Supplementary Online Content

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eTable 1. Polyglutamine disease-associated genes and primers.

Gene	Primer 1 (forward)	Primer 2 (reverse)	Mix
ATXN1	CCCCAACCGCCAACCCC	GTGGGATCATCGTCTGGTGGG	A
ATXN2	CGTTCCGGCGTCTCCTTGG	ACCGAGGAGGGAGCCGT	B
ATXN3	GTAATCTGTATCAGACTAACTGCTCTTG	GGGAATGAAGAATAATGTAAAGCAAAAATCAC	B
CACNA1A	CGTGTCCTATTCCCCTGTGATCC	CCTGGGTACCTCCGAGG	A
ATXN7	GAACTCCCTGGCGCCTCC	GATTCCACGACTGTCCCAGCAT	A
TBP	CCACAGCCTATTCAGAACACC	TGGGACGTTGACTGCTGAAC	B
HTT	ATGAAGGCCTTCGAGTCCCTCAAGTCCTTC	GGCGGTGGCGGCTGTTGCTGCTGC	A
ATN1	CCACCCACCAGTCTCAACACATC	CCAGTGGGTGGGGAAATGCTC	A
AR	ACCGAGGAGCTTTCCAGAAT	CTCATCCAGGACCAGGTAGC	B

eTable 2. Summary of polyglutamine disease-associated genes over the cohorts.

PDAG	Cohort	Allele	Mean	Median	Range	#Total
ATXN1	NESDA	short	29.2	29	19-35	930
		long	30.8	30	27-37	930
	NESDO	short	29.2	29	26-34	128
		long	30.9	30	28-39	128
	NEO	short	29.2	29	17-36	6438
		long	30.8	30	22-40	6438
	PROSPER	short	29.2	29	17-36	5633
		long	30.8	30	26-44	5633
	Leiden 85-plus	short	29.3	29	24-35	539
		long	30.8	30	28-38	539
	Total	short	29.2	29	17-36	13668
		long	30.8	30	22-44	13668
ATXN2	NESDA	short	21.9	22	13-23	930
		long	22.3	22	22-31	930
	NESDO	short	21.9	22	17-22	128
		long	22.4	22	22-30	128
	NEO	short	21.9	22	13-30	6389
		long	22.4	22	17-36	6389
	PROSPER	short	21.9	22	11-27	5548
		long	22.4	22	22-33	5548
	Leiden 85-plus	short	21.9	22	13-23	541
		long	22.4	22	22-31	541
	Total	short	21.9	22	11-30	13536
		long	22.4	22	17-36	13536
ATXN3	NESDA	short	18.8	20	13-28	929
		long	24.1	23	13-38	929
	NESDO	short	18.8	20	14-27	128
		long	25.0	25.5	14-31	128
	NEO	short	19.0	20	14-35	6494
		long	24.2	23	14-62	6494
	PROSPER	short	19.0	20	14-34	5544
		long	24.3	23	14-49	5543
	Leiden 85-plus	short	18.9	20	14-28	450
		long	24.4	24	14-38	450
	Total	short	19.0	20	13-35	13545
		long	24.2	23	13-62	13544
CACNA1A	NESDA	short	10.5	11	4-13	927
		long	12.5	13	4-15	927
	NESDO	short	10.7	11	4-14	128
		long	12.3	13	4-14	128
	NEO	short	10.5	11	4-14	6394
		long	12.5	13	4-22	6394
	PROSPER	short	10.6	11	4-14	5633
		long	12.5	13	7-17	5633
	Leiden 85-plus	short	10.7	11	4-14	533
		long	12.5	13	7-19	532
	Total	short	10.6	11	4-14	13615
		long	12.5	13	4-22	13614

PDAG	Cohort	Allele	Mean	Median	Range	#Total
ATXN7	NESDA	short	10.0	10	7-15	856
		long	10.8	10	9-17	856
	NESDO	short	10.0	10	7-13	125
		long	10.9	10	10-14	125
	NEO	short	10.0	10	5-13	6356
		long	10.8	10	7-30	6356
	PROSPER	short	10.1	10	7-16	5285
		long	10.8	10	10-25	5285
	Leiden 85-plus	short	10.1	10	7-14	413
		long	10.9	10	10-25	413
	Total	short	10.1	10	5-16	13035
		long	10.8	10	7-30	13035
TBP	NESDA	short	36.4	37	27-39	930
		long	37.9	38	33-43	930
	NESDO	short	36.1	36	29-38	128
		long	37.8	38	35-41	128
	NEO	short	36.4	37	23-40	6418
		long	37.9	38	30-45	6418
	PROSPER	short	36.3	37	26-40	5559
		long	37.9	38	30-47	5559
	Leiden 85-plus	short	36.3	37	27-39	550
		long	37.9	38	35-44	550
	Total	short	36.3	37	23-40	13585
		long	37.9	38	30-47	13585
HTT	NESDA	short	16.9	17	9-26	930
		long	20.0	19	15-33	930
	NESDO	short	16.9	17	10-24	128
		long	19.8	19	15-30	128
	NEO	short	16.9	17	6-31	6453
		long	20.1	19	11-40	6453
	PROSPER	short	16.9	17	9-29	5602
		long	20.2	19	10-38	5602
	Leiden 85-plus	short	17.0	17	9-25	557
		long	20.3	19	15-33	557
	Total	short	16.9	17	6-31	13670
		long	20.2	19	10-40	13670
ATN1	NESDA	short	12.3	14	7-19	931
		long	15.5	15	8-27	931
	NESDO	short	12.6	15	8-18	128
		long	15.6	16	8-21	128
	NEO	short	12.4	14	3-22	6467
		long	15.5	15	8-28	6467
	PROSPER	short	12.3	14	5-20	5633
		long	15.6	16	8-27	5633
	Leiden 85-plus	short	12.2	14	5-17	550
		long	15.5	16	8-25	550
	Total	short	12.4	14	3-22	13709
		long	15.5	15	8-28	13709

PDAG	Cohort	Allele	Mean	Median	Range	#Total
AR	NESDA	allele male	22.0	22	13-32	335
		short female	20.2	20	8-27	590
		long female	23.4	23	17-33	590
	NESDO	allele male	21.5	21	18-27	4978
		short female	20.2	20	15-25	78
		long female	22.8	22.5	19-32	78
	NEO	allele male	22.0	22	11-36	3010
		short female	20.3	20	8-29	3330
		long female	23.4	24	16-38	3330
	PROSPER	allele male	22.0	22	7-35	2663
		short female	20.4	20	7-29	2847
		long female	23.6	23	16-39	2847
	Leiden 85-plus	allele male	22.4	22	12-32	179
		short female	20.4	20	11-30	369
		long female	23.5	24	16-36	369
	Total	allele male	22.0	22	7-36	6236
		short female	20.3	20	7-30	7214
		long female	23.5	23	16-39	7214

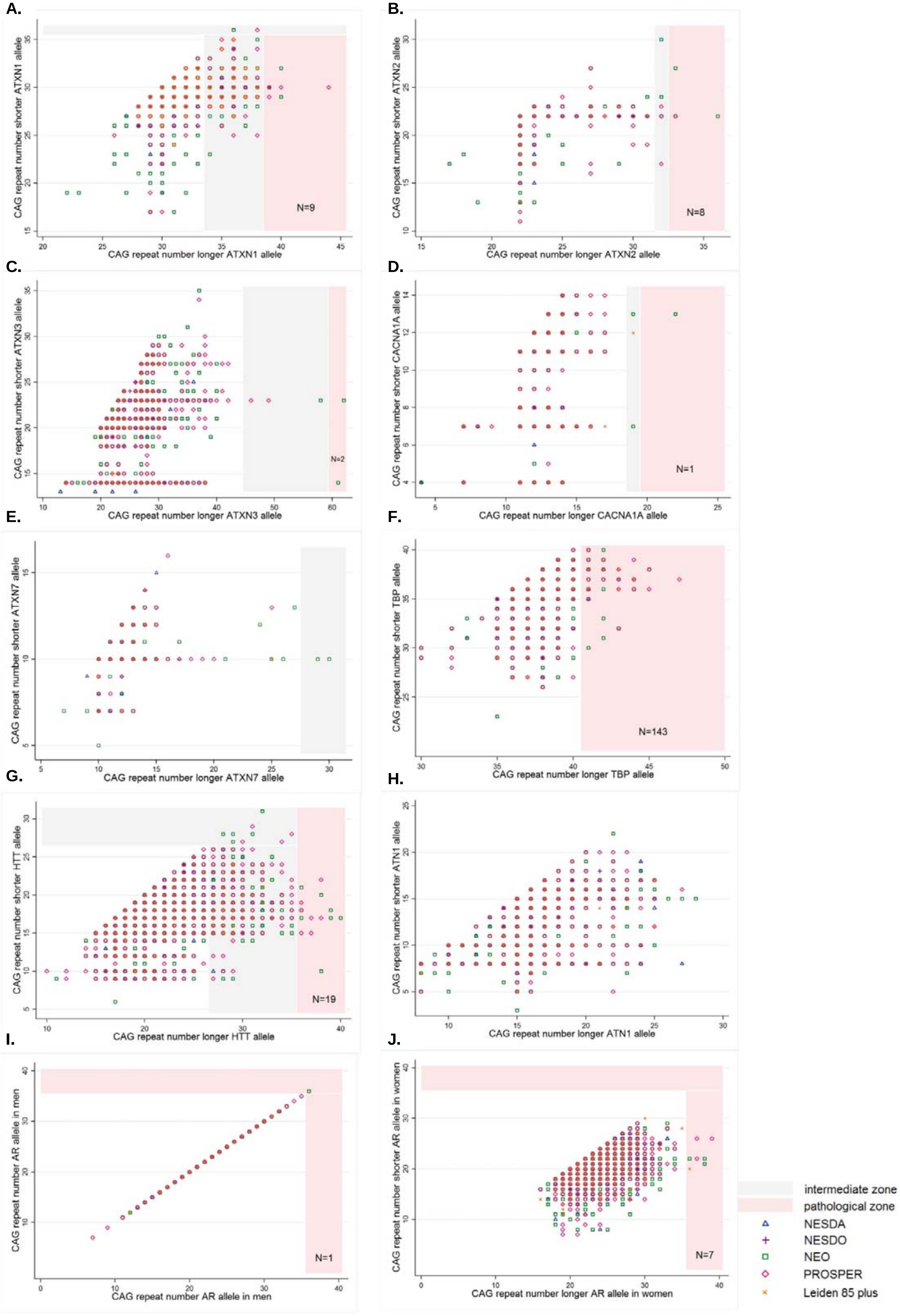
PDAG=polyglutamine disease-associated gene. NESDA=the Netherlands Study of Depression and Anxiety. NESDO=the Netherlands Study of Depression in Older Persons. NEO=the Netherlands Epidemiology of Obesity. PROSPER=the Prospective Study of Pravastatin in the Elderly at Risk.

eTable 3. Differences in characteristics between individuals with CAG repeat numbers within the pathological range and individuals with CAG repeat numbers within the normal range.

PDAG	Variable		Pathological (%)	Normal[a]	Total	P-value[b]
ATXN1	Cohort (n)	NESDA	0 (0.00)	930	930	.027
		NESDO	1 (0.78)	127	128	
		NEO	4 (0.06)	6434	6438	
		PROSPER	4 (0.07)	5629	5633	
		Leiden 85-plus	0 (0.0)	539	539	
	Sex (n)	male	4 (0.06)	6353	6357	.901
		female	5 (0.07)	7306	7311	
	Age (mean±SE)		67.9±1.79	64.2±0.11	64.2±0.11	.396
	BMI (mean±SE)		29.0±1.19	28.3±0.04	28.3±0.04	.639
	Country (n)	The Netherlands	5 (0.05)	9101	9106	.320
		Scotland	1 (0.04)	2455	2456	
		Ireland	3 (0.14)	2103	2106	
ATXN2	Cohort (n)	NESDA	0 (0.00)	930	930	.600
		NESDO	0 (0.00)	128	128	
		NEO	6 (0.09)	6383	6389	
		PROSPER	2 (0.04)	5546	5548	
		Leiden 85-plus	0 (0.00)	541	541	
	Sex (n)	male	6 (0.10)	6289	6295	.106
		female	2 (0.03)	7239	7241	
	Age (mean±SE)		60.8±3.18	64.1±0.11	64.1±0.11	.474
	BMI (mean±SE)		27.2±1.61	28.3±0.04	28.3±0.04	.550
	Country (n)	The Netherlands	8 (0.09)	9034	9042	.137
		Scotland	0 (0.00)	2419	2419	
		Ireland	0 (0.00)	2075	2075	
ATXN3	Cohort (n)	NESDA	0 (0.00)	929	929	.704
		NESDO	0 (0.00)	128	128	
		NEO	2 (0.03)	6492	6494	
		PROSPER	0 (0.00)	5544	5544	
		Leiden 85-plus	0 (0.00)	450	450	
	Sex (n)	male	1 (0.02)	6320	6321	.925
		female	1 (0.01)	7223	7224	
	Age (mean±SE)		57.5±3.50	63.9±0.11	63.9±0.11	.488
	BMI (mean±SE)		30.8±2.04	28.3±0.04	28.3±0.04	.469
	Country (n)	The Netherlands	2 (0.02)	9054	9056	.992
		Scotland	0 (0.00)	2423	2423	
		Ireland	0 (0.00)	2066	2066	
CACNA1A	Cohort (n)	NESDA	0 (0.00)	927	927	.890
		NESDO	0 (0.00)	128	128	
		NEO	1 (0.02)	6393	6394	
		PROSPER	0 (0.00)	5633	5633	
		Leiden 85-plus	0 (0.00)	533	533	
	Sex (n)	male	0 (0.00)	6327	6327	.351
		female	1 (0.01)	7287	7288	
	Age (mean±SE)		52	64.2±0.11	64.2	-
	BMI (mean±SE)		23.0	28.3±0.04	28.3	-
	Country (n)	The Netherlands	1 (0.01)	9050	9051	.777
		Scotland	0 (0.00)	2457	2457	
		Ireland	0 (0.00)	2107	2107	

PDAG	Variable		Pathological (%)	Normal[a]	Total	P-value[b]
TBP	Cohort (n)	NESDA	7 (0.75)	923	930	.631
		NESDO	1 (0.78)	127	128	
		NEO	62 (0.97)	6357	6418	
		PROSPER	66 (1.19)	5493	5559	
		Leiden 85-plus	7 (1.27)	543	550	
	Sex (n)	male	61 (0.95)	5258	6319	.353
		female	82 (1.13)	7184	7266	
	Age (mean±SE)		65.4±1.08	64.1±0.11	64.1±0.11	.254
	BMI (mean±SE)		27.7±0.38	28.3±0.04	28.3±0.04	.177
	Country (n)	The Netherlands	92 (1.01)	8987	9079	.037
		Scotland	19 (0.78)	2409	2428	
		Ireland	32 (1.54)	2046	2078	
HTT	Cohort (n)	NESDA	0 (0.00)	930	930	.501
		NESDO	0 (0.00)	128	128	
		NEO	12 (0.19)	6441	6453	
		PROSPER	7 (0.11)	5595	6502	
		Leiden 85-plus	0 (0.00)	557	557	
	Sex (n)	male	13 (0.20)	6336	6349	.055
		female	6 (0.08)	7315	7321	
	Age (mean±SE)		64.8±2.17	64.2±0.11	64.2±0.11	.833
	BMI (mean±SE)		27.2±0.96	28.3±0.04	28.3±0.04	.331
	Country (n)	The Netherlands	15 (0.16)	9118	9133	.527
		Scotland	2 (0.08)	2444	2446	
		Ireland	2 (0.10)	2089	2091	
AR ♂	Cohort (n)	NESDA	0 (0.00)	335	335	.899
		NESDO	0 (0.00)	49	49	
		NEO	1 (0.03)	3009	3010	
		PROSPER	0 (0.00)	2663	2663	
		Leiden 85-plus	0 (0.00)	179	179	
	Sex (n)	male	1 (0.02)	6235	6236	-
		female	-	-	-	
	Age (mean±SE)		63	64.3±0.16	64.3	-
	BMI (mean±SE)		21.2	28.1±0.05	28.1	-
	Country (n)	The Netherlands	1 (0.02)	4122	4123	.774
		Scotland	0 (0.00)	1190	1190	
		Ireland	0 (0.00)	923	923	

PDAG=polyglutamine disease associated gene. NESDA=the Netherlands Study of Depression and Anxiety. NESDO=the Netherlands Study of Depression in Older Persons. NEO=the Netherlands Epidemiology of Obesity. PROSPER=the Prospective Study of Pravastatin in the Elderly at Risk. BMI=body mass index. [a]) including the intermediate and normal range. [b]) determined by an independent sample t-test given a continuous variable or a chi-square test given a categorical variable.


A.
CAG repeat number shorter ATXN1 allele
CAG repeat number longer ATXN1 allele
N=9
B.
CAG repeat number shorter ATXN2 allele
CAG repeat number longer ATXN2 allele
N=8
C.
CAG repeat number shorter ATXN3 allele
CAG repeat number longer ATXN3 allele
N=2
D.
CAG repeat number shorter CACNA1A allele
CAG repeat number longer CACNA1A allele
N=1
E.
CAG repeat number shorter ATXN7 allele
CAG repeat number longer ATXN7 allele
F.
CAG repeat number shorter TBP allele
CAG repeat number longer TBP allele
N=143
G.
CAG repeat number shorter HTT allele
CAG repeat number longer HTT allele
N=19
H.
CAG repeat number shorter ATN1 allele
CAG repeat number longer ATN1 allele
I.
CAG repeat number AR allele in men
CAG repeat number AR allele in men
N=1
J.
CAG repeat number shorter AR allele in women
CAG repeat number longer AR allele in women
N=7
intermediate zone
pathological zone
△ NESDA
+ NESDO
□ NEO
◇ PROSPER
× Leiden 85 plus

eFigure. The distribution of the CAG repeat numbers in the polyglutamine disease-associated genes per allele and cohort. On the x-axis are the CAG repeat numbers in the longer allele and on the y-axis are the CAG repeat numbers of the shorter allele. Since the alleles are defined as ‘shorter’ or ‘longer’ relative to the size of the other allele, the shorter allele cannot be longer than the longer allele. The *AR* gen is linked to the X-chromosome. Therefore, men only have one *AR* allele.