ei finansiell kost-nytte analyse der ein brukte stokastisk modellering for å gjere greie for usikkerhet og variasjon i parametrane. Modellering av laktasjonskurver hadde ei data-driven tilnærming der ein brukte regresjonsmodellar med både faste og variable effektar inkludert. I tillegg vart det implementert spline-modellar i laktasjonskurvene for å ta høgde for den ikkje-lineære

naturen i ein laktasjon. Vidare vart det gjennomført ei evaluering av to diagnostiske testar for påvising av caprin artritt-encefalitt og byllesjuka antistoff. Resultat frå tankmelktesting og individuell serologisk testing vart samanlikna og vurdert med tanke på å bruke tankmelk i framtidig overvaking av desse to sjukdomane.

Materiale til studiane i denne avhandlinga kjem frå ulike kjelder og inkluderer mellom anna Geitekontrollen, Effektivitetskontrollen Geit, spørjeundersøkingar til melkegeitprodusentar som deltek i FG og til sauebønder som har tett kontakt med geitebesetningar, prøvesvar frå serologisk testing og tankmelktesting for byllesjuka og caprin artritt-encefalitt hos geit og serologiske testresultat frå sauer for påvising av byllesjuka.

Resultat frå studiane viser at FG i gjennomsnitt har ein positiv økonomisk effekt for bøndene over ein investeringshorisont på opp imot 10 år. Det vart utrekna netto nåverdi av investeringar i FG og desse vart stort sett positive over ein periode på mindre enn ti år. Vidare viste analysane av laktasjonskurver at total melkeytelse auka med over 20% frå før til etter sanering i FG når ein kontrollerte for den generelle utviklinga i melkeytelse uavhengig av FG. Vedrørande dei to tankmelk-test evalueringane for påvising av byllesjuka og caprin artritt-encefalitt i tankmelk, viste begge testane seg pålitelege nok til å brukast som ein første-steg test i overvaking av desse to sjukdomane.

Det kan også konkluderast med at utan den omfattande økonomiske støtta som FG fekk over dei årlege Jordbruksforhandlingane, så ville resultatane vore mykje mindre positive for melkegeitprodusentane. Det kunne også vist seg vanskelegare å rekruttere deltakarar til FG dersom ein stor andel av utgiftene til sanering måtte blitt dekkja av produsentane sjølve og ikkje gjennom tilskot frå FG slik situasjonen har vore i programmet. Når det er sagt, så er ikkje dei økonomiske tilskota aleine om å forklare suksessen til FG. Eigeninnsats og initiativ frå melkegeitprodusentane sjølve har vore avgjerande for å sikre smittefrie sanerte geitebesetningar. Andre suksessfaktorar vil

vere eit godt etablert samarbeid mellom praktiserande veterinærar, prosjektledelsen i FG, rådgjevarar i TINE SA og bøndene sjølve. Vidare er kravet om å følgje saneringsprotokollen til FG, som måtte vere godkjend av lokal veterinær, for å få utbetalt rekrutteringsbilag frå FG, eit viktig suksesskriterium.

FG har vist at det er mogleg å sanere tre alvorleg smittsame sjukdomar frå ein heil nasjonal populasjon av melkegeiter gjennom god styring og forutsigbarhet for dei involverte. Det vil vere naturleg å forvente at erfaringar og resultat frå FG kan brukast inn i planlegging av andre sjukdomskontrollprogram ikkje berre i Norge, men også i andre deler av verden og for andre artar enn geita.

List of acronyms

AIC	Akaike' Information Criteria
BIC	Bayesian Information Criteria
BTM	Bulk Tank Milk
CAE	Caprine Arthritis Encephalitis
CBA	Cost Benefit Analysis
CDF	Cumulative Distribution Factors
CLA	Caseous Lymphadenitis
DIM	Days In Milk
DPY	Day of Peak Yield
ELISA	Enzyme Linked Immunosorbent Assay
FG	Friskare Geiter
ECDG	Efficiency Control Database for Goats
GIS	Geographic Information System
GMRS	Goat Milk Recording System
HG	Healthier Goats disease eradication programme
MAP	Mycobacterium avium subspecies paratuberculosis
MV	Maedi-visna virus
NGHS	Norwegian Goat Health Service
NILF	Norwegian Agricultural Economics Research Institute
NPV	Net Present Value
NSG	Norwegian Association of Sheep and Goat Farmers
PERT	Program Evaluation and Review Technique
PY	Peak Yield
ROC	Receiver Operating Characteristic
SRLV	Small Ruminant Lentivirus
TY	Total milk Yield for a lactation period

List of papers

Paper I

Nagel-Alne GE, Simon-Nilsen M, Valle PS, Sølverød L. Caseous lymphadenitis infection in sheep flocks and risk of spread through pasture contact with infected goat herds in Malangen, Norway, (Submitted for publication in *Veterinary Record*)

Paper II

Nagel-Alne GE, Valle PS, Krontveit R, Sølverød L. (2015) Caprine arthritis encephalitis and caseous lymphadenitis in goats: use of bulk tank milk ELISAs for herd-level surveillance, *Veterinary Record* 176(7):173 doi:10.1136/vr. 102605

Paper III

Nagel-Alne GE, Krontveit R, Bohlin J, Valle PS, Skjerve E, Sølverød L. (2014) The Norwegian Healthier Goats program—Modeling lactation curves using a multilevel cubic spline regression model, *Journal of Dairy Science* 97: 4166-4173 doi: 10.3168/jds.2013-7228

Paper IV

Nagel-Alne GE, Asheim LJ, Hardaker JB, Sølverød L, Lindheim D, Valle PS. (2014) The Norwegian Healthier Goats programme – A financial cost–benefit analysis, *Preventive Veterinary Medicine* 114:96-105 doi: 10.1016/j.prevetmed.2014.02.002

Introduction

The presence of diseases has negative consequences for the productivity of affected animals and the production levels in dairy goats in Norway has been particularly affected by high prevalence of chronic infectious diseases.

The main aim of this thesis was to investigate how the Healthier goats disease eradication programme -Healthier Goats (HG) affected the enrolled dairy goat herds and to provide estimates for the cost and benefit of HG to the dairy goat farmers.

Dairy goat industry in Norway

Before the Second World War there were between 250.000 and 300.000 goats in Norway, distributed in approximately 27.000 small herds around the country. The goats were kept for milk and meat production without any organised production form at this time. After the Second World War, the number of goats decreased gradually and the dairy goat production became organised, with larger herds and the establishment of milk goat dairies in strategic areas in the vicinity of goat herds. In the first half of the 20th century, it was a challenge for the milk cow dairies to properly collect, store separately, and process goat milk. Therefore, the majority of the goat milk was processed on farms, while only 24% of the milk was handled by the milk cow dairies in 1939 (Geiteboka, 2002).

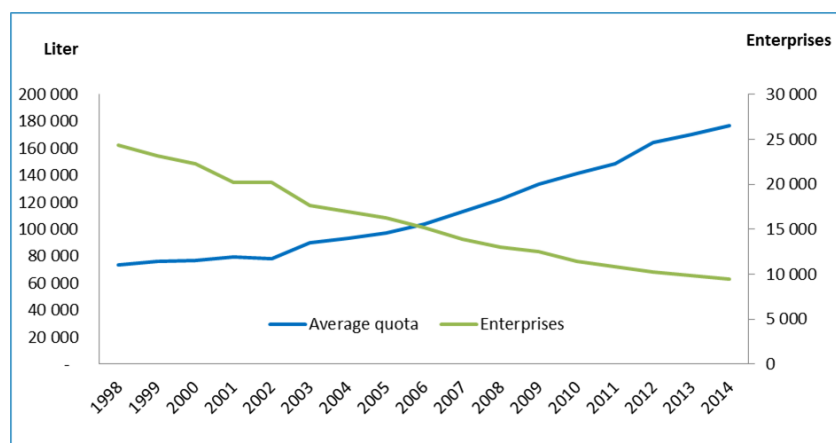
In 1947, the Norwegian Association of Sheep and Goat Farmers (NSG) was founded. One of their aims was to re-organise the dairy goat production and improve the utilisation of outlying fields in the production of dairy goat milk. Another important task for the NSG was the establishment of common alpine dairy farms, with the first initialised in 1957 where 180 dairy goats from 35 herds were milked through summer months. In 1985, more than 50 common alpine dairy farms had been established in all dairy goat producing areas in the country. But as a consequence of a reduced number of dairy goat farms and the closing down of regional dairies, the majority of the common alpine dairy farms were unsustainable and therefore closed down.

Along with the more efficient dairy goat production, the interest for milk yield and milk yield measures was raised, and in 1972, the TINE Goat Milk Recording System (GMRS) was established with routine measurements of milk yield and milk content, among others.

While the number of dairy goat herds has decreased, the average milk quota has increased the last 30 years. In 1991 the average milk quota was 29 000 L, while in 2014 it had reached 72 400 L. There were approximately 1000 dairy goat farmers in 1991, decreasing to 310 in 2014 (Figure 1).

Furthermore, the average total milk yield per lactation has increased from 550 Kg in 1991 to 727 Kg in 2013. The proportion of goat milk delivered and classified as “Premium quality milk” has also increased from 73.4% in 2009 to 92.4% in 2013 (TINE Rådgiving, 2013).

Figure 1 *Developments in goat milk quotas and the number of dairy goat farmers from 1991 to 2014.* Statistics, Norwegian Agriculture Agency, 2014.



Goats in a global perspective

According to the Food and Agriculture Organization of the United Nations (FAO) (2010) the world population of goats is about 921 million, and includes a total of 570 breeds. Asia has the largest population of goats of about 556 million (60%), followed by Africa (311 million) (Table 1). Europe accounted for only 2% of the goat population but many of the European breeds have been widely introduced into many Asian and African countries to improve milk yield (Devendra, 2012).

Table 1 *Goat population and their global distribution presenting figures for 1986 and 2010 together with the annual growth rate of number of goats in each region. Figures in millions. (Source FAO, 2010).*

Region	Year		% (2010)	Average growth rate (% per year)
	1986	2010		
Africa	105.4	310.7	33.7	2.8
Asia and Pacific	253.5	556.1	60.4	2.3
Europe	10.8	16.5	1.9	1.4
Latin America and the Caribbean	32.9	212.6	4.8	22.8
Near East	83.9	267.5	2.3	9.1
North America	1.8	3.0	0.1	1.7
Total	488.2	920.6	-	7.0

The extensive keeping of goats is important for smallholders in certain parts of the world including Africa and Asia (Devendra, 2012). Goat meat and milk plays an important role in nutrition and the socioeconomic wellbeing of the many rural people in developing and underdeveloped countries, where it provides basic nutrition and subsistence (Park and Haenlein, 2007).

Production of goat milk and dairy products like cheeses and yoghurt is also a valued part of the dairy industry in developed countries, where it provides diversity to consumer tastes, and supports people with medical afflictions, such as allergies and gastro-intestinal disorders, who need alternative dairy products (Haenlein, 1996 and 1997; Park, 1992 and 1994).

The intensive dairy goat industry is by and large limited to developed countries and is very small compared to the dairy cattle industry. The vast majority of milk produced on EU farms (96.8%) comes from cows, although in a number of the southern European Member States significant quantities of milk are also produced by sheep, goats and buffaloes (Eurostat, 2013). This difference in size of the dairy goat industry compared to dairy cattle may in part explain the smaller number of existing reports on dairy goat related issues.

The Goats Density Map produced by FAO (Figure 2) shows the global distribution of goats and clearly shows the high density of goats in Asia and Africa.

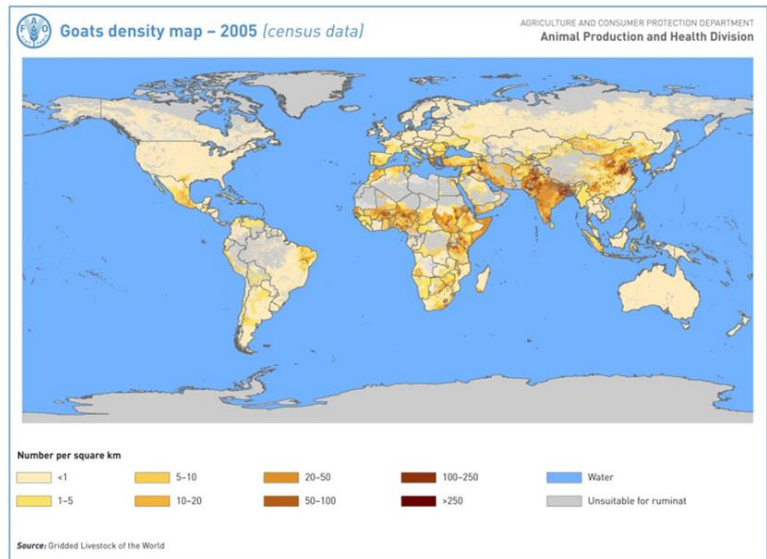


Figure 2 Worldwide distributions of goats according to the number of goats per km². (Source FAO, 2005).

The most important chronic infectious agents

Numerous reports describe the challenges and potential losses caused by different chronic infectious diseases in goat populations worldwide (Kruze, 2006; Adam et al., 1983; Brown and Olander, 1987).

Norway is no exception, and over the years towards 2000, a common understanding about the worsening of the health status of the Norwegian dairy goat population emerged. Registrations in the GMRS of dairy goats either euthanised or dead without a certain diagnosis became a worry.

Among veterinarians working with dairy goats in their practice and the dairy goat farmers themselves there was too little knowledge concerning the health status of the goats, but they worried that the presence of chronic infectious diseases was detrimental for the production and a burden for the dairy goat population (N. Leine, personal communication). With this in mind, a local project was established in 1999 with registrations from 17 dairy goat herds located in two areas with a high density of dairy goats (Valdres and Sunnmøre), (Leine, 2000). The project included routine pathological examinations of goats, detailed post mortem registrations on carcasses in slaughter

houses, registrations of live weight and slaughter weight, documentation of parasite infestations in the herds, registrations of reasons for culling and diagnosis in GMRS, blood sampling, and registrations from the environment and barn.

From this screening, it was concluded that respiratory diseases were highly prevalent, and the most important problems among the Norwegian dairy goats were caprine arthritis encephalitis (CAE), lung worms and caseous lymphadenitis (CLA). The pathological examinations showed that a majority of the goats had more than three serious diagnoses. Further, a large variability in both live weight and slaughter weight between herds and within herds were registered. The obvious variation between different age groups was thought to be due to chronic infections in animals in later lactations, resulting in a significant reduction in live weight. The presence of caprine paratuberculosis was a special worry as this is a notifiable disease creating restrictions on pasture use, livestock trade and for sending animals for slaughter.

With the presence of these major infections in the majority of the Norwegian goat population, it was assumed that there could be a substantial production volume being lost due to the infection burden. Other relevant factors contributing to production losses could be suboptimal feeding regimes, management practices as late weaning and the industry's lack of focus on the value of breeding for better milk quality and volume.

The results from the screening in the 17 dairy goat herds lead to a suggestion to establish a national eradication programme for CAE, CLA and caprine paratuberculosis in the Norwegian dairy goat population. Other countries as Sweden, Switzerland and France had established and accomplished programmes for control and eradication of CAE, so it was possible to learn from their experiences (Lindqvist, 1999). The idea to incorporate all three diseases in the same eradication programme was based on the knowledge regarding the way the three diseases spread and that they were all slow, chronic infections with very limited degree of in utero transmission.

Caprine arthritis encephalitis (CAE)

CAE was first recognized in the early 1970s and has emerged as a significant and costly disease of goats. The CAE virus is an enveloped, single-stranded ribonucleic acid virus in the lentivirus genus of the family *Retroviridae*. Other lentiviruses, or slow viruses, include the maedi-visna (MV) virus of sheep, equine infectious anaemia virus, the bovine immunodeficiency virus, the feline immunodeficiency virus and the human immunodeficiency virus. The MV virus and the CAE virus were historically considered to be similar but distinct viruses, with strong host species predilection for sheep and goats respectively. However, new research shows that this distinction does not hold and the two viruses are now classified together in the small ruminant lentivirus (SRLV) serogroup (Smith and Sherman, 2009). This classification of MV and CAE viruses has an impact on the way CAE can be controlled in populations with both sheep and goats.

The CAE virus is a cell-associated virus using the host cell machinery for the production of proviral deoxyribonucleic acid (Cheevers and McGuire, 1988). In general, it can be said that a CAE virus infection is considered to be lifelong, and serum antibodies to the virus, if not of colostrum origin, are considered synonymous with infection (Smith and Sherman, 2009).

The highest prevalence of CAE seemed to occur in countries with long established, intensive goat dairying industries, namely Canada, France, Norway and the United States. The seroprevalence has exceeded 65% in all these countries (Adams et al., 1983), while indigenous African goat breeds tested were free of infection. A study by Nord et al. (1998) showed that out of 51 tested dairy goat herds in Norway, 42% of the goats and 86% of the herds were infected. Further, in 2004, bulk tank milk (BTM) testing indicated that 88% of the Norwegian dairy goat herds had a CAE infection.

The CAE virus can be transmitted both vertically and horizontally and the most important vertical transmission is through ingestion of virus-contaminated colostrum or milk. The main route of horizontal infection is by direct or close contact with infected animals. The strong association between CAE infection and intensively managed dairy goat is largely due to management practices

that facilitate transmission of the virus from does to kids in the perinatal period, as well as horizontally between adults (East et al., 1987 and 1993; Greenwood et al., 1995). Additional potential sources of infection in kids during the perinatal period, include exposure to virus from birth fluids during kidding and the inhalation of infected aerosols from a coughing doe to the kid, as well as *in utero* infection, although this mechanism of spreading is not definitely documented (Adams et al., 1983). Iatrogenic transfer of CAE is also considered a possible transmission route, e.g. caused by the multiple uses of needles for vaccination. A number of traits common for goats are considered to contribute to the spread of CAE virus, including biting, eye licking in hot weather, leaking of milk to the environment and the presence of nasal discharge in common feed troughs. Although the contribution of these different factors to the transmission and spreading of the CAE virus is unknown, they should be taken into account when planning and implementing successful disease control program in a CAE infected population as stated by Greenwood et al., (1995) and Blacklaws et al., (2004).

Subclinical CAE infections occur, but the CAE virus can cause a range of signs in infected goats, including arthritis, neurological dysfunction, progressive paresis and indurative mastitis. The most common presentation of the disease is arthritis in sexually mature goats. The clinical signs may be subtle, but infected goats may have a reluctance or difficulty to raise or move, a stiff gait and swollen joints. The infection often progresses to a painful debilitating arthritis accompanied by a gradual weight loss and a rough hair coat (Smith and Sherman, 2009).

The diagnosis of CAE infection is based on a combination of clinical history of CAE in the herd, serological examination and/or PCR diagnostics, detection of synovial fluid abnormalities, and typical histopathological findings and post mortem examinations (Smith and Sherman, 2009). The most important diagnostic test for CAE screening is the detection of CAE specific antibodies. Serological testing of individuals or the use of BTM at herd level is the two main biological sources of material used when an ELISA test is applied. ELISAs are rapid tests, are relatively inexpensive and are also

suitable for a large number of samples. In Norway, commercially available ELISAs are used for the detection of CAE infection in goats.

The economic impact of CAE is linked to the considerable reduction in milk yield observed in infected does compared to uninfected ones, especially in later lactations (Martínez-Navalóna et al., 2013; Greenwood, 1995; Sanchez et al., 2001). Epidemiological studies assessing the economic impact of CAE infection in a dairy goat population are very few. Peterhans et al. (2004) states that CAE infection is thought to have a considerable economic impact on dairy goat production.

A sound method for controlling a CAE infection includes: 1) removal of adult animals and raising CAE-free kids, 2) periodical serological sampling for monitoring the prevalence during an ongoing control programme and 3) culling or segregation of seropositive animals to limit further spread of the infection (Smith and Sherman, 2009).

Caseous lymphadenitis (CLA)

CLA is a chronic contagious disease mainly affecting sheep and goats. It is caused by *Corynebacterium pseudotuberculosis* and the organism enters the goat's body through wounds or small breaks in the skin or mucous membranes, and eventually becomes located in regional lymph nodes (Smith and Sherman, 2009). The incubation period until abscesses are observed in superficial lymph nodes is typically between two and six months or longer (Ashfaq and Campbell, 1980). These abscesses may rupture and drain spontaneously with contamination of the environment and herd mates. Internal, visceral abscesses may also develop if the organism reaches the thoracic lymph duct or is inhaled.

Many of the external lymph nodes may be involved in the infection, especially lymph nodes of the head and neck because injuries from fighting and scratching commonly occur here (Ashfaq and Campbell 1979a and 1979b; Holstad, 1986; Schreuder et al., 1986). A slaughterhouse study by

Ghanbarpour and Khaleghiyani et al. from 2005 found the highest prevalence in the prescapular lymph node.

CLA occurs worldwide and is especially evident in commercial flocks (Connor et al., 2000; Paton et al., 2003 and Peel et al., 1997). Holstad (1986) reported CLA in 19 out of 36 herds (53%) tested in a prevalence study in northern Norway.

Clinical diagnosis of CLA is based on the presence of a firm to slightly fluctuant subcutaneous swelling in the anatomic location of lymph nodes (Burrell, 1981). In a herd with a history of caseous lymphadenitis, the clinical findings alone are considered presumptive evidence of infection. Without a herd history, laboratory assistance may be necessary for confirming a diagnosis. Detection of CLA specific antibodies by the application of ELISA tests is used in the diagnosis of CLA in the Norwegian goat population.

CLA infection is a potential zoonosis and human lymphadenitis has been reported especially from Australia (Peel et al., 1997; Mills et al., 1997). People at risk are slaughterhouse workers, farmers, shearers and veterinarians. Antibiotic treatment has not been rewarding because most antibiotics do not penetrate the encapsulated abscess and the organism itself may reside intracellularly. Surgical treatment, either by draining or removal of the affected lymph node, has been described (Ashfaq and Campbell, 1980), but the procedure involves a high risk of spreading infectious material to the environment and can be a hazardous for the personnel.

The eradication and control of CLA relies on the willingness of farmers to cull goats with abscesses and to purchase or raise new uninfected stock. *Corynebacterium pseudotuberculosis* is killed by commercial pasteurisation (Baird et al., 2005), so the separation of new-born kids from the dams and feeding them with pasteurised colostrum or milk replacer can be an adequate procedure in controlling CLA. An eradication programme in the Netherlands managed to successfully eradicate CLA in 53 herds by applying serological testing and culling of infected animals (Dercksen et al., 1996). The value of vaccination as an aid in controlling the disease has frequently been questioned (Smith

and Sherman, 2009). Vaccinated goats test false positive in an ELISA for antibodies (Sting et al., 1998), so a test and cull programme is difficult to implement when vaccination is applied in a population.

CLA is a disease of both sheep and goats, but under Norwegian conditions the disease has been regarded mostly a “goat problem”. This can in part be explained by the more obvious expression of the disease in goats than in sheep, as external abscesses are more common in goats (Brown and Olander, 1987). Sheep with CLA more frequently acquire internal abscesses and these are often only discovered at post mortem inspections in slaughterhouses and reported as unspecific abscesses.

In 2006, the Malangen Peninsula in Troms County in Norway came in focus due to the detection of a higher prevalence level of CLA in sheep herds than expected. These sheep herds were tested for CLA because they were located in close vicinity to dairy goat herds that were enrolled in HG, and they also shared pasture. It became a worry for the goat farmers in the area that sheep could re-infect their goats after disease eradication since there was contact between sheep and goats on pasture. To further investigate the risk of spread of CLA between sheep and goats, a local study was established to gain information on CLA infection in the sheep population in Malangen Peninsula and this study was included in the present PhD study.

Caprine paratuberculosis (Johne's disease)

Johne's disease is caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP) and is an economically important infectious disease of domestic and wild ruminants, primarily affecting the digestive tract. Johne's disease has been studied most intensively in cattle and the infection has similarities between the cattle and goats, with wasting and reduced milk yield. One of the most important differences between bovine and caprine paratuberculosis is the lack of profuse diarrhoea

in goats which in cattle is regarded as the cardinal sign of the infection (Juste and Perez, 2011; Cho et al., 2012; Mitchell et al., 2008).

Paratuberculosis was first described in cattle in 1865 (John and Frothingham, 1895) and in goats in 1916 (McFadyean and Sheather, 1916). It has a worldwide distribution and is regarded as one of the most costly diseases causing high economic losses to the dairy production globally (Hasonova and Pavlik, 2006).

In Norway, Johne's disease has been more prevalent in goats than in sheep and cattle (Djønne, 2003). A goat-specific strain is recognised in Norway (Collins et al., 1990) and the disease has previously been endemic in goats in the southern part of the country. Differences in prevalence in different parts of the country are assumed to be related to climatic conditions, influencing the survival of the causative bacterium. By 1982, the infection rate of paratuberculosis in individual animals had been reduced from 53% to 1% following the introduction of a compulsory vaccination program in 1967 (Saxegaard and Fodstad, 1985). Vaccination has largely reduced the prevalence of observed signs of the disease, but asymptomatic animals still shed MAP in their faeces (Djønne, 2003).

The primary mode of transmission of paratuberculosis is faecal-oral, with the organism shed in the faeces of infected adults and ingested by susceptible young stock. Neonates are considered to be the most susceptible for new infections.

There is no effective treatment against Johne's disease in goats. Even if clinical signs can be alleviated in individuals after antimicrobial treatment, there will be life-long shedding of bacteria in the faeces, and the organism can be found in tissues at necropsy (Smith and Sherman, 2009).

Paratuberculosis also has a potential zoonotic aspect, as a putative connection between MAP and Crohn's disease or granulomatous enteritis of humans has been suggested (Patterson and Allen, 1972). In 1984, the MAP organism was identified in tissues from four Crohn's disease patients and

Chiodini et al. (1984) suggested that MAP played an etiological role in Crohn's disease. This association remains controversial.

Three basic elements must be considered when planning for a successful control of paratuberculosis: 1) the identification and removal of infected animals from the herd, 2) reducing the rate of reinfection in susceptible uninfected young stock through improved sanitary measures and kid-rearing techniques, and 3) vaccination to increase host resistance to new infections (Smith and Sherman, 2009). The use of vaccination has some drawbacks related to the frequent development of a granulomatous nodule at the site of injection. Moreover, vaccinated goats can develop cross-reactivity to standard tuberculosis tests, thus complicating the testing procedures for regulatory programmes designed to control tuberculosis. Paratuberculosis is a notifiable disease in Norway and vaccination has been compulsory in areas where the disease until recently has been endemic.

Choice of control - Healthier Goats disease eradication programme

In 1998, the Norwegian Goat Health Service (NGHS) was established as a cooperation between the Norwegian Veterinary Association, the Meat and Poultry Association, the National Animal Health Inspection, the Norwegian Meat Cooperation, the Norwegian Association of Sheep and Goat Farmers and TINE Norwegian Dairies SA. The main aim of NGHS was to control important chronic infections in the Norwegian goat population and further establish and promote preventive measures to reduce the extent of diseases.

In 2000, a working group was established by *Innovation Norway* (Norwegian Government's instrument for innovation and development of Norwegian enterprises and industry) with members representing the dairy goat industry and farmers. The main task of this group was to explore the possibilities of increased value creation in the Norwegian dairy goat production. The group agreed that the first task to accomplish was to "make the Norwegian goat population healthier" through

eradication of prevalent chronic infections, in particular CAE, CLA and caprine paratuberculosis as these diseases were regarded as particularly onerous for the dairy goat production. The resulting work of this group was a suggestion to the Annual National Agricultural Negotiations in 2001 to establish a disease eradication programme, namely Healthier Goats (HG).

In 2001, the first phase of HG was established with monetary support to eradicate CAE, CLA and caprine paratuberculosis in twenty dairy goat herds. The first phase lasted from 2001-2004. The main focus was CAE eradication, but through the disease eradication protocol developed by NGHS in 2000, a method was established that incorporated CAE, CLA and caprine paratuberculosis in HG (Samarbeidsrådet for Helsetjenesten for geit, 2010).

In 2005, the second phase of HG started, lasting up to 2010. The goal of the second phase was 1) to screen all Norwegian dairy goat herds for CAE, CLA and caprine paratuberculosis, 2) to enrol at least 200 dairy goat herds and 3) to establish a control system to prevent and detect possible re-infections in herds that had completed the eradication.

The third and final phase involves continued disease eradication in remaining herds until 2014, with follow-up surveillance and advice until 2018 (Samarbeidsrådet for Helsetjenesten for geit, 2011).

The Cooperation Council for the NGHS is the steering group of HG, and the personnel involved in HG includes a project leader and field personnel, who are goat farm advisors from TINE Extension Services and veterinarians working as private practitioners in dairy goat herds and connected to HG through individual working agreements.

The methodology applied in HG works on the principle of culling the infected herd and recruiting an infection-free herd. Recruitment of kids to the herd happens either by “snatching” kids (removal of the kids directly at delivery) or by buying kids from herds that have already completed the eradication. All snatched kids are raised under controlled conditions at a separate location, and the

old herd is eventually slaughtered at the end of the lactation. Hygienic measures are implemented in farm buildings and nearby areas before the reintroduction of the snatched or purchased kids.

The HG programme relies on close cooperation with other organisations and in particular the Norwegian Food Safety Authority. Initially, CAE was not a notifiable disease but this was changed in 2010, laying restrictions on farms with CAE infection. Caprine paratuberculosis is listed as a notifiable disease, but CLA is not notifiable (Norwegian Parliament, 2002). As HG relies on state funds, it appears logical to have a close cooperation with the Food Safety Authority to secure the detection of possible re-infections and apply official restrictions on farms to hinder further spreading of the disease(s).

HG has been financed jointly by the government, the dairy industry and the dairy goat farmers following a cost-sharing agreement by the partners. Governmental monetary support to HG has been determined as part of the Annual National Agricultural Negotiations between farmer organisations and the Ministry of Agriculture and Food. Participation in HG has been, and still is, voluntary. However, from 2012, TINE Norwegian Dairies SA changed one major aspect by markedly lowering the price for goat milk from herds not enrolled in HG, thus creating a stronger economic incentive for non-enrolled farmers to participate.

By the end of 2014, all dairy goat herds that deliver goat milk to TINE Norwegian Dairies SA have completed eradication through HG; effectively 100% of the Norwegian dairy goat population.

Knowledge gaps

Before HG was initiated, the prevalence of CAE, CLA and caprine paratuberculosis in the Norwegian dairy goat population was not known. In addition, the prevalence of CLA in the Norwegian sheep population had not been studied systematically and this issue became a worry for the HG

programme because of the potential of spreading CLA from sheep with unknown infection status to goat herds that had undertaken infection clearance through HG.

Transmission of CAE is thoroughly described in the literature (Smith and Sherman, 2009), but when HG was initiated, information was lacking regarding the interspecies transmission of CLA between goats and sheep.

The knowledge regarding milk production levels during a lactation period for goats was also sparse prior to the initiation of the HG programme, as the milk recordings had not been explored by proper means. There are some studies of lactation curves in goats available (Macciotta et al. 2005a, 2007; Léon et al. 2012), but the majority of such studies are on dairy cattle (Macciotta et al. 2005b; Gipson and Grosman 1990; Silvestre et al. 2006) and also conducted after the initiation of the present project. In addition, information on the effect of infectious diseases, including CAE, CLA and caprine paratuberculosis, on goat's milk yields were limited. Although some reports exist, it is mostly the effect of CAE that has been studied (Martínez-Navalón et al. 2013; Kaba et al. 2012; Nord and Ådnøy 1997; Leitner et al. 2010; Greenwood 1995).

Limited knowledge regarding the interpretation of inconclusive diagnostic test results in the HG programme (CAE, CLA and caprine paratuberculosis) was also evident. Especially knowledge regarding the application of herd level testing in control and eradication programmes of dairy goat populations was sparse. Motha and Ralston (1994) reported that BTM testing could be used as an initial screening test to determine whether CAE is present in a goat herd or not, but the prevalence level in the material studied was much higher than would be expected from a population that has undergone disease eradication. Brinkhof et al. (2010) described the use of ELISA BTM testing as a promising tool for the detection of SRLV-infections in sheep and goats that warranted further field evaluation.

Accumulated data from HG, including diagnostic test results from the enrolled dairy goat herds, is an important source of information that should be explored. Reports, including cost-benefit analyses, on

similar disease eradication and control programmes as HG were lacking. The Norwegian BVD control and eradication programme (Valle et al., 2005) was used as a template in the establishment of the HG programme, albeit with limitations due to the obvious differences between the two programmes in terms of diseases and species involved. Thus, a major knowledge gap was to which extent the experience from the successful BVD programme could be used in the HG programme.

The present project started in 2006, a period where most of the abovementioned knowledge gaps were still open.

Aims and objectives

The main aim of the project leading to this thesis was to “establish an optimised programme for health control, animal welfare and food safety in the goat production, in order to adapt for a future-oriented and robust industry with quality products that meet the market demand.” This project was provided with financial support enabling the establishment of two PhD-studies, one of them described in this thesis. The other PhD study focused on animal welfare related aims (project number 179745 NORDAM-SAM) (Muri, 2012). The overall aim addressed in the current PhD-study is a general evaluation of the efficacy of the HG programme and was addressed under the following specific objectives:

1. Estimate the prevalence level of CLA in sheep herds in Malangen Peninsula, Norway, and evaluate the risk of spreading CLA between sheep and goats by contact on pasture (Paper I)
2. Estimate the performance (i.e. sensitivity and specificity) of the initial screening tests (BTM ELISA tests) applied in the HG programme for the herd level detection of CAE and CLA (Paper II)
3. Provide information on the effect of the HG programme on the milk yield potential by comparing milk yield levels before and after the implementation of HG (Paper III)
4. Perform a retrospective cost-benefit analysis of the HG programme at farm level based on observed effects on farms enrolled in HG versus unenrolled farms (Paper IV)

Materials and methods

Study population, sampling and recruitment

The target population was all the Norwegian dairy goat herds. The study population was selected from both HG enrolled and non-enrolled dairy goat herds. The four different objectives (studies) constituting this thesis, are all based on a range of different sources of material from the study population. The following sections describe the material in relation to each study.

Prevalence of CLA in sheep herds

A total of 46 sheep herds in Malangen Peninsula in Troms County, with altogether 4248 sheep, were blood sampled and clinically examined in the time period from October 2007 to October 2008.

Initially, 14 sheep farms located in close vicinity or with common borders to goat farms participating in HG were selected for blood sampling. The selection was also based on local knowledge regarding the use of common pastures for sheep and goat herds, personnel traffic between herds and the high density of sheep and goat farms in this area. Clinical examinations of the 4248 animals were conducted at the same time as the blood sampling. The parotid, submandibular, retropharyngeal, prescapular, mammary, prefemoral and popliteal lymph nodes were palpated. The texture, size and connection to underlying tissue were the parameters evaluated to detect abscesses indicating infection with CLA (Baird, 2007). A herd protocol was developed for registration of principal management practices relevant for the spread of CLA, including general hygiene level at the farm, procedures in relation to shearing, extent of hired shearers, among others. The protocol was piloted by two sheep farmers not located in the study area. The herd protocol registrations were collected from 13 of the sheep herds that were serologically tested and clinically examined in October and November 2007. The same sheep herds were blood sampled and retested in 2008 to be able to compare and detect possible changes in the CLA prevalence level. Voluntarily implemented sanitary

measures in the period from 2007 to 2008 were registered and related to changes in CLA prevalence estimates for the same period.

Application of Geographic Information System (GIS) in estimating risk

To be able to say something about the extent of contact on pasture between sheep and goats in the study area, a map covering Malangen Peninsula (in a scale of 1:50 000, provided by the County Governor in Troms County) was sent to sheep and goat farmers asking them to draw their pasture area onto the map. Map registrations from the sheep and goat farmers were plotted using the GIS analysis package ArcGIS®/Arc View 9.3 to visualise overlapping of pasture areas for sheep and goat herds (Figure 3).

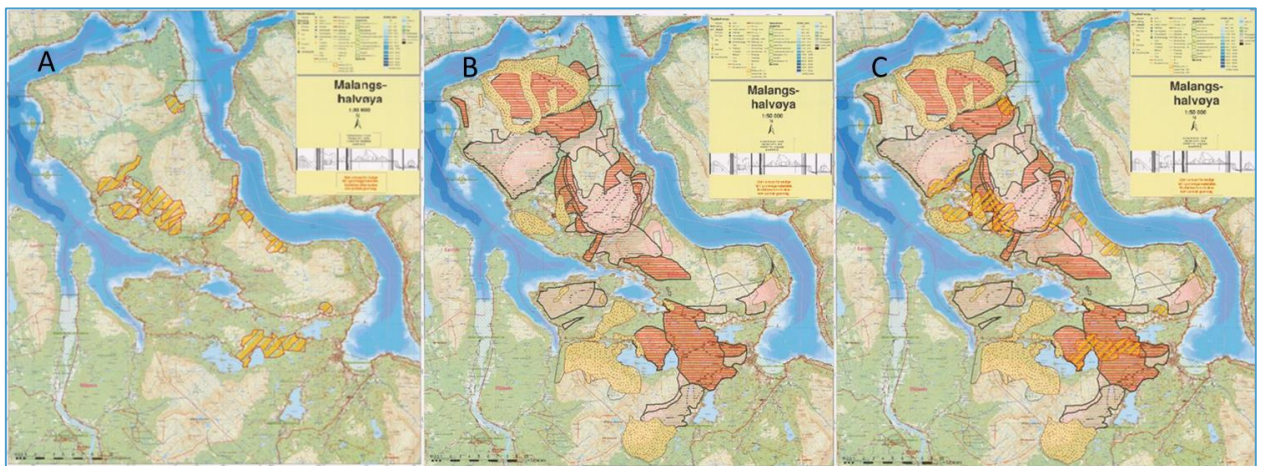


Figure 3. Maps used for registration of sheep and goat pasture areas in the Malangen Peninsula, Norway. A: map with goat pasture areas marked with orange/red stripes B: map with sheep pasture areas, yellow dots= free of caseous lymphadenitis infection, pink = <10% caseous lymphadenitis prevalence level, red = >10% caseous lymphadenitis prevalence level C: overlapping pasture areas for sheep and goats.

The pasture registrations were combined with serological test results for CLA in sheep herds. The sheep herds were categorised according to the prevalence level of CLA, with no CLA, less than 10% CLA and more than 10% CLA. The goat herds were all regarded as infected with CLA since the eradication of CLA by the HG programme had not yet started at the time of map registration.

Individual blood and bulk tank milk samples in the evaluation of two ELISA tests

To assess the suitability of testing bulk tank milk in the surveillance of CAE and CLA after disease eradication using ELISA diagnostic tests, field data on combined blood and bulk tank milk samples were gathered from dairy goat herds that have finished eradication and therefore represented an infection-cleared population of dairy goats. Serum and bulk tank milk samples from herds that were enrolled in HG and finished the disease eradication before 2010 were included in the study. Only herds where all milk producing animals were blood sampled and where bulk tank milk and blood samples were collected on the same day, were included. This material constituted the basis for evaluating the diagnostic performance of the bulk tank milk ELISAs for the herd level detection of CAE and CLA in infection-cleared dairy goat herds.

Individual data on milk yield recordings before and after enrolling in Healthier Goats

The data on individual daily milk recordings used for the estimation of milk yield changes were extracted from the GMRS and included data from 1999 to 2008. The data was separated into two categories depending on HG status; enrolled herds and non-enrolled herds (controls).

A set of inclusion criteria were applied for the study: 1) a minimum of three milk yield records in the GMRS per lactation, 2) the first milk yield record within 60 days after kidding, 3) herds must have enrolled in HG from 2002 through 2006, and 4) herds in the control category should not have enrolled in HG any earlier than 2009. Milk yields recorded before day 6 or after day 275 in lactation and milk records of less than 0.2 kg were excluded from the data set, as recommended by the International Committee of Animal Recording, ICAR (2012). The interval between consecutive milk recordings was 40 to 50 days.

To compare the milk yield in HG enrolled herds with that of control herds, while controlling for changes in milk yield over time due to other factors than HG, the data were further categorised along a time line. Every milk yield recording from the *enrolled* group was coded according to the time of recording in relation to the year of HG enrolment. The notation “early” was used for records from before HG enrolment (years 1999 to 2005) and “late” for records after HG enrolment (years 2003 to 2008). Depending on the actual year of enrolment in HG, different years were coded as early or late in different herds. Similarly, in the control herds, records from years 1999 to 2003 was considered as “early” and records from the years 2004 to 2008 were considered as “late”. This classification divided the data into four categories: *enrolled early*, *control early*, *enrolled late* and *control late*. There were 247 617 records in the original dataset from where 135 446 test-day records corresponding to 28 829 lactations of 9791 does in 43 herds were extracted.

Questionnaire to investigate the effect of Healthier Goats at farm level

Initial meetings were held with representatives from the NGHS, the Norwegian Agricultural Economics Research Institute (NILF) and the HG programme to identify elements related to the economic impact of the disease eradication that would be relevant to ask the farmers about. The questionnaire was developed in QuestBack® and was pre-tested by two farmers not participating in the study and by one veterinarian with extensive experience from dairy goat practice. The questionnaire was subsequently distributed to 19 farms applying the snatching method and to five farms applying the test-and-cull method in the disease eradication process. Twenty-two of these farmers received a link to the web-based questionnaire by email, while the remaining two received a paper version of the questionnaire by mail. The information from the respondents was merged with GMRS and ECDG data, and contributed to the establishment of best estimates of budget parameters. Quantitative data on farm effects of HG were collected with the questionnaire. This included longevity of the goats, feeding regimes, and the work-loads and investments associated with HG

participation. The qualitative data collected concerned the farmers' experience or perceptions of disease prevalence before and after disease eradication, as well as general effects of HG on the farm, including effects on the working environment and on the sustainability of the goat milk production.

Economic evaluation of Healthier Goats at farm level

From the initiation of the HG programme back in 2001, substantial knowledge regarding the dairy goat population and production in Norway has been generated. Prior to the initiation of HG, there were numerous anecdotes and beliefs about the detrimental effects of the three chronic, infectious diseases CAE, CLA and caprine paratuberculosis. When the application for governmental funding for HG was written, different accounting and quotes were developed to get an idea of the real costs of enrolling into HG. Regarding the time horizon from the starting point of HG and up to present, a continuous inflow of information, including different aspects of the HG programme, has built up a valuable knowledge base. This information includes health effects of enrolling in HG, costs of diagnostic testing, the impact on animal welfare, the real cost in terms of work hours necessary to secure a disease-free population, the risk of re-infection, and the cost of investing in new buildings among others (Figure 1).

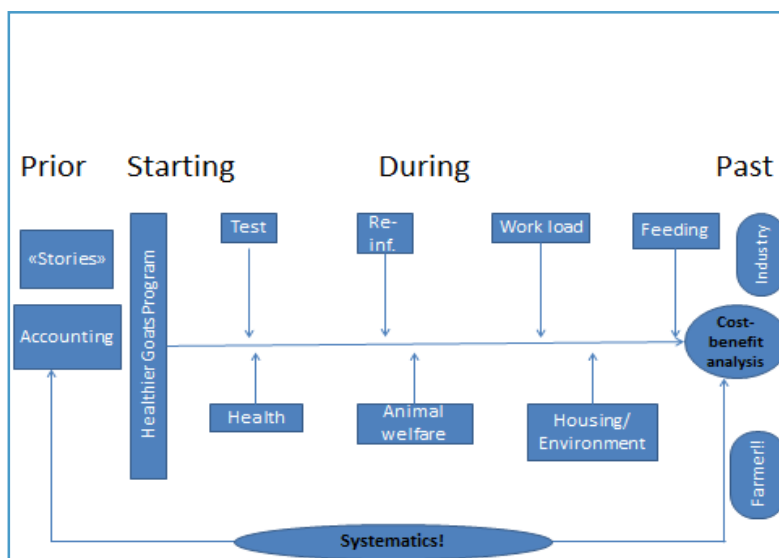


Figure 1. The information about the cost of diagnostic testing, risk of re-infection, amount of work load, cost of feeding, effect on health status and milk production, the effect on animal welfare and the cost of renewing housing and environment because of the Healthier Goats programme were collected systematically through the programme period.

A CBA was suggested as an appropriate tool to explore the effect of enrolling into HG. A CBA can be defined as a procedure for determining the profitability of e.g. disease control programmes over an extended time period (Dijkhuizen and Morris, 1997). There are two main kinds of CBA which, although closely related, are fundamentally different. These are financial CBA and economic/social CBA. Financial CBA is about the profitability and financial feasibility of a program to the key participants. Economic CBA simply addresses the question of whether the project is worthwhile to the society/nation as a whole (B. Hardaker, personal communication). A financial CBA at farm level was the chosen method to address the effect of HG on the goat farmers' economy.

Different methods of collecting relevant data to the study of the economic impact of the HG programme were identified. Initially, the TINE Extension Services' advisory personnel were asked to identify farms to include in the study sample; the reason for this approach was the local knowledge of these people about the information that was available from different farms. We needed to draw the sample from farms with bookkeeping information available in ECDG. The second inclusion criterion was a herd size of more than 30 goats in order to include herds that were representative of the actual size distribution of Norwegian dairy goat herds. We compared data from before and after enrolling in HG for 24 HG enrolled farms and from early and late years in 21 non-HG farms. The latter comparison was carried out to assess the development that could have been expected without enrolling in HG.

The number of records of herd-level data in GMRS and ECDG varied. Data from a minimum of two years before and two years after enrolling in HG were required, thus, GMRS and ECDG data from a minimum of five years were included. Data from GMRS and ECDG, together with information from the questionnaire described above, provided the necessary inputs to the CBA.

Data management and statistical analyses

The detailed description of data management and statistical analyses can be found in the respective papers. Thus, the methods applied to achieve the specific objectives for this project are only briefly described here.

Fisher's exact test

In paper I, the Fisher's exact test was applied as a significance test due to the very few observations (n=5) in one of the groups compared.

Summary statistics for the ELISA tests

The sensitivity, specificity, area under curve, and positive and negative predictive values of the two ELISAs applied for the diagnosis of CAE and CLA in the HG programme, were estimated using the *diagt* command in the statistical package STATA IC 11©. The *diagt* command displays various summary statistics for a diagnostic test, compared to a case's true disease status. Based on the results of the *diagt* analysis a plot of true positive rates (sensitivity) versus false positive rates (1-sensitivity) with trend line (calculated as moving average for two data points) was produced in Excel 2010®. This resembled a receiver operating characteristic (ROC) curve for visual assessment of the two tests evaluated.

Multilevel mixed effect cubic spline regression

In the modelling of the daily milk yield, the overall approach was to build a model that incorporated both fixed effects (days in milk [dim] and parity) and random effects (farm, individual goat and lactation number) to explore their effect on the resulting daily milk yield. Initial data management was conducted in Microsoft Office Excel 2007/2010 before transferring data to Stata IC 11©, where

the remaining data management and statistical analyses were performed. The *xtmixed* procedure for multilevel mixed-effects regression models was used in the statistical analyses of the data. The functional relationship between the outcome (milk yield on test day) and dim was further evaluated by exploring several different transformations of dim in the overall model, including linear spline, cubic spline and polynomial transformation. The Akaike's Information Criteria (AIC) and Bayesian Information Criteria (BIC) were used to compare and rank the models (Akaike, 1974; Schwarz, 1978; Raftery, 1995). The cubic spline regression model had the lowest AIC/BIC and was regarded as the best model to compare milk production in different categories.

Stochastic modelling

Several key parameters in the CBA were regarded as uncertain due to lack of full information, and furthermore there was variation across farms and time. Stochastic estimates were applied, in which the uncertainty was expressed as probability distributions to represent uncertain key parameters. We used PERT (Program Evaluation and Review Technique) distributions, a version of the β distribution which has been recommended by Vose (2000) for such cases. A PERT distribution is defined by the minimum, most likely and maximum values, and these were assessed using available data combined with expert opinions. The stochastic simulation model was built in Microsoft Office Excel 2007/2010 by using the add-in software risk analysis tool @RISK® 5.7/6.0 (Palisade, New York). The CBA stochastic model was used to generate distributions of NPV of farmers' net cash flows for enrolling versus not enrolling in the HG programme.

Summary of papers (study results)

Paper I

Prevalence estimates for caseous lymphadenitis (CLA) in sheep herds on the Malangen Peninsula, was established through serological testing using a commercially available ELISA. Furthermore, registration of principal management practices related to the spread of CLA was conducted together with map registrations of pasture areas for sheep and goat herds on the Malangen Peninsula. The serological prevalence estimates were compared with map registrations of common pasture areas to evaluate the potential risk of spreading CLA infection through contact on pasture between sheep and CLA infected goats. Fourteen sheep flocks in the closest vicinity to goat herds were sampled first in October 2007. The remaining 32 sheep flocks located further away from the goat herds were tested in 2008.

The herd prevalence level for CLA in sheep herds on the Malangen Peninsula was 72% and the within-herd prevalence ranged from 0% to 31%, with a mean within-herd prevalence of 8% among all the test-positive herds. Of the 4248 animals tested, 276 were CLA seropositive, giving an overall CLA prevalence of 6.4 % among all sheep in the Malangen Peninsula. The herd prevalence is higher in the group of 14 sheep herds in close vicinity to goat herds compared to the group of 32 sheep herds located at a greater distance to the goat herds; 86 % compared to 66 %, but no significant difference related to contact with goat herds was detected ($p = 0.286$, Fisher's exact test).

With only one exception, the Fisher's exact test reported no significant differences in the different management practices between the two groups of sheep herds; the low-prevalence group with <10% CLA and the high-prevalence group with $\geq 10\%$ CLA (p -values ranged between 0.21 - 1.00). The exception was that the low-prevalence group unexpectedly reported more "purchase of live animals" than the high-prevalence group, with a p -value of 0.028.

Map registrations demonstrated that sheep and goat herds had moderate overlapping of pasture areas. Among the 26 CLA seropositive sheep flocks with map registrations, 17 flocks had pasture areas that overlapped with goats' pasture. Furthermore, only one of the 13 seronegative sheep flocks had contact with goats on pasture. The Fisher's exact test detected a significant difference ($p = 0.001$) in CLA-status of the sheep flocks between the two groups (contact on pasture vs. no contact on pasture).

There was a significant relationship between a sheep herd being CLA infected and contact with CLA infected goats on pasture. Due to the high density of sheep and goats in the studied area, one should exercise caution in generalising the current findings to other parts of Norway with less dense contact between sheep and goats. The high herd prevalence level found in the sheep herds should be taken ad nota, and investigation of the CLA prevalence level in sheep herds in parts of Norway with a lower density of goats should be performed.

Paper II

The objective of this study was to evaluate the diagnostic performance of two ELISA tests applied to BTM as the first part of a two-step test scheme for the surveillance of CAE and CLA in goats. The herd-level BTM tests were assessed by comparing them with the test results of individual serological samples. The aggregated results from the serological testing and BTM test results were compared, and the ability of the BTM test to detect seropositive animals in herds with $\geq 2\%$ within-herd prevalence was evaluated. The potential for refining the cut-off levels for BTM tests used as surveillance tools in a population that has recently been cleared of infection was also investigated.

The results showed that the sensitivity and specificity of the CAE ELISA BTM test with respect to detecting $\geq 2\%$ within-herd prevalence was 72.7% and 86.6%, respectively. For the CLA ELISA BTM the sensitivity and specificity were 41.4% and 81.7%, respectively, for the same goal of detection.

The positive predictive values for the CAE ELISA BTM test at both 5% and 10% within-herd prevalence were poor, with a respective 22.2% and 37.6% ability to truly detect herds determined to have a positive serological status. Similarly, for the CLA ELISA BTM test, the positive predictive values at 5% and 10% within-herd prevalence were 10.7% and 20.1%, respectively. The negative predictive values of the CAE and CLA ELISA BTM tests at a 5% within-herd prevalence level indicated that 98.4% (CAE) and 96.4% (CLA) of the seronegative herds would be correctly classified by the bulk tank milk tests given the selected aggregated individual serological infection level.

Paper III

The aim of this study was to explore how control and eradication of CAE, CLA and caprine paratuberculosis by enrolling in HG affected the milk yield by comparing with herds not enrolled in HG. Lactation curves were modelled using a multilevel cubic spline regression model, where farm, goat and lactation ID (parity) were included as random effect parameters. The TY increased in the enrolled herds after eradication: fourth lactation TY were 634.2 kg and 873.3 kg in *enrolled early* and *enrolled late* herds, respectively, and 613.2 kg and 701.4 kg in the *control early* and *control late* herds, respectively. Furthermore, the TY for parity four increased by 239 kg from the *enrolled early* to the *enrolled late* category, while the corresponding increase in TY in the *control early* to *control late* was 88 kg. In other words, the total milk yield after HG enrolment was 63% higher compared to the total milk yield for the *control late* category.

DPY differed between enrolled and control herds. The DPY came on day 6 of lactation for parities 2, 3 and 4 in the *control early* category, indicating an inability of the goats to further increase their milk yield from the initial level. For the *enrolled late* category, on the other hand, the DPY came between day 49 and 56, indicating a gradual increase in milk yield after kidding.

The proportion of variance explained by herd, individual goat and lactation number was estimated for the four categories with parity included as a fixed effect (i.e. the variance components include all parities in each category). The proportion of explained variance was high ($P < 0.001$) at each level (herd, individual goat and lactation number), and highest at individual goat level, ranging from 21% to 25%, depending on category.

Paper IV

The aim of this study was to evaluate dairy goat farmers' profitability of participating in HG. The profitability was estimated in a financial CBA using partial budgeting to quantify the economic consequences of infectious disease control versus taking no action. The CBA model was used to generate distributions of NPV of farmers' net cash flows for enrolling versus not enrolling. This was done for milk quota levels of 30 000 L, 50 000 L and 70 000 L, and for both before and after the introduction of a reduced milk price for non-enrolled herds. The NPVs were calculated for time horizons of five, ten and 20 years using an inflation-adjusted discount rate of 2.8% per annum. The expected NPVs were found to be negative for all quota levels with a time horizon of five years. Evidently, five years was too short for farmers to recoup their investment costs. However, for horizons of ten and 20 years, the calculated expected NPVs were found to be positive for of the 50 000 L and 70 000 L quota levels, and only slightly negative for 30 000 L. Over a ten year horizon, with a quota of 30 000 L, the probability of a negative NPV was 55%. At quota levels of 50 000 L and 70 000 L the chance of having a negative NPV was reduced to 25% and 15%, respectively. Our results indicate that over 20 years, there was still a 5% chance of experiencing a negative NPV with a quota of 30 000 L. However, for the other quota alternatives the chances were only 1% and 0.6%, respectively.

The results show that participation in HG on average was profitable over a time horizon of ten years or longer for quota levels of 50 000 L and 70 000 L, although not without risk of having a negative

NPV. If farmers had to pay all the costs themselves, participation in HG would have been profitable only for a time horizon beyond 20 years.

In 2012, a reduced milk price was introduced for farmers not enrolled in HG, changing the decision criteria for farmers, and thus the CBA. When the analysis was altered to account for these changes, the expected NPV was positive over five years for the 50 000 L quota. This indicates an increased profitability of enrolling in HG, as the alternative with reduced milk price was not a sustainable choice. The sensitivity analysis showed that particular attention should be paid to work load and investment costs when planning for disease control programmes in the future, as these factors had the absolute highest (negative) correlation coefficient related to NPV output.

Discussion

The Healthier Goats Programme has from its beginning in 2001 focused on gaining and building knowledge regarding important aspects of disease eradication and control, like determining the prevalence estimates of the diseases and improving the diagnostic tools, among others. The objectives, methods and results of the studies included in this thesis have been described and discussed within the respective papers (I-IV). The discussion below gives some general comments on the materials and methods that formed the basis for this research project and finally a general discussion about the study results.

Methodological considerations

This thesis covers several scientific disciplines and therefore a range of diverse methods are applied to obtain the desired outcome. Paper I has a descriptive character with elements of risk evaluation, paper II deals with diagnostic test performance, whereas paper III is based on regression analysis and paper IV includes stochastic modelling and cost-benefit analysis.

Using maps for detecting animal contact on pasture

The mapping of mountain pasture areas by using information from each sheep farmer in Malangen was the method chosen to best describe the pattern of pasturing sheep and goats in this area. The local knowledge of the farmers and the use of a high-scale map were regarded as suitable tools for this task. There are potential errors in the resulting map registrations from at least two sources; the erroneous registration by the farmers and the fact that sheep and goats unnoticeably can use other pasture areas than the ones registered. These sources of potential errors were taken into account when the map registrations were transferred to ArcGIS®/Arc View 9.3 for further analysis. Outliers were removed from the analysis and follow-up questions to the farmers in case of uncertain registrations were conducted.

Test properties influencing prevalence estimates and diagnostic performance

Information about the prevalence of infectious diseases is of obvious importance in connection with controlling the diseases in question. In many countries, the prevalence of CLA is considered to be high. Although this has been thoroughly described in some sheep producing countries, e.g. Australia (Windsor, 2011), less information is available from European countries (Baird and Malone, 2010). When the initial screening for CLA in sheep herds in close vicinity to goat herds on the Malangen Peninsula revealed a higher prevalence than expected, precautionary measures were implemented and HG was halted until further information on the prevalence of CLA in sheep was available. Several reports (Dercksen et al., 2000; Voigt et al., 2012) highlight the importance of combining serological sampling with clinical examination in the diagnosis of CLA. In a production unit with sheep it is highly recommended to perform clinical examinations of all sheep at the time of shearing or at least once a year. It is also good practice to isolate animals showing signs of abscesses in regional lymph nodes (Baird and Malone, 2010). When the sheep herds in Malangen were screened for CLA, it was important to sample all adult animals in the herds to obtain a prevalence estimate that was as reliable as possible. The diagnostic test applied was commercially available and was used according to the producer's recommendations (ELITEST CLA #CK105A manufactured by Hyphen Biomed, France [<http://www.mvdiagnostics.co.uk/documents/CK105A02-08-07.pdf>]).

The sensitivity and specificity of the test applied can influence the prevalence level determined. Some of the herds had very few test positive animals compared to the number of animals tested, and this can be a result of false positive test results. The fact that the prevalence estimates are mere estimates, and not a determination of the true infection level in the herds, should have consequences for the interpretation of the test results. We did not adjust prevalence for test properties, as prevalence estimates was only a part of the HG programme.

For our study of CLA in sheep herds in Malangen, the main aim was to explore the sheep population with regard to CLA infection level and to combine this knowledge with the information about common pasture areas with goats. The screening for CLA in the sheep population in Malangen was the first systematic mapping of the presence of CLA in sheep in Norway. The study generated valuable information for the HG programme regarding the presence of CLA in sheep and an evaluation of the risk of spread of infection by contact on pasture.

Based on the new knowledge regarding the diseases involved, the HG programme changed the test regime, the prevalence level of the diseases and the choice of new diagnostic methods to develop. As the Norwegian dairy goat population changed from being heavily infected with one or more of the three diseases, to become a very low-prevalent (almost disease-free) population, the need for reliable diagnostic tests to be used in the surveillance for early detection of re-infected individuals, was crucial. Cost-effective diagnostic tests with appropriate sensitivity and specificity, adjusted for a low-prevalent population, was the defined need of the programme. Brinkhof et al. (2010) reported the use of milk and BTM for the early detection of SRLV-infected sheep and goats by using a commercially available ELISA test and concluded that the use of BTM bears a potential that should be investigated further. Motha et al. (1994) also reported that the use of BTM for the early detection of CAE infection in a herd can be a suitable method, but it warrants further testing at individual level to confirm the prevalence level.

In the study presented in Paper II, there was a need to investigate the agreement between serological test results and BTM test results to be able to evaluate the performance of the BTM ELISA tests in the detection of CAE and CLA. The use of ELISA sera results as gold standards is an inadequate way to validate the ELISA BTM milk results (Plaza et al., 2009). Despite ELISA tests being the most sensitive serological method available for diagnosing CAE and CLA infections, the sensitivity is not 100%, and as described by DeAndres et al. (2005), there is no gold standard to compare with in CAE and CLA diagnostics. With this in mind, the method for comparing serological test results with

BTM test results was based on the premise that a CAE or CLA seropositive goat is truly seropositive, but not necessarily truly infected. When this basis for comparison between serology and BTM was established, the “search” for an optimal cut-off level for tests from the low-prevalent population was initiated. The knowledge regarding the infection level and disease status in herds that were enrolled in HG and had completed eradication was substantial due to years of testing and the farmers’ awareness of disease, which was believed to be enhanced. With this background, it was thought to be adequate to have a diagnostic test with as high as possible specificity and therefore few false positives, even if this theoretically could result in missing truly positive individuals. The diagnostic performance analyses using the “diagt” command in STATA IC 11© gave relevant estimates to be used in the evaluation of the BTM ELISA tests for the diagnosis of CAE and CLA.

Choice of method for modelling milk yield

The most important factor when designing the study of milk yield in relation to disease eradication in HG was to find and apply a method that would explore the data on daily milk yield optimally. There are various methods developed in modelling daily milk yields and processing lactation curves. The Wood’s curve from 1967 has been used until recently and has been followed by the Wilmink model (1987) and the Ali and Schaeffer method (1987). A lactation curve can be defined as the mathematical representation of the physiological response of milk production throughout the milking period (Masselin et al., 1987), or as the graphical representation of daily milk yield against time after parturition (Sherchand et al., 1995). The mathematical functions applied for the presentation of lactation curves should allow a valid reflection of the milk production throughout the lactation period (León et al., 2012). The geometric shape (time of peak yield and persistency) and scale (initial and peak yield) parameters are important characteristics of a lactation curve. The abovementioned lactation curve models (Wood, Wilmink and Ali and Schaeffer) estimate fixed coefficients that describe the shape and scale of the lactation curve. Such models can be hampered

due to the bias introduced by the mathematical formula employed, resulting in reduced flexibility compared to other statistical methods specifically constructed for data adaptation. The decision that the model chosen for this study should represent the data structure as authentically as possible led to the choice of a data-driven mathematical method; the multilevel cubic spline based regression model. This model fitted the data significantly better than the other models tested, with different transformations of the dim parameter. Although polynomial regressions can fit data exhibiting non-linear trends, the polynomials can introduce bias because they tend to shoot up or down at end-points due to a strong influence of records at the end-points of a lactation period.

Linear splines allow for the estimation of the relationship between daily milk yield and dim as a piecewise linear function which connects through the knots. It has been shown that a linear spline can be used to fit many functions well (Gould 1993; Harrell 2001; Panis 1994). Cubic splines may be a better choice than linear splines when non-linear curves, such as lactation curves, are fitted (White et al., 1999). The introduction of both fixed and random effects in the model allowed us to study their influence on the outcome (Dohoo et al., 2009).

In recent years, multi-level spline regression models have been introduced to describe milk yield throughout the lactation in dairy cattle (Silvestre et al., 2006; Bohmanova et al., 2008; Schaeffer and Jamrozik, 2008). The use of spline functions in the study of lactation curves from dairy goats is more limited, but León et al. (2012) compared the use of a quadratic spline function with several parametric models and found that the quadratic spline function showed the best fit.

Non-linear regression models, such as Wood (1967), may be superior in terms of predictive abilities, since the statistical nature of such models allows for statistical inference. However, in a purely explorative study, these models are not only complex, but they can be difficult to run if a self-starter routine is absent or fails to estimate the starting values required for the estimation of such models (Pinheiro and Bates, 2000). With the use of multi-level cubic spline regression model in this study, the traditional shape of a lactation curve, with an ascending and descending phase was not obvious.

A possible reason for this is that the structural constraints imposed on the curve-fitting procedure by e.g. the traditional Wood's model are absent. Hence, the traditional lactation curve models, like Wood's (1967), might introduce bias and may be better suited for predictive modelling rather than data exploration, which was the main focus of this study.

Modelling uncertainty and variation using stochastic simulation

Financial CBA deals with cash flows, i.e. money paid and received by various parties. It includes all cash transactions when they occur, and excludes non-cash costs and benefits, such as depreciation or appreciation, or imputed costs and benefits. It includes an assessed valuation of assets and liabilities at the end of the programme. Typically, the analysis is broken down to show the financial flows for various agents or groups. In the case of the HG programme, these are the farmers, the government, processors and consumers. Measures of profitability may be computed for some or all of the parties by discounted cash flow methods. In this study, the financial CBA at farm level was conducted as mentioned before. The discount rate used may be the cost of credit or the opportunity cost of available funds. In the financial CBA conducted in this study, the discount rate was set as the inflation-adjusted average 10-years bond rate, 2.8%, and was appropriate since the NPV budget was calculated in constant 2009 prices.

Some conventions have grown up about how CBA should be conducted. CBA should ideally be done to compare two future scenarios, one with the project in question, and one without. It can be misleading to compare a future with the project with the past if the past situation is not going to remain unchanged into a future without the project. For the present financial CBA of HG, the comparison was done retrospectively between farms enrolled in HG and farms not enrolled. It might be claimed that the conduction of a retrospective study only can satisfy curiosity and will not bring essential information suitable for making future decision, as the decisions are already taken. On the other hand, a retrospective approach can enhance the precision of estimates in the model as more

information is available, thus the study could more accurately demonstrate the results from enrolling in HG versus not enrolling. Also, generating experience from already implemented projects, such as HG, would be interesting in the context of future decision-making in connection with similar projects.

In establishing the model for the financial CBA, the levels of the parameter estimates were crucial. Several key parameters were regarded as uncertain due to lack of full knowledge, and furthermore, there was variation across farms and time. In cases where there was no exact information available, expert opinions were asked for and combined with stochastic estimates, in which the uncertainty was expressed as probability distributions to represent uncertain key parameters. The PERT distribution was applied, as this type of distribution is described to be feasible when relying on expert opinions in the parameter estimation (Vose 2000). Uncertainty about a certain value can come from both variation about a parameter and actual uncertainty, i.e. there is lack of knowledge. The concept of “total uncertainty” introduced by Vose (2000) was applied for the present study which includes both uncertainty and variation in the same distribution. For parameters such as milk yield and feeding costs, there was little uncertainty, but the degree of variation between farms was not fully expressed, thus the two concepts were modelled together for all the uncertain parameters.

There were also issues in defining and representing stochastic dependencies between uncertain variables, the omission of which can give seriously erroneous results (Hardaker et al., 2004). The introduction of relevant correlation coefficients between dependent parameters in the model captured the potential presence of stochastic dependency. Correlation matrices were specified for the dependencies between herd size and work hours per goat, between herd size and level of investment, and between milk yields from one lactation to the next, as these were the dependencies recognised.

The output of the present study, the net financial results of implementing HG, were derived as cumulative distribution functions (CDFs) of NPV, which represent the present values of uncertain annual net cash flows to the chosen time horizon. The estimation of risk in relation to implementing

the HG programme can be derived from the CDFs of the NPV by using the resulting CDFs as a basis for choice, accounting for the farmers' individual attitude to risk. The probability of having a negative NPV is derived from the CDFs and thus provides a useful measure of riskiness.

General discussion about the study results

The evaluation of HG was conducted using an epidemiological and economical methodology.

Evaluation has different definitions depending on context. In a wide sense, it is explained as judging or determining the significance, worth, or quality of something. The term can be used similarly to *assess*, which can mean estimating the official value of something. To be able to perform an evaluation/assessment of the HG programme, it was deemed necessary to work in a systematic manner and to apply a particular framework to this task. In the following sections, the results from the evaluation of HG are discussed together with the current scientific knowledge.

Spread of CLA between goats and sheep through contact on pasture

Information on the prevalence of CLA in sheep herds was important to the HG programme because sheep and goat herds were believed to be in close contact in Malangen, with the risk of spreading CLA between the species, and particularly the risk of re-infecting goat herds that were enrolled in HG and had undertaken disease eradication.

There is limited information regarding the prevalence level of CLA in sheep herds in Norway. An exception is from a study of sheep herds on a small island near the Malangen Peninsula, describing an outbreak of CLA in a ram circle and an action plan for eliminating the infection (Hektoen, 2012). Thus, most of the information regarding the prevalence of CLA in sheep herds in Norway is based on data needed by HG for the mapping of sheep farms in the vicinity of goat herds. It is therefore not

possible to draw conclusions about the impact of contact between sheep and goats on the prevalence of CLA in sheep herds.

The results from the pasture map registrations indicate that there can be a higher chance of contracting CLA for a sheep herd if there is contact with CLA infected goat herds on pasture than if there is not. On the other hand, it is a difficult task to say anything about the causation, since all goat herds had CLA infection at the time of map registrations. A proper basis for comparison with sheep herds in contact with CLA negative goat herds has not been available in this study. Due to scarcity of scientific literature on the risk of spreading CLA between sheep and goats on pasture, we found no scientific reports to rely on in our interpretation of the results.

Bulk tank milk testing for early detection of CAE and CLA

The use of BTM for the detection of disease has been described for several diseases and species (Mazzei et al. 2005, Brinkhof et al. 2010, Armstrong et al. 2001, Nielsen et al. 2000, Lindberg et al. 1999, Saman et al. 1999, Motha and Ralston 1994, Plaza et al. 2009).

Surveillance of a supposed infection-free population, such as the Norwegian dairy goat population after the completion of HG, requires a cost effective test scheme for the detection of potential reinfections, which have occurred and still can occur.

In populations with a low prevalence of disease, the cut-off level has to be increased to obtain a desired high positive predictive value (the probability that given a positive test, the animal actually has the disease) (Dohoo et al., 2009). An increased cut-off level, together with an increased BTM sampling frequency, can then contribute to an efficient and cost-effective test regime, which is relevant in a surveillance situation after disease eradication. This issue was possible to address by investigating field data from the Norwegian dairy goat herds that had undergone disease eradication

with HG. As described by Brinkhof and others (2010), BTM varies in antibody constitution due to variations in the excretion from individual animals, milk volume and the dilution characteristics of individual antibodies for each animal. Due to this variation, a relatively high BTM sampling frequency was considered necessary. For the surveillance of CAE and CLA, it was decided to collect BTM samples from all dairy goat herds four times yearly following disease eradication in the HG programme (L. Sølverød, personal communication).

By comparing several cut-off levels for the BTM samples with individual serologic samples, the optimal cut-off level in a two-step surveillance situation was evaluated. For HG, the goal with the BTM tests was not to classify a herd as infected or non-infected, but to identify herds that require follow-up testing in step two (individual serological testing). Hence, the main goal was to identify herds that were likely to have prevalence above 2%, based on the test specificity of 98%.

After the establishment and completion of the HG programme, the prevalence of CAE and CLA (and caprine paratuberculosis) in the Norwegian dairy goat population has reached a level close to zero. However, herds are still under surveillance in order to detect new infections. The fact that the prevalence levels of CAE and CLA are well documented through serological testing through the HG programme enables the use of a herd-test in the surveillance of the diseases. Furthermore, the BTM test results should be compared with the clinical history of the herds to secure the correct diagnosis of CAE and CLA.

The HG programme regarded the refinement and identification of an optimal cut-off value for the CAE and CLA ELISA BTM tests as important in order to make the tests better suited for the current situation, with a low-prevalence level for CAE and CLA. The current results can be used as a part of a decision-making tool in the planning of a future surveillance programme both in the Norwegian dairy goat industry and in other goat populations that are considering the application of a two-stage test scheme, using BTM as the first step.

Differences were observed between the two tests investigated, in that the CAE ELISA BTM was better able to discriminate between positive and negative herds than the CLA ELISA BTM test was. However, both provided improved information about the tested herds. Herd structures and other characteristics that might affect the performance of a herd-level test will vary between populations, so further refinement of cut-off values to improve the predictive abilities of these two tests should be investigated within the population in question.

Healthier Goats and its impact on the milk yield level of dairy goats

There are several reports from the literature on the detrimental effect on milk production for all the three diseases that have been eradicated through HG (Smith and Cutlip, 1988; Burrell, 1981; Kruze et al., 2006). With that in mind, it seems logical to assume that freedom from these diseases would have a positive effect on milk production, i.e. an increased yield compared to a situation with the presence of these diseases. Particularly CAE has been described to impair milk yield in higher lactations, and to cause a “hard udder” soon after parturition (Robinson and Ellis, 1986; Greenwood, 1995; Martínez-Navalón et al., 2013). Factors that can influence the lactation curve shape includes breed, kidding season, age of doe, litter size, herd and feeding practices (Gipson and Grosman, 1990; Macciotta et al., 2005; Motaldo et al., 1997). Also, underlying pathological factors in the animal can influence the shape and scale of the lactation curve (Dematawewa et al., 2007). The categorisation of data into enrolled and non-enrolled, and according to the time of recording, allowed us to quantify the effects on the milk yield solely related to HG. There may be several other factors that can explain an increase in milk yield after disease eradication. In the present study, the highest level of clustering was found at the individual goat level; the proportion of variance was over 20%. Information about the breeding regimen and selection of breeding animals or breeding values were not available, but enrolled and control herds did have the same breeding system (data not shown). Herd level clustering was higher in the non-enrolled herds in the time period 2004-2008 than in the enrolled

herds after eradication (23% and 16%, respectively). This could indicate that the enrolled herds were more homogenous due to improved management and feeding regimes after disease eradication. Thus these are also factors that might contribute to improvement in milk yield. Farmers' motivations for joining HG have not been screened, and no potential systematic difference between early enrollers and late enrollers have been detected or incorporated in this study. Due to the fact that the eradication of the three diseases through HG is labour-intensive and requires substantial effort from the farmers, one might expect that the most motivated and best organised farmers may have enrolled first. These are not necessarily the farms with the highest prevalence of the three diseases. The TY after enrolling in HG was significantly higher than before enrolling. Estimated TY increased by almost 20% when the TY of the fourth parity of enrolled herds after eradication was compared to the TY of the fourth parity of the control herds in 2004-2008. In addition, there were obvious differences in the shape of the lactation curves between enrolled and control herds. It was only in the HG enrolled herds after eradication that an increase in milk production toward a PY at around 50 days after kidding was evident. A possible explanation for the very early DPY, (dim 6), in control herds from 1999-2003 and in the enrolled herds pre-eradication, could be that the goats were unable to increase milk production after kidding due to the detrimental effects of diseases. The control herds in the time period 2004-2008 provided us with information on the trend of milk production independent of HG. The control herds in the time period 1999-2003 and the enrolled herds pre-eradication were considered equal in terms of variation in genetic material, management practices and prevalence of diseases. Assuming that the controls and enrolled farms represent the same situation before HG enrolment, the comparison of controls and enrolled farms after HG would point out the effect of disease eradication (and other herd effects due to HG enrolment, as discussed above). The effect of improved management and feeding regimes on daily milk yield can be regarded as independent from the effect of freedom from disease, although the eradication of CAE, CLA and caprine paratuberculosis could affect the goats' ability to utilise feed optimally. However, with an

increased TY in the enrolled herds of more than 20% compared to the control herds, the effect of HG seems clear.

Healthier Goats and its financial impact on enrolled farms

The retrospective CBA of the Healthier Goats programme was based on observed trends and effects of having any or all of the three diseases, CAE, CLA and paratuberculosis, in the herd. It is important to have a fair comparison in the evaluation and search for beneficial financial effects of the HG programme. The control group constituted farms that were not enrolled and the resulting NPVs for the different milk quota levels (30 000L, 50 000L, 70 000L) reflects the result of implementing HG adjusted for the general development without enrolling in HG, as represented by the control herds. The results from the CBA showed that, over a five year time horizon, the high investments required for the farmers' participation in HG resulted in a negative expected NPV, regardless of the quota levels. With large investments in the initial period after enrolment, the farmers faced a high risk of a net loss over the first few years. On the other hand, over 10- and 20-year horizons, expected NPVs were positive both at 50 000 L and 70 000 L quota levels. Yet over a 10-year period there were significant risks of farmers making a loss at all quota levels, but especially at the lowest scale of production. Evidently, the control and eradication of CAE, CLA and caprine paratuberculosis has required farmers to take a long-term view, as in the short term they faced significant downside risks. Those risks were most serious for farmers with small herds, who may be least able to take a long-term view and to bear the risk of the investments. The discount rate was held constant in the modelling and reflected the situation with a low and stable interest rate, which Norway has experienced over several years. This has clearly contributed to make the programme more profitable and worthwhile undertaking. A higher discount rate, which might be appropriate for a farmer with substantial existing debts, would make the programme less profitable in expected value terms, and more risky.

Whether a goat farmer takes a short- or a long-term view of the investment may depend on personal circumstances, such as age or level of indebtedness and the upcoming capital needs of the farm and family. These factors represent the overall objectives a farmer has with his/her business. We did not study the farmers' decisions criteria, but we believe that an insight into these aspects would be useful when addressing disease control issues in the future.

In the scenario in which farmers were left without any reimbursement of the costs of control and eradication, and also had to pay for testing and analyses themselves, the expected NPV was negative over ten years, independent of the quota level. Thus, the importance of governmental support to make the programme financially attractive was demonstrated. Whether the prolonged period before gaining a positive NPV in the scenario without reimbursements would have affected farmers' decisions to enrol in the programme, has not been assessed. It seems likely that more farmers, if not most, would have been discouraged by the extended time horizon before the programme would be financially beneficial. Indeed, industry representatives claim that the governmental support has been crucial for the success. The farmers' assessment in this respect has not been studied.

The non-enrolled farms represented the general situation among the dairy goat farms without eradication of CAE, CLA and caprine paratuberculosis. They represented the same as the data from the enrolled farms prior to their enrolment in HG (own controls). The study by Hardeng et al. (2009) showed that the average milk yield was higher for the non-enrolled group than for the enrolled group prior to HG. This suggests that the loss in milk yield for the enrolled farms might have been even greater without HG. Hence, the difference between enrolled and non-enrolled farms, as described in our CBA model, may be an underestimation, meaning that the CBA model provided a somewhat conservative assessment of the benefits of HG.

The overall detrimental effects of CAE, CLA and caprine paratuberculosis on the productivity of dairy goats was difficult to measure or value. It was not possible to distinguish between the impacts of the individual diseases. With this in mind, caution is needed when comparing HG to disease control

programmes targeting only one or two of the diseases, as the costs of HG were spread across the elimination of all three diseases. However, with this reservation, we believe that HG is a relevant model for other disease control programmes, either in Norway or other countries, just as the Norwegian BVD control and eradication programme (Valle et al., 2005) was an important reference in the establishment of HG.

By initiating and implementing HG, a major disease burden has been removed from the Norwegian goat population, and consequently animal welfare has been improved (Muri, 2012). Because such benefits are hard to quantify in terms of monetary value, they are difficult to include in an economic comparison (Dijkhuizen and Morris, 1997) and therefore not captured in the present NPV calculations. However, the satisfaction of having a healthy herd with improved animal welfare and a reduction in potential human health risks are important factors when considering the full benefits of HG.

In 2012, the main focus of HG shifted towards recruiting the remaining farms, in order to complete the eradication in the entire Norwegian dairy goat population. Achieving that goal would lower the risk of re-infection of herds free from CAE, CLA and Johne's disease. The reduction in milk price was implemented to ensure enrolment of the total Norwegian dairy goat population in HG, and made non-enrolment an unsustainable alternative for the majority of the dairy goat farmers. The extra benefit of eventually obtaining a close to zero risk of re-infection, given all herds are cleared of the diseases, was not explicitly included in our analyses.

The subsidies saved by the government can be seen in relation to the governmental monetary support to HG, as the support to HG is a one-time payment per farm, and following this, the continuous subsidy payment may be reduced due to higher-yielding animals. We observe a theoretical opportunity for the government to recover the support to HG in less than five years, given that the quota system and regulations on subsidy payments remain unchanged. Hence, from a government point of view, it can be argued that providing money to HG could be seen as a good

investment. However, we did not undertake a social economic cost-benefit analysis of the programme; hence we did not assess HG from the viewpoint of the society as a whole, where effects as mentioned above belong.

Main conclusions

- There may be a higher chance of sheep flocks contracting CLA if there is contact with CLA infected goat herds on pasture, but more work is required to draw conclusions about this risk.
- The project results support the use of CAE and CLA ELISA BTM testing for surveillance in the Norwegian dairy goat population as well as other low-prevalent populations. This strategy has the potential of reducing the costs associated with controlling CAE and CLA.
- The increase in milk yield from before to after enrolling in HG demonstrates the positive impact of HG on the milk yield in Norwegian dairy goats.
- The Norwegian Healthier Goats programme was shown to be profitable for the farmers over a moderate time horizon.

Overall, the results from this project show that the Healthier goats programme has been beneficial for the Norwegian dairy goat population, and has contributed to increased knowledge which can be useful in the establishment of similar projects in the future.

Implications for future research

- Further investigation of the risk of spreading CLA in relation to pasture contact between sheep and goat should be conducted, and an investigation of the prevalence of CLA in sheep herds in other areas of Norway would be desirable.
- The persistence of the promising results from the eradication process relies on a high level of surveillance in the future. Therefore, further works needs to be performed on diagnostic tools, i.e. evaluation of the performance of existing systems and possibly also the development of other screening tests.
- A revision of the methodology applied in the establishment of lactation curve analyses for dairy goats (and cows) would be a natural continuation of the work done in modelling lactation curves by data-driven methods, i.e. spline regression.
- In relation to the financial CBA at farm level, it would be desirable to also include other stakeholders, like the dairy industry and the consumers, in a socioeconomic CBA of the Healthier Goats programme. Since the Healthier Goats programme to a large extent relies on resources from the community, it would be a reasonable task to evaluate the outcome of the Healthier Goats programme for the society as a whole.

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Appendix