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BIOMARKERS (NON-NEUROIMAGING)

The Down Alzheimer Barcelona Neuroimaging Initiative (DABNI): Ten Years of Progress in Understanding Alzheimer's in Down Syndrome

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Abstract

Background: Down syndrome (DS) is a form of genetically determined Alzheimer's disease (AD). Understanding the natural history and biomarker specificities in this population can offer insights into AD pathogenesis and potential treatment targets.

Methods: The Down Alzheimer Barcelona Neuroimaging Initiative (DABNI) is a prospective longitudinal cohort of adults with DS that builds on a population-based health plan screening for neurological conditions (Figure 1). Conducted at the Alzheimer-Down Unit, the study aims to elucidate the natural history of AD in DS through multimodal biomarker investigations and support clinical trials. Participants undergo neurological and neuropsychological evaluations, blood and cerebrospinal fluid collection, structural 3T brain MRI, PET imaging ([18F]FDG-PET, amyloid-PET or tau-PET), as well as electroencephalography and video-polysomnography examinations.

Results: The DABNI cohort included 1,135 participants with a mean age of 42.82 years (SD = 11.56), 46.3% of whom are female. At baseline, 673 participants were asymptomatic or cognitively stable, 113 had prodromal AD, 239 had AD dementia, and 110 were uncertain due to non-AD conditions. The cohort's intellectual disability level distribution was 20% mild, 50% moderate, 20% severe, and 7% profound. Over 10,000 visits have demonstrated that AD progression is rare before age

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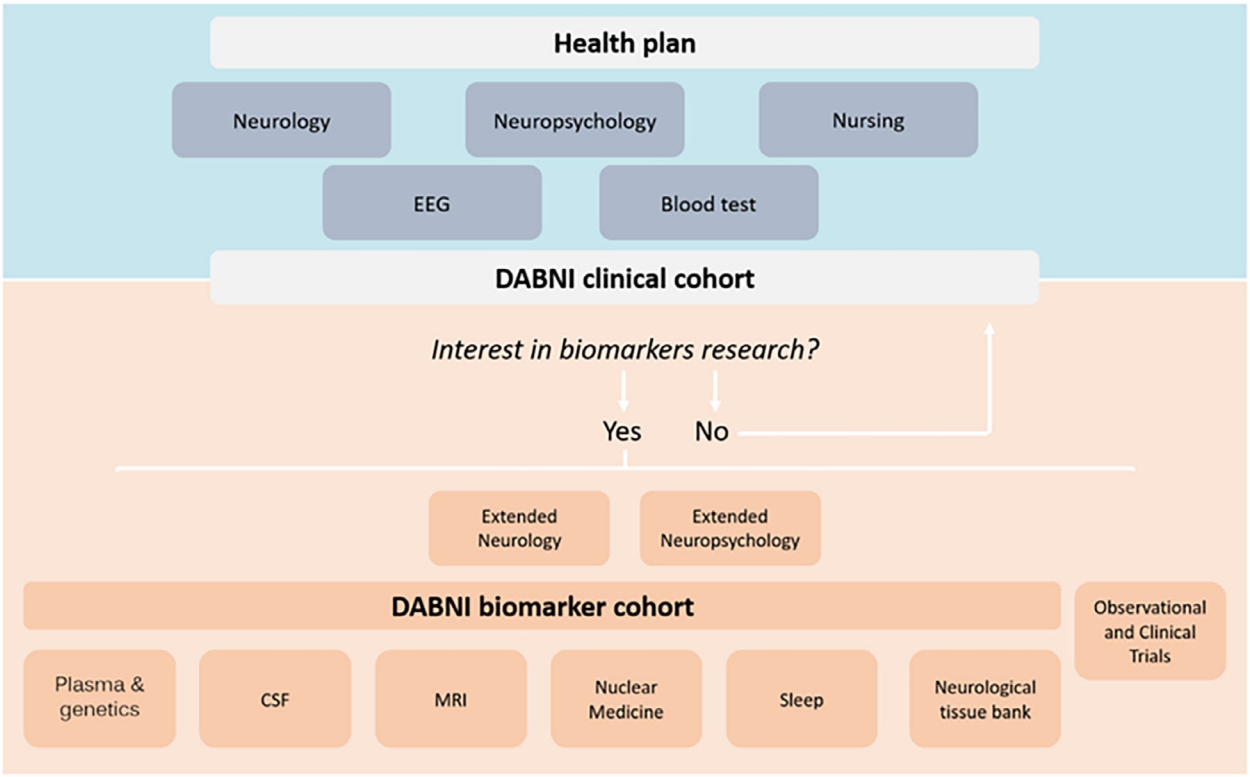
40, but high thereafter (57.5% of individuals over 50 progress within 5 years). Neuropsychological assessments and biomarkers have shown strong diagnostic performance for symptomatic AD, and a prolonged and predictable preclinical phase similar to autosomal dominant AD. The initiative is actively participating in three clinical trials and has yielded a robust body of work, with nearly 100 publications. Table 1 shows the number of clinical visits and biomarker studies in the whole sample and stratified by clinical diagnosis.

Conclusion: In 10 years, the DABNI study has become one of the largest multimodal initiatives on AD in adults with DS and has provided critical insights into disease progression and biomarkers, advancing interventions and clinical research

Figure 1. DABNI flowchart. The health plan run at the Alzheimer-Down Unit and the biomarker cohort, are integrated to optimize data collection and the participant pathway.



Abbreviations: EEG, Electroencephalogram; CSF, Cerebrospinal Fluid; MRI, Magnetic Resonance Imaging; DABNI, Down Alzheimer Barcelona Neuroimaging Initiative.

Table 1. DABNI clinical visits and biomarker studies in the whole sample and stratified by clinical diagnosis.

	Whole sample	Asymptomatic	Prodromal	Dementia	Uncertain
Clinical Visits					
Neurology Visits (total)	**6339**	**2860**	**662**	**2218**	**434**
Baseline (n)	1135	673	113	239	110
Longitudinal (n, mean time between visits [SD])	5204 [0.76 (0.80)]	2187 [1.02y (0.85)]	549 [0.66y (0.74)]	1979 [0.54 (0,66)]	324 [0.81y (0.86)]
Neuropsychology Visits (total)	**4101**	**2529**	**420**	**852**	**296**
Baseline (n)	1078	656	103	211	108
Longitudinal (n, mean FUP time [SD])	3023 [1.09 (0.75)]	1873 [1,2 (0.66)]	317 [0.98 (0,88)]	641 [0,88 (0,77)]	188 [1,18 (1,07)]
Fluid Biomarkers					
CSF total samples (n)	**383**	**157**	**83**	**113**	**30**
Baseline	316	123	68	100	25
Longitudinal	67	34	15	13	5
Blood total samples (n)	**1956**	**1109**	**217**	**509**	**121**
Baseline	753	427	85	177	64
Longitudinal	1203	682	132	332	57
Neuroimaging and nuclear medicine biomarkers					
MRI total (n)	**486**	**261**	**70**	**115**	**40**
Baseline	334	170	53	83	28
Longitudinal	152	91	17	32	12
FDG-PET total (n)	**235**	**111**	**39**	**67**	**18**
Baseline	190	85	32	57	16
Longitudinal	45	26	7	10	2
Amyloid-PET (FBP+Flute) total (n)	**204**	**114**	**30**	**48**	**12**
Baseline	182	104	24	42	12
Longitudinal	22	10	6	6	0
Tau-PET total (n) baseline	**60**	29	7	20	4
Sleep studies and EEG					
PSG	254	154	25	75	0
EEG	163	67	25	46	25
Baseline	152	65	22	41	24
Longitudinal	11	2	3	5	1

Abbreviations: SD, Standard Deviation; CSF, Cerebrospinal Fluid; MRI, Magnetic Resonance Imaging; FDG-PET, Fluorodesoxyglucose Positron Emission Tomography; FBP, Florbetapir; Flue, Flutemetamol; PSG, Polysomnography; EEG, Electroencephalogram.