

IMI1 Final Project Report Public Summary

Project Acronym: EPAD

Project Title: European Prevention of
Alzheimer's Dementia

Grant Agreement: 115736

Project Duration: 01/01/2015 – 31/10/2020

Executive summary

1.1. Project rationale and overall objectives of the project

According to the World Health Organization, an estimated 36 million individuals are currently living with dementia and it is expected to increase to 115 million by 2050. Alzheimer's disease (AD) is the leading cause of dementia globally. It affects around 7 million people in Europe. Clearly, the need to develop interventions for preventing Alzheimer's disease dementia has never been greater. Conventional drug development approaches for the treatment of Alzheimer's disease dementia have failed to produce success to date for a variety of reasons: the therapeutic targets may have been incorrect; the treatments may have been given too late in the disease process; phase 3 studies were undertaken before proof of concept was clearly demonstrated; and the utility of the clinical and biomarker endpoints that were incorporated in the trials were not understood as much as they might have been.

The European Prevention of Alzheimer's Dementia (EPAD) consortium, launched early 2015, is a research initiative designed to facilitate the development of new drugs for the secondary prevention of AD dementia by improving the understanding of the early stages of Alzheimer's disease and how it progresses to dementia and by establishing a clinical research infrastructure, including a large pool of research participants willing to participate in trials, to investigate new treatments that aim to prevent or delay the onset of clinical symptoms in people at risk of developing Alzheimer's disease.

Besides the development of the platform and the research activities, possible sustainability models for EPAD are studied to ensure adequate post-project continuation of products and services developed.

1.2. Overall deliverables of the project

The overall aim of EPAD was to define an accurate set of criteria for identifying Alzheimer's pathology early in the course of disease in people who have no or minimal associated symptoms and to develop a research platform that efficiently enables the undertaking of adaptive, multi-arm Proof of Concept studies for early and accurate decisions on the ongoing development of novel interventions, including drug candidates and drug combinations, for the prevention of AD dementia. The EPAD framework consists of three core structures – the EPAD Register, the Longitudinal Cohort Study (LCS), and the Proof-of-Concept Trial (PoC).

The first step was to identify approximately 24,000 participants from pre-existing European cohorts that will be available via the EPAD Register. The EPAD Register will serve as the main recruitment pool for the entire EPAD framework.

From the Register, initially approximately 3500 participants were selected for the EPAD LCS where participants will undergo a series of regular assessments of biomarker, clinical and cognitive status. The data collected in the LCS would contribute to the understanding of contributing factors of the onset of dementia, as well as providing pre-intervention/randomization data for participants randomized into the PoC.

From the LCS research participants will be identified and randomized into the EPAD PoC – a standing, double blind, adaptive clinical trial to evaluate potential treatments for the prevention of Alzheimer's dementia. Treatments that are effective in the PoC will be ready to proceed to phase III clinical trials. The EPAD trial platform infrastructure is fully operational, however, due to the lack of suitable interventions during the project's lifetime no clinical PoC was initiated.

1.3. Summary of progress versus plan since last period

EPAD has progressed as detailed in the following sections. The main area of focus during this reporting period was monitoring and implementing recruitment enhancement strategies of the Longitudinal Cohort Study to drive it towards a readiness cohort and finalization of the EPAD Proof-of-Concept Trial Platform Infrastructure. This achievement is the result of a continuous coordinated activity of the different Work Packages in EPAD.

In the final period progress can be summarized in four domains:

1. Cohort readiness
2. PoC Platform establishment and completion of an appendix protocol
3. Trial Delivery Centre (TDC) preparedness for PoC
4. Sustainability

Cohort Readiness

Through the work of the Balancing Committee and following several protocol amendments, recruitment prioritized and achieved greater proportions of research participants who, at baseline, were characterised as having prodromal Alzheimer's disease. This population represented those being sought by intervention owners who were in discussions with the CCSC and working on developing an appendix. Through 2019, the cohort expanded well and with the right balance in the population. Over 2,000 participants were screened by the end of the IMI period and new TDCs coming into the project performed very well and the cohort was certainly ready for both prodromal and preclinical studies had they eventuated in 2019/20.

PoC Platform establishment and completion of an appendix protocol

The legal, research governance and operational aspects of developing the master protocol, vendor contracts, sponsor oversight (including delegation of duties) was completed in 2019. This allowed confident progression of establishing two Appendix writing groups that added to the one that was set up in 2018 and was disbanded after the drug to be trialed did not progress in development. In 2019, one drug was pulled as finance could not be secured by the biotech and the second, in late 2019, as legal agreements could not be secured around an issue related to audit. Therefore, although the cohort, TDCs, master protocol and vast majority of research governance was in place towards the end of 2019, an inability to overcome a legal point led to no appendix protocol being completed and therefore no PoC trial commenced.

Trial Delivery Centre preparedness for PoC

With the expectation that in late 2019 or early 2020 a PoC trial would start in a prodromal population, new sites were rapidly opened through 2019 that, in particular, had good access to the right population either through extensive registers or from clinics. This led to the structure of the cohort matching the needs of the trial. Moreover, investigators and their teams attended several meetings and workshops about the master protocol and appendices to prepare for a rapid start up when the final appendix protocol was ready to initiate. The close working relationship with the Global Alzheimer's Platform continued during this period and has been sustained through 2020/21 as they collaborate with all sites in the TDC network to benefit from their brokerage with numerous sponsors.

Sustainability

Work package 7 had performed against all its deliverables through the course of the project, but the pressure brought by the end of the IMI period led to an increase in activity for the project sustainability which included thoughts on programme governance, funding models and continued brand management. All this was predicated on the likelihood of having a PoC launched and therefore

an ongoing funding source. When this option was removed, attempts were made to secure funding for key elements of the programme. This was achieved for 2 years for the maintenance of the database, biosamples and branding/communication but not for the ongoing follow up of research participants in the LCS. In early 2020 it was agreed that each site/country would need to seek funding for the follow up of their own participants. The whole programme was dependent on achieving the primary objective of starting a PoC trial, when this was not achieved, the foundation to any sustainability of the readiness cohort was removed and instead attention was focused on the sustainability of other key EPAD assets namely data, samples, brand and site network. Onboarding GAP to support the site network and a US-based grant allows the data, samples and brand to be maintained for another 2 years (ie., until mid-2022).

1.4. Significant achievements since last report

Each Work Package documented success against deliverables but by the nature of EPAD, the key achievements were attained through transversal work between work packages as listed in 1.3. By work package, the key highlights are:

WP1: The SAGs worked closely with the bioresource in Edinburgh and imaging core at VUMC to ensure that laboratory samples and imaging data were processed and stored optimally for future use.

WP2: Study statisticians oversaw the final curation of the LCS database with issuance of the final study report as well as optimised structure for making available on the ADDI platform (<https://www.alzheimersdata.org/about-addi>).

WP3: The viewing of live data for recruitment was optimised by creation and delivery of SEEPAD (Subject enrolment in EPAD) https://lcsgraphs.pr-epad.org/?api_key=81ef0cf19e8406c8c3900c5bd95ab75c# and completion of a PhD based entirely from within the EPAD Academy.

WP4: The cohort study delivered 2096 screened research participants. In the trial network, 29 TDCs were active and the Master Protocol and all aligned legal, governance and operational documents and structures were in place. The CCSC also reviewed 8 compounds by the end of the IMI period. At the 2019 AAIC in Los Angeles, a Presentation Booth further encouraged collaboration with both academic groups, funders and intervention owners further enhancing the global visibility of EPAD within the AD community.

WP5: Overseeing the 2019 Geneva GA (continuing year on year increases in attendance) and budgetary analysis to feed WP7 sustainability activities. The 2020 Edinburgh GA, although fully organized, had to be cancelled because of the COVID-19 pandemic.

WP6: Numerous webinars, newsletter releases, updating YouTube channel and increased presence on social media with additional 625 followers and 689,100 interactions.

WP7: Development of the EPAD Programme: a 5-Component Model including the Site Network, the Registers, the Cohort, the Trials and the Academy. For each Component, the purpose, the management structure and the potential funding sources were identified/ EPAD LCS: Funding has been awarded to secure storage of samples and data, and to maintain the systems and processes that have been established to facilitate open access to the data and samples, via www.epad.org/erap/ The EPAD Academy has successfully built a community of 66 AD Early Career Researchers.

WP8: Continued to provide ELSI inputs to all EPAD outputs as appropriate through CDEx as well as specifically completing survey on reporting of incidental findings as well as recruitment and disclosure materials for investigators to use as research participants transition from LCS to PoC.

1.5. Scientific and technical results/foregrounds of the project

The reality is that given that data curation and access was a late-stage delivery of the project from the LCS, the data releases V500.0, V1,500.0 and V500.1 were superseded by V.IMI once the programme closed – so foreground derived from data analysis is limited during the final reporting period, though with the data now on the ADDI Platform and being released since Q3 2020, there have been almost 200 data requests approved and almost 10 sample access requests. Several methodology and white papers were published during the IMI period on development and choice of the cognitive outcomes, the imaging protocol, the LCS methodology and the conceptual and scientific basis for EPAD. The key asset from the project was the data and the samples which were secured with 2 years of follow-on funding from the Alzheimer's Association.

As well as cohort methodology, the master protocol and platform structure has been developed but not yet published in peer reviewed journals, though the EPAD project does form an entire chapter in a textbook on AD Clinical Trials edited by Cummings et al (in publication). The developments within WP3 of PrePAD, SEEPAD and associated publications was a notable development of the project and one that built on and optimised work started in IMI-EMIF. The TDC network was established to contain the pre-eminent sites in Europe for AD research and this has been carried forward by GAP to be incorporated in their global trial network. It is worth noting that the global visibility of EPAD meant that attainment of all funding post-EPAD has come from the USA. Within the communications work package, the website and social media platforms have been maintained for at least 2 years to ensure that the EPAD community bound by public visibility has been secured. The model of engaging participants as partners has been clearly articulated through several outputs in WP8 which includes peer reviewed academic publications. A full bibliography of all academic outputs is provided in section 1.8.

1.6. Potential impact and main dissemination activities and exploitation of results

EPAD work and the input of each EPAD work package throughout the project has resulted in significant outcomes and contributions to the scientific community. The longitudinal data collected in the LCS has been made available at no cost to the entire research community through the official data releases V500.0, V500.1, V1500.0 and V.IMI. Additionally, the LCS biological samples (cerebrospinal fluid, urine, blood and saliva) can also be accessed not only by EPAD partners but also by external research groups.

The PREPAD/Velosity system can speed up recruitment of individuals for trials in AD and as such provide health benefits in the future. The implementation of PREPAD in cohorts across Europe could potentially increase competitiveness of Europe and makes Europe an attractive place for biopharmaceutical research and development.

Through the ongoing collaboration with industrial partners in EPAD, PREPAD has been presented to Pharma partners within and outside Europe, including the Global Alzheimer's Platform (GAP) consortium. The integrated registry approach developed in EMIF was applied and optimised during EPAD project and the learnings have catalysed development of new registers specific to AD in the UK (SBHR and Great Minds) and Germany (KOLN registry).

The disease modelling work performed by WP2 will improve the understanding of the Alzheimer's disease process over time, identifying important biomarkers which can be used to inform management of patients and new targets for drug development and help improve recruitment/selection into clinical trials for Alzheimer's Disease in Europe and worldwide.

EPAD has also created a platform trial structure that allows multiple arms to enter a single trial platform located in the EU to allow more efficient drug development in the EU. The knowhow in

developing such a platform can inform future initiatives of this nature that may also choose to expand the offering beyond secondary prevention studies to symptomatic and Phase 3 trials.

The work of the EPAD ethics, legal and social implications (ELSI) work-package (WP8) has undoubtedly contributed to overall IMI objectives in terms of ensuring the responsible development of novel Alzheimer's therapies and diagnostics in a way that is most able to contribute to the health of European citizens and societies. The findings of WP8 have contributed more widely in several ways:

- The model for the consent process for readiness studies has been discussed and developed in the UK Government's Accelerating Detection of Disease (ADD) initiative.
- The work on the longer-term impact on individuals of the move to targeted prevention in Alzheimer's disease (through the ACAR substudy) has been taken up within the international Advisory Group on Risk Evidence Education for Dementia (AGREED) group.
- The work on participant experience developed in the SPEAR sub-study has been fed into the development of work in the Canadian Consortium on Neurodegeneration and Aging, as well as the UK MRC's Deep and Frequent Phenotyping Study.
- EPAD ELSI activities have closely informed the development of work in the IMI AMYPAD study, and WP8 leads have contributed to ongoing work or advisory roles in a number of other IMI and H2020 projects, primarily the privacy and ethics working group of NEURONET but also RADAR-AD, MOPEAD and EHDEN.
- The uptake of WP8's work by the scientific and clinical community formed the basis for a successful application to the Brocher Foundation, Geneva for an international symposium on the Social and Ethical Consequences of the re-definition of Alzheimer's disease.

Additionally, EPAD scientific presentations and publications will be relevant for scientists worldwide.

The EPAD Project achieved global visibility through its scale and the successful delivery of the LCS. Moreover, active engagement work with the Biotechnology and Pharmaceutical Industry sector complemented the inherent private-public partnership of EPAD to raise awareness and demonstrate credibility of Europe as academic, industrial and operational leaders in the neurodegeneration field. This will be further enhanced with the anticipated substantial academic output from the LCS which will occur through 2021. The data from the EPAD LCS has been seen as an exemplar for free, rapid and open access by global organisations such as the Alzheimer's Disease Data Interoperability Programme (<https://www.alzheimersdata.org/about-addi>) and the Davos Alzheimer's Collaborative (<https://www.davosalzheimerscollaborative.org/>). This reputational success helps reinforce the ability and attitude of Europe to collaboration and delivery.

The trial delivery site network and the community that built up around this and the programme as a whole has facilitated collaboration with the Global Alzheimer's Platform which envisages a truly global AD site network for delivery of all types of clinical trials under a singular governance structure. The European ability to deliver complex protocols with very large number of participants per site has acted as a beacon for sponsors and other academics to seek to contract or collaborate with EPAD from 2020 onwards.

1.7. Lessons learned and further opportunities for research

The collaboration in a public private partnership (PPP) has added a significant value for the achievement of each work package's goals and it is also extendable to the whole EPAD project development. The good interaction between pharmaceutical industry and academic partners has enabled the generation and effective integration of scientific knowledge. From the overall EPAD perspective, we believe on the added value of this PPP on three different aspects:

- Sharing knowledge and best practice
- Deconstructing fear and mistrust on both sides of the partnership
- Recognition of shared objectives and values

Besides these, this PPP has also yielded benefits to each individual EPAD work-package listed in Section 2.5.

In summary though and in true Bayesian fashion, had we known then what we know now, what would we do differently?

The truth is, very little. Perhaps, had EPAD looked more closely at the offering and maintained its focus in the preclinical space as had been the original intent in IMI-EPOC-AD we would not have had downstream 'competition' from existing disease programmes. That was also the space where there was most uncertainty in disease models forming a bridge between programmes like DIAN (familial AD), ALFA and PREVENT (mid-life) and ADNI and AIBL (MCI, later life).

The Management Consultant guru Peter Drucker is famously quoted as saying that 'Culture eats Strategy for Breakfast', and whilst EPAD developed an amazing, internal 'EPADista' culture, this was not broadly shared with key decision makers especially outside of Europe. Whilst the collaboration and dialogue with GAP was purposeful throughout, the GAP and EPAD programmes evolved with different emphasis mid-way through the EPAD programme, isolating the developments somewhat from global developments and culture. These two major programmes are merging once more which will be of huge benefit for all under the umbrella of the Davos Alzheimer's Collaborative.

Finally, the legal and governance framework that EPAD existed within would not or could not change or flex to accommodate some of the more innovative aspects of the programme. Intervention owners were being asked to place their lead assets for AD into a platform that was being governed by a 3rd party sponsor. There was no 'proof of platform' to refer to, perhaps with a back-up compound that would have mitigated concerns about this set up for the ultimate decision makers in organisations who, in a historically unrewarding clinical area, may be risk averse. Had EPAD onboarded some assets to test the system, perhaps drugs that could be repurposed, drugs that had failed Phase 2 (or 3) in mild Alzheimer's dementia and prodromal, then we could have had real evidence as opposed to theoretical assurance that the system worked.

■ WP1- Scientific Challenges

From the academic side, the input and contribution of the experts in the field has provided a central rationale for the design of strategies, choice of best outcomes and suitable participants and criteria, based on the latest scientific evidence on Alzheimer's disease prevention. In turn, the private sector has provided extremely valuable expertise in the design and development of study protocols, as well as in the implementation and management of the study throughout the different TDCs.

In view of the WP1 achievements and knowledge gathered, and in line with the current status of research in the field of Alzheimer's disease prevention, EPAD recommends future research to focus on the following key points. First, future studies should address the pathophysiological mechanisms arising in the preclinical stage of AD, e.g., analysing biomarkers other than the core AD biomarkers (amyloid- β and tau). A better understanding of the pathological cascade would enable optimizing stratification of patients for trials and to progress towards precision medicine approaches. In this

regard, expanding the biomarkers outcomes in cohorts like EPAD would add great value for future projects. Besides, growing efforts are being put in place in studying non-pharmacological interventions as prevention strategies to avoid or delay the progress of the pathophysiological cascade in this early preclinical stage of the disease. Altogether, it will be crucial to maintain the longitudinal follow up in the EPAD cohort, to allow for further research on the progression of Alzheimer's disease- related pathology, the actual effect of risk and protective factors, and as a trial-ready cohort for testing therapeutic and preventive interventions.

■ **WP2 – Statistical/Methodology Engine Room**

From the WP2's point of view, the collaboration in a public private partnership has allowed access to the expertise of academic as well as non-academic partners, thus improving the understanding of the data being generated and how to best model them. Future studies could potentially focus on modelling digital and novel biomarkers and integrative modelling is required to further advance the field. Additionally, it is necessary to develop continued innovative analysis methods across cognitive endpoints. Finally, we believe it is important to continue to present the concept of a platform trial to potential intervention owners with the potential to start the PoC trial, as this is the one innovative aspect of EPAD that remains to be tested.

■ **WP3- EPAD Register**

Through the public private partnership WP3 could design the EPAD register and PREPAD and SEEPAD tools tailored to the needs of recruitment for clinical studies.

Limitation of the recruitment through registers was depletion of individuals needed for the clinical studies. A recommendation for a future public private partnership would be to use parent cohorts with active recruitment or recruitment through online registers with enrichment of individuals for key AD biomarkers

While currently screening was performed using existing data with a modest diagnostic accuracy for AD, implementation of blood testing for AD biomarkers in the pre-screening process may increase identification of individuals at high risk for AD. Thus, we believe this would be a very interesting research topic to further advance the field.

■ **WP4 – EPAD Studies**

Similarly, the EPAD public private partnership has allowed WP4 to bring together the best expertise from both industry and academia to build and design the EPAD LCS and the PoC Platform.

From WP4's perspective, new research could bring resources to follow up on the EPAD LCS in partner sites and countries. Additionally, an interesting partnership for the future could focus on data interoperability and sample management/access.

WP4 has compiled a set of recommendations and lessons learnt deriving from the EPAD public private partnership that could also be relevant to future collaborative projects with similar scopes.

- We recommend subcontracting all study sites and retaining more budget as contingency.
- We recommend establishing an LCS steering group and stick with the plans set up by this group.
- Running a disease-modelling observational cohort and a trial-ready cohort under the same protocol is probably not the best approach as the necessary trade-offs lead to compromises that are not conducive for obtaining the best outcomes for both objectives.
- Early 'proof of platform' for the PoC would have helped show and iron out any unforeseen issues with the design and governance. Waiting for the intervention owners to use the master protocol was maybe the excellent damaging the good.
- Provide a platform which can at the outset accommodate all trials as adjusting once project 'in-life' – e.g. the expansion programme proved hard to fit a quite fundamentally different model into an existing project structure.

- Secure high-level commitment from intervention owners and sponsor to the development of an appendix early in the course of appendix development.

■ **WP6 – Dissemination**

WP6 gathered several partners across multiple sectors, which led to the development of a powerful workstream. WP6 gained active contribution and input from 1 patient organisation, 2 EFPIA partners, 2 SMEs and 2 academic partners. Bringing together diverse partners provided expertise from a multitude of backgrounds. The heterogeneity of partners had positive impacts and added substantial value by leveraging best practices. We were able to learn from each other and share skills and knowledge across the WP.

Public private partnership allowed EPAD and WP6 to maximise exposure of the project and reach out to relevant target audiences efficiently. As an example, academic partners provided support to communicate the project and its results to the scientific community and to advertise EPAD at national and international meetings. Specific attention was paid to reach out to patient groups and national Alzheimer associations via the involvement of Alzheimer Europe. Bringing together partners dealing directly with study sites complemented each other in the production of communication tools and activities (i.e. understanding of the national needs and environment).

Public private partnership was key to achieve WP6 outcomes in connecting academic and pharma to come together and coordinate outreach to specific external stakeholders.

■ **WP8 – Ethical, Social and Legal Implications (ELSI)**

Similar to the other EPAD WPs, collaboration within a public private partnership has been valuable for the ELSI research group. The involvement from the start, and continued engagement, of senior representatives from EFPIA partners provided valuable insight into differences in approach and focus between academic and industry, while helping orient the work of the ELSI group towards tangible outcomes, and translate this work into action within the study.

In view of the achievements of the work package, WP8 suggest that further research is needed in the following areas:

- To understand the actual lived experience of risk – beyond studying the immediate impact of disclosure, to consider how people experience stigma and potential discrimination. This would build on our work exploring the hypothetical long-term impacts of living with information about increased risk of Alzheimer’s dementia.
- To consider how the implementation of biomarker-based personalised approaches to prevention can effectively engage with challenges associated with social justice and health equity.
- To address the strength of normative arguments related to early detection of dementia.
- To consider how large projects exploring Alzheimer’s and neurodegenerative disease can ensure a diverse range of participants, and to better understand and address barriers and facilitators associated with research participation.
- To consider how public and patient participation can be embedded in a sustainable way within institutions applying for and conducting IMI-funded research.
- To consider the challenges associated with questions of data governance and data access beyond individual projects, across multiple jurisdictions, as within IMI projects.
- To establish public and participant expectations related to ‘fair’ exchange and interaction within public private partnerships.

To build on, and capture our experience within EPAD, WP8 also suggest a series of recommendations for the future development of ELSI work within public-private partnerships, such as those funded through IMI:

- A dedicated work package or task on ethics with independence to operate within the study should be created. It should also be recognized, however, that the mandate of this group relates to the wider social and ethical context of the project.
- Relatedly, it is important that study leads and researchers recognize the distinction between obtaining regulatory approvals and developing a broadly ethical and socially responsible programme of work. To ensure this, the ELSI team should not have the final responsibility for drafting and submitting the paperwork to have studies approved by local ethical committees.
- The ELSI team should be multidisciplinary, reflecting the range of perspectives within the study as a whole, as well as societal stakeholders.
- Consideration should also be given to questions of diversity and inclusion in the incorporation of public and patient perspectives within studies.
- Strong support from the project leadership is critical for the success of the ELSI role, accompanied with visibility within the project and interaction at GAs.
- ELSI researchers, as well as those from the wider consortium, should attempt to engage constructively and collaboratively in a 'neighbourly' way.
- To ensure the visibility and continuity of the ELSI perspective, there is value in funding a dedicated research post for the duration of the study

To conclude, the EPAD management team (WP5) would like to provide a general set of recommendations that could be of use for future PPPs:

- Allow for greater equity of partnerships in both industry and academia with more flexible, centrally managed (PMO, Executive Committee), funding to ensure that partners who do not perform do not hold onto budget that should be used for other more active partners.
- EFPIA partners should have a minimum contribution in terms of in-kind, cash or FTE before acceding to a partnership as large and complex as EPAD.

Summary list of papers published by EPAD during the project duration

A total of 32 papers have been reported as published under the acknowledgement of EPAD. Additional papers have been submitted and some others are being prepared. The scientific articles have been published in high-impact journals (Table below).

Title	Journal	Doi
Development of interventions for the secondary prevention of Alzheimer's dementia: the European Prevention of Alzheimer's Dementia (EPAD) project	The Lancet Psychiatry	http://doi.org/10.1016/S2215-0366(15)00454-X
Ethical challenges in preclinical Alzheimer's disease observational studies and trials: Results of the Barcelona summit	Alzheimer's & Dementia	http://dx.doi.org/10.1016/j.jalz.2016.01.009
Recommended cognitive outcomes in preclinical Alzheimer's disease: Consensus statement from the European Prevention of Alzheimer's Dementia project	Alzheimer's & Dementia	https://doi.org/10.1016/j.jalz.2016.07.154
Detecting cognitive changes in preclinical Alzheimer's disease: A review of its feasibility	Alzheimer's & Dementia	https://doi.org/10.1016/j.jalz.2016.06.2365
Psychological, behavioral and social effects of disclosing Alzheimer's disease biomarkers to research participants: a systematic review	Alzheimer's Research & Therapy	https://doi.org/10.1186/s13195-016-0212-z
Ethical issues in the development of readiness cohorts in Alzheimer's disease research	Journal of Prevention of Alzheimer's disease	http://dx.doi.org/10.14283/jpad.2017.5
Brain Amyloid Pathology and Cognitive Function Alzheimer Disease Without Dementia?	JAMA	http://dx.doi.org/10.1001/jama.2017.6895
Evolution and future directions for the concept of mild cognitive impairment	International Psychogeriatrics	http://dx.doi.org/10.1017/S1041610217002812
Perspectives on Communicating Biomarker-Based Assessments of Alzheimer's Disease to Cognitively Healthy Individuals	Journal of Alzheimer's Disease	http://doi.org/10.3233/JAD-170813
The Rationale Behind the New Alzheimer's Disease Conceptualization: Lessons Learned During the Last Decades	Journal of Alzheimer's Disease	http://dx.doi.org/10.3233/JAD-170698
European Prevention of Alzheimer's Dementia Registry: Recruitment and prescreening approach for a longitudinal cohort and prevention trials	Alzheimer's & Dementia	https://doi.org/10.1016/j.jalz.2018.02.010
At, with and beyond risk: expectations of living with the possibility of future dementia	Sociology of health & illness	https://doi.org/10.1111/1467-9566.12731
On the personal utility of Alzheimer's disease-related biomarker testing in the research context	Journal of Medical Ethics	http://dx.doi.org/10.1136/medethics-2018-104772
Research participants as collaborators:	Dementia	https://doi.org/10.1177/1471301218789307

Title	Journal	Doi
Background, experience and policies from the PREVENT Dementia and EPAD programmes	(London)	
Secondary prevention of Alzheimer's dementia: neuroimaging contributions	Alzheimer Research & Therapy	https://doi.org/10.1186/s13195-018-0438-z
Ethical Arguments Concerning the Use of Alzheimer's Disease Biomarkers in Individuals with No or Mild Cognitive Impairment: A Systematic Review and Framework for Discussion	Journal of Alzheimer's Disease	http://dx.doi.org/10.3233/JAD-180638
European Prevention of Alzheimer's Dementia Longitudinal Cohort Study (EPAD LCS): study protocol	BMJ Open	http://dx.doi.org/10.1136/bmjopen-2017-021017
Multi-study validation of data-driven disease progression models to characterize evolution of biomarkers in Alzheimer's disease	Neuroimage Clinical	https://doi.org/10.1016/j.nicl.2019.101954
Medial temporal lobe atrophy and posterior atrophy scales normative values	Neuroimage Clinical	https://doi.org/10.1016/j.nicl.2019.101936
Associations Between Multimorbidity and Cerebrospinal Fluid Amyloid: A Cross-Sectional Analysis of the European Prevention of Alzheimer's Dementia (EPAD) V500.0 Cohort	Journal of Alzheimer's Disease	https://doi.org/10.3233/JAD-190222
Re-aligning scientific and lay narratives of Alzheimer's disease	Lancet Neurology	https://doi.org/10.1016/S1474-4422(19)30323-0
The European Prevention of Alzheimer's Dementia (EPAD) Longitudinal Cohort Study: Baseline Data Release V500.0	Journal of Prevention of Alzheimer's disease	https://doi.org/10.14283/jpad.2019.46
Prescreening for European Prevention of Alzheimer Dementia (EPAD) trial-ready cohort: impact of AD risk factors and recruitment settings	Alzheimer Research & Therapy	https://doi.org/10.1186/s13195-019-0576-y
Cognitive Functions as Predictors of Alzheimer's Disease Biomarker Status in the European Prevention of Alzheimer's Dementia Cohort	Journal of Alzheimer's Disease	http://dx.doi.org/10.3233/JAD-191108
Cognitive Dispersion is not Associated with Cerebrospinal Fluid Biomarkers of Alzheimer's Disease: Results from the European Prevention of Alzheimer's Dementia (EPAD) v500.0	Journal of Alzheimer's Disease	http://dx.doi.org/10.3233/JAD-200514
Involving research participants in a pan-European research initiative: the EPAD participant panel experience	Research Involvement and Engagement	https://doi.org/10.1186/s40900-020-00236-z
Prediction of Alzheimer's disease biomarker status defined by the 'ATN framework' among cognitively healthy individuals: results from the EPAD longitudinal	Alzheimer Research & Therapy	http://dx.doi.org/10.1186/s13195-020-00711-5

Title	Journal	DOI
Precision prevention of Alzheimer's and other dementias: Anticipating future needs in the control of risk factors and implementation of disease-modifying	Alzheimer's & Dementia	https://doi.org/10.1002/alz.12132
Evaluating the Alzheimer's disease data landscape	Alzheimer's & Dementia: Translational Research & Clinical Interventions	https://doi.org/10.1002/trc2.12102
The influence of diversity on the measurement of functional impairment: An international validation of the Amsterdam IADL Questionnaire in eight countries	Alzheimer's & Dementia: Diagnosis Assessment & Disease monitoring	https://doi.org/10.1002/dad2.12021
The relation between APOE genotype and cerebral microbleeds in cognitively unimpaired middle- and old-aged individuals	Neurobiology of Aging	https://doi.org/10.1016/j.neurobiolaging.2020.06.015
Application of the ATN classification scheme in a population without dementia: Findings from the EPAD cohort	Alzheimer's & Dementia	https://doi.org/10.1002/alz.12292