

# Infectious Salmon Anemia (ISA)

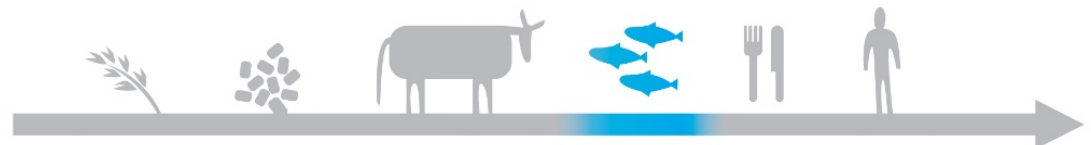
## Recent development and future control

Torfinn Moldal, Maria Aamelfot, Trude Lyngstad, Lars Qviller,  
Knut Falk, Edgar Brun and Brit Hjeltnes

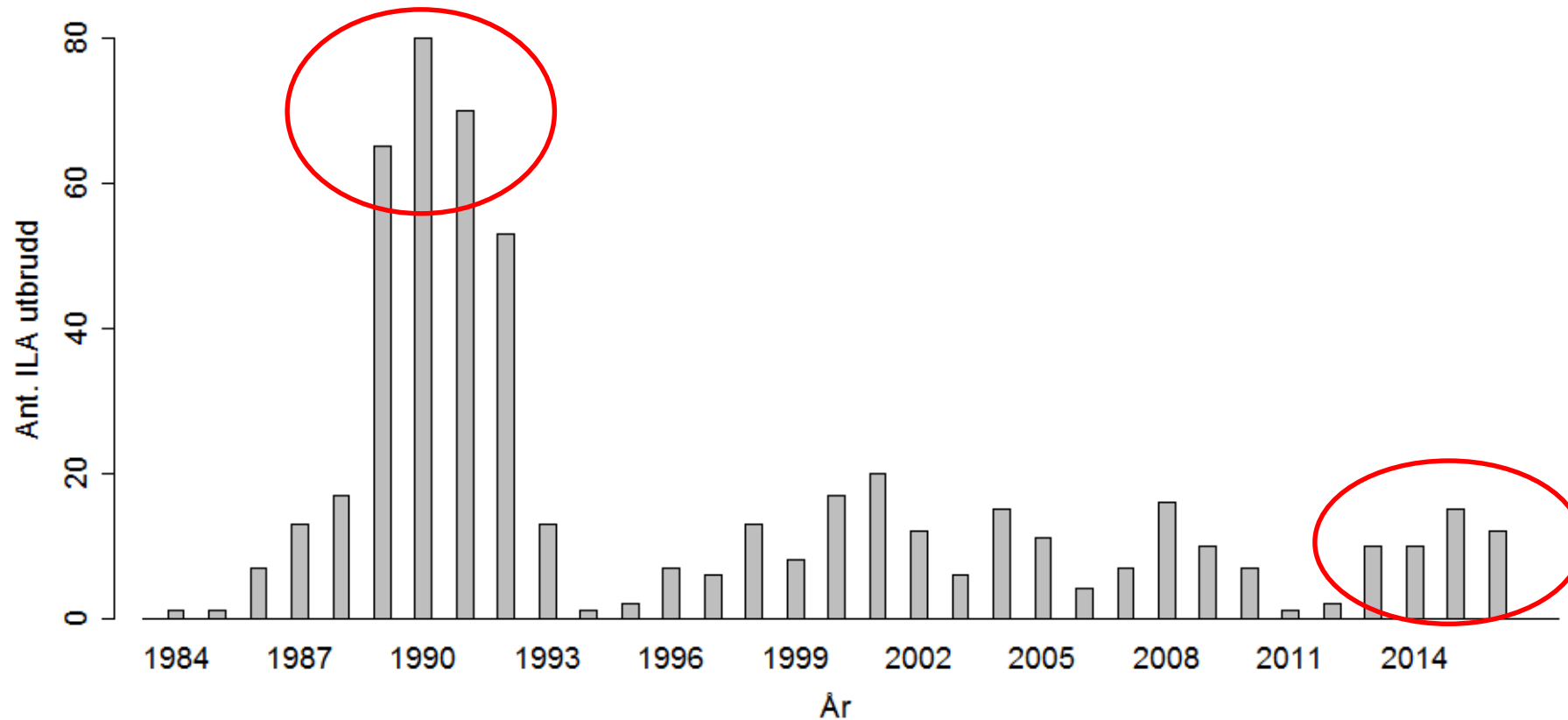
[torfinn.moldal@vetinst.no](mailto:torfinn.moldal@vetinst.no)



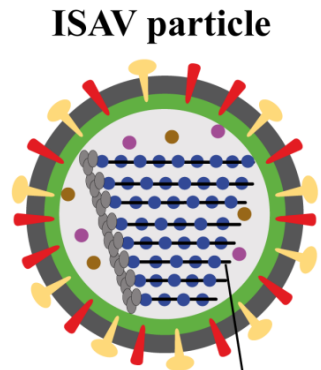
**Veterinærinstituttet**  
Norwegian Veterinary Institute



# Number of annual ISA-outbreaks in Norway



# Infectious Salmon Anemia Virus (ISAV)



Encoded amino acids

HPRO	KLQRNITDVKIRVDAIPPQLNQT FNTN QVEQPATSVLSNIFISM
	KLQRNITDVKIRVDA-----NQVEQPATSVLSNIFISM
	KLQRNITDVK-----PATSVLSNIFISM
	ELRRNITDVGIGVDAIPPQL-----NIFISM
	KLQRNITDVKIRVDAIPPQLNQT-----M
Selected HPRs	KLQRNITDVK-----TSVLSNIFISM
	KLQRNITDVKIRVDAIPPQLNQT-----L
	KLQRNITDVKIRVDAIPPQLNQT-----M
	KLQRNITDVKIRVDAI-----QVEQPATSVLSNIFISM
	KLQRNITDVKIRVDAIPPQLNQT-----FISM
	KLQRNITDVKIRVDAIPPQL-----ISM
	KLQRNITDVKIRVDAIPPQL-----SNIFISM

*Orthomyxoviridae*

Eight segments – ten proteins

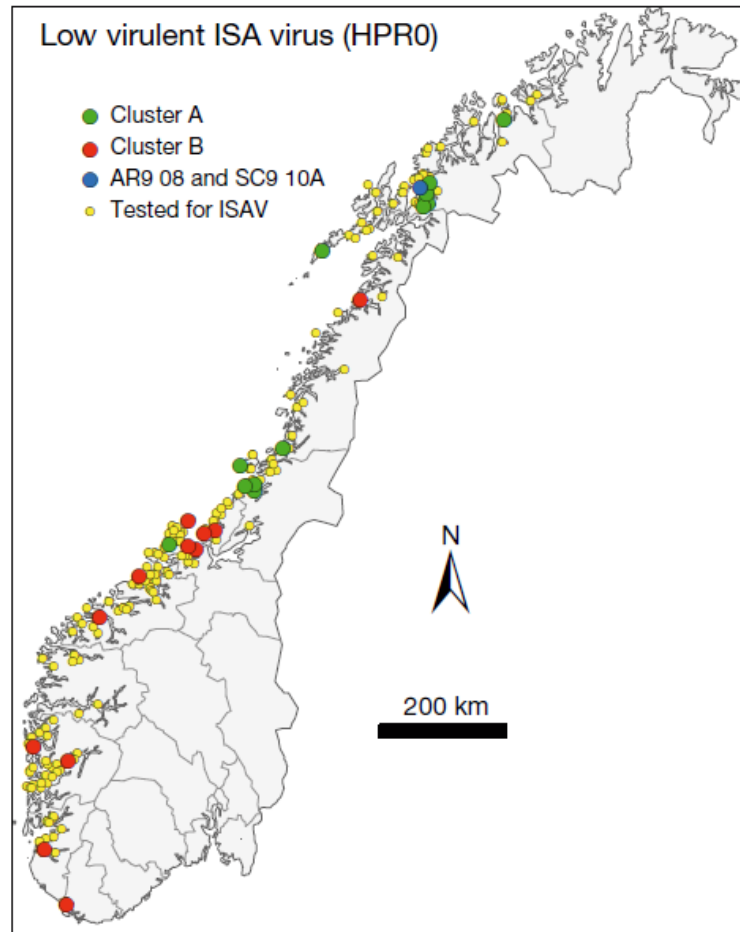
HE-gene of particular interest

Hyperpolymorphic region (HPR):

- ISAV HPRO (non-virulent)
- ISAV HPR $\Delta$  (virulent)



# ISAV HPRO is prevalent in healthy fish



Lyngstad *et al.*, 2012

Fresh water and sea

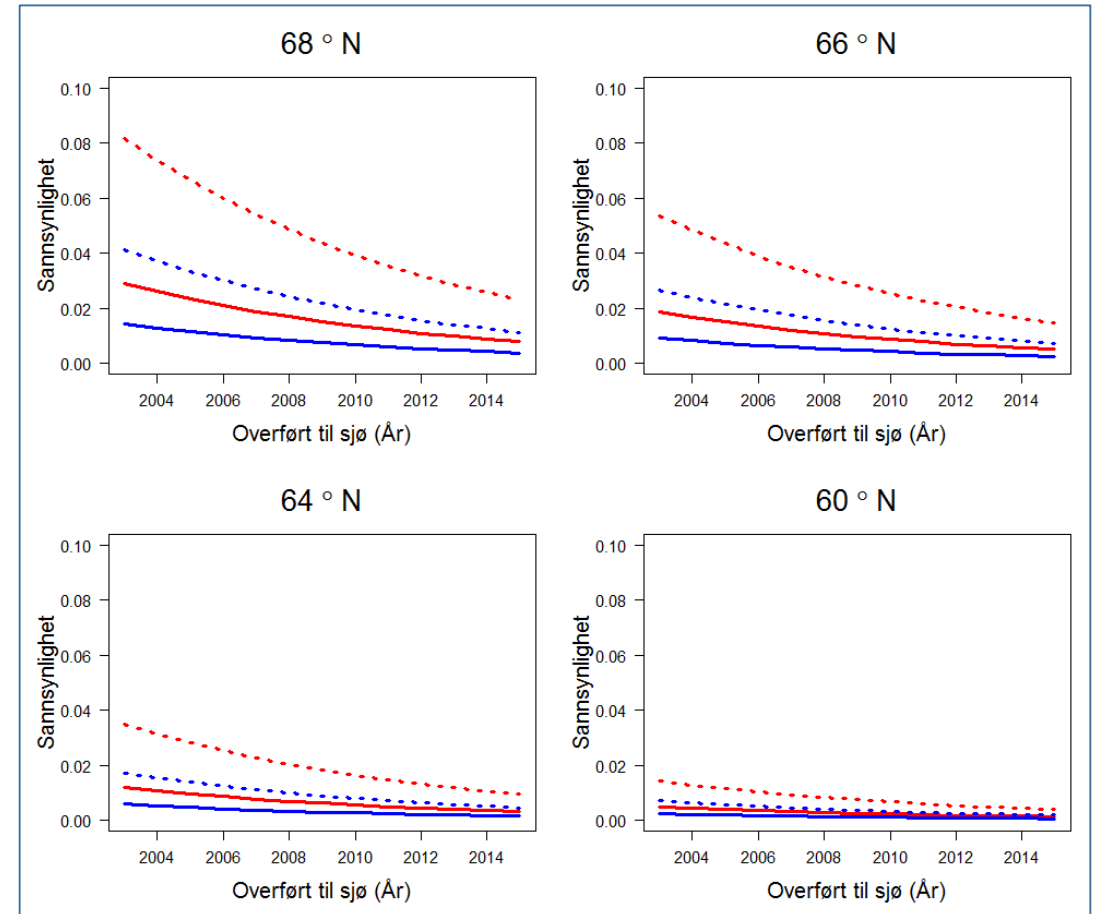
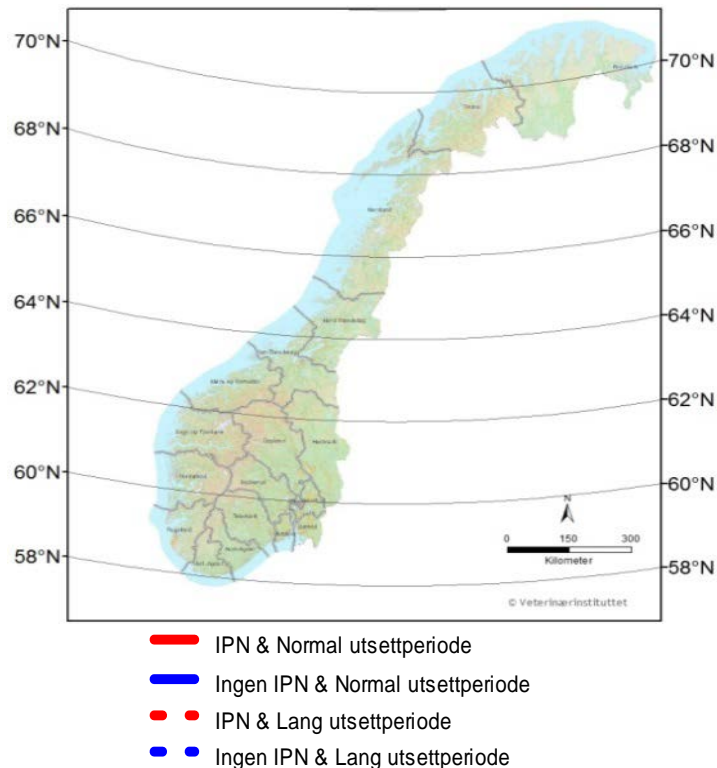
Juveniles, on-grown and broodstock

Geographic structure

Association with ISAV HPRΔ



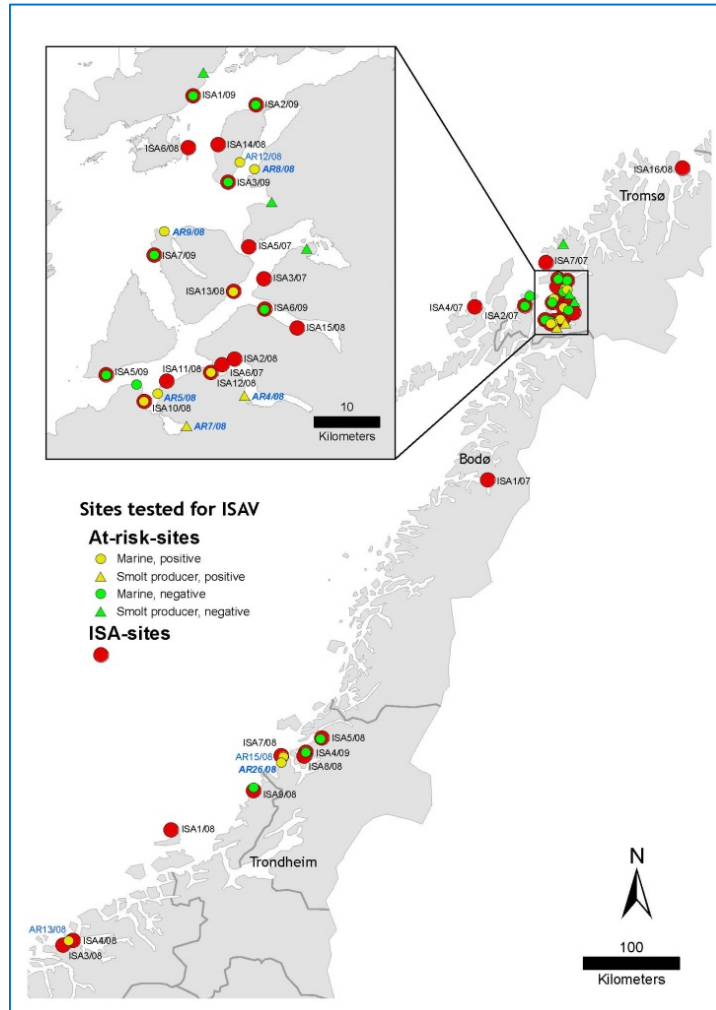
# Variables that may explain primary outbreaks



Work in progress by Lyngstad *et al.*



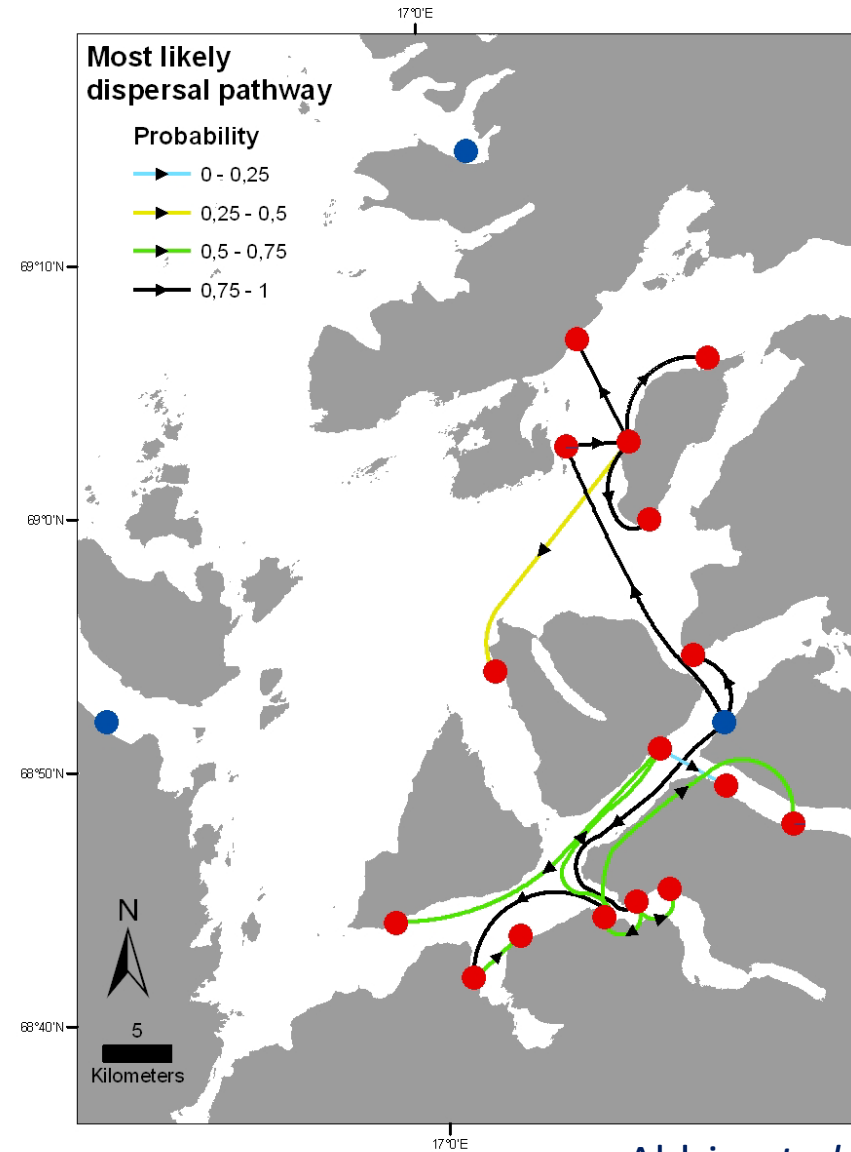
# Tracing of ISA-virus



Lyngstad *et al.*, 2011

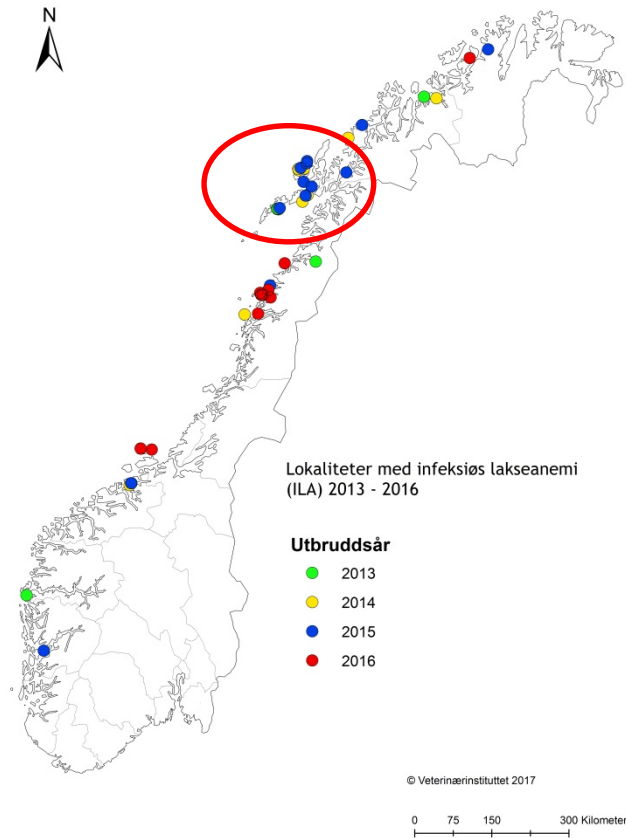


**Veterinærinstituttet**  
Norwegian Veterinary Institute



Aldrin *et al.*, 2011

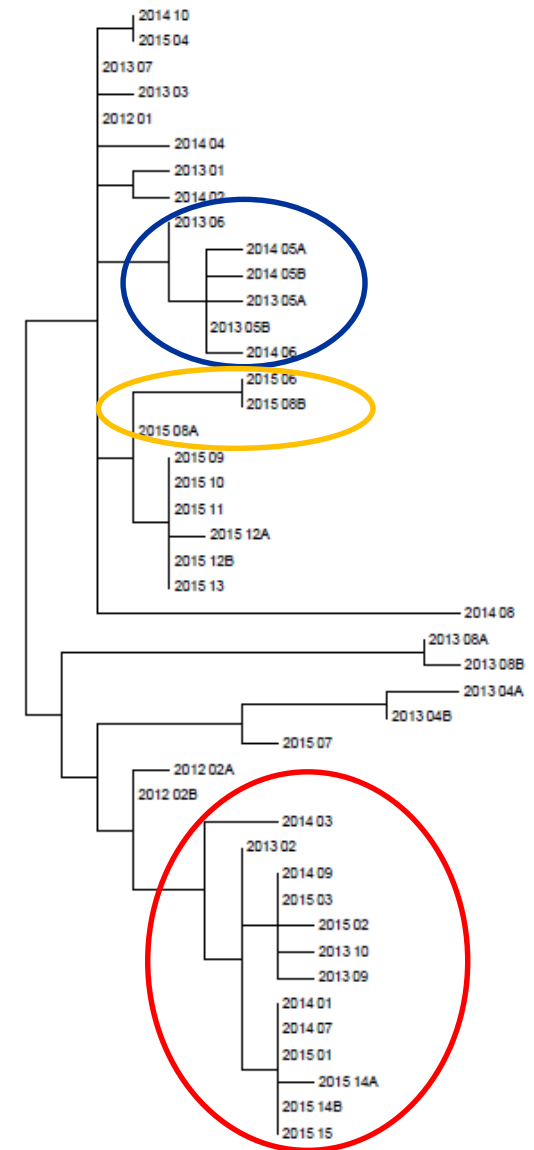
# Outbreaks during the last four years



Fish Health Report 2016

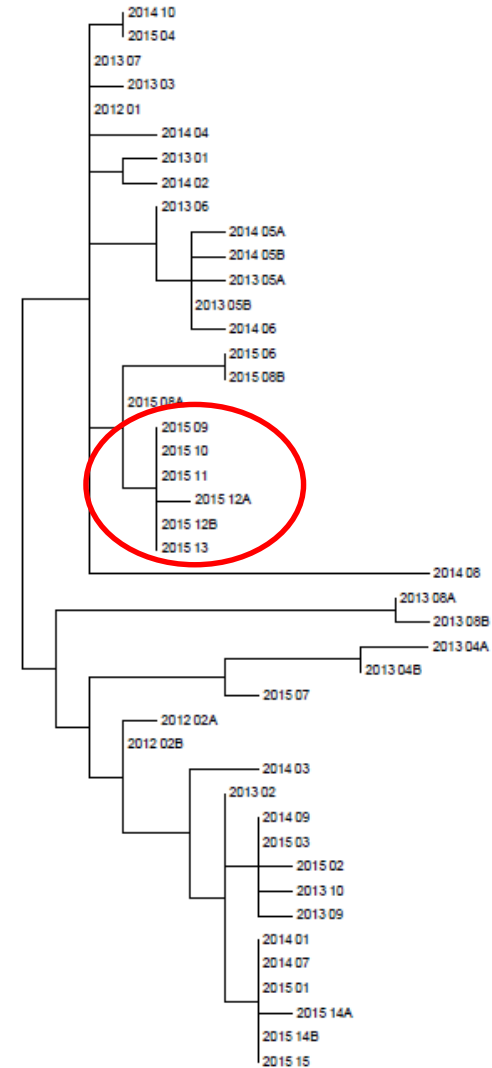
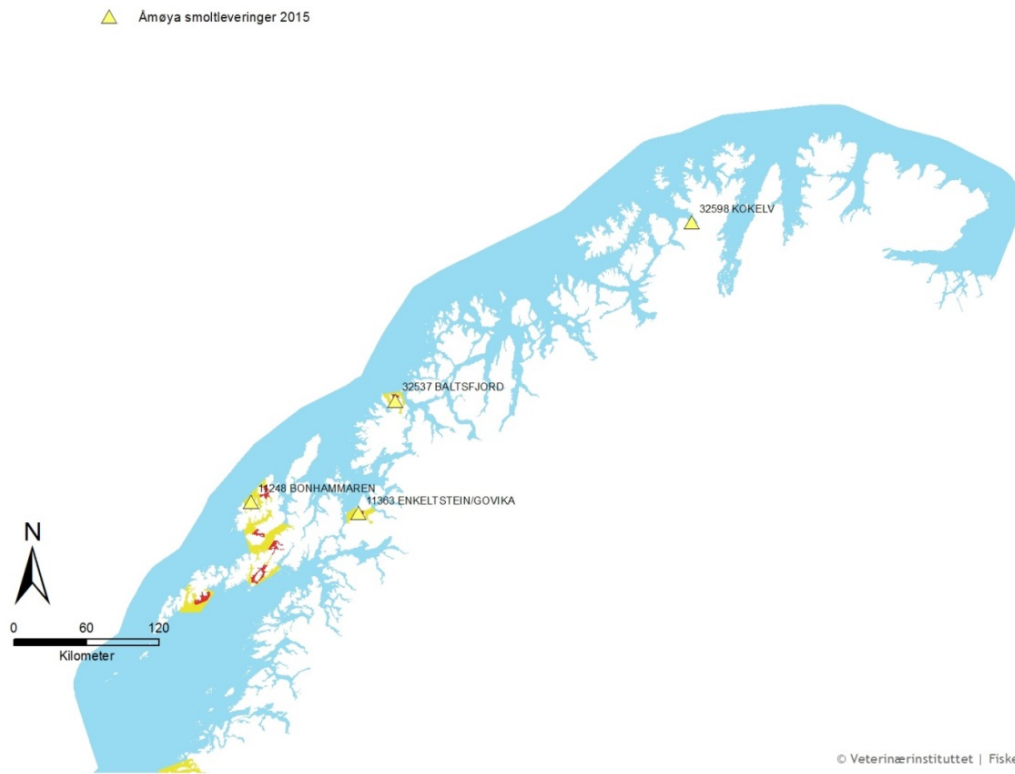


# Three epidemics in the same area





# ISA in smolt shortly after sea-transfer



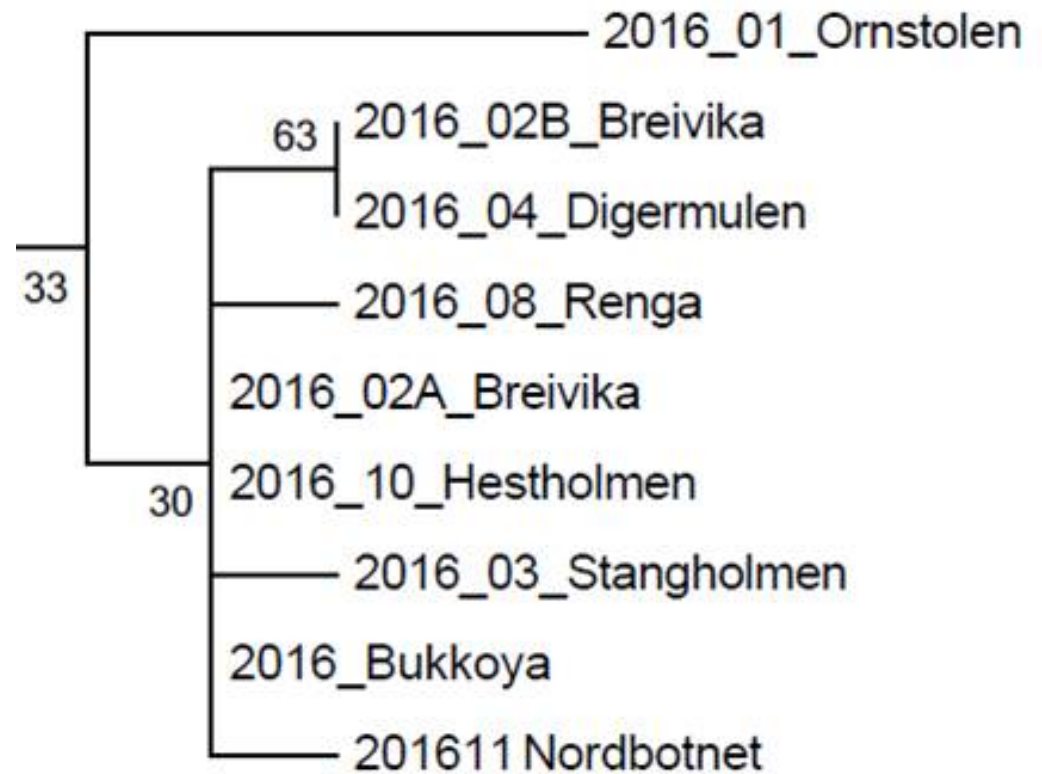
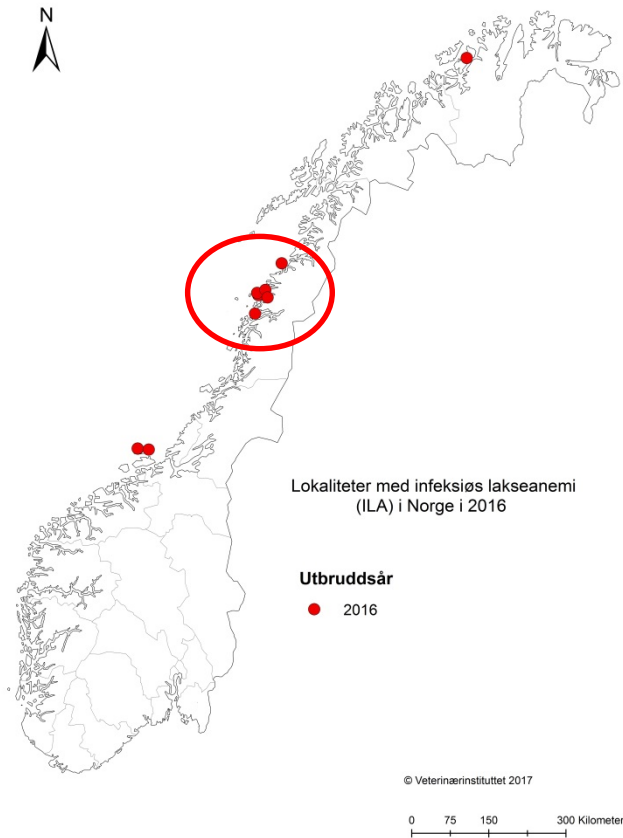
# ISAV HPRO to ISAV HPRΔ in the hatchery

DNA Sequences		Translated Protein Sequences	
Species/Abbrv	Group Name	*****	*****
1. P343_HPR_F		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
2. P351_HPR_F		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
3. P352_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
4. P354_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
5. P355_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
6. P357_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
7. P358_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
8. P401_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
9. P402_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	
10. P403_HPR		AGATGTTAAAAGATCAGGGTATGACGCAATCCCACTTCAGCTGAAACCATAATTCATAACAAACCAAGTAGAGCAACCTGCGACATCTGTGTGAGTAAACA	

Closely related ISAV HPRO and ISAV HPRΔ detected in February and June respectively



# ISA-outbreaks in 2016

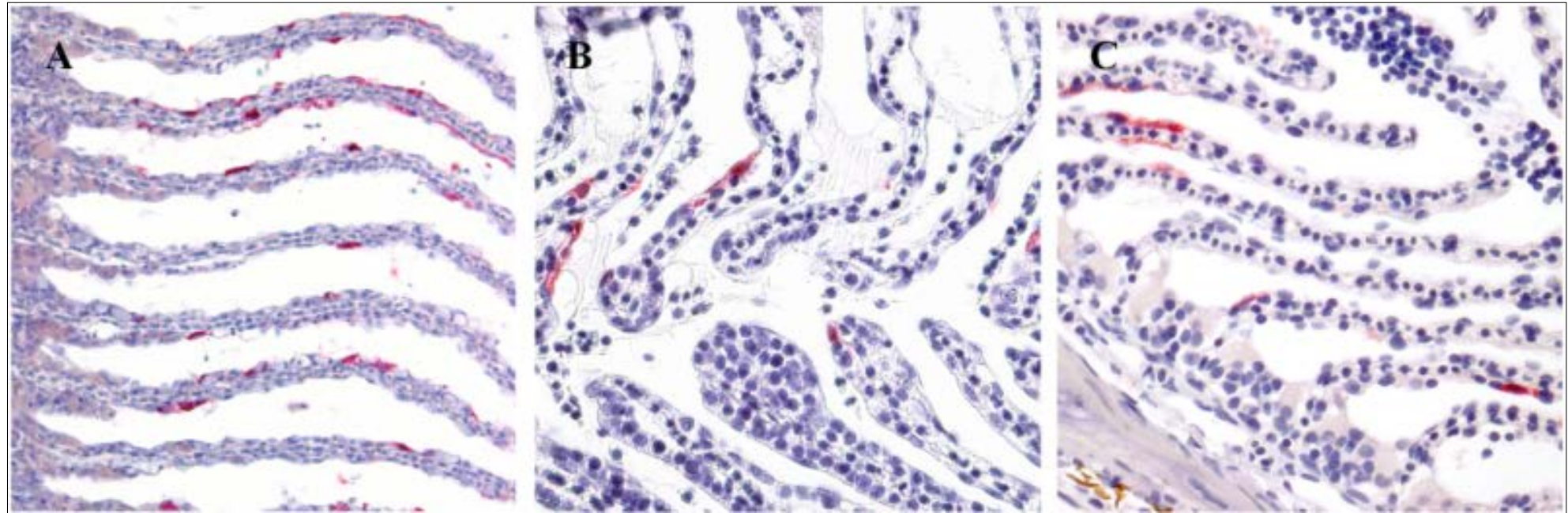


# Deletions in HPR are not compatible

ILAV HPRO	TDV	KIRLDAI	PPQL	NQT	FNTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Ørnstolen	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Brevika	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Stangholmen	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Bukkøya	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Digermulen	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Kvalvika	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Storstompan	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Renga	TDV	KIRLDAI			NTN	QVEQ	PA	TSVL	SNI	FISM	GVA
Hestholmen N	TDV	KIRLDAI	PPQL	NQT	FNT					M	GVA
Nordbotnet	TDV	KIRLDAI	PPQL								GVA



# ISAV HPR0 in mucosal surfaces (gills and skin)



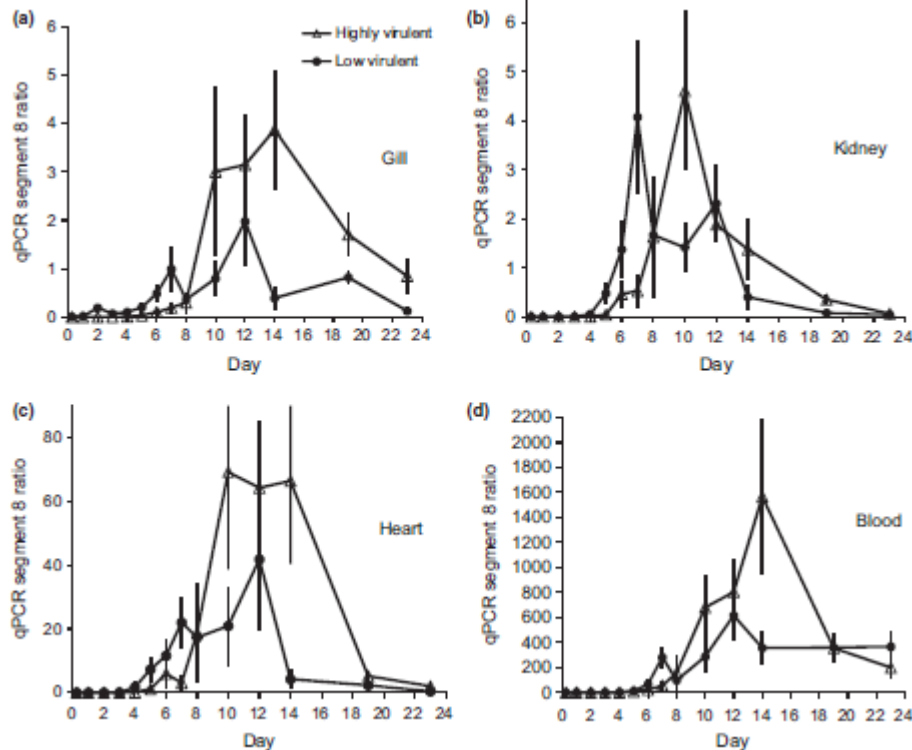
Aamelfot *et al.*, 2016



# Low- versus highly virulent ISAV HPRΔ

Mortality 20% versus 100% 23 DPI when challenged by immersion

Low-virulent ISAV HPRΔ initiated earlier infection, but reached lower maximum virus load than highly virulent ISAV HPRΔ



McBeath *et al.*, 2015



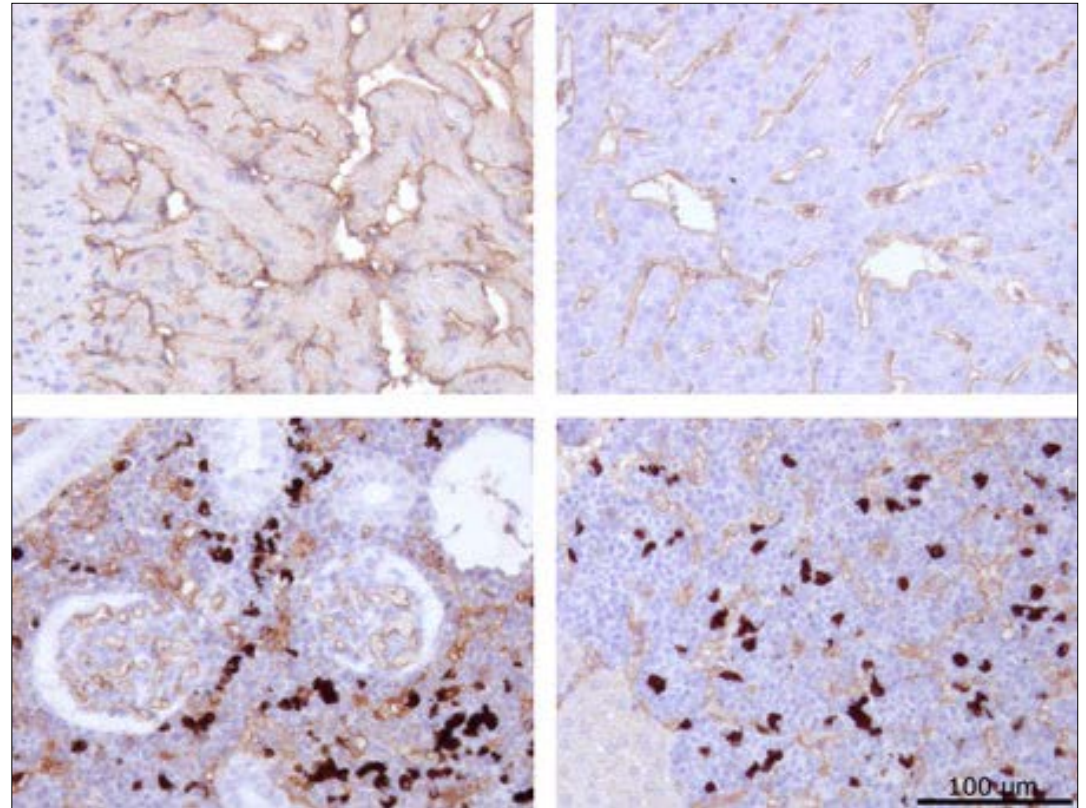
# Receptors and tissue tropism

ISAV bind to 4-*O*-acetylated sialic acid on the cell surface of

- endothelium
- erythrocytes
- epithelium

Species barrier

Potential carriers?



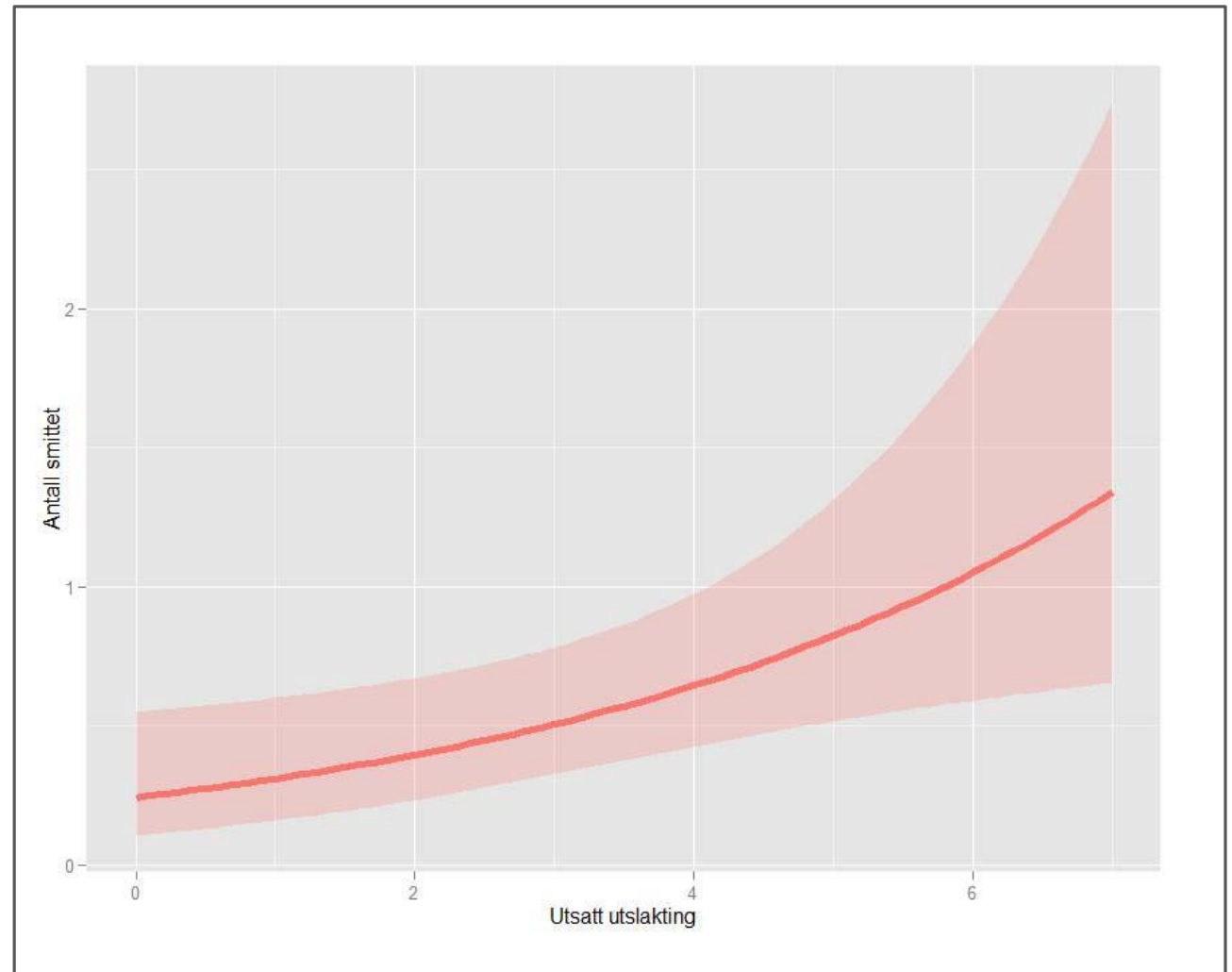
*Aamelfot et al., 2014*



# Management of ISA-outbreaks

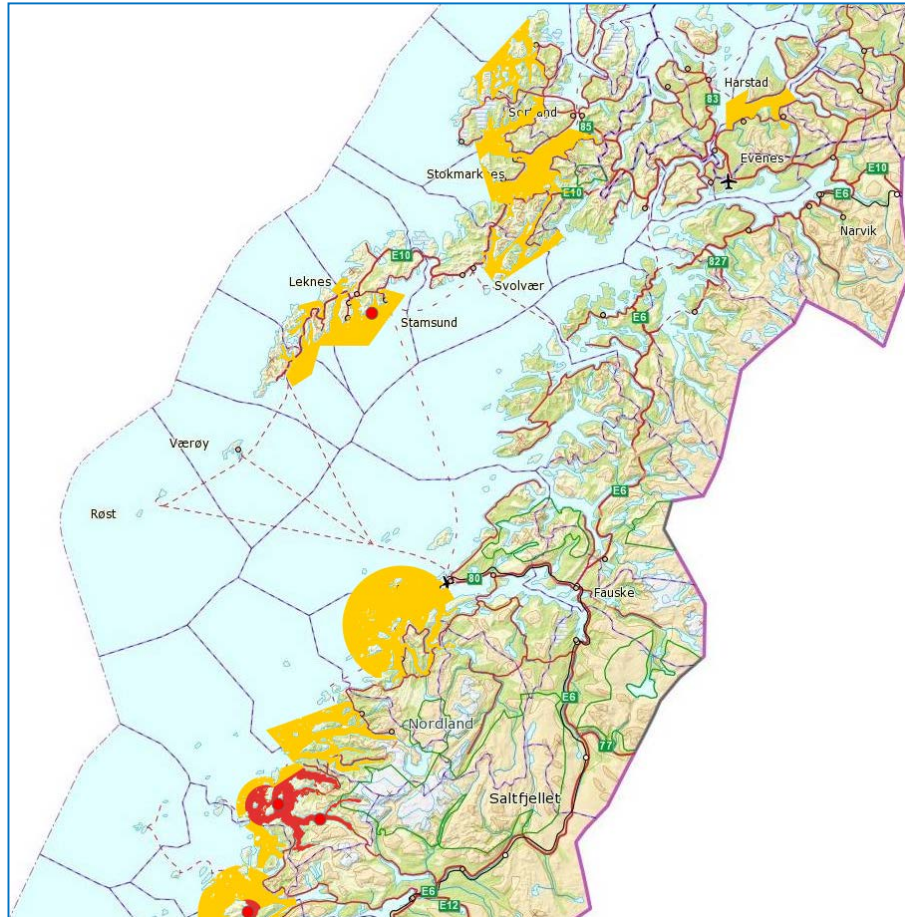
Will delayed removal of fish cause:

- longer period of shedding?
- more affected farms?





# Intensified health control and surveillance



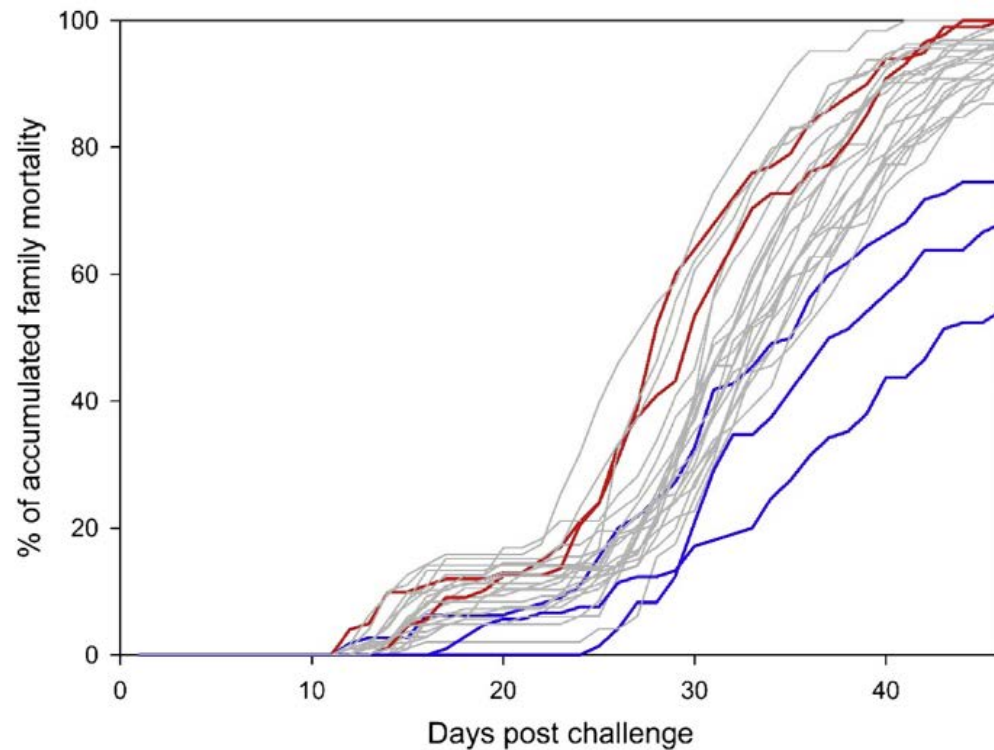
Control areas

Monthly inspections with  
sampling for ISAV-PCR

ISAV HPRΔ detected in at least  
two farms through active  
surveillance last year



# Variable susceptibility between family groups



Dettleff *et al.*, 2017

Large differences between family groups regarding mortality

Differences in virus replication and transcription of immune genes

Silent infections and carriers?



# Summary

ISAV HPR0 is prevalent in healthy fish

Transition from ISAV HPR0 to ISAV HPRΔ

IPN, long period of transfer to sea and latitude may explain primary outbreaks of ISA

Phylogenetic investigation is useful for tracing outbreaks

Receptors are essential for host tropism

Fast removal of fish is an important measure to limit outbreaks

Surveillance for early detection

