IMI2 821513 – NEURONET

Efficiently Networking European Neurodegeneration Research

WP1 Projects & Impact analysis

D1.6 Map of relevant initiatives and gap analysis v2

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Contents

Definitions and abbreviations

Partners of the NEURONET Consortium are referred to herein according to the following codes:

1. **SYNAPSE**: Synapse Research Management Partners SL
2. **NICE**: National Institute for Health and Care Excellence
3. **AE**: Alzheimer Europe
4. **JANSSEN**: Janssen Pharmaceutica NV
5. **LILLY**: Eli Lilly and Company Limited
6. **ROCHE**: F. Hoffman – La Roche AG
7. **TAKEDA**: Takeda Development Centre Europe LTD (*terminated partner*)
8. **SARD**: Sanofi-Aventis Recherche & Développement
9. **PUK**: Parkinson's Disease Society of the United Kingdom LBG
10. **TPIZ**: Takeda Pharmaceuticals International AG

Grant Agreement: The agreement signed between the beneficiaries and the IMI JU for the undertaking of the NEURONET project.

Project: The sum of all activities carried out in the framework of the Grant Agreement.

Work plan: Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.

Consortium: The NEURONET Consortium, comprising the above-mentioned legal entities.

Consortium Agreement: Agreement concluded amongst NEURONET participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

IMI: Innovative Medicines Initiative

ND: Neurodegenerative Disorders

WP: Work Package

Abstract

There are many research activities focused on Alzheimer's disease and other neurodegenerative diseases in the global research landscape. This deliverable aimed to map neurodegenerative disease research initiatives based on their strategic importance and carry out a gap analysis to identify gaps in our understanding of the evidence base and areas to prioritise for future research.

Using a framework of strategic importance, a survey was carried out of researchers to rate a list of initiatives on several variables and to add any initiatives they are aware of that are not on the list. People living with dementia and their supporters and health technology assessment and regulatory experts were consulted on gaps both generally and within the IMI neurodegenerative disease research portfolio and asked to identify priorities for future research.

The results of the mapping and gap analysis show that while there seems to be a busy landscape of neurodegenerative disease research, there is a need for better management, co-ordination, and communication of initiatives to achieve more impact. Furthermore, there are several gaps/areas where more research focus is needed to address the needs of various stakeholders, particularly those who are recipients of research outputs.

1 Introduction

The IMI portfolio of neurodegenerative disease research operates in a global environment. It is important to get the views of different stakeholder groups on their perception of gaps in neurodegenerative research both within the IMI portfolio and from a global perspective. Stakeholder engagement to inform research priorities increases the likelihood of producing research outputs that are relevant and beneficial to the recipients of those outputs(1). Therefore, it can inform priorities for future research, funding allocation and contribute to the evolution of the neurodegenerative disease research landscape.

2 Background

This is the second stage of an exercise to map the global research landscape for neurodegenerative diseases and to enable a gap analysis with the IMI project portfolio. In the first deliverable (D1.3), we identified several existing initiatives (e.g. IADRP, JPND Research Mapping) that had already carried out similar mapping exercises in recent years. Therefore, it was agreed not repeat the work already carried out by these initiatives, but to build upon the findings to understand where the IMI neurodegenerative disease portfolio fits in to the global research landscape. For the first deliverable, we used the results from the International Alzheimer's and Related Dementias Research Portfolio (IADRP) mapping exercise to perform an analysis of global neurodegeneration research activity in relation to key aspects including funding, disease focus and research classification. A gap analysis was also performed to assess the IMI neurodegenerative disease project portfolio in relation to the same dimensions.

3 Objectives

The objectives of this second stage of the global mapping exercise are:

- To assess the understanding of neurodegenerative disease researchers of the current global landscape of neurodegenerative disease initiatives[1].
- To understand where the gaps are in the evidence base and make recommendations on where research should be focused in the next 5 years.

[1] Initiatives that are generating knowledge or those that act as enablers for the generation of knowledge and action, such as funding initiatives and data platforms etc.

4 Methods

4.1 Mapping

An initial scoping review for neurodegenerative disease initiatives was undertaken to identify relevant neurodegenerative disease initiatives. It was not a comprehensive or systematic search of the global neurodegenerative disease landscape but aimed to provide an initial view of the landscape to inform discussions with stakeholders.

The following methods were used to identify neurodegenerative disease research initiatives:

- Targeted searches of key websites were conducted to identify potential neurodegenerative disease initiatives and publications/reports which name, list or describe neurodegenerative disease initiatives:
    - Google
    - Non-profit organisations relating the list of conditions for this task (e.g., The ALS Association, Alzheimer's Association etc.)
    - Major international and neurodegenerative disease funding bodies
- Snowballing from websites, publications and lists of initiatives:
    - Publications/reports identified through these searches were reviewed to identify neurodegenerative disease initiatives. Furthermore, references from key publications/reports were used to identify other relevant publications for review.
- The list of initiatives was shared with WP1 members, and they were asked to add any initiatives that they were aware of that were not identified through the searches

To enrich our understanding of the neurodegenerative disease research landscape, we invited members of the NEURONET Scientific Coordination Board (SCB) and Working Groups (WGs) to complete a survey based on a framework that we developed to define our concept of initiatives' strategic importance. This framework was informed by published literature(2) and discussions within WP1 along with members of the NEURONET SCB, and constitutes of the following variables:

- Scope
- Reach
- Innovation
- Long-term impact
- Funding
- Openness
- Influence

Respondents could assign their subjective evaluation of an initiative's perceived innovation, available funding, long-term impact, influence, and openness. These variables were presented to respondents as they are described in Figure 1 with a prompt to assign values using a four-point star system (e.g., for long-term impact, ★ would represent "not very impactful", with ★★★★ representing "very impactful") for each variable. There was no need for them to rate an initiative's scope or reach since these two variables were dependent on the disease area(s) targeted by the initiative and the geographical focus of the initiative, respectively. We invited respondents to add and evaluate any initiatives that we did not include on our shortlist.

As a further development, we invited these same members of the WGs and SCB to attend a two-hour mapping workshop, where we intended to host an open discussion to help elaborate on their evaluations and provide more qualitative feedback.

Figure 1. Criteria for defining strategic importance/value

4.2 Gap analysis

A consultation with the European Working Group of People with Dementia (EWGPWD) and their supporters was held on 13th October 2021 and was carried out across three virtual meetings in the context of public involvement.

The EWGPWD was launched by AE in 2012 and is composed entirely of people with dementia, who are nominated by their national Alzheimer's associations. The EWGPWD is currently chaired by Chris Roberts (UK – Wales) and has 14 members, some of them supported by family members, friends, or a person from the Alzheimer association. The goal of the EWGPWD consultations was to understand the views and perspectives of people with dementia and their supporters on biomedical research in the IMI2 Strategic Research Agenda; the research priorities and areas in the agenda; and identify any potential gaps in the agenda.

To facilitate discussions, the group was split in two smaller sub-groups and two consecutive meetings were carried out which focused on obtaining feedback from people with dementia, involving seven people in total (supported in some cases by a supported for translations). The perspectives of caregivers of people with dementia were sought in a separate meeting and involved four people. Pre-

reading documents, developed by Alzheimer Europe team members, were provided to the EWGPWD and supporters two weeks prior to the consultations, to help them prepare for the consultation. During the consultation, presentations were delivered by a NEURONET representative (Angela Bradshaw, AE; presentations can be seen in Annex II), after which feedback from the participants was prompted using a series of questions. The consultations were moderated and facilitated by Ana Diaz-Ponce and Dianne Gove, who jointly support the EWGPWD.

A two-hour virtual workshop with health technology assessment (HTA) and regulatory experts was held on 4 November,2021 to gain their perspectives on gaps and priorities for neurodegenerative disease research. There was a presentation delivered by NEURONET representatives (Fatima Salih, NICE and Nina Coll, SYNAPSE; presentation can be seen in Annex II), and the discussions were moderated by Fatima Salih (NICE), Nina Coll and Lewis Killin (SYNAPSE). A total of 10 experts participated in the workshop, and one expert who was unable to attend sent written feedback on the areas of discussion. A MIRO™ board was also used as a tool to facilitate the interaction between participants.

The participants had experience in assessment of treatments for neurodegenerative diseases and/or had a background of neurodegenerative disease research and therefore were familiar with challenges and gaps in research in this disease area. A pre-reading document was prepared by NICE and provided to the experts in advance of the workshop to give an overview of the project, the IMI neurodegenerative disease portfolio and areas of discussion.

Experts from the following organisations participated in the consultation:

- The Dental and Pharmaceutical Benefits Agency (TLV), Sweden
- European Network for Health Technology Assessment (EUnetHTA), EU
- NICE, UK
- Institute for Clinical and Economic Review (ICER), USA
- Danish Medicines Agency, Denmark
- Agency of Health Quality and Assessment of Catalonia (AQuAS), Spain
- The Norwegian Medicines Agency (NoMa), Norway
- AstraZeneca (Regulatory Affairs and Policy), EU
- Graduate School of Health Economics and Management, Catholic University of the Sacred Heart, Italy

While the focus of the workshops was slightly different depending on the stakeholder group, across the consultations, participants were asked to identify gaps in neurodegenerative disease research and priorities for future research.

Therefore, the collective views of these various stakeholders were the basis of the gap analysis, the results of which are summarised in Section 6 of this report. The consultation with the EWGPWD and their supporters was held first followed by the workshops with neurodegenerative disease researchers and HTA and regulatory experts, which were held in parallel. This allowed feedback themes from the consultation with the EWGPWD and their supporters, who are key stakeholders for neurodegenerative disease research, to be shared with other stakeholders and inform the discussions in the other two workshops. An overview of some of the key questions asked at the workshop and consultations is presented in Figure 2.

The consultation with neurodegenerative disease researchers reported in Section 4.1 also aimed to identify any gaps in our understanding of existing neurodegenerative disease initiatives so we can have a clearer view of the current research landscape.

EWGPWD and their supporters
•Are the four priorities for biomedical research in the IMI2 Strategic Research Agenda relevant and important to you? Why? •What other types and topics of biomedical research would you like to see prioritised? Why? •How do you feel about the research topics that have been addressed by IMI funded projects? Is there anything missing? What benefit would these new research topics bring to people with dementia? •How do you feel about the disease areas that have been addressed by IMI funded projects? Is there anything missing? What benefit would these disease areas bring to people with dementia?
HTA and regulatory experts
•Do you have any thoughts on the IMI neurodegenerative disease research portfolio and the priorities outlined in the IMI2 Strategic Research Agenda? Which do you think are the most important and why? •Looking at the list of research projects, are there any that seem particularly interesting or valuable from your perspective? If so, why? •What are the gaps and challenges that you have faced or expect to face in the assessment of treatments for neurodegenerative diseases? •What are the research areas that need to be prioritised to address these gaps?

Figure 2. Questions asked to identify gaps and priorities in consultation with EWGPWD and HTA and regulatory experts

5 Neurodegeneration research mapping results

5.1 Survey results

The survey was created as an Excel® proforma and Qualtrics® online survey to suit the respondents' preferences. There was no difference in content between the versions. Both versions of the survey were sent to the NEURONET SCB and WGs by email. We received 21 responses to the initiative evaluation survey. From the shortlist of 34 initiatives, seven new initiatives were added by the respondents: EPAD, AMYPAD, Interdem, WYLD, MJF Foundation, EDoN, EDPI. Of these, EPAD and AMYPAD were removed from the final analysis as they constituted studies rather than initiatives. Not all respondents returned information for all initiatives, resulting in four initiatives with no data: CBD Solutions, Clinical Research in ALS, and Related Disorders for Therapeutic Development (CReATe), Fox DEN: Data Exploration Network and the International Parkinson Disease Genomics Consortium.

For the 35 initiatives that were evaluated, star ratings were converted into numeric values (i.e., ★ to 1, ★★ to 2, etc.) and an average score for each variable was calculated for each initiative. Additionally, an overall score was calculated for each initiative by taking the average of these calculated values for each variable. The initiatives and scores are presented in Table 1 in descending order relative to the overall average. The number of responses (i.e., respondents providing ratings per initiative) is presented in the "responses" column. The four initiatives with the highest overall scores (scoring 3 or over, out of 4) were the CHDI foundation, IMI, Alzheimer's Disease Data Initiative (ADDI) and the Parkinson's Progression Markers Initiative (PPMI). The highest scores recorded for each individual variable are highlighted in light blue in the table.

A further analysis was carried out to calculate the average evaluation for each category based on initiative scope and initiative reach, presented in Table 2 to identify any patterns based on these variables. There is no clear differentiation in perceived influence based on reach, and it seems that respondents perceived Huntington's Disease initiatives to be more influential than other initiatives.

However, given the small number of initiatives considered for Huntington's disease and the small number of overall responses, this should be interpreted with caution.

Figure 3 illustrates one subset of the potential relationships between variables associated with strategic importance. Here, by interpreting an initiative's (perceived) amount of funding as an independent variable, it can be seen that its relationship to an initiative's influence is weaker ($r = 0.23$) than its relationship with openness, innovation, or long-term impact ($r = 0.33, 0.39, 0.48$, respectively). With few responses and data, it is not possible to draw strong inferential conclusions with this analysis, but this pattern raises the hypothesis that funding does not affect all aspects of an initiative's perceived strategic importance in a uniform way. Taken further, it could be argued that the strongest relationship - funding and long-term impact – reflects the extent to which an initiative is simply able to be present through sustained and dedicated funds.

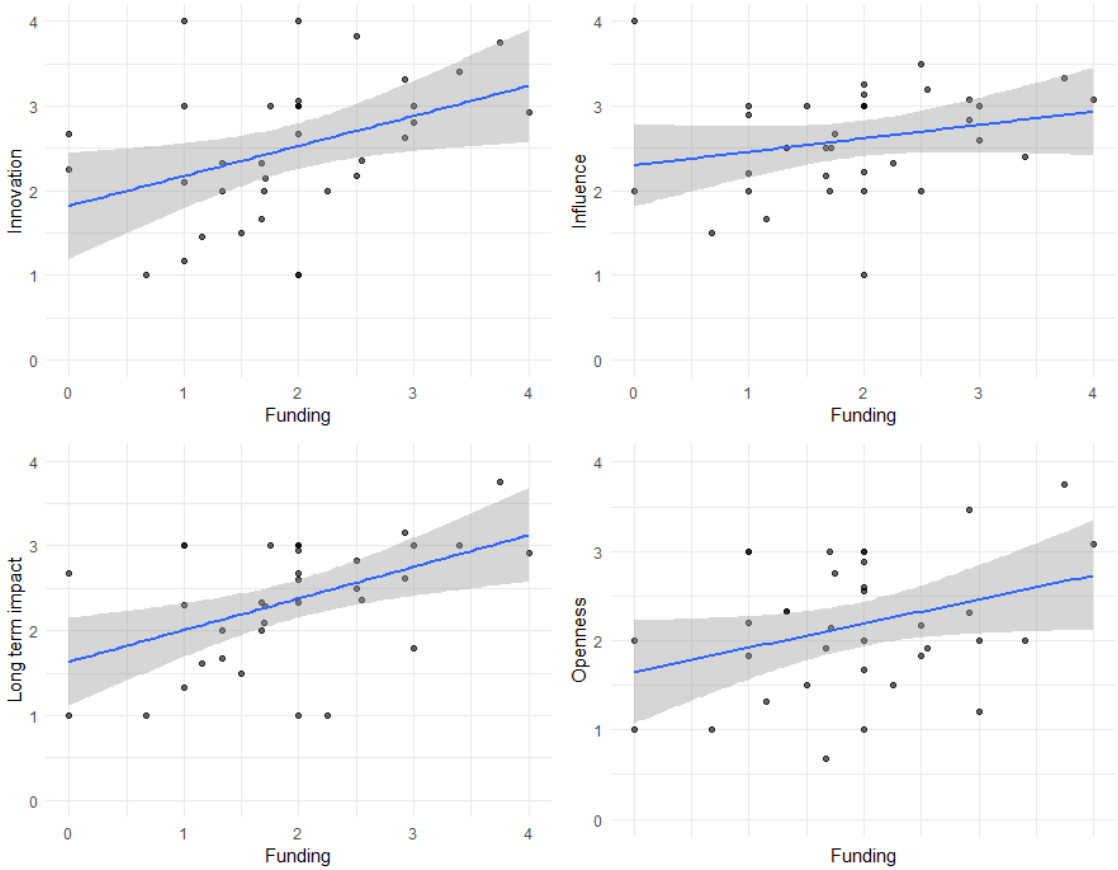

Figure 3. The relationship between initiatives' perceived amount of funding and variables associated with strategic importance

Table 1. Evaluations of neurodegenerative disease research initiatives.

Initiative	Scope	Reach	Responses	Influence	Innovation	Openness	Funding	Long term impact	Overall Average
CHDI Foundation	HD	Intl	4	3.33	3.75	3.75	3.75	3.75	3.67
Innovative Medicines Initiative (IMI)	NDD	Intl	13	3.08	2.92	3.08	4.00	2.92	3.20
Alzheimer's Disease Data Initiative (ADDI)	AD	Global	13	3.08	3.31	3.46	2.92	3.15	3.18
Parkinson's Progression Markers Initiative (PPMI)	PD	Intl	1	3.00	4.00	3.00	2.00	3.00	3.00
Dominantly Inherited Alzheimer Network (DIAN)	AD	Intl	6	3.50	3.83	2.17	2.50	2.83	2.97
Dementia Discovery Fund (DDF)	NDD	Intl	5	2.40	3.40	2.00	3.40	3.00	2.84
Alzheimer's Disease Neuroimaging Initiative (ADNI)	AD	Intl	16	3.13	3.06	2.88	2.00	2.94	2.80
MJF Foundation	PD	Natl	1	3.00	3.00	2.00	3.00	3.00	2.80
World Young Leaders in Dementia (WYLD)	AD	Global	1	3.00	4.00	3.00	1.00	3.00	2.80
Global Brain Health Institute (GBHI)	NDD	Global	5	3.25	3.00	2.60	2.00	2.60	2.69
Alzheimer's Drug Discovery Foundation	AD	Intl	13	2.83	2.62	2.31	2.92	2.62	2.66
European Huntington's Disease Network (EHDN)	HD	Intl	4	2.67	3.00	2.75	1.75	3.00	2.63
Davos Alzheimer's Collaborative	AD	Global	11	3.20	2.36	1.91	2.55	2.36	2.48
Dementias Platform UK	NDD	Intl	9	2.22	2.67	2.56	2.00	2.67	2.42
European Dementia Prevention Initiative (EDPI)	AD	Intl	1	2.00	3.00	2.00	2.00	3.00	2.40
Interdem	AD	Intl	1	2.00	3.00	3.00	1.00	3.00	2.40
Early Detection of Neurodegenerative Disease (EDoN)	AD	Intl	1	1.00	3.00	3.00	2.00	3.00	2.40
JPND	NDD	Global	5	2.60	2.80	1.20	3.00	1.80	2.28
Huntington's Disease Regulatory Science Consortium (HD-RSC)	HD	Intl	3	4.00	2.67	2.00	0.00	2.67	2.27
Accelerating Medicines Partnership: AD	AD	Natl	6	2.00	2.17	1.83	2.50	2.50	2.20
NEURONET	NDD	Intl	10	2.00	2.00	3.00	1.70	2.10	2.16
Global Alzheimer's Platform Foundation	AD	Global	7	2.50	2.14	2.14	1.71	2.29	2.16
World Dementia Council	NDD	Global	10	2.90	2.10	2.20	1.00	2.30	2.10
Tau Consortium	NDD	Intl	3	2.50	2.33	2.33	1.33	2.00	2.10

Global Alzheimer's Association Interactive Network (GAAIN)	AD	Global	12	2.18	2.33	1.92	1.67	2.33	2.09
Aligning Science Across Parkinson's (ASAP)	PD	Global	3	3.00	1.00	1.67	2.00	2.33	2.00
Accelerating Medicines Partnership: PD	PD	Natl	3	2.50	2.00	2.33	1.33	1.67	1.97
European Brain Council	NDD	Intl	4	2.33	2.00	1.50	2.25	1.00	1.82
Bluefield Project	FTD	Intl	2	3.00	1.50	1.50	1.50	1.50	1.80
Critical Path for Parkinson's	PD	Intl	3	2.50	1.67	0.67	1.67	2.00	1.70
Network of Centres of Excellence in Neurodegeneration (COEN)	NDD	Intl	2	3.00	1.00	1.00	2.00	1.00	1.60
European Alzheimer 's Disease Consortium (EADC)	AD	Intl	6	2.20	1.17	1.83	1.00	1.33	1.51
Critical Path for Alzheimer's Disease (CPAD)	AD	Intl	13	1.67	1.46	1.31	1.15	1.62	1.44
Genetic Frontotemporal dementia Initiative (GENFI)	FTD	Intl	4	2.00	2.25	1.00	0.00	1.00	1.25
AMP PD Knowledge Platform	PD	Intl	3	1.50	1.00	1.00	0.67	1.00	1.03

AD = Alzheimer's disease, *PD* = Parkinson's disease, *FTD* = Frontotemporal dementia, *HD* = Huntingdon's disease, *Intl* = international, *Natl* = national, *NDD* = neurodegenerative disease.

Table 2. Evaluations of neurodegenerative disease research initiatives according to their reach and scope.

	Influence	Innovation	Openness	Funding	Long term impact
Reach					
Global	2.86	2.56	2.23	1.98	2.46
International	2.58	2.47	2.12	1.84	2.27
National	2.50	2.39	2.05	2.28	2.39
Scope					
AD	2.45	2.67	2.34	1.92	2.57
PD	2.58	2.11	1.78	1.78	2.17
FTD	2.50	1.88	1.25	0.75	1.25
HD	3.33	3.14	2.83	1.83	3.14
NDD	2.63	2.42	2.15	2.27	2.14

AD = Alzheimer's disease, *PD* = Parkinson's disease, *FTD* = Frontotemporal dementia, *HD* = Huntingdon's disease, *NDD* = neurodegenerative disease.

A further consideration is that initiatives which are more known (i.e., those associated with a higher number of evaluations or responses) may in turn be associated with greater ratings of strategic importance. However, as demonstrated in Figure 4, the relationship between any aspect of an initiative's strategic importance does not appear to be associated with the extent to which it was well-known, with weak relationships between number of received responses and innovation (r = -0.02), influence (r = 0.09), long-term impact (r = 0.09) and openness (r = 0.18).

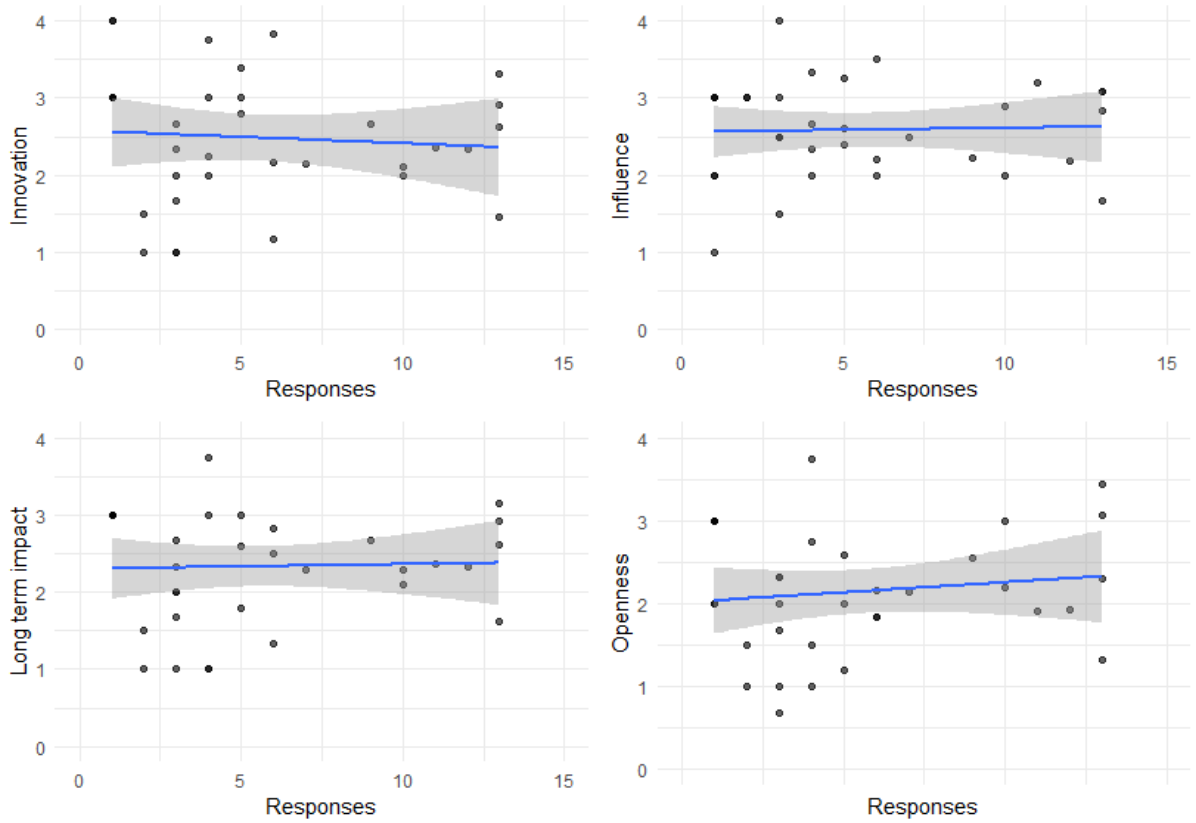

Figure 4. the relationship between number of responses received for initiatives and variables associated with strategic importance

5.2 Researcher workshop results

Seven researchers and members of EFPIA attended a research landscape and gap analysis workshop on the 2nd of November 2021.

Prior to the meeting, the attendees had received a copy of the evaluation survey to review and complete. During the meeting, facilitators from SYNAPSE and NICE used the MURAL whiteboard site to plot the average evaluation of initiative variables, representing influence, innovation, scope, funding, and reach. This map was created as a heuristic illustration and reference for discussion and is presented in Figure 5.

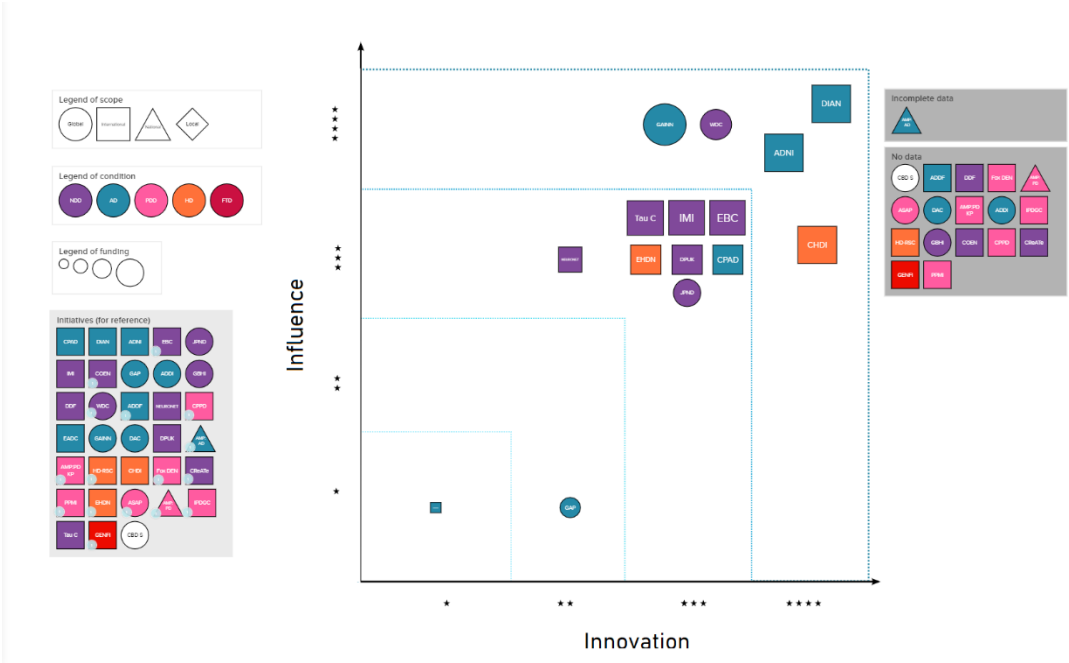

Figure 5. A map of NDD initiatives according to their funding size, innovation (x-axis) and influence (y-axis)

Overall, the group of researchers considered the mapping exercise to be useful, but, critically, felt its use was beyond plainly mapping or discussing the importance, influence, and impact of current initiatives. Instead, they felt this exercise underlined a necessity for change in how research initiatives are structured and supported, raising four key points.

Specifically, by being asked to comment on a long list of initiatives, and seeing a correlation between funding and impact, the group agreed that progress in the field of neurodegenerative disease research was hindered by a) initiative fragmentation and b) an absence of long-term sustained investment. However, even in the case of dedicated funding (i.e., resolving the lack of long-term, sustained investment), large initiatives tended to fail because of c) bad programme management, usually associated with unclear objectives, milestones, or achievements. As a potential solution, the group mentioned d) the benefit of short-term micro-projects, which seek to achieve focussed and clear objectives that address a specific neurodegenerative disease-related problem. In this way, clear achievements in a more limited area could progress the field of research further and faster than unwieldly initiatives.

6 Gap Analysis

6.1 Research focus

From the returned researcher survey and workshops, it was clear that the NEURONET consortium, WGs and SCB had limited insights into initiatives dedicated to neurodegenerative diseases outside of Alzheimer's disease with six Parkinson's disease initiatives, three Huntington disease initiatives and two Frontotemporal dementia initiatives. Multiple sclerosis, motor neuron disease, Lewy body dementia, corticobasal degeneration and prion diseases were not represented by any initiatives in the current mapping exercise.

The limited scope (in terms of disease area) was also highlighted in the consultations with the EWGPWD and their supporters. EWGPWD members commented that biomedical research is very important, but that they would like to see more research on non-Alzheimer's dementia. They emphasised the value of involving people with lived experience of disease in research, and called for improved communication of research results, in accessible, plain language, to participants, patients and the general public. Family caregivers of EWGPWD members stated that there is a need for interdisciplinary research exploring living with other health conditions along with dementia (e.g., cardiovascular disease) and that there should be more work that connects medical and social aspects of the disease. It was also highlighted that there was a strong focus on the preclinical or early stages of dementia, although they understood that it may be more complicated to do research with people in the more advanced stages of dementia.

Similarly, feedback from HTA and regulatory experts was that the projects in the portfolio do not reflect the range of neurodegenerative diseases encountered in clinical practice. This was also a finding in the first version of the mapping and gap analysis that was carried out by NEURONET (D1.3), in which there was a clear trend of a focus on Alzheimer's disease research both within the IMI neurodegenerative disease portfolio and across global research activities.

6.2 Data on natural history of the disease and disease mechanisms

In the HTA and regulatory workshop, it was highlighted that there should be more focus on collecting longitudinal background population-level data on cognitive function, to have a better understanding of the natural history of neurodegenerative diseases. This is important to understand normal cognitive function within this age group to be able to assess the impact of treatments aiming to slow down the progression of disease. We need a better understanding of the population that should undergo screening, since mild cognitive impairment is an ill-defined heterogenous condition that can have other causes that can be misdiagnosed as Alzheimer's disease in clinical practice.

Another aspect that is important to know yet remains unclear from an HTA perspective is the size of the target population for treatments per country. Furthermore, there is still a stigma around certain conditions like Alzheimer's and Parkinson's disease which we need to tackle when designing screening programmes.

6.3 Disease-modifying treatments

It was highlighted in the HTA and regulatory workshop, that there is a gap for disease-modifying treatments for neurodegenerative diseases and that while screening is important it is not meaningful unless we can offer people treatments that can change the course of the disease and improve outcomes.

6.4 Diagnostic tests

Participants in the HTA and regulatory workshop stated that diagnostic tests that are currently routinely used are not particularly predictive, prognostic, or in some instances pleasant (e.g., lumbar puncture for Alzheimer's disease). Therefore, there is a gap for less invasive, highly sensitive diagnostic tests.

6.5 Clinical trial endpoints and clinical outcomes

There is a need for better endpoints than those which are currently used in trials, not just to measure the effect of an intervention within a trial but also their relationship to long term outcomes for patients. More focus should be put on thinking of how patient-reported outcomes or user-generated data within trials could be used as a way for managed access/entry for products. The participants were aware that digital endpoints are being explored within the IMI neurodegeneration research projects but felt that there is still scope for improvement.

A finding of the IMI project, ROADMAP,(3) was that there was a mismatch of how Alzheimer's disease was diagnosed in clinical practice compared to the processes used in clinical trials. The clinical assessments that were done and how they were recorded in electronic health records and GP practices were mismatched to the instruments that were used in clinical trials and there were also regional variations. There was an attempt in the ROADMAP project to validate a disease progression model based on real world evidence but there were no repeat measurements to base this on (3). The reason for this is that in clinical practice, once a person was diagnosed with Alzheimer's disease by clinicians, they usually would not have repeat assessments of cognitive parameters. Therefore, there is a gap for data on long-term clinical outcomes in the real-world context. However, ROADMAP has set the stage for future research tools to inform and shape the next generation of research and advancements in the neurodegeneration field.

7 Challenges and priorities for specific groups

There were some additional key feedback themes beyond research gaps that were highlighted across the workshops. This additional feedback is reported in this section to give a fuller picture of the issues that were relevant to the respective stakeholders.

7.1 Consultation with EWGPWD and supporters

7.1.1 Public involvement

A strong theme from the EWGPWD and supporter consultation was the importance of involving people with lived experience of disease in biomedical research projects, and the value of considering disease in a holistic way, including social and psychological factors alongside biomedical aspects. They explained that there could be many benefits from involving people affected by disease in biomedical research, such as increasing the relevance of that research to real-world situations, identifying new, practical considerations for patient-facing materials, and enabling people affected by disease to act as advocates or champions for research.

7.1.2 Access to research and public involvement

The consultations also identified that people with dementia and their supporters experience challenges in accessing, participating in, and understanding the outputs of research. They spoke about being excluded from participation in research due to geographical location or language issues, despite a strong desire to be involved in research. They also highlighted that the results of research aren't always returned, and that there needs to be better communication of research, in plain language, and

to diverse audiences (including e.g., schools). In turn, this could both increase knowledge of and improve engagement in research.

7.1.3 Diagnosis and early detection

In terms of research priorities outlined in the IMI2 Strategic Research Agenda, while the participants felt that all the priorities and topics were important, the one that resonated particularly with both EWGPWD members, and their supporters was diagnosis and early detection. They explained that the nature and quality of diagnosis was critical ("the right diagnosis, at the right time") and that appropriate post-diagnostic support and counselling should always be offered.

7.1.4 Prevention and progression of dementia

Prevention was perceived as a very important topic but it was felt that it should extended beyond the point of diagnosis, with further research on the topic of delaying progression of dementia to the advanced stages.

7.2 Researcher workshop

7.2.1 Research communication

From the researchers' perspective, EFPIA and academia collaborations work well, but the research and its findings are probably not well communicated. There is also the question of how to get research findings faster into practice, for the benefit of patients. Currently this process usually takes over a decade and that is discouraging for everyone (patients and researchers).

7.2.2 Public involvement

In recent years it is becoming more and more common to get participants involved in designing the research studies they will participate in. This model of participants setting research priorities is represented by organisations such as the James Lind Alliance. They would aim, for example, to establish research objectives together with people with dementia to see if the research being planned is aligned with their needs and interests.

7.3 HTA and regulatory workshop

7.3.1 Public involvement and accessibility of research informing decision-making

Working with people living with neurodegenerative diseases and relevant organisations is important when communicating research and decision-making to share with the wider public. It is also important to engage with physicians and to educate them to explain the role of regulators and HTA bodies to ensure that the message is clearly communicated to people they treat.

While we can put a lot of effort into making sure that the language used is accessible, publications in journals behind paywalls are not accessible to the public. Furthermore, having information redacted in public documents because pharmaceutical companies are not willing to share the data until they disseminate it, is an issue which some HTA bodies encounter.

From a regulatory perspective, industry is responsible for sharing the results of studies in lay language to participants. As per EU Regulations, clinical data which were submitted by industry to support their marketing applications for human medicines under the centralised procedure and were assessed by the Committee for Medicinal Products for Human Use are now published on the European Medicines Agency (EMA) website. Furthermore, in 2022 with the release of the EMA database, CTIS, these summaries will be uploaded and made available. However, data will be shared on single studies, while HTA decisions are made based on the totality of the evidence and therefore the synthesised data should also be accessible.

7.3.2 Stakeholder alignment

Given the challenges associated with the assessment of treatments for neurodegenerative diseases, there is a need for regular interaction between HTA and regulatory agencies. There is also a need for alignment of HTA and regulatory bodies beyond timelines and processes, but on evidence standards.

The focus of regulatory bodies when carrying out assessments of treatments is the demonstration of statistically significant effects of treatment, but it is also important that minimum relevant clinical effectiveness is considered. A statistically significant treatment effect does not necessarily translate to clinical significance. An example of this for neurodegenerative disease is the 6-Minute Walking Test (6MWT) where there may be a statistically significant improvement observed but a struggle to translate this into clinical improvement in aspects like life expectancy or health-related quality of life.

From an HTA perspective it is important to think of price and value, and while regulators can authorise interventions that cause some improvement, there is an uncomfortable discussion around how much we should pay for them. Therefore, the alignment should not only be between regulators and HTA bodies but should also involve the pharmaceutical industry. A discussion with pharmaceutical companies around their reasonable expectation of price based on the value of their product for the market should be carried out early in the process to allow for timely access of treatments. Furthermore, pharmaceutical companies and researchers should engage more with HTA bodies and regulators for advice about the evidence needs and study designs that will lead to the highest quality of evidence.

7.3.3 Authorisation and post-authorisation considerations for treatments

Clear stopping rules of when to stop treatment (i.e., when disease has progressed to a point where treatment is not beneficial and not cost-effective) are needed when authorising treatments. This is usually requested by clinicians when administering very expensive drugs, so that they do not have the responsibility of making that decision on a case-by-case basis. It is also important to collect real-world data to inform when drugs should be withdrawn from the market post-authorisation or whether additional useful information could be generated.

8 Priorities for research

We recommend that the following areas are prioritised when thinking of future research in the next 5 years, based on the feedback collected from the various stakeholders that were consulted:

- **Approach to future research funding and management**: from the researcher workshops, it was clear that their preferred priorities for future research would be associated with a paradigm shift in how projects were proposed and funded. Specifically, rather than promoting one particular theme or area of research, the group commented that priorities and areas of investigation should generally focus on small or well-defined problems across themes, rather than supporting large, expensive initiatives with diffuse aims and ambitions. Taken in concert with the survey responses, this change in approach could be applied to those neurodegenerative disease conditions that were under-represented by this exercise.
- **Disease-modifying treatments:** a better understanding of disease mechanisms and the development of disease-modifying treatments for neurodegenerative diseases, given the current lack of available effective treatments for conditions like dementia is a high priority. Dementia has a high global disease burden and the number of people living with it is expected to continue to rise(4).
- **Public involvement and communication:** It is important to involve people living with neurodegenerative diseases and their supporters in planning and designing future research and to address any barriers that they may encounter e.g., in accessing and taking part in research. Efforts

need to be made to effectively communicate research activities, making it transparent and easily accessible and ensuring that research informs decision-making.

- **Observational data:** there is a need for more research efforts to collect background longitudinal data in populations on the change in cognitive function over time and to understand the patient population to target with screening programmes.
- **Clinical trial design:** when designing future clinical trials, it is important that they are aligned with clinical practice and that trial endpoints translate to long-term clinical outcomes. Furthermore, it is beneficial to engage with regulatory and HTA bodies at the stage of study design so they can advise on the best approach to generate high quality evidence.
- **Diagnostic tests:** there is a need for more research to develop less invasive, highly sensitive diagnostic tests so that patients can receive the correct diagnosis in a timely manner.
- **Broader research focus:** there is a need for research into a broader range of neurodegenerative diseases beyond Alzheimer's disease and earlier stages of disease. There is also a need for more interdisciplinary research, across different conditions and aspects of conditions that connect the medical, social, and psychological impact on people with neurodegenerative diseases.
- **Interaction between different stakeholders:** there is a need for better communication between researchers to avoid redundancy in research efforts. There is also a need for interaction and alignment between researchers, HTA bodies, and regulators and better communication of research outputs to patients and the public in general.

9 Discussion

This deliverable aimed to map the neurodegenerative disease research landscape according to the strategic importance/value of research initiatives and undertake a gap analysis of current research. The results of the mapping exercise show that our current understanding of key research activity in the neurodegenerative disease field to be comprehensive with only a few additional initiatives being suggested by respondents.

Researchers expressed a need for a paradigm shift in the management of research to ensure that it is more efficient and impactful. While the landscape of neurodegenerative disease research may seem busy with the number of initiatives undertaken, the fact that the impact of this research may not be felt could be a result of research fragmentation and working in isolation. Therefore, this highlights the importance of projects like NEURONET that support the communication between projects to integrate efforts being carried out.

The gap analysis identified several areas where the stakeholders consulted, perceived a need for more research. The feedback highlighted that there was scope for the IMI neurodegenerative disease research portfolio to broaden disease areas being studied, particularly beyond earlier stages of dementia and Alzheimer's disease. There is also a need for more interdisciplinary research across other conditions along with neurodegenerative diseases, and to explore social and psychological aspects.

HTA and regulatory experts highlighted challenges caused by gaps in knowledge in addition to a lack of alignment between trials' conduct and clinical practice. As they are mostly involved in later stages of research and utilise research outputs to determine the effectiveness and safety, and in the case of HTA experts, the cost-effectiveness of treatments, these gaps may hinder the decision-making process. Therefore, it is important that the evidence being generated by trials is fit for decision-making so that regulatory and HTA bodies can allow patients to access safe and effective treatments in a timely manner.

The wide range of feedback on gaps and priority areas that was collected from the gap analysis emphasises the importance of involving different stakeholder groups in research priority setting and decision-making to produce relevant and satisfactory outputs.

Our analysis has a few limitations. We did not receive a large number of responses to the survey of neurodegenerative disease researchers and the awareness of the different initiatives varied across the respondents, therefore it was not possible to make strong conclusions based on the responses. Furthermore, the ratings for each initiative relied on the perception of the respondents and are not meant to be taken as evidence of the initiative's strategic importance. However, the framework could be considered a starting point for taking this further and collecting data on the variables to quantify the strategic importance of initiatives in the future.

10 Conclusion

This deliverable sets out the second and final stage of a global mapping exercise and gap analysis and aimed to assess the strategic importance of key initiatives in the global neurodegenerative research landscape, in addition to research gaps and priorities from the perspective of different stakeholders. Based on the mapping and gap analysis, the results show that we have a good understanding of the current research landscape but that the awareness of global research initiatives across NEURONET researchers varied and that there is a need for more influential research. There is also scope for improvement to the approach to undertaking research, and there are several gaps in the evidence base that represent areas that need to be prioritised in future research.

11 References

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12 Annexes

Annex I –Survey completed by NDD Researchers

NEURONET Initiative Survey

Introduction

At NEURONET, we're interested in mapping the global neurodegenerative (ND) research landscape.

To help achieve this, we wanted to gain the perspectives of ND researchers from around the world to comment and report on what they consider to be the most important, relevant or upcoming initiatives in the field. From here, we're interested in understanding and revealing the gaps in our current evidence base and efforts, which will allow us to lay out priorities for future research.

In this survey, we will ask you to evaluate a shortlist of ND initiatives that we have drawn up. If you feel that we have missed some, you will have an opportunity to tell us what they are, and also rate them.

Please do not feel that you have to comment on **all** initiatives; you can return an evaluation for just the ones you know.

This survey will take **10 minutes** to complete.

Thank you for your time. We will be publishing the results of this work in our upcoming deliverable in Q1 2022.

Question 1 Where are you based?

- ○ Europe (1)
- ○ North America (2)
- ○ South America (3)
- ○ Asia (4)
- ○ Africa (5)
- ○ Oceania (6)

Question 2 What best describes your current field or place of work?

- ○ Academia (1)
- ○ SME (2)
- ○ Industry (3)
- ○ Regulatory/HTA (4)
- ○ Patient organisation (5)
- ○ Other (6)

Display This Question:

If What best describes your current field or place of work? = Other

Question 2b If you selected "Other" please specify here.

_____

Question 3

Please select the initiatives that you are familiar with.

- [ ] Accelerating Medicines Partnership: AD (AMP: AD) (1)
- [ ] Accelerating Medicines Partnership: PD (AMP: PD) (2)
- [ ] Aligning Science Across Parkinson's (ASAP) (3)
- [ ] Alzheimer's Disease Data Initiative (ADDI) (4)
- [ ] Alzheimer's Disease Neuroimaging Initiative (ADNI) (5)
- [ ] Alzheimer's Drug Discovery Foundation (ADDF) (6)
- [ ] AMP PD Knowledge Platform (7)
- [ ] Bluefield Project (8)
- [ ] CBD Solutions (9)
- [ ] CHDI Foundation (10)
- [ ] Clinical Research in ALS and RElated Disorders for Therapeutic Development (CReATe) (11)
- [ ] Davos Alzheimer's Collaborative (DAC) (12)
- [ ] Critical Path for Alzheimer's Disease (CPAD) (13)
- [ ] Critical Path for Parkinson's (CPAP) (14)
- [ ] Dementia Discovery Fund (DDF) (15)
- [ ] Dementias Platform UK (DPUK) (16)
- [ ] Dominantly Inherited Alzheimer Network (DIAN) (17)

- [ ] European Alzheimer's Disease Consortium (EADC) (18)
- [ ] European Brain Council (EBC) (19)
- [ ] European Huntingdon's Disease Network (EHDN) (20)
- [ ] Fox DEN: Data Exploration Network (21)
- [ ] Genetic Frontotemporal Dementia Initiative (GENFI) (22)
- [ ] Global Alzheimer's Association Interactive Network (GAAIN) (23)
- [ ] Global Alzheimer's Platform Foundation (GAP) (24)
- [ ] Global Brain Health Institute (GBHI) (25)
- [ ] Huntingdon's Disease Regulatory Science Consortium (HD-RSC) (26)
- [ ] Innovative Medicines Initiative (IMI) (27)
- [ ] International Parkinson Disease Genomics Consortium (28)
- [ ] Joint Programme Neurodegenerative Disease (JPND) (29)
- [ ] Network of Centres of Excellence in Neurodegeneration (COEN) (30)
- [ ] NEURONET (31)
- [ ] Parkinson's Progression Markers Initiative (32)
- [ ] Tau Consortium (33)
- [ ] World Dementia Council (34)
- [ ] I don't know any of these initiatives. (35)

Skip To: Question 4 If please select the initiatives that you are familiar with. = I don't know any of these initiatives.

Defining initiatives

We have created some variables that definite the value or quality of initiatives. They are based on a star rating, where four stars represents the positive extreme of a variable (e.g., *very innovative or very influential*).

Innovation: to what extent is the initiative looking at new problems (or old problems in a new way?) **Influence**: to what extent is the initiative setting or changing the research agenda? **Long-term impact**: to what extent do you perceive the initiative as having a lasting impact on the field? **Funding**: to what extent do you perceive the initiative to have funding at its disposal? **Openness**: to what extent is the initiative open to collaboration? Does it represent a "closed club"?

Question 4 How would you evaluate the initiatives you identified previously?

	Innovation	Influence	Long-term impact	Funding	Openness
Accelerating Medicines Partnership: AD (AMP: AD) (1)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Accelerating Medicines Partnership: PD (AMP: PD) (2)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Aligning Science Across Parkinson's (ASAP) (3)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Alzheimer's Disease Neuroimaging Initiative (ADNI) (36)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Alzheimer's Disease Data Initiative (ADDI) (37)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Alzheimer's Drug Discovery Foundation (ADDF) (38)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
AMP PD Knowledge Platform (39)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Bluefield Project (40)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)

CBD Solutions (41)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
CHDI Foundation (42)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Clinical Research in ALS and RElated Disorders for Therapeutic Development (CReATe) (43)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Davos Alzheimer's Collaborative (DAC) (44)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Critical Path for Alzheimer's Disease (CPAD) (45)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Critical Path for Parkinson's (CPAP) (46)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Dementia Discovery Fund (DDF) (47)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Dementias Platform UK (DPUK) (48)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Dominantly Inherited Alzheimer Network (DIAN) (49)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
European Alzheimer's Disease Consortium (EADC) (50)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
European Brain Council (EBC) (51)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
European Huntingdon's Disease Network (EHDN) (52)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Fox DEN: Data Exploration Network (53)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)

Genetic Frontotemporal Dementia Initiative (GENFI) (54)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Global Alzheimer's Association Interactive Network (GAAIN) (55)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Global Alzheimer's Platform Foundation (GAP) (56)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Global Brain Health Institute (GBHI) (57)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Huntingdon's Disease Regulatory Science Consortium (HD-RSC) (58)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Innovative Medicines Initiative (IMI) (59)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
International Parkinson Disease Genomics Consortium (60)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Joint Programme Neurodegenerative Disease (JPND) (61)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Network of Centres of Excellence in Neurodegeneration (COEN) (62)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
NEURONET (63)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Parkinson's Progression Markers Initiative (64)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
Tau Consortium (65)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)
World Dementia Council (66)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)

Question 4 Do you know of any other initiatives that we have not mentioned?

- ○ Yes (1)
- ○ No (2)

Skip To: End of Block If Do you know of any other initiatives that we have not mentioned? = No

Question 5 Please write the name of any initiatives that we may have missed below.
You can add up to 5.

- ○ Initiative 1 (1) _____
- ○ Initiative 2 (2) _____
- ○ Initiative 3 (3) _____
- ○ Initiative 4 (18) _____
- ○ Initiative 5 (19) _____

Question 6 How would you rate the initiatives that you have added?
In addition to the variables from the last page, scope and reach refer to disease area and geographic location, respectively.

	Innovation	Influence	Long-term impact	Funding	Openness	Reach	Scope

Initiative 1	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... Global (5)	▼ NDD (1 ... FTD (9)
Initiative 2	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... Global (5)	▼ NDD (1 ... FTD (9)
Initiative 3	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... Global (5)	▼ NDD (1 ... FTD (9)
Initiative 4	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... Global (5)	▼ NDD (1 ... FTD (9)
Initiative 5	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... ★★★★ (5)	▼ Don't know (1 ... Global (5)	▼ NDD (1 ... FTD (9)

Glossary

NDD: General or non-specific neurodegeneration, **AD**: Alzheimer's disease, **PD**: Parkinson's disease, **HD**: Huntingdon's disease, **MS**: Multiple sclerosis, **PrD**: Prion disease, **MND**: Motor neuron disease, **LBD**: Lewy body dementia, **FTD**: Frontotemporal dementia

Comments If you would like to add any comments, please do so here.

Annex II Presentations used in the consultation with the EWGPWD and their supporters, and the workshop with HTA and regulatory experts


NEURONET_IMI_D1.6 consultation_EWGPW


NEURONET_IMI_D1.6 consultation_supporte


NEURONET_IMI_D1.6 HTA and Regulatory v