JPND Research and Innovation Strategy Stakeholder Consultation Responses 2018

The 2019 Research and Innovation Strategy provides a roadmap for future investment in research to improve prevention, diagnosis, treatment and patient care for neurodegenerative diseases.

It builds on and updates the framework set out in the original Research Strategy that was released in 2012 to ensure that it continues to have impact in the research community and among policymakers. The new edition will be published following consultations with JPND's stakeholder communities.

The JPND Scientific Advisory Board, has identified common research goals that would benefit from joint action between countries to accelerate progress on solutions that can alleviate the symptoms, and lessen the social and economic impact of neurodegenerative disease (ND) for patients, families and health care systems.

The aim of this online public consultation was to gather views and opinions relating to an update to these priorities, since the release of JPND's original Research Strategy in 2012.

The Stakeholder Consultation was open from the 17th September 2018 until the 8th October 2018. All comments were read and analysed. All respondents in this document consented to their responses being published anonymously and as part of overall trends.

Overall trends:

- A good level of engagement, with a wide range of issues highlighted
- For each theme of the SRIA, at least 80% of respondents agreed with the stated priorities and activities
- Each response was carefully considered afresh and adjustments to the strategy document were made where the point was new or needed emphasis
- Majority of topics raised by stakeholders were already included
- Most comments arose from the Stakeholder consultation priorities which are shortened versions of the priorities listed in the strategy document. Therefore, many of the comments made by respondents were addressed in the longer strategy document
- For each theme respondents were asked 'Which priorities do you consider to be less important?'. Most respondents listed the letter(s) of the priority identified as least important so these have been collated into graphs. Full responses can be found in the appendix

To note

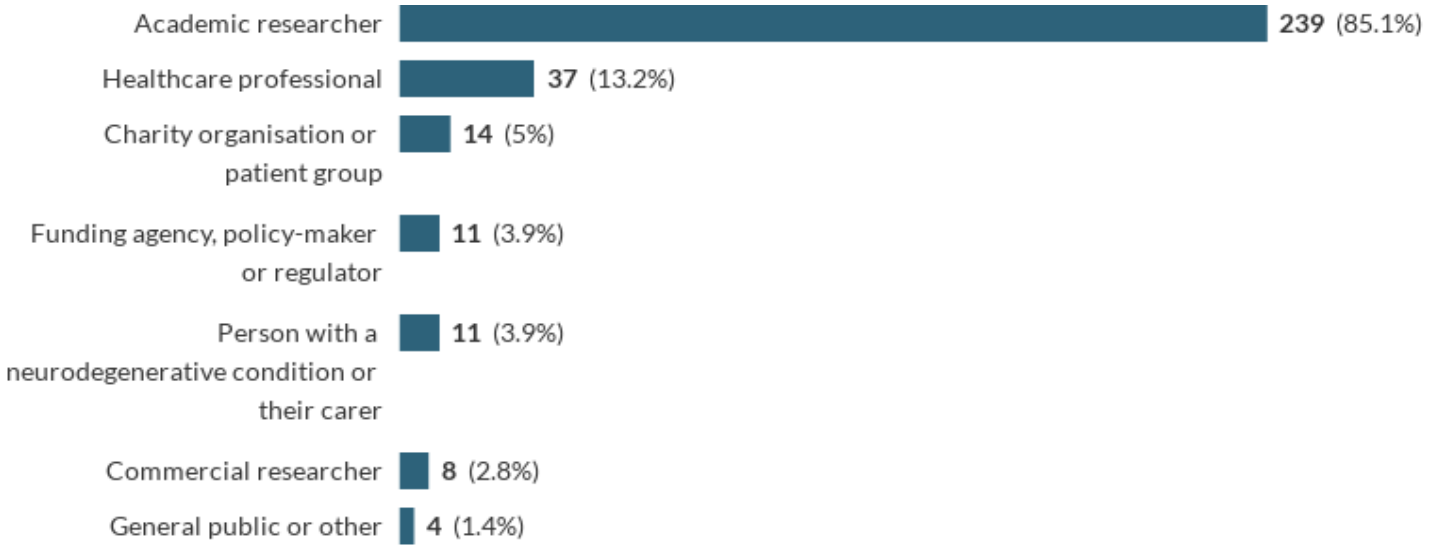
- The comments in this document are unedited responses to the JPND Stakeholder Consultation 2018 and do not represent the views of JPND
- The priorities and actions within each theme below have been shortened for the purpose of this consultation. The full abridged version was made available to all respondents

Contents

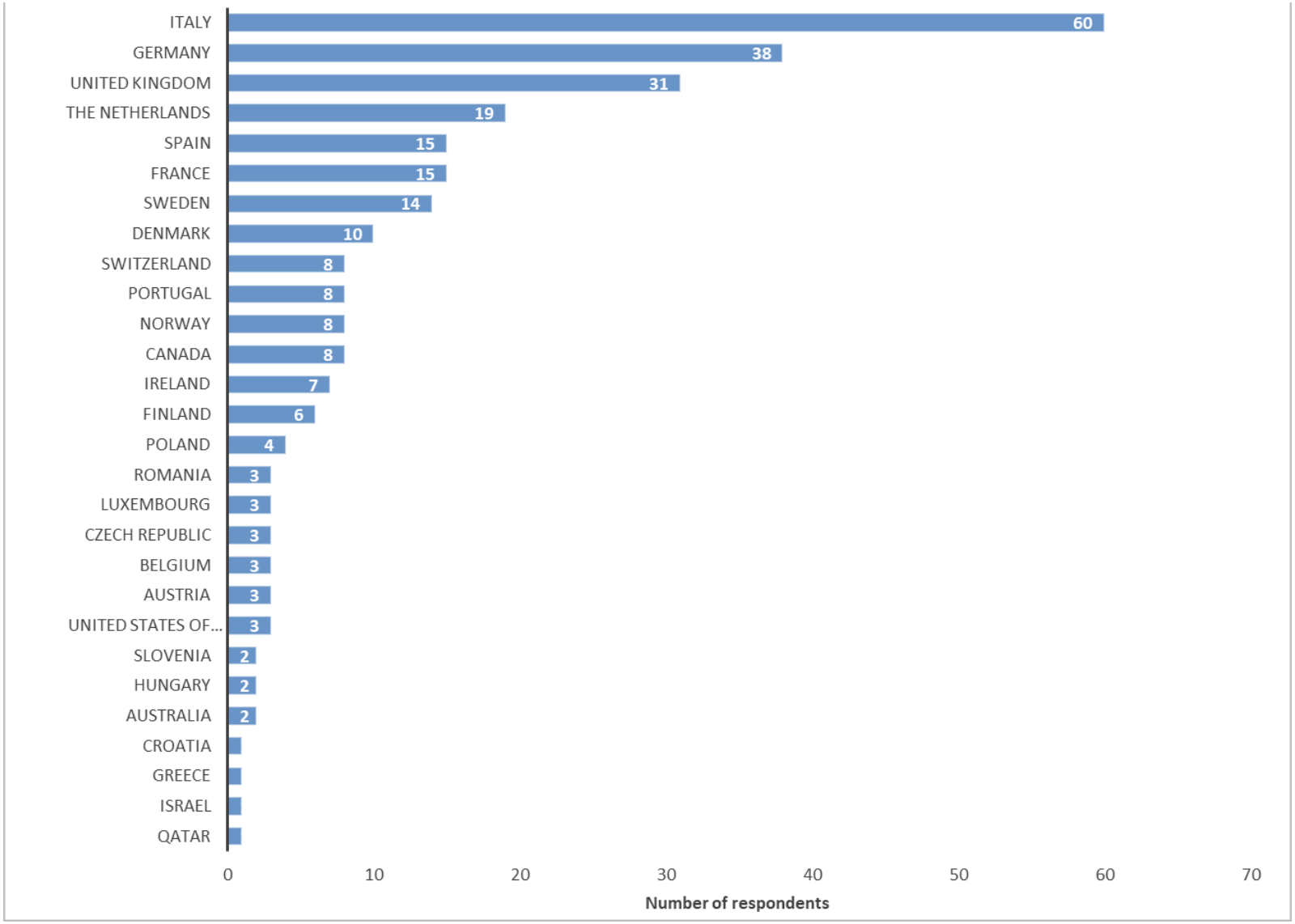
As part of the consultation we collected information on the title, sector and country of residence of each respondent.

Title

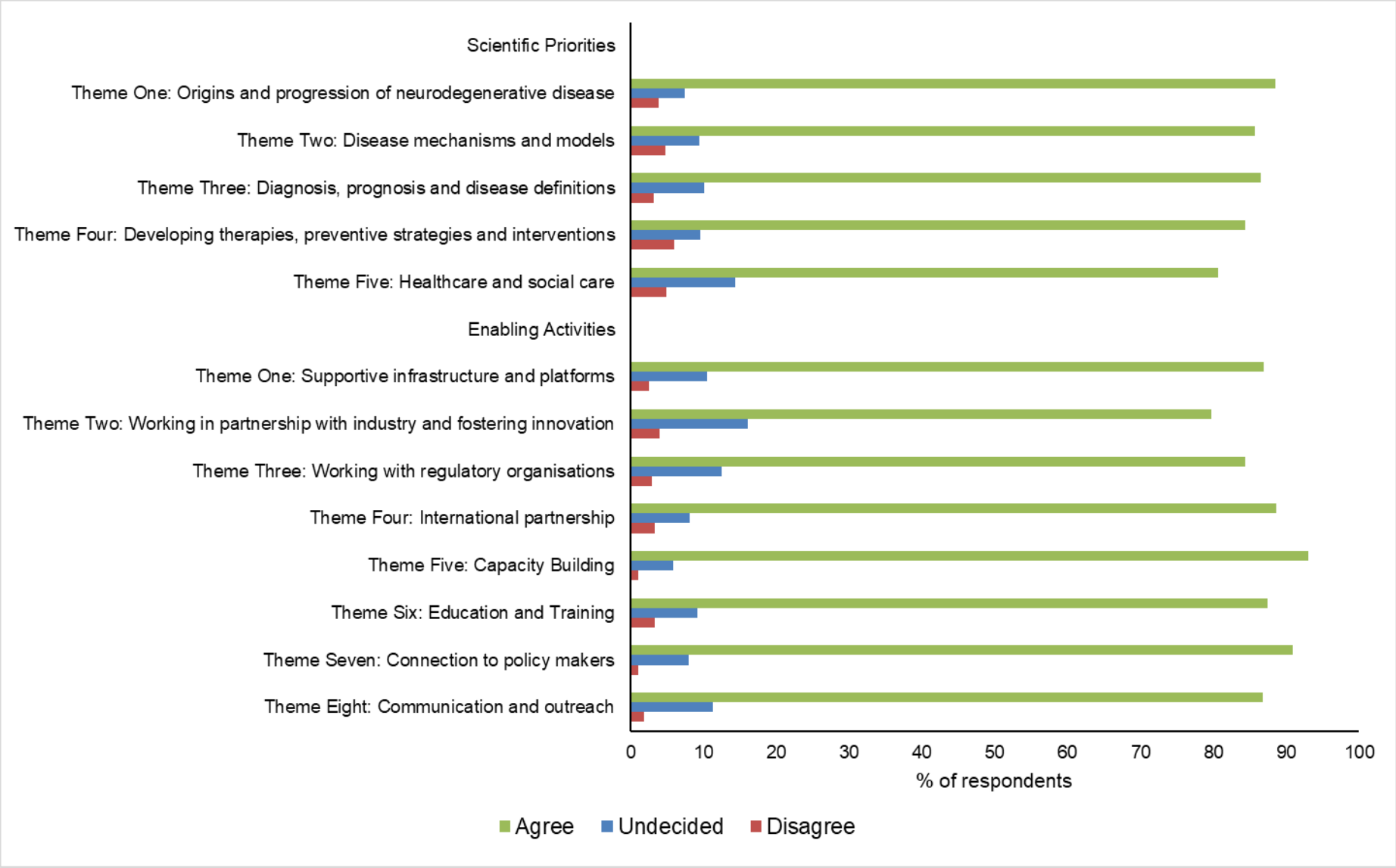
Select the category that best represents you or your organisation



Country of residence



Summary of respondents that agreed with stated priorities and activities



The consultation guided respondents through and requested feedback on the different Scientific Priorities and Enabling Activities of the JPND Research and Innovation Strategy. Respondents were asked to review the strategy and provide comments on each of the themes.

Scientific Priorities

Theme One: Origins and progression of neurodegenerative disease

This theme focuses on improving our knowledge about the fundamental causes of specific neurodegenerative diseases (ND). This includes identifying the factors that determine people's risk and resilience and better understanding the triggering events leading to the onset and progression of disease.

Within this theme JPND has identified the following research priorities:

A. Better understand the significance of recently discovered risk factors for ND.
B. Identify new genetic, environmental and social risk factors for ND.
C. Deepen understanding of the causes of different protein misfolding disorders, a feature common to many ND, taking account of new and evolving technologies.
D. Understand ageing and how this relates to the development of and resilience to ND.
E. Optimise the use of data from existing population-based and ND-relevant cohorts and where possible repurpose or enrich cohorts with ND specific measures.
F. Promote studies investigating synapse dysfunction and loss in cognitive decline.
G. Expansion of research on post-mortem tissues from brain banks
H. Advance knowledge of the interactions between ND with vascular and metabolic systems and the role of infection and inflammation.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

10. Do you agree with these research priorities?

10. a) Please comment on your response below:

Respondents were given the opportunity to comment on question 10. The majority of comments are from those who disagreed with research priorities.

Comment
Complete lack of reference to excitability disorders (epilepsy)
I think that A is difficult to address and may not be well founded. Conclusions are difficult to translate into treatments and many risk factors cannot be modified by patients. H, in contrast, is underestimated in my view in stimulating ND. It also lends itself to treatment hypotheses and thus commercial activity.
I think the point C should be raised to priority level 1. ND is a multifactorial conditions related to a large number of dysfunction in the cell.
REM sleep behavior disorder, a sleep motor disorder that arises in adulthood and herald by years the onset of the motor/cognitive symptoms of synucleinopathies is lacking
I agree with . The notion of resilience should however extend to the potential of humans to overcome the obstacles of ND - this should go beyond brain reserve and towards the notion of the human spirit - psychological and social reliance (the latter should go beyond social networks to meaningful social relationships and brain behaviour relationships that can be maintained. Cohort studies and data sharing may be trendy but at the individual level of hope and resilience it has far to go and may not be a useful way to spend research resources.
The list should comprise the molecular mechanisms of diseases. This should be the priority.
Neurobiological background of NDs should be widened beyond the protein folding problems and synapse dysfunction. Slow progress in the filed is partially caused by preconceived ideas about the pathophysiology that by now has proven wrong.
At its root AD and many other NDs are a chronic metabolic disorder. Risk factors almost perfectly overlap with those for other major chronic metabolic diseases. Those other diseases are quite effectively treated by targeting metabolism - statins+physical activity+diet and often anti hypertensive drugs is the most frequent treatment prescribed around the globe, providing a strong case that the metabolic aspect of AD is a very promising therapeutic target and remains a vastly underresearched topic. JPND historically spent some efforts in investigating the overlap between diseases and some other aspects which graze the topic. Looking at the current agenda, this topic has been degraded according to my counting to a sub-sub-sub topic (a part of aspect H -last aspect in the list - which itself is part of theme one. At the same time the field still continues to struggle with the basic understanding on how to link - on a mechanistic level - metabolic modifiable risk factors and ND.
What is missing: critical reflection on the pathologization of ageing by linking it closely to ND; ethical and social implications of risk factor diagnosis without efficient treatment, role of wellbeing and patient-reported QOL, tendency to have reductionistic perspective on ND, especially when age-related such as dementia

I think the priorities are generally fine However I some are very broad e.g. area H which covers vascular. metabolism/infection and immunity- Whereas are F synaptic dysfunction and cognitive decline is very specific. So some thought should go into this. This is why I ticked disagree so I could comment on this

11: What would you like to see included that isn't covered in the above priorities? (please explain below)

Keyword	Number of respondents	Comments
Alternative models (not animal models)	**3**	• Development of alternative models - replacing of animal testing • I would like to see more support of drug discovery by a focus on robust in vitro and in vivo models
Animal models	**11**	• Generation of better cellular and animal models of these diseases. • Include more translational research, improving models, involving large animal models, include predictive AI models. So much of our data stems from bad animal models and we need to have better ways to study the disease. Large animal models (including models that naturally develop neurodegenerative diseases will allow us better understanding of the disease. Artificial inteligence can help to understand pathways and may be able to generate new hypothesis based on large data sets. • Improve the methodological quality and predictive value of ND animal studies to facilitate translation to human clinical trials • Develop new research models: for example the model involving human cells growing in rodent brains need to be better analyzed. • 1. Precision medicine: a number of genetic mutations increasing ND risk have been clearly identified recently and should be taken into a deeper consideration. 2. Animal models better mimicking disease pathophysiology (synuclein, tau...) are required. Neurotoxin-based models are useless in terms of neuroprotection. • Animal models of social pathologies • developing new animal models relevant to onset and progress of ND diseases developing approaches of long term studies of the development and progression of disease on the animal model • Develop animal models of ND, to cover both genetic and environmental causes in a more realistic way • I would like to see more support of drug discovery by a focus on robust in vitro and in vivo models • - research dedicated to prevention - state of the art of ND research - more research on alternatives for animal models • better models of disease in particular in vivo models where they adhere to the known mechanisms and pathologies. Fundemental to understand the diseases and for final testing putative drugs • promote studies using model organisms

		• One should add the development or switch on existing mice models of neurodegeneration based only on the genetic risks that do not reproduce the disease and have delayed the progress in the field.
AI/network analysis	**9**	• Employ systems biology and machine learning approaches to identify molecular subtypes in ND, perform network analysis, and identify targetable pathways in each subtype • Include more translational research, improving models, involving large animal models, include predictive AI models. So much of our data stems from bad animal models and we need to have better ways to study the disease. Large animal models (including models that naturally develop neurodegenerative diseases will allow us better understanding of the disease. Artificial inteligence can help to understand pathways and may be able to generate new hypothesis based on large data sets. • Test breakthrough hypotheses as soon as they emerge Evaluate the interest of modelling and AI • 1.Develop diagnostic techniques for sub-diseases encompassed by existing syndromic labels. 2. I think H is important 3. Move to AI and big data approaches to image examination and classification • Mechanistic computational modelling of neurodegenerative disease pathogenesis has an important role to play in synthesising the data generated by the many foci listed above, not to mention the multiple parallel brain initiatives. Therefore it is strange not to see explicit mention of this as a necessary focus. • Alzheimer beginning recognition with support of artificial intelligence for support to care • Development of new Technology for the early in vivo identification of subjects affected of ND • (Further) development of methods of measurement based on human (materials). Development of alternatives for animal models. With the aim to shrink the translational gap between laboratory science and clinical use. • Develop better mathematical tools, statistical models to tackle the increasing amount of imaging data from multi-center studies. We need to share more the data, and make the analysis reproducible.
Molecular	**16**	• Orogon of the diseases at atomistic level • Rare diseases and molecular mechanisms • Molecular basis of neurodegeneration. This should include specific pathways activated in neurodegenerative diseases as well as failure of physiological pathways. • prevention measures based on more molecular and neuronal understanding • Neurobiological basis of NDs • Deepen understanding of the causes of mitochondrial (dys)function in ND; Epigenetics effects in ND

		• - novel molecular mechanisms that might be at the origin of ND - novel combinations of previously proposed mechanisms of ND - unifying cytoskeletal mechanisms perturbed in ND • I would like to explicitly see both pre- and postsynaptic dysfunction including axonal functionality in point F. This is because the synucleinopathies likely have their original process of aggregation starting at this site rich in native a-synuclein and these aggregates have to be brought back into the cell body by retrograde axonal transport. The Lewy neuritis may represent stalled retrograde axonal transport cargo. • Although it may be included within the aim of understanding aging, I think it is convenient to explicitly mention two important issues: 1st Advance studies investigating mitochondrial dysfunction and its contribution to synaptic dysfunction and neurodegeneration. 2nd Advance studies investigating dysfunction in DNA repair systems and its contribution to neurodegeneration. I consider that basic research in these issue is necessary to better understand neurodegenerative diseases. • 1. Unbiased drug screening. Screen drugs, already used in clinic for other pathologies, for their efficacy in preventing ND in animal models. This would accelerate the use in clinic. The idea is try something that work, and then you try to understand why. 2. Understand the molecular pathways through which exercise training and diet influences the progression of ND • Target known critical pathways for the pre-clinical development of treatment approaches • The molecular basis of the pathogenesis of the disease have a multifold nature and should be considered in a new olistic perspective. As an example, it could be useless to study factors triggering protein misfolding if one overlooks the network of cell pathways driving protein homeostasis. Priority should be given to molecular details underlying the disease. • The role of time-dependent accumulation of DNA damage as a main factor underlying aging and because aging is the main risk factor also neurodegeneration • Several ND's have a specific neuron type/brain area that apparently initiates the disease. Understanding the cause/mechanism will be the only way to specifically target the disease in its early stage
Genetic	**5**	• Use of Next generation techniques for early detection • Deepen understanding of the causes of mitochondrial (dys)function in ND; Epigenetics effects in ND • Identify new epigenetic risk factors • Considering recent evidence, it would be good to explicitly add epigenetic mechanisms. Focus on aspect of causality, as many changes might 'simply' accompany or follow pathological changes. Longitudinal analyses in aging cohorts. (multi)omics?
Other conditions	**9**	• Epilepsy. A common comorbidity and negative prognostic factor in AD • REM sleep behaviour disorder (RBD) as an early and prognostic marker of ND

		• Rare diseases and molecular mechanisms • THE DEVELOPMENT OF NEROPROTECTION IN TARDETED POPULATIONS SUCH AS REM SLEEP BEHAVIOR DISORDER AS FIRST MANIFESTATION OF PARKINSON'S DISEASE • preclinical symptom of ND like REM sleep behavior disorder • I think that the Batten Disease CLN3 should be included here. • Agree with those, would like to add that from all these perspectives sleep and specifically RBD is an important field
Disease progression	**2**	• Although included in pointF, need to put more emphasis on analysis of markers of disease progression (cognitive decline) and functional connectivity between brain subregions.
Need for novelty	**2**	• The priorities listed here are the "classical" priorities, i.e., have been the research focus for the last 10 years. A new way of looking at this would be to focus on brain diseases that are not associated with an increased risk of AD or other ND, e.g. epilepsy, why is it not one of the known risk factor for AD? • Thinking outside the box! We need a special research priority for people, who do not follow the common lines, but dare to think lateral. Best results are often those that surprise us.
Early diagnosis	**1**	• Development of methods for ND earlier diagnosis
Longitudinal cohorts	**7**	• Establish prospective and longitudinal cohorts of elderly healthy cases and early disease with detailed information on different brain pathologies using PET (amyloid, tau, UCB-J) and CSF biomarkers (synaptic markers, neuroinflammation, tau, amyloid, a-synuclein) • Due to the long term nature of ND we need planned long-term research: 1. Front forward studies starting at birth with power to answer questions about risk. 2. Reverse studies taking large numbers of octo-nonogenerians and asking why have they survived 3. Studies in level 2 &3 countries that are increasing wealth to investigate what factors are responsible for increased longevity • Treatment interventions both rehabilitation and drugs. Epidemiological studies, though this is indirectly covered under population studies but to design epi studies not just those based on existing database • Considering recent evidence, it would be good to explicitly add epigenetic mechanisms. Focus on aspect of causality, as many changes might 'simply' accompany or follow pathological changes. Longitudinal analyses in aging cohorts. (multi)omics? • The study of cohorts of sporadic forms of ND • Support cohort studies /registry studies on PRODROMAL Stages of ND - such as GBA carriers, REM Sleep behaviour disorder, LRRK2 carriers - Long term follow up of theses cohorts with in Depth phenotyping wilson disease missing • In addition to optimising the use of data from existing population-based and ND-relevant cohorts there is potential to use and link routinely-collected administrative data to enhance

		datasets and study the causes and progression of ND and the protective or modifiable factors.
Biomarker development	**9**	• 1) Development of molecular imaging biomarkers for neurodegenerative disorders. 2) Building databases of existing molecular imaging markers investigated in imaging centers in Europe. • Develop non-invasive methods (such as imaging) of the disease course and progression to develop early markers for ND and follow intervention • Promote studies on biomarkers to improve the diagnosis and prognosis of neurodegnerative disorders. • The role of biomarkers such as tau pathology in relation to diagnosis and prognosis • 1) validation of biomarker in clinical setting. 2)Pragmatic clinical trial on QOL outcome, effect on caregivers, ... • Biomarkers for ND • Consider adding biomarkers as a means to track diseases from their origin • Consider signatures/markers that allow tracking disease evolution from the origin
Biotechnology	**3**	• Regenerative medicine-new bionanotechnologies. • Biotechnological approaches to overcome ND • Technology in dementia specifically
Precision medicine	**2**	• 1. Precision medicine: a number of genetic mutations increasing ND risk have been clearly identified recently and should be taken into a deeper consideration. 2. Animal models better mimicking disease pathophysiology (synuclein, tau...) are required. Neurotoxin-based models are useless in terms of neuroprotection.
Inflammation	**5**	• In H. the role of infection and inflammation is mentioned. I would like to suggest a broader approach: the role of the derailed immune system (this also includes infection as well). Furthermore, I would like to advocate besides the immune system also take in to account the role of the microbiome (an important regulator of the immune system). Finally I would like to include the gut-brain axis as many ND patients suffer from intestinal problems. Finding solutions for this comorbidity will improve the quality of life of ND patients. • Advance knowledge on the interplay of peripheral immunity in ND • The role of inflammation and immune system on ND risk and progression • The interaction b/w the periphery and brain re 1. gut brain micro biomes axis/ inflammation immune systems and lifestyle
Metabolism	**5**	• Promote studies investigating the relationship between food, nutrition, metabolism and NDs • I would like to see a significantly stronger focus on metabolic research. This is relevant for origin & progression and Theme two. This topic should include further research in better understanding the molecular link between the modifiable AD/ND risk factors and disease etiology/pathology. This is important because those risk factors - as you are well aware of -

		are considered as main pillars on which future early intervention and prevention guidelines may have to be build. All experience from other disease areas suggests that those intervention will help to maximize benefit from pharmaceutical approaches - if there will be any for AD. We already learned a lot on risk factors, without a better molecular understanding - as difficult as this may be - benefit will remain severely shortened. • I assume diet is included in A & B • A clear task in the definition of multi factorial molecular mechanisms, integraring phenotypic profiling both at proteome and metabolome level
Vascular	**5**	• Role of energy shortage in the generation of ND (e.g., interaction between brain ischemia and senile plaques in generating symptomatic AD). • Studies on brain barriers to improve delivery of therapeutic agents to the brain • encourage specific studies to examine how dysfunctional brain microvessels trigger ND • The vascular component is strongly underrepresented in the topics. I would like to see one topic specifically focussing on the blood brain barrier. • research on vessel health, blood-brain barrier function, interaction metabolic diseases (metabolic syndrome) with brain's health
Risk factors	**7**	• Better understanding of ineraction between known risk factors such as cardiovascular disease and mood disorders, poor exercise and high cholesterol etc. • A more clear emphasis on the interrelationship between peripheral organs and the brain, particularly mechanisms linking food, physical exercise and psychological factors that can all contribute as risk/resilience factors • relates to the development of and resilience to ND ... for clarification purposes: from my understanding resilience is linked to the disease. Otherwise its about risk/resistance • Risk factors and overlapping of different ND asymptomatic. • For ALS, which is the ND I am familiar with, the thorough analysis of the vast literature made me convinced that search for causative risk factors is meaningless. I am afraid similar situation concerns also other NDs. I would suggest instead analyses of modifiable risk factors, which would be helpful in designing preventive strategies. There is practically no study with this goal, big enough to have a chance to reach conclusive results. • Clarify that environmental (or social) factors do include diet and life-style habits, as well as occupational exposures
Interactions/ comorbidities	**7**	• Identification of causality networks and its relationship with age-related comorbidities. • Identify common themes between different ND • Greater integration of social risk factors (isolation, poor support) and inflammatory, metabolic and vascular risk. Also, the role of infectious disease in ND would be a valuable priority given newer findings. • Comparative research between neurodegenerative diseases. What do they have in common and what are differences? Genetic disorders with full penetrance (like Huntington's disease

		and several ataxia's) are more likely to give opportunities for clinical trials as individuals that carry the mutation and will develop the disease can be identified. However most of the cases will be sporadic and therefore it will be important to look for commonalities between familial and sporadic neurodegenerative diseases. • Risk factors and overlapping of different ND asymptomatic. • The development of some ND is highly stimulated by other diseases. For instance, it is well known that diabetes mellitus increases the prevalence of AD and PD. Therefore, to design therapeutic strategies against it, I believe that we need to understand of the molecular linking these diseases. Hence, I think it could be good if JPND could cover these research lines. • The most important in my opinion is to improve the knowledge about the causes and progression of ND in people. We need to understand the risk factors and resilience in humans.
Gut-brain axis	**3**	• A more clear emphasis on the interrelationship between peripheral organs and the brain, particularly mechanisms linking food, physical exercise and psychological factors that can all contribute as risk/resilience factors • The interaction b/w the periphery and brain re 1. gut brain micro biomes axis/ inflammation immune systems and lifestyle
Infection	**3**	• Development and adverse events occurring during development (e.g. viral infection): Viral infection occurring at young age are not often considered as potentially involved in ND whereas they are in psychiatric conditions such as schizophrenia. Further research and development of EARLY biomarkers to allow recruitment in clinical trials at very early stage (pre-symptomatic) of subjects. Without reliable, easy and cheap biomarkers, even to identify subjects at risk that would need further screening to be definitely included in pre-symptomatic population, I fear that clinical trials recruiting patients that have already symptoms (advanced stage of neuronal dysfunction that cannot be reversed and possibly not even stopped) will continue to cost millions and fail. • Greater integration of social risk factors (isolation, poor support) and inflammatory, metabolic and vascular risk. Also, the role of infectious disease in ND would be a valuable priority given newer findings. • Among the point A (risk factors), specific attention to infections. On top, I think issue H would deserve more attention, given its link with ageing
Sex-specific mechanisms of ND	**4**	• Sex-specific mechanisms of ND; from a clinician's view the progression of disease is sex-specific and it needs to be clarified whether sex-specific mechanisms are at play, pathophysiologically • Sex-specific vulnerability should also be investigated • yes, I would like to see included more on the molecular and cellular mechanisms of neurodegeneration and on the relevance of sex and gender (the mention to social is not sufficient)

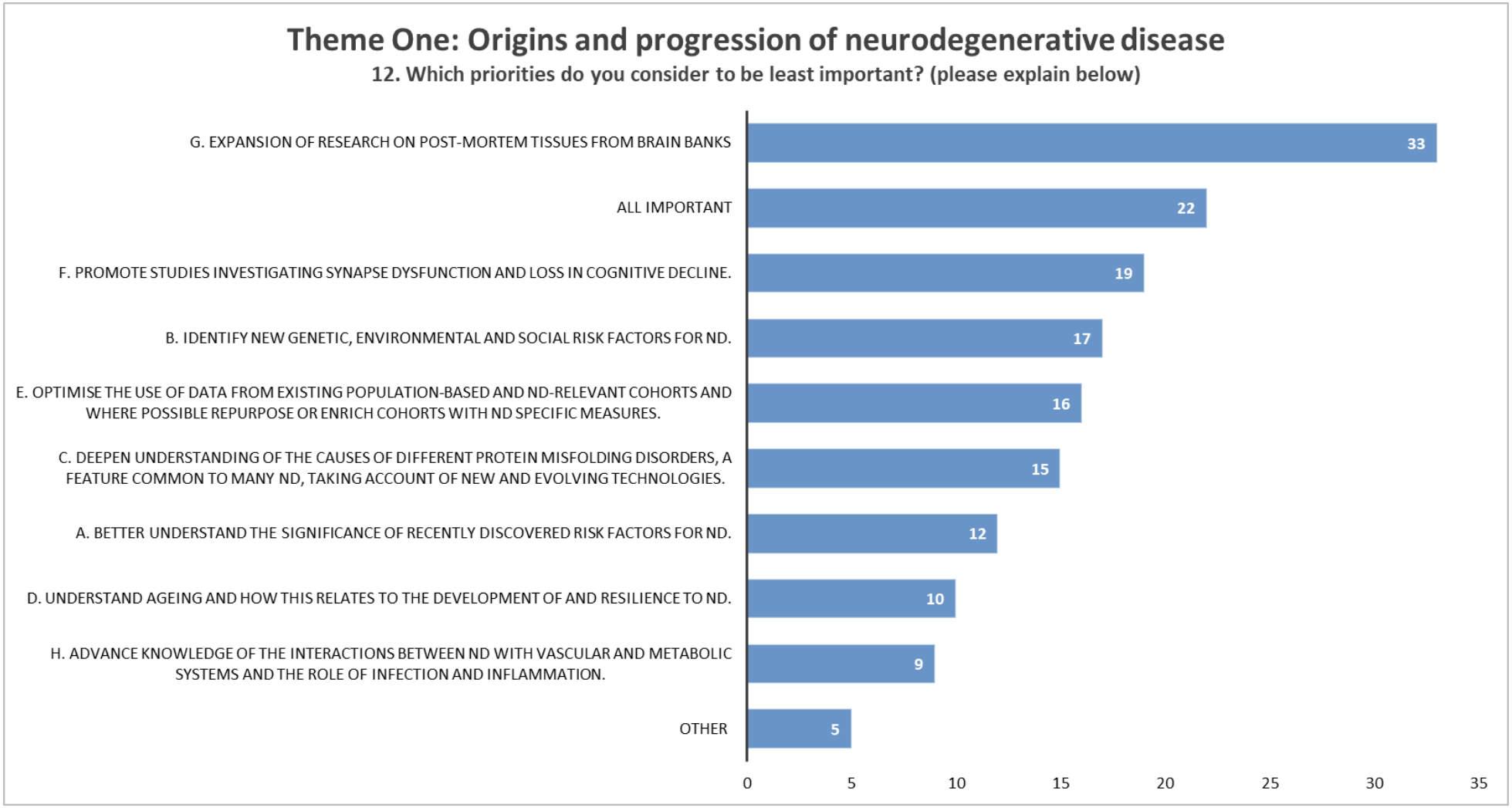
		• knowledge about gender differences
Other cohorts	**2**	• G should be extended to research on other tissue and body fluids • 1. Identification of subtypes within ND disorders (for example, Alzheimer's disease will have several subtypes; 2. Large scale CSF proteomic studies (>500 individuals) and gene-proteomic studies.
Subtypes		• 1. Identification of subtypes within ND disorders (for example, Alzheimer's disease will have several subtypes; 2. Large scale CSF proteomic studies (>500 individuals) and gene-proteomic studies.
Other		• There is nothing about rate of progression (e.g. cell to cell transmission,...): in clinical medicine, the rate of progression of a neurodegenerative disease is one of the most important factor for patients management. • The issue 'Developing therapies, preventive strategies and interventions' seems to be completely ignored/overlooked, at least in an explicit, understandable manner. • Neurodegeneration as a global disease, not brain-centered only • Economics implication and policy perspective on origin and progression • More fundamental blue sky research addressing the brain's multicellularity, i.e. how glial cells interact with neurons and vice versa. • Association of loss in cognitive decline and daily living of the patient • Consider developing and primary and secondary prevention trials • circuit mechanisms of ND, that is which types of neurons are affected when and how and how does it affect functionality of circuits • Cognitive functions • High-risk high gain innovative intervention strategies and/or technologies that enable high-throughput research and discovery • Positive psychological approaches to ND to include notions of hope, humour ,gratitude, transcendence flourishing etc and perhaps better study of brain behaviour -relationships and maintaining brain behaviour function RE E: Expansion of research on post-mortem tissues from brain bank -more work on people who function relatively well despite brain pathology and/or severe cognitive loss - societal influences on how the old old can live well without the stigma of dementia -ie-normalising dementia as a disability of age • Focus on how to assess drugs' effects on ND, which will enable the design of clinical trials that are short and cost-effective. • Establishing the biobank for ND • Understanding the mechanisms involved in other symptoms of ND, as psychiatric or dysautonomous ones that appear highly disabling for patients • Better understanding on prodromal ND • Quality of life in advanced dementia

		• 1.Develop diagnostic techniques for sub-diseases encompassed by existing syndromic labels. 2. I think H is important 3. Move to AI and big data approaches to image examination and classification • 1. Unbiased drug screening. Screen drugs, already used in clinic for other pathologies, for their efficacy in preventing ND in animal models. This would accelerate the use in clinic. The idea is try something that work, and then you try to understand why. 2. Understand the molecular pathways through which exercise training and diet influences the progression of ND • The involvement of people living with ND to include the experiences of ND • Understanding the affects of Anesthesia and other medical interventions • Eye tracking research with new parameters regarding pupil variation eye movement and blinking • A focus on a life course perspective Technological advances for identifying high risk and preclinical cases Better staging of disease; particularly for early identification of the declining process Development of accurate risk calculation scores/models • What it is missing, are novel and provocative hypotheses and this can only be derived from supporting research in the areas outlined in points C., D., F., G., and H. Hypothesis-less approaches, and correlation studies will only give answers by chance; even though chance has been a key contributor to the advancement of science in the past, we are running out of possibilities. • Psychological support. Many of ND disorders fall into the "rare" condition diagnosis. For most people, "rare" implies "severe". As a psychiatrist, I have often been called to interview people with psychiatric/ psychological problems related to the trauma of being diagnosed with a rare and/ or severe ND disorder. Furthermore, little is known about how psychological well being/ or lack thereof, intervenes in chronic inflamation/ progression of various ND disorders. • They are still not getting to the fundamental population underpinning of ND • Priorities that would include how to: - Understand how palliative and end-of-life care services impact Quality of Life for people with ND and when services should be introduced - Understand how people's coping mechanisms, factors and access to services relates to the development of and resilience to ND • Application of new methods to addressing mechanisms of neurodegenerative disease (not only under category C above) Explanation: previous mechanistic models led to numerous clinical trials for AD, but these have shows no sign of succeeding at phaseIII. New mechanistic insight is likely to now be achievable through application of the latest methodologies that were not available at the time the failed trials were envisaged, as cell mechanisms and signalling networks have in general been poorly understood. A more

		accurate mechanistic understanding of neurodegenerative diseases is likely to be critical for development of improved clinical strategies.

12: Which priorities do you consider to be less important? (please explain below)

N.B. some people responded with more than two letters. Some people responded with letters only (no comments).



Theme Two: Disease mechanisms and models

This theme focuses on improving our understanding of the biological basis underlying disease mechanisms and progression of neurodegenerative disease (ND). This includes the improvement of animal and cellular models of ND, together with taking advantage of developments in experimental medicine (investigations undertaken in humans).

Within this theme JPND has identified the following research priorities:

A. Develop novel animal models (ranging from worms to non-human primates) relevant to ND and take into account factors such as the progressive nature of ND, sex differences and ageing.
B. Establish cell-based models utilising innovative approaches to create disease specific and patient derived cell lines that better represent the complex pathology and interactions in ND.
C. Determine the role of new pathways proposed for ND pathogenesis e.g mechanisms of protein seeding (spreading).
D. Investigate traits, pathways, measures and biomarkers that are either common to, or specific for, different ND, spanning molecular-, cellular-, and systems-level approaches.
E. Identify the mechanism(s) that account for the effect of lifestyle factors on either promotion of resilience (e.g. educational enrichment in early life) or neurodegeneration.
F. Target emerging areas to better understand complex connections between biological systems that contribute to ND pathology (e.g develop models to investigate the contribution of the microbiome-gut-brain axis).
G. Elucidate the biological and environmental basis of behaviour and psychological symptoms in ND.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

13. Do you agree with these research priorities?

13. a) Please comment on your response below

Comments
I disagree on a focus on animal models.
This field of research has received large fundings for now >30 y with none or very little translation towards clinical practice and treatment
The aims "D & G" seem not to be very well defined.
we need more studies directly in humans - models are no good if the premise is wrong - only humans can tell us what is really happening and we could make better use of in vivo human research methods like imaging.
G seems the only worth cause in the list above
these models have been shown to have very little heuristic value,
This is already a research priority for a whole industry of endeavour with an army and infrastructure behind it. Public spending must focus on the ideas that are less likely to be funded by pharmaceutical industries and more likely to impact on the likes of people with dementia now.
1. animal models have been good for understanding animals not humans. Mechanistic studies are interesting but too greater reliance on these has led us astray 2. ND research is being technique led. Before genetics, now epigenetics, later big data.
"A" priority should be the last one (at least an intermediate one). Human models have much more translation potential than animal models
C - remove the requirement of NEW pathways, which most often wouldn't be true - as it already isn't true for the example 'seeding' E -do not limit to lifestyle factors, this should be modifiable risk factors.
In my opinion, the benefit of new animal models including non-human primates is overrated. Similar is research on iPSCs. Would not rate them with highest priority.
There is a lot of overlap with them 1 so I would merge topics
Without underpinning to population how can you understand the model?

14. What would you like to see included that isn't covered in the above priorities? (please explain below)

Keyword	Number of respondents	Comments
Cell based models	**12**	• I suggest a stronger focus on novel cell based models – organoids • single cell analysis and organoid systems • Within the priority of cell-based models, I would explicitly mention the generation of brain organoids from patient-specific pluripotent cell lines. • I would re-phrase B: Establish cell-based models utilising innovative approaches to create disease specific CELL LINES (INCLUDING YEAST, PRIMARY MAMMALIAN CELL LINES) and patient derived cell lines that better represent the complex pathology and interactions in ND • artificial organs as disease models • Human gene-editing technologies of IPSC to generate knowledge of well established genetic risk factors • possibly advocate and to try to support a global repository of all patient cells lines (iPSC) • Priority B: ND are too complex to be modeled in vitro without the appropriate context. Priority F: Not too much relevant in my opinion. • Special attention to allernative to animal models. Would it be possible to cowork with other fundamental research fields? brain-research in general • Learning from other brain-research areas than ND. more attention to alternatives for animal models • Assay of siimplified biochemical or cellular assays suitable for drug screening • The development of some specifically designed tube tests assays may provide clues to single out effects and factors that are convoluted (and masked) in bioloical assays.
Animal models	**5**	• There are many mouse models for Alzheimer's disease, stroke. However, to save costs and time, the desired pathology is generally induced when lab mice are 2 to 6 months old. (The average lifespan for the most commonly used lab mouse is 22 months.) Researchers might delete a key gene, for instance, or remove a particular organ (such as the ovaries) to induce a disease. This means that the effects of cellular ageing on disease progression are rarely taken into account. • Development of animal models of accelerated ageing • important to link with models from other brain research models • Maybe more important than to stress development of entire new animal models is to promote research that compares the mainstream genetic mouse lines to gain better insight into the pathological processed that may vary between the lines and between brain regions. • (I) DISEASE MECHANISMS AT THE CIRCUIT LEVEL. (II) COMPUTATIONAL MODELS. (III) NON CELL-AUTONOMOUS MECHANISMS OF ND, including the interactions between

		neurons, glia, immune cells, and vessel-associates cells. (IV) CROSS-SPECIES COMPARISONS OF PARTICULAR MECHANISMS AND THERAPEUTIC TARGETS. These comparative studies should be fostered because they are needed to clarify both the possibilities and the limitations of each particular model.
Human tissue	**1**	• More direct research in humans and humans tissues due to the fact that the neurodegeneration itself cannot be probably well modellize in animals (e.g. PD has a 10-20 years course which canno be accurately imited in an animal modell)
Longitudinal studies	**2**	• Promoting longitudinal studies in selected patient groups with imaging markers for ND • improved lonngitudinal scans of protein deposition, degeneration
Computational	**7**	• Mechanistic computational modelling of neurodenerative disease pathogenesis. Reuse of existing experimental data. • Mathematical or computer-based modelling of disease • develop comprehensive models using multi-modal and multiscale data. develop simulation based model (in silico ND). understand interindividual variability in symptoms and biological data. • Elucidate the biological and environmental basis of behaviour and psychological symptoms in ND with artificial intelligence support • Frameworks to integrate the data generated from the different models are needed to integrate the data, so this should also be included as a priority • (I) DISEASE MECHANISMS AT THE CIRCUIT LEVEL. (II) COMPUTATIONAL MODELS. (III) NON CELL-AUTONOMOUS MECHANISMS OF ND, including the interactions between neurons, glia, immune cells, and vessel-associates cells. (IV) CROSS-SPECIES COMPARISONS OF PARTICULAR MECHANISMS AND THERAPEUTIC TARGETS. These comparative studies should be fostered because they are needed to clarify both the possibilities and the limitations of each particular model. • Include the development of statistical and bioinformatic methodology to uncover biological mechanisms relevant to disease onset and progression
Molecular	**14**	• molecular mechanisms • Role of ATP and/or phosphocreatine shortage in determining or worsening ND • Elucidate the bounderies between physiological and pathological actions of molecular pathways implicated in ND. • The role of oxidative stress • Use of molecular imaging techniques to identify new targets • Better investigate the pathways, with related biomarkers, from prodromal ND (e.g. iRBD for LBD and MCI for AD) to full blown ND • The study of the changes and roles played by the different cell populations in brains: astrocytes, oligos, neurons microglia, perivascular macrophages and peripheral immune cells

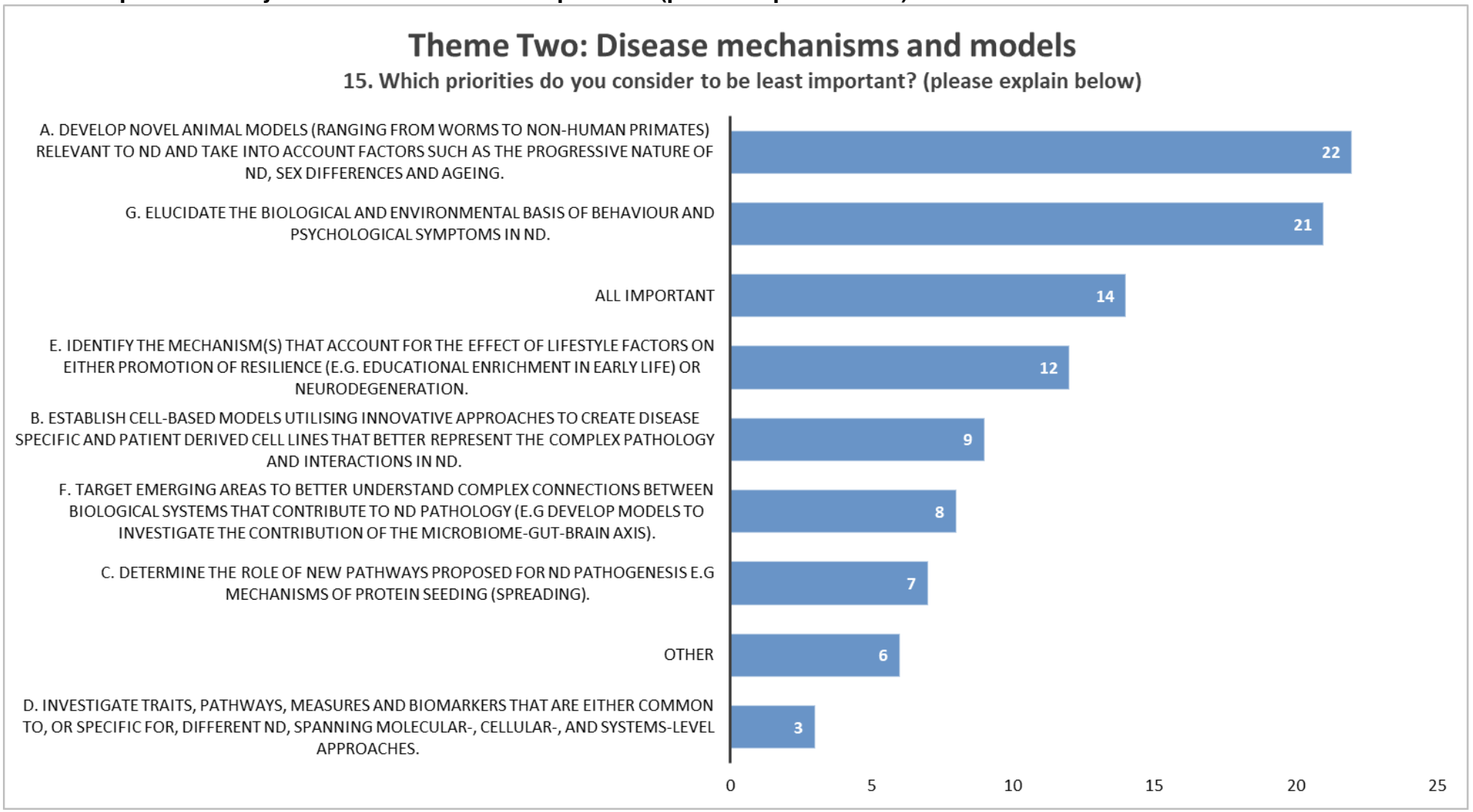
		• New mechanisms preceding protein spreading should be investigated. Spreading means that the pathology is already started. Focus should be given to mechanisms preceding to spreading and directly related to disease. • (I) DISEASE MECHANISMS AT THE CIRCUIT LEVEL. (II) COMPUTATIONAL MODELS. (III) NON CELL-AUTONOMOUS MECHANISMS OF ND, including the interactions between neurons, glia, immune cells, and vessel-associates cells. (IV) CROSS-SPECIES COMPARISONS OF PARTICULAR MECHANISMS AND THERAPEUTIC TARGETS. These comparative studies should be fostered because they are needed to clarify both the possibilities and the limitations of each particular model. • Multi factorial molecular investigations • I would like to include in explicit manner the contribution of oxidative stress • I will like to see point C expanded to also comprise the neuronal dysfunction caused by slowly progressive accumulations of misfiled proteins, e.g. a-synuclein and tau. Such dysfunction may be contributing to dysfunctional circuitries that cause symptomatology without have dead neurons. Such dysfunction and their downstream symptomatology may be accessible for therapeutic intervention. • Target disease mechansisms for the development of treatment approaches
Genetic	**3**	• genomic approach at early life can predict early diagnosis and prevention of ND • Integration of Omics for better understanding of complex pathogenetic mechanisms
Other conditions	**3**	• Evaluation of a specific sleep disorder, as REM sleep behavior disorder (RBD). There are several publications about the importance of RBD as prodromal disorder of alpha-synucleinopathies • Again, epilepsy. Most AD animal models have seizures • I am a grandmother to a child with Batten Disease CLN3 - I think the fact that he will have dementia in a very young age
Inflammation	**6**	• The role of autoimmune dysfunction in ND would be valuable, mechanistically. • Immunologic aspects • contribution of the immune system to pathogenesis of ND • Interaction of misfolded proteins from different origins (underlying disease and exempli gratia inflammation, infection) . • I think they are fine too but overlap with Theme1 - F could be broadened to include "peripheral" biological systems e.g. gut brain axis, but also immune/metabolic. More themes that integrate body and brain and genes/mechanism with. Personally I think immune systems should be explored more also sex differences • Include studies to better understand the link between neuroinflammation and neurodegeneration.

Biomarkers	**3**	• FINDING NOVEL PERIPHERAL BIOMARKERS FOR EARLY DIAGNOSIS AND PROGRESSION OF ND • I totally agree with the priorities, and in particular, I would foster studies leading to novel peripheral biomarkers for early diagnosis and for monitoring the progression of disease. • Focussing on single biomarkers is not sufficient. It's rather the array of combined biomarkers in a patient that should be most promising to reveal risk of outbreak and tailored therapeutic strategies for individual patients.
Vascular	**3**	• the role of the blood brain barrier in ND • more information on how vascular dysfunction affects the brain at a microvessel level
Lifestyle	**8**	• Especially for dementia, the interaction between lifestyle factors and disease (E) should be elaborated. • Adult neurogenesis and exercise increases • Further emphasis on the environmental risk factors and the way they may contribute to disease onset and progression • A more inclusive research on life-style factors that represents the full spectrum of risk factors in the population and modern society would be desirable. • But it is very difficult to understand for lay people. What about the influence of the invironment? • Investigate interactions of lifestyle and environmental factors • Point F: Human lifestyle factors to prevent the onset of the illness are, in my opinion, the most important key to understand and combat the neurodegenerative diseases ND
Common mechanism	**3**	• Additional research priority: Identify common mechanisms in ND • Shared pathways in different diseases. More general approaches to tackle the disease such as reduction of the levels of the toxic proteins. • A greater connection between psychiatric and neurodegenerative disorders as risk-resilience factors may likely be common
Need novel high risk work		• The key point is, that JPND does not promote high risk Projects JPND should have an additional Funding scheme for such high Risk Projects with say two to three partners. with a relatively low total budget - 250 000 - 300 000 for two to three years - rapid response approach
Sex differences	**2**	• clear reference to sex and gender • I think they are fine too but overlap with Theme1 - F could be broadened to include "peripheral" biological systems e.g. gut brain axis, but also immune/metabolic. More themes that integrate body and brain and genes/mechanism with. Personally I think immune systems should be explored more also sex differences
New technology	**2**	• Develop understanding of interaction between biological factors and PEMF (pulsed electromagnetic field therapy, also known as low field magnetic stimulation) resulting into specific models

		• Emphasis on new areas e.g. in the imaging field (from super-resolution to preclinical imaging and in between) is lacking here. Numerous recent advances are not being called for, but they could make a difference to our understanding.
Other		• See page 5 about exercise training and diet, which I am not sure is included in point E • Support for caregivers • Fully agree. Though researchers should try to follow 3R principle, politicians and regulators should be made aware that in vitro (even advanced - like organoids) cell systems are not enough to fully research ND (pathology, target finding, intervention strategies) taken from a system medicine approach • Again economics component is important to present the value underlying disease mechanisms and models • Developing therapies, preventive strategies and interventions. • what about ethical issues related to the biomarker / predicitve approach? impact on the health care system (e.g. WHO else will be interested in these results? insurance companies?) effect of lifestyle factors -> what about socioeconomic factors (e.g. poverty, migration) biological and environmental basis of behaviour and psychological symptoms -> means that a methodological discourse about translational research is needed (across the whole research spectrum from T0-T4/5) • Develop methods to translate findings from models to patients. • E F & G are important • In my opinion they cover all priorities especially the point D. • NEUROPROTECTIVE STRATEGIES • special focus on dementia with young onset. • the list covers most priorities, but something which target preclinical stage of ND would be important • Neurophysiological approach and cognitive neuroscience • The actual situation is far too confused and the large amount of data, however,still difficult to use in a translational way. We need a stronger translational effort • More emphasis on the contribution of aging as the main risk factor for ND. Now aging can be influenced by nutritional interventions and by drugs this opens new perspectives to prevent and delay onset and progression of ND. • Add a topic on metabolism, unless you've added it to Theme one (see previous comments). • Identify the mechanism(s) that account for the effect of lifestyle factors that when implicated at a non-idividual Level nut at a socital might prevent neurodegeneration as e.g dementia. • please do not orget clinical approaches, e.g. quantitative approches in human sleep research • Learning from other brain-research areas than ND. more attention to alternatives for animal models

		• I would add to (G.) that we need to go further than the "biological and environmental basis of behaviour & psychological symptoms in ND", to the complex, bio-psycho-social aspects of it. • Development of novel therapies, repurposing of drugs, exploring treatment options that are of little interest to pharmaceutical industry (vitamins, nutritional measures). • point G should include also the interpersonal/social aspects (bio-psycho-social model of BPSD) • Would like to see priority E expanded to include a priority on identifying the mechanisms of environmental factors (e.g. pollution, radiation, exposure to chemicals etc.)

15. Which priorities do you consider to be less important? (please explain below)



Theme Three: Diagnosis, prognosis and disease definitions

This theme focuses on enhancing research relating to the definition and classification of neurodegenerative disease (ND), discovering new improved diagnostic techniques and identifying new biomarkers. Ultimately, this research will enable earlier and more accurate diagnosis of these diseases including the ability to predict disease progression and monitor the impact of therapies and interventions.

Within this theme JPND has identified the following research priorities:

A. Standardise disease definitions, diagnostic criteria, assessment tests and procedures for ND, developing and validating new ones where required.
B. Develop and validate new diagnostic criteria and procedures in a way that supports their implementation from the population level through to primary care and specialised clinical settings.
C. Harmonise and standardise existing biomarkers and develop, validate and standardise new biomarkers (e.g. molecular, imaging, functional, cognitive).
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

16. Do you agree with these research priorities?

16. a) Please comment on your response below

Comments
As already mentioned in 2012, the JPND program has never founded any research on idiopathic REM sleep behavior disorder, whereas 92% of affected patients convert to Parkinson disease, Lewy Body dementia and multiple system atrophy. This is the most specific clinical sign preceding these synucleinopathies. I have been chocked to observe that European efforts have been completely absent since JPND onset in this direction, leaving individual centers alone and poorly founded, whereas a common, translational program would be easy (an international RBD study group had been established alone and without founds for 10 years, having led to send the DNA and clinical data to Canada, by lack of European fundings, and having generate a massive delay for this disorder. Meanwhile, patients have converted.. This is something the JPND really missed.
Diagnosis and disease definition does include genetic analyses and the identification of known genes. This is not reflected in the priorities.
without therapy the diagnosis is not so useful
These priorities look to me essentially as the same mantra we heard during the last ten years.
Given the move to earlier diagnosis and a focus on prevention, there needs to be greater attention to research on the value of biomarkers for assessing prognosis as well as providing diagnostic information
A: needs critical reflection on expert consensus, unclear role of patient perspective, C: not only about biomarker development, but also needs standards regarding disclosure
I think that standardisation and development novel criteria (A+B) is not the most salient anymore ;a lot of progrss has been made.
Ever more refined definitions don't help patients with cognitive decline and does not help therapy and treatment. ND disorders are intrinsically heterogeneous, which is a property associated with and caused by aging.
Standardise outcome measures that take patient and caregiver preferences and reelvance into account

17. What would you like to see included that isn't covered in the above priorities? (please explain below)

Keyword	Number of respondents	Comments
AI/data	**13**	• 1. AI for image classification 2. Big data for integrating chemical, anatomical, physiological and genetic data to look for patient groupings that show homogeneity in the integrated clinical and biological sphere - looking for disease signatures to influence diagnostic classification. • The data collected in clinical studies should be stored in standardised formats so that future re-use of suitably anonymised clinical data is facilitated. • Need consistent collection of clinical and phenotypic data. Need consistent collection of biological samples including for generation of cell lines • Longitudinal aging cohorts, including healthy individuals at baseline (some of which convert to MCI/AD) along the course of the study. Use of big data? Machine learning? • ad c: Please include results from workinggroup call on Harmonization Imaging. And include epidemiological data (big data, brain voxels) • Harmonise and standardise data preprocessing adn data analyses methods. • Develop and validate new diagnostic criteria with artificial intelligence and deep learning new possibilities for practical research • Work should also be done to develop common data elements (CDEs) for ND. • use of large genomic data sets to explore risk factors for sporadic neurodegenerative diseases • Include digital technology in standardising diagnosis in order to have more objective and sensitive tools. • Technology. We need to interlace new technologies, both static & mobile, into future research. Better data transfers, better monitoring tools, an interactive world where we can do better, and be better than current social-network support groups and/ or chatrooms. • Need to harmonise without creating massive amounts of new technological investment in the process
Longitudinal studies	**3**	• 1) Multinational European prospective and longitudinal cohorts of elderly healthy cases and early disease with detailed information on different brain pathologies using PET (amyloid, tau, synaptic density etc) and CSF biomarkers (synaptic markers, neuroinflammation, tau, amyloid, a-synuclein etc). 2) Compare in vivo biomarkers with neuropathological outcomes (e.g. tau PET imaging with tau immunihistochemistry). • follow-up of well defined cohorts suffering pro ND or preclinical symptoms of ND • Longitudinal aging cohorts, including healthy individuals at baseline (some of which convert to MCI/AD) along the course of the study. Use of big data? Machine learning?
Genetics	**2**	• Identification of known disease genes and improvement of current genetic test procedures. • Genetic studies aiming at a better stratification of patients

Imaging	**3**	• Use of multi-modality imaging to obtain quantitative parameters that are characteristic for the disease • Develop novel technologies (e.g. imaging technology) to improve biomarker sensitivity • I think imaging deserves a separate point. The new imaging approaches important to both preclinical and clinical evaluations are becoming a necessary tool to validate any approach in ND diseases.
Early detection	**6**	• Focus on early detection and diagnosis • Possible preclinical biomarkers • There should be more focus on early diagnosis and early biomarker discovery. • More stress on the #1 problem in the field, lack of tools/methods for early diagnosis • There is no specific mention of early diagnosis/detection i.e. years before overt clinical symptoms. It may be generically covered under B, but could perhaps do with being called out explicitly.
Prognosis	**6**	• what is missing is the prognostic issue in ND. Dementia, parkinson's disease and also ALS can have different progression and prognosis can be difficult. On the other hand people with the disease can be in need to get info about, not the progression in itself but also into time perspective of the progression. Some effort should be done to develop prognosis criter • Implementation of follow-up studies to confirm or disprove the first diagnosis of neurodegenerative disease • A more definite focus on linking clinical disease subtypes with specific pathogenic pathways. For example, this seems really necessary to do in the case of Parkinson's disease. Without this kind of endeavour it will be impossible to personalise the trials of disease-modifying therapies in the future. • Determinants of prognosis • The problem of overlapping and how can we monitor such a patient ? Monitoring is extremely important because this is the only way to haveresults • Develop and validate better prognostic models
Definitions	**8**	• Reconciliation of research and clinical definitions of AD would be helpful. • An organic system of diagnosing ND, similar to DSM-V for psychiatric diseases. • Confirming in vivo diagnoses postmortem is a prerequisite for establishing valid biomarkers. Pure clinical diagnoses suffer from insufficient validation and can mislead the research community in the long term. Because this type of research is more challenging due to the need for interdisciplinary collaboration and building up a complex infrastructure, it would be highly desirable if the JPND would put more emphasis on and provide support for this field.

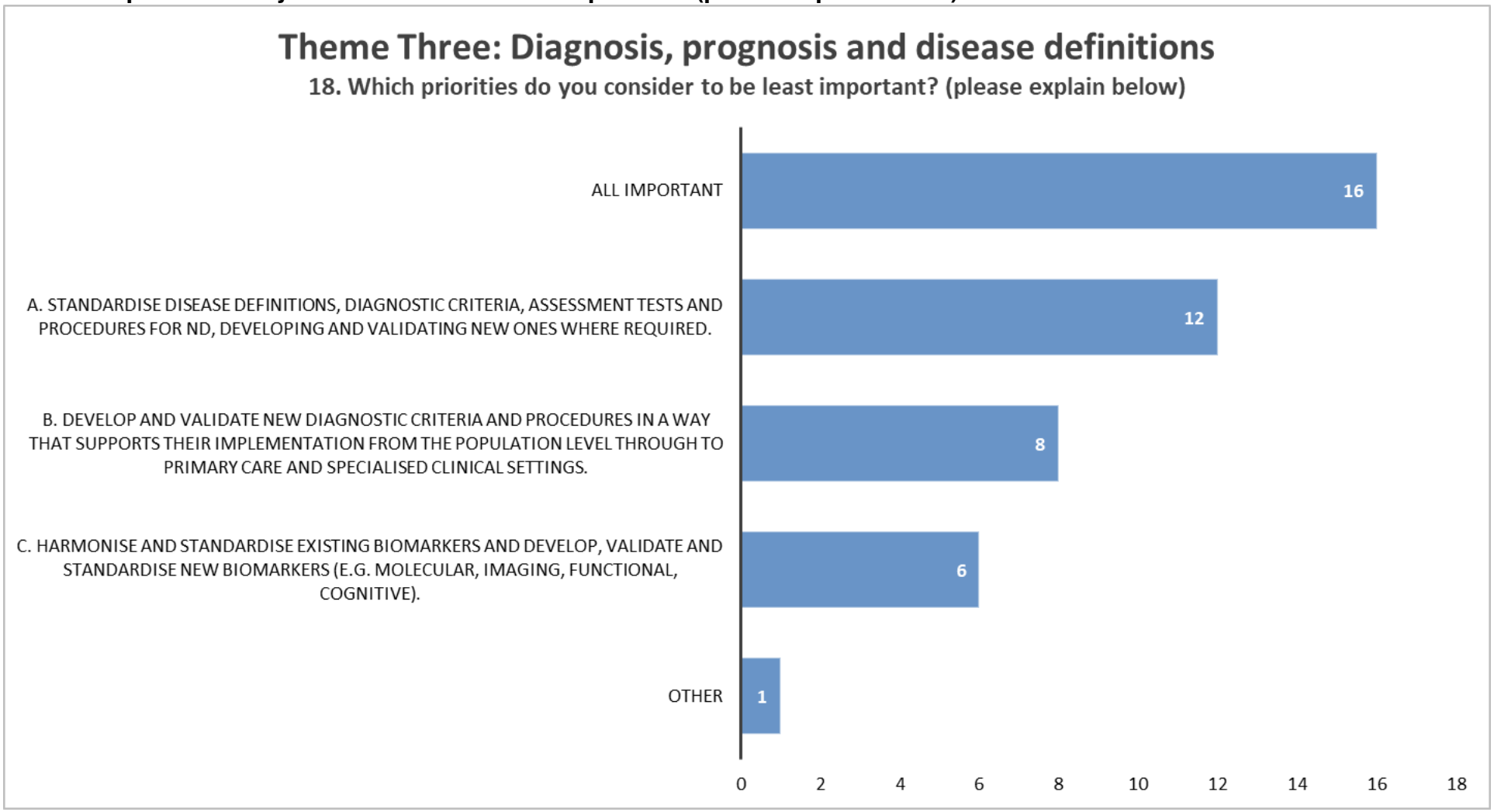
		• Staging criteria. The cancer world has developed different treatments at different disease stages, and uses stage in clinical trial design. Systems for clinical staging need to be developed for neurodegenerative disease. • Continuous update. Definition - test – redefinition • Clinical tools to dissect the complex pathological components behind AD-related dementia. This challenge probably is more interesting than trying to convert the AD status in a yes/no paradigm (unrealistic) • Include points for standardising definitions of preclinical as well as early disease stages (ie the state of mild cognitive impairment and its associated terms)
Open data		• epidemiology should have more attention. Sharing of knowledge as well.
Cost effectiveness	**2**	• Study and compare (!) the cost-effectives of each of these measures for standard use in the clinic or population level. • Cost effectiveness studies on diagnostic tools –

Biomarker	**13**	• integrate vascular disease and risk markers explicitly into all of the above - you have them from two JPND funded projects but they need to be explicit. • Standardise disease definitions and criteria for the diagnosis of prodromal ND along with the harmonization of existing biomarkers in this cohorts • I would sepparate the standarization of known biomarkers from the development of new biomarkers. A specific call on new biomarkers should be considered. • Biomarker development should include novel, yet unleveraged, sources, e.g. tear fluid. • Other eye tracking biomarkers compared with the existing • Focus on new biomarkers --> particularly blood-based, also markers for DLB, tauopathy/TDP43/FUS and for inflammation and synapse loss (i.e. other disease processes). distinguish diagnostic biomarkers from prognostic biomarkers and theragnostic biomarkers (not necessarily the same). Prepare for a future where medication for Alzheimer is available - diagnostic landscape will change tremendously. • A specific mention of neurophysiological markers • Are motor symptoms an early marker for cognitive decline? Which motor aspects (including dual tasking) are then of most importance and how should these be assessed? To clearly define the level of ADL difficulties/limitations that support the diagnosis major neurocognitive disorder, i.e. dementia. • Harmonise and standardise existing biomarkers are very important point. • In my opinion is very important to identify biomarkers that are disease-specific (like AD, PD, etc...). This study would allow an early diagnosis of the disease. • Among the biomarkers, RBD must be included • Finding and validating a blood biomarker for AD and neurodegeneration • QC by cross-check that all investigators generate and interpret data using standardize procedures • C: not only about biomarker development, but also needs standards regarding disclosure • Develop newborn screening procedures and protocols as a key diagnostic tool • 1. Prognostic markers (not mentioned in A-b-c 2. Definition of endophenotypes (subtypes within a disorder) • It is important to find clinical functional biomarkers, to validate and standardize.

Other		• all of these priorities are difficult as in many disorders that go under a single identity e.g. Alzheimer's disease, there may be multiple disorders with different causes. • The weight on biomedical models within this whole survey so far is perhaps not justified • I am expecting from JPND to found massively research on idiopathic REM sleep behavior disorder, in order to increase the number of patients diagnosed (transnational registries, epidemiology, increasing the knowledge of EU citizens and healthcare), create large European cohorts, with fine follow up (genetic, omics, clinical, radiological) and rapid inclusion into all neuroprotective programs (GBA supplements, antibodies anti alpha syn, effect of life style changes including sport, food, coffee, uric acid...). There seems also to be unequal effort, with AD being well funded, whereas Parkinson disease and especially Lewy body dementia and multiple systemic atrophy have been poorly funded, despite the burden and deaths linked to these devastating disorders. • Current ND clinical trial processes are too slow and so the expllicit translation of point A to assist in speeding up trials would be useful • Development of measures using modern psychometrics such as Rasch measurement theory and Iterm response theory to accurately capture patient data • validating tools or questionnaire is culturally adapted one • supports their implementation -> means that FUNDING for implementation projects is NEEDED, usually only the development/ validation of new tools will be funded. this also means that a discourse about patient centered outcomes is needed, otherwise its "only" an increase of the number of early diagnosed patients, but NOT which impact a dementia related diagnose has on hers/his live (LINK to theme 4 & 5 needed) • Standardise the studies on modifiable risk factors, in particular the neuromuscular stress. NDs are rare diseases and require big cohorts investigated according to common rules. • Interaction with brain stimulation • Include co-morbidities • under B: please specificy better clinical criteria and differentiate from other criteria (e.g. neuroimaging, EEG,...) • I agree, but we should not forget that a personalized-medicine should be included. • identification of new biomarkers for the patient follow-up to undertand the efficacy of "treatment" • Standardise impact of disease for the patient's life (prognostic models), especially with regards to cognition • on B above - the value of criteria and procedures for whom? The loos of personhood in the race to diagnose is not well understood by a majority of people who are quick to develop biomarkers and make diagnoses. The lack of understandings of personhood in the way A-C are phrased is a point in case. • Again economic to quality relative value of investments

		• more about course and influence of comorbidity and intercurrent health problems on course and progression • I agree, item B should be done for RBD, and item C should include polysomnography as a biomarker (see Högl et al, Nat Rev Neurol 2018) • Not sure if the suggested themes include early diagnostics or affordable early diagnstics • there are only 3 themes here therefore they are much broader and less specific than the previous themes - so perhaps a more specific subheadings and focus would benefit. • Multi factorial molecular definition in the different tasks • Ethical dilemmas of early diagnosis and no treatment. • CHARACTERIZE PARAMETERS THAT WILL ALLOW TO CHARACTERIZE THE PHENOTYPE AS PRECISE AS POSSIBLE, ACCORDING TO THE NETWORK MEDICINE GUIDELINES • Promote framework for market access of medicine and medical devices in EU • For the priority Harmonise and standardise existing biomarkers further research should be build on the results from the JPND Working Group call 2016 on harmonisation • To eplore in the different neurodegenerative disorders (namely Dementias and Parkinsonian Syndromes) the subtypes with slow progression comparing them with the standard subtypes and fast progressing subtypes • Would like to see a priority on research that explores how to shorten the time required for diagnosing a person with ND (specifically MND, MSA) and research on the best ways to deliver a diagnosis of ND from the perspective of the person with ND that can then be used to inform and educate health care professionals. • The Research Roadmap for Dementia Prevention, Diagnosis, Intervention and Care published by the UK Alzheimer's Society recommends research to define "a ‘timely’ and ‘quality’ diagnosis of dementia ... to enable informed decision-making", to understand reasons for not seeking a diagnosis, and "the most effective ways to communicate a diagnosis". These areas may be addressed under the health care and social care theme of the Strategy, but if not there may be potential to support research about the process of seeking and receiving a diagnosis under theme three. The Roadmap also notes the importance of the "acceptability, cost-effectiveness and real-world outcomes of innovations in diagnostics", which goes beyond validation of criteria and tests.

18. Which priorities do you consider to be less important? (please explain below)



Theme Four: Developing therapies, preventive strategies and interventions

This theme focuses on the research needed to transform the treatment of neurodegenerative disease (ND). This includes the development of new therapies, intervention and prevention strategies (e.g. lifestyle modifications), defining better methods of care or a combination of these approaches at different intervention times.

Within this theme JPND has identified the following research priorities:

A. Improve the validity of model systems used for target identification and therapeutic development to increase the likelihood of translation to clinical benefit.
B. Investigate the differences and similarities in the susceptibility to neurodegeneration across specific neuronal subpopulations to reveal novel targets that may promote resilience and increase neuronal plasticity.
C. 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.
D. Develop disease modifying approaches, where appropriate, that slow, reduce, or clear the proteinopathy that underpins ND.
E. Promote regenerative strategies to restore function for ND where specific neuronal deficits are implicated.
F. Develop novel systems for delivery and targeting of drugs/biological agents to sites in the brain and other parts of the nervous system.
G. Promote research to consolidate and expand methods for the clinical assessment of human disease.
H. Encourage theoretical and empirical research and education regarding the use of non-pharmacological interventions such as cognitive training.
I. Encourage socio-economic studies that address ethical issues around how novel drugs are developed for ND; e.g., how best to undertake early phase clinical studies in 'at-risk' or presymptomatic individuals.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

19. Do you agree with these research priorities?

19. a) Please comment on your response below

Comments
Again, I cannot see a sentence about treating pre-PD and pre-dementia (idiopathic RBD, not just MCI)
Mostly agree, but there is an excessive focus on protein misfolding and the neuron at the expense of targeting ND pathways that involve other components of the neurovascular unit (glia, microglia, and vascular cells) and other pathways including inflammation.
I think that the development of novel strategies for the delivery of drugs to specific brain districts should have priority 1.
I do not copy that themes H and I have the same priority as the others as H and I does not "solve the issue" but more deals with the point how to cope with the disease and how to accept it.
Is it really true that there is a "proteinopathy that underpins ND"? This statement seems to suggest that ND is always primarily a proteinopathy. That may be the case for certain ND, but there is another school of thought that dysfucction of the proteostatic network is just one, albeit important, factor in the onset and progression of neurodegenerative disease. We must be wary of an echo chamber approach to deciding research priorities. Those that argue the hardest are not necessarily correct. It would be better to foster a broader set of etiopathogenic mechanisms until we are surer of what is happening.
Priorities are highly influenced by age-dependent NDs. However, recent highly relevant innovations were based on other NDs without high priority (SMA, Duchenne).
There are no mechanisms or drugs known being beneficial in ND! Therefore I suggest to further strengthen the basic research for mechanisms and drug candidates.
I guess that the main priority should focus on better animal models to accurately test disease-modifying therapies.
This is repeating the previous. Drug development strategies have clearly defined steps which should be recapitulated here for development of any therapy. All general points should be moved back to Themes 1 and 2.
This is a very broad list - I would suggest the goals set out here actually represent three or four categories - identifcation of new molecular targets; alternatives to drug development; trialling and recruitment; social and ethical challenges
many overlap with early mentioned Themes (e.g. 2) - not always clear focus on therapy and prevention
I think this is a very broad list, which is difficult to get through and keep overview.
I think the priorities are too narrow in relation to Health science research and current gaps of knowledge. It should be more balanced between interventions that focus on drugs versus non-pharmacological interventions. The focus is too strong on drugs. Why is the focus on enncouraging the development of psychosocial interventions, paying attention to the promotion of social inclusion and carer involvement ?
encourage studies that investigate community-based interventions, taking the needs of primary care into account
These priorities are too narrowly focussed on pharmacological interventions. Prevention comes down to reducing biomarker levels with the implicit and unproven assumption that this translates to clinical outcomes. JPND would benefit from a broader prioritisation of prevention. See latest development in Lancet Commission, NASEM report and WHO: http://www.who.int/mental_health/neurology/dementia/action_plan_2017_2025/en/

20. What would you like to see included that isn't covered in the above priorities? (please explain below)

Keyword	Number of respondents	Comments
Non-pharmacological – cognitive training	**10**	• Therapies based on devices instead of drugs • Try rehabilitation protocols with brain stimulation • Among non-pharmacological interventions I would mention not only cognitive training but also physical exercise • Include neurocognitive and psychiatric testing, for attention, memory, sleep disturbances, anxiety and depression to renew the driving licence. This will help to indirectly collect the presence of early symptoms of neurodegeneration and to avoid driving in people that developed dramatic cognitive deficits. • encourage more on preventive and non pharmacological approach • More understanding of systemic interactions between social and physiological risk factors, and identifying points for interventions in lifestyle. • Specific research into how to meaningfully seek stakeholder involvement of people with dementia in this research theme in a gap here. There is so little attention here focussed on so many psychosocial interventions (Cognitive training is the least evidenced approach) that instantly alleviate suffering and are desperately in need of an evidence base - but are complex because outcome measures are under developed and evaluation is thus complex. This is research that needs to happen and will not be funded by drug companies. The number one 'intervener' in any therapy where a person with dementia is living in the community is the family system. There is so much potential - mainly because of the under developed nature of services for people with dementia - to impact on this group positively and to evaluate the results of such intervention rigorously. However this group - the number one supporters of people with dementia are ignored completely. This is unconscionable. • eHealth strategies that support recovery and slow progression • Reg. H: Considering the evidence I suggest you mention cognitive rehabilitation instead of cognitive training. • Would like to see Priority H expanded to include research into psychological support and coping mechanisms.
Non-pharmacological – Other tech	**4**	• There is a need for a totally new approach taking into account disease modifiers, including social and psychological as well as lifestyle factors • The use of molecular imaging for monitoring disease progression and response to therapy, and also its use for predicting response to therapy. • The language and focus is quite biomedical and clinical which may limit engagement from broader disciplines including social science that can contribute to the development and implementation of interventions. We welcome the inclusion of non-pharmacological research and interventions and note that this extends beyond cognitive training and ethics, to include

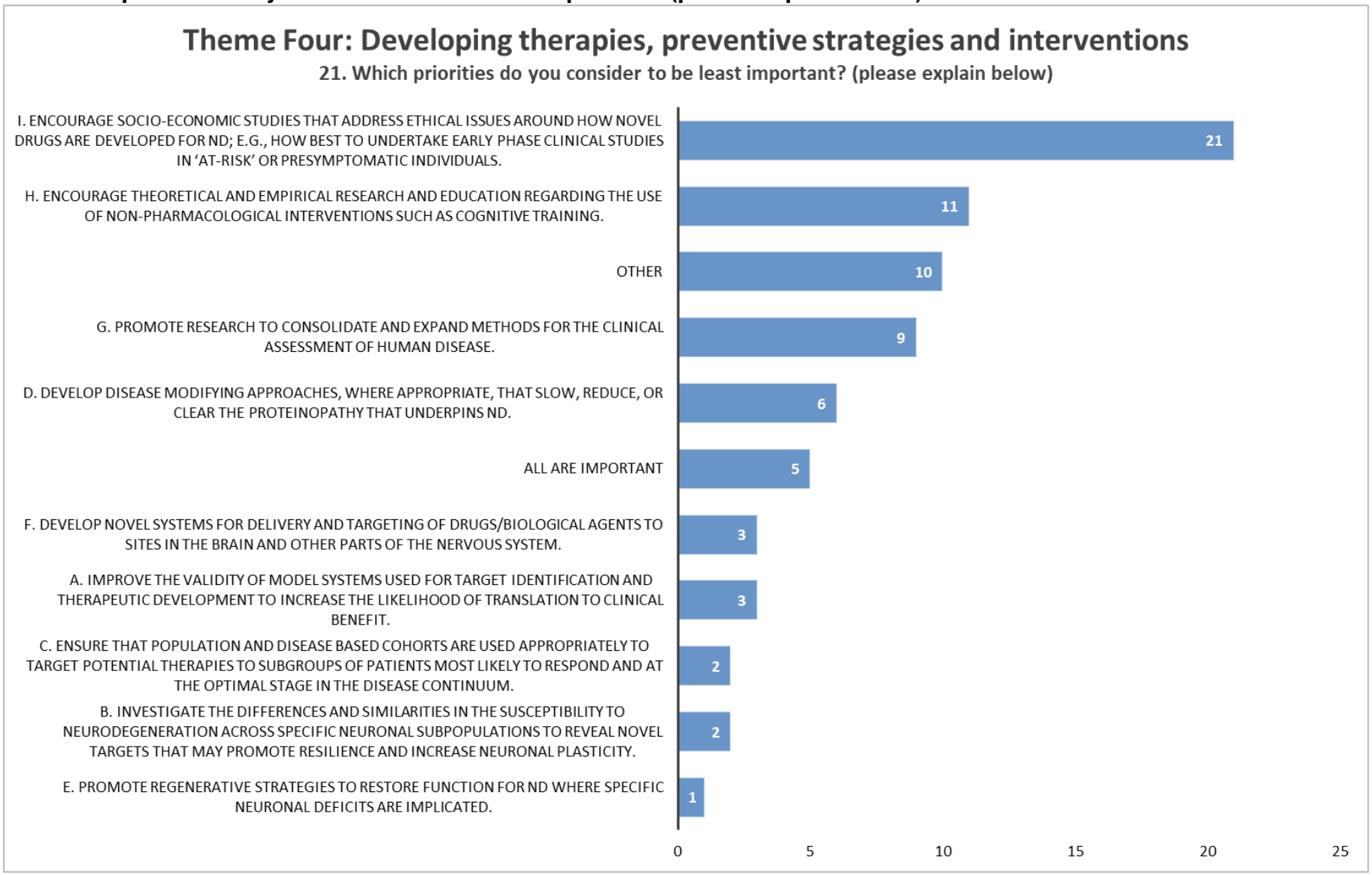
		lifestyle modifications and broader protective factors which must be considered within a socio-economic context. • Role/training of carers in non-pharmacological therapies.
Non-pharmacological – Diet	**6**	• Effect of nutrition on treatment and prevention of neurodegeneration. -Evaluation of outcome measures for trials in early stages of dementia. • Diet, in general, and specific nutrients and metabolites thereof seem to be quite overlooked, or at least not mentioned in a sufficiently explicit manner. • What is the optimal dietary intervention to slow the progression of ND?. • The existing evidence for lifestyle programs at least urges further investigation, including testing multifactorial interventions. Often trials are not feasible (event though World Wide Fingers), so better developed proxy outcomes are needed. Also, the biological effect of lifestyle modifications on disease markers as well as comorbidity (.eg. vascular brain pathology) needs investigation. Finally, best ways of public advocating of preventive strategies and risk communication need to be evaluated. See also report of the JPND meeting on Public Health in ND (Paris). • Could include use of Traditional Chinese Medicines (or complementary medicines) in #H • Prevention strategies especially, nutrition and pesticides in our nutrition is not mentioned here. How to educate populations regarding nutrition and to avoid pollutants in our diet.
Reducing risk	**4**	• The list above suggests secondary prevention for at risk groups but need also to consider primary prevention at population basis • Implement public health measures to reduced risk factors associated to ND (diet, physical activity....etc) • promote preventive measures • Investigation of novel risk factors for ND in the view of possible prevention and intervention (exercise, cardiovascular disease, hypertension).
Genetic	**3**	• use of genetic data to infer directions and effect sizes of novel treatments • Gene therapies targeting protein aggregation • I think that prevention, predisposition (including the genetic point of view) and very early signs should be the most investigated.
Drug development	**8**	• Support basic research of new drugs • Facilitate and support small "proof of concept" explorative phase I studies in selected population of patients with ND • Drug design • Research aiming at finding novel therapeutic targets involving the brain immune system. Glial cells are under-investigated when it comes to development of therapeutic strategies. In particular, much fewer studies investigate astrocytes compared to microglia. • Develop tool compounds for novel pathways recently associated with NDs

		• Consider including the development of strategies for the delivery of novel therapeutics • Make specific mention to synergistic multi-drug therapies.
Drug repurposing	**5**	• Make use of already identified critical pathways towards the development of innovative treatment approaches. • Reformulation of old drug to improve their phamacologic efficacy. • Foster research into repurposing of licensed drugs with known safety profiles for ND, Facilitate development and set-up of multinational IIT for therapeutic interventions in ND • people should be stratified according to their vascular risk and symptoms in all drug trials; trials of repurposed agents should be encouraged.
Animal models	**2**	• Since the validity of the animal or cellular models is a real problem, there is a need to support early studies in humans • Development of better preclinical methods for monitoring the treatment response.
Other models	**1**	• Encourage the creation of in silico models (eg healthy vs disease neuron network) to test potential therapies
Personalised	**2**	• Promote personalised therapies based on data from digital biomarkers with AI,ML and DL. Make J&J smarter with neurogenesis...campaign newborn neurons with exercise, MIND diet...within J&J. With low budget you could become a lot of data related to ND and J&J shall become smarter. • Personalized medicine should be added as well. Adding to this studies on alternatives for RCT for examples n=1 longitudinal studies, should be included as well. In addition, subtypes of ND patients could be defined to explain (lack of) responsiveness to interventions
Biomarkers	**3**	• Develop biomarkers that guide and predict success of interventions • identify biomarkers of early stage ND that could be use as endpoints in clinical trials • Bioinformatics data in ND for new biomarkers discovery
AI	**1**	• Alzheimer use of multivariate mathematical for detecting the causes of Alzheimer, with Artificial Intelligence and deep learning support
Blood brain barrier	**2**	• Blood-Brain-Barrier passage of drugs / biological agents
Other		• In my experience industry is better suited than academia to developing therapies. My view is that academia should focus on the discovery of disease mechanisms and potential targets of therapy, whereas actual therapeutic leads are more effectively developed by industrial-academic collaborations (e.g. the Innovative Medicines Initiative). • the ND patients suffer from many sleep problems which impact on them but also on their care person (who cannot sleep either, or is injured, or must face nocturnal confusion). In addition, the role of physiological sleep in facilitating the cleaning of the brain from abnormal peptide, as well as consolidating memory and reducing metabolic and cardiovascular risks for the brain has been increasingly recognized. It is major to include sleep research, in all its aspects

		(prevention, care, caregiver) in this JPND program, in addition to the idiopathic RBD problem, not addressed yet by the JPND. • Too many priorities. The list could easily be shortened. • IDENTIFICATION OF EARLY STAGE OF THE DISEASE, AS IN REM SLEEP BEHAVIOR DISORDER • there is a significant overlapp here with what IMI with neurodegeneration SGG can be doing, we need to synergize the two . Key for translation is also to make available rare human samples and possibly iPSC lines. Of key importance would be to validate markers that in 3 or 6 month could provide a hard measure of disease progression to enable clinical studies would need early stage patient registries • The term " socio-economic studies" is very broad and I would prefer explicit use of high impact studies such as "RTCs with concurrent cost effectiveness analyses" or "health technology assessment" or "systematic review and model-based economic evaluations" • Much of the basic data we use in ND resaerch is old. Brain maps, cellular definitions, interactions etc were all generated several decades ago. Focus in the more recent past has been technique driven. We need alot more core data. • Include patient's perspective on c • Looking for target cells and phenotypes behind aetiological risk factors and those involved in disease progressionriteria for the use oand impact of medical trials • More research on the link between neurodevelopmental dysfunction and neurodegeneration • prevention strategies (e.g. lifestyle modifications) -> what about socioeconomic factors? increase the likelihood of translation to clinical benefit -> see earlier comment about the need of a methodological discourse regarding translational research, incl. implementation science non-pharmacological interventions such as cognitive training -> by highlighting CT dementia will be seen primarily from a cognitive perspective, which ignores that at the same time there is a broad/international discourse related to relational and social health care approaches what about the 'social cognition' concept and its impact? when using the term 'interventions', it should be clear that ALL healthcare professionals develop interventions, not only medical professionals • Preclinical and clinical trials. A. in vitro models, B. small animls, C. large animals, D. clinical trials phase I, etc. • Several of these approaches (disease-modifying, regenerative, ...) should me associated with approaches allowing earlier diagnosis of ND, in order to improve substantially their potential efficiency • I think it would be good if you could add a research line to specific study the development of inhibitors of protein misfolding and aggregation • I think animal model systems have proved to be less informative than thought. Unsure how to create cohorts in a situation where diagnosis is imperfect. F will be very important in the long

		run. If mechanisms and biology underpin diagnosis then treatment of asymptomatics will be very important. • Trials with "neuroprotective" drugs in idiopathic RBD patients that represent presymptomatic individuals are mandatory • h,h, i are key along with strong emphasis on neurotrophic factors • Work with regulatory agencies to define the clinically significant benefit Define realistic incremental benefits (as it has been done in cancer) • Developing intervention and therapies strategies which included prodromal ND, including a better stratification of such patients (e.g. early converters vs late converters) • Focus on mechanisms responsible for suppression of symptom expression (resilience) as possible avenue to control of symptoms for a pathology that may not (yet) be avoided. (if not already covered by "E") • There is a need to focus on preclinical and prodromal progression, and measures of early symptoms, in populations at increased risk such as individuals with Down syndrome or with other genetic conditions, to enable proof of principle trials of treatments for prevention of NDs • Gender specific research • I think we do not have a problem with rodent animal models and their applicability to the human diseases as such, but rather with the idea to treat NDs with approaches that tackle only one aspect of the diseases, whereas NDs are often systemic diseases. • Here there are too many themes B seems specific whereas D is broad. There could be focus on immune mechanisms. I There could perhaps be integration to understand how lifestyle interventions integrate with biological mechanisms therapeutically with age- • The stated treatment priorities are too narrow. There is a need to include pharmacological approaches other than those for clearing proteopathies. More specifically, there is a need to also consider symptomatic therapies that may represent a significant improvement over the existing ones. These can benefit patients with an already severe disease within a short time frame. They are also likely to synergise with approaches requiring active patient participation, such as exercise or cognitive training. • Develop and promote adaptive designs for the early identification of treatment (in)efficacy. Development of patient-centered outcomes.

21. Which priorities do you consider to be less important? (please explain below)



Theme Five: Healthcare and social care

This theme focuses on research into the treatment, support and care of individuals with neurodegenerative disease (ND) together with their carers and families. Researchers should employ conceptually sound approaches to seek 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, and to consider comorbid conditions that often affect the delivery of treatment and care.

Within this theme JPND has identified the following research priorities:

A. Evaluate current and potential pathways to diagnosis, treatment, care and support relevant to ND globally, particularly by reference to effectiveness, cost-effectiveness and equity of access.
B. Investigate the interplay of biological, environmental, social, economic and other factors in the determination of cognitive decline and behavioural and psychological symptoms.
C. Determine the critical factors that affect disability and health-related QoL and wellbeing in ND, including evaluating approaches to better support carers.
D. Focus on a person-centred approach to care where those affected by ND are involved in the planning, development and monitoring of their own care and individual health needs and resources.
E. Promote research into end-of-life and palliative care for ND patients.
F. Investigate the ability of assisted living and health technologies to address the needs of individual patients with ND and their carers.
G. 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.
H. Conduct studies to determine how to improve access to formal care to reduce the unmet needs of individuals outside the formal care system.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

22. Do you agree with these research priorities?

22. a) Please comment on your response below

Comments
Not within the scope of the JPND program in my opinion.
These social care issues do for sure help current patients but do not give patients a perspective that their diseases will be cured at some point in the future. So I do not see that Theme Five should have the same priority than Themes 1-4.
Funds are limited, thus they should be used fully to advance our knowledge on the pathogenesis, diagnosis and therapy of ND. This in turn will by itself improve patients' well-being and care.
the problem is that most older people with ND receive very poor social care from very overstretched and poorly thought out but expensive services. there has to be a better way of looking after our older people. When did any social studies actually translate into policy change that benefited the whole country? I would like to see money spent on social research translating more effectively into better quality of life for the population as a whole.
The text is vague and weak. It avoids to recognize the huge burden of ND diseases to families and society. In many cases it is repetition of previous Themes.
by nature of dementia it is impossible to obtain meaningful data on quality of life of patients with the present methods. Thus donstream research into cost-effectiveness and Qalys can not be done in a meaningful way.
In this case, a sustainability plan for dementia care in the context of the increase of prevalence and the reduction of the population is mandatory in my opinion.
The topics above read as if compiled 10 years ago, as if nothing would have happened in the meantime. I'm missing here a specified focus on the novel care challenges faced by the MCI patient population with solid disease diagnosis. Care should be wildly different for an unspecified MCI diagnosis compared with a MCI-AD diagnosis. At the same time, the generational background and hence needs of MCI-AD versus dementia populations differ.
C. is too much detached from diagnosis, D. havn't seen yet really research on F., B. does fit better in other research themes, such as 2, 4
I think rehabilitation efforts should be stressed, which is vastly different from the construct care which applies to nursing per se. I think well-being should encompass both physical and psychological well-being. In several countries in Europé, none is without the formal care system.
I think JPND should focus on biomedical research that addresses causes for NDs and their proper

23. What would you like to see included that isn't covered in the above priorities? (please explain below)

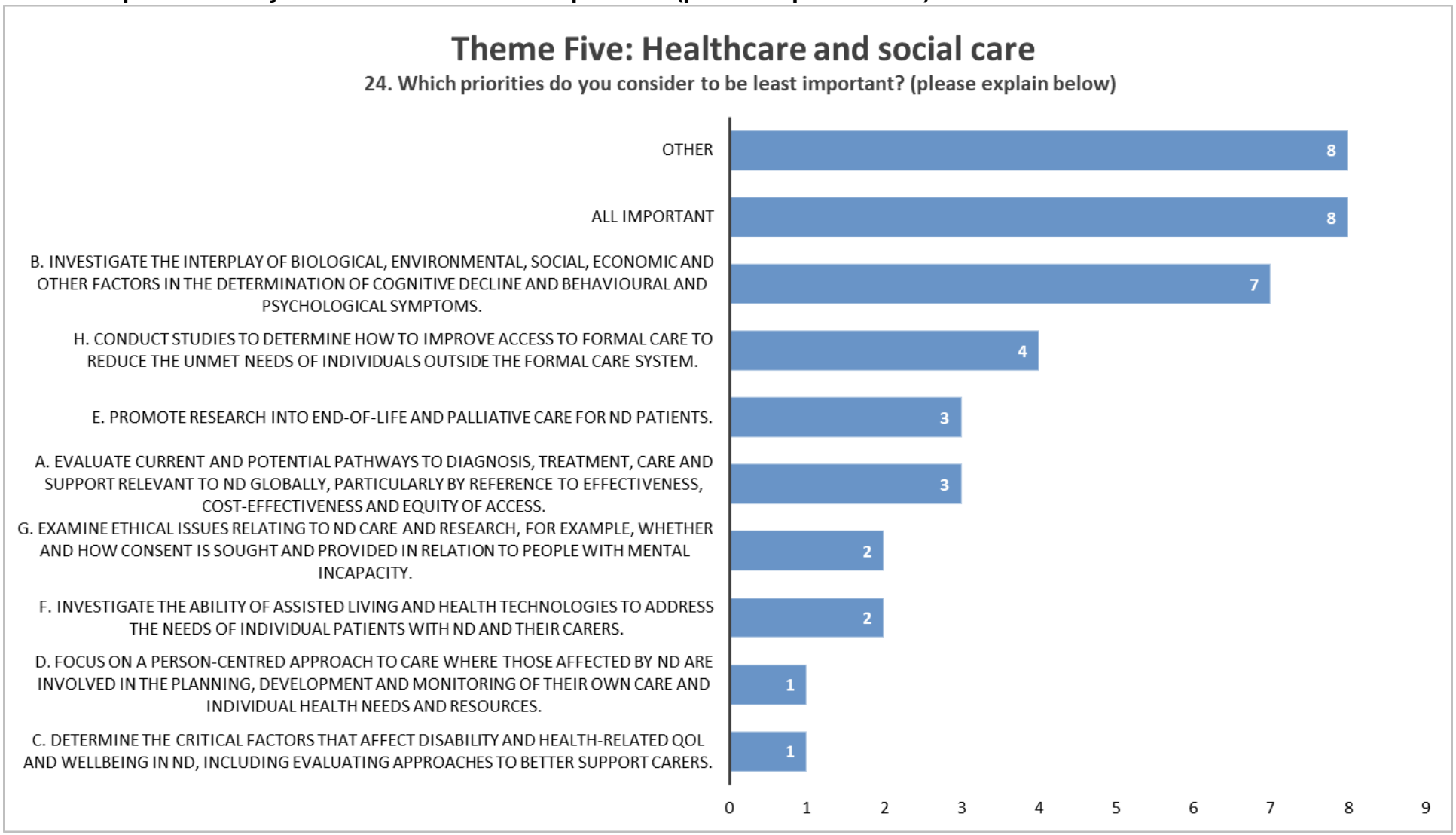
Keyword	Number of respondents	Comments
Do not like section/Poor research quality	**3**	• Extremely important, but the reality is that this kind of research of often of mediocre quality. I would agree to funding it, but the quality criteria would have to be really stringent. • I'd like to see this section removed. • I would rather shift this field of Topics to DG Sante or Horizon Europe JPND should Focus on the above listed Topics 1-8
Caregiver burden	**6**	• There should be research in the empowerment of relatives from patients with ND. In most European Countries relatives carry a huge burden in ND. • I like the person focused approach. A real problem is access to formal care which can be very difficult and costly. Another important problem that has to be taken into account is that of the informal carers and their burden. • The role of caregivers should be analysed • more attention on carers
Training/communication	**8**	• Life style interventions including training program for medical students, doctors and patients should be added as well. • Questions around how changes in community engagement and awareness (public health) enable people with dementia to live well at home and avoid/delay admission to long term care. • Dissemination of research advances to patients' associations. • one priority missed, in my opinion is the workforce in health and social care. Research regarding impact of care on health and social care workforce can be usefull in order to enhance professionnals attitude and skills in dealing with the ND burden. • Comparisons of the social care system across countries to evaluate what works best • I suggest you to focus more explicitly on rehabilitation. ND increasingly considered as a disability/a biopsychosocial condition might entail a strenghtened focus on rehabilitation, both as a guiding philosophy and as a practical framework for care. Research on dementia and citizenship is needed Research on communication and interaction is needed
Palliative care	**3**	• I am sure the most important part is palliative care, which you have stressed much to little. The only answer to euthanasia and a changed valuebase in our societies when the costs for patients with ND will increase is sound palliative care and not any biomedical research. • Would like to see priorities on : - research that explores health economics and QoL benefits of health and social care palliative care interventions - Research into assisted decision making for

		people with ND who may need support (e.g. people with dementia) specifically in relation to legislation at national and EU level and how health and social care services could provide appropriate support for people particularly when receiving palliative care services and at end-of-life - All research that addresses the identified priorities should include people with ND, family/carers and health and social care professionals in an advisory capacity on relevance and guiding the research undertaken
Technology	**4**	• Promote innovative research and development of connected tools to allow home living and increase quantifiable knowledge of everyday life issues of ND patients • Potenziate new assistive technology such as BCI, telemedicine robotic • develop pragmatic clinical trial using real world data • Determine the critical factors that affect disability in Alzheimer with use of mathematics and multivariate analysis fo understand more on its genesis
Population	**3**	• Heath care and Epidemiology have probably much to offer in following population trends and finding correlations with environmental and nutritional factors • a realistic study on a midterm sustainability plan for dementia care for EU countries. • Target population which take care about ND patients should be taken in account. No overlap of Themes should be allowed.
Person centred approach	**4**	• Focus on th eneeds of persons with dementia (and particular attention for dementia with early onset and specific types of dementia). Focus on what you can do yourself - how to maintain your own life/ live at home. With attention for e-health possibilities. • The user-involvement in developing the health and social care • Focus on a person-centred approach to care at all Level at the health-care system, e.g the developpment of "Dementia friendly hospital" and involve those affected by ND in the planning, development and monitoring of their own care and individual health needs and resources.
Cross discipline	**1**	• More of B we need to integrate across disciplines - so healthcare and social care are not considered completely separate to actual biological mechanisms of disease. D should also include person centred integration with research

Other		• Again too many priorities. Makes the proposal a bit unfocused. • maybe mention treatment of BPSD specifically • Investigate what is realistic and workable. Make it simple so that it is easy to understand for everyone. • Some pragmatic and easily translatable research • This may be partially covered by D but investigate different models of care that may differ by economic conditions including teleclinic approaches. • Development of animal models for social pathologies • Psychological and Social diagnostics has been ignored to date -yet if we don't understand the science behind how individuals their family and staff behave - and their differing needs we will never understand what works for who when and where /under what environmental an organisational system- or what does not work - and the economics (implementation economics) of this • I do not agree with the focus on QALY / health-related QoL as a major outcome as it is mentioned here, mainly b/c it relies heavenly on measures of QoL for people with dementia (difficult discourse/results/comparabiltiy / proxy etc.); b/c so far treatment strategies have not been able to show significant improvements in QALY; b/c across studies heterogeneous (non significant) results regarding the idea to 'improve QoL' I'm missing the discourse about positive outcomes, meaningful outcome from the perspective of the person living with dementia, methodological issues regarding fluctuation and self-report etc. I'm missing the stimulus to conduct pragmatic trials, stepped-wedge or SMART or MOST trials, participatory / consumer oriented research; to require process evaluation to inform implementation, what about tailored implementation strategies or hybrid designs? the discourse about 'producing evidence and therefore to implement evidence-based strategies' is not the most innovative approach and stays behind the international discourse about the need to develop / use innovative research methods what about funding of research that addresses ethical issues (e.g. capacity to consent within cohort studies; or process consent strategies; or impact on life after the diagnosis etc.) • Standardization of QoL assessment • research in the field of social care should take into account the specific professions (e.g. there is often a lack of research in the role of nurse in ND). • The Batten Disease CLN3 starts with blindness, then Epilepsy, then as very young, they will have dementia • There's no specific mention on the impact of multi-morbidities on any of the above priorities. • Standardising of care for certain disorders rather than Postcode lottery • Rehabilitation - Exercise - For example why is not activity level/performance or physical performance included in the following: Investigate the interplay of biological, environmental, social, economic and other factors in the determination of cognitive decline and behavioural and

		psychological symptoms. - - Importantly, when grading the evidence for exercise in people with PD, most studies have had cognitive imapirments as an exclusion criteria. Moreover, phsycial functioning should also be included. • I think better connection between these and theme 4 is needed • ompare care models for different ND • this part is very diverse and not very specific, G: important issue regarding research, treatment and end-of-life decisions, but also varies across different ND in its problematic, needs to be specified more • Anticipating on future needs,wishes and scenario's • Priority B should be updated to include 'physiological' factors as in the case of Parkinson's for instance. • mong other priorities that could be included would be: a focus on stigma reduction, building health systems that have capacity to meet the needs of people with dementia, implementation research, the use of non-pharmacological treatment • The list of priorities seems to me, again, excessively comprehensive. Despite that all aspects have relevance, I would make a further selection. Some priorities are too dependent on geopolitics or too philosophical: cost-effectiveness, equality, QoL, health resources, ethical issues and mental capacities • Conduct studies on innovative intervention. Conduct studies on enabling intervention. We are trying to find part time job for people with dementia. It is amazing to see the positive effect from people with dementia and the family carer. I believe there are more amazing and innovative intervention in the world.

24. Which priorities do you consider to be less important? (please explain below)



Enabling activities

Theme One: Supportive infrastructure and platforms

This theme focuses on 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 advances in computational power and intelligence and increasing recognition of the strength of effective research collaboration and partnerships.

Accordingly JPND should seek to:

A. Encourage integration and harmonisation of data and materials and promote an open-access approach to sharing and pooling of data and resources.
B. Establish standardised methods, platforms and tools for data collection and analysis.
C. 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.
D. Provide coherence to the global investment in cutting-edge but high-cost areas, such as proteomics and computational biology, to establish centres or networks at the national or international level.
E. Ensure wider access to high-quality biomaterials (e.g. brain tissue, from ND patients and from age-matched controls) provided through biobanks.
F. Link and better exploit existing cohorts, patient registers and sample/data collections.
G. Establish national and global registers of people with both common and rare forms of ND.
H. Promote registers of patients with cognitive impairment, with minimum requirements for entry, to reflect real-world situations.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

25. Do you agree with these research priorities?

25. a) Please comment on your response below

Comments
To my point of view, JPND should better support research projects with a clearly defined role than plateforms or harmonizations of methods that could be generally done without this support and/or not just dedicated to ND
This strategy will lead to the point that current centers will grow within themselves but does not help to ensure the access of the scientific community to this infrastructure.
Investment in computational biology is welcome, however rather than establishing more dedicated centers for computational biology, of which there are already many, it would be better to a) embed computational biologists within experimental neurodegenerative research teams and b) provide more support for computational modelling within neurodegenerative disease research institutes. This would encourage greater interaction between experimentalists and computationalists and increase the impact of computational modelling on neurodegenerative disease research.
This is an ill-defined list of generic measures. Again, funds should be saved for scientific research, not organizational matters or ill-defined priorities.
DO NOT Establish national and global registers of people with both common and rare forms of ND if this is NOT embedded within an ethical discourse (society) and a clear defined intention. BE aware of WHO will use this information for what kind of purposes. NO way: Promote registers of patients with cognitive impairment the list above sounds like: do whatever might be possible WITHOUT considering its impact on society, the person affected by the disease of the professionals who interact with these patients and their families. I do not see, that there is a program that address the 'impact' of theses ideas on our health care system and which supporting interventions may be needed
Too much of a top-down approach draining money from creative bottom-up approaches
what is missing: critical reflection on existing hurdles regarding data harmonization and also ethico-legal issues related to usage of patient data/registers etc.

26. What would you like to see included that isn't covered in the above actions? (please explain below)

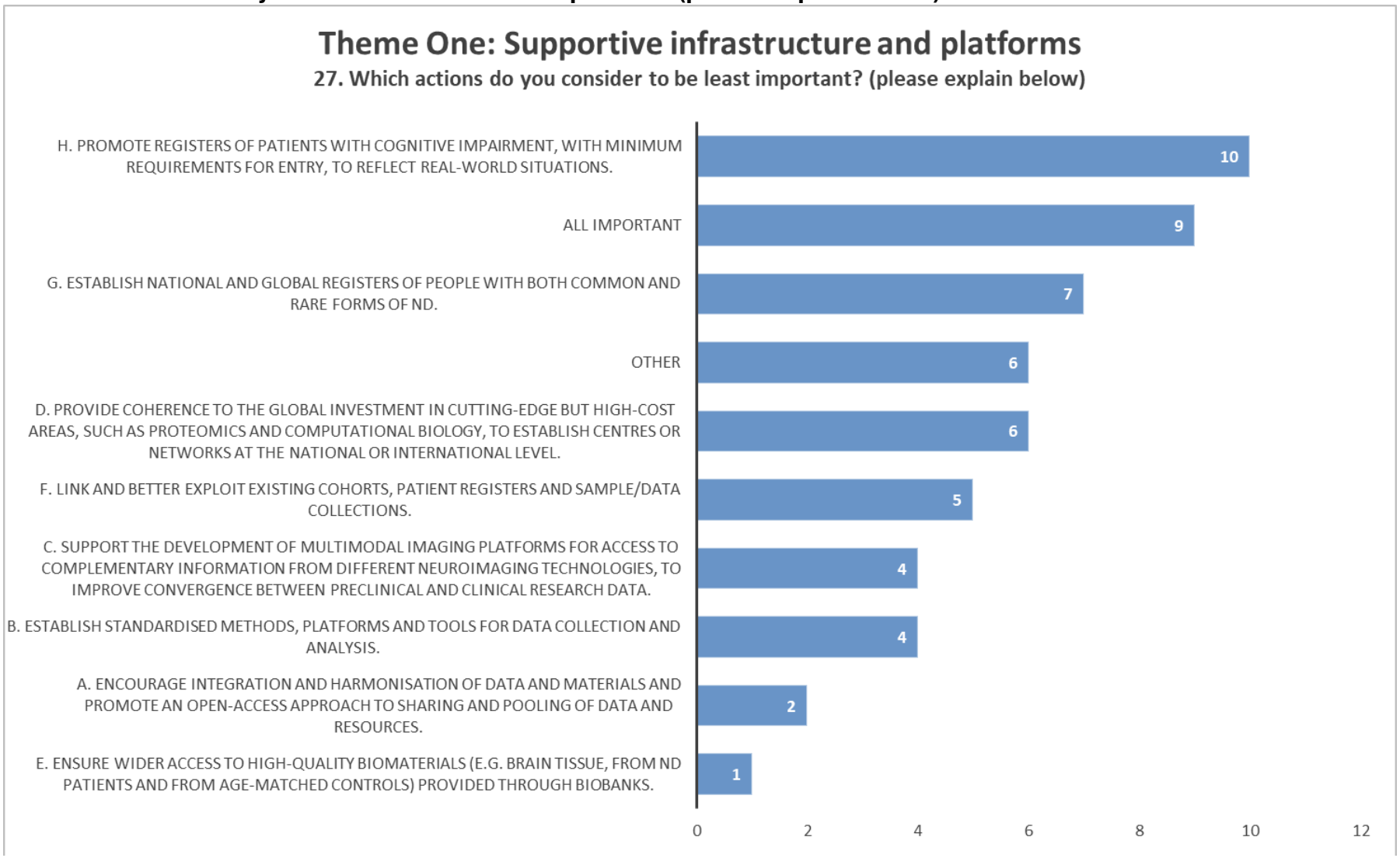
Keyword	Number of respondents	Comments
Promotion of open access/open science	**12**	• Re A: may be JPND could oblige every beneficient to place the results in the open repository? • given push for open-access accept pre-print publications in grant applications • I think that open access and other best practices for open science should be not only promoted but actually enforced. • Promotion of the access of the scientific community to already existing infrastructure. • Establish networks of researchers sharing the same interests • support an open access data sharing Platform worldwide with realworld patients data. • Actions to promote unbiased publishing, i.e. pressure and encouragment to publish also negative results. • I suggest being more explicit on point F. Data collection should include accessibility to industry databases on published trials • Open to all scientific Community, not only to particular groups in big centers. • Direct support for the development of standards and best practices that enable data sharing in terms of metadata and infrastructure • All research should be published using Open platforms. • As noted under theme one in the scientific priorities, there is potential to enhance existing cohorts and datasets through linkage of routinely-collected administrative data, and this would benefit from a culture of data sharing and standardised methods.
Data mining/AI	**2**	• I am not sure if priority B would cover this. But one of the problems for data analysis, especially when talking on meta-analysis, is the quality and relevance of data. Efficient methods of data mining are much needed, in order to cut out a vast amount of "unuseful" data, and also help to more efficiently channel resources to what is important (whatever this is) • Develop AI understanding of the patterns of the diseases. Registration cannot be an objective in the area of digitalization.
Data protection regulations	**5**	• what about privacy/ data protection / who has access to which data, when for what purposes? • privacy as for STDs... • What about the conflict between open platforms and sharing data contra Data protection and security? • Establishment of a JPND Network wide data privacy protection concept, which acknowledges the specific needs of the different participating countries

New repository	**11**	• To start decoding in a comprehensively/integrated manner the DNA/EPigenome from all ND cases avaiables in Europe ASAP • Specific promotion of genetic and epigenetic platforms and registers. The cost of storing, maintaining and analysing whole genome sequence data is huge, and not easily sustained by individual research groups. National and international infrastructure is needed so that the millions of research funds invested in this technology can be used most effectively. • Network for early drug/biomarker development (common imaging, EEG, neuropsychological evaluation methods and homogeneization) • Anticipation of change - how to incorporate new methodologies into existing cohort studies without abandoning valuable longitudinal data. Also, newer methods for analysis and modeling of epigenetic data across cohorts. Also, aggregation of data from individuals with post mortem verification of pathology (i.e., MRI, biomarkers, cognition from now-deceased patients with dementia) would be helpful for many projects. • Creating registers is a very difficult business. Much better to keep data where they are initially collected and stored - the hospitals - and then interrogate them in a distributed manner. Novel informatics - the relationship between medicine and informatics is largely underdeveloped and yet Googl ena Amazon among others are very keen to exploit medical data Cooperation is needed • proteomics and computational biology are important and expensive. This should be extended to other fields, such as imaging and clinical studies. • Importance should be given also on the establishment of neurophysiologic datasets (EEG in particular) that are easy to collect and provide valuable information. • Provide support to create a bank of relevant iPSC from patients that can be available to researchers • Registers of patients to understand the real world situation are important, but it is necessary to have an automatic system in agreement with hospitals, for both visits and recovery. The problem is that there are many situations in which the patients are not registered appearing a low prevalence, but the illness is present even in high percentages • a collection should reflect the complexity of the factors influencing disease onset and progression and should not be limited to biological or cognitive data but should include data regardng life style, psychological and social aspects • Establish centers or networks on development of patient-derived neuronal and non-neuronal cell lines.
Animal model repository	**3**	• create tools facilitating the appropriate models to research

Education	**5**	• Tools to educate Ethics boards on the importance of inclusion of those with cognitive impairment in research studies and processes of consent for those with cognitive impairment • Engage medical doctors in the activities proposed as they are essential to attain many of these objectives and are often overloaded in the clinical practice to commit to these programs. • Promote better integration of traditional scientific approaches with the social sciences. • Education & knowledge transfer are things which need to be better, deeper and wider understood. Cutting edge technologies & progresses should be better and more often vulgarized.
International collaboration	**7**	• There is no mention of working effectively with other organisations with similar goals. No mention of sharing of negative outcomes/issues of reproducibility. • Linking of research on socio-economic and ethical aspects across initiatives and countries, to enable ongoing learning rather than individual projects starting again from scratch • link more to existing international infrastructures from JPND projects and data • These themes require a Hugh amount of Money and can only be established with a Joint effort of DG R§D, DG Connect and DG Sante and DG Growth, may be with IMI • Establish national and global registers of people with both common and rare forms of ND with Alzheimer disease. • link and better exploit existing databases at the EU level but also where possible globally
Other	**16**	• in E generation and availability of lymphoblastoid cell lines and potentially banked fibroblasts from subjects with genetic characterisation (genome-wide genotyping or sequencing) should be attempted - these can be hugely valuable. For G the Enroll study in HD is a great example of a global register. • "Bona fide" scientific research. • Create new homes for eldery near J&J Labs to investigate and to do research in real-world situations. Eldery people can living for free... • Some more emphasis should be placed in rare forms of ND, such as for instance multiple system atrophy • Again, we should demand redefinition and testing. • More emphasis on people with young onset dementia • for A and B, build on existing coodination/standardisation efforts at national levle (like CATI in France) and expand across europe E and G are very much part of theme4 • Include prodromal ND in the harmonisation process • Points E-G should be given higher priorities • Point D - I would include metabolomics • Try to align with existing initiatives (EMIF-AD, DPUK) rather than develop novel ones

		• In the following point, the exclusive emphasis on multimodal imaging is somewhat puzzling: "C. 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." Convergence between preclinical and clinical research data is not dependent on multimodal imaging technologies. For example, the resolution of in vivo brain imaging technologies is not good enough in small animal models of disease. • Assist countries in the EU to influence their governments to increase prioritisation for ND research nationally - • Support development of complementary molecular platforms tailored to addressing ND mechanisms

27. Which actions do you consider to be less important? (please explain below)



Theme Two: Working in partnership with industry and fostering innovation

Many different commercial organisations engage with ND research, ranging from 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 and commercial domains is essential to deliver novel approaches to diagnosis, treatment and care. There are also opportunities to bring innovative and targeted products to market through partnerships with small and medium enterprises with expertise in specific areas. Effort is needed to:

A. Facilitate high-quality 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.
B. Promote innovation within a multi-partner international funding framework by fostering a risk-taking approach and streamlining the pathway to accessing and exploiting innovative discoveries.
C. Develop approaches to give companies visibility and access to science opportunities emerging from academic research at the earliest stages, fostering co-development of innovation across sectors.
D. Foster a genuine collaborative culture with and between industry sectors, reflecting the emerging trend for industry to conduct less discovery science in-house.
E. 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.
F. Continue collaborative, academic-industry partnerships for system level approaches to the study of the taxonomy of ND and for the development of new pharmaceuticals.
G. Encourage data and resource exchange between industry, clinical centres and academia, on both science and regulatory issues.
H. Support knowledge transfer between sectors, encouraging secondments and people exchange alongside development of shared campuses to support innovation.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

28. Do you agree with these research priorities?

28. a) Please comment on your response below

Comments
There is a paragraph missing regarding publishing and IP rules. It cannot be the case, that university groups just supply industry with results and ideas and have nothing in return!
to many words to explain simple thing - supporting collaboration between academia and industry. Technology transfer has clear steps and these should be addressed here.
This theme does not need any extra support as is already quite healthy.
Too political statements. Pretty impractical in my opinion
unclear how public money invested will be paired by industry, problem of patenting and intransparency, - this sections jeopardize various "research" goals, should be better separated as extra initiative
Make sure that academic independency is retained, it is difficult even without input from commercial partners
Partnerships between academia and industry are no good by themselves but should be encouraged where appropriate. The currently forced marriages are not per se promoting good science. G. This should be clearly bi-directional then.
The objectives are useful but there is a lot of overlap with the IMI programme here.
Need to encourage appropriate TWO WAY industrial linkage. Academia is not industries R&D department

29. What would you like to see included that isn't covered in the above actions? (please explain below)

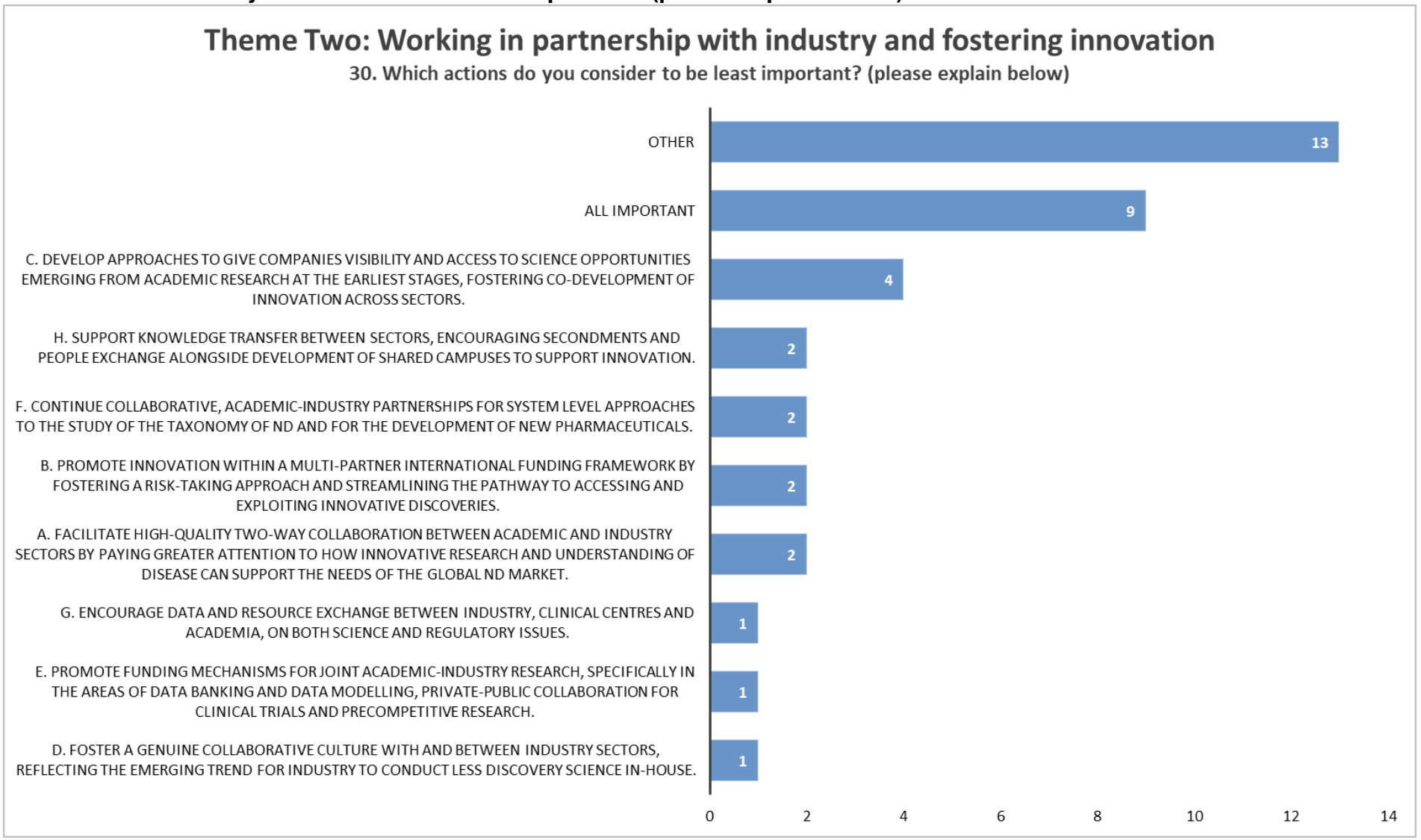
Keyword	Number of respondents	Comments
Avoid overlap with IMI	**2**	• D and E are generally overlapping with IMI efforts, JPND and IMI should be better coordinated • but avoid overlap with IMI.
Industry not interested	**2**	• I'm not convinced that industry is as willing to share valuable data and methods. • My gues is that industry calls the tunes
Other ideas for promoting collaboration	**17**	• There are a lot of pious aims listed - the ones that may deliver are those that encourage major academic and engineering/informatics collaboration (not small projects) Get politicians to resolve these issues with major agreements and incentives - public health is a very political issue. • Promote swarm intelligence. There are enough technologies to work together whole over the world. Complex diseases like ND have the best results with swarm intelligence. • Addressing valleys of death in translating idea to product/service. Innovation transfer to industry. • Encourage industrial support for IITs in drug repurposing for rare and frequent ND • industry sectors -> if health CARE is meant as well than the word 'provider' should be added (specifically since we are heading toward participatory / consumer oriented research) Continue collaborative, academic-industry partnerships -> research to increase the mechanism/function/application of translational research is needed NOT only for for the development of new pharmaceuticals, BUT also within fundamental/clinical/healthcare and health service research Support knowledge transfer -> assuming knowledge circulation/ dissemination is meant here (knowledge transfer is an 'old term') I'm missing funding for implementation science / research projects (e.g. large scale implementation) • These above statements are boring me. They are too political from my point of view and pretty impractical. A real project-driven collaborative translational research fueled by real investment and fair IP sharing is the only interesting scenario to boost public private cooperation. • Very important: Encourage data and resource exchange between industry, Clinical centres and more • Funding of novel and innovative therapeutic approaches! Aligning interests of academic and industrial researchers in 2-way partnerships. • Some form of enciouragement for the industry to interact with researchers in poorer areas instead of focusing almost exclusively on already well supported research centres in rich areas. • what about the companies motivation as they want to earn from their products contra researchers motivation for knowledge production?

		• taking into account the differences in rules and regulations for partnership with industry with different MS. Stimulating Private Partnership is important • There need to be clearer mechanisms for ensuring long-term public benefit from public-private partnerships - not just supporting the ND marker, but also supporting the sustainability of social healthcare systems • Due to their current large profits of the Pharma/Biotech industry, finding mechanisms to promote their participation in research which does not necessary aims for innovation from a commercial point of view, but which would improve the possibilities for drug development, e.g. research on non-patentable compounds. • Likewise integration of EU countries which have excellent industrial pernerships with those that do not. • Create a general fund supported by pharma companies to support independent research on neurodegenerative diseases • More collaboration between academy and care home industry. • Foster a genuine collaborative action for Alzheimer with economic, industrial, neurophysiologists and mathematics, for the first real understanding
Mention SMEs/startups	**3**	• Co-funding of academia and industry should be restricted to small-and-medium enterprises (SMEs) • The list is not very precise with very general statements: for example, if an accademic is starting its "start up": can he gets money from you to further develop its new drug? Is this under A) or rather E)? • Develop mobility between academia and industry Also consider SMEs
Require applicants to have an industry/private partner	**2**	• I hope basic research also will be encouraged and you will not impose the obligatory condition to have a conection with indutry.

Publication of results	**3**	• Securing publication regardless of results - to combat the current publication bias. Focus on the reliability and validity of research and on if results can be reproduced. Developing research guidelines securing a better reliability and reproductability. • A timely access of industry data to the academic field is important.
Other		• eHealth inclusion • Industry are not always interested in working on areas of highest priority to people with dementia and now they have huge power to set research agendas. we have seen a huge race towards supportive technologies for people with dementia with very little return. At all costs technology must be in service to the research agenda and not the other way around - the pendulum has already swung too far in the opposite direction. • Regarding patient's QoL in drug develop between academic and industry fields. • Facilitate the work with Industry on pre-BD stages, including the idiopathic RBD stage, which may not interest the industry (which often wants rapid results) because of changes over 5 years. • Intellectual protection of new therapeutic strategies deriving from academic research to ensure future access to the patients • Validation of data from preclinical models in human tissue and materials should be supported. • Academics need to publish their work to thrive; industry prefers to patent innovative findings that can be used to develop novel therapies; therefore for industry publishing id detrimental. Academics collaborating with industry must be acknowledge for their work in collaboration with industry, even without publishing. • Better animal models are required to further satisfy industry needs • Many of the roadblocks here are local. How can JPND help increase knowledge translation by navigating all the legal and agreement files involved? • Just always hesitant to engage industry at too early a stage • collaboration with indunstries should not be at the expense of the development of basic/translational research • A joint platform to encourage inter-connectivity between professionals, researchers and other stakeholders. Information is key, but also the speed at which information travels. We need to be better prepared for the future. • Point H is the most important up to me: knowledge transfer and people exchange is not always easy • Accompany researchers with intellectual property • All actions are fine, but JPND support should not be limited to these partnership studies. • Build transdisciplinary research teams.

		• Would like to see a research priority that promotes research that collaborates with enterprise to allow person with ND to stay of place of choice especially when receiving palliative care services and at end-of-life

30. Which actions do you consider to be less important? (please explain below)



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. Maintaining the highest standards of ethics and governance will promote public confidence, as will the provision of up to date and clear guidance.

The following actions are needed to facilitate translation:

A. Promote interactions between researchers, clinicians, industry, patients, carers, families and regulatory organisations to inform key data collection and study design considerations at the earliest stages possible.
B. Promote the standardisation of procedures around the control and consent of patient data.
C. Work with regulators to integrate patient preference and patient-reported outcome information into all relevant stages of research and therapeutic development.
D. Re-examine research governance and regulation in relation to the unique aspects of ND; e.g., concerning studies in presymptomatic individuals.
E. Ensure that regulatory guidance is aligned with financial incentives and the practicalities of designing rigorous, definitive and statistically powerful clinical trials.
F. Encourage the acceptance of alternate trial designs where appropriate, optimising the use of resources and reducing the time to trial completion.
G. Promote the creation of support networks, public/private consortia and/or portals or hubs to disseminate best practices in regulation.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

31. Do you agree with these research priorities?

31. a) Please comment on your response below

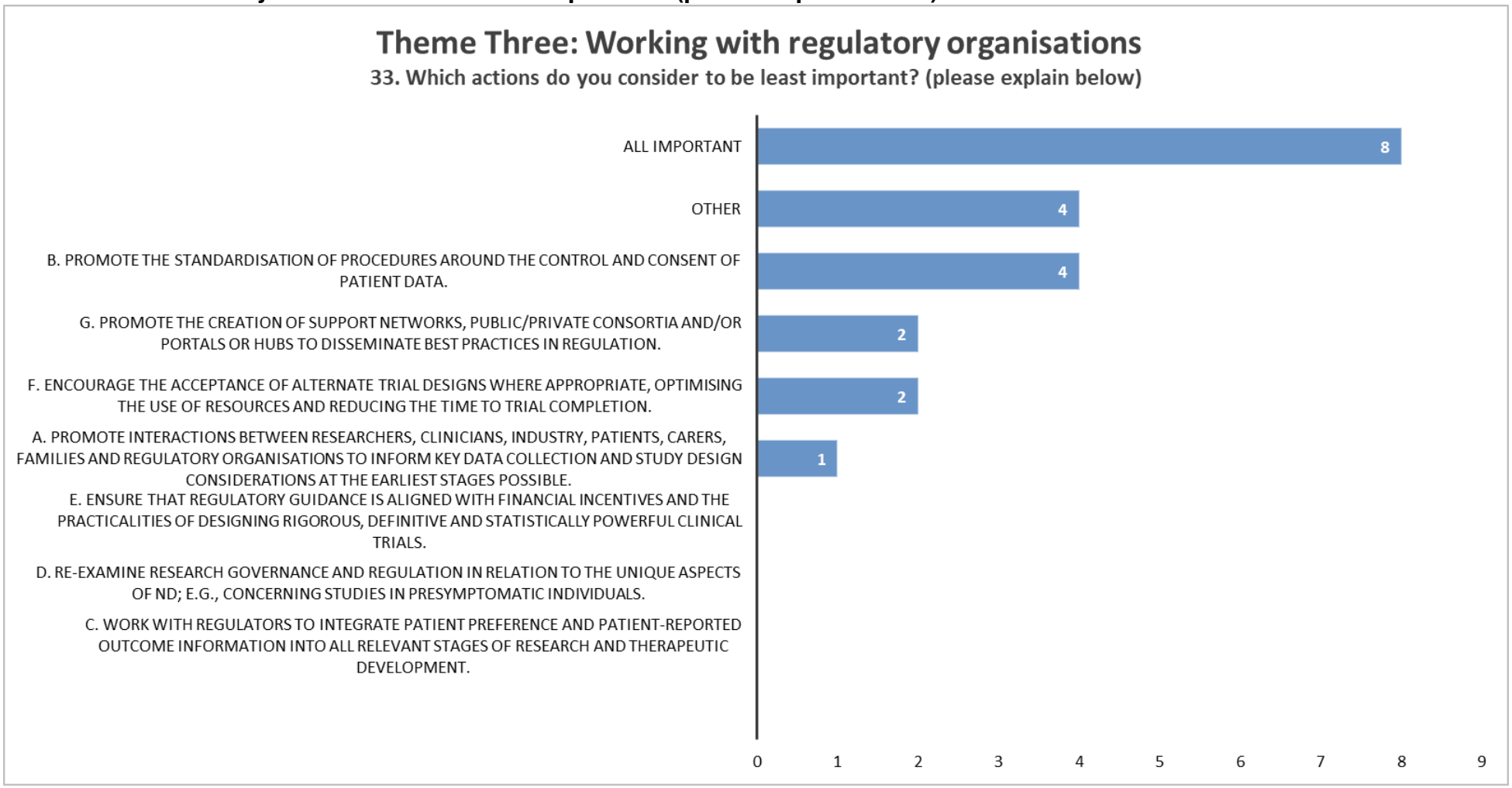
Comments
Too early engagements are contraproductive when they consume too much time. Another 'trend' that may disappear again.
Theme 3 does not cover approaches how regulatory procedures can be simplified and abolished but seem to promote more the establishment of even more regulations.
many aims sound repetitive or even legally unrealistic (e.g. Eu wide standardisation of consent)
This is a very time consuming and tedious process and should not be covered by JPND. Central organisations such as the academic professional societies should deal with these issues such as the EAN, EPA, EBC, FENS
We need less regulation not more. To use secondary data in the other aims if these things are created as above it will be impossible.

32. What would you like to see included that isn't covered in the above actions? (please explain below)

Keyword	Number of respondents	Comments
Standardise regulatory processes/reduce bureaucracy	**10**	• reduce the burden of regulations++ (we now need special "administrative" people to write EU grants. This is not how I see a grant application. - allow rapid, futility trials • Theme 3 does not cover approaches how regulatory procedures can be simplified and abolished but seem to promote more the establishment of even more regulations. • the reality is that clinical trials are a nightmare from a regulatory perspective - anything that can be done to streamline these and make them easier for patients and trialists would help. too much beaurocracy. • Reconcile differences in regulatory processes between different national requirements. • Decreasing bureaucracy of clinical research • Provide guidance on the conduct of international IITs - too much time goes here into set-up and problem-solving, because even experienced researchers and CROs do not oversee the administrative obstacles of such enterprises • Regulatory agencies need to be educated to smooth regulatory pathways for CNS neurodegenerative diseases. • It's not clear if the above priorities include working to harmonise the viewpoints of different regulators (e.g. EMA, FDA, PMDA, MHRA if it diverges from EMA post Brexit). If therapeutics are found to be effective in 'at risk' populations data protection/IP regulations may need revising to accommodate the very long trials that will be required to demonstrate efficacy. • Integration of the priorities in the procedure of JPND and particularly creating the preconditions in a multilateral context.
Database/clinical records alignment	**2**	• Build strong foundations of research useful clinal records and everything will follow • Work on procedures to share and access patient data from healthcare providers for scientific studies.
Negative data publication	**2**	• would like to suggest that results of trials should be shared even if with negative results. Also the nnouncement about results should be under regolatory organizations since it can induce a false hope in patients and families. • The pressure and encouragement to combat the heavy publication bias on under-powered positive results and hide solid evidence of negative results should be one issue on the list.
Other		• genuine attention paid to juvenile and rare forms of NDs that can get forgotten • Standardise rules and radiation safety requirements for conducting imaging studies with radiopharmaceuticals in Europe • Again swarm intelligence shall create possibilities on opportunities in a "thinking ouside the bow" - way.

		• The action # D (Re-examine research governance and regulation in relation to the unique aspects of ND; e.g., concerning studies in presymptomatic individuals) is crucial • use complementary and traditional medicines • E. and F. should be a priority having in mind that we are pretty unsuccessful • Design of new clinical trials covering the specific needs of ND. This is of utmost importance. • Exploring mechanisms for making pilot studies mainstream • Patient advisory boards should be part of all scientific programs • NGOs and their role not mentioned. • Be responsive to the time and complexity inherent in human studies of chronic disease development. Consider to protect investment in mechanisms for longer term development. • Point A is every important. • Create (inter)natonal user/client panel(s) that provide(s) input into (and 'judges') JPND-funded projects. • Integration of these actions in the calls is necessary • Involving the users in the implementation process • A fast-track for various ND disorders should be jointly promoted at the level of transnational stakeholders. • In EU, 28 MS enhance involvement in consultative/regulatory bodies within the EU framework HTA • Action of evaluation of cooperation of industry in the healthcare

33. Which actions do you consider to be less important? (please explain below)



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:

A. Utilise resources and infrastructures outside Europe; e.g., connecting with large-scale initiatives that provide access to major genetic or epidemiological samples, datasets or emerging technologies.
B. Promote alignment with groups collecting data relevant to ND research, such as the World Health Organisation's Global Dementia Observatory.
C. 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.
D. Widen our understanding of how cultural differences affect the management of health delivery and social care.
E. Promote closer global alignment of patient and public involvement (PPI) and ethics activities.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

34. Do you agree with these research priorities?

34. a) Please comment on your response below

Comments
The strategy seems to support the interaction between larger centers (which may already cooperate anyway) but does not target the interaction of smaller centers or individual researchers.
Same as previous page. Only point "C" of the above list is relevant and should be promoted.
These sounds for me too much blabla. The topics mentioned here are so diverse, there appears to be no concept here!
I guess that resources and know-how available within the EU scenario will suffice
I believe that a priority should be to create a meaningful alignment in Europe first before engaging large scale initiatives outside Europe. In other words it is not just how many but how properly you manage datasets.
This is the very last step if the tasks of diagnosis and treatment are solved. right now it is of less importance and should not drain money from more important research areas
PPI involvement is or perhaps should be more local. Alignment may generate barriers
To make this a theme on its own is not relevant. The best way to promote international partnership is to make it easier for JPND to include partners outside EU.
I am worried that some of these activities will be a waste of resources

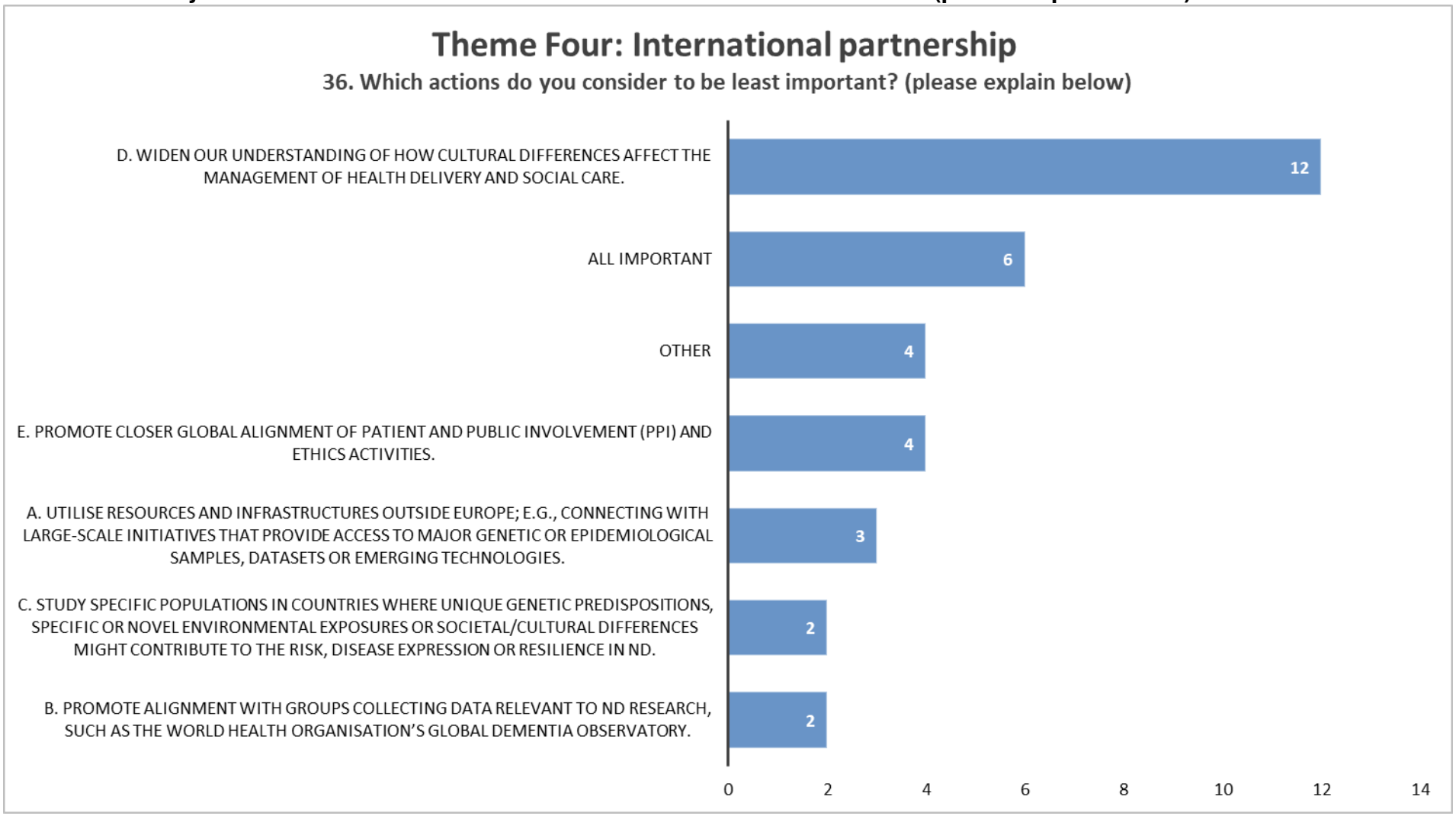
35. What would you like to see included that isn't covered in the above actions? (please explain below)

Keyword	Number of respondents	Comments
Share data	**3**	• create opportunities to collaborate and share data across boarders • Advocacy at the regulatory level to ensure that data can be exchanged between Europe and the rest of the world.
Collaborations – joint grants	**7**	• open JPND for collaborations with US, China, Japan and others matching grants - may be this is already possible and I missed this. Cooperation with Canada is already possible • nternational engagement is obviously going to be very important. Could your strategy also have a role to promote international funding opportunities to your UK researcher network where relevant, perhaps also promoting/influencing researchers to apply for research into JPND priorities through international funding programmes? Promotion of global alignment of research priorities might also be a priority similar to the priority E of promoting alignment of PPI and ethics activities. • Regarding funding for research, it is a lot more difficult to obtain funding for collaborations between Europe and the US. It would be very beneficial for grant agencies from both countries to facilitate providing grants for these international collaborations. Due to increasing reliance on multi-center neuroimaging data, it is necessary to make funding for international collaborations (between Europe and outside of Europe) a lot easier to implement in practice. • Support the international interaction of individual researchers. • Please do not limit the number of partners participating in a project. • Promote funding for pre-clinical/clinical research projects between European Research groups and non-European groups. • Develop partnership with IMI
European focus	**6**	• Point A is important, but to work with this in Europe is important • E: promote is nog enought, it is essential! • Ensuring free movement of researchers, funding and data across UK borders post Brexit. • Making funding easier for international research collaborations - the current JPND processes seems unnecessarily complicated and with too many demands for number of countries, spread between different health care systems etc. Possibly keeping good researchers from investing time in the calls. Focus should be on research quality and novelty + reproducebility. • Stimulate collaboration within Europe as well.
LMIC	**3**	• Specific inclusion and mention of low and middle income countries and the opportunity for partners from these countries to be included in JPND applications. • Evaluate the impact of poverty in developing ND • Helping to get access to Dementia knowledge networks to low GDP countries.

Russia		• Reach out to the east, particularly Russia
Form international partnerships	**7**	• Repetitive now but tI hink there should be specific funding to establish better international partnerships b/w countries that are investing prioritising ND research and those that are not – • Utilise resources and infrastructures outside Europe and in particular in China and Africa, as sources of new data useful for improvements • Focus on partnership outside Europe only where Europe "is not enough" (topics with less priority, when necessary to include larger sampling) • Other groups collecting data related to ND research include the US National Institutes of Health (NIH) funded Alzheimer's Disease Centers (ADRCs) and Vascular Cognitive Impariment and Dementia (VCID) initiatives. It may be helpful to specifically mention these groups as they are large resources outside of Europe that would be important to synergize with. • Investigations of traditional medicines in eg Africa • Include mediators for international collaborations with sufficient experience from each participating country • Promote collaboration with under-represented countries that will act as a research foundation for the future, and to improve healthcare delivery
PPI	**5**	• elop tools for interaction on equal levels for patient and careres and researchers in order to enhance the PPI in all research Projects. • PPI is essential in order to be successful in the uptake of the research results. it therefore shouldn't be promoted but be as an essential part of the JPND procedure. To focus on the different SRIA scientific priorities / enabling activities it might be helpful to share out these priorities among the JPND member states in order to utilise the budget of the member states efficiently and to ensure a maximum return on investment in ND research • Patient groups/associations should be able to be included in the call as regular partners and have a budget attached to their contribution. "Everyone" wants patient input and contribution but "no one" wants to budget for it and pay for our time. • Would JPND make section E available to public to help advise on public involvement?? • some link to patient associations
Other	**11**	• A-C very important • Keep in mind that smaller consortia are usually more effective than large consortia. • I don't know, the larger the scale od the studies the bigger the difficulties in obtaining reliable data. • Allow second rounds of funding for ongoing projects (more effective than solely funding new projects) • Being the environment probably an important factor probably also influencing the genetics, I would direct the majority of the efforts toward european studies and a minority to specific

		populations in countries with unique genetic predispositions (which might be very different from our genetics) • Expand D to include our understanding around stigma and fear of receiving a diagnosis of ND, specifically relating to life-limiting dementia, Motor Neurone Disease and Multiple System Atrophy • Promote also meetings and congresses • Improved understanding of cultural, dietary, and other differences in determinants or risk factors for ND. and Establish clear goals for public involvement. • Get international standard clinically useful phenotype collection for research and everything else follows

36. What would you like to see included that isn't covered in the above actions? (please explain below)



Theme Five: Capacity Building

Across all three research domains of JPND there are certain areas that lack capacity and need to be strengthened to ensure future opportunities can be realised. Approaches to capacity building already used within JPND countries or internationally should be shared, with a view to identifying approaches that might be adapted to the specific needs identified below.

Accordingly, JPND needs to:

A. Encourage research networks across and between disciplines and researchers, both within individual countries and internationally.
B. Improve the training of clinical researchers, and translational specialists and ensure that their role is recognised and sustained.
C. Promote a culture of open science, data sharing and dissemination between global initiatives and teams developing resources for ND research.
D. Increase the numbers of neurodegeneration researchers, especially those with expertise in health economics, public health surveillance, statistics, computational biology, bioinformatics, electrophysiology and disease model development.
E. Support interdisciplinary research within existing frameworks and build new alliances across science and other research areas (e.g. physics, engineering, artificial intelligence).
F. Promote capability and improve the quality of digital technologies and devices (e.g. wearables) in terms of patient monitoring, risk prediction, diagnosis, clinical trials and treatment in large populations.
For further details on the above points please see the full version of the JPND Research and Innovation Strategy by clicking here.

37. Do you agree with these research priorities?

37. a) Please comment on your response below

Comments
Same as previous pages.
I believe that improving training is outside of the scope of the JPND. Training of the next generation of scientists is critical and would deserve a dedicated programme.
This kind of effort to create networks and interdisciplinary collaboration from above will not promote research on NDs very much. Much better return for the investment would be to give more funding to high-quality research programs. They will included all these aspects without external guidance.

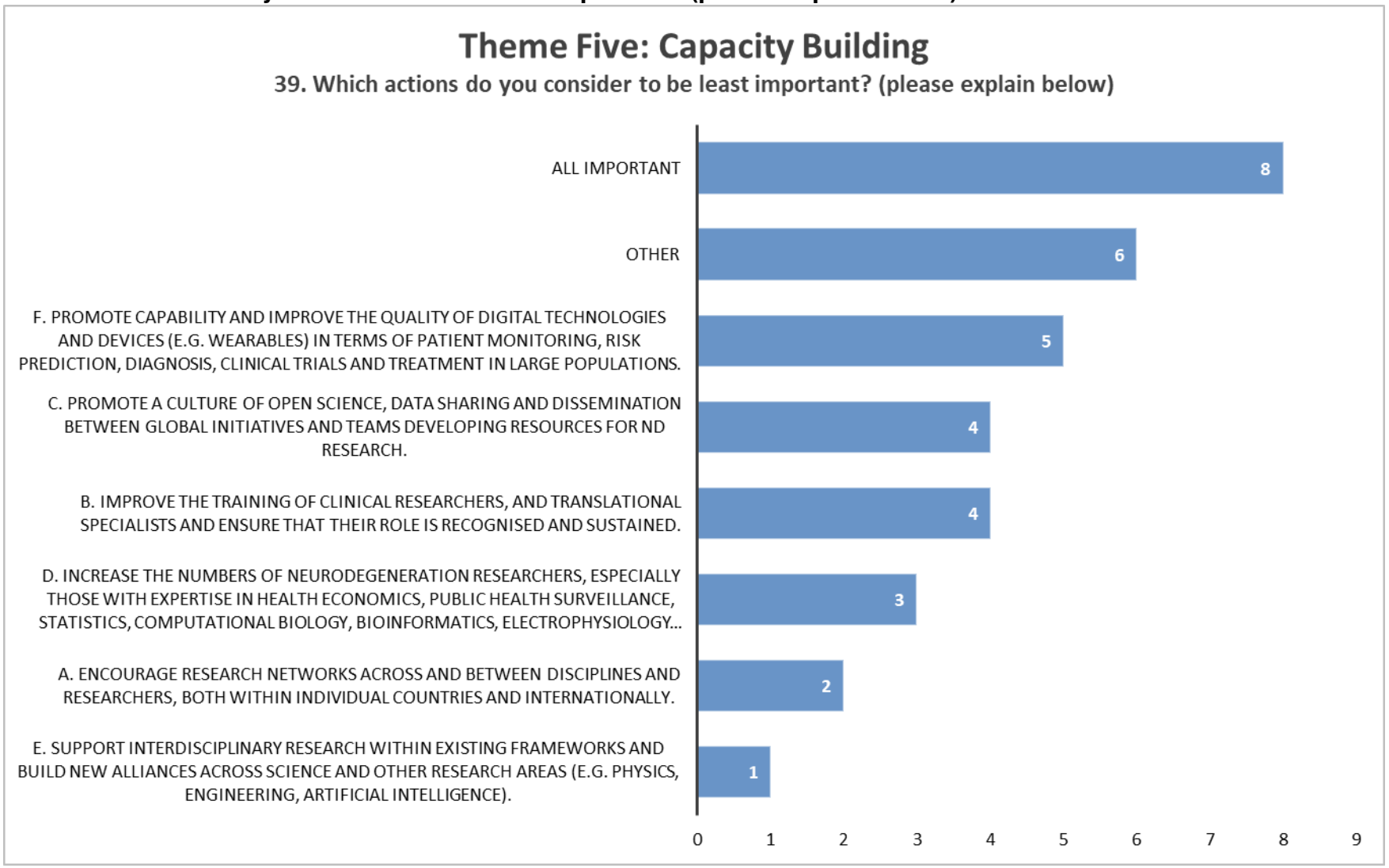
38. What would you like to see included that isn't covered in the above actions? (please explain below)

Keyword	Number of respondents	Comments
Open science/ Data sharing	**6**	• Open science and data sharing should be not only promoted but actually enforced. • Please keep in mind that open data sharing will be an issue for novel therapeutic approaches, particularly if these novel approaches tend to be successful. Industry will insist on patenting first and on keeping the data confidential. • Promote a culture of open science also with all the culture in the mankind, because always inter science offered the best results
Collaboration between basic science and clinical	**5**	• Promote the exchange between basic and clinical research. • Reenforcement of continous collaborations between specialized health care centres for ND and universities • Foreground the integration of the social sciences into any research study. • interdisciplinary research should be really interdisciplinary and include partnership with researchers in humanities and psychology
Amendment to B	**3**	• I hope by clinical researchers ALL professions are meant neurodegeneration researchers -> I'm missing gero-psy, nursing and occupational therapy (so far they are not very present in ND research) but are very much needed • There is no mention of allied health professionals within this - are these included when referring to clinical researchers? They are a very important group given that they provide much of the ongoing longer term care for many patients. Engaging them with basic scientists and a range of other disciplines is also going to be essential. • Regarding this point: "B. Improve the training of clinical researchers, and translational specialists and ensure that their role is recognised and sustained". This goal should be pursued jointly, and in a dialogue with, other organisations that are already working along the same directions (e.g. the International Parkinson and Movement Disorders Society, and equivalent organisations related to other disease areas).
Amendment to D	**8**	• Clinical neurodegeneration researchers are the key to success and therefore should be included in D. • In the statements about interdisciplinary working and increasing the numbers of researchers, important to acknowledge the involvement of those working in social care and the importance of building research capacity. • I would add neuroimaging in D • If you are increasing the number of researchers (D) the system should be ready to create stable work positions, including in Academia. Now we have a major problem to offer relevant positions to talented researcher after their postdoctoral position.

		• Would like to see Priority D expanded to include increase in neurodegenerative researchers in legal, health and social care, psychology and pharmacology. It may be useful for JPND to think about how they could accredit organisations/research networks that are aligned with ways of working. • chemists are not included in the list of expertise to be promoted, even though it is from chemists that we expect new ideas for new drugs • D lacks mention of molecular mechanisms/signalling networks/protein function
Non pharmacological	**4**	• Promote capability of product design. For the future there is a need for other forms than only pills...new technologies ask for new product design. • Improve data modeling and analysis from continuous monitoring via wearable devices. Establish better guidelines for psychosocial monitoring. • Connect developers with digital technologies and devices with people working with the patients (most devices are for academic use only with no consideration of practical use for the patient) • AI and machine Learning training courses for clinicians
Training	**10**	• facilitate Research Training for medical doctors by allowing them (financially supported) to allocate more time for research • Specific training ND programs for medical students, PhD students and doctor • I think capacity building in ethics, including for researchers, would be an essential addition to this - both because dementia and ND research raises specific challenges, but also because of the changing technologies and disease definitions associated with new therapeutic approaches • important to ensure the skills base for researchers is kept broad. With the advent of more translational studies there is less opportunity for more basic scienctific experiemtnation. This shift has been quite dramatic and it is important to keep the basic sciecne skills and the discovery research active to maintain the supply of new candidate pathways and drugs etc • The promotion of early career scientists (possibly through specific calls only open to this group) • I think diversity in the research community is needed - more clinician researchers from different backgrounds - allied health / therapies/ engineering / data science. Need political scientists/ global health researchers etc • In relation to the priority B, I would think that JPND should improve also training of non-clinical or pre-clinical researchers, on clinical aspects, to ensure that their role is relevant and valued in clinics • Involvement of young scientists? Organisation of JPND conferences PPI-stakeholders committee • Promote capacitybuilding of palliative care research, training pallliative care researchers and support building research centers.

Other		• These activities are particularly important in rare populations at genetic risk of NDs • Promote complementary interactions between groups in studying genetic forms of ND • Multidisciplinary projects should be encouraged by funding opportunities • Develop strategies able to support young and emergent researcher • A better definition of how we will be training the next generation of neuroscientists focused on ND research • E. Lacks basic mathematics (beyond statistics) which might be the most important discipline missed. • Legal gets in the way of network research! • No mention and 'curiosity, but also hypothesis-driven' basic research to explore new, 'out of the box' strategies and ideas. The way it is described it looks very much like a restricted (pre-established') circle. • Point E is very important - and to let the world notice the name Batten Disease CLN and what this disease to with a child • I think that we need to explore new ways of staffing clinical trials and more centres • Ensuring free movement of researchers, funding and data across UK borders post Brexit. • promote, stimulate; provide evidence (numbers of neurologists needed?) • Expertise in user involvement • Reflection on how many of these gaols conflict with aims for public-industry partnership! • I would like to see a European funding scheme on NDs that is not relying so much on the specific requirements of the national funding agencies. This often consumes a lot of time • Equality diversity and inclusion within JPND

39. Which actions do you consider to be less important? (please explain below)



Theme Six: Education and Training

There is considerable heterogeneity in awareness amongst 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 and social care. It will also help to promote public health messaging, and lead to greater involvement in care. This strategy will help to reduce stigma and misunderstanding that surround these conditions.

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

A. Expand the clinical education and training of health and social care professionals who interact with ND patients.
B. Promote appreciation amongst health and social care professionals of the benefits of research participation.
C. Undertake research to improve and implement effective health education to promote broader awareness about ND across all generations and sectors of society.
D. Understand how to create changes in behaviour in the population through strategies aimed at mitigating risk factors associated with an unhealthy lifestyle and lessening the chance of developing ND.
E. Develop systems for education and training that support recognition frameworks for researchers who share methods and data in a '*team science*' environment.
F. Promote opportunities to engage neurosurgeons in ND research to reinforce translational medicine.
G. Provide education for families and carers on new or existing technologies or devices that can promote freedom and independence of ND patients.
For further details on the above points please see the full version of the JPND Research and Innovation Agenda by clicking here.

40. Do you agree with these research priorities?

40. a) Please comment on your response below

Comments
In the ideal world these are good goals, but may be a bit too far off what is required now? Do we know that 'changing behaviour' really impacts on risk reduction? More research is required first.
Education does not only apply to the clinical sector. It is important as well to support basic researchers and to education them in standard clinical procedures / the clinical picture of diseases and their diversity.
This should not be a part of a research program.
Should be united with the Theme Five.
G Education for families and carers should not only concern tehcnologies but also the course of the disease, prepare for a decision making role when the person with ND becomes incapacitated etc
This theme should be more directed to efforts on increasing public awareness and understanding of NDs. In other words, more efforts are needed to make science understandable to the general public and to combat the present epidemic of misinformation in the general discussions.
Too far A and B from E and F and more G, it's a MESS

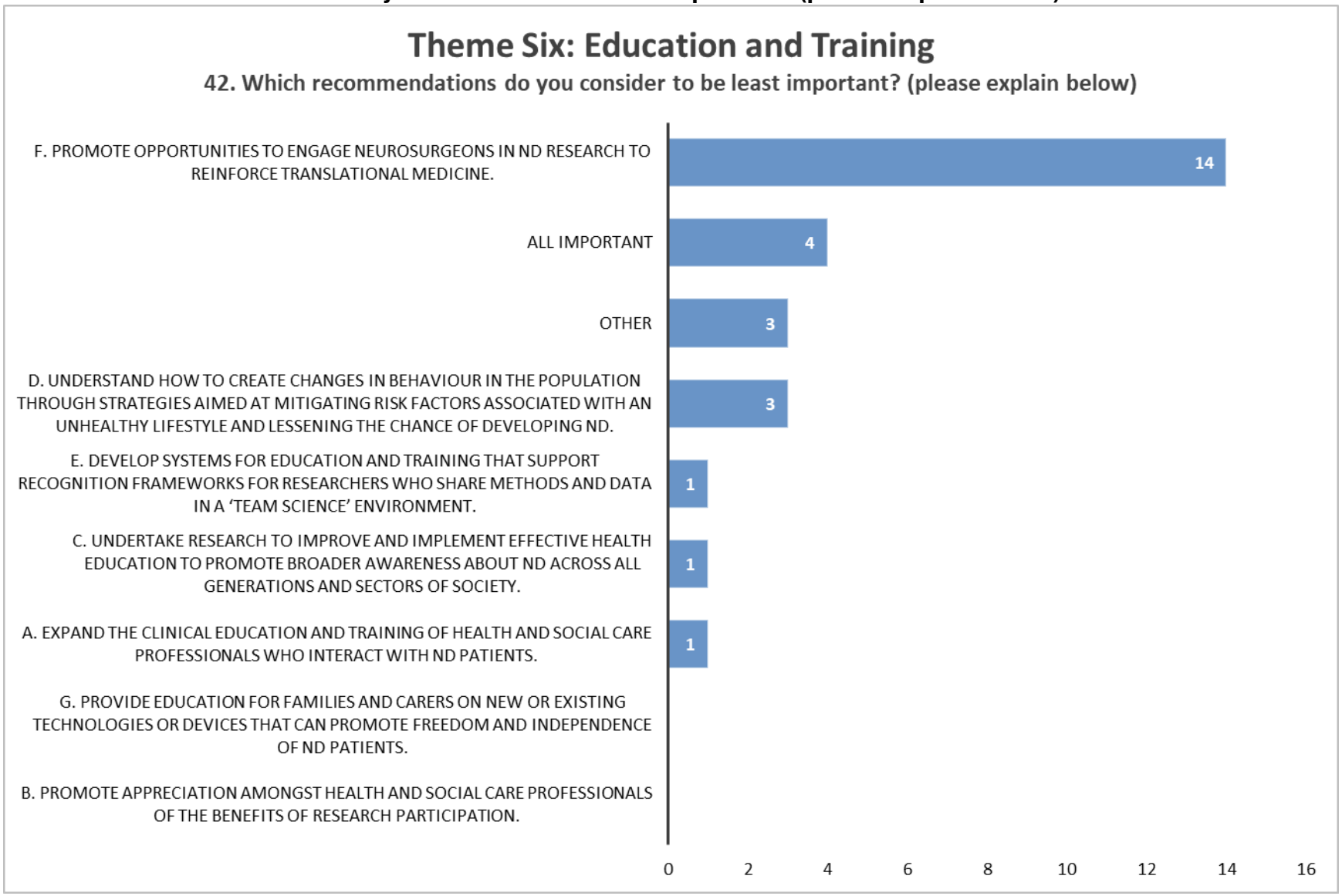
41. What would you like to see included that isn't covered in the above recommendations? (please explain below)

Keyword	Number of respondents	Comments
Support ECRs/PhD training	**7**	• Promote specific PhD programmes within this field • Support for early career researchers (clinical and non-clinical) • I miss targeting (under)graduate students (bio)medical sciences • E is very important - integrating education research culture across all sectors - not just health and social care ? • Palliative care is not included in undergraduate programs for physicians at universities. • within the reccommendation A. i would suggest that the topic of ND should considered as an area in training starting from the University Level with a specific curricula in.
Support clinician training	**10**	• Promote opportunities for clinicians in general to be involved in ND research, to enable translational medicine • Provide education for dotors and other healthcare professionals on new or existing technologies or devices • Should include support for traininig of clinical researchers. Should emphasize multidisciplinary training. • Expanding the clinical education and training of health and social care professionals is improtant but often overlooked are the specific dementia care skills that staff need to implement evidence. Dementia is recognised as a risk factor in health care but there is a limited evidence base on the kind of dementia skills practitioners can use to improve care outcomes. This is an overlooked area of education and training • Why is F limited to neurosurgeons? All MDs working in the field of neurology, neurosurgery, neurophysiology, neuropathology, neuroradiology etc. should be encouraged • Perhaps worth mentioning education & training for patients and healthcare workers about CSF sampling for diagnosis and monitoring disease progression. Opportunities to learn from different EU countries with very different attitudes to this topic. • More implementing than only promoting. Education is very important to implement research results. More attention to this in a stronger way than only promoting • Provide education and training in future care planning Provide education and training in spiritual care • E is very important - integrating education research culture across all sectors - not just health and social care ?
Patient education	**6**	• missing: education and training for patients -- focus ony on care takers and professionals is very problematic and conflict with early mentioned aims of increasing PPI; resilience, patients' wellbeing

		• G: We need to including people with ND in this research, to enhance inclusion and protecting their rights - they are often main users of technology - or the use of tehchnology has great implications for them • expand preclinical education • Patient, caregivers and public as co-researchers • E is very important - integrating education research culture across all sectors - not just health and social care ? • JPND to provide opportunities for people with ND, family and carers to interact with researchers and health care professionals so that they can provide more person-centered research that informs practice through education and informs policy.
Public engagement	**7**	• Better public education and engagement so far greater proportion of people with NDs participate in some form of research • dissemination towards non-scientific audience • We need to work closer to patient's associations, including better dissemination strategies • Promote appreciation amongst the general Public of the benefits of research and that all new knowledge is based on research in order to give us evidence to believe in. • Need to understand and educate about the potential for stigma in early disease and risk states • I would like to include the direct information to populations, with a special regard to predisposed subjects and at risk, to let them understand the importance to change everyday habits from the very beginning of their life and for the life of their sons
Interdisciplinary	**7**	• Education of basic neuroscientists in the clinical picture of neurodegenerative disorders. • There is a need for improving the understanding of clinical researchers in basic and translational research. I would recommend to include the facilitation of such training programs into the JPND agenda. • Stronger focus on training of interdisciplinary research (biology, math, physics) • Promote double competencies (eg NDD/IA, NDD/informatics...) • Promote interdisciplinary research and education between computational/engineering/statistical modeling and clinical/anatomical/imaging research. • F is particularly important. These translationally active physician need to have the necessary time to stay involved with the scientific questions and challenges. • Promote appreciation amongst health and social care professionals of the benefits of research participation, ALSO IN ECONOMICAL AND MANAGEMENT PROFESSIONS
Other		• not clear what is meant: effective health education???? studies about effective education programs show the same heterogeneous results as the one dementia research (e.g. psycho-social approaches). Overall: a methodological reflection of 'effective' / evidence based' is NEEDED

		• promote joint or joined up clinics - too much in ND is silo'd - better joint clinics between stroke and ND since so much of ND is vascular and at least vascular is treatable. • Education without practice /implementation to deliver has no evidence base for this (dementia) complex condition. There is a huge gap in research on the bio-psychosocial management of challenging behaviour /BPSD for people living at home (70% in some countries) yet no funders see this as a priority – sadly • Building the capacity of consumers to participate/advise research. Building the capacity of researchers to engage with consumers along the lifecycle of a project. • standardise successful life style to be pormoted as preventive measure; including diat, social interaction and physical/ mental training. Similarly to diabetes or cardiovascular. Think that other mental diseases may share mechanisms with proteinopathies and perform trials of such life style changes as augmentation. • Make J&J smarter to engage all employees in a campaign to create more newborn neurons...make J&J 100 T neurons smarter with exercise, MIND diet, brain games... • Focus on research that is easy to implement and that is meaningful for the patients and their carers • I would leave this Topic again to the professional societies and Lobby organisations.- JPND should cooperate with them • Could also add e-learning to the list. • link research with education (involve educational organisations in research) as essential part of research in order to implement. • Again Equality, diversity and inclusion lacking in these statements

42. Which recommendations do you consider to be less important? (please explain below)



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. 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 quality of life, 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. Second, there is a need for national policy frameworks to ensure that research outcomes ultimately will lead to effective implementation in public health policy.

The following activities will be needed to enhance the progress made to date and help address ongoing challenges:

A. Strengthen the commitment of national governments to support ND research.
B. Expand the adoption of national plans for ND (general or specific).
C. Increase national earmarked budgets for transnational research.
D. Better facilitate resources, funds and data exchange across borders.
E. Adopt and harmonise evidence-based policies and best practices at the national level.
F. Promote effective communication between researchers and policy makers.
G. Increase awareness and understanding of the societal impact of ND.
For further details on the above points please see the full version of the JPND Research and Innovation Agenda by clicking here.

43. Do you agree with these research priorities?

43. a) Please comment on your response below

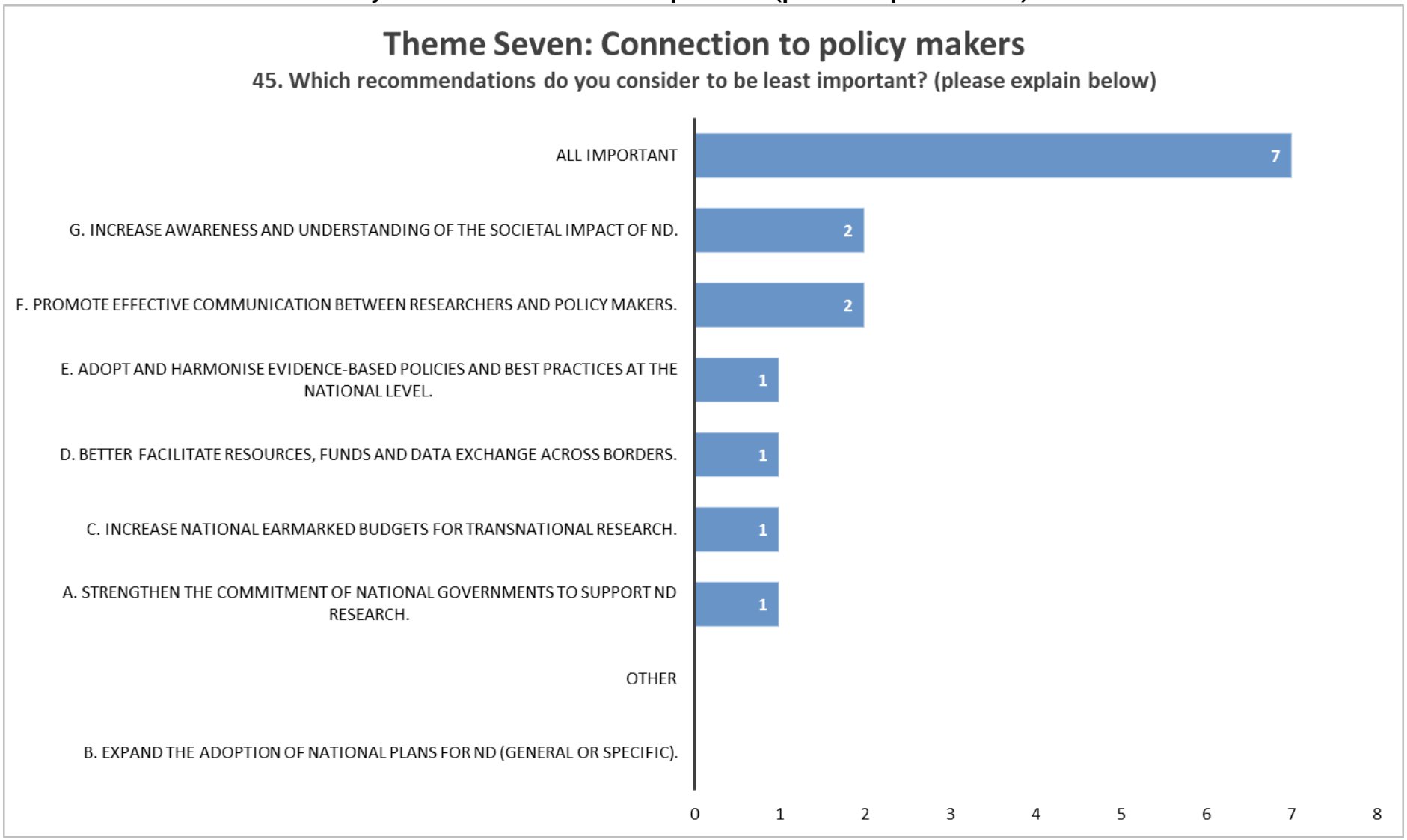
Comments
Should be united with Theme 3

44. What would you like to see included that isn't covered in the above recommendations? (please explain below)

Keyword	Number of respondents	Comments
Statements to general	**2**	• very general statements: which influence do you have on goverments? How do want to reach goal A) for example? • Again it looks like vague political statements to me. Not a clear path to implementation herewith.
Scientist – policy maker partnership	**2**	• Researcher secondments with policy makers have been very successful with other disciplines in bridging the divide between policy and research. • Promote effective communication between researchers and policy makers with the support of journals, media, movies, common information, etc.
Link with non-gov agencies	**1**	• Link to strategic non-government organisations (ie UN, WHO, ADI) to further support research and promote/disseminate findings
Don't spend money on policy	**1**	• some aims are repetetive to earlier mentoned goals. various goals are not part of Research but about poloicy, so why is money spend for policy making?
Policy makers	**10**	• Policy makers should be connecting themselves already - do they have adequate input from Academies, Research agencies etc - they are aware of the cost implications. A real professional campaign with political champion is needed • Take policy makers in your swarm intelligence platform. most of them have no feeling with ND.... • effective communication between researchers and policy makers -> what about Health Policy Fellowships? • Better understanding on why policy makes ignore research findings that can be applied to care; over and above the fact that research can be slow whilst policy runs ahead sometimes unpredictably. • We expect that PD becomes priority in policy makers • policy makers are also sensitive to economic issues. I suggest to include the topic of cost effectivness as part of the benefit in developping new strategies or approches to ND disease • The policymakers are more concerned about the impact of an increased number of ND patients and its cost on the valuebase of society, rather than on the molecular causes. Thus, more stress on palliative care to get the policymakers ear. • Expand identified priority F to include encouraging and providing opportunities to produce policy briefs and dissemination opportunities with appropriate policy makers in relation to their research.

EU countries	**6**	• Expand the commitment of national governments to support ND research, especially in EU countries that, so far, have not actively participated in JPND calls. Increase national earmarked budgets for basic and translational research on NDs. • Critical but some EU countries are doing this to a much greater degree than others EU influence on national policy is central • In addition to JPND, the European Commission should continue to have calls for proposals favouring ND research. These calls should be complementary to those issued by JPND.
Other		• dementia friendly societies • Establish costs associated with ND AND mitigation of costs associated with research and treatment developments. • Convergence on national agencies within JPND priorities • better awareness of the role of early life factors like education in preventing ND in later life - this is political as much as medical • It is important to train researchers to give REALISTIC statements, what will be possible in the future. Unless policy makers and the public will be disappointed, and in the end they will not give money in the future anymore. Train researchers to admit that they have been wrong. • Require implementation plans as a part of the research project • Focus the funding on true translational approaches instead of just pouring more funding into basic academic research only. • Extremely important Scientists and clinicians have to improve their skills how to inform the decision makers and the public in General science into the kindergarden and early School years. more science channel on TV • Increase understanding of the general public around the nature of diseases that are progressive and ultimately terminal • Point E seems important for evidence-based guidelines even though, on the other hand, precision medicine is the actual evolution • Promote a public responsibility to support patient associations/representatives. It is in every ones interest to have strong and well representative associations for the patient groups. In order to be able to contribute and be a voice on the different arenas the associations needs financial support. This should be a public responsibility. • societal impact and social-economic trans action cost • G should be the top one, the impact does not seem to be fully appreciated • Each EU-member country should join JPND and support ND research

45. Which recommendations do you consider to be less important? (please explain below)



Theme Eight: 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 reduced the stigma attached to ND. To promote communication and outreach with a wide range of stakeholders, JPND continues to:

A. Disseminate ND research outcomes to all stakeholder communities in an effective, balanced and consistent manner to assist successful translation into policy and practice.
B. Consult the JPND PPI Stakeholder Advisory Board regarding JPND initiatives and research outcomes.
C. Increase awareness and support for ND research amongst decision makers in participating countries.
D. Encourage JPND-funded researchers to engage in dissemination and outreach activities as appropriate.
E. Promote the development of innovative tools to facilitate communication between individuals with ND, their families and carers, healthcare professionals, and care service providers.
F. Continue to support dialogue with stakeholder communities on a national and international level.
For further details on the above points please see the full version of the JPND Research and Innovation Agenda by clicking here.

46. Do you agree with these research priorities?

46. a) Please comment on your response below

Comments
I would merge themes 7 and 8.
Patient and Public Involvement should be a separate activitiy. PPi is much more than described and is more than consultation.
Again, there are a lot of initiatives in Europe already so better align with them.

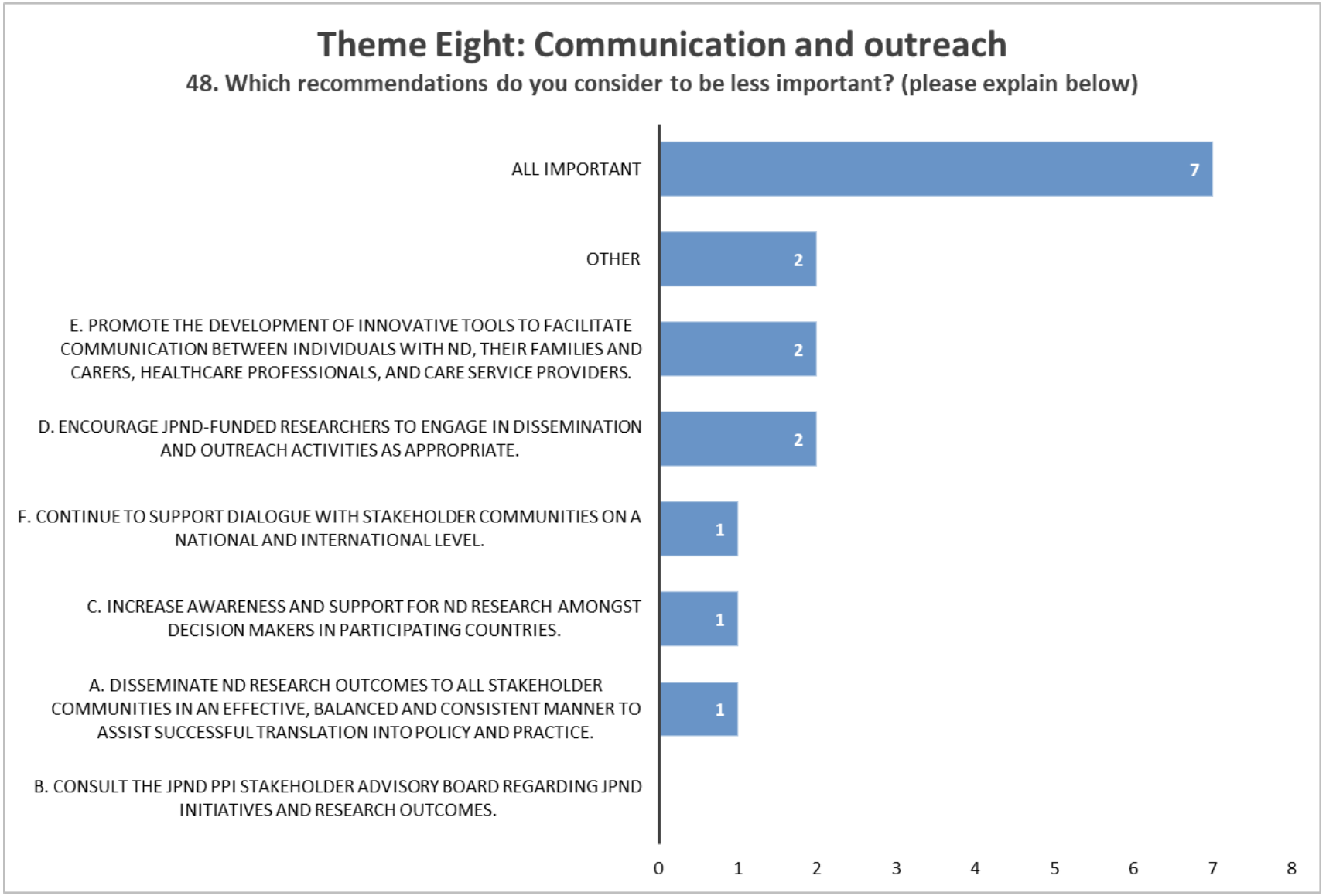
47. What would you like to see included that isn't covered in the above recommendations? (please explain below)

Keyword	Number of respondents	Comments
Public engagement	**10**	• Again, we need to really go to the basics. We take it for granted that the general public knows what a neurodegenerative disorder is. General media and school education on neurodegenerative disorders, symptoms, care policy etc.. should be promoted. • public lecctures to pre-aging population to raise awarance. • Promote new vision of NDD for lay audience • Widely disseminate public relations materials to the public about the value of research. • Efforts to educate public and even the press regarding all-too-frequent claims about "breakthroughs" in science. Perhaps something equivalent to the old "Good Housekeeping Seal of Approval" (an American phenomenon as far as I know, but I'm sure other similar endorsements exist. Perhaps some sort of public forum evaluating credibility of outlandish claims? • Support public orientated information • The most important issue is to make ND research more understandable and desirable in the eyes of the general public. • Develop a concept of how to communicate projects and results in a easy accessible manner for the general public. • Could also use PPI as a mechanism for dissemination and communication, to promote participation and increase awareness of research outcomes. This could link to D - encouraging researchers to engage in dissemination. They could make very good use of their PPI stakeholders to support this activity. • Public engagement initiative at a European level to promote awareness of ND, importance of research and how it can support practice.
Political engagement	**4**	• Political lobbying • Encourage JPND-funded researchers to engage in dissemination and in great Congresses and networks of information • Stronger requirement for the involvement of people affected by ND and groups/charities that represent them throughout the research process, from development of the concept and design of proposals to engagement in undertaking research (not only as study participants), as well as dissemination and broader consultation.
B	**3**	• Develop validTools how to implement advice from the JPND PPI Stakeholder Advisory Board regarding JPND initiatives and research outcomes. • As for B. More elaborate (inter)natonal user/client panel(s) that provide(s) input into (and 'judges') JPND-funded projects. • PPI must be a separate enabling activity

Other		• Outreach to other fields of neuroscience, psychiatry and neurology • Communication for least-developed countries...investigate what we can do for these countries with low budgets and possibilities. Traditional neuroimaging is not realistic and what can we do about awareness and ND in these countries ? • Explain necessity of animal research for such complex diseases as ND diseases to stakeholders and public. • the Stroke Alliance for Europe is a well joined up series of organisations promoting care of patients with cerebrovascular disease - you could partner with them to broaden your reach in ND as well. Great added value all round. • The KEY thing is to get a foundation of uniform collection of phenotypic data to together with biological samples in a clinically useful framework. Biological samples should include pbmcs to future proof for investigation of personalised med • Disseminate ND research outcomes to translate ... -> is not enough. I'm missing funding for large scale implementation strategies (which should be part of each national dementia strategy, but are not funded at all). IF change of performance and patient related outcome is the goal of this topic Furthermore implementation strategies need to be tailored regarding the intervention / the context / the system to be effective / efficient. So far almost no funding opportunities on national levels • Maybe JPND could also engage with Scientific Publishers since its becoming a huge problem that researchers first have to find Funding for performing the research and writing manuscripts. And then also are almost forced to also pay publishing fees that are increasing to huge amounts. • understand that sleep medicine and sleep research is of paramount importance to improving disease understanding, treatment and modification in ND, train your clinicians and scientists, increase public awareness and poitics, namely role of RBD • E and F. are very important, but it remains unclear where the research part is in it, • Seek more stakeholders • Balance of publication, patent protection and commercialization is important. • Monitoring and spreading results, is now unsatisfactory. Monitoring and final results are not seen by experts. • include review panel more during monitoring. • Missing in these activities are the voices of people living with ND. The communication and dissemination of research should include them as well as including them as stakeholders at the table supporting decision making on priorities • The involvement of Review Panel in the monitoring phase of JPND research projects? • I strongly agree all these points to prevent as much a possible ND and I would suggest to plan some special program dedicated to subjects predisposed or at risk of developing ND. After

		the arousal of the illness, it could be worth to develop a precision medicine approach for health and social care research including a person-centred approach to care. • This and the previous 4 sections are in volume a major part of the questionnaire but will have very limited influence on individual lives unless the basic and medical scientist with informaticiens and computer scientists don't solve some of the fundamental issues of causes and mechanisms of a range of dementias and other neurodegenerative conditions • Prioritize research activities published in peer-reviewed journals

48. Which recommendations do you consider to be less important? (please explain below)



Appendix

Question 12 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**12**	• A and B sound similar and could be combined. • A and B have been flogged to death. I have commented on cohort studies. • Topic A could benefit from some specification. Genetics (both monogenetic, oligogenetic and polygenic causes) could deserve more attention. • "A. Better understand the significance of recently discovered risk factors for ND": without knowing what these risk factors are (and how significant they are), it is difficult to estimate the concrete impact of this sort of research. "D. Understand ageing and how this relates to the development of and resilience to ND." (a) ND can also affect young people; (b) Perhaps this item should be incorporated into some other one (e.g. topic H, because ageing greatly increases the risk of vascular and metabolic comorbidities). "H. Advance knowledge of the interactions between ND with vascular and metabolic systems": The H2020 Health programme has had several calls on comorbidities, and projects have certainly been awarded to study how vascular, metabolic or infectious comorbidities impact on the development of neurodegenerative disease. It is important to avoid overlap between the H2020 and the JPND funding schemes. • There is a large body of research on the genetic risks for ND, including the developing different technologies accordingly, but this is one of the areas, which has been less efficient. Too many data generated, but very few answers, if any. On the other hand, mostly every environmental negative pressure that has been studied has been linked to ND, but very few have contributed to determine any causative/mechanistic role. Using any method for analysis, you can predict causative correlation in all cases you could analyse, with no possibility to eliminate false negatives. • "A. Better understand the significance of recently discovered risk factors for ND": without knowing what these risk factors are (and how significant they are), it is difficult to estimate the concrete impact of this sort of research. "D. Understand ageing and how this relates to the development of and resilience to ND." (a) ND can also affect young people; (b) Perhaps this item should be incorporated into some other one (e.g. topic H, because ageing greatly increases the risk of vascular and metabolic comorbidities). "H. Advance knowledge of the interactions between ND with vascular and metabolic systems": The H2020 Health programme has had several calls on comorbidities, and projects have certainly been awarded to study how vascular, metabolic or infectious comorbidities impact on the

		development of neurodegenerative disease. It is important to avoid overlap between the H2020 and the JPND funding schemes.
B	**17**	• A and B sound similar and could be combined. • A and B have been flogged to death. I have commented on cohort studies. • I do not see the strong focus on genetics if we cannot combine it with function! • Genetic risk factor, because I believe ND is a combination of nature and nurture and a systems medicine approach (t.i. integration of genetics with environmental triggers) might help to find new targets for prevention and treatment. • All are important, however as for the obesity debate, we are looking to cure something that we are in part driving by life style. Too little focus is placed on changing the source. • search for genes/genetic risk factors synapse dysfunction • This type of epidemiological/big data research depends on a clinical diagnosis which is often incorrect without confirmation by newer diagnostic procedures, e.g. amyloid or tau PET • However, far too much funding is being given to genetics that is not providing the expected useful information. It costs too much and is little useful • G: better to invest in searching for early phenotypes of ND A and B: redundant F: Synaptic dysfunction and loss represent too-late phenotypes in ND-linked cognitive decline • Points B e C, because they are epiphenomenon of a ND in progress. I mean that even in the case of a familial form of ND, the effect of a mutated gene, or the presence of aggregated proteins, is not evident until aging. This suggest that they are not the cause but the consequence of other primary trigger events (aging, inflammation, oxidative stress, etc) that also cause protein aggregation or allow the manifestation, the effect of a mutated gene. • B. genetic has been, widely for 30 and more years studied without valid results. the gap between familial and sporadic ND is huge. Any of the ND environmental and social risk factors for ND. C. Deepen understanding of the causes of different protein misfolding disorders, a feature common to many ND IS MAINLY AN EPIPHENOMENON and not the cause • Genetic risk factors • G: better to invest in searching for early phenotypes of ND A and B: redundant F: Synaptic dysfunction and loss represent too-late phenotypes in ND-linked cognitive decline • Points B e C, because they are epiphenomenon of a ND in progress. I mean that even in the case of a familial form of ND, the effect of a mutated gene, or the presence of aggregated proteins, is not evident until aging. This suggest that they are not the cause but the consequence of other primary trigger events (aging, inflammation, oxidative stress, etc) that also cause protein aggregation or allow the manifestation, the effect of a mutated gene. • B. genetic has been, widely for 30 and more years studied without valid results. the gap between familial and sporadic ND is huge. Any of the ND environmental and social risk factors for ND. C. Deepen understanding of the causes of different protein misfolding disorders, a feature common to many ND IS MAINLY AN EPIPHENOMENON and not the cause

C	**15**	• C This process is already reasonably well understood from a therapeutic perspective • Deepen understanding of the causes of different protein misfolding disorders, a feature common to many ND, taking account of new and evolving technologies • Not sure how much more post-mortem tissue studies are going to help unless technology allows examination of the whole brain at the resolutions used for hippocampus and other select regions examined by pathologists with speed and efficiency • disproportional focus on protein deposition and misfolding • Any related to the candidate or aprioristic hypotheses. i.e. synapse dysfunction, misfolding disorders, etc • Favouring focus on multiple mechanisms beyond neurodegenerative pathology (protein folding, amyloid, tau burden) will be important to focus on in the next five years. As described above, this includes focus on environmental and social factors, vascular disease, the resilience mechanisms. • An emphasis on protein misfolding does not seem such a priority given the poor results obtained so far after many years of research on the subject • c - this is already a high priority for the industry and brain researchers, not sure it could benefit additional through JPND focus • C Again, the main cause seems to be downstream of protein misfolding and mainly as a consequence of aging. Multiple research studies and heavy funding on protein misfolding have not identified any successful therapeutic strategy or disease modifying agents • Points B e C, because they are epiphenomenon of a ND in progress. I mean that even in the case of a familial form of ND, the effect of a mutated gene, or the presence of aggregated proteins, is not evident until aging. This suggest that they are not the cause but the consequence of other primary trigger events (aging, inflammation, oxidative stress, etc) that also cause protein aggregation or allow the manifestation, the effect of a mutated gene. • B. genetic has been, widely for 30 and more years studied without valid results. the gap between familial and sporadic ND is huge. Any of the ND environmental and social risk factors for ND. C. Deepen understanding of the causes of different protein misfolding disorders, a feature common to many ND IS MAINLY AN EPIPHENOMENON and not the cause • Again, the main cause seems to be downstream of protein misfolding and mainly as a consequence of aging. Multiple research studies and heavy funding on protein misfolding have not identified any successful therapeutic strategy or disease modifying agents • Points B e C, because they are epiphenomenon of a ND in progress. I mean that even in the case of a familial form of ND, the effect of a mutated gene, or the presence of aggregated proteins, is not evident until aging. This suggest that they are not the cause but the consequence of other primary trigger events (aging, inflammation, oxidative stress, etc) that also cause protein aggregation or allow the manifestation, the effect of a mutated gene. • B. genetic has been, widely for 30 and more years studied without valid results. the gap between familial and sporadic ND is huge. Any of the ND environmental and social risk factors for ND. C.

		Deepen understanding of the causes of different protein misfolding disorders, a feature common to many ND IS MAINLY AN EPIPHENOMENON and not the cause
D	**10**	• F is a very global and basic question, which in my view will not contribute a lot to dealing with the specifics of the disease, unless it is targeted to the specific synaps relevant for a particular ND. D important risk factor for many diseases, not only ND, so not sure/convinced that JNPD should have a focus on that • this priority has much longer focus than a decade but would drain significant resources from the programme. • "A. Better understand the significance of recently discovered risk factors for ND": without knowing what these risk factors are (and how significant they are), it is difficult to estimate the concrete impact of this sort of research. "D. Understand ageing and how this relates to the development of and resilience to ND." (a) ND can also affect young people; (b) Perhaps this item should be incorporated into some other one (e.g. topic H, because ageing greatly increases the risk of vascular and metabolic comorbidities). "H. Advance knowledge of the interactions between ND with vascular and metabolic systems": The H2020 Health programme has had several calls on comorbidities, and projects have certainly been awarded to study how vascular, metabolic or infectious comorbidities impact on the development of neurodegenerative disease. It is important to avoid overlap between the H2020 and the JPND funding schemes. • this priority has much longer focus than a decade but would drain significant resources from the programme. • "A. Better understand the significance of recently discovered risk factors for ND": without knowing what these risk factors are (and how significant they are), it is difficult to estimate the concrete impact of this sort of research. "D. Understand ageing and how this relates to the development of and resilience to ND." (a) ND can also affect young people; (b) Perhaps this item should be incorporated into some other one (e.g. topic H, because ageing greatly increases the risk of vascular and metabolic comorbidities). "H. Advance knowledge of the interactions between ND with vascular and metabolic systems": The H2020 Health programme has had several calls on comorbidities, and projects have certainly been awarded to study how vascular, metabolic or infectious comorbidities impact on the development of neurodegenerative disease. It is important to avoid overlap between the H2020 and the JPND funding schemes.
E	**16**	• all these points are important, but points E and G are purely technical and could be included in any of the the other priority points • E+G- not that helpful and much has been invested in cohorts • these are fishing expeditions • G - that's a very small and extremely focused but tiny topic, which however can swallow enormous funding. Brains had been available for long and studies on brains can be conducted as part of the other topics. One should fund aims to answer questions, one should not fund mere tools without a

		clear question. E - correlation only research has been helpful in the past. It might already has seen its peak impact in AD/ND research. It does not belong within the theme one 'origins & progression of ND' • Poorly defined
F	**19**	• Animal models so far not very revealing? • I do understand that investigate synapse dysfunction and loss in cognitive decline, it is less important that investigate the real mechanims that induces synaptic disfunction.. • Point F is too narrow. There are many other specific problems, which are related to NDs, so the best strategy is to leave the decision, which problem to study, to researchers themselves. • In my opinion, priorities F, G and H are not as relevant as the remaining ones. For instance, regarding brain banks, it is hard to differentiate between disease mechanisms and the outcome of chronic medication. • In my opinion the point F is not a priority as the loss in cognitive decline is only the final effect of neurodegenerative diseases and these studies will not help the understanding of the pathology. • F and G, F less relevant and G unclear benefits • point F seems too specific. There are other narrow research fields which are not listed. • F. We have spent a lot of time on this already and it does not bring us forward in isolation. • I do not see that "synapse dysfunction" should be treated with the same priority as "Deepen understanding of the causes of different protein misfolding disorders" • Promote studies investigating synapse dysfunction and loss in cognitive decline. • Synapse dysfunction seems relatively downstream in comparison with the other priorities. • F is a very global and basic question, which in my view will not contribute a lot to dealing with the specifics of the disease, unless it is targeted to the specific synaps relevant for a particular ND. D important risk factor for many diseases, not only ND, so not sure/convinced that JNPD should have a focus on that • need less further investigation • F seems very specific and different to the others
G	**33**	• it is always difficult to sort out primary and secondary events in pm tissue and issues of confounding eg by medication cause problems with deducing new knowledge. • The post-mortem samples, correspond to a after death time point in the disease with can lead to mechanisms that are so far from the early disease events that are of little value. • all these points are important, but points E and G are purely technical and could be included in any of the the other priority points • In my opinion, priorities F, G and H are not as relevant as the remaining ones. For instance, regarding brain banks, it is hard to differentiate between disease mechanisms and the outcome of chronic medication. • F and G, F less relevant and G unclear benefits

		• G. since post mortem tissue is so scarce and also because the ND will be so widespread at the time of death that it will be difficult to differentiate origins from later host response mechanisms • G Findings likely to reflect consequences not causes of disease • E+G- not that helpful and much has been invested in cohorts • Post-mortem analysis • Expansion of research on post-mortem tissues from brain banks. I think less important to investigate brain tissues because they may be related to a late stage of disease, with less significant indications about the real causes of the disease. • Expansion of research on post-mortem tissues from brain banks • Expansion of research on post-mortem tissues from brain banks. This research must be done by universities. • Postmortem research because it is too late in the pathology. One wants to have better understanding of earlier events. • G - that's a very small and extremely focused but tiny topic, which however can swallow enormous funding. Brains had been available for long and studies on brains can be conducted as part of the other topics. One should fund aims to answer questions, one should not fund mere tools without a clear question. E - correlation only research has been helpful in the past. It might already has seen its peak impact in AD/ND research. It does not belong within the theme one 'origins & progression of ND' • Post mortem tissues can be problematic as they are end stage disease and problems with post mortem artefact, • G.: It gives only static information, while the causes of NDs are highly related to dynamic processes in the living brain. • Hard to tell, they are all equally important. However, priority G: "Expansion of research on post-mortem tissues from brain banks" may be less important for studies looking at the origin of NDs if the brains would include individuals with the end-stage of the disease. • G: better to invest in searching for early phenotypes of ND A and B: redundant F: Synaptic dysfunction and loss represent too-late phenotypes in ND-linked cognitive decline • Post mortem studies • The G priority is less important since post mortem data are already availble and they can be collected at the end of the disease so they are not informative about origin or progression or at least there is a limited benefit for this topic. • G: better to invest in searching for early phenotypes of ND A and B: redundant F: Synaptic dysfunction and loss represent too-late phenotypes in ND-linked cognitive decline • It gives only static information, while the causes of NDs are highly related to dynamic processes in the living brain. • priority is less important since post mortem data are already availble and they can be collected at the end of the disease so they are not informative about origin or progression or at least there is a limited benefit for this topic.

		• As post-mortem studies may not be able to provide sufficient information on origin and progression of the disease that could be gained by focusing on other research areas.
H	**9**	• might not be likely to result in major break throughs. • In my opinion, priorities F, G and H are not as relevant as the remaining ones. For instance, regarding brain banks, it is hard to differentiate between disease mechanisms and the outcome of chronic medication. • "A. Better understand the significance of recently discovered risk factors for ND": without knowing what these risk factors are (and how significant they are), it is difficult to estimate the concrete impact of this sort of research. "D. Understand ageing and how this relates to the development of and resilience to ND." (a) ND can also affect young people; (b) Perhaps this item should be incorporated into some other one (e.g. topic H, because ageing greatly increases the risk of vascular and metabolic comorbidities). "H. Advance knowledge of the interactions between ND with vascular and metabolic systems": The H2020 Health programme has had several calls on comorbidities, and projects have certainly been awarded to study how vascular, metabolic or infectious comorbidities impact on the development of neurodegenerative disease. It is important to avoid overlap between the H2020 and the JPND funding schemes. • "A. Better understand the significance of recently discovered risk factors for ND": without knowing what these risk factors are (and how significant they are), it is difficult to estimate the concrete impact of this sort of research. "D. Understand ageing and how this relates to the development of and resilience to ND." (a) ND can also affect young people; (b) Perhaps this item should be incorporated into some other one (e.g. topic H, because ageing greatly increases the risk of vascular and metabolic comorbidities). "H. Advance knowledge of the interactions between ND with vascular and metabolic systems": The H2020 Health programme has had several calls on comorbidities, and projects have certainly been awarded to study how vascular, metabolic or infectious comorbidities impact on the development of neurodegenerative disease. It is important to avoid overlap between the H2020 and the JPND funding schemes. • There is no priority that I consider unimportant, but H seems to me slightly less important. • H refers to aspects that can be included in most or all other categories and does not need to be a separate category
All important	**22**	
Other	**5**	• All of this is less important that studies to translate what we know about prevention into health strategy and general vernacular. • The animal model is less important than human model in ND • lack of novelty • There is a large body of research on the genetic risks for ND, including the developing different technologies accordingly, but this is one of the areas, which has been less efficient. Too many data generated, but very few answers, if any. On the other hand, mostly every environmental negative

		pressure that has been studied has been linked to ND, but very few have contributed to determine any causative/mechanistic role. Using any method for analysis, you can predict causative correlation in all cases you could analyse, with no possibility to eliminate false negatives. • I'm afraid that most academics will give a biased answer that serves their own research interest.

Question 15 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**22**	• As outlines, focus on animal models. • I suggest that "A" is treacherous. Certainly in the case of Alzheimer's the models have created self-fulfilling prophesies about the amyloid cascade hypothesis. • I doubt that we need more animal models. Possible exception being large animal models. We have enough transgenic mice and they usually have been more of a distraction than a real advancement • Develop novel animal models Translation is sometimes very poor • I think less important to develop new animal models • A B less important than C D E • we have a lot of existing models so investment in new ones may be less justifiable • Develop novel animal models, as big amounts of money have been spent on this area without any major impact for the cure of ND within the last 25 years. Mice are not men and ND are multisytstematic disorders, so transfer of findings is difficult. • A Animal models remove the complexity of human disease. We need paradigms that embrace that complexity • Animal models in general. People are the best models of human disease. • Development of animal models: although I have used them widely myself, the translatability of findings from animal models to humans is deceivingly limited, particularly if it comes to complex wired organs as the brain. The understanding of cellular mechanisms is likely to be more rewarding in a translational aspect. • cell models, worm models gut-brain axis • Cell-based or animal models are mainly depending on genetic modifications. Given the low percentage of autosomal disorders as causes for dementia, cellular and animal models, A, B, and C seems to be less important for the majority of People with dementia. • 1. I am unsure what animal models tell us about abnormal human brain function - but I am probably still out on a limb with this opinion 2. Cell models seem appropriate to looking for mechanisms and sorting out if misfolded proteins are causes or effects or both of disease initiation and progression
B	**9**	• A B less important than C D E • I question the generalizability and translatability of these. • B. Cell-based models fail to reproduce in situ complexity. • Priorities B, F and G are not so appealing as the remaining ones. We need better animal models and mechanistic approaches.

		• Cell-based or animal models are mainly depending on genetic modifications. Given the low percentage of autosomal disorders as causes for dementia, cellular and animal models, A, B, and C seems to be less important for the majority of People with dementia. • cell models can be misleading
C	**7**	• If I am correct there is already enough research on this topic...? • Mechanisms of protein seeding, too narrow focused • Cell-based or animal models are mainly depending on genetic modifications. Given the low percentage of autosomal disorders as causes for dementia, cellular and animal models, A, B, and C seems to be less important for the majority of People with dementia. • Protein spreading to me seems less relevant as protein aggregation is only a last step in the process of degeneration, when it is already (too) late to halt the ND • oint C. Again, protein aggregation is an epiphenomenon. Once a ND is in progress, understanding mechanisms of protein aggregation cannot help to modify disease progression. • C. Determine the role of new pathways proposed for ND pathogenesis e.g mechanisms of protein seeding IS NOT RELEVANT AT ALL
D	**3**	• Biomarkers are only usefull if they are placed in some biological context. Therefore it is important to understand and not only identify biological markers. • (D) - poorly defined
E	**12**	• Aims "E & F" might not likely result I breakthroughs. • research into lifestyle factors. On one hand it will by the nature of these modulators need such an amount of money and persons that these resources are missing in more promising fields. On the other hand it might lead to imposing lifestyle against the inborn diversity of lifestyle choices. • In my opinion we still do not understand enough ND to even think finding the eventual influence of lifestyle • E and G are to little specific in the field of ND. Might be of interest in case of late stage patient care and to provide sustainable end-of-life solutions but hopefully we will eventually have an imporved causal understanding leading to treatment
F	**8**	• Aims "E & F" might not likely result I breakthroughs. • cell models, worm models gut-brain axis • Priorities B, F and G are not so appealing as the remaining ones. We need better animal models and mechanistic approaches. • F: I think the microbiome-gut-brain axis is a bit overestimated in NDs.
G	**21**	• G. The underlying biology is too complex at present. • F and G are risky research lines. Unless they are very focused, there is a high risk to invest money and obtained none translational results • G - it may be more useful if applied to the development of clinical trial end-points which accelerate trials.

		• I assume that targeting the cause of the disease will also target side effects so I see that "Elucidate the biological and environmental basis of behaviour and psychological symptoms in ND." is less important. • Examples in the above mentioned reseach priorities are focused on aggregation diseases. This covers only a few of relevant NDs. Priority G is very diffuse. • I think that G does not fit very well to theme 2 • In my opinion the point G is too vague and ambitious. • Priorities B, F and G are not so appealing as the remaining ones. We need better animal models and mechanistic approaches. • G - based on decades of past research it doesn't look promising to address it from this angle. Most progress made over the last decades came from research that originally had nothing to do with ND (e.g. hippocampal function, enriched environment etc..). I consider this compared to the others as low priority for JPND. • i am not sure that this specific set of symptoms warrants a separate bullet. Or alternatively - all symptom categories could get their own bullet. • E and G are to little specific in the field of ND. Might be of interest in case of late stage patient care and to provide sustainable end-of-life solutions but hopefully we will eventually have an imporved causal understanding leading to treatment • Priority G may be considered less important as it addresses the basis of the symptoms in ND and does not deal with the causes of the disease.
All important	**14**	
Other	**1**	• There should be a high bar for biomarker studies. How much money has already been spent searching for biomarkers without much to show for it? • Examples in the above mentioned reseach priorities are focused on aggregation diseases. This covers only a few of relevant NDs. Priority G is very diffuse. • I find the inclusion of highly diverse models useful. • I hope environment is not necessarily only limited to social (e.) or gut-brain axis. Could also include for example radiation etc. • The animal models, although very important, should be taken cautiously due to some differences at the level of metabolic pathways, life style etc etc • priotities might be covered to dedicated research centra? Be shure only research is funded where international collaboration is necessary

Question 18 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**12**	• As outlines, focus on animal models. • Standardize disease definitions. Thankfully a patient with AD or with PD or with idiopathic RBD is already diagnosed as so for a long time. Biomarkers are "fashion" but they do not treat patients: I would like now to see more efforts given to preventive treatments. • standardization is neither easy neither necessary • Personally, I do not find much difference between A and B (they are both about refining diagnostic criteria and related practices):
B	**8**	• B and C. Most of ND can be considered as neurodegenerative proteinopathies overall, sharing a number of common charactersitics particularly in late stages of disease progression • Develop new diagnostic criteria, better harmonise what is already there • Personally, I do not find much difference between A and B (they are both about refining diagnostic criteria and related practices):
C	**6**	• The new biomarker work, except in specific instances of disease where the cause is known and the biomarker therefore proximal to cause (eg measuring HTT in CSF in Huntington's disease). I think a lot of time and money has been spent in this area already and we have a few good biomarkers are available which we should use. • Standardize disease definitions. Thankfully a patient with AD or with PD or with idiopathic RBD is already diagnosed as so for a long time. Biomarkers are "fashion" but they do not treat patients: I would like now to see more efforts given to preventive treatments. • B and C. Most of ND can be considered as neurodegenerative proteinopathies overall, sharing a number of common charactersitics particularly in late stages of disease progression • Bio markers. Just use a gnome wide bio marker such as gene expression or other omits. The number of independent biomarkers will be few. Individual candidate biomarkers are expensive • (C) has the potential to restrict research and diagnostic improvements in the future • Single marker exploitation •
All important	**16**	• All are criticially important. Revised disease definitions based on new research insights (specifically, the multi-pathology contribution to dementia) should be incorporated into overall JPND research strategy and objectives
Other	**1**	• Harmonisation is an important goal, but may be particularly challenging from a political perspective.

		• none, however, biomarkers get a lot of attention but instead clinical parameters are much more important for the patient and should be the leading parameter in diagnostics. • Standardization seems to be a very important priority to ensure we are all measuring the same thing • None - but need to define "biomarkers" carefully as diagnostic, prognostic, or disease stage biomarkers • AI harmonisation and validation that is not based on adequate disease classification seems 2nd order. A pill for dementia is clearly a bankrupt idea. So proper classification that has to include all features - clinical and laboratory is of primary importance. • We probably have enough biomarkers but need to pool them together and select the best subsets by means of more advanced strategies • A and B are to be done by the European professional societies such as the EAN, EPA or FENS - may be they are allowed to apply to JPND

Question 21 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**3**	• A: I realize that this promise of translation did not become true, in the last 30 years. I would not put money there. • The model system used is relatively low, the point A is quite accessory to other points related to develop (novel) models
B	**2**	
C	**2**	• The issue of selective neuronal vulnerability has been around for quite some time and at present has lost appeal, at least to some extent. Cell based neuroregenerative approaches are hard to implement in realistic terms and difficult to translate to clinical use
D	**6**	• Aim "D. Develop disease modifying approaches, where appropriate, that slow, reduce, or clear the proteinopathy that underpins ND." is the only priority that really matters here, but the other ones might to different degrees help to accomplish that one. • D needs much more work before clearance of abnormal proteins is tried again • D, this strategy has not proved effective at least in Alzheimer's disease • G belongs to theme 3, it is not "developing therapies, preventative strategies and intervensions" D appears to have been evaluated and led to multiple failed phase III trials, at least for AD. Maybe it should anyway include "and ameliorates outcomes in model systems"?
E	**1**	• D because it is based on wrong assumptions. E, F make sense only after the identification of the correct targets
F	**3**	• In my opinion the point F is not a priority as it is almost useless to counteract the final effect in the brain if all pathways are activated. • D because it is based on wrong assumptions. E, F make sense only after the identification of the correct targets
G	**9**	• G- but may be I don't understand what is really meant here • Priority G is not clear how it can contribte to ND challenge. it is a very broad topic and not clear . • G belongs to theme 3, it is not "developing therapies, preventative strategies and intervensions" D appears to have been evaluated and led to multiple failed phase III trials, at least for AD. Maybe it should anyway include "and ameliorates outcomes in model systems"?
H	**11**	• Priorities H and I does not "solve the issue" but more deals with the point how to cope with the disease and how to accept it. This is not a development of a therapy. • H priority in my opinion is less important as it can only delay the diseasem it cannot be a cure.

		• H, although I consider it important. I'm simply not sure if it needs to be comparably funded.
I	**21**	• Priorities H and I does not "solve the issue" but more deals with the point how to cope with the disease and how to accept it. This is not a development of a therapy. • Seems unclear • I Seems like a waste of money trial will be voluntary • it's totally misleading to support "socio-economical" studies to solve ethical issues - for ethical issues, ethical and ethico-empirical research is needed. • is I think obsolete - these studies already run. we should now focus on including participants. • secondary to treatments • The last point is really non important if an effective intervetion becomes available • Priority I shouldn't be considered for funding purposes as it represents a shortcut for potential misuse and has overemphasised focus on pharmacology of ND • Point I interesting but "mens sana in corpore sano" is well known since 2000 years and more
All are important	**5**	
Other	**10**	• H and I are most important • Again, proteinopathy seems a rather reductionistic approach. • All items have a medical model underlying their writing and I would encourage more multidisciplinary approach to ensure we are working towards translation • D and E should be on top having in mind that we have millions of patients without effective treatments... • Search for novel drugs has been unfruitful so far - we have a few drugs that work moderately well on a third of people with Alzheimers type dementia. But we have 3 therapeutic modalities which have promising results and have had virtually no investment. If this does not make a priority - what does! • High priority should be give to much more frequent diseases • working on at high risk individuals, to better identify the risk factors and associated features but most importantly to work in term of prevention. Thus try to develop research in identify pathways altered in at risk subjects and develop strategies to target these individuals, preventing or minimising the progress of the pathology. • After the onset, the neurodegenerative diseases are hardly curable and difficult to study. • FOR ND, IN THE EU, DIFFERENT FROM THE USA, THE SOCIO-ECONOMIC SEEMS TO BE NOT SO IMPORTANT, FOR THE HUGE DIFFERENCES IN THE HEALTH CARE SYSTEMS

Question 24 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**3**	• A, B, C, D and H are out of this scope • A and B as they are completely addressed previously. Others need to be rewritten.
B	**7**	• A, B, C, D and H are out of this scope • B- is redundant with previous priorities • A and B as they are completely addressed previously. Others need to be rewritten. • B- as this seems to be partially covered by a prior topic in another theme • overlaps with topics mentioned in other themes. • Care is more important
C	**1**	• A, B, C, D and H are out of this scope
D	**1**	• A, B, C, D and H are out of this scope
E	**3**	• E. End of life, palliative care - I'm unclear on what needs to be addressed in this area. • E : a lot of research is already dedicated to end of life care regardless of the diagnosis. Although I agree that it would probably be useful to study it within a context of ND but not convinced of the added value. So if ressources are tight (and only then) could this be seen as a minor priority
F	**2**	• End of life, palliative care - I'm unclear on what needs to be addressed in this area.
G	**2**	• G This is not unique to neurodegeneration disorders
H	**4**	• A, B, C, D and H are out of this scope • H is the less important • Seems overly ambitious
I	**2**	• This question needs refinement we need research that addresses how people with dementia and co-morbid conditions can access appropriate health care. This requires changes in how non dementia services adapt to provide care to people with dementia
All are important	**8**	
Other	**8**	• These are "good thoughts", but basically we now need a ND preventive treatment, and to put the money an energy there. For example, the problem of end of life is not specific to ND, so I do not see why it should be covered by the JPND. I would save the money for prevention. • These priorities are arguably covered relatively well by other funders • Worried that the net is being spread too wide at a time when a number of fundamental issues must first be addressed

		• Ethical issues related to ND • Randomised controlled studies for psychosocial therapies /care programmes are definitely not the way to go - they result in waste of research resources. Large scale cale implementation research and measurement of positive outcomes will remain an important agenda for this stream • All the above ones. • not important • JPND should not fund Research Health care or social care

Question 27 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**2**	• "open access" to large data sets is difficult if enforced, because it allows some people harvesting the fruits of others.
B	**4**	• B, F, G, and H are the same, and need to be one point. • standardising is doomed to failure for obvious reasons of access and quality. So a move to big data methods is vital • I think the drive toward standardization, harmonization, etc. is a two-edged sword. We must assure that individual labs have free rein to pursue "idiosyncratic" methods.
C	**4**	• C. It looks to be less important but probably i am biased.. D. Most of this is already available i think. • I think a and particularly b are important. Phenotype of risk and progression are limit8ng factors. We need strong foundations on which everything else is built. G should follow from b and so shouldn't be prioritised on its own. Registries without biological samples are useless. F also follows from b. Imaging is expensive so I don't support c. Use omits biomarkers. • C. 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. (already commented upon) D. Provide coherence to the global investment in cutting-edge but high-cost areas, such as proteomics and computational biology, to establish centres or networks at the national or international level. (does this mean that only one centre in each country is going to receive support from JPND for carrying out proteomics of computational biology? Because I do not think that this would be a good idea).
D	**6**	• C. It looks to be less important but probably i am biased.. D. Most of this is already available i think. • Proteomics. Complex, not sure it is interesting • These kind of organizations are rigid and often not functional. Best collaboration happens bottom-up.
E	**1**	
F	**5**	• I am unsure that aims F-H will really lead to novel important findings. Usually data is different retrospective cohorts are too diverse, and registries does not include enough in depth data on different brain pathologies. • B, F, G, and H are the same, and need to be one point. • I think a and particularly b are important. Phenotype of risk and progression are limit8ng factors. We need strong foundations on which everything else is built. G should follow from b and so shouldn't be prioritised on its own. Registries without biological samples are useless. F also follows from b. Imaging is expensive so I don't support c. Use omits biomarkers.

		• A better and more coordinated collection of cohort data is needed.
G	**7**	• I am unsure that aims F-H will really lead to novel important findings. Usually data is different retrospective cohorts are too diverse, and registries does not include enough in depth data on different brain pathologies. • B, F, G, and H are the same, and need to be one point. • Registers of patients with cognitive impairment. These are already covered in other headings with a little tweaking of the definitions (eg G). • I think a and particularly b are important. Phenotype of risk and progression are limit8ng factors. We need strong foundations on which everything else is built. G should follow from b and so shouldn't be prioritised on its own. Registries without biological samples are useless. F also follows from b. Imaging is expensive so I don't support c. Use omits biomarkers. • I would combine priorities G and H
H	**10**	• H. I am allergic to the new buzz word 'real world' - overused these days. Seriously - this would be too ambitious to be achieved. • I am unsure that aims F-H will really lead to novel important findings. Usually data is different retrospective cohorts are too diverse, and registries does not include enough in depth data on different brain pathologies. • B, F, G, and H are the same, and need to be one point. • Point H seemd to be too specific. Why only patients with cognitive impairment? • I would combine priorities G and H
All important	**9**	
Other	**6**	• All of the above • Emphasize importance of specific subgroups/cohorts of patients with cognitive impairment, as setting and characteristics of patient cohort may determine course and natural history of cognitive impairment • In general, I regard the approach to sharing and pooling of data and resources as highly important, but the experience in the last decades has shown that this interferes with today's competitiveness of groups.... • the list is very long and wide: it is impossible to disagree, but I am not sure it is useful to have so many goals. • Speaking of cooperation, and making structures which sometimes are not efficient • I think B, F and G are incredibly important and necessary for research to progress, but there is a dilemma here in that if the diagnosis and definition research in Theme 3 has not advanced sufficiently, investment could be made in data collection systems which become obsolete or less useful than they need to be. It's a chicken and egg type challenge as you do need better records of disease to support all research. Is there confidence that records and data collection could be set up in a meaningful way without further progress in Theme 3 priorities?

Question 30 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**2**	• Theoretical cooperation University - Industry. Pfizer stopped research on Alzheimer and no reaction from any one. It must get solicitation
B	**2**	
C	**4**	• C - they will find out of emerging research through usual channels of peer publications • Maybe point C. I would tell the opposite: Give academic research visibility to the companies and access to their data...
D	**1**	
E	**1**	
F	**2**	• FGH points difficult to practice for the different mission of a private industry and public research centers
G	**1**	• FGH points difficult to practice for the different mission of a private industry and public research centers
H	**2**	• FGH points difficult to practice for the different mission of a private industry and public research centers
All are important	**9**	
Other	**13**	• Most are beauty (and empty) words. I cannot deprioritize anything... • Industry is interested in making money. We are interested in maintaining health. You want the two to overlap. I cannot see this is possible. • JPND differs from H2020, since it accepts, also projects in basic sciences (without industry output). I hope it will still be possible. • In general, joint academic-industry research is important, however, it's usually only on the molecular level with no inclusion of patient's perspective. • Fostering a culture of collaboration seems somewhat in conflict with trade practices in big pharma. • Co-funding of academia and industry should be restricted to small-and-medium enterprises (SMEs) • Foster a genuine collaborative culture with and between industry sectors, reflecting the emerging trend for industry to conduct less discovery science in-house. • All the fostering and encouraging will be a slow process. Mandating and incentivising would be more likely to succeed.

		• The partnership with industries is necessary, but it is important to control commercial interests and marketing power. • Organising activities specified in the Theme 2 is a quite complex task, which requires strong information sharing effort/support. • In general, there is too much emphasis in the program for the company involvement. The real problem in Europe is the lack for funding for cutting-edge basic science that will lead to true scientific breakthroughs, which then on they own weight will surely create collaboration between universities and the industry.

Question 33 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**1**	• F is not realistic.... so far A special call on alternative designs???
B	**4**	• B. Consent is subject to national rules. In this domain, things have been more an more complicated in the last 30 years, without protecting better the patients. So please do not add a new strate here. • B already exists • B. Looks pretty impractical. At the end of the day, all protocols must be aligned with local and EU regulations and IRB criteria
C	**-**	
D	**-**	
E	**-**	
F	**2**	• F is not realistic.... so far A special call on alternative designs???
G	**2**	
All are important	**8**	
Other	**4**	• Take into consideration the feasibility when choosing the topics. For most projects it is not feasible • Regulatory organization sometimes are politically oriented instead of scientifically interested. • Promote the standardisation of procedures around the control and consent of patient data • Would like to see: - Priority that ensures alignment of health and social care strategies at national level with JPND strategies and research priorities - Include in Priority A charity organisations and not-for-profit organisations working with or on behalf of people with ND and their family and carers.

Question 36 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**3**	
B	**2**	
C	**2**	
D	**12**	• Vague • Option D. I do not think cultural differences should ever make any difference in treating disease. Diseases do not care about cultural differences, why should we?! • D and E appear to be less important to me, because the use of the presumably limited ressources must be bundled. • Again, this point seems "good thoughts" but not useful here • an aspect which applied to healthcare in general and is not specific for neurodegeneration • This needs to be reworded, the learning comes from understanding what is common/effective in all cultures and what is context specific. It needs to be explicit that increasing understanding is only relevant if it can inform directly how services are adapted for people living with dementia and are proven to be effective. • C & D. This topics are misplaced in my opinion.
E	**4**	• D and E appear to be less important to me, because the use of the presumably limited ressources must be bundled. • not sure I fully understand the value of this - we must accept ethical values may differ globally
All are important	**6**	
Other	**4**	• Forced cooperations • B to e much less important than a • I think the number of consortium partners should not be limited from above

Question 39 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**2**	• B : does not seem necessary to me A : yes it is important but should not be a so restrictive criteria as it is currently with JPND • "A" statement looks vague. Especially to be the top one.
B	**4**	• B : does not seem necessary to me A : yes it is important but should not be a so restrictive criteria as it is currently with JPND
C	**4**	• I believe this is quite present already.
D	**3**	• I do not agree with D: There is no need to increase the NUMBERS of neurodegenerative researchers, but there is a need to increase the QUALITY of the already existing researchers! Invest in training not in numbers!!
E	**1**	
F	**5**	• F. Wearables: this point is "fashion" and already receives a lot of money from the industry/start up. No need in my opinion that the JPND finances that.
All are important	**8**	
Other	**6**	• In line E. science should be replaced by neuroscience, as the other research fields are also science... • I have so far agreed with all and have not yet commented. However I worry a bit about too large initiatives when it comes to something, such as e.g. bioinformatics, and worry that D. is missing some topics; some areas are included while others are not. We certainly should promote increased numbers of ND researchers across the board, but could also include here to bring in e.g. cell and synapse biologists, among others, next to the topics now included in D. • The same comment as in the previous sheet. The number of partners and eligibilty criteria should not be too narrow. • D: The biomedical approaches to treat ND deserve absolute priority. • Propagation of information without validation from reality

Question 42 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**1**	
B	**-**	
C	**1**	
D	**3**	• D - this is likely to be driven by more common disorders such as CVD and diabetes so to some degree no need to double fund • Option D seems overly ambitious. People are already flooded with advice on how to change lifestyles. In any case, it is now abundantly clear that the same healthy lifestyles are good to promote general health
E	**1**	
F	**14**	• I don't see a major role for neurosurgeons in NDs and don't understand why this profession is highlighted specifically • I don't see an important role for neurosurgeons specifically. I don't see a need to prioritise their education over other clinical researchers from other disciplines such as geriatrics, psychiatry, neurology or family medicine/general practitioner. • The role of neurosurgery in the future of ND seems to be quite open for the next decade. • Not sure why F is only focused on neurosurgeons? • very specific don't get it • Point F is an odd bird in the list.
G	**-**	
All are important	**4**	
Other	**3**	• In line E. science should be replaced by neuroscience, as the other research fields are also science... • Awareness about ND is the key item to disseminate to the entire community. • They are all broad and general - to date the emphasis on technology rather that interpersonal care has been an obstacle. Also much of the research in demetia is about relationships (inter-dependence) not independence and the dementia frineds concept has in some cases served to push people into the disease model rather than the disability model.

Question 45 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**1**	• "A. Strengthen the commitment of national governments to support ND research". "C. Increase national earmarked budgets for transnational research". It is not clear to me what these points mean and what consequences they will have on the budget available for ND research within each country. Also smaller-scale projects within each country are in need of support, because such projects make it possible for a larger number of laboratories and clinics to actively engage in ND research (and not just a few stellar ones...).
B	**-**	
C	**1**	• "A. Strengthen the commitment of national governments to support ND research". "C. Increase national earmarked budgets for transnational research". It is not clear to me what these points mean and what consequences they will have on the budget available for ND research within each country. Also smaller-scale projects within each country are in need of support, because such projects make it possible for a larger number of laboratories and clinics to actively engage in ND research (and not just a few stellar ones...).
D	**1**	
E	**1**	
F	**2**	• F. is currently impractical. First, you should increase the educational level of EU politicians. Then you can start "F" implementation.
G	**2**	• Already accomplished
All are important	**7**	
Other	**-**	

Question 48 – full responses

For each theme the question: 'Which priorities do you consider to be less important? (please explain below)' was asked. Most respondents commented that they thought particular priority/priorities were the least important. These responses were collated into the bar charts included in the main report above. These appendices display the full responses to this question.

Priority	Number of respondents	Comments
A	**1**	
B	**-**	
C	**1**	• should be grants and budget for this from EU
D	**2**	• D - they should not need any more encouragement than that which is normal in leading research institutes • D - important to consider opportunity costs and social media is now primary source of information so best to have good comms folk do this supported by researchers
E	**2**	• "E" looks out of topic herewith. It is not seems to me that the scope of ND programs is to develop "dissemination tools".
F	**1**	
All are important	**7**	
Other	**2**	• Themes 7 and 8 should not be separate topics as they belong together. • More could be said about engagement with people living with dementia as partners in communication and dissemination