



"Wildlife health status in Norway" More than a need an obligation!

Why?

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European Veterinary Specialist
Head of Food Safety & Emerging Health Threats
Associate Professor





Veterinærinstituttet
Norwegian Veterinary Institute

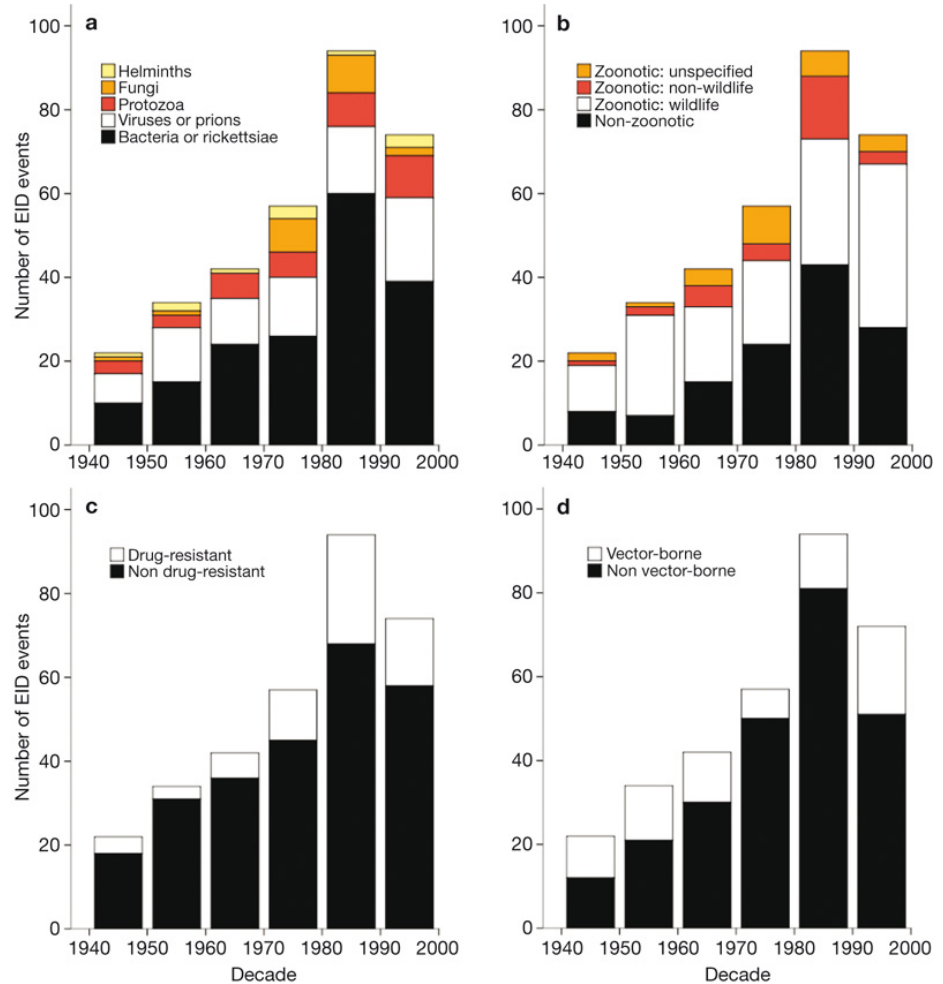


*Why must ALL wildlife
experimental field work cover
wildlife health?*



EID – EMERGING INFECTIOUS DISEASES

- EID events are dominated by zoonosis (60.3% of EIDs)
- **The majority of these (71.8%) originate in wildlife** (for example, severe acute respiratory virus, Ebola virus), and are increasing significantly over time.
- 54.3% of EID events are caused by bacteria or rickettsia, reflecting a large number of drug-resistant microbes.



1986	First case of BSE United Kingdom
1993	Hantavirus (Sin Nombre Virus) United States
1994	Hendra virus Australia
1997	First human cases of avian influenza H5N1 Hong Kong Menangle virus Australia
1998	Nipah virus Malaysia
1999	West Nile Virus United States
2003	Monkeypox, First case of BSE United States
2009	Human H1N1 pandemic United States, many countries worldwide

[Nature](#), 2008 Feb 21;451(7181):990-3.

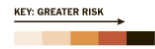
Global trends in emerging infectious diseases.

[Jones KE](#), [Patel NG](#), [Levy MA](#), [Storeygard A](#), [Balk D](#), [Gittleman JL](#), [Daszak P](#).

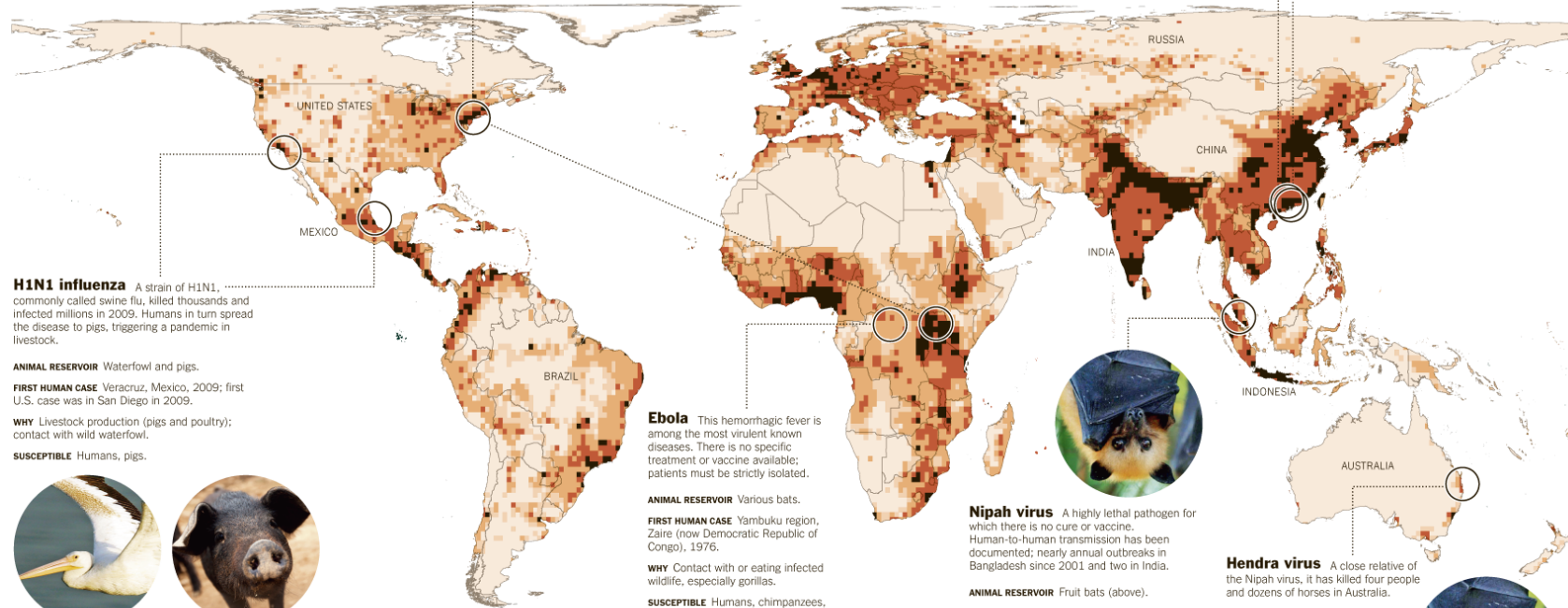


Hot Spots for Emerging Diseases

Map shows an analysis of the future likelihood of infectious diseases originating in wildlife that have the potential to infect humans.



Factors in the analysis included population density, proximity to and variety of wildlife, and climate.



West Nile virus A mosquito-borne illness that causes symptoms in about a fifth of those exposed. One in 150 becomes severely ill with encephalitis.

ANIMAL RESERVOIR Various birds, especially robins in the U.S.

FIRST HUMAN CASE West Nile district of Uganda, 1937; first U.S. case was in Queens in 1999.

WHY IT EMERGED International air travel.

SUSCEPTIBLE HOSTS Humans; birds, especially crows; horses.



SARS A severe viral respiratory infection that quickly spread from China to more than two dozen countries. The outbreak was contained, and since 2004 no new cases have been reported.

ANIMAL RESERVOIR Horseshoe bats.

FIRST HUMAN CASE Guangdong Province, China, 2003.

WHY Wildlife markets and trade; global travel.

SUSCEPTIBLE Humans, civets (inset, left).



Bird flu A deadly strain of the avian influenza virus called H5N1 has spread to humans via contact with live or dead poultry.

ANIMAL RESERVOIR Wild waterfowl.

FIRST HUMAN CASE Hong Kong, 1997. It re-emerged widely in 2003 and 2004.

WHY Global expansion of intensive poultry farming; contact with infected birds.

SUSCEPTIBLE Humans, poultry, cats.

H1N1 influenza A strain of H1N1, commonly called swine flu, killed thousands and infected millions in 2009. Humans in turn spread the disease to pigs, triggering a pandemic in livestock.

ANIMAL RESERVOIR Waterfowl and pigs.

FIRST HUMAN CASE Veracruz, Mexico, 2009; first U.S. case was in San Diego in 2009.

WHY Livestock production (pigs and poultry); contact with wild waterfowl.

SUSCEPTIBLE Humans, pigs.



Ebola This hemorrhagic fever is among the most virulent known diseases. There is no specific treatment or vaccine available; patients must be strictly isolated.

ANIMAL RESERVOIR Various bats.

FIRST HUMAN CASE Yambuku region, Zaire (now Democratic Republic of Congo), 1976.

WHY Contact with or eating infected wildlife, especially gorillas.

SUSCEPTIBLE Humans, chimpanzees, gorillas, duikers (small African antelopes, below right).



Nipah virus A highly lethal pathogen for which there is no cure or vaccine. Human-to-human transmission has been documented; nearly annual outbreaks in Bangladesh since 2001 and two in India.

ANIMAL RESERVOIR Fruit bats (above).

FIRST HUMAN CASE Sungai Nipah, Negri Sembilan, Malaysia, 1998.

WHY Large-scale livestock production; presence of orchards on pig farms; date palm sap harvest (eating contaminated sap is a significant cause of infection).

SUSCEPTIBLE Humans, pigs, horses, dogs, cats.

Hendra virus A close relative of the Nipah virus, it has killed four people and dozens of horses in Australia.

ANIMAL RESERVOIR Fruit bats.

FIRST HUMAN CASE Hendra, a suburb of Brisbane, Australia, 1994.

WHY Urban encroachment of wild habitats.

SUSCEPTIBLE Humans, horses, dogs.





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Photo: Norwegian Institute for Nature Research (NINA)



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Norwegian Veterinary Institute



"Wildlife health **diseases** status in Norway"
More than a need an obligation!

"Wildlife health **diseases** status in Norway"
More than a need an obligation!





Understanding the concept of «health»

- In veterinary medicine, health has been defined as “a state of physical and psychological well-being and of productivity, including reproduction” and “health indices” refer to easily observed parameters that can be used as a guide to the animal’s or group’s state of health (e.g., food intake, fecal output, body weight).
- It has recently been proposed to redefine health as “the ability to adapt and to self-manage”
- If it is unable to mount a protective response, reducing the potential for harm and restoring an (adapted) equilibrium, damage remains and may result in illness. Accordingly, measuring health is challenging and requires tools for assessing an individual’s capacity to cope and to adapt.
- It is also important to differentiate between the health status of individuals and that of populations.



Understanding the concept of «disease» (Wobeser 2003)

1. Is measured in terms of **impairment of function** rather than by the death of individuals.
2. **Factors that cause disease** may be either **intrinsic**, such as an inherited defect in an animal's vascular plumbing or degenerative changes associated with aging, or **extrinsic**, such as a virus, bacterium, or contaminant that enters its body and causes injury.
3. Disease may result from **factors acting alone or in combination**.
4. Many **different functions** may be impaired.



Harmonisation of the Care and Use of Animals in Field Research

Gardermoen, 21 – 22 May 2008

A consensus document from the participants

Introduction

An international consensus meeting was held in May 2008 at Gardermoen, Oslo, to discuss the care and [Ingen tittel]als in field research. A total of 52 participants from Norway (43), Great Britain (4), Canada (2), Germany (2) and Sweden (1) attended.

The specific aims of the meeting were:

- to provide a forum for dialogue between stakeholders (regulators, researchers and animal welfarists).
- to increase focus on "the 3Rs" (*Replacement, Reduction, Refinement*) of Russell & Burch (http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm).

The meeting was jointly organised by:

- The Norwegian Animal Research Authority (www.fdu.no).
- The Norwegian Institute for Nature Research (www.nina.no).
- The Norwegian Polar Institute (www.npolar.no).
- Norecopa (Norway's national platform for the 3Rs, www.norecopa.no).

The presentations held at the meeting are available on Norecopa's website. Norecopa aims to advance the 3Rs in animal research and testing, and facilitate cooperation between stakeholders. A further aim of the meeting was therefore to identify tasks for Norecopa in the area of field research. Although research on captive wild animals also raises ethical and welfare issues, this subject was not addressed at the meeting.

This document summarises the participants' views on field research and the potential for implementation of the 3Rs in the field. It is a consensus document that has been circulated to all participants for approval.

WELFARE 12

COOPERATION 1

HEALTH 1

DISEASE 0

SURVEILLANCE 0



THE PROBLEM

SOLUTIONS

THE VET's SOLUTIONS

THE BIOLOGIST's SOLUTIONS

THE ECOLOGIST's SOLUTIONS



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Time for paradigm shifts ?

FOCUS ON WILDLIFE HEALTH

BIOLOGIST
ECOLOGIST

FOCUS ON WILDLIFE DISEASE

VETERINARIAN

NO FOCUS

POLITICIAN



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Time for paradigm shifts ?



OPEN SEA SEAL AERIAL SURVEYS



Estimation of harp seal pup production in the Greenland Sea using spatial analysis on aerial survey data

Arnt-Børre Salberg*, Garry B. Stenson†, Tore Haug*, and Kjell T. Nilssen*

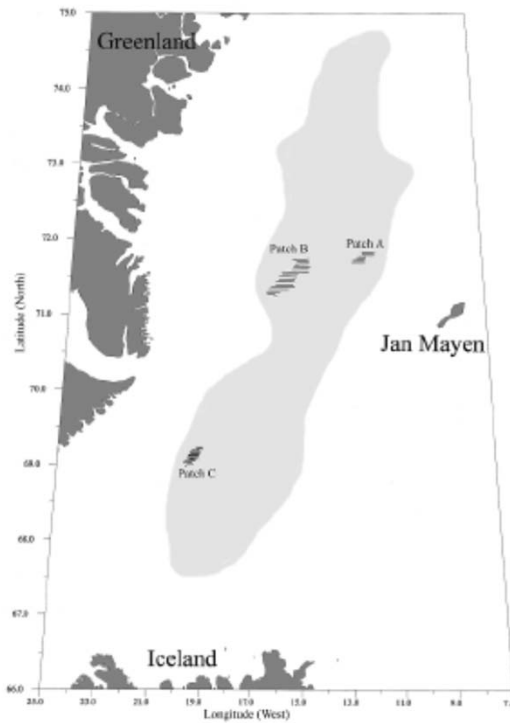


Figure 1: Survey area in the Greenland sea with three seal patches [A, B, and C]: Shaded area indicate where fixed-wing reconnaissance surveys were flown.





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Ryser-Degiorgis *BMC Veterinary Research* 2013, **9**:223
<http://www.biomedcentral.com/1746-6148/9/223>



REVIEW

Open Access

Wildlife health investigations: needs, challenges and recommendations

Marie-Pierre Ryser-Degiorgis

"Growing human population, globalization, climate change and a number of ecological perturbations have resulted in an increasing number of emerging diseases. Given this context, the role of wildlife in human and domestic animal disease emergence has become widely recognized as a factor **we can no longer afford to ignore**. Thus, **wildlife health surveillance has become an integral component in the identification and management of potential threats to human and animal health**"

Has it?

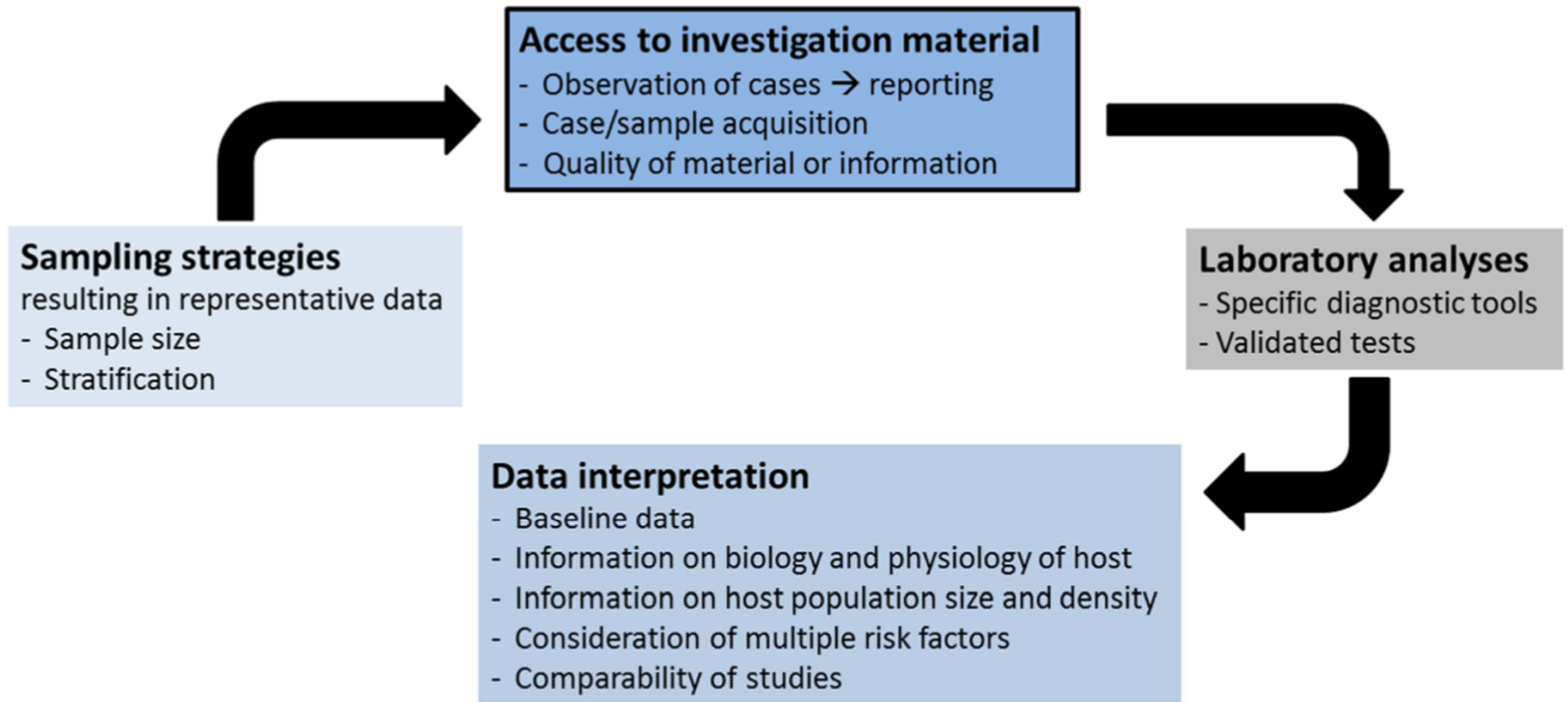


Figure 3 Challenges inherent in wildlife health investigations.



INSTITUTIONAL CHALLENGES

-  Norwegian Ministry of Justice and Public Security
-  Norwegian Ministry of Climate and Environment
-  Norwegian Ministry of Education and Research
-  Norwegian Ministry of Foreign Affairs
-  Norwegian Ministry of Trade, Industry and Fisheries
-  Norwegian Ministry of Agriculture and Food
-  Norwegian Ministry of Health and Care Services
























ECONOMICAL CHALLENGES



NILU Norsk institutt for luftforskning
Norwegian Institute for Air Research

folkehelseinstituttet

NIVA
Norsk institutt for vannforskning

HAVFORSKNINGSINSTITUTTET
INSTITUTE OF MARINE RESEARCH

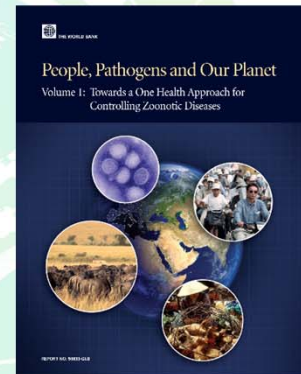
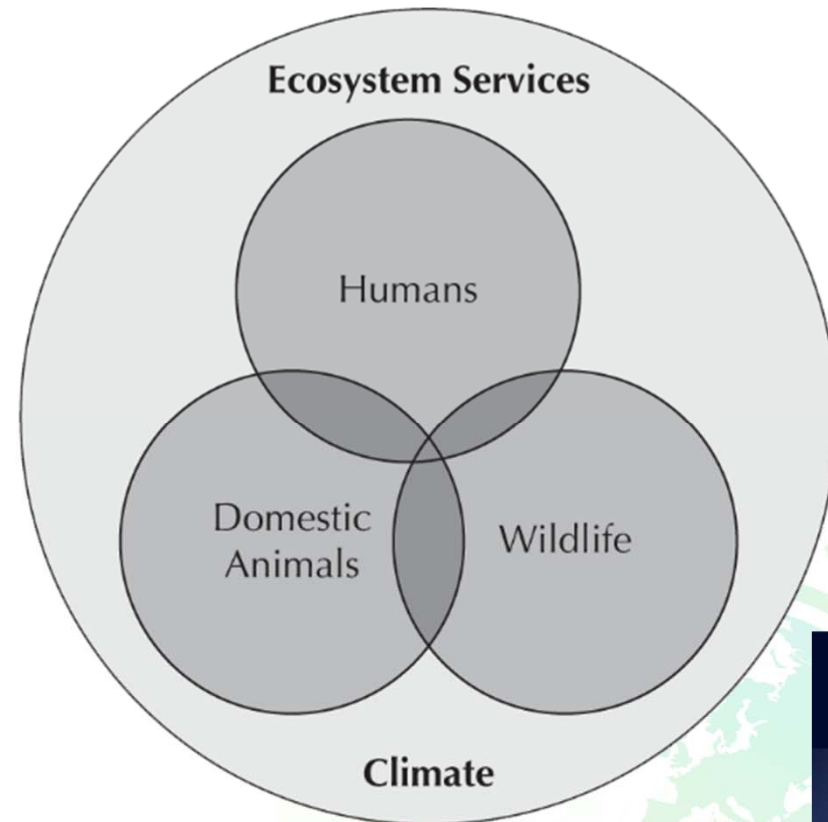
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Norwegian Veterinary Institute

NORSK-POLARINSTITUTT

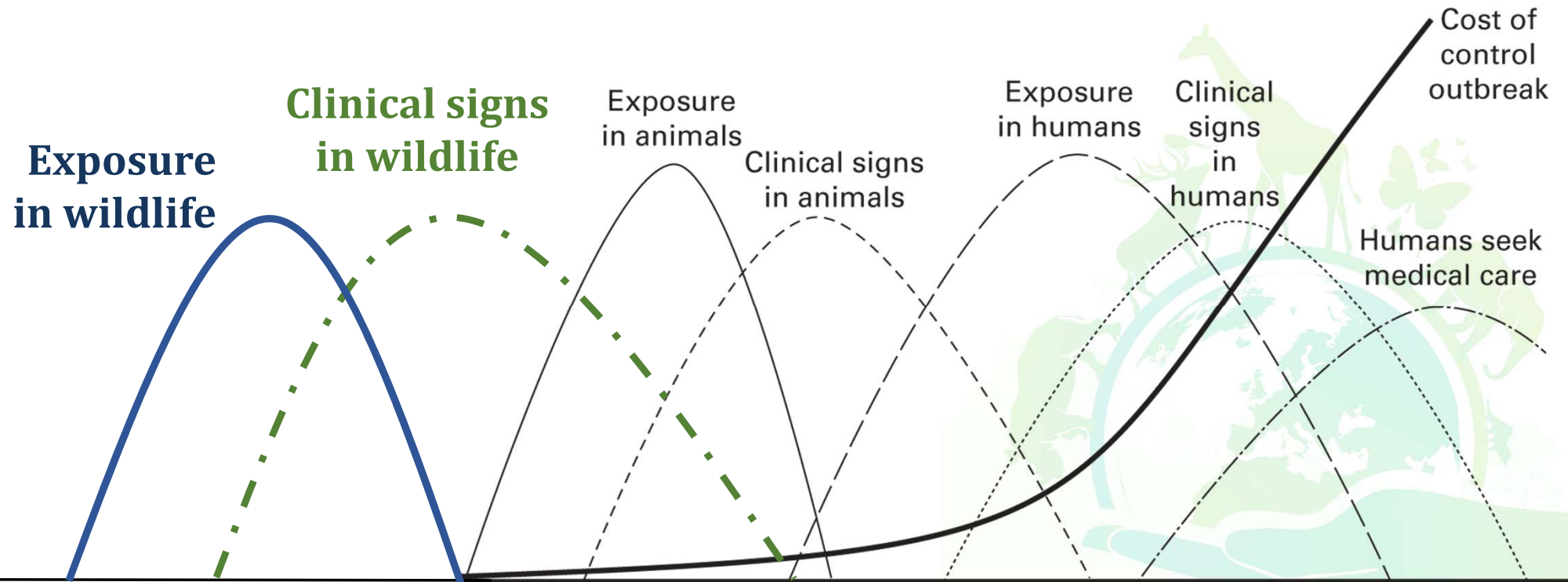
NINA
Norwegian Institute for Nature Research

Norwegian Meteorological Institute





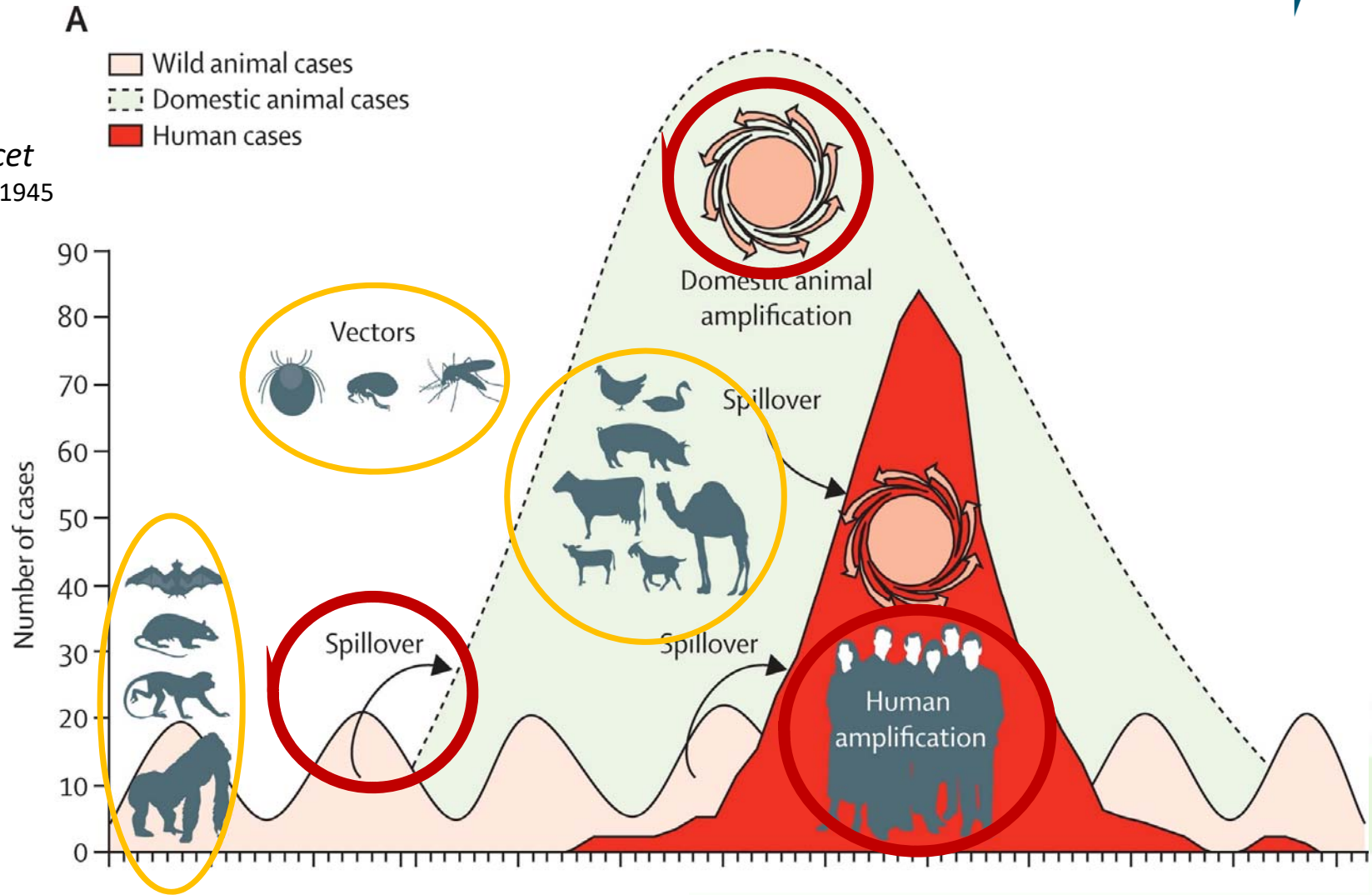
The most famous Venn diagram in the world

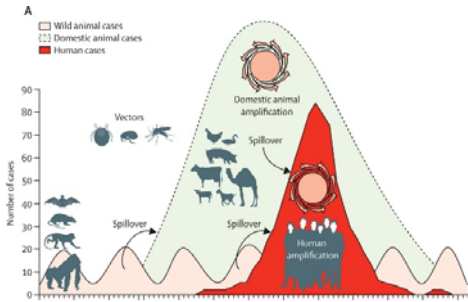


Source: Adapted from IOM (2009).



Karesh et al., 2012. The Lancet
Volume 380, Issue 9857, Pages 1936-1945





- Health & Welfare
- Conservation
- Population dynamic
- Financial aspects

Wildlife
itself

- Risk of zoonosis & EIDs
- Increase knowledge & awareness

Humans

Environment

- Environmental indicators
- Sentinel species
- Ecosystem maintenance

Domestic
animals

- Transmission of pathogens
- Confounders
- Diagnostic solutions



INTEGRATE HEALTH SURVEILLANCE in FIELDWORK

- Ownership....**Norway vs me?**
- **OPEN ACCESS!!!!!!!**
- Coordinated / centralized data/sample **banks**
- **Continous** sampling of **standardized samples** (blood, hair, feces, etc)
- Better use of **big-data** and **advanced** molecular techniques?
- **Multidisciplinary** «surveillance programs»?
- Integration in **scandinavian/european** solutions?



DANGER

DON'T RUN



BEWARE!

**DEEP
SHAFTS**



**DON'T WALK
BACKWARDS**



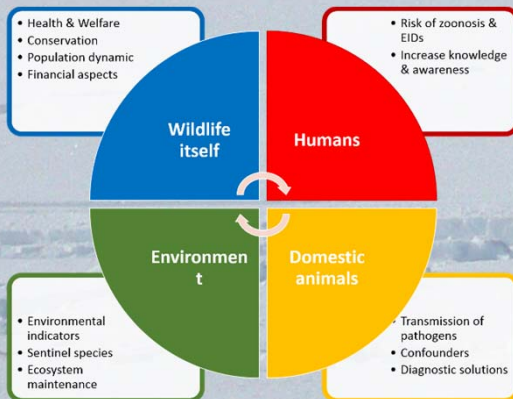
UNMARKED HOLES



DEPARTMENT OF
MINES AND ENERGY

Some health issues to think of...

disease?





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First challenge.... **DEFINITION**



An **emerging disease** is one that has appeared in a population for the first time, or that may have existed previously but is rapidly increasing in incidence or geographic range.





First challenge.... **DEFINITION**

Emerging infectious disease

Newly identified & previously unknown infectious agents that cause public health problems either locally or internationally

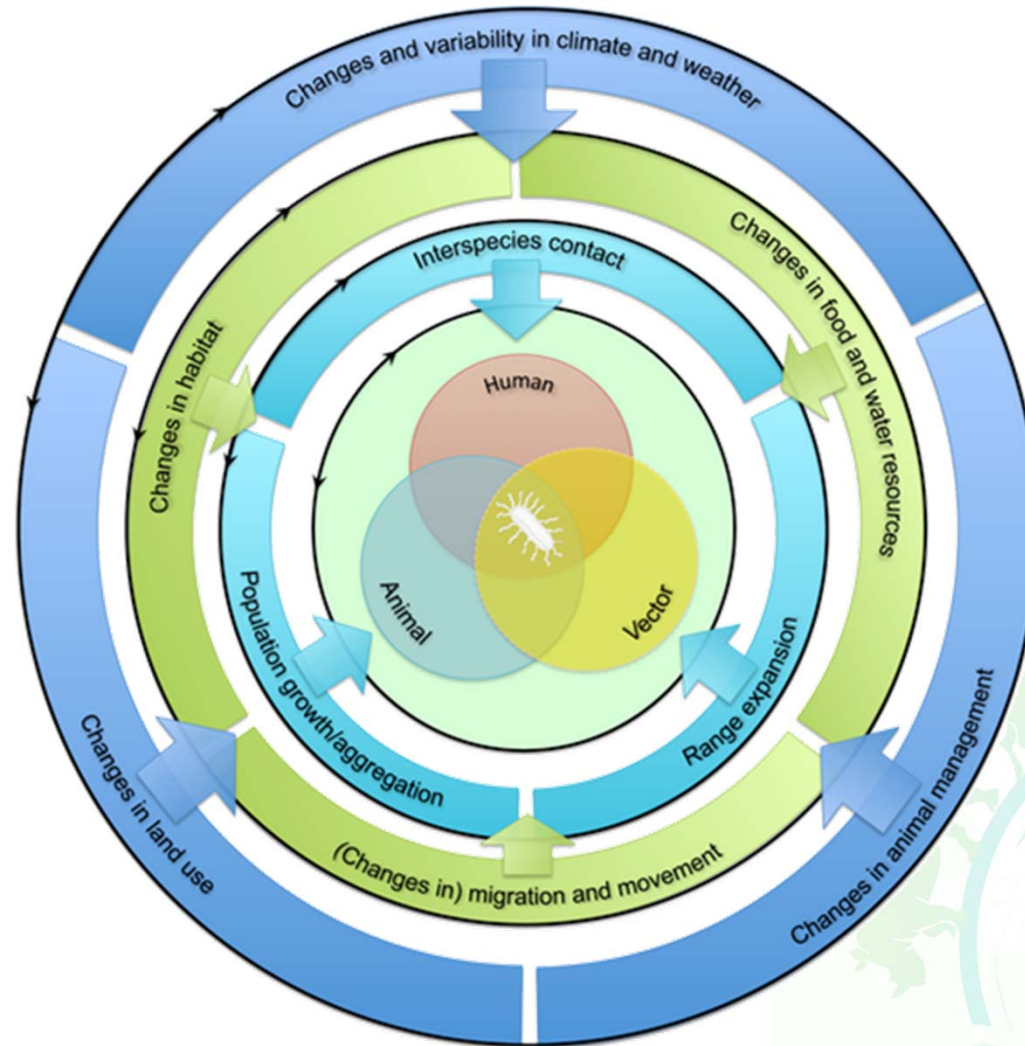
Re-emerging infectious disease

Infectious agents that have been known for some time, had fallen to such low levels that they were no longer considered public health problems & are now showing upward trends in incidence or prevalence worldwide





A quickly changing ecosystem



Gortazar C, Reperant LA, Kuiken T, de la Fuente J, Boadella M, et al. (2014) Crossing the Interspecies Barrier: Opening the Door to Zoonotic Pathogens. PLoS Pathog 10(6): e1004129. doi:10.1371/journal.ppat.1004129
<http://journals.plos.org/plospathogens/article?id=info:doi/10.1371/journal.ppat.1004129>

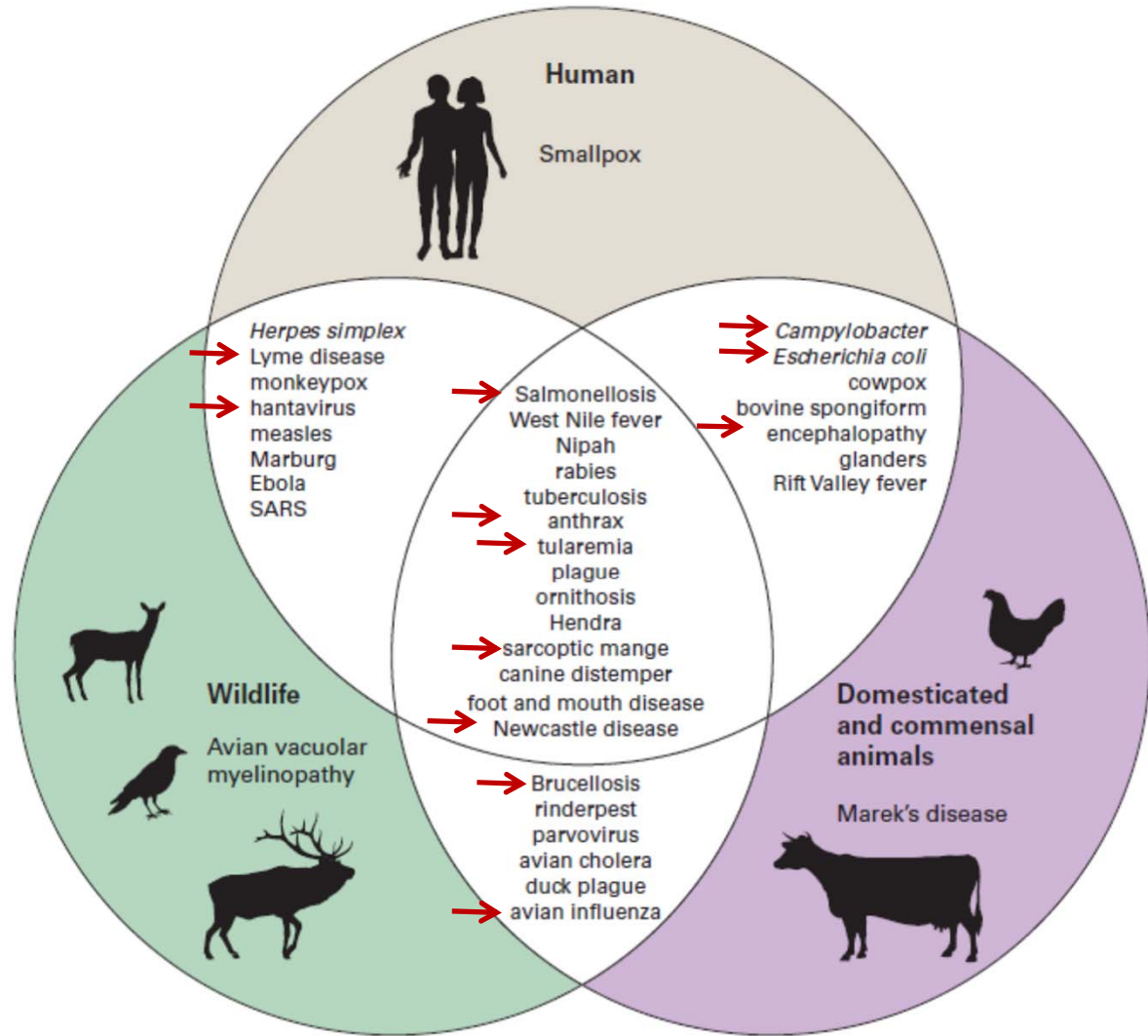
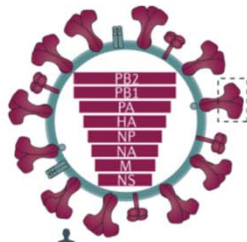
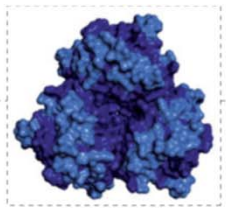


Figure 6.1 Examples of linkages between important infectious diseases of wildlife, domestic animals, and humans. (Modified from Dudley and Woodford⁴¹).

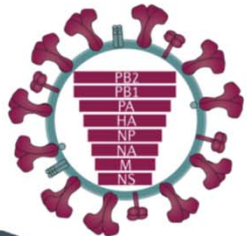
INFLUENZA VIRUS



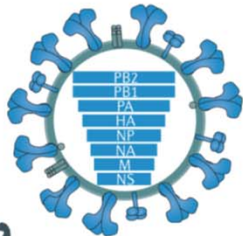
1918 H1N1



1918 H1N1 HA



Classical swine H1N1

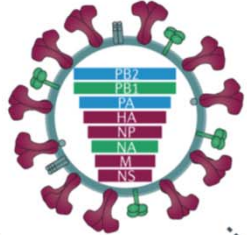


North American avian

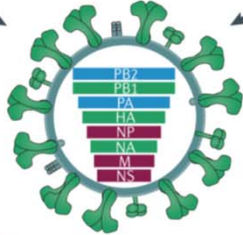


Human H3N2

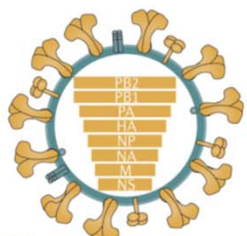
Antigenically similar HA owing to lack of selection pressure in pigs or drift in pig-specific antigen sites



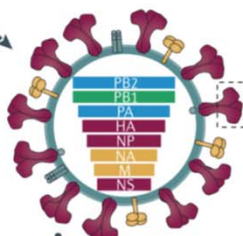
North American swine H1N2



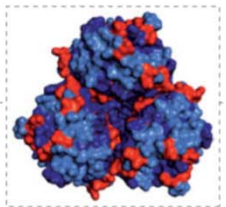
North American swine H3N2



Eurasian 'avian-like' swine H1N1



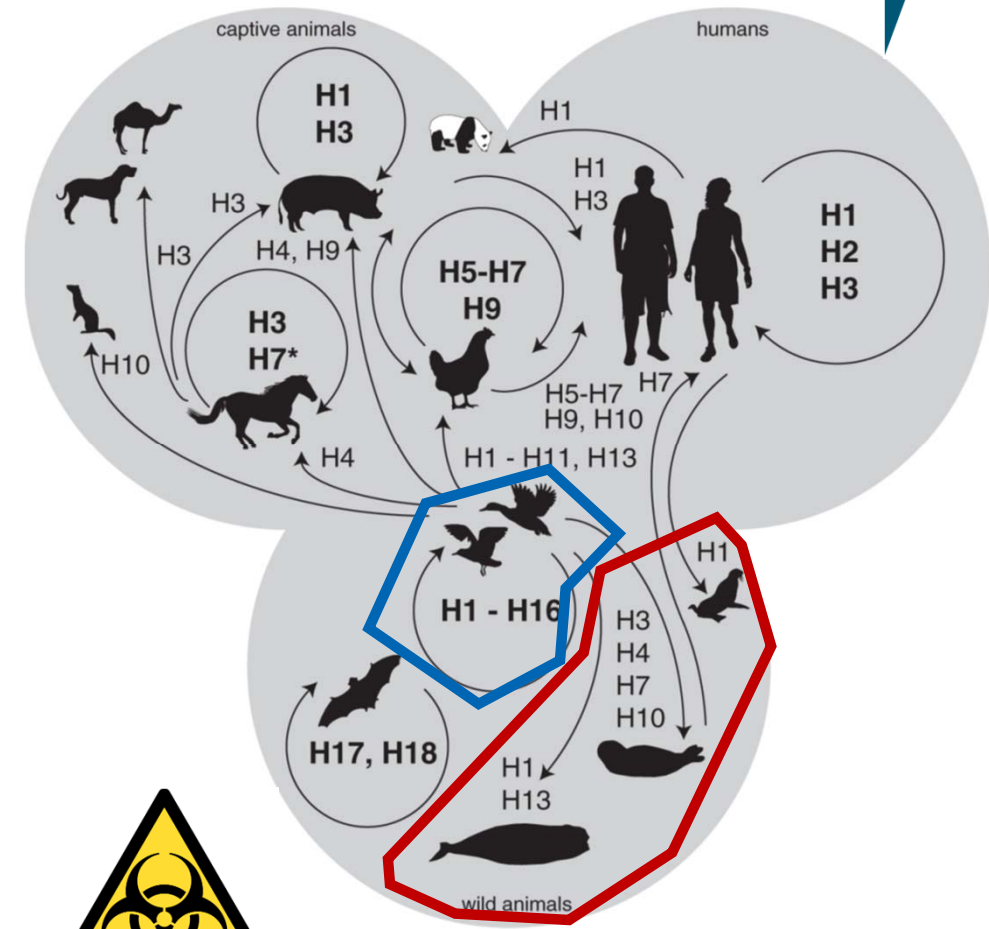
Emergence of the novel H1N1



2009 H1N1 HA

'Antigenically frozen' HA capable of producing a new pandemic

K.R. Short et al. / One Health 1 (2015) 1-13





H10N7



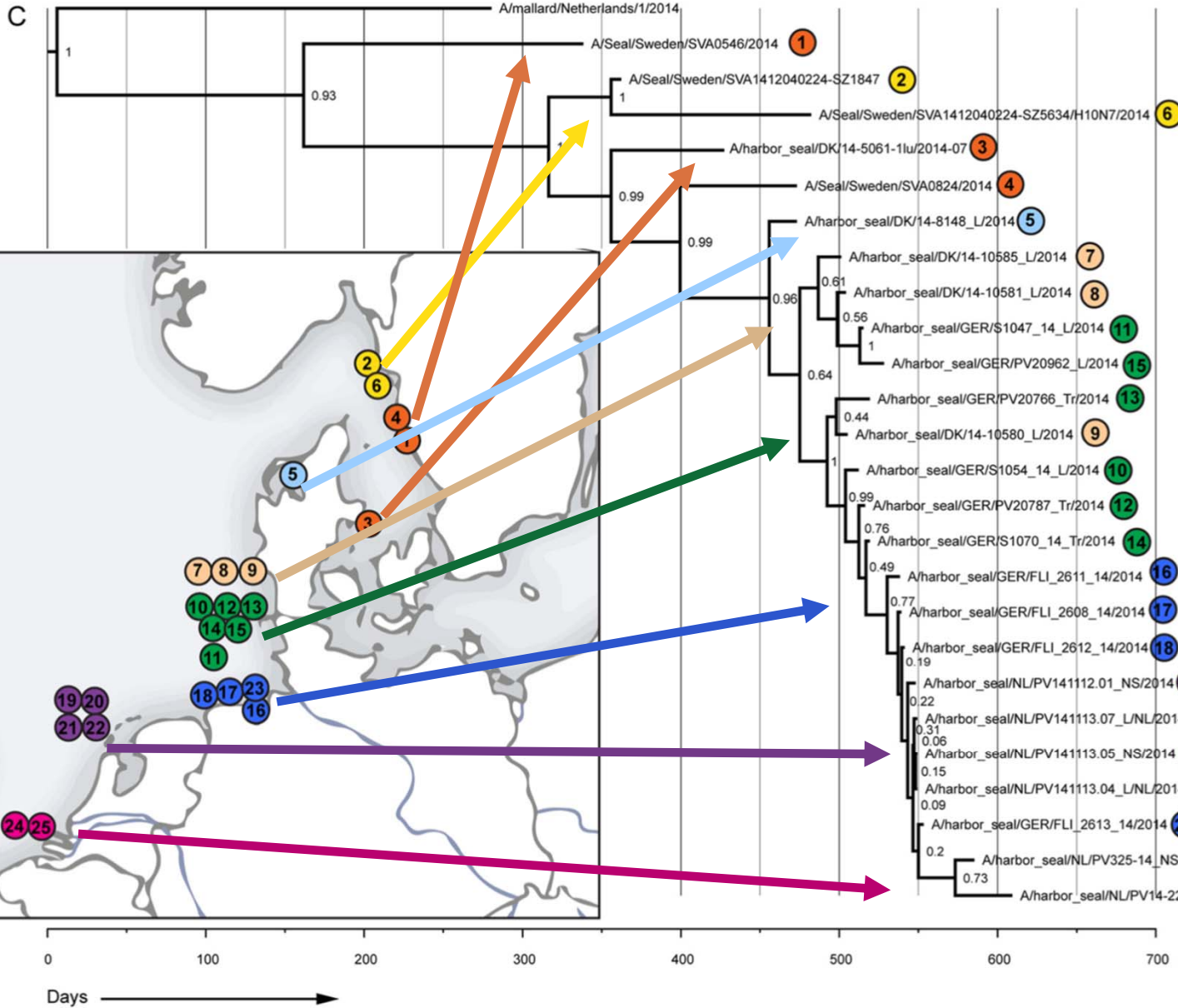
425 deaths
March - October 2014

152 deaths (Anholt)
June-August 2014

Approx. 1400 deaths
September- November 2014

First cases in the Netherlands
November 2014

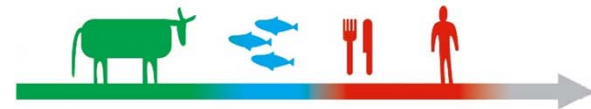




Spatiotemporal Analysis of the Genetic Diversity of Seal Influenza A(H10N7) Virus, Northwestern Europe

Rogier Bodewes,^{1*} Siamak Zohari,² Jesper S. Krog,³ Matthew D. Hall,⁴ Timm C. Harder,⁵ Theo M. Bestebroer,⁶ Marco W. G. van de Bildt,⁶ Monique I. Sponken,⁶ Lars E. Larsen,⁶ Ursula Siebert,⁶ Peter Wohlsein,⁶ Christina Puff,⁶ Frauke Seehusen,⁶ Wolfgang Baumgärtner,⁶ Tero Härkönen,⁶ Saskia L. Smits,⁶ Sander Herfst,⁶ Albert D. M. E. Osterhaus,^{6,11} Ron A. M. Fouchier,⁶ Marion P. Koopmans,^{6,8} Thijs Kuiken⁶

**Mutating
as it swims...**





RESEARCH ARTICLE

Influenza A (H10N7) Virus Causes Respiratory Tract Disease in Harbor Seals and Ferrets

Judith M. A. van den Brand¹*, Peter Wohlsein²*, Sander Herfst¹, Rogier Bodewes¹,
Vanessa M. Pfankuche², Marco W. G. van de Bildt¹, Frauke Seehusen², Christina Puff²,
Mathilde Richard¹, Ursula Siebert³, Kristina Lehnert³, Theo Bestebroer¹,
Pascal Lexmond¹, Ron A. M. Fouchier¹, Ellen Prenger-Berninghoff⁴, Werner Herbst⁴,
Marion Koopmans¹, Albert D. M. E. Osterhaus^{1,2}, Thijs Kuiken¹*,
Wolfgang Baumgärtner²*,

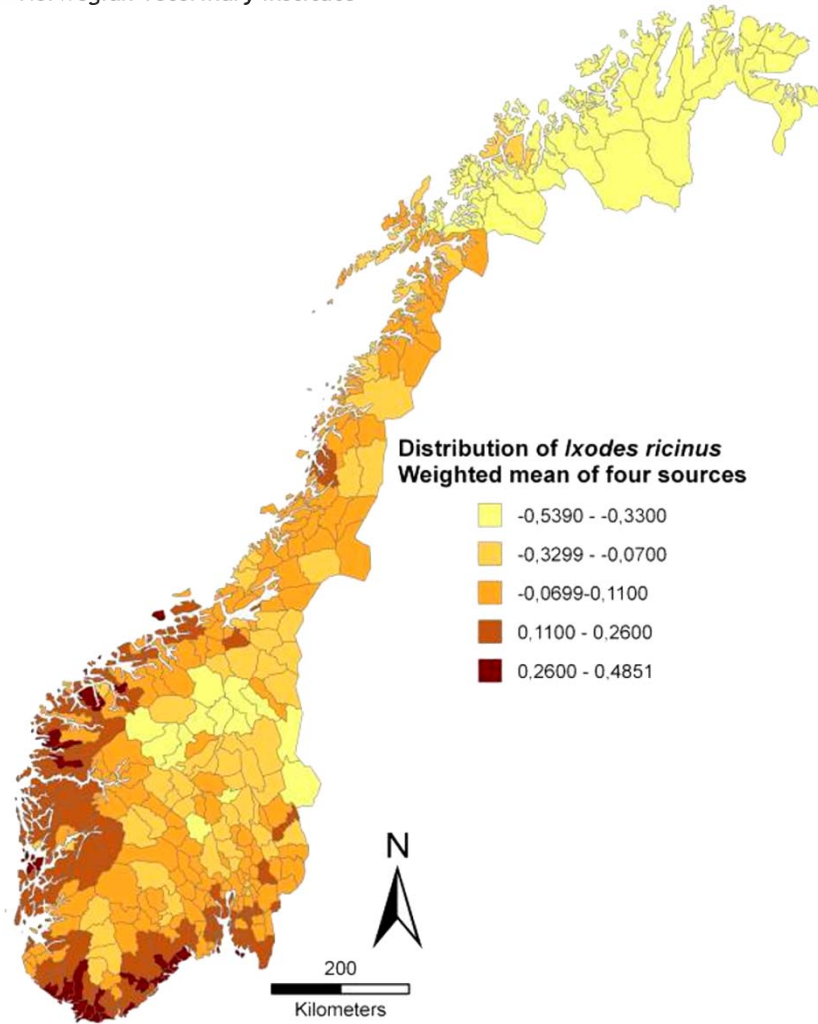


- Productive infection of ferrets indicates that seal/H10N7 may **possess a zoonotic potential**



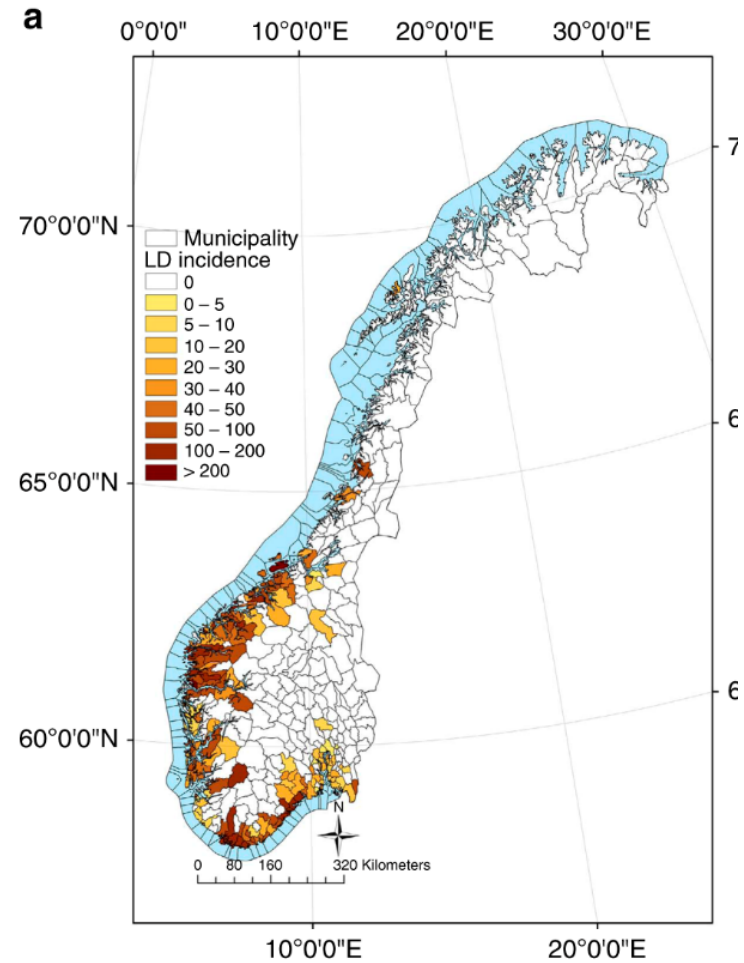


Ixodes ricinus
Ixodes persulcatus



Contrasting emergence of Lyme disease across ecosystems

Atle Mysterud¹, William Ryan Easterday¹, Vette Malmer Stigum¹, Anders Bjørnsgaard Aas^{1,2}, Erling L. Meisingset³ & Hildegunn Viljugrein^{1,4}

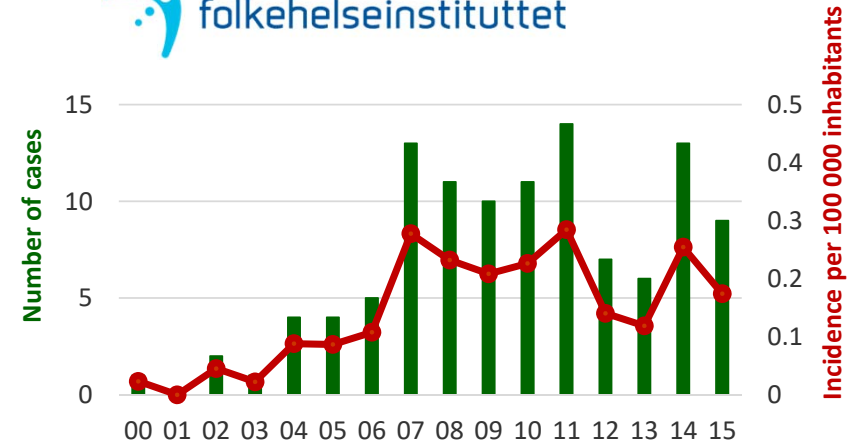
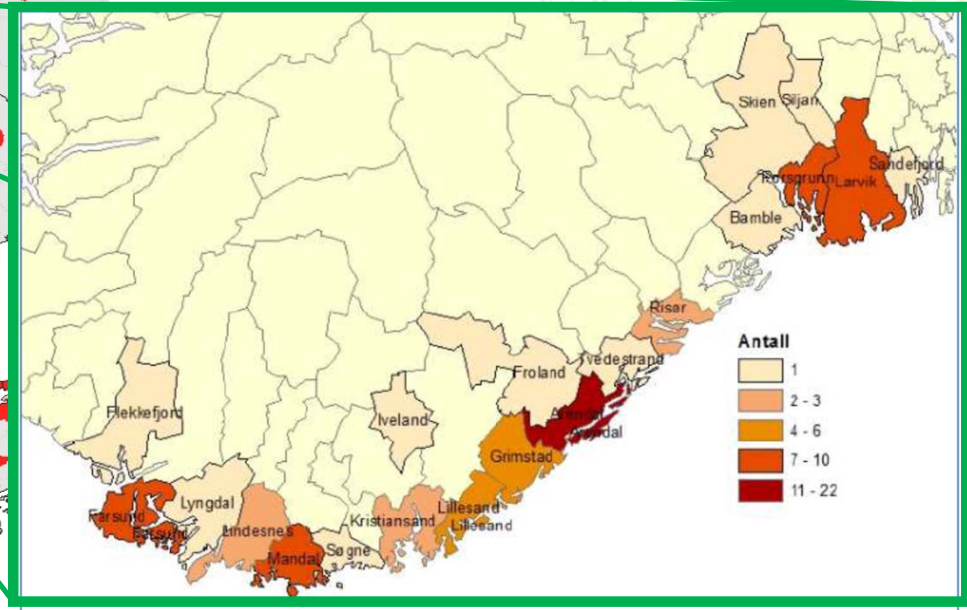
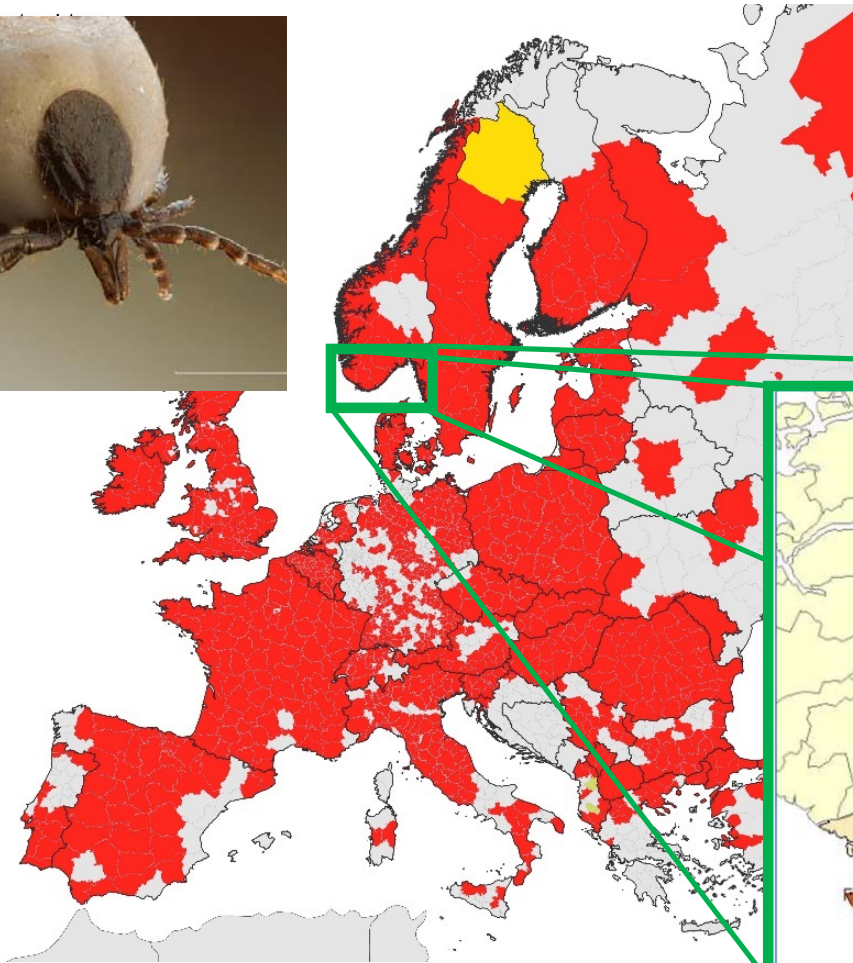




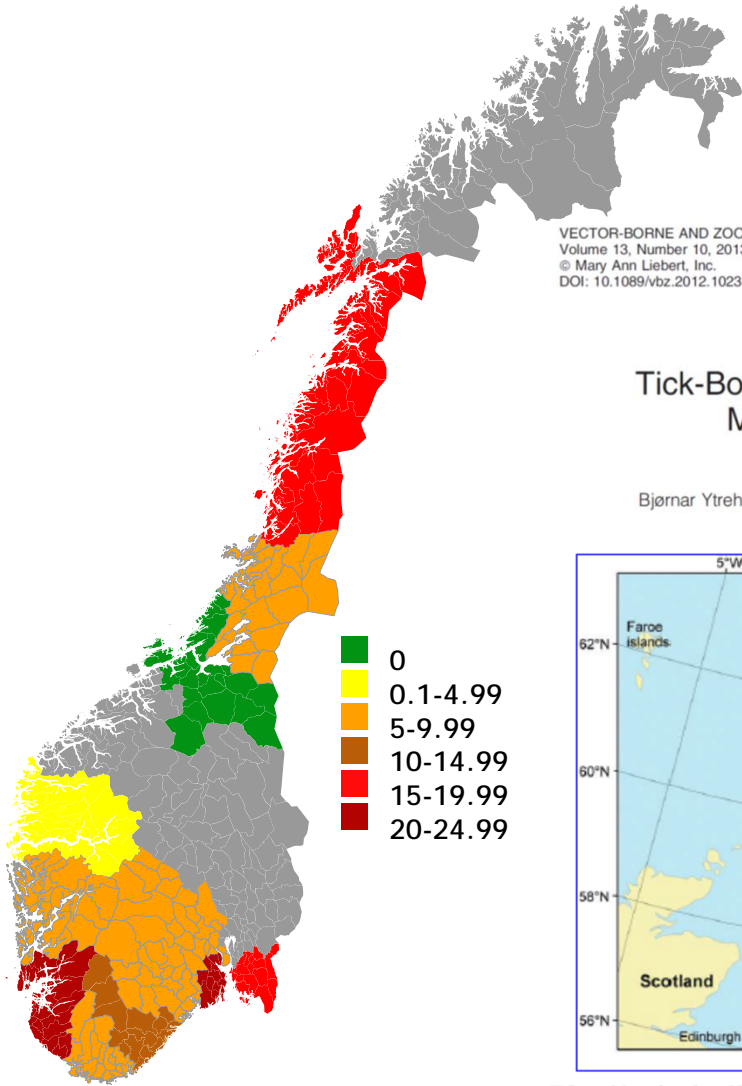
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TBE



- Ricks moving northwards
- TBE found in ticks in areas without humans cases



VECTOR-BORNE AND ZOO NOTIC DISEASES
Volume 13, Number 10, 2013
© Mary Ann Liebert, Inc.
DOI: 10.1089/vbz.2012.1023

Tick-Borne Encephalitis Virus and Louping-III Virus May Co-Circulate in Southern Norway

Bjørnar Ytrehus,¹ Kirsti Vainio,² Susanne G. Dudman,² Janice Gilray,³ and Kim Willoughby³

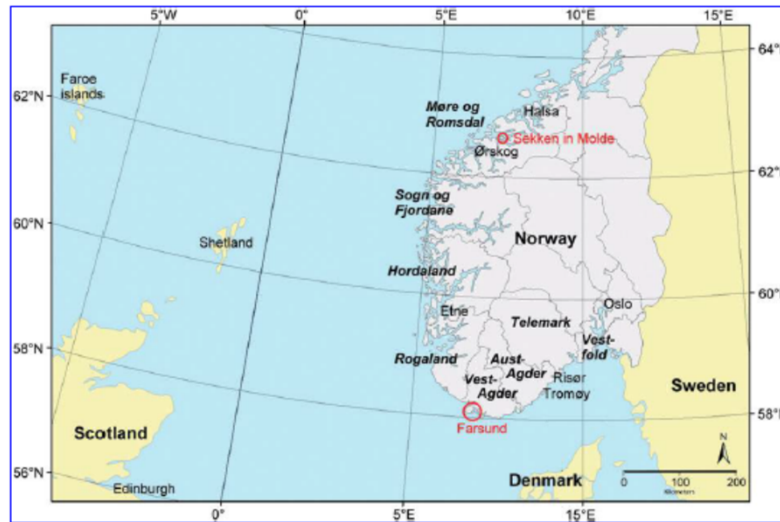


FIG. 1. Map of southern Norway. Sekken in Molde and Farsund are marked with circles. (Color image available online at www.liebertpub.com/vbz)



- Is TBE present in cervids?
- Can cervids be used as sentinel species (*early warning systems*)



- National health surveillance program for cervids and muskox
- 2000-2015 = >6000 animals sampled
- **2013 collection chosen for study**
- **755 animals from 15 regions**

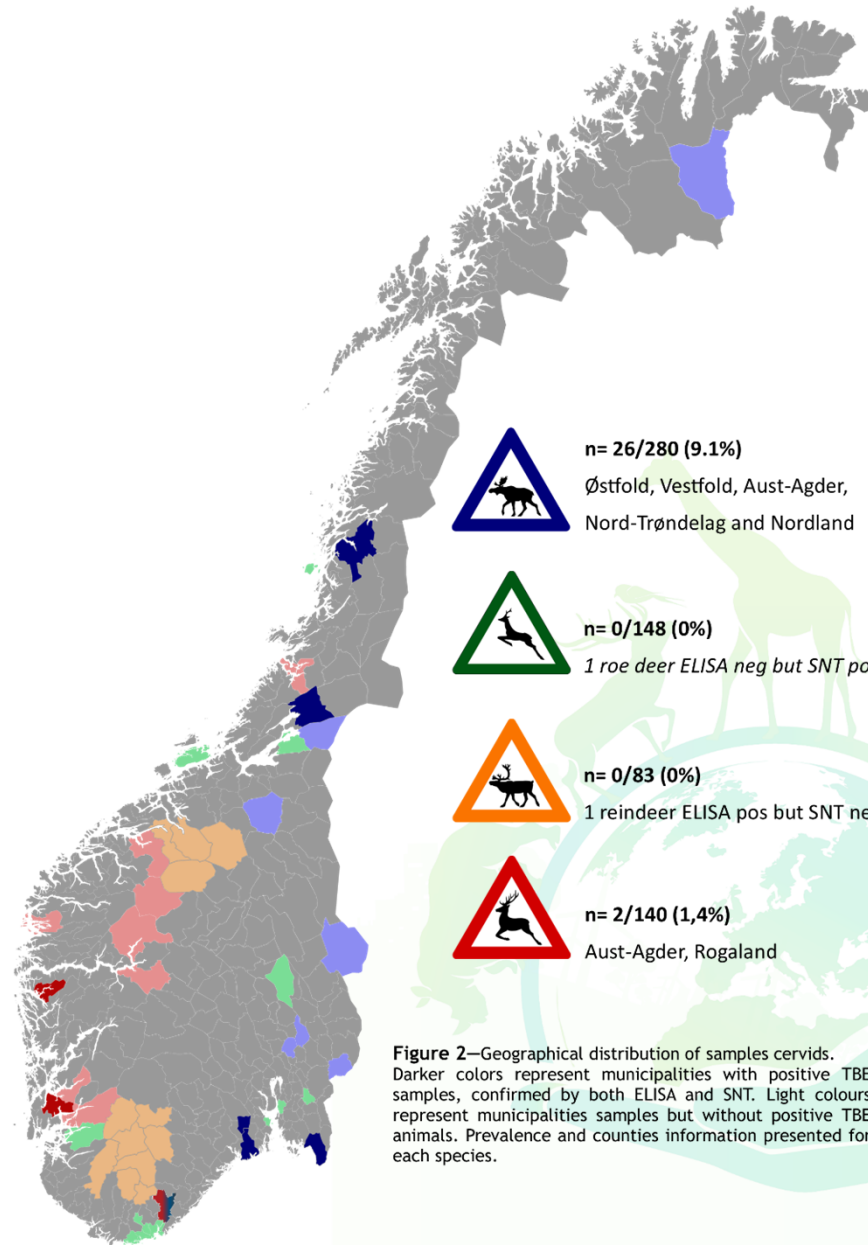


Figure 2—Geographical distribution of samples cervids. Darker colors represent municipalities with positive TBE samples, confirmed by both ELISA and SNT. Light colours represent municipalities samples but without positive TBE animals. Prevalence and counties information presented for each species.

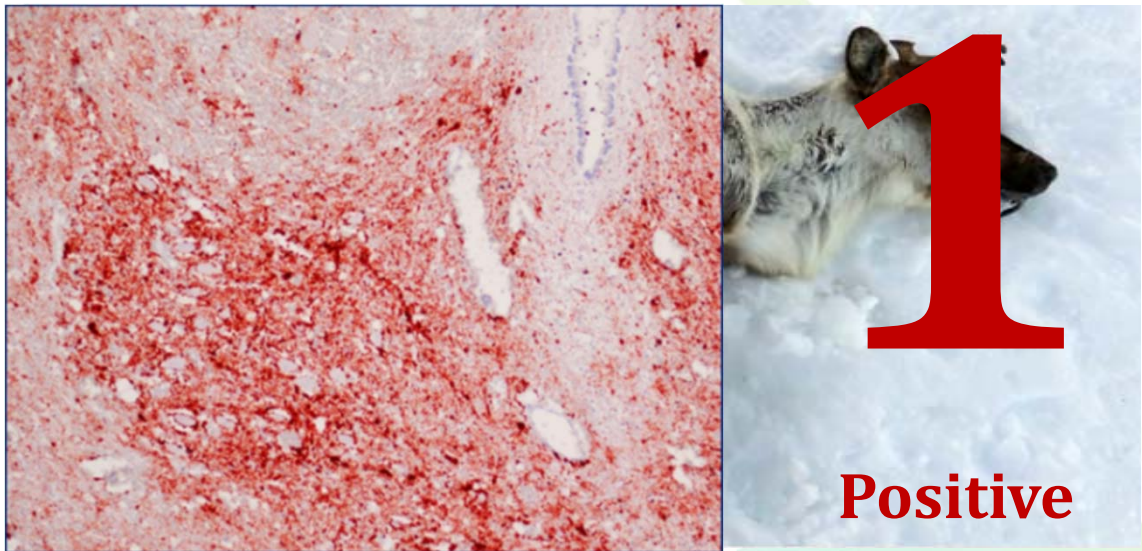
CWD Surveillance in Norway 2004-2015

Species	Number tested
Red deer (<i>Cervus elaphus</i>)	820
Moose (<i>Alces alces</i>)	130
Roe deer (<i>Capreolus capreolus</i>)	183
Reindeer (<i>Rangifer tarandus tarandus</i>)	
semi-domestic	966
wild	10
Fallow deer (<i>Dama dama</i>) – farmed	12
Musk oxen (<i>Ovibos moschatus</i>)	42
Total	2163

Last 3 years: Less than 20 animals tested a year



- **March 2016 - Nordfjella mountains**
- **Free-ranging reindeer (*Rangifer tarandus tarandus*)**
- **GPS, Darts, left the herd, locomotion problems**
- **Died within a short time**



Positive

Photo: Norwegian Institute for Nature Research (NINA)

- **May 2016 – Selbu area (300km from Nordfjella)**
- **2 pregnant females, 13-14 years old**
- **One shot because of abnormal behavior**
- **One found dead in good body condition**
- **Oct 17 - 1 more**

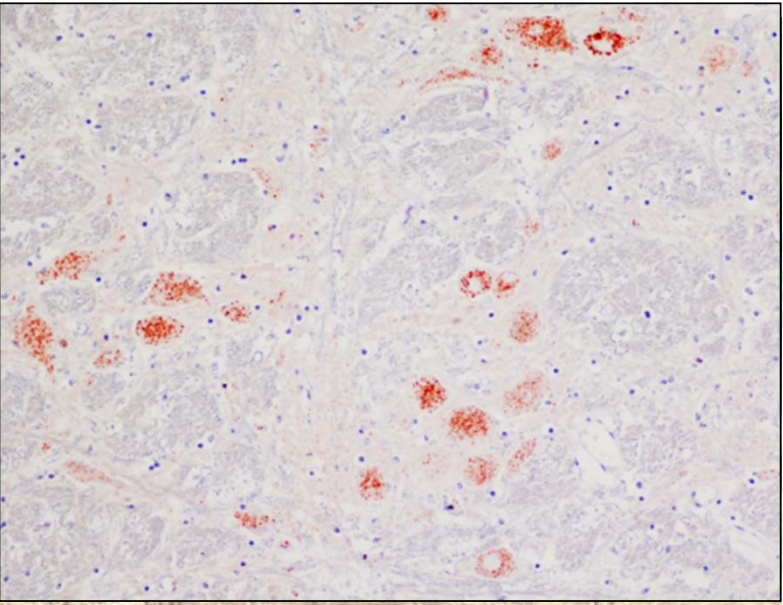


Photo: Jarle Fuglem

+3

Positive

- Aug16-Oct 17- Nordfjella mountains
- Free-ranging reindeer (*Rangifer tarandus tarandus*)



+6

Positive

CWD Surveillance in Norway 2016-2017

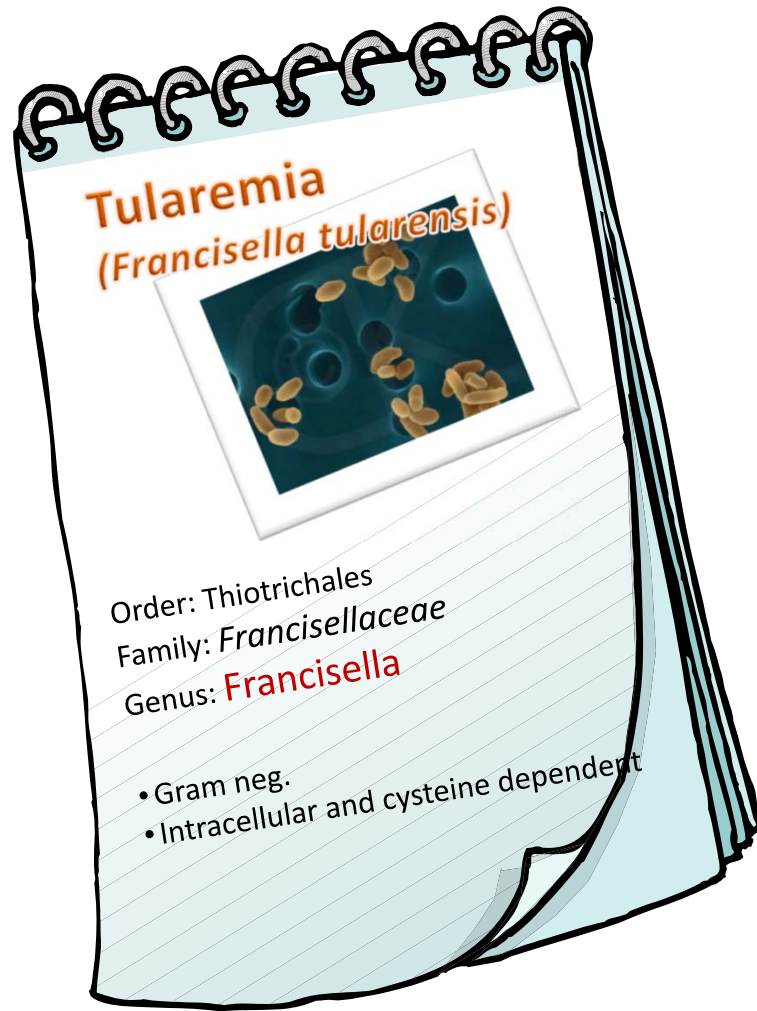
Species	2004-2015	2016	2017
Red deer (<i>Cervus elaphus</i>)	820	2593	1571
Moose (<i>Alces alces</i>)	130	4396	3466
Roe deer (<i>Capreolus capreolus</i>)	183	479	1296
Reindeer (<i>Rangifer tarandus tarandus</i>)			
semi-domestic	966	1737	3567
wild	10	838	2309
Fallow deer (<i>Dama dama</i>) – farmed	12	0	0
Total	2121	10043	12208/21000

Results delivered within 48H





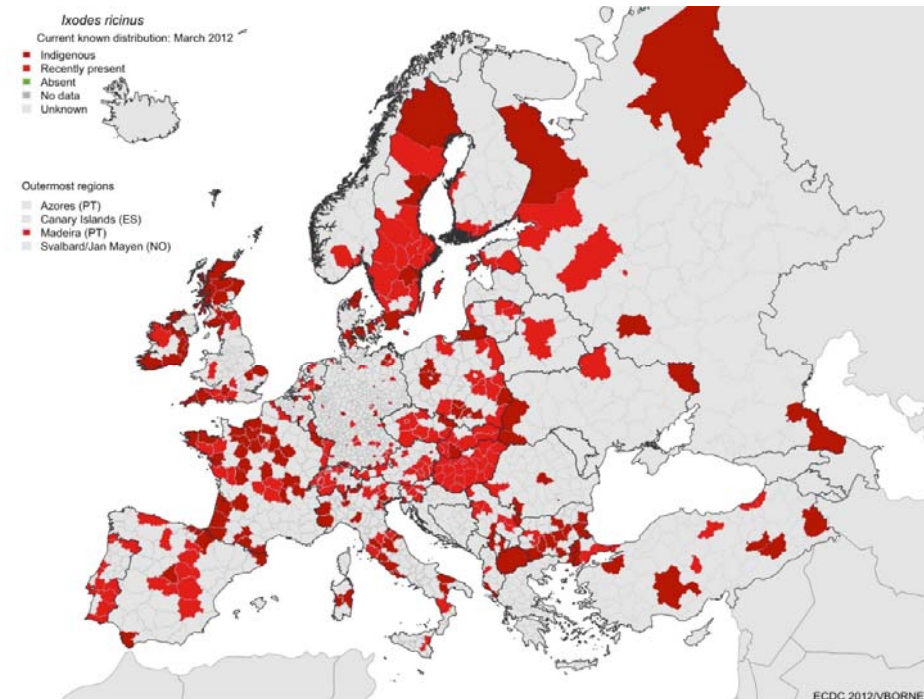
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ZOONOTIC



- Present: rodents, hare, beaver (reservoir unclear)
- In people: autumn and winter, specially when rodent population increases
- Transmission:
 - Direct contact with infected/diseases animals (mice, hunting)
 - Indirect contact: Inhalation of contaminated dust (cottage-cleaning etc.)
 - Drinking water (most common local source)
 - Insects (ticks, mosquitos)
 - **No transmission from person to person**
- Symptoms:
 - Lymphadenopathia associated to infection site
 - Infection and inflammation in mouth and pharynx
 - Eye-infection + local lymph nodes
 - Pneumonia
 - Enteritis (typhoid form)
- Mortality in rodents: appr. 100 %





RAPID COMMUNICATIONS

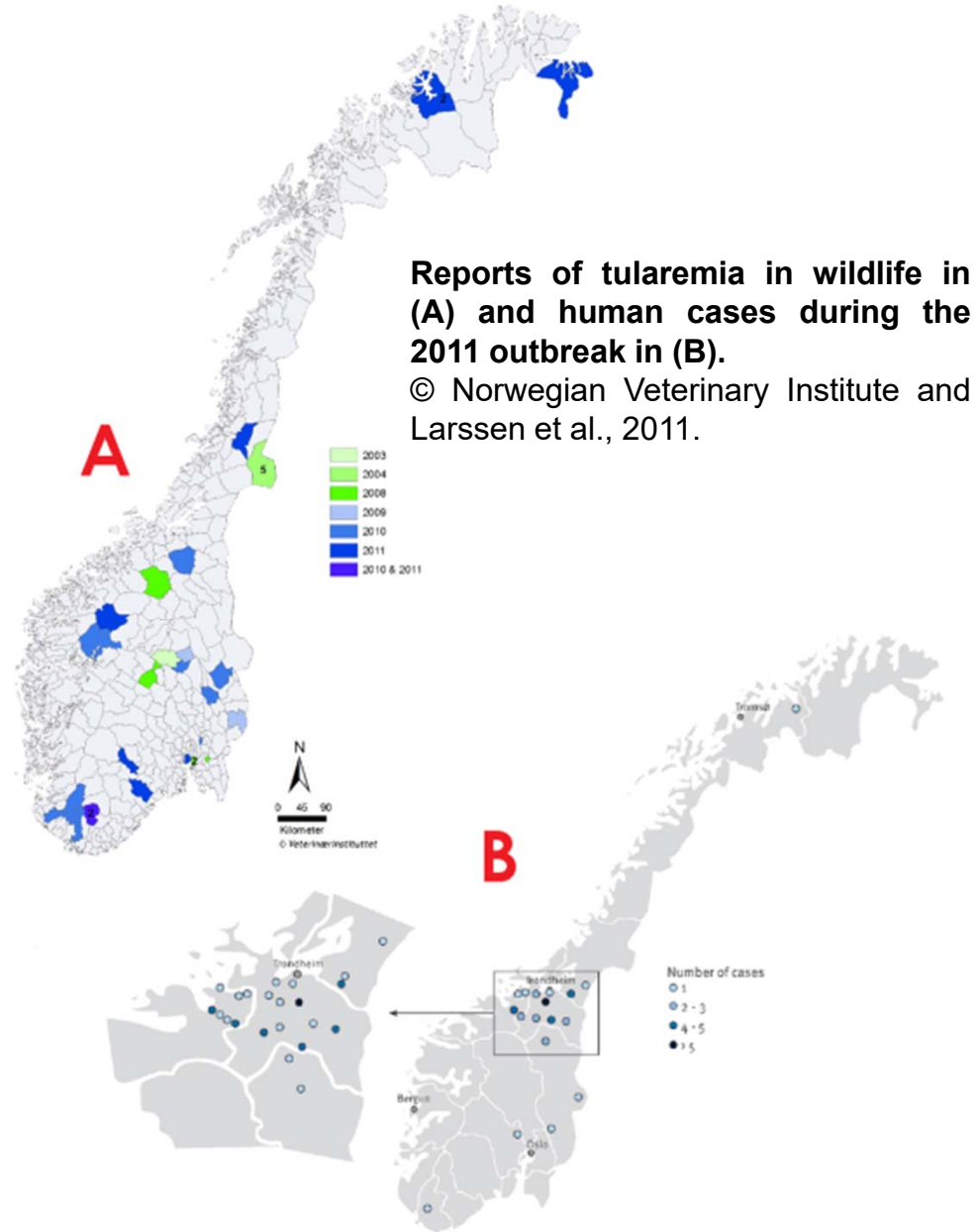
Outbreak of tularaemia in central Norway, January to March 2011

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Article published on 31 March 2011





Nyheter

Hare smittet jeger og jakthund med harepest (tularemi)



Published: 17.10.2012 10:07 Sist endret: 17.10.2012 10:07

Veterinærinstituttet påviste nylig harepest hos en hare som ble tatt i los av en jakthund. Både hunden og jegeren ble smittet. Veterinærinstituttet ønsker innsending av blodprøver fra hunder som blir syke etter jakt på hare eller annet vilt.

I dette tilfellet ble hunden syk med nedsatt matlyst og slapphet et par dager etter at den hadde tatt en hare i los. Sykdommen varte i 2-3 dager, og undersøkelse av blodprøver fra hunden viste at den hadde blitt smittet med harepest. Jegeren som slaktet haren ble syk fire dager senere med influensa-lignende symptomer og svulne lymfeknuter i armhulen.

Harepest eller tularemi forårsakes av bakterien *Francisella tularensis*. Bakterien er svært smittsom, og kan overføres gjennom direkte kontakt med sjuke eller døde dyr. I Norge blir tularemi oftest diagnostisert hos hare, og de fleste tilfellene ses på ettersommeren og høsten. Sjukdommen er også påvist hos lemen her i landet. Også andre smågnagere kan smittes med *Francisella tularensis*.

Det hender iblant at harer som viser tidlige symptomer på sjukdom (går tregt i los), blir tatt av hu harer utgjør en stor smittefare for jegeren, og må ikke slaktebehandles. De bør håndteres med h Veterinærinstituttet for laboratorieundersøkelse. Ta kontakt med det lokale Mattilsynet.



ARTIKKEL

Harepest - overføres fra lemen og andre smågnagere

I år med mye lemen og mus i naturen, bør du være ekstra forsiktig med å drikke vann direkte fra naturen. Smågnagere kan overføre harepest (tularemi).

OPPDATERT 20.10.2017

Skriv ut

Send på e-post

HAR DU FUNNET EN FEIL?

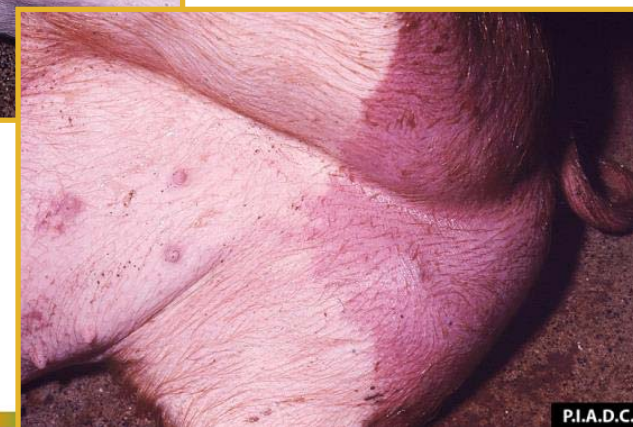
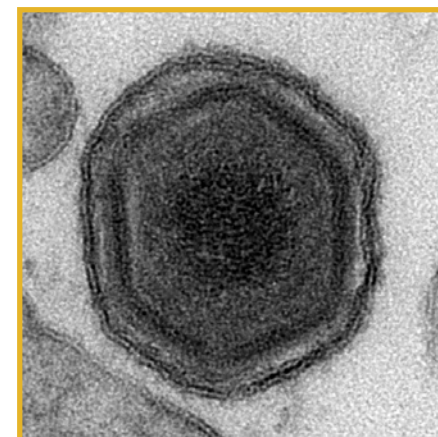
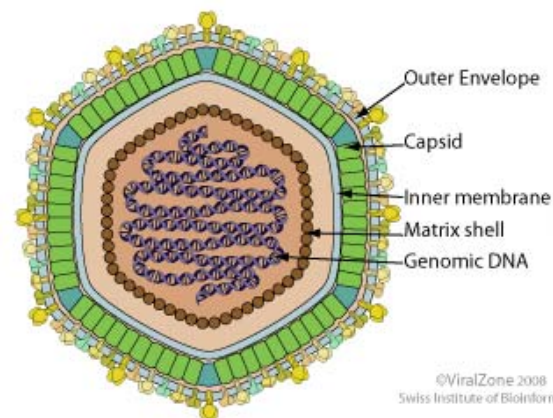
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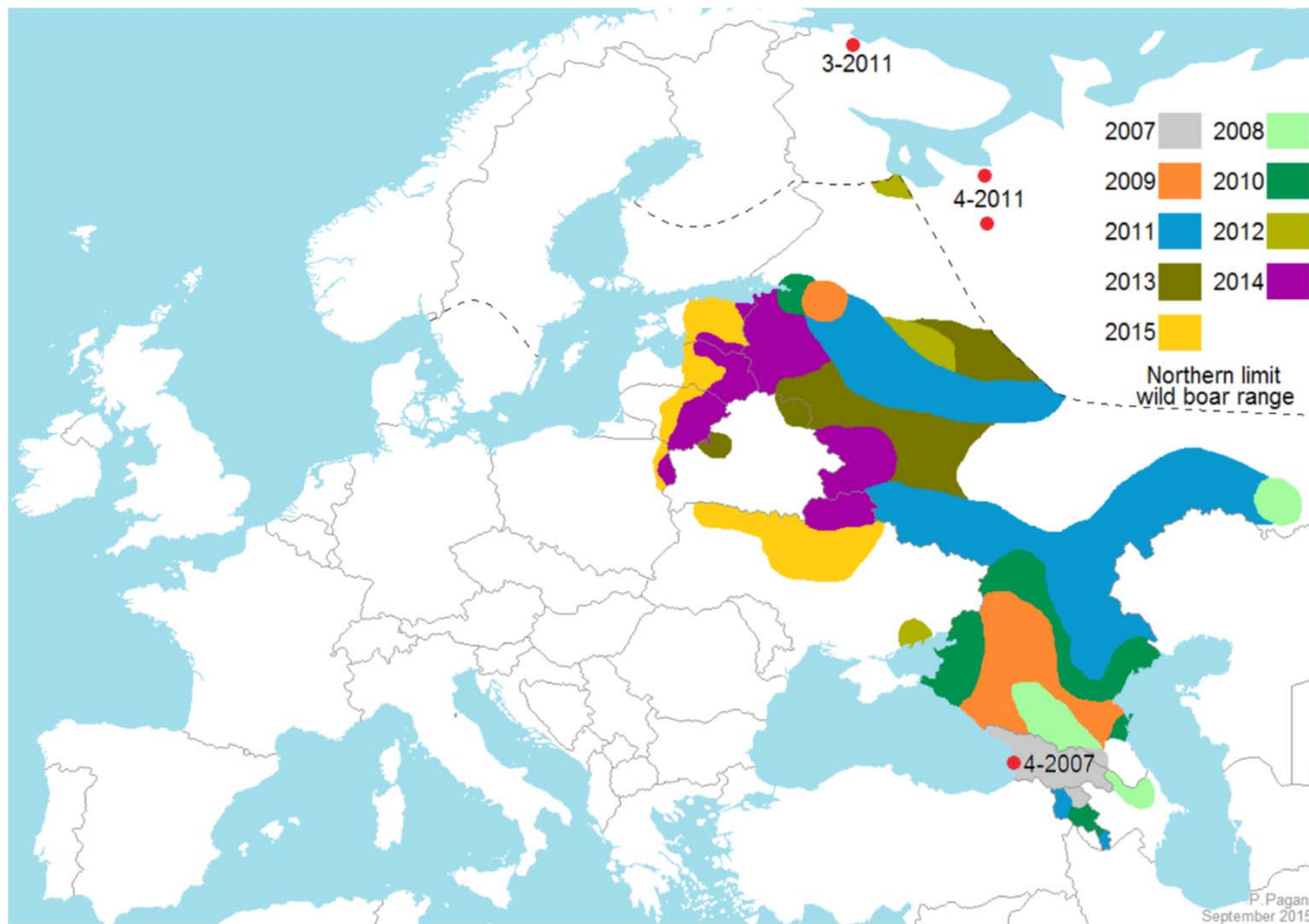




African Swine Fever Virus

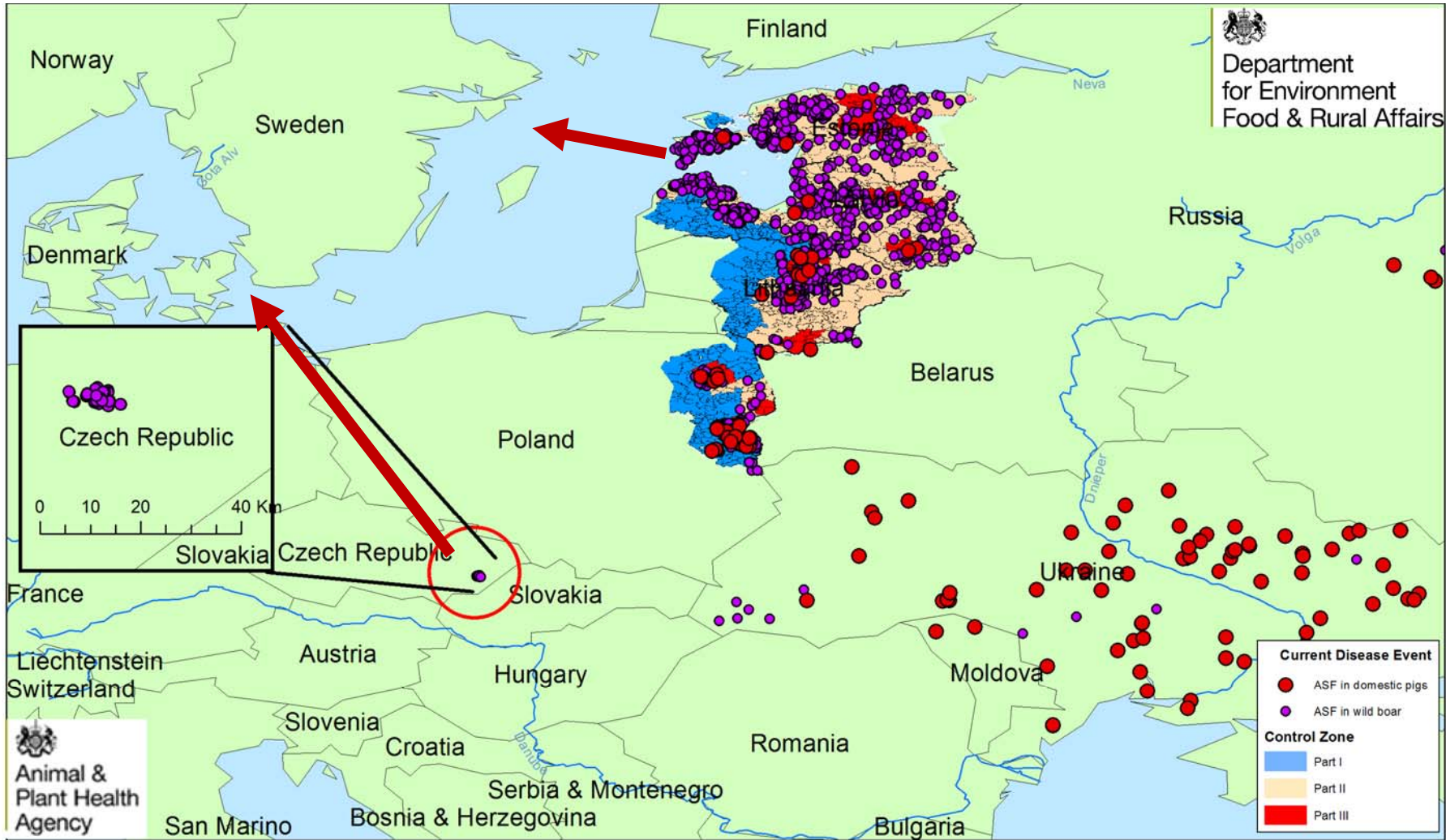
- Highly contagious viral disease of swine
- Asfarviridae
 - Enveloped DNA virus
 - Transmitted by arthropods
- Isolates vary in virulence
 - High virulence: up to 100% mortality
 - Low virulence: seroconversion
- Highly resistant
 - At least 30 days in pens
 - >140 days in some pork products





Map 1: Progression in Eurasia of the ASF outbreaks reported to the OIE from April 2007 to August 2015





Recent African Swine Fever outbreaks domestic pigs and wild boar in 2017 [Inset: wild boar cases in Czech Republic]

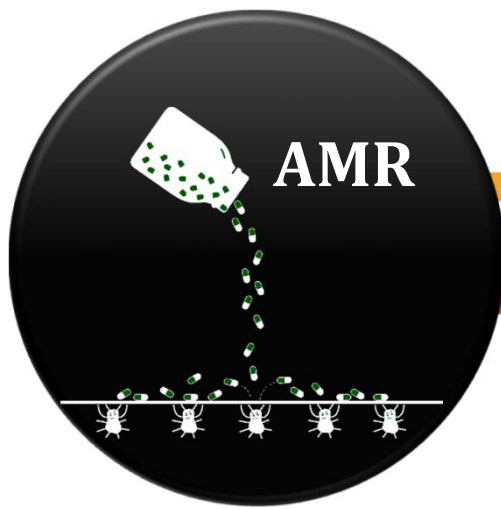
Date prepared 26/07/2017





AMR

Knowledge of AMR in wildlife in Norway is very limited



Wildlife, among others, can be a good indicator to study AMR dynamics

Antibiotic resistance is one of the biggest threats to global health, food security, and development today

Antibiotic resistance can affect human or animal, of any age, in any country





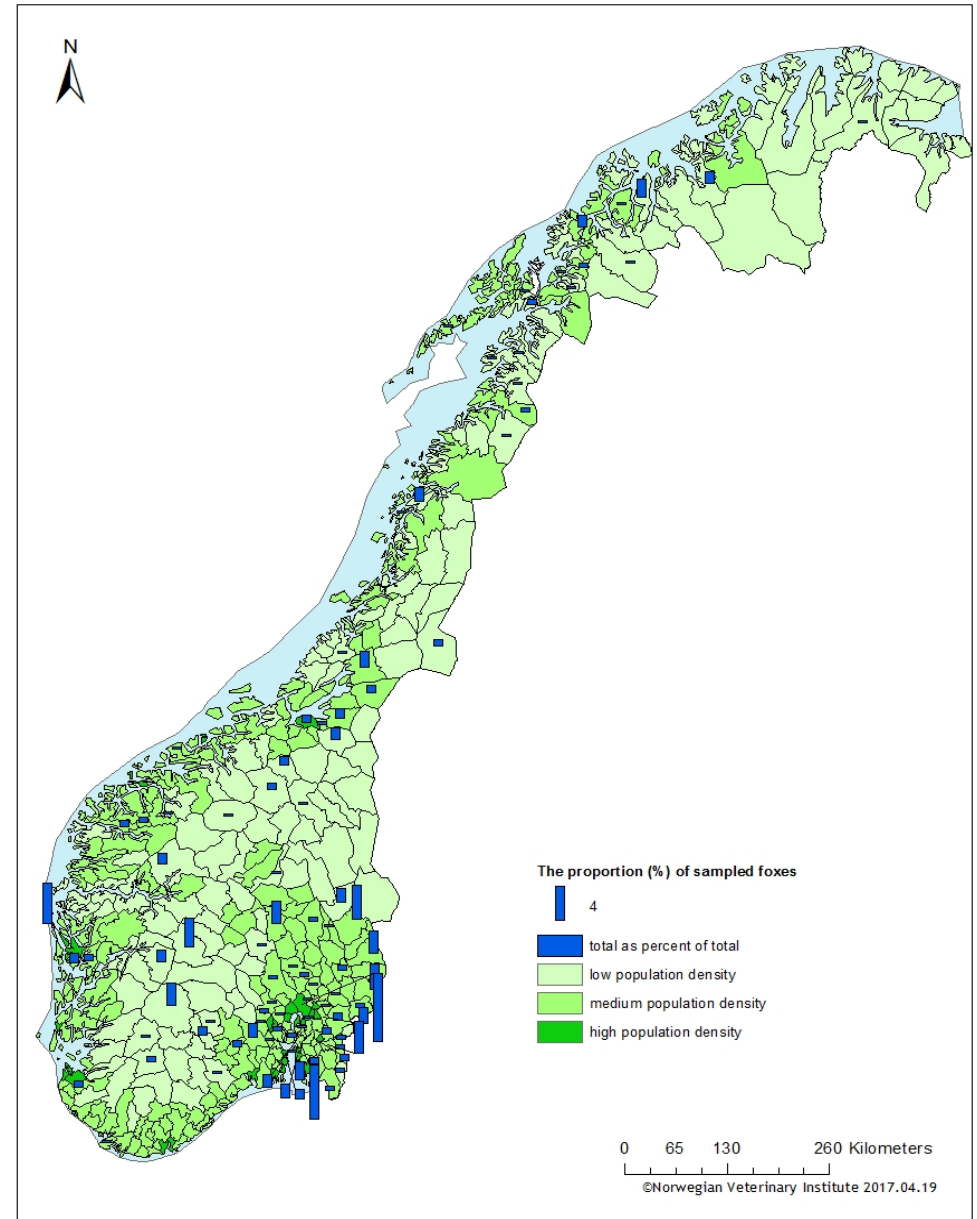
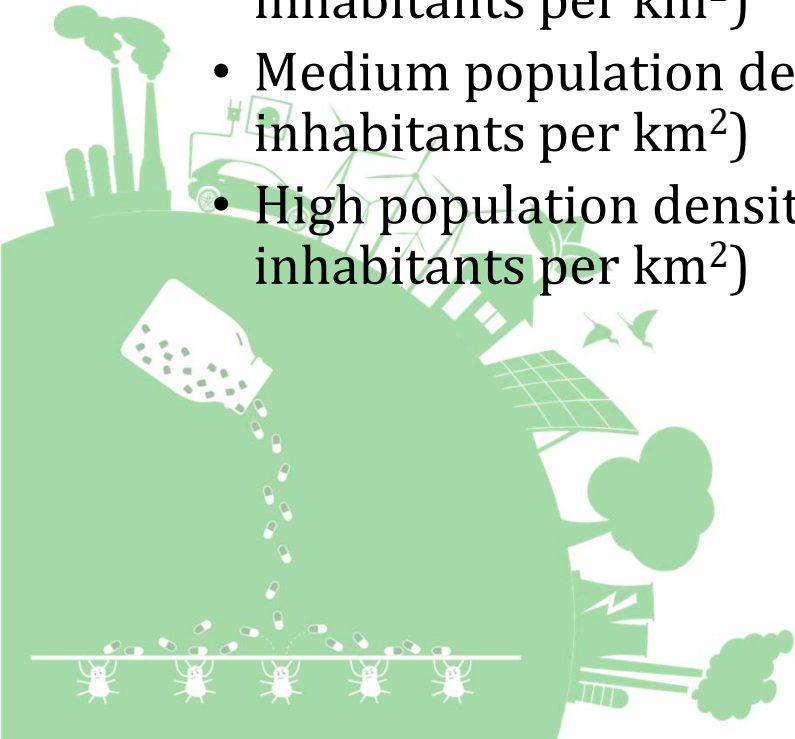
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Sample collection

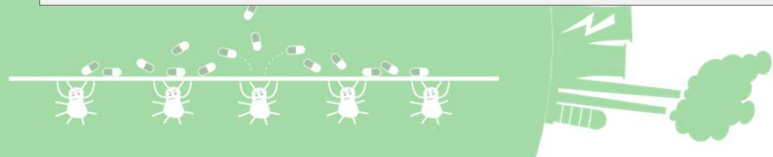
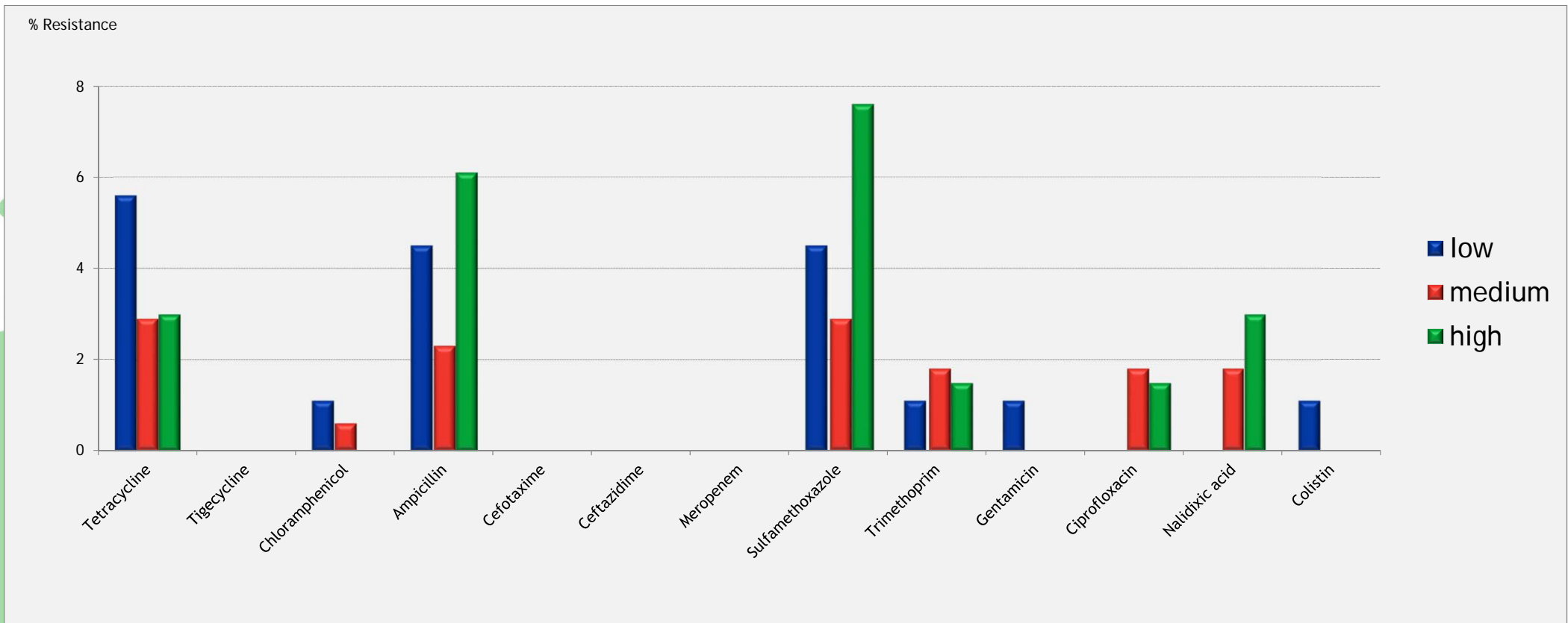
- **Geographical distribution of sampled foxes (N=387)**

- Low population density (<5 inhabitants per km²)
- Medium population density (5-200 inhabitants per km²)
- High population density (>200 inhabitants per km²)





Phenotypic resistance in indicator *E. coli*



2650 humans
61 000 km²





©Zairon



Distribution of resistance genes

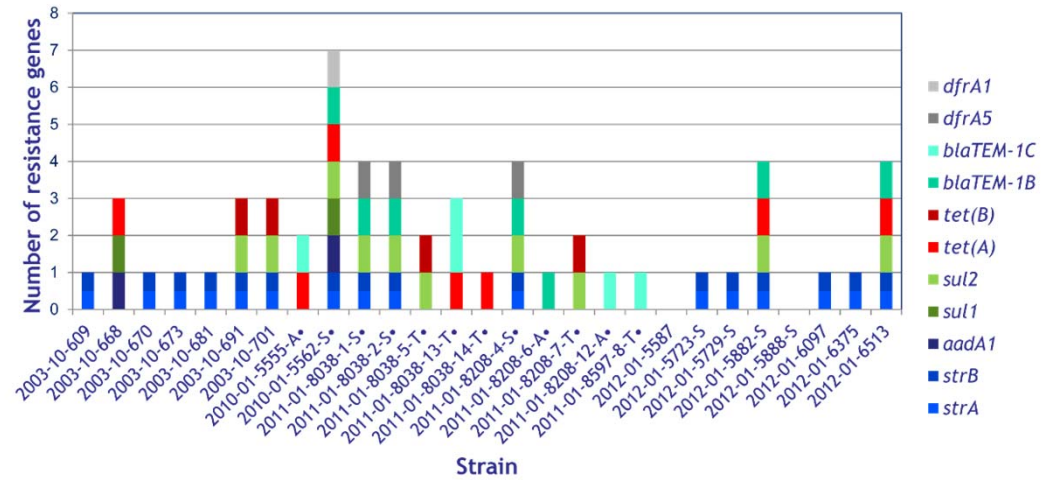


Figure 1. Isolates included in the study and their genotypic resistance profile. Strains marked with “•” are isolated from Svalbard reindeer.

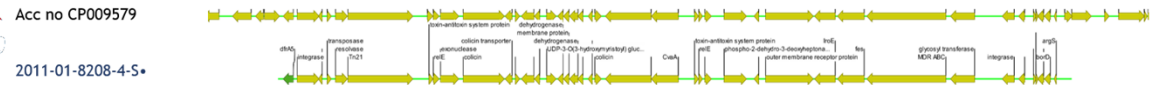
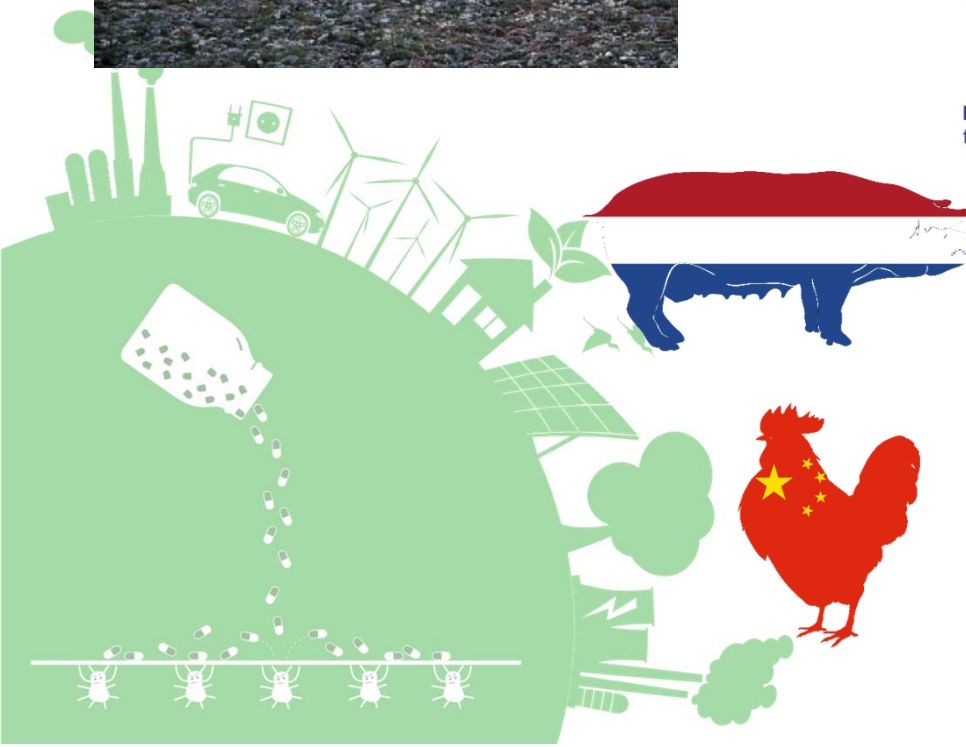


Figure 4. Structure of conjugative resistance plasmid originating from *E. coli* (2011-01-8208-4-S) from Svalbard reindeer and map of 36 kb region (below) with 99% identity to part of plasmid FAP1 plasmid 1 (CP009579) isolated from pig faeces in the Netherlands.

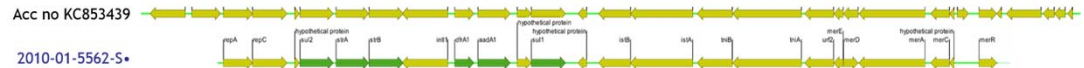


Figure 3. Structure of conjugative resistance plasmid originating from *E. coli* (2010-01-5562-S) from Svalbard reindeer and map of a 19 kb region (below) containing resistance genes with 99% identity to part of plasmid pACN001-F (KC853439) isolated from poultry in China

Identification of virus causing recent seal deaths

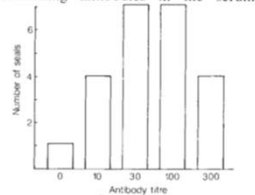
SIR—We recently reported the isolation of a herpesvirus and a virus tentatively classified as a picornavirus, from organs of harbour seals (*Phoca vitulina*), which had died during recent outbreaks of acute disease with high mortality in the North and Baltic seas. We suggested that further evidence for the causative role of these viruses for the outbreaks should come from serological studies on samples collected from animals during and after the outbreaks.

In virus-neutralization assays, we now show that, although virus-neutralizing antibodies against both viruses are present in sera from harbour seals in endemic areas, there is no correlation between the occurrence of disease symptoms and the development or rise of antibody titres against either virus. We also show that the immunization of young harbour seals in the seal orphanage in Pieterburen, The Netherlands, with inactivated preparations of either of these viruses, which did elicit virus neutralizing antibodies, fail to protect the animals against fatal disease (manuscript in preparation). These data suggest that these two virus infections, rather than being the primary cause of the disease outbreaks, are opportunistic infections occurring in animals suffering from another disease.

In a further attempt to identify the primary cause of the outbreaks, which on the basis of epizootiological observations is generally believed to be infectious, we extended our serological studies to other viruses of carnivores known to cause similar disease symptoms. For this reason, and as it had been noted by Drs A. Bergman and B. Klingeborn (National Veterinary Institute, Uppsala, Sweden) that the postmortem findings observed are often similar to those of canine distemper virus (CDV) infections in dogs, we carried out CDV serology on serum samples collected from seals in The Netherlands, Denmark, Germany, Sweden and the United Kingdom. We tested all the samples in the virus-neutralization test described previously (see table). We tested 21 serum samples from harbour seals collected in 1984 in the seal orphanage in Pieterburen after the outbreak of acute disease caused

by Phocid herpesvirus 1*. All these samples are negative in this assay (titres <10). Also, 16 samples collected from seals in March 1988 in the orphanage just before the start of the outbreaks were negative.

From May 1988, the first orphan seals born this year were brought into the orphanage and kept in separate groups of 10 to 15 animals. We force-fed these animals to exclude lactogenic transmission of antibodies. Once the first symptoms started to occur, we detected CDV-neutralizing antibodies in the serum



Development of CDV-neutralizing antibody titres within 14 days in orphan seals seronegative at admission to the Pieterburen orphanage. Of 23 baby seals brought to the orphanage between 3 July and 8 August clinically healthy and without CDV-neutralizing serum antibodies, 22 developed CDV neutralizing antibodies with titres of 10–300 within 14 days, and they all developed disease symptoms in this period (see figure).

Most of the baby seals brought to the orphanage after 9 August showed disease symptoms and were seropositive on arrival. Serum samples collected from grey seals (*Halichoerus grypus*), which had been in the orphanage during the outbreak and survived the disease, showed CDV-neutralizing antibody titres ranging from 10,000 to 30,000. From one of these animals, a serum sample collected before the outbreak in March 1988 was available and this proved to be negative. Of seven serum samples collected from harbour seals in Denmark which had died with acute symptoms in May 1988, two showed antibody titres of 10 and 1,000 respectively. Of 35 samples collected in July and August 1988 from harbour seals in

Germany at different stages of the disease, 23 were seropositive (titres 10–30,000; \bar{x} =100). Eight serum samples from harbour seals suffering from the disease in Sweden in August 1988 were tested. All except the serum from one baby seal show CDV-neutralizing antibody titres ranging from 10 to 30,000 (\bar{x} =138). Finally, all eight serum samples from harbour seals in a seal sanctuary in the United Kingdom which had survived the disease show CDV-neutralizing antibody titres ranging from 30 to 3,000 (\bar{x} =363).

These serological data clearly show that an infection of CDV, or a closely related morbillivirus, occurred in the respective seal populations after April 1988. That the antibodies found were not directed against measles virus (MV), a closely related morbillivirus was shown in an MV-specific haemagglutination-inhibition assay in which CDV neutralizing sera were negative. That a few samples were not positive may be because they were taken mainly during the acute stage of the disease when no anti-CDV antibodies had yet developed. The results obtained with the paired serum samples from individual animals in the orphanage show that the infection coincided with the occurrence of the disease symptoms. Furthermore, the clinical symptoms observed during the outbreaks, which affected respiratory, gastrointestinal, central-nervous and cutaneous systems, are similar to those of canine distemper, which is also frequently accompanied by secondary viral and bacterial infections.

We therefore conclude that the primary cause of the disease outbreaks of seals is infection with CDV or a closely related morbillivirus. The failure so far to isolate the virus from organs of affected animals may be explained by the fact that no isolation techniques were used which favour the isolation of CDV. We have now started *in vivo* and *in vitro* virus-isolation procedures to compare properties of the virus with those of CDV isolates from dogs. Because in seal sanctuaries there is an urgent need for a preventive vaccine, and the use of live vaccines is in general inadvisable for wild animals, we have now started to evaluate in seals the value of a subunit iscom CDV vaccine, recently shown to be effective in dogs⁵.

A. D. M. E. OSTERHAUS
National Institute of Public Health and
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E. J. VEDDER

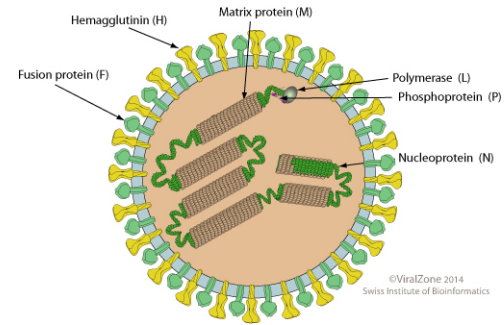
Seal Orphanage, Pieterburen,
The Netherlands

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	CDV-neutralizing serum antibody titres ≥ 10 in harbour seals.						
	Year	1984		1988			
	Month	M	A	M	J	J	A
The Netherlands* (Pieterburen orphanage)	(–)† (+)	0/21‡ 0/1	0/16 20/21	0/5	1/14 20/21	8/33 43/52	8/17 43/52
Denmark	(+)			2/7			
Germany	(–) (+)				2/10 10/12	3/4 10/10	
Sweden	(+)						7/8
United Kingdom	(+)						8/8

*Serum samples obtained from Drs E. Vedder (NL), P. Grauballe (D), E. Vedder (D), B. Klingeborn (S) and S. Anderson (UK). †(–): Clinically healthy, (+): Clinically ill. ‡Number positive/number tested.

Morbillivirus



- In **April 1988**, an epidemic swept through breeding colonies of **European harbor seals** (*Phoca vitulina vitulina*) around the coasts of the North, Baltic and Irish seas **killing up to 18,000** of this species and possibly a few hundred sympatric grey seals, *Halichoerus grypus* (Heide-Jorgensen et al., 1992).





Another Phocine Distemper Outbreak in Europe

Trine Jensen,¹ Marco van de Bildt,¹ Hans Henrik Dietz,²
Ths. Holmen Andersen,² Anne Sofie Hammer,² Thijs Kuiken,³
Albert Osterhaus^{1,3}

The seal population of Northern Europe was able to recover from the 1988 phocine distemper epidemic that killed about 18,000 seals. However, starting at the beginning of May 2002, unusually high mortality among harbor seals (*Phoca vitulina*) was noted on the shores of Anholt, an island off the east coast of Denmark. Since then, 182 of about 900 animals, both adult and juvenile, died with clinical signs of respiratory and nervous disease. About 440 seals have been found dead on the east coast of Denmark, and the disease also appears to have spread to Sweden, where 100 seals were reported dead along the west coast (1). Most recently, over 10 seals were found moribund or dead along the coast of the Netherlands in the second half of June. The clinical signs observed were reminiscent of those in seals that died in 1988 of infection with a morbillivirus (2), subsequently identified as PDV, a new member of the genus (3).

We performed necropsies on seven seals (four adults, one subadult, and two juveniles) in variable states of decomposition found at Anholt or on the nearby Danish mainland and on one freshly dead juvenile seal from Vlieland, an island off the Dutch coast. Tissue samples (lung, kidney, bladder, and brain) were examined for morbillivirus nucleic acid by reverse-transcriptase polymerase chain reaction (RT-PCR), with a set of universal morbillivirus primers, P1 (5'-ATGTTTATGATCACACGGGT-3') and P2 (5'-ATTGGGTGACACCACTTGTC-3'), that are based on conserved sequences in the phosphoprotein (P) gene. Tissue samples from three Danish seals (two adults and one juvenile) and the Dutch seal were positive, giving the expected products of 429 base pairs (bp). Selected fragments of the PCR products were sequenced for phylogenetic analysis. The resulting sequences closely matched (>97% homology) those of PDV isolates from harbor seals in 1988 and were distinct from those of canine distemper virus (CDV) and other members of the genus Morbillivirus (Fig. 1). Except for one nucleotide change in the P gene fragment, the sequences obtained from Denmark and the Netherlands were identical, indicating that seals from widely separated regions of Northern Europe were infected by the same virus. Serum samples were tested for morbillivirus-specific immunoglobulin M (IgM) antibody by antibody-capture enzyme-

linked immunosorbent assay (ELISA), with goat antibody to dog IgM-coated plates and peroxidase-labeled CDV antigen for detection. The goat antibody to dog IgM preparation specifically captures seal IgM, as was shown in routine serological tests for CDV infection. Two adult Danish seals and the Dutch seal had IgM antibodies, showing re-

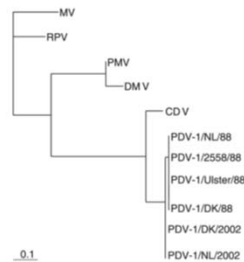


Fig. 1. Phylogenetic tree based on a 370-bp Morbillivirus P gene fragment. The maximum likelihood tree was generated with the SEQBOOT and DNAML program of the Phylip 3.75 software package with 100 bootstraps. When available, GenBank accession numbers are given in parentheses. MV, measles virus, Edmonston strain (M89920); RPV, rinderpest virus, RBOK strain (X68311); DMV, dolphin morbillivirus (Z47758); PMV, porpoise morbillivirus strain 53 (8); CDV, canine distemper virus, Onderstepoort strain (AF305419); PDV-1/NL/88, phocine distemper virus 1 (AF525289); PDV-1/DK/88 (X75960); PDV-1/2558/88 (X65512); PDV-1/Ulster/88 (D10371); PDV-1/DK/2002 (AF525287) and PDV-1/NL/2002 (AF525288).

cent infection. These findings, together with the known severity of PDV infection in harbor seals (4), indicate that PDV infection is the cause of ongoing harbor seal mortality in Northern Europe.

In 1988, the disease spread rapidly from Anholt in April to the Wadden Sea by May, to the southern Baltic Sea by July, and to the waters around the United Kingdom by August, killing about 18,000 animals (5). The current sequence of events parallels the early pattern of the 1988 outbreak. The rapid spread of this high-mortality disease may be

explained by the migratory behavior of harbor seals, which may travel hundreds of kilometers within days. The effect of the current PDV epidemic will depend on the overall resistance and specific immunity of the Northern European seal population. The recovery of seal numbers in the Wadden Sea from about 4000 in 1989 to 17,000 in 2000 (6), indicates that, at the very most, one-fifth of the current seal population may have specific immunity to PDV resulting from the 1988 epidemic. Furthermore, for the past 10 years, we have systematically tested all Wadden Sea seals [harbor and gray (*Halichoerus grypus*)] admitted to the Seal Rehabilitation and Research Center in the Netherlands for serum antibodies to PDV by ELISA confirmed by VN assay. Of the 736 animals tested (95% of whom were less than 1 year of age), over 95% were seronegative. All positive titers involved recently weaned pups, and most probably represent passive antibody derived from mothers that had survived the 1988 epidemic. Since 1997, 197 seals also were tested by virus isolation and/or RT-PCR with consistently negative results. Collectively, these data indicate that PDV has not been circulating in this population for at least 10 years, corroborating the prediction of Grenfell *et al.* by mathematical modeling (7) that PDV would be eliminated from the Northern European harbor seal population after 1988. The recent reappearance of PDV in this largely susceptible Northern European seal population may allow its rapid spread with devastating consequences. During the previous epidemic, thousands of seal carcasses littered beaches of the North Sea and adjacent waters. The responsible ministries and nongovernmental organizations of the respective countries involved are now discussing preparations for the possible consequences if history is repeated.

References and Notes

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¹Seal Rehabilitation and Research Center, Hoofdstraat 94A, NL-9968 AG Pieterburen, Netherlands. ²Danish Veterinary Institute, 2 Hangovej, DK-8200 Aarhus N, Denmark. ³Erasmus MC, Institute of Virology, Dr. Molewaterplein 50, 3015 GE Rotterdam, Netherlands.

Morbillivirus

- A **second and equally devastating** epidemic occurred among European harbor seals in 2002, with a similar temporal and geographic range to the 1988 event (Jensen *et al.*, 2002; Harkonen *et al.*, 2006).
- In that summer of 2002, **thousands of dead harbor seals were again found in the Kattegat and Skagerrak and along North Sea coasts** (Harding *et al.* 2002).
- In the North Sea the grey seal, which was exposed but **did not show overt infection or mortality**

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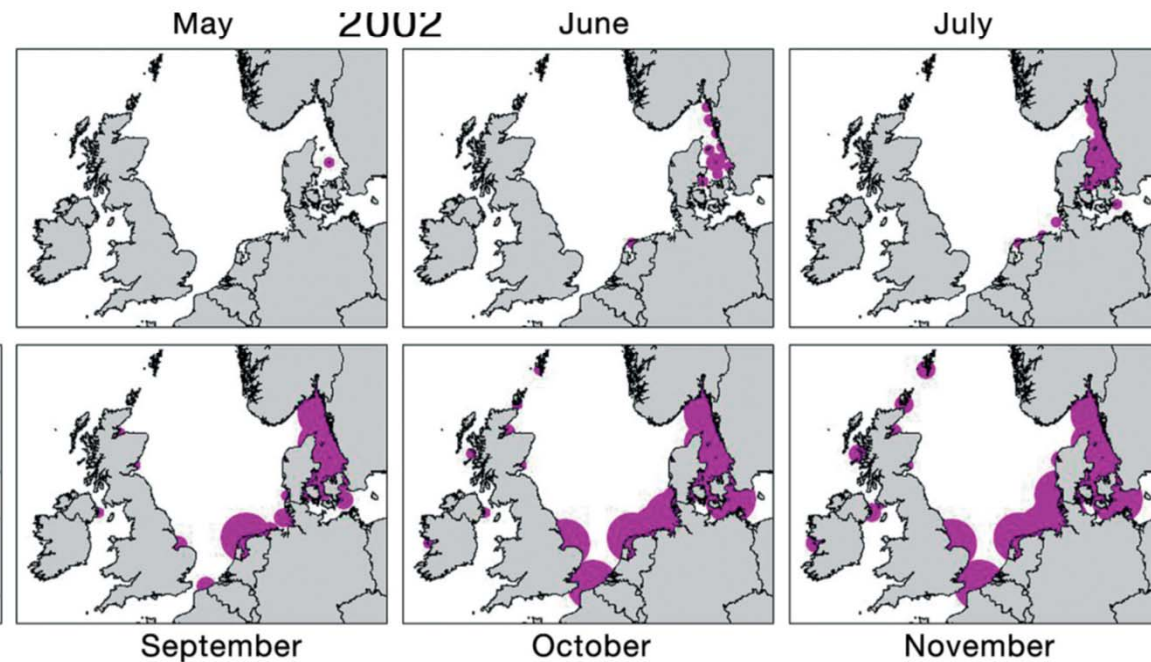
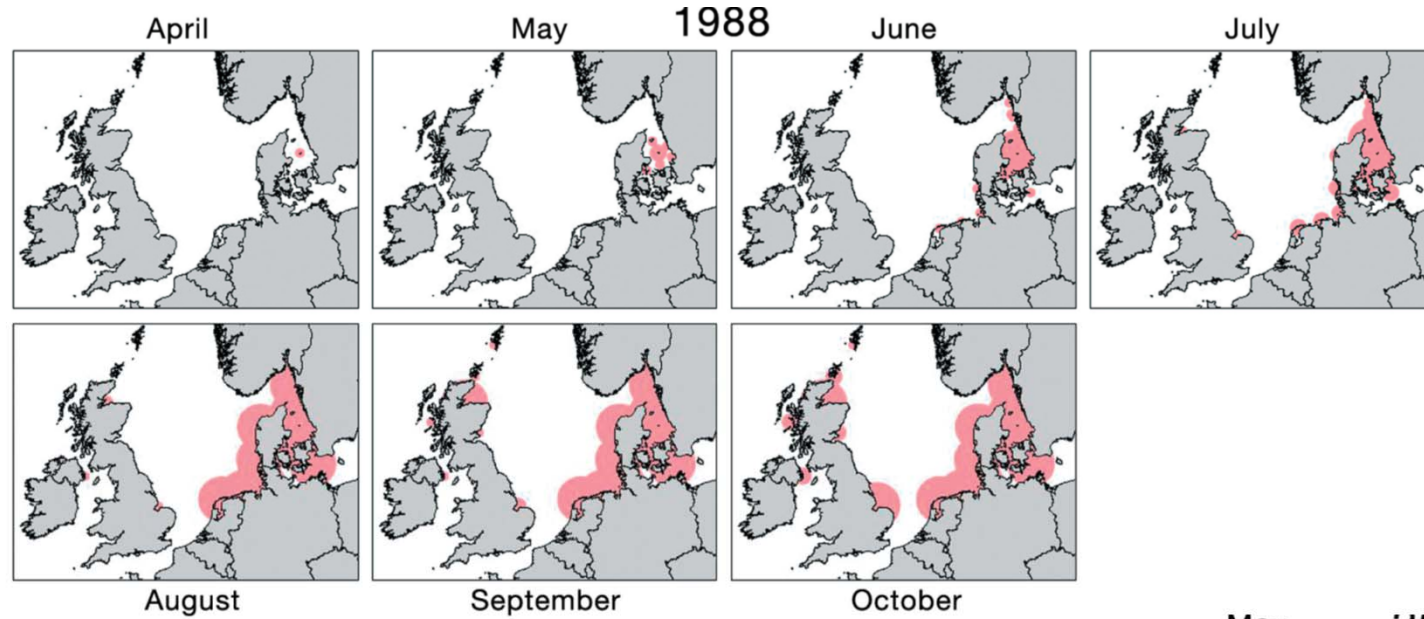


- The initial cases of PDV in both outbreaks were identified in the Danish and Swedish Kattegat with the Danish island of Anholt being the breeding colony where the first cases were reported. The reason for this remains unclear.



A review of the 1988 and 2002 phocine distemper virus epidemics in European harbour seals

Tero Härkönen^{1*}, Rune Dietz², Peter Reijnders³, Jonas Teilmann², Karin Harding⁴,
Ailsa Hall⁵, Sophie Brasseur³, Ursula Siebert⁶, Simon J. Goodman⁷,
Paul D. Jepson⁷, Thomas Dau Rasmussen², Paul Thompson⁸





Conservation concerns?



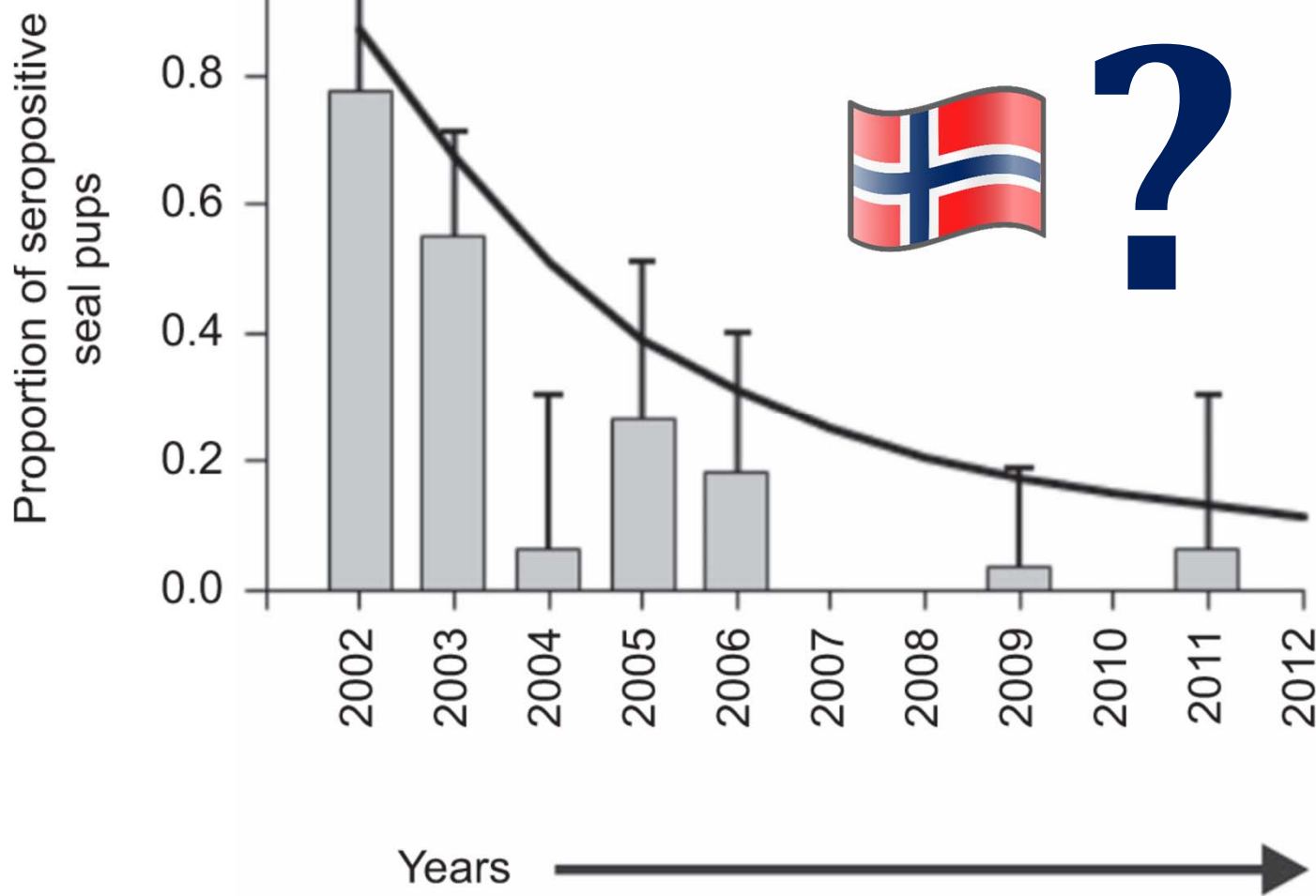
ORIGINAL ARTICLE

Prevalence of phocine distemper virus specific antibodies: bracing for the next seal epizootic in north-western Europe

Rogier Bodewes¹, Danny Morick², Marco WG van de Bildt¹, Nynke Osinga², Ana Rubio García², Guillermo J Sánchez Contreras², Saskia L Smits^{1,3}, Leslie AP Reperant¹, Thijs Kuiken¹ and Albert DME Osterhaus^{1,3}



Next outbreak in?





Veterinærinstituttet
Norwegian Veterinary Institute



**A GLOBAL WORLD
means GLOBAL PROBLEMS**



Veterinærinstituttet
Norwegian Veterinary Institute

Wildlife health as a driver of One Health research.

- **Long term** rather than ad hoc cooperation
- Needed combination of **health + ecology + biology + social sciences**
- Financial mechanisms for integrated research still **missing**
- **International networking** on wildlife of paramount importance (compare & standardize!!!)
- **Wildlife as SENTINEL species** brings added value, early detection and may reduce outbreak costs
- Wildlife as **ONE HEALTH driver** (outside “major outbreaks”) remains a **difficult** concept to communicate and lobby for





Veterinærinstituttet
Norwegian Veterinary Institute

**The way
forward ?...**

Tusen takk!

