neuroSHARE: Measurement of Neurodegenerative Diseases in SHARE Survey

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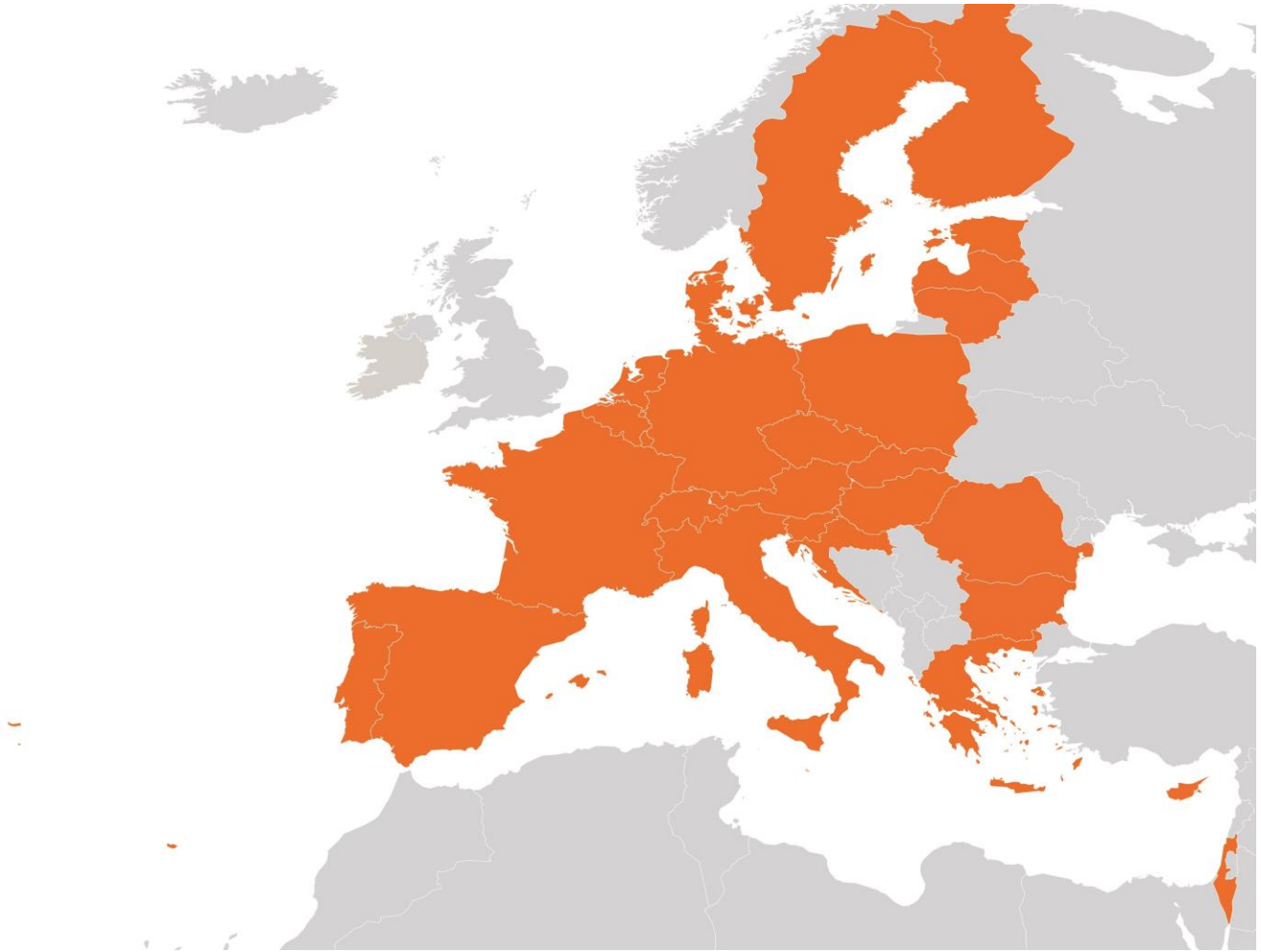
Agenda

1. Introduction to SHARE & neuroSHARE
2. neuroSHARE consent, sample, results
3. Medical validation
4. Cognition in neuroSHARE and SHARE & HCAP
5. Future plans & conclusions

Survey of Health, Aging, and Retirement in Europe (SHARE)

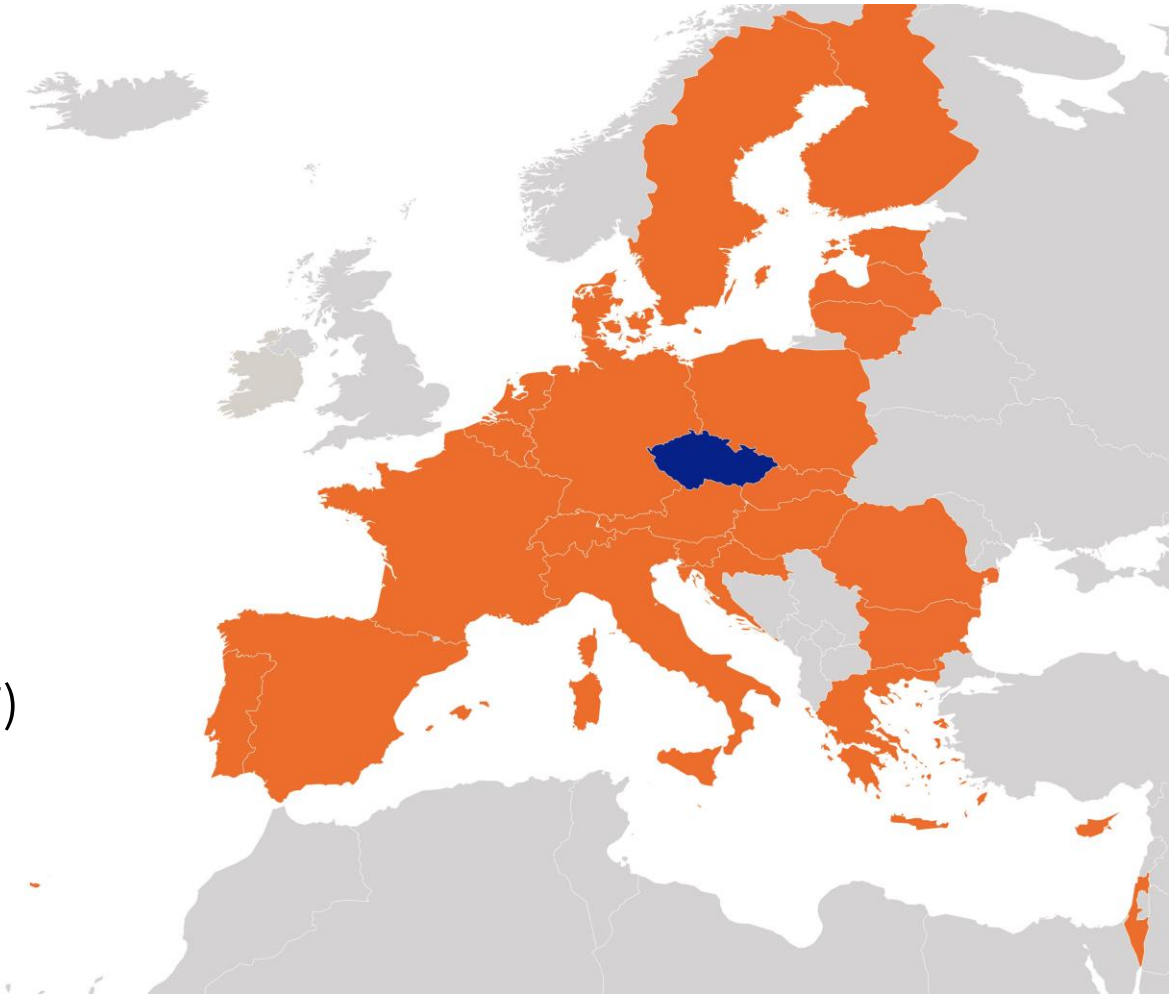
- Representative sample 50+
- 600 000 interviews
- 140 000 respondents
- 23 000 users
- 28 countries
- Harmonized with HRS
- Multidisciplinary
- Panel: 10 waves



SHARE-CZ

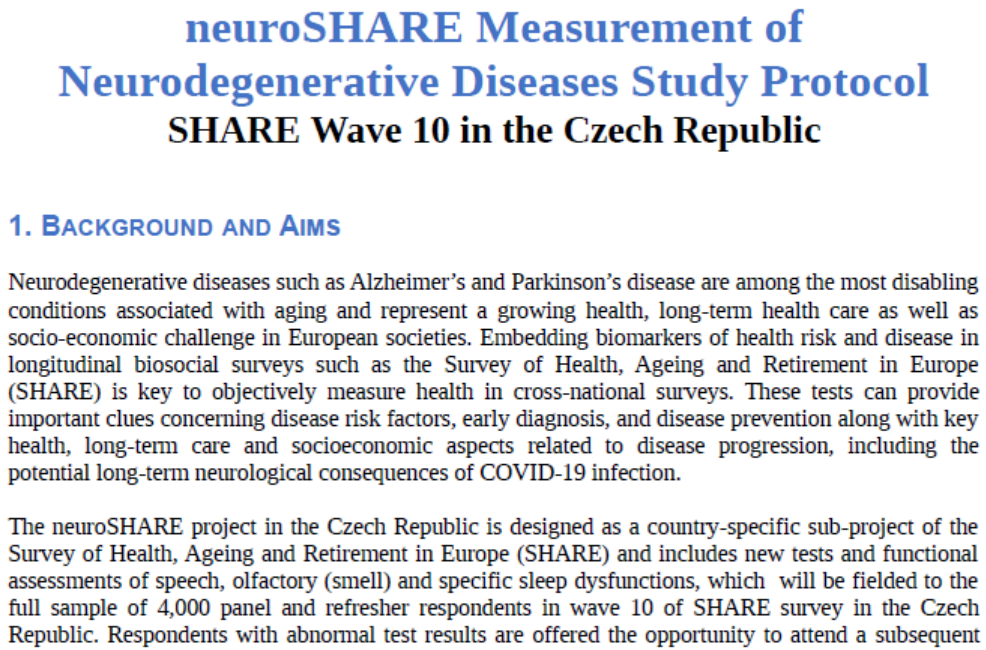
- Czech Republic
- Since 2006
- 5000 sample

- HCAP in wave 9
- **neuroSHARE in wave 10**
- Biomarkers and linkage in wave 11 (2027)
  - Incl. exposomes, geolocations, life history
- HCAP 2 in 2028



The neuroSHARE module

- Part of 10th SHARE wave *only* in SHARE-CZ
- **Task: capture signs of *early* neurodegeneration**
- **Clinical validation**
- First ever study in a representative sample
- Cost-effective, noninvasive, scalable



neuroSHARE Measurement of Neurodegenerative Diseases Study Protocol

SHARE Wave 10 in the Czech Republic

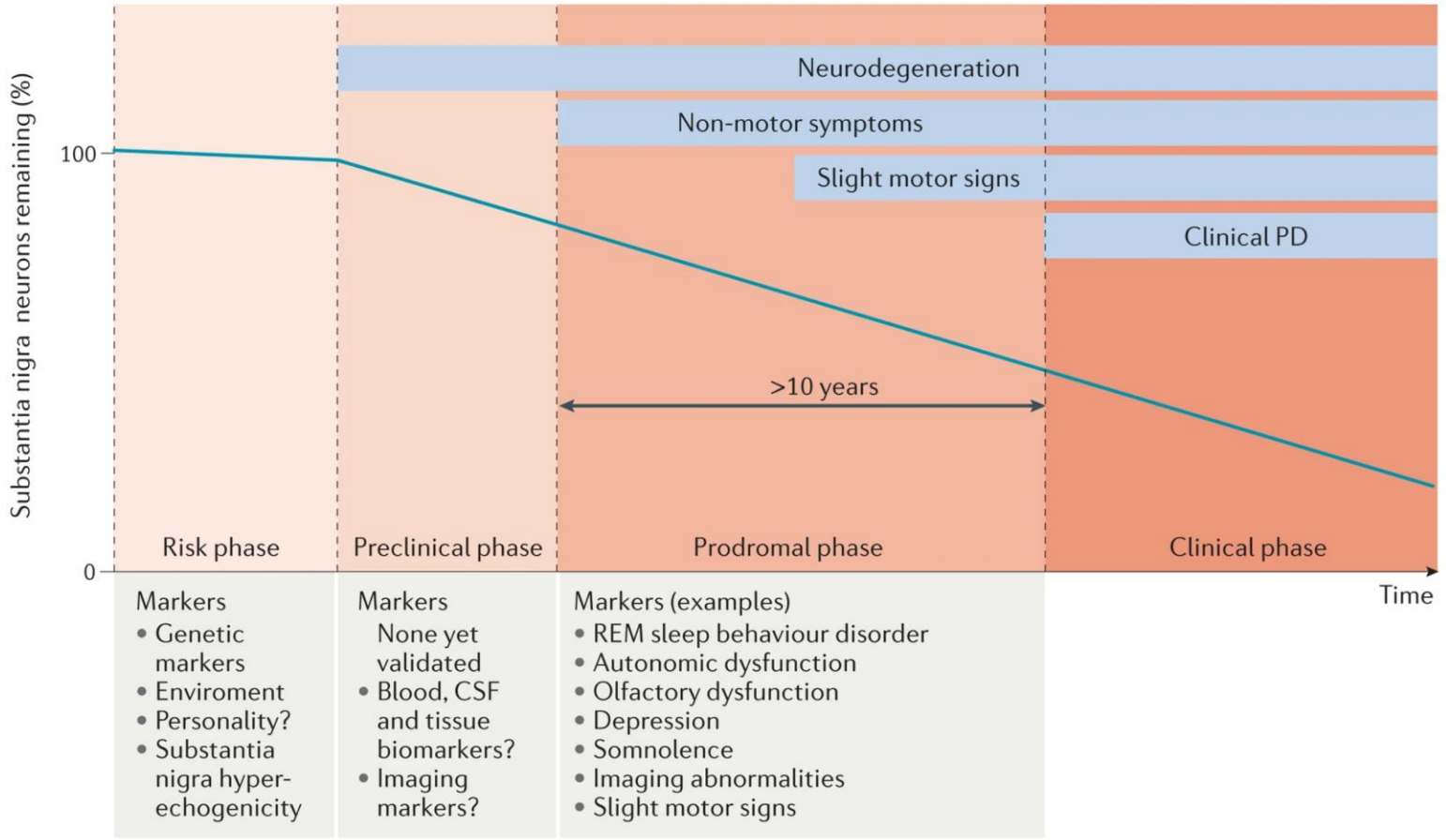
1. Background and Aims

Neurodegenerative diseases such as Alzheimer's and Parkinson's disease are among the most disabling conditions associated with aging and represent a growing health, long-term health care as well as socio-economic challenge in European societies. Embedding biomarkers of health risk and disease in longitudinal biosocial surveys such as the Survey of Health, Ageing and Retirement in Europe (SHARE) is key to objectively measure health in cross-national surveys. These tests can provide important clues concerning disease risk factors, early diagnosis, and disease prevention along with key health, long-term care and socioeconomic aspects related to disease progression, including the potential long-term neurological consequences of COVID-19 infection.

The neuroSHARE project in the Czech Republic is designed as a country-specific sub-project of the Survey of Health, Ageing and Retirement in Europe (SHARE) and includes new tests and functional assessments of speech, olfactory (smell) and specific sleep dysfunctions, which will be fielded to the full sample of 4,000 panel and refresher respondents in wave 10 of SHARE survey in the Czech Republic. Respondents with abnormal test results are offered the opportunity to attend a subsequent

neuroSHARE motivation

- **Capturing signs of early (prodromal) phase of parkinsonism**
- Age group 50-80
- Clinically extremely important



Postuma & Berg 2016, Advances in markers of prodromal Parkinson disease, Nature Reviews Neurology.

neuroSHARE implementation

- A set of three *standardized* tasks of approx. 20 minutes in total
- Standard CAPI format

speech test
(set of speech tasks)

smell test
(olfactory testing kit)

sleep test
(brief questionnaire)

+ brief questionnaire focused on conflicting conditions (such as stuttering, Covid, …)

- **Tasks sensitive to the presence of *early* neurodegeneration**

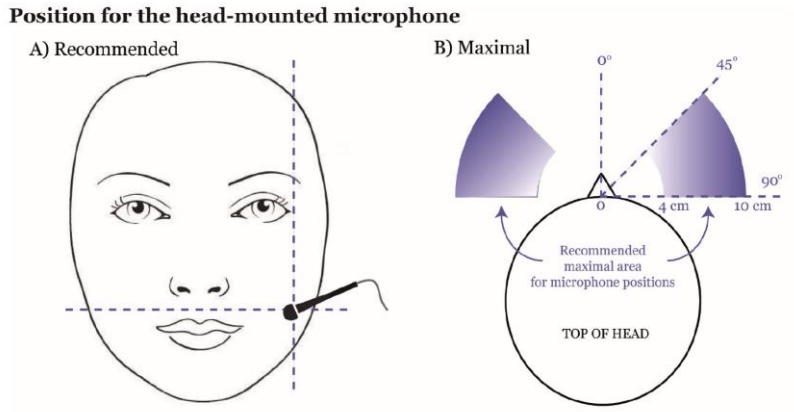
neuroSHARE tasks - speech

1. Prolonged phonation of vowel /a/ - 2x
2. Fast syllable repetition, /pa/-/pa/-/pa/ - 2x
3. Reading passage (using cards)
4. Retelling a narrated story
5. Monolue on arbitrary topic

Subtle speech impairment (motor movement)

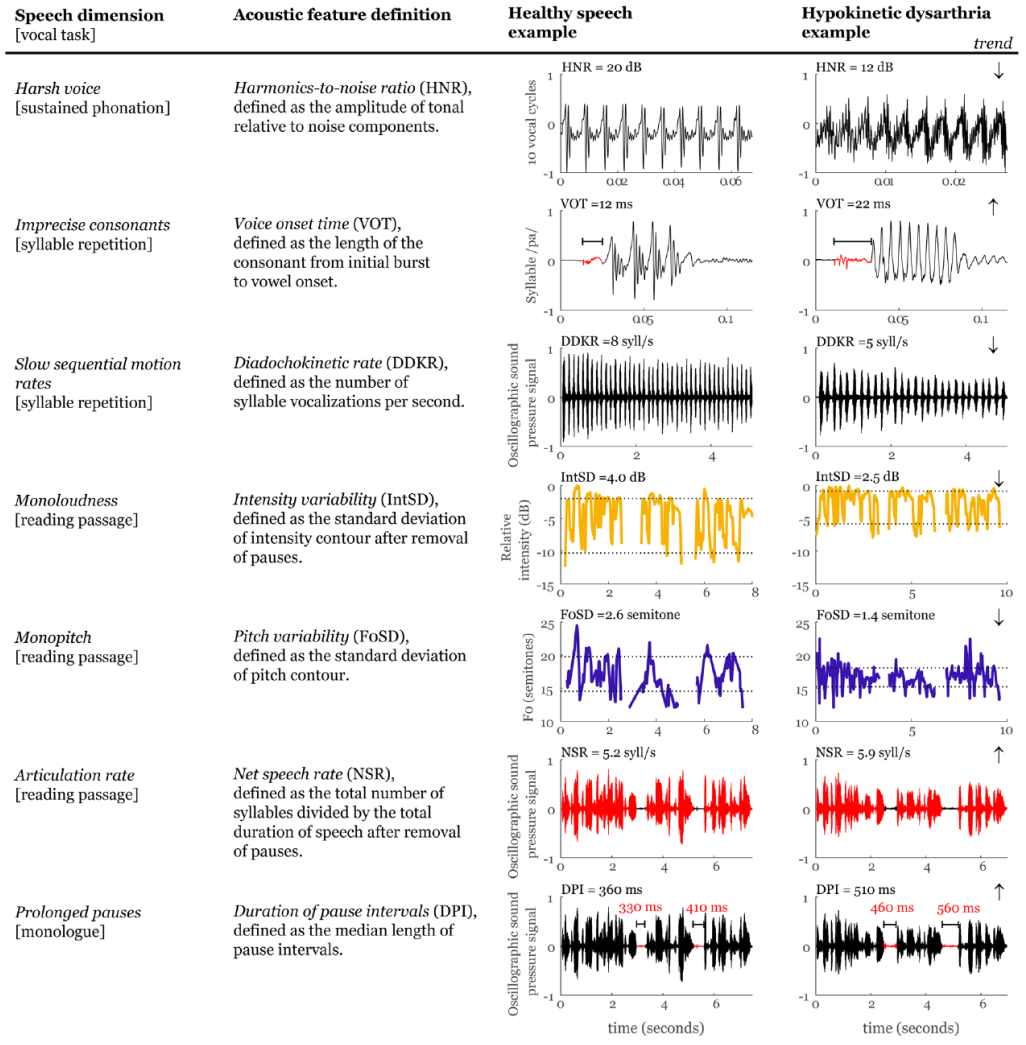
Subtle speech & language impairment (congition)
Less control

- Total time 10 min.
- Managed by a developed CAPI application
  - Recording, guidelines, data transfer…



neuroSHARE tasks – speech – markers

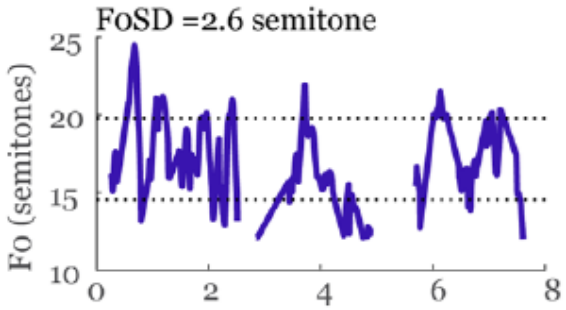
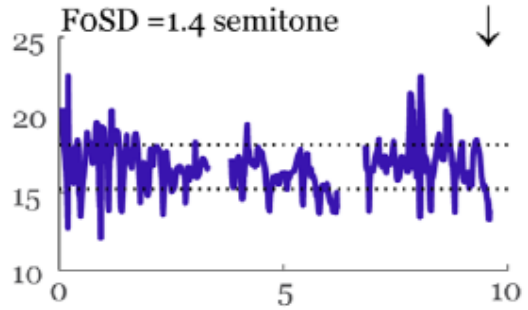
- Capturing speech impairment in prodromal PD
- Automatically computed from raw data
- Team expertise



Rusz et al. 2021, Speech Biomarkers in Rapid Eye Movement Sleep Behavior Disorder and Parkinson Disease, Ann Neurol.
Rusz et al. 2024, From prodromal stages to clinical trials: The promise of digital speech biomarkers in Parkinson's disease, Neur Biob Rev.

neuroSHARE tasks – speech – markers

- Capturing speech impairment

Speech dimension [vocal task]	Acoustic feature definition	Healthy speech example	Hypokinetic dysarthria example *trend*
Monopitch [reading passage]	*Pitch variability* (FoSD), defined as the standard deviation of pitch contour.		

Sleep Behavior Disorder and Parkinson Disease, Ann Neurol.
Rusz et al. 2024, From prodromal stages to clinical trials: The promise of digital speech biomarkers in Parkinson's disease, Neur Biob Rev.

neuroSHARE tasks – smell

- Standard HCAP olfactory test (HRS, ELSA)

- Task 1: Smell sensitivity
- Task 2: Recognition of five scents

- Marker: total smell score
- Low values indicate smell impairment

neuroSHARE tasks – smell (motivation)

- Impaired smell might indicate damage to cranial nerve, which can be caused by neurodegeneration
- Very early marker (90% in early-stage PD)

neuroSHARE tasks – sleep

- A brief, standardized questionnaire for detecting signs of REM sleep behavior disorder (RBD).

- Marker: total sleep score
- High value indicates probable RBD.

REM Sleep Questionnaire (RBD-SQ) to Be Filled by Respondent (if unable, filled together with the INTERVIEWER)

ne_sleep_q

The following questions are related to your sleep.
Please answer yes or no to the following questions:
(Please check one box on each row)

		Yes	No
1)	I sometimes have very vivid dreams.	☐1	☐2
2)	My dreams frequently have an aggressive or action-packed content.	☐1	☐2
3)	The dream contents mostly match my nocturnal behavior.	☐1	☐2
4)	I know that my arms or legs move when I sleep.	☐1	☐2
5)	It thereby happened that I (almost) hurt my bed partner or myself.	☐1	☐2
	I have or had the following phenomena during my dreams:		
6a)	speaking, shouting, swearing, laughing loudly	☐1	☐2
6b)	sudden limb movements, “fights”	☐1	☐2
6c)	gestures, complex movements, that are useless during sleep, e.g., to wave, to salute, to frighten mosquitoes, falls off the bed	☐1	☐2
6d)	things that fell down around the bed, e.g., bedside lamp, book, glasses	☐1	☐2
7)	It happens that my movements awake me.	☐1	☐2
8)	After awakening I mostly remember the content of my dreams well.	☐1	☐2
9)	My sleep is frequently disturbed.	☐1	☐2
10)	I have/had a disease of the nervous system (e.g., stroke, head trauma, Parkinsonism, RLS, narcolepsy, depression, epilepsy, inflammatory disease of the brain).	☐1	☐2

neuroSHARE tasks – sleep (motivation)

- A clinically diagnosed RBD (via polysomnography) is *the largest* risk factor of prodromal PD.

BRAIN

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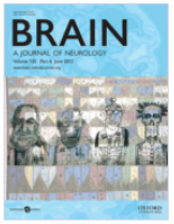


Volume 135, Issue 6
June 2012

JOURNAL ARTICLE

How does parkinsonism start? Prodromal parkinsonism motor changes in idiopathic REM sleep behaviour disorder Get access >

R. B. Postuma, A. E. Lang, J. F. Gagnon, A. Pelletier, J. Y. Montplaisir

Brain, Volume 135, Issue 6, June 2012, Pages 1860–1870,
https://doi.org/10.1093/brain/aws093

Movement Disorders — Official Journal of the International Parkinson and Movement Disorder Society

Review

MDS research criteria for prodromal Parkinson's disease

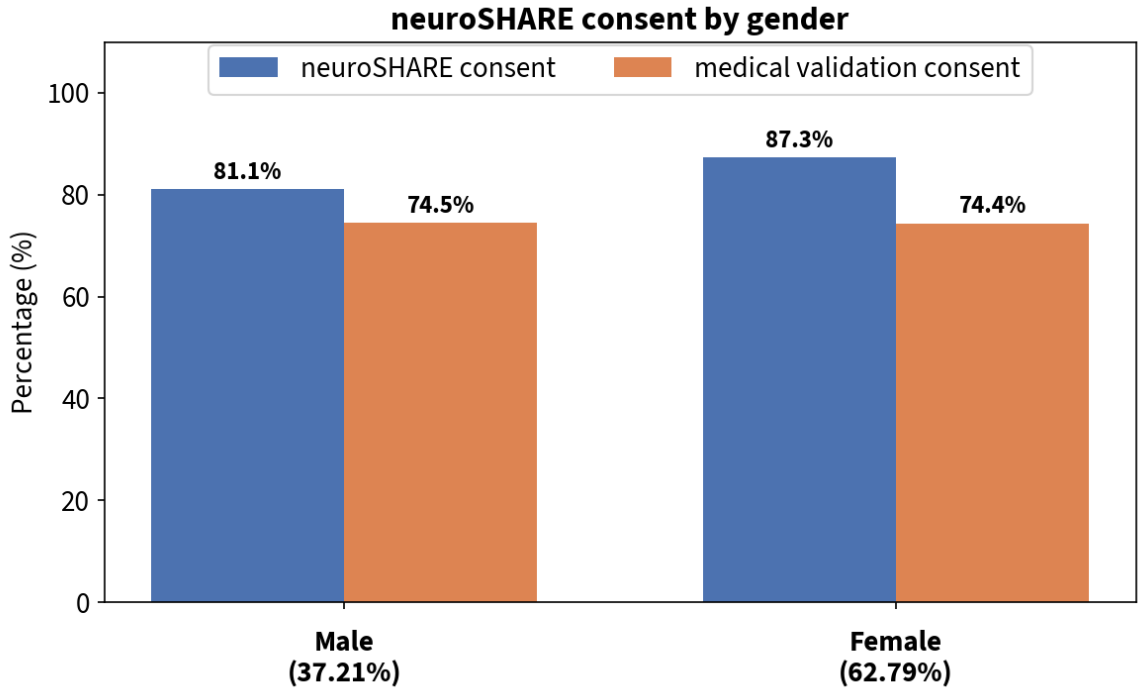
Daniela Berg MD, Ronald B. Postuma MD, MSc, Charles H. Adler MD, PhD, Bastiaan R. Bloem MD, PhD, Piu Chan MD, PhD, Bruno Dubois MD, PhD, Thomas Gasser MD, Christopher G. Goetz MD, Glenda Halliday PhD, Lawrence Joseph PhD, Anthony E. Lang OC, MD, FRCPC, Inga Liepelt-Scarfone PhD, Irene Litvan MD, Kenneth Marek MD, José Obeso MD, PhD, Wolfgang Oertel MD, C. Warren Olanow MD, FRCPC, Werner Poewe MD, Matthew Stern MD, Günther Deuschl MD

First published: 16 October 2015 | https://doi.org/10.1002/mds.26431 | VIEW METRICS

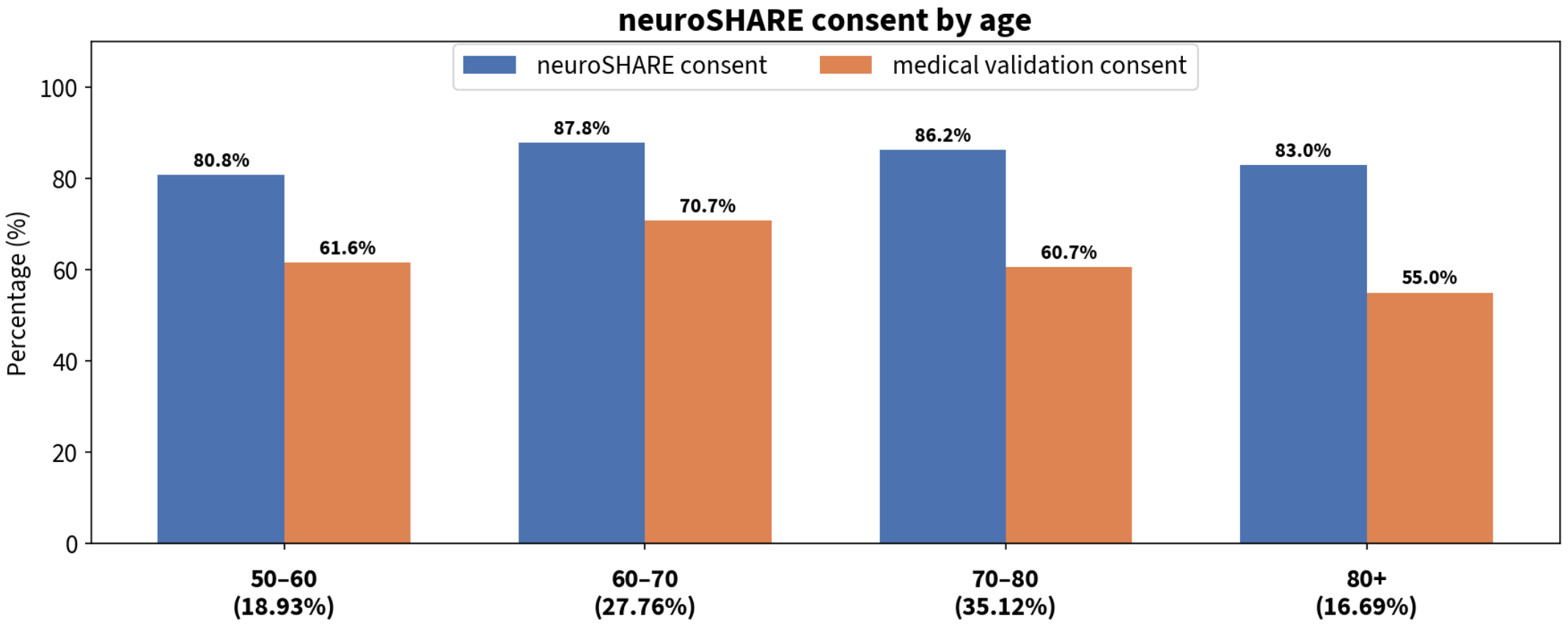
neuroSHARE consent rates

- Two consents:
  - Consent to participate in neuroSHARE
  - Consent with medical assessment

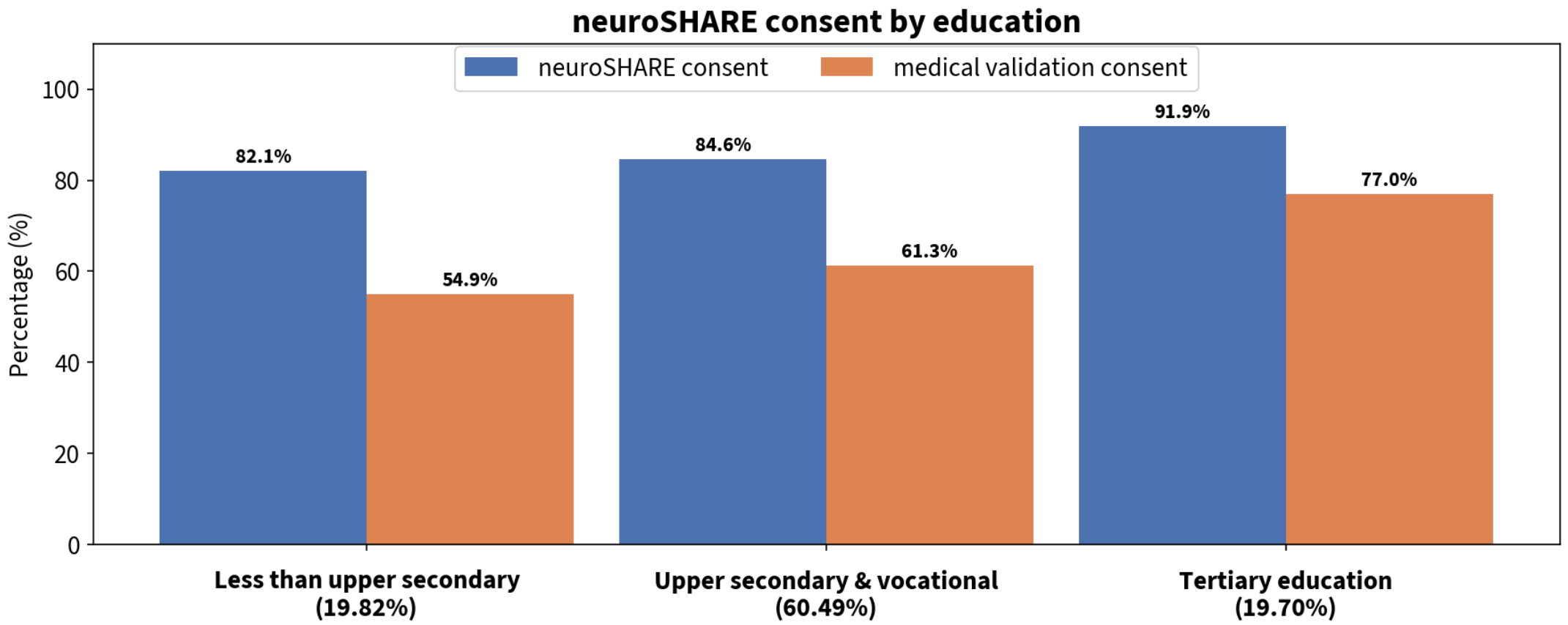
- Consent to participate in neuroSHARE: **85.0%**
- Consent with medical assessment: **74.5%**



Consent by age

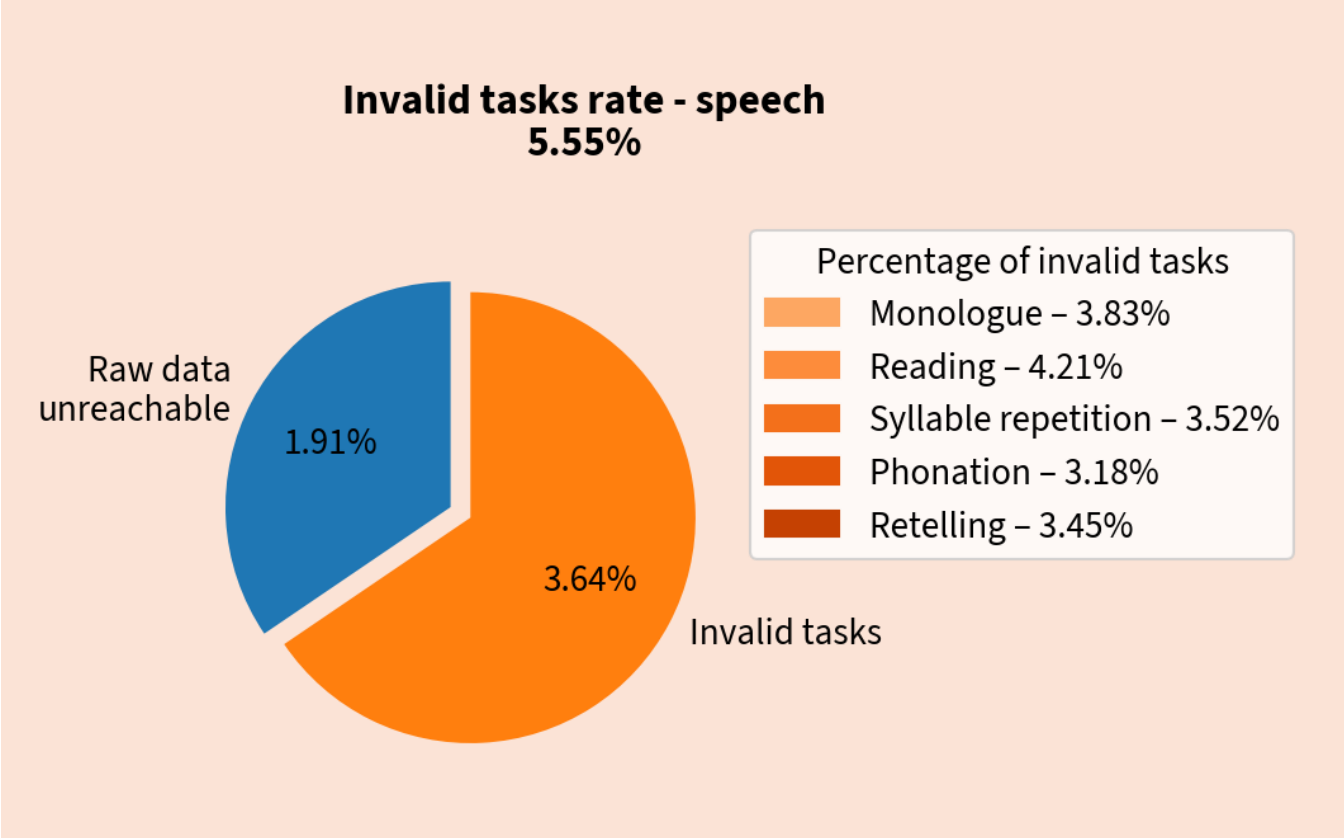


Consent by education



Invalid tasks rate

Invalid – outcome markers could not be computed, answers are missing
Data still preliminary

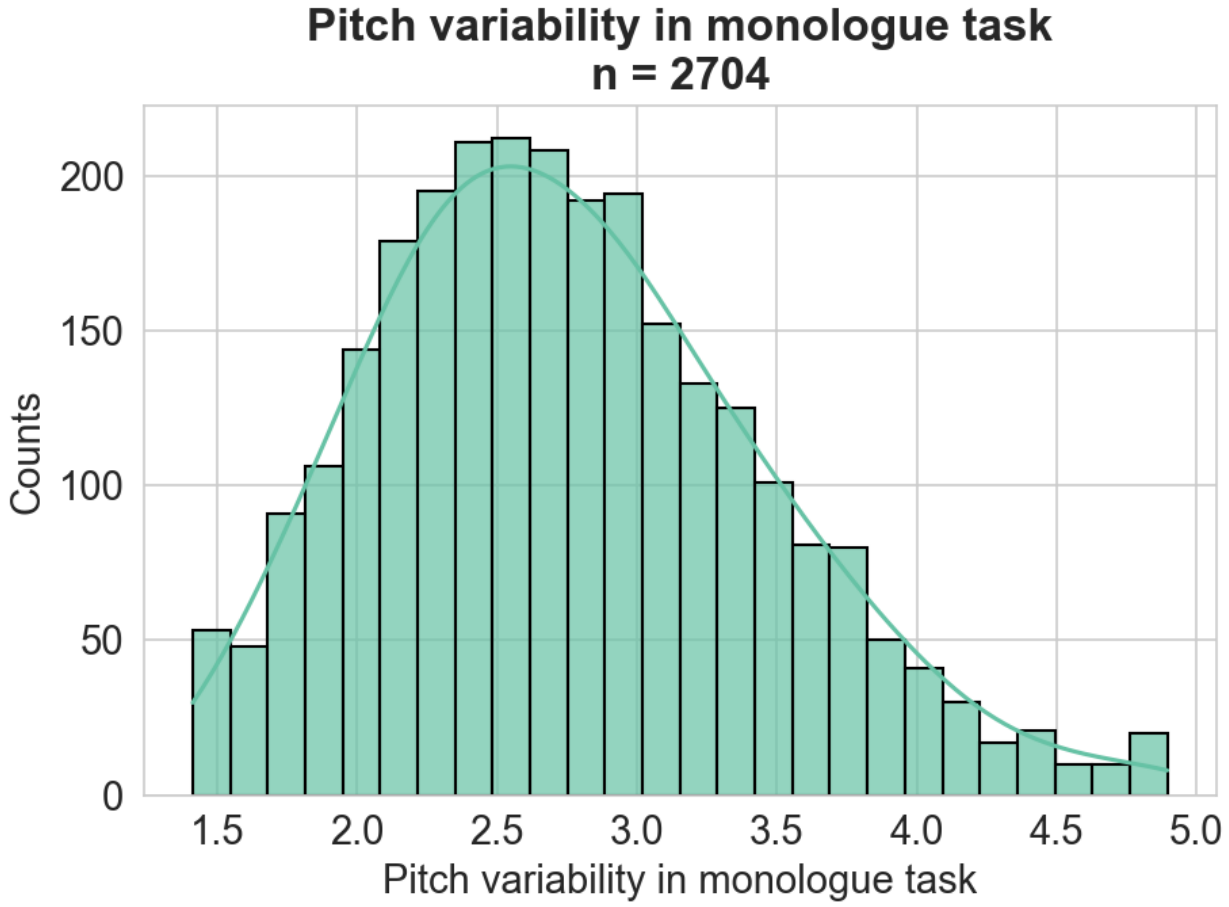


- Invalid smell tasks: **1.0%**
- Invalid sleep tasks: **0.7%**

Results examples - speech marker

- Lower pitch variability indicates vocal folds control and ability impairment – early PD sign
- **Impairment at values < 1.7** (evidence from the literature and PD cohort at the clinic)

Rusz 2021, Speech Biomarkers in Rapid Eye Movement Sleep Behavior Disorder and Parkinson Disease, Ann Neurol.



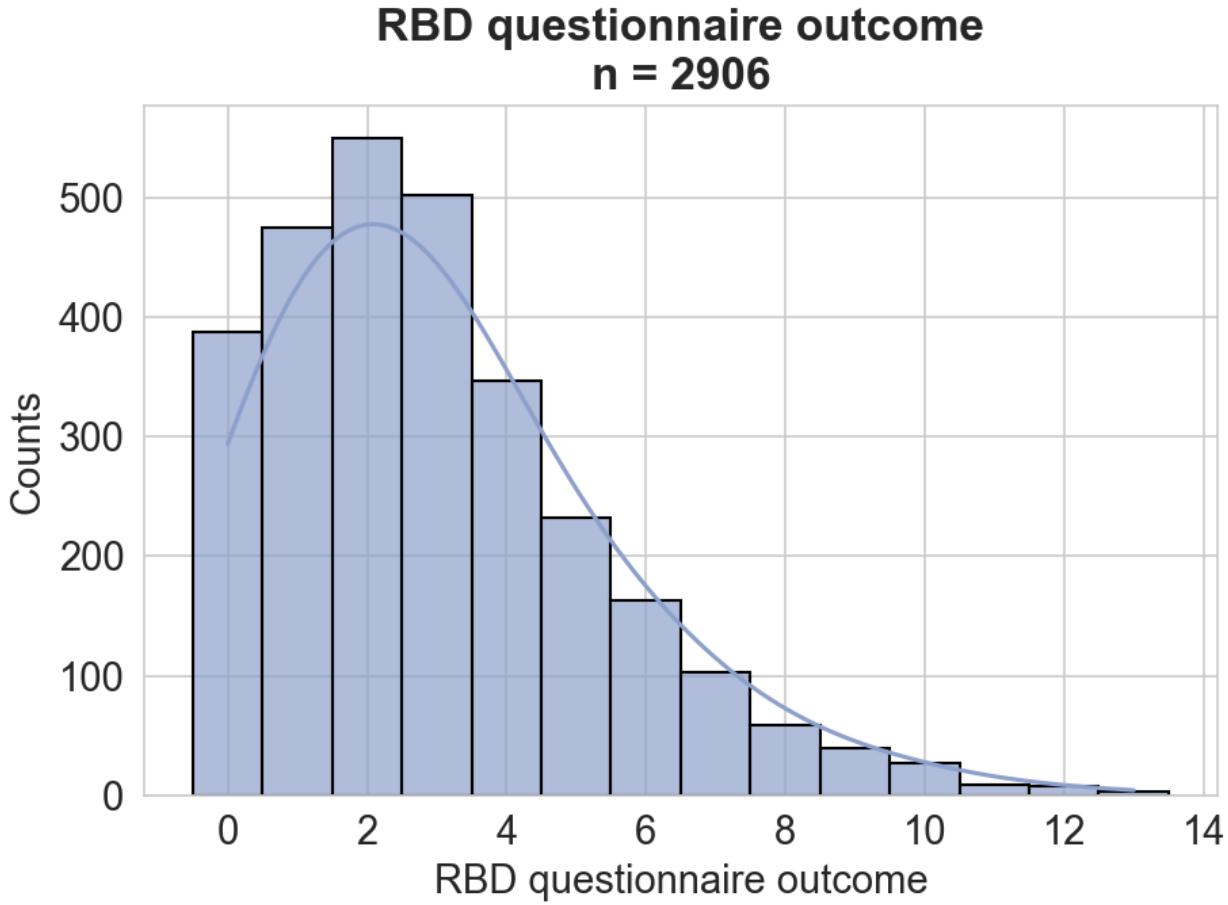
Results examples - smell marker

- Number of errors when recognizing the five scents

- **Subtle smell loss == 2**
- **Smell loss > 2**

Results - sleep marker (presence of RBD)

- The RBD sleep questionnaire score
- **Risk of RBD presence at > 5**
- Higher percentage of positive results than literature suggests (RBD prevalence 1-2% in population 60+)



Stiasny-Kolster et al. 2007, The REM sleep behavior disorder screening questionnaire—A new diagnostic instrument, Mov Disord.
Bušková et al. 2019, Validation of the REM sleep behavior disorder screening questionnaire in the Czech population, BCM Neurol.

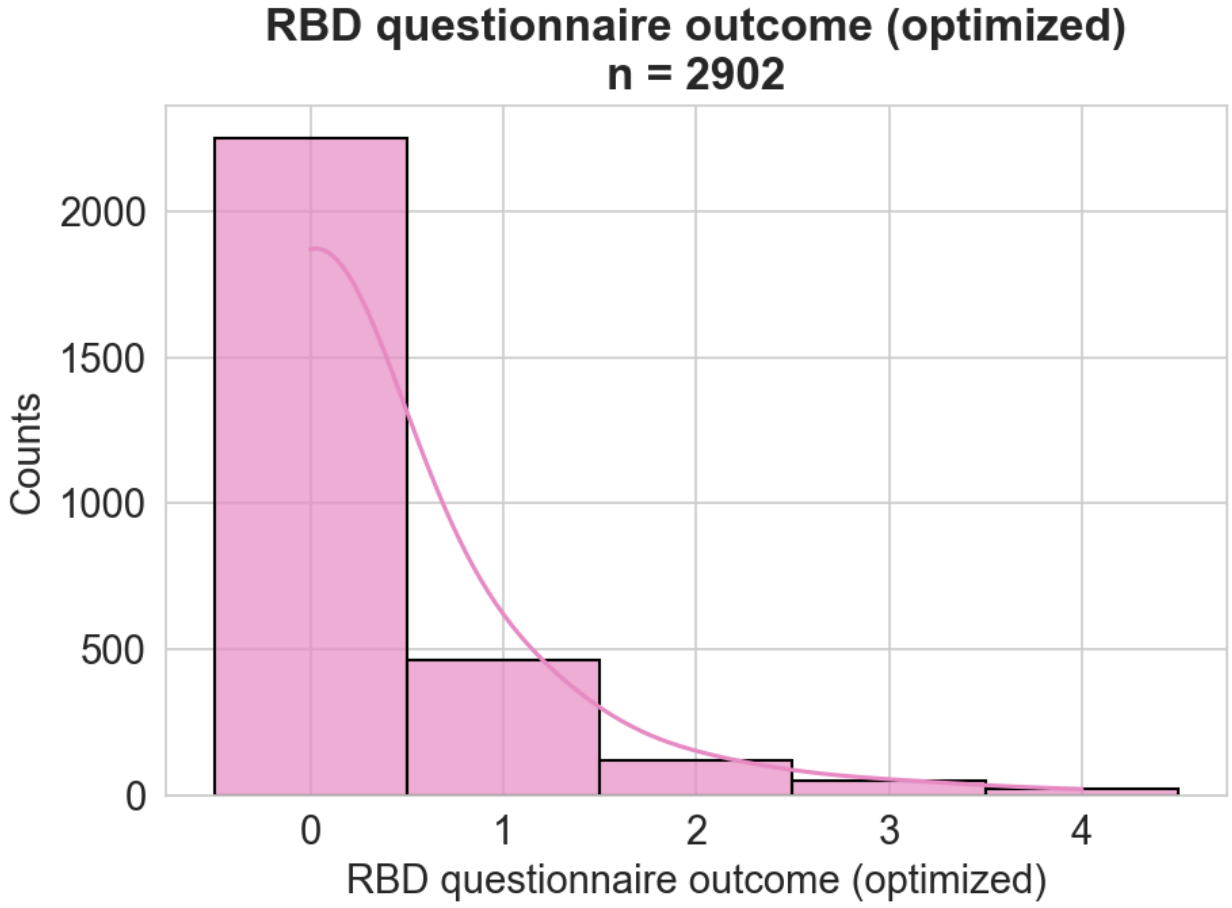
Sleep marker - optimized (presence of RBD)

- Optimized version without too broad questions
- Based on results of RBD cohort at the neurological clinic

- **Risk of RBD presence at > =2**

- More accurate correspondence with the estimated prevalence.

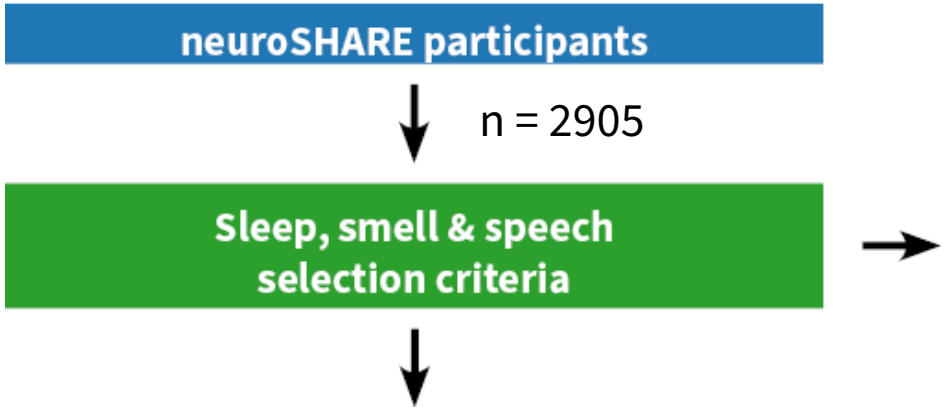
Stiasny-Kolster et al. 2007, The REM sleep behavior disorder screening questionnaire—A new diagnostic instrument, Mov Disord.
Bušková et al. 2019, Validation of the REM sleep behavior disorder screening questionnaire in the Czech population, BCM Neurol.



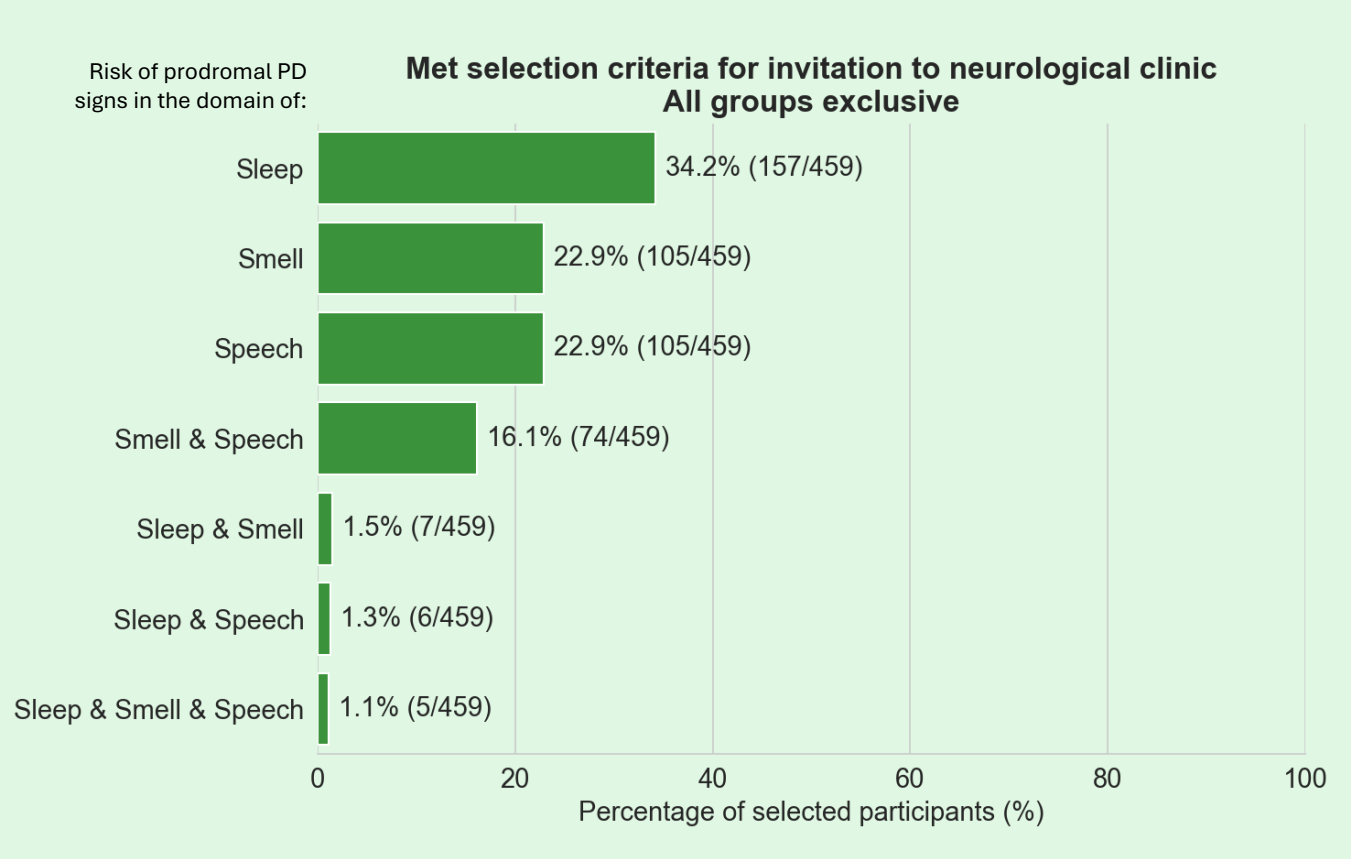
Selection of respondents for medical validation

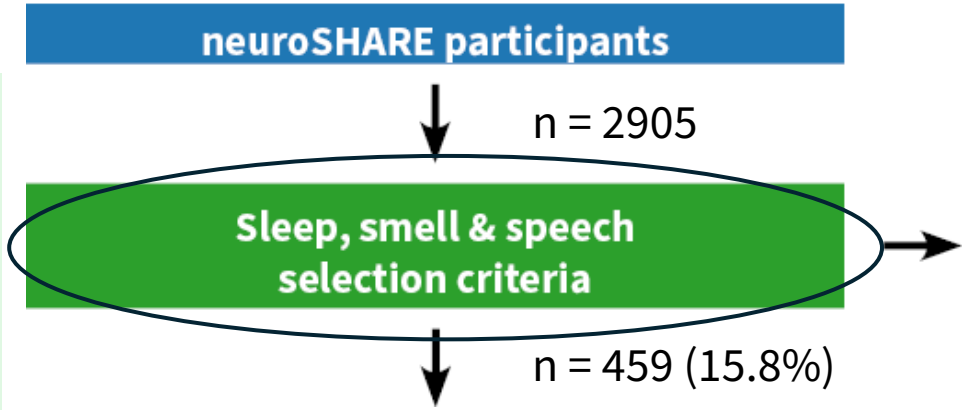
Selection of respondents for medical validation

- Participants with a high-risk scores from sleep, smell, and speech domains are selected.



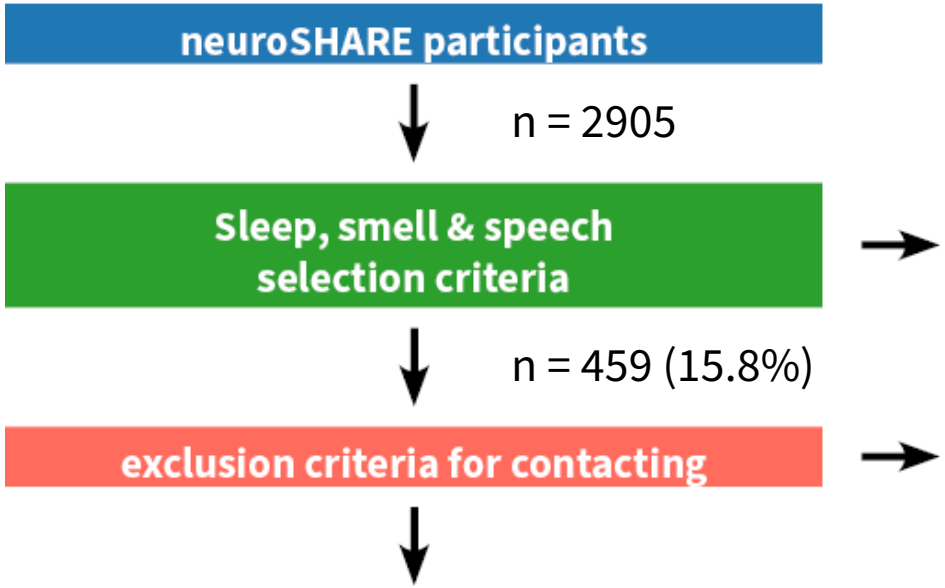
Selection of respondents for medical validation



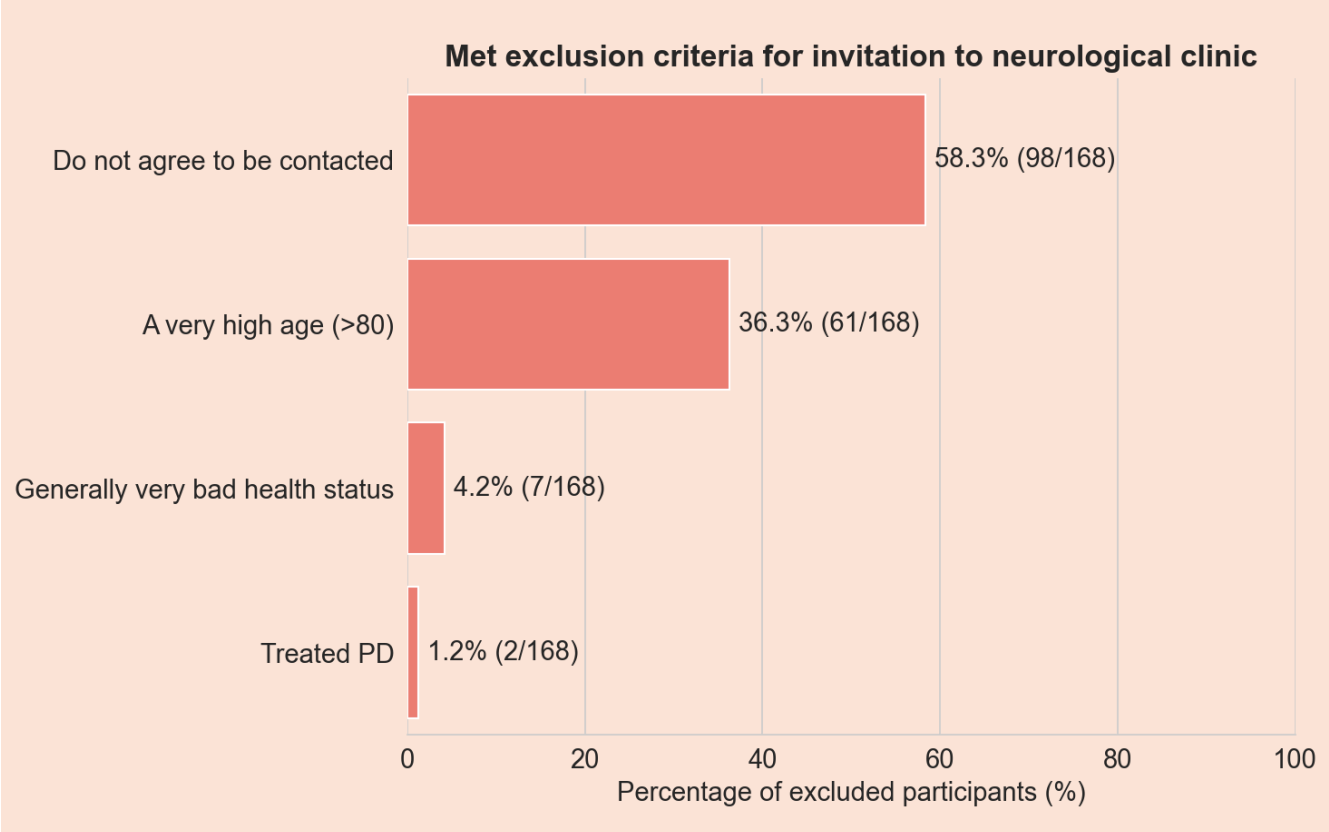


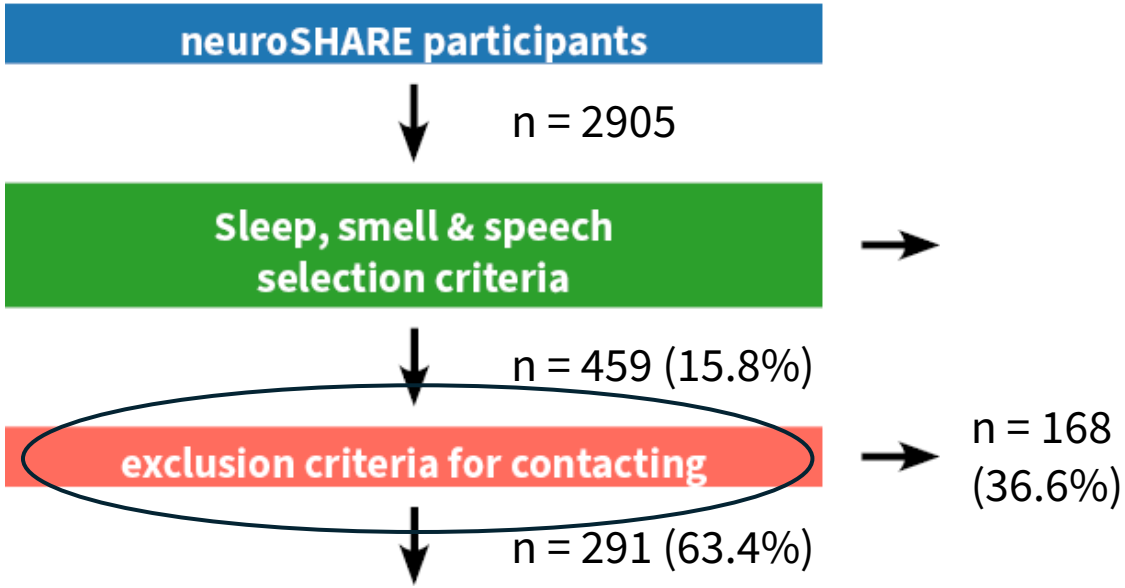
Selection of respondents for medical validation

- From the selected participants, those meeting the exclusion criteria for prodromal PD are excluded.



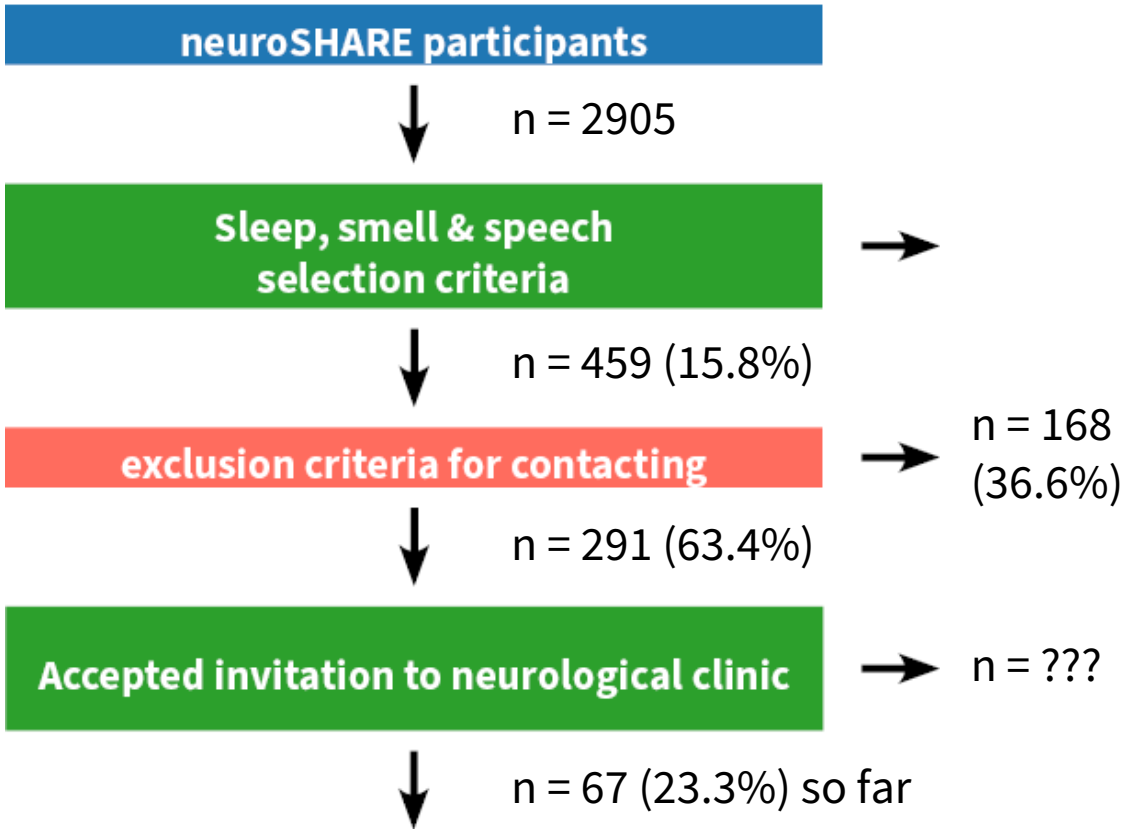
Selection of respondents for medical validation



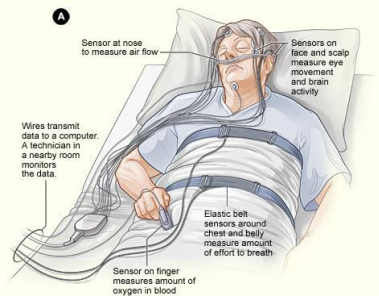


Selection of respondents for medical validation

- Selected participants which were not excluded are contacted by the neurological clinic via phone call.
- Summary about rejection and reasons of rejection is being prepared.



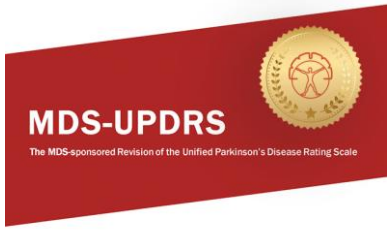
neuroSHARE clinical validation



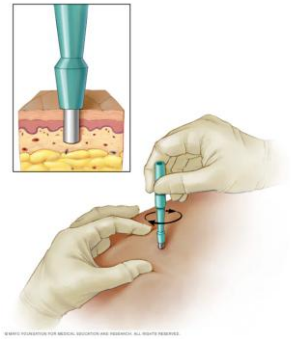
Polysomnography

DaTscan + MRI

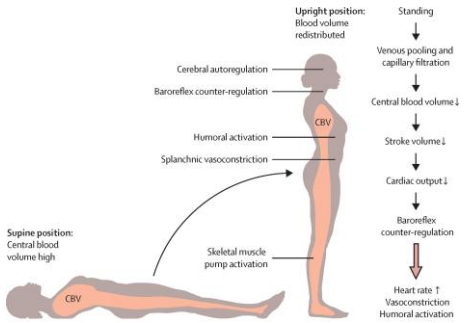
Olfactory test



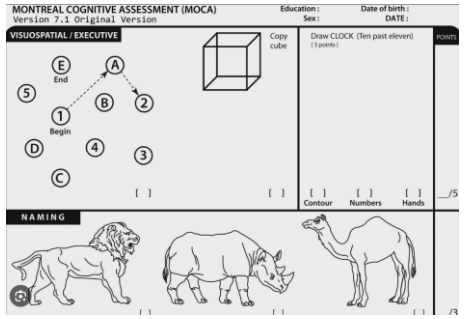
Unified Parkinson Disease Rating Scale + speech examination



Skin biopsy



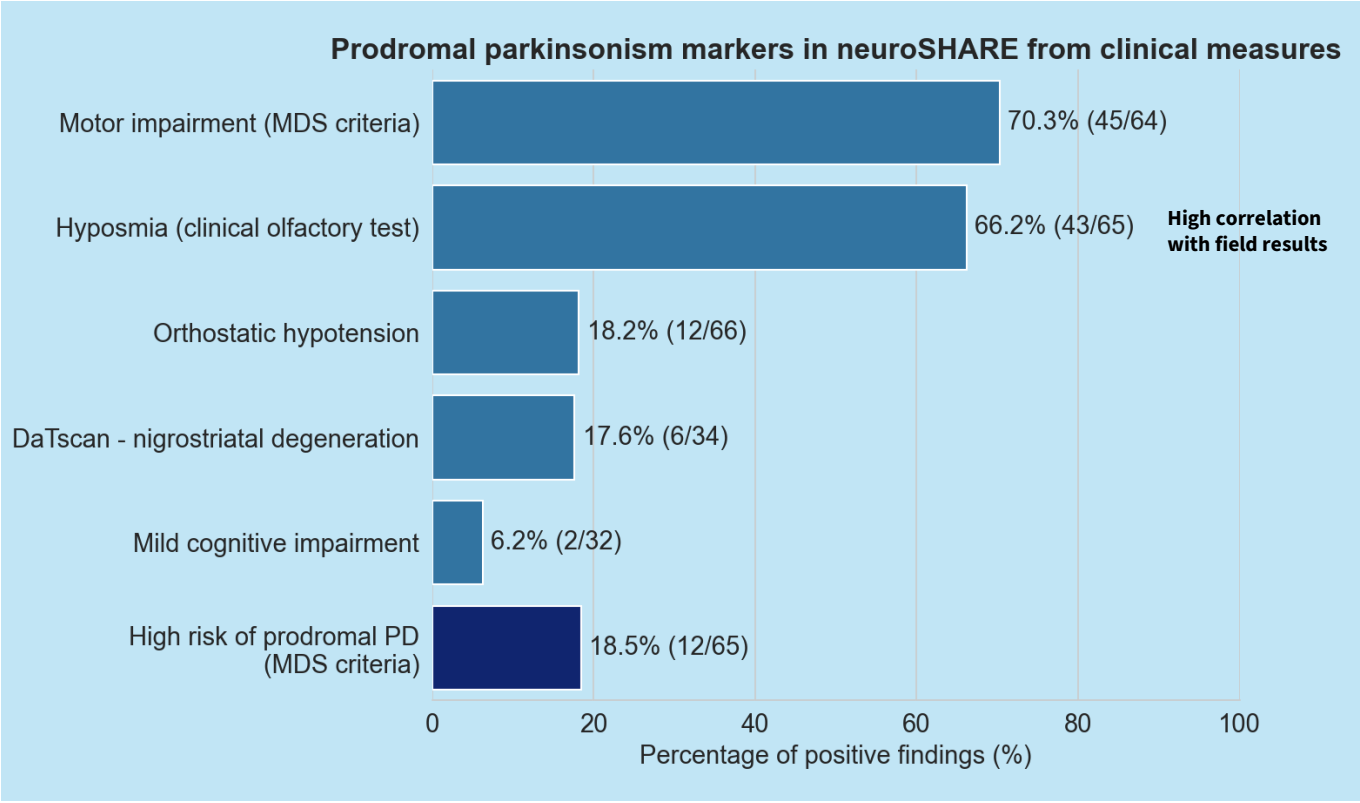
Orthostatic test

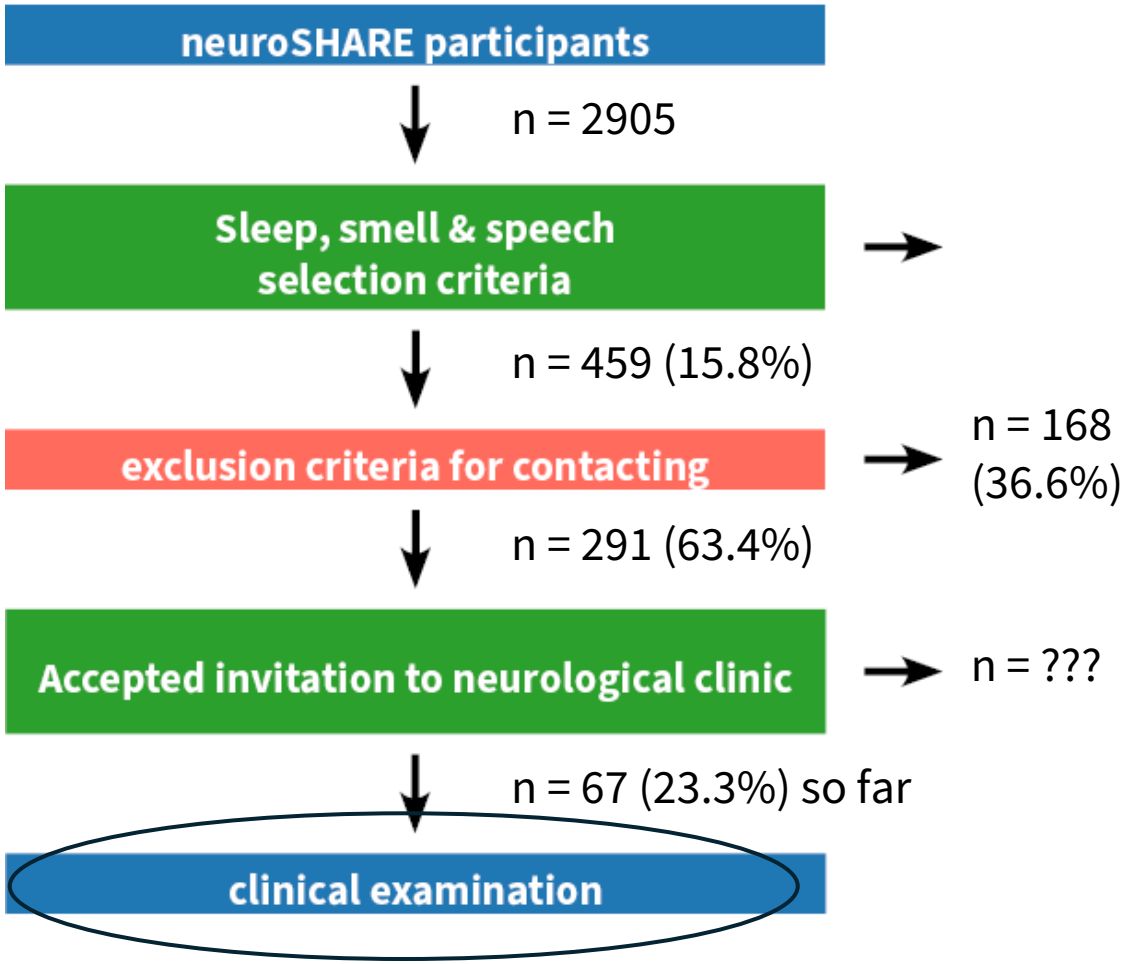


MoCA

Depression, neuropsychologic, and memory scales

Medical validation results





Berg et al. 2015, MDS research criteria for prodromal Parkinson's disease, Mov Disord.

neuroSHARE cognition

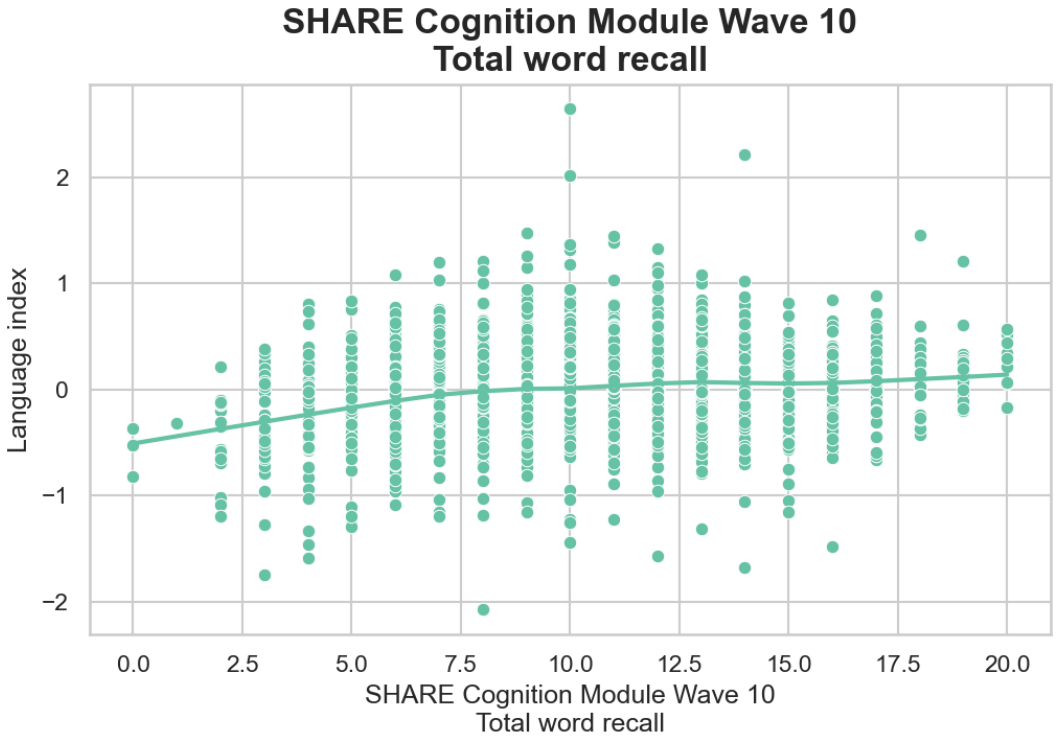
- Computed from monologue and retelling tasks automatically using natural language processing.
- Capture lexical and syntactic richness and complexity of uttered sentences – focused mostly on cognition.
- Not used as criteria for medical validation in neuroSHARE.

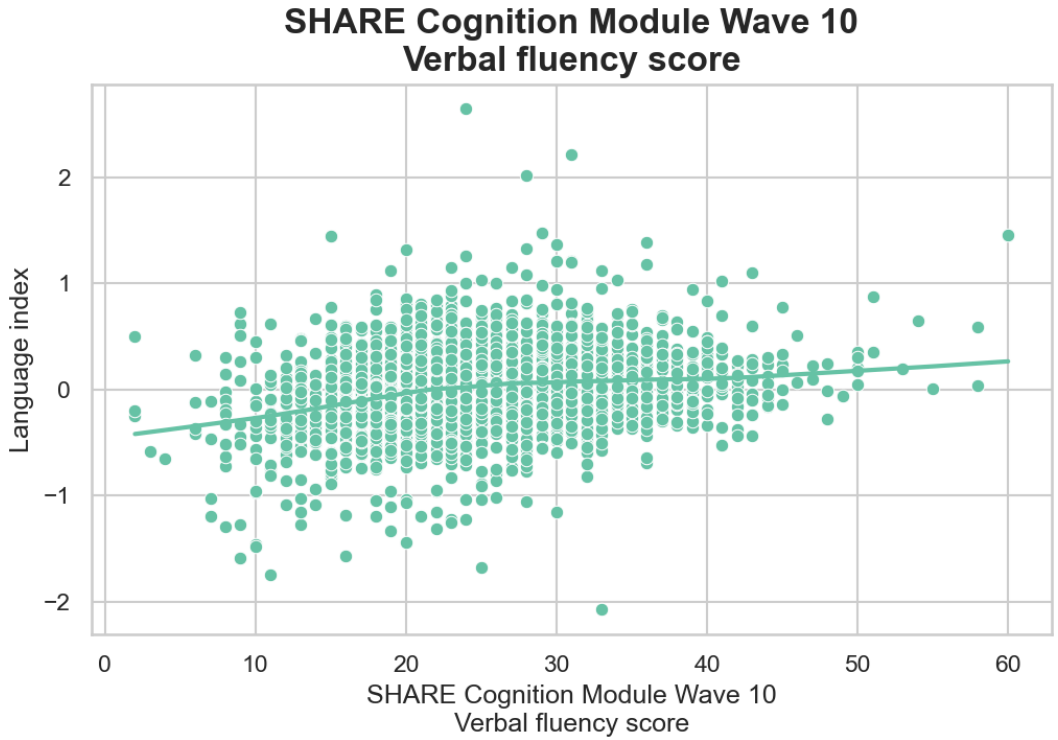
Šubert et al. 2022, Linguistic Abnormalities in Isolated Rapid Eye Movement Sleep Behavior Disorder, Mov Dis.

	Language dimension	Feature description	Healthy speech	Mild cognitive impairment	trend
Linguistic features	***Content richness***	*Content words*, reflect a tendency to prioritize or neglect content-bearing words	*Content words* = 0.55 (-) *...cats are definitely funny animals, and I love them...*	Content words = 0.67 (-) *...I like funny cats. I like dogs, horses too...*	↑
	Grammatical components	*Function words*, evaluate the tendency to use or neglect fuction words, representing the grammatical and syntactic role in a sentence.	Function words = 0.44 (-) *...cats are definitely funny animals, and I love them...*	Function words = 0.33 (-) *...I like funny cats. I like dogs, horses too...*	↓
	Vocabulary range	*Moving-average type-token ratio (MATTR)*, evaluates the richness of vocabulary by exploring unique and repeated words.	MATTR = 1 (-) *...cats are definitely funny animals, and I love them...*	MATTR = 0.78 (-) *...I like funny cats. I like dogs, horses too...*	↓
	Phrase patterns	*N-grams*, assesses the recurrence of phrases against the generation of new ones by monitoring repeated bi-, tri-, and four--grams.	N-grams = 0 (-) *...cats are definitely funny animals, and I love them...*	N-grams = 0.11 (-) *...I like funny cats. I like dogs, horses too...*	↑
	Sentence length	*Mean length of utterance*, evaluate the mean number of words used in a sentence.	Mean length of utterance = 9 (-) *...cats are definitely funny animals, and I love them...*	Mean length of utterance = 4.5 (-) *...I like funny cats. I like dogs, horses too...*	↓
	Sentence development	*Coordinate clauses*, evaluate the sentence development with coordinate clauses.	Coordinate clauses = 1 (-) *...cats are definitely funny animals, and I love them...*	Coordinate clauses = 0 (-) *...I like funny cats. I like dogs, horses too...*	↓

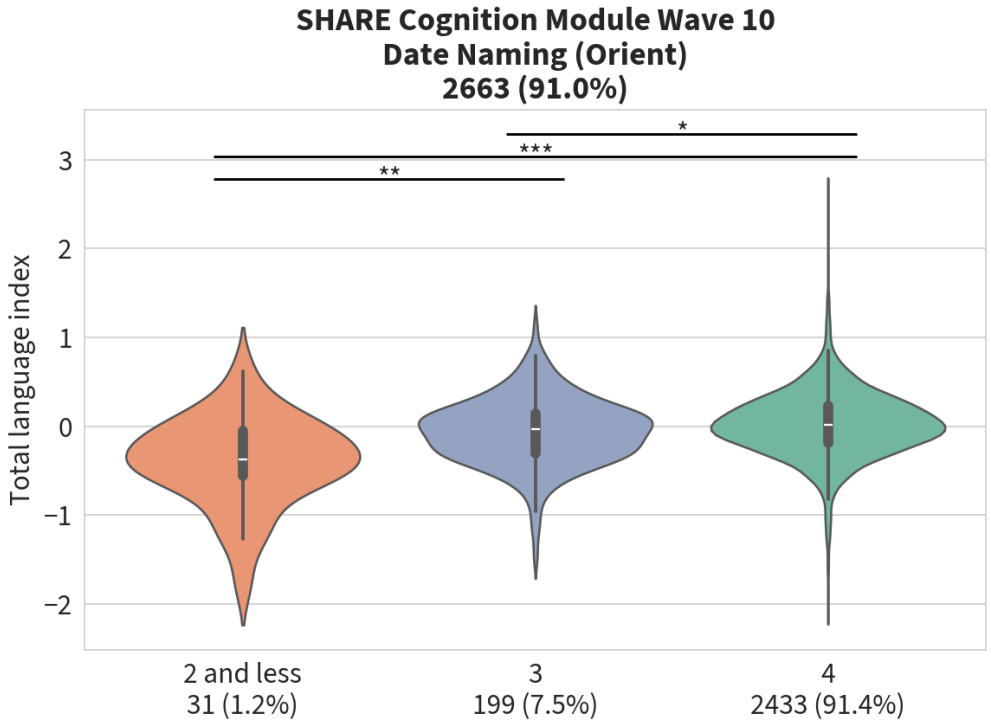
Cognition in neuroSHARE and SHARE

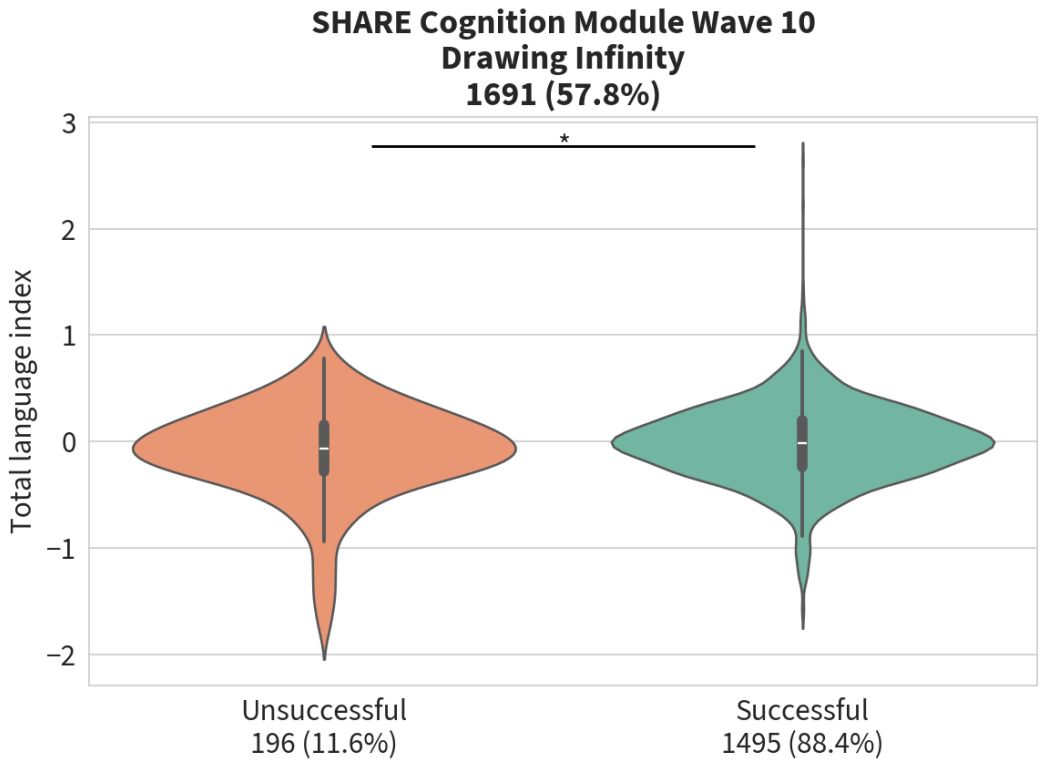
- Relationship between neuroSHARE language and core SHARE congition module in Wave 10





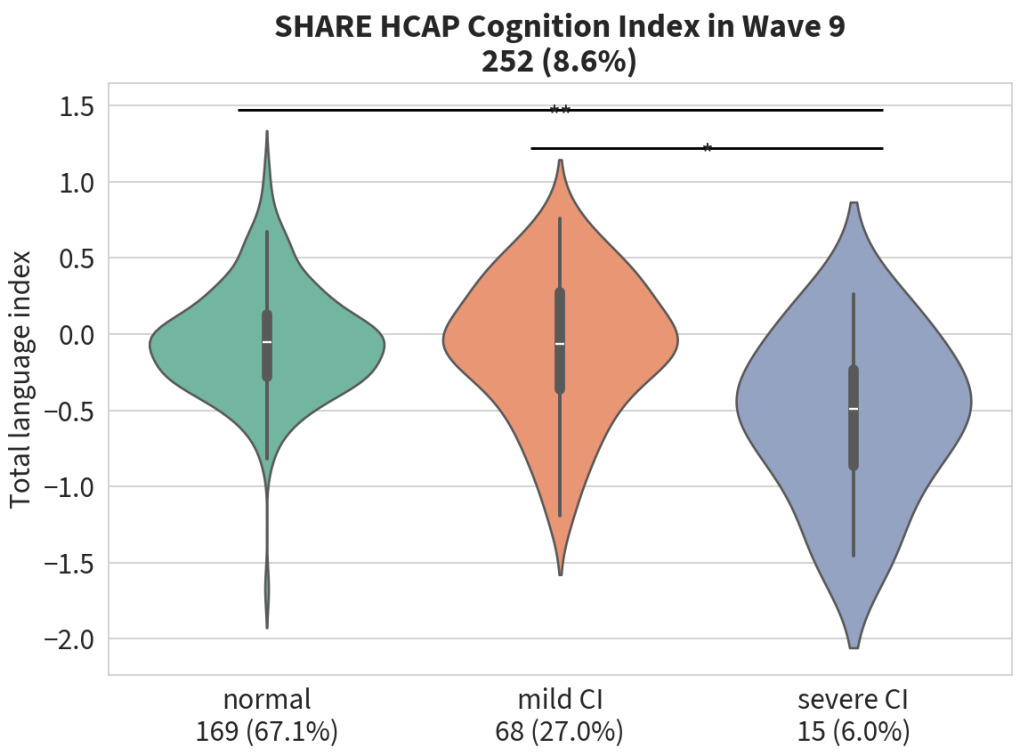
Cognition in neuroSHARE and SHARE

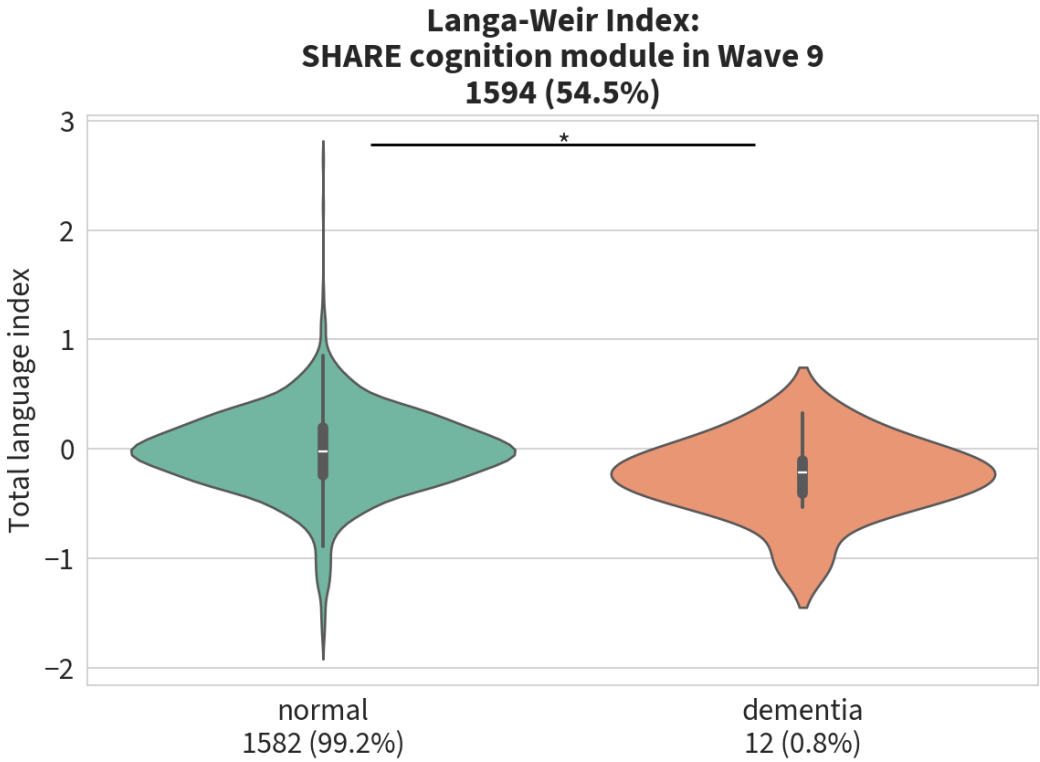




Cognition in neuroSHARE, SHARE and HCAP

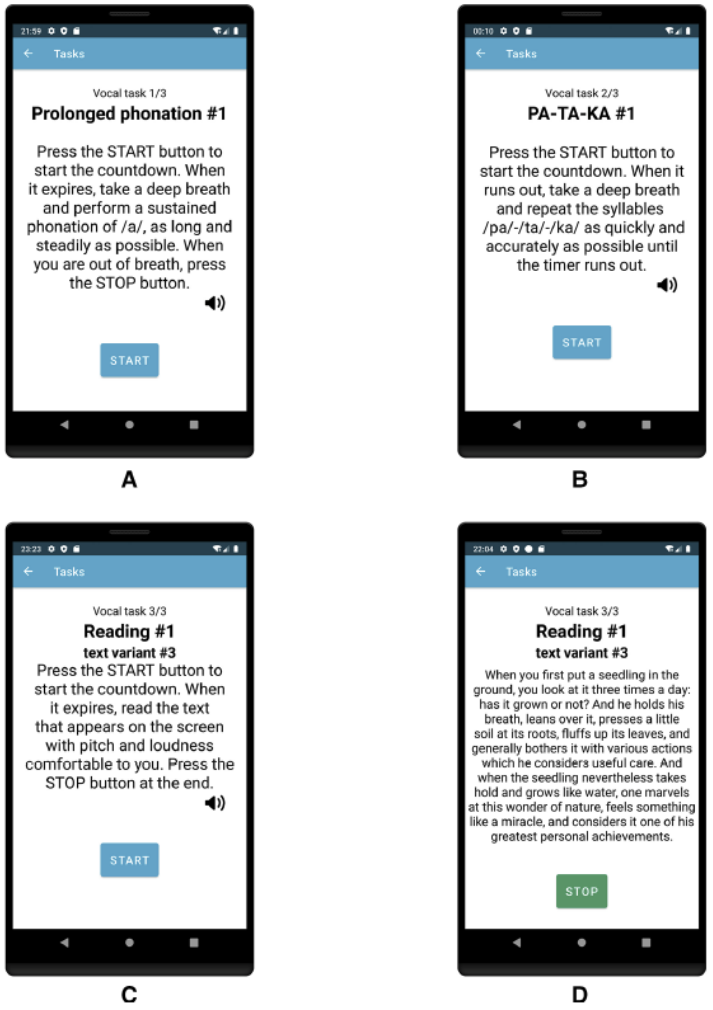
- These two indices are used to compute dementia prevalences
- HCAP data are still preliminary





Future plans

- **neuroSHARE Remote**
  - SHARE Switzerland wave 11
  - Remote version of neuroSHARE using web platform
  - Cost-effective, practical, self-administered

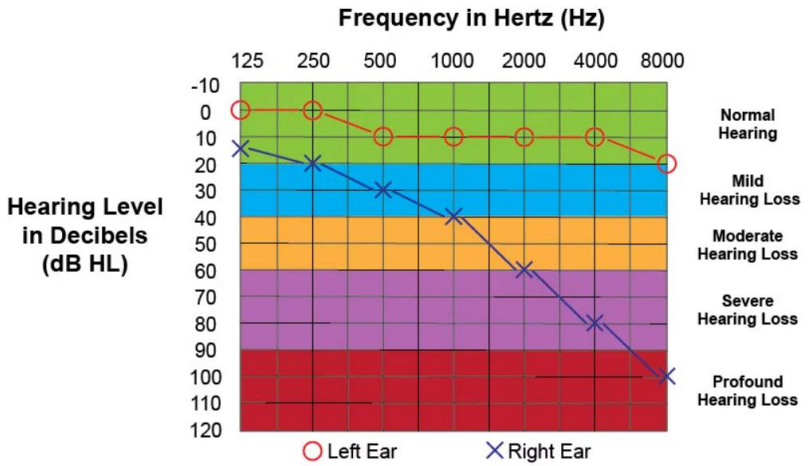


Future plans

- **neuroSHARE Remote**
  - Additional tasks
    - Facial movements during speech
    - Hearing
  - Multilingual environment
  - Focus on cognition

- Extensions to a broader spectrum of neurodegenerative conditions, i.e., dementia

Cheeks			
Cheek Surface Variability	Surface Left/Right	The standard deviation of the image entropy of difference between cheek areas of two consecutive video frames. Describes changes in the cheek area during cheek raising and relaxation.	
Mouth			
Upper Lip Elevation/ Depression	Euclidean Central	The standard deviation of the distance between the upper lip and the nose tip normalized by the distance between medial eye corners. Represents movement of the upper lip.	
Lower Lip Elevation/ Depression	Euclidean Central	The standard deviation of the distance between the lower lip and the nose tip normalized by the distance between medial eye corners. Represents movement of the lower lip.	
Mouth Corner Adduction/Abduction	Euclidean Left/Right	The standard deviation of the distance between the mouth corner and the nose tip normalized by the distance between medial eye corners. Represents changes of the mouth shape.	
Jaw			
Jaw Elevation/ Depression	Euclidean Central	The standard deviation of the distance between the chin and the nose tip normalized by the distance between medial eye corners. Represents movement of the mandible.	



Conclusions

- Successful implementation of neuroSHARE

- The data is still preliminary but promising
- **neuroSHARE as a supportive tool for early neurodegeneration presence in the population**

- **Intriguing potential of the unique combination of:**
  - neuroSHARE (Wave 10)
  - HCAP 1 & 2 (Wave 9, 11)
  - Biomarkers (Wave 11)
  - Linkage to health registers, life history, exposomes, geolocations (Wave 11)

- Slight adaptation of the tests based on validation results might be necessary

Thanks for attention

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