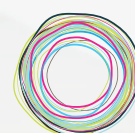


# JPND Research and Innovation Strategy



Tackling the challenge of Alzheimer's  
and other neurodegenerative diseases  
in Europe and beyond



**JPND**  
research

EU Joint Programme – Neurodegenerative Disease Research

# Acknowledgments

JPND would like to thank everyone who gave up their valuable time to contribute to the original 2012 Research Strategy and to this update in 2019. We are particularly grateful to members of the JPND Scientific Advisory Board<sup>1</sup> whose discussions and inputs shaped the strategy prior to consultation with our stakeholders, comprising funding agencies, charities and patient groups, industry and academic researchers, healthcare professionals, patients, carers and the general public.

Delivery and publication of this document was made possible through JPsustaiND<sup>2</sup>, a Horizon 2020 Coordination and Support Action funded by the European Commission.

The JPND Research and Innovation Strategy was developed by Work Package 3 of JPsustaiND, led by the Medical Research Council (MRC, UK). The MRC team consisted of Dr Catherine Moody (WP lead, MRC Programme Manager), Dr Simon Fisher (JPND Programme Manager) and Rachel Harris (JPND Science Officer). We were grateful for the administrative support at the workshops provided by Emilie Haignere (Inserm Transfert) and Ness O'Sullivan (MRC).

JPND Research and Innovation Strategy: published 2019  
UK Medical Research Council  
ISSN 2632-0223 / (ISSN 2632-0231 online version)

Cover photo credit within 'JPND domains' brain image, lower right: Photo by Ewa Jezierska of the JPND-supported project MeetingDem, showing the Meeting Centre in Wrocław, Poland.

---

1. SAB membership is shown in Annex C

2. Coordination Action in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases. Project ID 681043.  
[Link to full project details.](#)

# Contents

	Foreword from the Chair	4
	Executive Summary	5
1.	Introduction	8
2.	Current research landscape	9
3.	Scientific Priorities	10
	Theme 1: The origins and progression of neurodegenerative diseases	11
	Theme 2: Disease mechanisms and models	13
	Theme 3: Diagnosis, prognosis and disease definitions	15
	Theme 4: Developing therapies, preventive strategies and interventions	16
	Theme 5: Health and social care	18
4.	Enabling Activities	20
	Theme 1: Supportive infrastructure and platforms	21
	Theme 2: Partnership with industry and fostering innovation	22
	Theme 3: Working with regulatory organisations	24
	Theme 4: International partnership	25
	Theme 5: Capacity building	26
	Theme 6: Education and training	27
	Theme 7: Connection to policy makers	28
	Theme 8: Communication and outreach	29
5.	Delivery of the Research Strategy	30
6.	Impact	31
7.	Evaluation	32
8.	Conclusion	33
Annexes		
A.	Glossary	34
B.	Workshops and Consultations	36
C.	Governance of JPND	38
D.	Supporting Documents	39

## Foreword from the Chair

I am delighted and honoured to present the updated JPND Research and Innovation Strategy, which lays out a global collective ambition to conquer the 'grand' challenge of age-related neurodegenerative diseases and dementia.

JPND's Scientific Advisory Board has retained the format of the original strategy, first published in 2012, while rigorously examining and updating each theme to account for evolving scientific advances and emerging research priorities. JPND recognises that neurodegenerative diseases affect people in every country right across the world. Correspondingly, I am glad that there is now widespread recognition of the need for solutions to tackle the considerable suffering and distress experienced by persons living with these debilitating conditions, their relatives and carers.

JPND seeks to align and build upon national programmes to increase the impact and effectiveness of research undertaken within the participating countries and the European Commission, and to identify common goals that would benefit from transnational collaborations. JPND's membership now includes 28 European countries together with Australia and Canada. Recently, promising collaborations have been made with the United States and contacts have been initiated with Asian countries. Thanks to the enduring trust that has been built among these countries over the last ten years, research across Europe and beyond is better coordinated and the landscape less fragmented, adding value and reducing duplication. Ultimately, our goal is to improve the scientific understanding of neurodegenerative diseases, provide innovative approaches for their prevention, diagnosis and treatment, and ensure that individuals receive optimal care and quality of life at all stages of their illness, wherever they live.

Based on recommendations from our Scientific Advisory Board and input from the stakeholder consultation, this Research and Innovation Strategy is one of the three pillars of the JPND joint programming initiative, together with a shared global foresight and a light and efficient management structure. This Research and Innovation Strategy is the basis for present and future JPND actions and a key reference point for national and organisational strategic plans. It provides a common framework for future investment that addresses how countries can effectively improve prevention, diagnosis, treatment and patient care for neurodegenerative diseases.

We look forward to working together to implement our strategy over the coming years, to advance the global research effort, create opportunities for breakthroughs and ultimately transform outcomes for patients and their families.



Professor Philippe Amouyel  
Chair of JPND Management Board



# Executive Summary

## Background and Purpose of the JPND Research and Innovation Strategy

Neurodegenerative diseases (ND) are debilitating and largely untreatable conditions that are strongly linked with age. Amongst these disorders, the dementias are responsible for the greatest burden of global disease, with 50 million people worldwide living with Alzheimer's disease and related disorders. By 2050 in Europe alone, total direct and informal care costs for Alzheimer's and Parkinson's disease are estimated to surpass €350 billion per year, indicating that ND represent one of the leading medical and societal challenges of our time.

JPND is a major collaborative research initiative established to tackle the problems posed by ND and to accelerate progress in the search for solutions. JPND aims to align and build upon national programmes to increase impact and effectiveness of research and to identify common goals that would benefit from joint action. This Research and Innovation Strategy represents a framework for future implementation and investment that addresses how the global research effort can most effectively be harnessed to improve prevention, diagnosis, treatment and patient care for these debilitating conditions.

## Scientific Priorities

To achieve impact will require encouragement of novel as well as multidisciplinary approaches. There is a need to strengthen and extend existing capabilities across the full spectrum of basic, clinical, health and social care, and translational research. Research will need to take account of gender and sex-related differences and to consider their relevance across all domains. JPND has identified the following thematic priorities for future research:

### » The origins and progression of neurodegenerative disease

A major challenge is to improve knowledge about the causes and progression of ND and the factors that determine a person's risk and resilience. Efforts to identify the origins of ND should place greater emphasis

on understanding disease phenotypes within the broader scientific and life course context and gaining insights from a wider range of relevant diseases. The significance of recently discovered risk factors needs to be determined and research is required to identify new genetic, epigenetic, environmental and social modulators. A better appreciation is needed of the role of ageing in chronic disease and the relationship to ND development and resilience.

### » Disease mechanisms and models

A more complete understanding of the underlying disease mechanisms is required to underpin the development of new diagnostic and therapeutic approaches and identify appropriate time windows for intervention. Success in this area will require novel and improved existing animal and cellular models of ND, taking advantage of insights from human experimental medicine. Greater emphasis should be placed on reverse translation from ND patients to develop more predictive models and on research to determine the role of new pathways in ND pathogenesis.

### » Diagnosis, prognosis and disease definitions

Standard clinical assessments fail to capture the evolving complexity of ND, necessitating refinement and updating of current diagnostic criteria. The various forms and subtypes of ND require better definition in both 'presymptomatic' and 'symptomatic' states, given that abnormal processes underlying these disorders occur many years before the onset of clinical disease. New or improved diagnostic tools and identification of novel biomarkers are required to enable earlier, and more accurate detection or diagnosis of ND, including the ability to predict disease outcome and progression and monitor the impact of therapies and interventions. Standardisation and harmonisation across such tools and assessments will be critical to ensure the comparability of results and to support cross-centre studies.

### » Developing therapies, preventive strategies and interventions

To advance the field and transform treatment and care for people with ND requires work on a range of fronts and a willingness to embrace innovative

approaches. This may include a combination of strategies at different intervention time points, including multi-drug therapies, technological and social interventions, together with lifestyle modifications and care approaches. Further research on preventive strategies and interventions will help to lessen the risk of developing ND or help promote the capacity of the brain to resist neurodegeneration. To accelerate translation of basic findings to clinical benefit, the validity of model systems used for target identification and therapeutic development needs improvement. Longer-term approaches should be pursued, that promote regenerative strategies and develop novel systems for drug delivery and targeting to specific sites in the brain and nervous system.

#### » Health and social care

In general, there is inefficient and inequitable co-ordination between healthcare and social care systems in individual countries. Research should employ conceptually sound approaches to understand the factors that contribute to social inclusion, civic participation, dignity, health-related quality of life (QoL) and wellbeing for individuals with ND and their families. It is crucial for findings to be validated in real world settings, taking account of acceptability, cost-effectiveness and the complex ethical issues relating to ND care. A patient-centred approach to care should be adopted, with appreciation of the various factors that affect the rate of clinical progression. Assisted living technologies may help address the needs of individual patients with ND and their carers in both early and moderate disease stages, in effective, cost-effective and equitable ways. Further research should also be undertaken to inform palliative and end-of-life care.

### Enabling Activities

A number of cross-cutting activities will be needed to progress the scientific themes outlined above:

#### » Supportive infrastructure and platforms

In seeking to create an enabling environment for ND research, there is a need to encourage integration and harmonisation of data and materials, and to promote

an open-access approach to sharing and pooling of data and resources. The ability to do this is aided by recent advances in informatics and artificial intelligence (AI) and increasing recognition of the strength of effective research collaboration and partnerships. Standardised methods and tools for data collection and analysis should be adopted for example, to address the requirements of high-throughput technology platforms and biobanking, and to better connect and exploit existing cohorts, patient registers and sample/data collections.

#### » Partnership with industry and fostering innovation

Many different commercial organisations engage with ND research, ranging from the pharmaceutical, diagnostic, biotechnology, bioinformatics, imaging and digital health sectors, through to assisted living and healthcare providers. Connection between and across academic and industry domains is essential to deliver novel approaches to diagnosis, treatment and care. Innovation should be promoted within a multi-partner international funding framework by fostering a risk-taking approach, encouraging co-development of research across sectors and supporting knowledge transfer and innovation between sectors.

#### » Working with regulatory organisations

Effective translation of research into meaningful and beneficial treatments for patients requires dialogue and co-operation with key transnational and national regulatory agencies. Greater interaction with regulators should be encouraged, particularly to integrate patient needs at all stages of therapeutic development and to assist the standardisation of procedures around the control and consent of patient data. Regulatory support networks should be promoted to disseminate best practices in regulation, to define typical clinical development and address potential bottlenecks at an early stage.

#### » International partnership

It is now well recognised that the unmet clinical need and societal impact of ND is a global issue, and opportunities exist for JPND to link to worldwide research efforts in this area. Such co-operation should be strategically directed and offer clear benefit to

JPND's objectives. This includes utilising resources and infrastructure outside of Europe and better connecting global patient public involvement (PPI) and ethics activities.

#### » Capacity building

Across ND research certain areas lack capacity and need to be strengthened to ensure that future opportunities can be realised. Accordingly, networks should be established across and between disciplines and researchers to bring innovative thinking to the field. Approaches to capacity building already used within JPND countries or internationally should be shared to reveal practices that might be adapted. Areas may include encouraging a culture of open science and improving the quality and capability of AI and digital technologies for use in home monitoring, risk prediction, diagnosis and clinical trials.

#### » Education and training

There is considerable heterogeneity in awareness amongst clinicians, healthcare professionals and related stakeholder groups about the ways that people are affected by ND. An evidence-led educational approach will help to embed a research culture across the full spectrum of health, social and palliative care and help to promote public health messaging. Recommendations include education and training on the needs of ND patients with specific conditions, the value of research participation and the use of new or existing technologies or devices to promote patient independence.

#### » Connection to policy makers

JPND provides a single international framework to highlight important current and emerging issues for policy consideration at the national level. Two translational gaps in ND-related policy are to prioritise implementation of new technologies or practices towards those patients and carers who need them the most and to implement research outcomes effectively into public health policy. To enhance the progress made to date and address ongoing challenges, the commitment of national governments to supporting ND research needs to be strengthened and work is needed to better

facilitate the exchange of data, funds and resources across borders.

#### » Communication and outreach

The research agenda for ND must connect and engage with a wide range of sectors and stakeholders for effective translation into policy and practice. JPND will ensure that all stakeholder communities are well informed about ongoing ND research and its outcomes, increasing awareness and support for ND research among decision makers, patients, carer organisations and the public. This should also help to increase research participation and lower the stigma associated with ND.

### Delivery of the Research and Innovation Strategy

This Research and Innovation Strategy provides a framework of opportunities for countries participating within and beyond JPND. Member countries will use it both as the basis for co-operative action that realigns or links national investments for increased impact, and for decisions on the provision of joint funding to support new research of international scientific quality.

### Summary

JPND provides a framework to address the major societal challenge of ND, which cannot be resolved through national research programmes alone. This document updates the common vision of 30 JPND member countries, first published in 2012. It provides a strategic approach to support world class research and innovation to promote exploitation of scientific opportunities, confront barriers to progress, and define novel approaches to prevention, intervention and care. The recommendations address the full spectrum of research and associated approaches necessary to achieve impact. JPND is working alongside other stakeholder groups towards delivering this Research and Innovation Strategy. The ultimate goal is to undertake research for translation into new interventions to improve the health and wellbeing of patients with ND, their families and carers, as well as economic and societal benefit in Europe and beyond.

# I. Introduction

Neurodegenerative diseases (ND) are debilitating and largely untreatable conditions that are strongly linked with age and lead to disability and reduced quality of life (QoL). Worldwide, around 50 million people are estimated to be living with Alzheimer's disease and related disorders, the most frequent class of ND, and that number is expected to almost double every 20 years<sup>3</sup>. In addition to affecting the lives of patients, relatives and carers, by 2050 in Europe alone, total direct and informal care costs for Alzheimer's and Parkinson's disease are estimated to surpass €350 billion per year<sup>4</sup>.

JPND<sup>5</sup> is a major collaborative research initiative that aims to tackle the problems posed by ND as effectively as possible and to accelerate progress in the search for solutions. The objectives of JPND are to align and build upon national programmes to increase impact and effectiveness of research undertaken within participating countries, and to identify common goals that would benefit from joint actions between these countries and the European Commission. Ultimately, JPND seeks to improve the scientific understanding of ND, provide new approaches for their prevention, diagnosis and treatment and ensure effective provision of health and social care, so that individuals receive optimum care and optimised QoL at all stages of their illness.

The development of a Strategic Research and Innovation Agenda is central to the JPND initiative, establishing a platform for future transnational activity and serving as a reference point for developing national and organisational strategies and plans. Innovation is a core theme throughout, as a key driver of increased investment in research and development. The strategy represents a framework for future implementation and investment that addresses how the global research effort, can most effectively be harnessed to improve prevention, diagnosis, treatment and patient care for these debilitating conditions.

JPND first published its Research Strategy<sup>6</sup> in 2012 based on a comprehensive series of activities, including themed workshops, stakeholder meetings and a consultation on the key recommendations. Implementation of the strategy to date has been hugely successful, not least with the mobilization of €131 million of JPND transnational funding across 91 projects. In the intervening period, there have been numerous scientific and technological advances, as well as new infrastructure and global developments. Examples include the use of artificial intelligence (AI) technologies for medical care and research, the explosion of capability in digital health and the growth in public-private partnerships. The JPND SAB carried out an update which is integrated within this document and includes advice from focused workshops to identify the emerging opportunities and challenges in the areas of precision medicine and public health and a survey on the use of non-human primates for ND research<sup>7</sup>. To validate the report, key opinion leaders were interviewed and a comprehensive online consultation was carried out to canvas the views of stakeholder groups. Overall, the process aimed to capture a refreshed overview of the research landscape and updated recommendations for use by JPND as a roadmap for future research activity.

3. Prince M et al. Alzheimer's Disease International. World Alzheimer Report 2015. The Global Impact of Dementia. An analysis of prevalence, incidence, costs and trends. World Alzheimer's Report.

4. Maresova P et al. (2016) Alzheimer's and Parkinson's Diseases: Expected Economic Impact on Europe-A Call for a Uniform European Strategy. J Alzheimers Dis. 54(3):1123-1133.

5. 30 countries belong to JPND: the EU Joint Programme – Neurodegenerative Disease (JPND)

6. The first research strategy was also known as the Strategic Research agenda (SRA)

7. The outputs from these workshops and the survey on the use of non-human primate are available in Annex B.

## 2. Current research landscape

During 2016/17, JPND carried out a new exercise to map national and global research and infrastructure relevant to ND. This followed the methodology of the initial survey of the landscape completed in 2011, however the scope was extended to seven further countries, the level of detail on smaller investments was enhanced and JPND transnational awards were included. The end result is a more complete and up to date picture of ND research funding.

The primary aim of the research<sup>8</sup> mapping was to provide an objective view of the scale and scope of research activity in ND and provide a snap-shot of research projects, initiatives and resources in JPND member countries that were receiving funding on 1st January 2016. This information will be used by JPND in conjunction with this Research and Innovation Strategy to identify gaps and opportunities and clarify medium to long-term biological, medical, social and public health research needs, objectives and priorities.

To summarise the outputs, 2011 data (baseline) were compared with new data collected in 2016 to provide a view on any changes in the research landscape and spend on ND research before and after the publication of the 2012 JPND Strategic Research Agenda and its subsequent implementation. Key changes in the research landscape were found to be as follows:

- » Notably since 2011, an approximate two-fold increase in annual spending on clinical and health & social care research as a proportion of total funding was reported, with a small decrease in basic research spend.
- » An increase in spend on Alzheimer's disease (AD), Parkinson's disease (PD) and motor neurone diseases (MND) as a proportion of total funding was identified since 2011, while there was a significant reduction in research in the general neurodegenerative disease category.
- » Greater involvement of JPND member countries in larger research projects was observed, with 81% of countries contributing to at least one investment greater than €500k, representing a 15% increase from 2011. JPND calls were a major factor in this change.
- » The total research portfolio was calculated at €2,217 million (€566 million/year) from 2,672 projects, representing a 53% increase on overall annual investment reported in 2011 (€370 million/year). Annual spending on investments over €500k increased by 55% (€150 million/year), with a similar increase (48%, €46 million/year) observed for investments under €500k since 2011.
- » Accounting for the growth in JPND membership since the last mapping exercise, the research portfolio only from those countries (20 countries and the EC) that participated in both exercises was compared. This identified a 34% increase (€124 million/year) in annualised investment since 2011.

8. 27 of the JPND member countries and the European Commission participated in the mapping exercise



### 3. Scientific Priorities

JPND aims to accelerate progress in research into the causes, prevention and treatment of ND, the care and quality of life for patients, and to facilitate its translation into practice and policy.

The JPND Research and Innovation Strategy sets out research priorities that take account of scientific, health and social importance and tractability. To achieve impact requires novel and multidisciplinary approaches, and to strengthen and extend the existing capabilities across the full spectrum of basic, clinical and health and social care and translational research.

Research will need to take account of gender and sex-related differences and to consider their relevance across all domains, from biological understanding of disease through to pathways for care. Progress will be dependent upon the promotion of both researcher-led and more strategically driven activities. Since new scientific discoveries often emerge from unexpected sources, novel thinking and innovation will need to be encouraged and recognised to accelerate development of new and effective therapies.

Below, specific scientific themes and, within these themes, priorities for future research are identified.

#### Theme One:

The origins and progression of neurodegenerative diseases

#### Theme Two:

Disease mechanisms and models

#### Theme Three:

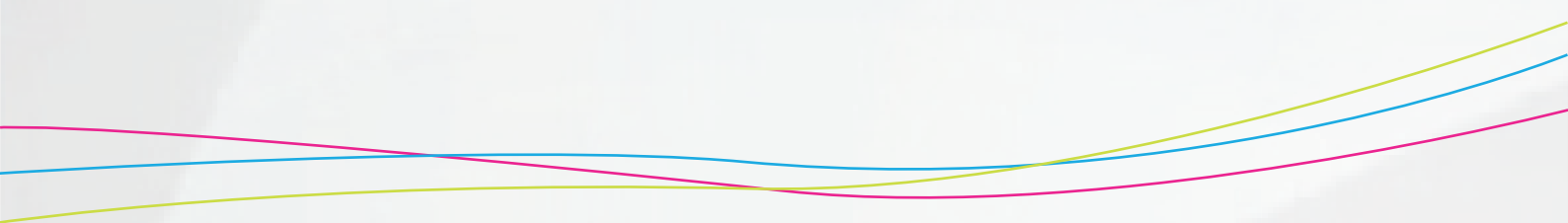
Diagnosis, prognosis and disease definitions

#### Theme Four:

Developing therapies, preventive strategies and interventions

#### Theme Five:

Health and social care



## Theme One:

### The origins and progression of neurodegenerative diseases

A major challenge is to improve knowledge of the causes and progression of ND in people, together with the factors that determine their risk and resilience. This requires studies in humans that are informed by data from experimental models (Scientific Priorities, Theme Two).

Efforts to identify the origins of ND should place a greater emphasis on understanding disease phenotypes within the broader scientific and life course context. This may include examining the pathogenesis of rarer ND to provide mechanistic insights, gathering information on a population health basis and recognising the value of research across a wider range of relevant diseases<sup>9</sup>.

A key point is the existence of multiple entry points to ND onset and progression. Similarly, many factors are likely to contribute towards enhancing our understanding of the processes underlying ND. Priorities are to:

» Understand the significance of recently discovered risk factors and uncover new genetic, epigenetic,

environmental and social risk factors for ND, including the identification of 'at-risk' populations.

More specifically there is a need to:

- Systematically identify the genetic variability underlying ND and its influence on disease onset and rate of decline, including re-interpretation of the significance of known risk factors by triangulation of the available information with more recent genetic and other data.
- Improve methods to determine the impact of risk factors throughout the life course.
- Undertake mapping of the transcriptome, proteome and epigenome of the human brain and other relevant tissues (e.g. blood), in both healthy individuals and people with ND, acknowledging tissue, region specific and temporal changes.
- Improve understanding of phenotypic variability in ND, including the role of sex and gender.
- Establish population-based and longitudinal studies of populations incorporating integrated and in-depth phenotyping that link clinical, real world and lifestyle data beyond traditional biological

9. For example, improved survival in conditions such as cancer and HIV, due to treatment advances provides an emerging opportunity to investigate ND development in the context of these pre-existing conditions.



domains (e.g. information such as co-morbidities, drug interactions and behaviour, including sleep, exercise and social engagement). To achieve this, existing cohorts should be sustained or enhanced or new cohorts created from susceptible groups, including underrepresented populations (e.g. low socio-economic and minority ethnic groups). Studies which recruit in middle-age or earlier will help identify risk factors which in turn will inform preventive strategies.

- Promote the creation of cohorts of patients with both rare and common ND. In-depth phenotyping should be standardised across studies. Sampling and data collection from these cohorts should include cerebrospinal fluid (CSF), blood, saliva, urine, fibroblasts, neuroimaging and cognitive assessment data. Increased availability of post-mortem analyses from cohorts should be achieved by linking with systems for brain donation and banking.
- » Deepen understanding of the phenotypic, biochemical and genetic determinants of different proteinopathies, which are a feature common to many ND, taking account of new and evolving technologies (e.g. gene-editing).
- » Take a more holistic, 'geroscience' approach to encompass the understanding of ageing in the context of chronic disease, and in turn the relationship to ND development and resilience. To achieve this, there is a need to:
  - Develop cohorts of successfully ageing individuals that include clinical evaluation, exposure and lifestyle, social history, neuroimaging, and sample collection for use in comparative studies.
  - Better understand the interplay between genetic and environmental factors and what contributes to resilience.
  - Promote research into the molecular mechanisms of ageing in model systems (e.g. DNA repair systems).
  - Identify ageing processes that are shared by or interact with ND, including the role of mitochondrial dysfunction and oxidative stress and other upstream processes that derail cellular function across multiple systems.
- Define the phenotype of the 'physiological' ageing process at the cellular, synaptic, system, cognitive, functional and social levels and understand how this changes across the life course.
- Identify environmental, social and behavioural modulators of ageing and ND with the ultimate aim of determining protective and resilience factors.
- » Develop research areas to obtain additional insight and understanding, including:
  - Elucidate the contribution of non-coding regulatory RNA to ND onset and progression (e.g. viruses, transposable elements and other factors affecting the transcriptome).
  - Optimise the use of data from existing population and ND-relevant cohorts and where possible repurpose or enrich these with ND specific measures.
  - Promote studies investigating presynaptic and postsynaptic dysfunction and loss in cognitive decline.
  - Expand research on ND using both post-mortem tissue from brain banks and living tissue collected during surgery.
  - Embrace novel single cell analysis techniques to understand the disease process at the level of the individual cell. Also important is to understand the interactions between neurons and other cell types (e.g. astrocytes and microglia) that may affect the onset and progression of ND.
  - Advance knowledge on the relationship between ND with vascular and metabolic systems and the role of infection and systemic inflammation in the context of early and late-life comorbidity.
  - Use of AI technologies to understand the role of mechanistic pathways and for example, to interrogate imaging, neurophysiological, biochemical mapping data.

## Theme Two:

### Disease mechanisms and models

To develop new diagnostic and therapeutic approaches, and identify the appropriate time windows for intervention, as well as establish predictive disease models, a more complete understanding of the biological basis underlying disease mechanisms and progression is needed. This will require, in parallel with further assessment of current ideas, the development and testing of new hypotheses and the creation of specific strategies to investigate novel ND pathways in animal and cellular models. Integral to success will be the improvement of these models, taking advantage of developments from human experimental medicine (e.g. multimodal imaging, combined with 'omics technologies). Models should not be expected to capture the full extent of the human conditions but may provide important insights into the mechanistic pathways underlying ND. Accordingly, priorities are to:

- » Develop novel animal models that are relevant to ND and take into account factors such as the progressive nature of ND, comorbidities, sex differences and ageing. Consideration must be given to:
  - Genetic background, generational aspects and other influences on phenotype.
  - Compensatory mechanisms and their influence on ND processes.
  - Validation of mechanisms across different model organisms ranging from worms to non-human primates (see Box 1), to consolidate results by triangulating phenotypic changes due to risk gene expression and drug effects.
  - Development of new tools (e.g. new methods for gene-editing, more sensitive metabolomic and proteomic tools) and methodologies so that models have more physiologically relevant levels of target gene expression.
  - Standardisation of testing and the development of reporter technologies that allow real-time monitoring of the progression of disease pathology.
  - Sharing technologies and increasing access to centralised data repositories of validated models, DNA sequences from genetic models and whole transcriptome expression data.

#### Box 1.

**Non-human primates (NHP):** The use of NHP models, in the view of JPND, should be considered only where there are no available and validated alternative methods to understand relevant ND mechanisms or targets, for example to understand higher brain function through multimodal analysis at the physiological or cognitive level. The following conditions or questions should be addressed:

- » The research should be methodologically rigorous and of the highest scientific quality
- » Are the potential effects of the NHP research justified by a high likelihood of scientific, medical or societal benefit?
- » Is there strong scientific justification that the research aims cannot be achieved using another species or alternative approaches (e.g. human cell models, organoids)?
- » The research should comply fully with relevant European<sup>10</sup>, national or local regulations and codes of conduct, extending to collaborative research conducted in non-JPND countries.
- » Available measures for Replacement, Reduction and Refinement (the 3R's) have been applied throughout the care and use of NHPs including the study design.
- » Measures are put in place to ensure that NHP data, models and tissues are accessible to the scientific community, including publishing null or negative data.

- Placing greater emphasis on reverse translation from ND patients to develop more predictive models and phenotypes, including identification of translational biomarkers (e.g. imaging, biochemical, behavioural and other functional biomarkers).
- Promoting the translation of research findings from model systems to specific clinical measures involving investigative medicine and human physiology approaches.

10. In the EU, research involving the use of NHPs is governed by Directive 2010/63/EU on the protection of animals used for scientific purposes, adopted through national legislation from 01/01/2013. A recent scientific opinion on 'The need for non-human primates in biomedical research, production and testing of products and devices' by the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) was updated in May 2017.

- » Establish cell-based models utilising innovative approaches to create disease-specific and patient derived cell lines that better represent the complex pathology, cytoarchitecture and interactions in ND. These may involve the use of embryonic stem cells<sup>11</sup>, induced pluripotent stem (iPS) cells, trans-differentiation technologies or 3D cell models (e.g. brain organoids). Standardised cell collections and guidelines for comparing cell lines are needed to improve reproducibility and model validity.
- » Evaluate whether computational models of ND pathogenesis could be used to test hypotheses and examine the interplay between multiple interacting mechanisms.
- » Determine the role of new pathways proposed for ND pathogenesis. For example, explore the relationship of mechanisms of protein seeding encompassing genetic, propagation and aggregation models of toxic proteins with emerging knowledge on phase transitions of intrinsically disordered proteins.
- » Investigate traits, pathways, measures and biomarkers that are either common to, or specific for, different ND, spanning molecular-, cellular-, and systems-level approaches. This should take advantage of new techniques such as sophisticated live imaging of genetically labelled single cells or relevant pathways and their behaviour within a network.
- » Examine ND mechanisms, such as physiological versus maladaptive plasticity, non-cell- autonomous mechanisms, microglial and astroglial responses and the interplay between central and peripheral inflammatory processes, in addition to the well-studied areas of protein aggregation, neuronal dysfunction and death. For example, understand mechanistically how genetic risk variants for ND onset are manifested in changes to biological pathways.
- » Identify neuronal substrates or other mechanism(s) that account for the effect of lifestyle factors on either promotion of resilience (e.g. educational enrichment or social engagement) or neurodegeneration. This should include consideration of compensatory mechanisms and the concepts of cognitive and brain reserve as well as the effect of psychological and social resilience.
- » Target emerging areas to better understand complex connections between biological systems that contribute to ND pathology. Examples include:
  - Modelling cerebrovascular pathology and blood brain barrier dysfunction.
  - Interactions between the peripheral and central immune system.
  - Disruption of normal sleep patterns.
  - Develop models to investigate the contribution of the microbiome-gut-brain axis.
  - Understanding the role of metabolic dysfunction.
- » Elucidate the biological and environmental basis of behaviour and psychological symptoms in ND via the development of cognitive test batteries in humans that can be reverse-translated to relevant animal models.



11. The regulations concerning research using human embryonic stem cells vary across JPND member countries (refer to EuroStemCell for further details), and the participation in related JPND activity will respect all relevant national frameworks. If applicable, for EU Commission funding, the regulations and ethical principles of the Horizon 2020 Framework Programme, including the statement by the Commission concerning Article 19 (L 347/114 dated from 20/12/2013) will be respected.

## Theme Three:

### Diagnosis, prognosis and disease definitions

Standard clinical assessments lack sufficient accuracy to capture the complexity of common ND, necessitating refinement of the current diagnostic criteria. Conceptually, disease development should be seen as a continuum, rather than as distinct stages. The abnormal processes underlying ND occur many years prior to the onset of symptoms and therefore the various forms and subtypes of ND need definition in both 'presymptomatic' and symptomatic states. It is expected that subclassification based on variability in disease progression may lead to the identification of distinct pathological mechanisms. Correspondingly, further work is needed in the following areas:

- » disease definition and classification.
- » discovering new or improved diagnostic techniques and methods that are validated against established diagnostic tests.
- » identification of new biomarkers that are validated against high quality, widely used biomarkers.

The above should include novel devices for early detection to be used as biomarkers or diagnostics (e.g. electrophysiological recordings, behavioural measurements) and other tests with functional read-outs. This will enable earlier and more accurate detection or diagnosis of ND, help to predict disease outcome and development and facilitate the monitoring of disease progression, with or without interventions. To delineate the best approach and to determine those people who are most likely to develop ND, it will be necessary to identify extensively characterised 'risk phenotypes' to study the wider population as well as already-known 'at-risk' groups. Further classification of disease and stratification of patient cohorts will in turn be assisted by the development of new diagnostic techniques; for example, new imaging methodologies, including their analysis with AI and machine learning approaches, as well as genomic, proteomic and metabolomic technologies and telemedicine.

In particular, effort is needed to:

- » Standardise disease definitions, diagnostic criteria, assessment tests and procedures for ND, developing and validating new versions where required.

- » Develop and validate new diagnostic criteria and procedures in a way that supports their implementation from the population level through to primary care, as well as specialised clinical settings.
- » Harmonise and standardise existing biomarkers and develop, validate and standardise new biomarkers (molecular, imaging, functional, cognitive), including markers of inflammation, astrogliosis, microglia activation and synaptic disruption across disease progression. Biomarkers for ND are needed that:
  - Enable early diagnosis and to predict progression from a presymptomatic to symptomatic phase and beyond.
  - Provide information about the presymptomatic stage at the molecular and network level.
  - Provide surrogates for progression, prognosis and treatment effects.
  - Enable insight into protective vs. causative factors, at the level of genomics and the immune system.
  - Exhibit favourable stability profiles during sample collection, processing and storage to enable the development of robust diagnostic assays.
  - Link disease mechanisms and functional endpoints, including disease-related Quality of life (QoL) thereby promoting bidirectional translation between human-and animal-based studies.



## Theme Four:

### Developing therapies, preventive strategies and interventions

Transforming treatment and care for people with ND requires work on a range of fronts, including the definition of clinically useful methods for early diagnosis and to inform prevention advice. To advance the field, researchers need to be open to developing completely novel approaches that include pharmacological and non-pharmacological (e.g. technological, social) interventions. A combination of strategies at different intervention time points is likely to be required, such as multi-drug therapies combined with changes to lifestyle or care approaches. It is important to take account of acceptability to the patient and to recognise that ways are needed to manage symptoms in order to improve the quality of life of people who live with ND. The input of scientists with an understanding of physiological psychology will enrich this area, for example to understand effects on sleep or emotions.

Preventive strategies for ND can be seen to exist at two different though complementary levels, those that reduce the possibility of developing disease (e.g. physical exercise, nutrition, vascular health) and those that enhance the capacity or reserve of the brain to resist neurodegeneration (e.g. bilingualism, psychological therapy, social engagement). Further research is necessary on both preventive strategies and interventions at the population or individual level (see Box 2).

Close collaboration with industry is obviously essential for successful translation of basic research to clinical therapies (Enabling Activities, Theme Two). Optimal development strategies and trial design should recognise that typically, models of ND reflect a single pathway rather than modelling the disease itself (Scientific Priorities, Theme Two). Validated biomarkers and surrogate endpoints are needed to help identify therapies with potential clinical benefit. Priorities are to:

- » Improve the validity of model systems used for target identification and therapeutic development to increase the likelihood of translation to clinical benefit. This can be achieved by multimodal validation of targets in terms of drug effects, biomarker response and clinical readouts.

#### Box 2.

**Prevention and Intervention:** Epidemiological evidence indicates that certain lifestyle choices can affect the onset and development of ND: for example, the strongest evidence for possible causal associations with dementia are, across the life course, those of low education, midlife hypertension, midlife obesity, smoking, social engagement, physical inactivity, frailty and diabetes. There is a gender dimension to lifestyle choices that relates to cultural values and social attitudes, which is largely an unrecognised influencing factor. A remaining challenge is the complexity and cost of confirming epidemiological data in randomized interventional trials, versus the more pragmatic approach of advocating for a 'healthy lifestyle'. For individuals with ND, the large heterogeneity underlying these diseases indicates that personalised intervention strategies, both in medicine and in care, may be needed to achieve the best outcomes across patient subgroups and at each stage of the disease. Emphasis on the following areas would best advance research progress:

- » Promote studies investigating intervention and prevention strategies based on an understanding of known or novel risk or protective factors. Specifically, studies targeting both biological and psychosocial factors are needed to identify and overcome barriers to the adoption of evidence-based health promotion strategies to encourage behaviour change at the population level and lessen the risk of developing ND.
- » Use animal models to confirm risk factors identified from epidemiological data.
- » Develop advanced computational modelling approaches to stratify individuals based on their putative risk of developing ND or potential response to an intervention or therapy.
- » Determine approaches to measure the impact of lifestyle or public health interventions across populations, in 'at risk' individuals and those already having ND. For example, studies are needed to better understand factors and interventions that could maintain or improve cognitive functioning in elderly ND patients.
- » Encourage the development of psychosocial interventions, paying attention to the promotion of social inclusion and carer involvement. These interventions should avoid negative side-effects that reduce a person's ability to retain dignity and make positive contributions to society. Improved methodologies are also required to assess such interventions.

- » Investigate the differences and similarities in the susceptibility to neurodegeneration across specific brain cell subpopulations to reveal novel targets that may promote synaptic/neuronal resilience and increase neuronal plasticity.
- » Ensure that population and disease based cohorts are used appropriately to target potential therapies to subgroups of patients most likely to respond and at the optimal stage in the disease continuum. Approaches should use tools that are culturally appropriate for the populations being studied.
- » Develop disease modifying approaches, that slow, reduce, or clear proteins such as amyloid, tau and alpha synuclein since proteinopathy is considered an important factor in the onset and progression of ND. This will require resolution of complex issues relating to delivery, dose selection and risk/benefit analysis.
- » Promote regenerative strategies to restore function, such as stem cell and gene therapeutics for disorders where specific neuronal deficits are implicated (e.g. in Parkinson's disease, Huntington's disease and motor neurone diseases). Therapies that slow ND progression may offer a better window for these regenerative strategies, particularly if introduced before significant pathology is evident.
- » Develop novel systems for delivery and targeting of drugs/biological agents to sites in the brain (including crossing the blood brain barrier) and other parts of the nervous system. These could, for example, include nanoparticles, liposomes, peptides, cells, viruses, pumps, as well as targeting based on antisense technologies.
- » Promote research to consolidate and expand methods for the clinical assessment of human disease, to cover:
  - clinical trial design;
  - new and more effective cognitive and functional assessments;
  - disease-stage specific cognitive and behavioural assessments, including the prodromal stage, and the impact of phenotypic heterogeneity on these tests;
  - endpoints that capture the complex activities of daily living;
  - novel imaging agents to measure proteinopathy, neuronal loss, synapse loss, synaptic connectivity, microglial and astrocytic activation.
- » Encourage theoretical and empirical research and education regarding the use of non-pharmacological interventions such as cognitive stimulation and rehabilitation, physical training or neuromodulation approaches. This should include research into psychological support and coping mechanisms. Research should aim to better understand underlying mechanisms of action, how to measure outcomes and any interaction with pharmacological interventions.
- » Encourage socio-economic studies that address ethical issues around how novel drugs are developed for ND; for example, how best to undertake early phase clinical studies in 'at-risk' or presymptomatic individuals. Correspondingly, the ethical and regulatory implications of treating someone at risk of developing, but not certain to develop, disease need to be carefully considered and will likely be dependent upon the risks and benefits of each individual therapy.



## Theme Five:

### Health and social care

The nature, availability and quality of health and social care for individuals with ND varies considerably within different countries; however, in general, there is inefficient and inequitable co-ordination between healthcare, social care and other systems. Accordingly, an evaluation of the strengths and weaknesses of formal and informal care approaches, technologies and infrastructures should be considered as a prelude to implementing new, evidence-based, systems. Research should employ conceptually sound approaches to understand factors within these systems that contribute to social inclusion, civic participation, dignity, health-related QoL and wellbeing for individuals with ND and their families, and consider comorbid conditions that often affect the delivery of treatment and care.

It is crucial for research findings to be validated in real world settings, taking account of acceptability and cost-effectiveness. The development of care approaches should be tailored to advances in clinical understanding of the different types or stages of disease. Across all research efforts, sufficient consideration must be given to cross-cultural issues and diversity, particularly when developing instruments and implementing intervention strategies. Priorities are to:

- » Evaluate current and potential pathways to diagnosis, treatment, symptom management, care and support relevant to ND globally, particularly by reference to effectiveness, cost-effectiveness and equity of access. In some circumstances, this may require development of key evaluative tools, for example improved outcome measures, including functional assessments and tools that measure quality-adjusted life years (QALY) and costs. Mixed-method approaches should be employed.
- » Determine the critical factors that affect disability and rehabilitation, health-related QoL and wellbeing in ND, including the effects of: comorbidity, nutrition and frailty; interaction with family carers and communities, physical and social environments; and health, social care and housing systems.
- » Investigate the interplay of physical health, biological, environmental, social, economic and other factors in the determination of cognitive decline and behavioural and psychological symptoms. This should include approaches to better recognise the needs, preferences and goals in managing symptoms in both individuals with ND and their carers. Research should involve carer-centred and carer-mediated interventions, in order to maximise health-related QoL and general wellbeing.
- » Evaluate the most effective and cost-effective ways of implementing evidence-based therapeutic strategies on a broad basis. An understanding of what factors affect the rate of clinical progression as well as scientific modelling will be important. Consideration should be given to the relationship between multiple risk factors for ND, interactions with comorbid conditions and impact on life expectancy. Research should take advantage of specialist expertise in implementation science, which provides a source of information on anticipated and real barriers and takes account of the needs and setting of the individual.



- » Focus on a person-centred approach to care research where those affected by ND are involved in the planning, development and monitoring of their own care and individual health needs, goals and resources. Careful consideration should be given to modes of communication and interaction which should include a discussion about what constitutes a meaningful outcome for the person living with ND. At the same time, the benefits and potential disadvantages of advance care planning by individuals and families affected by ND will need to be examined.
- » Promote research into end-of-life and palliative care for ND patients. This should include an assessment of the transferability of current end-of-life care and hospice care models into social care situations, the ethical issues involved, and the core criteria of effectiveness, cost-effectiveness and equity.
- » Investigate the ability of assisted living and health technologies to address the needs of individual patients with ND and their carers, in both early and moderate disease stages, in effective, cost-effective and equitable ways. For example, this might include information and communications technology (ICT) approaches, providing alerts to alleviate memory loss and improve adherence to medication, the development of new digital technologies for monitoring symptoms and to provide remote support, and the design of smart homes and the wider environment to improve QoL and prolong independent living. Options to facilitate 'living well with dementia' (e.g. environmental adaptations) are important considerations for patient and public involvement (PPI) input.
- » Examine ethical issues relating to ND care and research; for example, whether and how consent is sought and provided in relation to people with mental incapacity, assessment of how the level of disease risk is defined to allow intervention in preclinical populations, and how dignity might be preserved in patients with ND.
- » Conduct studies to determine how to improve access to formal care and to reduce the unmet needs of individuals outside the formal care system (e.g. individuals cared for at home) and their carers.

## 4. Enabling Activities

JPND's goal is to create an enabling environment to facilitate research in key areas. To progress the scientific themes outlined in Section 3 in an effective way will require a range of supporting activities, which will depend on the nature of the science, as outlined below.

### Theme One:

Supportive infrastructure and platforms

### Theme Two:

Partnership with industry and fostering innovation

### Theme Three:

Working with regulatory organisations

### Theme Four:

International partnership

### Theme Five:

Capacity building

### Theme Six:

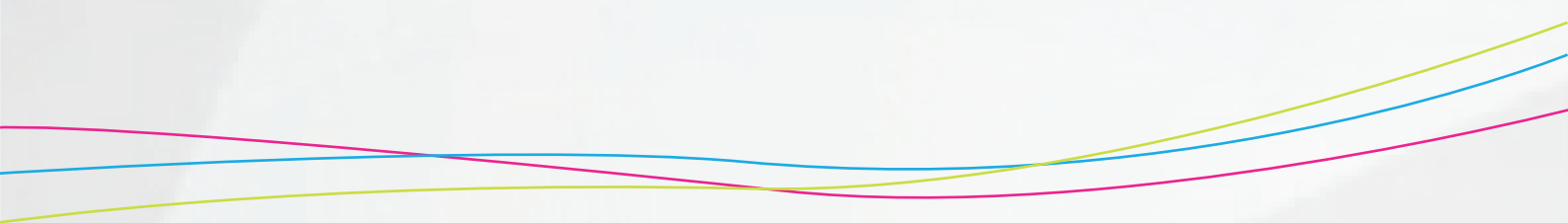
Education and training

### Theme Seven:

Connection to policy makers

### Theme Eight:

Communication and outreach



## Theme One:

### Supportive infrastructure and platforms

There are opportunities to harmonise many aspects of ND research and to develop an integrative approach across the dimensions of basic, clinical, healthcare and social science. The ability to do this is aided by recent progress in informatics and increasing recognition of the strength of effective research collaboration and partnerships.

An important advance with major potential is the advent of AI as a tool across all domains of research, from discovery science to medical diagnostics and monitoring, to care support and beyond. AI will need careful adaptation for ND research, taking account of the ethical, legal and societal implications of the technology.

JPND will seek to explore synergies with existing platforms/infrastructures, such as the 2018 European Strategy Forum on Research Infrastructures Roadmap and the Human Brain Project. Accordingly, JPND intends to:

- » Encourage integration and harmonisation of data and materials and promote an open-access approach to sharing and pooling of data and resources. Progress will benefit from the introduction of state of the art data architecture/ tagging methods, taking account of ethical, legal, privacy and data protection issues<sup>12</sup>.
- » Establish standardised methods, platforms and tools for data collection and analysis, with particular attention to neuroimaging and clinical, cognitive, functional, behavioural and perceptual/motor assessment, including measures of QoL. Certain areas, such as cognitive assessment, would benefit from the development of standardised guidelines. This is an example where advances in AI may facilitate future analysis.
- » Support the development of multimodal imaging platforms for access to complementary information from different neuroimaging technologies, to improve convergence between preclinical and clinical research data. This will help both to better define brain structure-function relationships and underlying disease mechanisms, as will the use of multi-tracer PET imaging, for example to visualise amyloid and tau in the same individual.
- » Provide coherence to the global investment in cutting-edge but high-cost areas, such as genome sequencing, proteomics, metabolomics, imaging, clinical studies and computational biology, in order to establish national or international centres or networks that can provide broad access to a critical mass of expertise.
- » Ensure wider access to high-quality biomaterials (e.g. brain tissue, CSF and cells from ND patients and age-matched controls) from brain and tissue banks operating standardised procedures and promoting ethical best-practices in sample collection, handling and curation.
- » Link and better exploit existing cohorts, patient registers and sample/data collections. This will require the development and implementation of new software and technologies to improve the capture and sharing of information, which should encourage external research groups to undertake secondary analyses of population data.
- » Establish national and global registers of people with both common and rare forms of ND. Two such examples are the Swedish national registries of motor neurone disease and Parkinson's disease.
- » Promote registers of patients with cognitive impairment, with minimum requirements for entry that reflect real-world situations. This is because most current cohorts are drawn from specialised populations and are not fully representative.

12. The General Data Protection Regulation (GDPR, Regulation 2016/679) was designed to harmonize data privacy laws across Europe and strengthen data protection for individuals within the EU. It replaces the 1995 Data Protection Directive 95/46/EC and became enforceable in May 2018.

## Theme Two:

### Partnership with industry and fostering innovation

Many different commercial organisations engage with ND research, ranging from the pharmaceutical, diagnostic, biotechnology, bioinformatics, imaging and digital health sectors to assisted living and healthcare providers, including the care home industry. Connection between and across academic, clinical and commercial domains, together with consultation of patients and carers, is essential to deliver novel approaches to diagnosis, treatment and care.

Greater awareness is required of the respective capabilities and needs of each sector, as well as legal and organisational frameworks that promote and incentivise the formation of long-term partnerships. There are also opportunities to bring innovative<sup>13</sup> and targeted products to market through partnerships with small and medium enterprises (SMEs) with specific expertise in areas where large pharma does not have in-house capability.

Effort is needed to:

- » Facilitate high-quality, intellectual property-protected, two-way collaboration between academic and industry sectors by paying greater attention to how innovative research and understanding of disease can support the needs of the global ND market. Current trends suggest that biomedical innovation is promoted by a range of factors, such as:
  - University-hospital-business collaborations;
  - Industry clusters;
  - Private equity and other financial support;
  - Entrepreneurship;
  - Confidence in data and reproducibility.
- » Promote innovation within a multi-partner international funding framework by fostering a risk-taking approach and streamlining how innovative discoveries are accessed and exploited. JPND recognises that true innovation needs to embrace a higher risk of failure.
- » Develop approaches to enhance the visibility of science opportunities emerging from academic research and to give companies access at the earliest stages to encourage co-development of innovation across sectors.
- » Foster the genuine collaborative culture with and between industry sectors and associated initiatives, which reflects the emerging trend for industry to conduct less discovery science in-house. This could include promoting the benefits of academic-industry interchange, sponsoring biotechnology partnering sessions, identifying 'innovation leads' for projects and encouraging networking between academic technology transfer and biopharma business development professionals.
- » Promote funding mechanisms for joint academic-industry research, specifically in the areas of data banking and data modelling, private-public collaboration for clinical trials and precompetitive research.
- » Continue collaborative, academic-industry partnerships for system level approaches to the study of the taxonomy of ND and for the development of new pharmaceuticals, targeting multiple components of the relevant mechanistic pathways, as opposed to focusing on individual drug targets.
- » Encourage data and resource exchange between industry, clinical centres and academia, on both science and regulatory issues, for example, by:
  - Promoting generation of collaborative platforms for data collection and retrieval. This will enable wider access to quality annotated pathology data and radiology images at scale, along with linkages to health data, experimental models and biomaterials, including post-mortem material.

13. Readers are referred to the European Commission definition for the term 'innovation': An innovation is the implementation of a new or significantly improved product (good or service), or process, a new marketing method, or a new organisational method in business practices, workplace organisation or external relations..

- Facilitating academic access to compounds and toxicity/safety data from stalled or terminated drug-development programmes, to promote drug repurposing.
  - Encouraging mechanisms to enable the adoption of common standards for legal agreements between industry and academia.
  - Sponsoring meetings between patent attorneys and business development/ technology transfer officers from industry and academia.
- » Support knowledge transfer and innovation between sectors, encouraging secondments and people exchange alongside development of shared campuses.

Regarding imaging technologies, ambient and assisted living (AAL) and information and communication technology (ICT) approaches, a number of global initiatives are already in place to promote development. However, there needs to be greater emphasis on addressing the challenge of ND and dementia in particular, as opposed to ageing in general. Economic evaluation is always essential for proposed interventions. With the advent of new digital/ICT solutions available to assist ND research, it may also help to identify novel business models that offer sustainability for SMEs. An example is to identify the potential financial savings to be made through prolonging care provision at home.

## Theme Three:

### Working with regulatory organisations

Effective translation of academic and commercial research into meaningful and beneficial treatments for patients requires dialogue and co-operation with key transnational and national regulatory agencies, as well as harmonisation across organisations. This ensures that regulation is easily understood by researchers, clinicians, drug developers and patients and is proportionate both to patient risk and current understanding of the field.

Maintaining the highest standards of ethics and governance will promote public confidence, as will the provision of up-to-date and clear guidance. For example, ethical issues relating to developing approaches to identify individuals with increased risk of ND, at a time before diagnosis when no disease modifying treatments are available.

The following actions are needed to facilitate translation:

- » Promote interactions between researchers, clinicians, industry, patients, carers, families and regulatory organisations to inform key data collection and study design requirements at the earliest stages possible, to reduce potential bottlenecks to successful translation of therapies. Specifically, interactions might include meetings between scientists and regulators to discuss key examples and prospective issues that are particularly associated with ND.
- » Promote the standardisation of procedures around the control and consent of patient data.
- » Make negative results from basic, clinical and health and social care studies available in the public domain to accelerate progress and avoid unnecessary duplication.
- » Work with regulators to integrate patient preference (including risk/benefit perspectives), goals and patient-reported outcome information into all relevant stages of research and therapeutic development.
- » Re-examine research governance and regulation in relation to the unique aspects of ND; for example, concerning studies in presymptomatic individuals, in relation to stratified subgroups, and those with mental incapacity.
- » Ensure that regulatory guidance is aligned with financial incentives and the practicalities of designing rigorous, definitive and statistically powerful clinical trials. Relevant considerations include:
  - Patenting frameworks;
  - The costs of lengthy trials to establish clinical benefit;
  - The inclusion of surrogate/proxy endpoints that may provide short-term biological proof of therapeutic benefit in the absence of long-term clinical outcome.
- » Encourage the acceptance of alternate trial designs where appropriate, for example adaptive trials that allow ongoing modification of design throughout data collection, optimising the use of resources and reducing the time to trial completion.
- » Promote the creation of support networks, public/private consortia and/or portals or hubs to disseminate best practices in regulation, to define typical clinical development pathways, and lessen the delays in commencing experimental medicine or intervention studies. This should include integration and harmonisation of data and materials and working towards a universal definition and criteria for sharing these resources.

## Theme Four:

### International partnership

It is now well recognised that the unmet clinical need and societal impact of ND is a global issue, and opportunities exist for JPND to link to worldwide research efforts in this area. Such co-operation should be strategically directed and offer clear benefit to JPND's objectives. Linkages might operate at different levels, for example, activity to:

- » Utilise resources and infrastructures outside Europe; for example, connecting with large-scale initiatives in other countries that provide access to major genetic or epidemiological samples, datasets or emerging technologies.
- » Promote alignment with groups collecting data relevant to ND research, such as the World Health Organisation's Global Dementia Observatory.
- » Study specific populations in countries where unique genetic predispositions, specific or novel environmental exposures or societal/cultural differences might contribute to the risk, disease expression or resilience in ND.
- » Widen our understanding of how socio-economic and cultural differences affect the management of health delivery and social care.
- » Promote closer global alignment of PPI and ethics activities for example, through transnational umbrella organisations such as research charities which advocate for the needs of ND patients and their families.



blue indicates countries contributing data to the JPND Research Mapping Exercises conducted in 2011 and 2016

## Theme Five:

### Capacity building

Across ND research certain areas lack capacity and need to be strengthened to ensure that future opportunities can be realised. Approaches to capacity building already used within JPND countries or internationally should be shared, with a view to identifying strategies that might be adapted to the specific needs identified below. Accordingly, JPND needs to:

- » Encourage better networking across and between disciplines and researchers, both within individual countries and globally including low- and middle-income countries. There should be promotion of existing effective capacity building models and consideration of novel approaches to incentivise and reward fruitful collaboration.
- » Improve the training of clinical researchers, and translational specialists and ensure that their role is recognised and sustained. In parallel, encourage basic scientists to gain exposure to the clinical/ translational approach (and vice versa) and to integrate this understanding throughout their research.
- » Promote a culture of open science, data sharing and dissemination between global initiatives and teams developing resources for ND research, and build connections to increase awareness and transfer of knowledge. This should include streamlining contractual and legal issues relating to data access and learning from other fields.
- » Recognise the changing face of science communication. Adoption of open access publishing has increased the pre-publication of data pending peer review. Additionally, there is now the facility to use AI to search literature and databases at speed.
- » Increase the numbers of neurodegeneration researchers, especially those with expertise in health economics, public health surveillance, computational biology, bioinformatics, electrophysiology and disease model development. In the biomedical field, opportunities should be sought to attract those with a background in conjoint disciplines, such as neurophysiology, developmental neurobiology, immunology and metabolism.
- » Support interdisciplinary research within existing frameworks and build new alliances across science and other research areas (e.g. physics, engineering, materials science, digital technologies, computer science, ND patient-friendly architecture) to introduce novel approaches and interventions for ND. International research forums should be promoted to share data, encourage innovative thinking and interdisciplinarity.
- » Promote capability and improve the quality of AI, digital technologies and devices (e.g. home monitoring, wearables, wireless sensors) for use in patient monitoring, risk prediction, diagnosis, clinical trials and treatment in large populations. This will ensure that these technologies are taken beyond the 'proof of concept' stage, to optimise and standardise their use in biomedical, clinical and social research applications.



## Theme Six:

### Education and training

There is considerable heterogeneity in awareness amongst clinicians, other healthcare professionals and related stakeholder groups, including ethics committee members, about the ways that people are affected by ND. An evidence-led educational approach will help to embed a research culture across the full spectrum of health and social care, including palliative care. It will also help to promote public health messaging and reduce the stigma and misunderstanding that surround these conditions.

A good understanding of ND and awareness of the available evidence-based care will ensure that patients are treated in the most effective and acceptable way. Mainstream clinical education for the appropriate professions (nurses, physiotherapists, doctors, social workers, etc.) should include access to specialist training in ND to cover disease management across the full range of relevant disciplines, including ethics and sociology.

Specific recommendations for education and training in relation to ND are to:

- » Expand the clinical education and training of health and social care professionals who interact with ND patients, considering the specific needs that are characteristic of these conditions and the available evidence-based options for treatment.
- » Promote appreciation amongst health and social care professionals of the benefits of research participation in order to improve recruitment to longitudinal and clinical studies and to increase donation of human tissue for research.
- » Undertake research to improve and implement effective health education to promote broader awareness of ND across all generations and sectors of society which includes carers, families, the wider public and those working in service industries.
- » Understand more clearly how to create changes in behaviour in the population (at the early- and mid-life stages) through strategies aimed at mitigating risk factors associated with an unhealthy lifestyle, in order to lessen the chance of developing ND.
- » Within education and training, promote recognition frameworks for researchers who share methods and data in a 'team science' environment. Operating through large collaborative multi-disciplinary projects, team science is the best approach to tackle the most challenging aspects of the field.
- » Provide education for families and carers on new or existing technologies or devices (e.g. mobile apps, wearable location tracking devices) that can promote greater freedom and independence of ND patients, at the same time addressing safeguarding concerns.

## Theme Seven:

### Connection to policy makers

JPND provides a single international framework through which to highlight important current and emerging issues for policy consideration at the national level. One of the key aims of JPND is to promote compatibility between the policy approaches of different countries. Effective policies should be evidence- and analysis-based, and it is critical that consultations with people living with ND and their carers are built into the process of policy formulation.

Historical, political, regional and cultural considerations have resulted in different policy approaches across countries. For example, healthcare provision may be organised privately or be government-provided or both. In the years since JPND was created, a number of countries have implemented national ND-related strategies, leading to a significant improvement in the alignment and efficiency of ND research. However, more commitment from policy makers is needed to extend this progress and meet some of the most pressing research needs in the field. New and existing policy frameworks need to be considered to enable research to be conducted across the full range of healthcare structures, for example, research in primary care, general hospitals, care homes and specialised centres.

For instance, one area in which there continues to be a clear need to undertake research is in the assessment of the effectiveness of different health and social care models and approaches. Indeed, reducing the segmentation of the care sector and evaluating alternative strategies for long-term care could improve service, cost-effectiveness and efficiency.

In this context, there are two key translational gaps in ND-related policy where national policy makers can take action to improve the impact of research, and the QoL, for patients, carers and their families. First, better links with technology developers are needed to ensure that the benefits of new technologies and practices are being extended to the patients and carers who most need them. Examples include developments in the areas of telemedicine, assisted living and delivery of services. Second, there is a need for national policy frameworks to ensure that research outcomes – for example, evidence

indicating the best pathway of care for a specific stage of a particular ND – ultimately will lead to effective implementation in public health policy.

The attention of policy makers should also be drawn to the special considerations that arise from issues of consent and data disclosure in the context of diminished mental capacity in ND. The following activities will be needed to enhance the progress made to date and help address ongoing challenges:

- » Strengthen the commitment of national governments to support ND research.
- » Expand the adoption of national plans for ND (general or specific).
- » Increase national earmarked budgets for transnational research.
- » Better facilitate resources, funds and data exchange across borders.
- » Adopt and harmonise evidence-based policies and best practices at the national level.
- » Promote effective communication between researchers and policy makers.
- » Increase awareness and understanding of the societal impact of ND.

## Theme Eight:

### Communication and outreach

The research strategy for ND must connect and engage with a wide range of sectors and stakeholders for effective translation into policy and practice. It is crucial that individuals living with ND and their carers are well-informed about ongoing ND research and its outcomes. Involvement of patients, their relatives and carers should be considered in the planning and conduct of clinical, health and social care research to ensure the inclusion of relevant study endpoints and QoL perspectives. In this context, JPND has established a Stakeholder Advisory Board for PPI, and has adopted mechanisms to provide rapid feedback and advice from the broad PPI stakeholder community during JPND calls and other actions.

The promotion of effective communication between patients, carers, and health and social care practitioners (alongside Education and Training; Theme Six) is known to increase the number of people joining registers. Research participation remains an urgent need, since clinical trials around the world are currently seeking tens of thousands of volunteers. Public understanding around ND can be promoted by adopting unambiguous language such as ‘brain health’ within public health messaging. Additionally, wider knowledge and awareness can help to reduce the stigma that society may attach to neurodegenerative conditions.

The JPND website serves as a focal point for communication and dissemination to a wide range of sectors across different digital content types (fact sheets, videos, blogs etc). The website provides a searchable database of ND research capability and new tools to build research capacity (e.g. the first Global Database of Cohorts for ND). Regular news-feeds and social media (e.g. Twitter) updates reach a large number of stakeholders who have expressed an interest in the initiative, and this will continue throughout JPND’s life-span.

To promote communication and outreach with a wide range of stakeholders, JPND continues to:

- » Disseminate ND research outcomes to all stakeholder communities in an effective, balanced and consistent manner to assist successful translation into policy and practice. A range of methods should be used as appropriate (e.g. webinars and communication of expert views to the press through science media centres).
- » Consult the JPND PPI Stakeholder Advisory Board regarding JPND initiatives and research outcomes.
- » Increase awareness and support for ND research amongst decision makers in participating countries.
- » Encourage JPND-funded researchers to engage in dissemination and outreach activities as appropriate, thereby increasing awareness and support for ND research among patients, patient organisations and the public.
- » Promote the development of innovative tools to facilitate communication between individuals with ND, their families and carers, healthcare professionals, and care service providers, to increase social inclusion and reduce the stigma associated with ND.
- » Continue to support dialogue with stakeholder communities on a national and international level.

## 5. Delivery of the Research Strategy

### Timeframe and Framework for Delivery

The Research and Innovation Strategy establishes a framework of opportunities for countries involved in JPND and which are willing to participate in joint actions. Starting from recommendations made within the strategy, working groups and taskforces will establish short-, medium- and long-term priorities and specify what actions, instruments and resources are required for implementation. JPND will seek to implement its strategy in the most effective manner, whether through co-operative activities that realign or link national investments to achieve increased impact, or through the provision of new funding. This may involve either the use/adaptation of existing instruments and initiatives or the launch of new activities, such as data sharing to increase interdisciplinary or cross-sector research.

A guiding principle for delivering the objectives identified within the strategy will be that research investment is provided in a competitive environment that supports research of the highest scientific quality. In this way, public funding will be used efficiently to ensure the best outcomes for patients, carers and families affected by ND.

### Stakeholder Engagement

A key indicator of the success of JPND will be direct communication and engagement with all stakeholders, including patient organisations, industry representatives and policy makers. Supporting key stakeholders with appropriate information at relevant times will maximise both the support for JPND and the involvement of participating member countries in the collaboration. As an integral part of JPND, a broad, multi-national stakeholder community will be created to encourage stakeholder engagement and address unmet needs. Stakeholder engagement will enable co-operation, interaction, communication, dissemination, knowledge transfer, networking, and consultation on plans and initiatives.

JPND has identified its stakeholder groups as key influencers (politicians, decision makers); scientific researchers (public and commercial); research funding organisations; health policy makers; patient interest groups; regulators; healthcare professionals; the media; and the public.

## 6. Impact

Over the coming decade JPND aims to achieve the following:

- » The development of new therapeutic approaches and interventions for ND, including preventive strategies for at-risk individuals, which could also lead to new business and commercial opportunities.
- » Research elements relevant to ND to be embedded more routinely in health service and care infrastructures.
- » The delivery of evidence-based policy relevant to ND with efficient uptake of research outputs.
- » A positive influence on treatment, care and QoL for patients with ND and their carers.
- » Raise the profile to de-stigmatise ND.
- » Increased visibility at the political level of the burden of ND and the benefits of research.
- » Catalysis for the development of national and organisational strategic plans in JPND countries.
- » Increased annual funding invested by JPND member countries based on the transnational JPND Research and Innovation Strategy.
- » Increased investment in global R&D for ND, across academic and commercial sectors.
- » Increased capacity in ND research, through linkage both to conjoint disciplines and to other international activities.
- » Recognition of the importance of integration and harmonisation of data and materials.
- » Adoption of an open access approach to sharing data and resources and towards publication.

## 7. Evaluation

To assess the JPND initiative regarding its direct outputs, early effects and long-term impacts, a monitoring and evaluation framework was constructed in 2012 and recalibrated in 2016 including a set of key performance indicators.

Indicators are categorised according to the information they provide for the monitoring and evaluation process: input, output, outcome and impact. Two types of indicators were identified following JPND's workplan and defined as:

1. Type A indicators related to the process of joint programming
2. Type B indicators associated with the scientific and societal orientation of JPND research on ND.

The framework was built in close consultation and collaboration with JPND stakeholders and has aligned JPND's objectives (on both scientific and policy levels) with the scientific priorities and enabling activities presented in the Research and Innovation Strategy. The set of key performance indicators will be updated for every monitoring cycle.

Monitoring and evaluation of the initiative will occur at different, but interrelated, levels with the approach focussing on the initiative's process and progress on its aims, such as delivery of the scientific objectives and interaction between the scientific community and wider society.

## 8. Conclusion

Launched a decade ago, JPND was the very first 'joint programming' initiative, dedicated to ND set up by the European Commission under the auspices of the member countries to tackle the 'grand' challenges Europe has to face during this century. Investment in ND research and infrastructure has increased significantly in Europe, resulting in international recognition that can largely be attributed to the foresight and global initiatives of JPND since its inception. At the same time, JPND membership has expanded and efforts continue to engage countries and extend international reach. It is estimated that by 2030, 75 million people worldwide will be living with Alzheimer's disease and related disorders, the most frequent class of ND, indicating the magnitude of the problem. The framework established by JPND places the scientific community in a stronger position to advance research and accelerate discovery.

Only by mobilising large numbers of researchers to work in the field and providing substantial governmental support for research, will solutions be found rapidly. Made possible by trust and fair exchanges, research across Europe and beyond is now better coordinated and the landscape less fragmented, adding value and reducing duplication. This Research and Innovation Strategy sets out JPND's collective and holistic ambition to identify effective means to prevent, treat or slow the progression of ND. Over the next 5-10 years, this strategy will guide future transnational research, foster innovative breakthroughs, and lessen the societal and economic impact of ND. JPND's goal is to transform the lives of patients, families and carers - and to do this as soon as possible.

# Annexes

## A. Glossary

**Ambient and assisted living (AAL):** Use of intelligent products and provision of remote services to allow people to live in their preferred environment by increasing their autonomy and assisting them, their carers and families in carrying out activities of daily living.

**Animal models:** Living animals that reproduce all or some aspects of a condition or part of a disease pathway and which are used during investigation into human disease. They are used both to test understanding of disease pathways and to provide the tools for developing therapeutics.

**Artificial intelligence (AI):** The theory and development of computer systems able to perform tasks normally requiring human intelligence.

**Astrocyte:** A star-shaped support cell of the central nervous system.

**Biomarker(s):** Short for biological marker: A characteristic that is measured or evaluated as an indicator of a biological (or cognitive) state, e.g. to evaluate the presence or progression of disease or a response to treatment.

**Blood brain barrier:** A semipermeable membrane separating the blood from the cerebrospinal fluid, and constituting a barrier to the passage of cells, particles, and large molecules.

**Cerebrospinal fluid (CSF):** A colourless liquid that surrounds the brain and the spinal cord and provides a mechanical barrier against shock, immunological protection and regulates cerebral blood flow.

**Clinical trial:** A scientifically controlled study that is carried out in consenting human beings to evaluate the safety and effectiveness of a therapy.

**Comorbidity:** The presence of one or more disorders in addition to (in this case) neurodegenerative disease.

**Disability:** Following the World Health Organisation model, disability is an umbrella term for impairments, activity limitations and participation restrictions. It denotes the negative aspects of the interaction

between an individual (with a health condition) and that individual's contextual factors (environmental and personal).

**Epidemiological:** The study of the incidence, distribution, and control of diseases and other health problems.

**Epigenetics:** The study of changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself.

**Gene-editing:** The deliberate alteration of a selected DNA sequence in a living cell. CRISPR-Cas9 is a widely used gene-editing method.

**Geroscience:** The science of aging and age-related disease

**Liposomes:** A spherical sac of phospholipid molecules enclosing a water droplet, especially as formed artificially to carry drugs or other substances into the tissues.

**Machine-learning:** A field of artificial intelligence that uses statistical techniques to give computer systems the ability to progressively improve performance on a specific task from data, without being explicitly programmed.

**Mechanistic pathway:** The components involved in a physiological process, their relationship and interactions with each other.

**Metabolomics:** The scientific study of chemical processes involving metabolites, the small molecule intermediates and products of metabolism.

**Microbiome:** This comprises all of the genetic material within the entire collection of microorganisms in a specific niche, e.g. the human gut.

**Microglia:** A support cell in the central nervous system that functions primarily as an immune cell.

**Nanoparticles:** Particles between 1 and 100 nanometres in size with a surrounding interfacial layer.

**Neurodegenerative disease (ND):** an umbrella term for a range of conditions primarily involving neurodegeneration, which is the progressive loss of

structure or function of neurones, including death of neurones. ND included in the JPND initiative are Alzheimer's disease and other dementias (AD), Parkinson's disease (PD) and PD-related disorders, prion disease, motor neurone diseases (MND), Huntington's disease (HD), spinocerebellar ataxia (SCA) and spinal muscular atrophy (SMA).

**Neuromodulation:** the alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents.

**Neuron:** A specialist cell found in the nervous system responsible for transmitting information by electrical and chemical signalling.

**Non-coding regulatory RNA:** An RNA molecule that is not translated into a protein.

**Non-pharmacological interventions:** Prevention strategies and treatments that do not involve the use of chemical agents; for example, physical or behavioural therapy or initiatives that promote meaningful activity or social interaction.

**Organoids:** Small, self-organized three-dimensional tissue cultures that are commonly derived from stem cells. Organoids can be used to study aspects of that organ, in this case the brain, in a tissue culture dish.

**Patient and public involvement (PPI):** An active partnership between patients and/or members of the public and researchers. PPI is distinct from participation in research.

**PET imaging:** Positron-emission tomography is a functional imaging technique used to observe metabolic processes in the body.

**Pharmacological intervention:** Prevention strategies and treatments that involve the use of chemical agents e.g. medication.

**Phenotype:** The set of observable characteristics of an individual resulting from the interaction of its genotype with the environment.

**Precision medicine:** The targeting of specific elements responsible for pathology in a given individual at a particular point in time. The term incorporates the use of tools for stratification of patients based on risk of disease, or response to treatment using diagnostic tests or techniques.

**Proteinopathy:** Any disease (especially a neurodegenerative disease) caused by a malformed protein.

**Proteomics:** The study of the proteome which is the entire set of proteins that is, or can be, expressed by a genome, cell, tissue, or organism at a certain time.

**Quality of life (QoL):** An individual's total wellbeing including all emotional, social and physical aspects.

**Reverse translation:** The use of human/clinical data to inform and refine laboratory or animal-based research.

**Stem cells:** Stem cells are biological cells that can differentiate into other types of cells and can divide to produce more of the same type of stem cells. This includes embryonic stem cells and induced pluripotent stem (iPS) cells.

**Stratification:** The process of dividing patients into more specific classes or groups with the idea that their response to treatment will be more uniform (and so easier to assess).

**Telemedicine:** The remote diagnosis and treatment of patients by means of telecommunications technology.

**Transcriptome:** The set of all RNA molecules in one cell or a population of cells. It is sometimes used to refer to all RNAs, or only messenger (mRNA).

**Translation:** The continuum of the process from scientific discovery through to its application;

**Transposable element:** A DNA sequence that can change its position within a genome, sometimes creating or reversing mutations and altering the cell's genetic identity and genome size.

## B. Workshops and Consultations

### B.1 Precision Medicine

Precision medicine<sup>14</sup> is an emerging approach that encompasses disease prevention, diagnosis and treatment that takes into account individual variability in genes, biological/molecular characteristics together with environmental and lifestyle factors.

Key recommendations from the JPND workshop on Precision Medicine for ND included:

- » Standardise data collection and storage protocols using appropriate quality control to permit pooling of data to enhance reproducibility.
- » Establish common standards for data sharing and provide guidelines for data access and management to promote cross initiative data exchange.
- » Promote data sharing by simplifying data access procedures with an emphasis on building in interoperability from the beginning to promote the integration and harmonisation of data.
- » Integrate digital technologies (e.g. wearable sensors, mobile apps) and move towards optimising these for medical and clinical application.
- » Promote the use of real world data and encourage the adoption of common standards, defining its quality and content indexing to improve discoverability.
- » Develop a precision medicine approach for health and social care research including a person-centred approach to care and elements relating to PPI.
- » Expand the number of trained data competent scientists including developing expertise in data modelling in neurodegeneration research.

The full workshop report can be found at [www.neurodegenerationresearch.eu/wp-content/uploads/2018/09/JPND-Precision-Medicine-Workshop-Final-Report.pdf](http://www.neurodegenerationresearch.eu/wp-content/uploads/2018/09/JPND-Precision-Medicine-Workshop-Final-Report.pdf)

### B.2 Public Health

The emphasis in public health<sup>15</sup> is on interventions for health protection, health promotion and healthcare. These are all activities concerning the rational use of limited resources for the best possible health and wellbeing through the entire life course. Progress in achieving population health is dependent on translation into actions, interventions or behaviours at the individual level or change through policy and legislation at the population and societal level.

Key recommendations from the JPND workshop on Public Health in ND included:

- » Promote research on newly identified risk factors while in parallel improving the approaches used to determine the impact of these factors throughout the life course.
- » Optimise and improve the utilisation of data from current cohorts and where possible repurpose or enrich existing cohorts with ND-specific, and social measures.
- » Encourage greater diversity within longitudinal studies of populations including hard to reach and underrepresented populations.
- » Adopt a broader perspective to ND research by gaining insight from overlapping pathologies, operating across traditional scientific boundaries embracing the wider concepts of health and society.
- » Promote equality of access to care, prevention and education when formulating public health strategies.

14. Precision medicine relates to the targeting of specific elements responsible for pathology in a given individual at a particular point in time. The term incorporates the use of tools for stratification of patients based on risk of disease, or response to treatment, using diagnostic tests or techniques. Precision, 'personalised' and stratified medicine are overlapping terms that are part of the same continuum. The EU has adopted the term 'personalised medicine'.

15. Public health refers to organised measures to harness the best evidence on prevention, treatment and management of health conditions to optimise population health. It includes the integration of primary, secondary and tertiary prevention for policy, service and societal outcomes.

- » Improve consistency and confidence in public health communication including research to understand the attitudes to ND risk and how society prioritises dementia.
- » Ensure greater emphasis on PPI within research to understand the key priorities and outcomes for patients and carers including decision-making relating to end of life care and other ethically sensitive topics.

The full workshop report can be found at [www.neurodegenerationresearch.eu/wp-content/uploads/2018/09/JPND-Public-Health-Workshop-Final-Report.pdf](http://www.neurodegenerationresearch.eu/wp-content/uploads/2018/09/JPND-Public-Health-Workshop-Final-Report.pdf)

### B.3 Consultation on the use of NHPs in ND Research

To contribute to the update of the JPND Research and Innovation Strategy, a small-scale consultation of academic researchers and industry representatives from 16 countries was conducted on the use of non-human primates (NHPs) in ND research. The objective of the consultation was to understand the applicability of NHPs to ND research.

Findings were as follows:

- » Respondents identified that NHP-ND research takes place in Europe, North America and Asia, with most studies focused on Alzheimer's disease and Parkinson's disease. Pharmaceutical industry use was reported to be mainly in advanced preclinical testing to evaluate drug safety, however, some companies adopted strategies that were less dependent on NHPs.
- » Participants gave a range of scientific justifications for the use of NHPs in ND research, including improved translation to humans, their suitability for studying the complexity and higher cognitive functions affected in ND and the ability of NHPs to overcome technical limitations of smaller animal models.
- » Respondents largely took the view that NHP-ND research could be justified ethically where studies were methodically rigorous, focused on important medical questions and where no alternatives were available. However, 14% of respondents held the view that there was no justification for NHP-ND research.
- » Limitations of using NHPs in research, were reported to include small sample sizes, high costs, ethical concerns and the inability of NHPs to model all aspects of human disease, although in general these issues were not specific to ND research.
- » Regarding reduction or replacement of the use of NHPs for ND research, there was no consensus. For the future, 23% of respondents anticipated that experimental advances with complex organoids or the use of sophisticated computer models of disease potentially could reduce or replace the use of NHPs.
- » Areas recommended for greater worldwide cooperation were the development of shared international standards for the use of NHPs and the advancement and adoption of alternatives. NHP users had several practical suggestions, which included the development of specialised research centres and sharing of tissues, models and data between researchers to optimise the use of NHP resources.
- » Regulatory or legal issues were not considered to constrain necessary and important research involving NHPs, although researchers perceived some countries as having stricter regulations than others.

## C. Governance of JPND

The management structure of the JPND initiative comprises a Management Board (MB), an Executive Board (EB), Steering Committee(s), a Scientific Advisory Board and a Secretariat.

### » Management Board

The MB is the decision-making body of JPND. Established in June 2009, it works within the terms of reference adopted by all participating countries. It is composed of a (non-voting) Chair and Vice Chair and a maximum of two representatives of each JPND member country.

### » Executive Board

The EB supports MB in all aspects concerning the preparation and implementation of decisions. Its membership comprises the Chair and Vice-Chair of the MB plus three other MB members.

### » Steering Committee

JPND has a Steering Committee to advise EB. Separate ad-hoc Steering Committees are set up when JPND is in receipt of a major EC award such as JPcofuND or JPsustaiND.

### » Secretariat

The Secretariat organises the day-to-day management of JPND and implements those tasks assigned to it by the MB and EB. The Secretariat and specific Work Packages tasked to develop, implement, communicate and evaluate the Research and Innovation Strategy and JPND have been funded through a Coordination Action from the EC, known by the acronym JPsustaiND. In addition, JPco-fuND, a five-year initiative (2014-2019) supports co-funded calls and other JPND activities. The EC has recently awarded JPco-fuND2 (2019-2024, Project ID: 825664) a further ERA-NET award.

### » Scientific Advisory Board

The SAB is an independent advisory body consisting of 14 internationally recognised experts (Box 3), spanning the domains of basic, clinical and social and health services research. Its primary role is to offer advice to MB regarding the SRA and other scientific issues.

#### Box 3.

##### Scientific Advisory Board

Professor Thomas Gasser  
Chair, University of Tübingen

Professor Martin Rossor,  
Vice-Chair, University College London

Professor Stefano Cappa  
Institute for Advanced Studies, Pavia

Professor Jesus de Pedro Cuesta  
Epidemiología Instituto de Salud Carlos III, Madrid

Professor Bruno Dubois  
Hopital Pitié Salpêtrière, Paris

Dr Brian Fiske  
Michael J. Fox Foundation for Parkinson's Research

Professor John Hardy  
University College London

Dr Eric Karran,  
Neuroscience Center at AbbVie

Professor Martin Knapp  
London School of Economics and Political Science

Dr Thomas Rooney  
Sanofi

Professor Charles Scerri  
University of Malta, Alzheimer Europe

Professor Philip Scheltens  
VU University Medical Center, Amsterdam

Professor Myrra Vernooij-Dassen  
UMC St Radboud, Nijmegen

Professor Bengt Winblad  
Karolinska Institutet, Stockholm

## D. Supporting Documents

### Workshop Reports

Precision Medicine Workshop

<http://www.neurodegenerationresearch.eu/wp-content/uploads/2018/09/JPND-Precision-Medicine-Workshop-Final-Report.pdf>

Public Health Workshop

<http://www.neurodegenerationresearch.eu/wp-content/uploads/2018/09/JPND-Public-Health-Workshop-Final-Report.pdf>

### Consultation Reports

Consultation of the use of NHPs in ND research

[www.neurodegenerationresearch.eu/initiatives/the-2018-jpnd-research-and-innovation-strategy/workshops/consultation-on-non-human-primates/](http://www.neurodegenerationresearch.eu/initiatives/the-2018-jpnd-research-and-innovation-strategy/workshops/consultation-on-non-human-primates/)

Public Consultation

<http://www.neurodegenerationresearch.eu/initiatives/the-2018-jpnd-research-and-innovation-strategy/stakeholder-consultations/>

### Mapping Exercise

Mapping Exercise Report 2016

[www.neurodegenerationresearch.eu/initiatives/mapping-exercise/2016-report/](http://www.neurodegenerationresearch.eu/initiatives/mapping-exercise/2016-report/)

Research Database

[www.neurodegenerationresearch.eu/search-our-database/](http://www.neurodegenerationresearch.eu/search-our-database/)

