



Enroll-HD:

A Prospective Registry Study in a Global Huntington's Disease Cohort

A CHDI Foundation Project

Enroll-HD Periodic Dataset (PDS#3)

Statistical Analysis Report

Version 1.0

03 October 2017

QUALITY CONTROL AND QUALITY ASSURANCE STATEMENT AND SIGNATORIES

Statistical Analysis

The results presented in this report were generated in accordance with Statistical Analysis Plan (SAP) [Enroll-HD-SAP_1-2016-R1-for PDS3].

The above referenced SAP was prepared by Nilza Gonçalves and Daisy de Abreu.

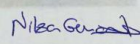

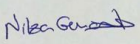
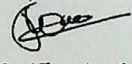

Analytical scripts generated to perform analyses outlined in the SAP were prepared by Ana Raquel Fernandes, and validated and approved by a second statistician, Nilza Gonçalves. Analyses were performed by Ana Raquel Fernandes and validated and approved by a second statistician, Nilza Gonçalves.

Statistical Report

The current statistical report was prepared by Ana Raquel Fernandes. The report was reviewed by two statisticians Nilza Gonçalves and Daisy Abreu, to confirm accuracy of transposition of values from statistical software output into final report (including tables, figures and text).

The final report was reviewed and approved by Joaquim J. Ferreira and Jennifer Ware.

Signatures

	Name	Company/Institution	Signature & Date
	Name	Institution	(YYYY-MM-DD)
SAP preparation:	Nilza Gonçalves	AIDFM	 2017/10/14
SAP approval:	JOAQUIM FERREIRA	AIDFM	11 OCT 2017 
Analytical script preparation:	Ana Fernandes	AIDFM	Ana Fernandes 2017/10/11
Analytical script approval:	Nilza Gonçalves	AIDFM	 2017/10/11
Performance of analyses:	Ana Fernandes	AIDFM	Ana Fernandes 2017/10/11
	Daisy Abreu	AIDFM	Daisy Abreu 2017/10/14
Statistical report preparation:	Raquel Lobo	AIDFM	Raquel Jose Ladeira Lobo 2017/10/11
	Ana Fernandes	AIDFM	Ana Fernandes 2017/10/11
Statistical report validation (value cross-check):	Ana FERREIRA	AIDFM	Ana Ferreira 2017/10/11
	Daisy Abreu	AIDFM	Daisy Abreu 2017/10/14
Review and approval of final statistical report:	JEN WARE	DIRECTOR, EXP. DESIGN, CHDI	 2017-10-04
	JOAQUIM FERREIRA	AIDFM	11 OCT 2017 

Contents

ENROLL-HD STUDY	5
Enroll-HD Study Objectives	5
Objective 1	5
Objective 2	5
Objective 3	6
Enroll-HD Study Design	6
Design.....	6
Population.....	6
Inclusion Criteria	6
Exclusion Criteria.....	7
Enroll-HD Assessments	8
ENROLL-HD PERIODIC DATASET #3 (PDS#3).....	10
Enroll-HD Periodic Dataset Quality Control.....	10
Enroll-HD Periodic Dataset De-Identification Control	11
ENROLL-HD PERIODIC DATASET STATISTICAL ANALYSIS	11
ENROLL-HD PERIODIC DATASET #3 STATISTICAL RESULTS.....	12
Data Characterization	12
Who's in?	12
What's in?	24
Where?.....	44
Discontinuations	76
APPENDIX.....	78

ENROLL-HD STUDY

The goal of Enroll-HD is to build a large and rich database of clinical information and biorepository that will serve as a basis for future studies aimed at developing tools and biomarkers for progression and prognosis, identifying clinically relevant phenotype characteristics and establishing clearly defined endpoints for interventional studies.

Enroll-HD Study Objectives

Objective 1

To provide a platform to support the design and conduct of clinical trials by:

- providing a resource to identify, develop and qualify novel assessment tools, clinical endpoints and biomarkers,
- collecting longitudinal data to inform disease modelling studies, and facilitating the identification of potential trial participants informing the selection of potential trial participants using data to estimate and quantify slopes/rates of disease progression (providing “run-in” data).

Objective 2

To improve the understanding of the dynamic phenotypic spectrum and the disease mechanisms of HD by:

- collecting natural history data covering the cognitive, behavioral and motor domains permitting estimates of rates of progression in HD and allowing insights into the neurobiology of HD,
- collecting data and biologic samples to identify genetic and environmental factors influencing and/or modifying the HD phenotype and disease progression, and
- promoting interrogatory studies that may provide clues to the pathogenesis of HD.

Objective 3

To promote the development of evidence-based guidelines to inform clinical decision making and improve health outcomes for the participant/family unit by:

- assisting in the identification of beneficial interventions (clinical, pharmaco-therapeutic, non-pharmacologic),
- facilitating the dissemination and implementation of currently proposed best clinical practices,
- providing a platform for conducting outcome research, and
- promoting exploratory data analysis projects that may identify processes to further improve the healthcare of affected individuals and their families.

Enroll-HD Study Design

Design

Observational, prospective, multi-national, multi-centre study without experimental treatment

Population

Participants include individuals 18 years or older who are HD gene expansion mutation carriers independent of the phenotypical manifestation or the stage of HD and controls who do not carry the HD expansion mutation and who comprise the comparator study population. For individuals under the age of 18 years, those with clinically diagnosed features of HD in the setting of a confirmatory family history or a positive genetic test result may be included in this study.

Inclusion Criteria

Individuals eligible to participate in Enroll-HD are classified into two major categories:

- Carriers: This group comprises the primary study population and consists of individuals who carry the HD gene expansion mutation.
- Controls: This group comprises the comparator study population and consists of individuals who do not carry the HD expansion mutation.

These two major categories can be further subdivided into six different subgroups of eligible individuals:

- Manifest¹ HD: Carriers with clinical features that are regarded in the opinion of the investigator as diagnostic of HD.
- Pre-Manifest HD¹: Carriers without clinical features regarded as diagnostic of HD.
- Genotype Unknown: This group includes a first or second degree relative, i.e., related by blood to a carrier, who has not undergone predictive testing for HD and therefore has an undetermined carrier status.
- Genotype Negative: This group includes a first or second degree relative, i.e., related by blood to a carrier, who has undergone predictive testing for HD and is known not to carry the HD expansion mutation.
- Family Control: Family members or individuals not related by blood to carriers (e.g., spouses, partners, caregivers).
- Community Controls: Individuals unrelated to HD carriers who did not grow up in a family affected by HD. Data collected from community controls will be used for generation of normative data for sub-studies.

Exclusion Criteria

- Individuals who do not meet inclusion criteria.
- Individuals with choreic movement disorders in the context of a negative test for the HD gene mutation.
- For Community Controls: those individuals with a major central nervous system disorder will be excluded (e.g. stroke, Parkinson disease, Multiple Sclerosis, etc.).

¹ Disease categorization into pre-manifest and manifest vary between experts/studies, however the categorization used in Enroll-HD study is the standard used for HD.

Enroll-HD Assessments

Table 1 – Enroll-HD Assessments

Assessments	Core	Extended	Optional
Written informed consent/ parental permission/assent	x		
Creation of the unique HDID	x		
Review of Inclusion/Exclusion Criteria	x		
Local diagnostic laboratory CAG report (if available)	x		
Investigator and research genotyping determined classification of participant	x		
Socio-demographic information	x		
HD Clinical Characteristics (HDCC)	x		
Medical history	x		
Co-morbid conditions	x		
Current therapies Pharmacotherapy Nutritional supplements Non-pharmacologic therapies	x		
Reportable event monitoring	x		
UHDRS '99 Motor	x		
UHDRS '99 Diagnostic Confidence Index	x		
UHDRS '99 Total Functional Capacity	x		
UHDRS '99 Function Assessment Scale	x		
UHDRS '99 Independence Scale	x		
Problem Behaviors Assessment-Short (PBA-s)	x		
Hospital Anxiety/ Depression Rating Scale (HADS)		x	
Snaith Irritability Scale (SIS)		x	
Columbia Suicide Severity Rating Scale (CSSR)		x	
Symbol Digit Modality Test	x		
Stroop Word Reading	x		
Categorical Verbal Fluency	x		
Stroop Color Naming	x		
Stroop Interference		x	
Trail Making A & B		x	
Letter Verbal Fluency		x	
Mini Mental State Examination (MMSE)		x	
Global Clinical Impression		x	
Timed Up and Go (TUG)		x	
30-second Chair Stand Test		x	
Short Form Health Survey-12 (SF-12)		x	
Companion Quality of Life Questionnaire		x	
Client Services Receipt Inventory (CSRI)		x	
Work Productivity and Activity Impairment-Specific Health Problem Questionnaire (WPAI-SHP)		x	

Assessments	Core	Extended	Optional
Research Genotyping (conducted at the first visit for all new participants to the study or for participants from previous studies for whom a research genotype is not available)	x		
Family History			x
Biospecimens for biobanking			x

ENROLL-HD PERIODIC DATASET #3 (PDS#3)

Enroll-HD Periodic Dataset #3 was release in December 2016 and data was extracted on October 21, 2016 from a larger dataset based on predefined requirements (Figure 1).

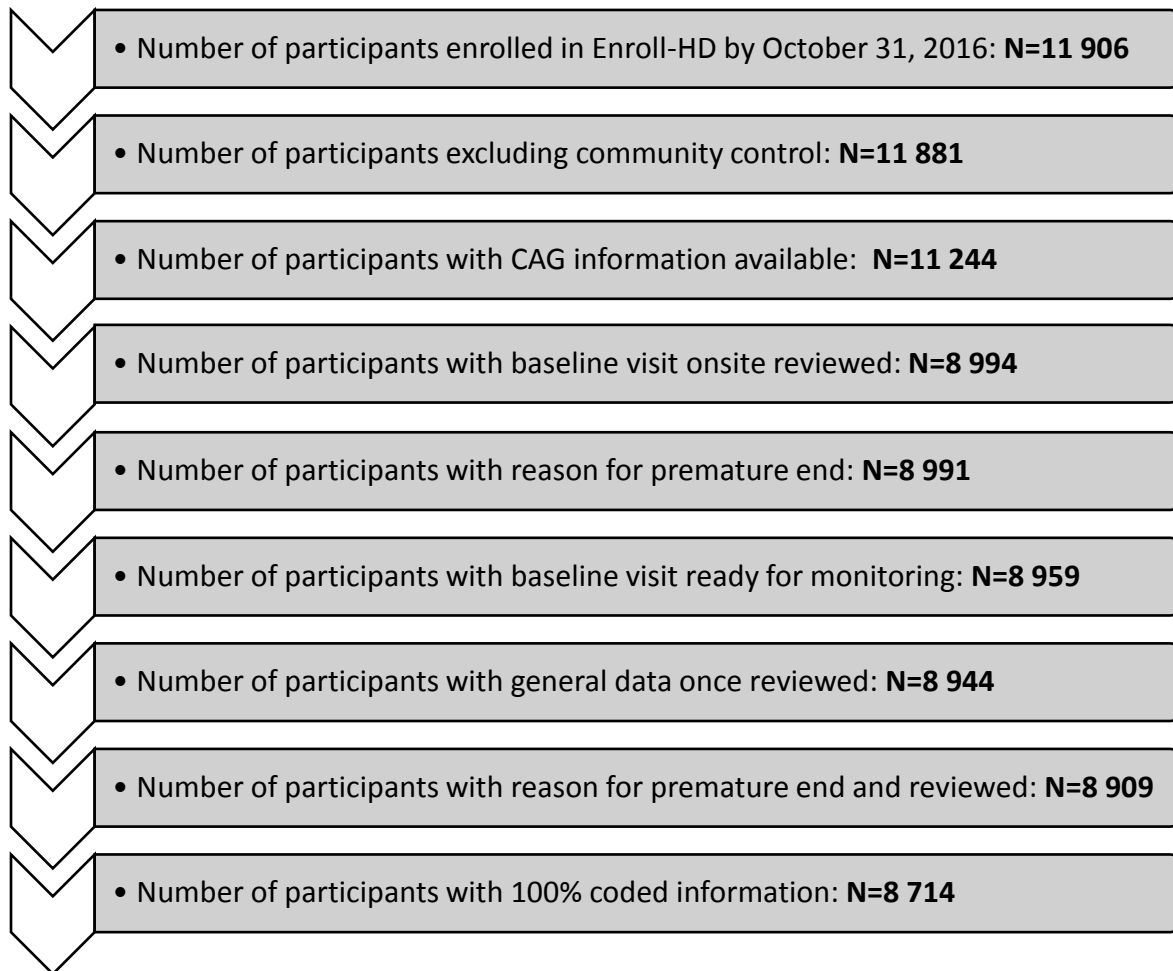


Figure 1 – Flow chart showing requirements for participant exclusion from the dataset (ref. Enroll-HD Data Handling Manual – PDS3#)

Enroll-HD Periodic Dataset Quality Control

Enroll-HD PDS#3 was submitted to a Quality Control (QC) process. This process was planned and defined as a system of checks to assess and maintain the quality of the data being

compiled. QC procedures were designed to provide routine technical checks to measure and control the quality of the data to ensure data consistency, integrity, correctness and completeness; and to identify any errors and omissions.

Enroll-HD Periodic Dataset De-Identification Control

Enroll-HD PDS#3 was submitted to a De-Identification process to guarantee confidentiality of data and identity management, dealing with de-identifying individuals in a system and controlling their privacy within that system or database. The De-Identification process took in consideration the methods supported by the HIPAA Privacy Rule, namely “Expert Determination” and “Safe Harbor”.

The De-Identification process consisted in identifying variables that could possible identify participants, determine minimal values to aggregate data in order to eliminate unique cases and, finally, to determine the actual probability of re-identification for each participant.

ENROLL-HD PERIODIC DATASET STATISTICAL ANALYSIS

Purpose of the report

The statistical analysis presented in this report intends to provide descriptive information on the Enroll-HD PDS#3 data.

Scope of the report

Data characterization was segmented into ‘Who’s in?’, ‘What’s in?’ and ‘Where?’. The first question answers about the number of participants, the second question address Enroll-HD population characterization concerning basic information and the last question discriminates the information by regions.

Statistical analysis was performed through descriptive analysis following a Statistical Analysis Plan previously approved. For continuous variables mean, standard deviation, median, range,

maximum and minimum were calculated, and for categorical variables, absolute and relative frequencies were calculated.

Analyses were limited to the generation of descriptive statistics only.

ENROLL-HD PERIODIC DATASET #3 STATISTICAL RESULTS

Data Characterization

Who's in?

Enrollment information

A total of **8714 participants** were included in the Enroll-HD periodic dataset #3, of which **465** (5.3%) are considered dropouts.

Participant categorization

All participants are categorized into one of the five categories: 1) HD manifest, 2) HD pre-manifest, 3) Genotype negative, 4) Genotype unknown, and 5) Family Control. All participants classified as 'Genotype unknown' were then re-categorized into one of three categories according to the following definitions:

- Genotype negative: research genotyping larger CAG allele < 36;
- Pre-manifest: research genotyping larger CAG allele ≥ 36 and investigator classification (in the enrollment form) not set to manifest. Alternatively to the investigator judgment, the judgment based on motor signs ('certainty') not set to 4 (Diagnostic Confidence Level from the UHDRS) ;
- Manifest: research genotyping larger CAG allele ≥ 36 and investigator classification (in the enrollment form) set to manifest. Alternative to the investigator judgment, the judgment based on motor signs ('certainty') set to 4.

Table 2 – Enroll-HD participant information

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family control (‘hdcat=5’)
Participants enrolled (n; %)	8714 (100%)	1862 (21.4%)	4752 (54.5%)	1089 (12.5%)	1011 (11.6%)

Table 3 – Enroll-HD participant information

	All	HDGEC’s (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
Participants enrolled (n; %)	8714 (100%)	6614 (75.9%)	2100 (24.1%)

Figure 2 – Participant category at baseline (NB: participants in the category ‘genotype unknown’ have been reclassified on the basis of undisclosed centralized research genotyping results)

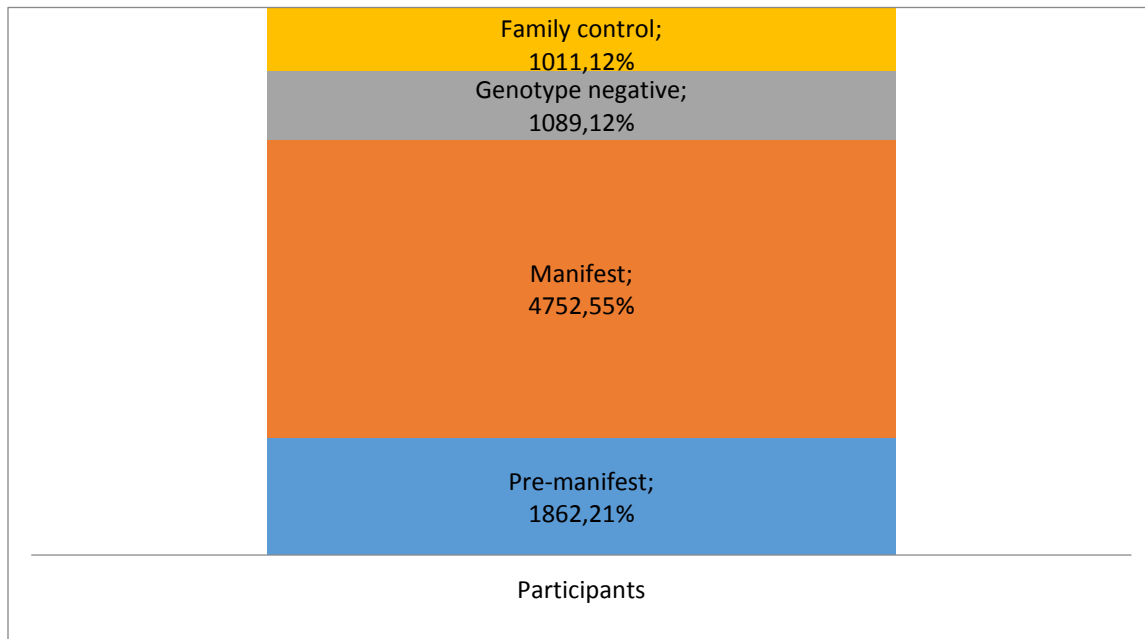
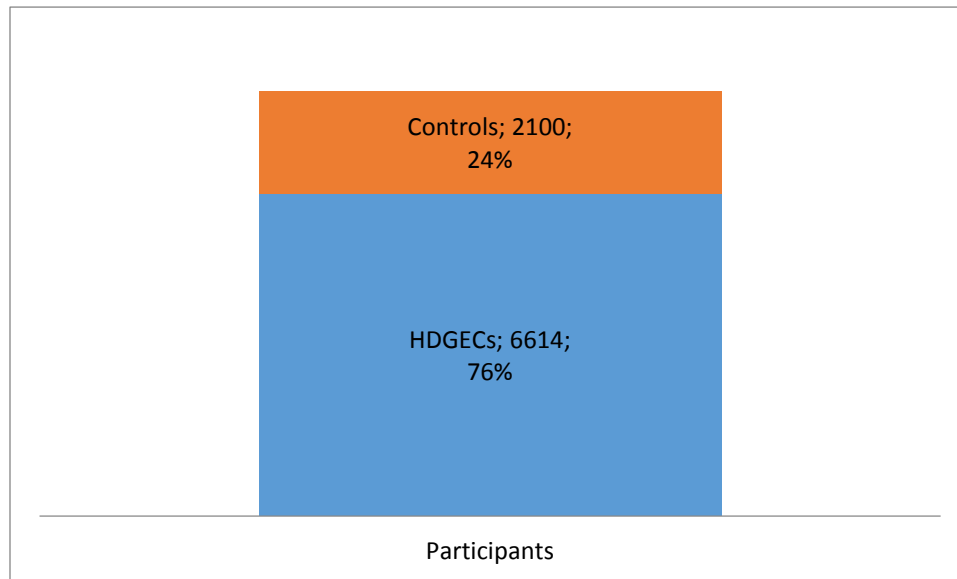


Figure 3 – Participant HD status category (NB: participants in the category ‘genotype unknown’ have been reclassified on the basis of undisclosed centralized research genotyping results)



Demographics characterization

Table 4 – Participant characterization at baseline visit

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family control (‘hdcat=5’)
Age (‘age’)	8714	1862	4752	1089	1011
(n; mean±sd)	49.1±13.9	40.4±12.0	52.9±12.6	42.9±14.4	54.1±12.5
(median; minimum; maximum)	50.0 (17.0; 91.0)	40.0 (17.0; 82.0)	53.0 (17.0; 91.0)	42.0 (17.0; 86.0)	55.0 (17.0; 84.0)
NA	-	-	-	-	-
Gender (‘sex’) (n males (‘sex=m’); % male)	3884 (44.6%)	729 (39.2%)	2342 (49.3%)	365 (33.5%)	448 (44.4%)
NA	1	-	-	-	1
ISCED Education level (‘isced’):					

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family control (‘hdcat=5’)
ISCED 0 (‘isced=0’) (n; %)	17 (0.2%)	-	13 (0.3%)	2 (0.2%)	2 (0.2%)
ISCED 1 (‘isced=1’) (n; %)	276 (3.2%)	11 (0.6%)	219 (4.6%)	20 (1.8%)	26 (2.6%)
ISCED 2 (‘isced=2’) (n; %)	1388 (16.0%)	223 (12.0%)	954 (20.2%)	106 (9.8%)	105 (10.4%)
ISCED 3 (‘isced=3’) (n; %)	2633 (30.3%)	489 (26.3%)	1565(33.1%)	294 (27.0%)	285 (28.2%)
ISCED 4 (‘isced=4’) (n; %)	1572 (18.1%)	393 (21.1%)	781 (16.5%)	205 (18.9%)	193 (19.1%)
ISCED 5 (‘isced=5’) (n; %)	2598 (29.9%)	692 (37.2%)	1102(23.3%)	434 (39.9%)	370 (36.7%)
ISCED 6 (‘isced=6’) (n; %)	198 (2.3%)	53 (2.8%)	91 (1.9%)	26 (2.4%)	28 (2.8%)
NA	32	1	27	2	2
Ethnicity (‘race’):					
Caucasian (‘race=1’) (n; %)	8089 (92.9%)	1744 (93.8%)	4473 (94.1%)	952 (87.4%)	920 (91.0%)
American Black (‘race=2’) (n; %)	89 (1.0%)	10 (0.5%)	52 (1.1%)	18 (1.7%)	9 (0.9%)
Hispanic /Latino Origin (‘race=3’) (n; %)	158 (1.8%)	23 (1.2%)	75 (1.6%)	31 (2.8%)	29 (2.9%)
Other (‘race=6’) (n; %)	131 (1.5%)	31 (1.7%)	66 (1.4%)	23 (2.1%)	11 (1.1%)
American Indian (‘race=8’) (n; %)	89 (1.0%)	15 (0.8%)	20 (0.4%)	37 (3.4%)	17 (1.7%)
Mixed (‘race=15’) (n; %)	93 (1.1%)	26 (1.4%)	34 (0.7%)	22 (2.0%)	11 (1.1%)
Asian (‘race=16’) (n; %)	62 (0.7%)	11 (0.6%)	31 (0.7%)	6 (0.6%)	14 (1.4%)
NA	3	2	1	-	-

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family control (‘hdcat=5’)
Marital status (‘maristat’):					
Single (‘maristat=1’) (n; %)	1671 (19.2%)	438 (23.5%)	921 (19.4%)	279 (25.6%)	33 (3.3%)
Partnership (‘maristat=2’) (n; %)	781 (9.0%)	308 (16.5%)	264 (5.6%)	138 (12.7%)	71 (7.0%)
Married (‘maristat=3’) (n; %)	4946 (56.8%)	955 (51.3%)	2628 (55.3%)	555 (51.0%)	808 (79.9%)
Divorced (‘maristat=4’) (n; %)	874 (10.0 %)	119 (6.4%)	647 (13.6%)	77 (7.1%)	31 (3.1%)
Widowed (‘maristat=5’) (n; %)	304 (3.5%)	18 (1.0%)	192 (4.0%)	28 (2.6%)	66 (6.5%)
Legally separated (‘maristat=6’) (n; %)	133 (1.5%)	24 (1.3%)	96 (2.0%)	11 (1.0%)	2 (0.2%)
NA	5	-	4	1	-
Employment (‘jobclas’):					
Full-time employed (‘jobclas=1’) (n; %)	2720 (31.3%)	1019 (54.8%)	557 (11.7%)	626 (57.7%)	518 (51.3%)
Part-time employed (‘jobclas=2’) (n; %)	792 (9.1%)	275 (14.8%)	274 (5.8%)	131 (12.1%)	112 (11.1%)
Self employed (‘jobclas=3’) (n; %)	231 (2.7%)	64 (3.4%)	76 (1.6%)	50 (4.6%)	41 (4.1%)
Not employed (‘jobclas=4’) (n; %)	4957 (57.0%)	503 (27.0 %)	3837(80.9%)	278 (25.6%)	339 (33.6%)
NA	14	1	8	4	1
Residence (‘res’) :					

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family control (‘hdcat=5’)
Rural (‘res=1’) (n; %)	472 (5.4%)	104 (5.6%)	223 (4.7%)	67 (6.2%)	78 (7.7%)
Village (‘res=2’) (n; %)	1389 (16.0 %)	292 (15.7%)	800 (16.8%)	148 (13.6%)	149 (14.8%)
Town (‘res=3’) (n; %)	3166 (36.4 %)	648 (34.8%)	1856 (39.1%)	324 (29.8%)	338 (33.5%)
City (‘res=4’) (n; %)	3681 (42.3 %)	817 (43.9%)	1870 (39.4%)	549 (50.5%)	445 (44.1%)
NA	6	1	3	1	1

*NA are omitted from the total 100%

Table 5 – Participant characterization at baseline visit

	All	HDGEC’s (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
Age (‘age’)	8714	6614	2100
(n; mean±sd)	49.1±13.9	49.4±13.7	48.3±14.6
(median; minimum; maximum)	50.0 (17.0; 91.0)	50.0 (17.0; 91.0)	50.0 (17.0; 86.0)
NA	-	-	-
Gender (‘sex’)			
(n males (‘sex=m’); % male)	3884 (44.6%)	3071 (46.4%)	813 (38.7%)
NA	1	-	1
ISCED Education level (‘iscd’):			
ISCED 0 (‘iscd=0’) (n; %)	17 (0.2%)	13 (0.2%)	4 (0.2%)

	All	HDGEC's (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
ISCED 1 (‘isced=1’) (n; %)	276 (3.2%)	230 (3.5%)	46 (2.2%)
ISCED 2 (‘isced=2’) (n; %)	1388 (16.0%)	1177 (17.9%)	211 (10.1%)
ISCED 3 (‘isced=3’) (n; %)	2633 (30.3%)	2054 (31.2%)	579 (27.6%)
ISCED 4 (‘isced=4’) (n; %)	1572 (18.1%)	1174 (17.8%)	398 (19.0%)
ISCED 5 (‘isced=5’) (n; %)	2598 (29.9%)	1794 (27.2%)	804 (38.4%)
ISCED 6 (‘isced=6’) (n; %)	198 (2.3%)	144 (2.2%)	54 (2.6%)
NA	32	28	4
Ethnicity (‘race’):			
Caucasian (‘race=1’) (n; %)	8089 (92.9%)	6217 (94.0%)	1872 (89.1%)
American Black (‘race=2’) (n; %)	89 (1.0%)	62 (0.9%)	27 (1.3%)
Hispanic /Latino Origin (‘race=3’) (n; %)	158 (1.8%)	98 (1.5%)	60 (2.9%)
Other (‘race=6’) (n; %)	131 (1.5%)	97 (1.5%)	34 (1.6%)
American Indian (‘race=8’) (n; %)	89 (1.0%)	35 (0.5%)	54 (2.6%)
Mixed (‘race=15’) (n; %)	93 (1.1%)	60 (0.9%)	33 (1.6%)
Asian (‘race=16’) (n; %)	62 (0.7%)	42 (0.6%)	20 (1.0%)
NA	3	3	-
Marital status (‘maristat’):			
Single (‘maristat=1’) (n; %)	1671 (19.2%)	1359 (20.6%)	312 (14.9%)
Partnership (‘maristat=2’) (n; %)	781 (9.0%)	572 (8.7%)	209 (10.0%)

	All	HDGEC's (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
Married (‘maristat=3’) (n; %)	4946 (56.8%)	3583 (54.2%)	1363 (64.9%)
Divorced (‘maristat=4’) (n; %)	874 (10.0 %)	766 (11.6%)	108 (5.1%)
Widowed (‘maristat=5’) (n; %)	304 (3.5%)	210 (3.2%)	94 (4.5%)
Legally separated (‘maristat=6’) (n; %)	133 (1.5%)	120 (1.8%)	13 (0.6%)
NA	5	4	1
Employment (‘jobclas’):			
Full-time employed (‘jobclas=1’) (n; %)	2720 (31.3%)	1576 (23.9%)	1144 (54.6%)
Part-time employed (‘jobclas=2’) (n; %)	792 (9.1%)	549 (8.3%)	243 (11.6%)
Self employed (‘jobclas=3’) (n; %)	231 (2.7%)	140 (2.1%)	91 (4.3%)
Not employed (‘jobclas=4’) (n; %)	4957 (57.0%)	4340 (65.7%)	617 (29.5%)
NA	14	9	5
Residence (‘res’) :			
Rural (‘res=1’) (n; %)	472 (5.4%)	327 (4.9%)	145 (6.9%)
Village (‘res=2’) (n; %)	1389 (16.0 %)	1092 (16.5%)	297 (14.2%)
Town (‘res=3’) (n; %)	3166 (36.4 %)	2504 (37.9%)	662 (31.6%)
City (‘res=4’) (n; %)	3681 (42.3 %)	2687 (40.7%)	994 (47.4%)

	All	HDGEC's (<i>'hdcat=2 & 3'</i>)	Controls (<i>'hdcat=4 & 5'</i>)
NA	6	4	2

*NA are omitted from the total 100%

Figure 4 – Participants characterization at baseline visit (Age [*'age'*]). The boxplot present quartiles ($Q_{0.25}$, median, $Q_{0.75}$), minimum and maximum of the variable in study. Outliers are plotted as individual points.

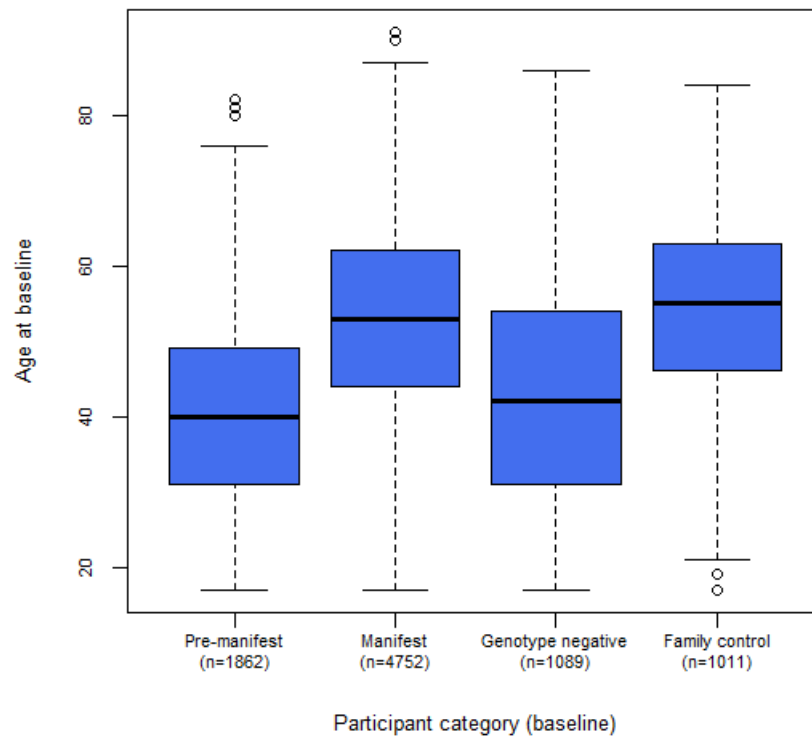


Figure 5 – Participants characterization at baseline visit per HDGEC’s [`'hdcat=2&3'`] (Age [`'age'`]). The boxplot present quartiles ($Q_{0.25}$, median, $Q_{0.75}$), minimum and maximum value of the variable in study. Outliers are plotted as individual points.

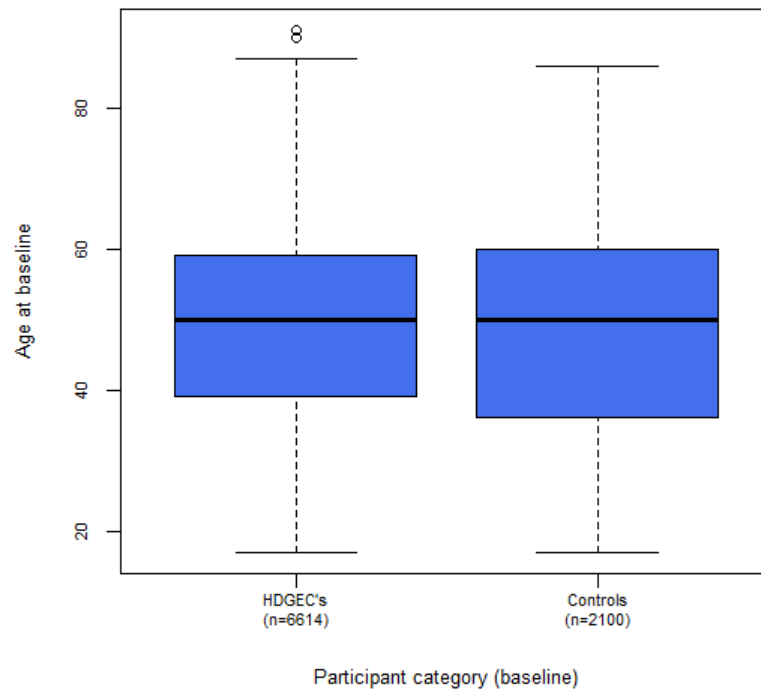


Table 6 – Body Mass Index (BMI [`'bmi'`]) characterization

	All	Pre-manifest (<code>'hdcat=2'</code>)	Manifest (<code>'hdcat=3'</code>)	Genotype negative (<code>'hdcat=4'</code>)	Family control (<code>'hdcat=5'</code>)
BMI (<code>'bmi'</code>)	8477	1831	4588	1064	994
(n; mean±sd)	26.1±5.7	26.4±5.5	25.1±5.1	27.5±6.4	28.8±6.2
(median; minimum; maximum)	25.1 (10.8; 67.8)	25.4 (10.9; 59.4)	24.4 (10.9; 63.2)	26.2 (10.8; 67.8)	27.8 (13.0; 58.1)
NA	237	31	164	25	17

Table 7 – Body Mass Index (BMI ['bmi']) characterization

	All	HDGECs (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
BMI ('bmi')	8477	6419	2058
(n; mean±sd)	26.1±5.7	25.5±5.3	28.1±6.3
(median; minimum; maximum)	25.1 (10.8; 67.8)	24.7 (10.9; 63.2)	27.0 (10.8; 67.8)
NA	237	195	42

*NA are omitted from the total 100%

HD Stages

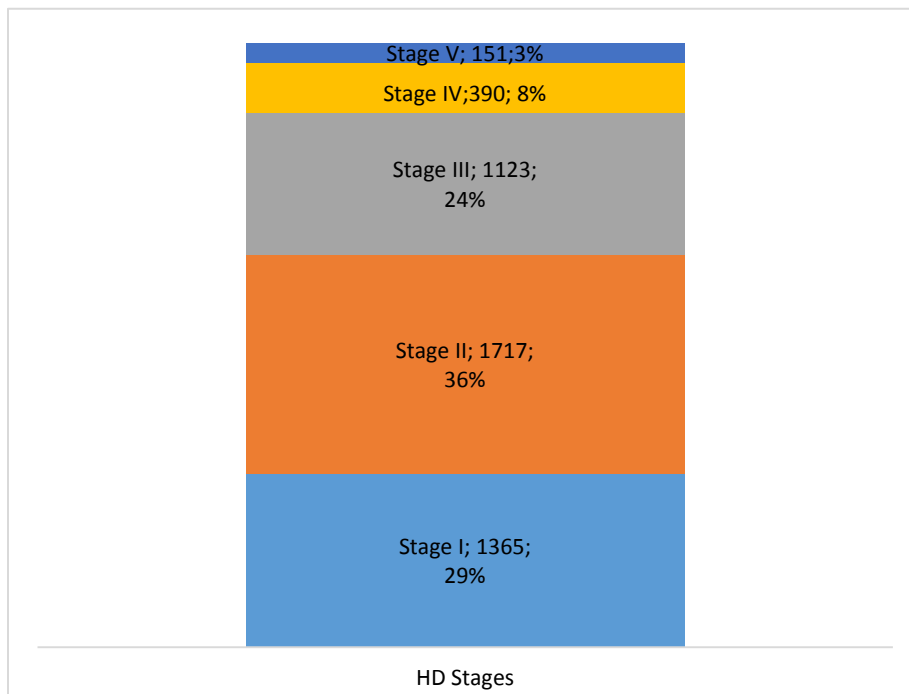
HD stages were defined based on TFC score ('tfcscore') at baseline, based on the categories defined by Shoulson (1981)²:

- Stage V (TFC Score: 0), Stage IV (TFC Score: 1-2), Stage III (TFC Score: 3-6), Stage II (TFC Score: 7-10), Stage I (TFC Score: 11-13)

These stages were applied to all HD manifest participants, with exception for those who have missing value for TFC score at baseline (n=4746, NA=6).

1. Shoulson, I. (1981). Huntington disease: Functional Capacities in patients treated with neuroleptic and antidepressant drugs. *Neurology* 1981;31;1333-1335.

Figure 6 – HD stages at the baseline visit



What's in?

Research genotype information

Different formulas can be used to estimate disease burden, in this report the formula used was following :

$$- \text{Disease Burden} = (\text{CAG} - 35.5) * \text{age}^3$$

Table 8 – CAG characterization according the centralized research genotyping

	All	Pre-manifest (‘hdcats=2’)	Manifest (‘hdcats=3’)	Genotype negative (‘hdcats=4’)	Family control (‘hdcats=5’)
Participants with CAG information (n; %)	8714 (100%)	1862 (21.4%)	4752 (54.5%)	1089 (12.5%)	1011 (11.6%)
Allele 1 CAG repeat length (smaller allele) (‘caglow’)	8714	1862	4752	1089	1011
(n; mean±sd)	18.1±3.1	18.5±3.1	18.5±3.3	16.9±2.1	16.9±2.0
(median; minimum; maximum)	17.0 (8.0; 29.0)	18.0 (9.0; 29.0)	17.0 (8.0; 29.0)	17.0 (9.0; 29.0)	17.0 (9.0; 25.0)
NA	-	-	-	-	-
Allele 2 CAG repeat length (larger allele) (‘caghigh’)	8714	1862	4752	1089	1011
(n; mean±sd)	38.0±10.7	42.4±2.8	44.1±4.0	20.3±3.7	20.1±3.7
(median; minimum; maximum)	42.0 (12.0; 71.0)	42.0 (36.0; 61.0)	43.0 (36.0; 71.0)	19.0 (12.0; 35.0)	19.0 (12.0; 35.0)
NA	-	-	-	-	-

³ Penney JB Jr, Vonsattel JP, MacDonald ME, Gusella JF, Myers RH. (1997) CAG repeat number governs the development rate of pathology in Huntington's disease. Ann Neurol. 41(5):689-92

Disease burden

('dburden')	6614	1862	4752		
(n; mean±sd)	372.6±119.7	261.4±83.6	416.1±102.3	-	-
(median; minimum; maximum)	376.0 (14.0; 1192.5)	258.5 (14.0; 630.0)	412.5 (24.5; 1192.5)		
NA	-	-	-		

Table 9 – CAG characterization according the centralized research genotyping per HDGEC's

	All	HDGECs (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
Allele 1 CAG repeat length			
Smaller allele ('caglow')	8714	6614	2100
(n; mean±sd)	18.1±3.07	18.5±3.2	16.9±2.1
(median; minimum; maximum)	17.0 (8.0; 29.0)	17.0 (8.0; 29.0)	17.0 (9.0; 29.0)
NA	-	-	-
Allele 2 CAG repeat length			
Larger allele ('caghigh')	8714	6614	2100
(n; mean±sd)	38.0±10.7	43.6±3.8	20.2±3.5
(median; minimum; maximum)	42.0 (12.0; 71.0)	43.0 (36.0; 71.0)	19.0 (12.0; 35.0)
NA	-	-	-
Disease burden ('dburden')			
(n; mean±sd)	6614	6614	-
(median; minimum; maximum)	372.6±119.7	372.6±119.7	

NA	376.0 (14.0; 1192.5)	376.0 (14.0; 1192.5)
	-	-

Figure 7 – CAG larger allele ('caghigh') distribution per participant category ('hdcat'). The boxplot present quartiles (Q_{0.25}, median, Q_{0.75}), minimum and maximum of the variable in study. Outliers are plotted as individual points.

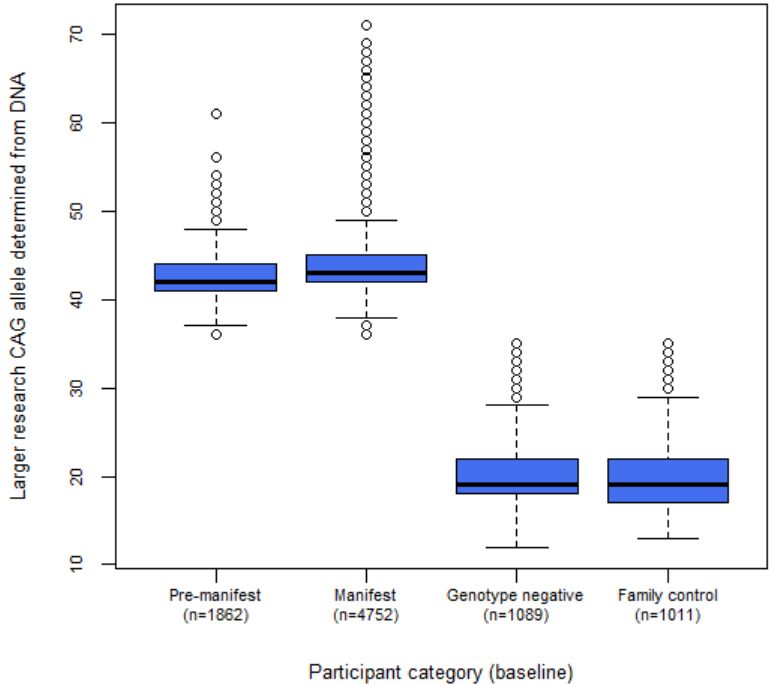


Figure 8 – CAG larger allele ('caghigh') distribution per HDGEC's. The boxplot present quartiles ($Q_{0.25}$, median, $Q_{0.75}$), minimum and maximum of the variable in study. Outliers are plotted as individual points.

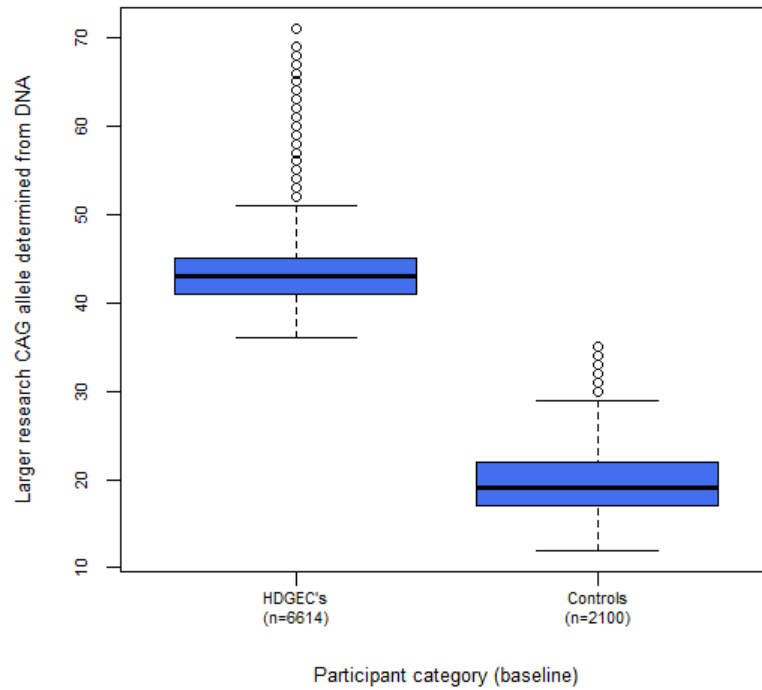


Figure 9 – CAG small allele ('caglow') distribution per participant category ('hdcat'). The boxplot present quartiles ($Q_{0.25}$, median, $Q_{0.75}$), minimum and maximum of the variable in study. Outliers are plotted as individual points.

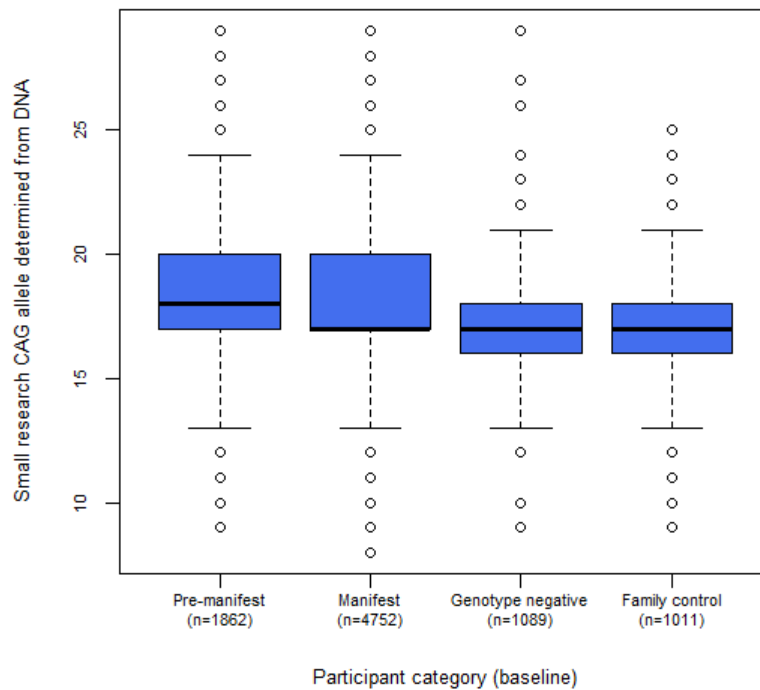


Figure 10 – CAG small allele ('caglow') distribution per HDGEC's. The boxplot present quartiles ($Q_{0.25}$, median, $Q_{0.75}$), minimum and maximum of the variable in study. Outliers are plotted as individual points.

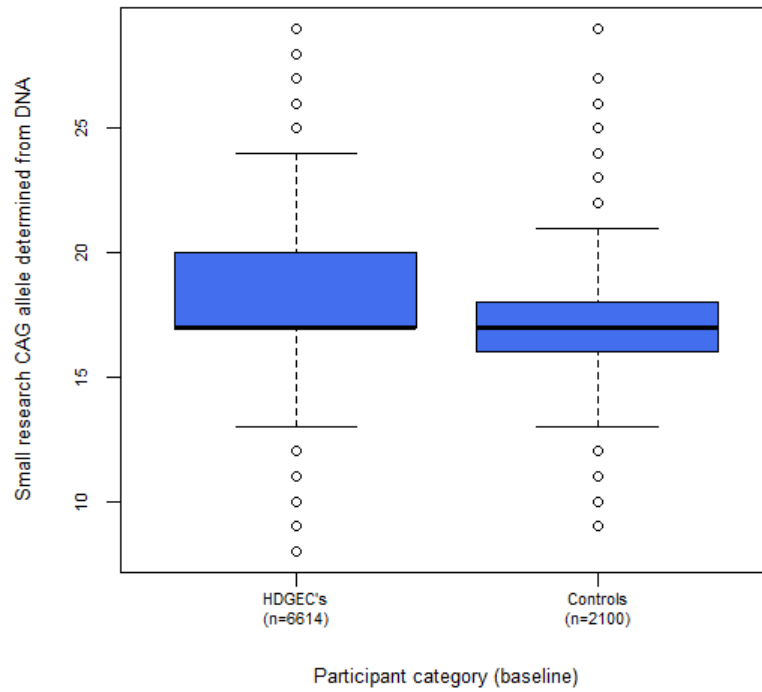


Figure 11 – CAG larger allele ('caghigh') distribution per participant category ('hdcat')

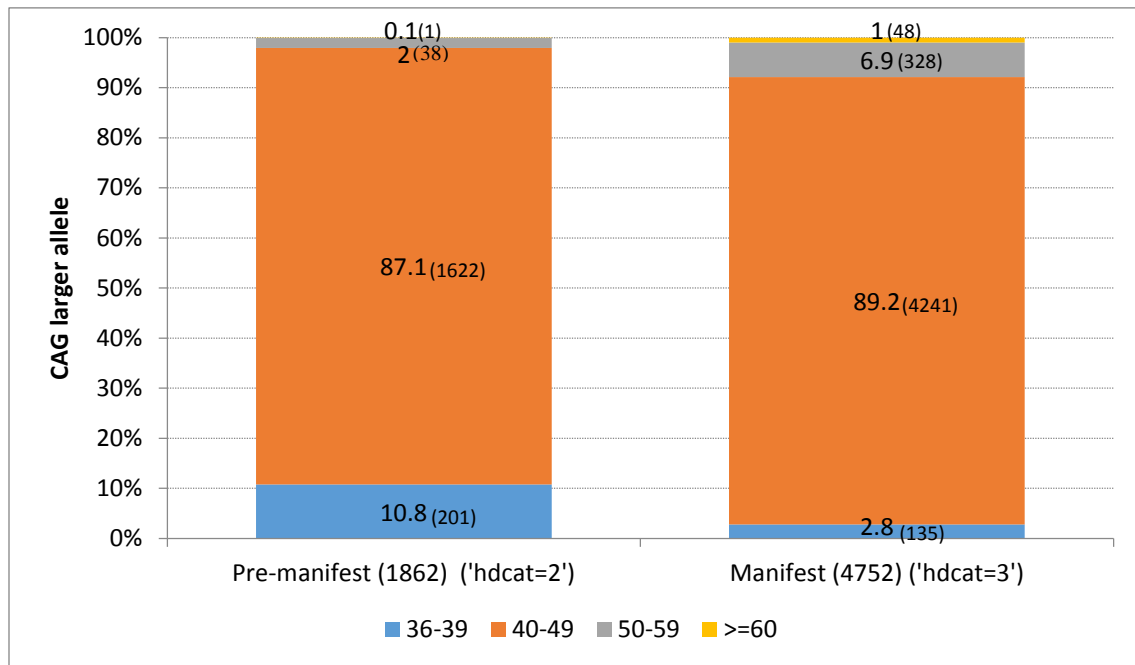
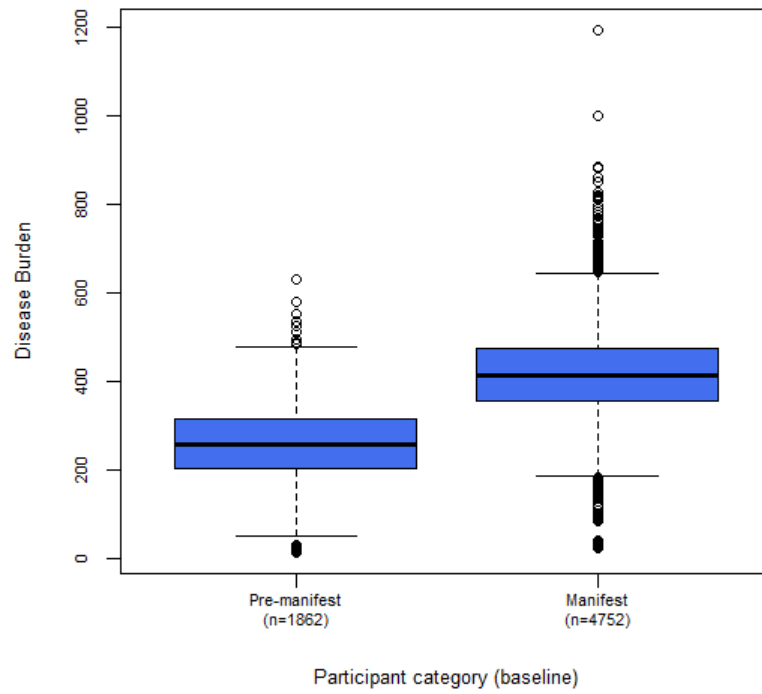


Figure 12 – Disease Burden ('dburden') per participant category ('hdcat'). The boxplot present quartiles ($Q_{0.25}$, median, $Q_{0.75}$), minimum and maximum of the variable in study. Outliers are plotted as individual points.



Participant information

Figure 13 – Consumption habits per participant category ('hdcat')

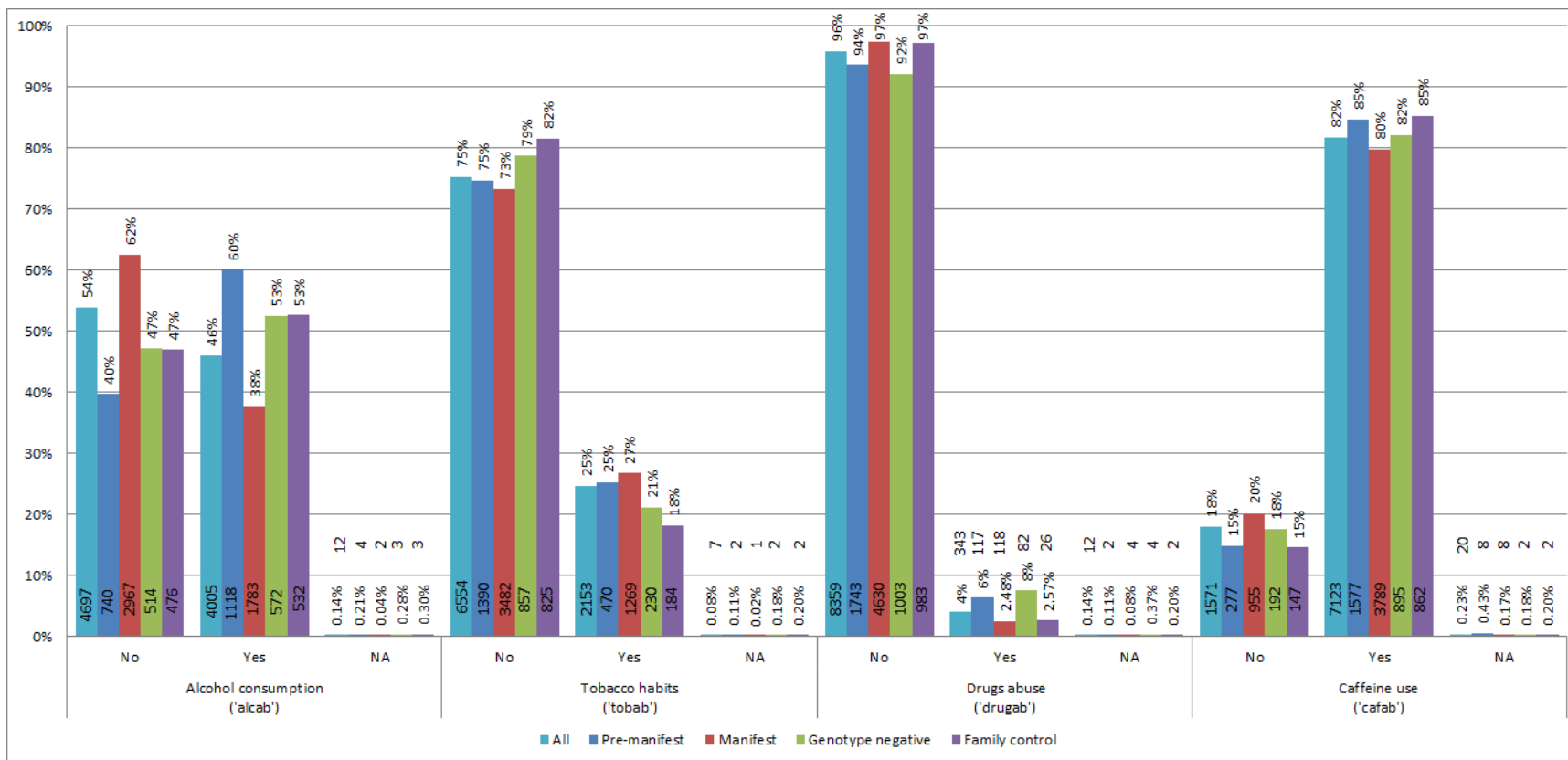


Figure 14 – Consumption habits per HDGEC’s category

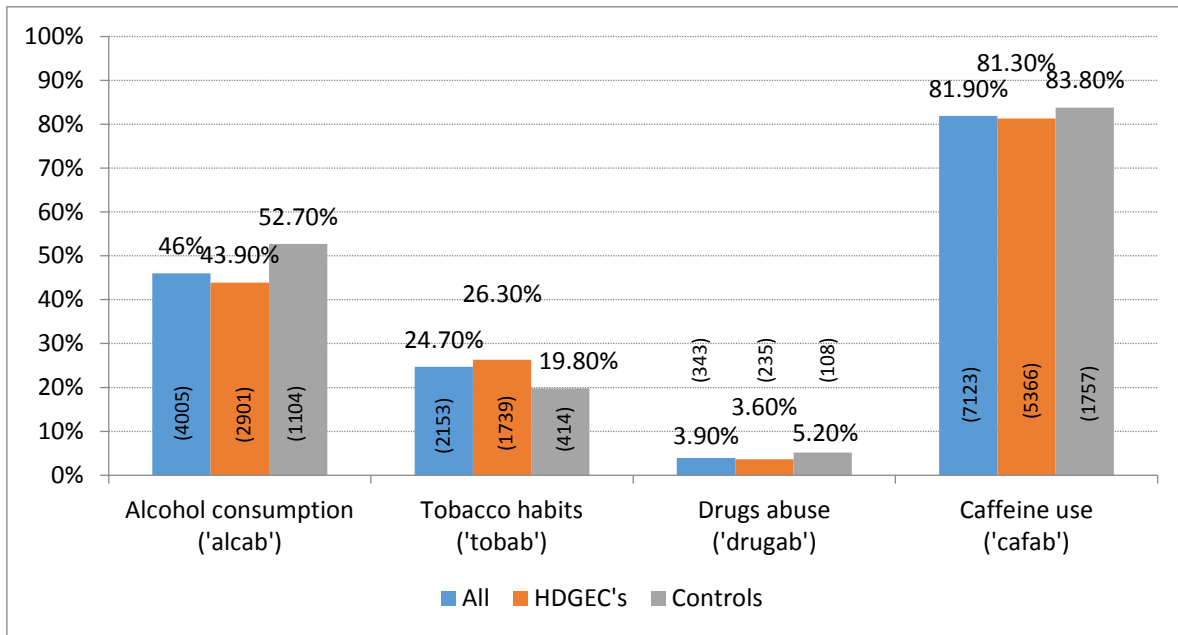


Figure 15 – Pharmacotherapy ('Pharmacotx'), Non-pharmacotherapy ('Nonpharmacotx') and Nutritional Supplements ('Nutsuppl') usage per participant category ('hdcat')

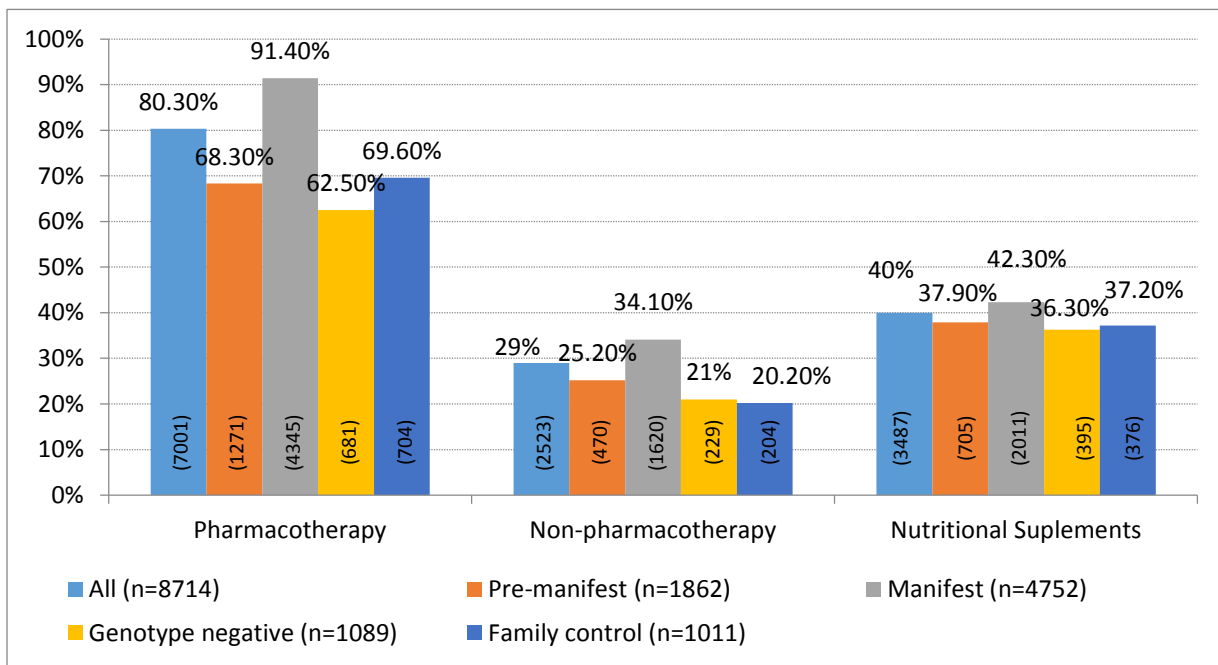


Figure 16 – Pharmacotherapy ('Pharmacotx'), Non-pharmacotherapy ('Nonpharmacotx') and Nutritional Supplements ('Nutsuppl') usage per HDGEC's

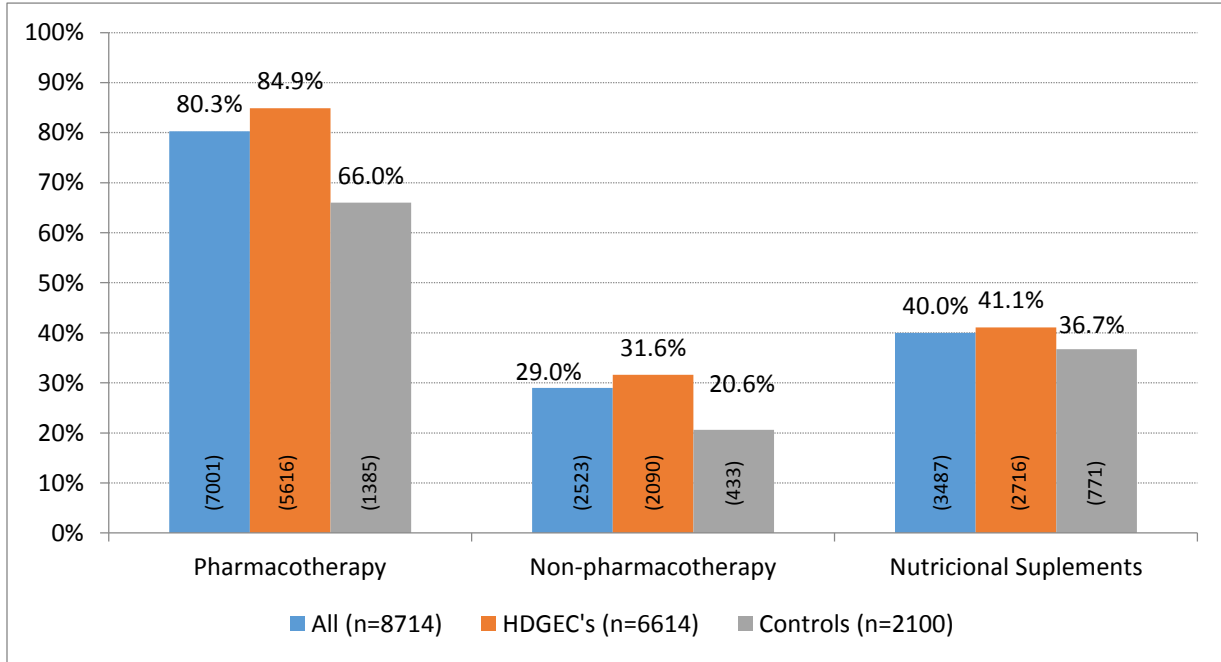


Figure 17 – Presence of Comorbidities ('Comorbid') per participant category ('hdcat')

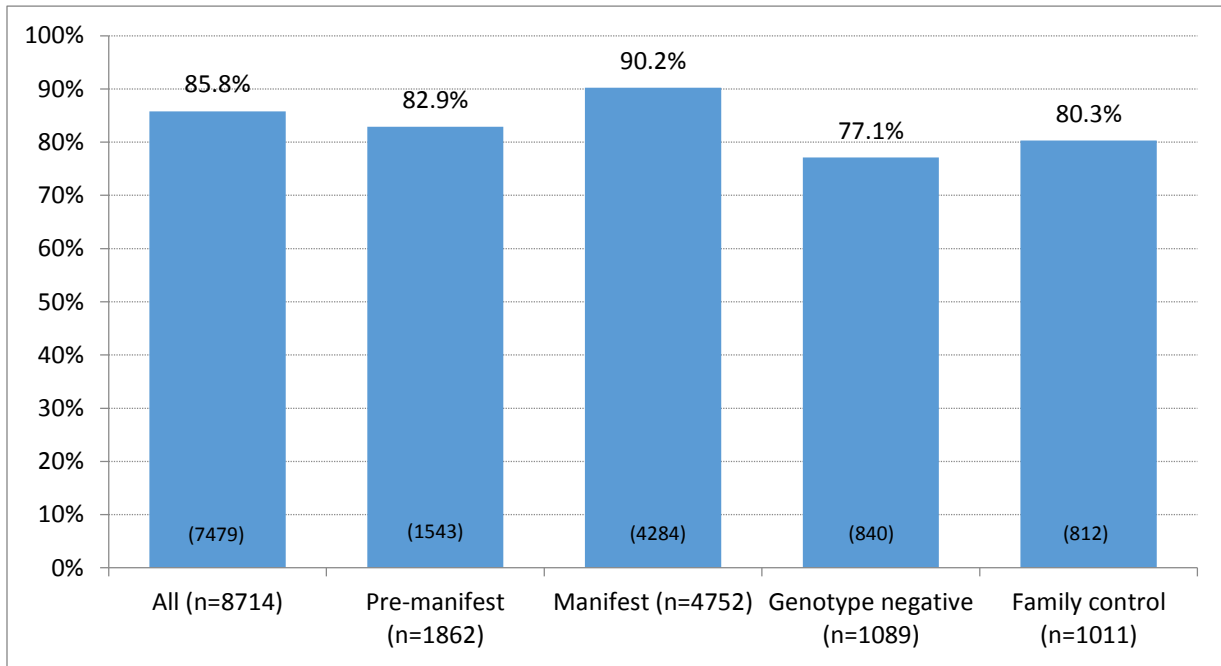
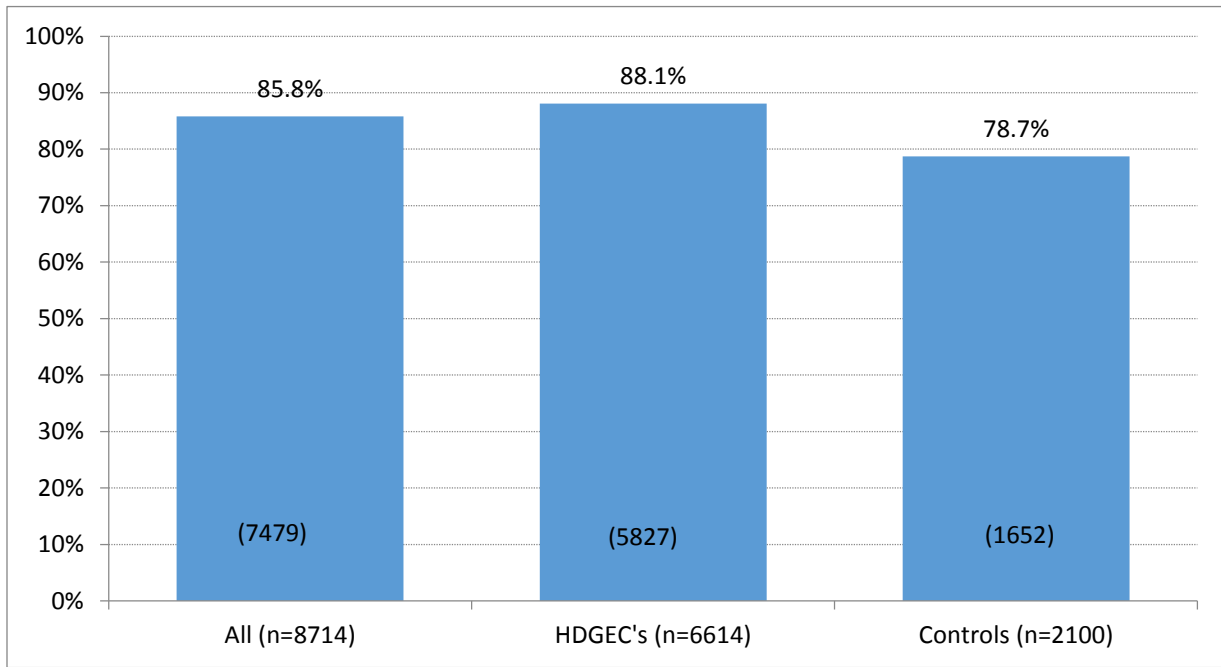


Figure 18 – Presence of Comorbidities ('Comorbid') per HDGEC's



Clinical evaluation (baseline information)

Table 10 – Clinical evaluation at baseline per participant category ('hdcat')

	All	Pre-manifest ('hdcat=2')	Manifest ('hdcat=3')	Genotype negative ('hdcat=4')	Family ('hdcat=5')	Control
UHDRS '99 Motor ('motscore')	8670	1856	4723	1083	1008	
(n; mean±sd)	22.8±24.9	3.5±5.3	39.7±22.2	2.0±4.0	1.6±2.9	
(median; minimum; maximum)	14.0 (0.0; 120.0)	2.0 (0.0; 70.0)	36.0 (0.0; 120.0)	0.0 (0.0; 69.0)	0.0 (0.0; 21.0)	
NA	44	6	29	6	3	
UHDRS '99 DCL ('diagconf')						

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family (‘hdcat=5’)	Control
0 (n; %)	2670 (30.7%)	973 (52.3%)	16 (0.3%)	823 (75.6%)	858 (85.0%)	
1 (n; %)	925 (10.6%)	521 (28.0%)	33 (0.7%)	225 (20.7%)	146 (14.5%)	
2 (n; %)	309 (3.5%)	226 (12.1%)	55 (1.2%)	25 (2.3%)	3 (0.3%)	
3 (n; %)	234 (2.7%)	119 (6.4%)	104 (2.2%)	11 (1.0%)	0 (0.0%)	
4 (n; %)	4571 (52.5%)	23 (1.2%)	4541 (95.6%)	5 (0.5%)	2 (0.2%)	
NA	5	-	3	-	2	
UHDRS ‘99 Total Functional Capacity (‘ tfcscore ’)	8702	1858	4746	1088	1010	
(n; mean±sd)	10.1±3.7	12.7±1.1	7.8±3.7	12.9±0.7	12.9±0.6	
(median; minimum; maximum)	12.0 (0.0; 13.0)	13.0 (0.0; 13.0)	8.0 (0.0; 13.0)	13.0 (1.0; 13.0)	13.0 (4.0; 13.0)	
NA	12	4	6	1	1	
UHDRS ‘99 Function Assessment Scale (‘ fascore ’)	8535	1832	4613	1081	1009	
(n; mean±sd)	20.7±6.4	24.6±1.4	17.3±7.0	24.9±1.0	24.9±0.7	
(median; minimum; maximum)	24.0 (0.0; 25.0)	25.0 (0.0; 25.0)	19.0 (0.0; 25.0)	25.0 (5.0; 25.0)	25.0 (13.0; 25.0)	
NA	179	30	139	8	2	
UHDRS ‘99 Independence Scale (‘ indep scl ’)	8703	1861	4744	1088	1010	
(n; mean±sd)	86.0±18.7	98.7±4.6	75.0±19.2	99.5±3.1	99.7±2.1	
(median; minimum; maximum)	95.0 (5.0; 100.0)	100.0 (25.0; 100.0)	80.0 (5.0; 100.0)	100.0 (45.0; 100.0)	100.0 (65.0; 100.0)	
NA		1		1	1	

	All	Pre-manifest (<i>'hdc</i> cat=2)	Manifest (<i>'hdc</i> cat=3')	Genotype negative (<i>'hdc</i> cat=4')	Family (<i>'hdc</i> cat=5')	Control
	11		8			
Cognitive Assessment: symbol digit modality test (total correct) (<i>'sdmt1'</i>)	8310	1851	4374	1079	1006	
(n; mean±sd)	35.5±18.8	49.4±12.7	22.6±13.5	52.2±11.8	47.9±11.6	
(median; minimum; maximum)	36.0 (0.0; 101.0)	50.0 (0.0; 101.0)	21.0 (0.0; 92.0)	53.0 (0.0; 92.0)	49.0 (0.0; 94.0)	
NA	404	11	378	10	5	
Cognitive Assessment: verbal fluency test (category) completed (total correct) (<i>'verfct5'</i>)	8534	1847	4605	1081	1001	
(n; mean±sd)	16.2±7.5	21.1± 5.9	11.8±6.0	21.7±5.7	21.5±5.5	
(median; minimum; maximum)	16.0 (0.0; 55.0)	21.0 (1.0; 55.0)	11.0 (0.0; 42.0)	22.0 (3.0; 48.0)	21.0 (7.0; 44.0)	
NA	180	15	147	8	10	
Cognitive Assessment: stroop colour naming test (total correct) (<i>'scnt1'</i>)	8461	1846	4545	1073	997	
(n; mean±sd)	56.1±24.0	72.5±15.5	40.9±19.4	76.4±14.9	73.1±14.3	
(median; minimum; maximum)	58.0 (0.0; 400.0)	73.0 (0.0; 136.0)	41.0 (0.0; 400.0)	76.0 (0.0; 140.0)	73.0 (0.0; 129.0)	
NA	253	16	207	16	14	
Cognitive Assessment: stroop word reading test (total correct) (<i>'swrt1'</i>)	8448	1848	4527	1074	999	
(n; mean±sd)	72.4±29.6	92.2±19.7	53.9±24.3	96.6±18.3	93.5±17.4	

	All	Pre-manifest (<i>'hdc</i> cat=2)	Manifest (<i>'hdc</i> cat=3')	Genotype negative (<i>'hdc</i> cat=4')	Family (<i>'hdc</i> cat=5')	Control
(median; minimum; maximum)	75.0 (0.0; 199.0)	94.0 (0.0; 177.0)	54.0 (0.0; 199.0)	98.0 (0.0; 168.0)	94.0 (0.0; 160.0)	
NA	266	14	225	15	12	
Cognitive Assessment: stroop interference test (total correct) (<i>'sit1'</i>)	7511	1733	3836	1013	929	
(n; mean±sd)	32.9±15.6	43.2±11.4	23.4±12.0	44.4±15.1	40.5±10.8	
(median; minimum; maximum)	33.0 (0.0; 374.0)	43.0 (0.0; 93.0)	23.0 (0.0; 100.0)	44.0 (0.0; 374.0)	40.0 (0.0; 119.0)	
NA	1203	129	916	76	82	
Cognitive Assessment: trailmaking test (Part A: total correct) (<i>'trla2'</i>)	6454	1557	3112	937	848	
(n; mean±sd)	24.4±4.7	24.8±6.4	24.0±4.6	24.8±2.0	24.7±2.6	
(median; minimum; maximum)	25.0 (0.0; 250.0)	25.0 (0.0; 250.0)	25.0 (0.0; 25.0)	25.0 (0.0; 2767.0)	25.0 (0.0; 25.0)	
NA	2260	305	1640	152	163	
(Part B: total correct) (<i>'trlb2'</i>)	6333	1553	3000	935	845	
(n; mean±sd)	22.7±7.9	24.5±4.3	20.8±10.5	24.4±3.6	24.5±3.2	
(median; minimum; maximum)	25.0 (0.0; 240.0)	25.0 (0.0; 117.0)	25.0 (0.0; 240.0)	25.0 (0.0; 29.0)	25.0 (0.0; 26.0)	
NA	2381	309	1752	154	166	
Cognitive Assessment: verbal fluency test (letters) completed (total correct) (<i>'verfit05'</i>)	6676					
	30.8±16.3	1560	3343	933	840	
	31.0 (0.0; 94.0)					

	All	Pre-manifest (<i>'hdcats=2'</i>)	Manifest (<i>'hdcats=3'</i>)	Genotype negative (<i>'hdcats=4'</i>)	Family (<i>'hdcats=5'</i>)	Control
(n; mean±sd)	2038	40.0±13.1	21.2±13.2	41.6±13.3	40.4±12.3	
(median; minimum; maximum)		40.0 (7.0; 84.0)	19.0 (0.0; 77.0)	41.0 (0.0; 91.0)	40.0 (8.0; 94.0)	
NA		302	1409	156	171	
PBA-s - depression score (<i>'depscore'</i>)	8621	1856	4668	1088	1009	
(n; mean±sd)	4.6±6.2	4.5±6.1	5.2±6.5	3.1±5.2	3.3±4.9	
(median; minimum; maximum)	2.0 (0.0; 48.0)	2.0 (0.0; 41.0)	3.0 (0.0; 48.0)	1.0 (0.0; 32.0)	1.0 (0.0; 44.0)	
NA	93	6	84	1	2	
PBA-s - irritability score (<i>'irascorscore'</i>)	8680	1854	4732	1086	1008	
(n; mean±sd)	2.6±4.5	2.1±3.7	3.5±5.1	1.2±2.8	1.4±2.7	
(median; minimum; maximum)	0.0 (0.0; 32.0)	0.0 (0.0; 32.0)	1.0 (0.0; 32.0)	0.0 (0.0; 21.0)	0.0 (0.0; 28.0)	
NA	34	8	20	3	3	
PBA-s - psychosis score (<i>'pyscore'</i>)	8613	1855	4664	1085	1009	
(n; mean±sd)	0.2±1.5	0.1±1.1	0.4±1.9	0.1±1.1	0.0±0.3	
(median; minimum; maximum)	0.0 (0.0; 32.0)	0.0 (0.0; 18.0)	0.0 (0.0; 32.0)	0.0 (0.0; 18.0)	0.0 (0.0; 9.0)	
NA	101	7	88	4	2	
PBA-s - apathy score (<i>'aptscore'</i>)	8626	1853	4676	1088	1009	
(n; mean±sd)	2.4±4.0	1.2±2.7	3.7±4.7	0.5±1.7	0.4±1.5	
(median; minimum; maximum)	0.0 (0.0; 16.0)	0.0 (0.0; 16.0)	1.0 (0.0; 16.0)	0.0 (0.0; 12.0)	0.0 (0.0; 16.0)	
NA	88	9	76	1	2	
PBA-s - executive function score (<i>'exfscore'</i>)	8602	1850	4657	1086	1009	
(n; mean±sd)	2.5±4.9	1.3±3.1	3.8±5.8	0.8±2.5	0.6±2.2	

	All	Pre-manifest (‘hdcats=2’)	Manifest (‘hdcats=3’)	Genotype negative (‘hdcats=4’)	Family (‘hdcats=5’)	Control
(n; mean±sd)	0.0 (0.0; 32.0)	0.0 (0.0; 28.0)	1.0 (0.0; 32.0)	0.0 (0.0; 25.0)	0.0 (0.0; 24.0)	
(median; minimum; maximum)	112	12	95	3	2	
NA						
MMSE score (‘mmsetotal’)	5650	1265	2844	833	708	
(n; mean±sd)	26.8±3.9	28.6±1.7	24.9±4.6	29.0±1.5	28.8±1.5	
(median; minimum; maximum)	28.0 (0.0; 30.0)	29.0 (16.0; 30.0)	26.0 (0.0; 30.0)	30.0 (19.0; 30.0)	29.0 (18.0; 30.0)	
NA	3064	597	1908	256	303	
HADS-SIS – anxiety subscore (‘anxscore’)	5378	1244	2565	814	755	
(n; mean±sd)	5.6±4.1	5.6±4.1	6.0±4.3	5.0±3.8	5.2±3.5	
(median; minimum; maximum)	5.0 (0.0; 21.0)	5.0 (0.0; 21.0)	5.0 (0.0; 21.0)	4.0 (0.0; 21.0)	5.0 (0.0; 18.0)	
NA	3336	618	2187	275	256	
HADS-SIS – depression subscore (‘hads_depscore’)	5370	1241	2559	814	756	
(n; mean±sd)	4.7±4.0	3.7±3.6	6.1±4.2	2.9±3.1	3.7±3.2	
(median; minimum; maximum)	4.0 (0.0; 21.0)	3.0 (0.0; 21.0)	6.0 (0.0; 21.0)	2.0 (0.0; 18.0)	3.0 (0.0; 19.0)	
NA	3344	621	2193	275	255	
HADS-SIS – irritability subscore (‘irrscore’)	5374	1241	2561	816	756	
(n; mean±sd)	5.3±4.3	5.2±4.1	6.0±4.6	4.2±3.6	4.3±3.1	
(median; minimum; maximum)	5.0 (0.0; 24.0)	4.0 (0.0; 23.0)	5.0 (0.0; 24.0)	4.0 (0.0; 21.0)	4.0 (0.0; 16.0)	
NA	3340	621	2191	273	255	

*For graphical illustration of these figures see appendix 1.

Table 11 – Clinical evaluation at baseline

	All	HDGECs (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
UHDRS ‘99 Motor (‘motscore’)	8670	6579	2091
(n; mean±sd)	22.8±24.9	29.5±25.0	1.8±3.5
(median; minimum; maximum)	14.0 (0.0; 120.0)	26.0 (0.0; 120.0)	0.0 (0.0; 69)
NA	44	35	9
UHDRS ‘99 DCL (‘diagconf’)			
0 (‘diagconf=0’) (n; %)	2670 (30.7%)	989 (15.0%)	1681 (80.1%)
1 (‘diagconf=1’) (n; %)	925 (10.6%)	554 (8.4%)	371 (17.7%)
2 (‘diagconf=2’) (n; %)	309 (3.5%)	281 (4.3%)	28 (1.3%)
3 (‘diagconf=3’) (n; %)	234 (2.7%)	223 (3.4%)	11 (0.5%)
4 (‘diagconf=4’) (n; %)	4571 (52.5%)	4564 (69.0%)	7 (0.3%)
NA	5	3	2
UHDRS ‘99 Total Functional Capacity (‘fcscore’)	8702	6604	2098
(n; mean±sd)	10.1±3.7	9.2±3.9	12.9±0.7
(median; minimum; maximum)	12.0 (0.0; 13.0)	10.0 (0.0; 13.0)	13.0 (1.0; 13.0)
NA	12	10	2
UHDRS ‘99 Function Assessment Scale (‘fascore’)	8535	6445	2090
(n; mean±sd)	20.7±6.4	19.4±6.8	24.9±0.8
(median; minimum; maximum)	24.0 (0.0; 25.0)	22.0 (0.0; 25.0)	25.0 (5.0; 25.0)

	All	HDGECs (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
NA	179	169	10
UHDRS ‘99 Independence Scale (‘indepscl’)	8703	6605	2098
(n; mean±sd)	86.0±18.7	81.7±19.6	99.6±2.7
(median; minimum; maximum)	95.0 (5.0; 100.0)	85.0 (5.0; 100.0)	100.0 (45.0; 100.0)
NA	11	9	2
Cognitive Assessment: symbol digit modality test (total correct) (‘sdmt1’)	8310	6225	2085
(n; mean±sd)	35.5±18.8	30.6±18.1	50.1±11.9
(median; minimum; maximum)	36.0 (0.0; 101.0)	28.0 (0.0; 101.0)	51.0 (0.0; 94.0)
NA	404	389	15
Cognitive Assessment: verbal fluency test (category) completed (total correct) (‘verfct5’)	8534	6452	2082
(n; mean±sd)	16.2±7.6	14.5±7.3	21.6±5.6
(median; minimum; maximum)	16.0 (1.0; 55.0)	14.0 (0.0; 55.0)	21.0 (3.0; 48.0)
NA	180	162	18
Cognitive Assessment: stroop colour naming test (total correct) (‘scnt1’)	8461	6391	2070
(n; mean±sd)	56.1±24.0	50.0±23.2	74.8±14.7
(median; minimum; maximum)	58.0 (0.0; 400.0)	49.0 (0.0; 400.0)	75.0 (0.0; 140.0)
NA	253	223	30
Cognitive Assessment: stroop word reading test (total correct) (‘swrt1’)	8448	6375	2073
(n; mean±sd)	72.4±29.6	65.0±28.8	95.1±18.0

	All	HDGECs (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
(median; minimum; maximum)			
NA	75.0 (0.0; 199.0)	64.0 (0.0; 199.0)	96.0 (0.0; 168.0)
	266	239	27
Cognitive Assessment: stroop interference test (total correct) (‘sit1’)	7511	5569	1942
(n; mean±sd)	32.9±15.6	29.6±15.0	42.6±13.4
(median; minimum; maximum)	33.0 (0.0; 374.0)	29.0 (0.0; 100.0)	42.0 (0.0; 374.0)
NA	1203	1045	158
Cognitive Assessment: trailmaking test (Part A: total correct) (‘trla2’)	6454	4669	1785
(n; mean±sd)	24.4±4.7	24.2±5.3	24.8±2.3
(median; minimum; maximum)	25.0 (0.0; 250.0)	25.0 (0.0; 250.0)	25.0 (0.0; 27.0)
NA	2260	1945	315
(Part B: total correct) (‘trlb2’)	6333	4553	1780
(n; mean±sd)	22.7±7.9	22.1±9.0	24.4±3.4
(median; minimum; maximum)	25.0 (0.0; 240.0)	25.0 (0.0; 240.0)	25.0 (0.0; 29.0)
NA	2381	2061	320
Cognitive Assessment: verbal fluency test (letters) completed (total correct) (‘verflt05’)	6676	4903	1773
(n; mean±sd)	30.8±16.3	27.2±15.8	41.0±12.8
(median; minimum; maximum)	31.0 (0.0; 94.0)	26.0 (0.0; 84.0)	40.0 (0.0; 94.0)
NA	2038	1711	327
PBA-s - depression score (‘depscore’)	8621	6524	2097
	4.6±6.2	5.0±6.4	3.2±5.0

	All	HDGECs (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
(n; mean±sd)	2.0 (0.0; 48.0)	3.0 (0.0; 48.0)	1.0 (0.0; 44.0)
(median; minimum; maximum)	93	90	3
NA			
PBA-s - irritability score (‘irascore’)	8680	6586	2094
(n; mean±sd)	2.6±4.5	3.1±4.8	1.3±2.7
(median; minimum; maximum)	0.0 (0.0; 32.0)	1.0 (0.0; 32.0)	0.0 (0.0; 28.0)
NA	34	28	6
PBA-s - psychosis score (‘psyscore’)	8613	6519	2094
(n; mean±sd)	0.2±1.5	0.3±1.7	0.1±0.8
(median; minimum; maximum)	0.0 (0.0; 32.0)	0.0 (0.0; 32.0)	0.0 (0.0; 18.0)
NA	101	95	6
PBA-s - apathy score (‘aptscore’)	8626	6529	2097
(n; mean±sd)	2.4±4.0	3.0±4.4	0.5±1.6
(median; minimum; maximum)	0.0 (0.0; 16.0)	0.0 (0.0; 16.0)	0.0 (0.0; 16.0)
NA	88	85	3
PBA-s - executive function score (‘exfscore’)	8602	6507	2095
(n; mean±sd)	2.5±4.9	3.1±5.3	0.7±2.4
(median; minimum; maximum)	0.0 (0.0; 32.0)	0.0 (0.0; 32.0)	0.0 (0.0; 25.0)
NA	112	107	5

	All	HDGECs (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
MMSE score (‘mmsetotal’)	5650	4109	1541
(n; mean±sd)	26.8±3.9	26.1±4.3	28.9±1.5
(median; minimum; maximum)	28.0 (0.0; 30.0)	27.0 (0.0; 30.0)	29.0 (18.0; 30.0)
NA	3064	2505	559
HADS-SIS – anxiety subscore (‘anxscore’)	5378	3809	1569
(n; mean±sd)	5.6±4.1	5.9±4.2	5.1±3.7
(median; minimum; maximum)	5.0 (0.0; 21.0)	5.0 (0.0; 21.0)	4.0 (0.0; 21.0)
NA	3336	2805	531
HADS-SIS – depression subscore (‘hads_depscore’)	5370	3800	1570
(n; mean±sd)	4.7±4.0	5.3±4.2	3.3±3.1
(median; minimum; maximum)	4.0 (0.0; 21.0)	5.0 (0.0; 21.0)	3.0 (0.0; 19.0)
NA	3344	2814	530
HADS-SIS – irritability subscore (‘irrscore’)	5374	3802	1572
(n; mean±sd)	5.3±4.3	5.8±4.5	4.2±3.4
(median; minimum; maximum)	5.0 (0.0; 24.0)	5.0 (0.0; 24.0)	4.0 (0.0; 21.0)
NA	3340	2812	528

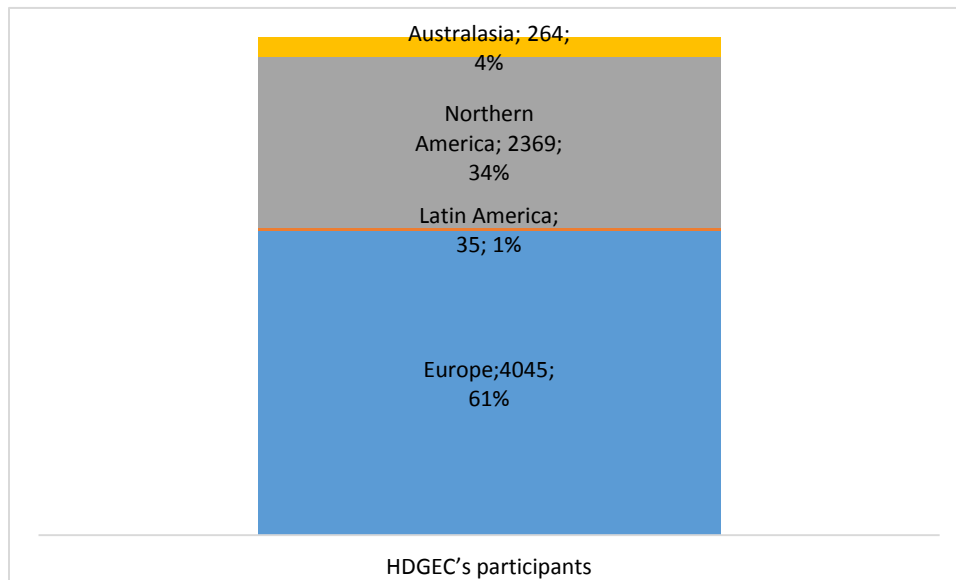
Where?

Participants by region (baseline information)

Figure 19 – Number of participants per region ('region') at baseline

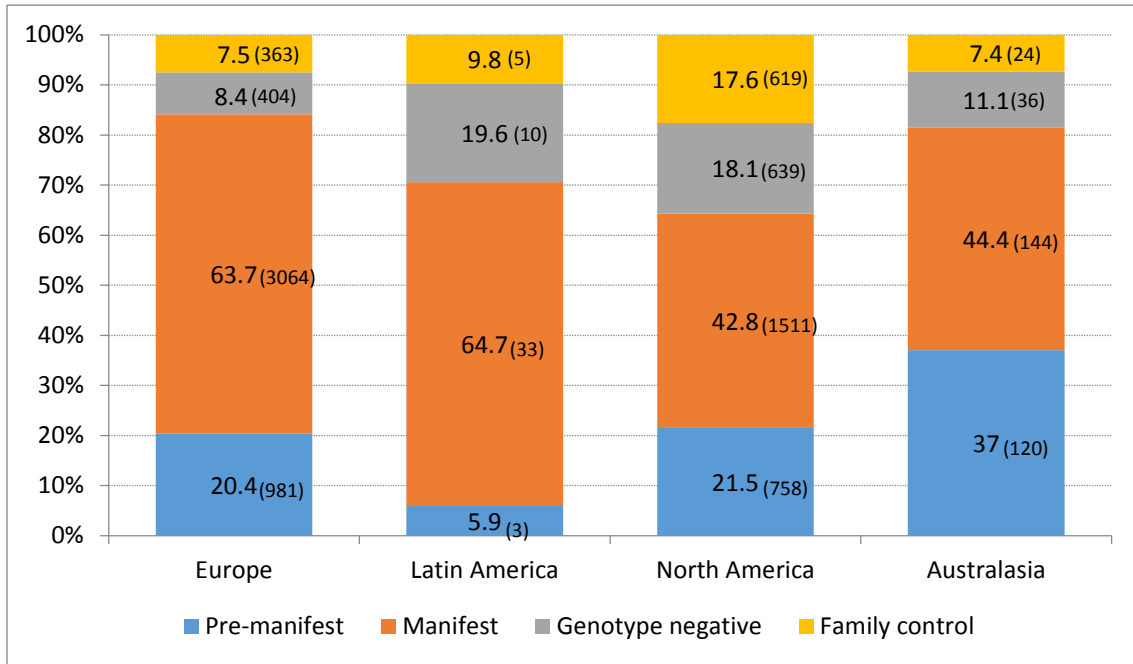


Figure 20 – Number and percentage of HDGEC's participants per region ('region') at baseline



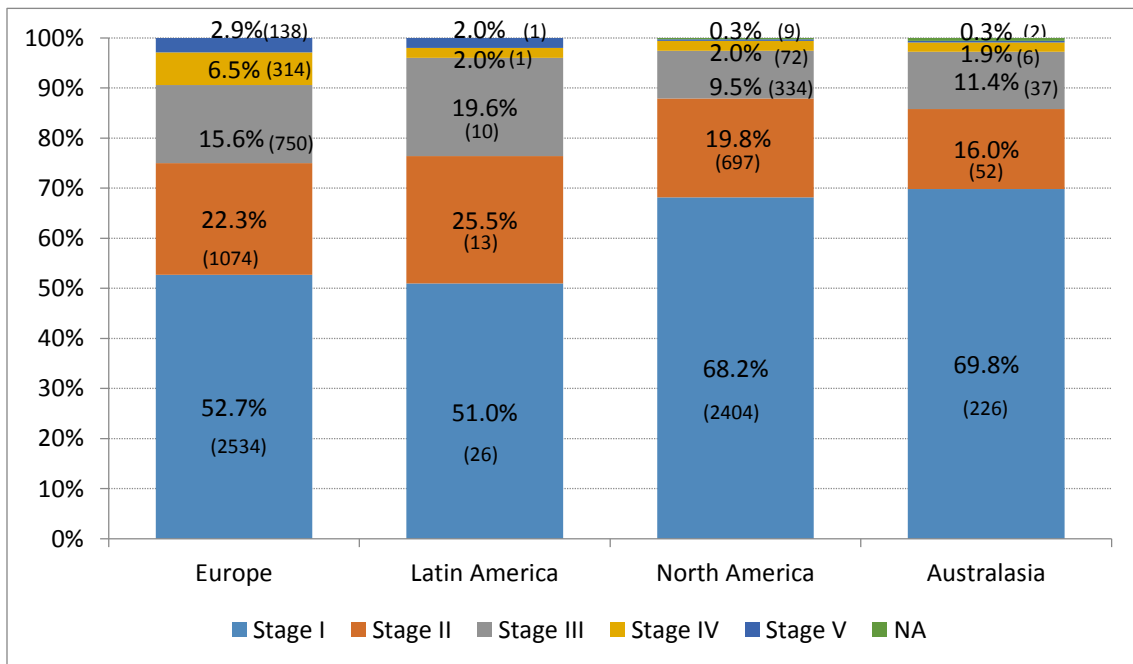
Participant characterization per region (baseline information)

Figure 21 – Participants as classified at enrollment per region ('region') per participant category ('hdcap')



HD Stages

Figure 22 – HD stages at the baseline visit per region ('region')



Participant information

Figure 23 – Pharmacotherapy ('Pharmacotx'), Non-pharmacotherapy ('Nonpharmacotx') and Nutritional Supplements ('Nutsuppl') usage per region ('region')

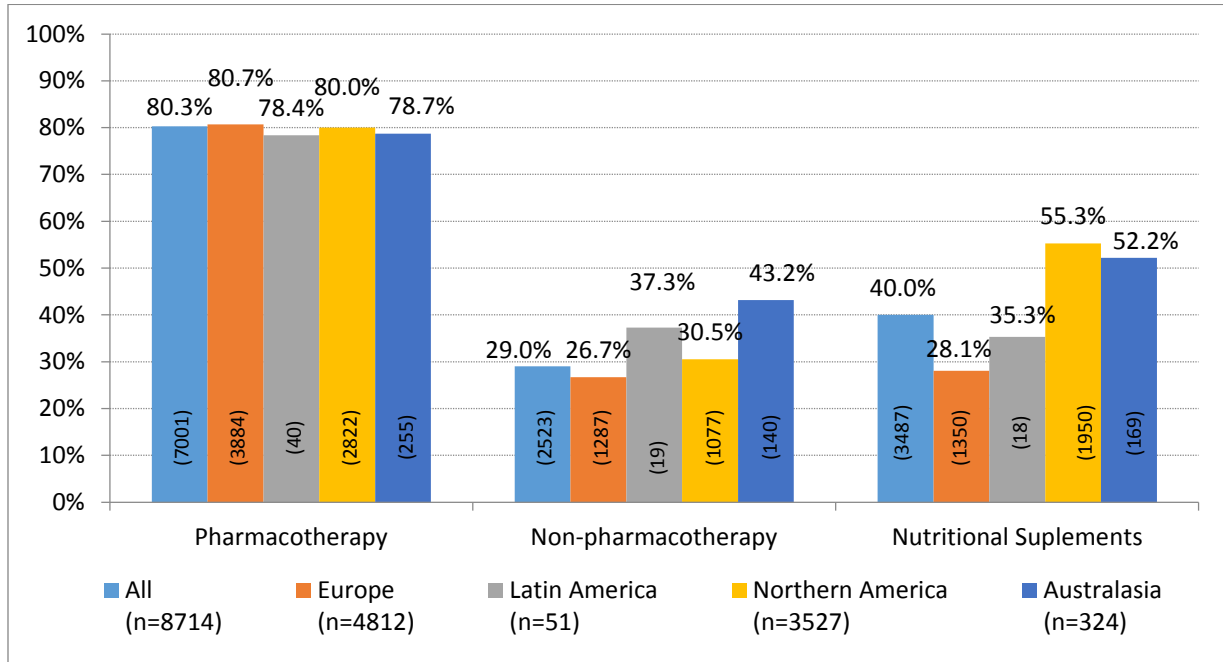


Figure 24 – Pharmacotherapy ('Pharmacotx'), Non-pharmacotherapy ('Nonpharmacotx') and Nutritional Supplements ('Nutsuppl') usage per participant category ('hdcat'): region Europe ('region=Europe')

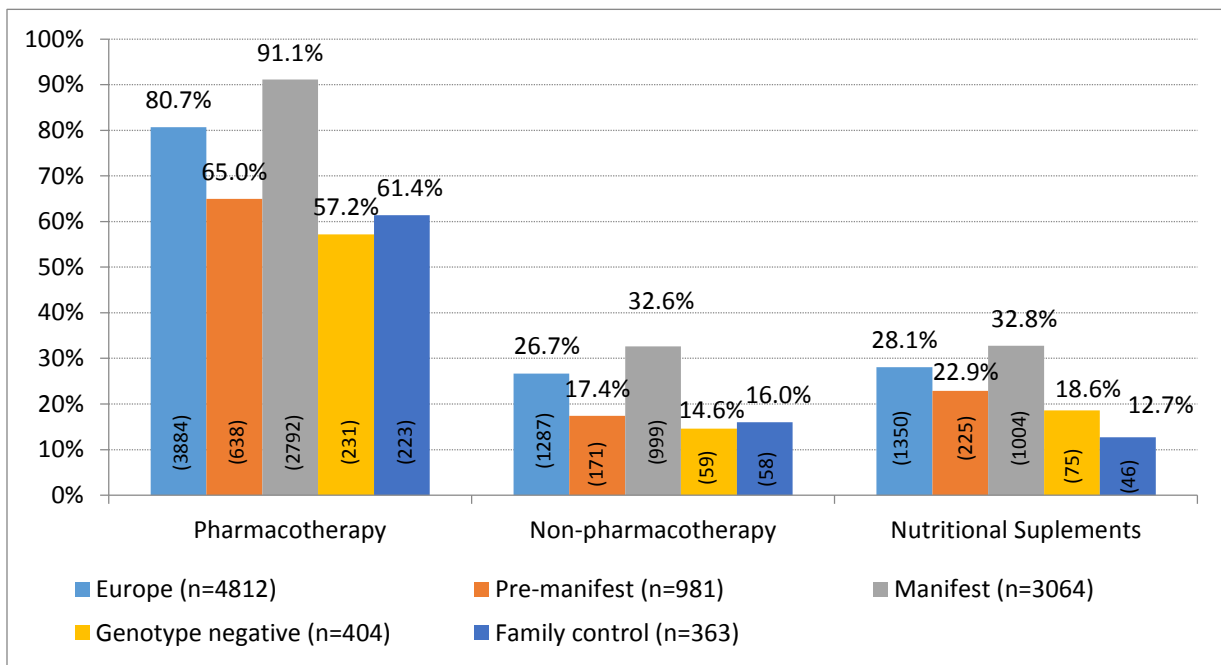


Figure 25 – Pharmacotherapy ('Pharmacotx'), Non-pharmacotherapy ('Nonpharmacotx') and Nutritional Supplements ('Nutsuppl') usage per participant category ('hdcat'): region Latin America ('region=Latin America')

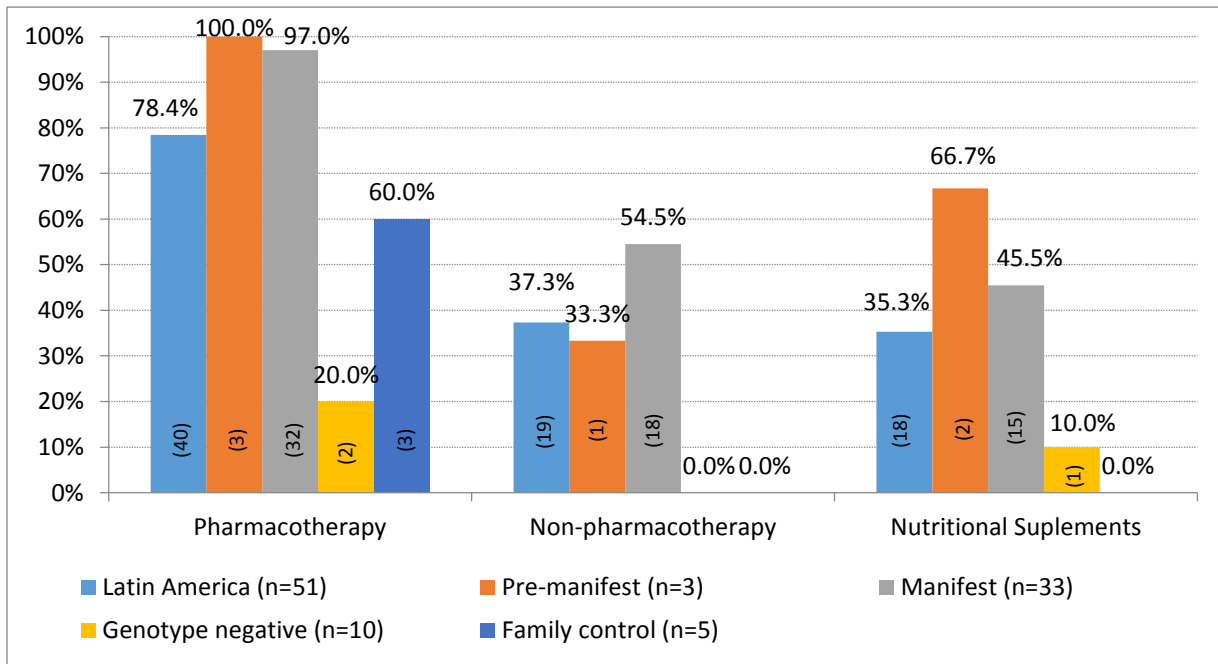


Figure 26 – Pharmacotherapy ('Pharmacotx'), Non-pharmacotherapy ('Nonpharmacotx') and Nutritional Supplements ('Nutsuppl') usage per participant category ('hdcat'): region Northern America ('region=Northern America')

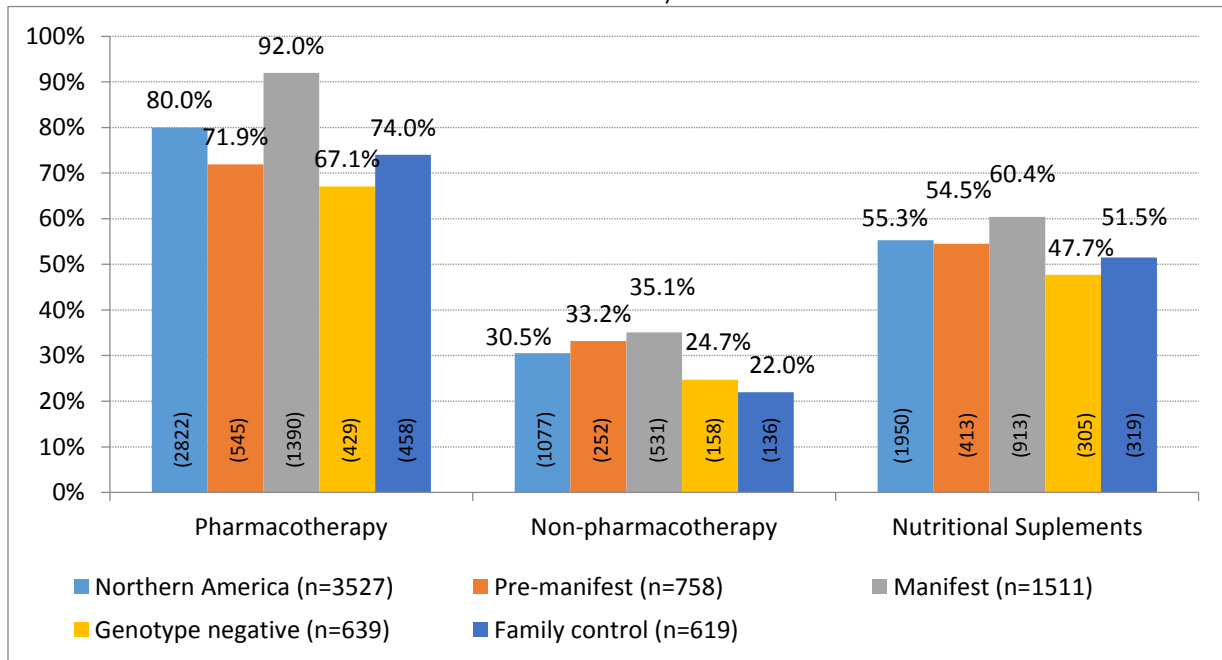


Figure 27 – Pharmacotherapy ('Pharmacotx'), Non-pharmacotherapy ('Nonpharmacotx') and Nutritional Supplements ('Nutsuppl') usage per participant category ('hdcac'): region Australasia ('region=Australasia')

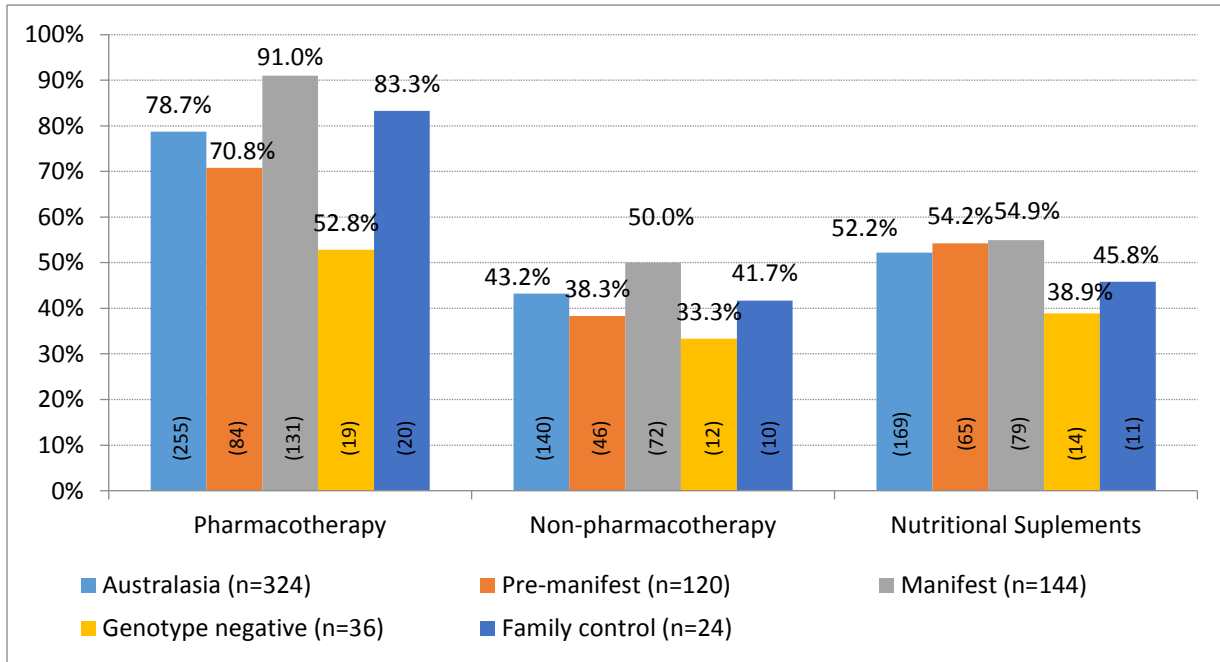


Figure 28 – Presence of Comorbidities ('Comorbid') per region ('region')

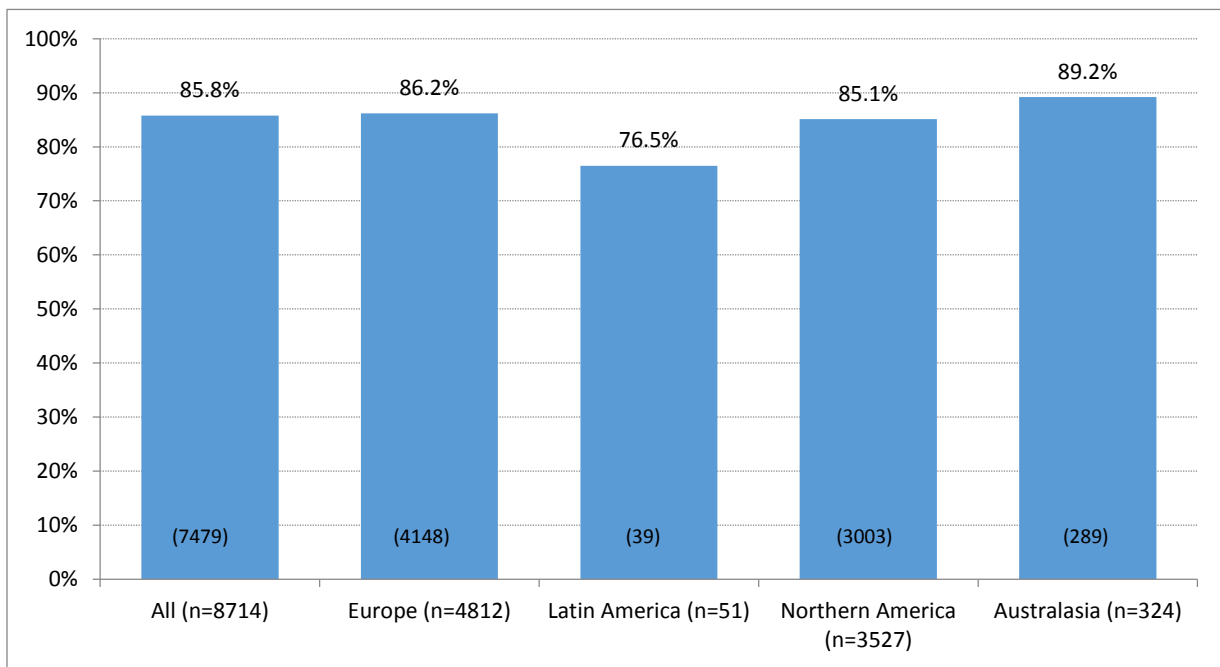
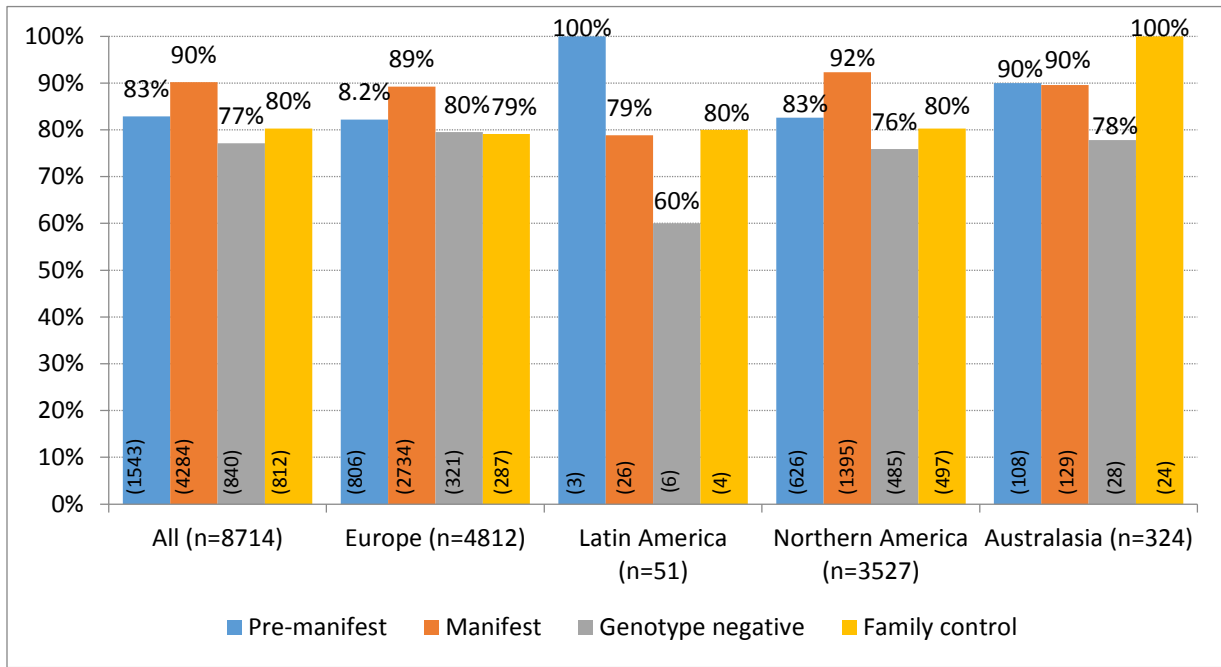


Figure 29 – Presence of Comorbidities (‘Comorbid’) per region (‘region’) and HD category (‘hdcat’)



Research genotype information

Table 12 – CAG characterization according the centralized research genotyping per region (‘region’)

	All	Europe	Latin America	Northern America	Australasia
Participants with CAG information (n)	8714	4812	51	3527	324
Allele 1 CAG repeat length (smaller allele) (‘caglow’)	8714	4812	51	3527	324
(n; mean±sd)	18.1±3.07	18.2 ± 3.1	17.7 ± 3.1	18.0 ± 3.0	18.2 ± 3.0
(median; minimum; maximum)	17.0 (8.0; 29.0)	17.0 (8.0; 29.0)	17.0 (10.0; 29.0)	17.0 (8.0; 29.0)	17.0 (9.0; 29.0)
NA	-	-	-	-	-
Allele 2 CAG repeat length (larger allele)	8714	4812	51	3527	324

('caghigh')					
(n; mean±sd)	38.0±10.7	39.9 ± 9.3	38.9 ± 15.2	35.2 ± 11.8	38.5 ± 9.6
(median; minimum; maximum)	42.0 (12.0; 71.0)	42.0 (12.0; 71.0)	43.0 (17.0; 71.0)	41.0 (15.0; 71.0)	42.0 (15.0; 60.0)
NA	-	-	-	-	-
Disease burden ('dburden') (HDGEC's)	6614	4045	36	2269	264
(n; mean±sd)	372.6±119.7	378.6 ± 119.7	450.2 ± 151.0	364.1 ± 118.2	342.5 ± 118.0
(median; minimum; maximum)	376.0 (14; 1192.5)	382.5 (14.0; 1192.5)	443.2 (227.5; 812.5)	364.0 (21.0; 883.5)	339.0 (25.0; 703.0)
NA	-	-	-	-	-

CAG larger allele ('caghigh') was categorized into the following classes:

- 36-39, 40-49, 50-59, >=60.

Figure 30 – CAG larger allele ('caghigh_1') distribution for HD manifest participants ('hdcat=3') per region

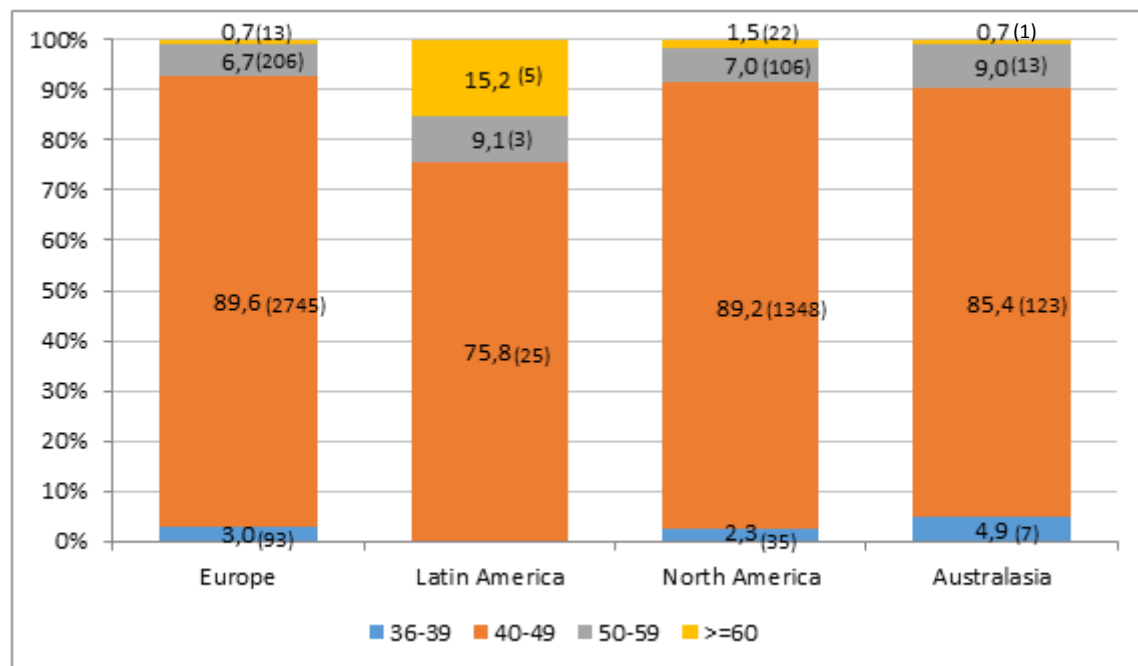


Figure 31 – CAG larger allele ('caghigh_1') distribution for HDGEC's participants ('hdcat_1') per region ('region')

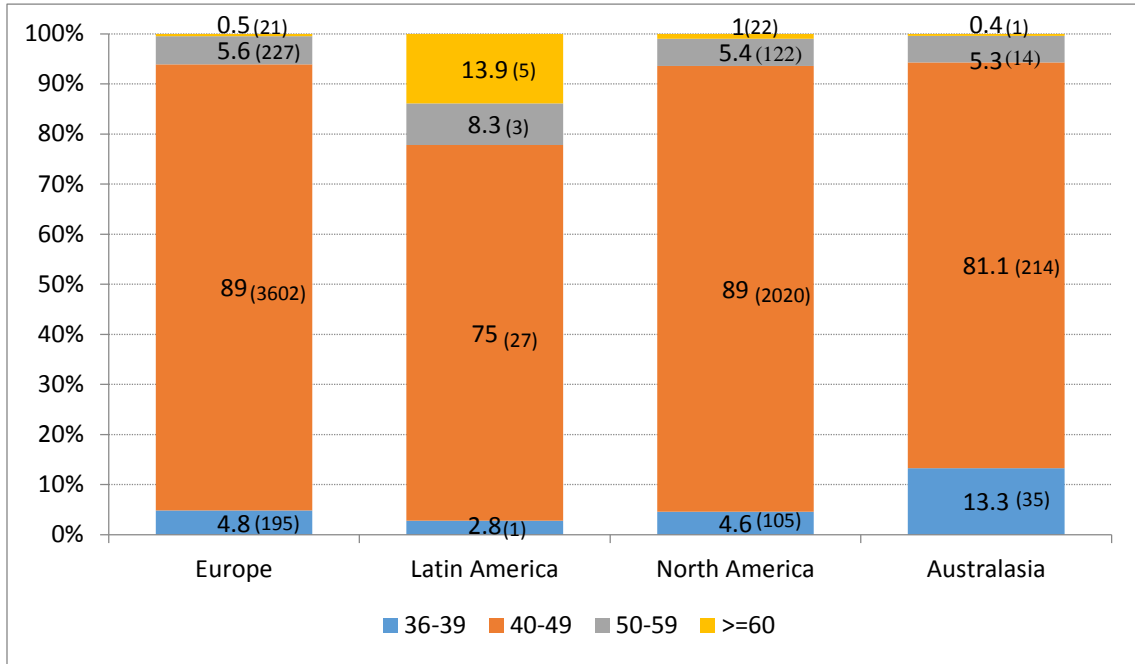


Figure 32 – CAG larger allele ('caghigh_1') distribution for All participants per region ('region')

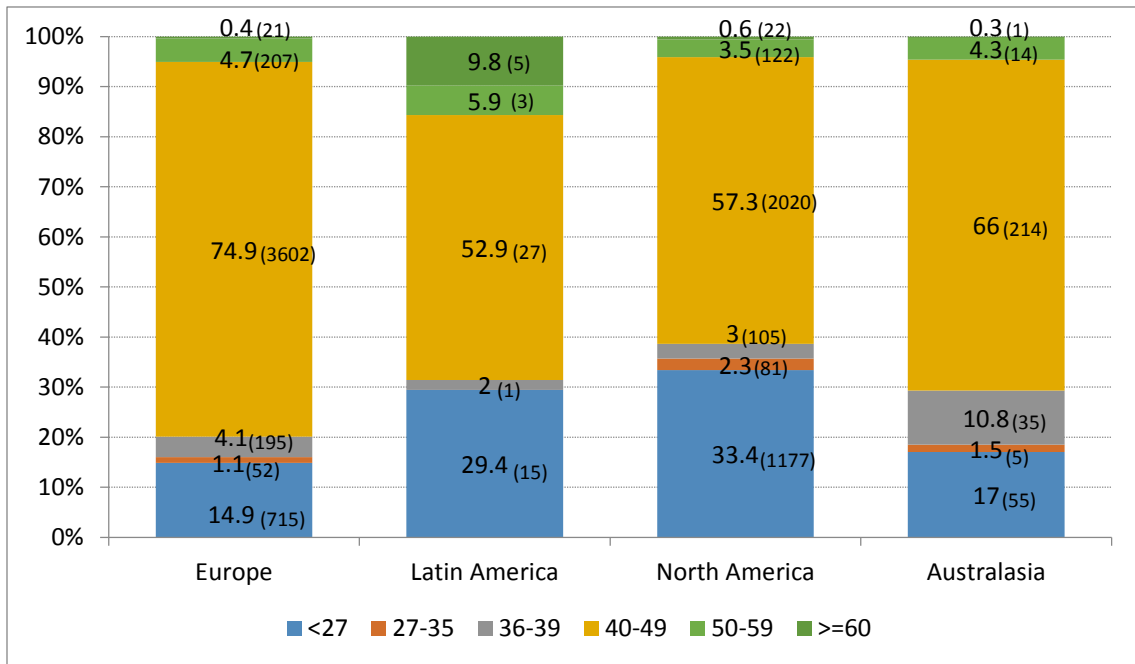


Table 13 – Clinical evaluation at baseline per region: EUROPE ('region=Europe')

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
UHDRS ‘99 Motor (‘motscore’)	4787	978	3044	402	363
(n; mean±sd)	27.4±27.0	3.0±5.3	41.8±23.8	1.5±2.7	1.1±2.4
(median; minimum; maximum)	21.0 (0.0; 120.0)	1.0 (0.0; 70.0)	38.0 (0.0; 120.0)	0.0 (0.0; 20.0)	0.0 (0.0; 21.0)
NA	25	3	20	2	-
UHDRS ‘99 DCL (‘diagconf’)					
0 (‘diagconf=0’) (n; %)	1251 (26.0%)	561 (57.2%)	13 (0.4%)	340 (84.2%)	337 (92.8%)
1 (‘diagconf=1’) (n; %)	332 (6.9%)	243 (24.8%)	15 (0.5%)	50 (12.4%)	24 (6.6%)
2 (‘diagconf=2’) (n; %)	140 (2.9%)	108 (11.0%)	24 (0.8%)	8 (2.0%)	0 (0.0%)
3 (‘diagconf=3’) (n; %)	115 (2.4%)	57 (5.8%)	55 (1.8%)	3 (0.7%)	0 (0.0%)
4 (‘diagconf=4’) (n; %)	2971 (61.8%)	12 (1.2%)	2954 (96.5%)	3 (0.7%)	2 (0.6%)
NA	3	-	3	-	-
UHDRS ‘99 Total Functional Capacity (‘tfcscore’)	4810	980	3063	404	363
(n; mean±sd)	9.4±4.1	12.7±1.1	7.5±3.9	12.9±0.6	12.8±0.7
(median; minimum; maximum)	11.0 (0.0; 13.0)	13.0 (2.0; 13.0)	8.0 (0.0; 13.0)	13.0 (2.0; 13.0)	13.0 (4.0; 13.0)

	All	Pre-manifest (<i>'hdc</i> at=2')	Manifest (<i>'hdc</i> at=3')	Genotype negative (<i>'hdc</i> at=4')	Family Control (<i>'hdc</i> at=5')
NA	2	1	1	-	-
UHDRS '99 Function Assessment Scale (<i>'fasc</i> ore')	4641	952	2929	398	362
(n; mean±sd)	19.4±7.2	24.6±1.7	16.4±7.4	24.9±0.8	24.8±0.8
(median; minimum; maximum)	23.0 (0.0; 25.0)	25.0 (0.0; 25.0)	18.0 (0.0; 25.0)	25.0 (11.0; 25.0)	25.0 (13.0; 25.0)
NA	171	29	135	6	1
UHDRS '99 Independence Scale (<i>'indep</i> scl')	4807	981	3059	404	363
(n; mean±sd)	82.2±20.8	98.7±4.9	72.5±20.4	99.7±2.2	99.6±2.8
(median; minimum; maximum)	90.0 (5.0; 100.0)	100.0 (25.0; 100.0)	75.0 (5.0; 100.0)	100.0 (65.0; 100.0)	100.0 (65.0; 100.0)
NA	5	-	5	-	-
Cognitive Assessment: symbol digit modality test (total correct) (<i>'sdmt</i> 1')	4531	976	2795	401	359
(n; mean±sd)	31.4±19.2	49.2±13.0	20.6±13.7	51.0±12.1	45.8±12.6
(median; minimum; maximum)	29.0 (0.0; 94.0)	50.0 (0.0; 86.0)	19.0 (0.0; 90.0)	52.0 (11.0; 91.0)	47.0 (0.0; 94.0)
NA	281	5	269	3	4
Cognitive Assessment: verbal fluency test (category) completed (total correct) (<i>'verfct</i> 5')	4693	973	2959	401	360
(n; mean±sd)	15.1±7.8	21.3±5.9	11.3±6.1	22.0±5.8	21.9±6.0
(median; minimum; maximum)	15.0 (0.0; 45.0)	21.0 (1.0; 45.0)	11.0 (0.0; 42.0)	22.0 (3.0; 43.0)	22.0 (7.0; 44.0)
NA	119	8	105	3	3

	All	Pre-manifest ('hdcat=2')	Manifest ('hdcat=3')	Genotype negative ('hdcat=4')	Family Control ('hdcat=5')
Cognitive Assessment: stroop colour naming test (total correct) ('scent1')	4651	975	2916	400	360
(n; mean±sd)	51.1±24.8	71.9±15.0	38.3±20.3	75.6±14.0	70.9±14.4
(median; minimum; maximum)	51.0 (0.0; 400.0)	72.0 (0.0; 124.0)	38.0 (0.0; 400.0)	75.0 (28.0; 132.0)	72.0 (0.0; 112.0)
NA	161	6	148	4	3
Cognitive Assessment: stroop word reading test (total correct) ('swrt1')	4640	975	2903	401	361
(n; mean±sd)	67.3±31.1	92.3±19.4	51.3±25.3	97.9±17.9	94.9±19.2
(median; minimum; maximum)	69.0 (0.0; 155.0)	94.0 (0.0; 155.0)	51.0 (0.0; 123.0)	100.0 (24.0; 140.0)	98.0 (0.0; 139.0)
NA	172	6	161	3	2
Cognitive Assessment: stroop interference test (total correct) ('sit1')	4079	920	2450	380	329
(n; mean±sd)	30.4±15.6	43.4±11.0	22.0±12.2	44.4±11.1	39.7±10.3
(median; minimum; maximum)	30.0 (0.0; 100.0)	44.0 (0.0; 86.0)	21.0 (0.0; 100.0)	44.0 (6.0; 76.0)	40.0 (11.0; 72.0)
NA	733	61	614	24	34
Cognitive Assessment: trailmanking test (Part A: total correct) ('trla2')		804	1951	341	303
(n; mean±sd)	3399	25.0±8.4	23.6±5.4	24.6±3.0	24.3±3.9
(median; minimum; maximum)	24.1±6.0	25.0 (0.0; 250.0)	25.0 (0.0; 25.0)	25.0 (0.0; 25.0)	25.0 (0.0; 25.0)
NA	25.0 (0.0; 250.0)	177	1113	63	60
(Part B: total correct) ('trlb2')	1413	800	1874	341	303
(n; mean±sd)	3318	24.5±4.9	19.8±9.9	24.2±4.1	23.9±4.7

	All	Pre-manifest (<i>'hdcat=2'</i>)	Manifest (<i>'hdcat=3'</i>)	Genotype negative (<i>'hdcat=4'</i>)	Family Control (<i>'hdcat=5'</i>)
(median; minimum; maximum)	21.8±8.3	25.0 (0.0; 117.0)	25.0 (0.0; 240.0)	25.0 (0.0; 25.0)	25.0 (0.0; 26.0)
NA	25.0 (0.0; 240.0)	181	1190	63	60
	1494				
Cognitive Assessment: verbal fluency test (letters) completed (total correct) (<i>'verflt05'</i>)	3658	821	2184	349	304
(n; mean±sd)	27.4±16.0	39.7±12.9	19.4±12.7	39.3±12.9	38.3±12.0
(median; minimum; maximum)	26.0 (0.0; 91.0)	40.0 (7.0; 83.0)	17.0 (0.0; 72.0)	40.0 (9.0; 91.0)	38.0 (8.0; 76.0)
NA	1154	160	880	55	59
PBA-s - depression score (<i>'depscore'</i>)	4732	978	2989	403	362
(n; mean±sd)	4.9±6.3	4.3±5.9	5.4±6.6	3.3±5.2	3.5±5.1
(median; minimum; maximum)	2.0 (0.0; 48.0)	2.0 (0.0; 41.0)	3.0 (0.0; 48.0)	1.0 (0.0; 30.0)	1.0 (0.0; 27.0)
NA	80	3	75	1	1
PBA-s - irritability score (<i>'irascore'</i>)	4789	977	3047	403	362
(n; mean±sd)	3.0±4.8	2.1±3.7	3.8±5.3	1.3±2.7	1.5±2.8
(median; minimum; maximum)	1.0 (0.0; 32.0)	0.0 (0.0; 32.0)	1.0 (0.0; 32.0)	0.0 (0.0; 20.0)	0.0 (0.0; 24.0)
NA	23	4	17	1	1
PBA-s - psychosis score (<i>'psyscore'</i>)	4722	977	2982	401	362
(n; mean±sd)	0.3±1.7	0.1±0.7	0.4±2.1	0.1±0.9	0.0±0.1
(median; minimum; maximum)	0.0 (0.0; 32.0)	0.0 (0.0; 12.0)	0.0 (0.0; 32.0)	0.0 (0.0; 13.0)	0.0 (0.0; 2.0)

	All	Pre-manifest ('hdcat=2')	Manifest ('hdcat=3')	Genotype negative ('hdcat=4')	Family Control ('hdcat=5')
NA	90	4	82	3	1
PBA-s - apathy score (‘aptscore’)	4733	976	2992	403	362
(n; mean±sd)	3.1±4.5	1.2±2.7	4.4±4.9	0.6±1.7	0.5±1.6
(median; minimum; maximum)	0.0 (0.0; 16.0)	0.0 (0.0; 16.0)	2.0 (0.0; 16.0)	0.0 (0.0; 12.0)	0.0 (0.0; 12.0)
NA	79	5	72	1	1
PBA-s - executive function score (‘exfscore’)	4711	972	2976	401	362
(n; mean±sd)	3.1±5.5	1.2±2.9	4.3±6.3	0.9±2.5	0.7±2.0
(median; minimum; maximum)	0.0 (0.0; 32.0)	0.0 (0.0; 28.0)	1.0 (0.0; 32.0)	0.0 (0.0; 18.0)	0.0 (0.0; 14.0)
NA	101	9	88	3	1
MMSE score (‘mmsetotal’)	2745	563	1688	277	217
(n; mean±sd)	26.1±4.7	28.8±1.7	24.4±5.1	29.0±1.6	29.0±1.5
(median; minimum; maximum)	28.0 (0.0; 30.0)	29.0 (16.0; 30.0)	26.0 (0.0; 30.0)	30.0 (21.0; 30.0)	29.0 (19.0; 30.0)
NA	2067	418	1376	127	146
HADS-SIS – anxiety subscore (‘anxscore’)	2707	606	1552	277	272
(n; mean±sd)	5.7±4.1	5.3±3.9	6.0±4.2	4.9±3.8	5.5±3.7
(median; minimum; maximum)	5.0 (0.0; 21.0)	5.0 (0.0; 21.0)	5.0 (0.0; 21.0)	4.0 (0.0; 17.0)	5.0 (0.0; 18.0)
NA	2105	375	1512	127	91
HADS-SIS – depression subscore (‘hads_depscore’)	2702	604	1547	277	274
(n; mean±sd)	5.4±4.3	3.8±3.8	6.6±4.3	3.3±3.4	4.7±3.5

	All	Pre-manifest (‘hdcats=2’)	Manifest (‘hdcats=3’)	Genotype negative (‘hdcats=4’)	Family Control (‘hdcats=5’)
(median; minimum; maximum)	5.0 (0.0; 21.0)	3.0 (0.0; 21.0)	6.0 (0.0; 21.0)	2.0 (0.0; 18.0)	4.0 (0.0; 19.0)
NA	2110	377	1517	127	89
HADS-SIS – irritability subscore (‘irrscore’)	2703	605	1546	278	274
(n; mean±sd)	5.7±4.4	5.3±4.2	6.2±4.7	4.5±3.8	4.6±3.3
(median; minimum; maximum)	5.0 (0.0; 24.0)	5.0 (0.0; 23.0)	6.0 (0.0; 24.0)	4.0 (0.0; 21.0)	4.0 (0.0; 16.0)
NA	2109	376	1518	126	89

Table 14 – Clinical evaluation at baseline per region: LATIN AMERICA ('region=Latin America')

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
UHDRS ‘99 Motor (‘motscore’)	51	3	33	10	5
(n; mean±sd)	31.4±27.5	0.7±1.2	48.3±18.5	0.4±1.0	0.0±0.0
(median; minimum; maximum)	37.0 (0.0; 96.0)	0.0 (0.0; 2.0)	47.0 (9.0; 96.0)	0.0 (0.0; 3.0)	0.0 (0.0; 0.0)
NA	-	-	-	-	-
UHDRS ‘99 DCL (‘diagconf’)					
0 (‘diagconf=0’) (n; %)	15 (29.4%)	2 (66.7%)	0 (0.0%)	8 (80.0%)	5 (100.0%)
1 (‘diagconf=1’) (n; %)	3 (5.9%)	1 (33.3%)	0 (0.0%)	2 (20.0%)	0 (0.0%)
2 (‘diagconf=2’) (n; %)	1 (2.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)
3 (‘diagconf=3’) (n; %)	1 (2.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0 (0.0%)
4 (‘diagconf=4’) (n; %)	31 (60.8%)	0 (0.0%)	31 (93.9%)	0 (0.0%)	0 (0.0%)
NA	-	-	-	-	-
UHDRS ‘99 Total Functional Capacity (‘tfcscore’)	51	3	33	10	5
(n; mean±sd)	9.7±3.7	13.0±0.0	7.9±3.4	13.0±0.0	13.0±0.0
(median; minimum; maximum)	11.0 (0.0; 13.0)	13.0 (13.0; 13.0)	8.0 (0.0; 13.0)	13.0 (13.0; 13.0)	13.0 (13.0; 13.0)

	All	Pre-manifest ('hdcat=2')	Manifest ('hdcat=3')	Genotype negative ('hdcat=4')	Family Control ('hdcat=5')
NA	-	-	-	-	-
UHDRS '99 Function Assessment Scale ('fascore')	51	3	33	10	5
(n; mean±sd)	19.5±6.5	25.0±0.0	16.5±6.3	24.9±0.3	25.0±0.0
(median; minimum; maximum)	21.0 (0.0; 25.0)	25.0 (25.0; 25.0)	18.0 (0.0; 25.0)	25.0 (24.0; 25.0)	25.0 (25.0; 25.0)
NA	-	-	-	-	-
UHDRS '99 Independence Scale ('indep scl')	51	3	33	10	5
(n; mean±sd)	82.7±19.0	100.0±0.0	73.3±17.5	100.0±0.0	100.0±0.0
(median; minimum; maximum)	85.0 (20.0; 100.0)	100.0 (100.0; 100.0)	75.0 (20.0; 100.0)	100.0 (100.0; 100.0)	100.0 (100.0; 100.0)
NA	-	-	-	-	-
Cognitive Assessment: symbol digit modality test (total correct) ('sdmt1')	51	3	33	10	5
(n; mean±sd)	27.5±20.6	54.3±5.7	17.2±15.0	42.5±19.3	49.4±9.7
(median; minimum; maximum)	23.0 (0.0; 67.0)	56.0 (48.0; 59.0)	12.0 (0.0; 53.0)	47.0 (6.0; 67.0)	50.0 (36.0; 59.0)
NA	-	-	-	-	-
Cognitive Assessment: verbal fluency test (category) completed (total correct) ('verfct5')	51	3	33	10	5
(n; mean±sd)	13.4±7.2	20.0±7.0	10.4±5.6	17.8±6.6	20.6±6.3
(median; minimum; maximum)	12.0 (0.0; 32.0)	23.0 (12.0; 25.0)	10.0 (0.0; 24.0)	16.5 (9.0; 32.0)	17.0 (15.0; 28.0)
NA	-	-	-	-	-

	All	Pre-manifest ('hdcat=2')	Manifest ('hdcat=3')	Genotype negative ('hdcat=4')	Family Control ('hdcat=5')
Cognitive Assessment: stroop colour naming test (total correct) ('scent1')	51	3	33	10	5
(n; mean±sd)	46.2±24.6	65.0±5.0	34.5±21.2	65.2±17.2	74.2±5.2
(median; minimum; maximum)	45.0 (0.0; 94.0)	65.0 (60.0; 70.0)	35.0 (0.0; 80.0)	61.0 (36.0; 94.0)	74.0 (66.0; 80.0)
NA	-	-	-	-	-
Cognitive Assessment: stroop word reading test (total correct) ('swrt1')	51	3	33	10	5
(n; mean±sd)	60.7±30.5	81.0±3.6	46.4±27.2	85.9±18.8	92.2±8.1
(median; minimum; maximum)	64.0 (0.0; 100.0)	80.0 (78.0; 85.0)	46.0 (0.0; 100.0)	92.0 (41.0; 100.0)	92.0 (81.0; 100.0)
NA	-	-	-	-	-
Cognitive Assessment: stroop interference test (total correct) ('sit1')	37	3	19	10	5
(n; mean±sd)	29.3±14.7	38.7±7.5	19.7±10.8	37.6±11.8	43.4±12.7
(median; minimum; maximum)	28.0 (1.0; 55.0)	39.0 (31.0; 46.0)	19.0 (1.0; 40.0)	37.5 (18.0; 55.0)	51.0 (23.0; 52.0)
NA	14	-	14	-	-
Cognitive Assessment: trailmanking test (Part A: total correct) ('trla2')	34	3	18	8	5
(n; mean±sd)	24.4±2.2	25.0±0.0	23.9±2.9	25.0±0.0	24.8±0.4
(median; minimum; maximum)	25.0 (15.0; 25.0)	25.0 (25.0; 25.0)	25.0 (15.0; 25.0)	25.0 (25.0; 25.0)	25.0 (24.0; 25.0)
NA	17	-	15	2	-
(Part B: total correct) ('trlb2')	34	3	18	8	5
(n; mean±sd)	20.8±7.8	24.3±1.2	17.3±9.5	24.9±0.4	24.8±0.4

	All	Pre-manifest (<i>'hdcat=2'</i>)	Manifest (<i>'hdcat=3'</i>)	Genotype negative (<i>'hdcat=4'</i>)	Family Control (<i>'hdcat=5'</i>)
(median; minimum; maximum)	25.0 (0.0; 25.0)	25.0 (23.0; 25.0)	24.0 (0.0; 25.0)	25.0 (24.0; 25.0)	25.0 (24.0; 25.0)
NA	17	-	15	2	-
Cognitive Assessment: verbal fluency test (letters) completed (total correct) (<i>'verflt05'</i>)	35	3	17	10	5
(n; mean±sd)	26.3±15.8	35.0±6.2	14.0±7.4	37.3±16.2	41.2±5.2
(median; minimum; maximum)	25.0 (4.0; 66.0)	33.0 (30.0; 42.0)	13.0 (4.0; 36.0)	36.0 (6.0; 66.0)	42.0 (36.0; 48.0)
NA	16	-	16	-	-
PBA-s - depression score (<i>'depscore'</i>)	51	3	33	10	5
(n; mean±sd)	5.1±6.2	8.3±9.3	5.2±5.1	5.1±9.6	2.2±3.3
(median; minimum; maximum)	3.0 (0.0; 31.0)	4.0 (2.0; 19.0)	4.0 (0.0; 18.0)	0.5 (0.0; 31.0)	1.0 (0.0; 8.0)
NA	-	-	-	-	-
PBA-s - irritability score (<i>'irascore'</i>)	51	3	33	10	5
(n; mean±sd)	2.1±3.9	2.7±2.9	2.5±4.5	1.3±2.5	0.4±0.5
(median; minimum; maximum)	0.0 (0.0; 19.0)	1.0 (1.0; 6.0)	0.0 (0.0; 19.0)	0.0 (0.0; 6.0)	0.0 (0.0; 1.0)
NA	-	-	-	-	-
PBA-s - psychosis score (<i>'psyscore'</i>)	51	3	33	10	5
(n; mean±sd)	0.6±2.2	0.0±0.0	0.9±2.6	0.0±0.0	0.0±0.0
(median; minimum; maximum)	0.0 (0.0; 12.0)	0.0 (0.0; 0.0)	0.0 (0.0; 12.0)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
NA	-	-	-	-	-

	All	Pre-manifest (<i>'hdcat=2'</i>)	Manifest (<i>'hdcat=3'</i>)	Genotype negative (<i>'hdcat=4'</i>)	Family Control (<i>'hdcat=5'</i>)
PBA-s - apathy score (<i>'aptscore'</i>)	51	3	33	10	5
(n; mean±sd)	1.7±3.0	1.0±1.7	2.4±3.5	0.3±0.7	0.4±0.9
(median; minimum; maximum)	0.0 (0.0; 12.0)	0.0 (0.0; 3.0)	0.0 (0.0; 12.0)	0.0 (0.0; 2.0)	0.0 (0.0; 2.0)
NA	-	-	-	-	-
PBA-s - executive function score (<i>'exfscore'</i>)	51	3	33	10	5
(n; mean±sd)	2.3±4.3	0.0±0.0	3.5±4.9	0.0±0.0	0.0±0.0
(median; minimum; maximum)	0.0 (0.0; 16.0)	0.0 (0.0; 0.0)	0.0 (0.0; 16.0)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
NA	-	-	-	-	-
MMSE score (<i>'mmsetotal'</i>)	36	3	19	9	5
(n; mean±sd)	26.1±4.2	28.7±1.5	23.7±4.4	28.6±1.9	29.2±0.4
(median; minimum; maximum)	28.0 (15.0; 30.0)	29.0 (27.0; 30.0)	24.0 (15.0; 30.0)	29.0 (24.0; 30.0)	29.0 (29.0; 30.0)
NA	15	-	14	1	-
HADS-SIS – anxiety subscore (<i>'anxscore'</i>)	37	3	19	10	5
(n; mean±sd)	5.5±4.1	6.3±1.5	5.6±3.7	6.1±5.8	3.4±3.0
(median; minimum; maximum)	5.0 (0.0; 16.0)	6.0 (5.0; 8.0)	6.0 (0.0; 13.0)	4.5 (0.0; 16.0)	3.0 (0.0; 8.0)
NA	14	-	14	-	-
HADS-SIS – depression subscore (<i>'hads_depscore'</i>)	37	3	19	10	5
(n; mean±sd)	5.5±4.0	8.3±4.5	6.2±4.1	4.2±4.0	4.0±2.3
(median; minimum;					

	All	Pre-manifest (‘hdcats=2’)	Manifest (‘hdcats=3’)	Genotype negative (‘hdcats=4’)	Family Control (‘hdcats=5’)
maximum)	6.0 (0.0; 14.0)	8.0 (4.0; 13.0)	6.0 (0.0; 14.0)	4.0 (0.0; 10.0)	5.0 (0.0; 6.0)
NA	14	-	14	-	-
HADS-SIS – irritability subscore (‘irrscore’)	37	3	19	10	5
(n; mean±sd)	5.1±3.9	9.3±3.5	4.9±4.1	4.4±3.6	4.8±2.8
(median; minimum; maximum)	5.0 (0.0; 13.0)	9.0 (6.0; 13.0)	5.0 (0.0; 13.0)	4.0 (0.0; 12.0)	6.0 (1.0; 8.0)
NA	14	-	14	-	-

Table 15 – Clinical evaluation at baseline per region: NORTHERN AMERICA ('region=Northern America')

	All	Pre-manifest (<i>'hdc</i> at=2')	Manifest (<i>'hdc</i> at=3')	Genotype negative (<i>'hdc</i> at=4')	Family Control (<i>'hdc</i> at=5')
UHDRS '99 Motor (<i>'motscore'</i>)	3510	755	1504	635	616
(n; mean±sd)	17.0±20.4	4.4±5.3	35.7±18.3	2.3±4.6	1.9±3.1
(median; minimum; maximum)	7.0 (0.0; 107.0)	3.0 (0.0; 44.0)	33.0 (0.0; 107.0)	0.0 (0.0; 69.0)	0.0 (0.0; 19.0)
NA	17	3	7	4	3
UHDRS '99 DCL (<i>'diagconf'</i>)	1289 (36.6%)	333 (43.9%)	3 (0.2%)	453 (70.9%)	500 (81.0%)
0 (<i>'diagconf=0'</i>) (n; %)	543 (15.4%)	252 (33.2%)	18 (1.2%)	159 (24.9%)	114 (18.5%)
1 (<i>'diagconf=1'</i>) (n; %)	153 (4.3%)	104 (13.7%)	29 (1.9%)	17 (2.7%)	3 (0.5%)
2 (<i>'diagconf=2'</i>) (n; %)	110 (3.1%)	58 (7.7%)	44 (2.9%)	8 (1.3%)	0 (0.0%)
3 (<i>'diagconf=3'</i>) (n; %)	1430 (40.6%)	11 (1.5%)	1417 (93.8%)	2 (0.3%)	0 (0.0%)
4 (<i>'diagconf=4'</i>) (n; %)	2	-	-	-	2
NA					
UHDRS '99 Total Functional Capacity (<i>'tfcscore'</i>)	3518	755	1507	638	618
(n; mean±sd)	10.9±3.1	12.6±1.1	8.4±3.2	12.8±0.8	12.9±0.5
(median; minimum; maximum)					

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
NA	13.0 (0.0; 13.0)	13.0 (0.0; 13.0)	9.0 (0.0; 13.0)	13.0 (1.0; 13.0)	13.0 (9.0; 13.0)
	9	3	4	1	1
UHDRS ‘99 Function Assessment Scale (‘fascore’)	3519	757	1507	637	618
(n; mean±sd)	22.4±4.7	24.7±1.0	19.1±5.7	24.9±1.0	24.9±0.5
(median; minimum; maximum)	25.0 (0.0; 25.0)	25.0 (17.0; 25.0)	21.0 (0.0; 25.0)	25.0 (5.0; 25.0)	25.0 (20.0; 25.0)
NA	8	1	4	2	1
UHDRS ‘99 Independence Scale (‘indepscl’)	3521	757	1508	638	618
(n; mean±sd)	90.8±14.3	98.6±4.4	79.5±15.5	99.5±3.2	99.7±1.6
(median; minimum; maximum)	100.0 (5.0; 100.0)	100.0 (70.0; 100.0)	80.0 (5.0; 100.0)	100.0 (45.0; 100.0)	100.0 (85.0; 100.0)
NA	6	1	3	1	1
Cognitive Assessment: symbol digit modality test (total correct) (‘sdmt1’)	3413	752	1411	632	618
(n; mean±sd)	40.6±16.9	49.9±12.4	26.3±12.1	53.2±11.1	49.1±10.9
(median; minimum; maximum)	43.0 (0.0; 101.0)	51.0 (0.0; 101.0)	25.0 (0.0; 92.0)	53.0 (0.0; 92.0)	50.0 (1.0; 92.0)
NA	114	6	100	7	1
Cognitive Assessment: verbal fluency test (category) completed (total correct) (‘verfct5’)	3469	751	1472	634	612
(n; mean±sd)	17.6±6.9	20.8±5.9	12.8±5.5	21.6±5.5	21.2±5.2
(median; minimum; maximum)	18.0 (0.0; 55.0)	20.0 (7.0; 55.0)	12.0 (0.0; 34.0)	21.0 (3.0; 48.0)	21.0 (7.0; 43.0)
NA		7	39	5	7

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
	58				
Cognitive Assessment: stroop colour naming test (total correct) (‘sct1’)	3439	748	1456	627	608
(n; mean±sd)	62.7±21.4	73.5±16.2	46.0±16.6	77.1±15.1	74.4±14.2
(median; minimum; maximum)	64.0 (0.0; 140.0)	74.0 (24.0; 136.0)	45.0 (0.0; 120.0)	77.0 (0.0; 140.0)	74.0 (39.0; 129.0)
NA	88	10	55	12	11
Cognitive Assessment: stroop word reading test (total correct) (‘swrt1’)	3436	750	1450	627	609
(n; mean±sd)	79.0±26.4	92.4±20.4	58.8±21.7	96.2±18.4	92.8±16.4
(median; minimum; maximum)	81.5 (0.0; 199.0)	94.0 (6.0; 177.0)	58.0 (0.0; 199.0)	97.0 (0.0; 168.0)	93.0 (37.0; 160.0)
NA	91	8	61	12	10
Cognitive Assessment: stroop interference test (total correct) (‘sit1’)	3104	695	1250	588	571
(n; mean±sd)	36.3±15.3	43.6±12.0	26.2±11.4	44.8±17.5	40.9±11.1
(median; minimum; maximum)	36.0 (0.0; 374.0)	44.0 (8.0; 93.0)	25.0 (0.0; 93.0)	44.0 (0.0; 374.0)	40.0 (0.0; 119.0)
NA	423	63	261	51	48
Cognitive Assessment: trailmanking test (Part A: total correct) (‘trla2’)	2740	636	1034	553	517
(n; mean±sd)	24.7±2.5	24.6±3.3	24.6±3.0	24.9±1.1	24.9±1.5

	All	Pre-manifest (<i>'hdcats=2'</i>)	Manifest (<i>'hdcats=3'</i>)	Genotype negative (<i>'hdcats=4'</i>)	Family Control (<i>'hdcats=5'</i>)
NA	25.0 (0.0; 27.0)	25.0 (0.0; 25.0)	25.0 (0.0; 25.0)	25.0 (0.0; 27.0)	25.0 (0.0; 25.0)
	787	122	477	86	102
(Part B: total correct) (<i>'trib2'</i>)	2702	636	1001	551	514
(n; mean±sd)	23.7±6.4	24.5±3.5	22.3±9.5	24.5±3.4	24.8±2.0
(median; minimum; maximum)	25.0 (0.0; 240.0)	25.0 (0.0; 26.0)	25.0 (0.0; 240.0)	25.0 (0.0; 29.0)	25.0 (0.0; 25.0)
NA	825	122	510	88	105
Cognitive Assessment: verbal fluency test (letters) completed (total correct) (<i>'verflt05'</i>)	2698	622	1030	539	507
(n; mean±sd)	35.3±15.5	40.5±13.3	24.9±13.5	43.4±13.2	41.4±12.4
(median; minimum; maximum)	35.0 (0.0; 94.0)	40.0 (9.0; 84.0)	23.0 (0.0; 77.0)	43.0 (0.0; 82.0)	40.0 (8.0; 94.0)
NA	829	136	481	100	112
PBA-s - depression score (<i>'depscore'</i>)	3514	755	1502	639	618
(n; mean±sd)	4.2±6.0	4.7±6.4	5.0±6.5	2.9±5.0	3.2±4.8
(median; minimum; maximum)	2.0 (0.0; 44.0)	2.0 (0.0; 41.0)	2.0 (0.0; 41.0)	0.0 (0.0; 32.0)	1.0 (0.0; 44.0)
NA	13	3	9	-	1
PBA-s - irritability score (<i>'irascore'</i>)	3516	754	1508	637	617
(n; mean±sd)	2.2±4.0	2.1±3.7	3.0±4.8	1.1±2.9	1.3±2.6
(median; minimum; maximum)	0.0 (0.0; 32.0)	0.0 (0.0; 32.0)	1.0 (0.0; 32.0)	0.0 (0.0; 21.0)	0.0 (0.0; 28.0)
NA	11	4	3	2	2

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
PBA-s - psychosis score (‘psyscore’)	3517	756	1505	638	618
(n; mean±sd)	0.2±1.2	0.2±1.5	0.2±1.3	0.1±1.2	0.0±0.4
(median; minimum; maximum)	0.0 (0.0; 20.0)	0.0 (0.0; 18.0)	0.0 (0.0; 20.0)	0.0 (0.0; 18.0)	0.0 (0.0; 9.0)
NA	10	2	6	1	1
PBA-s - apathy score (‘aptscore’)	3518	754	1507	639	618
(n; mean±sd)	1.5±3.2	1.3±2.9	2.6±4.0	0.5±1.8	0.4±1.5
(median; minimum; maximum)	0.0 (0.0; 16.0)	0.0 (0.0; 16.0)	0.0 (0.0; 16.0)	0.0 (0.0; 12.0)	0.0 (0.0; 16.0)
NA	9	4	4	-	1
PBA-s - executive function score (‘exfscore’)	3517	755	1505	639	618
(n; mean±sd)	1.8±3.9	1.5±3.5	2.9±4.7	0.7±2.5	0.5±2.3
(median; minimum; maximum)	0.0 (0.0; 28.0)	0.0 (0.0; 20.0)	0.0 (0.0; 28.0)	0.0 (0.0; 25.0)	0.0 (0.0; 24.0)
NA	10	3	6	-	1
MMSE score (‘mmsetotal’)	2603	593	1030	514	466
(n; mean±sd)	27.6±2.9	28.5±1.7	25.9±3.4	29.0±1.4	28.7±1.6
(median; minimum; maximum)	29.0 (8.0; 30.0)	29.0 (16.0; 30.0)	27.0 (8.0; 30.0)	30.0 (19.0; 30.0)	29.0 (18.0; 30.0)
NA	924	165	481	125	153
HADS-SIS – anxiety subscore (‘anxscore’)	2357	524	886	492	455
(n; mean±sd)	5.7±4.2	6.2±4.4	6.0±4.4	5.0±3.9	5.1±3.5
(median; minimum; maximum)	5.0 (0.0; 21.0)	5.0 (0.0; 21.0)	5.5 (0.0; 21.0)	4.0 (0.0; 21.0)	4.0 (0.0; 17.0)

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
NA	1170	234	625	147	164
HADS-SIS – depression subscore (‘hads_depscore’)	2355	523	886	492	454
(n; mean±sd)	4.0±3.6	3.7±3.6	5.4±4.0	2.7±2.9	3.2±2.8
(median; minimum; maximum)	3.0 (0.0; 20.0)	3.0 (0.0; 17.0)	5.0 (0.0; 20.0)	2.0 (0.0; 15.0)	3.0 (0.0; 16.0)
NA	1172	235	625	147	165
HADS-SIS – irritability subscore (‘irrscore’)	2358	523	888	493	454
(n; mean±sd)	5.0±4.1	5.2±4.1	5.9±4.7	4.1±3.5	4.1±3.1
(median; minimum; maximum)	4.0 (0.0; 24.0)	4.0 (0.0; 23.0)	5.0 (0.0; 24.0)	3.0 (0.0; 21.0)	3.0 (0.0; 16.0)
NA	1169	235	623	146	165

Table 16 – Clinical evaluation at baseline per region: AUSTRALASIA ('region=Australasia')

	All	Pre-manifest (<i>'hdcat=2'</i>)	Manifest (<i>'hdcat=3'</i>)	Genotype negative (<i>'hdcat=4'</i>)	Family Control (<i>'hdcat=5'</i>)
UHDRS '99 Motor (<i>'motscore'</i>)	322	120	142	36	24
(n; mean±sd)	16.2±20.0	2.7±3.9	33.4±18.7	2.2±4.1	2.2±3.4
(median; minimum; maximum)	6.0 (0.0; 94.0)	1.0 (0.0; 19.0)	30.0 (1.0; 94.0)	1.0 (0.0; 19.0)	1.0 (0.0; 15.0)
NA	2	-	2	-	-
UHDRS '99 DCL (<i>'diagconf'</i>)					
0 (<i>'diagconf=0'</i>) (n; %)	115 (35.5%)	77 (64.2%)	0 (0.0%)	22 (61.1%)	16 (66.7%)
1 (<i>'diagconf=1'</i>) (n; %)	47 (14.5%)	25 (20.8%)	0 (0.0%)	14 (38.9%)	8 (33.3%)
2 (<i>'diagconf=2'</i>) (n; %)	15 (4.6%)	14 (11.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)
3 (<i>'diagconf=3'</i>) (n; %)	8 (2.5%)	4 (3.3%)	4 (2.8%)	0 (0.0%)	0 (0.0%)
4 (<i>'diagconf=4'</i>) (n; %)	139 (42.9%)	0 (0.0%)	139 (96.5%)	0 (0.0%)	0 (0.0%)
NA	-	-	-	-	-
UHDRS '99 Total Functional Capacity (<i>'tfcscore'</i>)					
(n; mean±sd)	323	120	143	36	24
(median; minimum; maximum)	10.9±3.2	12.8±0.8	8.6±3.5	12.8±1.3	12.9±0.3

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
maximum)	13.0 (0.0; 13.0)	13.0 (9.0; 13.0)	9.0 (0.0; 13.0)	13.0 (5.0; 13.0)	13.0 (12.0; 13.0)
NA	1	-	1	-	-
UHDRS ‘99 Function Assessment Scale (‘fascor’) (n; mean±sd)	324 22.0±5.3	120 24.8±0.7	144 18.6±6.4	36 24.6±1.9	24 25.0±0.2
(median; minimum; maximum)	25.0 (0.0; 25.0)	25.0 (21.0; 25.0)	21.0 (0.0; 25.0)	25.0 (14.0; 25.0)	25.0 (24.0; 25.0)
NA	-	-	-	-	-
UHDRS ‘99 Independence Scale (‘indep scl’) (n; mean±sd)	324 90.6±15.2	120 99.2±3.1	144 79.8±16.9	36 98.8±7.5	24 100.0±0.0
(median; minimum; maximum)	100.0 (20.0; 100.0)	100.0 (80.0; 100.0)	80.0 (20.0; 100.0)	100.0 (55.0; 100.0)	100.0 (100.0; 100.0)
NA	-	-	-	-	-
Cognitive Assessment: symbol digit modality test (total correct) (‘sdmt1’) (n; mean±sd)	315 38.9±16.4	120 48.3±12.0	135 26.2±12.4	36 48.7±13.3	24 49.1±9.4
(median; minimum; maximum)	40.0 (0.0; 84.0)	48.5 (20.0; 84.0)	25.0 (0.0; 74.0)	48.5 (7.0; 69.0)	49.0 (30.0; 69.0)
NA	9	-	9	-	-
Cognitive Assessment: verbal fluency test (category) completed (total correct) (‘verfct5’) (n; mean±sd)	321 17.5±7.2	120 21.1±5.5	141 12.5±5.6	36 22.4±7.5	24 21.3±4.0
(median; minimum; maximum)	18.0 (1.0; 40.0)	20.5 (6.0; 35.0)	12.0 (1.0; 29.0)	23.0 (4.0; 40.0)	21.0 (15.0; 32.0)
NA	3	-	3	-	-

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
Cognitive Assessment: stroop colour naming test (total correct) (‘scnt1’)	320	120	140	36	24
(n; mean±sd)	60.1±20.0	70.2±15.3	45.7±14.8	73.6±19.8	73.0±12.5
(median; minimum; maximum)	60.5 (0.0; 104.0)	71.0 (20.0; 100.0)	46.0 (14.0; 95.0)	77.0 (0.0; 98.0)	72.0 (56.0; 104.0)
NA	4	-	4	-	-
Cognitive Assessment: stroop word reading test (total correct) (‘swrt1’)	321	120	141	36	24
(n; mean±sd)	76.7±24.1	89.5±17.2	59.5±20.4	91.7±20.3	91.3±13.6
(median; minimum; maximum)	79.0 (18.0; 137.0)	89.5 (50.0; 137.0)	59.0 (18.0; 126.0)	94.0 (21.0; 122.0)	91.0 (64.0; 124.0)
NA	3	-	3	-	-
Cognitive Assessment: stroop interference test (total correct) (‘sit1’)	291	115	117	35	24
(n; mean±sd)	33.9±13.1	39.7±10.8	24.4±10.6	41.5±9.9	41.1±10.0
(median; minimum; maximum)	33.0 (0.0; 76.0)	39.0 (11.0; 76.0)	23.0 (0.0; 62.0)	41.0 (8.0; 58.0)	41.0 (25.0; 58.0)
NA	33	5	27	1	-
Cognitive Assessment: trailmanking test (Part A: total correct) (‘trla2’)	281	114	109	35	23
(n; mean±sd)	25.0±0.1	25.0±0.0	25.0±0.1	25.0±0.0	25.0±0.0
(median; minimum; maximum)	25.0 (24.0; 25.0)	25.0 (25.0; 25.0)	25.0 (24.0; 25.0)	25.0 (25.0; 25.0)	25.0 (25.0; 25.0)
NA	43	6	35	1	1
(Part B: total correct) (‘trlb2’)	279	114	107	35	23
	24.9±13.4	24.6±2.8	25.2±21.6	25.0±0.0	25.0±0.0

	All	Pre-manifest (‘hdcats=2’)	Manifest (‘hdcats=3’)	Genotype negative (‘hdcats=4’)	Family Control (‘hdcats=5’)
(n; mean±sd)	25.0 (0.0; 240.0)	25.0 (1.0; 25.0)	25.0 (0.0; 240.0)	25.0 (25.0; 25.0)	25.0 (25.0; 25.0)
(median; minimum; maximum)	45	6	37	1	1
NA					
Cognitive Assessment: verbal fluency test (letters) completed (total correct) (‘verflt05’)	285	114	112	35	24
(n; mean±sd)	33.5±15.7	39.7±13.3	23.3±13.7	37.3±12.9	46.3±11.2
(median; minimum; maximum)	34.0 (3.0; 78.0)	39.0 (8.0; 78.0)	19.0 (3.0; 65.0)	35.0 (16.0; 63.0)	45.0 (22.0; 70.0)
NA	39	6	32	1	-
PBA-s - depression score (‘depscore’)	324	120	144	36	24
(n; mean±sd)	4.2±5.0	4.3±5.2	4.1±4.9	4.7±5.7	3.5±4.6
(median; minimum; maximum)	2.0 (0.0; 24.0)	3.0 (0.0; 23.0)	2.0 (0.0; 22.0)	3.5 (0.0; 24.0)	2.0 (0.0; 18.0)
NA	-	-	-	-	-
PBA-s - irritability score (‘irascore’)	324	120	144	36	24
(n; mean±sd)	2.0±3.5	1.8±3.0	2.2±4.2	1.8±2.3	1.8±2.2
(median; minimum; maximum)	0.0 (0.0; 28.0)	0.0 (0.0; 15.0)	0.0 (0.0; 28.0)	0.0 (0.0; 8.0)	1.0 (0.0; 8.0)
NA	-	-	-	-	-
PBA-s - psychosis score (‘pyscore’)	323	119	144	36	24
(n; mean±sd)	0.2±1.3	0.0±0.0	0.3±1.8	0.4±1.7	0.0±0.0
(median; minimum; maximum)	0.0 (0.0; 16.0)	0.0 (0.0; 0.0)	0.0 (0.0; 16.0)	0.0 (0.0; 10.0)	0.0 (0.0; 0.0)

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
NA	1	1	-	-	-
PBA-s - apathy score (‘aptscore’)	324	120	144	36	24
(n; mean±sd)	1.4±2.7	0.8±1.8	2.2±3.4	0.3±0.8	0.7±1.5
(median; minimum; maximum)	0.0 (0.0; 12.0)	0.0 (0.0; 9.0)	0.0 (0.0; 12.0)	0.0 (0.0; 4.0)	0.0 (0.0; 6.0)
NA	-	-	-	-	-
PBA-s - executive function score (‘exfscore’)	323	120	143	36	24
(n; mean±sd)	1.6±3.6	0.8±2.0	2.5±4.7	1.4±3.3	0.5±2.0
(median; minimum; maximum)	0.0 (0.0; 28.0)	0.0 (0.0; 9.0)	0.0 (0.0; 28.0)	0.0 (0.0; 16.0)	0.0 (0.0; 10.0)
NA	1	-	1	-	-
MMSE score (‘mmsetotal’)	266	106	107	33	20
(n; mean±sd)	27.0±2.9	28.0±1.8	25.2±3.2	28.5±2.1	28.4±1.4
(median; minimum; maximum)	28.0 (13.0; 30.0)	28.0 (22.0; 30.0)	26.0 (13.0; 30.0)	29.0 (22.0; 30.0)	28.0 (26.0; 30.0)
NA	58	14	37	3	4
HADS-SIS – anxiety subscore (‘anxscore’)	277	111	108	35	23
(n; mean±sd)	4.9±3.7	4.8±3.5	5.1±4.1	4.6±3.3	4.9±3.2
(median; minimum; maximum)	4.0 (0.0; 20.0)	4.0 (0.0; 15.0)	4.0 (0.0; 20.0)	5.0 (0.0; 12.0)	4.0 (0.0; 10.0)
NA	47	9	36	1	1
HADS-SIS – depression subscore (‘hads_depscore’)	276	111	107	35	23
(n; mean±sd)	3.3±3.3	2.8±2.8	4.7±3.8	1.7±2.2	2.0±1.9

	All	Pre-manifest (‘hdcats=2’)	Manifest (‘hdcats=3’)	Genotype negative (‘hdcats=4’)	Family Control (‘hdcats=5’)
(median; minimum; maximum)	2.5 (0.0; 18.0)	2.0 (0.0; 14.0)	4.0 (0.0; 18.0)	1.0 (0.0; 8.0)	2.0 (0.0; 8.0)
NA	48	9	37	1	1
HADS-SIS – irritability subscore (‘irrscore’)	276	110	108	35	23
(n; mean±sd)	4.9±3.7	4.7±3.7	5.6±4.0	3.7±2.8	4.7±3.1
(median; minimum; maximum)	4.0 (0.0; 21.0)	4.0 (0.0; 18.0)	5.0 (0.0; 21.0)	3.0 (0.0; 12.0)	5.0 (0.0; 11.0)
NA	48	10	36	1	1

Discontinuations

Table 17 – End of study or reportable events

	All	Pre-manifest (‘hdcat=2’)	Manifest (‘hdcat=3’)	Genotype negative (‘hdcat=4’)	Family Control (‘hdcat=5’)
End of study:	465 (5.3%)	38 (2.0%)	305 (6.4%)	46 (4.2%)	76 (7.5%)
Reasons (‘dsterm’):					
Event or intercurrent illness (‘dsterm=1’)	27 (5.8%)	-	27 (8.9%)	-	-
Primary care physician’s, site investigator’s request (‘dsterm=2’)	8 (1.7%)	-	6 (2.0%)	2 (4.3%)	-
Participant’s request (‘dsterm=3’)					
Lost to follow up (‘dsterm=4’)	245 (52.7%)	19 (50.0%)	154 (50.5%)	21 (45.7%)	51 (67.1%)
Institucionalized (‘dsterm=5’)	102 (21.9%)	17 (44.7%)	51 (16.7%)	20 (43.5%)	14 (18.4%)
Other (‘dsterm=6’)					
	32 (6.9%)	-	32 (10.5%)	-	-
	51 (11.0%)	2 (5.3%)	35 (11.5%)	3 (6.5%)	11 (14.5%)
Reportable events (‘evtnum’):	112	3	105	3	1

Table 18 – End of study reportable events

	All	HDGEC's (‘hdcat=2 & 3’)	Controls (‘hdcat=4 & 5’)
Premature discontinuation:	465 (5.3%)	343 (5.2%)	122 (5.8%)
Reasons (‘dsterm’):			
Event or intercurrent illness (‘dsterm=1’)	27 (5.8%)	27 (7.9%)	-
Primary care physician’s, site investigator’s request (‘dsterm=2’)			
Participant’s request (‘dsterm=3’)	8 (1.7%)	6 (1.7%)	2 (1.6%)
Lost to follow up (‘dsterm=4’)	245 (52.7%)	173 (50.4%)	72 (59.0%)
Institucionalized (‘dsterm=5’)			
Other (‘dsterm=6’)	102 (21.9%)	68 (19.8%)	34 (27.9%)
	32 (6.9%)	32 (9.3%)	-
	51 (11.0%)	37 (10.8%)	14 (11.5%)
Reportable events (‘evtnum’):	112	108	4

APPENDIX: Clinical outcomes distribution by HD category and CAP score.

Notes

Boxplots: Outlying data points are represented by 'o' and '*' symbols, the former representing values $\pm 2 \times$ interquartile range (IQR), the latter representing values $\pm 3 \times$ IQR (i.e., extreme outliers).

Scatterplots: These figures feature data from HDGEC participants only.

1. Total Motor Score analysis

Figure 33: distribution of total motor score by HD category

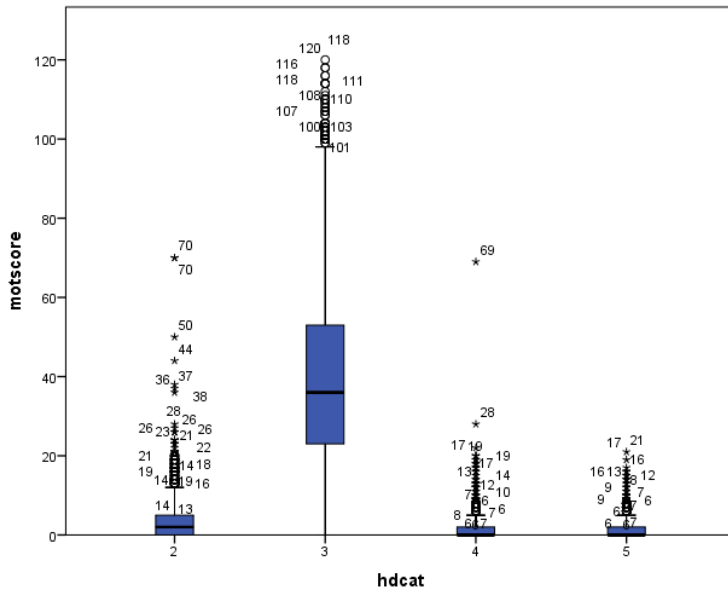
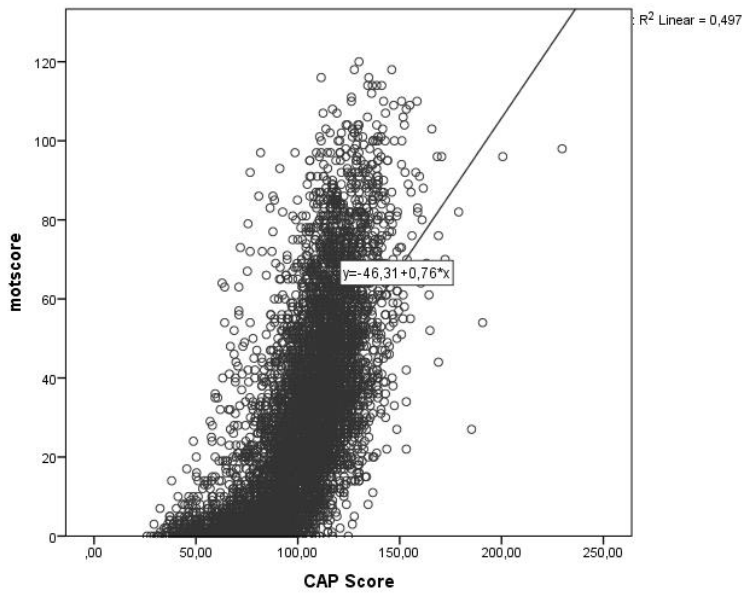


Figure 34: distribution of total motor score by CAP score



2. Diagnosis Confidence Level analysis

Figure 35: distribution of diagnosis confidence level by HD category

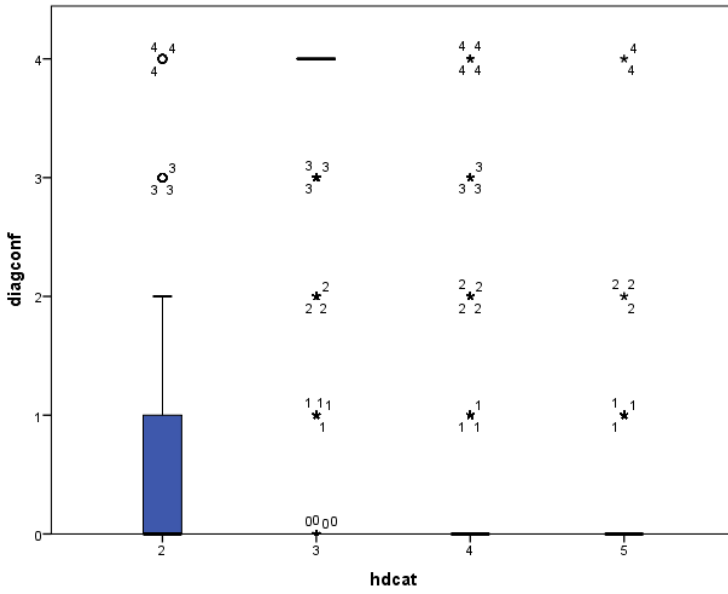
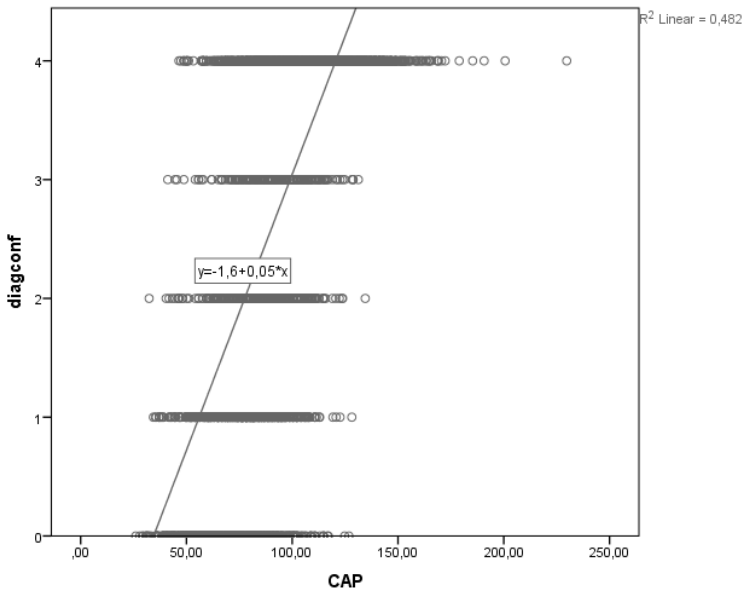


Figure 36: distribution of diagnosis confidence level by CAP score



3. Total Functional Capacity

Figure 37: distribution of total functional capacity by HD category

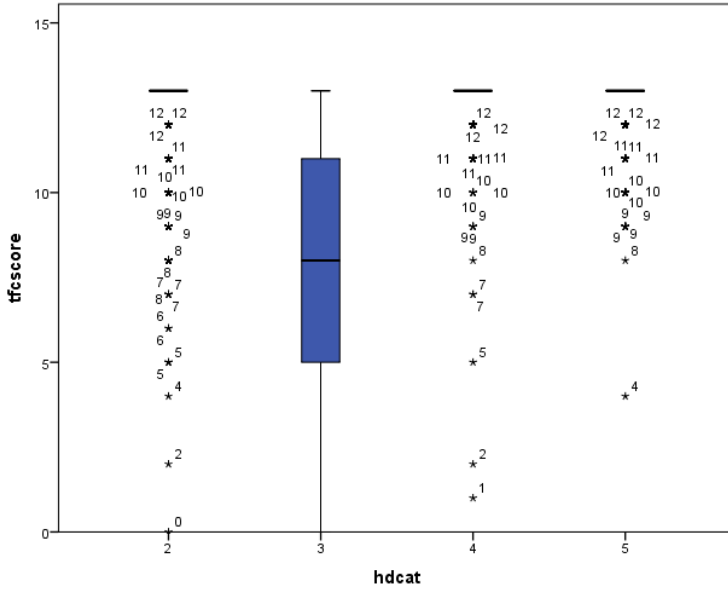
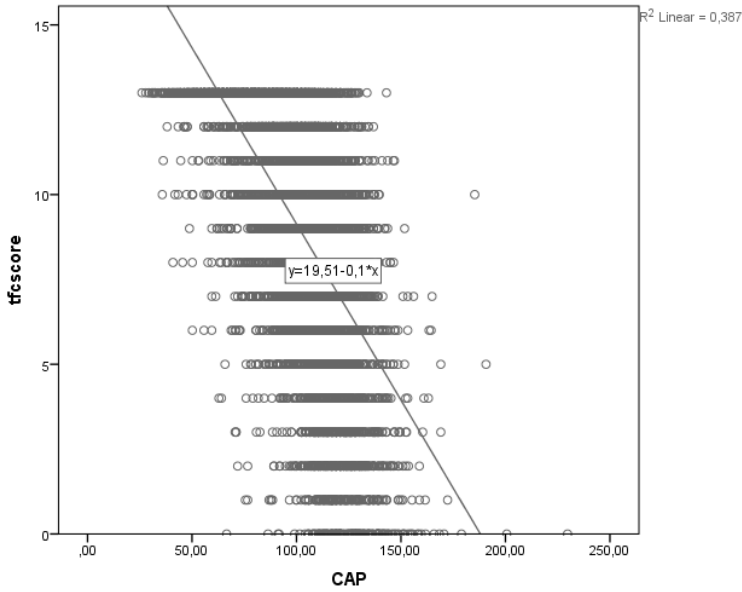


Figure 38: distribution of total functional capacity by CAP score



4. Functional Assessment score

Figure 39: distribution of functional assessment score by HD category

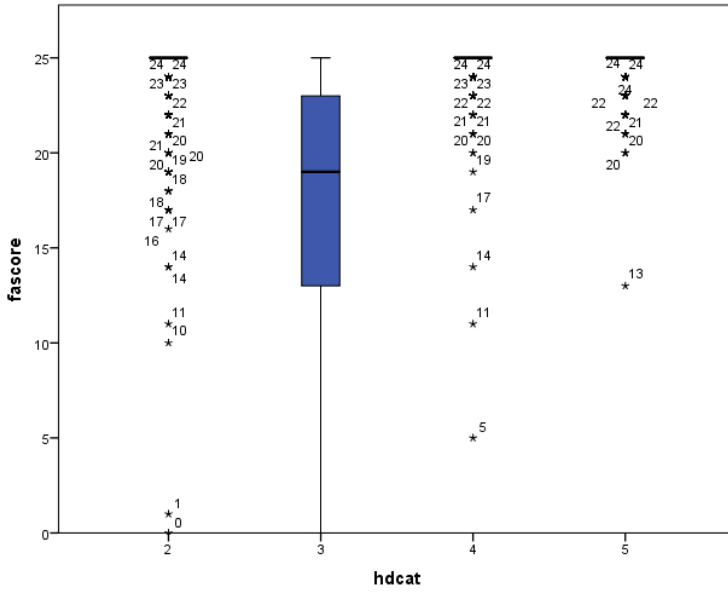
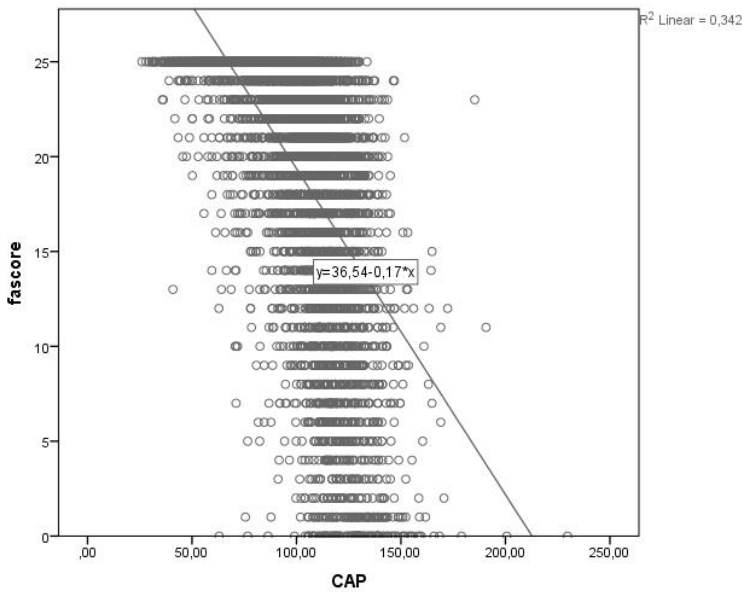


Figure 40: distribution of functional assessment score by CAP score



5. Independent scale

Figure 41: distribution of independent scale by HD category

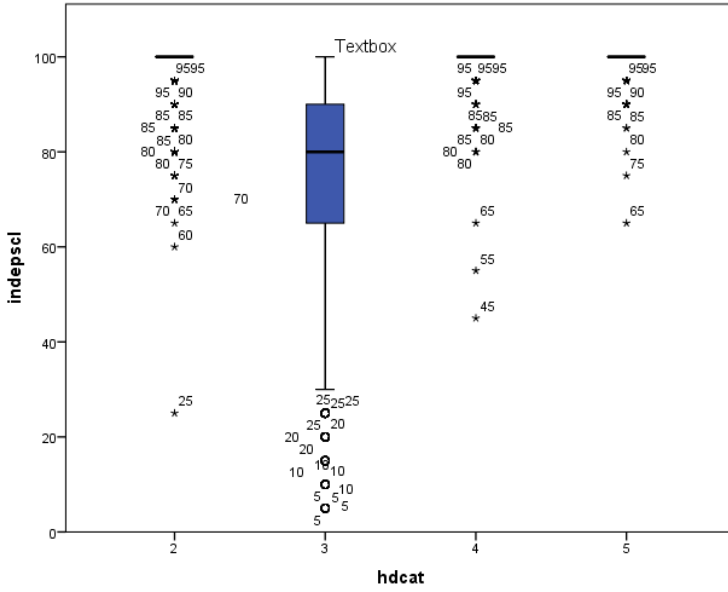
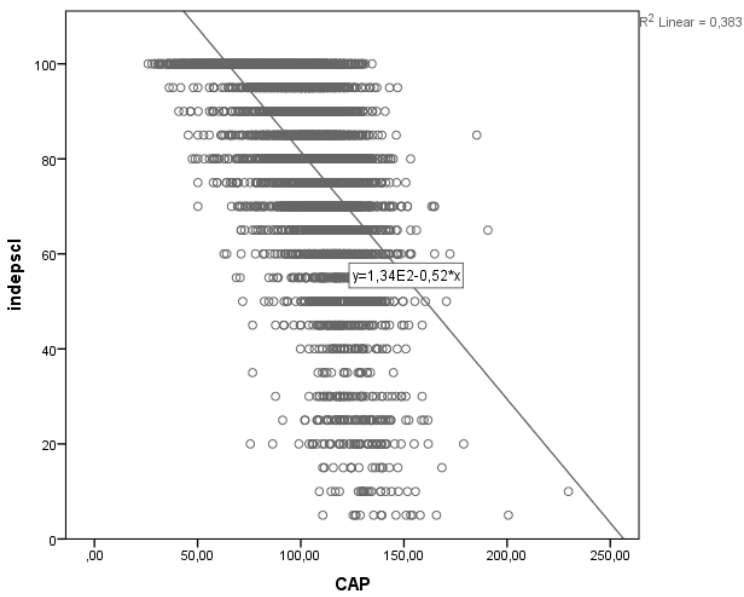


Figure 42: distribution of independent scale by CAP score



6. Symbol digit modality test

Figure 43: distribution of symbol digit modality test by HD category

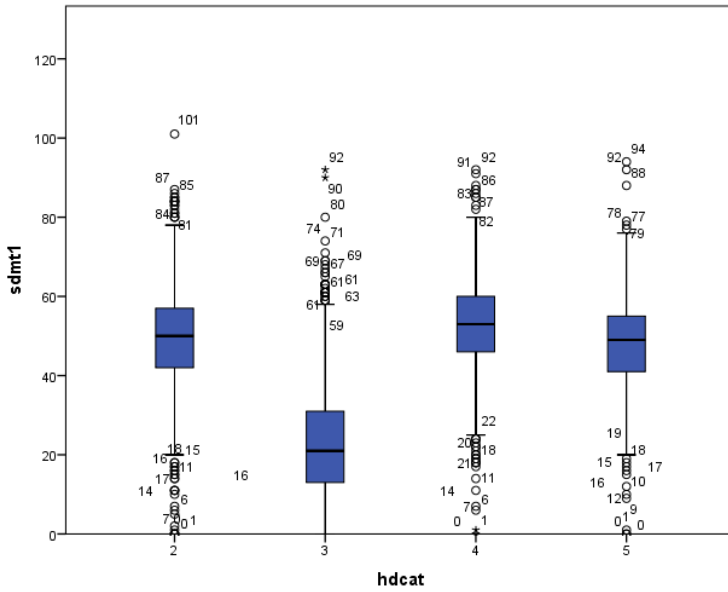
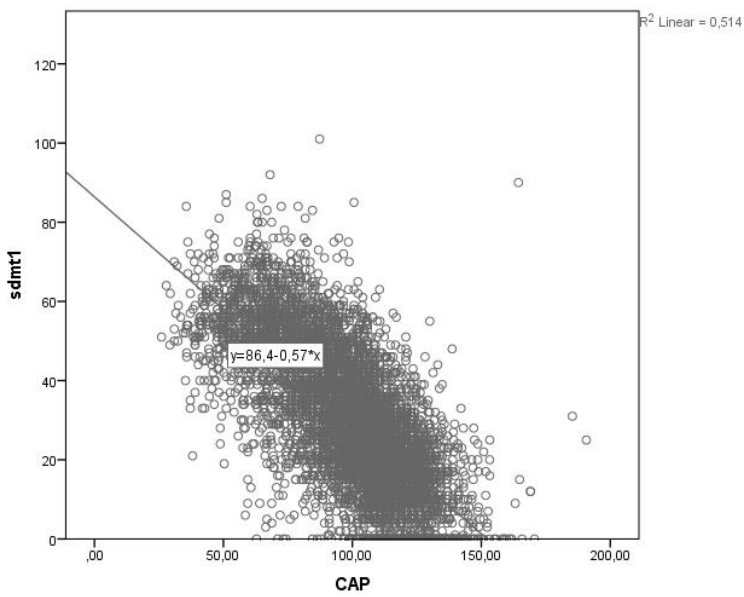


Figure 44: distribution of symbol digit modality test by CAP score



7. Categorical Verbal Fluency (Total correct (1 min))

Figure 45: distribution of verbal fluency capacity test by HD category

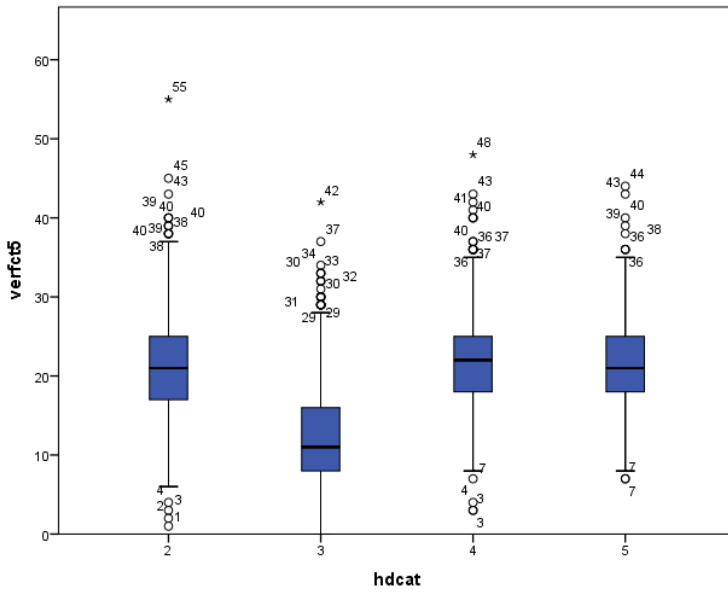
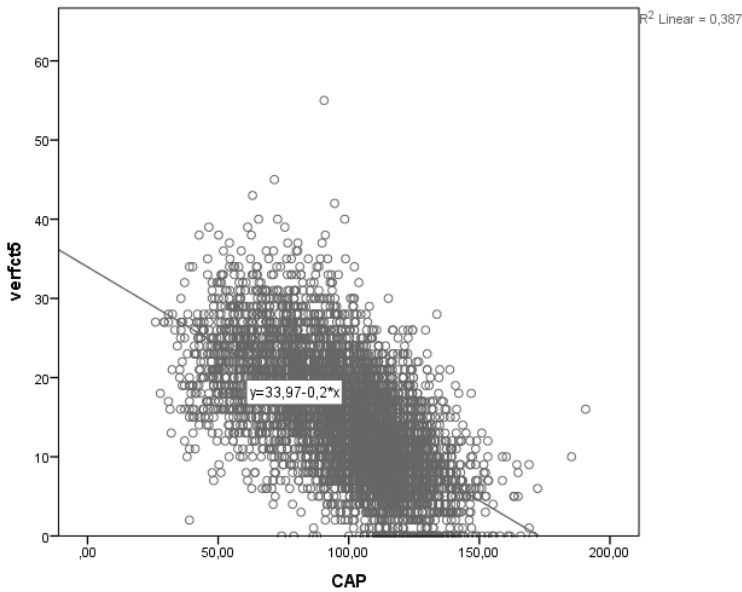


Figure 46: distribution of verbal fluency capacity test by CAP score



8. Stroop Color Naming (total correct)

Figure 47: distribution of Stroop Color Naming by HD category

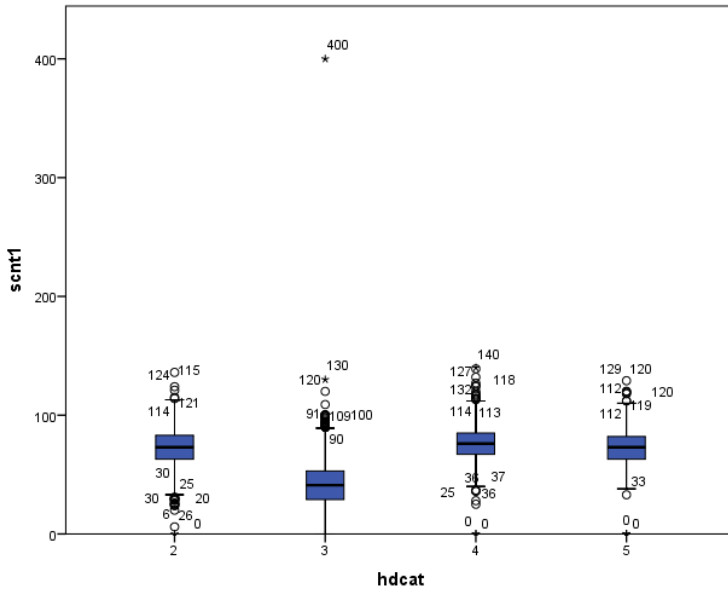
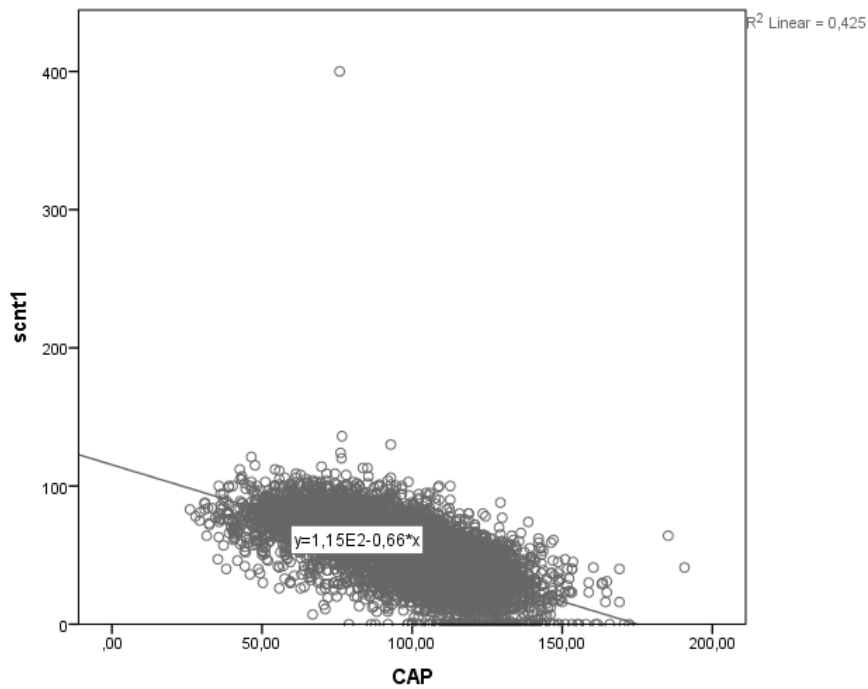


Figure 48: distribution of Stroop Color Naming by CAP score



9. Executive function_PBA-s

Figure 49: distribution of Executive function by HD category

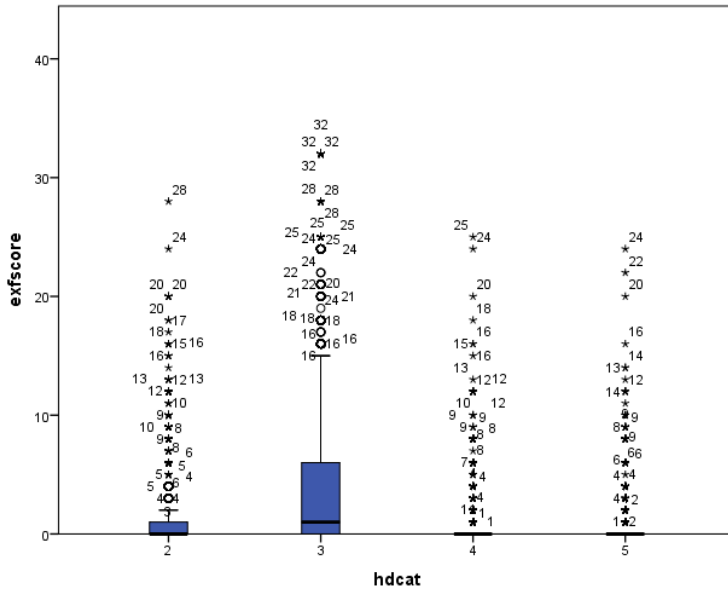
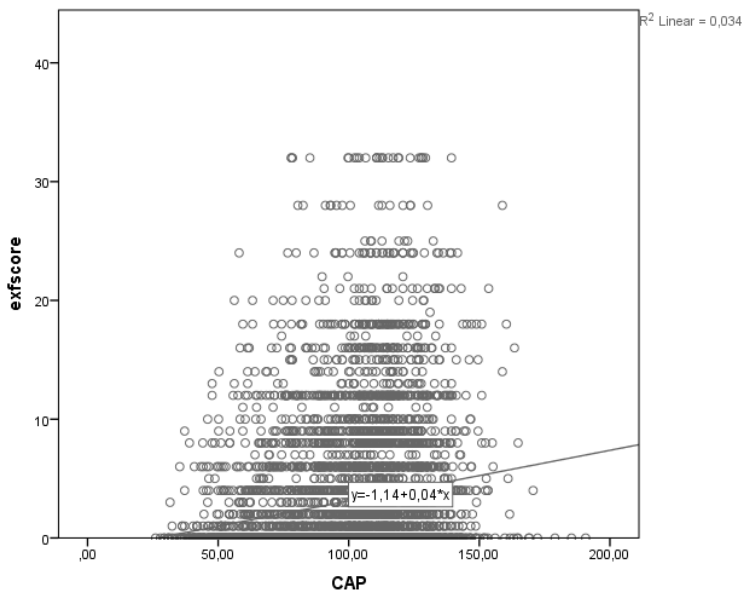


Figure 50: distribution of Executive function by CAP score



10. Minimental Score (MMSE)

Figure 51: distribution of MMSE by HD category

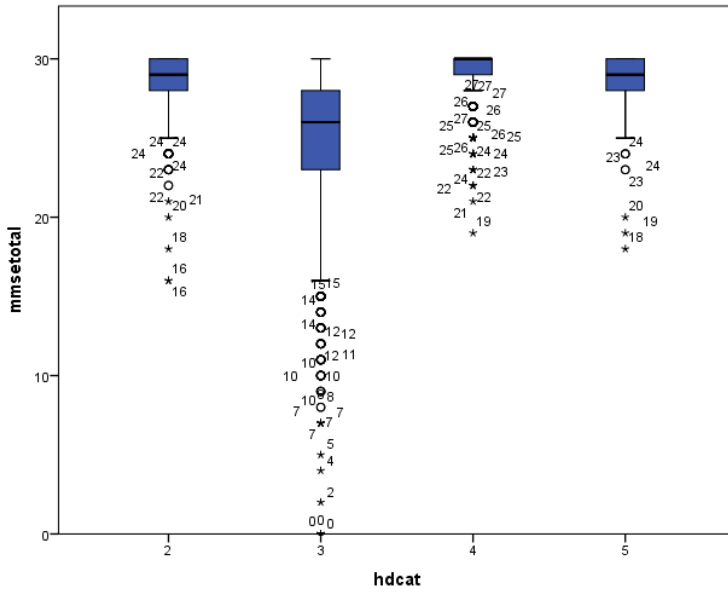
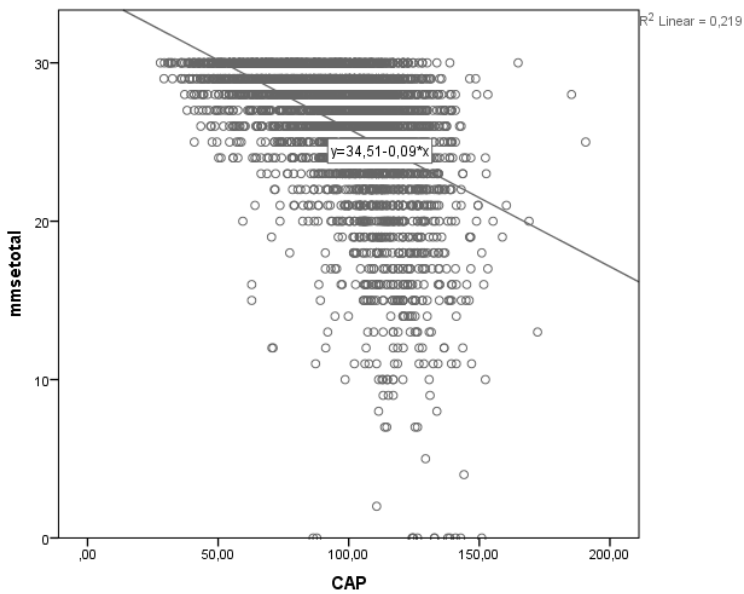


Figure 52: distribution of MMSE by CAP score



11. Anxiety subscore_HADS-SIS

Figure 53: distribution of Anxiety subscore by HD category

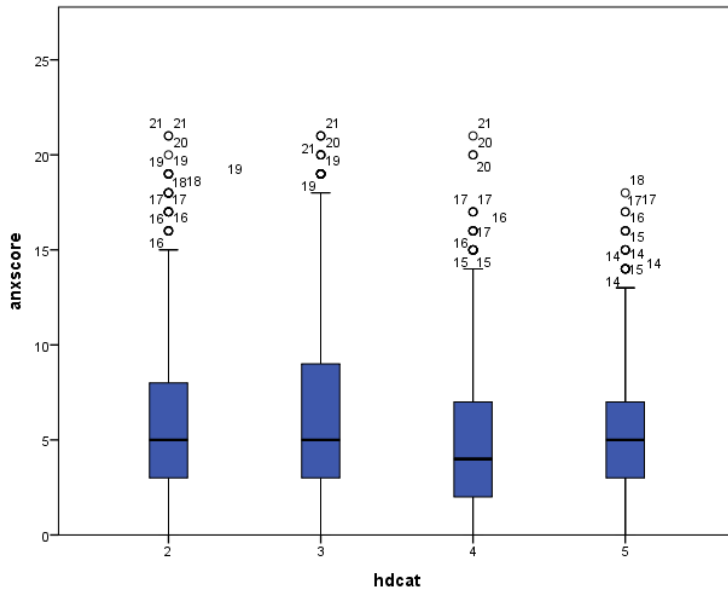
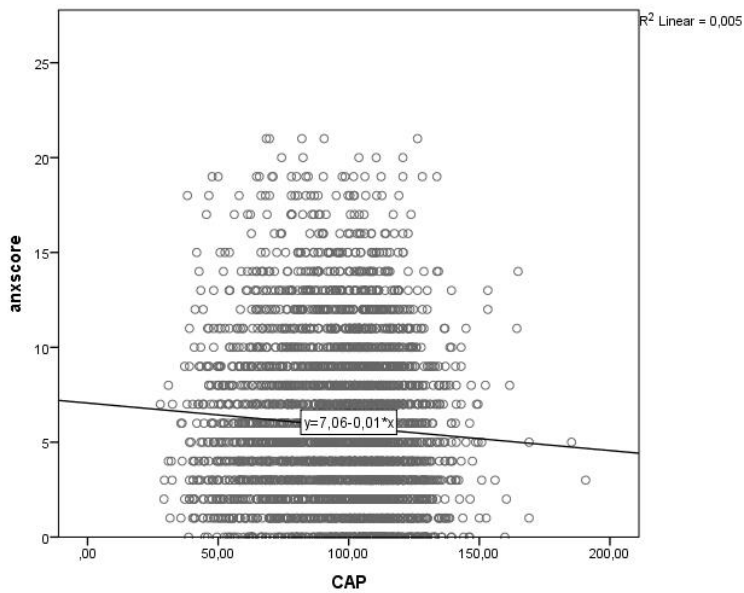


Figure 54: distribution of Anxiety subscore by CAP score



12. Depression subscore

Figure 55: distribution of depression subscore by HD category

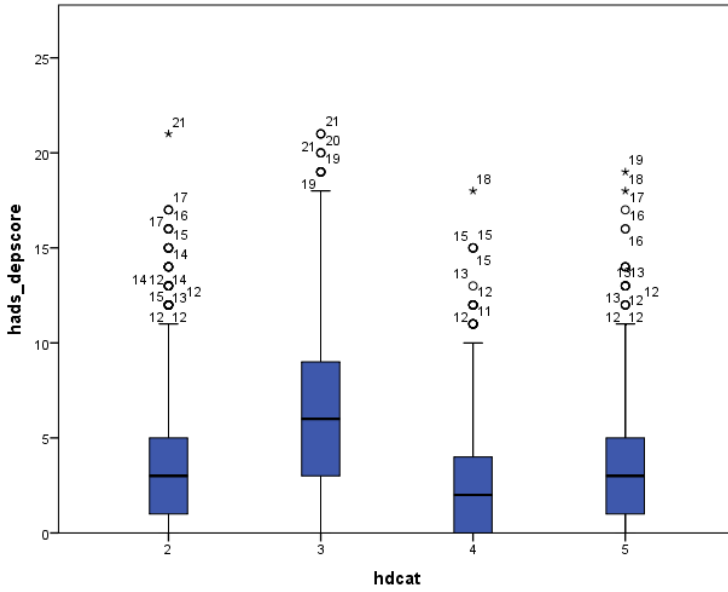
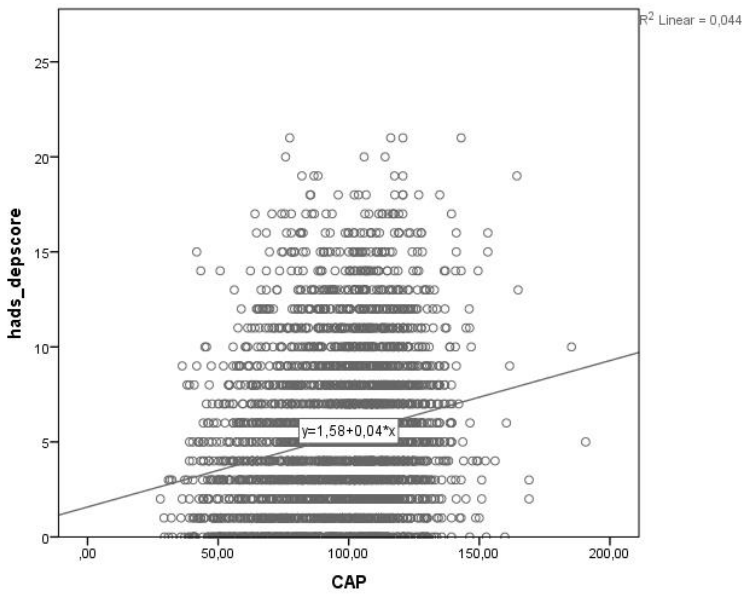


Figure 56: distribution of depression subscore by CAP score



13. Irritability subscore_HADS-SIS

Figure 57: distribution of Irritability subscore by HD category

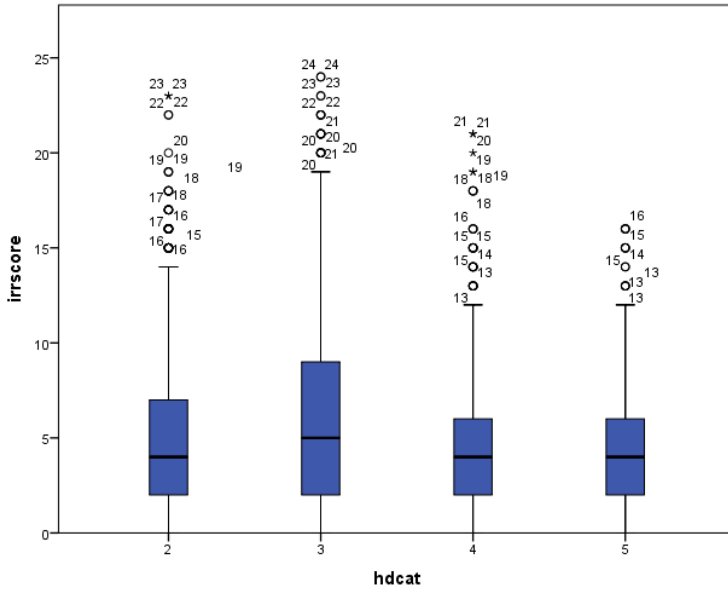
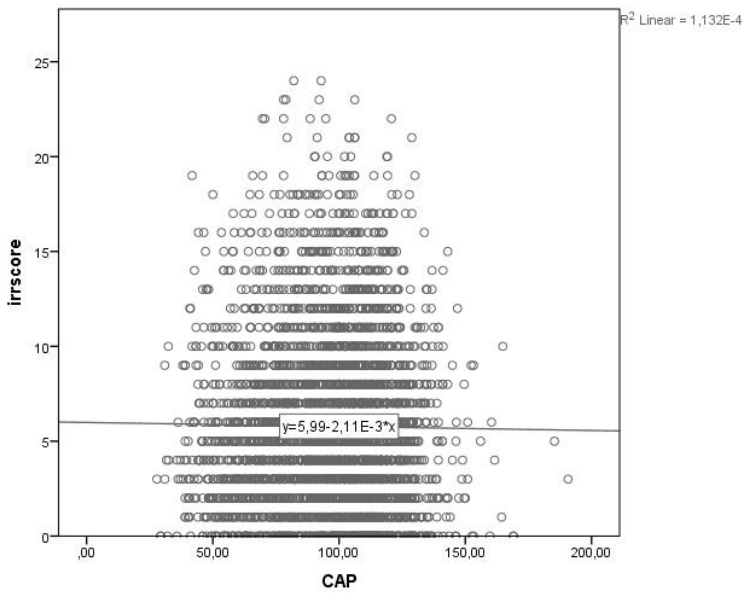


Figure 58: distribution of Irritability subscore by CAP score



14. Letter Verbal Fluency (total correct)

Figure 59: distribution of Letter Verbal Fluency by HD category

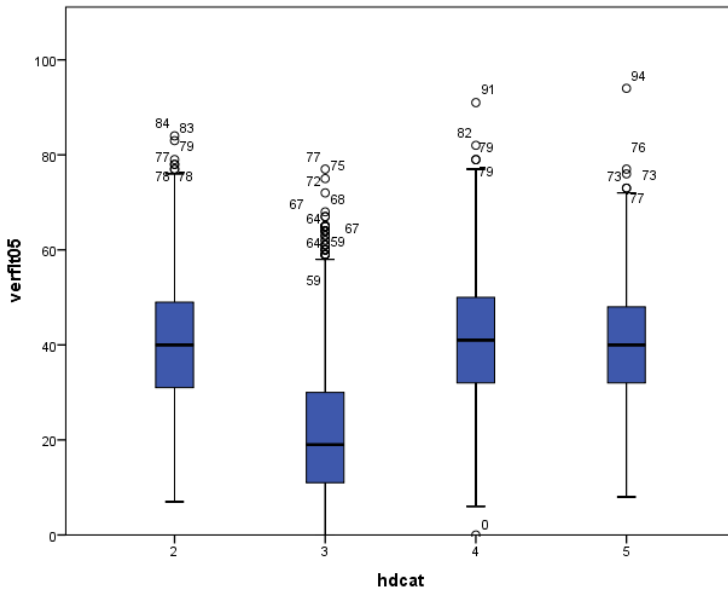
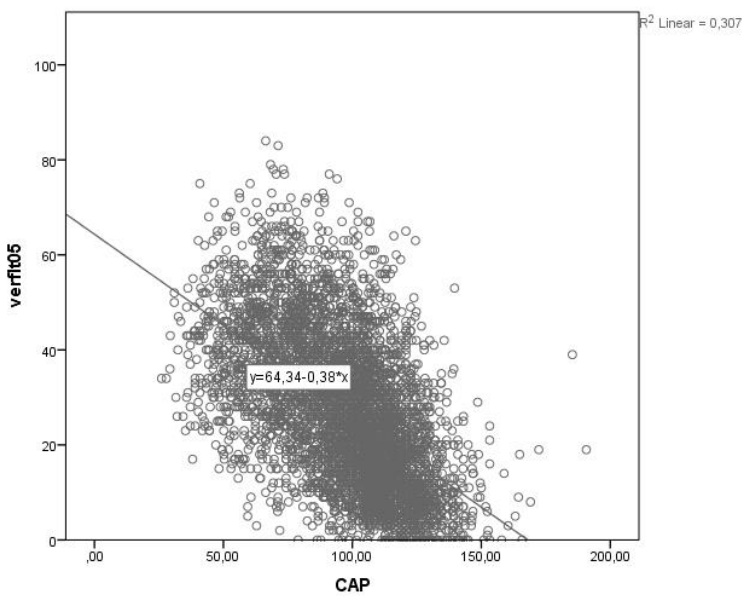


Figure 60: distribution of Letter Verbal Fluency by CAP score



15. Depression subscore_HADS-SIS

Figure 61: distribution of Depression subscore by HD category

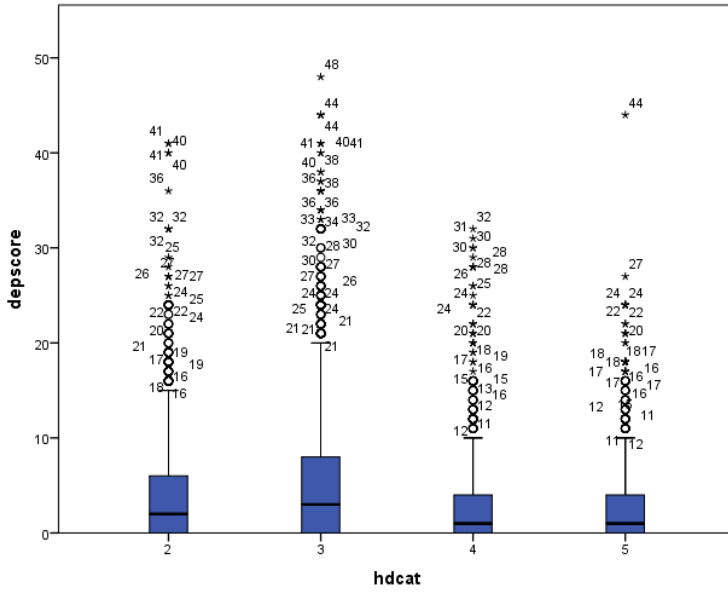
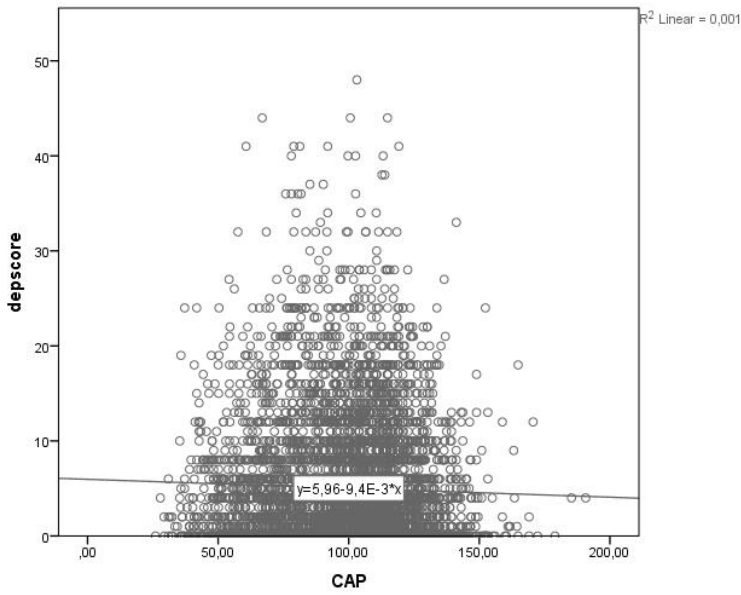


Figure 62: distribution of Depression subscore by CAP score



16. Irritability/aggression score_PBA-s

Figure 63: distribution of Irritability/aggression score by HD category

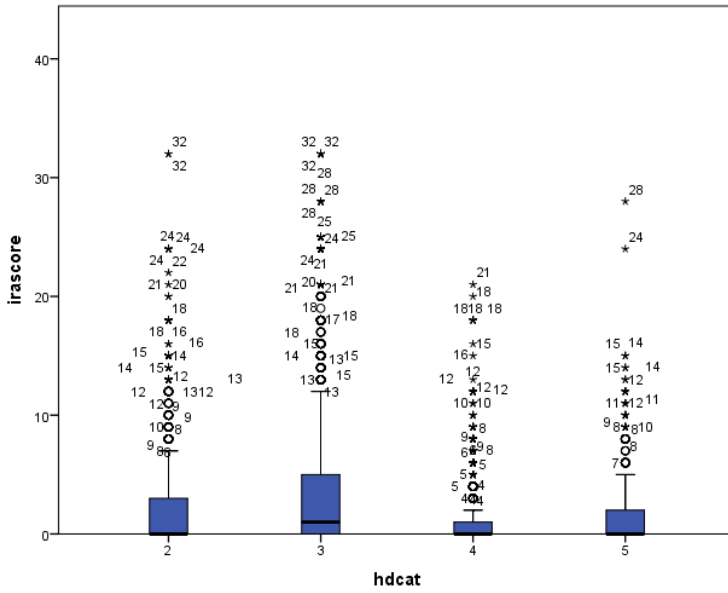
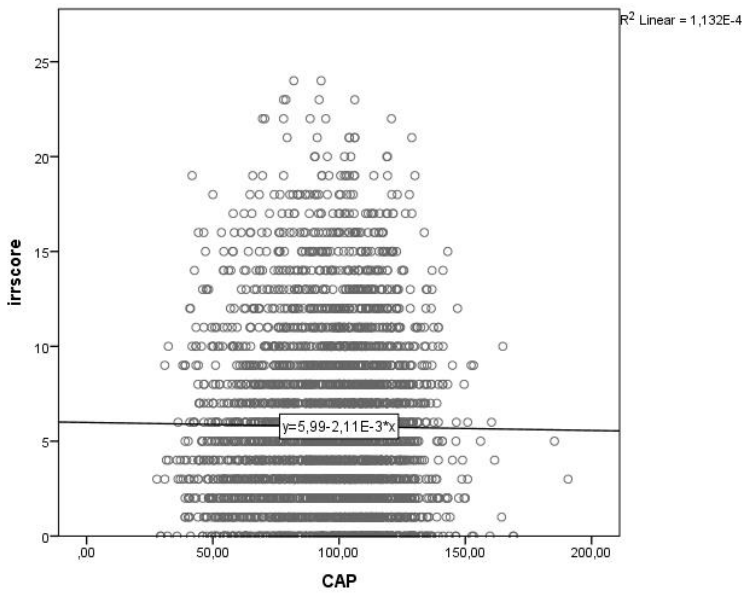


Figure 64: distribution of Irritability/aggression by CAP score



17. Psychosis score_PBA-s

Figure 65: distribution of Psychosis score by HD category

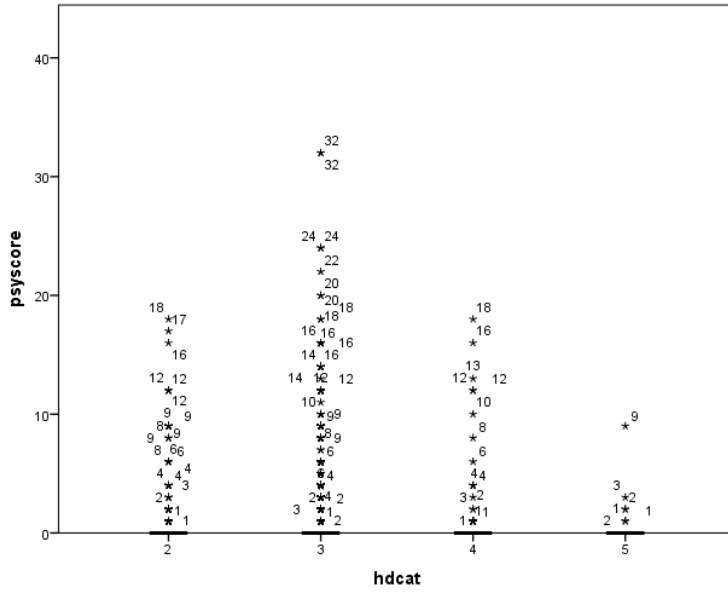
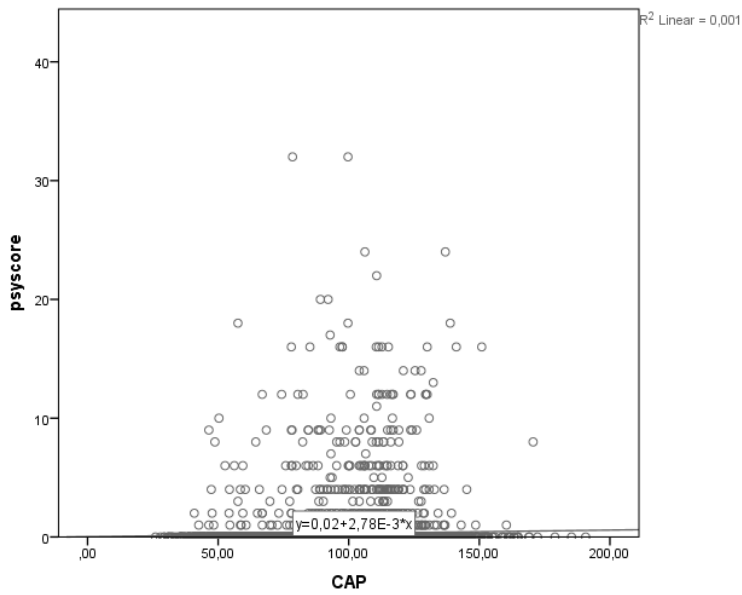


Figure 66: distribution of Psychosis score by CAP score



18. Apathy score_PBA-s

Figure 67: distribution of Apathy score by HD category

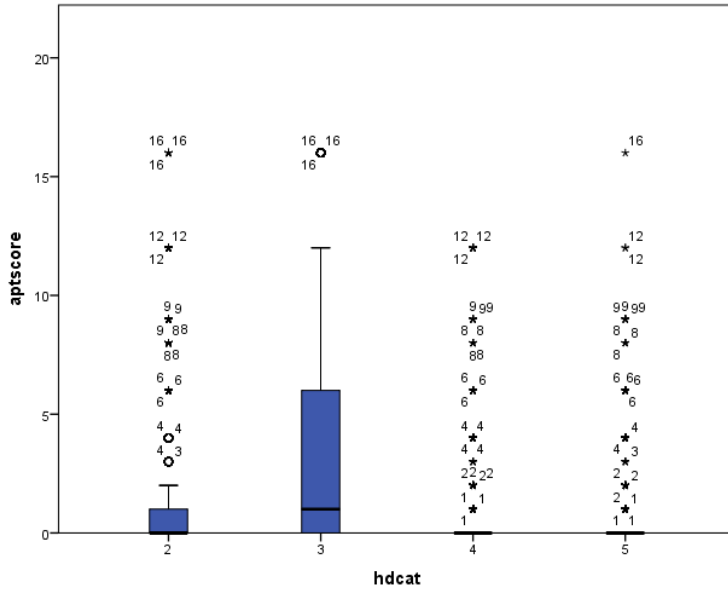
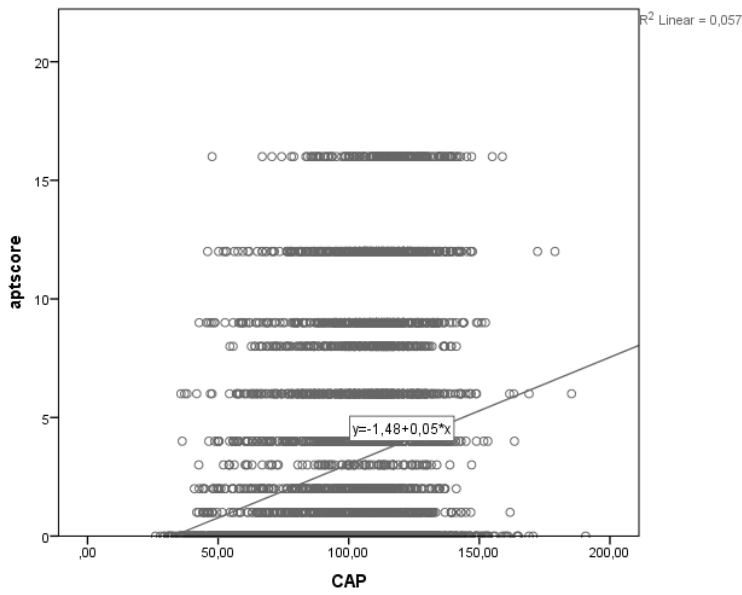


Figure 68: distribution of Apathy score by CAP score



19. Stroop Word Reading (Total correct)

Figure 69: distribution of Stroop Word Reading by HD category

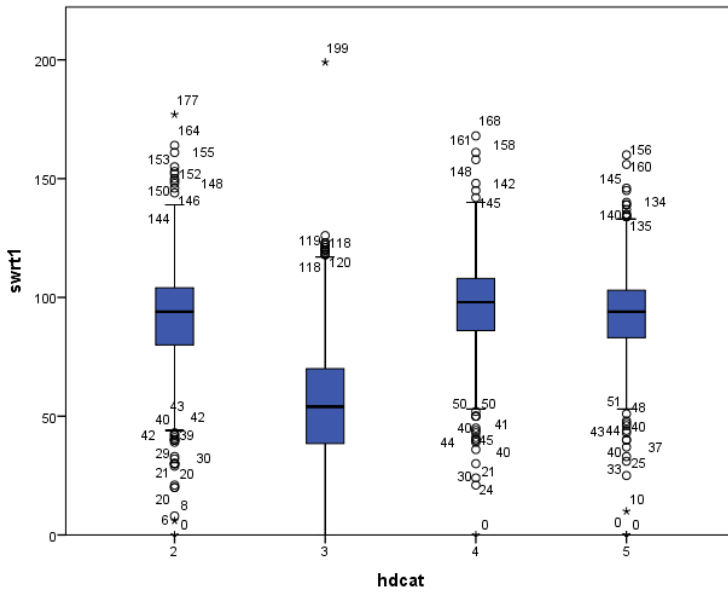
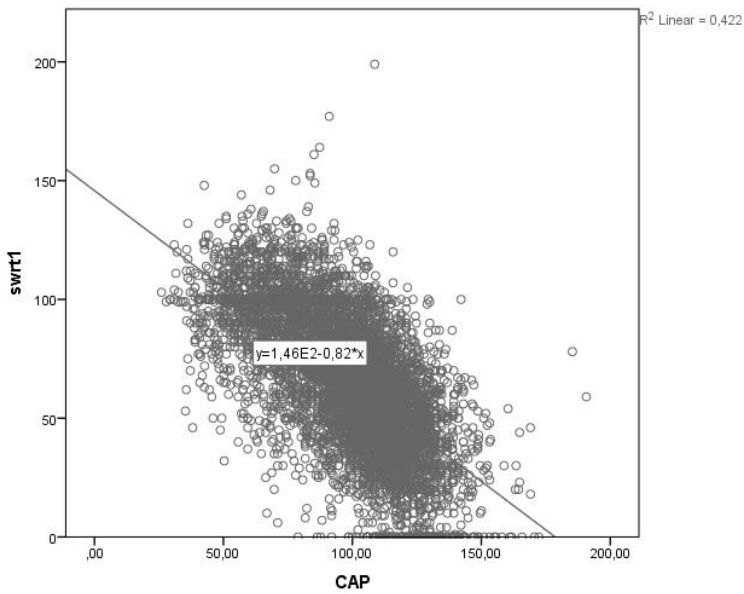


Figure 70: distribution of Stroop Word Reading by CAP score



20. Stroop Interference (Total correct)

Figure 71: distribution of Stroop Interference by HD category

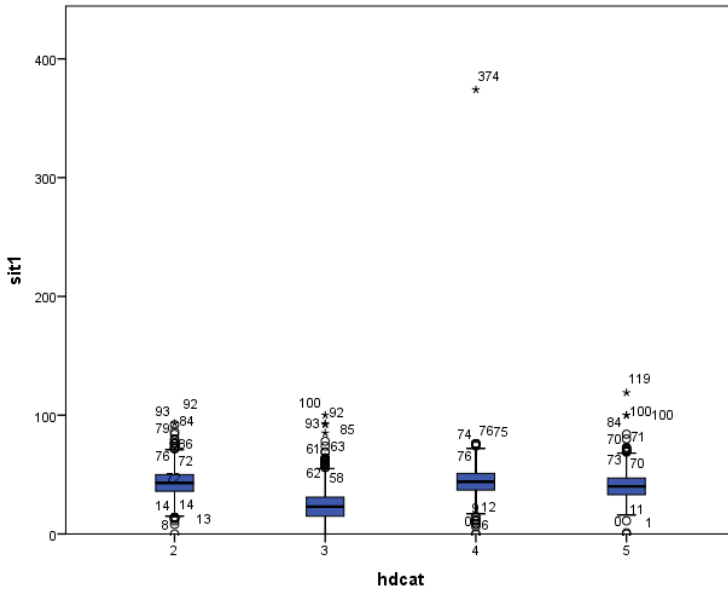
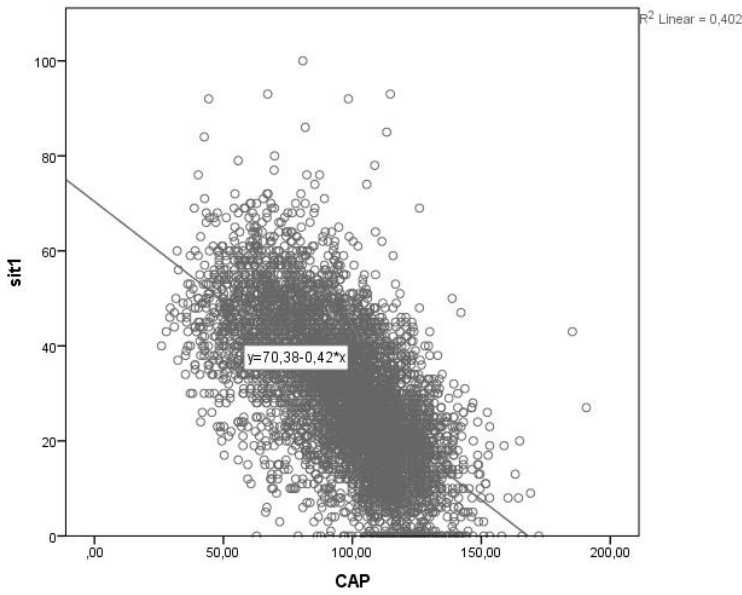


Figure 72: distribution of Stroop Interference by CAP score



21. Trail Making A (Total correct)

Figure 73: distribution of Trail making test A by HD category

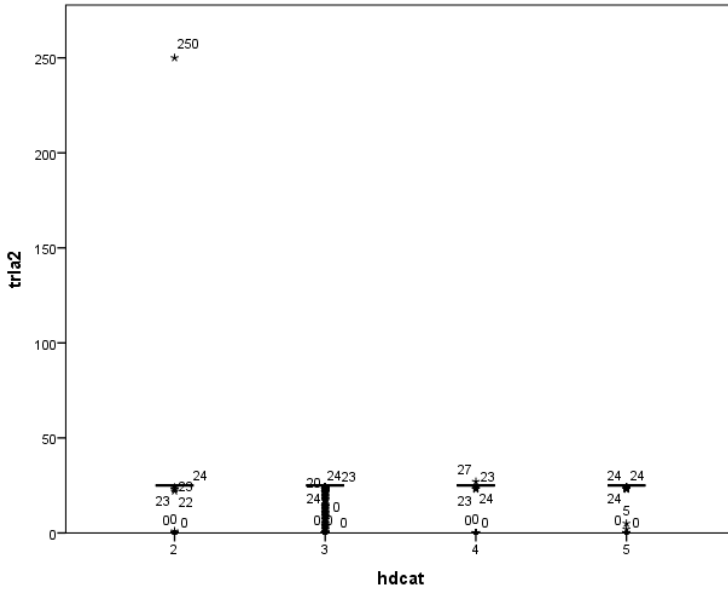
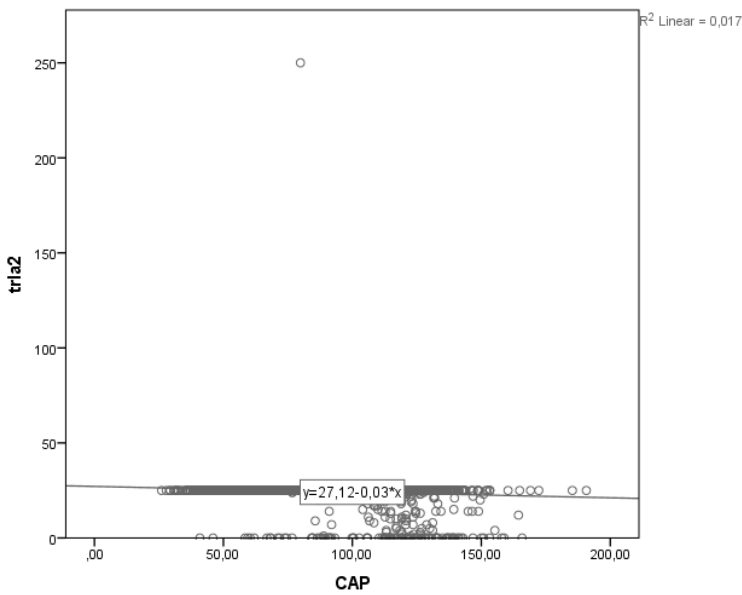


Figure 74: distribution of Trail making test A by CAP score



22. Trail Making A (Total correct)

Figure 75: distribution n of Trail making test B by HD category

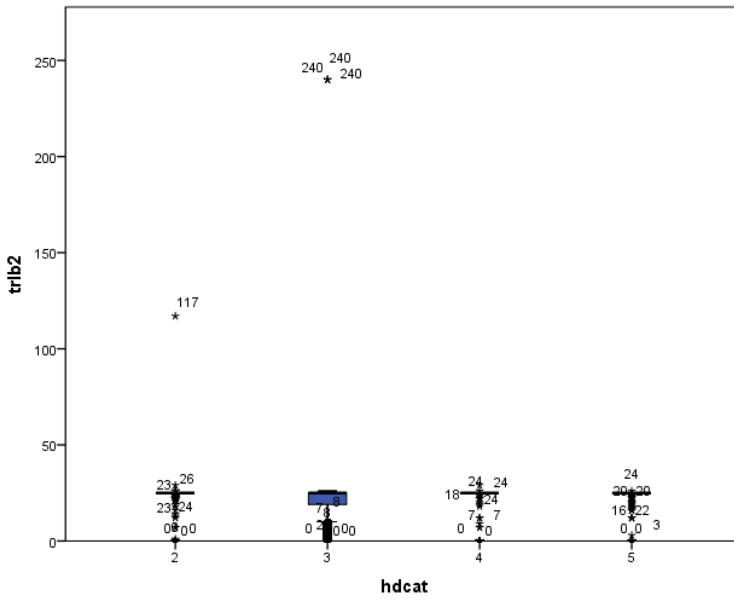


Figure 76: distribution of Trail making test B by CAP score

