Effect of a DNA and oil-adjuvanted vaccines for pancreas disease on spinal cross-stitch pathology development, growth and economic impact of commercially reared Atlantic salmon

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Elanco

Introduction[1,2]

- New manifestation of vertebral deformity first noted in Norway in 2016

- «Cross-stitch vertebrae»

- Found in bigger harvest sized fish with no previous history of deformities

- More prevalent in S0's than in S1's

- Cross-stitch vertebrae pathology recently described

- Multivalent oil-based PD vaccines suggested as predisposing factor[3]

- Fish welfare concerns, especially with the more severe manifestations (scores 3-4)[3]

- Mechanism behind this pathological manifestation unknown

1. C. Trangerud, et al., 2020. Vertebral column deformity with curved cross-stitch vertebrae in Norwegian seawater-farmed Atlantic salmon, *Salmo salar* L. Journal of Fish Diseases. 43, 379-389.
2. H. Holm, et al., 2020. A pathomorphological description of cross-stitch vertebrae in farmed Atlantic salmon (*Salmo salar* L.). Aquaculture. 526, 735382.
3. G. Baeverfjord (Nofima), personal communication

Introduction cont…- Cross-stitch vertebrae
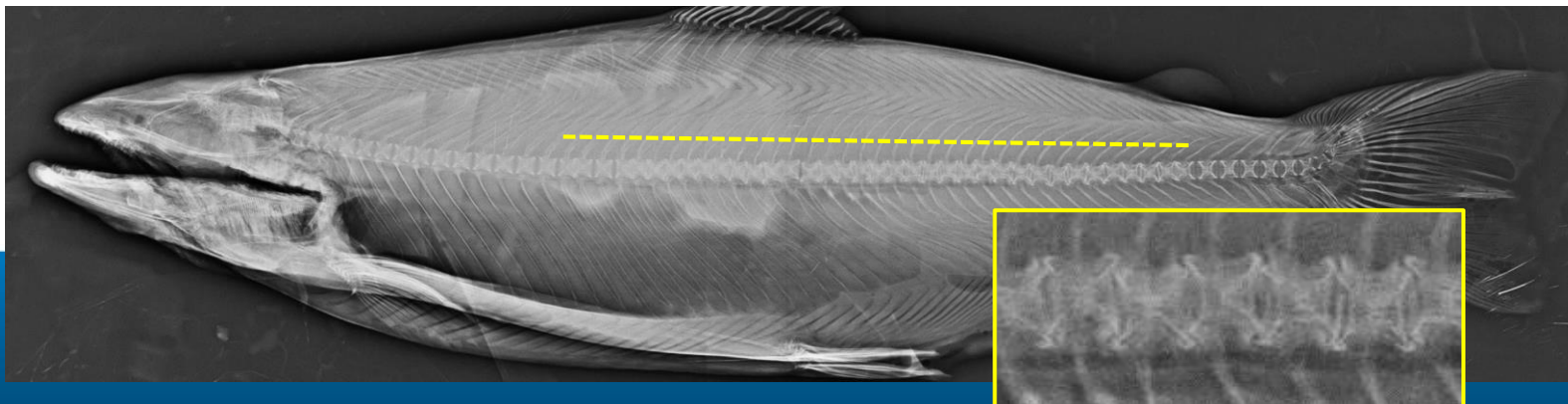
Study objective

To evaluate and compare relative field safety and efficacy of two different immunization strategies against pancreas disease (PD) in Atlantic salmon in Norway using licensed vaccines
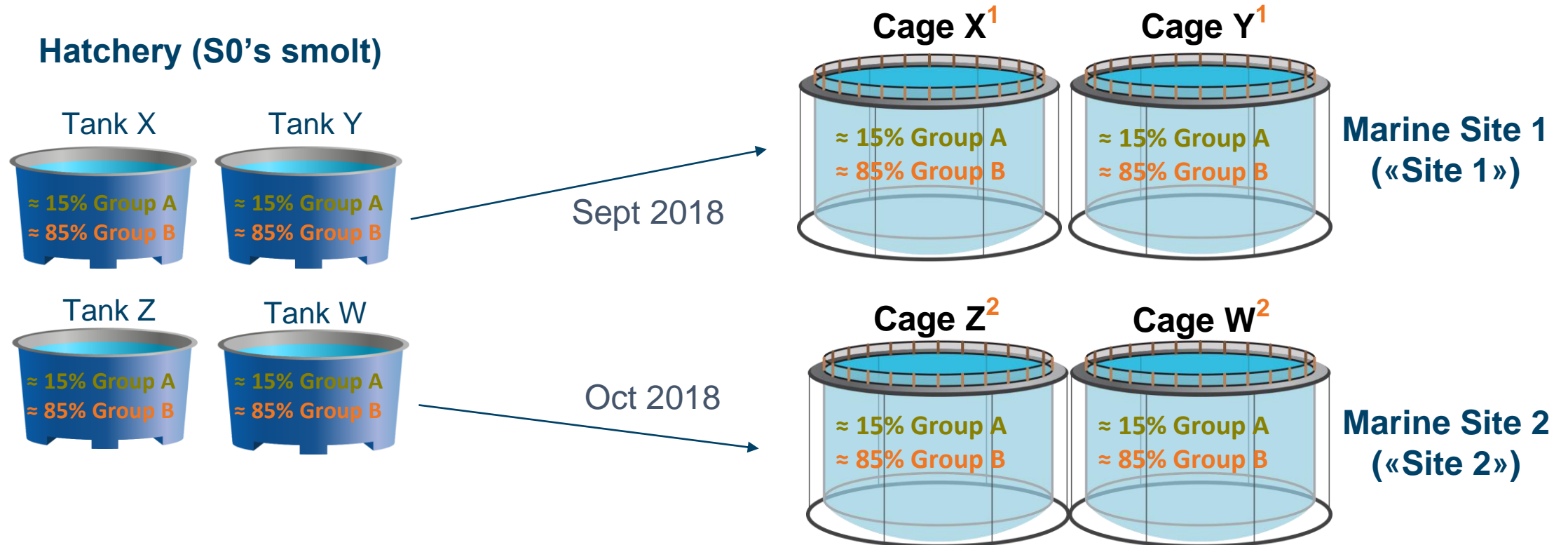
The vaccines used

Group ID	Vaccines used (administration / dose volumes)
Group A	AFC; DNA PD vaccine (i.m. / 0.05ml) + 6 component OA vaccine (i.p. / 0.05ml)
Group B	7 component OA PD vaccine (i.p. / 0.1ml)

AFC – Adipose Fin Clipped for group identification

i.m. – administered intramuscularly

i.p. – administered intraperitoneally
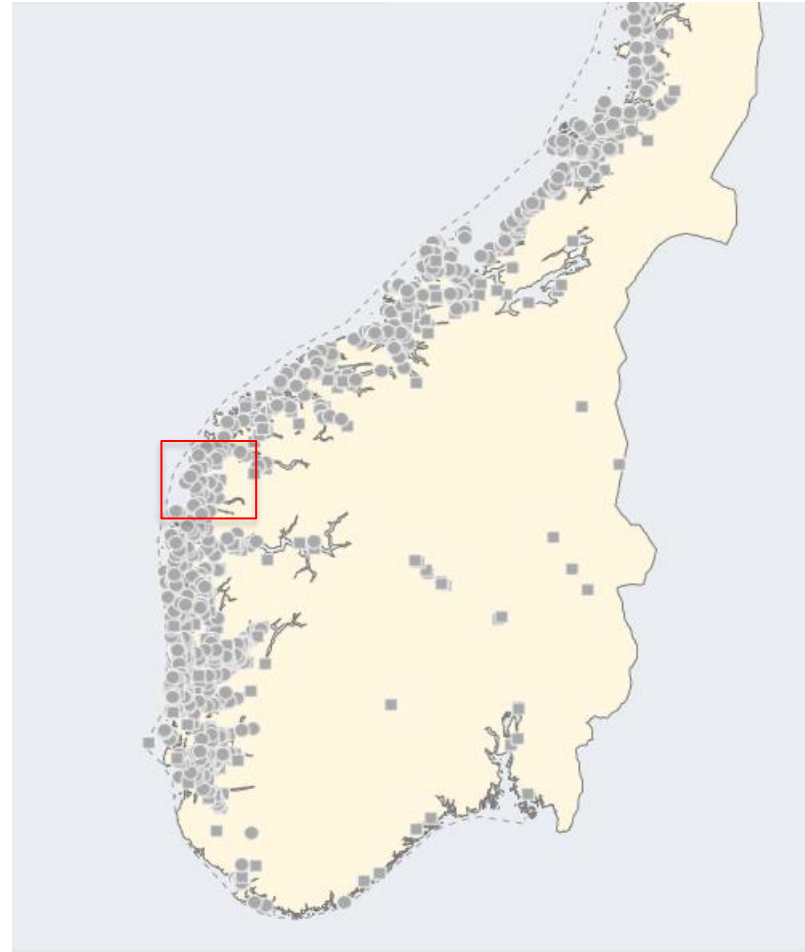
OA – Oil Adjuvanted

Study design

"Marked & Mixed" (M&M) design. Each rearing unit contained
15% ≈ 28 500 fish (**Group A**) and 85% ≈ 161 500 fish (**Group B**).

Hatchery (S0's smolt)

Tank X   Tank Y
≈ 15% Group A
≈ 85% Group B

Tank Z   Tank W
≈ 15% Group A
≈ 85% Group B

Sept 2018

Oct 2018

Cage X[1]   **Cage Y[1]**
≈ 15% Group A
≈ 85% Group B

Marine Site 1 («Site 1»)

Cage Z[2]   **Cage W[2]**
≈ 15% Group A
≈ 85% Group B

Marine Site 2 («Site 2»)

[1] Sampled pre slaughter ≈ 12 months post sea transfer
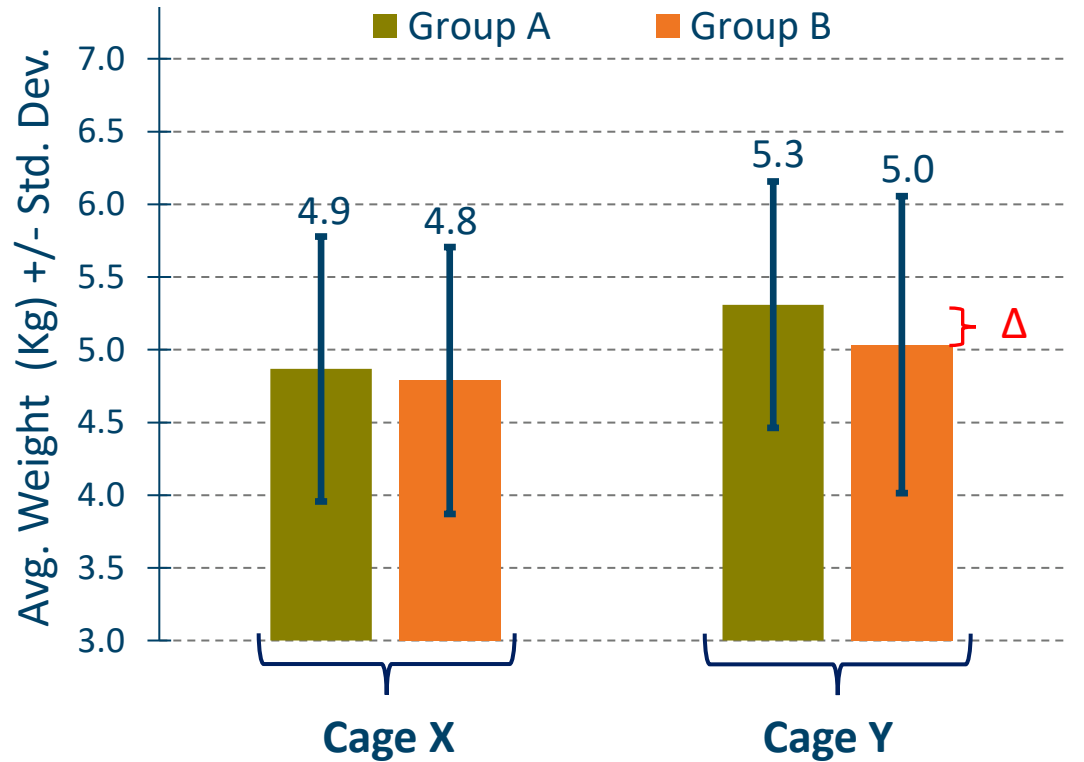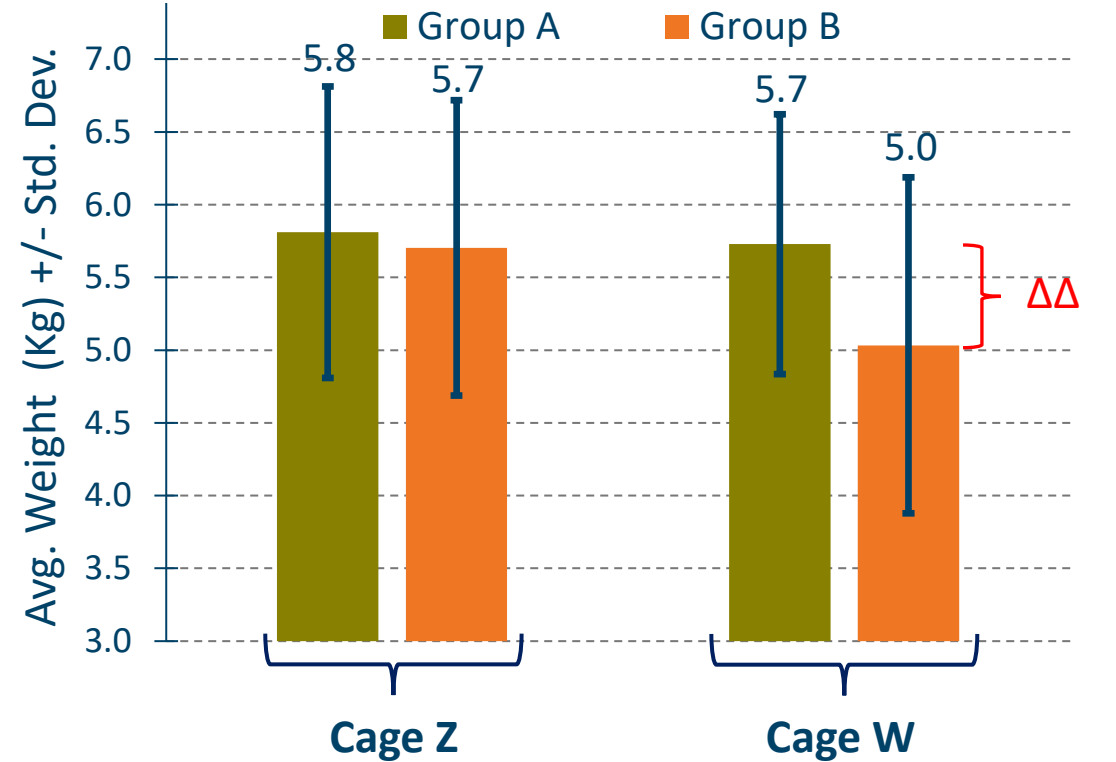[2] Sampled during slaughter ≈ 14 months post sea transfer

Geographical location

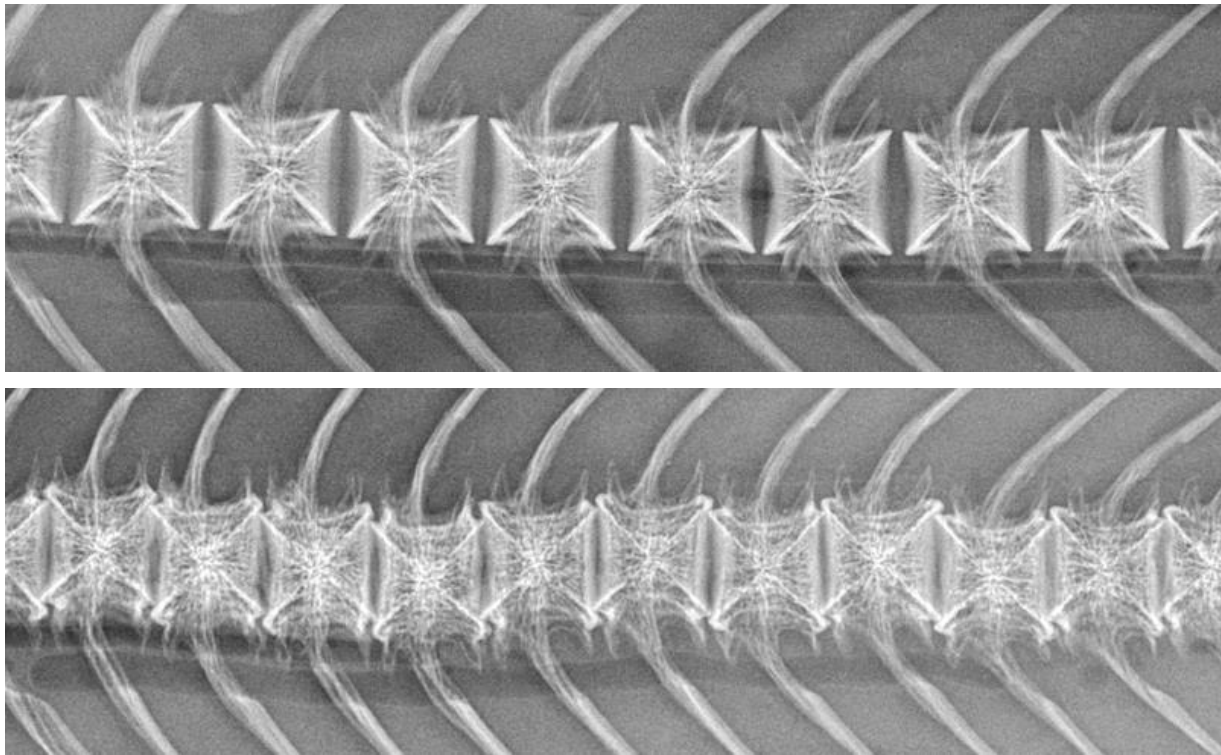# Weights pre-slaughter (Site 1) and during slaughter (Site 2)

Site 1

Avg. Weight (Kg) +/- Std. Dev.

Group A   Group B

Cage X: 4.9   4.8
Cage Y: 5.3   5.0   Δ

Δ ≈ 0,3kg /6%; p<0.05

Site 2

Avg. Weight (Kg) +/- Std. Dev.

Group A   Group B

Cage Z: 5.8   5.7
Cage W: 5.7   5.0   ΔΔ

ΔΔ ≈ 0,7kg /14%; p<0.0001

Δ and ΔΔ denote significant differences in weight between the groups (ANOVA).
(n= 99 to100 fish per group per cage).

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Normal vertebrae (top) and with cross-stitch pathology (bottom)[1]

CS Severity Score	0	1	2	3	4
No. Affected Vertebrae	0	1 - 5	6 - 10	11 - 30	31+

Prevalence and severity of cross-stitch pathology*

Chart axis label: Presence of CS deformity (%)

Site 1 — Group A: a** (1%), Group B: b (13%)

Site 2 — Group A: a** (8%), Group B: b (31%)
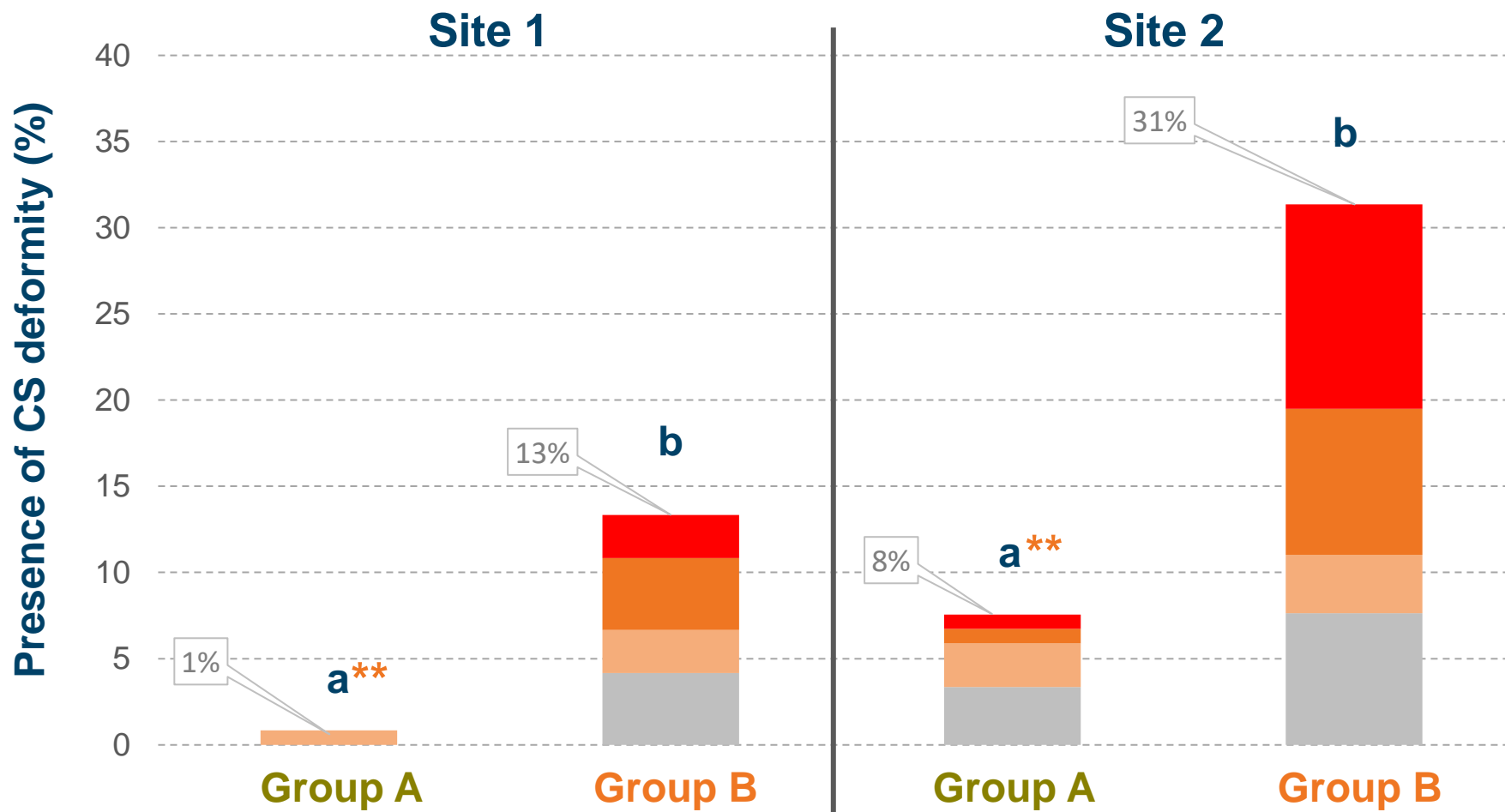
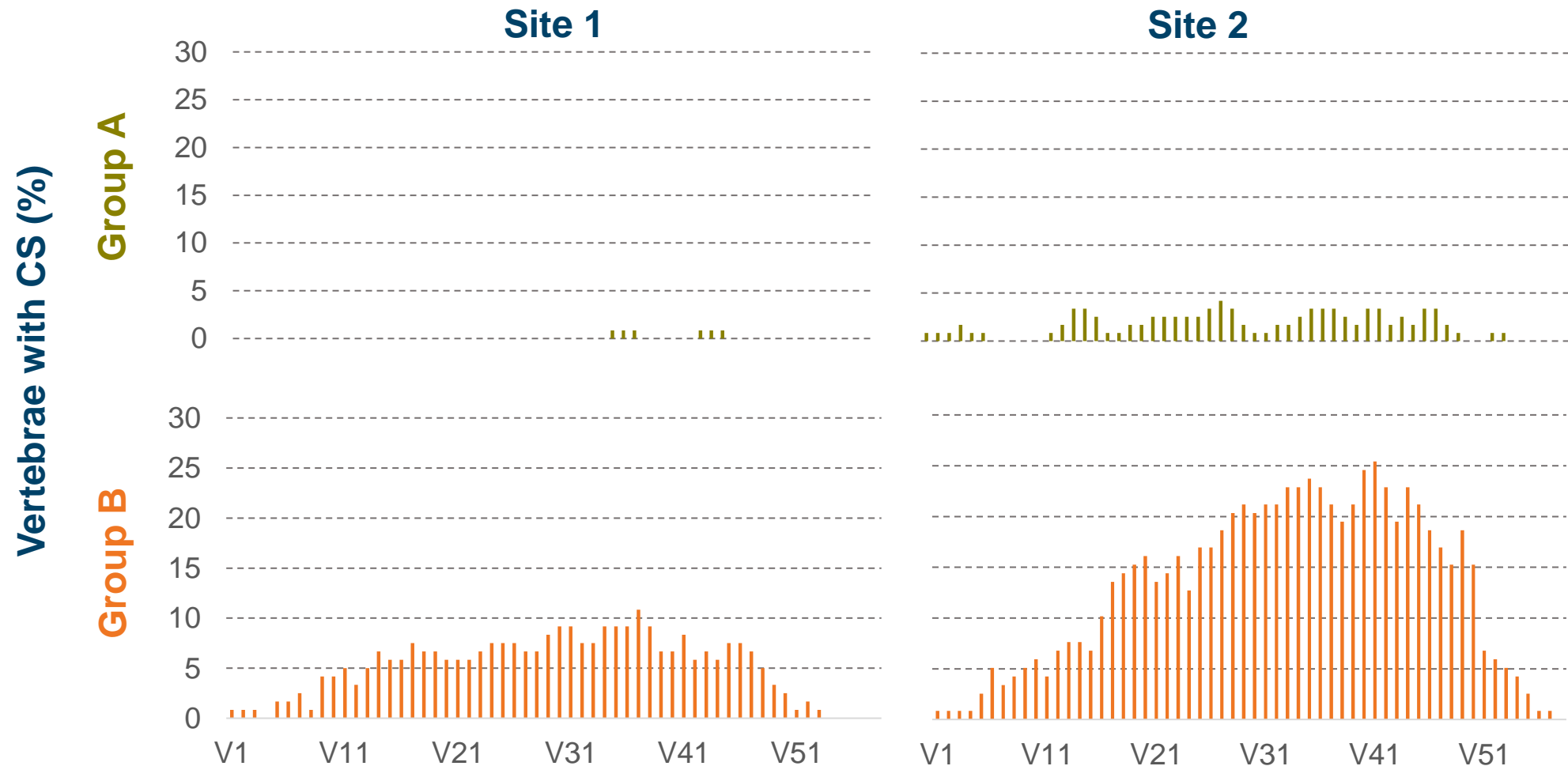| Cross stitch score	No. of affected vertebrae
4	31+
3	11 − 30
2	6 − 11
1	1 − 5
0	0

* Graph shows average per site and vaccine group. Different letters (a, b) denote significant differences in prevalence (<0.0001; n=118 to120 per group per site). The evaluation and scoring was performed in a blinded manner.

** The OA vaccine used in Group A (without a PD component) used alone in similar study was shown to produce 6,7% prevalence with cross-stitch pathology (Ref; https://www.vetinst.no/rapporter-og-publikasjoner/faglige-vurderinger-og-horingssvar)

Prevalence of the vertebrae (V) with cross-stitch pathology
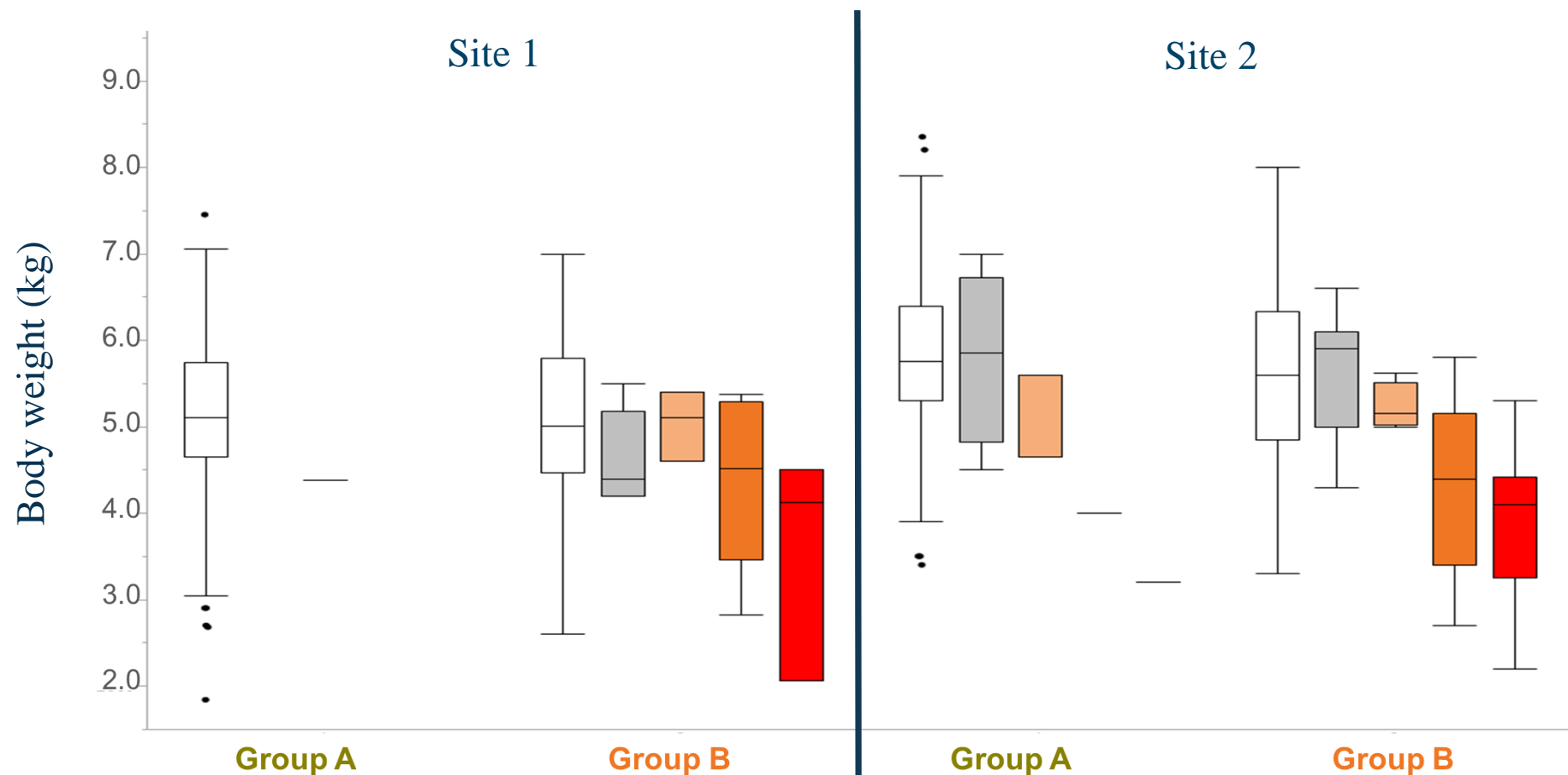*(n = 118 to 120 fish per group per site)*

From anterior (V1) to posterior (V57)

Effect of cross-stitch pathology on growth

Cross stitch score	Avg. neg. effect on growth	P-value
0	-	-
1	- 0.12 kg	p= 0.42
2	- 0.35 kg	p= 0.009
3	- 1.12 kg	p< 0.001
4	- 1.75 kg	p< 0.001

*Linear regression with robust variance estimation (compared to score "0"). n= 118 to 120 fish per group per site (59-60 fish per group per cage)

Economic impact of vaccine regimes
*References where similar modelling has been used*

- J.M. Pettersen, O.B. Brynildsrud, R.B. Huseby, K.M. Rich, A. Aunsmo, B.B. Jensen, M. Aldrin, 2016. The epidemiological and economic effects from systematic depopulation of Norwegian marine salmon farms infected with pancreas disease virus. Preventive Veterinary Medicine 132: 113 - 124

- J.M. Pettersen, K.M. Rich, B. Bang Jensen, A. Aunsmo, 2015. The economic benefits of disease triggered early harvest: A case study of pancreas disease in farmed Atlantic salmon from Norway. Preventive Veterinary Medicine121: 314-324.

- A. Aunsmo, P.S. Valle, M. Sandberg, P.J. Midtlyng, T. Bruheim, 2010. Stochastic modelling of direct costs of pancreas disease (PD) in Norwegian farmed Atlantic salmon (Salmo salar L). Preventive Veterinary Medicine 93: 233-241.

- A. Aunsmo, 2009. Health related losses in sea farmed Atlantic salmon - quantification, risk factors and economic impact. PhD thesis, Norwegian School of Veterinary Science.

Economic impact of vaccine regimes
Methodology

- A partial budget model was adapted to compare the effect of the two vaccine groups on production and economy[1]

- All sample weights assumed as actual harvest weights

- Differences in weights between the groups (95% CI)

- Salmon price «head-on gutted» (HOG) per slaughter weight category were calculated and averaged for 2019[2]

- Weight categories assigned using normal distribution with coefficient of variation (CV) of 22% in both groups[3]

- Only effects of weight differences included in model
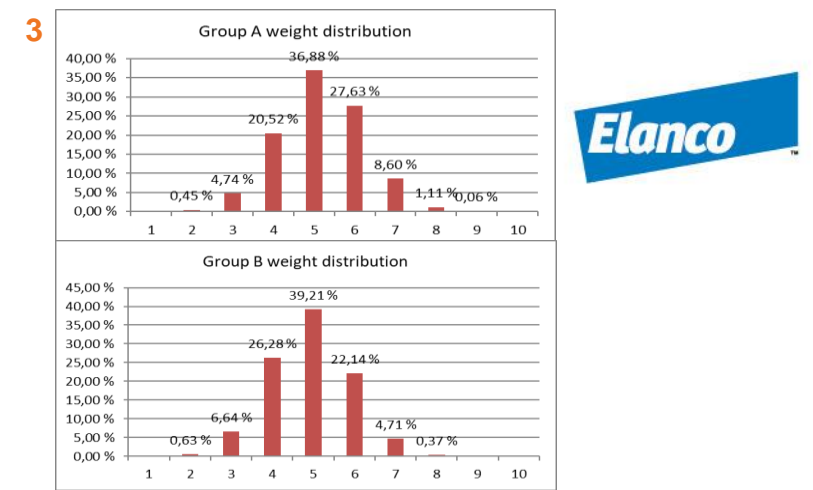
Other input variables	
Vaccine cost per fish – group A	5.47 NOK
Vaccine cost per fish – group B	2.93 NOK
No of smolts used in model	1 million
Average costs of feed/kg[4]	11.70 NOK
Harvest & sales cost/kg HOG[4]	3.72 NOK
Mortality based on industry average[4]	17%
Production cost/kg[4]	45.54 NOK
Historical 2019 avg. salmon prices/kg (HOG)[2]	57.96 NOK

[1] A. Aunsmo, et al. 2010. Stochastic modelling of direct costs of pancreas disease (PD) in Norwegian farmed Atlantic salmon. Prev Vet Med.93(2-3):233-41

[2] https://salmonprice.nasdaqomxtrader.com/public/report?1

[4] https://fiskeridir.no/Akvakultur/Tall-og-analyse/Loennsomhetsundersoekelse-for-laks-og-regnbueoerret/Matfiskproduksjon-laks-og-regnbueoerret

Effects of different growth and thereby harvest weight of the two vaccine groups analyzed in a model comparing production of 1 mill. stocked fish using Norwegian 2019 salmon prices and costs

Vaccine group	Values	Harvest weight (gram)	Price HOG NOK/ kg	Volume tons	Production cost NOK/ kg	Result in mill. NOK
Group A	mean	5430	59.32	3866	45.54	49.4
Group B	mean	5141	58.47	3660	46.29	41.0
	95% CI*	(4895 - 5298)	(58.00 - 58.93)	(3549 - 3772)	(47.11 - 45.51)	(35.1 – 46.9)
Δ value (B-A)	mean	-289	-0.85	-206	0.75	-8.4
	mean %	-5.3%	-1.4%	-5.3%	+1.6%	-17.0%
	95% CI*	(-445 to -132)	(-1.32 to -0.39)	(-317 to -94)	(1.57 to -0.03)	(-14.3 to 2.6)

* 95% confidence interval from analyses on weight and projected in the partial budget model

Conclusions

➢ Fish in Group A had significantly greater weights than those in Group B in Cages Y ($p<0.05$) and W ($p<0.0001$)

➢ Cross-stitch pathology significantly (3.9 to 13-fold) more prevalent in Group B compared to Group A ($p<0.0001$)

➢ The OA vaccine used in Group A has been reported to cause similar levels of cross-stitch pathology when used on its own, suggesting that the DNA PD vaccine is not contributing to the cross-stitch pathology

➢ There was a significant effect of cross-stitch severity scores 2-4 on reduced fish weight ranging from average growth penalty of 0.35 kg (score 2; $p=0.009$) to 1.75 kg (score 4; $p<0.001$) compared to unaffected fish (Score 0)

➢ There was an indirect, strong effect of vaccine group on fish weight through cross-stitch scores ($p<0.001$)

➢ Based on the overall average differences measured in this study and input of one million smolts using Norwegian 2019 average costs and sales prices, the salmon producer could have expected to end up with a profit increase (EBIT) of 17% by having selected the Group A vaccine alternative

Thank you for your attention!