Poster P10.051.C

PREVALENCE AND GEOGRAPHIC DISTRIBUTION OF THE *C9ORF72* REPEAT EXPANSION AMONG NORWEGIAN ALS PATIENTS

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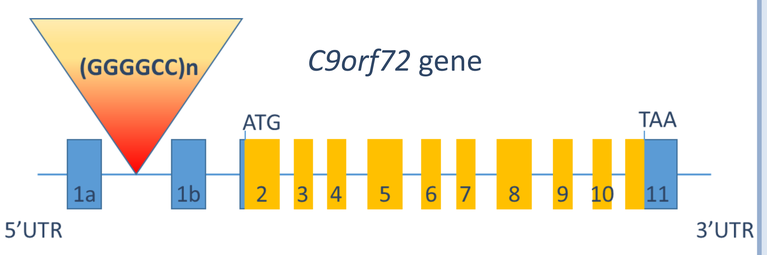
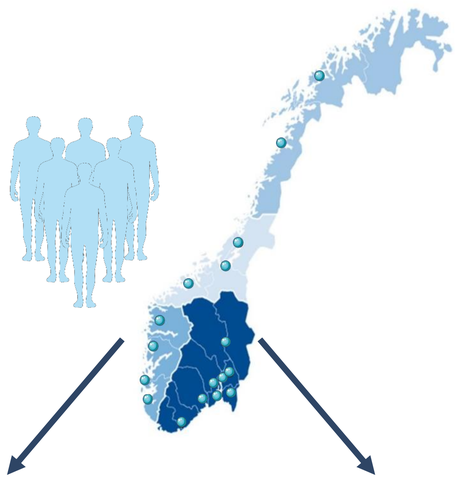
Background

- ✓ Amyotrophic lateral sclerosis is a fatal neurodegenerative disease that affects motor neurons
- ✓ Approximately 10% of the patients are categorised as familial ALS (fALS). The remaining 90% are categorised as simplex ALS (sALS).
- ✓ One of the most common genetic cause of Amyotrophic Lateral Sclerosis (ALS) is a hexanucleotide repeat expansion $(GGGGCC)_n$ in the non-coding region of the *C9orf72* gene. This also may cause Frontotemporal dementia (FTD).
- ✓ In Europe, this expansion accounts for 34% of the familial ALS cases and approximately 6% of simplex ALS cases, geographic variation is seen.

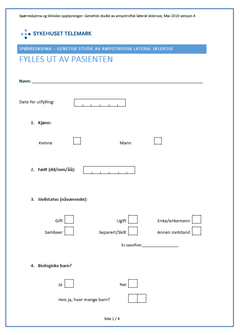


Methods

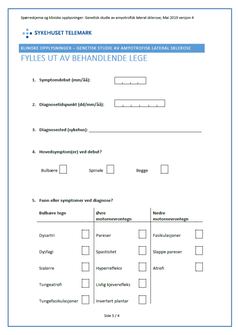
Patients diagnosed with ALS is recruited from all over Norway



2-part questionnaire

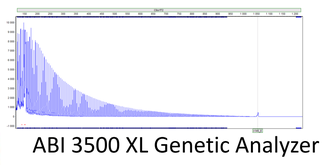


First part concerning known family history answered by the patient



Second part concerning clinical information answered by recruiting neurologist

C9orf72 repeat expansion analysis



ABI 3500 XL Genetic Analyzer

Asuragen AmplideX® PCR/CE *C9orf72* kit

No. of repeats	
2-24	Normal repeat size
25-60	Intermediate repeat size
61 - >4000	Pathogenic repeat size, causes ALS/FTD with age-dependent penetrance

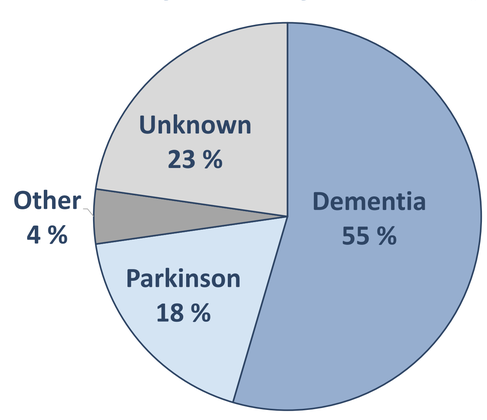
Ref: GeneReviews

Results: Clinical characteristics

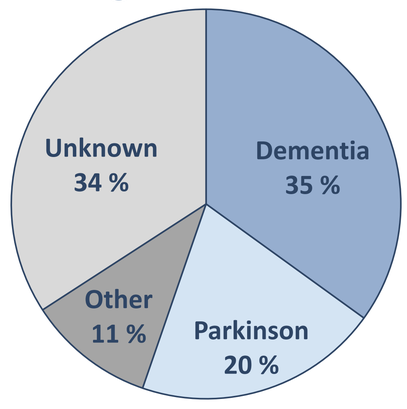
Patients	with *C9orf72*	without *C9orf72*	Total
Patients included, n (%)	44 (9.8)*	406 (90.2)	450
Familial ALS, n (%)	22 (50)	45 (11.1)	67 (14.9)
Simplex ALS, n (%)	22 (50)	361 (88.9)	383 (85.1)
Age of onset (mean)	61.3	63.7	63.4
Relatives with NMD or NDD**, n (%)	22 (50)***	124 (30.5)***	146 (32.4)
Cognitive impairment, n (%)	4 (9.1)	33 (8.1)	37 (8.2)

* 43 full and 1 intermediate repeat expansions, ** Neuromuscular or neurodegenerative diseases

***Family history of NMD/NDD among relatives

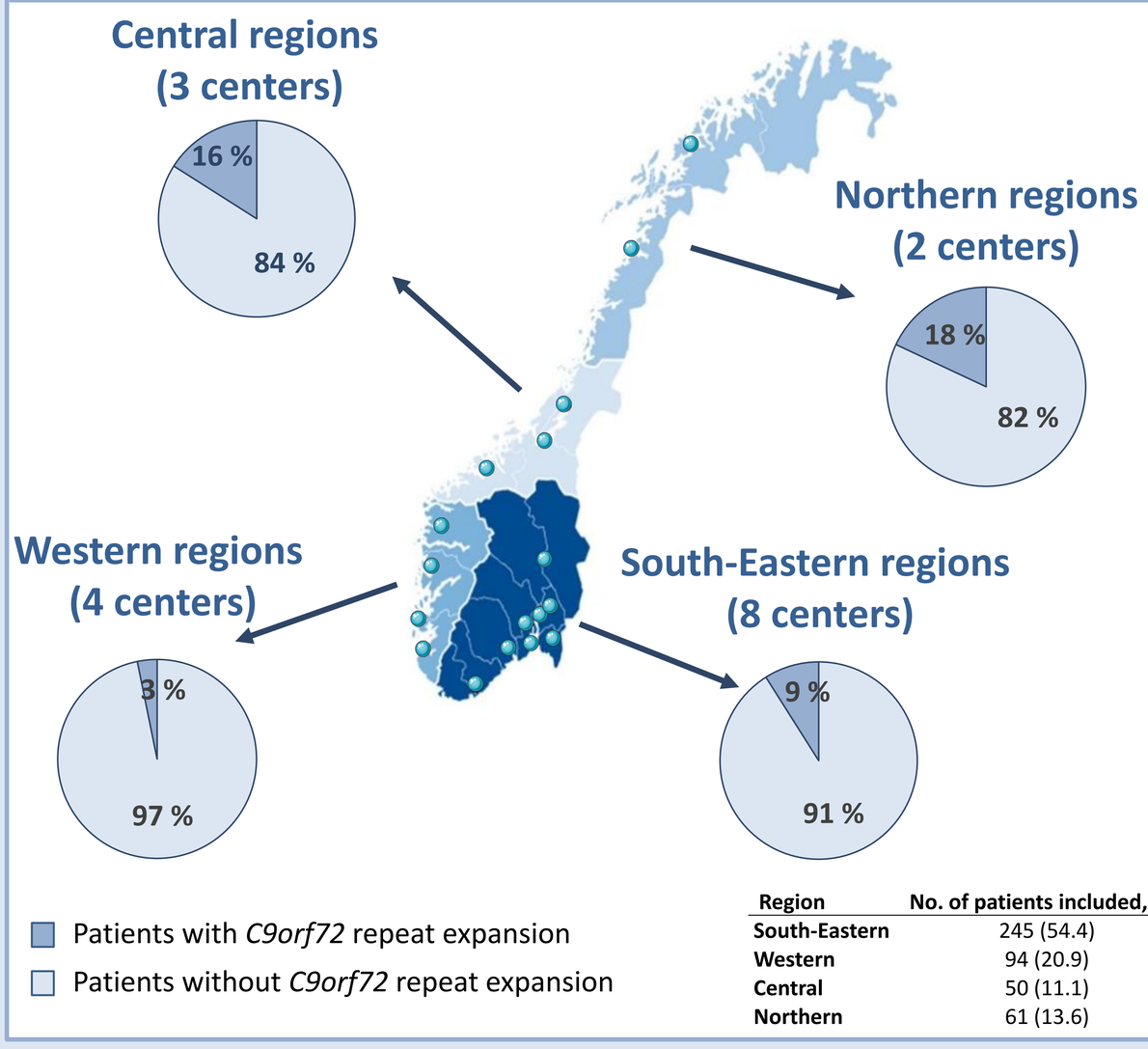


Relatives of patients with *C9orf72* repeat expansion with NMD or NDD



Relatives of patients without *C9orf72* repeat expansion with NMD or NDD

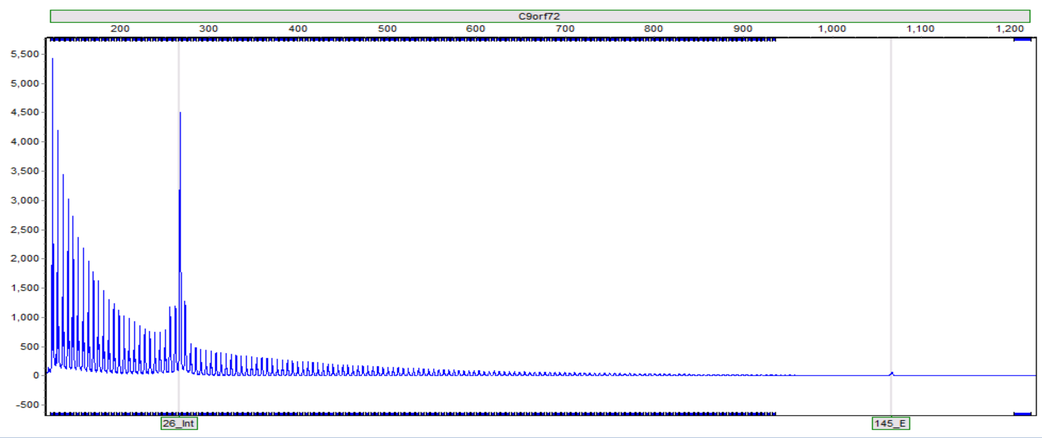
Results: Geographic variation of the C9orf72 expansion



Region	No. of patients included, (%)
South-Eastern	245 (54.4)
Western	94 (20.9)
Central	50 (11.1)
Northern	61 (13.6)

Result: Interesting case

One patient had both an intermediate (26) and a full expansion repeat (>145) in *C9orf72*



Conclusion:

- ✓ The pathogenic C9orf72 repeat expansion was identified in 32.8% of the familial ALS cases and 5.5% simplex ALS cases.
- ✓ 50% of those with a *C9orf72* repeat expansions had relatives with NMD or NDD. Dementia were the most common type.
- ✓ There is a tendency of a higher frequency of *C9orf72* repeat expansion in the central and norther regions.

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The authors declare no conflicts of interest