Alzheimer Europe

EPAD

European Prevention of
Alzheimer's Dementia Consortium

Special supplement to issue 23 of Dementia in Europe magazine (November 2016)

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Front cover photo: Delegates at the EPAD "Science, Collaboration and Progress" consortium meeting (Edinburgh, 19-21 May 2015)

Introduction

I am very pleased to welcome the readers of our Dementia in Europe magazine to this special supplement about the EPAD project.

This truly innovative initiative is a research collaboration between 36 partners from academia and industry to improve the chance of successfully preventing Alzheimer's dementia and to better understand early aspects of Alzheimer's disease before dementia develops.

I am delighted that Alzheimer Europe is a full partner in this consortium and a co-leader of the project's "Dissemination" work package, which has developed communication and branding tools, as well as various channels to deliver project news and activities. We are also participating in the work package entitled "Ethical, Legal and Social Implications", which provides guidance on a number of key ethical issues raised by the project such as informed consent, privacy, disclosure of at-risk status and data sharing.

I am glad to say that the work in both our groups as well as the project as a whole is proceeding very well. This is due to the excellent cooperation between the participating researchers. Since our very first meeting in Paris in January 2015, there has been a remarkable sense of solidarity among the partners and the development of a true EPAD community or even EPAD family. I am convinced that this will continue to be a key element in EPAD's ultimate success!

The special supplement begins with a general overview of how EPAD was conceived and what it hopes to achieve and we thank the project leaders Craig Ritchie, Serge Van der Geyten and José Luis Molinuevo who share their ideas behind the project and their enthusiasm for its expected results. The important ethical and legal considerations which are guiding the project are presented by Richard Milne and Wouter Deneyer.

We have also included a report from a special colloquium which EPAD organised in Barcelona in May 2016: the presentations by Craig Ritchie, Miia Kivipelto and Maria Escrivà showed that involvement and motivation have a prodigious impact on recruiting and retaining research participants and we are hoping that their good practices will be shared and imitated by other trial delivery centres within the project as well as by the wider research community. This will certainly be reflected in our future communication activities – particularly as recruitment for the EPAD Proof of Concept study is now well underway.

The two first volunteers recruited for the study are Julie Duffus from Edinburgh and Maria Carme Garcia from Barcelona and we have included short interviews with both of them in this special supplement. We are very grateful for their commitment and willingness to share their experience so far and their expectations from participating in the EPAD project. It is thanks to volunteers like Julie and Maria Carme and their invaluable contributions that we hope to deliver real benefits to all people who are at risk of developing Alzheimer's dementia.

We also feature an interview with Pierre Meulien, the Executive Director of the Innovative Medicines Initiative (IMI) which funds the EPAD collaboration. It is encouraging to see how our funders share our enthusiasm for the project and its results. In addition, Pierre Meulien gives an overview of the entire IMI Alzheimer's portfolio and a preview of some future projects.

I hope you will find this special supplement on the EPAD project interesting and that you will share our interest and commitment to this important and unprecedented research endeavour. Preventing the development of dementia in biomarker-positive people would be a fantastic step forward in our fight against Alzheimer's disease. The EPAD project and its novel trial concept will hopefully help speed up the drug discovery progress and bring us closer to this ambitious aim.

Jean Georges
Executive Director, Alzheimer Europe


Jean Georges

The EPAD machine: how it works

The EPAD project consists of many elements that all need to function efficiently in order to successfully achieve its objectives. The three main project leaders explain how this is being accomplished.


Craig Ritchie

How and why was EPAD conceived?

Craig Ritchie: Ongoing failures to turn massive scientific advances into clinical therapeutics for Alzheimer's disease forced the academic and pharmaceutical communities to reflect on whether we were approaching trials the right way. This reflection led to a realisation that many elements of trial design and delivery were suboptimal and we could not fix one problem at a time. Rather we needed to make wholesale changes to use adaptive trial designs, build a readiness cohort, generate "in-house" data for optimal disease modelling and establish the most "state-of-the-art" centres of excellence for trial delivery.

EPAD came into existence because of two key factors – firstly the IMI funding stream backed the idea to put in place wholesale innovations as described above, and secondly, the proposal resonated with academics and pharmaceutical companies who really put their weight, know-how and investment into the project. This dates back to 2014 when we pulled the proposal together to officially launch the project in January 2015.

What has been achieved to date? What's coming up next?

Craig Ritchie: Since January 2015 we have met every critical timeline we set for ourselves. We knew we couldn't rush the science, the methods and the "back-office" functions of data management, legal and governance and funding. Though as well as the tangible achievements, the most important is undoubtedly the building of the "EPAD Family"; there is an on-going sense of joint vision, ownership, camaraderie and "fun" in delivering EPAD to this point. We have probably held more teleconferences than is healthy, but we also have already (and on schedule) recruited over 20 research participants and opened almost all the first wave trial delivery centres.

Next, we accelerate recruitment substantially and work hard on developing the Proof of Concept protocol and appendices to be starting the trial as envisaged towards the end of 2017. We also look forward to spreading the word to the broader academic community as well as through Alzheimer Europe's leadership of our communication and dissemination work package – the broader public.


120 delegates attended EPAD's "Initiation and Delivery" General Assembly (Barcelona, 17-19 May 2016)

What are the biggest challenges facing the project?

Serge Van der Geyten: The complexity of a project such as EPAD brings with it its own unique challenges. In EPAD, however, we prefer to see these not so much as challenges but rather opportunities to change the status quo and make a real difference for people living with dementia.

In recent years we have come to understand that our best chances for slowing or even stopping Alzheimer's disease are to intervene early when the disease has not progressed far enough to cause irreversible damage in sensitive areas in the brain. That brings with it the need to develop accurate screening tools to identify who is at risk for developing dementia due to Alzheimer's disease and should be treated. It is clear that in the current social and economic environment we will not be able to afford treating everyone expressing the earliest signs of developing Alzheimer's disease pathology without at least a minimal level of confidence that these people are on a trajectory to develop dementia due to Alzheimer's disease. Linked to this EPAD has the immense opportunity to help shape the regulatory and payer environment, so that as a society we are ready to make the new Alzheimer disease's therapies available to the patient community as soon as these become available.

On a different note, EPAD is currently funded until the end of 2019. Considering that clinical trials in preclinical and prodromal AD take on average 2–4 years it is clear that these studies will still be ongoing when the funded part of the project ends. This means that EPAD, although only just started, already has to make sure robust sustainability plans are in place from the project's outset. This will allow EPAD to not only continue in the post-IMI funding period but expand even more, so the platform is ready to accept more interventions for testing from 2019 and beyond.

How is EPAD cooperating with other projects?

Serge Van der Geyten: EPAD is collaborative by nature and closely involved with other initiatives in the AD field; these include for example the IMI Alzheimer's Disease Research Platform, the Global Alzheimer's Platform (GAP) Foundation, and the Dementias Platform UK (DP-UK).


Serge Van der Geyten

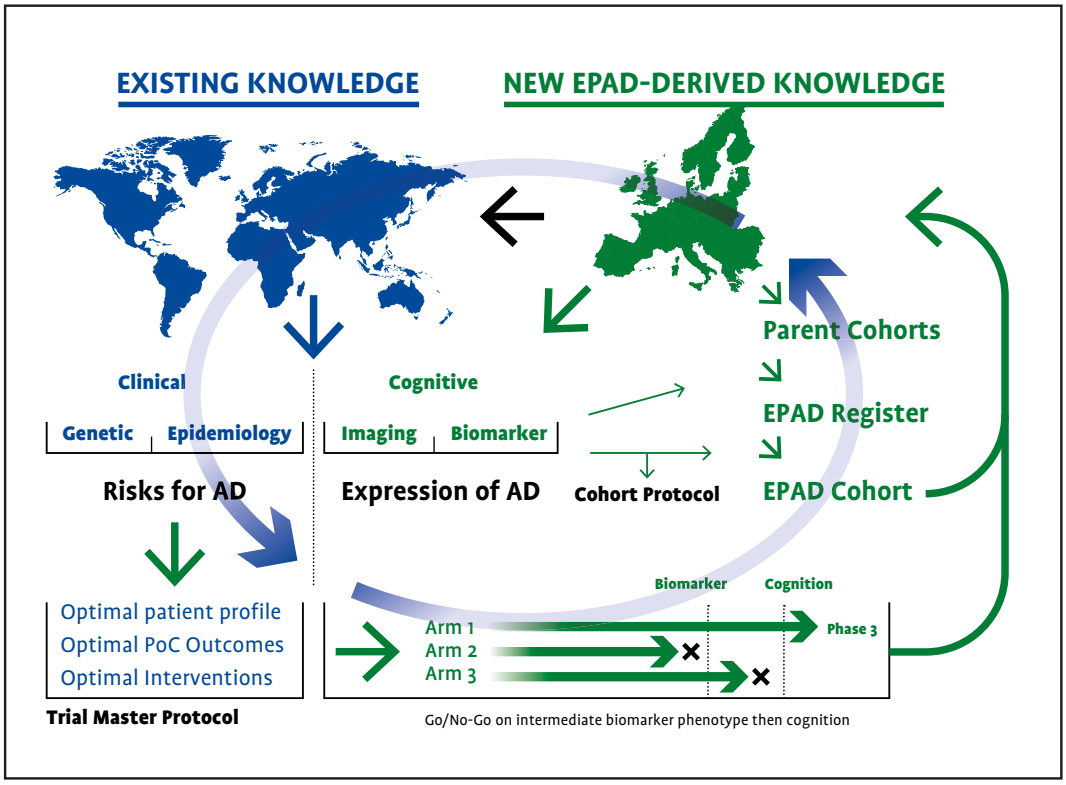
IMI Alzheimer's Disease Research Platform: The EU-based IMI AD Platform was launched in March 2015 to facilitate collaboration between three of IMI's leading AD projects: EPAD, EMIF (European Medical Information Framework) and AETIONOMY. Some of the work that is happening under the IMI AD Platform umbrella is, for example:

- building a data discovery tool (PREPAD) that allows finding suitable research participants for the EPAD LCS study from existing population-based cohorts and memory clinics from across Europe (EMIF+EPAD)
- identification of new disease mechanisms and potential targets for AD drug development (AETIONOMY + EPAD)

As of September 2016 EPAD will start collaborating with the IMI2 AMYPAD (Amyloid Imaging in the Prevention of Alzheimer's Disease) project to explore the utility of PET amyloid imaging in risk stratification and patient selection in clinical trials.

> "In a global context, EPAD is working together with other initiatives in the US, Canada, Australia and Japan to set up a global platform for conducting clinical trials across the AD spectrum."
>
> *Serge Van der Geyten*


José Luis Molinuevo



Global Alzheimer's Platform (GAP): In a global context EPAD is working together with other initiatives in the US, Canada, Australia and Japan to set up a global platform for conducting clinical trials across the AD spectrum with a unified goal to bring new therapies for Alzheimer's disease to patients faster.

In addition to these already formalised collaborations, EPAD is continuously exploring new opportunities to enhance our understanding of Alzheimer's disease and develop new treatments. To that end, EPAD has developed a research access process that will allow interested parties to submit a research proposal to the EPAD consortium (more information coming soon via the EPAD website: http://ep-ad.org/).

> "We have already (and on schedule) recruited over 20 research participants and opened almost all the first wave trial delivery centres."
>
> *Craig Ritchie*

How are people with dementia involved in EPAD?

José Luis Molinuevo: The main goal of EPAD is to develop a sustainable pan-European scientific, analytical and adaptive trial delivery platform specifically and uniquely developed with the singular aim of undertaking Proof of Concept (PoC) trials for the prevention of Alzheimer's dementia. This will be achieved through creating a pan-European register of people representing the whole Alzheimer's risk spectrum, many of whom will be invited to be part of the longitudinal cohort study (LCS). The LCS functions as a trial readiness cohort, from which participants will be invited to participate in the PoC. From the perspective of EPAD design, people with dementia will not be participating, since the main aim is to prevent dementia. Nevertheless, their voice is important, and working closely with Alzheimer Europe in communicating, creating panels to understand people's need, leveraging from their knowledge and experience, ensures that EPAD will be developed in close agreement with the needs of people with dementia.

Will EPAD's work continue after the end of the funding period?

José Luis Molinuevo: The short answer is YES. The aim of EPAD is to develop a sustainable platform for undertaking Proof of Concept (PoC) trials for the

prevention of Alzheimer's dementia. Explicitly, the project aims to develop an infrastructure allowing performing PoC trials for the prevention of Alzheimer's dementia that should remain after the initial IMI funding period and therefore we have to make it sustainable. This is the reason why EPAD has a whole work-package dedicated to sustainability. Sustainability plans have already started and if they are ultimately successful, EPAD will continue – in Europe at least – as a permanent infrastructure to prevent Alzheimer's. We all believe that EPAD is a game-changer that is in great demand by both scientists and society. It should therefore continue to benefit European society and, on a much larger scale, also the US, Australian, Canadian and Japanese societies, since they are building sister initiatives.

> *"EPAD will be developed in close agreement with the needs of people with dementia."*
>
> *José Luis Molinuevo*

First meeting of the EPAD consortium partners (Paris, 15 January 2015)

The EPAD Work Packages

Work Package 1: Scientific Challenges

WP1 integrates the scientific input to the project and addresses the central questions in AD disease modification that will drive the design of the EPAD adaptive clinical trial: who are the subjects, how should they be assessed, and with what should they be treated?

Objectives

- to define a spectrum of individuals at risk of developing dementia due to AD
- to define the evaluation criteria for inclusion of participants into the EPAD Register, EPAD Cohort and EPAD Trial, and the relevant biomarkers, clinical assessments and endpoints
- to assess and select potential trial mechanisms and compounds, through a Clinical Candidate Selection Committee
- to establish and coordinate four Scientific Advisory Groups (SAGs) referring to key scientific areas that gather the needed, high-level scientific knowledge to support decisions made in WP1

Work Package 2: Statistical/ Methodology Engine Room

This WP is the anchor for knowledge management and receives all data from the EPAD Register, Cohort and Trial for analysis, to continually inform disease modelling and adaptive trial design decisions. WP2 will gather the tools and resources that will be used for disease modelling, assess and prepare them for exploitation and set up procedures to design the adaptive trial.

Objectives

- to develop and optimise disease modelling and simulation software supporting risk modelling and adaptive clinical trial design and updates
- to develop disease and risk modelling capacity based on existing and acquired data via EPAD Cohort and Trial activities informing scientific assessment in WP1 and trial design updates
- to build the interventional adaptive trial design and needed methodology, providing updates to the design, analysis of new interventions and of existing compounds

Work Package 3: Parent Cohorts and EPAD Register

WP3 will create and maintain an EPAD Register, in the form of full "fingerprinting" of Parent Cohorts (approximately 24,000 participants).

Objectives

- to provide the methods and tools to identify, characterise and select Parent Cohorts suitable for contributing to the EPAD Register
- to provide the methods and tools to identify and select suitable participants from Parent Cohorts to build the EPAD Register, enabling the appropriate data discovery/sharing capacity and underpinning policies
- to define operational processes and arrangements for maintenance and replenishment of the EPAD Register

Work Package 4: EPAD Cohort and EPAD Trials

WP4 will initially focus on selection and certification of the EPAD trial delivery centres (TDCs) and establish the EPAD Cohort Protocol early in the project. Subsequently, the design and execution of the Proof of Concept (PoC) study will be their main focus. WP4 will oversee the execution of the protocols for the EPAD Cohort and Trials and work with National/ Regional Leads and Clinical Research Organisations (CROs) on qualification, establishment and training of the EPAD trial delivery centres.

Objectives

- to establish certified EPAD TDCs across Europe capable of recruiting the required number of subjects for the EPAD Cohort and Trial
- to establish the EPAD Cohort and related data flows, databasing infrastructure, quality control/assurance and monitoring procedures

- to sign off the EPAD Cohort Protocol and implement it
- to sign off the EPAD Trial Master Protocol and Appendices implement them
- to establish a Principal Investigators Network supporting EPAD Cohort and Trial activities

Work Package 5: Project Management

WP5 provides professional project management to EPAD ensuring successful completion of the project.

Objectives

- to set up a project management structure that ensures efficient operational and timely execution of the project
- to guarantee project is executed according to the work plan and scientific activities are managed efficiently
- to manage resources, procedures and tools for ensuring that all expected results are delivered on time, with an adequate quality level and within cost, including risk management and quality control procedures on deliverables
- to ensure effective communication and work dynamics between Participants to help drive the whole Consortium as a team towards successful completion of the project

Work Package 6: Dissemination

This WP will lead and coordinate external dissemination activities, outreach to specific external stakeholders and the public health campaign with special emphasis on the importance of AD prevention. WP6 will also assess the impact and effectiveness of dissemination activities.

Objectives

- to develop a dissemination and communication plan including objectives, target audiences, tools and activities
- to develop and update the needed tools to implement the planned dissemination activities
- to carry out a variety of dissemination activities aiming at maximising exposure of the project while optimising the project's perception among the different target audiences

Work Package 7: Business Model and Sustainability

WP7 will analyse markets, stakeholders, incentives and schemes for pre-competitive intellectual property handling, in order to develop a viable business plan for sustainability of the EPAD "machine" and network of centres beyond the time frame of the project.

Objectives

- to study existing and emerging public-private partnership collaborative models that can be useful for the EPAD sustainability
- to analyse the stakeholder types intervening in EPAD, their interests and incentives towards sustainability
- to analyse and develop procedures for a pre-competitive space that caters to a variety of companies and therapies
- to analyse and develop procedures that enable the EPAD infrastructure of TDCs to be sustained over time
- to develop a solid business plan that enables transition of EPAD to the post-project phase for long term sustainability

Work Package 8: Ethical, Legal and Social Implications

WP8 will carefully study critical ethical, legal and social issues (ELSI) pertaining to the project and provide guidance on informed consent, privacy, disclosure of findings and data sharing.

Objectives

- define an EPAD ethics and information governance framework for recruiting from existing cohort studies
- develop a robust strategy for involving research subjects in the development of ethics procedures and research protocols
- investigate the ethical, legal and social implications of disclosure of biomarker results and the associated risk of AD dementia
- evaluate and compare the feasibility and impact of large-scale biomarker-testing within national health care systems
- investigate and advise on the recruitment of subjects for Phase 2 trials from existing cohort studies

EPAD in pictures: snapshots from events in 2014 and 2015

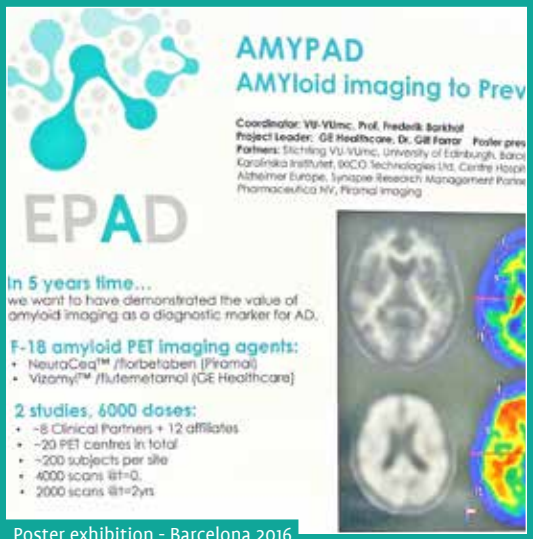
The EPAD mascot - Edinburgh 2015

Poster exhibition - Barcelona 2016

Consortium meeting - Edinburgh 2015

Consortium meeting - Edinburgh 2015

Alzheimer Europe conference - Ljubljana 2015



Poster exhibition - Barcelona 2016

Consortium meeting - Edinburgh 2015

Ethical and legal considerations in the EPAD project

EPAD's work with people at risk of developing dementia has resulted in a unique ethical and legal framework. Richard Milne from the Institute of Public Health at the University of Cambridge looks at the ethical issues, while the legal considerations are explained by Wouter Deneyer, external counsel acting on behalf of Janssen Pharmaceutica NV, coordinator of the EPAD consortium.

What are the main ethical concerns in the EPAD project? How do they differ from other projects?

Richard Milne: EPAD is a fascinating project to be involved in because of the really complex range of ethical and societal questions that it raises. The innovative structure of the project, which joins together a register, cohort and clinical trials, means that specific ethical questions linked with each of these come together and get combined in new ways. Add to that the broader ethical challenges connected with doing research on Alzheimer's dementia, and it gets even more interesting. Because of this, EPAD has a dedicated ethics workgroup, led by Edo Richard, Shirlene Badger, Luc Truyen and Carol Brayne. In this workgroup we have spent a lot of time working through the whole project to identify what concerns need to be addressed when.

Three topics really distinguished EPAD from many other projects. The first was that EPAD recruits participants entirely from existing research studies or clinical registers, and recruits across a "risk spectrum" for Alzheimer's dementia, from lower to higher risk groups. We worked with the legal team and the group developing technical aspects of EPAD recruitment to develop an approach that means that EPAD researchers, and potential participants, do not know where on that spectrum a participant is.

Second, we looked at how to ensure that participants understand the whole of EPAD when they give their consent to take part in research. Everyone going into the EPAD cohort needs to know the detail of what they're going to be asked to do in the study – what the tests and examinations involve, how long they take, and what risks are associated with them. However, they also need to know that they may eventually be asked to take part in a clinical trial and that this might involve learning that they are in a higher risk group for developing Alzheimer's dementia. Providing people with both specific detail and a general overview ensures that people are properly informed about what EPAD involves.

The third question that we have looked at in a lot of detail is managing the return of research results to participants, particularly the disclosure of Alzheimer's dementia risk to some people later in the project. This is one of the big challenges facing Alzheimer's disease research at the moment. Our ability to predict someone's risk of developing Alzheimer's dementia is not good enough to use routinely in the clinic. It also isn't clear what the value of doing so would be when there are no treatments available that are known to effectively reduce risk. However, researchers


Richard Milne

> "We looked at how to ensure that participants understand the whole of EPAD when they give their consent to take part in research."
>
> *Richard Milne*

need to identify "high risk" people for clinical trials so that they can see if drugs are able to reduce this risk. These people will be told why they're being contacted, so will learn that their test results may mean they are at increased risk of developing dementia. A lot of our work at the moment revolves around making sure that EPAD participants are aware what this information can and can't tell you, and developing a process for risk communication.

How will EPAD's new participant panel work?

Richard Milne: The success of EPAD relies on the continued support and involvement of the participants who give up their time to take part in research. It's really important that the voice of these participants is also heard in decision-making about the future of the project. The Participant Panel is our plan to make this work, and we're planning to have it up and running by spring 2017. It builds on the success of similar initiatives in some of the studies feeding into EPAD, including the PREVENT study.

The panel will involve local groups at each of the EPAD centres. These small groups will meet regularly and provide feedback on what it's like to take part in EPAD, and how it might be improved. A representative from this local group will then represent that centre on a central EPAD Participant Panel. This panel will meet alongside the annual scientific meeting of EPAD – providing an opportunity for researchers to interact with panel members, and for panel members to attend planning meetings for the project. One member of the panel will formally represent EPAD participants within the governance of the project.


Wouter Deneyer

What is involved in disseminating and sharing data and samples from the EPAD longitudinal cohort study?

Wouter Deneyer: One of the main goals of EPAD is to share its main findings as much as possible with the scientific community in order to foster research on Alzheimer's disease. From a legal viewpoint, these findings are identified as "foreground". The term foreground under IMI includes not only intellectual property rights, but also data, information, know-how, and other outputs resulting from the activities under an IMI project.

There are two ways a (third) party can access such foreground. Either it can wait until the foreground is disseminated (published) or it can request an (individual) "access right" to the party owning the foreground.

As a standard, the IMI requires each participant to disseminate its foreground as soon as practicable but not later than one (1) year after the end of the EPAD project. The EPAD Project Agreement includes a detailed process for these dissemination activities, under the supervision of a "Publication Approval Committee".

The IMI also foresees that parties can request access to foreground for research purposes. For non-EPAD participants, this is in principle possible after the end of the project by making a request to the party owning the foreground and by agreeing with that party the terms of such access.

One of the key deliverables of the EPAD project is the EPAD longitudinal cohort study. This is a non-interventional (observational) study which is to include about 6,000 participants in sites all over Europe. Once the first participants had joined the longitudinal cohort study, it became clear that there is a scientific need to share data and samples generated in this study earlier than the timelines normally foreseen in IMI projects for third party sharing.

This is the reason why the EPAD participants are installing a procedure permitting third parties (like researchers working for universities or institutions not participating in EPAD) to access data and samples originating from the EPAD longitudinal cohort study already during the project, to the extent certain conditions are complied with.

In summary, the researcher will have to complete an online application form providing more detail about the scope of its intended research, the resources, and the goals. An EPAD committee will then decide on whether the access can be granted. An important condition to grant such access is that from an ethical perspective (for instance, informed consents) the data and/or samples can be shared with the requesting third party and can be made subject to the contemplated research.

> "The EPAD Project Agreement includes a detailed process for dissemination activities, under the supervision of a Publication Approval Committee."
>
> *Wouter Deneyer*

EPAD colloquium focuses on communication and engagement

On 17 May, the EPAD project held a colloquium to inform its partners of communication activities and ongoing efforts to engage public support for the project.

The "EPAD loyalty programme: sharing experiences across Europe" colloquium took place on 17 May 2016, during the project's General Assembly in Barcelona. Dr José Luis Molinuevo, Scientific Director of the Barcelonabeta Brain Research Center (BBRC), welcomed the audience and emphasised the importance of motivating people to become involved in research. He hoped that EPAD could develop local initiatives that would keep research participants informed and interested throughout the project lifetime and beyond.

Changing the way we communicate about AD

The first speaker was Jean Georges, Executive Director of Alzheimer Europe and co-leader of EPAD's Dissemination work package (WP6). He explained that WP6 has five main objectives:

- coordinate external dissemination activities, including publication and dissemination strategies
- outreach to specific external stakeholders
- develop a campaign on the importance of prevention of Alzheimer's dementia
- develop a communication plan and raise awareness of project aims and results
- develop branding for the project

The team members have already delivered a communication plan, including project branding and policies, as well as a report on communication tools and materials. Various EPAD partners have presented the project at scientific conferences such as the CNS Summit, AAIC and CTAD, but also at Alzheimer Europe's 2015 Annual Conference and its Alzheimer's Association Academy.

The WP6 team is now updating the communication strategy, in order to raise awareness of EPAD and its processes and change the way we communicate about Alzheimer's dementia and Alzheimer's disease. The new strategy will also facilitate the creation of an "EPAD community" among the research participants: the WP6 members are developing tools to update participants on the progress of the project

Colloquium speakers (L-R) Jean Georges, Maria Escrivá, Craig Ritchie, Miia Kivipelto.

and will also seek to identify good practices by mapping the communication and retention strategies of the EPAD partners.

Involving people leads to high retention rates

Prof. Ritchie (Professor of the Psychiatry of Ageing at the University of Edinburgh) described the activities of the PREVENT project, a mid-life cohort study of some 300 people between the ages of 40–59.

The project aims to identify biological and psychological factors which may increase the risk of dementia in later life. Once these factors are identified, the researchers will select people at high risk and intervene in the process. Interventions might be lifestyle changes or measures to affect the risk of an individual developing dementia. The study is still recruiting and is jointly managed by Imperial College London and the Universities of Cambridge, Edinburgh and Oxford.

Prof. Ritchie noted that a two-year review conducted in February 2016 showed an almost perfect retention rate of 99%. He attributed this excellent result to a very open and transparent approach of the project team toward the participants: they are fully involved in all aspects of the trial and have come to consider themselves as collaborators rather than merely test subjects. The project website was specifically designed to be "non-clinical" and attracts many visits from participants, who are also active on dedicated social media accounts and blogs.

Prof. Ritchie was convinced that this approach should be emulated in the EPAD trial centres and gave a simple summation of the initial requirements: "Be nice. Listen. Be honest. Be available."

Providing information and results in simple language

He was followed by Prof. Miia Kivipelto (Professor of Clinical Geriatric Epidemiology at Karolinska Institutet, Sweden), who presented "FINGER's best practices: building an innovative research platform for adaptive interventions to prevent dementia".

The FINGER study (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability) ran during 2009–2014 with a group of 1,260 Finnish people aged 60–77 who were at risk of developing dementia. The non-pharmacological study featured nutrition, exercise, cognitive training and social activity, as well as monitoring of metabolic and vascular risk factors over two years. The results showed that multidomain intervention is effective in reducing or preventing cognitive decline.

It was equally clear that the trial participants were very pleased to be involved in the project. In general, their motivation was based on helping researchers to find a cure. Prof. Kivipelto added that people were also grateful for the comfort and care they received and appreciated the provision of information and results in simple language.

Making participants feel like heroes

The final speaker was Ms Maria Escrivá, Communication Specialist at the BBRC in Barcelona, who presented ongoing activity around the ALFA (Alzheimer's & Families) study.

A joint project of BBRC and Fundació Pasqual Maragall, ALFA is a biomarker study and also a primary prevention study in healthy adult children of people with Alzheimer's disease. The researchers' initial recruitment efforts focused on traditional sources such as hospitals, medical specialists and patient groups.

However, these were unsuccessful so the researchers decided to hold a public press conference and place ads in the local media. The result was a flood of positive responses that led to the creation of a registry with over 6,500 people. After screening, the researchers created the ALFA parent cohort, from which some 800 participants will be selected for the two arms of the clinical trial.

Like their British and Finnish counterparts, the Spanish "volunteers" are very enthusiastic about being part of the study. The research team has launched a loyalty programme that includes face-to-face meetings, news updates via dedicated channels and events that are increasingly popular. Ms Escrivá said that the volunteers "are treated like heroes, because our work would be impossible without them".

Presenting the first participants of the EPAD study

Julie Duffus joined the EPAD study in May 2016 and was followed by Maria Carme Garcia in July. Along with the other participants, they will undergo regular health checks that include blood tests, brain scans and mental agility tests. In this article, they speak about their experiences with dementia and how they got involved in the EPAD project.

Julie Duffus

Tell us a little bit about yourself: who is Julie?
I was born in Preston but have moved around for most of my life. My husband and I lived in Cheshire for over 25 years and then moved to Scotland to be nearer to my husband's mother. We have two grown up children – a son who lives in Manchester and a daughter who lives down the road in Edinburgh.

How did you first hear about the EPAD project?
I have a keen interest in dementia research because both my mum and dad had Alzheimer's disease. It was heart breaking to watch how the disease changed their personalities and robbed them of their independence. My mum Beryl was diagnosed first – she started showing symptoms of memory loss in her early 80s and it was confirmed that she had Alzheimer's disease. She passed away in 2005. Around four years later, my dad Bert was also diagnosed with dementia. He deteriorated quickly and passed away in 2012. He had donated his brain to the BRACE clinic in Bristol and it was removed immediately following his death. The post mortem test results revealed he was suffering from Dementia with Lewy Bodies as well as Alzheimer's. I first heard about the EPAD project through my participation in another dementia study – the Prevent project. I became involved with Prevent after registering with Join Dementia Research, where volunteers are matched with research projects.

Why is it important for people to participate in clinical trials?
Although I don't have any symptoms of Alzheimer's, I know that researchers need to study a spectrum of people to identify risk factors that might trigger the disease. I hope that my contribution will in some way help scientists to find better ways of diagnosing the disease and potentially, one day, to prevent it. By taking part in this study, I hope I can help others who are affected by this horrible disease.

Maria Carme Garcia

Tell us a little bit about yourself: who is Maria?
I am 61 years old and retired. I live in Barberà del Vallès, about 20km from Barcelona. I am the daughter and granddaughter of people with Alzheimer's disease.

Although I did not know it at the time, I experienced dementia at a young age because both my father and grandfather had it. For neither case could anyone tell us what was happening, we were only told it was related to advanced age. I remember that I used to get angry with my father when he did unusual things due to mood changes. He was diagnosed only a short time before his death.

When my father died, an uncle developed the disease, then another uncle, an aunt and another aunt. It is said that dementia is not genetic, but at home we have had many cases.

How did you first hear about the EPAD project?
It was through my doctor at the Foundation Pasqual Maragall, where I am involved in the ALFA Study. I offered myself as a volunteer for the same reason that I decided to collaborate with the Foundation: because I am surrounded by many people affected by dementia. Moreover, Alzheimer's is a disease that has not been studied enough and it is largely unknown.

Why is it important for people to participate in clinical trials?
My motivation is to think that as more people participate, the more possibilities we will have to find a solution for brain diseases. Everywhere I go, I talk about the importance of the study and I try to act as an advocate.


Julie Duffus


Maria Carme Garcia

An interview with Pierre Meulien, IMI Executive Director

EPAD is one of a number of dementia projects supported by the Innovative Medicines Initiative (IMI). In this interview, Executive Director Pierre Meulien introduces IMI's wider dementia portfolio and gives a preview of some of the projects in the pipeline.


Pierre Meulien

innovative medicines initiative

EPAD is one of several IMI-funded dementia projects. What is IMI's overall vision on these projects?

So far, IMI has launched five projects on dementia (including EPAD) and more are in the pipeline. IMI has a strong focus on dementia because it is so complex, and the risk of failure is so high, that there is now widespread recognition that no company or even country can tackle this alone. In addition, it is an area with a huge unmet medical need and where the burden on society is particularly high. As a public-private partnership, IMI is well placed to bring together the top people from universities, pharmaceutical companies, small biotechs, and (of course) patient organisations in large-scale, international collaborative projects focused on specific challenges in dementia research and drug development.

Ultimately, IMI's goal is to make a very concrete contribution to efforts to deliver treatments to prevent and even cure dementia, and as such our projects address a range of challenges in dementia research.

For example, AETIONOMY is paving the way towards a new approach to the classification of Alzheimer's and Parkinson's diseases, thereby improving drug development and increasing patients' chances of receiving a treatment that works for them. EMIF is developing a common information framework of patient-level data that will link up and facilitate access to diverse medical and research data sources, opening up new avenues of research, particularly in the fields of Alzheimer's disease and obesity. Together with EPAD, AETIONOMY and EMIF form the IMI Alzheimer's Disease Research Platform – by collaborating, they hope to be able to deliver results faster.

Elsewhere, IMI's first Alzheimer's project, PharmaCog, studied tools and methods to improve our ability to identify successful new medicines as early as possible in the drug development process. Finally, IMI's newest Alzheimer's project, PRISM, which got underway earlier this year, aims to unravel the causes of social withdrawal, a common early symptom of Alzheimer's disease and other neurological conditions.

How does IMI encourage the involvement of people with dementia in research?

Our experience shows that patients can contribute to many aspects of research, including study design, communication and project governance. Most importantly, they help to ensure that projects address the needs and concerns of patients. With this in mind, IMI has always encouraged patients, carers and their representatives to get involved in our projects, and we have guidance for both patients and other researchers on best practice in this area on our website. More broadly, IMI's EUPATI project provides patients and carers and their advocates with extensive training on medicines research and development. As a result, EUPATI trainees are well equipped with the skills and knowledge needed to engage effectively as full as equal partners in medical research and drug development.

> "So far IMI has launched five projects on dementia (including EPAD), and more are in the pipeline."
>
> *Pierre Meulien*

When it comes to dementia, we are delighted that Alzheimer Europe is an active participant in so many of our dementia projects. In the case of EPAD, this is particularly significant as while early intervention trials can appear controversial to some, they nevertheless have the potential to dramatically slow down the pace of dementia onset.

Looking to the future, we will soon launch a new project on Alzheimer's disease and patient engagement. The project will work to identify the most effective ways of identifying and engaging with people who are in the very earliest stages of Alzheimer's, with the hope that this will add to our understanding of the early stages of the disease, help patients access support, and facilitate recruitment for clinical trials.

How important is international cooperation in dementia research?

International cooperation is essential if we want to make meaningful progress on a disease as complex as dementia. That is why IMI has a Memorandum of Understanding with the Global Alzheimer's Platform, and why we are in contact with other global players working on dementia, including the World Dementia Council, the World Health Organization, and the Accelerating Medicines Partnership (AMP).

> "International cooperation is essential if we want to make meaningful progress on a disease as complex as dementia."
>
> *Pierre Meulien*

Will IMI continue to fund dementia projects in the future?

Absolutely! We have a number of projects in the pipeline that will get underway in the coming months. These address issues such as the link between inflammation and Alzheimer's disease, the value of amyloid imaging in diagnosis and research, the genetic risks of Alzheimer's, and how we can harness big data to improve Alzheimer's care and prevention.

What's more, IMI has committees called Strategic Governing Groups (SGGs) in a variety of areas, including neurodegeneration. The SGG on neurodegeneration is extremely active and has a lot of plans for the future, so watch this space!

About the Innovative Medicines Initiative

The Innovative Medicines Initiative (IMI) is working to improve health by speeding up the development of, and patient access to, the next generation of medicines, particularly in areas where there is an unmet medical or social need. It does this by facilitating collaboration between the key players involved in healthcare research, including universities, pharmaceutical companies, other companies active in healthcare research, small and medium-sized enterprises (SMEs), patient organisations, and medicines regulators. This approach has proven highly successful, and IMI projects are delivering exciting results that are helping to advance the development of urgently-needed new treatments in diverse areas.

IMI is a partnership between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA) and IMI has a budget of EUR 3.3 billion for the period 2014–2024.

www.imi.europa.eu
@IMI_JU

Cooperation with other projects

EPAD cooperates with several other IMI-funded dementia projects and is also a stakeholder in the Global Alzheimer's Platform. Cooperation helps the European projects to deliver results faster, but also allows the EPAD partners to share results and best practices on a global level.

Current projects

AETIONOMY is paving the way towards a new approach to the classification of neurodegenerative diseases, particularly Alzheimer's and Parkinson's diseases, thereby improving drug development and increasing patients' chances of receiving a treatment that works for them. www.aetionomy.eu

EMIF is developing a common information framework of patient-level data that will link up and facilitate access to diverse medical and research data sources, opening up new avenues of research, particularly in the fields of Alzheimer's disease and obesity. www.emif.eu

IMI Alzheimer's Disease Research Platform

In March 2015, IMI and the AETIONOMY, EMIF and EPAD projects announced the creation of the "IMI Alzheimer's Disease Research Platform", in order to facilitate collaboration between the three projects and help them to deliver results faster.

The platform also gives the projects global reach, through IMI's Memorandum of Understanding with the Global Alzheimer's Platform (GAP). This is an agreement to cooperate on developing a global, standing, trial-ready platform for Alzheimer's drug development with partners in Australia, Canada, Japan and the US.

Future cooperation

EPAD will be working in close cooperation with AMYPAD. This IMI-funded project began operating on 1 October 2016 and includes many EPAD partners, including Alzheimer Europe.

AMYPAD

The "Amyloid imaging to prevent Alzheimer's disease" project (AMYPAD) aims to improve the diagnostic workup of patients suspected to have Alzheimer's disease and their management. The partners aim to improve knowledge of the natural history of AD in a pre-symptomatic stage, in order to better select patients for trials. In addition, they will monitor changes in beta amyloid deposition in the brain, in order to quantify the impact of novel therapies. www.amypad.eu

According to IMI Executive Director Pierre Meulien, there are more dementia projects in the pipeline. It seems likely that some of them will have objectives that relate to EPAD's work. The EPAD partners look forward to cooperating with all initiatives to improve the lives of people with dementia and their families.

This includes the new MOPEAD project. "Models of patient engagement for Alzheimer's disease" will create an effective interface between existing projects in order to identify and test models of efficient earlier identification of mild AD dementia and prodromal AD patients. The project will also seek to raise awareness of Alzheimer's disease, memory complaints, and cognitive decline risks.

The EPAD partners

ACADEMIA

EFPIA

SMEs

Patient Organisation

Other Industry

Alzheimer Europe

EPAD

European Prevention of Alzheimer's Dementia Consortium

For the latest information on the EPAD project, please visit our website http://ep-ad.org/

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