

WP1 Projects & Impact analysis

D1.3 Map of relevant initiatives and gap analysis v1

Lead contributor	Diana O'Rourke (02 – NICE)
Other contributors	Jacoline Bouvy (02 – NICE) Katy Harrison (02 – NICE) Pall Jonsson (02 – NICE) Angela Bradshaw (03 – AE) Nina Coll (01 – SYNAPSE) Carlos Diaz (01 – SYNAPSE) Emma Dodd (06 – ROCHE) Laurent Pradier (08 – SANOFI)

Contents

Document history	3
Definitions and abbreviations	4
Abstract.....	5
1 Introduction	6
2 Background	6
3 Methods.....	6
4 Neurodegeneration research mapping.....	8
4.1 Global neurodegeneration research.....	8
4.1.1 Research Resources	13
4.2 European neurodegeneration research.....	14
4.2.1 Previous research frameworks	14
4.2.2 IMI ND portfolio	14
5 Gap Analysis.....	17
6 Research mapping.....	22
6.1 Research tools and mapping initiatives	22
7 Discussion.....	26
8 Conclusion.....	27
9 References	28
10 Annexes.....	29
10.1 Annex I - IADRP Research Classification - Common Alzheimer's and Related Dementias Research Ontology' (CADRO)	29
10.2 Annex II - JPND Research Classification	31
10.3 Annex III - FP7-Health funded projects related to neurodegenerative disorders (2007 – 2011)	32

Document history

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V0.2	02/03/2020	First draft
V0.3	10/03/2020	Second draft including comments from work package
V0.4	24/03/2020	Draft including consortium comments
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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
8. **SARD:** Sanofi-Aventis Recherche & Développement
9. **PUK:** Parkinson's Disease Society of the United Kingdom LBG

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

Alzheimer's disease and other neurodegenerative disorders are a major global health burden and represent a high priority for global research and development activities. IMI operates within this global research landscape, funding a number of neurodegenerative disease projects. This deliverable aimed to map the global research landscape for neurodegenerative diseases to understand where the IMI neurodegenerative portfolio fits in globally and to enable a gap analysis with the IMI project portfolio.

Using results from the International Alzheimer's and Related Dementias Research Portfolio (IADRP) mapping exercise which compiles information on international Alzheimer's and Alzheimer's related dementia research, we performed an analysis of global neurodegeneration research activity in relation to key aspects including funding, disease focus and research classification. A gap analysis was then performed to assess the IMI neurodegenerative diseases project portfolio in relation to the same dimensions.

The results demonstrated that the scale and volume of global research in comparison to the IMI portfolio is considerable. There was a clear focus on Alzheimer's disease research, both globally and within the IMI portfolio. However, the IMI portfolio does not comprehensively cover the whole range of research activities that are covered globally, suggesting that many gaps in the IMI portfolio are being addressed outside the IMI context. Furthermore, the gap analysis demonstrates the importance of a coordination mechanism for the IMI portfolio, to ensure its outputs achieve maximum impact and to support the IMI neurodegeneration portfolio in connecting with international research activity.

1 Introduction

The IMI portfolio of neurodegenerative research projects operates in a global environment. Worldwide, many research and development efforts are dedicated to studying different neurodegenerative diseases. As initiatives outside of IMI might be funding research similar or complementary to that being conducted by the IMI neurodegenerative diseases project portfolio, it is important to understand where the IMI ND portfolio fits in globally and to see if any gaps identified in the IMI ND project portfolio might well be addressed by research efforts funded outside of the IMI context.

2 Background

The United States' National Institutes of Health (NIH) is the largest public funder of biomedical research in the world ((National Institutes of Health (NIH), n.d.). Between 2014 and 2020, it provided \$17.3 billion in funding for research in neurodegenerative disease (NIH - Research Portfolio Online Reporting Tools, 2019). Over a similar period (2014-2018), the European Commission invested €3.2 billion - which is approximately \$3.5 billion - into brain research under the Horizon 2020 programme ((European Commission, n.d.).

Between 2009 and 2013, the number of research articles about brain and neuroscience represented approximately 16% of the world's total publication output. In 2013, over 70% of global brain and neuroscience research was published by researchers from Europe and the USA (Elsevier Research Intelligence Analytical Services, 2014). If the number of publications is indicative of the amount of funding for a field, these figures suggest that there has been an increase in funding for neurodegeneration research. However, due to a time lag between funding and publication of research findings, figures may not be indicative of current funding status. Between 2009-2013 global publications in neurodegeneration increased by 3.9% annually (Elsevier Research Intelligence Analytical Services, 2014). Furthermore, the EU Joint Action on Neurodegenerative Diseases (JPND) mapping exercises performed in 2011 and 2016 found that funding for neurodegenerative research had increased by 34% (€370 million to €494 million) in those years (JPND, 2018).

3 Methods

Deliverable D1.3 aimed to provide a mapping exercise of the global neurodegeneration research portfolio, and to perform a gap analysis with the IMI project portfolio. Several existing initiatives have already carried out similar mapping exercises in recent years. Therefore, Neuronet did not repeat the work already carried out by these initiatives but rather, built upon it.

One of these initiatives, the [International Alzheimer's and Related Dementias Research Portfolio \(IADRP\)](#) compiles information on international Alzheimer's and Alzheimer's related dementia¹ research investments and projects. The types of information collected includes project/resource title, funding year, awardee organisation and country, and funding organisation and country. All research is coded by primary disease/condition and then further categorised by the '[Common Alzheimer's and Related Dementias Research Ontology](#)' (CADRO) system to enable the comparison of projects and resources across multiple funders using a common terminology (see [Annex I](#) for full details). The CADRO is organised around 7 major categories:

- Category A. Molecular Pathogenesis and Physiology of Alzheimer's Disease and Alzheimer's Disease-related Dementias
- Category B. Diagnosis, Assessment and Disease Monitoring
- Category C. Translational Research and Clinical Interventions
- Category D. Population Studies
- Category E. Dementia Care and Impact of Disease
- Category F. Research Resources
- Category G. Consortia and Public Private Partnerships
- Category H. Brain Aging and Common Mechanisms related to Dementias

The results are presented in a searchable database of over 30,000 Alzheimer's disease and related dementias research projects funded from 2008 onwards, including all clinical trials, patents and repositories (e.g. links to databases of biomarkers) that are related to the selected projects. It should be noted that the IADRP has a US focus due to the data collection approach that it uses. As the IADRP uses the 2016 JPND mapping exercise as a source, it does not capture all current EU research projects. However, IADRP includes up-to-date information from US federal and state funding agencies, such as the NIH and National Institute on Aging (NIA). It also includes historical NIH and NIA projects dating back to 2008, many of which will have since finished.

For the global mapping, we first searched the IADRP database for all research activity they have mapped in Alzheimer's disease and Alzheimer's related dementias (excluding Vascular dementia/dysfunction which is out of scope of the Neuronet project). We chose this database as it is the most comprehensive mapping tool available for neurodegeneration research. Furthermore, the database also includes the results from a 2016 mapping exercise undertaken by JPND and therefore should have a comprehensive overview of international research efforts in neurodegenerative diseases.

Using the available tools, we analysed the search results in relation to the following dimensions:

- Projects by Awardee country
- Projects by Primary Disease / Condition
- Funding² by Primary Disease / Condition
- Projects by research classification (CADRO category)
- Funding^{iError! Marcador no definido.} by research classification (CADRO category)
- Population study projects and funding^{iError! Marcador no definido.} by Primary Disease / Condition

¹Alzheimer's Disease, Frontotemporal Dementia, Lewy Body Dementias, Multiple Dementias, Vascular Dementia/Dysfunction

² US Dollars only

- Project related clinical trials and links/repositories by Primary Disease / Condition
- Project related clinical trials and links/repositories by research classification (CADRO category)

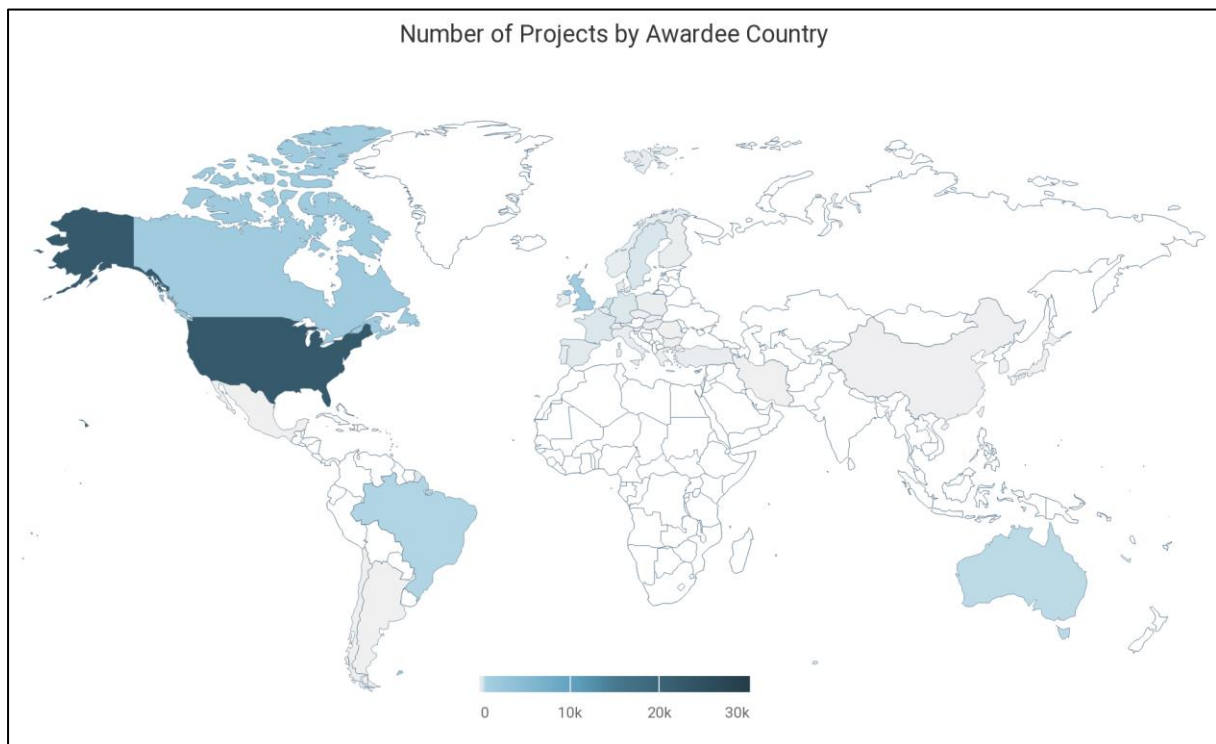
An analysis of the IMI neurodegenerative diseases project portfolio was also performed in relation to the same dimensions. The results of these analyses were then used to undertake a gap analysis, comparing both the IADRP and IMI portfolios with respect to these key dimensions.

4 Neurodegeneration research mapping

4.1 Global neurodegeneration research

Overall the total IADRP portfolio (excluding Vascular dementia/dysfunction) includes 28,066 Alzheimer's disease and Alzheimer's disease related dementias research projects. 81% (22,659) of projects are located in the USA compared to just 4.8% (1,350) in EU member states (figure 1). This large divergence between the number of EU projects compared to the number of US projects maybe partly the result of differences in the sampling methodology used for EU and US funded research (see Methods).

Figure 1. Map of the total number of projects by Awardee country (Iadrp.nia.nih.gov, n.d.)



The majority of projects are related to Alzheimer's disease (n=17,927, 64%) and Multiple Dementias (n=7,029, 26%) (figure 2). These conditions also received the highest proportion of funding - 71% (\$7 billion) and 20% (\$2 billion) respectively (figure 3). However, a brief assessment of the data indicated that 'Multiple Dementias' includes projects relating to other conditions, such as amyotrophic lateral sclerosis and Parkinson's disease.

Analysis of the primary research classification of projects showed that projects categorised as 'Category A: Molecular Pathogenesis and Physiology of Alzheimer's disease/Alzheimer's disease

related dementias' represented the highest proportion of projects in the database (n=10,491, 37%). Within this Category, 20% (n=2,076) are related to Amyloid beta (figure 4). This category also represented the highest proportion of research investment with 34% (\$3.4 billion) of total funding (US only) (figure 5).

The IADRP database contains records of cohort and population studies (cross-sectional, cross-national, prospective, and longitudinal – categorised using the CADRO as Category D). There are 1,021 projects in this category of which 61% (n=618) were in 'Multiple Dementias' with 60% (\$420.6 million) of funding (US dollars only) (figure 6).

The IADRP database also includes details of research resources which are related to the projects. For the 28,066 projects, there are 1,751 related Clinical Trials, 187 Patents and 884 Links/Repositories. The majority of clinical trials and links/repositories are in Alzheimer's disease (n=1,207, 69% and n=700, 79% respectively) (figure 7). Analysis of these resource types by research category shows that the majority fall into 'Category C: Translational Research and Clinical Interventions' (n=1,059, 60% of clinical trials and n=548, 62% of links/repositories) (figure 8).

Figure 2. Proportion of projects by Primary Disease / Condition (ladrp.nia.nih.gov, n.d.)

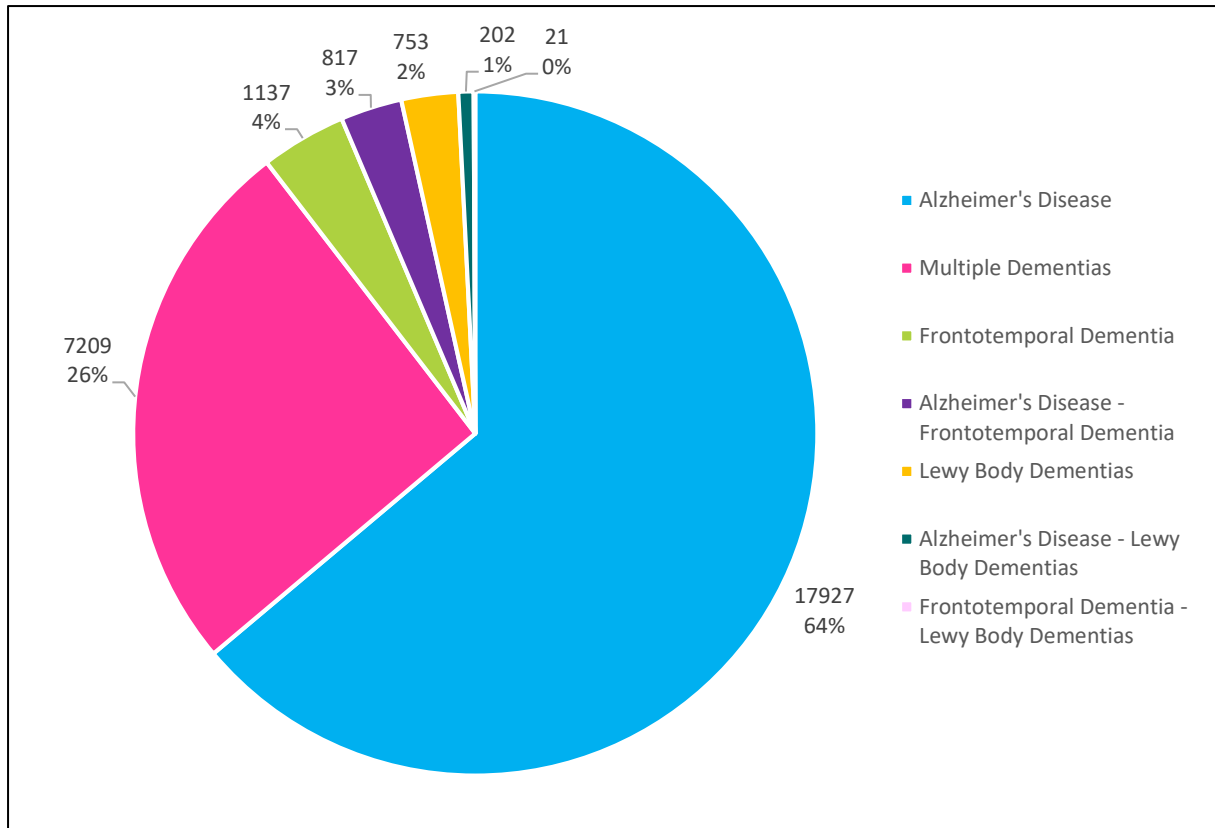


Figure 3. Proportion of funding by Primary Disease / Condition (ladrp.nia.nih.gov, n.d.)

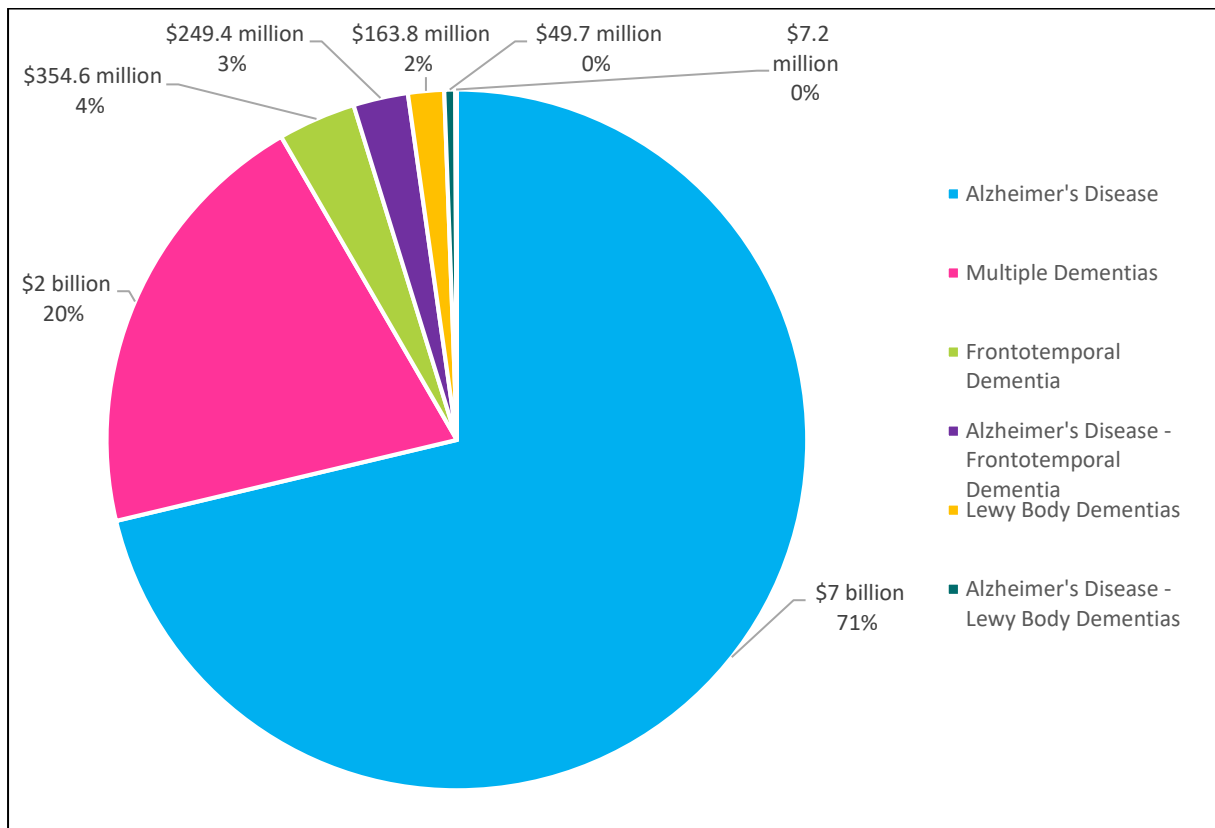


Figure 4. Proportion of projects by CADRO category (ladrp.nia.nih.gov, n.d.)

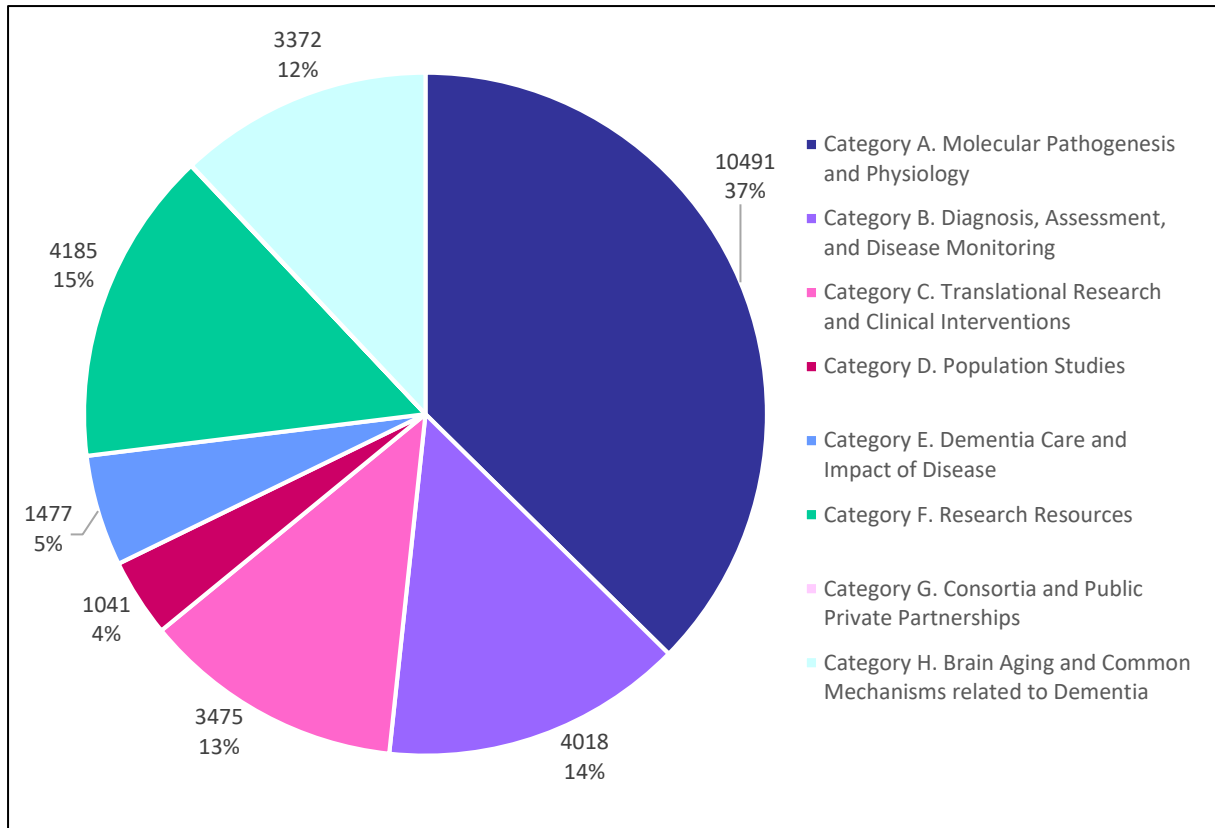


Figure 5. Proportion of funding by CADRO category (ladrp.nia.nih.gov, n.d.)

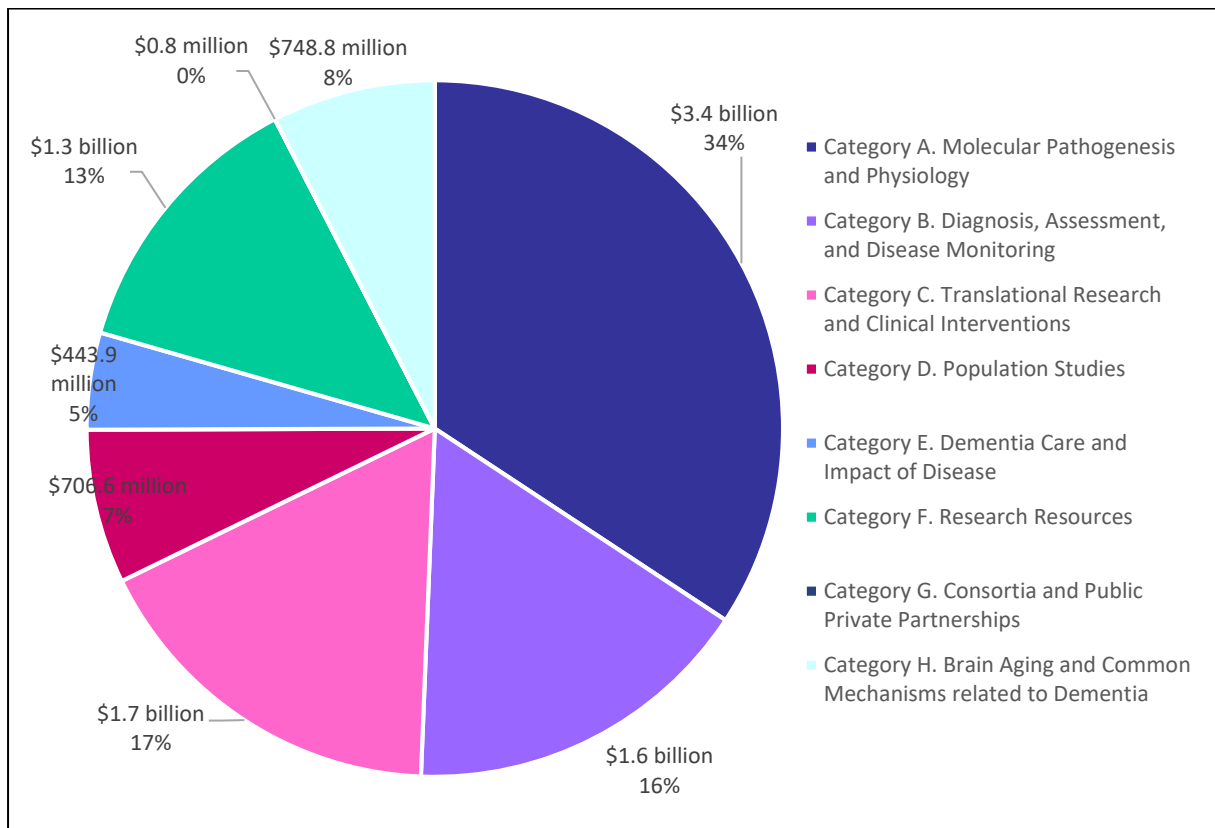


Figure 6. Proportion of population studies projects and funding by Primary Disease / Condition (ladrp.nia.nih.gov, n.d.)

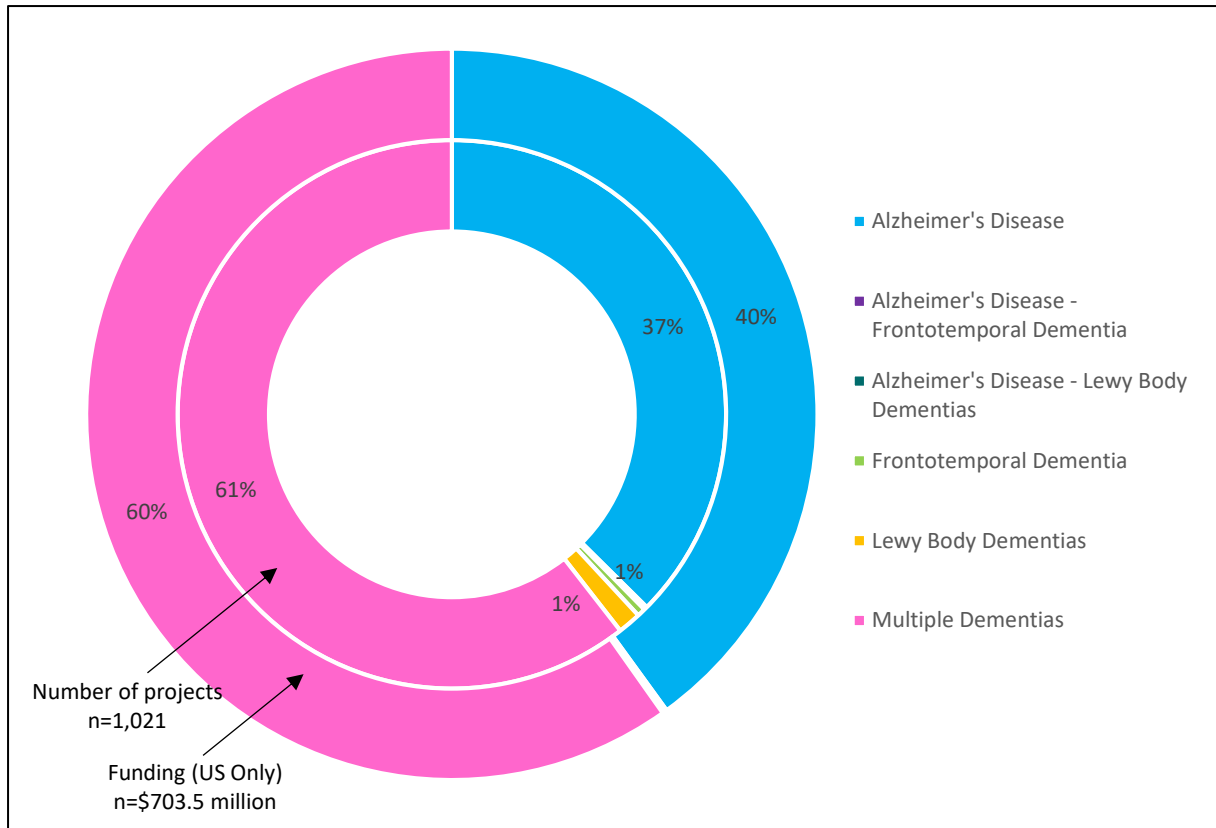


Figure 7. Proportion of 'clinical trials' and 'links/repositories' by Primary Disease / Condition (ladrp.nia.nih.gov, n.d.)

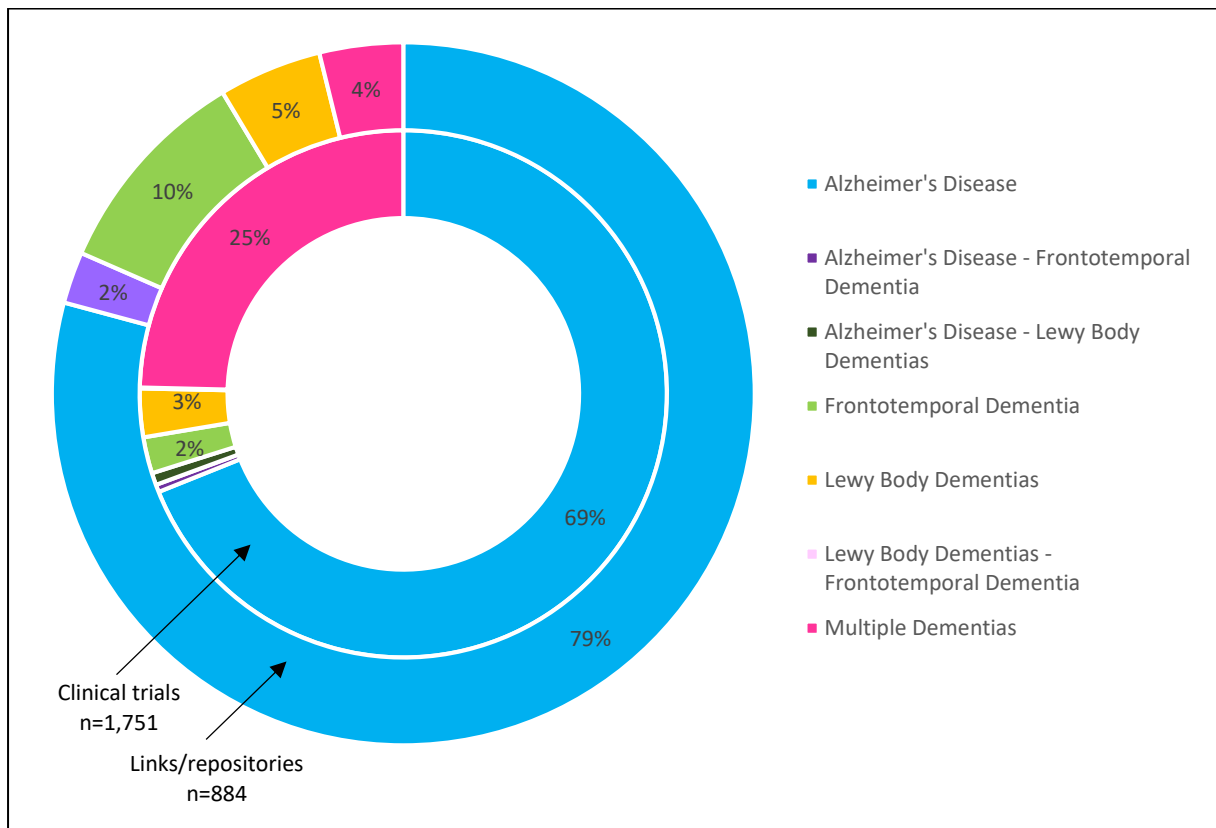
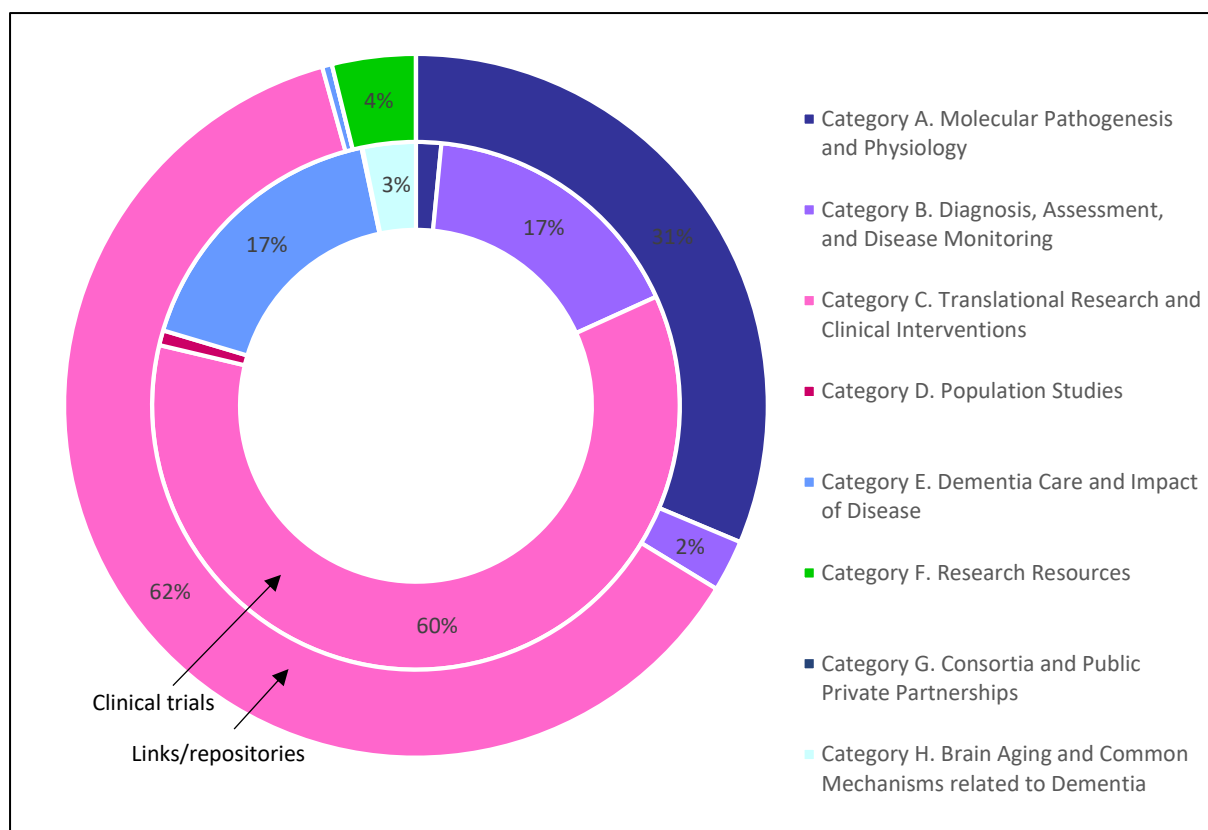


Figure 8. Proportion of ‘clinical trials’ and ‘links/repositories’ by CADRO category (Iadrp.nia.nih.gov, n.d.)



4.1.1 Research Resources

The IADRP provides links to both generic [research resources](#) (e.g. ClinicalTrials.gov) as well as resources related to the projects in the database. These are summarised into the following categories, including examples of specific resources provided (Iadrp.nia.nih.gov, n.d.):

Category	Number of resources	Example
Basic Mechanisms	12	Alzforum – Antibodies https://www.alzforum.org/antibodies Database containing information about antibodies relevant to the study of Alzheimer’s disease and related neurodegenerative diseases.
Genetic Studies	22	NIA Genetics of Alzheimer’s Disease Data Storage (NIAGADS) https://www.niagads.org Genetics repository including 64 datasets, 84,220 samples and 33.9 billion genotypes for Alzheimer’s disease and related dementias.
Diagnostic and Biomarkers	6	Alzheimer’s Disease Neuroimaging Initiative (ADNI): http://adni.loni.usc.edu Link to the ADNI study which aims to develop biomarkers as predictors of Alzheimer’s Disease.
Population Studies	10	Global Alzheimer’s Association Interactive Network (GAAIN): http://gaain.org/

		Open access, federated Alzheimer's disease data discovery platform which includes 480,914 subjects from 51 GAAIN data partners.
Translational Research	13	Agora - Discover Alzheimer's Disease Genes: https://agora.ampadportal.org/genes Publicly available online tool containing data on AD-associated genes and a list of candidate drug targets.
Clinical Research	5	Dominantly Inherited Alzheimer's Network (DIAN): https://dian.wustl.edu An international partnership undertaking research into Dominantly Inherited Alzheimer's disease (DIAD), including a long-term observational study, basic science studies and clinical trials.
Bio-repositories/Biobanks	11	NINDS Human Cell and Data Repository (NHCDR): https://nindsgenetics.org Contains cell sources including fibroblasts and/or induced pluripotent stem cells for Alzheimer's Disease, Amyotrophic Lateral Sclerosis, Ataxia-telangiectasia, Frontotemporal Lobar Degeneration, Huntington's Disease, Parkinson's Disease, and healthy controls. The NHCDR provides tools for analytics, searching and ordering for all components of the repository.
Special Research Focus: Traumatic Brain Injury-Dementia Research	11	Federal Interagency Traumatic Brain Injury Research (FITBIR): https://fitbir.nih.gov An informatic system developed to share data across the entire TBI research field.

4.2 European neurodegeneration research

4.2.1 Previous research frameworks

The EU has funded research into neurodegenerative diseases through both the 6th (FP6: 2002-2006) and 7th (FP7: 2007-2013) research frameworks. Under the FP7-Health theme, 16 projects were funded in the area of neurodegeneration with a total funding of €110 million (between 2007-2011) (See [Annex III](#) for further details) (Ilcuk.org.uk, 2011). Projects were mainly focused on Alzheimer's disease, Parkinson's disease and neurodegenerative disease in general, and covered areas such as biomarkers, underlying mechanisms of the diseases and therapies for memory loss.

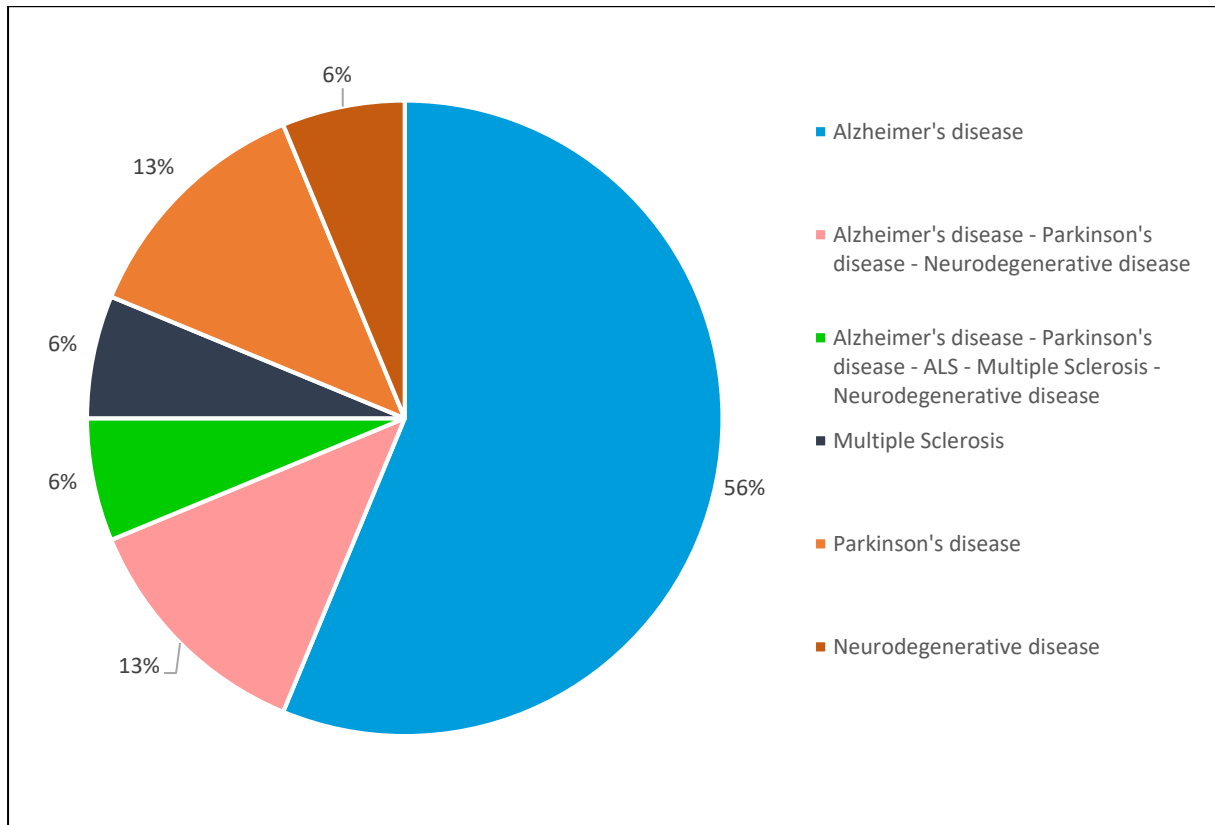
4.2.2 IMI ND portfolio

Currently, the IMI neurodegenerative disease portfolio includes 16 projects. These projects cover a number of neurodegenerative disease conditions (figure 9). Three quarters (n=12) of projects are exclusively in Alzheimer's disease or in Alzheimer's disease and another condition(s).

The total funding for projects in the Portfolio is €295.8 million which includes IMI funding of €136.4 million. 85% (€251.1 million) of the total funding for the portfolio is for projects in Alzheimer's disease or in Alzheimer's disease and another condition(s) (figure 10).

The projects in the portfolio have been classified according to the research categorisation system used by IADRP ([Annex I](#)). The 3 main categories covered by the portfolio are Category A: Molecular Pathogenesis and Physiology (37%), Category B: Diagnosis, Assessment and Disease Monitoring (38%) and Category C: Translational Research and Clinical Interventions (13%) (figure 11). The amount of funding for these categories differed slightly with Category B receiving 66% (€194.2 million) and Category A 26% (€76.8 million) of the total budget for the portfolio (figure 12).

Figure 9. IMI ND portfolio – Proportion of projects by Disease / Condition³



³ In conditions covered by the Neuronet project

Figure 10. Proportion of funding by Disease / Condition³

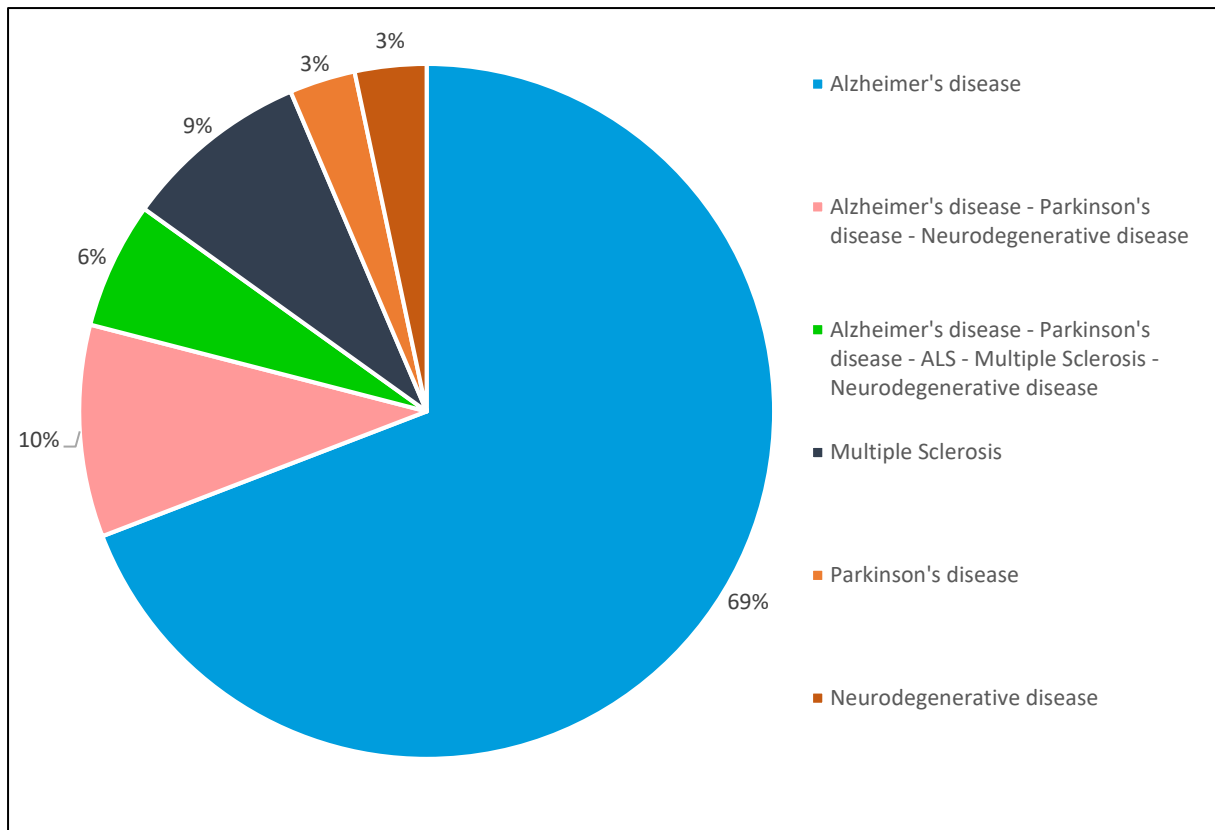


Figure 11. IMI ND portfolio - Proportion of projects by CADRO category

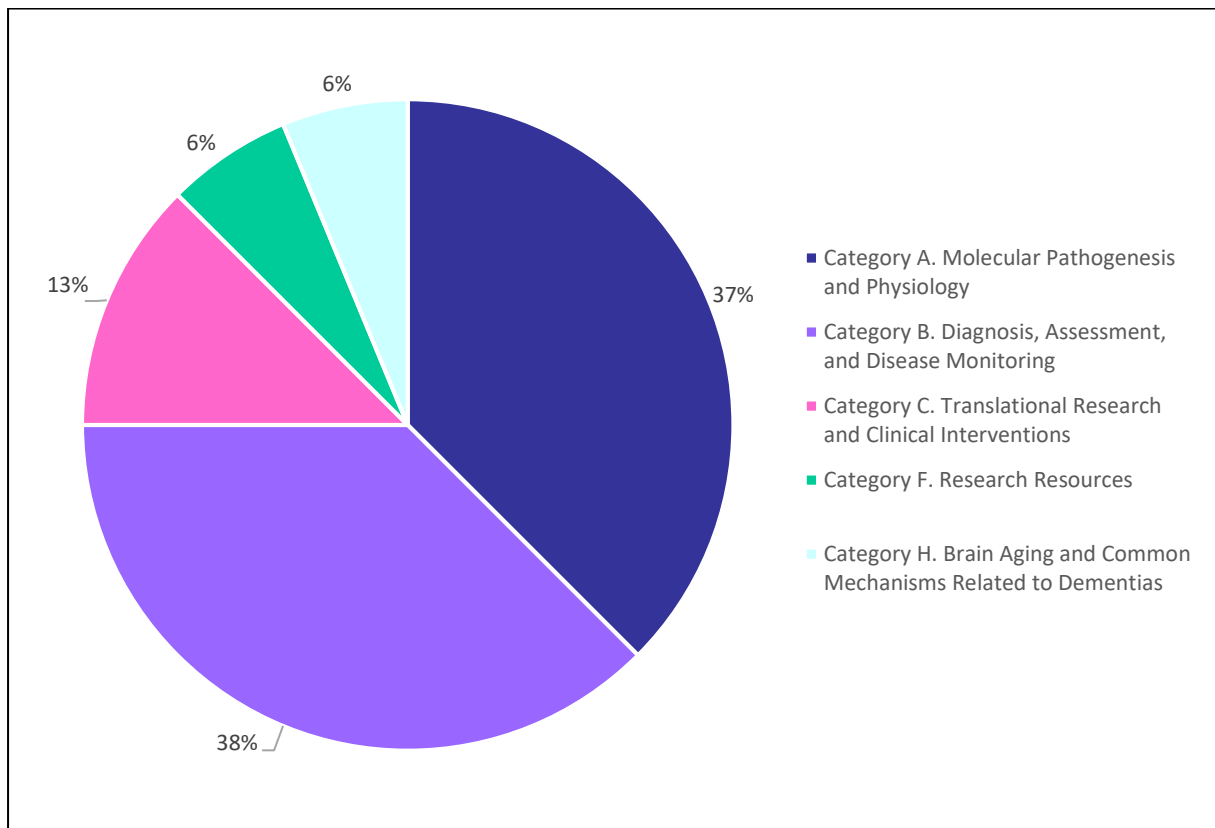
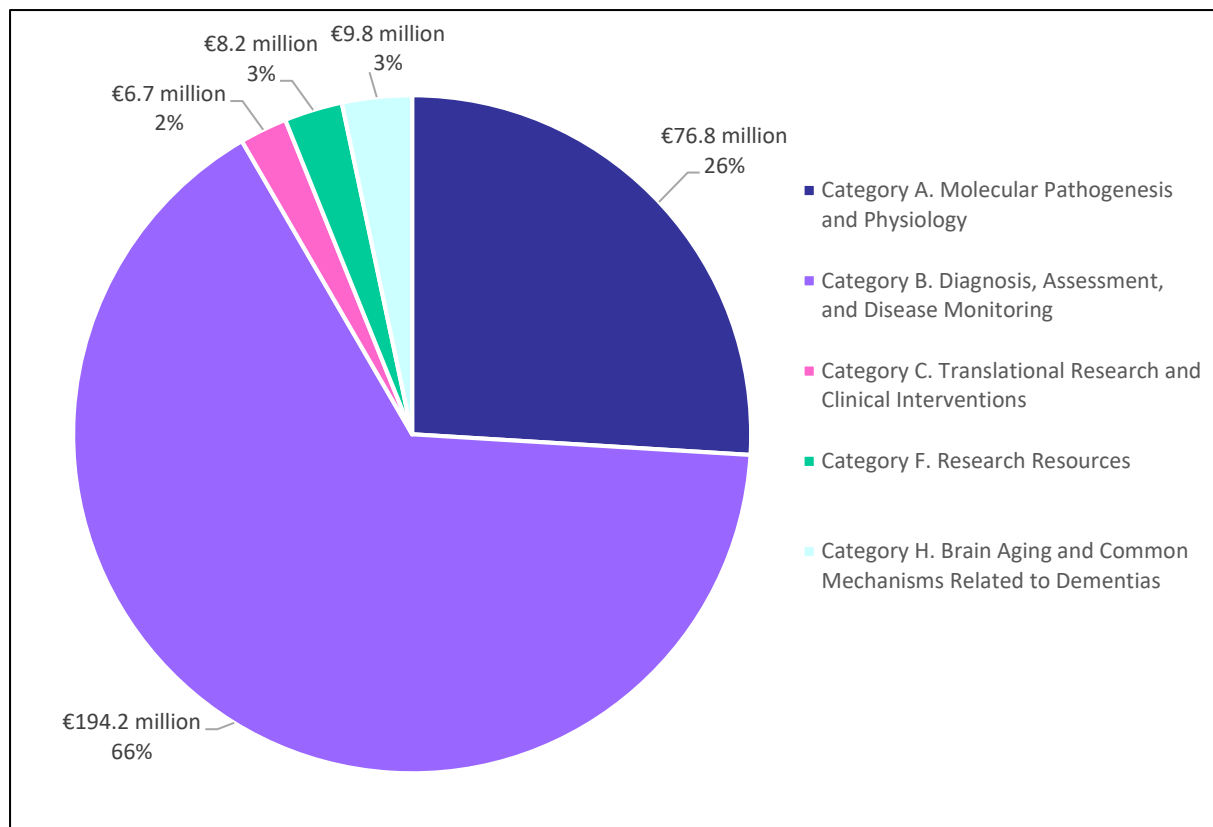


Figure 12. IMI ND portfolio - Proportion of funding by CADRO category



5 Gap Analysis

The volume of global research activity in Alzheimer's disease and Alzheimer's related dementias is considerable. Overall, the total IADRP portfolio includes over 28,000 projects with funding of \$9.9 billion (US only). These projects include small pump-priming grants, fellowships and project grants as well as a small number of public-private consortia. In contrast, the IMI neurodegeneration portfolio and its predecessor, FP7-Health, each include 16 projects with funding of €295.8 million (\$322.2 million) and €110 million (\$119.8 million) respectively.

In terms of research by disease, there are differences between the IADRP portfolio and both the IMI and FP7-Health portfolios. Across IADRP, the highest percentage of projects were in Alzheimer's disease (n=17927, 64%) followed by other forms of Alzheimer's related dementias⁴ (n=9,120, 32%). The percentage of projects exclusively in Alzheimer's disease was similar in the IMI portfolio (n=9, 56%). However, only 25% (n=4) of projects in the FP7-Health portfolio were exclusively in Alzheimer's (figure 13). Both the IMI ND portfolio and the FP7-Health portfolio cover neurodegenerative conditions, such as Parkinson's disease and multiple sclerosis, that haven't been coded individually in the IADRP database which could explain some of these differences.

⁴ Multiple Dementias, Frontotemporal Dementia, Lewy Body Dementias, Frontotemporal Dementia - Lewy Body Dementias

Figure 13. Comparison of the number of projects by disease / condition

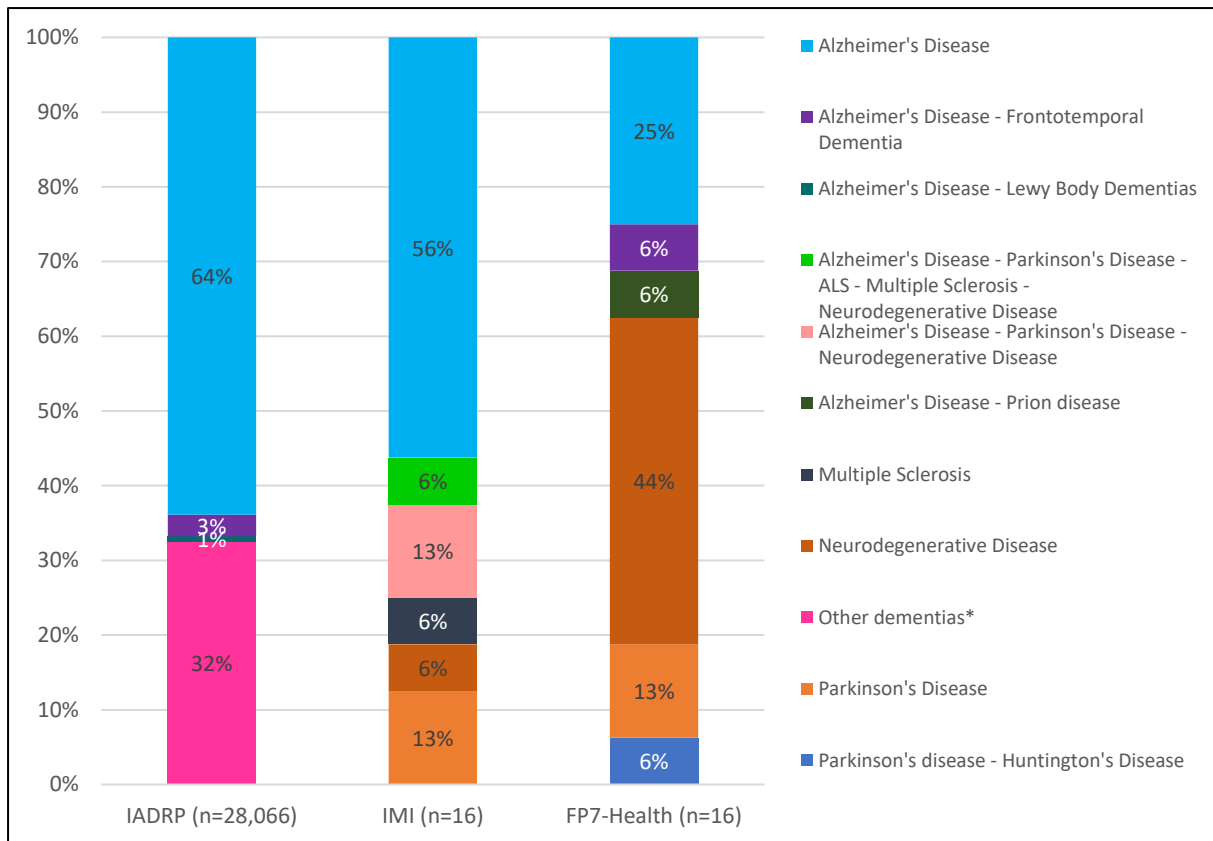
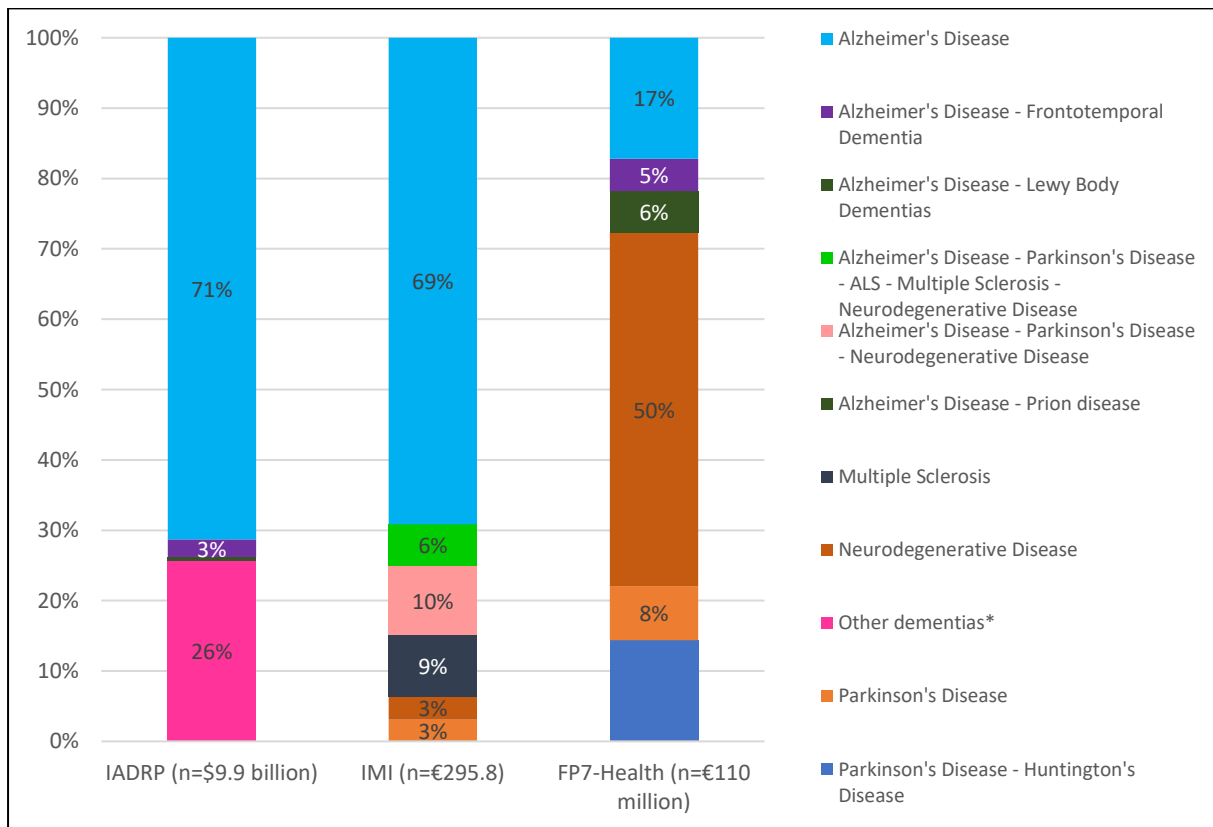


Figure 14. Comparison of the funding of projects by disease / condition



* Multiple Dementias, Frontotemporal Dementia, Lewy Body Dementias, Frontotemporal Dementia - Lewy Body Dementias

The actual levels of funding allocated by disease differ between the IADRP portfolio and the IMI and FP7-Health portfolios due to the differences in the overall levels of funding for the portfolios. Analysis of the percentages of funding that are allocated by disease shows that a similar percentage of funding has been invested in Alzheimer's disease related projects in both the IADRP (71%) and IMI portfolios (69%). In contrast, just 17% was allocated to Alzheimer's disease related projects in the FP7-Health portfolio. The majority of funding for FP7-Health neurodegeneration projects was for neurodegenerative disease, representing 50% (€55.3 million) of total funding (figure 14).

Figure 15 shows a comparison of the primary research classification of projects in the IADRP and IMI portfolios, based on the CADRO categories used by the IADRP. The IADRP portfolio covers the whole range of research categories compared to the IMI portfolio. However, this is largely due to the comparatively small number of projects in the IMI portfolio (which entirely focuses on public-private partnerships) compared to the IADRP portfolio, which includes projects ranging from single investigator, pump-priming grants from research charities to large, transnational consortium grants awarded by national funding bodies. Both the IADRP and IMI portfolios include a similar percentage of projects which focus on the Molecular Pathogenesis and Physiology of Alzheimer's disease and related dementias (Category A) – 37% and 38% respectively. However, the proportion of funding allocated to this category differs slightly between the portfolios at 34% of the IADRP total funding and 26% of the IMI portfolio total funding. Whilst the remaining projects are more evenly distributed amongst the remaining categories in the IADRP portfolio, a further 38% of projects in the IMI portfolio (representing 66% of total funding) are focused on Diagnosis, Assessment, and Disease Monitoring (Category B). (figures 15 and 16).

As part of an asset mapping exercise for the IMI portfolio, Neuronet has collected details regarding any cohort studies that are or have been undertaken by the projects. These results have been compared to the figures for the numbers of 'population studies' from the IADRP database (figure 17). The majority of population studies in the IADRP portfolio are related to multiple dementias (61%). In contrast, 88% of cohort studies in the IMI portfolio are related to Alzheimer's Disease. However, these differences are likely due to the small number of projects and studies within the IMI portfolio.

Neuronet has also collected details of clinical trials being undertaken by the projects in the IMI portfolio. A comparison of this information with the data on clinical trials related to the projects in the IADRP portfolio shows that a similar proportion of clinical trials are in Alzheimer's Disease (69% in the IADRP and 75% in the IMI portfolio) (figure 18).

Figure 15. Comparison of the number of projects by CADRO category

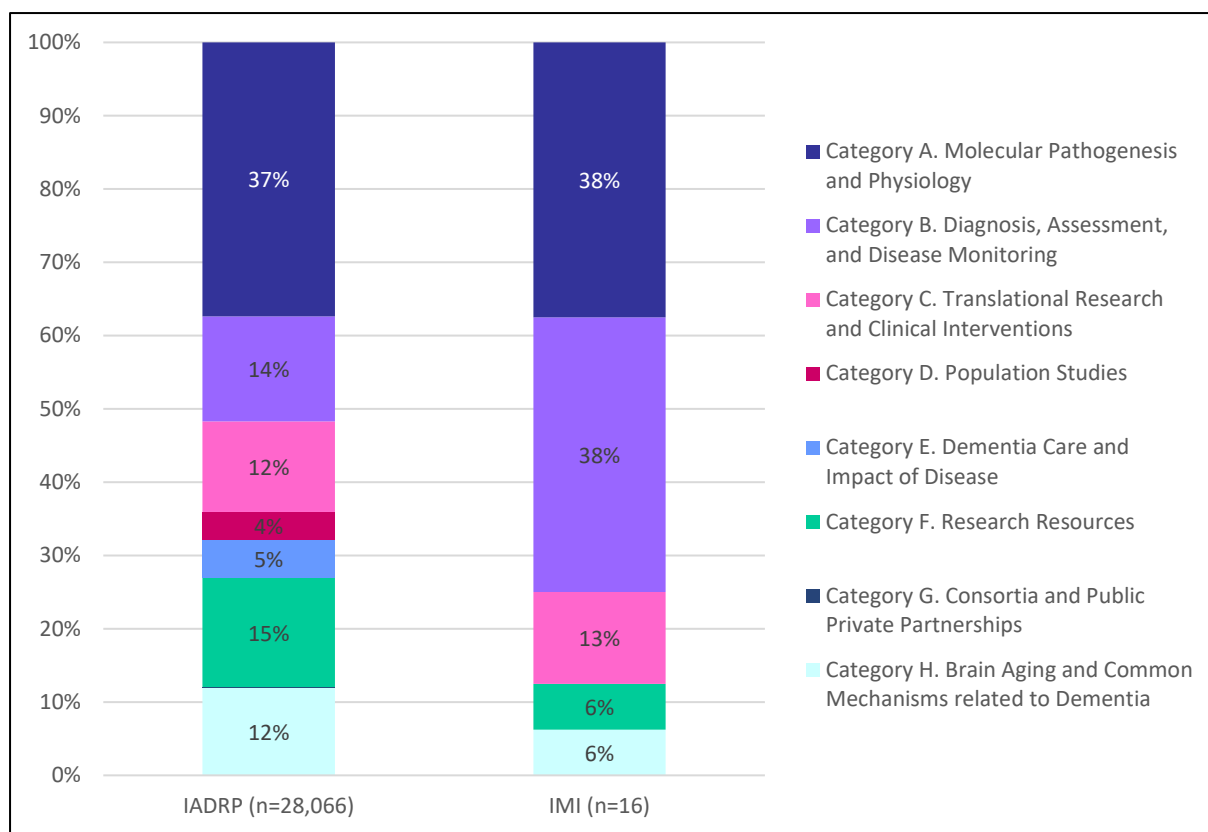


Figure 16. Comparison of the funding of projects by CADRO category

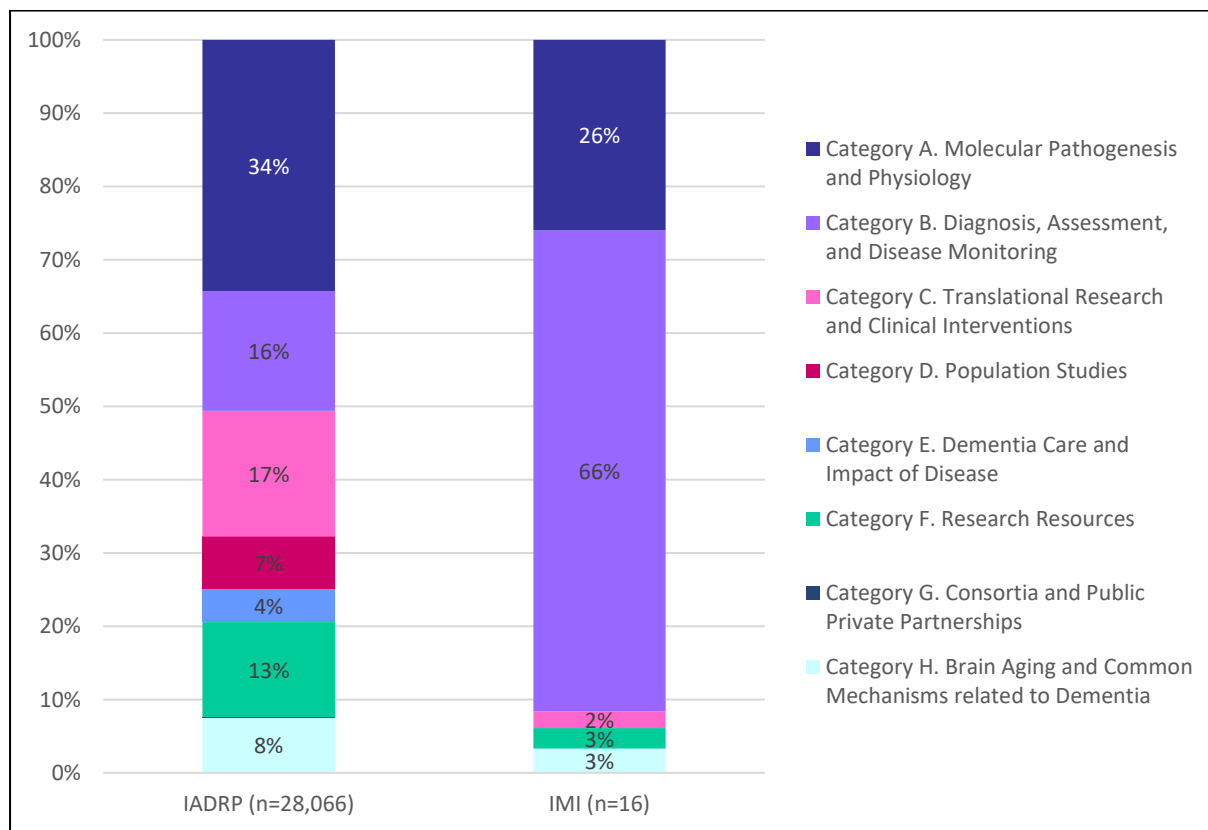


Figure 17. Comparison of 'population studies' by disease / condition

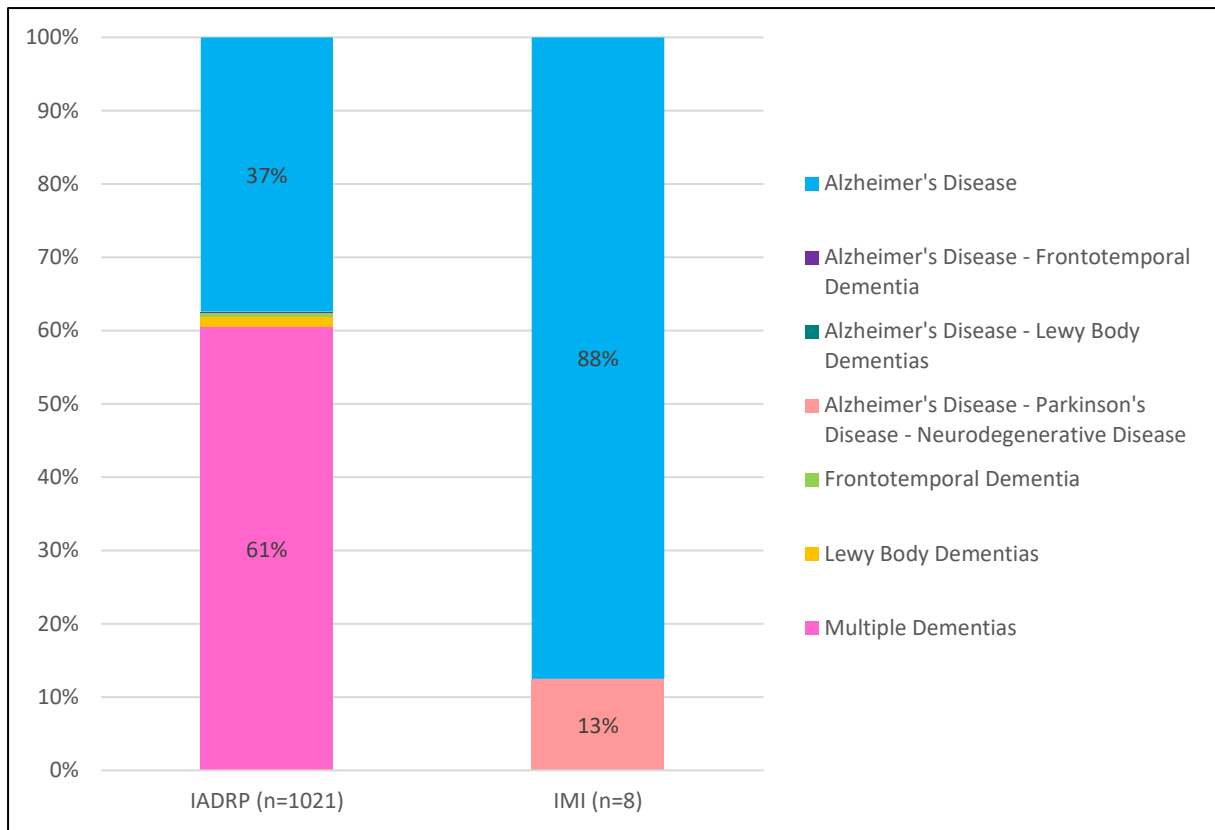
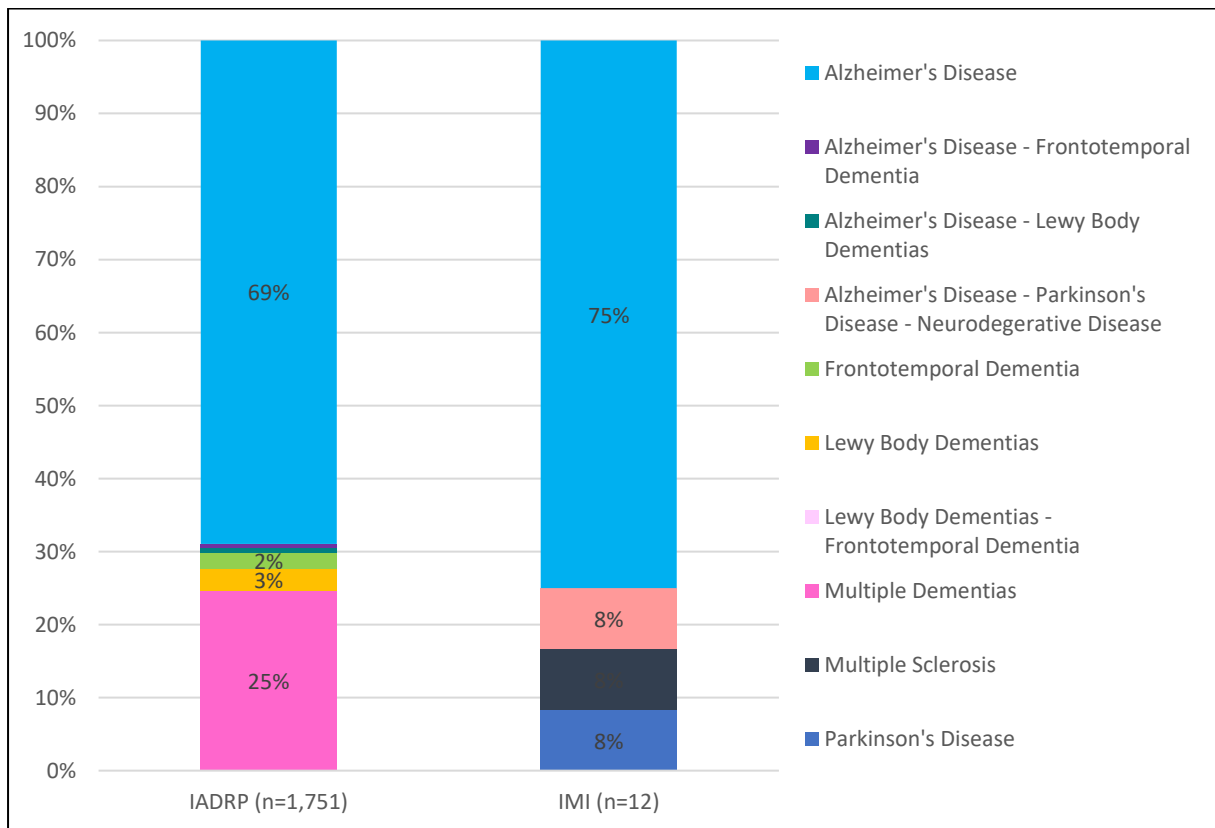


Figure 18. Comparison of 'clinical trials' by disease / condition



6 Research mapping

6.1 Research tools and mapping initiatives

We performed a pragmatic, web-based search to identify available databases of neurodegeneration research activity internationally. The results of this search are summarised in Table 1 below. The examples provided in the table present a snapshot of the available tools and initiatives for mapping global research in ND. No comprehensive research mapping initiative was identified. The databases and tools which were found all contain different levels of detail and information and with overlapping disease areas, timeframes, and different approaches to evidence sources. There was also a lack of information relating to research in particular geographies due to confidentiality or lack of transparency e.g. China.

Table 1. Summary of research tools and mapping initiatives

Tool / Initiative	Description
All disease types	
WORLD RePORT	<p>This is an interactive mapping database which highlights biomedical research investments and partnerships from 10 of the world's largest funding organisations (including the US National Institutes of Health (NIH), European Commission (EC) and UK Medical Research Council (MRC)). The database contains over 300,000 records which can be searched by keyword (e.g. disease or research area) and the results filtered by location, funding and research organisation.</p> <p>Search results are displayed on a geographical map showing the numbers of projects by country. The results can also be exported as an Excel file, including Title, Country, Start/End dates, and Funding amount and Currency. Project abstracts and collaborations (e.g. multiple organisations involved in a project) can be displayed for individual projects.</p> <p>The database is limited because it only includes projects funded by a limited number of funding organisations. Projects are also recorded by 'Research Organisation' resulting in duplication of project results where projects have more than one participant (e.g. consortia).</p>
Disease specific	
International Alzheimer's and Related Dementias	<p>The IADRP was launched in 2010 as a collaboration between the United States' National Institute on Aging and the Alzheimer's Association. It provides a searchable database of over 30,000 Alzheimer's disease and related dementias⁵ research projects (and related resources) funded by 40+</p>

⁵ Alzheimer's Disease, Frontotemporal Dementia, Lewy Body Dementias, Multiple Dementias, Vascular Dementia/Dysfunction

Tool / Initiative	Description
Research Portfolio (IADRP)	<p>public and private organisations from more than 10 countries worldwide. The database also displays data from the JPND mapping exercise (see below).</p> <p>All projects in the database have been classified using the ‘Common Alzheimer’s and Related Dementias Research Ontology’ (CADRO) research classification system to enable the comparison of projects using common terminology (see Annex I).</p> <p>The database can be filtered using keyword searches and by primary disease, research classification or other project-related categories. The results can be exported as an Excel file. The website also enables users to view ‘Related research resources and links’ (clinical trials, patents and repositories) or to create graphs and maps for different variables of interest.</p> <p>Records are self-completed by research projects therefore there is potential for differences in the way that projects are categorised e.g. primary disease or research categorisation.</p> <p>A brief assessment of the exported search results also indicated some further issues/limitations:</p> <ul style="list-style-type: none"> • The database includes some non- Alzheimer’s disease and related dementias conditions (e.g. Parkinson’s disease or Multiple sclerosis) which have been ‘coded’ as ‘Multiple Dementias’, making it difficult to search for these conditions specifically. • Projects are individually recorded by funding year rather than 1 project for the whole period of funding. • Funding amounts are recorded in the currency recorded by the projects therefore you are unable to compare funding amounts across countries. • There was some duplication of records e.g. projects included from the JPND database (see below) which were already recorded in the IADRP database.
EU Joint Programme – Neurodegenerative Disease Research (JPND)	<p>In 2011 and 2016, JPND undertook a global mapping exercise of ND⁶ research initiatives. The aim of the exercise was to understand the scale and scope of research activity in ND amongst JPND member countries (30 countries worldwide) and those funded by the European Commission.</p> <p>Information for the 2016 exercise was collected via an electronic survey. As part of the data collection exercise, all projects were assigned to 1 of 3 research classifications (see Annex II). All data were checked and validated to ensure it met the inclusion criteria and that there was no duplication of projects, studies or resources.</p>

⁶ Alzheimer’s disease, Alzheimer’s disease related dementias, Parkinson’s disease (PD) and PD-related disorders, Prion disease, Motor neurone diseases (MND), Huntington’s disease (HD), Spinocerebellar ataxia (SCA) Spinal muscular atrophy (SMA)

Tool / Initiative	Description
	<p>The results of the mapping exercises were summarised in 2 written reports. They were also included in an online searchable database containing almost 5,000 records. The database can be filtered using keyword searches and by 'Resource' (e.g. Biobanks, Capital infrastructure, Population Cohorts etc.), Disease and Country. The results can be exported as an Excel file. Individual project records can also be displayed online, including project abstracts where available. All funding amounts are recorded in Euros.</p> <p>Records are self-completed by research projects therefore there is potential for differences in the way that projects are categorised. However, the data validation process should mean that there is a certain level of consistency and accuracy in the results.</p>
Huntington Study Group	<p>The Huntington Study Group (HSG) facilitates clinical research trials and studies in Huntington disease. It provides a searchable list of all HSG trials and studies.</p>
Huntington's Disease Global Ecosystem Map (HD GEM)	<p>HD GEM is an interactive map of the Huntington's disease ecosystem. It includes details on advocacy groups, clinical trials, pharmaceutical companies and research organisations and the linkages between these.</p> <p>The Ecosystem is focused primarily on North America and therefore doesn't take into account work being undertaken by organisations in other countries.</p>
ALS Association	<p>The ALS Association provides funding to research projects across the world. The website provides an interactive world map of funded projects. There is also a keyword search function with additional filters, such as Year and Location. Project details can be viewed for all relevant projects including a summary of the project, funding amount, dates active, lead researcher etc.</p> <p>The website also included a clinical trial search function focusing on ALS and MND.</p>
Parkinson's disease map	<p>The University of Luxembourg, in collaboration with the Systems Biology Institute, Tokyo have developed an online, freely available map for Parkinson's Disease. The map provides a visual interface drawn from published research, showing all Parkinson's disease molecular mechanisms and their interactions. It also offers research functionalities, such as the ability to overlay experimental data and the identification of drug targets.</p>
Overview of Cohort Studies in Parkinson's disease	<p>This reports the findings of a study to identify observational cohort studies in clinical Parkinson's disease. The study identified 44 cohort studies in Parkinson's disease. Supplementary material is available in an Excel sheet providing details on study characteristics (e.g. location, sample size, disease stage) and assessments undertaken for each cohort.</p>
Country-based	

Tool / Initiative	Description
USA - Research Portfolio Online Reporting Tools (RePORT)	<p>The Research Portfolio Online Reporting Tools provide access to reports, data and analyses of NIH research activities, including information on NIH expenditures and the results of research.</p> <ul style="list-style-type: none"> • RePORTER: this tool enables you to search using keywords or other project related information such as project dates and research organisation. The search results can be displayed by Project (full details of projects including abstract, funding, results etc.), Publications, Patents and Clinical studies. There is also a geographical mapping function and various data visualisation tools. • NIH Awards by Location & Organization: this tool allows you to search for NIH funded projects by year, organisation and location. The data can be exported as an Excel file. • Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC): provides annual data (2015 – 2020) on NIH funding levels for 288 research/disease categories. The data can be exported as an Excel file.
UK Research and Innovation (UKRI) gateway	<p>The gateway provides a searchable database of UK publicly funded research. Projects can be searched using keywords and filtered by Project Status, Funding amount, Start date etc. The search results can be exported as an Excel file.</p>
Canadian Research Information System	<p>This system enables you to search for Canadian Institutes of Health Research grants and awards. The database can be searched by Research subject (using keyword searches), investigator, location, funding (type and years), Program and Institute/theme. The search results can be displayed as a detailed list which can be exported as an Excel file, or as high level statistics by country, region or institution.</p>
Other	
MAPPING NCD (Mapping Chronic Non-Communicable Diseases Research Activities and their Impact)	<p>This EU-funded project mapped research funding activities undertaken by public, private and voluntary organisations at a European Union (EU) and Member State level. The project covered 5 disease areas, including mental health.</p> <p>The results for the top-funded mental health projects in the five largest European Union (EU) Member States (MSs) showed that Alzheimer’s disease and schizophrenia received the majority of funding. Mental health research outputs accounted for around 6% of all biomedical research and 40% of mental health scientific publications worldwide. Of 10 mental health diseases included, Alzheimer’s disease, depression and schizophrenia papers made up 57% of the output (2002-2013).</p>
Project Ecosystem: Mapping the global	<p>A study was undertaken to map global funding of mental health (including neurodevelopmental disorders) research between 2009 and 2014, based on</p>

Tool / Initiative	Description
mental health research funding system	funding acknowledgements in journal articles. The focus of the study was on who the major mental health research funders are and what they fund. The study found that neurodegenerative and cognition disorders were 1 of the 3 clinical conditions most commonly covered by research papers.
Brain Science: Mapping the Landscape of Brain and Neuroscience Research	The report focuses on brain research between 2009 and 2013. Based on citations and articles, it describes brain and neuroscience research in terms of research output by country, impact, and collaboration, as well as examining the extent of cross-disciplinary mobility of researchers.

7 Discussion

This deliverable aimed to map and analyse global neurodegeneration research activity in order to undertake a gap analysis with the IMI neurodegeneration project portfolio. The results of the IADRP mapping exercise show that levels of global research activity in Alzheimer’s disease and Alzheimer’s disease related dementias are considerable, with almost 30,000 research projects and a total funding of almost \$10 billion. Global research in this field covered the full range of research categories, including basic research into the underlying mechanisms of Alzheimer’s disease (37%), diagnosis, assessment and disease monitoring (14%), and translational research (13%).

A comparative analysis of these results with those of the IMI project portfolio suggests that there are many similarities. In particular, the majority of both global (64%) and IMI (56%) projects were focused on Alzheimer’s disease research. However, whilst the largest proportion of global research funding is targeted at projects looking at the underlying mechanisms of the disease (34%), a larger proportion of IMI project funding is associated with research related to the development and testing of tools and methods for the diagnosis, assessment and monitoring of disease (66%). This finding demonstrates the importance of ensuring the IMI neurodegeneration portfolio has a coordinated mechanism such as Neuronet to ensure its outputs are disseminated internationally. Conversely, it will be important to ensure awareness of global activity for IMI and its projects, to avoid duplication of research efforts and to explore synergies. Given the large amount of research taking place globally, there is a huge potential for the uptake of the outputs developed by the IMI neurodegeneration portfolio in order to maximise its impact.

The global focus of research activity on Alzheimer’s Disease relative to other neurodegenerative diseases is reflective of the difference in the prevalence and global health burden of different neurodegenerative disorders. Of the neurodegenerative disorders in our analysis, Alzheimer’s Disease and other dementias have by far the highest global health burden. In 2017, the global level of all-age Disability Adjust Life Years (DALYs) was 30.5 million (95% uncertainty intervals (UIs) 28.5 to 32.6 million) for Alzheimer’s Disease and other dementias, compared to 5.6 million (95% UI 5.2 to 6.1 million) for Parkinson’s Disease, 1.1 million (95% UI 0.9 to 1.2 million) for multiple sclerosis and 0.9

million (95% UI 0.8 to 1 million) for motor neuron diseases (GBD 2017 DALYs and HALE Collaborators, 2018). Furthermore, Alzheimer's Disease and other dementias make up the highest proportion of total DALYs – 1.22% (1.14-1.3%) - compared to Parkinson's Disease (0.22% (0.2-0.24%)), multiple sclerosis (0.043% (0.038-0.048%)) and motor neuron diseases (0.035% (0.032-0.036)).

Our analysis has several limitations. The database used to map global activity has a strong US and English language focus, largely due to the sampling methodology used. It also does not provide an exhaustive picture of global neurodegenerative activity as it is mainly focused on dementia. The scope of neurodegenerative diseases covered by the IMI project portfolio is more broad. Furthermore, the research classification system used to categorise projects was developed specifically for Alzheimer's disease and related dementias and therefore may not be fully applicable to the projects in the IMI portfolio. In relation to the IMI portfolio, the relatively low number of projects currently covered means that it is difficult to make reliable comparisons with research being undertaken on a global scale. Furthermore, the scope of the IMI programme, with its focus on medicines and its public-private nature is more limited than the research in the IADRP database.

8 Conclusion

This deliverable sets out the first stage of a global mapping exercise aimed at assessing the position of the IMI neurodegenerative portfolio in relation to the global neurodegenerative research landscape. Based on a comparative analysis, the results show that there are clear areas of overlap and gaps between the global and IMI neurodegenerative research activities. Both globally and at an IMI level, neurodegenerative diseases research is primarily focused on Alzheimer's Disease, reflecting its high global health burden.

Our gap analysis suggests that gaps not currently covered by the IMI portfolio are potentially being addressed outside the IMI context. Therefore, we also provide an overview of existing mapping exercises and databases that allow IMI and researchers to easily identify international research efforts.

It is clear from the work presented in this analysis that the scope, amount of funding invested, and number of projects in the IMI neurodegeneration project portfolio is relatively limited compared to international research activity. However, as collaborative research projects involving the participation of multiple institutions across Europe, the IMI neurodegeneration project portfolio represents strategic action to tackle major public health challenges. A coordination mechanism, such as Neuronet, can therefore help optimise the impact of the IMI neurodegeneration project portfolio by increasing the awareness of global research efforts (through this deliverable), by providing support for dissemination of key assets produced by the projects and to help ensure a wide uptake internationally of the outputs of the IMI neurodegeneration project portfolio. To enable this, Neuronet will consider how it can facilitate adding the IMI neurodegeneration projects to the IADRP database so that they are part of the global picture for Alzheimer's Disease and related dementias research.

9 References

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10 Annexes

10.1 Annex I - IADRP Research Classification - Common Alzheimer's and Related Dementias Research Ontology' (CADRO)⁷

Category A. Molecular Pathogenesis and Physiology of Alzheimer's Disease and Alzheimer's Disease-related Dementias

1. Amyloid beta
2. Tau
3. Presenilin Biology
4. ApoE and Lipid Neurobiology
5. Other Proteinopathies
6. Autophagy, Endocytosis and Membrane Trafficking
7. Circuits and Synapses
8. Cell Death
9. Immunity and Inflammation
10. Metabolism and Bioenergetics
11. Vascular Etiology
12. Neuroendocrine Mechanisms
13. Molecular Mechanisms of Neuroprotection and Resilience
14. Gut-Brain Axis and Microbiome
15. Sleep and Circadian Rhythm
16. Environmental Factors
17. Genetics
18. Other Pathogenic Mechanisms

Category B. Diagnosis, Assessment, and Disease Monitoring

1. Fluid Biomarkers
2. Imaging Biomarkers
3. Traditional assessments (including cognitive, behavioral, functional reflecting changes in affective, social, decision-making, language/ speech, sensory and motor functions)
4. Personal assessments (using wearable and mobile technology including cognitive, behavioral, functional reflecting changes in affective, social, decision-making, language/ speech, sensory and motor functions)
5. Re-Purposed Biomarkers
6. Emerging Biomarkers
7. Multimodal Biomarkers
8. Novel Analyses, Methodologies and Techniques for Biomarker Discovery and Validation
9. Other

Category C. Translational Research and Clinical Interventions

1. Research Resources and Enabling Technologies to Accelerate Therapy Development
2. Identification and Validation of Novel Targets
3. Drug Discovery (small molecules and biologics), including assay development

⁷ Developed by the National Institute on Aging and the Alzheimer's Association

4. Non-clinical Drug Development (small molecules and biologics), including toxicology studies
5. Non-clinical Proof of Concept for Non-Pharmacological Interventions
6. Clinical Trial Design, including Recruitment/ Retention Strategies
7. Early-stage Clinical Drug Development (Phase I and Phase II Clinical Trials)
8. Late-stage Clinical Drug Development (Phase II/III and III Clinical Trials)
9. Non-Pharmacological Interventions
10. Clinical Therapy Development for the Neuropsychiatric Symptoms of Dementia
11. Clinical Ethics
12. Other

Category D. Population Studies

Category E. Dementia Care and Impact of Disease

1. Identifying, Assessing and Improving Care and Quality of Life for Persons with Dementia
2. Identifying, Assessing and Improving Quality of Life and Care by provided by Family or Informal Caregivers
3. Environmental Modifications and Technology Assisted Monitoring and Care
4. Health Disparities (Assess Inequality/equity (e.g., access and quality of care))
5. Socioeconomic Impact of Dementia
6. Other

Category F. Research Resources

1. Alzheimer's Disease Centers
2. Other Types of Cores or Centers (e.g., P01s, U01s, etc..)
3. Professional and Career Development
4. Repositories, Bioinformatics and Resources
5. Infrastructure (including equipment, construction, technology, etc..)
6. Disease Models
7. Other

Category G. Consortia and Public Private Partnerships

1. Consortia
2. Public Private Partnership

Category H. Brain Aging and Common Mechanisms Related to Dementias

1. Brain Aging
2. Common Mechanisms Related to Dementias

10.2 Annex II - JPND Research Classification

Basic: Aetiological and underpinning research and research relating to detection, screening, diagnosis or development of treatments and therapeutic interventions carried out in model systems or preclinical settings (i.e. not in human patients)

Clinical: Research relating to detection, screening, diagnosis, prevention or treatment of disease or promotion of patient well-being, conducted in/on (live) humans, and patient-oriented at some level.

Health and social care: Research relating to care or management of disease, provision and delivery of health and social care services (including health economics, health policy, research governance etc.), and the social or societal impact of disease.

10.3 Annex III - FP7-Health funded projects related to neurodegenerative disorders (2007 – 2011)

Project	Disease	Funding (€)
ADAMS: Genomic variations underlying common behaviour diseases and cognition trait in human populations	Alzheimer's disease	5,678,333
DOPAMINET: Molecular networks of dopaminergic neurons in chordates	Parkinson's disease	3,831,030
EURIPIDES: European research initiative to develop Imaging Probes for early In-vivo Diagnosis and Evaluation of response to therapeutic substances	Neurodegenerative disease	9,086,523
LUPAS: Luminescent polymers for in vivo imaging of amyloid signatures	Alzheimer's disease Prion	6,475,643
MEMOLOAD: Neurobiological mechanisms of memory loss in Alzheimer's disease	Alzheimer's disease	3,928,486
MEMOSAD: Memory loss in Alzheimer disease: underlying mechanisms and therapeutic targets	Alzheimer's disease	4,023,079
MEMSTICK: Synaptic mechanisms of memory loss: novel cell adhesion molecules as therapeutic targets	Neurodegenerative disease	4,138,676
MITOTARGET: Mitochondrial dysfunction in neurodegenerative diseases: towards new therapeutics	Neurodegenerative disease	10,332,037
MOLPARK: Molecular mechanisms of neuronal restoration: novel approaches for Parkinson's Disease	Parkinson's disease	4,590,740
NANOGNOSTICS: Quantum dot-based highly sensitive immunoassays for multiplexed diagnostics of Alzheimer's disease	Alzheimer's disease	5,281,158
NEUGENE: Advanced gene therapy tools for treatment of CNS-specific disorders	Neurodegenerative disease	4,026,267

NEURO.GSK3: GSK-3 in neuronal plasticity and neurodegeneration: basic mechanisms and pre-clinical assessment	Alzheimer's disease Frontotemporal dementia	5,082,027
NEUROCYPRES: Neurotransmitter cys-loop receptors: structure, function and disease	Neurodegenerative disease	14,640,209
NEUROPRO: Oligopeptidase inhibitors in brain function and dysfunction: towards new therapeutic strategies for neuroprotection	Neurodegenerative disease	6,290,178
NEUROSTEMCELL: European Consortium for Stem Cell Therapy for Neurodegenerative Diseases	Parkinson's disease Huntington's disease	15,842,632
PLASTICISE: Promotion of plasticity as a treatment for neurodegenerative conditions	Neurodegenerative disease	6,767,728