The European Prevention of Alzheimer's Dementia (EPAD) Programme

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Overview of Presentation

- Brief summary of the EPAD Project and Progress

- The V500.0 Dataset
  - Rationale
  - Results

- The next 5 years for EPAD

The European Prevention of Alzheimer's Dementia Consortium

EPAD
European Prevention of Alzheimer's Dementia Consortium

Academia

THE UNIVERSITY of EDINBURGH
UNIVERSITY OF OXFORD
barcelonaβeta Brain Research Center
Karolinska Institutet
VUmc VU University Medical Center Amsterdam
UNIVERSITY OF CAMBRIDGE
MRC Biostatistics Unit
UNIVERSITÉ DE GENÈVE
Radboudumc
CARDIFF UNIVERSITY PRIFYSGOL CAERDYDD
Hôpitaux de Toulouse
Erasmus MC
Inserm
University of Leicester
Fraunhofer FHR
UNIKLINIK KÖLN

SMEs

SYNAPSE
Berry Consultants Statistical Innovation
aridhia
IXICO

Patient Organisation

Alzheimer Europe

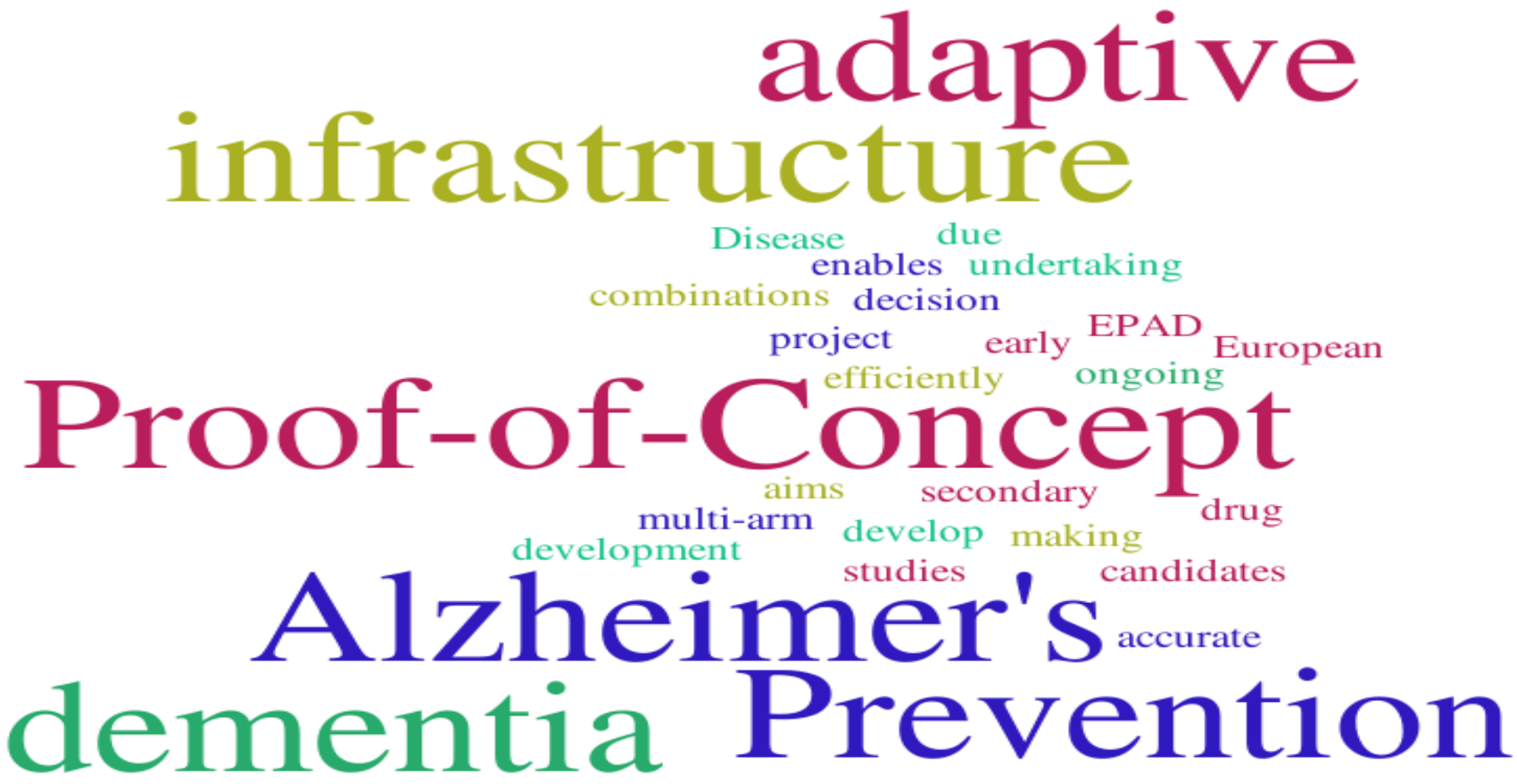
Other industry

QUINTILES
Araclon Biotech GRIFOLS

EFPIA

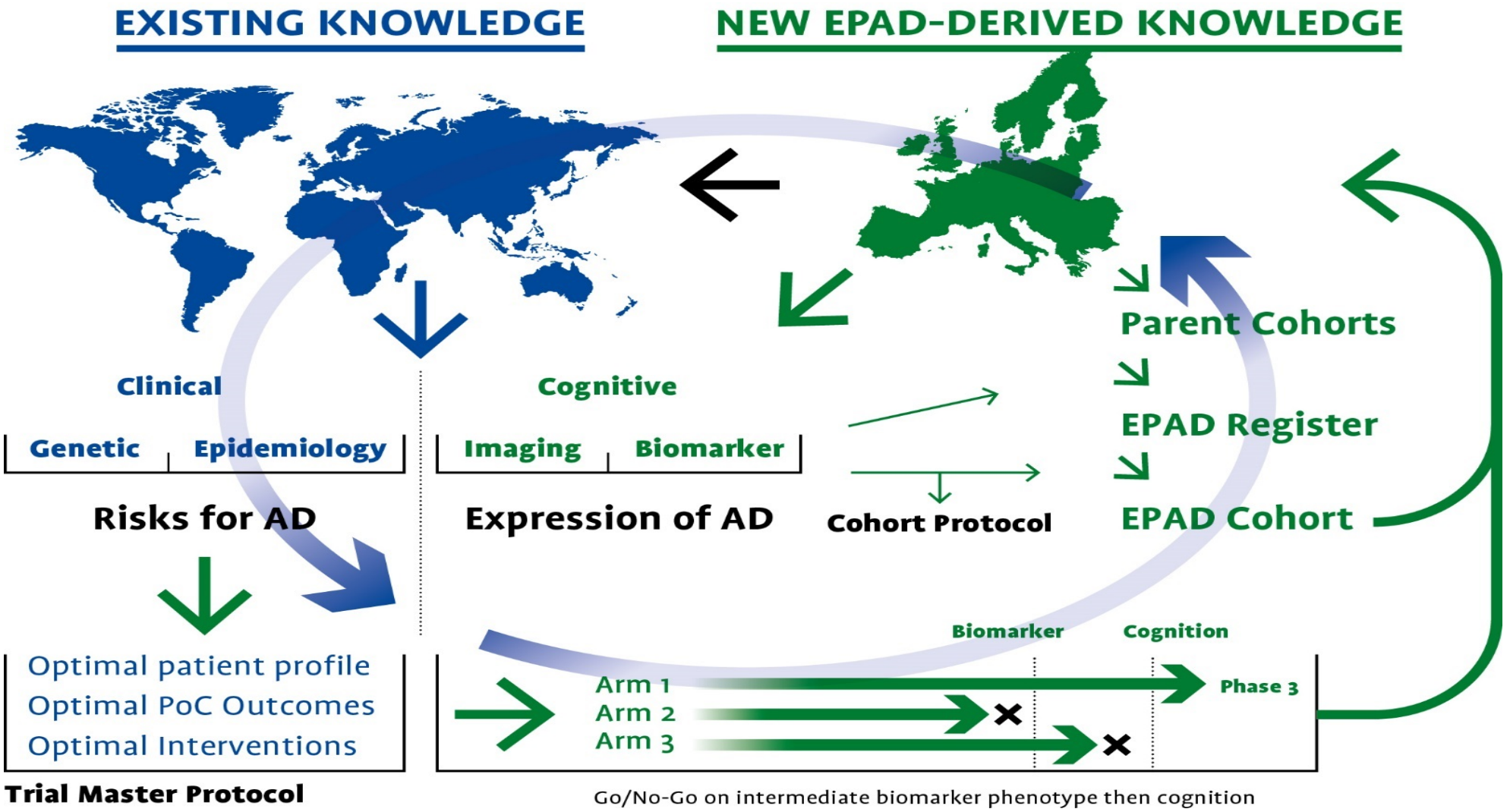
janssen
Eisai
SANOFI
NOVARTIS
Boehringer Ingelheim
Lilly
Lundbeck
Takeda
Roche
AC IMMUNE
Biogen
AMGEN
Pfizer
Inspired by patients. Driven by science.

The EPAD Objectives

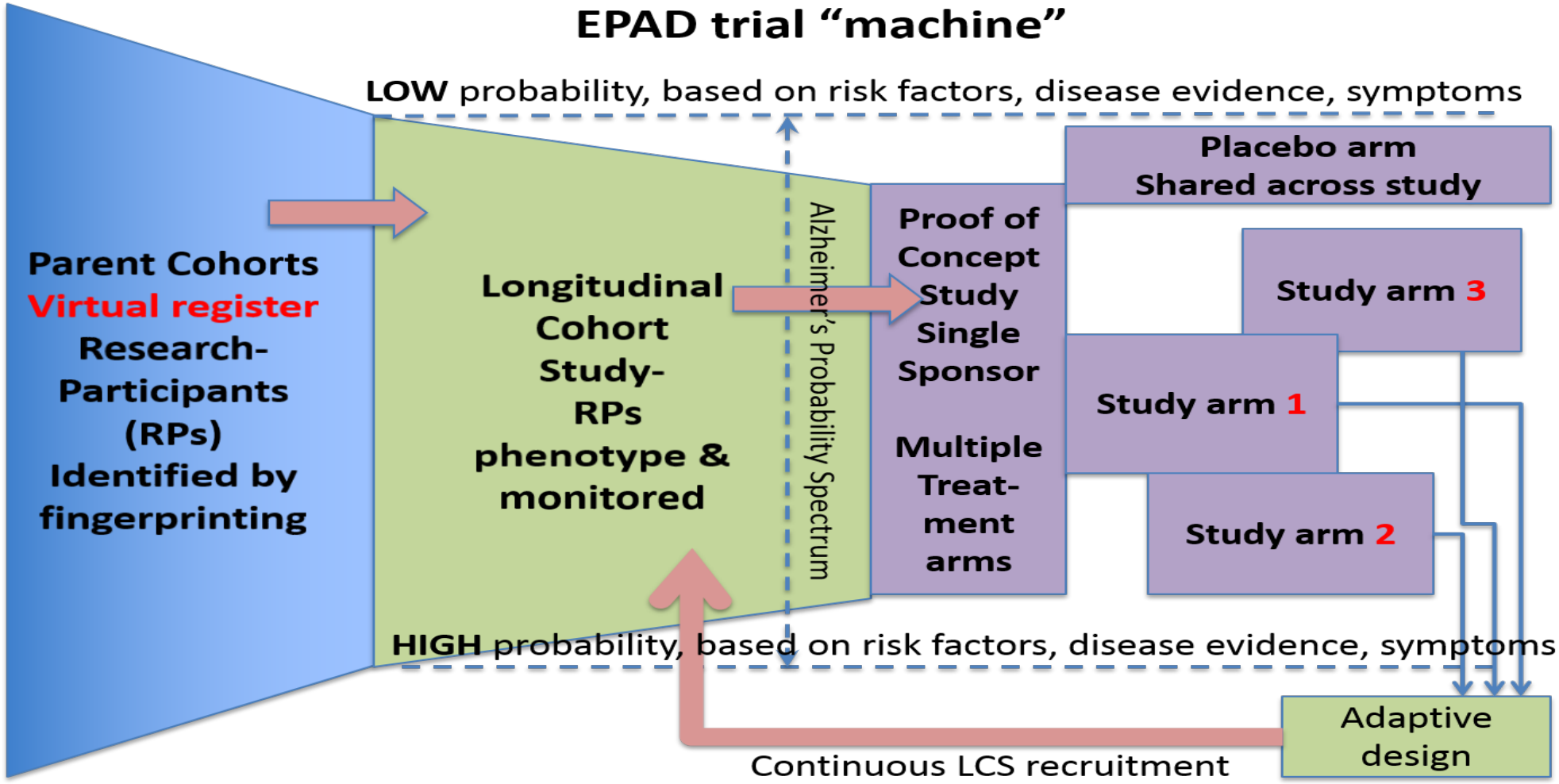


The EPAD Project

EPAD
European Prevention of Alzheimer's Dementia Consortium



EPAD Programme Overview



EPAD Longitudinal Cohort Study

- Readiness
- Disease Modeling
- Run In Data

EPAD Neuropsychological Examination (ENE)

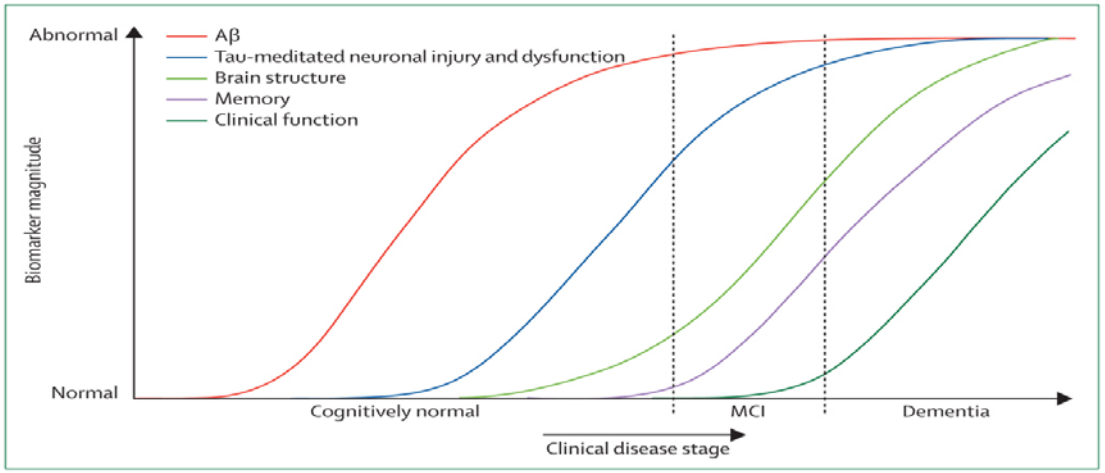
COGNITIVE OUTCOMES

PRIMARY: RBANS - Repeatable Battery for the Assessment of Neuropsychological Status

- Verbal Episodic Memory: List Learning & Story Memory
- Visual Episodic Memory: Figure recall
- Visuospatial/Constructional: Figure Copy & Line Orientation
- Language: Picture Naming
- Attention/Executive Functioning: Semantic Fluency, Digit Span, Coding

SECONDARY: Cognitive Outcomes

- Dot Counting
  - (working memory, NIH Examiner, secondary)
- Flanker
  - (choice reaction time and set-shifting, NIH Examiner, secondary)
- Name/Face Pairs
  - (paired associate learning, University of California, San Francisco, secondary)
- Four Mountains Task
  - (allocentric space, Cambridge Cognitive Neurosciences, exploratory)
- Virtual Reality Supermarket Trolley
  - (navigation in egocentric space, University College London, exploratory)

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Alzheimer's & Dementia ■ (2016) 1-10

Alzheimer's & Dementia

Perspective

Recommended cognitive outcomes in preclinical Alzheimer's disease: Consensus statement from the European Prevention of Alzheimer's Dementia project

Karen Ritchie[a,b,*,1], Michael Ropacki[c,1], B. Albala[d], John Harrison[e,f], Jeffrey Kaye[g], Joel Kramer[h], Christopher Randolph[i], C. W. Ritchie[j]


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Alzheimer's & Dementia ■ (2016) 1-25

Alzheimer's & Dementia

Review Article

Detecting cognitive changes in preclinical Alzheimer's disease: A review of its feasibility

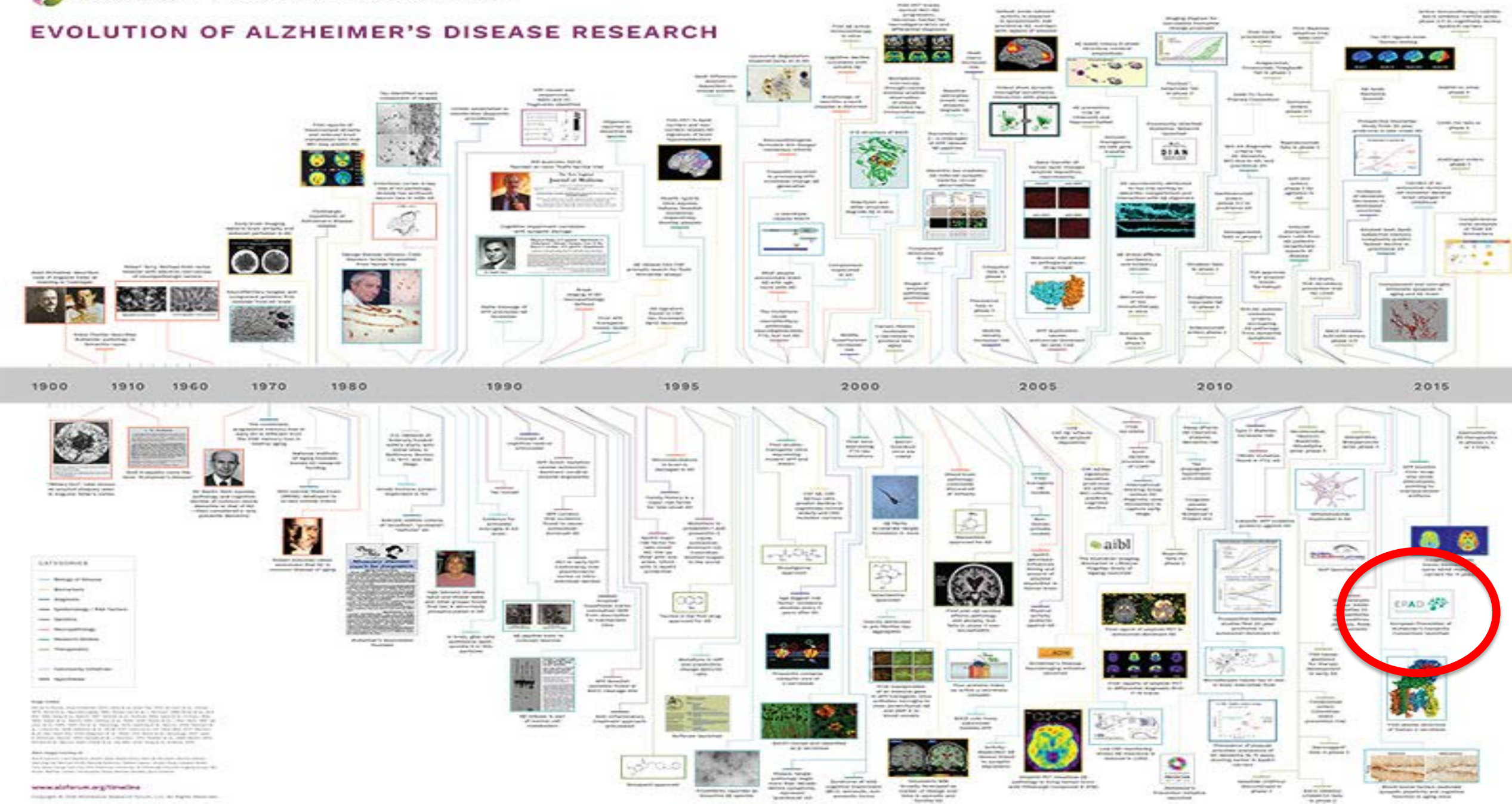
M. Mortamais[a,b,1], J. A. Ash[c,1], J. Harrison[d,e], J. Kaye[f], J. Kramer[g], C. Randolph[h], C. Pose[a], B. Albala[i], M. Ropacki[j], C. W. Ritchie[k], K. Ritchie[a,b,*]

Biomarker Outcomes

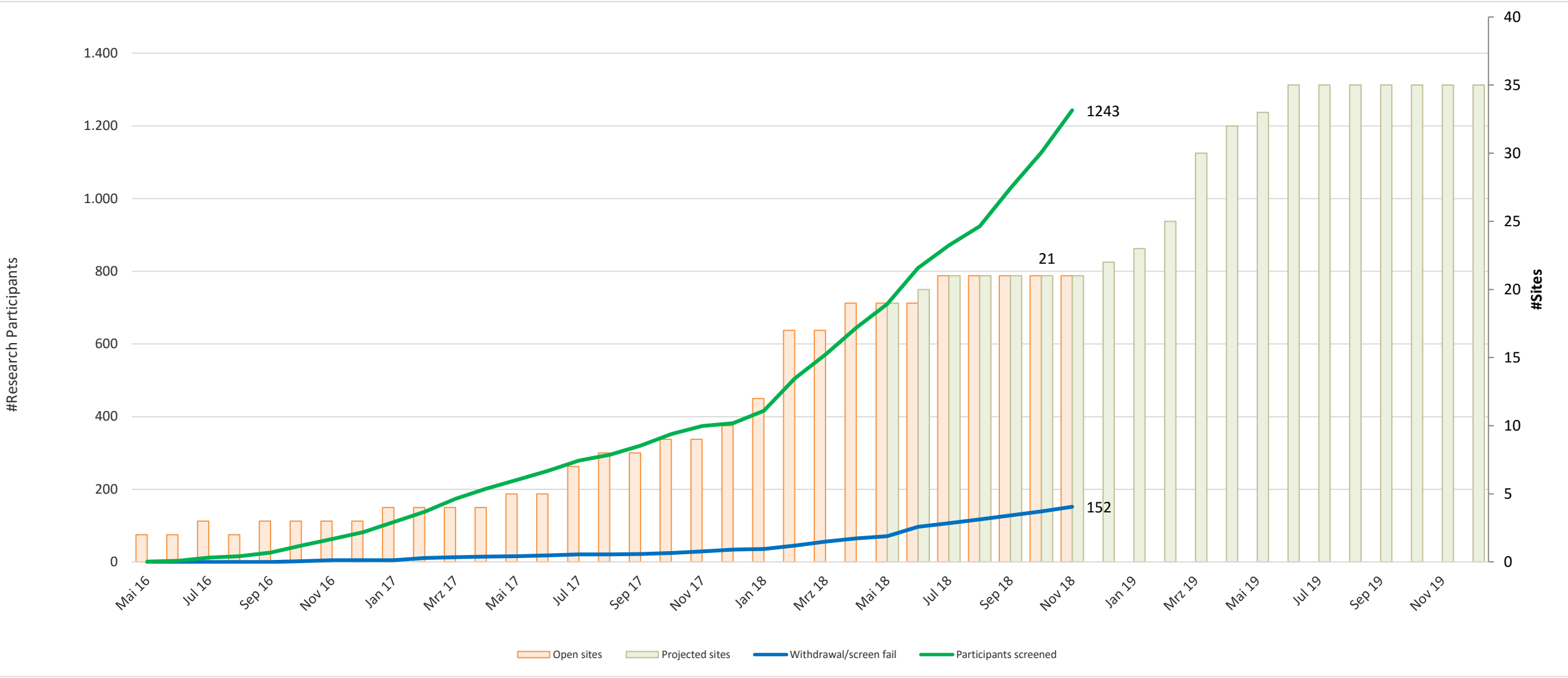
- Secondary outcomes
  - CSF biomarker outcomes: Aβ, t-tau, p-tau Blood, urine, saliva for genomics and assessment of emerging biomarkers
  - Neuroimaging outcomes
    - Structural MRI
      - Cortical thickness, deep grey matter volumes
      - Fractional anisotropy (FA) of temporal lobe, diffusion kurtosis (multi b-value DTI), network alterations
    - Functional MRI
      - Global & parietal CBF
      - Changes within the default-mode network & relation with hippocampal activity (rsfMRI)
      - Bolus arrival time (multi-delay ASL)
      - Network analysis (rsfMRI)
    - PET Amyloid Imaging (AMYPAD)

ALZFORUM Celebrating 20 Years of Alzforum (1996 - 2016)

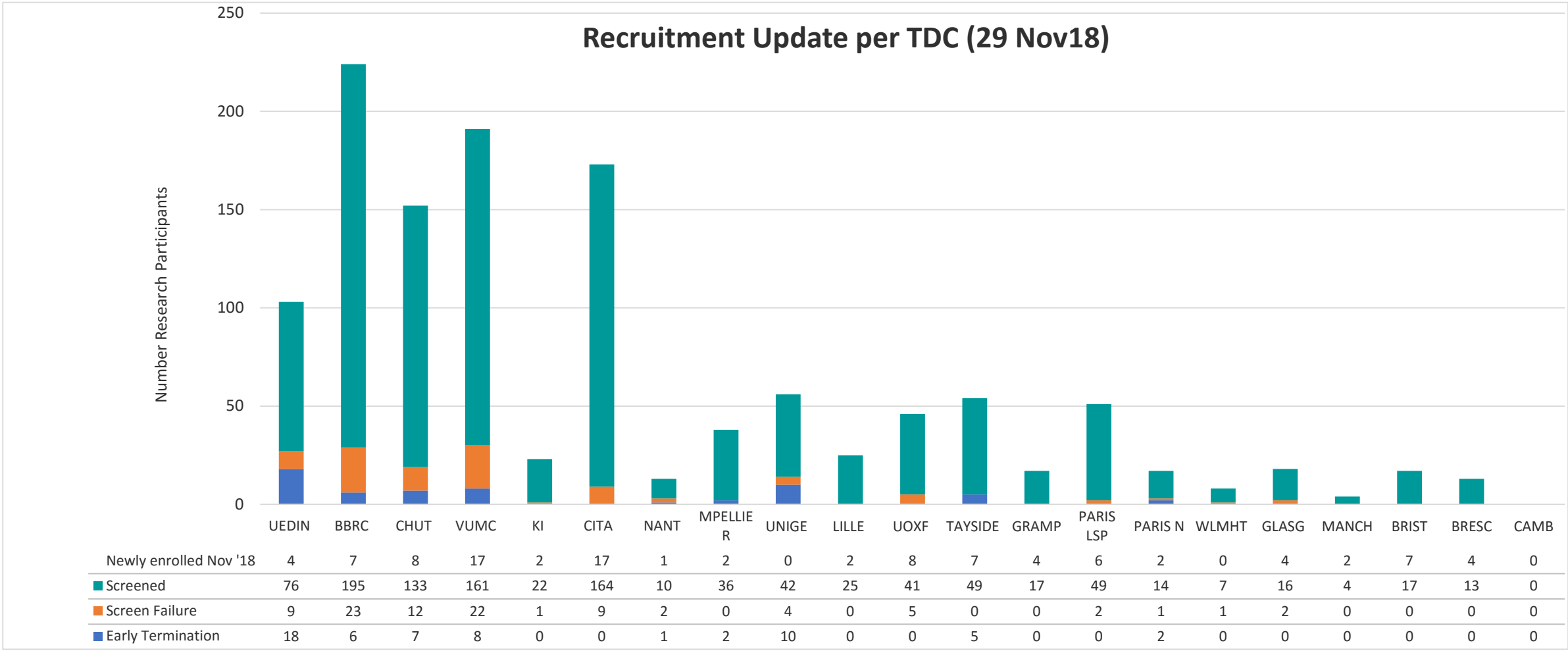
EVOLUTION OF ALZHEIMER'S DISEASE RESEARCH



EPAD Longitudinal Cohort Study Recruitment update



Regional Summary – 20 Nov 18



	UEDIN	BBRC	CHUT	VUMC	KI	CITA	NANT	MPELLIER	UNIGE	LILLE	UOXF	TAYSIDE	GRAMP	PARIS LSP	PARIS N	WLMHT	GLASG	MANCH	BRIST	BRESC	CAMB
Newly enrolled Nov '18	4	7	8	17	2	17	1	2	0	2	8	7	4	6	2	0	4	2	7	4	0
Screened	76	195	133	161	22	164	10	36	42	25	41	49	17	49	14	7	16	4	17	13	0
Screen Failure	9	23	12	22	1	9	2	0	4	0	5	0	0	2	1	1	2	0	0	0	0
Early Termination	18	6	7	8	0	0	1	2	10	0	0	5	0	0	2	0	0	0	0	0	0

The EPAD V500.0 Dataset

- **Rationale**
  - Perpetual recruitment so had to create interim data locks
  - Transparency on data set being used by researchers
    - Aids comparisons of research outputs and meta-analysis
  - Operationally more coordinated
    - Imaging, biomarker and genetic data embedded in main dataset

- **V** = Version
- **500** = the number of sequentially recruited research participants in dataset
- **.0** the study visit the dataset includes up to

- Summer 2019 – expect on basis of current recruitment V1500.0 and V500.1
- 6 month within consortium priviliged access then all data on open data access platform – still to be agreed exact details

The EPAD V500.0 Dataset

- Results[1]

  – All outputs grouped by CDR and Amyloid Status
    - (CSF Aβ <1,000pgml defined as Amyloid Positive)

  – Key variables
    - **Demographics and ApoE status**
    - **Cognition**
    - MRI Imaging (Volumes – Fazeka and Scheltens Scores)
    - Other Clinical – Functional, Sleep, Depression and Anxiety

[1]Ritchie CW et al. **The European Prevention of Alzheimer's Dementia (EPAD) Longitudinal Cohort Study: Baseline Data Release V500.0. (In Press)** ***JPAD*** **2018**

EPAD V500.0 Demographics and ApoE Status

	Total Sample (n=500)	CDR 0 Amyloid – (n=251)	CDR 0 Amyloid + (n=117)	CDR 0.5 Amyloid – (n=37)	CDR 0.5 Amyloid + (n=37)
Age (mean/SD)	66.4(6.7)	64.8(5.9)	65.9(6.5)	69.5(7.6)	71.8(6.6)
Gender					
Female	261(52.2%)	140(54%)	60(23%)	19(7%)	13(5%)
Male	236(47.2%)	111(47 %)	57(24%)	18(8%)	24(10%)
Marital Status					
Married/cohabiting	375	198(59%)	87(26%)	26(7%)	27(8%)
Divorced	54	19(40%)	15(32%)	7(15%)	6(13%)
Single	36	18(60%)	6(20%)	3(10%)	3(10%)
Widowed	32	16(59%)	9(33%)	1(4%)	1(4%)
Years of Education (mean/SD)	14.0(3.7)	14.2(3.6)	13.9(3.8)	13.7(3.7)	14.1(3.9)
Family History (%+)					
Yes	334(67%)	177(71%)	84(71%)	20(54%)	20(54%)
No	166(33%)	74(71%)	34(29%)	17(46%)	17(46%)
ApoE Status					
ApoEe4 Positive (n,%)	190(38%)	91(48%)	59(31%)	6(3%)	21(11%)
ApoEe4/4 (%)	19(10%)	2(11%)	11(58%)	1(5%)	4(21%)
ApoEe4/- (%)	171(90%)	89(52%)	48 (28%)	5(3%)	17(10%)

EPAD V500.0 Associations with Amyloid Positivity[1]

	Univariate Analysis			Multivariate Analysis[2]		
Variable	OR	95% CI	p-value	OR	95% CI	p-value
Age	**1.03**	**1.00 – 1.06**	**0.02**	1.03	0.99 – 1.06	0.07
$Gender_{male}$	1.31	0.9 – 1.92	0.16	1.20	0.80 – 1.80	0.38
Years of Education	0.99	0.93 – 1.03	0.61	1.01	0.95 – 1.06	0.74
Family History +	1.19	0.81 – 1.75	0.37	1.57	0.99 – 2.50	0.12
ApoEe4 +	**2.24**	**1.52 – 3.29**	**<0.0001**	**2.18**	**1.44 – 3.31**	**<0.0001**
CDR 0.5	**1.74**	**1.08 – 2.79**	**0.02**	1.60	0.89 – 2.90	0.12
$RBANS_{total}$	**0.98**	**0.96 – 0.99**	**0.03**	0.98	0.97 – 1.01	0.12

[1]Amyloid Positivity defined as CSF Aβ value <1,000pg/ml
[2]Adjusted for all other variables in the model i.e. age, gender, years of education, family history, ApoE status, CDR score and $RBANS_{total}$

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EPAD V500.0 Summary (2)

- Data release to consortium due December 2018
  - P100 Vermunt Study enrolment from parent cohorts
  - P143 Ropacki Cognitive data summary
  - P165 Stirland Amyloid Status and Co-morbidities
  - LBP54 Bauermeister Psychometric Methodologies (DPUK)
  - OC38 Ritchie V500.0 Presentation

  Imaging analysis ongoing within VUMC under Barkhof

- V500.0 **global** release summer 2019
- V500.1 consortium release December 2019
- V1500.0 consortium release summer 2019
  - (presentations CTAD San Diego)

- EPAD Longitudinal Cohort Study Recruitment improving month by month

Next Steps

- PoC planned to start in 2019
- Cohort balance optimised for readiness
- Site opening to reach over 30 in 2019
- Initiate sustainability plans
- Establish l'Academie for all new knowledge and scientific oversight of EPAD2

Acknowledgements

The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115736, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.