Vitenskapskomiteen for mat og miljø
Norwegian Scientific Committee for Food and Environment

VKM Report 2021: 01

Mitigations options after detection of Chronic Wasting Disease in the Hardangervidda Wild Reindeer Area – a basis for future management strategies

Original title:

VKM Rapport 2021: 01
Handlingsrommet etter påvisning av skrantesyke (Chronic Wasting Disease, CWD) på Hardangervidda – grunnlag for fremtidige forvaltningsstrategier

Vitenskapelig uttalelse fra Vitenskapskomiteen for Mat og Miljø (VKM)

20.01.2021

ISBN: 978-82-8259-403-5
ISSN: 2535-4019
Norwegian Scientific Committee for Food and Environment (VKM)
P.O. Box 222 Skøyen
0213 Oslo
Norway

Phone: +47 21 62 28 00
Email: vkm@vkm.no

vkm.no

Cover photo: Olav Strand

Citation: VKM, Bjørnar Ytrehus, Maria G. Asmyhr, Helge Hansen, Atle Mysterud, Erlend B. Nilsen, Olav Strand, Michael A. Tranulis, Jørn Våge, Georg Kapperud, Knut Madslien, Eli K. Rueness, Yngvild Wasteson (2021) Mitigation options after detection of Chronic Wasting Disease in the Hardangervidda Wild Reindeer Area – a basis for future management strategies. Scientific Opinion from the Norwegian Scientific Committee for Food and Environment. VKM Rapport 2021:01, ISBN: 978-82-8259-403-5 ISSN: 2535-4019. Norwegian Scientific Committee for Food and Environment (VKM), Oslo, Norway.

Mitigations options after detection of Chronic Wasting Disease in the Hardangervidda Wild Reindeer Area – a basis for future management strategies

Preparation of the opinion

The Norwegian Scientific Committee for Food and Environment (Vitenskapskomiteen for mat og miljø, VKM) appointed a project group to write a draft for a scientific opinion. The project group consisted of two VKM members, one VKM employee and five external experts. Two external referees commented on and reviewed the manuscript. The Scientific Committee, represented by a multidisciplinary approval group, evaluated and approved the final opinion.

Authors of the opinion

Members of the project group that contributed to the drafting of the opinion (in alphabetical order after chair of the project group):

Bjørnar Ytrehus – Chair of the project group and member of the Panel on Microbial Ecology. Affiliation: 1) VKM; 2) Department for Biomedicine and Veterinary Public Health, Swedish University of Agricultural Sciences, Uppsala.

Maria G. Asmyhr – Member of the project group and project leader from the secretariat of the Scientific Committee. Affiliation: VKM.

Helge Hansen – Member of the project group. Affiliation: County Governor of Trøndelag.

Erlend B. Nilsen – Member of the project group and member of the Panel on Alien Organisms and trade in Endangered Species (CITES) in VKM. Affiliation: 1) VKM; 2) Norwegian Institute for Nature Research (NINA).

Atle Mysterud – Member of the project group. Affiliation: 1) University of Oslo (UiO)

Olav Strand - Member of the project group. Affiliation: 1) NINA

Michael A. Tranulis - Member of the project group. Affiliation: 1) Norwegian University of Life Sciences (NMBU)

Jørn Våge - Member of the project group. Affiliation: 1) Norwegian Veterinary Institute (NVI)

Members of the multidisciplinary approval group

Georg Kapperud – Member of the Panel on Biological Hazards in VKM. Affiliation: 1) VKM; 2) NMBU; 3) Norwegian Institute of Public Health (NIPH)

Knut Madslien – Member of the Panel on Animal Health and Welfare in VKM. Affiliation: 1) VKM; 2) NVI

Eli K. Rueness – Member of the Panel on Alien Organisms and Trade in Endangered Species (CITES) in VKM. Affiliation: 1) VKM; 2) UiO

Yngvild Wasteson – Leader of the Panel of Microbial Ecology in VKM. Affiliation: 1) VKM; 2) NMBU

Acknowledgment

VKM would like to thank Hildegunn Viljugrein (NVI) for her help with data analyses and interpretation in Chapters 2.10 and 2.11. VKM will also thank the Morten Tryland (University of Tromsø) and Sylvie L. Benestad (NVI) for their valuable comments and critical review of the draft of the opinion. VKM emphasizes that the reviewers are not regarded as responsible for the content in the published opinion. In accordance with VKM's procedures for approval of risk assessments (VKM 2018) did VKM receive the comments from the peer reviewers before the multidisciplinary approval group conducted a final review, approved the opinion, and before the opinion was finalized for publication.

Competence of VKM experts

Persons working for VKM, either as appointed members of the Committee or as external experts, do this by virtue of their scientific expertise, not as representatives for their employers or third-party interests. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

Translated version

The current version of the report is translated from the original report, which was written in Norwegian. The translation was done by chair of the project group, Bjørnar Ytrehus in December 2021 – March 2022. In the event of conflict between the two versions, the Norwegian version will prevail.

Table of Contents

Sammendrag

Bakgrunn

Skrantesyke (Chronic Wasting Disease, CWD) er en prionsykdom som rammer hjortevilt. Prioner er proteiner dannet av kroppens egne celler. Proteinene er foldet feil og har en tredimensjonal struktur som gjør at de forårsaker sykdom og kan overføres mellom individer. Skrantesyke ble først beskrevet i Colorado i USA på slutten av 1960-tallet. Siden da har sykdommen spredt seg blant hvithale-, mul- og wapitihjort over store deler av Nord-Amerika, og er introdusert til Sør-Korea. Sykdommen er dødelig, dyrene opparbeider ikke immunitet, og det finnes ingen behandling eller vaksine. I enkelte områder i USA med høy forekomst av skrantesyke, ser en nedgang i hjorteviltbestanden. Sykdommen er svært vanskelig å håndtere. Infiserte dyr kan bære og skille ut smitte over lang tid uten å vise tegn på sykdom, og prionene som skilles ut i miljøet er smittefarlige i mer enn 5 år. Det finnes ingen holdepunkter for at skrantesyke kan smitte fra hjortedyr til mennesker, men en ønsker i størst mulig grad å unngå at mennesker blir eksponert for prioner.

Utbruddet av skrantesyke i Nordfjella i 2016, var det første i Europa og det første blant reinsdyr. Det ble satt inn en rekke tiltak, blant annet ble hele den berørte villreinbestanden i sone 1 av Nordfjella avlivet vinteren 2017-2018. Målet var å begrense og om mulig utrydde skrantesyke i Norge.

Den 3. september 2020 ble det imidlertid felt en villreinbukk på Hardangervidda som testet positivt for skrantesyke. På bakgrunn av det, ga Mattilsynet og Miljødirektoratet VKM i oppdrag å oppdatere kunnskapsstatus om skrantesyke og vurdere mulighetene for å håndtere sykdommen.

Metoder

Vi gjorde litteratursøk i vitenskapelige databaser etter relevante forskningsarbeider publisert mellom 2018 og 2020. Vi beskrev avsluttede og pågående forskningsprosjekter som er relevante for forvaltning av skrantesyke i Norge.

Analyseresultater av skrantesyke og overvåkningsdata for villrein ble satt inn i en smitteoppdagelsesmodell og en bestandsestimeringsmodell og brukt til å estimere forekomst på Hardangervidda.

Sannsynligheten for fravær av smitte i andre bestander av hjortevilt ble vurdert når det var datagrunnlag for det. For mange bestander var imidlertid datagrunnlaget for dårlig til å gjennomføre slike vurderinger.

Videre har vi beskrevet den smittede villreinbukken fra Hardangervidda, inkludert alder og genetisk profil.

Vi har også beskrevet karaktertrekk ved villreinbestanden på Hardangervidda og dens habitat, samt konnektiviteten mellom denne bestanden og ulike hjorteviltbestander.

På bakgrunn av litteratursøk, overvåkingsresultater og modellering vurderte VKM de tre aktuelle forvaltningsstrategiene for hvordan den nåværende situasjonen med skrantesyke på Hardangervidda kan håndteres; ingen tiltak, begrense sykdommen, og utrydde sykdommen.

Resultater

Nye internasjonale studier

Kunnskapsoppdateringen avdekket ikke ny forskning som i vesentlig grad endrer forutsetningene for hvordan skrantesyke kan håndteres i Norge. Kunnskapsgrunnlaget som er beskrevet i tidligere VKM-rapporter er fortsatt relevant. Det har derimot kommet en del studier som styrker og utdyper tidligere etablert kunnskap.

Forsøk hvor hvithalehjort har blitt infisert med skrantesykeprioner, viser at den minste dosen smittestoff som trengs for å gi sykdom er svært liten (0,0000001-0,0000003 g hjernemateriale eller tilsvarende mengde spytt fra et sykt individ).

Studier der en har gravd ned prionholdig hjerne i jord under naturlige forhold med nedbør og vekslende temperaturer, viser at prionene beholder evnen til å forårsake sykdom etter mange år i miljøet. En studie av sammenhengen mellom jakttrykk på bukker og forekomsten av skrantesyke, konkluderer med at hard beskatning av voksne bukker kan holde forekomsten lav. Simuleringsstudier basert på modeller for hvordan skrantesyke oppfører seg hos hvithalehjort, viser at effekten av tiltak avhenger av hvilken fase av et utbrudd man gjennomfører tiltaket i. I en tidlig fase er det en viss mulighet for at et utbrudd kan stanses ved at man tar ut alle infiserte dyr før de rekker å smitte nye, men allerede når fem dyr er smittet, vil det som regel gå mot fullt utbrudd.

Lærdom fra Nordfjella

I perioden april 2016 til våren 2018 ble 2424 reinsdyr undersøkt for skrantesyke i Nordfjella sone 1. Av de 19 dyrene som testet positivt, var det 13 bukker og seks simler, ingen kalver og bare én halvannet åring. Voksne bukker hadde 2,7 ganger så høy sannsynlighet for å være positive som simler. Sannsynligheten for infeksjon økte med økende alder på de voksne bukkene. Tilsvarende mønster er sett hos hvithale- og mulhjort i Nord-Amerika. Genetiske sammenlikninger av reinsdyr fra Nordfjella med og uten skrantesyke, viste at to av de fem genvariantene av priongenet (*PRNP*) var overrepresentert hos de positive individene. Dette indikerer at ulike varianter av *PRNP* - genet gir ulik mottakelighet for skrantesyke. Upubliserte studier viser at undersøkte villreinbestander har stor andel av de variantene som gir størst mottakelighet, mens det er større andel med lav mottakelighet blant tamrein.

Verken laboratorieundersøkelsene som ble gjort av skrantesyke-positive villrein fra Nordfjella eller epidemiologien ved utbruddet, avdekket noen forskjeller mellom skrantesyke hos villrein i Norge og skrantesyke slik den opptrer hos hvithale- og mulhjort i Nord-Amerika. Podeforsøk på

klatremus avdekket imidlertid at prionisolatet fra Nordfjella ga lengre inkubasjonstid enn kjente isolater fra Nord-Amerika. Dette indikerer at skrantesyken hos villrein i Nordfjella forårsakes av en prionstamme som inntil nå har vært ukjent for vitenskapen, men gir ikke grunnlag for å hevde at denne vil oppføre seg annerledes enn nordamerikanske isolater. Det er altså fortsatt slik at modeller og kunnskap fra Nord-Amerika, sammen med den relevante kunnskapen vi opparbeider oss i Norge, gir det beste grunnlaget for framtidig håndtering av skrantesyke.

Hardangervidda

Over 4000 villrein fra Hardangervidda har blitt undersøkt for skrantesyke, hvor ca. 70 % er undersøkt i både hjerne og svelglymfeknute. Etter jakta i 2020, estimeres forekomst av skrantesykeinfeksjon til å være 1-2 voksen bukk (95 % sikkerhetsintervall: 0-10 individer). Antallet infiserte simler og ungdyr kan ikke estimeres med sikkerhet pga. få prøver. Hvis man går ut fra at smittemønsteret er som i Nordfjella, kan det være 3-5 infiserte individer (95 % sikkerhetsintervall: 1-19 individer) i bestanden som helhet, men estimatene er usikre. Selv om beregningene er usikre, viser de at sykdommen er oppdaget i en tidlig fase av det som kan være starten på et større utbrudd av skrantesyke.

Det er beregnet sannsynligheter for fravær av smittede dyr i villreinbestanden i Nordfjella sone 2/Raudafjell og i tamreinflokken på Filefjell. Basert på prøvene analysert fram til 4. desember 2020 er sannsynligheten hhv. 82 % og 84-91 % for at man ville ha oppdaget smitte selv med bare få (3-4 eller flere) smittede dyr til stede.

Det er så langt ikke regnet ut tilsvarende sannsynligheter for andre villreinbestander, tamreinflokker og bestander av hjort, elg og rådyr.

Reinsbukken på Hardangervidda som fikk påvist skrantesyke hadde en slaktevekt på 58 kg og var åtte år gammel. Genetiske analyser viser at den med stor sannsynlighet kommer fra Hardangervidda-bestanden og ikke fra Nordfjella. Det ble bare påvist skrantesykeprioner i lymfeknuten og ikke i hjernen, noe som tilsier at bukken var i tidlig fase av sykdommen. De diagnostiske undersøkelsene avdekket ingen forskjeller i smittestoffet mellom dette dyret og de skrantesykepositive dyrene fra Nordfjella. Flere forhold peker likevel i retning av at bukken ble smittet på Hardangervidda, og ikke i Nordfjella; den lave hyppigheten av vandringer over Riksvei 7, de genetiske analysene som viser at bukken stammer fra Hardangervidda, og at den var i tidlig fase av sykdommen.

Vurdering av strategier for håndtering

VKM har tidligere (2017) skissert at det er tre strategier for å håndtere skrantesyke. I rapporten diskuteres disse i lys av kunnskapsgrunnlaget presentert i de tre tidligere VKM-rapportene (2016, 2017 og 2018), og kunnskapsoppdateringen i denne rapporten.

Ingen tiltak

Ingen tiltak vil med stor sannsynlighet føre til økt forekomst av skrantesyke på Hardangervidda og spredning til andre bestander av villrein, tamrein og annet hjortevilt. Det finnes ikke

vitenskapelig grunnlag for å hevde at sykdommen vil forsvinne av seg selv. Etter hvert som forekomsten øker, vil graden av miljøsmitte øke. Dette vil øke spredningshastigheten og gjøre at miljøet er smittefarlig i lang tid framover. Konsekvensen av ukontrollert spredning av skrantesyke vil være økt dødelighet og dårlig dyrevelferd i berørte reinbestander. Vi må også forvente spredning til andre hjorteviltarter. I et langt tidsperspektiv må vi forvente nedgang i berørte hjorteviltbestander. Effekten vil sannsynligvis variere fra art til art avhengig av bl.a. hvor sosiale dyra er. Økende miljøsmitte vil medføre økt eksponering for prioner for andre arter, inkludert menneske.

Utrydde smitte

Siden det ikke finnes anvendbare testmetoder som gjør at smittede dyr kan identifiseres mens de er i live, og ingen behandling eller vaksine, så er det bare mulig å fullstendig *utrydde smitte* ved å utrydde den infiserte bestanden. En slik strategi vil også innebære at det berørte området legges brakk og holdes tomt for hjortedyr inntil miljøsmitten er borte. Effekten av tiltaket avhenger av om det allerede finnes smitte i andre bestander og av om miljøsmitten forsvinner i løpet av brakkleggingen.

Om villreinbestanden på Hardangervidda utryddes, forsvinner en betydelig andel av det genetiske reservoaret til villreinen i Europa. Villreinen er også en art som har stor betydning for økosystemet på Hardangervidda, og om den forsvinner må en forvente økologiske ringvirkninger. Det å avlive så mange viltlevende flokkdyr på kort tid, vil være en betydelig dyrevelferdsmessig utfordring.

Begrense smitte

Strategien begrense smitte innebærer å gjøre tiltak som holder forekomsten innen villreinbestanden så lav som mulig og minimerer sannsynligheten for videre spredning. De samlede effektene av mange ulike tiltak vil være avgjørende for hvilken effekt man oppnår. Mange samtidige og sterke tiltak påbegynt i løpet av kort tid, dvs. mens forekomsten ennå er lav, vil ha størst mulighet for å lykkes med å begrense forekomsten. Om tiltakene er effektive, så finnes det en liten mulighet for at de kan medføre at sykdommen utryddes.

Strategien *begrense smitte* er spesielt aktuell når man opplever stor grad av usikkerhet, og hvor videre kunnskapsinnsamling på sikt vil gjøre usikkerheten vesentlig mindre. En slik strategi kan med stor fordel kombineres med en planmessig adaptiv forvaltning med løpende, systematisk kunnskapsinnsamling som brukes til å justere tiltakene underveis. En slik læringsbasert tilnærming krever styrket overvåking både av forekomsten av skrantesyke og andre veterinærmedisinske og økologiske variabler som kan påvirkes av tiltakene som gjennomføres.

Rapporten beskriver en rekke mulige tiltak. Under strategien *begrense smitte* er de antatt mest effektive tiltakene å minimere andelen bukk og redusere totalbestanden. Muligheten for å lykkes med å begrense forekomst og spredning gjennom å ta ut bukk er størst om tiltaket gjennomføres så snart som mulig (innen ett år). Reduksjon av bestanden har usikker effekt på andel infiserte og spredningsraten innad i bestanden, men vil sannsynligvis begrense forekomsten av

miljøsmitte og muligheten for spredning til andre bestander. Det er i denne strategien viktig å ikke redusere bestanden så mye at man i framtiden ikke får nok prøver til å vurdere om tiltakene lykkes. Det er foreløpig ikke beregnet hvilket bestandsnivå som gir best kombinasjon av begrensing av smitte, prøveuttak og bevaring av bestanden.

Reduksjon av menneskelig ferdsel på deler av Hardangervidda, vil kunne gi reinen større tilgjengelig areal og dermed senke tettheten og redusere sannsynligheten for at dyra eksponeres for miljøsmitte. Et omfattende skifte i områdebruken vil kunne hindre at dyra utsettes for allerede akkumulert miljøsmitte, men kan samtidig gjøre at eventuelle infiserte dyr sprer smitten til andre deler av vidda. Gjerder mellom Hardangervidda og omkringliggende områder kan forhindre inn- og utvandring av rein, noe som er viktig for å unngå spredning til andre bestander. Tiltakene for å styre villreinens arealbruk vil ha størst effekt om de påbegynnes nå og gjennomføres i løpet av kort tid (tre år).

Et tiltak kan være å avlive rein som viser tegn til klinisk sykdom. Et slikt tiltak har få negative konsekvenser, er rimelig og enkelt å gjennomføre og kan potensielt ta ut smittede dyr, noe som i så fall gir redusert forekomst og spredning.

Sannsynligheten for at villrein eksponeres for miljøsmitte er størst på salteplasser, ved kadavre av infiserte dyr og steder hvor dyra trenges tett sammen. Tiltak som gjør at salteplasser ikke er tilgjengelige, vil gjøre sannsynligheten for eksponering for miljøsmitte betydelig mindre for både villrein, annet hjortevilt og sau. Slakteavfall representerer også en potensiell smittekilde som mennesker kan påvirke. Tiltak for å unngå eksponering for og akkumulering av miljøsmitte vil begrense smitte mest effektivt om de gjennomføres så snart som mulig.

Ulike hjorteviltarter har lite direkte kontakt, og miljøsmitte vurderes som viktig for overføring av skrantesyke mellom arter. I tillegg til antall smittede dyr blant villreinen og forekomst av punktkilder som f.eks. salteplasser, som brukes av flere arter, vil graden av overlappende områdebruk avgjøre sannsynligheten for smitteoverføring. Denne kan minimeres ved å redusere bestandene av hjort, elg og rådyr i tilgrensende områder til lav tetthet (ned mot ett dyr per km^2) og skyte ut delbestander som lever innenfor villreinens leveområder. En har størst mulighet til å begrense spredning dersom tiltaket gjennomføres så snart som mulig.

Sannsynligheten for at sau kan spre skrantesyke vurderes som lav, og tettheten av sau er relativt lav i de områdene av Hardangervidda som brukes mest av villreinen. Dette gjør at en reduksjon av sauetallet eller et beiteforbud for sau vurderes til å ha liten eller ingen effekt på forekomsten og spredningen av skrantesyke. Dette gjelder særlig dersom mulighetene for indirekte kontakt mellom sau og villrein på salteplassene minimeres.

Konnektiviteten mellom enkelte av villreinbestandene og tamreinflokkene, og innad mellom tamreinflokkene, er stedvis svært stor. Mange av tiltakene rettet mot villrein vil med tilpasning også være aktuelle for å forebygge spredning av skrantesyke til, fra og mellom tamreinflokker. Dette kan være reduksjon av flokkstørrelsen, redusert bukkeandel og/eller andre tiltak som påvirker sannsynligheten for utveksling av dyr. Omfanget og hastigheten av tiltak må vurderes ut fra lokale forhold og grad av forbindelse/nærhet til påvist skrantesyke.

Det er mulig å avle på rein for å senke mottakeligheten for skrantesyke. Dette kan gjøres ved å ta prøver av bukker og velge ut de som har en *PRNP*-variant som er assosiert med lav mottakelighet for infeksjon. Dette vurderes ikke som praktisk gjennomførbart for en stor villreinbestand, men kan være gjennomførbart i små flokker og tamreindrift.

Konklusjon

Påvisning av skrantesyke hos én villrein på Hardangervidda vanskeliggjør bekjempelsen av denne svært alvorlige, smittsomme og dødelige dyresykdommen i Norge. Hardangervidda er leveområde for Europas største bestand av villrein og et utbrudd av skrantesyke her vil få alvorlige konsekvenser. I tillegg vil et utbrudd gi høy sannsynlighet for spredning til andre bestander av rein og annet hjortevilt. Vi må forvente alvorlige konsekvenser også for disse, selv om utbrudd kan arte seg forskjellig hos ulike arter. Det vil være svært krevende å stanse spredningen.

Situasjonen er vesentlig endret fra situasjonen med funn av skrantesyke hos tre villrein i Nordfjella sone 1, behandlet i en tilsvarende rapport i 2017. For det første viser funnet utenfor Nordfjella at smitten kan finnes i enda flere bestander. Det gjør det usikkert om tiltak rettet mot bestanden på Hardangervidda vil kunne utrydde sykdommen fra Norge.

For det andre er villreinbestanden på Hardangervidda større og dermed har større betydning enn bestanden i Nordfjella sone 1, og området bestanden utnytter er betydelig større, vanskeligere å avgrense og kontrollere. Det gjør tiltak for å begrense eller utrydde sykdommen mer krevende å gjennomføre og sannsynligheten for å lykkes mindre.

Det er påvist smitte hos ett dyr av over 4000 undersøkte villrein fra Hardangervidda. Forekomsten vurderes dermed som svært lav, og vi har sannsynligvis oppdaget smitten tidlig i forløpet av et utbrudd. De tiltak man velger å gjennomføre, må gjennomføres innen kort tid om de skal ha størst mulig sannsynlighet for å gi ønsket effekt.

Summary

Background

Chronic wasting disease (CWD) is a prion disease affecting cervids such as deer species, moose (*Alces alces*) and reindeer (*Rangifer tarandus*). Prions are abnormally folded proteins that are transmissible and able to induce abnormal folding of specific proteins naturally occurring in cells, thus resulting in a transmissible disease. CWD was initially described in the late 1960s in Colorado, US. Since then, the disease has spread extensively among white-tailed deer (*Odocoileus virginianus*), mule deer (*Odocoileus hemionus*) and wapiti (*Cervus canadensis*) in North America. The disease was also introduced to South Korea. CWD is always fatal, infected animals do not develop immunity and there is currently no available treatment or vaccine.

In the US, population declines of deer have been observed in some areas of high prevalence. Infected animals may carry and transmit prions long before they display any symptoms of the disease, so called "silent carriers". In addition, prions can persist in the environment for prolonged periods, retaining infectivity. These factors pose challenges to effective management of the disease. There are currently no data suggesting that CWD could transfer from cervids to humans, however it is still recommended to avoid human exposure to CWD prions.

CWD was first discovered in Europe in 2016, in the Nordfjella area in Southern Norway. This was also the first outbreak of CWD in reindeer. Targeted management strategies were initiated, culminating in the removal of the entire population of reindeer in Nordfjella zone 1, during winter 2017-18. The overall goal of this strategy was to restrict the spread of the disease and if possible, eradicate CWD from Norway.

On September 3, 2020, a reindeer male shot on Hardangervidda, Norway, was diagnosed with CWD. Based on this, the Norwegian Food Safety Authority and the Norwegian Environment Agency commissioned VKM to prepare an updated status report on CWD in Norway, including an assessment of various management strategies.

Methods

For this report, VKM searched the literature for papers published between 2018 and 2020, describing both finalized and ongoing research projects of relevance to CWD management in Norway.

Diagnostic and population surveillance data for wild reindeer were used for estimating CWD prevalence on Hardangervidda.

For some other cervid populations we assessed the probability of absence of CWD. However, for the majority of populations there were not enough data available to conduct such analyses.

VKM describes the CWD case on Hardangervidda, including an age-estimate of the diagnosed reindeer bull and *PRNP* genotype. We describe the characteristics of the wild reindeer population on Hardangervidda and its habitat, as well as the level of connectivity between this population and other populations of cervids.

Based on the literature searches and the results from surveillance and modeling, we evaluate the three management strategies outlined as alternatives for handling the current situation: a) no measures; b) control the disease; and c) eradicate the disease

Results

Recent international studies

The synthesis of CWD research published since previous VKM-reports revealed no new information that changes the prerequisites for handling CWD in Norway. As such, the information provided in previous VKM-reports is still relevant today. However, the results of several recent studies strengthen and builds on previous knowledge.

Experiments where white-tailed deer have been infected with CWD-prions shows that the oral infective dose is very low (0,0000001-0,0000003 grams of brain material or a similar amount of saliva from an individual with terminal disease) compared to previous experiments.

Studies have shown that brain material infected with prions and buried in soil under natural conditions, such as rain and changing temperatures, remains infectious for many years.

One study concludes that removal of a substantial proportion of adult males may maintain low occurrence of CWD.

Simulation studies of CWD in white-tailed deer show that the effects of management strategies are dependent on the phase of the disease outbreak. In an early phase, there is a minor possibility of stopping the outbreak by removing all infected animals before they pass the disease on to other animals. However, then five or more animals are infected the outbreak will continue to grow.

New knowledge gained from Nordfjella

Between April 2016 and spring 2018, 2424 reindeer from Nordfjella zone 1 were tested for CWD. Among these animals, 19 were positive for CWD: 13 adult males and 6 females, but no calves and only one yearling. Adult males had a 2.7 % higher probability of being infected compared to females. In males, the probability increased with increasing age. A similar sex and age distribution has previously been observed among white-tailed deer and mule deer in North America.

Then comparing the genetic profile of Nordfjella reindeer with and without CWD, two of the five variants of the prion protein gene (*PRNP*) were overrepresented among the CWD-positive

animals. These results indicate that the different *PRNP*-variants cause different susceptibility to CWD.

The initial diagnostic tests performed in 2016-2018 indicated that the CWD prion isolates from wild reindeer in Nordfjella were identical to isolates from North America. However, a recent inoculation study of bank voles showed that the Nordfjella isolates resulted in a longer incubation period than North American isolates, thus indicating that the Nordfjella CWD is caused by a new strain of CWD prions, not previously known to science.

Hardangervidda

To date, more than 4000 animals from Hardangervidda have been tested for CWD. Of these, 70 % have had both brain and lymph nodes tested. The prevalence of CWD is estimated to be 1-2 adult males (95 % confidence interval: 0-10 individuals) after the 2020 hunting season. The prevalence among females and sub-adults cannot be estimated with certainty, due to lack of positive cases. However, if the age and sex distribution is similar to the one in Nordfjella (mentioned above), there may be 3-5 infected animals (95 % confidence interval: 1-19 animals in the total population. Notably, these estimates are highly uncertain. However, they do show that the disease has been discovered at an early stage of what could be the initial phase of a larger outbreak of CWD.

The probability of absence of CWD infected animals was calculated for the Nordfjella wild reindeer population zone 2/Raudafjell and the domestic reindeer population in Filefjell. Based on the samples analyzed until December 4, 2020, the probability is 82 % and 84-91 % respectively, that one would have detected CWD even with very few (3-4 or more) infected animals present.

So far, such calculations have not yet been carried out for populations of wild reindeer, semi-domesticated reindeer, and populations of red deer (*Cervus elaphus*), moose and roe deer (*Capreolus capreolus*).

The CWD infected reindeer male from Hardangervidda weighed 58 kg and was eight years old. Genetic analyses show that the most probable origin of the male is Hardangervidda. CWD prions were detected in the retropharyngeal lymph nodes, but not in the brain, which indicates that the animal was in an early phase of the disease.

Diagnostic tests did not reveal any differences between the CWD prions in this animal compared with CWD-positive animals from Nordfjella. Several conditions indicate that the animal most likely contracted the infection on Hardangervidda and not in Nordfjella; the well documented low frequency of migration between these areas across highway 7 (riksvei 7), the results of the genetic analyses and that the animal was in an early phase of the disease.

Assessment of management measures

VKM has previously (2017) outlined three strategies for handling CWD. We discuss these strategies based on the information presented in past VKM-reports (2016, 2017, 2018) as well as the more recent research presented in the current report.

Strategy: No measures

Based on current evidence, a strategy of no measures will very likely lead to an increasing prevalence of CWD in the Hardangervidda wild reindeer herd and spread of the disease to other populations of wild and semi-domesticated reindeer. There is no scientific evidence suggesting that the disease will peter out on its own. With increasing prevalence, environmental contamination will accumulate, further increasing the rate of spread. The environmental infection will persist for a long time (multiple years).

The consequences of an uncontrolled spread of CWD will be increased mortality and poor animal welfare in the affected reindeer populations. We must also expect spread to other species of cervids. Long-term consequences are expected to be population declines in the cervid populations; however the effect will probably vary among species dependent on factors such as social population structure. Increasing environmental contamination will cause increased prion exposure also for other species, including humans.

Strategy: Eradicate CWD

In the absence of vaccines, treatment and tests that can efficiently identify infected animals while still alive, the only way to eradicate CWD with certainty is to remove (cull) the affected population and keep the Hardangervidda free from cervids until testing reveals that there is no longer any disease present in the environment. How effective these measures will be depends on whether CWD is present in other populations and whether a fallowing period efficiently clears any vestiges of the disease.

To eradicate the wild reindeer population on Hardangervidda will also eradicate a significant part the genetic reservoir of the European wild reindeer population. The wild reindeer plays an important role in the Hardangervidda ecosystem, thus one can expect ecological consequences by such removal. To cull a large number of wild animals like the Hardangervidda herd within a short time frame will also pose a significant challenge in regard to animal welfare.

Strategy: Controlling CWD

The strategy of controlling CWD comprises various measures to keep CWD prevalence within the wild reindeer population as low as possible while minimizing the probability of spread. The collective effectiveness of several measures will determine the overall success of the strategy. Simultaneously initiating these measures within a short time frame (while the disease prevalence is still low) should offer the best opportunity to successfully control the occurrence of CWD. Through the combined effect of these measures, there may also be a possibility, albeit low, of successfully eradicating the disease.

The "limit" strategy is particularly relevant in situations where there is a high level of uncertainty, and where continued sampling would significantly contribute to reducing uncertainty. It would be advantageous to combine this strategy with a plan for adaptive management, including continuous and systematic collection of data to guide adjustment of measures while gaining

better knowledge about the situation. A learning-based approach requires strengthened surveillance of CWD prevalence and the initiation of other measures, the effects of which (veterinary and ecological) should be closely monitored.

The most effective measure for controlling CWD is to minimize the proportion of males and to reduce the total number of animals in a population. Reducing the proportion of males will have a greater chance of restricting prevalence and spread if it is carried out as soon as possible (within one year). While it is uncertain how a reduction of population size will affect the number of infected animals and the rate of spread within the population, it will most likely decrease the level of environmental infection and diminish the probability of spread to other populations. Importantly, the optimal population size for achieving the combined goals of controlling the disease, conserving the population and sufficient sample collection to assess the effect of initiated measures, is not known.

Reducing human activity in parts of Hardangervidda would offer the animals access to a larger area, and thus result in lower densities. Moreover, a geographical shift in area use would prevent the animals from being exposed to accumulated environmental contamination. However, at the same time it could lead to already-infected animals spreading the disease to other parts of Hardangervidda. Fences between Hardangervidda and surrounding areas can prevent reindeer migration and thus contribute to avoiding spread of CWD to other populations. Measures directed towards altering reindeer area use will be more effective if initiated now and finalized within a short time period (3 years).

Culling reindeer exhibiting clinical symptoms is a cheap and straightforward measure that can potentially remove infected animals, thus reducing disease prevalence and spread.

Areas with salt licks, cadavers, slaughter waste (offal) and other places where animals are commonly gathered together are the most probable places where wild reindeer may be exposed to environmental infection. Initiating measures to reduce accessibility of salt licks will reduce the probability of exposure to environmental infection for reindeer, other cervids and sheep. Measures for avoiding exposure to and accumulation of environmental infection are expected to be most effective if they are carried out as soon as possible.

Direct contact between different species of cervids is rare, thus environmental infection is considered important for transfer of CWD between species. To reduce the probability of transfer of the disease, which is affected by the amount of shared habitat, one can reduce the density of populations of deer, moose and roe deer in the areas surrounding reindeer habitat as well a completely remove populations within reindeer habitat. The probability for successful limitation of spread is greater if these measures are carried out as soon as possible.

The probability that sheep may spread CWD is assessed as low, and the density of sheep is relatively low in the areas most commonly used by wild reindeer on Hardangervidda. As such, a reduction in the number of sheep or a prohibition of sheep grazing is assessed as having a small or no impact on the prevalence and spread of CWD. This is particularly true if the possibilities of indirect contact between sheep and wild reindeer at salt licks are minimized.

The connectivity between some of the wild reindeer populations and the semi-domesticated reindeer populations, as well as among semi-domesticated reindeer populations are at times significant. Many of the measures directed towards wild reindeer are also relevant for preventing spread of CWD to, from, and between semi-domesticated reindeer populations. Such measures could be a reduction in population size, a reduced proportion of males and or other measures affecting the exchange of animals. The scope and how quickly to initiate measures should be assessed based on local conditions and the degree of connectivity to CWD-infected populations.

It is possible to breed reindeer to reduce susceptibility to CWD by taking samples of males and selecting animals that display a *PRNP*-variant associated with low susceptibility for CWD infection. This approach would not be suitable in a large population of wild reindeer but could possibly be carried out in a small population and in semi-domesticated reindeer herds.

Conclusions

The detection of CWD in one wild reindeer on Hardangervidda complicates the combat against this fatal disease in Norway. A CWD outbreak on Hardangervidda will have serious consequences for the wild reindeer population and increases the probability of spreading CWD to other populations of reindeer and cervids. While CWD may affect different species in various ways, the consequences of extensive outbreaks are expected to be serious.

Compared to the situation described in the VKM (2017) report, where three wild reindeer in Nordfjella had been diagnosed with CWD, the current situation is very different. Firstly, a case of CWD outside Nordfjella shows that the disease may be found in additional populations. It is therefore uncertain whether measures targeting the Hardangervidda population would be sufficient to eradicate CWD from Norway.

Secondly, the wild reindeer population on Hardangervidda is significantly bigger and thus plays a greater ecological role than the Nordfjella zone 1 population. The population exploits a larger geographical area and is therefore harder to delimit and control. Consequently, it is more challenging to carry out measures for controlling and/or eradicating the disease, and the probability of actually succeeding is lower.

It is important to note that CWD has been detected in one out of more than 4000 wild reindeer from Hardangervidda tested for the disease. The occurrence of CWD is therefore assessed as very low, and the disease was probably discovered in an early phase of an outbreak. If the measures selected are to have the highest possible probability of being effective, they must be carried out within a short timeframe.

Key words: VKM, Chronic Wasting Disease, CWD, Cervids, Hardangervidda, Prion

Background from the Norwegian Food Authority and the Norwegian Environment Agency

Chronic Wasting Disease (CWD) was diagnosed on a wild reindeer bull on Hardangervidda on the 10th of September 2020. The disease has previously been diagnosed in Nordfjella Wild Reindeer Area, and VKM has published several scientific opinions related to this.

After this new detection on Hardangervidda, the Norwegian Food Authority and the Norwegian Environment Agency are in need of an assessment of new knowledge about this disease and risk factors for spread of the disease both within and out of the Wild Reindeer Area.

In principle, there are three alternative strategies for management of classic CWD in Norway: No intervention, control the pathogen or eradicate the pathogen. We regard the strategy of no intervention as not applicable but do although recognize that there is a need to elucidate consequences of not doing anything.

As it is urgent to get answers on certain questions, we have chosen to divide this task in two phases. Attached is the mandate for the request on Phase 1 concerning CWD from the Environment Agency and the Food Authority. Key words for questions in Phase 2 are food safety, wildlife management and so on. We will get back to this.

We want the report written in Norwegian with an extended summary in English, since the report receives great interest both locally and nationally. We do although wish that the report is translated to English with an extended summary in Norwegian on a later point of time*.

We retrieved 18 stakeholder responses on the published draft of the request, and we have, in dialogue with VKM, performed some adjustments from the original draft in the following terms of reference.

Terms of Reference from the Norwegian Food Authority and the Norwegian Environment Agency

1. Knowledge update
   1.1. An update of new knowledge about the disease, including epidemiology, aetiology and pathogenesis, that has been published since publication of previous VKM reports.
   1.2. Status of on-going national and known, relevant international research projects related to CWD.
   1.3. Prevalence estimates for CWD in the wild reindeer population of Hardangervidda
   1.4. Estimation of probability of freedom from disease in populations of cervids that have or may have had relevant contact with wild reindeer from the CWD-positive populations (Hardangervidda and Nordfjella Zone 1) and eventually also other relevant populations.
2. The case on Hardangervidda
   2.1. Information about the diagnosed case
   2.2. Comparison with previous cases in Norway and internationally
   2.3. Consider potential origins of the diagnosed disease, including when, how and where the animal may have become infected
3. Conditions concerning the wild reindeer population on Hardangervidda and its home range that can be important for the management of CWD
   3.1. Environment (including available pastures, factors affecting the herd, etc.)
   3.2. Geography and area use (including contact with other populations etc.)
   3.3. Characterization of the population (including population development, demography, condition, health status etc.)
4. Strategies

In principle, there are three alternative strategies for management of classic CWD in Norway: No intervention, control the pathogen or eradicate the pathogen.

   4.1. What are the overarching possible consequences of these three strategies in the short and long term?
      4.1.1. Veterinary
      4.1.2. Ecological
5. Detailed consideration of the strategies control and eradicate the pathogen
   5.1. Controlling the pathogen – consideration of different measures with regard to limit spread of the pathogen within and out of Hardangervidda, and within Norway.
      5.1.1. Expected effect
      5.1.2. Time perspectives related to the measures
         5.1.2.1. how quickly should they be instigated
         5.1.2.2. how long time will it take before one can expect an effect of the measures
         5.1.2.3. how enduring will the effect be

5.1.3. Critical success criteria
5.1.4. Veterinary and ecological consequences
5.1.5. Uncertainties

5.2. Eradicating the pathogen – consideration of measures with regard to eradicate the pathogen from Hardangervidda and Norway

5.2.1. Expected effect

5.2.1.1. how quickly should they be instigated
5.2.1.2. how long time will it take before one can expect an effect of the measures
5.2.1.3. how enduring will the effect be

5.2.2. Critical success criteria
5.2.3. Veterinary and ecological consequences
5.2.4. Uncertainties

6. Knowledge gaps and uncertainties

6.1. Knowledge gaps

6.2. Uncertainties actualized by the detection on Hardangervidda

6.3. Which knowledge is most important to retrieve in short time in order to reduce uncertainty about the strategies for control and eradicate the pathogen

6.4. The need for further surveillance of CWD in all cervids in Norway

1 Literature search and choice of literature

We have previously performed comprehensive reviews of the scientific literature from USA and Canada (VKM, 2017; 2018). To update these, we performed searches in ISI-Web of Science Core Collection on the term «chronic wasting disease» for the years 2018-2020. The search returned 216 results on the 15th of October 2020. One of us (AM) scanned all titles for information about spread and impact of CWD on wildlife populations in USA and Canada. We furthermore performed searches in PubMed on the term «prion» combined with names of scientists leading research groups working with CWD in the years of 2018-2020: «Aiken J» (8), «McKenzie D» (9), «Hoover E» (14), «Mathiason C» (10), «Telling G» (16), «Gilch S» (12), «Cross P» (0), «Storm D» (0), «Samuel M» (1), «Greenlee JJ» (16) and «Bartz J» (13). One of us (BY) scanned all titles for information about infection, pathogenesis and environmental persistence. We also performed PubMed searches on «CWD» and «*PRNP* variation», «Chronic wasting disease» and "pathogenesis» and «CWD», «Chronic wasting disease» and «tonsil» and «CWD», «Chronic wasting disease» and «test and cull» and «CWD», and finally «classic scrapie» and «*PRNP*» and «selection». One of us (JV) scanned all titles for information about spread and impact of CWD with relevance for the report. In addition, all the co-authors went through their own reference libraries to find literature relevant for the current report.

2 Knowledge update

2.1 CWD knowledge update

2.1.1 Prions

Information about prions and prion diseases is provided in previous VKM-reports about CWD (VKM, 2017; 2018). Some relevant background information about this subject is also provided in an attachment to this report (Appendix II). In summary:

- Prions are unique pathogens, different from virus, bacteria, fungi and parasites
- Prions are particular resistant and can remain infectious over long time in the environment.
- Prions can be shed from infected animals that do not show clinical signs of the disease.
- To confirm with absolute certainty that a sample contain/not contain prions, demands long-lasting and expensive trials including experimental infection of animals
- Prion disease can be diagnosed by demonstrating the presence of the prion disease marker PrP^{Sc}. This is regarded as an unequivocal sign of prion disease even in the absence of experimental infection. Tests for CWD and other prion diseases rely on the demonstration of PrP^{Sc}.
- Prions are found in different variants that in experimental infections are excreted in different strains.
- Investigations have shown that the prion strains found in wild reindeer (*Rangifer tarandus*), moose (*Alces alces*) and red deer (*Cervus elaphus*) in Norway, are different from each other and different from the strains that has been found in North America.
- Prions transmit poorly or not at all between species, but CWD prions are transmitted between several species of the Cervidae.

2.2 CWD and other prion diseases

Background knowledge about prion diseases in animals is described in Appendix II. In the table below (2.2-1), we provide an overview of these prion diseases and their occurrence in Norway. Contagious (naturally transmitted) variants are marked with red letters. Classic scrapie in sheep and CWD in wild reindeer are the only naturally transmitted prion diseases that have been diagnosed in Norway. "Naturally transmitted" or "contagious" does in this context mean a disease where an infected animal shed infectious material in amounts sufficient to be infective for other animals, either through direct contact or through the environment.

There are, as previously stated (VKM, 2017), no vaccines available that protect against CWD. Recent publications indicate that vaccine development still is going on (Abdelaziz et al., 2017;

Abdelaziz et al., 2018; Taschuk et al., 2017). On-going research is also aiming to develop treatment options for prion disease (Abdelaziz et al., 2019). There is however, no reason to expect that we will see a breakthrough that will provide vaccines or treatment options for neither humans nor animals in the near future.

Table 2.2-1. Occurrence of prion diseases in Norway. Variants that are transmitted under natural conditions are marked with red letters

Species	Disease	Notes and occurrence
Humans	Sporadic CJD[1]	Stable incidence, 4-6 cases in Norway annually
	Variant CJD	Not recorded
	Familiar (inherited) CJD	Not recorded
	Iatrogen CJD	Not recorded
Sheep and goat	Scrapie	Last record in 2009
	Nor98/Atypical	Stable occurrence, 5-14 cases annually
Cattle	Mad cow disease (BSE)[2]	Not recorded
	Atypical L-strain	Not recorded
	Atypical H-strain	One case in 2015 in a 15-year-old cow
Reindeer	Chronic Wasting Disease (CWD)	Diagnosed in 20 wild reindeer
	Atypical CWD	Not recorded
Moose	CWD	Not recorded
	Atypical CWD	Eight cases, seven cows and one bull. Mean age 15 years for the cows
Red deer	CWD	Not recorded
	Atypical CWD	One case, 2017, 16 year old hind

[1]CJD is an acronym for Creutzfeldt-Jakob's disease

[2] Other species: Feline spongiform encephalopathy (FSE) that is caused by the BSE-prion was diagnosed in a domestic cat in Norway in 1994. The individual was probably infected from cat food produced in Great Britain.

Prion disease in mink (Transmissible mink encephalopathy, TME) has never been diagnosed in Norway and is not listed in the table. One case of atypical scrapie was diagnosed in goat in 2006. That a case is «diagnosed» imply that the test was performed with conventional and approved (EU and OIE) methods. We have not included testing by PMCA- or RT-QuIC-methods or experimental infection, which are more sensitive, but not are used for routine diagnostics.

2.3 Chronic Wasting Disease in the Nordic countries

A recent publication describing experimental infection in rodents (bank voles) showed that the prion variant found in Nordfjella is a strain different from those described in North America (Nonno et al., 2020). This study included prions from three moose (described in Pirisinu et al. (2018) and two wild reindeer from Norway (one of them described in Benestad et al. (2016)). Below we summarize the investigations necessary to compare prion strains, as well as the results of the prion isolation from Norwegian reindeer and moose.

Prions are categorized into strains depending on three levels of investigations. A fourth level of investigation is occasionally included.

Level I: Disease characteristics and occurrence in the primary host

- Species, distribution, incidence, age- and gender distribution among infected animals and their clinical signs of disease
- Genetic characterization of the *PRNP* (prion protein gene)
- Characterization of PrP^{Sc} aggregates in brain, brain stem and lymphoid organs and their distribution (lesion profile)
- PrP^{Sc} type: Fragmentation pattern of PrP^{Sc} in gel electrophoresis and Western blot.

Comment: These methods provide a foundation for differentiation between prion variants and prion diseases. Based on such investigations it was possible to conclude that the variant of CWD observed in wild reindeer from Nordfjella was distinctly different from CWD observed in moose in Norway. However, these methods did not enable differentiation between CWD in wild reindeer in Norway and CWD as it is observed in white-tailed and mule deer in North America.

Level II: Experimental infection in bank voles and transgenic mice

Prions can be studied in inoculation trials of bank voles (*Myodes glareolus*) and transgenic (genetically modified) mouse lines. Only after such experiments will scientists be able to categorize an isolate to a strain. The length of the incubation period at first, second and third passage of the pathogen is crucial. A passage is in this context a complete course of infection in an individual host. The researchers study how the prions change after having gone through more and more infection courses (passages). In addition to the detailed investigations described in level I, the prions' ability to cross-species transmission is tested. Such analyses have some limitations, as they not are performed in the primary host (reindeer), but are although important, especially with regard to evaluation of zoonotic risk (transmission to humans).

Comment: Level II investigations showed that there are differences between the CWD strain from Nordfjella and those found in North America. There was an obvious difference in incubation period in bank voles, where the voles inoculated with the Nordfjella isolate, lived much longer

before they developed disease compared to those inoculated with known isolates from North America. Of seven bank voles inoculated with material from Norwegian wild reindeer, only one got sick, and then after 776 days. In comparison, 38 of 40 bank voles inoculated with material from Norwegian moose got sick after 300-500 days. Expected incubation period at first passage of CWD in bank voles is between 150 and 350 days, based on experiences with North American CWD isolates. After the third passage in bank voles, the incubation period after inoculation with the CWD isolate from Norwegian wild reindeer stabilized on 105±9 days, while the corresponding periods 76±3 and 175±36 for the two Norwegian moose isolates. In comparison, an isolate from CWD in a Canadian moose stabilized on an incubation period on 32±2 days after three passages (Nonno et al., 2020). In addition, subtle differences were discovered between the two moose isolates. The interpretation of this is that there are two CWD strain in moose in Norway that cause the same or a similar disease.

Level III. Experimental infection in the primary host, closely related species and livestock grazing in the same areas

These investigations are important when we need to describe the pathogenesis and occurrence of the disease in the primary host (in the current case the wild reindeer). Animals with different genotypes of the *PRNP*-gene need to be inoculated, and both inoculations directly in the brain and through the gastrointestinal tract need to be performed. The latter is crucial to provide a realistic model of natural infection. Such experiments are time- and resource-consuming, but they provide essential information. It is the only way to get conclusive knowledge about the clinical signs of infection with the actual prion strain; for example how the disease develop in animals with different *PRNP*-genotypes, and how and in which amounts the pathogen is excreted from the host in the different phases of the disease.

See page 28 for further description of on-going inoculation trials in sheep.

Level IV. Experimental infections in primates

This kind of inoculation trials is only done in very few instances and only to elucidate which risk the prion strain constitute for humans. Such research is only performed after thorough ethical evaluation and justification and is not performed at Norwegian research institutions.

Defining a prion strain:

A prion strain is a prion isolate that after inoculation in genetically identical mice cause reproducible and characteristic signs of disease (incubation period length, PrP^{Sc} distribution, PrP^{Sc} type etc.). These properties of the prion isolate are relatively stable over time and through many passages. It is thought that these traits are "inherited" through subtle variations in the three-dimensional folding of the prion protein aggregates (Collinge and Clarke, 2007).

Diagnosing CWD in moose and red deer

Almost concomitantly with the outbreak of CWD in Nordfjella, CWD was discovered in moose in Norway. However, the characteristics of these cases diverged from what was previously observed in CWD in North America (Pirisinu et al., 2018).

In the examined moose, PrP^{Sc} were only observed within the brain, and the lesion profile (see above) diverged from the profile observed in diseased reindeer from Nordfjella and what was described in CWD in North America. In addition, the animals were old. In the eight cases found in Norway, the age varied between 12 and 20 years, with a mean of approximately 15 years. In January 2021 an adult moose bull was diagnosed with CWD, but this individual is not age determined yet. In addition to these cases, the same (a similar or identical) disease has been diagnosed in Sweden (four cases) and Finland (two cases). As in the majority of Norwegian cases, all these are old females.

Nonno and co-workers (2020) showed that the three examined moose from Norway had two different strains of pathogens, i.e. two of the moose had a similar strain, while the third had another one. The dispersed findings of moose with diagnosed CWD in the Nordic Countries indicate that this is a prion disease with a sporadic epidemiology, similar to the atypical variants in cattle (atypic BSE) and sheep (atypic scrapie) (Appendix II).

In 2017, we also found CWD in a 16-year-old red deer hind in Møre og Romsdal (Vikoren et al., 2019). Examination of this case showed that the lesion profile and the Western blot profile clearly was different from the findings in moose and wild reindeer. As in the moose, the prions were only found within the brain. Further investigations are needed to map the occurrence of this disease in Norway and elsewhere in Europe.

Conclusion:

During the last four years, CWD has been diagnosed in three different species of cervids in Norway, revealing four different prion strains that previously was unknown to science. In addition, CWD is diagnosed in moose in Sweden and Finland. In the table below, we summarize the characteristics of the prion diseases diagnosed in Norwegian cervids.

Table 2.3-1 Characteristics of prion diseases in Norwegian cervids

Species	Reindeer	Moose	Red deer[1]
Characteristics of contagious variants (reindeer)			
Several cases in the same herd/location	✓	✗	✗
Diagnosed in young animals	✓	✗	✗
Prions demonstrated outside the central nervous system	✓	✗	✗

Species	Reindeer	Moose	Red deer[1]
Characteristics of atypical variants (moose & red deer)			
Prions demonstrated only within the central nervous system	✗	✓	✓
Only adult, most often old animals	✗	✓	16 years of age
Dispersed solitary cases	✗	✓	-

1 There is currently currently only observed one case in red deer

2.4 Infection, incubation period and pathogenesis of CWD

Hoover et al. (2017) inoculated white-tailed deer (*Odocoileus virginianus*) with brain homogenate from CWD positive individuals of the same species. The inoculate was given as a spray to the nasal cavity and as a homogenate to the oral cavity. The animals were euthanized and necropsied after 24 and 72 hours, one, two, three, four and sixteen months. There were individuals with *PRNP*-genotypes associated with high, medium and low susceptibility to CWD infection (Wolfe et al., 2007).

The study shows that uptake of prions through the mouth and pharynx is the first step of an infection. Furthermore, the replication of the prions happens in lymphoid tissues, initially in those associated with mouth and pharynx, and subsequently in other parts of the body. The development was slower in individuals with lower genetic susceptibility but did follow a similar course.

At which dose CWD prions causes natural infection in cervids has been unknown, and if such a "minimum infective dose" can be reached through cumulative accumulation of small doses, or if the dose has to reach a certain threshold before an infection is established. Henderson et al. (2017) did a study where white-tailed deer were given either brain homogenate from moribund white-tailed deer with CWD, or saliva that contained a certain amount of prions. Among the experimental animals were individuals with *PRNP*-genotypes associated with high, medium and low susceptibility to CWD infection (see Chapter 2.8).

The study showed that minimum infective dose is less than previously assumed, but that it has to reach a certain threshold level. An amount of 300 ng (i.e., 0,0000003 g) brain or a corresponding amount of saliva, divided on three doses of 100 ng given over three weeks was sufficient to establish infection. The animals were not infected when the same dose was given in ten doses of 30 ng over twelve weeks. In this experiment, that probably mimic natural infection better than previous experiments, the length of the incubation period was two to three years.

The length of the incubation period can vary considerably and is influenced by multiple factors. In a study (Moore et al., 2016) where clinically healthy reindeer had either direct or indirect contact with reindeer inoculated with prions from white-tailed deer and mule deer (*Odocoileus hemionus*), were two out of four animals with direct contact only positive in lymphoid tissues

when they died/were euthanized after 30 to 57 months of exposure. Two out of two reindeer that were in indirect contact were still alive after 33 and 50 months of exposure, but these were also infected and positive in CNS. None of these animals showed clinical signs of CWD. A possible interpretation is that CWD can progress slowly when reindeer are naturally exposed to prions that originate from white-tailed deer and mule deer.

2.5 The ability of prions to persist in the environment

Evidence available from North America show that cervids can become infected without being in direct contact with infected animals, i.e. that they ingest or inhale infective material that is found in the environment (Mathiason et al., 2009; Miller et al., 2004). It has also been observed that sheep have acquired infection with scrapie prions from the environment many years after the last observation of disease in the area (Georgsson et al., 2006).

An important aspect of CWD is that prions persist in the environment and that susceptible animals can acquire infection therefrom. In the initial phases of an outbreak, transmission from animal to animal is regarded as most important, but after a while, indirect transmission via environmental contamination increases (Almberg et al., 2011). North American experts often express that it is the long-lasting environmental persistence that make mitigation of CWD so difficult when the disease prevalence first have reached a certain level within a population (Miller and Fischer, 2016).

A recent study indicate that repeated freezing/thawing lower the amount of detectable prions in faeces, while desiccation seem to have little effect (Tennant et al., 2020). Analyses of faeces collected from the ground in the same study emphasize that faeces from animals with CWD is a source of environmental contamination. The study also indicates that examination of faecal samples collected from the ground can provide information about the level of environmental contamination in areas with high prevalence.

Kuznetsova and co-workers (2018) have performed inoculation trials that show that high levels of humic acid, a natural constituent of organic substance in soil, cause loss of prion infectivity. In a recent paper (Kuznetsova et al., 2020) show that when prions are mixed and stored with soil over long time (under stable conditions with stable, low temperature) detection of the prions with Western blot becomes increasingly difficult. The amount of detectable prions diminished most in clay-rich soils typical for Canadian prairie, while the decrease was less pronounced in what the researchers characterize as sand-rich podsol soil collected in Scandinavia and soil types typical for the boreal and tundra areas of North America. However, when susceptible laboratory animals were inoculated with the different soil samples, no difference in infectivity was observed. The researchers' interpretation is that the prions probably get bound to the surface of soil particles (adsorbed) with strong affinity, and thereby become «invisible» with this method of analysis, but that the particle-prion-complexes anyway preserve their infectivity and pathogenicity.

This experiment show that it is challenging to interpret analyses of prions in environmental samples, at least when these are performed with immunoblot methods. These results cannot

necessarily be extrapolated to studies where other methods are utilized, for example RT-QuIC and PMCA (see chapter 2.9.2), but results from comparable studies performed with such methods are currently not available. The study also confirm previous knowledge about the binding of prions to soil particles, and the differences between soil types with regard to binding ability and character (VKM 2017 og 2018). This may suggest, as mentioned in previous VKM reports, that Scandinavian soils to a lesser degree bind prions, resulting in faster wash out of the prions from superficial to deeper soil layers where they are less accessible for animals. The on-going analyses of Norwegian soil samples can probably provide more knowledge about this (See descriptions about on-going research in chapter 2.9).

In a long-term experiment performed in Scotland, brain material containing BSE prions was buried in clay-rich and sand-rich soil (Somerville et al., 2019). The soil was exposed for natural weather, but the run-off was collected. The locality had much precipitation, both as rain and snow (10 – 260 mm/month) and ambient temperature was from -11 to 28°C, i.e. conditions similar to those in Norway. The study confirm that prions preserve their ability to infect and cause disease even after years in decomposing brain tissue. The study also showed that prions leach out of a carcass and can be found in the soil around and below it, and that small amounts of prions are found in run-off water from such an infected carcass.

2.6 Population dynamics and spread of CWD in North America

2.6.1 Hunting pressure and CWD in mule deer bucks

Miller et al. (2020a) studied the development of the CWD prevalence in mule deer in relation to number of sold hunting licenses, as an estimate of hunting pressure, in twelve areas in the northwestern part of Colorado in 2000-2018. These areas have had endemic CWD since 2002 and are managed in a similar manner. The hunting areas cover six populations of mule deer. Retropharyngeal lymph node samples from 19105 animals were tested.

The authors conclude that a sufficient hunting pressure can stabilize the CWD prevalence on a low level, especially if the prevalence is low in the first place. They show that the prevalence of CWD increases if the population proportion of older bucks increases. As discussed by the authors, they describe how a *decrease* in hunting pressure is associated with an *increase* in CWD prevalence, and not how an increase in hunting licenses could have caused a decrease in CWD prevalence. It is unknown why the prevalence of CWD decreases when a high proportion of old bucks are harvested.

2.6.2 CWD in farmed red deer in Quebec, Canada

Previous studies has shown that European red deer is susceptible to CWD (Schwabenlander et al., 2013). In 2020 CWD was diagnosed in red deer of European origin in a deer farm in Quebec, Canada (Gagnier et al., 2020). At the point of time when CWD was diagnosed, the disease had probably been present for a period of 1,5 years. Professional hunters culled CWD 534 white-tailed deer in the area closest to the farm to reduce population density and to provide samples

for testing (7,5 km buffer zone; 401 km^2 control area). In addition, 447 white-tailed deer and 21 moose were culled by hunters in a surveillance area and 2584 in an area outside the closest zone. No cases of CWD were discovered in wild cervids.

2.6.3 Management of CWD in Illinois, USA

The first cases of CWD were reported simultaneously from Illinois and Wisconsin (Manjerovic et al., 2014) and major efforts to combat CWD were initiated, including spatially targeted harvest (see VKM 2017, chapter 9.2.4 og 10.1.4). These measures were in action in the period 2003-2007, but were abandoned in Wisconsin due to heavy resistance. After leaving the spatially targeted harvest approach, an increase in CWD prevalence was observed in the relevant areas of Wisconsin. In Illinois, the active management was continued (Hedman et al., 2020), and analyses show that the strategy have been successful in keeping CWD prevalence on a low level over a long period.

2.6.4 «Mark, test and cull»

To explore the possibilities for targeted lowering of CWD prevalence in a population of mule deer in Colorado, USA, an experiment with so-called "test and cull" was performed (Wolfe et al., 2018). Mule deer in a limited area were immobilized, marked, sampled, and thereafter released. If the test indicated CWD, the individual animal was recaptured and culled. The study involved testing of 1251 tissue samples (from tonsils) from over 700 animals. The study period was about 4,5 years and the test and cull did result in a significant decrease of CWD prevalence in males. No difference was observed in females. The different result between the genders was explained by differences in sampling frequency. The authors point out that they, through changes in sampling procedure, perhaps could have reached a corresponding reduction of CWD prevalence also in females. It is, however, pointed out that the method is expensive and labour-intensive, and that it can cause increased stress load on animals that are subjected to repeated immobilizations.

2.6.5 Simulations of CWD dynamics

An overview of the various models to aid understanding of and to mangae CWD was published by (Escobar et al., 2020). Furthermore, agent-based modelling tools have been designed to estimate the probability of discovering CWD as well as the development of CWD prevalence in populations of white-tailed deer (Belsare et al., 2020a; Belsare et al., 2020b; Belsare and Stewart, 2020). These models show that the success of of mitigation is dependent on the phase of the CWD outbreak. In these studies, CWD outbreaks are divided in to a pre-establishment phase (< 1 % prevalence), a transition phase (1-3 % prevalence) and an endemic phase (≥ 3 % prevalence) (Belsare et al. 2021). Simulations indicate that introduction of CWD (through an infected animal) may not necessarily result in an outbreak. This is mainly achieved by removing infected animals before they have transmitted the infection to new individuals. However, when more than five individuals are infected, the situation will most likely develop into an outbreak,

since the probability of harvesting all infected animals through hunting then will be low (Belsare et al., 2021). In the initial phase of an outbreak, transmission will mainly occur directly between animals, while uptake from the environment become increasingly more important in the endemic phase (Almberg et al., 2011).
It is well documented that CWD is difficult to eradicate from a landscape once an endemic phase is reached, because of the environmental contamination, among other factors (Uehlinger et al., 2016). In the USA, most CWD outbreaks have been discovered in the transition phase, and eradication is no longer considered a feasible alternative (Belsare et al., 2020a; Belsare et al., 2020b).

2.6.6 Population impacts of CWD

Estimates indicate an annual decline of 10 % in populations of white-tailed deer (Edmunds et al., 2016) and 20 % in mule deer (DeVivo et al., 2017) in endemic areas with over 20 % prevalence in Wyoming. We are not aware of empirical data on the long-term population impact in USA and Canada, including how much reduction of hunting pressure can counteract the effects of CWD. There is uncertainty about how strongly CWD will affect the population dynamics in the Norwegian populations of cervids. The impact of CWD on the populations will rely on the relative balance between the basic reproduction ratio of the infection (also called basic reproduction number, R_0), how long the course of infection lasts (among other factors related to variation in the *PRNP*-gene), the rate of reproduction and other mortality in the population(s) (Mysterud and Edmunds, 2019). White-tailed deer and roe deer are regarded as having a very high reproduction potential, mule deer and moose an intermediary and reindeer and red deer a low reproduction potential. Consequently, at a given R_0 and length of infection course, the population impact of CWD should be expected to be stronger in reindeer. We are, however, not currently able to provide a valid estimate of population effects, since we do not know R_0 and length of infection course. It is, however, evident that a high prevalence of CWD will affect the populations particularly by reducing survival of adult females, and that this will lead to a reduced population gain to harvest and/or population reduction.

2.7 Epidemiology of CWD in wild reindeer in Nordfjella Zone 1

A tota lof 2424 wild reindeer from Nordfjella wild reindeer management area were tested for CWD from March 2016 to May 2018 (table 2.7-1). Among these, 13 males and 6 females were CWD positive, which imply a strong male preponderance (68,4 vs. 31,6 %) among the CWD positive animals, in spite of female majority in the population (Mysterud et al., 2019a). We refer to chapter 2.11.1 for a description of the methodological challenges of estimating prevalence (proportion of infected animals) based on the available samples of brain and lymph node tissue.

Pattern of infection

Based on the numbers presented in Table 2.7-1 we have calculated a demographic pattern of infection describing to which degree different age classes of males and females are infected

relative to what is expected based on the composition of the population. No calves and only one yearling (male) tested positive for CWD. Estimates provide a prevalence of 1.6 % (95 % credible interval, CrI: 1,4 %, 1,8 %) in adult males and 0,5 % (95 % CrI: 0,5 %, 0,7 %) in adult females (≥ 2 years of age) from the 10th of August 2017 to the 1st of May 2018 in Nordfjella Zone 1. These estimates are not adjusted for test sensitivity not being 100 %, implying that false negative test results can occur with the methods used to test for CWD (Chapter 2.11.1). If we adjust for test sensitivity, were 1,8 % (95 % CrI: 1,5, 2,6) of the adult males and 0,6 % (95 % CrI: 0,5 %, 0,9 %) of the adult females infected with CWD. Adult males had 2,7 (95 % CrI: 1,0, 7,2) times higher probability of acquiring a positive test result than adult females. Infected males were from 1,5 to 8,5 years of age. The probability of CWD infection increased with increasing age for adult males, and the proportion was 3,0 % for males that were above five years of age.

This striking demographic pattern of CWD infection in wild reindeer is something that can be actively utilized in the management, both for detection (Mysterud et al., 2020a) and for combatting disease. Such a mitigation approach is particularly relevant at low occurrence of CWD. Population management that allows a high proportion of adult males can cause an exponential growth of the prevalence (see chapter 2.6.1.1 - Miller et al., 2020). A similar demographic pattern of infection is described in white-tailed deer (Heisey et al., 2010; Samuel and Storm, 2016) and mule deer (Miller and Conner, 2005) in USA and Canada (Rees et al., 2012). It is common to observe 2-3 times higher prevalence in adult males compared to adult females in both these species. Even though the material from Nordfjella is small, the similarity with much larger data sets from different areas of USA and Canada provide evidence that warrant an expectation of a higher proportion of CWD infected males than females.

Data on the demographic pattern of CWD infection in wapiti/elk (*Cervus canadensis*) is more limited, but do not indicate any difference in CWD prevalence between the genders (Argue et al., 2007; Monello et al., 2014; Sargeant et al., 2011).

Routes of transmission

There are several documented routes of transmission for CWD between individual cervids (see previous VKM reports about CWD for a more thorough review). In lab experiments on muntjac (*Muntiacus reevesi*) intrauterine transmission was documented (Nalls et al., 2013), and seeding activity consistent with presence of prions has been found by PMCA in foetal tissues from infected dams (Selariu et al., 2015). In the eradicated herd of Nordfjella Zone 1, all the six infected females were three to four years old and consequently too young to be mothers for the majority of the infected males. The infected animals were also examined for genetic relationships, and the infected animals were not more closely related than expected by coincidence. There is hence no evidence supporting that transmission from mother to calf was an important route of transmission among wild reindeer in Nordfjella Zone 1 (Mysterud et al., 2019a).

Interpretations concerning routes of transmission

In early phases of a CWD epidemic with low prevalence, it is assumed that transmission mainly occur directly from animal to animal and not indirectly via the environment (Almberg et al., 2011). It is not well documented why males experience a two to three time's higher prevalence than females in several species of cervids, or why prevalence increases with age among males in Nordfjella.

h2.7- 1. Overview of all reindeer tested for CWD during the outbreak in Nordfjella Zone 1, 2016-18. In 2016 the registrations did not differentiate between Zone 1 and Zone 2, and the number hence include approximately 35 animals from Zone 2. In total, information about age class was missing in 68 and information about gender in 94 of the tested animals. (Mysterud et al., 2019).

Source	Gender	Age Class				
		Unknown	Calf	Yearling	Adult	Sum
Fallen stock 2016	Male				5	5
	Female			1	2	3
	Unknown	12				12
Hunting 2016	Male	1	40	13	97	151
	Female	2	36	20	117	175
	Unknown		4		3	7
Fallen stock	Male	1		1	35	37
2017	Female			1	1	2
	Unknown	2		4	2	8
Hunting 2017	Male	2	67	36	221	326
	Female		45	19	193	257
	Unknown	35	2	1	4	42
Fallen stock	Male		1		13	14
2017-18	Female			1	3	4
	Unknown	8	1			9
Eradication 2017-18	Male		133	100	319	552
	Female		157	122	560	839
	Unknown	5	6		5	16
Sum	Male	4	241	150	690	1085
	Female	2	238	164	876	1280
	Unknown	62	13	5	14	94
CWD-positives	Male			1	12	13
	Female				6	6

2.8 Genetic susceptibility, including *PRNP*-genetics in Norwegian cervid populations related to data from the outbreak in Nordfjella

Prion diseases are caused by a change in the three-dimensional folding of the prion protein. The gene that code for the prion protein is called *PRNP.* Variations in *PRNP* occur with different frequency in different species but may have a large impact on the occurrence and susceptibility

to CWD and other prion diseases (see appendix II for a description of *PRNP*-genetics and scrapie management in sheep). The text below is partially based on an article about this subject published in the magazine Villreinen by Michael A. Tranulis, Jørn Våge and Knut Røed, the 12th of June 2020).

Animals have two copies of genes, one from each of their parents. The gene copies are called alleles (or gene variants) and each pair can be either similar or different. An animal with two similar alleles is called *homozygote* for that gene, while an animal with two different alleles is called a *heterozygote.* If the alleles are called A and B, there are three possible combinations: AA, AB and BB. If A is associated with higher susceptibility to a pathogen than B, you can range the combinations like this with regard to susceptibility: AA = very susceptible, AB = susceptible, BB = less susceptible. To gain knowledge about this, you have to perform surveys of susceptibility under natural conditions or experimental infection trials.

2.8.1 Genetic susceptibility in Nordfjella

After the eradication of the wild reindeer population in Nordfjella Zone 1 in 2018, the variation in the *PRNP* gene of CWD test positive and test negative animals. The study (Güere et al., 2020) revealed 5 alleles/gene variants of *PRNP,* and 14 different combinations (genotypes) of these. The gene variants were named A, B, C, D and E. Variant C had never been described in reindeer before. Gene variant A was most common, and it is assumed that this is the wild type allele of the reindeer.

Among the CWD positive animals, 74 % had gene variants A and C in combination or double dose, while these genotypes were only found in 19 % in a demographically matched group of 101 test negative animals. This shows that animals with the gene combinations AA, AC and (probably) CC were most susceptible for the prion strain found in Nordfjella. The gene variant B was found in double dose in 12 % of the negative animals, but not in any of the positives. This indicates that the B allele is associated with lower susceptibility, though four positive animals had the gene variant combination AB and one positive case had the BC genotype.

All the positive cases in Nordfjella Zone 1 had one of these gene variant combinations: AA (53 %), AB (21 %), AC (21 %) or BC (5 %). In the CWD negative animals, these combinations were found in 51 %. With other words: Approximately half (49 %) of the wild reindeer in Nordfjella had gene variants that were not found among the positive cases. Such a skewed distribution show a genetic effect on the susceptibility of CWD, but the low number of animals, only 19 cases, leads to cautiousness in the interpretation of these findings. The results do although provide a background for a tentative ranking of susceptibility for CWD as follows: A and C gives increased susceptibility, while B, D and E variants are less susceptible than A and C. It can be mentioned that the C variant is found in 4,5 % of the negative animals and in 13 % of the infected ones, i.e. more than three times more frequently.

The examined wild reindeer from Nordfjella can consequently be grouped like this:

I. Very susceptible: AA, AC, CC (19 %)

II. Susceptible: AB, BC, AD, AE, CD, CE (53 %)
III. Less susceptible: BB, BD, BE, DD, DE, EE (28 %)

The ranking is tentative and rely on several assumptions, for example that the gene variants A and C cause increased susceptibility also when they are present in a single dose. That five positive cases exhibit this combination provide some support for such an assumption. The assumption that the D and E gene variants can cause reduced susceptibility has a weaker foundation. After detection of CWD on Hardangervidda, the examination of the reindeer bull showed that it had genotype AD.

2.8.2 Genetic susceptibility in other reindeer populations

By utilizing the same categories, we can compare the occurrence of *PRNP* gene variants in different populations of wild and semi-domesticated reindeer, and through that estimate the degree of susceptibility for a population.

An on-going survey (Güere and co-workers, unpublished), shows that all wild reindeer populations investigated so far have a large proportion of very susceptible or susceptible animals. The results also show that this proportion is smaller in semi-domesticated reindeer, and several will be grouped as less susceptible. This is valid for semi-domesticated reindeer both in South Norway and in Finnmark.

In a recently published study from Canada, the variation in *PRNP* in North American caribou (*R. tarandus* subsp.) was studied (Arifin et al., 2020). The study found that a variation (138N) that is assumed to have lower susceptibility for CWD had low prevalence in caribou populations that had relatively high risk of spatial overlap with infected cervid populations[1]. This probably constitute a risk for spread of CWD to caribou in the western part of North America. The gene variant 138N has never been found in Norwegian reindeer.

Chafin et al. (2020) show that the frequencies of *PRNP*-variants change with age in white-tailed deer. This indicates that some variants are selected in areas with endemic CWD, by disposing for higher survival rates. A previous study also showed selection on *PRNP* in wapiti (Monello et al., 2017)). The biological impact of such selection is probably minor, since we not yet know if any gene variants provide full protection against CWD.

2.8.3 The sheep and its potential role in pathogen transmission

The potential role of sheep in transmission is comprehensively reviewed in a previous VKM report (2018). Compared to Nordfjella, there is much less sheep on Hardangervidda south of the road

[1] Translator's note: Directly translated, the original text stated as follows: "The study found that a variation (138N) that is assumed to have low susceptibility to CWD, had low occurrence in populations of caribou that had overlapping area use with other, infected populations of cervids." The translator has modified this statement to be more in line with the text in Arifin et al., 2020.

Rv7. According to public registrations (Organisert beitebruk, NIBIO/Kilden) 25.540 ewes and lamb (and 757 goats) were released on pasture. The sheep density is hence relatively low (10 per km^2) within the defined pasture areas for sheep (about 3000 km^2). Large areas in the central part of Hardangervidda are however not registered as pasture areas belonging to any pasture cooperative, including the areas that are most frequently used by female reindeer (Kvenna – Songa).

2.8.4 Predators and CWD

The relationship between predation and occurrence of CWD is highly complicated. It has been shown that prion infected cervids in North-America experience a higher probability of predation (Edmunds et al., 2016; Krumm et al., 2010; Miller et al., 2008).

Predators and scavengers can theoretically also contribute to the geographical spread of CWD, either by having prions in their intestines or by transporting carcass remains from infected cervids (VKM, 2017). It has not been documented that spread ever has occurred in any of these ways.

Wild et al. (2011) established a mathematical model describing how predation by wolves would affect the occurrence of CWD in a closed population of American cervids (*Odocoileus* spp.). This study is commented in VKM 2017.

2.9 Current state in national and international research projects on CWD

2.9.1 Completed projects

- *CWD in wild reindeer in Nordfjella*. Collected samples from Nordfjella Zone 1 has enabled analyses of the demographic pattern of infection in wild reindeer in Nordfjella (Mysterud et al., 2019a), and how individuals with different genotypes (*PRNP*) has different probability for acquiring CWD infection (Güere et al., 2020). This is a co-operation between Norwegian Institute of Nature Research (NINA), the Norwegian Veterinary Institute (NVI), University of Oslo (UiO) and Norwegian University of Life Sciences (NMBU).
- *CWD in other cervids*. Analysis of collected material has led to detection of atypical CWD in moose (Pirisinu et al., 2018) and red deer (Vikøren et al., 2019). It has been called attention to how sporadic CWD should lead to changes in form of a more differentiated management of CWD in the EU (Mysterud et al., 2020a).
- *Development of methods for efficient surveillance*. Researchers from NINA, UiO and NVI have estimated the probability of discovering infection, given tissue samples that have currently been collected and the sensitivity of the tests applied (Viljugrein et al., 2019). Hunting strategies designed to increase the detection of CWD have also been developed (Mysterud et al., 2020a).

- *Describing the efforts of CWD management*. NINA has in collaboration with UiO described the practical challenges of taking out a large number of animals in Nordfjella Zone 1. (Mysterud and Rolandsen, 2018; Mysterud et al., 2019b). The same group has also quantified to which degree fences around Nordfjella Zone 1 functioned according to their purpose (Mysterud and Rolandsen, 2019). NINA has also estimated the populations of red deer and moose around Nordfjella to provide basic knowledge necessary to reduce the risk of CWD transmission ("spillover") between species (Solberg et al., 2019).
- *Impacts of CWD management efforts.* NINA and UiO have highlighted how fragmentation can be utilized to prevent the spread of CWD (Mysterud et al., 2020c). Furthermore, to which degree a ban on feeding of wild cervids actually would result in less feeding is described (Mysterud et al., 2019c). The side effects of measures have also been studied, including for example description of the movements of the wild reindeer during the eradication process in Nordfjella, and how this type of disturbance led to an increased risk of spread of CWD (Mysterud et al., 2019a).
- *Other factors that can promote spreading of CWD*. Hunters come into contact with cervids with CWD in a very different way than other parts of the population. NINA and UiO has analysed the pattern of settlement and movements of large game hunters to study the risk of spread, and the significance of preventive measures among hunters (Mysterud et al., 2020b).

2.9.2 Ongoing projects

- *Sheep and CWD: The research project «Reindeer CWD prion ecology: risk of dissemination by sheep».* A four-year project (supported by the Norwegian Research Council) aiming to investigate if sheep are susceptible to the prions that infected the wild reindeer in Nordfjella. NMBU and NVI conduct an experimental inoculation of sheep, both per orally and directly to the brain. A work package in this project is led from NINA, analysing spatial overlap between sheep and wild reindeer on salt licks.
- *How is spontaneous prion disease initiated – can the cervids provide the answer?* This is a cooperative project between NMBU, NVI and Oslo University Hospital, Rikshospitalet studying age-related changes in the brain of moose with a focus on old individuals, where the risk of CWD is highest. The project will also include analyses of CWD positive brain tissue for comparison.
- *«The red deer in Nordfjella»* is led by UiO and Norwegian Institute for Bioeconomy (NIBIO), in cooperation with NINA, and is funded by the Environment Agency. This project is performing a survey of the habitat use of red deer in the areas around Nordfjella and effects of management measures aimed on deer. In phase 1 (2017-2019) was 30 red deer marked with GPS collars. In phase 2 (2020-2021) marking of further 20 red deer is planned. It is studied to which degree feeding still causes aggregation of red deer in Lærdal (Skjelbostad, 2020).
- «Population estimates of red deer and moose as a basis for CWD detection» (2019-2021) is led by NINA in cooperation with UiO and NVI and is funded by the Environment

Agency. The aim of the project is to develop methods for estimation of numbers of red deer and moose in the municipalities, divided on age group (calves, yearling, adults) and gender, to enable estimation of probability of CWD detection and other management purposes.

- «Moose in Trøndelag» is led by NINA and funded by the Environment Agency. The project's aim is to study the moose population in the areas of Trøndelag where atypical CWD was diagnosed in three moose cows. The project will follow a group of GPS collared individuals belonging to different gender and age groups in a period of ten years from the project initiation in 2017. So far has 76 moose been marked. NINA co-operates with among others NVI about sampling. In 2017 and 2018, for example, rectal biopsies were collected. Data will also be used in the on-going collaboration between NINA and UiO on subjects related to CWD. Themes that will be researched are among others seasonal migrations of moose bulls and cows, how stable their use of home ranges is dispersion of young animals, calf production and mortality of calves and adults apart from hunting. Other investigations will also be included in the project, as analyses of genetic kinship among marked and unmarked moose, including the CWD positive moose.
- «Demography among fallen stock of moose and red deer» is led by NINA and performed in cooperation with UiO and NVI as a part of the Surveillance program for CWD. This part of the surveillance program, funded by the Environment Agency, was started in 2020. It is based on a cooperation between hunters and about 40 municipalities that submit mandibles from fallen stock and animals felled during ordinary hunting. The age distribution among fallen stock is presumed to be significantly different from the age distribution among cervids shot during hunting. Better knowledge of the age distribution will enable us to say more about the relationship between occurrence of atypical CWD and age. Data on the age of fallen stock and hunted animals will also contribute to better estimates of the probability of freedom from CWD for different cervid populations.
- «Salt licks as transmission hot spots for CWD and gastrointestinal nematodes» («The Salt Lick Project») is based on collection of soil- and vegetation samples and camera traps from selected salt licks in Nordfjella, Knutshø and Forolhogna, and collection of faecal samples and tissue samples from wild reindeer, red deer, moose and sheep in the same areas. The project is funded by the Environment Agency and lead by NINA. The aim is to elucidate how permanent salt licks can have an impact on the parasite fauna and the area use of wild reindeer, to describe the occurrence of prions and parasites in soil on salt licks and to describe the properties of the soil in Norwegian mountains and how these properties can affect persistence and spread of prions.

  The sample collection started in 2017 and is still going on. Analyses of soil samples show that parasites are much more abundant on the salt lick than outside. This indicates that the salt licks are important hot spots for infection with pathogens with a faecal-oral route of transmission. The results can be extrapolated, to some extent, to the epidemiology of CWD, which also has a faecal-oral transmission.

A research group at the University of Alberta use PMCA to analyse the soil and vegetation samples from Nordfjella for prions. Answers on the first round of these analyses is expected in the spring of 2021.

As a part of the project, analyses of soil characteristics and analyses of mineral levels in livers from wild reindeer in the three regions is performed. The data from these investigations is still under analysis, but it is clear that the soil in the salt licks is profoundly changed compared with undisturbed soil from the same areas. Among other things, the level of many minerals (iodine, manganese, copper, zinc) is increased, and the pH levels is much higher than normal. The soil samples are dominated by sand and organic material and contain only small proportions of clay. In Nordfjella, however, there are salt lick soils with a clay content close to 12 % of the mineral fraction. These investigations will provide background for considering if establishment of salt licks has created a soil environment that facilitates transmission of prions.

It is also evident that the amount of plant nutrients like phosphate, nitrate, ammonium and sulphate is increased in the soil of the salt licks. This will probably cause increased growth and nutritional content of the plants on the salt licks, even after cessation of use, so that ruminants will be attracted to the sites for many years.

Analyses of mineral levels in the liver of wild reindeer has not revealed any obvious insufficiencies or intoxications.

Analyses of camera trap images taken on the salt licks has shown how the cervids use the spot, and it is documented that they ingest or lick on soil. Analyses of how the salt licks affect wild reindeer area use are still pending.

- «Inoculation studies with Norwegian CWD isolates»: Isolates from Norwegian cervids with confirmed CWD has been performed in various bioassays, including inoculations on transgenic mice and bank voles. The different models represent individual species, meaning that the mice through gene modification have the ability to produce cellular prion protein (PrP^C) from the species we want to study pathogenesis in (for example sheep, cattle, humans or cervids). In contrast, bank vole inoculation is a model that not is manipulated genetically, and the voles only produce their own species-specific prion protein.
  Such inoculation studies are time-consuming. The results are published continuously, and studies in bank voles (Nonno et al., 2020) demonstrated three hitherto unknown CWD strains, two in moose and one in wild reindeer in Norway. NVI cooperates with laboratories both in Europe and North America in these studies.
  Strains from prions isolated from Norwegian cervids have not previously been characterized in bioassays. It is hence important to use these tools to explore the risk of spillover from one species to another, i.e. the possibility that they can cause disease in other species, including humans. Inoculation of cervids has so far not been possible but is under review.

- «Diagnostics, development of methods and establishment of a CWD test for use on live cervids»: By virtue of being the national reference laboratory for prion diseases in animals and the OiE reference laboratory for CWD, is NVI continuously doing research to improve diagnostic methodology. In addition to the tests used routinely to detect prions in the brain and in lymph nodes, are new, very sensitive techniques established: RT-QuIC and PMCA. These are utilized in several of the cooperative projects where Norwegian research groups investigate CWD. They will in addition be important for detection in live animals, and the project is establishing a protocol for such testing.

- «Examine the occurrence of CWD prions in peripheral tissues of Norwegian cervids with confirmed CWD by help of the very sensitive detection methods RT-QuIC and PMCA. » This is a project that starts up in 2021 (Funding: Reindriftens utviklingsfond): RT-QuIC and PMCA are molecular biological techniques that enable detection of minute amounts of prions. Easily explained, the methods are based on breaking up the aggregates of misfolded proteins (by "quaking", i.e., shaking, or ultrasound) and adding PrP^{C}. If a sample contain aggregates, i.e., prions, will the process cause PrP^{C} to become misfolded into PrP^{Sc}. By measuring how much PrP^{Sc} that is formed, one gets a quantitative measurement of how much prions the sample contained. The techniques are not yet validated for use as diagnostic tools for detection for CWD but are used in research. NVI leads this two-year project and cooperates with three groups in Italy: Besta Institute Milan, ISS Roma and Laboratory of prion biology, Trieste. The aim is to reveal the tissue distribution of the different prion strains. Knowledge from this study is important for the understanding of the pathogenesis of CWD. It is furthermore important to establish if these tests are able to detect small amounts of prions in peripheral tissues, like muscle. The ability of CWD prions to cause disease in humans (zoonotic potential) is yet unknown and it is important to get knowledge about possible sources for exposure.

2.10 Prevalence estimates for the wild reindeer population on Hardangervidda

It is possible to estimate the proportion of infected animals in a population as "number of animals with infection/total number of tested animals", a so-called test prevalence. It is then assumed that the tested animals constitute a representative sample of the population. This is demanding in real life. First, you need to estimate the number of animals in the total population, you only test a sample of animals (mainly the hunting bag), and different categories have different probability for infection. In addition, different tissue types have been tested (lymph nodes/brain tissue) where there is variable probability for detection through the course of the disease.

NVI has, in co-operation with NINA and UiO, developed a model tool for estimation of prevalence (Ch. 2.10.1).

2.10.1 Methods for estimation of CWD in wild reindeer populations

In principle, the models are supposed to elucidate two conditions: 1) Uncertainty related to total population size, and 2) uncertainty related to detection of CWD based on the samples and tests that are available.

1) Population estimation model. This model estimates how many individuals there are in each demographic category (i.e. calves, yearlings and adults of each gender) of a wild reindeer population (Nilsen and Strand, 2018). The model collates typical surveillance date of wild reindeer as 1) winter surveys of total number of reindeer, 2) calf surveys performed in summer (calf per female adult and yearling), 3) hunting statistics, and 4) structural surveys after hunting, i.e. composition with regard to age and gender in the period where the herds gather during the mating season.

2) Probability model for detection of infection. This model estimate the probability for detection of CWD prions in a given individual based on which tissue that is tested and test regime (Viljugrein et al., 2019). As the tests do not have 100 % sensitivity, not all infected animals are detected. The kind of antigen tests[2] (TeSeE SAP ELISA-test from Bio-Rad) that are used, have a so-called analytical test sensitivity of 92,5 % (81,8 – 97,9) for brain tissue (obex, a part of the brainstem) and 98,8 % (93,5 – 99,97) for lymph nodes (Hibler et al., 2003). These numbers describe how often a positive CWD sample actually is diagnosed as a positive and not as a false negative sample.

The performed testing is assumed to have close to 100 % specificity, meaning that false positive tests are very rare. The specificity is furthermore ensured by a procedure where positive tests need to be validated by another analysis (Western blot is most commonly used) before the sample is confirmed as positive (Hazard et al., 2018). Some of the brain samples have «low quality» due to advanced[3] decomposition (rotting). In samples from the brain, the prions are first found in the brain stem (obex). It is, however, challenging to decide if such partially decomposed samples originate from other parts of the brain, where the probability for detection of infection is lower (lower sensitivity). The model therefore includes an uncertainty for animals in the early phase of infection, where only brain samples including obex will contain prions.

The model does hence take into account the development of the infection in the animal and when PrP^{Sc} can be expected to be detected in lymph nodes and brain tissue. This implies that the test sensitivity does not increase linearly with time since infection, as the increase of PrP^{Sc} starts

[2] Translator's note: The original text used the term "antistofftester", which translates to "antibody tests", but since the ELISA test detects PrP^{Sc} *antigens* in the sample by the help of specific antibodies, "antigen test" is a more correct term.

[3] Translator's note: The original text used the term "begynnende" which translates to "beginning", but recognition of tissue structures is not a major problem before the decomposition is "advanced".

before the increase in brain tissue, from zero up to analytical test detectability[4] (as shown in Figure 2.10.1-1 from Viljugrein et al., 2019).

It is possible to estimate prevalence of infection based on observations, but that will not take into account that the test sensitivitiy are not 100 %. To include this, assumptions must be made about the course of disease from the initial infection until death, since the sensitivity of different tissues will change as the disease progresses. In the estimations it is assumed that period of disease from infection to death is 2-3 years. This assumption is based on knowledge about the development of CWD in other cervid species, and from inoculation trials performed on semi-domesticated reindeer in Canada with *PRNP*-genotypes similar to wild reindeer in Langfjella in Norway. CWD has an incubation period of 1,5-2,5 years in mule deer (Fox et al., 2006) and 2-5 years in wapiti, depending on variation in the gene coding for prion protein (*PRNP*) (Moore et al., 2018).

Two CWD inoculation trials have been performed on reindeer with different *PRNP* variants (Mitchell et al., 2012; Moore et al., 2016). We do currently not have reliable knowledge about the length of the incubation period for animals infected with prions in Norway. The youngest animals in which PrP^{Sc} was detected in Nordfjella were a 1,5-year-old male with positive lymph node and a 2,5-year-old male with positive brain tissue and lymph node. This foundation indicate that an incubation period of 2-3 years is a reasonable assumption.

We do not know where in the course of infection an infected individual is, but we can provide an expected distribution of the test sensitivity for a given sample from an infected individual by repeatedly (for example 1000) drawing a random point of time in the course of infection. This can also be done on a population level. For the prevalence estimation, we made a probability distribution of mean test sensitivity. This was done by drawing 30 individuals 1000 times with a random distribution along the course of infection (1 month after infection to clinically ill/dead; H. Viljugrein, unpublished data). Based on this, the test sensitivities for lymph node and brain samples were estimated to a mean of 81 % (standard deviation 5,4) for samples consisting of both lymph node and brain tissue and to a mean of 56 % (standard deviation 7,3) for samples from brain tissue alone.

[4] Translator's note: The original text used the term "analytisk testsensitivitet" that translates to "analytical test sensitivity", while "analytical test detectability" seem to be closer to Viljugrein et al., 2018

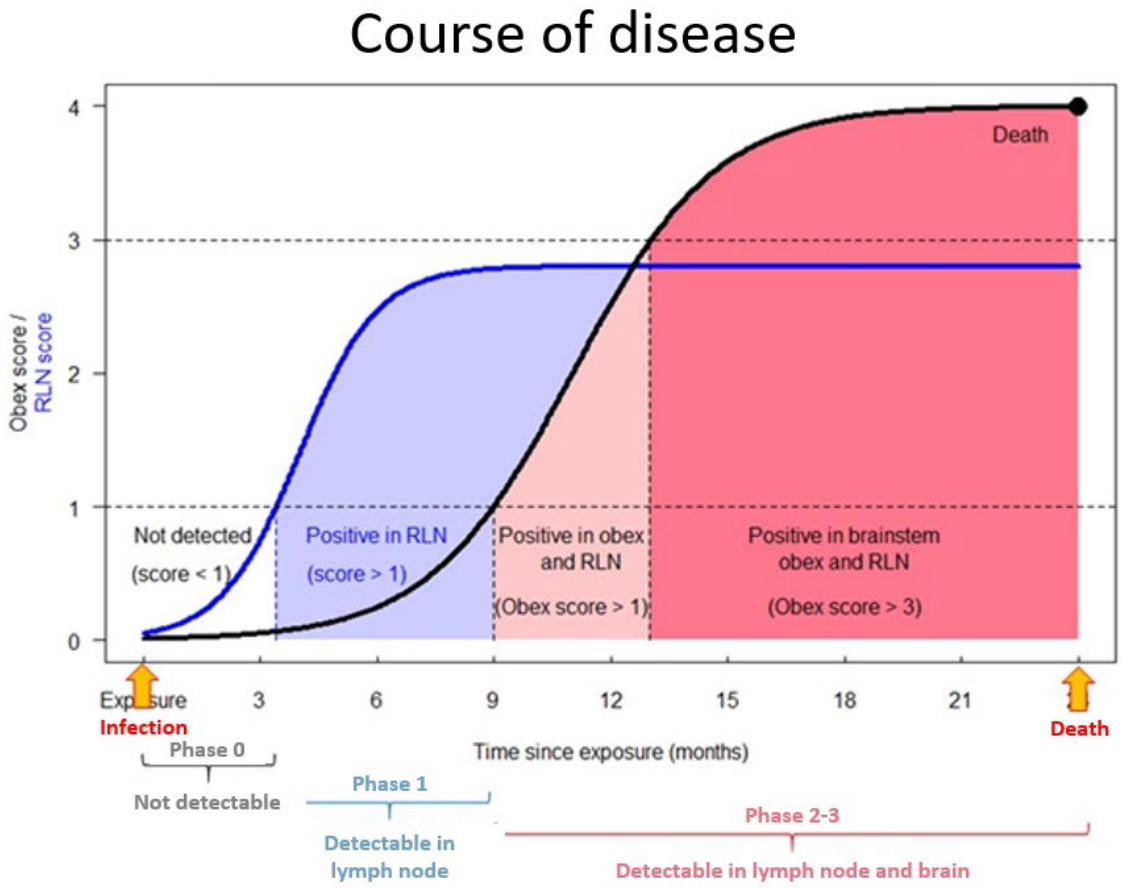

Figure 2.10.1-1 Model for the association between time since infection and detectability[4] in lymph nodes (RLN) and brain tissue (obex)

3) Estimation of prevalence. Data used for population size and test sensitivity are included as random distributions specified with estimated mean and standard deviation, i.e. we introduce an uncertainty in population size and test sensitivity (from point 1 and 2 above). NVI is now using a variant of the prevalence estimation method presented in Viljugrein et al. (2019) og Mysterud et al. (2019a).

«True» prevalence (prevalence taking test sensitivity into account) is constructed as a state-space model (same approach as for the population size estimation model), where an unknown number of infected individuals is specified as a function of test sensitivity and number of individuals with positive tests. The number of individuals with positive test is provided as a hypergeometric model around the number of individuals that are in a phase of the disease course where it is possible to detect infection by testing (discerns between lymph nodes and brain). Number of infected individuals can be estimated in total and for gender and age categories separately. The model is estimated in a so-called learning based (Bayesian) analysis by help of the modeller language jags in the R-package rjacs in the analysis program R.

2.10.2 Prevalence estimates and estimated numbers of CWD infected reindeer on Hardangervidda

Based on the population numbers and the disease detection model (Ch. 2.10), prevalence can be estimated based on available data (Tabell 2.10.2-1).

Notably, in an early phase of an outbreak, random events can have a large influence on the demographic pattern, i.e. that it is uncertain if more males than females are infected. At such low prevalence, one cannot without reservations presume that there are 2-3 times as high proportion of infected individuals among males as among females, as was observed in Nordfjella (Ch. 2.7), even though it is a clear expectation as the prevalence increases.

Before the hunting in 2020 was the population estimated to 9250 [95 % interval: 8800, 9770] reindeer on Hardangervidda based on surveillance data from NINA, including 3850 adult females [3750, 4000] and 1650 [1570, 1800] adult males (Figure 2.10.2-1). The population estimates will be updated and change slightly when new data (calf surveys, structural survey after hunting and minimum survey winter) are included in the model. The population estimates have relatively greater impact the smaller the population is in relation to how many animals that are tested. Uncertainty in the estimation of number of animals in the population can contribute to relatively large uncertainty about estimated number of infected animals based on an estimated prevalence.

Initially, the estimations are only based on data from males that were tested the last two years, since most of the samples originate from males (Table 2.3.2-1). Prevalence is then estimated for 2019, and the result used as prior distribution for the estimate for 2020. The prevalence estimate for 2020 is dependent on how much the prevalence of is weighted into the update of the model for 2020. To put more weight on the samples tested in 2020 compared with that tested previously, we increase the variation of the prior. We calculate the prevalence without taking into account the test sensitivity that is different between animals that are tested with material from brain only versus those tested with brain and lymph node separately. In addition, by taking into account the test sensitivity (mean +/- standard deviation), a "true" combined prevalence is estimated. Having only one positive male, this provide us with a CWD prevalence of 0,20 % among adult males on Hardangervidda. For comparison, in Nordfjella were 1,8 % of the males infected (Ch. 2.7). Note that the model estimates prevalence for the population before hunting in 2020 (Table 2.10.2-3), i.e. including the CWD positive male. Consequently, this provides us with a 95 % probability for 0-10 infected adult males on Hardangervidda, where the most probable number is 1-2 infected males (Table 2.10.2-2).

If there are infected adult females and yearlings on Hardangervidda, these will be added to the estimated males. Based on the number of adult females that was tested in 2020 (Table 2.10.2-1), it is expected that we with 95 % certainty would discover at least one infected individual if the prevalence among females was 0,6 % and the test sensitivity 80 %. It is consequently expected that the prevalence at least is below 0,6 % for adult females. Based on a presumption that adult females has half the probability and yearlings a quarter of the probability of being infected as adult males, it is estimated that there are in total 1-19 remaining CWD infected reindeer on Hardangervidda.

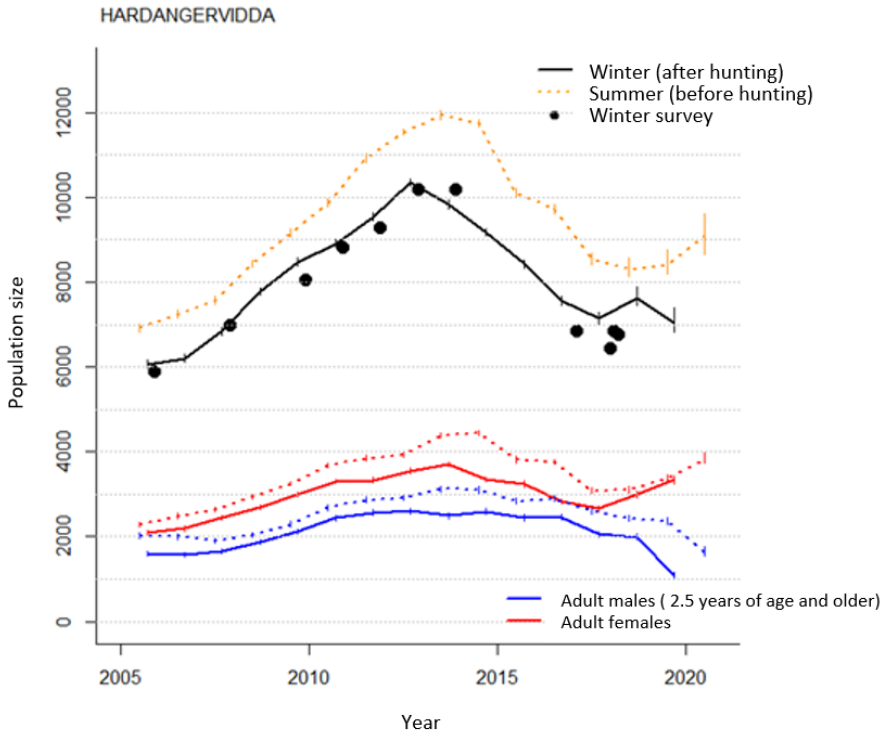

Figure 2.10.2-1 Estimated population numbers for wild reindeer on Hardangervidda based on surveillance data from NINA for the period 2000-2019.

Table 2.10.2-1. Number of animals tested for CWD on Hardangervidda in 2019-2020. In total, above 4000 animals have been tested (Data collected per 01.12.2020. Animals that are recognized as belonging to the Nordfjella population but shot on hunting licenses for Hardangervidda have been removed[5]. Some animals belonging to Hardangervidda but registered on neighbouring municipalities have been added. Further adjustments due to erroneous registrations of animals on other districts may occur.)

Year	Calves	Year-lings	Adult female	Adult male	Un-known	Sum	Proportion with lymph node sample
2016	70	23	24	17	269	403	88 %
2017	6	110	205	294	325	940	9 %
2018	8	47	98	361	44	558	73 %
2019	3	12	17	783	381	1091	78 %
2020	13	95	262	422	358	1115	75 %
Sum/mean	100	287	606	1877	638	4247	

[5] Translator's note: The areas north of the highway RV7 do administratively belong to Hardangervidda reindeer area, but are normally not used by reindeer belonging to the Hardangervidda population, but rather animals that belong to the reindeer herd of Nordfjella Zone 2. Consequently, reindeer shot in this area has been removed from the harvest numbers used in the estimates.

Higher proportion of lymph node samples in 2016 than in 2017 is caused by laboratory sampling of reindeer killed by lightening.

Table 2.10.2-2 Estimated prevalence among adult males on Hardangervidda in the fall of 2020 (H. Viljugrein, unpublished data). «True» prevalence, in contrast to CWD prevalence in lymph node and brain tissue, take into the account that infection is not detectable in the early phase of the disease (test sensitivity is not 100 % (see model for detection of disease)).

	Mean	**Median**	**0,025 % lower limit[1]**	**0,975 % upper limit[1]**
	Adult males:			
CWD prevalence lymph node	0,16 %	0,11 %	0,04 %	0,53 %
CWD prevalence brain tissue	0,11 %	0,08 %	0,03 %	0,37 %
«True» prevalence adult males	0,20 %	0,13 %	0,06 %	0,66 %
Number of infected adult males	3,3	2	1	11
	All categories of reindeer included:			
«True» prevalence totally, by use of prior[2]	0,09	0,06	0,03	0,30
Total number of infected animals (by use of prior in relation to prevalence in adult males)	5,9	4	2	20

[1] In a 95 % credibility interval.

[2] This means that a precondition (prior) is included that presume that the prevalence in adult females is half and the prevalence in yearlings is a quarter of the prevalence in adult males. This presumption is not necessarily correct at this low prevalence (see main text).

2.11 Probability of freedom from disease in population of cervids

We have partly used the same tools as in the estimation of prevalence (Ch. 2.10) to estimate probability of freedom from CWD, i.e. the population estimation model and the probability model for detection of infection that are on an *individual* level. In addition, a model have been developed to statistically estimate the probability of freedom from CWD infection in a (Mysterud et al., 2020a; Viljugrein et al., 2019). This methods builds on an approach called «Stochastic scenario tree models», that is used in cases where information from testing of different samples is compiled (Martin et al., 2007). It is presumed that the demographic pattern of infection is

similar to Nordfjella Zone 1, i.e. three times larger probability for CWD infection in an adult male compared to an adult female, and half the probability for a yearling compared with an adult female.

2.11.1 Methods to estimate probability of freedom from CWD

To document freedom from CWD in a population is in general much more demanding than to estimate the proportion of infected animals when this has been detected (Ch. 2.10). It is not possible to reach 100 % certainty for absence of infected animals in a population of wild cervids. The reason is that not all animals in the population will be tested and that some animals will be in the early phases of disease, where the probability of detection is lower with the diagnostic tests currently used (Ch. 2.10). It is only possible to estimate the probability of freedom from CWD *at a given level,* which in veterinary epidemiology is called "design prevalence" (Cannon, 2002).

The prevalence you want to detect can for example be set to 1 % infected animals in a population or ten infected individuals in a population. In areas surrounding Nordfjella Zone 1, the design prevalence has been assigned to an absolute number of infected individuals in a population (Viljugrein et al., 2019; Mysterud et al., 2020).

The level is selected based on knowledge of epidemiology and an assessment about which risk that is acceptable, by not detecting infected individuals below this prevalence level. The model use «learning-based» statistics (Bayesian models). As more reindeer are tested and no infected animals detected, will the probability for freedom from CWD in the population increase. Initially, a presumption is made about the probability for the population being infected or not, based on knowledge of the geographical proximity to infected population, among other factors. In situation where no such specific knowledge is available, it is common practice to choose a probability of 50 %, i.e., that the probability of presence is equal to the probability of freedom from infection.

Consequently, the probability for *freedom* from infection in Nordfjella Zone 1/Raudafjell initially (for 2015) was assigned to 50 %. With other words, it was regarded as equally probable that the population was *free* as *not free* from CWD. Now, with CWD detected on Hardangervidda, is it natural to presume that the probability of infection in Zone 1/Raudafjell was larger already in 2015. The probability of freedom from CWD, still in 2015, is consequently adjusted to a lower level, from 50 % to 25 %. The probability of freedom on 25 % is then not a calculated estimate. It is a number which, based on an assessment, is assigned to a lower level now that we know that CWD is found also south of Zone 2, and that the case on Hardangervidda is presumed to be associated with the outbreak in Nordfjella Zone 1. The choice indicate that it is presumed that the probability of freedom from CWD is lower than the 50 % chosen previously.

When testing is continued over several years, there is a danger for introduction of infection as time goes by. In these estimations, the *probability of introduction of CWD* is set at a relatively high level for the period before the population in Nordfjella Zone 1 was eradicated (May 2018). After the eradication of the population, and thereby the source of infection, is this probability

lower (from the hunting period of 2018). If the danger for introduction of CWD is high from a year to another, as it will be if an outbreak is allowed to evolve unhindered on Hardangervidda, will it in principle never be possible to reach a high probability of freedom in neighbour populations. The probability of introduction over years of testing is so far not adjusted to a higher level after the detection of CWD on Hardangervidda. As no real data is available that can provide estimates for this probability, it is necessary to evaluate if this probability has to be changed along the road. The estimates for probability of freedom from CWD can consequently change with time, based on increased knowledge and data.

2.11.2 Probability of freedom from CWD in Nordfjella Zone 2/Raudafjell

Nordfjella Zone 2 and Raudafjell are two different management areas for wild reindeer. The exchange of animals, in particular adult males, is so large that estimation is performed for the two areas together. The infection level we want to detect (the design prevalence) is set to four infected animals (increased from two in 2016 to four in 2020). Based on this model, we estimate that the probability of having fewer than four CWD infected animals in Nordfjella Zone 2/Raudafjell after the hunting season of 2020 is 82 % (95 % percentile interval: 79 %, 84 %).

That the probability of freedom from CWD is lower than previously presented estimates, is due to the adjustment of the presumed probability of freedom from CWD in 2015 from 50 % to 25 % after the detection of CWD on Hardangervidda (see the discussion above, Ch. 2.11.1).

Samples were collected from 84 animals during the hunting in 2020: 10 yearling, 35 adult females, 30 adult males and 9 calves/animals with unknown age. The proportion of individuals where the lymph node was examined was 89 %. Estimated population before hunting in 2020 was 600 (95 % credible interval, CrI: 570, 642), including 250 (95 % CrI: 235, 264) adult females and 120 (95 % CrI 114, 132) adult males.

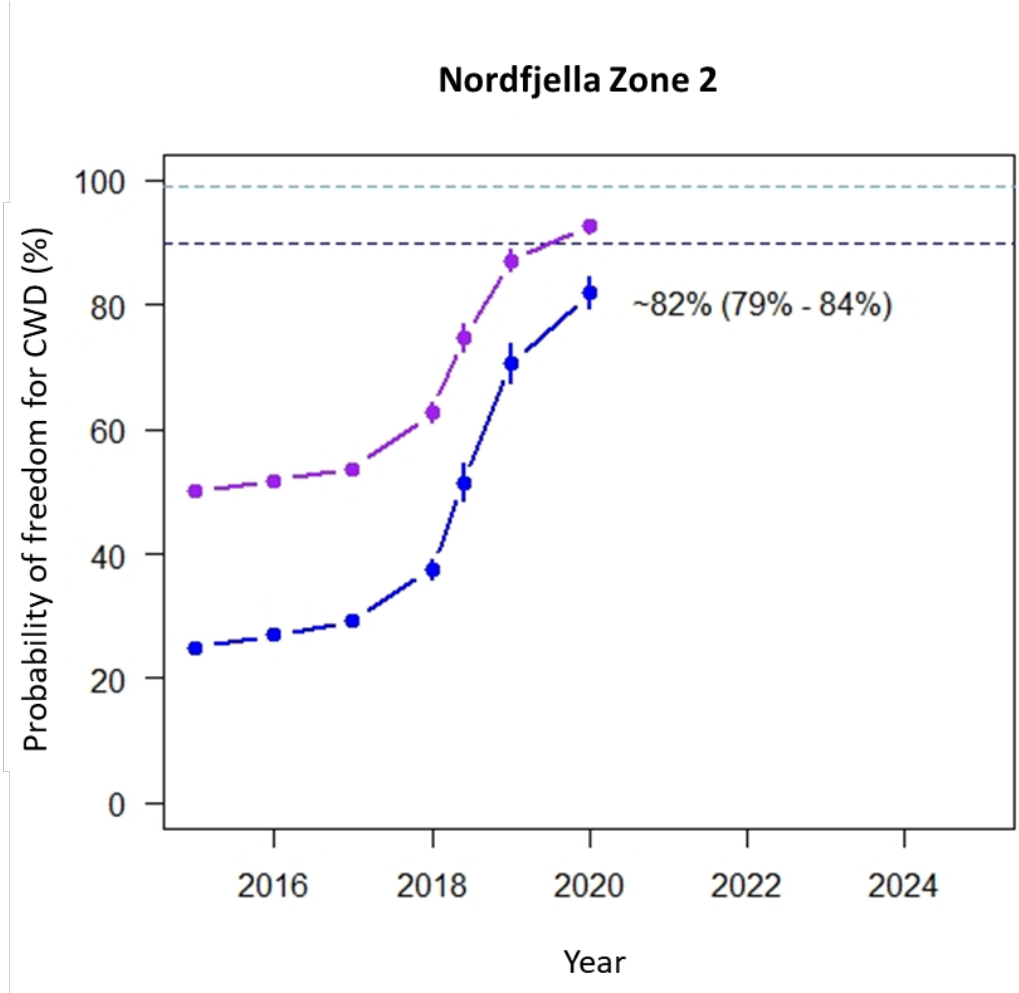

Figure 2.7.2-1. Estimated probability of freedom from CWD in Nordfjella Zone 2/Raudafjell as more reindeer are tested and no infection detected. It is currently a probability of 82 % that there is fewer than four CWD infected animals, provided an initial probability of freedom on 25 %. The lilac curve shows the development when this probability was assigned to 50 % in 2015. The probability was adjusted to 25 % (blue curve) after detection of CWD on Hardangervidda.

2.11.3 Probability of freedom from CWD in Filefjell

NVI leads the development of an in-house method for estimation of probability of freedom from CWD in populations of semi-domesticated reindeer (Viljugrein et al., 2021). The Norwegian Food Authority has required the same level of detection of disease in Filefjell as in Nordfjella Zone 2, i.e. the design prevalence is set with an aim of detecting from two (from 2016), three (from (2018) to four (from 2020) infected animals. The same model for disease detection is used in both cases, but there are certain differences in the calculations and the adaption to modern reindeer husbandry. Filefjell has currently only a few adult males in the population, and the opportunities for observation of animals with clinical signs of disease are much better, especially in the period around slaughter. The animals are when chased into a corral, and animals with deviating characteristics or behaviour are taken out and slaughtered. Observations from North America indicate that animals with CWD often die in situations with increased (Williams, 2005).

This may have been the case when the disease was detected in Nordfjella, as the animal was stressed when its herd was followed by a helicopter (Benestad et al., 2016).

The herders of Filefjell reinlag slaughter adult females when they have reached an age of ten years. In addition, females will be slaughtered at ages between from the age of two to nine years if they show signs of disease, including poor body condition, bad coat, ugly antlers, lameness, deviating behaviour, have wounds/inflammation, bad teeth or look unhealthy (information from Asgrim Opdal, Filefjell reinlag). The disease detection model for semi-domesticated reindeer takes into account that adult females in the group with deviations may have a higher probability of infection compared with females in the group without (Viljugrein et al., 2021).

Based on knowledge from North America we know that CWD is characterized by a long incubation period and a relatively short period of one to four months of distinct clinical signs of disease before death ensues (Johnson et al., 2011).

When a disease course of two to three years is presumed, the probability of an infected female being selected to the group female with deviations (and thereby is slaughtered and tested) instead of being left in the group of females without deviations (and not get tested). Given that there is an infected female in the age group, we can estimate a relative risk for infection in a random animal the group with deviations compared to a random animal in the group without deviations. There is no exact knowledge about the length of the incubation period in relation to the length of the period with clinical signs in wild reindeer infected with species-specific prion strains. Furthermore, individuals with different variants of the prion protein gene (*PRNP*) are expected to have different length on both the incubation period and the period with clinical signs of disease (Johnson et al., 2011). The model hence includes potential variation in the length of the period with clinical signs and simulates how different variations in the length of the incubation period relative to the length of the period with clinical signs, can have an impact on the surveillance.

Animals that are taken out as clinically suspicious, i.e., showing deviations, outside the slaughter period are given a higher weight than animals that are selected as ordinary slaughter animals. (Jennelle et al., 2018; Walsh and Miller, 2010).

The model is not differentiating between clinical signs specific for CWD relative to other diseases. By including a higher probability of CWD in the group with deviations, we take into account the information that is available from a herd of semi-domesticated reindeer, which in contrast to wild reindeer is followed and/or herded large parts of the year. Both when it is moved between grazing areas, and when it is observed on a daily basis from snowmobiles during the winter. Compared to wild reindeer, it is then probable that a larger proportion of infected semi-domesticated reindeer will be identified as animals with deviations, and thereby tested.

Using the model adapted for semi-domesticated reindeer, and with a given number of animals in different groups (age class, females with or without deviations, found dead/euthanized, clinically

suspicious) tested in the years from 2016 to 2020, the preliminary calculations indicate that the mean probability of detection of three or more infected animals 88 % after slaughter in 2019. The means of the estimate vary between 84 and 91 % depending on varying presumptions about the length of the clinical period in relation to the incubation period.) This relates to a prior probability of freedom from CWD in Filefjell assigned to 50 % in 2015 (Ch. 2.11.3).

The estimates vary much. The variation is reflect uncertainty (stochastic distribution) about the length of the clinical period relative to the length of the incubation period, how animals found dead/euthanized and clinically suspicious individuals are weighted relative to ordinary slaughter animals and the test sensitivity.

2.11.4 Probability of freedom from CWD in other populations of reindeer

There is still uncertainty around the CWD status for many of the wild and semi-domesticated reindeer areas in the country. Currently, the probability of freedom from CWD has not been estimated for other reindeer populations. Table 2.11.4-1 provides an overview of approximate population size, hunting harvest and number of samples collected from the different wild reindeer management areas in Norway. Analyses of the probability of freedom from infection are currently not finished. The work is thoroughly begun for populations of semi-domesticated reindeer. We have compiled an overview of collected material, number of harvested animals, number of slaughtered animals and number of tested samples per the 4th of December 2020[6] in Table 2.11.4-1 – 2.11.4-2.

Table 2.11.4.-1 The table shows cumulative and mean annual harvest (cumulative/mean) for the period 2016-2019 and number of samples tested for CWD categorized to a wild reindeer management area per 4th of December 2020 (http://apps.vetinst.no/skrantesykestatistikk/NO/#omrade). Please note that the

[6] Translator's note: The original text said 2021, but according to the Table (and logically) 2020 is correct.

harvest data are given up to and including 2019, while samples tested for CWD is presents the number of samples tested until and including the 4th of December 2020.

Wild reindeer management area	Approx. pop. size	Area (km^2)	Harvest (cum./ annual mean)	Samples tested[1]			
				Number of samples	Proportion brain only	Proportion brain + lymph node	Proportion lymph node only
Setesdal Ryfylke	3500	6154	1542/386	506	23 %	75 %	2 %
Setesdal Austhei	2000	2400	346/87	99	28 %	72 %	0 %
Skaulen - Etnefjell	60	486	47/12	50	36 %	60 %	4 %
Våmur-Roan	240	406	185/46	56	23 %	73 %	4 %
Brattefjell-Vindeggen	500	357	417/104	252	31 %	68 %	1 %
Blefjell	140	186	105/26	44	30 %	70 %	0 %
Hardangervidda	7000	8136	5210/1303	4116	40 %	59 %	1 %
Norefjell-Reinsjøfjell	700	314	1042/261	424	56 %	43 %	1 %
Oksenhalvøya	12	80	0/0	2	100 %	0 %	0 %
Fjellheimen	440	1705	254/64	153	31 %	69 %	0 %
Nordfjella	450	3004	576/170[2]	2781[3]	6 %	94 %	<1 %
Lærdal-Årdal	120	488	20/5	39	24 %	76 %	0 %
Vest-Jotunheimen	400	985	72/18	85	23 %	76 %	1 %
Sunnfjord	125	700	50/13	27	48 %	52 %	0 %
Førdefjella	100	700	37/9	20	63 %	32 %	5 %
Svartebotnen	55	99	30/8	22	41 %	59 %	0 %
Reinheimen-Breheimen	2900	4551	2815/704	1243	28 %	72 %	0 %
Snøhetta	2700	3345	2462/616	1209	34 %	66 %	<1 %
Rondane nord	1000		1584/396	808	34 %	65 %	1 %
Rondane sør	2500						
Sølnkletten	800	1330	816/204	238	29 %	70 %	1 %
Tolga Østfjell	2000	453	data not available	40	23 %	77 %	0 %
Forollhogna	1700	1843	1491/373	623	62 %	38 %	<1 %
Knutshø	1500	1776	798/200	414	46 %	53 %	1 %

[1]A number of tested samples are still not categorized after which reindeer management area they originate from. These samples are marked with municipality. The actual number of tested samples is consequently slightly larger than showed in this table. [2]Harvest number for Zone 2 from 2018 to 2020. [3]All Nordfjella in the period from 2016 to 2020, i.e. including the eradication of the subpopulation in Zone 1.

Table 2.11.4.-2 Sami reindeer pasture districts and semi-domesticated reindeer herds in Southern Norway, numbers of animals slaughtered, and samples tested. The table list the herd size in the spring per the 1st of April 2020, cumulative number of animals slaughtered from the 31st of March 2019 to 1st of April 2020 and number of samples tested for CWD per district/herd per the 25th of November 2020.

Pasture district/ reindeer herd	Size of herd in Spring (1st of April 2020)	Pasture area (km^2)	Slaughtered individuals 2019/2020	Samples tested			
				Total number of samples[2]	Proportion brain only	Proportion brain + lymph node	Proportion lymph node only
Filefjell rein-lag	3231	2000	2075	2183	4 %	96 %	0 %
Fram reinlag	2926	1500	1959	2177	2 %	98 %	0 %
Lom tamrein AS	2350	1265	1895	1574	1 %	99 %	0 %
Vågå tamrein AS	2274	1357	1631	1645	1 %	99 %	<1 %
Rendal renselskap	1150	1859	210*	564	6 %	94 %	<1 %
Trollheimen	1576	2235	773	477	30 %	70 %	0 %
Essand rein-beitedistrikt	4338	2324	2075	598	25 %	75 %	0 %
Riast/ Hylling reinbeite-distrikt	4965	1929	3093	2138	23 %	77 %	0 %
Femund rein-beitedistrikt[1]	Common winter pasture	1103	Common winter pasture	1609	25 %	75 %	0 %
Elgå reinbeite-distrikt	2885	1007	966	1796	5 %	95 %	<1 %
Færen	1636	2429	617	782	14 %	86 %	0 %
Skjækra	1840	2380	702	624	82 %	18 %	<1 %
Luru	2299	2729	609	748	48 %	52 %	0 %
Sum Southern Norway	25.695			16745	13 %	87 %	<1 %

[1.] Common winter pasture for Riast/Hylling and Essand reindeer pasture areas

[2.] Including diseased, injured and traffic killed reindeer

Sources: County Governor of Trøndelag (Næringsutøvernes melding om reindrift for driftsåret 2019/2020), Norwegian Agriculture Agency (Ressursregnskapet for reindriftsnæringen) and Norwegian Veterinary Institute (Skrantesykestatistikk).

2.11.5 Probability of freedom from CWD in other populations of cervids

A previous report (VKM, 2018) considered spread of CWD from infected cervids (red deer, moose and roe deer) in the areas surrounding Nordfjella Zone 1 as a relevant scenario. The probability of presence of infected red deer in the populations in Lærdal and Aurland was then considered as "relatively high in this context". This assessment was based on the high population density and the red deer's documented use of pastures and salt licks in the zone.

Our assessment is that the finding of a CWD infected reindeer on Hardangervidda increase the uncertainty about the probability of freedom from CWD in populations of red deer, moose and roe deer within and around Hardangervidda, and strengthen the need for surveillance and monitoring in these populations.

3 The case on Hardangervidda

3.1 Information about the detected case

A wild reindeer male (id 20-CD7187) shot during hunting on Hardangervidda, in Vinje municipality, on the 3rd of September 2020 was diagnosed with CWD at NVI. Samples from submitted brain tissue tested negatively with ELISA (both TeSeE® ELISA SAP, Bio-Rad, Hercules, CA, USA and IDEXX HerdChek BSE-Scrapie AG Test, IDEXX Laboratories, Westbrook, USA), while retropharyngeal lymph node tissue tested positively in the same tests. Examination of both tissue types with Western blot (TeSeE® Western Blot, Bio-Rad, Hercules, CA, USA) and immunohistochemistry with antibodies L42 and SAF84, confirmed the results from the ELISA analysis of retropharyngeal lymph node. The animal had *PRNP*-genotype AD (confer Chapter 2.8.1).

Examination of dental sections performed at NINA determined that the male was 8 years of age.

The animal's weight was registered as 58 kg in the National Cervid Data Base (Hjorteviltregisteret).

While the examination of the lymph node and brain samples was performed, the management authorities collected the remains of the animal for further investigations. Tests performed with additional lymphoid tissue (mandibular lymph node) and brain tissue samples gave results consistent with the results based on the samples submitted by the hunter.

Analyses performed at Section for Medical Genetics at NMBU by use of DNA microsatellites (N=18) (pers. comm. Knut H. Røed) compared the genotype profile of this individual with comparable analyses of reindeer from Hardangervidda (N=46), Setesdal-Ryfylke north (N=33), Nordfjella Zone 2 (N=54) and Nordfjella Zone 1 (N=42). By help of the software GeneClass2 (Piry et al., 2004) preliminary assessments has been performed about the probability of the reindeer male's origin from the different reindeer populations, using a Monte-Carlo re-sampling (Paetkau et al., 2004). The proportion of the re-samplings that placed the case to the different reference populations was 0,156 for Hardangervidda, 0,031 for Setesdal-Ryfylke, 0,018 for Zone 2 and 0,036 for Zone 1.

If it is presumed that the animal belong to one of the mentioned reference populations (without «re-sampling algorithm) (Rannala and Mountain, 1997), the estimated probability of the case originating from the Hardangervidda population is 98,23 %, while the probability for an origin in Setesdal-Ryfylke, Zone 2 or Zone 1 is only 0,08, 0,46 og 1,24 %, respectively.

3.2 Comparison with previous cases in Norway and internationally

There were no diagnostic dissimilarities (ELISA, Western blot and immunohistochemistry) between prions from the case and the nineteen wild reindeer from Nordfjella Zone 1 in which PrP^{Sc} was detected. In more than half of these animals from Zone 1 (10 of 19) PrP^{Sc} was only

detected in the lymph node sample, while the other half had PrP^{Sc} both in the lymph node and the brain sample.

Further characterization of the Hardangervidda case necessitates inoculation trials in mouse models or cervids. As described by Benestad et al. (2016) diagnostics tests (ELISA, Western blot and immunohistochemistry) could not differentiate between prions from the index case from Nordfjella and the two characterized CWD strains in North America. The difference between the North American strains and the isolate from the first case were first revealed after inoculation trials (Nonno et al., 2020).

3.3 Consideration of potential origins of detected disease, including when, where and how the animal has achieved the infection

- The finding of only one CWD infected reindeer on Hardangervidda make the epidemiological situation unclear. It is natural to interpret the case as a part of the same outbreak as Nordfjella, for example through exchange of animals between Nordfjella and Hardangervidda, as it is unlikely that we have to independent outbreaks of CWD so close to each other in time and space. Genetic analyses, however, indicate that the affected individual most probably originated from Hardangervidda and not Nordfjella (see Ch. 3.1). This may imply that the CWD positive reindeer not wandered from Nordfjella itself. The animal had PrP^{Sc} in the retropharyngeal lymph node and not in the brain sample, indicating that it was in an early phase of the infection. If we presume that the infection course lasts 2-3 years, it is most probable that the animal was infected on Hardangervidda. We can not exclude that the individual wandered up to Nordfjella Zone 1, got infected, and thereafter wandered back, but as described in Chapter 4.3.3 has such wandering events not occurred frequently.

4 Conditions relating to the wild reindeer population on Hardangervidda and its home range that can be of importance for handling of CWD

4.1 Background and history

Hardangervidda, covering 8200 km^2, is beyond comparison the largest wild reindeer area of Norway and home to the largest wild reindeer population in the country. The geographically central areas of Hardangervidda consist of large, relatively pristine areas, while the margins of the area are influenced by major infrastructure development and in some periods much human disturbance. Human encroachment and disturbance have over time contributed to significant fragmentation, causing the old core areas for the reindeer to become more isolated from surrounding wild reindeer areas. This is well documented for the areas between the road Rv7 and Geitryggen in Nordfjella, where the reindeer once had migration routes to and from the northern mountain areas and the eastern and central areas of Hardangervidda. Reindeer hunting drives and archaeological locations in this area indicate that reindeer has been caught here through the last 7-8.000 years. In the High Middle Ages (1130-1350) large numbers of reindeer were caught, but this ceased at the end of the 13th century (Indrelid and Hufthammer, 2011).

From the middle of the 18th century, several attempts were made on establishing reindeer husbandry on Hardangervidda, often by use of herds of semi-domesticated reindeer from the areas around Røros. These droves had variable extent and duration, but the practice continued until after the Second World War, during which the prohibition of travel on Hardangervidda after the heavy water sabotage at Vemork in 1943 caused a mix between the semi-domesticated reindeer herds and the wild reindeer. The three remaining reindeer herding companies suspended their activity on Hardangervidda in 1956 and -57 (Bitustøyl and Mossing, 2019).

The history of Hardangervidda is currently reflected in the genetics of the wild reindeer population. There are major differences between the genetic composition in the medieval material from Sumtangen and the current wild reindeer population (Røed et al., 2014).

The genetic composition has changed, partly as a consequence of bottlenecks the population has been through, and partially as a consequence of repeated periods with interbreeding with semi-domestic reindeer. The current Hardangervidda population is consequently a mixture of feral semi-domesticated reindeer and the reindeer that once lived in Langfjella in the Middle Ages and earlier (Kvie et al., 2019; Røed et al., 2014).

The wild reindeer population on Hardangervidda constitute more than 30 % of the current European wild reindeer, and has hence large ecological and cultural value (Bråtå et al., 2015; Andersen and Hustad, 2004)

4.2 Environment (including pasture resources, influencing factors etc.)

Hardangervidda is Europe's largest mountain plateau. A large part (3422 km^2) of this mountain area is protected as either national park or protected areas (landskapsvernområder). (Skaupsjøen/Hardangerjøkulen landskapsvernområde on 551km^2 and Møsvatn Austfjell landskapsvernområde on 299 km^2). Hardangervidda National Park was established in 1981, and consideration for the wild reindeer was the main reason for the protection. The natural and cultural values of the landscape are considered unique in Norwegian and European context. About half of the protected areas are public land, while approximately 70 % of the wild reindeer area is privately owned (Direktoratet for Naturforvaltning, 2003). Hence, a corresponding proportion of the harvest rights to this large area is in private hands. Local mountain administration boards (fjellstyrer) manage public land and hunting rights.

There is significant human activity on Hardangervidda, and the area has a well-developed network of trekking paths (Gundersen et al., 2020). Roads and hydropower installations characterizes the southeastern part of the area. Private hunting and fishing cabins are found all over Hardangervidda. Traditional mountain dairy farming has vanished, but in Nore og Uvdal, Hol and Eidfjord municipals are notable areas used as pastures for sheep.

Large predators are in reality eradicated from Hardangervidda, also from the National Park. The wild reindeer population is currently managed through hunting. Hardangervidda is hence a severely altered ecosystem, and the health of the animals (condition, parasite load and occurrence of disease) can be viewed in light of the artificial circumstances of life that the wild reindeer is living under.

4.3 Geography and area use (including contact with other populations etc.)

4.3.1 Area use and contact with other wild reindeer herds

Multiple projects have marked reindeer on Hardangervidda with radio- or GPS collars. This work started in 2001 and has provided a continuous data series (except from 2006) describing the area use of collared females. Unfortunately, comparable data describing the area use of males do not exist. The reason for this is that the research has been focussed on the impact of human encroachment and disturbance and collaring of females has hence been prioritized. During the study period has 126 females been marked with GPS-transmitters on Hardangervidda. Additionally, similar projects have been performed in Setesdal Ryfylke, Setesdal Austhei and in Nordfjella, and a minor number of animals have been GPS-collared in Vest-Jotunheimen (Table

4.3.1-1). In the Setesdal areas, 17 males have been marked, too. Some males has also been marked in Nordfjella Zone 2 after the detection of CWD in Nordfjella Zone 1.

The area use of the wild reindeer has lately gained increased attention in both research and management (Andersen and Hustad, 2004). Several local GPS-collaring projects and surveys have been performed (Nilsen and Strand, 2018; Panzacchi et al., 2014; Panzacchi et al., 2015; Strand et al., 2015a; Strand et al., 2011; Strand et al., 2015b). We have used the results from these investigations to evaluate the degree of contact between wild reindeer populations in Langfjella. Corresponding evaluations has been done for the semi-domesticated reindeer herds that can come in touch with these wild reindeer populations.

Table 4.3.1-1 Number of collar-marked reindeer in Langfjella in the period 2001-2020

	Sum	GPS female	VHF female	GPS male	VHF male
Hardangervidda	159	126	33	0	0
Setesdal Ryfylke	65	39	9	17	0
Setesdal Austhei	28	24	4	0	0
Nordfjella	48	43	0	5	0
Brattefjell vindeggen	4	4	0	0	0
Nordfjella Zone 2	20	10	0	10	0

4.3.2 Reindeer area use on Hardangervidda

The reindeer on Hardangervidda show what we can call a nomadic behaviour. The western part of the area is characterized by larger precipitation and has qualities as bare ground pastures[7]. The western areas do also have a topography with elevated areas that are important pastures for the reindeer during summer. The eastern parts have more of a character of a mountain plateau with a dry inland climate. Consequently, the central and eastern areas are dominated by lichen-rich vegetation and function as winter pastures for the Hardangervidda reindeer (Falldorf, 2013; Skogland, 1990a)

The grazing needs of the animal affect their area use, and the grazing pattern change through a year, something that in turn contribute to seasonal variation in home range size and population density. The radio-collared females has in general used a very limited area between the rivers Kvenna and Songa (Strand et al., 2015a). In the autumn, they use a much larger area, but there are still large areas in the western and north-northeastern parts of the Hardangervidda that rarely are used at this time of year. The area use is most dispersed during winter, and is then

[7] Translator's note: «Bare ground pastures» are pastures used when the ground is not covered with snow, i.e., in the late spring, summer and autumn until the snow falls.

A parenthesis with the text «(selv i vinterhalvåret?)» is omitted, as it is interpreted as a comment meant to be deleted before publishing.

most influenced by snow coverage and access to pasture lichens (Falldorf, 2013; Strand et al., 2015a). Which areas the animals use in the calving period has changed profoundly over some decades. From the beginning of the 1980s through to the 1990s[8] documented Terje Skogland that the females calved in the western and northwestern parts of Hardangervidda, had their early summer pastures, and nursed their young calves in Veigdalen. Since that period the calving areas have moved eastwards, and the females have in the last decades mostly calved in the areas west of Møsvatn, having had their early summer pastures and nursing areas around Songa and in Kvennadalen (Strand et al., 2015a).

GPS-marking of females on Hardangervidda has provided solid documentation on the area use of parts of this population, but corresponding data are missing for males (see table 4.3.1-1). Reindeer are strongly polygamic and live in partially gender segregated herds (Skogland, 1990a).

The males in general leave the nursing herds (that consist of females, calves and juveniles) in the first part of the winter (December – March). Through the last part of the winter, the spring and summer do the males group with other males in their own herd. Not before the end of the summer, but before the rut, do the males re-join with the nursing herds. The males do not display the same anti-predator behaviour as the females with their vulnerable calves.

The males are less shy and more opportunistic in their area use and do hence utilize areas on the edges of the area and areas with rich spring- and summer pastures. These differences in area use are to some extent visible in the calf surveys that are performed in June and July. The herds of males then roam the areas south of Songa watercourse down towards the border areas to Setesdal Ryfylke. There are also large differences between the genders with respect to herd size through the year. The typical herd of males on Hardangervidda in June and July consists of less than 50 individuals, while the females aggregate far larger herds within a relatively small area in the central parts of Hardangervidda. This pronounced herd behaviour, where the reindeer on Hardangervidda is concentrated in small areas through parts of the summer, can constitute a substantial risk factor for spread of infection.

4.3.3 Contact towards other wild reindeer areas: Nordfjella

Because of changes in human area use (Ch. 4.3.1), the wild reindeer population on Hardangervidda is currently more isolated from surrounding wild reindeer populations in Nordfjella, Norefjell- Reinsjøfjell, Blefjell, Brattefjell Vindeggen and the Setesdal areas than previously. The old mass trapping sites have been used as indicators of old migration routes and are together with GPS-data from collar-marked reindeer used to test the impact of human encroachment and disturbance (Jordhøy, 2007; Panzacchi et al., 2013). These investigations show that road, buildings, tourist cabins etc. has contributed to cessation of use of these old migration routes (Panzacchi et al., 2015). The best evidence for this has been found in the area

[8] Translator's note: The original formulation was «Fra begynnelsen av 1980-tallet og fram gjennom 1990-tallet», meaning «From the beginning of the 1980s and forward through the 1990s».

between the railroad from Oslo to Bergen and the road Rv7. This area is administratively a part of the Hardangervidda wild reindeer area, but is occasionally used by reindeer that normally live in the areas between the railroad and Geitryggen (Zone 2 in Nordfjella). The importance of Rv7 as a barrier for the wild reindeer has attracted much attention. A designated operation has had the area under surveillance since 2001. In addition to marking of animals, has the Norwegian Nature Inspectorate (SNO) run surveillance with snowmobile patrols in the field since 2007 (Strand et al., 2015b). Since 2007 and until the detection of CWD in Nordfjella, procedures were installed to ensure that the road was closed for ordinary traffic if a larger herd of reindeer (more than 1000 animals) was in the areas close to the road. The aim of this was to ease their use of the areas north of Rv7 and their migration between Hardangervidda and Nordfjella. Due to this, attention has been large around the wild reindeer's use of the areas close to Rv7, and it can be stated with high certainty that there not has been any large exchange between the Hardangervidda and the Nordfjella populations in this period. Last time a large number of animals from Hardangervidda used an area north of Rv7, was during the winter of 2007, when 300-1000 animals from Hardangervidda stayed north of Rv7 between January and April (Strand et al., 2015b).

The probability for exchange of animals between Hardangervidda and Zone 2 in Nordfjella is also related to the area use of the wild reindeer in Zone 2. This area only to a little extent used by reindeer in Nordfjella until the beginning of the 2000s. The population in Nordfjella did for a large part stay in Zone 1. During the years between 1997 and 2000, a large proportion (1000-1500 animals) migrated from Zone 1 to Zone 2 over Geitryggen. Many of these drew back to Zone 1 the next 3-4 years, but approximately 500 animals continued to use Zone 2. These animals did relatively soon also start to use the areas south of the railroad between Oslo and Bergen. (Strand et al., 2011). The herds in this area has been followed with GPS-transmitters since 2007. The data series show that the reindeer here have used areas also on the southern side of the glacier Hardangerjøkulen, and that they have reached Rv7. It is important to emphasize that this happened after the visit of the animals from Hardangervidda during the winter of 2007, and that we do not have data on the area use of males in this area, apart from the periods they have been in herds with collar-marked females.

4.3.4 Contact towards east: Norefjell-Reinsjøfjell and Blefjell

Hardangervidda has to large potential contact areas towards east, Dagalitangen og Lufsjåtangen. Dagalitangen is partially connected with Norefjell-Reinsjøfjell, but both low-elevation forest areas, roads and buildings on Dagalitangen are efficient barriers. Dagalitangen holds important winter pastures, but the human impact in the area is so profound that the area currently is reckoned as lost for the wild reindeer on Hardangervidda. Reindeer males are observed Dagalitangen, but this is probably animals from Norefjell–Reinsjøfjell. The exchange probabilities between the wild reindeer areas are small, but it cannot be excluded that single animals or small herds can cross these barriers.

Imingfjell is still used as winter pasture for wild reindeer from Hardangervidda (Jordhøy and Strand, 2009). This is well documented by data from GPS-collared females on Hardangervidda.

The possibilities for migration between Hardangervidda and Blefjell over Lufsjåtange are considered as larger than over Dagalitangen to Norefjell-Reinsjøfjell.

4.3.5 Grungedalstangen

This is a wild reindeer hunting ground[9] that administratively is a part of Hardangervidda wild reindeer area but has a subpopulation that for the most part is separated from the Hardangervidda population and has been managed as a separate population with independent allotment of hunting cards for decades. The management goal is to maintain a winter population of approximately 40 animals.

4.3.6 Contact towards east: Brattefjell-Vindeggen and the Setesdal areas

South of Hardangervidda are the old migration routes towards Brattefjell-Vindeggen more or less completely closed by building of holiday cabins and roads. In the 1960s and early in the 1980s, when the wild reindeer population of Hardangervidda was very large, local knowledge indicate that significant dispersion from Hardangervidda to Brattefjell-Vindeggen occurred. Locally, it is reckoned that dispersion from Hardangervidda contributed to the establishment of a separate wild reindeer population here. The contact area between Brattefjell-Vindeggen and Hardangervidda is nowadays characterized by built-up areas and much human activity. The probability of exchange of animals between these areas is regarded as low. It can, however, not be excluded that solitary animal cross between the areas, since there is little knowledge about the area use of reindeer males.

The road E134 and areas built up with holiday cabins along it provide a strong barrier towards south and Setesdal-Ryfylke. There are, however, still a number of reindeer that travel between Hardangervidda and Setesdal-Ryfylke. This is mostly males that normally stay in Setesdal-Ryfylke, but in some periods of the year use areas on Hardangervidda. NINA has collar-marked wild reindeer in Setesdal-Ryfylke since 2006. In total, 39 females and 17 males have been marked in this area (Strand m fl. 2019). In addition, 24 females from Setesdal Austhei are marked with GPS-transmitters. The results from these marking projects show that there still is a certain exchange of animals between the two reindeer areas of Setesdalen. They also show that the males to a much higher extent cross barriers (like roads) and that they to a larger degree wander between populations. The marking projects have revealed that there are several relevant crossing areas that seem to be highly relevant with regard to exchange, for example the uplands north of Hovden (Strand et al., 2019; Strand et al., 2011).

Build-up along E134 has gradually diminished the migration potential in these areas. Currently, mainly males cross this axis and periodically use areas that administratively belong to Hardangervidda. Until the 1980s did also nursing herds from Setesdal-Ryfylke use winter

[9] Translator's note: Small reindeer hunting management unit.

pastures north of E134 in some periods (Strand et al., 2011). A varying number of males that most probably have wandered into Hardangervidda from Setesdal-Ryfylke are annually shot in Røldal. Both local knowledge and data from collar-marked reindeer in this area have estimated where the reindeer most probably will choose to cross the barrier along E134. The most relevant areas of exchange are west of Haukeliseter, but it should be emphasized that the whole distance between Vågsli and Dyrskar are areas where reindeer can cross between Setesdal-Ryfylke and Hardangervidda.

4.3.7 Connectivity north of Nordfjella

Figure 4.3.4-1 depicts known, potential contact areas between Hardangervidda and surround wild reindeer management areas and semi-domesticated reindeer herds in Langfjella. Table 4.3.4-1 describes the potential for contact between wild reindeer management areas and semi-domesticated reindeer areas in Langfjella.

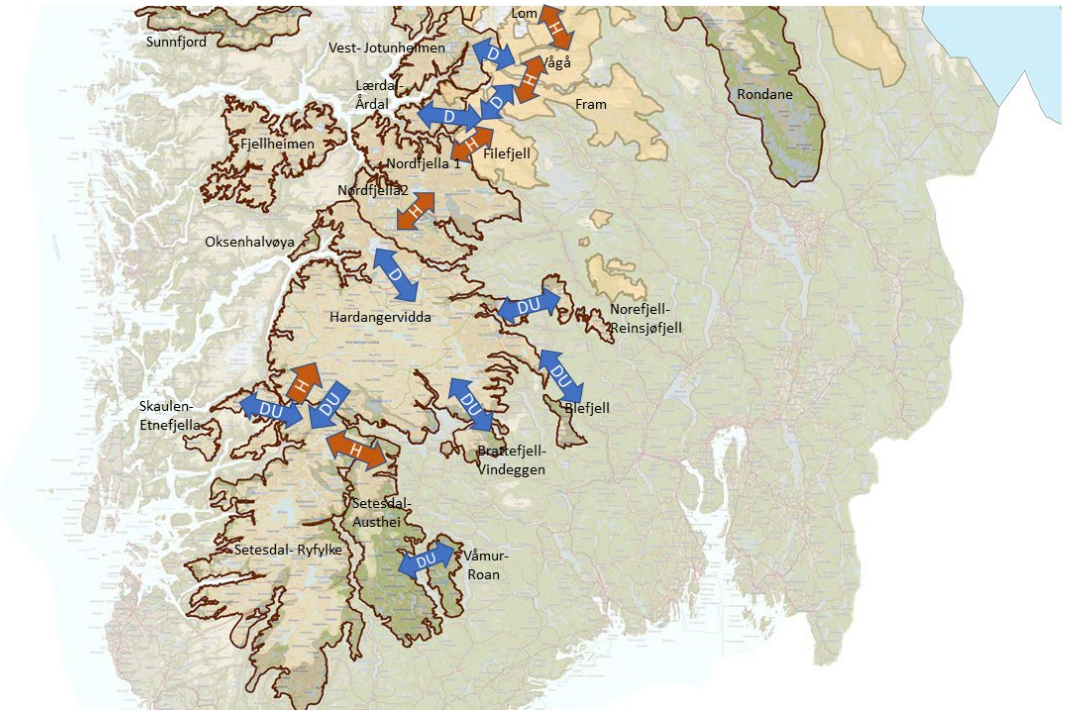

Figure 4.3.4-1 Map over the Langfjella region in southern Norway and known, potential contact areas between Hardangervidda and surrounding wild reindeer management areas and semi-domesticated reindeer herds in Langfjella (see Appendix III for details, H = frequent contact, D = direct and documented contact and DU = potential direct but not documented contact).

Table 4.3.4-1 Matrix that describe the potential for contact between wild reindeer management areas and semi-domesticated reindeer areas in Langfjella. The matrix differentiates between immigration and emigration and should be viewed horizontally. It is for example documented frequent[10] contact from Setesdal-Ryfylke to Hardangervidda, while crossing of reindeer from Hardangervidda to Setesdal-Ryfylke not is documented (DU).

	Setesdal-Ryfylke	**Setesdal Austhei**	**Skaulen-Etnefjell**	**Våmur- Roan**	**Brattefjell-Vindeggen**	**Blefjell**	**Hardanger-vidda**	**Norefjell-Reinsjøfjell**	**Oksenhalvøya**	**Fjellheimen**	**Nordfjella 1**	**Nordfjella 2**	**Lærdal-Årdal**	**Vest-Jotunheimen**	**Raudafjell**	**Filefjell**	**Fram**	**Vågå**	**Lom**
Setesdal-Ryfylke	--	**D**	**DU**	U	**I**	U	**H**	U	U	U	U	U	U	U	U	U	U	U	U
Setesdal Austhei	**D**	--	U	**I**	**I**	U	**I**	U	U	U	U	U	U	U	U	U	U	U	U
Skaulen Etnefjell	**DU**	**I**	--	U	U	U	**I**	U	U	U	U	U	U	U	U	U	U	U	U
Våmur Roan	**I**	**DU**	U	--	U	U	U	U	U	U	U	U	U	U	U	U	U	U	U
Brattefjell-Vindeggen	U	**I**	U	**I**	--	U	**I**	U	U	U	U	U	U	U	U	U	U	U	U
Blefjell	U	U	U	U	U	--	**DU**	U	U	U	U	U	U	U	U	U	U	U	U
Hardanger-vidda	**DU**	**I**	**DU**	U	**I**	**I**	--	**I**	U	U	**I**	**DU**	U	U	U	U	U	U	U
Norefjell-Reinsjøfjell	U	U	U	U	U	U	**DU**	--	U	U	U	U	U	U	U	U	U	U	U
Oksen-halvøya	U	U	U	U	U	U	U	U	--	U	U	**I**	U	U	**I**	U	U	U	U
Fjellheimen	U	U	U	U	U	U	U	U	U	--	U	U	U	U	**I**	U	U	U	U
Nordfjella Sone1	U	U	U	U	U	U	**I**	U	U	U	--	**D**	U	U	U	**D**	**I**	U	U
Nordfjella Sone2	U	U	U	U	U	U	**DU**	U	**I**	U	**D**	--	U	U	**D**	**I**	**U**	U	U
Lærdal-Årdal	U	U	U	U	U	U	U	U	U	U	I	U	--	**DU**	U	**D**	**D**	**I**?	**U**
Vest-Jotunheimen	U	U	U	U	U	U	U	U	U	U	U	U	**DU**	**--**	U	**I**	**D**	**D**	**D**
Raudafjell	U	U	U	U	U	U	U	U	**I**	**I**	**I**	**D**	U	U	--	U	U	U	U
Filefjell	U	U	U	U	U	U	U	U	U	U	**H**	**I**	**D**	**I**	U	--	**D**	**I**	**I**
Fram	U	U	U	U	U	U	U	U	U	U	U	U	**D**	**D**	**D**	**D**	--	**H**	**H**
Vågå	U	U	U	U	U	U	U	U	U	U	U	U	**I**	**D**	**U**	**I**	**H**	--	**H**
Lom	U	U	U	U	U	U	U	U	U	U	U	U	**I**	**D**	U	**I**	**H**	**H**	--

H = frequent contact, D = direct and documented contact, DU = potential but not documented contact, I = potential but unlikely direct contact or potential contact via an area with documented contact, U = no or very unlikely contact, ? = unknown/not assessed

[10] Translator's note: The original text was "direkte" which means "direct", but this disagree with the letter "H" in the legend and the table, which translates to "frequent".

4.4 Conditions relating to the population (including population development, demography, condition and health status)

4.4.1 Management and management goals

The wild reindeer populations in Norway were at a minimum around the year of 1900. New legislation and introduction of hunting quotas did over time decrease overharvesting, and the population grew until the end of the 1950s. The population increase led to significant overgrazing on Hardangervidda and in the Snøhetta area. Since then, the wild reindeer population on Hardangervidda been through at least two periods of significant overgrazing. In these periods, considerable discrepancy arose about the measures used in the population management. These conflicts were a direct cause of the emergence of the local management we know today. Concurrently, new management goals were established that aimed to stabilize the growth in the wild reindeer populations Local management plans were made that established aims of improving the condition of the animals and pastures. The proportion of males was very low until the end of the 1980s. Changes in harvesting and gender- and age-specific hunting quotas did over time contribute to a reestablishment of the male segment, and most Norwegian wild reindeer populations do currently have a close to natural gender distribution (Solberg et al., 2017). This is very pronounced on Hardangervidda, where the male proportion was as low as 5 % in the 1980s, but where we until the CWD outbreak in Nordfjella and a planned reduction of the male segment, had about 20 % adult females (three year and older) in the population after the hunting season (Solberg et al., 2017).

A major difference between wild reindeer management and the management of moose and red deer is that stabilization of population growth has been a goal over a long period. The management goals for an individual population, and which measures that should be taken to reach them are formulated in the resolutions of the working plan for the respective wildlife management area. The legal basis for these working plans lies in paragraph 27 in the regulation on management of cervids (forskrift om forvaltning av hjortevilt) and can be approved by the relevant wild reindeer management board (villreinnemnda[11]). To be given the rights to wild reindeer hunting and management, the area needs to be approved as a wild reindeer hunting ground. Since the beginning of the 1980s has the management goal on Hardangervidda been to maintain a winter population of approximately 10.000 animals. Over time, this has proved difficult as there has been and partially is significant variation in the numeric data the population management is built on. Similarly, there is significant variation in the relationship between population size, hunting quotas and to what degree hunting quotas are filled. In total has these

[11] Translator's note: The Wild Reindeer Boards are regional public boards where members and deputies are appointed by the Norwegian Environment Agency. The appointments are made on the basis of proposals from each municipality that has wild reindeer land, for a female and a male candidate within the individual board's area of activity. The boards receive instructions from the Environment Agency and their activity and authority is described in regulations given by the Environment Agency (Source: www.villrein.no).

factors caused more variation in the population size on Hardangervidda than desired. During the last 25 years, the maximum summer population level reached 14.000 and the minimum 6.000. In line with this has the hunting quotas varied a lot, from very high levels to protection. These challenges has given the local managers considerable experience with very variable and deviating hunting quotas, for example hunting quotas that in reality have allowed unlimited hunting on calves.

The management goals that are approved in the current working plan for Hardangervidda wild reindeer management are comprehensive, but can be summarized in the following main goals:

- Ensure a viable wild reindeer population that provide a continuous harvestable surplus.
- Ensure protection of the wild reindeer area against unnecessary encroachment and human disturbance.
- Conserve the unique properties the wild reindeer area/population have by means of its size.
- Conserve and develop the wild reindeer as a resource for stakeholders and the societies surrounding the mountain plateau.

Under each of these main goals, several concrete objective areas and measures are defined that shall ensure that the goals are reached (Bestandsplan for Hardangervidda 2017- 2021).

For example:

- Objectives for area management and area use.
- Objectives for pastures, condition and health.
- Objectives for population size and calf production.

Hardangervidda did previously have a population goal that defined objectives for the size of the winter population. In large, this objective varied between 9.000 and 12.000 animals. Based on experience it is difficult to achieve annual censuses of the winter population on Hardangervidda, and discussion about the size of the population has characterized the management through decades. The wild reindeer management committee[12] (villreinutvalget) has abandon this objective for population size and have since 2017 aimed for a calf production of 2000-2500 calves. To reach this objective, there has also been an aim to maintain a 40 % proportion of females after the hunting season, and that the total population before calving not shall exceed 12.000 animals. An important reason for the introduction of this aim is the recognition of how limited the opportunities are for population regulation through ordinary hunting if the calf production exceeds 3.000 animals. The limitation relates to the fact that the number of shot animals has varied around 30 % of the hunting quota the last years, and that an increase in the

[12] Translator's note: The Wild Reindeer Management Committees are associations of stakeholders like landowners and other groups of local people, often within one or a few municipalities.

hunting quotas above 10.000 hunting cards only to a limited degree can be expected to increase the harvest.

4.4.2 State of the population

The wild reindeer population on Hardangervidda has over a long period been affected by the density dependent food limitation that emerged as a consequence of the population growth in the 1960s and 1980s (Loison and Strand, 2005; Skogland, 1990b). The goals of increased quality of the population have only partially been reached. The calf censuses on Hardangervidda show that there is less interannual variation in number of calves per 100 females and juveniles (K/SU) now than before. The mean recruitment rate is although somewhat low compared with other wild reindeer areas (Kjørstad et al., 2018). The quality of the wild reindeer populations and their home ranges has received renewed attention with the introduction of the Quality Norm for Wild Reindeer in spring 2020. According to this, the wild reindeer populations are required to have a minimum condition measured as slaughter weight in calves (corrected for date and gender) and a minimum number of adult males and females. The Norm also include requirements with regard to the quality of the lichen pastures and the degree of disturbance in areas with important functions for the wild reindeer (Kjørstad et al., 2018). In addition, the Norm has requirments of maintenance of genetic variation and abscence of notifiable diseases.

The results from the population monitoring on Hardangervidda shows that the management until the last years hunting quotas succeeded in building up a substantial proportion of adult males in the population. This was changed by the need for increased harvesting of this segment in order to collect samples for surveillance of CWD. The slaughter weights are, however, very low and the poorest in Norway (Kjørstad et al., 2018; Solberg et al., 2017). There may be several reasons for the low slaughter weights, and both demographic effect of orphanage due to shooting of mothers from their calves in the fall, long-lasting effects of food limitation, high densities on summer pasture and, in addition, high parasite load (Handeland et al., 2019) can alone or in interplay explain the low slaughter weights.

Handeland et al. (2019) found that half-year-old calves and juveniles on Hardangervidda were infected with substantial amounts of warble fly and nasal bot fly larvae. They emphasized that the high density in summer may have caused a high parasite load with negative effects on the slaughter weights of the calves. In the fall of 2019 a large outbreak of footrot was registered on Hardangervidda (Madslien et al., 2020). Lameness was observed in a large number of animals, first and foremost in calves but also in adult females, showed signs of lameness during the hunting season and the subsequent structural survey. Hunters reported about 100 animals (adult females and calves) with footrot during the hunting this year. Footrot has been reported previously in this population, but not with the high prevalence seen in 2019. Structural surveys performed in the fall of 2019 and through the winter (March and April) of 2020, indicate a loss of calves on more than 60 % during these months, something that may have contributed to the low net decrease in population size on Hardangervidda from 2019 to 2020.

In the last two years has the harvest on Hardangervidda been directed towards surveillance of CWD. Due to this, it was only permitted to shoot adult males in 2019, while the hunting quota in 2020 consisted of 50 % adult males and 50 % optional category animal. The last years' structural surveys show a decline in the post-hunting population proportion of adult males from approximately 20 % during the five-year period before 2019, to 6 % in 2020. The adult female segment has more or less been spared in these years. Consequently, the production and the growth of the population has been maintained in spite of the intensive sampling that has been performed. The last populations estimate, made before hunting in 2020, was on 9250 (with estimated credibility interval on 8800-9770 animals). According to the structural surveys performed this year, did the population consist of 23 % calves, 63 % adult females and juveniles, 8 % young males and 6 % adult females (three-year-old or above).

4.4.3 The phenomenon of antler gnawing

Widespread antler gnawing has been documented among wild reindeer in Langfjella (Mysterud et al., 2020d). It is remarkable that this occur while the antler still is attached to the animal. This is a well-known phenomenon and was referred to in a professional journal already in 1973. The work is the first to document the extent of this in different wild reindeer populations in Norway. The intensity of antler gnawing is highest on Hardangervidda and in Nordfjella and based on images it seems to have increased in occurence in the last decades. Based on images of herds on Hardangervidda from the period of 2004-2006, extremely high levels of antler gnawing are documented in 68,2 % of the animals, while it during the winter survey of 2020 was observed in as much as 93,2 % of the animals. Gnawing on felled antlers is relatively common among cervids and often thought to be associated with mineral deficiencies. A hypothesis has been formulated, proposing that this «antler cannibalism» may have been a mechanism that contributed to the emergence of contagious CWD in Langfjella.

5 Strategies

5.1 Three principal strategies

We have previously reviewed three strategies for how an outbreak of CWD can be approached (VKM, 2017):

- No measures
- Eradication of disease
- Control disease

In the following chapters are these strategies discussed in light of the updated knowledge reviewed in this report as well as information presented in previous VKM-reports. A strategy is defined as an approach or a plan made to reach a goal. Strategy is often considered as an overarching mode of approach, and it is often necessary to define a set of measures to follow up the chosen strategy. In this report these measures are described in detail in Chapter 6.

The three strategies will here be reviewed considering the situation that has emerged on Hardangervidda, which deviates from the situation in Nordfjella Zone 1, for example because the wild reindeer population on Hardangervidda is substantially larger. The wild reindeer population on Hardangervidda is Europe's largest wild reindeer population, and protection of the wild reindeer was an important background for the decision of protection when Hardangervidda National Park was created in 1981. The areas this population lives in are much larger and considerably more difficult to delineate and control. These circumstances will not only affect the assessment of the ecological consequences of the different strategies in short and long term, but will also affect the probability for the success of the different strategies.

The discussion about strategies does not include further discussion of the strategy that apply to atypical, not naturally transmitted CWD (strategy 1b in VKM, 2017). Based on current knowledge we can with a high degree of certainty conclude that the CWD strain detected in a reindeer on Hardangervidda, can be considered as a classic, contagious CWD corresponding to CWD in white-tailed and mule deer in North America. Classic CWD is so far detected in 20 wild reindeer in Norway (table 2.2-1), while atypical CWD not is detected in wild reindeer (Chapter 2.2).

We describe the timing of the different measures using the following three experssions: "As soon as possible" indicates that the measure should be accomplished at first opportunity and within a year to maximize the effect. "In short time" describe that the measure should be accomplished without unnecessary delay, but that the effect probably not will be substantially reduced if action is taken within two to three years. "Over a longer period of time" characterize measures that should be installed as soon as possible, but still will have the desired effect if they are completely implemented after a time period of four to eight years.

Due to constraints in space and time, the discussion of consequences on animal health and welfare in the following chapters mainly focus on health and disease. Animal welfare aspects are not adequately treated. Zoonotic aspects are not part of the mandate for the report, and are consequently not reviewed. The constraints in space and time have also caused the description of "ecological consequences" to focus on cervid ecology, though many of the measures will have consequences beyond this.

In the scientific literature about management models it is emphasized that an approach where

1) actions are based on the currently best available knowledge
2) the management strategy is designed so that the measures can be adjusted systematically as new knowledge become available, and
3) measures are accomplished in a way that increases the knowledge,

is appropriate when there is high degree of uncertainty about the effects of different measures. When these guiding points are followed in a purposeful and systematic fashion, and there is a concrete plan about generation of new knowledge applicable for adjustments of management plans and strategies, the approach is characterized as adaptive or learning-based management (Williams et al., 2010). It is important to note that it is this systematic approach to generation of new knowledge that separates adaptive management from other management models where the effects of different measures only are passively monitored. To ensure that new knowledge becomes available, the management strategy has to be designed som that it actually generates knowledge. This includes systematic collection of data, but also that certain measures sometimes are selected because they more efficiently create knowledge than other measures. Choice of harvesting strategy will for example not only affect the probability of controlling or eradicating the disease, but will also affect how rapidly new knowledge about the occurrence of the disease is generated (Mysterud et al., 2020a). Experience indicates that the success of such a kind of management relies on acceptance among those affected by the measures (McFadden et al., 2011; Rist et al., 2013). Independent of which strategy that finally is chosen, it is mandatory to not postpone choice of strategy and measures only because the uncertainty is high (Milner-Gulland and Shea, 2017). By postponing choice of strategy until all relevant uncertainties are reduced, the probability of actually reaching the goal of controlling (strategy 3) or eradicating (strategy 2) the disease may be drastically reduced (Chapter 6.1.1.2).

5.2 Strategy 1: No measures

All reindeer with documented CWD in Norway have so far been characterized as classic, contagious CWD (Table 2.2-1), and it is consequently highly probable that further transmission of infection will occur if no management measures are made. Empiric knowledge from North America show that there is no reason to assume that CWD will disappear spontaneously without intervention (see Chapter 2.5 og 2.6). Taking into the high degree of connectivity between cervids populations across country borders, spread of CWD out of Norway will be difficult to avoid.

In this context is hunting with ordinary quotas regardes as "No measures". The increased harvest of adult males that was accomplished in 2019 and 2020 is, on the contrary, regarded as a measure.

- If no measures are performed against CWD, the disease will spread within the wild reindeer population on Hardangervidda
- Even with the limited current connectivity between the Norwegian populations of wild reindeer, it is probable that CWD will spread to the nearest wild reindeer population. We do not know when, but the case on Hardangervidda indicate there is a potential for this to happen soon.
- There is substantial danger for spread of CWD to semi-domesticated reindeer herds (Chapter 4.3).
- Depending on the degree of species barriers, we can expect spread to other wild cervids and farmed red deer (Chapter 2.11.5).
- We can, in an early phase of uncontrolled spread of CWD and based on available models, expect that CWD mainly is transmitted directly from animal to animal. Looking at a longer time perspective, environmental contamination will be substantial (Chapter 2.5). This implies that the basic reproduction ratio, R_0, increases and that the environment potentially contains infective material for a long period of time (Chapter 2.5).
- In a long perspective and based on the knowledge we have about the population impacts on mule deer, white-tailed deer and wapiti, we must expect negative effects on population level, in particular mediated through decreased survival of adult females (Chapter 2.6; VKM 2017). The occurrence of the disease, and thereby its effects, will vary from species to species depending on degree of social behaviour and population dynamics.

5.2.1 Main animal health and ecological consequences

In a long time perspective, uncontrolled spread of CWD will cause increased occurrence of disease with long-lasting negative effects on animal welfare and increased mortality in affected reindeer populations. In addition, we have to expect spread to other populations of cervids and corresponding effects in these, even if there may be variations between the species. Together with increasing environmental transmission, this will imply that other species, including humans, will be increasingly exposed for CWD prions.

5.3 Strategy 2: Eradicate disease

In a situation where we on the population level lack an efficient and feasible testing method that differentiates between infected and non-infected live animals, and no treatment or vaccine exist,

eradication of the infected population may be the only opportunity for eradication of the disease and minimizing the probability of spread. After an eradication this strategy will also imply that the area is fallowed[13] until we with reasonable certainty can expect that any infective material in the environment is eliminated. Subsequently, reindeer may potentially be reintroduced to the area.

When such a mode of action is used to manage a disease in wildlife, advantages and disadvantages have to be balanced carefully, since the consequences of the measure are very large. Such a measure will only be rational and efficient if there is appropriate certainty for the following:

- That the disease is established in the population and that a larger outbreak of CWD is unavoidable if the whole population is not eradicated.
- That the disease is not already present in other populations.
- That substantial environmental accumulation of accessible infective material has not occurred to the degree that it will cause reemergence of disease after a fallow period.
- That the pathogen causes a disease corresponding to CWD in white-tailed and mule deer in North America.
- That geographical spread will occur within short time and with great certainty if eradication of the population is not accomplished.
- That other measures will not be appropriate to limit the increase in occurrence in the population and the probability of spread out of the area.

5.3.1 Main animal health and ecological consequences

The ecological consequences of eradication of the wild reindeer on Hardangervidda will be large. The population is the largest in Europe and constitute an important genetic reservoir for the European wild reindeer (Chapter 4). To remove a large species that to such a subtstantial degree interact with other species, will most probably also have significant impacts on the ecosystem. The exact characters and magnitudes of consequences are not assessed in this report.

Animal health consequences are primarily the animal welfare implications during the eradication process. Dependent on choice of method, the animals will be exposed to stress. If such an operation should be performed, it will be important to evaluate the experiences from the corresponding process in Nordfjella Zone 1.

[13] Translator's note: Fallowed = left idle, in the current context meaning that the area is left without any reindeer or other potential CWD host populations.

5.4 Strategy 3: Control the disease

This strategy implies that a certain level of disease is accepted, but that measures simultaneously are accomplished to i) keep the occurrence in the wild reindeer population on Hardangervidda as low as possible to minimize the impacts of the disease and ii) to limit the probability of spread from Hardangervidda to other populations.

The different measures can be performed with varying intensities, related to which level of contamination and disease that is regarded as acceptable and the considered time perspective. Extensive and powerful measures will slow down the development of CWD on Hardangervidda and surrounding populations. This can be appropriate in a phase where work is performed that aims to reduce uncertainty, for example surveillance providing more knowledge about the occurrence of CWD in other areas. Measures accomplished in an early phase will in general have a larger effect than the same measures applied at a later point of time. Few and less intrusive measures will probably cause minor impacts on occurrence of disease and probability of spread. In a long-time perspective, the *cumulative effects* of the different measures determine if we manage to limit disease occurrence to a level regarded as acceptable.

Depending on degree of success, rapid implementation of extensive measures aiming to control occurrence may be succeeded by a strategy of eradication.

The strategy of controlling disease includes multiple measures that can be used indivdually or in concert (see Chapter 6). These measures span from different harvest strategies (for example 6.1.1 – Reduction of the population; 6.2.1 Change of gender proportion) to reduction of barriers or disturbance that currently restrict the area use of the reindeer on Hardangervidda (Chapter 6.1.4). The presumed most efficient measures relate to harvest of a large number of animals and will consequently have substantial ecological and potential animal health consequences.

The strategy of controlling disease may be appropriate when a high degree of uncertainty is perceived, and further collection of data will over time cause a substantial decline in the uncertainty. As described in Chapter 2.10.2, the estimates indicate that there most probably are very few infected animals left on Hardangervidda after the hunting season in 2020. In such an early phase, stochastic events may have a major influence on whether an implemented measure lead to control or eradication of the disease.

Continuation of the substantial harvest of adult males is a moderate controlling measure. The proportion of adult males (three years and older) in the population has already been lowered from 20 % in the years before 2019 to approximately 6 % after the hunting season in 2020. This provides us with a good starting point for a further reduction of the proportion down towards 0-3 % adult males (three years and older) during 2021. A rapid harvest of males may have a marginal probability of eradicating the disease if the actual prevalences lies in the lower part of the estimated occurrences, but will limit an outbreak even if the prevalence is higher. Continuation of a high annual harvest of males will contribute to a stable low proportion of adult males in the population and can lower R_0. Calculations in Appendix IV are made for males that are two year and older.

Another, more encroaching measure is to reduce the whole population towards a genetic sustainable level in combination with a lasting low proportion of males. It is currently difficult to state exactly how many individuals that are necessary for maintenance of a genetically viable population (for example to avoid inbreeding depression).

5.4.1 Main animal health and ecological consequences

The ecological consequences of a substantial reduction of the wild reindeer population on Hardangervidda will be similar to the consequences of eradication of the population (see above). Many of the measures described in Chapter 6 can however be accomplished without extensive ecological consequences (see below).

Accomplishment of the measures may also create an impact through the disturbance they cause. Repeated disturbance, especially in winter, may cause reduced grazing time, increased energy expenditure and thereby reduced condition at a critical period of the year. A challenge with winter harvest operations is that the herds on Hardangervidda typically will be large and that they through the late fall and winter consist of both females and males. For example, during the structural survey in 2020 two mixed herds were observed, one counting 1500 and the other 1900 animals and thereby together constituting 40-50 % of the current population.

It will hence be very demanding to perform a selective harvest of adult males in these herds, as the proportion of adult males (three year and older) currently is as low as 6 %. Selective harvesting will under these circumstances be very time-consuming and lead to major disturbance of a large number of animals. A harvest of adult males will be less challenging and enchroaching in periods where the adults male walk alone, for example in the spring period and during the summer. Disturbance during a harvest may also increase the probability for geographic spread of CWD if sufficient caution is not exerted (Mysterud et al., 2020e).

5.4.2 Control or eradication of disease in the context of learning-based management

Uncertainty can be divided into lack of knowledge and uncertainty caused by environmental variation and stochastic events (Bolam et al., 2019). Lack of knowledge is caused by incomplete understanding or incomplete information about natural phenomena and processes and can be reduced if targeted research and learning-based management create new knowledge. Uncertainty associated with coincidences and environmental variation, cannot be reduced by increased research, but will influence the probability of success of different measures. An adaptive and learning-based approach is based on the fact that the situation with CWD on Hardangervidda in 2020 is more complex than the situation in Nordfjella in 2016-17. A complicating uncertainty is the lack of good evidence for freedom from CWD in surrounding wild reindeer areas and other cervid populations. By using an adaptive approach, we recognize that the uncertainties currently are too large (see Chapter 7) to make a long-term management plan for Hardangervidda. However, even when a detailed long-term plan cannot be made, the overarching adaptive approach has to have a long-term horizon. Contrary to a strategy founded

on one large measure, as in Nordfjella, will such a learning-based approach be based on a set of large and small measure that together constitute elements of a learning process. In an adaptive management will the measures be adjusted continuously and systematic as knowledge increase. The systematic character of such an approach reduces the processual uncertainty (which often is substantial). Such a model does not exclude that a decision to eradicate the complete reindeer population on Hardangervidda is reached at a later point in time. Not all measures are necessarily crucial for disease control but they contribute to a set of measures whose cumulative effect increase the probability of reaching the goals.

To succeed, a learning-based strategy relies on increased surveillance and monitoring of both ecological and animal health and welfare parameters, including CWD testing. Such a learning-based approach can be used both if the long-term goal is eradication (Strategy 2) or control (Strategy 3) of CWD.

6 Further consideration of the strategies control and eradicate CWD

6.1 Controling disease – consideration of different measures with regard to control of spread of disease within and out of Hardangervidda, and in Norway

6.1.1 Reduction of the population on Hardangervidda

As mentioned in Chapter 5.4, population reduction to control CWD can be achieved through various measures. A sizeable harvest will, in addition to an effect on disease control, also increase the number of samples available for testing and thereby the ability to estimate CWD prevalence (or freedom from CWD). A harvest that is higher than the population growth will, however, not be sustainable over time, especially not if adult females are harvested. If this is done, we may reach a phase where the harvest must be reduced, causing a reduction in number of samples and the ability to monitor the development in infection prevalence. It is consequently important to balance the disease limitation against the capability to follow the epidemiological development. Large variations in number of samples can make efficient estimation of infection prevalence impossible (Walton et al., 2016).

6.1.1.1 Expected effect on the disease

Reduction of population density can contribute to disease control in several ways. This is thoroughly described in previous VKM reports (VKM, 2017). We recapitulate shortly:

- Less infected individuals. Reduction of a population will lower the absolute number of infected animals. This may decrease the risk for geographic spread of CWD to new areas.
- Reduced environmental contamination. Lowered number of infected reindeer will result in less environmental contamination and thereby diminish the probability for transmission to red deer and moose (see Chapter 2.5).
- Increased recruitment of calves. A decline in population density may increase recruitment, ie. that a higher proportion of the females get calves. Harvesting can then be increased and the proportion of infected animals reduced (Potapov et al., 2012). This effect is considered to be small.
- Shortened life span. Increased harvesting pressure in the period of population reduction cause a decrease in expected life length for all infected animals, and consequently a reduction of the R_0.
- Decreased R_0. It is uncertain if a reduced population density will cause a substantial decrease in the R_0 within the wild reindeer population (see VKM, 2017). Modelling of CWD in USA suggest frequency dependent transmission (Jennelle et al., 2014; Wasserberg et

al., 2009), ie. transmission occurring independently from the population density. Reduction of the cervid population density has not caused a change in R_0 (Conner et al., 2007; Uehlinger et al., 2016). Contact rates between cervids are sometimes density dependent (Cross et al., 2013; Habib et al., 2011), but it is uncertain if this is enough to have an impact on the R_0. An empirical work found higher CWD prevalence in areas with high population density of white-tailed deer as a spatial correlation (Storm et al., 2013).

Based on knowledge from white-tailed and mule deer in North America it is most probable that a reduction in population density have little effect on R_0, and that this alone not will be an efficient measure for reduction of R_0. However, data supporting this are not present for reindeer populations.

The expected effect on the disease is that a reduction of the population may have a lasting effect through a decrease in the probability for geographic spread. Reduction in R_0 due to shorter life span will, however, increase when the harvest is reduced again.

The time perspective for a population reduction in order to control disease will depend on whether the goal is reduced probability for geographic spread or reduced infection within the population. If the aim is to reduce spread and reduce infection in a short-time perspective, the action should be performed before the prevalence is too high.

A *critical success factor* is that the an eventual population reduction has to be performed in a way that prevent that the wild reindeer is chased out of the area and mix with other populations (Mysterud et al., 2020a).

Animal health and welfare and ecological consequences of a reduced population size on Hardangervidda will vary depending on the size of the reduction. A moderate reduction of the size of the population will primarily affect the economy and the culture associated with the wild reindeer on Hardangervidda. The genetic diversity may be reduced if a larger proportion of animals are culled, but exactly where this level lies is currently not estimated. After some time, a population reduction is expected to improve the condition and increase the calf production (calving rate and calf survival).

The wild reindeer population on Hardangervidda is in poor condition, it suffers from substantial parasite load, and it has experienced a large outbreak of footrot (in 2019). Hence, a population reduction has been discussed as a way of improving the conditions for this population and is expected to exert a positive influence on the body condition.

It is *uncertain* how much the population has to be reduced before the expected effects occur. It is furthermore uncertain how much and if the R_0 is changed by a population reduction alone. It is expected that the contact rates are changed, but it is uncertain if this affects R_0 sufficiently to prevent prevalence increase.

6.1.2 Change age- and gender composition on Hardangervidda

Several has proposed that increased harvest of adult males as a measure for control of CWD (Jennelle et al., 2014; Miller et al., 2020b; Potapov et al., 2012; Uehlinger et al., 2016). Increased harvest of adult males is the only approach where hunting with a certain probability can contribute to a decline in the R_0. Modellings of various transmission paths consistently indicate that intense hunting of adult males provides the greatest probability for control of CWD. We are then talking about a harvest approaching 80 % of the males (Potapov et al., 2016). A new empirical study of mule deer (Miller et al., 2020a) is reviewed in detail (Chapter 2.2.1.1). That study found that decreased harvesting of mule deer males caused a subsequent rapid increase in infection prevalence.

The expected effect on disease with a large harvest of males will consequently be that the R_0 decreases. Hard hunting pressure on males will normally imply both a change of the gender ratio and age structure, ie. higher proportion of females and a lower proportion of large males in the population.

The time perspective for a major harvest of males is one year, under the presumption that there are only a few infected males. If so, the measure can increase the probability for eradication of CWD. It can also be an appropriate measure for a longer period (Two years and further) in order to decrease prevalence. If they work according to the theory, the measures will provide an immediate effect, but it will be difficult to evaluate if the effect is as theorethically expected.

A shortened life length among infected males will be an important effect of intense hunting. A hard hunting pressure on the whole population cannot be maintained over a long period of time, as harvesting will be larger than recruitment. Intense hunting over long time is however possible among the adult males, since each male can mate with many females and the proportion of males consequently means little for the population growth rate.

A *critical success factor* is that it will be challenging to find a balance in the harvesting of adult males that is sustainable over time. It is hence mandatory with good models that annually are calibrated with the actual harvest, and that the effect of the harvest is simulated with population data from Hardangervidda to demonstrate how big the harvest of males need to be to achieve a sufficient reduction in R_0.

Animal health and welfare and ecological consequences of the measure are:

Calving rate: In a polgynous species as the wild reindeer can the gender ratio normally be extremely skewed without influencing the proportion of animals that become pregnant. It is expected that yearlings can substitute a substantial part of the mating. It is no clear expectation of a reduced calving rate with a low proportion of adult males in the population, but it cannot be excluded.

Calving time: A low proportion of large males can delay the rut and thereby cause late calving period. Experiments on semi-domesticated reindeer in Finland indicate that these effects are

small, ie. only 4-5 days when only yearlings were used for mating (Holand et al., 2004). However, the studied herd in Finland received feeding, was in good body condition and were kept in a small area. It cannot be excluded that the effects are larger in a wild population. A low proportion of large males is expected to delay the calving period, but how profound this effect will be in the Hardangervidda population is not known in detail.

Rutting period and body condition: It has been argued that late calving is a cause of low body condition in females, as they nurse their calves to a later date in the fall. In a study of Finnish semi-domesticated reindeer did mating three weeks apart only lead to ten days difference in calving date and reduced calf weigh in the fall, while the females that were mated late, had similar body weights as the year before (Holand et al. 2006). This is also the theorethical expectation; that the females rather reduce the investment in their offspring than putting their own survival at risk.

Adult males dig up food to the females: It has been claimed that an important function of adult males is to dig away snow to provide access to pasture for the females. Thera are no scientific studies of this, and it is regarded as less probable that this will cause a measurable impact after a reduction in the proportion of males.

Uncertainties: It is uncertain which mechanism that actually cause lower prevalence growth when there are few adult males in the populations. It is uncertain to which degree contact rates between individuals in addition change with changing gender ratio and age structure among the males.

It is likely that encroaching measures can cause unexpected effects, and that these may cause unintended negative consequences.

6.1.3 Change the area use of wild reindeer on Hardangervidda and the connectivity to surrounding wild reindeer populations

How the wild reindeer use Hardangervidda varies a lot during a year. This is partly a consequence of the nomadic behavior of the species and natural circumstances like the temporospatial access to pasture, but also a consequence of human traffic and disturbance (see Chapter 4). The newly introduced Quality Norm for Wild Reindeer formulates criteria for the wild reindeer areas and the quality of the wild reindeer populations (Kjørstad et al., 2018). The management of Hardangervidda has for a long period implemented and considered measures that may improve the area use of the wild reindeer.

A changed area use can be achieved either by reduction in the number of animals and/or a change in the population's age and gender composition. The scientific base and the consequences of these measures is described in detail in Chapter 6.1.1 and 6.1.2 above. Below we discuss changes in area use as a consequence of measures that increase or decrease the area available for the wild reindeer.

This can be achieved for example by minimizing human disturbance, so that the wild reindeer is encouraged to extended area use, or by putting up fences that prevent reindeer from moving into surrounding areas used by other wild reindeer populations.

The expected effect on the disease: Reduction of barriers (human activity) may contribute to a reduction of functional density and thereby the contact rate between infected and non-infected individuals[14]. Barriers that prevent connectivity to other areas and populations will contribute to prevention of spread of infection with animals[15]. The probability of exposure for environmental contamination will be reduced when the population is diluted. If the wild reindeer changes its area use considerably, so that it no longer use the same areas it used to, will the population avoid eventual accumulated environmental contamination. However, this can also introduce environmental contamination to new areas.

The time perspective of installing new and reducing old barriers to induce changes in areas use, reflects that this is a work- and time-consuming measure that involves various stakeholders on Hardangervidda. Based on experience will some time (one or more years) be needed before the measures are implemented. The processes should hence be initiated as soon as possible. It is expected that the measures will exert an effect as soon as they are installed and be efficient as long as they are in operation.

A critical success factor in the areas where the aim is to encourage the wild reindeer to utilize a larger area, will be to reduce human activity sufficiently. In the areas where the aim is to reduce connectivity, either within Hardangervidda or on its borders, experience from Nordfjella show that such measures can be effective. A major effort is, however, demanded both in shape of continuous follow-up and investments.

Animal health and welfare and ecological consequences of these measure are among others the large negative effect fences can have on a natural environment by constructing negative barriers for other animal life, and increase mortality of among other species galliform birds when they collide with or entangle in such installations (Hayward and Kerley, 2009).

Uncertainties: There is a clear connection between the area use of wild reindeer and disturbance/distance to human infrastructure. It is expected that this will influence the efficiency

[14] Translator's note: The original text said «…kan bidra til å redusere tettheten og dermed kontakten mellom smittede individer» which translates directly to «may contribute to a reduction of density and thereby the contact between infected individuals». The words "functional" and "and non-infected" are added by the translator.

[15] Translator's note: The original text said «Barrierer som hindrer konnektivitet til andre områder og villreinbestander vil bidra til å hindre at dyr fra andre bestander bringer med seg smitte ut av området.» which may be directly translated to «Barriers that prevent connectivity to other areas and wild reindeer populations will contribute to prevent that animals from other populations carry pathogens out of the area.». The sentence has been changed by the translator to a more general statement.

of this measure. The degree of success will also rely on a sufficient reduction of the human activity and disturbance level. The area use of wild reindeer is also affected by the population size.

6.1.4 «Mark, test and cull» infected individuals

To remove infected animals selectively from a population demands that they can be tested while still alive, and that they simultaneously are marked in such a way that they subsequently can be tracked and culled. We have provided the knowledge basis for such a measure in Chapter 2.2.1.4. Only one case (Wolfe et al., 2018) of such a «test and cull» effort is described. This was an effort performed in a small population of free-ranging mule deer in Colorado, USA. The study from Colorado included testing and culling performed over several years (Wolfe, 2018).

The expected effect on disease is that such a measure probably will reduce the prevalence of CWD. The management authorities have planned radiocollaring of about 50 animals on Hardangervidda. Testing of such a low number will however not be sufficient to significantly improve disease prevalence estimation or reduce infection prevalence[16].

A critical success factor for use of the method on wild reindeer would be to have opportunities to perform immobilization efficently, probably by use of helicopter. It is likely that such a method could be useful if a smaller number of animals is to be tested.

The time perspective of such a measure will vary depending on which group(s) of animals it should include.

Animal health and welfare and ecological consequences of selection and culling of CWD-infected animals will vary with the extent of the measure. Animal welfare aspects of marking were reviewed in a risk assessment from VKM (2013, Doc.no 11/804-Endelig) where the contemporary practice of immobilizing and radiocollaring of reindeer was evaluated. The assessment concluded that the protocol for reindeer appeared safe and could be recommended, and that no documented long-term effects have been documented. Experiences from wild reindeer marking indicates that the animals easily are running scared when they are approached by helicopters. The herds can run long distances at high speeds. The flight response seems to increase with repeated approaches by helicopter (Pers. Comm. Roy Andersen, NINA). Such an increasing flight response is presumably associated with stress.

[16] Translator's note: The original sentence was written: «Forvaltningsmyndighetene har planlagt radiomerking av noen titalls dyr (n = 50) på Hardangervidda, men testing av et slikt antall vil ikke ha en vesentlig effekt på å avdekke forekomst av sykdommen, og heller ikke på muligheten for å kunne redusere prevalensen av sykdommen.» that may be directly translated into «The management authorities have planned radiocollaring of some tens of animals (n = 50) on Hardangervidda, but testing of such a number will not have an appreciable effect on the revelation of occurrence of the disease, and neither on the opportunity for been able to reduce prevalence of disease.»

The study (Wolfe et al. 2018) empasized that an animal may experience strain when immobilization are repeated in a «test and cull» situation. Consideration of animal welfare aspects ought to be included in a comprehensive evalutation of the necessity of such a measure. This should elucidate potential impacts both on the individual and population level.

The uncertainty about the effects of such a measure are substantial, as no available studies describe and evaluate the use of selective culling used as a measure in large populations. The uncertainty includes both reduction of CWD infection and eventual negative impacts on animal welfare.

6.1.5 Prevent and limit spread of CWD to and from semi-domesticated reindeer

The detection on Hardangervidda increase the uncertainty about presence of CWD also in other areas, in particular areas surrounding Nordfjella. The connectivity between populations of reindeer or between wild reindeer and other populations of cervids increase the probability for spread of CWD. The overview provided in Chapter 4.3.4 show that the connectivity between the wild reindeer populations and semi-domesticated reindeer herds and between semi-domesticated herds in some places is very high.

Many of the measures for wild reindeer are in principle also relevant for the reindeer herding industry, even if they may look different. All measures that reduce the probability of animals dispersing out of their normal range should be considered. This may include reduction of herd size, reduction of proportion of adult males and/or measures that physically influences the exchange of animals. The extent of measures must be considered on the basis of local circumstances. Which measures that should be applied must be considered in relation to the development of the occurrence of CWD on a larger scale.

The measures mentioned above will not have any *expected effects* on the occurrence of CWD among wild reindeer on Hardangervidda but can prevent spread from Hardangervidda and eventually other infected populations to semi-domesticated reindeer, and from semi-domesticated reindeer and further on.

The time perspective of these measures is that they should be implemented as soon as possible but are most urgent for the semi-domesticated reindeer herd closest to Hardangervidda and Nordfjella. The different measures will exert their effect at different points of time, but many of them will have an immediate effect. The preventive effect will last as long as the measures are adhered to and maintained.

Degree of adherence and number of accomplished measures will be decisive for which degree of prevention or limitation of spread the measures will generate.

Animal health and welfare and ecological consequences are treated in the chapters that describe corresponding measures for wild reindeer.

Uncertainty: It is uncertain if CWD is present in the cervid populations and the semi-domesticated reindeer herds. It is also uncertain if the effect of the described measures is sufficient to completely prevent spread to and from the semi-domesticated reindeer herds.

6.1.6 Measures directed against surrounding populations of other cervids

The gene that code for the prion protein is mapped for various species of cervids (Cullingham et al., 2020; Robinson et al., 2012). This gene is sufficiently similar within the Cervidae that there is a danger for transmission of prions between different species in the family. In USA and Canada CWD is found in free-ranging mule deer, white-tailed deer and wapiti, and a few moose. It is regarded as likely that infection has been transmitted between these species on several occasions. Different species of cervids do rarely have direct contact. It is hence presumed that environmental contamination constitutes the largest probability of transmission between species (VKM, 2017). On Hardangervidda, this probability will increase with the number of infected reindeer. More infected individuals imply more environmental contamination and increased are use overlap with roe deer, red deer and moose. In particular red deer and moose are present in the areas used by reindeer on Hardangervidda. We may differentiate between small-scale measures, like the ones applied around salt licks, and measures that have a more general impact on the overlap in habitat use. In this paragraph we discuss reduction of overlapping area use in a more large-scale context and reduction of population densities of moose and red deer.

Expected effect on disease: The probability for transmission of CWD to red deer and moose is smaller the less animals that use an area shared with infected reindeer. There is no documented knowledge about how low the population density of cervids has to be to reach an acceptable probability of transmission between species, ie. it is not possible to know for sure how much the populations of moose and red deer have to be reduced to minimize the probability for transmission. A course assessment of what a low population density is, imply that we have to reach close to one animal per square kilometer forest/mire, or even lower. The number is based on general knowledge about the variation of cervid density in Norwegian municipalities, and what is perceived as low population density. It is important to emphasize that the number not is based on any data on probability of transmission of disease.

It is also relevant with targeted eradication of populations of moose and red deer that to a larger extent than others use the mountain areas of Hardangervidda.

Time perspectives: The measure should, based on a precautionary principle, be initiatied as soon as possible, or as soon as it is clear that CWD has gained foothold in wild reindeer on Hardangervidda. The probability of transmission will decline as soon as the population densities of cervids are reduced in areas that overlap with the home range of the wild reindeer on Hardangervidda. The effect of the measures will be reduced by population growth at any time of the process, and continuous efforts are needed to keep the populations low.

Critical success factors: One critical success factor is that the population actually is reduced to the level necessary to provide the desired effect.

Animal health and welfare and ecological consequences: The measure will presumably have limited and local consequences, as the cervid populations are large and viable.

Uncertainties: We do currently not know for sure that transmission of infection to other species of cervids will occur, so the rationale of the measure relies on a precautionary principle.

6.1.7 Targeted culling of animals that show signs raising clinical suspicion

Estimated prevalence of CWD on Hardangervidda is low (Chapter 2.10). In Nordfjella Zone 1 did only the first CWD-positive reindeer show obvious clinical manifestations of disease. If the situation on Hardangervidda is comparable, we search for very few clinically ill animals, and the opportunity to perform a targeted culling will be strongly limited due to the low probability of spotting them. Simultaneously, we are in a situation where coincidences and stochastic events may ply a large role. Scientific evidence from North America shows that CWD-infected animals easier are felled by predators, killed in traffic accidents or shot by hunters. This may be related to subtle, not easily recognized behavioral changes. On Hardangervidda will it occasionally be possible to observe many animals over a long period of time (hours). In such a situation, very experienced reindeer hunters may have a certain success in pointing out animals with CWD, given that they given unlimited authoritizaton to do so. This would be a relatively simple and inexpensive measure to implement in combination with other kinds of surveillance of the wild reindeer, and it will create few negative consequences.

The expected effect on disease of culling an infected animal is high, as these animals represent the largest known source of infection with CWD, in particular in a situation with low prevalence and limited environmental combination. The problem with CWD is that infected animals shed prions long before they show clinical manifestations of disease. Targeted culling is however not that efficient that it can eradicate the disease completely.

Time perspective: The effect will be largest if the measure is implemented as soon as possible and, if possible, continuously developed. As any removal of an infected animal from the populations will lower the probability of transmission, a culling will have an immediate and lasting effect.

Critical success factors: It will be adequate if hunters are allowed to cull cervids showing clinical manifestations of disease, even when these belong to species or are individuals that the respective hunter not posess a hunting permit for. Observation and eventual culling of animals that raises suspicion of disease can be facilitated during various ranger inspection missions and population monitoring and surveillance, as an important success factor will be that as many of such observations as possible result in culling of suspicious animals.

Some of the suspicious animals that are culled will probably suffer from other conditions than CWD. Such cullings will represent unintended, but positive *animal health and welfare and ecological* consequences for the populations. Culling of suspicious animals may in addition lead to lowered R_0 for other parasite and infectious diseases, and that chronically ill animals are releaved of the strain and suffering that the disease cause.

Uncertainties: It is uncertain how many animals with clinical manifestations that exist, and to which degree we will manage to cull them, indicating the uncertainty about which effect that is achieved if a targeted culling is performed. However, the large risk associated with the presence of such animals in the population, should be given much weight when considering the uncertainties with such a measure.

6.1.8 Measures that reduce environmental transmission

The theme for the report VKM 2018 was for a large part environmental transmission. It described that permanent salt licks that cervids have access to, probably are very important hot spots for transmission of CWD. The reason for this this is that very many animals visit these places, and because the animals lick on surfaces and ingest soild when they are there. The probability of excretion of prions from infected animals is consequently high in that location, and so is the probability of exposure for this infectious material for other animals.

Recently published research on excretion of prions and their persistence in soild (see Chapter 2.4 and 2.5) confirm that this is a sound assessment. The preliminary findings in the Salt Lick Project (see Chapter 2.9.1.1) support the assessment of salt lick sites as potential hot spots for transmission of disease.

The second important hot spot for transmission of CWD that is reviewd in VKM 2018, are carcasses of infected animals and the soil below and around them. Recent research strengthens also this assessment (see Chapter 2.5).

Other places where wild reindeer gather on Hardangervidda may also have increased environmental contamination. This may be snowdrifts where they gather in hot weather and potentially banks where the animals gather to drink wather or passes and isthmuses that many animals pass through. The occurrence of such sites and how they are used (how many animals, how long time used, which activity) is to our knowledge not mapped.

The low prevalence that is estimated for Hardangervidda, indicates that we probably are in an early phase of an outbreak (see Chapter 2.6.1.5). The amounts of infective material in the environment are then regarded to be sparse.

To prevent wild reindeer from access to permanent salt licks is anyway an important measure if accumulation of and exposure to prions shall be prevented as much as possible.

Measures applied to render carcasses and offal inaccessible for cervids are also important to reduce the probability of environmental contamination and exposure.

Measures directed towards reduction of population size and/or density (see Chapter 6.1.1 and 6.1.3) may decrease the number of animals on salt licks and other gathering sites, and thereby lower the probability of transmission through the environment.

The expected effect of minimizing the cervids' access to permanent salt licks will be that we relatively easily minimize transmission from an obvious environmental source.

The effect of measures directed towards treatment of carcasses and offal, will also contribute to minimization of the probabilities of environmental transmission.

How much these measures actually will mean, depends on several unknown factors, among them how many animals that actually are infected, how much prions eventual infected animals excrete (on for example the salt licks), and how much prions prions that exist in a wild reindeer that die from/with CWD. In the current situation, we should expect that the effect is numerically small, but that it although can make a difference.

The effect of eventual measures to prevent use of other gathering sites than salt licks will depend on how many animals that use these places, how long and often they stay there and what they do. With the current prevalence, we should expect that the effect is relatively small, among other causes because the animals will move to other places that fill the same needs.

Time perspective: Measures that prevent environmental transmission from salt licks and carcasses should be initiated as soon as it is practically feasible, as it is obvious that they will minimize environmental transmission, have few negative consequences and are (relatively) uncomplicated to accomplish. Measures directed against other gathering sites must be considered individually and after a more detailed mapping of the occurrence and character of such places. The effect of the measures will occur immediately and provide a lasting reduction of the potential for environmental transmission.

Critical success factors will be that we manage to map and handle the gathering sites so that we either minimize environmental contamination or prevent the cervids' access to it (and thereby exposure).

Animal health and welfare consequences of the measures directed against salt lick sites will in addition to the effect on prion transmission, also minimize transmission of nematodes and other pathogens with a fecal-oral route of transmission. The measures will also reduce the frequency and degree of contact between livestock and cervids and between different species of cervids, and thereby lower the probability of transmission of pathogens between them. To decrease the availability of carcasses may interrupt the transmission cycle for parasites that are found in cervids (*Toxoplasma, Cryptosporidium,* tapeworms).

Ecological consequences of preventing access to permanent salt licks may possibly include changes in the grazing behavior of both livestock and wildlife. Insufficient sal supply can possibly stimulate to increased animal movement. Decreased availability of carcasses will influence the access of food for all larger scavengers and may possibly have consequences for the ecology of these species. Smaller animals will although get access – maybe to a larger degree.

Uncertainties: There are several uncertainties concerning this assessment. We lack knowledge about the prevalence of CWD on Hardangervidda, and the necessity and the effect of the

measures related to salt licks and carcasses will for a large part be associated with how many animals that are infected. There is, however, little doubt that this measure has effect against environmental transmission. There is little published knowledge about the impact of removal of salt licks on grazing pattern and welfare of sheep. Even if many sheep farmers express that having sheep at pasture without being able to use salt licks will cause major inconvenience, our impression is that there is great variation in their experiences. This may of course be related to local conditions like herd management, sheep density, available pasture, topography etc.

We do not have any knowledge about the importance of gathering sites other than salt licks and can hence not assess how important it is to perform measures directed towards these.

6.1.9 Selective breeding based on genotype

Appendix I describes management of classic scrapie through breeding. This has been successful in many European countries. A prerequisite is that the various genotype variants susceptibility to the relevant pathogen is known. Subsequent to the outbreak in Nordfjella were several variants of the *PRNP* gene investigated (Chapter 2.8). Comparable to the situation concerning scrapie in sheep, there are clear differences in susceptibility to CWD in reindeer. Gene variant A and C seem t increase susceptibility, while gene variant B probably is least susceptible. Consequently, such a strategy would imply to aim at an increased prevalence of the B variant. In the wild reindeer subpopulation in Nordfjella Zone 1 was the B variant found in 34 % of the animals, and in 11 % was the variant present in double dose (homozygous). A breeding program would specifically aim at an increased proportion of animals with the BB genotype, as these are considered least susceptible. It is important to note that these animals have reduced susceptibility, and not are completely resistant against infection. In some semi-domesticated reindeer herds is the prevalence of the B variant close to 70%, something that will could be an aim for such a breeding program. The high prevalence among semi-domesticated reindeer may also indicate that the B allele not is associated with negative traits, something that is consistent with the experiences from comparable programs in sheep (see Appendix I). It must be emphasized that breeding as described here, must be complemented by monitoring of important phenotypic traits as growth and occurrence of disease. Marker-assisted breeding, as such programs are called, can also cause a reduction of genetic variation. In general, however, is the genetic variation high in reindeer compared to other cervids in the Norwegian fauna.

Breeding programs like this are often based on selection of males, typically with the BB genotype in the described current case with reindeer. By using such males will the frequency of the B variant increase, as all offspring of these males will carry at least one copy of the B variant.

6.1.10 Reduction of number of sheep grazing on Hardangervidda

Knowledge about susceptibility of sheep for CWD is reviewed in VKM 2016 (Chapters 2.1.9.1 and 3.4) and the eventual role for sheep in spread of disease is thoroughly discussed in VKM 2018. A summary is provided in Chapter 2.8.3.

The expected effect of a reduction in number of sheep grazing on Hardangervidda or a ban on sheep grazing is considered minor or absent. This is based on the low probability of spread of CWD with sheep[17], the relatively low numbers of sheep grazing, and the fact that there are few sheep grazing in the areas that are most used by wild reindeer. This is especially true if contact between wild reindeer and sheep is minimized by measures preventing environmental transmission at salt lick sites as described in Chapter 6.1.9.

This assessment is based on the presumption that sheep are not susceptible for natural infection with CWD prions from cervids and hence only function as passive carriers of the pathogens.

The uncertainty associated with this is related to this presumption, and if evidence show that infection in sheep although occur, will the assessment be incorrect.

6.1.11 Introduction of predators

It has been suggested several times that the abscence of large predators is a factor that may facilitate establishment and spread of CWD among cervids. This was also discussed in VKM 2017 Chapter 4.4. There are no new scientific reports on the theme CWD and predators, and it is currently not possible to substantiate an effect of variable predators on occurrence of CWD in Norway. A review of knowledge status is provided in Chapter 2.8.4.

The expected effect on CWD of introduction of predators as wolf or wolverine to Hardangervidda is unclear.

Implementation of such a measure should only be done when evidence substantiates that predators can limit spread of CWD under Norwegian conditions. It is expected that an eventual effect by such a measure would arise gradually.

Critical biomedical success factors will be that the predators maintain a selection pressure on infected animals, and that they themselves not spread prions out of the area. There is a long list of other critical success factors that ought to be present if this measure should be implemented. In Norway, the large predators are regulated according to a compromise settlement («rovdyr-forliket») made in Stortinget (the Norweegian parliament). Geographically, Hardangervidda lies south of the current zone for wolverines and far west for the wolf zone, and major political amendments would be needed if this should be implemented. It is not within our mandate to consider these sociopolitical circumstances.

Animal health and welfare consequences: Introduction of wolverine and wolf can cause an increase in pathogens that have their intermediate stage(s) in the tissues of reindeer and predators as final hosts, as for example tape worms and tissue cyst-forming coccidia. On the

[17] Translator's note: The original statement was «Basert på den lave sannsynligheten for at sau kan spre skrantesyke,» which translates to «Based on the low probability for sheep being able to spread CWD,…»

other side may predators selectively remove animals that suffer from other diseases than CWD. It is for example tempting to think that animals with grave footrot would have been killed rapidly if wolverines or wolves were present. We do, however, the relative importance of spread from animals with footrot compared to infection from environmental sources, but it seems plausible that removal of diseased animals decreases the pathogen exposure for susceptible individuals.

Ecological consequences: Colonization by wolves will certainly have considerable consequences on a number of matters concerning the cervid populations on and around Hardangervidda, in addition to the eventual effects on CWD. Having wolves in the mountains, is not compatible with the current use of same areas as pasture for sheep, and cessation of grazing will also have consequences on the ecology of Hardangervidda.

Uncertainties: There are many uncertainties in this consideration. To introduce predators for control or even eradication of CWD, has never been tried. We do for example not know how selective wolverines or wolf will be, escpecially when animals are in the early stages of the disease. We also do not know to which extent the predators will be restricted to hunt wild reindeer as prey, or how the presence of large predators will affect the behavior and area use of wild reindeer.

6.2 Eradicating of the pathogen – consideration of measures with regard to eradicate the pathogen from Hardangervidda and Norway

As described in Chapter 5.3 and in VKM 2017 Chapter 10.1.3 eradication of the whole infected wild reindeer population is the strategy that provide the largest probability of eradication of the disease.

The expected effect of eradication depends on the fulfillment of the criteria described in Chapter 5. Only then may the measure result in eradication of the disease.

Time perspective: The probability of eradication of disease will be larger the earlier the measure is implemented. Removal of all infected animals will have immediate effect, and if this is done will CWD probably not become established on Hardangervidda.

We cannot with certainty conclude that such a measure has succeeded in eradicating the disease before several years after a reintroduction of wild reindeer, ie. that new animals not are infected from the environment or that the infection is spread within and from other populations.

A critical success factor for this measure is that it is possible to prevent infection of the reestablished population from environmental contamination or by spread from other populations of cervids. A prerequisite to succeed in eradicating CWD from Norway by eradicating the wild reindeer on Hardangervidda, is that we with sufficient certainty can exclude that the prions are present in other populations of cervids.

Animal health and welfare and ecological consequences of this measure are described in Chapter 5.

Uncertainty about occurrence of environmental contamination, persistence of prions in the environment and occurrence of CWD in other populations of cervids, create doubt about the achievability of eradication of CWD from Hardangervidda and Norway through eradication of the wild reindeer population.

7 Uncertainties

7.1 Important uncertainties in the current assessment

CWD on Hardangervidda is a typical complex problem where the probability of different outcomes of events is influenced by an intricate interplay of many factors (SAPEA, 2019). This creates uncertainty on many levels of the current assessment.

Some uncertainties are more fundamental and significant for this assessment than others. Below we list a prioritized list of five uncertainties with a short description of the effect they have on the assessment:

7.1.1 Knowledge gap concerning the occurrence of CWD in other populations of reindeer and other cervids:

In the assessments of the situation in Nordfjella Zone 1 given by VKM in 2016-2017, it could be assumed that if the pathogen only was present in that area, an eradication of this population would provide a decent chance for successful eradication fo the pathogen, if we only went to action rapidly and with great force. We now know that the pathogen is present in at least one additional population, but we have insufficient knowledge to assess if it also is present in other populations of reindeer or other cervids. This increases the uncertainty about the possibility of eradication of CWD from Norway through measures directed towards the wild reindeer on Hardangervidda.

7.1.2 Knowledge gaps concerning occurrence on Hardangervidda:

The uncertainty of the estimates of prevalence in the Hardangervidda population, in particular among the females, cause a small degree of uncertainty about if we at all have an outbreak, (ie. if there are several infected animals). Our lack of knowledge about which phase this outbreak is in constitute an even larger uncertainty (i.e., how many infected animals are there). This knowledge gap creates uncertainty about the time perspective, ie., how urgent it is to implement measures, and how strongly we need to apply measure to reach the desired aims. How and when measures should be applied and which consequences they create will vary depending on our approach very much, i.e., if we choose to base our management on the presumption that only a few males are infected, or if we presume that several males, females and juveniles carry CWD prions.

7.1.3 Knowledge gap concerning transmission and infection with the actual CWD prion strain in Norwegian cervids:

New knowledge that show that the prions found in Norwegian wild reindeer represent a new strain, increase the uncertainty about to which degree we can presume that an outbreak of CWD

will have the same course and consequences as the outbreaks in white-tailed and mule deer in North America. Data from the outbreak in Nordfjella Zone 1 do on one hand show great similarity with what is described from North America. On the other hand, knowledge about small differences concerning pathogen transmission may turn out to be important for choice and design of measures. A transmission that is more efficient and a shorter disease course could make it more relevant with rapid and strong measures, while less efficient transmission and longer disease course would give us more time to act.

7.1.4 Lack of knowledge concerning environmental contamination and persistence of prions:

We do miss some knowledge concerning where there is environmental contamination and how the relevant prions will persist over time in a Norwegian mountain environment. This implies that we lack knowledge about how environmental transmission may have an impact on the outcome of different strategies and measures.

7.1.5 Lack of knowledge about environmental factors that affect the occurrence of CWD:

We have not found knowledge that provide evidence to support the assumption that environmental conditions (population density, demography, nutrition, anthropogenic disturbance, etc.) are factors that dispose the wild reindeer on Hardangervidda (and in Nordfjella) for outbreaks of CWD. This uncertainty underlines the need for a holistic approach where the measures, in addition to minimizing the occurrence of CWD, must be implicated in a way that optimize conditions for life for a future wild reindeer population.

8 Conclusions

The detection of CWD in a wild reindeer on Hardangervidda complicate the management of this serious infectious disease in Norway. Hardangervidda is the home range for Europe's largest remaining population of wild reindeer. An outbreak of CWD on Hardangervidda will have large serious consequences for this population and will constitute a high risk of spread to other populations of reindeer and other cervids. It will be very demanding to prevent further spread of the disease.

The situation is substantially different from the situation after detection of CWD in three wild reindeer in Nordfjella Zone 1, described in a similar report in 2017. Firstly, this implicates a substantially increased uncertainty about the occurrence of the disease. Secondly, the wild reindeer population on Hardangervidda is larger and consequently economically more important. The population uses a considerably larger area and is more difficult to delineate and control compared to Nordfjella.

8.1 Knowledge update

1.1-1.2 The understanding of CWD

Since 2018, American and Canadian studies have not provided new knowledge about epidemiology, etiology and pathogenesis that necessitates major revisions of the assessments in previous VKM reports concerning CWD. On the contrary, new studies confirm the knowledge the previous assessments were built on. We have, however, gained access to published analyses of data concerning CWD in wild reindeer in Nordfjella.

Inoculation trials in bank vole and transgenic mice show that the CWD isolates from the Nordfjella outbreak are not identical to the North American. This strengthens the hypothesis that the prion strain that caused the outbreak among wild reindeer in Nordfjella, not originate from North America.

That the isolate from Norway are characterized as a new prion strain increase the uncertainty in the consideration of the knowledge based on research on CWD in North America, and to which degree this is extrapolatable to Norwegain conditions. Laboratory investigations, epidemiological descriptions and genetic analyses do although show that the CWD in wild reindeer in Nordfjella displayed characteristics similar to CWD in white-tailed and mule deer in North America. There is consequently no reason to presume that CWD in wild reindeer in Norway will be very different from CWD as it is described in the available scientific literature.

1.3 Prevalence estimates in the wild reindeer population on Hardangervidda

Over 4000 wild reindeer from the Hardangervidda population have been examined for CWD. About 70 % of them are examined both in brain and retropharyngeal lymph node. The prevalence of CWD is estimated to 1-2 adult males (95 % credibility interval: 0-10 individuals)

after hunting in 2020, but the number of infected adult females and juveniles cannot be estimated with certainty because of insufficient number of samples. If we presume that the infection pattern is similar to the pattern in Nordfjella, the whole population may include 3-5 individuals (95 % credibility interval: 1 – 19 individuals), but these estimates are uncertain. Even though the estimates are uncertain, they show that the disease is discovered in an early phase of what can be a larger outbreak of CWD. In such an early phase, will there still be a small probability of eradication of CWD through comprehensive measures without eradicating the whole population, but this opportunity will vanish as the number of infected animals and the environmental contamination increase.

1.4. Consideration of the probability of abscence of infection in populations of cervids

Probabilities of abscence of infected animals in the wild reindeer subpopulation in Nordfjella Zone 2/Raudafjell and in the semi-domesticated reindeer herd on Filefjell are estimated. Based on the samples analyzed until the 4th of December 2020 is the probabilities for detection of disease with only few (3-4 or more) infected individuals present 82 % and 84-91 %, respectively.

The knowledge base is insufficient for estimation of similar probabilities of absence of CWD in other populations of cervids. The probability of absence will vary with the degree of contact with Nordfjella Zone 1 and Hardangervidda.

2. The case on Hardangervidda

The wild reindeer on Hardangervidda with detected CWD had a slaughter weigh of 58 kg, an estimated age of 8 years and *PRNP*-type A/D. The performed examinations provide identical results as for CWD-positive wild reindeer from Nordfjella. The finding is consequently interpreted as a part of the same outbreak as in Nordfjella. Genetic analyses show that the male most probably originated from Hardangervidda and not from Nordfjella. The animal had PrP^{Sc} only in the retropharyngeal lymph node and not in the brain sample. Under the presumption that the course of infection is 2-3 years, this indicates that it was in an early phase of the infection. Consequently, it is most probable that this male was infected on Hardangervidda.

3. Special conditions concerning Hardangervidda and the wild reindeer population there

The wild reindeer population on Hardangervidda represent great values in an ecological perspective and an important genetic capital for European reindeer. Then Hardangervidda National Park was established in 1981, protection of the wild reindeer was a major motivation behind the decision.

Surveillance data and research show that the wild reindeer population on Hardangervidda is in bad condition. The animals has substantially lower nutritional condition than other wild reindeer populations, and the population has suffered from high occurrence of the disease footrot and high parasite load. The movement pattern show that the wild reindeer only is using a small part of what theorethically should have been accessible area. The actual population density is high,

especially in the summer. This is attributed to landscape encroachment and human disturbance that scare away the wild reindeer.

4. Strategies

No measures.

If no measures against CWD are put in action, we will expect that the coming years will bring:

- Increase in the occurrence and, as time go by, a larger outbreak on Hardangervidda.,
- Spread to surrounding wild reindeer populations.
- Increased environmental contamination, diminishing the potential for future limitation and eradication.
- Increased occurrence of CWD cause increased probability of human exposure.

In a longer time perspective, the following events should be expected to occur:

- Spread to semi-domesticated reindeer herds.
- Spread to other cervid species.
- Increased occurrence of CWD, providing an increased probability of spread out of Norway.

In this context is hunting with ordinary quotas regarded as «No measures», while the increased harvesting of adult males that was implemented in 2019 and 2020, should be regarded as a measure.

Control disease.

How strongly the conservation value of the wild reindeer population is weighted against the value of minimizing the risk of spread of CWD, decides which measures that should be selected. We have not considered the societal and administrative aspects of the measures. How much emphasis that is placed on uncertainty, for example about the CWD occurrence in other areas, will also play a decisive role.

Measures for control of occurrence of CWD may have as their main goal to:

- keep the level as low as possible to minimize transmission[18] and thereby the occurrence and impact of the disease within the wild reindeer herd on Hardangervidda

[18] Translator's note: The original sentence was «holde nivået så lavt som mulig for å minimere smitterate» which literally is translated to «keep the level as low as possible to minimize infection rate» where «smitterate» in the text above have been translated to R_0. However, as R_0 not necessarily will change if the «level» (interpreted as «prevalence») is reduced, «smitterate» is translated to «transmission» in this context.

and/or

- limit spread of the disease out of Hardangervidda and within Norway.

The selection of measures depends on which of these two aims that are most prioritized. Several measures can be implicated at variable scales. Few and mild measures will probably only have little effect on disease occurrence and probability of spread. Comprehensive and powerful measures will be able to slow the development of CWD on Hardangervidda and spread to surrounding populations. This may be appropriate in a phase where we work actively to gather information that will reduce uncertainty. Measures intiated in an early phase will have a larger effect than similar measures initiated at a later point of time, when the prevalence and thereby the infection pressure has increased. In a longer time perspective will the *combined effect* of different measures decide whether the disease is limited to a level that is regarded as acceptable.

Rapid implementation of comprehensive measures to limit occurrence may also be a foundation for subsequent measures that aim to eradicate the disease.

Eradicate disease.

It is unlikely to succeed in eradication of CWD from Hardangervidda unless the infected population is removed. It is not clear if removal of the infected population is sufficient to eradicate the disease from Norway (see uncertainties).

That eradication of the disease should ensue as a consequence of control measures, i.e. by coincidental removal of all infected animals, is unlikely even when powerful measures are implemented, as long as culling of whole population not is accomplished. This marginal probability of coincidental disease eradication only excist when the prevalence is very low and the measures are initiated in a very early phase (see Appendix IV).

If a healthy population subsequently is to be established in the area, must removal of animals and management of transmission hot-spots be done before too much environmental contamination build up. To eradicate the population can prevent spread from Hardangervidda if the measure is implemented soon. The effect and necessity of such a measure relies on the following criteria:

- That we with sufficent certainty can say that the disease is established in the population, and that a larger outbreak of CWD is unevitable if not the whole population is eradicated.
- That the disease not already is present in other populations (in Norway[19]).

[19] Translator's note: «In Norway» is added by the translator, as occurrence of CWD for example in North America presumably not interfere with the situation on Hardangervidda.

- That the environment is not so heavily contaminated that the disease will reemerge after fallowing.
- That the pathogen will cause disease similar to CWD in white-tailed and mule deer in North America.
- That geographical spread will occur within a short time period and with large certainty if eradication is not accomplished.
- That other measures not sufficiently will manage to prevent increased occurrence within the population and limit the probability of spread out of the area.

The zoonotic aspect is not considered in this assessment.

5. 5. Detailed consideration of the strategies control disease and eradicate disease

The most powerful measures for control and potentially eradication of the disease in this phase of an outbreak will be to (1) substantially reduce the proportion of adult males in the winter population and/or (2) strongly reduce the population. The effect of the measures will increase the more rapidly they are implemented. Accomplishment of the measures may lead to extensive and repeated disturbance of the wild reindeer. This may have negative ecological and animal welfare consequences. A challenge that is particularly associated with winter harvesting, is that a considerable proportion of the reindeer will roam in large, mixed herds. A selective harvest of adult males will be less encroaching when the males roam by themselves, i.e. in the spring and summer.

Changed demographic structure in the Hardangervidda population

The proportion of adult males (three years of age and older) has already been decreased from 20 % after hunting in the years before 2019 down to approximately 6 % after hunting in 2020. A measure with moderate negative consequences is to further reduce the proportion down to 0-3 % adult males (three years of age and older) in 2021. Harvest of a substantial proportion of adult males can remove a relatively high proportion of infected animals, and a lower proportion of males and lower mean age among males can contribute to decreased R_0. This may be accomplished without major consequences for calf production, but may have other negative and unintentional effects, as delayed calving. It is uncertain if a low proportion of adult males reduce the R_0 enough to completely stop the increase in prevalence.

Reduction of number of reindeer on Hardangervidda

A harvest that is larger than the population growth will reduce the absolute number of infected individuals and by that reduce environmental contamination and the probability of spread to other wild reindeer areas. An increased harvest can also provide a weak compensatory increase in the calving rate, and thereby and increase in the proportion of uninfected individuals. Such a harvest may possibly also contribute to a reduced prevalence, not only in the number of infected animals. An increased harvest will shorten the mean life length, and consequently also the prion shedding period of infected animals. This effect will only last as long the measure is in action. A

continuous harvest of higher number of females than the number of recruited females cannot be sustained over time without population reduction. These effects occur whether the R_0 itself is density or frequency dependent. It is, however, uncertain if reduced population density will cause a substantial decrease in the direct transmission between individuals, since the herd behaviour of wild reindeer implies that the animals are in close contact also at decreased densities.

Targeted culling of suspicious animals

A low threshold for culling animals that show clinical signs that raise suspicion of CWD can remove infected individuals and thereby reduce the level of infection in the population. At low prevalences, the removal of such animals may have a large impact on the R_0. This measure cannot eradicate the disease but is relatively easy to implement and have few negative consequences.

Another measure that could theoretically result in a selection of diseased animals would be to introduce predators as wolverine or wolf to Hardangervidda. The effect of this is very uncertain, and it is not regarded as a relevant measure.

Testing and culling of positive individuals

Individuals that get marked with GPS-collars can be tested for CWD, and positive animals subesequently be culled or taken out for research. This is considered feasible only with small and easily delimited groups of animals.

Measures preventing environmental transmission

Measures that prevent cervids from use of permanent salt licks and other places they gather, and handling that prevent access to carcasses and offal, will reduce exposure for environmental contamination and by that reduce the R_0. This will also limit transmission of other contagious diseases and parasites.

The environmental contamination per area will be diluted when the density is reduced through harvesting. Reduced exposure can also be achieved if the reindeer start to use areas where reindeer have not been present for a long time. The latter can be facilitated by reduction of barriers and minimizing human disturbance.

Measures directed towards other pasture animals

There are relatively few sheep in the parts of Hardangervidda that are most used by wild reindeer. The role of sheep in CWD transmission is unclear, and the benefit from reduction of number of sheep or prohibition of grazing in the area is uncertain.

Measures directed towards other wild reindeer populations

Measures that reduce the population size and/or number of adult males in surrounding areas, can prevent wild reindeer from roaming over to Hardangervidda and thereafter return. Low

population density and low proportion of adult males will also facilitate that the herds stay within their home range. The probability of spread will be reduced by reduction of connectivity between the Hardangervidda population and other wild reindeer populations. This can be accomplished by construction of barriers.

Measures directed towards other populations of cervids

Infectious CWD has been detected in red deer, moose, wapiti, white-tailed deer and mule deer in USA and Canada. We regard it as highly likely that red deer, moose and roe deer are susceptible for CWD prions from wild reindeer. Different species of cervids do rarely get into direct contact, and environmental transmission will be the most probable route between wild reindeer and other cervids. Handling of hot-spots for disease transmission (see above) will consequently be of high importance with regard to reduction of the probability of transmission to other cervid species. The fewer individuals of other cervids species that have overlapping area use with infected wild reindeer, the smaller is the probability of transmission. A harvest that reduce the population density of red deer, moose and roe deer in the areas around Hardangervidda, is conseauently a measure that can prevent spread. It should be considered if subpopulations of moose and deer that have a particularly large overlap in area use ought to be eradicated.

Measures within the semi-domesticated reindeer husbandry

The connectivity between wild reindeer populations and semi-domesticated reindeer herds is high in several areas. There is also high connectivity between different semi-domesticated reindeer herds. Measures that decrease number and density of animals, provide low mean age and low proportion of adult males, prevent access to hot-spots for disease transmission, decrease connectivity, increase culling of clinically suspicious individuals and strengthen the control with the position of the animals, will prevent and limit the probability for spread to and between the semi-domestic reindeer herds.

1. Knowledge gaps and uncertainties

There is currently a lack of knowledge about the occurrence of CWD within and outside Hardangervidda at a level that is critical for this report. If an adaptive, learning-based management model is chosen, it is mandatory to make a plan to lower this uncertainty. In such a management model, it is not necessarily decided if the strategy is to strongly limit the occurrence and spread of the disease, or to eradicate it. In a short time-perspective, the measures under these two strategies will be quite similar, so that there are no contradictions between them.

A systematic and strategic knowledge collection is a prerequisite for an adaptive, learning-based management model, if this is to be implemented. This will provide us with regular evaluation of the results of the measures, both with regard to the effect on the disease and with regards to other consequences.

9 Knowledge gaps

Chapter the knowledge gap relates to	Description of the knowledge gap	What is needed to fill the knowledge gap?
2. Knowledge update	Genetic susceptibility	Surveillance that provides more complete overview of the *PRNP*-variation in Norwegian cervids. This will, however, not provide knowledge about the role of the different gene variants in disease development.
	Infection, incubation period and pathogenesis of CWD	Detailed descriptions of findings in CWD-positive wild reindeer from Nordfjella. Inoculation trials with Norwegian prion strains in wild reindeer, moose, red deer and roe deer with different *PRPNP*-variants.
	Infection, incubation period and pathogenesis of CWD	Inoculation trials to elucidate the zoonotic potentia of different CWD strains – to enable management of cervids and potential for human exposure for CWD prions.
	Infection, incubation period and pathogenesis of CWD	Susceptibility for other species
	Prions' ability to persist in the environment	Studies of how long Norwegian prion strains persist and remain infective under relevant environmental conditions.

Chapter the knowledge gap relates to	Description of the knowledge gap	What is needed to fill the knowledge gap?
	The potential role of sheep	Inoculation trials with prion isolates from Norwegian wild reindeer on sheep with different *PRNP*-variants. Exploration of the possibilities for different carrier states in sheep.
	Predators and CWD	Empirical studies of the impact of wolf and wolverine on the occurrence of CWD.
	Infection in females and juveniles	Harvest of adult females and juveniles is necessary to be able to estimate CWD occurrence.
	Infection in adult males	Harvest of adult males is necessary to explore if more animals are infected, since the current estimate (with 95% uncertainty) includes zero adult females.
	Negative and unintended effects of measures	Increased surveillance, among other variables including slaughter weights and calving dates.
4. Conditions relating to the wild reindeer population on Hardangervidda	Genetics	Estimates have to be made about how small the population can be over time without causing a reduction in genetic diversity.

Chapter the knowledge gap relates to	Description of the knowledge gap	What is needed to fill the knowledge gap?
5. Strategies	Basic reproduction ratio R_0 and harvest	It should be modelled to which degree harvest can reduce R_0 efficiently enough to control or eradicate CWD without eradication of the complete population.
	Genetic effects of harvest for disease control	It should be modelled how reduction of the Hardangervidda population through different harvest measures impact the genetic diversity of wild reindeer in Norway.
6. Detaliled consideration of the strategies control and eradicate disease	Measures to prevent geographic spread	GPS-marking of wild reindeer to improve surveillance of herds of females and to enable modelling of probability of spread with adult males.
	Measures to minimize environmental transmission	The presence and localisation of hot-spots of transmission, i.e. salt lick sites, carcasses and other relevant sites where wild reindeer aggregate.
	Measures against environmental contamination	The degree of environmental contamination (relies on how long CWD has circulated in the area and how many animals that have been/are infected)
	Measures directed towards other cervids	GPS-marking should be performed to enable evaluation of arial overlap with infected wild reindeer.

Chapter the knowledge gap relates to	Description of the knowledge gap	What is needed to fill the knowledge gap?
	Measures directed towards other cervids	Clarify prevalence in other cervids and semi-domesticated reindeer.

10 Referanser

Abdelaziz D.H., Abdulrahman B.A., Gilch S., Schatzl H.M. (2019) Autophagy pathways in the treatment of prion diseases. Current Opinion in Pharmacology 44:46-52. DOI: https://doi.org/10.1016/j.coph.2019.04.013.

Abdelaziz D.H., Thapa S., Abdulrahman B., Lu L., Jain S., Schatzl H.M. (2017) Immunization of cervidized transgenic mice with multimeric deer prion protein induces self-antibodies that antagonize chronic wasting disease infectivity in vitro. Scientific Reports 7:10538. DOI: 10.1038/s41598-017-11235-8.

Abdelaziz D.H., Thapa S., Brandon J., Maybee J., Vankuppeveld L., McCorkell R., Schätzl H.M. (2018) Recombinant prion protein vaccination of transgenic elk PrP mice and reindeer overcomes self-tolerance and protects mice against chronic wasting disease. Journal of Biological Chemistry 293:19812-19822. DOI: 10.1074/jbc.RA118.004810.

Almberg E.S., Cross P.C., Johnson C.J., Heisey D.M., Richards B.J. (2011) Modeling Routes of Chronic Wasting Disease Transmission: Environmental Prion Persistence Promotes Deer Population Decline and Extinction. PLoS ONE 6:e19896. DOI: 10.1371/journal.pone.0019896.

Anderson R.M., Anderson, B., May, R.M. (1992) Infectious Diseases of Humans: Dynamics and Control OUP Oxford.

Argue C.K., Ribble C., Lees V.W., McLane J., Balachandran A. (2007) Epidemiology of an outbreak of chronic wasting disease on elk farms in Saskatchewan. Canadian Veterinary Journal 48:1241-1248.

Arifin M.I., Staskevicius A., Shim S.Y., Huang Y.-H., Fenton H., McLoughlin P.D., Mitchell G., Cullingham C.I., Gilch S. (2020) Large-scale prion protein genotyping in Canadian caribou populations and potential impact on chronic wasting disease susceptibility. Molecular Ecology 29:3830-3840. DOI: https://doi.org/10.1111/mec.15602.

Babelhadj B., Di Bari M.A., Pirisinu L., Chiappini B., Gaouar S.B.S., Riccardi G., Marcon S., Agrimi U., Nonno R., Vaccari G. (2018) Prion Disease in Dromedary Camels, Algeria. Emerging Infectious Diseases 24:1029-1036. DOI: 10.3201/eid2406.172007.

Belsare A., Gompper M., Keller B., Sumners J., Hansen L., Millspaugh J. (2020a) Size matters: Sample size assessments for chronic wasting disease surveillance using an agent-based modeling framework. MethodsX 7:100953. DOI: https://doi.org/10.1016/j.mex.2020.100953.

Belsare A., Millspaugh J.J., Mason J.R., Sumners J., Viljugrein H., Mysterud A. (2021) Getting in front of chronic wasting disease: model-informed proactive approach for managing an emerging wildlife disease. Frontiers in Veterinary Science in press.

Belsare A.V., Gompper M.E., Keller B., Sumners J., Hansen L., Millspaugh J.J. (2020b) An agent-based framework for improving wildlife disease surveillance: A case study of chronic wasting disease in Missouri white-tailed deer. Ecological Modelling 417:108919. DOI: https://doi.org/10.1016/j.ecolmodel.2019.108919.

Belsare A.V., Stewart C.M. (2020) OvCWD: An agent-based modeling framework for informing chronic wasting disease management in white-tailed deer populations. Ecological Solutions and Evidence 1:e12017. DOI: https://doi.org/10.1002/2688-8319.12017.

Belt P.B., Muileman I.H., Schreuder B.E., Bos-de Ruijter J., Gielkens A.L., Smits M.A. (1995) Identification of five allelic variants of the sheep PrP gene and their association with natural scrapie. Journal of General Virology 76 (Pt 3):509-17. DOI: 10.1099/0022-1317-76-3-509.

Benestad S.L., Mitchell G., Simmons M., Ytrehus B., Vikoren T. (2016) First case of chronic wasting disease in Europe in a Norwegian free-ranging reindeer. Veterinary Research 47:88. DOI: 10.1186/s13567-016-0375-4.

Benestad S.L., Sarradin P., Thu B., Schonheit J., Tranulis M.A., Bratberg B. (2003) Cases of scrapie with unusual features in Norway and designation of a new type, Nor98. Veterinary Research 153:202-8.

Biacabe A.G., Laplanche J.L., Ryder S., Baron T. (2004) Distinct molecular phenotypes in bovine prion diseases. EMBO Rep 5:110-5. DOI: 10.1038/sj.embor.7400054.

Bitustøyl K., Mossing A. (2019) Reinen på hardangervidda – sterkt blanda med tamrein, https://www.villrein.no/aktuelt/reinen-p-hardangervidda-sterkt-blanda-med-tamrein.

Bolam F.C., Grainger M.J., Mengersen K.L., Stewart G.B., Sutherland W.J., Runge M.C., McGowan P.J.K. (2019) Using the Value of Information to improve conservation decision making. Biological Reviews 94:629-647. DOI: https://doi.org/10.1111/brv.12471.

Bolton D.C., McKinley M.P., Prusiner S.B. (1982) Identification of a protein that purifies with the scrapie prion. Science 218:1309-11.

Bossers A., Schreuder B.E., Muileman I.H., Belt P.B., Smits M.A. (1996) PrP genotype contributes to determining survival times of sheep with natural scrapie. Journal of General Virology 77 (Pt 10):2669-73. DOI: 10.1099/0022-1317-77-10-2669.

Brandner S., Raeber A., Sailer A., Blattler T., Fischer M., Weissmann C., Aguzzi A. (1996) Normal host prion protein (PrPC) is required for scrapie spread within the central nervous system. Proceedings of the National Academy of Sciences 93:13148-51.

Bruce M.E., Will R.G., Ironside J.W., McConnell I., Drummond D., Suttie A., McCardle L., Chree A., Hope J., Birkett C., Cousens S., Fraser H., Bostock C.J. (1997) Transmissions to mice indicate that 'new variant' CJD is caused by the BSE agent. Nature 389:498-501. DOI: 10.1038/39057.

Bueler H., Aguzzi A., Sailer A., Greiner R.A., Autenried P., Aguet M., Weissmann C. (1993) Mice devoid of PrP are resistant to scrapie. Cell 73:1339-47.

Cannon R.M. (2002) Demonstrating disease freedom-combining confidence levels. Preventive Veterinary Medicine 52:227-249.

Casalone C., Zanusso G., Acutis P., Ferrari S., Capucci L., Tagliavini F., Monaco S., Caramelli M. (2004) Identification of a second bovine amyloidotic spongiform encephalopathy: molecular similarities with sporadic Creutzfeldt-Jakob disease. Proceedings of the National Academy of Sciences 101:3065-70. DOI: 10.1073/pnas.0305777101.

Chafin T.K., Douglas M.R., Martin B.T., Zbinden Z.D., Middaugh C.R., Ballard J.R., Gray M.C., Don White, Jr., Douglas M.E. (2020) Age structuring and spatial heterogeneity in prion protein gene (PRNP) polymorphism in white-tailed deer. Prion 14:238-248. DOI: 10.1080/19336896.2020.1832947.

Collinge J., Clarke A.R. (2007) A General Model of Prion Strains and Their Pathogenicity. Science 318:930. DOI: 10.1126/science.1138718.

Conner M.M., Miller M.W., Ebinger M.R., Burnham K.P. (2007) A meta-bacic approach for evaluating management intervention on chronic wasting disease in mule deer. Ecological Applications 17:140-153. DOI: https://doi.org/10.1890/1051-0761(2007)017[0140:AMAFEM]2.0.CO;2.

Cross P.C., Creech T.G., Ebinger M.R., Manlove K., Irvine K., Henningsen J., Rogerson J., Scurlock B.M., Creel S. (2013) Female elk contacts are neither frequency nor density dependent. Ecology 94:2076-2086. DOI: 10.1890/12-2086.1.

Cullingham C.I., Peery R.M., Dao A., McKenzie D.I., Coltman D.W. (2020) Predicting the spread-risk potential of chronic wasting disease to sympatric ungulate species. Prion 14:56-66. DOI: 10.1080/19336896.2020.1720486.

DeVivo M.T., Edmunds D.R., Kauffman M.J., Schumaker B.A., Binfet J., Kreeger T.J., Richards B.J., Sch„tzl H.M., Cornish T.E. (2017) Endemic chronic wasting disease causes mule deer population decline in Wyoming. Plos One 12:e0186512. DOI: 10.1371/journal.pone.0186512.
Doherr M.G. (2003) Bovine spongiform encephalopathy (BSE) infectious, contagious, zoonotic or production disease? Acta Vet Scand Suppl 98:33-42.
Dudas S., Czub S. (2017) Atypical BSE: Current Knowledge and Knowledge Gaps. Food Saf (Tokyo) 5:10-13. DOI: 10.14252/foodsafetyfscj.2016028.
Edmunds D.R., Kauffman M.J., Schumaker B.A., Lindzey F.G., Cook W.E., Kreeger T.J., Grogan R.G., Cornish T.E. (2016) Chronic Wasting Disease drives population decline of white-tailed deer. Plos One 11:e0161127. DOI: 10.1371/journal.pone.0161127.
EFSA B., Panel. (2014) Scientific Opinion on the scrapie situation in the EU after 10 years of monitoring and control in sheep and goats. EFSA J 12:155.
Eloit M., Adjou K., Coulpier M., Fontaine J.J., Hamel R., Lilin T., Messiaen S., Andreoletti O., Baron T., Bencsik A., Gaelle Biacabe A., Beringue V., Laude H., Le Dur A., Vilotte J.L., Comoy E., Deslys J.P., Grassi J., Simon S., Lantier F., Sarradin P. (2005) BSE agent signatures in a goat. Veterinary Record 156:523. DOI: 10.1136/vr.156.16.523-b.
Ersdal C., Ulvund M.J., Benestad S.L., Tranulis M.A. (2003) Accumulation of pathogenic prion protein (PrPSc) in nervous and lymphoid tissues of sheep with subclinical scrapie. Veterinary Pathology 40:164-74.
Escobar L.E., Pritzkow S., Winter S.N., Grear D.A., Kirchgessner M.S., Dominguez-Villegas E., Machado G., Townsend Peterson A., Soto C. (2020) The ecology of chronic wasting disease in wildlife. Biological Reviews 95:393-408. DOI: https://doi.org/10.1111/brv.12568.
European Food Safety A. (2017) The European Union summary report on surveillance for the presence of transmissible spongiform encephalopathies (TSE) in 2016. EFSA J 15:e05069. DOI: 10.2903/j.efsa.2017.5069.
Falldorf T. (2013) Habitat use of wild Reindeer (Rangifer t.tarandus) in Hardangervidda, Norway.
Fox K.A., Jewell J.E., Williams E.S., Miller M.W. (2006) Patterns of PrPCWD accumulation during the course of chronic wasting disease infection in orally inoculated mule deer (Odocoileus hemionus). Journal of General Virology 87:3451-3461. DOI: https://doi.org/10.1099/vir.0.81999-0.
Gagnier M., Laurion I., DeNicola A.J. (2020) Control and Surveillance Operations to Prevent Chronic Wasting Disease Establishment in Free-Ranging White-Tailed Deer in Québec, Canada. Animals: an open access journal from MDPI 10:283. DOI: 10.3390/ani10020283.
Georgsson G., Sigurdarson S., Brown P. (2006) Infectious agent of sheep scrapie may persist in the environment for at least 16 years. Journal of General Virology 87. DOI: 10.1099/vir.0.82011-0.
Goldmann W., Hunter N., Foster J.D., Salbaum J.M., Beyreuther K., Hope J. (1990) Two alleles of a neural protein gene linked to scrapie in sheep. Proceedings of the National Academy of Science USA 87:2476-80.
Goldmann W., Hunter N., Smith G., Foster J., Hope J. (1994) PrP genotype and agent effects in scrapie: change in allelic interaction with different isolates of agent in sheep, a natural host of scrapie. Journal of General Virology 75 (Pt 5):989-95. DOI: 10.1099/0022-1317-75-5-989.
Groschup M.H., Lacroux C., Buschmann A., Luhken G., Mathey J., Eiden M., Lugan S., Hoffmann C., Espinosa J.C., Baron T., Torres J.M., Erhardt G., Andreoletti O. (2007) Classic scrapie in sheep with the ARR/ARR prion genotype in Germany and France. Emerging Infectious Diseases 13:1201-7. DOI: 10.3201/eid1308.070077.

Gundersen V., Rauset G.R., Panzacchi M., van Moorter B., Strand O. (2020) Villrein-ferdselsanalyser på Hardangervidda- - Anbefalinger og tiltak, in: NINA (Ed.), NINA.
Güere M.E., Våge J., Tharaldsen H., Benestad S.L., Vikøren T., Madslien K., Hopp P., Rolandsen C.M., Røed K.H., Tranulis M.A. (2020) Chronic wasting disease associated with prion protein gene (PRNP) variation in Norwegian wild reindeer (*Rangifer tarandus*). Prion 14:1-10. DOI: 10.1080/19336896.2019.1702446.
Habib T.J., Merrill E.H., Pybus M.J., Coltman D.W. (2011) Modelling landscape effects on density–contact rate relationships of deer in eastern Alberta: Implications for chronic wasting disease. Ecological Modelling 222:2722-2732. DOI: https://doi.org/10.1016/j.ecolmodel.2011.05.007.
Hagenaars T.J., Melchior M.B., Windig J.J., Bossers A., Davidse A., van Zijderveld F.G. (2018) Modelling of strategies for genetic control of scrapie in sheep: The importance of population structure. PLoS One 13:e0195009. DOI: 10.1371/journal.pone.0195009.
Handeland K., Davidson R.K., Viljugrein H., Mossing A., Meisingset E.L., Heum M., Strand O., Isaksen K. (2019) Elaphostrongylus and Dictyocaulus infections in Norwegian wild reindeer and red deer populations in relation to summer pasture altitude and climate. International Journal for Parasitology: Parasites and Wildlife 10:188-195. DOI: https://doi.org/10.1016/j.ijppaw.2019.09.003.
Hayward M.W., Kerley G.I.H. (2009) Fencing for conservation: Restriction of evolutionary potential or a riposte to threatening processes? Biological Conservation 142:1-13. DOI: https://doi.org/10.1016/j.biocon.2008.09.022.
Hazard E.P.o.B., Ricci A., Allende A., Bolton D., Chemaly M., Davies R., Esc mez P.S.F., Giron‚s R., Herman L., Koutsoumanis K., Lindqvist R., N›rrung B., Robertson L., Ru G., Sanaa M., Skandamis P., Snary E., Speybroeck N., Kuile B.T., Threlfall J., Wahlstr"m H., Benestad S., Gavier-Widen D., Miller M.W., Telling G.C., Tryland M., Latronico F., Ortiz-Pelaez A., Stella P., Simmons M. (2018) Scientific opinion on chronic wasting disease (II). EFSA Journal 16:e05132. DOI: 10.2903/j.efsa.2018.5132.
Hedman H.D., Varga C., Brown W.M., Shelton P., Roca A.L., Novakofski J.E., Mateus-Pinilla N.E. (2020) Spatial analysis of chronic wasting disease in free-ranging white-tailed deer (Odocoileus virginianus) in Illinois, 2008-2019. Transboundary and Emerging Diseases online early. DOI: 10.1111/tbed.13901.
Heisey D.M., Osnas E.E., Cross P.C., Joly D.O., Langenberg J.A., Miller M.W. (2010) Linking process to pattern: estimating spatiotemporal dynamics of a wildlife epidemic from cross-sectional data. Ecological Monographs 80:221-240.
Henderson D.M., Tennant J.M., Haley N.J., Denkers N.D., Mathiason C.K., Hoover E.A. (2017) Detection of chronic wasting disease prion seeding activity in deer and elk feces by real-time quaking-induced conversion. Journal of General Virology 98:1953-1962. DOI: 10.1099/jgv.0.000844.
Hibler C.P., Wilson K.L., Spraker T.R., Miller M.W., Zink R.R., DeBuse L.L., Andersen E., Schweitzer D., Kennedy J.A., Baeten L.A., Smeltzer J.F., Salman M.D., Powers B.E. (2003) Field validation and assessment of an enzyme-linked immunosorbent assay for detecting chronic wasting disease in mule deer (*Odocoileus hemionus*), white-tailed deer (Odocoileus virginianus), and Rocky Mountain elk (*Cervus elaphus nelsoni*). Journal of Veterinary Diagnostic Investigation 15:311-319.
Holand Ø., Weladji R.B., Gjøstein H., Kumpula J., Smith M.E., Nieminen M., Røed K.H. (2004) Reproductive effort in relation to maternal social rank in reindeer (*Rangifer tarandus*). Behavioral Ecology and Sociobiology 57:69-76. DOI: 10.1007/s00265-004-0827-0.
Hoover C.E., Davenport K.A., Henderson D.M., Denkers N.D., Mathiason C.K., Soto C., Zabel M.D., Hoover E.A. (2017) Pathways of Prion Spread during Early Chronic Wasting Disease in Deer. Journal of Virology 91:15. DOI: 10.1128/jvi.00077-17.

Hunter G.D. (1972) Scrapie: a prototype slow infection. Journal of Infectious Diseases 125:427-40.
Ikeda T., Horiuchi M., Ishiguro N., Muramatsu Y., Kai-Uwe G.D., Shinagawa M. (1995) Amino acid polymorphisms of PrP with reference to onset of scrapie in Suffolk and Corriedale sheep in Japan. Journal of General Virology 76 (Pt 10):2577-81. DOI: 10.1099/0022-1317-76-10-2577.
Indrelid S., Hufthammer A.K. (2011) Medieval mass trapping of reindeer at the Hardangervidda mountain plateau, South Norway. Quaternary International 238:44-54. DOI: https://doi.org/10.1016/j.quaint.2010.09.008.
Jellinger K.A. (2012) Interaction between pathogenic proteins in neurodegenerative disorders. Journal of Cellular and Molecular Medicine 16:1166-83. DOI: 10.1111/j.1582-4934.2011.01507.x.
Jennelle C.S., Henaux V., Wasserberg G., Thiagarajan B., Rolley R.E., Samuel M.D. (2014) Transmission of Chronic Wasting Disease in Wisconsin White-Tailed Deer: Implications for Disease Spread and Management. PLOS ONE 9:e91043. DOI: 10.1371/journal.pone.0091043.
Jennelle C.S., Walsh D.P., Samuel M.D., Osnas E.E., Rolley R., Langenberg J., Powers J.G., Monello R.J., Demarest E.D., Gubler R., Heisey D.M. (2018) Applying a Bayesian weighted surveillance approach to detect chronic wasting disease in white-tailed deer. Journal of Applied Ecology 55:2944-2953. DOI: https://doi.org/10.1111/1365-2664.13178.
Johnson C.J., Herbst A., Duque-Velasquez C., Vanderloo J.P., Bochsler P., Chappell R., McKenzie D. (2011) Prion Protein Polymorphisms Affect Chronic Wasting Disease Progression. PLOS ONE 6:e17450. DOI: 10.1371/journal.pone.0017450.
Jordhøy P. (2007) Gamal jakt- og fangstkultur som indikatorar på trekkmønster hjå rein i Sør-Noreg. Kartlagde fangstanlegg i Rondane, Ottadalen, Jotunheimen og Forollhogna, in: NINA (Ed.), NINA Rapport. pp. 41.
Jordhøy P., Strand O. (2009) Lufsjåtangen og Dagalitangen på Hardangervidda. Kunnskap og utfordringar i høve til villreintrekk og menneskseleg arealbruk, in: NINA (Ed.), NINA Rapport pp. 77.
Kjørstad M., Bøthun S.W., Gundersen V., Holand Ø., Madslien K., Mysterud M., Myren I.N., Punsvik T., Røed K.H., Strand O., Tveraa T., Tømmervik H., Ytrehus B., Veiberg V. (2018) Miljøkvalitetsnorm for villrein, NINA. pp. 193.
Krumm C.E., Conner M.M., Hobbs N.T., Hunter D.O., Miller M.W. (2010) Mountain lions prey selectively on prion-infected mule deer. Biology Letters 6:209-211. DOI: 10.1098/rsbl.2009.0742.
Kuznetsova A., Cullingham C., McKenzie D., Aiken J.M. (2018) Soil humic acids degrade CWD prions and reduce infectivity. PLOS Pathogens 14:e1007414. DOI: 10.1371/journal.ppat.1007414.
Kuznetsova A., McKenzie D., Cullingham C., Aiken J.M. (2020) Long-Term Incubation PrP(CWD) with Soils Affects Prion Recovery but Not Infectivity. Pathogens (Basel, Switzerland) 9:311. DOI: 10.3390/pathogens9040311.
Kvie K.S., Heggenes J., Bårdsen B.-J., Røed K.H. (2019) Recent large-scale landscape changes, genetic drift and reintroductions characterize the genetic structure of Norwegian wild reindeer. Conservation Genetics 20:1405-1419. DOI: 10.1007/s10592-019-01225-w.
Laplanche J.L., Chatelain J., Westaway D., Thomas S., Dussaucy M., Brugere-Picoux J., Launay J.M. (1993) PrP polymorphisms associated with natural scrapie discovered by denaturing gradient gel electrophoresis. Genomics 15:30-7. DOI: 10.1006/geno.1993.1006.
Loison A., Strand O. (2005) Allometry and variability of resource allocation to reproduction in a wild reindeer population. Behavioral Ecology 16:624-633. DOI: 10.1093/beheco/ari037.

Madslien K., Våge J., das Neves C., Hagelin J., Handeland K., Vikøren T. (2020) Helseovervåkingsprogrammet for hjortevilt og moskus (HOP) 2019, Veterinærinstituttet.
Manjerovic M.B., Green M.L., Mateus-Pinilla N., Novakofski J. (2014) The importance of localized culling in stabilizing chronic wasting disease prevalence in white-tailed deer populations. Preventive Veterinary Medicine 113:139-145.
Martin P.A., Cameron A.R., Greiner M. (2007) Demonstrating freedom from disease using multiple complex data sources. Preventive Veterinary Medicine 79:71-97.
Mathiason C.K., Hays S.A., Powers J., Hayes-Klug J., Langenberg J., Dahmes S.J., Osborn D.A., Miller K.V., Warren R.J., Mason G.L., Hoover E.A. (2009) Infectious Prions in Pre-Clinical Deer and Transmission of Chronic Wasting Disease Solely by Environmental Exposure. PLOS ONE 4:e5916. DOI: 10.1371/journal.pone.0005916.
McFadden J.E., Hiller T.L., Tyre A.J. (2011) Evaluating the efficacy of adaptive management approaches: Is there a formula for success? Journal of Environmental Management 92:1354-1359. DOI: https://doi.org/10.1016/j.jenvman.2010.10.038.
Miller M.W., Conner M.M. (2005) Epidemiology of Chronic Wasting Disease in free-ranging mule deer: Spatial, temporal, and demographic influences on observed prevalence patterns. Journal of Wildlife Diseases 41:275-290. DOI: 10.7589/0090-3558-41.2.275.
Miller M.W., Fischer J.R. (2016) The First Five (or More) Decades of Chronic Wasting Disease: Lessons for the Five Decades to Come, The 81st North American Wildlife and Natural Resources Conference, Wildlife Management Institute, Pennsylvania, USA, Pittsburgh, Pennsylvania, USA.
Miller M.W., Runge J.P., Holland A.A., Eckert M.D. (2020a) Hunting pressure modulates prion infection risk in mule deer herds. Journal of Wildlife Diseases 56:781-790. DOI: 10.7589/jwd-d-20-00054.
Miller M.W., Swanson H.M., Wolfe L.L., Quartarone F.G., Huwer S.L., Southwick C.H., Lukacs P.M. (2008) Lions and Prions and Deer Demise. PLOS ONE 3:e4019. DOI: 10.1371/journal.pone.0004019.
Miller M.W., Williams E.S., Hobbs N.T., Wolfe L.L. (2004) Environmental sources of prion transmission in mule deer. Emerg Infect Dis 10. DOI: 10.3201/eid1006.040010.
Miller W.L., Miller-Butterworth C.M., Diefenbach D.R., Walter W.D. (2020b) Assessment of spatial genetic structure to identify populations at risk for infection of an emerging epizootic disease. Ecology and Evolution 10:3977-3990. DOI: https://doi.org/10.1002/ece3.6161.
Milner-Gulland E.J., Shea K. (2017) Embracing uncertainty in applied ecology. Journal of Applied Ecology 54:2063-2068. DOI: 10.1111/1365-2664.12887.
Mitchell G.B., Sigurdson C.J., O'Rourke K.I., Algire J., Harrington N.P., Walther I., Spraker T.R., Balachandran A. (2012) Experimental Oral Transmission of Chronic Wasting Disease to Reindeer (*Rangifer tarandus tarandus*). PLOS ONE 7:e39055. DOI: 10.1371/journal.pone.0039055.
Monello R.J., Galloway N.L., Powers J.G., Madsen-Bouterse S.A., Edwards W.H., Wood M.E., O'Rourke K.I., Wild M.A. (2017) Pathogen-mediated selection in free-ranging elk populations infected by chronic wasting disease. Proceedings of the National Academy of Sciences 114:12208-12212. DOI: 10.1073/pnas.1707807114.
Monello R.J., Powers J.G., Hobbs N.T., Spraker T.R., Watry M.K., Wild M.A. (2014) Survival and population growth of a free-ranging elk population with a long history of exposure to Chronic Wasting Disease. Journal of Wildlife Management 78:214-223.
Moore S.J., Kunkle R., Greenlee M.H., Nicholson E., Richt J., Hamir A., Waters W.R., Greenlee J. (2016) Horizontal Transmission of Chronic Wasting Disease in Reindeer. Emerging Infectious Diseases 22:2142-2145. DOI: 10.3201/eid2212.160635.
Moore S.J., Vrentas C.E., Hwang S., West Greenlee M.H., Nicholson E.M., Greenlee J.J. (2018) Pathologic and biochemical characterization of PrPSc from elk with PRNP polymorphisms

at codon 132 after experimental infection with the chronic wasting disease agent. BMC Veterinary Research 14:80. DOI: 10.1186/s12917-018-1400-9.
Mysterud A., Edmunds D.R. (2019) A review of chronic wasting disease in North America with implications for Europe. European Journal of Wildlife Research 65:26. DOI: 10.1007/s10344-019-1260-z.
Mysterud A., Hopp P., Alvseike K.R., Benestad S.L., Nilsen E.B., Rolandsen C.M., Strand O., Våge J., Viljugrein H. (2020a) Hunting strategies to increase detection of chronic wasting disease in cervids. Nature Communications 11:4392. DOI: 10.1038/s41467-020-18229-7.
Mysterud A., Madslien K., Viljugrein H., Vikøren T., Andersen R., Güere M.E., Benestad S.L., Hopp P., Strand O., Ytrehus B., Røed K.H., Rolandsen C.M., Våge J. (2019a) The demographic pattern of infection with chronic wasting disease in reindeer at an early epidemic stage. Ecosphere 10:e02931. DOI: https://doi.org/10.1002/ecs2.2931.
Mysterud A., Rauset G.R., Van Moorter B., Andersen R., Strand O., Rivrud I.M. The last moves: The effect of hunting and culling on the risk of disease spread from a population of reindeer. Journal of Applied Ecology n/a. DOI: https://doi.org/10.1111/1365-2664.13761.
Mysterud A., Rivrud I.M., Gundersen V., Rolandsen C.M., Viljugrein H. (2020b) The unique spatial ecology of human hunters. Nature Human Behaviour 4:694-701. DOI: 10.1038/s41562-020-0836-7.
Mysterud A., Rolandsen C.M. (2018) A reindeer cull to prevent chronic wasting disease in Europe. Nature Ecology and Evoloution 2:1343-1345. DOI: 10.1038/s41559-018-0616-1.
Mysterud A., Rolandsen C.M. (2019) Fencing for wildlife disease control. Journal of Applied Ecology 56:519-525. DOI: https://doi.org/10.1111/1365-2664.13301.
Mysterud A., Strand O., Rolandsen C.M. (2019b) Efficacy of recreational hunters and marksmen for host culling to combat chronic wasting disease in reindeer. Wildlife Society Bulletin 43:683-692. DOI: https://doi.org/10.1002/wsb.1024.
Mysterud A., Strand O., Rolandsen C.M. (2020c) Embracing fragmentation to save reindeer from disease. Conservation Science and Practice 2:e244. DOI: https://doi.org/10.1111/csp2.244.
Mysterud A., Viljugrein H., Solberg E.J., Rolandsen C.M. (2019c) Legal regulation of supplementary cervid feeding facing chronic wasting disease. The Journal of Wildlife Management 83:1667-1675. DOI: https://doi.org/10.1002/jwmg.21746.
Mysterud A., Ytrehus B.r., Tranulis M.A., Rauset G.R., Rolandsen C.M., Strand O. (2020d) Antler cannibalism in reindeer. Scientific Reports 10:22168.
Nalls A.V., McNulty E., Powers J., Seelig D.M., Hoover C., Haley N.J., Hayes-Klug J., Anderson K., Stewart P., Goldmann W., Hoover E.A., Mathiason C.K. (2013) Mother to offspring transmission of Chronic Wasting Disease in Reeves' muntjac deer. Plos One 8:e71844. DOI: 10.1371/journal.pone.0071844.
Nilsen E.B., Strand O. (2018) Integrating data from several sources for increased insight into demographic processes: Simulation studies and proof of concept for hierarchical change in ratio models. Plos One 13:e0194566.
Nodelijk G., van Roermund H.J., van Keulen L.J., Engel B., Vellema P., Hagenaars T.J. (2011) Breeding with resistant rams leads to rapid control of classical scrapie in affected sheep flocks. Veterinary Research 42:5. DOI: 10.1186/1297-9716-42-5.
Nonno R., Di Bari M.A., Pirisinu L., D'Agostino C., Vanni I., Chiappini B., Marcon S., Riccardi G., Tran L., Vikøren T., Våge J., Madslien K., Mitchell G., Telling G.C., Benestad S.L., Agrimi U. (2020) Studies in bank voles reveal strain differences between chronic wasting disease prions from Norway and North America. Proceedings of the National Academy of Sciences 117:31417. DOI: 10.1073/pnas.2013237117.

Oesch B., Westaway D., Walchli M., McKinley M.P., Kent S.B., Aebersold R., Barry R.A., Tempst P., Teplow D.B., Hood L.E., et al. (1985) A cellular gene encodes scrapie PrP 27-30 protein. Cell 40:735-46. DOI: 10.1016/0092-8674(85)90333-2.

Ortiz-Pelaez A., Bianchini J. (2011) The impact of the genotype on the prevalence of classical scrapie at population level. Veterinary Research 42:31. DOI: 10.1186/1297-9716-42-31.

Paetkau D., Slade R., Burden M., Estoup A. (2004) Genetic assignment methods for the direct, real-time estimation of migration rate: a simulation-based exploration of accuracy and power. Molecular Ecology 13:55-65. DOI: https://doi.org/10.1046/j.1365-294X.2004.02008.x.

Panzacchi M., Van Moorter B., Gundersen V., Jordhøy P., Strand O. (2014) Managing wildlife in a human dominated world or managing man into the wild? Experiences from the last remaining populations of wild mountain reindeer. Hystrix: The Italian Journal of Mammalogy 25:2-3.

Panzacchi M., Van Moorter B., Jordhøy P., Strand O. (2013) Learning from the past to predict the future: using archaeological findings and GPS data to quantify reindeer sensitivity to anthropogenic disturbance in Norway. Landscape Ecology 28:847-859. DOI: 10.1007/s10980-012-9793-5.

Panzacchi M., Van Moorter B., Strand O., Loe L.E., Reimers E. (2015) Searching for the fundamental niche using individual-based habitat selection modelling across populations. Ecography 38:659-669. DOI: https://doi.org/10.1111/ecog.01075.

Pirisinu L., Tran L., Chiappini B., Vanni I., Di Bari M., Vaccari G., Vikøren T., Madslien K.I., Våge J., Spraker T., Mitchell G., Balachandran A., Baron T., Casalone C., Rolandsen C., Røed K., Agrimi U., Nonno R., Benestad S. (2018) Novel Type of Chronic Wasting Disease Detected in Moose (Alces alces), Norway. Emerging Infectious Disease journal 24:2210. DOI: 10.3201/eid2412.180702.

Piry S., Alapetite A., Cornuet J.-M., Paetkau D., Baudouin L., Estoup A. (2004) GENECLASS2: A Software for Genetic Assignment and First-Generation Migrant Detection. Journal of Heredity 95:536-539. DOI: 10.1093/jhered/esh074.

Potapov A., Merrill E., Lewis M.A. (2012) Wildlife disease elimination and density dependence. Proceedings of the Royal Society B: Biological Sciences 279:3139-3145. DOI: 10.1098/rspb.2012.0520.

Potapov A., Merrill E., Pybus M., Lewis M.A. (2016) Chronic Wasting Disease: Transmission Mechanisms and the Possibility of Harvest Management. PLOS ONE 11:e0151039. DOI: 10.1371/journal.pone.0151039.

Prusiner S.B. (1993) Prion encephalopathies of animals and humans. Development in Biological Standardization 80:31-44.

Prusiner S.B. (1994) Inherited prion diseases. Proceedings of the National Academy of Sciences of the United States of America 91:4611-4.

Prusiner S.B. (1998) Prions. Proceedings of the National Academy of Sciences of the United States of America 95:13363-83.

Prusiner S.B., Bolton D.C., Groth D.F., Bowman K.A., Cochran S.P., McKinley M.P. (1982) Further purification and characterization of scrapie prions. Biochemistry 21:6942-50.

Prusiner S.B., Hadlow W.J., Garfin D.E., Cochran S.P., Baringer J.R., Race R.E., Eklund C.M. (1978) Partial purification and evidence for multiple molecular forms of the scrapie agent. Biochemistry 17:4993-9.

Rannala B., Mountain J.L. (1997) Detecting immigration by using multilocus genotypes. Proceedings of the National Academy of Sciences of the United States of America 94:9197-9201. DOI: 10.1073/pnas.94.17.9197.

Rees E.E., Merrill E.H., Bollinger T.K., Hwang Y.T., Pybus M.J., Coltman D.W. (2012) Targeting the detection of chronic wasting disease using the hunter harvest during early phases of an outbreak in Saskatchewan, Canada. Preventive Veterinary Medicine 104:149-159.
Rist L., Felton A., Samuelsson L., Sandström C., Rosvall O. (2013) A New Paradigm for Adaptive Management. Ecology and Society 18.
Rivera N.A., Brandt A.L., Novakofski J.E., Mateus-Pinilla N.E. (2019) Chronic Wasting Disease In Cervids: Prevalence, Impact And Management Strategies. Veterinary Medicine (Auckland, NZ) 10:123-139. DOI: 10.2147/VMRR.S197404.
Robinson S.J., Samuel M.D., O'Rourke K.I., Johnson C.J. (2012) The role of genetics in chronic wasting disease of North American cervids. Prion 6:153-162. DOI: 10.4161/pri.19640.
Røed K.H., Bjørnstad G., Flagstad Ø., Haanes H., Hufthammer A.K., Jordhøy P., Rosvold J. (2014) Ancient DNA reveals prehistoric habitat fragmentation and recent domestic introgression into native wild reindeer. Conservation Genetics 15:1137-1149. DOI: 10.1007/s10592-014-0606-z.
Samuel M.D., Storm D.J. (2016) Chronic wasting disease in white-tailed deer: infection, mortality, and implications for heterogeneous transmission. Ecology 97:3195-3205.
Sargeant G.A., Weber D.C., Roddy D.E. (2011) Implications of chronic wasting disease, cougar predation, and reduced recruitment for elk management. Journal of Wildlife Management 75:171-177.
Schreuder B.E., van Keulen L.J., Smits M.A., Langeveld J.P., Stegeman J.A. (1997) Control of scrapie eventually possible? Vet Q 19:105-13. DOI: 10.1080/01652176.1997.9694752.
Schwabenlander M.D., Culhane M.R., Hall S.M., Goyal S.M., Anderson P.L., Carstensen M., Wells S.J., Slade W.B., Armién A.G. (2013) A case of chronic wasting disease in a captive red deer (Cervus elaphus). Journal of Veterinary Diagnostic Investigation 25:573-6. DOI: 10.1177/1040638713499914.
Science Advice for Policy by European A. (2019) Making Sense of Science Under Conditions of Complexity and Uncertainty, Berlin.
Selariu A., Powers J.G., Nalls A., Brandhuber M., Mayfield A., Fullaway S., Wyckoff C.A., Goldmann W., Zabel M.M., Wild M.A., Hoover E.A., Mathiason C.K. (2015) In utero transmission and tissue distribution of chronic wasting disease-associated prions in free-ranging Rocky Mountain elk. The Journal of General Virology 96:3444-3455. DOI: 10.1099/jgv.0.000281.
Skjelbostad I.N. (2020) Use of spatial clusters by red deer (*Cervus elaphus*) to identify transmission hot spots in a Chronic Wasting Disease context Master thesis, University of Oslo, Oslo.
Skogland T. (1990a) Comparative Social Organization of Wild Reindeer in Relation to Food, Mates and Predator Avoidance. The Quarterly Review of Biology 65:386-386. DOI: 10.1086/416923.
Skogland T. (1990b) Density dependence in a fluctuating wild reindeer herd; maternal vs. offspring effects. Oecologia 84:442-450. DOI: 10.1007/BF00328158.
Solberg E.J., Rivrud I.M., Nilsen E.B., Veiberg V., Rolandsen C.M., Meisingset E.L., Mysterud A. (2019) Bestandsreduksjon av elg og hjort i Nordfjellaregionen i perioden 2019-2020. NINA rapport 1667:1-111.
Solberg E.J., Strand O., Veiberg V., Andersen R., Heim M., Rolandsen C.M., Solem M.I., Holmstr›m F., Jordh›y P., Nilsen E.B., Granhus A., Eriksen R. (2017) Hjortevilt 1991-2016: Oppsummeringsrapport fra Overvåkingsprogrammet for hjortevilt. NINA rapport 1388:1-125.
Somerville R.A., Fernie K., Smith A., Bishop K., Maddison B.C., Gough K.C., Hunter N. (2019) BSE infectivity survives burial for five years with only limited spread. Archives of Virology 164:1135-1145. DOI: 10.1007/s00705-019-04154-8.

Storm D.J., Samuel M.D., Rolley R.E., Shelton P., Keuler N.S., Richards B.J., Van Deelen T.R. (2013) Deer density and disease prevalence influence transmission of chronic wasting disease in white-tailed deer. Ecosphere 4:art10. DOI: https://doi.org/10.1890/ES12-00141.1.
Strand O., Gundersen V., Jordhøy P., Andersen R., Nerhol I., Panzacchi M., Van Moorter B. (2015a) Villrein og ferdsel i Rondane; Sluttrapport fra GPS-merkeprosjektet 2009-2014, in: NINA (Ed.), NINA Rapport
Strand O., Gundersen V., Thomassen J., Andersen R., Rauset G.R., Romtveit L., Mossing A., Bøthun S., Ruud A. (2019) GPS villreinprosjektet i Setesdal-Ryfylke – avbøtende tiltak, in: NINA (Ed.), NINA rapport. pp. 111.
Strand O., Jordhøy P., Mossing A., Knudsen P.A., Nesse L., Skjerdal H., Panzacchi M., Andersen R., Gundersen V. (2011) Villreinen i Nordfjella. Status og leveområde, in: NINA (Ed.), NINA Rapport pp. 71.
Strand O., Jordhøy P., Panzacchi M., Van Moorter B. (2015b) Veger og villrein. Oppsummering – overvåking av Rv7 over Hardangervidda, in: NINA (Ed.), NINA Rapport pp. 47.
Taschuk R., Scruten E., Woodbury M., Cashman N., Potter A., Griebel P., Tikoo S.K., Napper S. (2017) Induction of PrPSc-specific systemic and mucosal immune responses in white-tailed deer with an oral vaccine for chronic wasting disease. Prion 11:368-380. DOI: 10.1080/19336896.2017.1367083.
Tennant J.M., Li M., Henderson D.M., Tyer M.L., Denkers N.D., Haley N.J., Mathiason C.K., Hoover E.A. (2020) Shedding and stability of CWD prion seeding activity in cervid feces. PLoS ONE 15. DOI: 10.1371/journal.pone.0227094.
Tranulis M.A. (2002) Influence of the prion protein gene, Prnp, on scrapie susceptibility in sheep. APMIS 110:33-43.
Tranulis M.A., Benestad S.L., Baron T., Kretzschmar H. (2011) Atypical prion diseases in humans and animals. Topics in Current Chemistry 305:23-50. DOI: 10.1007/128_2011_161.
Tranulis M.A., Osland A., Bratberg B., Ulvund M.J. (1999) Prion protein gene polymorphisms in sheep with natural scrapie and healthy controls in Norway. Journal of General Virology 80 (Pt 4):1073-7. DOI: 10.1099/0022-1317-80-4-1073.
Uehlinger F.D., Johnston A.C., Bollinger T.K., Waldner C.L. (2016) Systematic review of management strategies to control chronic wasting disease in wild deer populations in
North America. BMC Veterinary Research 12:1-16. DOI: 10.1186/s12917-016-0804-7.
VKM. (2017) CWD in Norway – a state of emergency for the future of cervids (Phase II). Opinion of the panel on Biological Hazards, ISBN: 978-82-8259-266-6, Oslo, Norway.
VKM, Bjørnar Ytrehus, Danica Grahek-Ogden, Olav Strand, Michael Tranulis, Atle Mysterud, Marina Aspholm, Solveig Jore, Georg Kapperud, Trond Møretrø, Truls Nesbakken, Lucy Robertson, Kjetil Melby, Taran Skjerdal. (2018) Factors that can contribute to spread of CWD – an update on the situation in Nordfjella, Norway. Opinion of the Panel on biological hazards. ISBN: 978-82-8259-316-8. Norwegian Scientific Committee for Food and Environment (VKM), Oslo, Norway.
VKM. (2016). CWD in Norway. Opinion of the Panel on biological hazards, ISBN: 978-82-8259-216-1, Oslo, Norway
Vikoren T., Vage J., Madslien K.I., Roed K.H., Rolandsen C.M., Tran L., Hopp P., Veiberg V., Heum M., Moldal T., Neves C.G.D., Handeland K., Ytrehus B., Kolbjornsen O., Wisloff H., Terland R., Saure B., Dessen K.M., Svendsen S.G., Nordvik B.S., Benestad S.L. (2019) First Detection of Chronic Wasting Disease in a Wild Red Deer (Cervus elaphus) in Europe. Journal of Wildlife Diseases 55:970-972.
Viljugrein H., Hopp P., Benestad S.L., Nilsen E.B., Våge J., Tavornpanich S., Rolandsen C.M., Strand O., Mysterud A. (2019) A method that accounts for differential detectability in mixed samples of long-term infections with applications to the case of chronic wasting

disease in cervids. Methods in Ecology and Evolution 10:134-145. DOI: https://doi.org/10.1111/2041-210X.13088.
Viljugrein H., Hopp P., Benestad S.L., V†ge J., Mysterud A. (2021) Risk-based surveillance to establish freedom of chronic wasting disease in semi-domestic reindeer. Manuscript.
Walsh D.P., Miller M.W. (2010) A weighted surveillance approach for detecting chronic wasting disease foci. Journal of Wildlife Diseases 46:118-35. DOI: 10.7589/0090-3558-46.1.118.
Walton L., Marion G., Davidson R.S., White P.C.L., Smith L.A., Gavier-Widen D., Yon L., Hannant D., Hutchings M.R. (2016) The ecology of wildlife disease surveillance: demographic and prevalence fluctuations undermine surveillance. Journal of Applied Ecology 53:1460-1469. DOI: https://doi.org/10.1111/1365-2664.12671.
Wasserberg G., Osnas E.E., Rolley R.E., Samuel M.D. (2009) Host culling as an adaptive management tool for chronic wasting disease in white-tailed deer: a modelling study. Journal of Applied Ecology 46:457-466. DOI: https://doi.org/10.1111/j.1365-2664.2008.01576.x.
Wild M.A., Hobbs N.T., Graham M.S., Miller M.W. (2011) The role of predation in disease control: a comparison of selective and nonselective removal on prion disease dynamics in deer. Journal of Wildlife Diseases 47:78-93. DOI: 10.7589/0090-3558-47.1.78.
Williams B.K., Nichols J.D., Conroy M.J. (2010) Analysis and management of animal populations. Academic, San Diego.
Williams E.S. (2005) Chronic Wasting Disease. Veterinary Pathology Online 42:530-549. DOI: 10.1354/vp.42-5-530.
Williams E.S., Young S. (1980) Chronic wasting disease of captive mule deer: a spongiform encephalopathy. Journal of Wildlife Diseases 16:89-98.
Wolfe L.L., Spraker T.R., Gonzalez L., Dagleish M.P., Sirochman T.M., Brown J.C., Jeffrey M., Miller M.W. (2007) PrPCWD in rectal lymphoid tissue of deer (*Odocoileus* spp.). Journal of General Virology 88:2078-82. DOI: 10.1099/vir.0.82342-0.
Wolfe L.L., Watry M.K., Sirochman M.A., Sirochman T.M., Miller M.W. (2018) Evaluation of a test and cull strategy for reducing prevalence of chronic wasting disease in mule deer (*Odocoileus hemionus*). Journal of Wildlife Diseases 54:511-519. DOI: 10.7589/2018-01-015.

Appendix I

Breeding programs for reduction/eradication of classic scrapie

In sheep is the susceptibility for classic scrapie mainly determined by three variants (alleles) of VRQ, ARQ og ARR (Belt et al., 1995; Bossers et al., 1996; Goldmann et al., 1990; Goldmann et al., 1994; Laplanche et al., 1993). The presence of the VRQ-allele in a sheep breed makes the sheep very susceptible for classic scrapie. Animals with the ARQ-allele are less susceptible, while those who have the ARR-allele have very low susceptibility (Tranulis, 2002), especially if it present in double dose (homozygous ARR/ARR). This knowledge provide the basis for a strategy for reduction and eventual eradication of classic scrapie through systematic breeding on the sheep with highest resistance (Schreuder et al., 1997). This idea got an early foothold in in the Netherlands. A program with voluntary genotype testing was started already in 1998 and made compulsory from 2004 to 2011 (Hagenaars et al., 2018). Great Britain and France were also early, implementing a similar approach in their sheep breeding in 2001. In 2003, EU launched a control- and surveillance program combined with breeding on gene variants with low susceptibility. A review of this program has been presented by EFSA (EFSA, 2014).

Even though classic scrapie not is regarded as a direct threat for humans, it was known that sheep (inoculation trials) and goat (Eloit et al., 2005) could be affected by classic BSE (mad cow disease), that is dangerous to humans, and that this disease could be confused with scrapie. This paved the way for high priority of the reduction/eradication program for classic scrapie.

The breeding programs for classic build on the same principle as vaccination programs, where the aim is to achieve so-called herd immunity, where R_0 is less than 1, i.e. that a diseased individual in average infects less than one susceptible individual, and the disease gradually diminish. If R_0 remain larger than 1, will the disease occurrence increase (Anderson, 1992). When the number of vaccinated individuals in a population is larger than a certain level, will R_0 become smaller than 1. In a similar manner will R_0 for classic scrapie get lower than 1 if the proportion of less susceptible animals (with the ARR-allele) reaches a certain level, and then will the occurrence of the disease decline. Such breeding programs have proved to be very efficient, in particular in combination with good disease surveillance and preventive measures against disease transmission, for example to decrease contact between herds and prevent/avoid transport of live animals between areas (EFSA, 2014).

The effects of the breeding programs to reduce classic scrapie have been particularly appreciable in Great Britain, France and the Netherlands. The Dutch results are well studied, and analyses show that when the frequency of the ARR-allele in the sheep population reach 70 %, will R_0 become less than 1, and a decline in the occurrence (Hagenaars et al., 2018; Nodelijk et al., 2011; Ortiz-Pelaez and Bianchini, 2011). For example, in the Netherlands in 2005 were there about 1,8 cases of classic scrapie per 1000 examined sheep when the prevalence of the ARR-allele was approximately 37 %. Five years later was the ARR-frequency increased to 65 %, and the occurrence of classic scrapie reduced to less than 0,1 case per 1000 examined sheep. Since

2011 have only few cases of classic scrapie been detected in the Netherlands, and years may go by between each time the disease is diagnosed. This does not imply that the disease is eradicated once for all: If the numbers of very susceptible individuals once again rise, this will imply an increase in probability of development of disease, as the susceptible sheep easily will develop disease after exposure to infective material in the environment or infected imported animals (Hagenaars et al., 2018). As long as the proportion of less susceptible animals is high, however, will large outbreaks be prevented, though solitary cases may occur from time to time. This situation is analoguous to what we know from vaccines. A good vaccine is said to provide 60 to 90 % protection. Statistically, this means that among 100 infected individuals will between 10 and 40 develop disease, while the rest is protected. If we compare the susceptibility for classic scrapie in the most sensitive sheep (the VRQ/VRQ variant), with the least susceptible ones (ARR/ARR variant), will the latter have a degree of protection of more than 99 %. This is known because many thousands of cases of classic scrapie has been investigated through the last 25 years, and only a few solitary cases of sheep with the ARR/ARR gene variant has been observed (Groschup et al., 2007; Ikeda et al., 1995).

As described above are there clear *PRNP*-genetic effects in reindeer in Nordfjella, where some individuals are less susceptible than others (Güere et al., 2020). However, we do not have evidence that indicates that any of them are nearly as protective as the ARR-allele in sheep. Even a substantially lower degree of protection than 99 % may although have a large effect on the occurrence of an infectious disease, and can thereby limit the extent of new outbreaks.

Appendix II

Prions and prion diseases

Prions

The American researcher Stanley B. Prusiner studied the brain of prion-infected hamsters in the late 1970s. He reached the conclusion that the infectious agent was not a virus, which was widely believed, but an aggregate of protein, and he coined the term prion (Bolton et al., 1982; Prusiner et al., 1982; Prusiner et al., 1978). The name was constructed from «protein-based infectious particle» (Prusiner, 1998). A series of important discoveries followed, including that the prions consisted of proteins that were produced by the animal and not by an alien organism (Oesch et al., 1985). It was one of the host's own genes that coded for the protein that was named the prion protein (PrP). It was shown that PrP is found in almost all cells in the body in a normal form called PrP^{C} (C for cellular). When prion diseases develop, PrP^{C} become flattened and much less soluble. This form is called PrP^{Sc} (Sc for scrapie) and tend to stick together in aggregates that the cells of the body does not manage to break down.

Prion diseases are consequently characterized by a severe change in the shape of one of the body's own proteins. There are several neurodegenerative diseases (Jellinger, 2012), so-called protein aggregation diseases, where certain proteins change properties and accumulate within or around cells. The most well known are Alzheimer's disease, Parkinson's disease, Huntington's disease and Amyotrophic Lateral Sclerosis (ALS). Even though the prion diseases are categorized as protein aggregation diseases, they differ in one important aspect: The protein aggregates that are formed in a prion disease are infectious, i.e., that the disease can be transmitted from one individual to another.

Early in the 1990s were transgene mice developed that were deficient of the gene coding for PrP^{C}. These mice seemed to grow and develop without major problems and gave the researchers an important opportunity to test the theory of Prusiner. According to his model, the mice should be completely resistant against prion infection, since they missed the protein that is affected and cause the large damages associated with prion disease. This proved right (Bueler et al., 1993). The mice without PrP^{C} (often called PrP-knockout, since the gene is «knocked out») remained healthy even after exposure to large doses of prions, while mice with normal PrP^{C} turned sick and died. Several elegant experiments were published on this theme (Brandner et al., 1996).

Other findings that emphasised the crucial role of PrP in the development of these diseases, was that heritable prion diseases without exception was associated with gene changes (mutations) in the PrP-gene (*PRNP*) that caused the disease (Prusiner, 1994). It was also revealed that naturally occurring variations in this gene decided how susceptible sheep were for scrapie (Goldmann et al., 1990; Laplanche et al., 1993; Tranulis, 2002; Tranulis et al., 1999). This is the background for the investigation of variation in *PRNP* in order to clarify eventual differences in susceptibility for prion

disease in animals. In sheep and goats, gene variants have been found that are less susceptible for classic scrapie, and by selective breeding on these have the occurrence been substantially reduced (more comprehensive review of *PRNP*-genetics relevant for CWD is presented in Appendix I).
The prions are smaller than the smalles viruses, and their ability to resist physical and chemical attacks are extraordinary. Prion contamination of the environment can hence be a long-lasting problem.

Prion diseases occur in humans and some species of ruminants. The diseases are lethal and occur in several syndromes but do always cause progressive brain damage (neurodegeneration). There is so far no vaccine or treatment. Another common denominator is that they are experimentally transmissible. It has in this way been shown that they cause disease in other species, for example rodents, in inoculation trials (Prusiner, 1993).

Mad Cow Disease (BSE)

Classic Mad Cow Disease (BSE-C) is an apprehensive prion disease in cattle, which unintentionally has been transmitted to other species, including humans. In humans, BSE-C cause variant Creutzfeldt-Jakob's Disease (vCJD) after ingestion of meat products contaminated with BSE-C-infective material (Bruce et al., 1997). Variant CJD, which never have been observed in Norway, is registered as cause of death in 232 patients, including 178 in Great Britain. BSE-C was also the cause of prion disease affecting several species of Felidae (including domestic cats) and ruminants in zoological gardens, as the animals were fed with meat or bone meal from animals infected with BSE-C (Doherr, 2003). Although BSE-C could be transmitted to many species, transmission from cattle to cattle was not observed. The large extent of the epidemic was instead due to infection through their feed. After radical measures, among them prohibition of use of bone meal supplement in feed intended for ruminants, is the occurrence of BSE-C reduced from over 35.000 cases in 1992 to occasional solitary cases today. The last two cases in Great Britain were detected through active surveillance in 2015 (Somerville et al., 2019).

As a consequence of the extensive surveillance that was implemented to map the occurrence of BSE-C were two unusual variants of prion disease in cattle discovered in 2004 (Biacabe et al., 2004; Casalone et al., 2004). A comprehensive review of these, which now are called BSE-H and BSE-L, and comparison with other, unusual prion diseases in animals and humans is presented by Dudas and Czub (2017) and Tranulis et al. (2011). (Dudas and Czub, 2017; Tranulis et al., 2011). Important characteristics are that they only have been described in old animals, and that these variants are not transmitted under natural circumstances. Both BSE-H and BSE-L are hence considered to be sporadic diseases. Among cattle that are eight year or older, the incidence is estimated to approximately two cases per million cattle per year. In Norway, BSE-H was detected in 2015 in a Scottish Highland cow that was 15 years of age.

Scrapie

Scrapie in sheep and goat was the only animal prion disease we knew for several hundred years. The disease was efficiently transmitted, and many animals died (Hunter, 1972). Descriptions dating 300 years back describe which nuisance the disease was for European sheep production. Scrapie was not transmitted to other domestic animals (except from goat) and meat from sheep with scrapie was eaten by humans.

The first documented case of scrapie in Norway was detected in 1981. The occurrence increased and reached a summit in 1996, with 31 affected (Tranulis et al., 1999). Investigations showed that many animals could be infected in each herd (Ersdal et al., 2003). Powerful and controversial measures were implemented to reduce and eventually eradicate the disease. These were effective, and the last outbreak in Norwegian sheep was diagnosed in 2009 (Scrapie surveillance, NVI).
Towards the end of the 1990s, some cases of scrapie were observed in Norway that were characterized by unusual brain lesions and occurred in sheep with other genetic traits than the typical cases (Tranulis et al., 1999). Thorough investigations showed that this was a «new» disease in sheep, and it was named atypical/Nor98 scrapie (Benestad et al., 2003). The designation Nor98 refers to the discovery in Norway. Contrary to typical scrapie, which now is called «classic scrapie», is atypical scrapie reckoned to be a non-infectious variant (Tranulis et al., 2011). This imply that the disease can emerge spontaneously, without transmission to other individuals. This major difference is of great importance for the management. Atypical scrapie occur in many countries (European Food Safety, 2017) and has a stable incidence in Norway. Five to 15 cases are observed each year. Atypical scrapie is also observed in goat.

Chronic wasting disease (CWD)

In 1967 a disease characterized by wasting was observed in mule deer in Colorado, USA. None of the animals that developed clinical disease survived, and the disease spread. At first was the disease believed to be caused by malnutrition and ill-thrift, and it was given the descriptive name Chronic Wasting Disease (CWD). It did later become clear that CWD belonged to the same group of diseases as scrapie in sheep (Williams and Young, 1980). As in sheep did the transmissability lead to such a large number of cases that the disease not could be neglected. Both CWD and scrapie emerged in farm situations with very high animal densities, where disease transmission was efficient.
In the 40 years from 1980 to today has the distribution of CWD increased to embrace 26 US states and three Canadian provinces (Rivera et al., 2019). The disease is no longer limited to farmed deer, but has infected many populations of free-ranging mule deer, white-tailed deer, wapiti and some individual American moose (*Alces alces*).

Camel Prion Disease (CPD)

In addition to scrapie and CWD is another prion disease of animals described. It was discovered in dromedars (*Camelus dromedarus)* in 2016 and got the name Camel Prion Disease (CPD) (Babelhadj et al., 2018). This disease, that is of unknown origin, is widespread in Algeria, but is not discussed further in this report.

Appendix III

Measures to prevent connectivity in semi-domesticated reindeer

North of Nordfjella lies the pastures of several semi-domesticated reindeer herds. The closest, Filefjell reinlag (FRL) has implemented and continues a range of measures to prevent introduction of CWD to their own herd, but also to avoid further spread of potential infection to the neighbour herds Fram reinlag, Lom Tamrein AS and Vågå tamrein AS.

Before the eradication of the subpopulation of wild reindeer in Nordfjella Zone 1 was invasion of herds of male reindeer common. The animals crossed from Nordfjella wild reindeer area over the road RV52 and roamed in and around the valley Mørkedalen in spring. This area included salt lick sites that were used by both wild and semi-domesticated reindeer. FRL put great effort into chasing the wild reindeer herds back to Zone 1 before their own reindeer migrated to the area from their calving grounds.

An important accomplished measure in this context is the barrier fence in Mørkedalen on the western side of RV52. This fence function as a barrier that delimits FRL's bare ground pastures[20] from Nordfjella Zone 1. The bare ground pastures are in use from April-May to November-December. As long at this fence is standing and properly maintained, will it function as a disease transmission barrier against eventual CWD infected wild reindeer in Nordfjella, and it will prevent that stray animals from Filefjell wander into contaminated areas in Zone 1. However, parts of the fence are covered by snow in the winter (Mysterud og Rolandsen 2019), and the fence will not function as an impassable barrier after a re-introduction in Nordfjella Zone 1.

In the northern part of the pasture areas of FRL (and Fram reinlag) occasional adult males wander in and out from Lærdal/Årdal wild reindeer area. The origin of this wild reindeer population is reindeer that were introduced from Nordfjella Zone 1.

In December FRL moves their herd in a south-east direction towards the slaughter facilities at Golsfjellet and thereafter towards rich lichen pastures around Hedalen and Vassfaret. It should be noted that FRL by this maintain a potential route of spread of CWD between Nordfjella Zone 1 and cervid populations far south in Hallingdal and Valdres.

The FRL herd was consequently in direct and frequent contact with the wild reindeer in Nordfjella Zone 1. The direct contact with the population on Hardangervidda is probably minor or negligible. FRL do also have contact with wild reindeer in Lærdal-Årdalsfjella, where little is known about CWD status. Semi-domesticated reindeer from FRL are also in contact with semi-domesticated

[20] Translator's note: Pastures used in the period of the year without snow cover.

reindeer in the Fram, Lom and Vågå herds and with red deer, moose and roe deer in a large area.

Fram reinlag has its summer pastures between the lakes Vangsmjøsa, Tyin and Bygdin. Reindeer from this herd may get in contact with reindeer from FRL by crossing the road FV35 between the Tyin crossroads and Tyin at the same time as reindeer from Filefjell can cross E16. Reindeer can probably also wander from the Fram pastures to areas further west, i.e. in Lærdal-Årdalsfjella, and wild reindeer from that area can move into the Fram pastures.

Fram may also loose reindeer over the road between Tyinholmen and Eidsbugarden towards the wild reindeer area Vest-Jotunheimen or towards the pasture areas of the Lom and Vågå herds. During wintertime Fram are herding their animals in the areas towards Synfjellet and Ormtjernkampen (Langsua National Park). Based on this pattern can we conclude that there is some indirect connectivity between Nordfjella Zone 1 and Fram, while the connectivity between Fram and Hardangervidda probably is minor/negligible.

Lom tamrein AS herd their animals within Jotunheimen, and their pasture areas border Vest-Jotunheimen and the areas of Reinheimen-Breheimen wild reindeer area that lies in Skjåk municipality. Wild reindeer males occasionally wander into their areas from Skjåk. This is in particular old males that search for better pastures. Lom is also bordering Fram reinlag and Vågå Tamrein AS, and may in some year experience some mixing with these herds. Reindeer from other herds are either taken out and driven home to their home pastures, or if they not are too many, slaughtered on the site. When larger groups of animals get mixed, are they gathered in corrals, split and herded back. In CWD context does consequently Lom have indirect contact with Nordfjella Zone 1 via the wild reindeer in Lærdal-Årdalsfjella. Lom may also function as a route of spread between that wild reindeer population, the Fram and Vågå herds and the wild reindeer area Reinheimen-Breheimen.

Vågå tamrein AS is not bordering any wild reindeer area, but may loose some animals to Fram and Lom. They may also receive stray animals from Fram that swims over lake Bygdin, or reindeer from Lom that cross borders. The connectivity between Nordfjella Zone 1 and Hardangervidda is consequently minor/negligible.

There is considerable larger degree of mixing between herds from different areas in the Sami reindeer pasture districts in Trøndelag and the north-eastern part of Innlandet County. In connection with collection before slaughtering are reindeer from neighbour districts or Sami societies in Sweden identified and separated. These are either driven back to the district they belong to with animal transports, or if the number is too large or the distance not too large, herded back.

Appendix IV:

The probability of removing all CWD infected individuals on Hardangervidda at different prevalences and harvest strategies.

Our current understanding of the situation on Hardangervidda is that CWD was discovered in a pre-establishment phase[21]. In this phase are there few infected individuals, and direct transmission between individuals is presumed to be more important than environmental transmission. Random events can influence the development in short term. It is expected that coincidences to some degree will decide if an individual infected animal at all will transmit the infection, or if an individual by coincidence transmit the infection to many (Belsare et al., 2021). This is determined not least by how long the animals are allowed to live. Intensive harvesting in an early phase may successfully remove the infected individuals by coincidence. These probabilities are already estimated for Hardangervidda (Mysterud et al., 2021).

In a short time perspective, willl uncertainties concerning the estimates of CWD prevalence greatly affect choices and cause considerable uncertainties about the effects of measures. Uncertainty in estimation of prevalence will currently overshadow uncertainties concerning and random events affecting prevalence growth. It is hence not considered relevant to model disease dynamics for different measures accomplished within a short time frame (one to two years from now on).

What can be done to make probable the short-term consequences of measures, is to estimate simple probabilities of removal of all CWD infected animals provided different scenarios for CWD prevalence (Chapter 2.10.2). These calculations were based on the following scenarios for CWD prevalence on Hardangervidda (CWD+ = CWD-positive individuals):

- Scenario 1: 2 CWD+ adult males
- Scenario 2: 3 CWD+ adult males, 1 CWD+ adult female
- Scenario 3: 9 CWD+ adult males, 3 CWD+ adult females, 1 CWD+ yearling
- Scenario 4: 18 CWD+ adult males, 6 CWD+ adult females, 1 CWD+ yearling

This takes into account some of the variation in CWD prevalence that may be relevant on Hardangervidda. The most probable numer is one to two infected adult males (Scenario 1), but it is impossible to estimate CWD prevalence or make absence of CWD probable in the female segment of the population due to insufficient number of samples. Under the presumption that the demographic pattern of infection is relatively similar to what was found in Nordfjella Zone 1 (Chapter 2.7), may there be for example 13 infected animals (Scenario 3) on Hardangervidda.

[21] Translator's note: The original text translates to «establishment phase», but «pre-establishment phase» is used here to be in line with the text in Chapter 2.6.5.

Scenario 4 describes potential CWD prevalence after a few years, if we await the situation and not implement measures.

It is important to notice that these simulations are very simple and only useful for illustration of principles and making probably which hunting strategies that probably can and probably cannot have the desired effect (removal of all infected animals). The simulations were performed using estimated population size on Hardangervidda before the hunt in 2019 (withouth taking into account the uncertainties in this estimate), and it is assumed that the probability of removal is similar between the different harvest strategies of adult males, adult females and calves.

«Ordinary hunting» is successful in taking out all infected animals only in 3 % of the simulations, even if only two CWD-positive males were present in the population (Scenario 1). With other words: It will be unrealistic to believe that we with ordinary hunting quotas (harvest rate of 20 %) by coincidence manage to remove all infected adult females on Hardangervidda.

If there are some infected animals among the adult females (Scenario 3 and 4), and the goal is to remove all infected animals, we will soon approach complete eradication of the population. Genereally speaking, this illustrates that the measure only will succede if the infection only is present among the adult males (Scenario 1), and a radical harvest of this segment of the population is accomplished. If infected females are found, will the thought of line about eradication of the disease by coincidental removal of infected animals, be regarded as less realistic.

Table 1: Overview of the probability of removal of all CWD-positive individuals (CWD+) in a population of the same size as the Hardangervidda population provided different hunting strategies (Str. 1 to 7):

It is not certain how many CWD-positive reindeer that are present on Hardangervidda. Consequently, we have looked on different Scenarios of prevalence of infection (presented in the text above). Population size estimates before the hunting season of 2019 are used in the estimations. Harvest is then the proportion of a given segment of the population that is culled. Harvest of yearlings follows the harvest of adult females. Gender ratio = number of adult males/numbers of adult females.

Parameter		**Harvest strategies**							
		Ordinary	**Str. 1**	**Str. 2**	**Str. 3**	**Str. 4**	**Str. 5**	**Str. 6**	**Str. 7**
	Harvest in %								
Adult males		20	70	90	100	100	100	100	100
Adult females		20	50	60	70	80	90	95	98
Calves		13	13	24	40	60	80	95	95
	Population size								
	Before hunting	After hunting							
Adult males	2356	1883	706	237	0	0	0	0	0
Adult females	3376	2700	1694	1005	674		339	169	67
Male yearlings	665	532	331	266	202	133	67	33	13
Female yearlings	723	578	358	289	218	144	72	38	15
Calves	1286	1121	1120	978	770	516	259	64	64
Total population	8406	6814	4209	3118	2195	1467	737	304	159
Gender ratio	1:1.43	1:1.43	1:2.40	1:5.7	NA	NA	NA	NA	NA
	Probability of removing all CWD-positive animals using different harvest strategies								
Scenario I*		0.03	0.53	0.8	1	1	1	1	1
Scenario II*		0.01	0.18	0.45	0.76	0.75	0.88	0.91	0.98
Scenario III*		0	0.01	0.06	0.17	0.34	0.65	0.83	0.94
Scenario IV*		0	0	0.01	0.1	0.28	0.46	0.72	0.86

Source: (Mysterud et al., 2021).

* Scenario I: 2 CWD+ adult males
* Scenario II: 3 CWD+ adult males, 1 CWD+ adult female
* Scenario III: 9 CWD+ adult males, 3 CWD+ adult females, 1 CWD+ yearling
* Scenario IV: 18 CWD+ adult males, 6 CWD+ adult females, 1 CWD+ yearling