IHI workshop on neurodegenerative diseases

Event report

21 March 2025 Innovative Health Initiative

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1 About this report

On 21 March 2025, the Innovative Health Initiative organised a workshop examining project outcomes, challenges and opportunities regarding neurodegenerative diseases in Europe and how public-private partnerships could help answer some of the complex questions surrounding these diseases.

Dementia and neurodegenerative diseases affected 14 million people in Europe in 2019, and they are one of the leading causes of dependency and disability among older people[1]. Since 2000 there has been an increase in deaths caused by Alzheimer's disease and other dementias, yet 65% of health care professionals and 80% of the general public think that dementia is a normal part of ageing[2].

New innovative technologies and therapies could help to diagnose Alzheimer's disease faster, understand it better, and slow or even halt its progress[3]. Public-private partnerships are a key vehicle to transform cutting-edge scientific knowledge into concrete patient outcomes[4]. The last year has seen significant advancements as new, game-changing treatments and diagnostics emerge. But they also come with challenges regarding implementation in the care systems and access for patients. The need for innovation in this field remains huge.

The Innovative Medicines Initiative has funded more than 20 projects so far that are tackling Alzheimer's disease[5][6], and the Innovative Health Initiative is following in those footsteps. The workshop examined how the public-private partnership model has worked in various IMI and IHI projects, and identified hot topics and key areas where public-private research could have an impact in the future, building on what has been delivered so far.

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[1] https://www.alzint.org/u/World-Alzheimer-Report-2024.pdf

[2] https://www.alzint.org/u/World-Alzheimer-Report-2024.pdf

[3] https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2023.1321225/full

[4] https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2023.1321225/full

[5] https://www.ihi.europa.eu/projects-results/health-spotlights/impact-dementia

[6] https://www.efpia.eu/news-events/the-efpia-view/blog-articles/imi-impact-collaboration-is-key-to-dementia-challenge/

2 Executive summary

The number of people living with dementia, mostly due to Alzheimer's disease, has been estimated at more than 50 million globally. However, most of those affected are in the early stages of the disease, suggesting that there is a window of opportunity to tackle it.

Participants at IHI's workshop discussed the pressing need for both a new, effective drug to tackle Alzheimer's disease and solutions that could improve quality of life for people living with Alzheimer's. They spoke about how a more positive, "brain health" approach should be adopted that could reduce the risks that a person will develop Alzheimer's.

Public-private partnerships such as those funded under IHI and IMI are the perfect vehicle to drive innovative research in this field. Collaborative projects involving industry, universities, SMEs, patient organisations and more create neutral platforms supporting trusted environments for knowledge exchange, encouraging joint capacity building and bridging innovation gaps for the public good.

Early engagement with regulators is crucial to ensure that innovative results achieve maximum impact. Early and active participation with patient organisations is also essential to ensure that the resulting innovations are useful for and wanted by patients.

Innovators must strive to ensure that they are creating outputs that will be accepted and implemented by the healthcare ecosystem and community. Hospitals and healthcare practitioners are often change-averse so researchers should consider how they can be incentivised to adopt new innovative treatments. Where appropriate, training and educational programmes should be set up to facilitate use of new innovations.

The clinical trial capacities of Europe remain limited because of fragmented regulatory landscapes and operational challenges. The workshop heard of the urgent need to adopt novel trial approaches such as platform trials to accelerate drug development. Advanced modelling approaches could also play a role. Identification of more trial endpoints, specifically those that matter to patients, was flagged as a priority, and the need for new biomarkers was also highlighted. More solutions for data interoperability and harmonising data standards (including metadata) to ensure full leverage of existing resources and knowledge were pinpointed as key to ensuring success.

3 Key takeaways

- Public-private partnerships such as IHI and IMI deliver a particular value to address challenges in neurodegeneration as a neutral convener, bringing a wide range of stakeholders around the table to produce impactful science.
- Collaboration can bridge the innovation gap, build real-world evidence to support decision making and advance new therapies.
- When it comes to diagnosis and disease interception, it’s essential to think beyond research and include a regulatory component to improve impact.
- Integrating results into healthcare is complicated. Doctors tend to be overloaded and many still believe that dementia is normal ageing. Healthcare professionals must be trained to use new tools.
- Some success stories are emerging because companies can progress biomarkers developed precompetitively into the regulatory pathway.
- Carrying out clinical trials in Europe is difficult because of the fragmented regulatory landscape. Europe is becoming less attractive as a place to run trials.
- There is an urgent need for novel trial approaches such as platform trials, but more clarity is needed regarding moving from the pre-competitive space to the competitive space.
- There is also a need for all kinds of trial endpoints, and these trial endpoints must be linked to the long-term endpoints that matter to patients.
- More biomarkers are vital.
- More solutions for data interoperability and data standards (including metadata) are needed. Digital tools will only work if accepted by patients, so a consensus is needed regarding which ones can be used by clinicians.
- In order to achieve longevity and sustained impact of project outputs, resources are needed, and IHI and IMI projects should also inform each other about research outputs to avoid duplication of work.
- IMI and IHI projects have global impact – for instance, work done by AETIONOMY is now feeding into a precision medicine hospital in the Middle East.
- The industry is ready to use advanced modelling in clinical trials, as well as other key innovations like knowledge graphs, modelling of disease progression and digital tools.
- Implementation science will enable health innovations to enter the health ecosystem. The PROMINENT project focuses on how health economics can pave the way for new Alzheimer’s treatments to reach citizens.
- It is vital that hospitals can easily take up tools developed in IHI and IMI projects. Many hospitals are change-averse so how can change be incentivised?
- New financial models for future treatments for Alzheimer’s disease are needed. Innovative solutions (e.g. healthcare bonds) should be developed which can be delivered in timeframes that are attractive to politicians.

- A drug that works is needed, and the community should take inspiration from the example of obesity drugs.
- Dialogues about new research projects should involve patients and people with lived experience at the earliest stages.
- Researchers should not only focus on disease progression but also on the factors affecting quality of life.
- Dementia sits on the border between healthcare and social care – input from both sectors is needed.
- Increased efforts need to be made to involve communities that are often not present in research.
- GDP is driven by brain health, and everyone will benefit from better brain health
- A more positive, brain health approach is needed.

4 Setting the scene

Every year, almost 10 million new cases of dementia arise[7], resulting from a variety of diseases and injuries that affect the brain. Dementia is the seventh leading cause of death and it affects memory, thinking, and the ability to perform daily activities. It is also the area of medicine with the highest attrition rate in bringing innovations to the market[8].

The workshop's first session explored the challenges that stand in the way of neurodegenerative research and innovation that public-private partnerships (PPPs) such as the Innovative Health Initiative (IHI) could address. Several speakers emphasised the unique value that PPPs such as IHI bring to this field. They spoke about the importance of collaboration to bridge implementation gaps, the need for real-world evidence to boost understanding and support decision-making, and how new therapies and diagnostics should be advanced.

To kick-start the discussion at the workshop, Kevin Quaid, a person who is living with Parkinson's and dementia with Lewy bodies and is the Chair of Alzheimer Europe's European Working Group of People with Dementia, spoke about the need for research into neurodegenerative diseases and the importance of involving people with lived experience.

“Dementia is more common than anyone realises, but people who get an accurate and timely diagnosis can still lead an active and productive life. Technologies are there to help, but there is a lack of knowledge about the different dementia types,” he told the workshop.

“The fact that more drugs are coming onto the market means that we are entering a new era. We need to double our efforts in research and in finding that cure.” He stressed that researchers should always ask people with lived experience rather than assuming what they need.

Miia Kivipelto of the Karolinska Institutet, shared the point of view of the doctors that implement the outputs from research and innovation in practice. She emphasised that although we are living through “exciting times” in the field of Alzheimer's research, there are large implementation gaps that need to be resolved. Early detection, prevention, precision and combination treatments will be the focus of future disease management and need to be implemented in the clinic. But as people with neurodegeneration are all different, so are the healthcare systems, and one size does not fit all.

Simon Lovestone of Johnson & Johnson (J&J) Innovative Medicine Janssen Research and Development, highlighted how projects of the Innovative Medicines Initiative, now IHI, have been highly productive and collaborative research endeavours, but stressed the importance of going further and faster. Johnson & Johnson (J&J) Innovative Medicine Janssen Research and Development teamed up with Gates Ventures to create the Global Neurodegeneration Proteomics consortium (GNPC) which gathered 40 000 samples, generating data from 300 million protein assays from 23 contributors[9].

A second phase is currently being planned, expanding to other pharmaceutical companies and other collaborators. All the researchers at the workshop were warmly invited to join. At present, proteomics and the understanding of proteomes at population level is an area of high interest and it

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[7] https://www.who.int/news-room/fact-sheets/detail/dementia

[8] https://www.sciencedirect.com/science/article/abs/pii/S1474442211700047?via%3Dihub

[9] (Note: The GNPC's V1 Harmonized Data Set (HDS) is accessible to the broader research community as a shared, global resource via the AD Data Initiative's (ADDI) data platform, the AD Workbench (for approved use/users) as of July 15th, 2025[9]).

is ripe for driving innovation. The GNPC and the UK biobank (now also including data from 300 thousand proteomics) represent huge datasets. A challenge for driving innovation which could be picked up by IHI is the analysis of these datasets, as well as the enrichment of this and other data collections with data from more diverse populations.

Violeta Stoyanova-Beninska of the European Medicines Agency (EMA) stressed the importance of developing a better understanding of disease and patient population heterogeneity, their molecular etiology and pathways. Additionally, to progress proof-of-concept studies there is a need for better non-clinical models that are representative of what happens in the clinic. Further challenges lie in the understanding of how to better use digital tools and how to fully exploit the richness of available data.

George Vradenburg of the Davos Alzheimer's Collaborative told the workshop participants that conventional thinking around neurodegenerative diseases needs to shift. He emphasised the need to look at a person's entire life course. "We should be talking about brain health, not brain disease," he said, and called for more research into maternal health and the impact of the first few years of life on a growing brain. "We only have one brain for the whole of our lives," he said.

The workshop participants reflected on how complex the brain is, and how unique biological challenges such as the blood-brain-barrier can make it difficult to progress innovations in this field. Simon Lovestone stressed that the complexity of the brain should not be viewed as an unsurmountable obstacle, but rather as a "spur for innovation". Zivjena Vucetic of Beckman Coulter Diagnostics also recognised disease complexity as a key challenge in the development of diagnostics for neurodegenerative diseases, but pointed out that this did not stop progress in the equally complex field of cancer diagnostics.

The European context

Tim Raemaekers of the Combatting Diseases Unit of the European Commission's DG Research and Innovation stressed that "brain science has been a long-standing priority for the EU," but at the same time noted that "Europe is good at producing excellent science but it is less good at transforming the results into technologies and products." Public-private partnerships could help address some of the ecosystem challenges that prevent real-world impact.

Raemaekers introduced the workshop participants to the upcoming European Partnership for Brain Health, which is due to start in 2026. The new partnership will form a bridge between the public and private sector to make advances in brain health, and the European Commission wants the new partnership to work in synergy with IHI to leverage public-private investment towards the greatest gains.

George Vradenburg remarked that the challenge of tackling Alzheimer's disease and other neurodegenerative diseases is not a Europe-only problem, but a "global issue" and that the global South should not be forgotten.

Detecting Alzheimer’s disease earlier

The earlier Alzheimer’s disease can be detected, the better for the patient, the workshop participants heard, and it was hinted that one day it might even be possible to prevent Alzheimer’s disease altogether.

Miia Kivipelto of the Karolinska Institutet stressed that the time has come to shift the research focus towards early-stage Alzheimer’s and how to spot the early signs of disease. She spoke about how 45% of all dementias are linked to modifiable risk factors and how, if the public and clinicians were more aware and knowledgeable about this, steps could be taken to reduce the number of people who go on to develop full-blown dementia.

“We need to move the focus and attitude towards the earlier phases. How can we make people more aware of risk factors?” she asked.

The promise of biomarkers

Blood-based biomarkers, digital markers and multimodal biomarkers might serve as important diagnostic tools for the early detection of disease as well as for guiding the patient journey over the years as the disease progresses. Zivjena Vucetic spoke about the key challenges in bringing biomarker-based diagnostic innovations to the patients.

“It’s difficult for us to pinpoint the right biomarkers. From a diagnostic development perspective, we need to focus on a critical few biomarkers that we can bring from research to the market,” she told the workshop participants. A public-private partnership could speed up the funnel of research to bedside, driving progress towards the better definition of disease subtypes and towards fostering the incorporation of multi-modal diagnostics to attain a more holistic and system-level understanding of disease complexity. Further challenges include clinical and regulatory bottlenecks, and that healthcare systems are not ready to take up innovations, e.g. in the case of multimodal biomarkers. More post-approval studies are needed to confirm clinical utility and cost-effectiveness.

Marta Vidorreta Diaz De Cerio of Siemens Healthineers also spoke about how the use of minimally invasive biomarkers could revolutionise the treatment of Alzheimer’s by enabling early detection and ongoing disease monitoring, positively impacting patient care and outcomes, while reducing costs. She highlighted how the PREDICTOM project is investigating novel innovative approaches to Alzheimer’s diagnostics, starting from early disease screening. Here the consortium is using a combined approach looking at genetic (e.g. ApoE) and epigenetic (microbiome) risk factors, including digital cognitive assessments and fingerprick blood sampling to measure Alzheimer’s disease-related biomarkers such as *pTAU217*. Fingerprick sampling is cost effective: it can be done at home and the dried samples can be shipped easily, thereby simplifying logistics and reducing costs for both diagnosis and disease monitoring. Importantly, it will make diagnosis and disease monitoring easier for patients living in remote areas.

Violeta Stoyanova-Beninska said that the EMA is eager to use new biomarkers but they must be proven to be of a high quality.

“From a regulatory point of view we very much want to make use of biomarkers but what we always want to know is: are they validated? Can they really show a correlation with clinical outcomes? Only then can we accept to use them instead of clinical outcome measures,” she told the workshop participants.

New approaches to clinical trials

In the past two decades, 99% of clinical trials for Alzheimer’s have failed, Zivjena Vucetic said, and there are no existing models that accommodate some of the more adaptive clinical trials that we see in oncology. She pointed to a need for reform in clinical trial designs for Alzheimer’s, highlighting the potential of platform trials.

“We should do some pilot programmes to embed new diagnostic tools in the real world early on, to test if our healthcare systems can take them on, rather than going through long development cycles only to find that they don’t work in the real world,” she said.

Vucetic said that collaboration with regulators was necessary to allow the inclusion of more real-world evidence and better define endpoints, a view which was echoed by Stoyanova-Beninska of the EMA.

“Regarding innovative and alternative trial designs, it’s important that regulators and the people involved in drug development agree which trial designs will bring us in the fastest way and the most efficient way towards the answers to the questions that we have,” said Stoyanova-Beninska.

“Early dialogue is very important. Many of the clinical and nonclinical data that have been generated could have been different if we had had an early dialogue to decide which models are useful, which endpoints are useful for clinical trials and what can be reduced and avoided.”

The value of the PPP

Most of the participants at the workshop were either previously or currently involved in an IMI or IHI project, and all were familiar with working in a public-private partnership (PPP). Throughout the session, participants mentioned how collaboration can: i) bridge implementation gaps, ii) build real-world evidence to increase understanding and support decision making, and iii) advance precision, prevention and novel combination therapies.

Miia Kivipelto outlined how the public-private model exemplified by IHI and IMI could help to close the gap between the exciting results that are appearing in laboratories and real-world clinical uses. PPPs such as IHI are ideal instruments to deliver necessary real world evidence, facilitating collaborations that can go further and faster by building on the knowledge of previous projects to co-create new solutions.

Simon Lovestone emphasised that the collaborations fostered by IMI/IHI opened up doors that were firmly shut when the industry worked alone. “We need partners, and one of the many things that IHI has done is to provide those partners in some extraordinarily successful projects from which we’ve learned a huge amount,” he said.

Violeta Stoyanova-Beninska of EMA stressed the value of PPPs such as IHI in fostering early dialogue and engagement with regulators, to ensure that the data that reaches the regulators are generated using the right models and endpoints.

George Vradenburg suggested that an initiative in neurodegeneration similar to the Operation Warp Speed (OWS) PPP initiated by the United States government could be beneficial and could be enabled by IHI. During the pandemic, Operation Warp Speed facilitated and accelerated the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics and diagnostics.

REMAINING CHALLENGES

As the first session of the workshop wrapped up, the participants reflected on the challenges that need to be addressed in neurodegenerative disease research. The five main issues are outlined below:

- Disease complexity
- Bringing innovations to healthcare and the patient – and not just in Europe
- Biomarkers and endpoints – vital to identify and validate correctly the critical ones
- Regulatory bottlenecks – important to have early dialogue
- Clinical trial design

4 Diagnosis and disease interception

Gill Farrar of GE Healthcare launched the discussion on diagnosis and disease interception by outlining the impact of the AMYPAD project, in particular describing how achieving one of the project's regulatory goals delivered longer lasting impact than they had imagined.

The goal of AMYPAD was to show how effective positron emission tomography (PET) was in providing evidence for the accumulation of beta amyloid deposits in the brain and to develop methods for the harmonisation of imaging read-outs using different PET tracers. One of the key outputs of the project – a biomarker qualification opinion for a method using a Centiloid scale to quantitatively evaluate the burden of amyloid deposition – was achieved thanks to the push for regulatory impact that was included as a formal project deliverable after the interim review of the project.

Farrar outlined how clinicians usually looked at PET scans and drew subjective conclusions on how developed a person's Alzheimer's pathology was according to what they could see, based on a positive/negative dichotomy.

AMYPAD evaluated whether a Centiloid scale could be used to quantify the burden of amyloid detected by PET scans, moving from a simple yes/no answer to a continuous measure that could better reflect the status and changes in amyloid deposition, opening up huge opportunities. The scale also has clinical utility e.g. in anti-amyloid trials. The AMYPAD researchers stress tested how the Centiloid methodology could be used for this purpose "to the nth degree," and strongly benefitted from constructive feedback from the European Medicines Agency (EMA), Farrar said.

> *" I would emphasise the importance of thinking beyond the research elements of your project and have a deliverable that has a regulatory component because it brought credibility to the AMYPAD project."*
>
> – **GILL FARRAR, GE HEALTHCARE LIFE SCIENCES**

Their interactions with the EMA were very helpful: "They were very constructive, they knew exactly what they needed and we were able to go away and produce that work," said Farrar. "When the biomarker qualification opinion was adopted, early last spring (2024), it created enormous visibility for the AMYPAD team. We've been invited to conferences in the US, it led to some very prestigious publications and we've had two PhDs awarded on the back of the work we've done."

Frederik Barkhof of the Amsterdam University Medical Centre, who co-led AMYPAD, noted that AMYPAD built lasting infrastructures, saying: "the AMYPAD community still work together on EPAD and AMYPAD data with the help of ADDI, producing new impactful outputs."

AMYPAD built on the data cohorts and data infrastructure developed by its sister IMI project, EPAD, combined with data from other pre-existing cohorts. Barkhof stressed the importance of making all the cohort data harmonised and interoperable.

Strong leadership and a pre-competitive spirit was essential for successful outcomes. The project built on the pre-existing EPAD infrastructure and on other pre-existing cohorts, to which further PET data was added. Raj Long of Gates Ventures commented on how the outcome of AMYPAD is a concrete demonstration of how, with the right push, it is possible to go successfully through the regulatory journey.

Emilio Merlo-Pich (International Foundation Big Data and Artificial Intelligence for Human Development- iFAB) from the project PRISM added that AMYPAD had a large amount of data and resources available already, which made it possible to achieve their regulatory goal. For other projects that are pursuing innovative tools and may have similar ambitions, there is often a need for further industry investment (funding and know-how) beyond the duration of a project for reaching such achievements.

After hearing about AMYPAD, the participants discussed the opportunities for improving diagnosis and disease interception. Better definition of disease subtypes, the need for multimodal biomarkers and diagnostics, and taking advantage of AI were highlighted as areas where impact could be achieved and more research is needed.

In light of the many different innovative solutions that are becoming available, work on harmonisation and standardisation of test results is of paramount importance. Harmonisation and standardisation of blood-based biomarkers were noted as key areas where public-private projects could play an important role. The lack of availability of tracers needed to carry out e.g. *tau* imaging was mentioned as a key problem. If a *tau* therapeutic were to become available tomorrow, the workshop participants heard, it could not actually be used in a hospital setting because there isn't enough *tau* PET being manufactured. This is a critical issue that may delay or even prevent access to necessary new drugs.

Blood-based biomarkers could address that, the audience heard. "The use of blood-based biomarkers to triage 80% of people out of needing an amyloid PET scan is the way to go on that," said Farrar.

> *"Making a brain health check-up every year as common and routine as the check-ups for the rest of your body is critical."*
>
> – **GEORGE VRADENBURG, DAVOS ALZHEIMER'S COLLABORATIVE**

Although biomarkers show great promise, there is an implementation challenge – how to integrate them into healthcare systems.

Another point raised was that more should be done to bring the knowledge generated by research to the clinic, so that it will have maximum impact. Outputs and results from research must be better implemented into clinical practice (a positive example was given for Sweden). While regulatory approval is needed for the use of a biomarker in drug development, it is not a strict requirement for adoption in clinical practice, although it can be beneficial. Digital technologies are nowadays often sent to the market without qualification, but a participant questioned if these technologies would then provide the data needed by the clinicians.

Lessons in implementation could be taken from the world of cardiology, which was in a similar situation 30 years ago, one participant suggested. Simon Lovestone stressed the importance of taking explicitly a precision neuroscience approach to clinical trials, since this will help with the uptake of biomarkers in the clinics. Miia Kivipelto stated that understanding the facilitators and barriers to implementation of biomarkers in clinical practice is a goal of the IHI AD-RIDDLE project.

Another issue in relation to implementation is that doctors are few and overloaded: it is a challenge to introduce these innovations into the clinical workflow without creating an extra burden. At the same time, it is necessary to provide continuous education to healthcare workers.

There is still a stigma surrounding Alzheimer's disease, and doctors often believe that it is part of normal ageing. There is a massive need for more education and increased awareness, Paola Barbarino of Alzheimer's Disease International stressed.

To catch Alzheimer's disease early, regular health checks for the brain should become the norm, the participants heard. "Making a brain health check up every year as common and routine as the check ups for the rest of your body is absolutely critical. We have to introduce this in primary care," said George Vradenburg.

5 Clinical studies and trials

The discussion on clinical studies and trials was opened by Craig Ritchie (Scottish Brain Sciences) of the EPAD project who reflected on how EPAD aimed to set up a platform for phase two clinical trials for Alzheimer's disease drugs. Although the platform was created, the project did not reach its goal of testing a drug out on the platform, due to the strong element of competitiveness that arose.

"Here again we are talking about the need for novel trial designs, platform trials and basket trials. We've been there. But the reason that we couldn't set up a platform trial with EPAD was that the moment you bring an asset in, you move from pre-competition to strong competition and that's a very difficult thing to overcome," said Serge Van der Geyten of Johnson & Johnson, who was also co-lead of EPAD. "The question is how can we move from the pre-competitive space (which IHI and IMI does beautifully) into the competitive space?"

Despite that challenge, EPAD left a strong legacy. Its data were among the first to be fed into the ADDI platform (co-designed with the EPAD community) and have been seminal for the work of AMYPAD. EPAD created a huge community of "Epadistas" which nurtures early career researchers and is still going strong.

> *"The moment you bring an asset in, you move from pre-competition to strong competition and that's a very difficult thing to overcome. How can we move from the pre-competitive space to the competitive space?"*
>
> – **SERGE VAN DER GEYTEN, JOHNSON & JOHNSON**

Cristina Sampaio of the CHDI Foundation made the point that platform trials have only been carried out successfully in rare diseases and that at CHDI they created a platform for Huntington disease trials but that companies did not find it attractive. Platforms have been created for Parkinson's trials for instance but only for repurposed drugs and using classical designs.

Frederik Barkhof mentioned the Oxford platform trial in multiple sclerosis (MS), using repurposed compounds and an imaging biomarker with early reading while continuing to recruit, so that if a read-out is positive, it is possible to jump to Phase III. This is why platform trials may be challenging in Alzheimer's disease, where there is strong competition between companies and alternatives should be explored.

Discussions mentioned several different types of novel trial design – adaptive, combination, and decentralised for instance – and that these could become the next generation of clinical trial designs. The workshop participants also reflected on the fact that one third of the pipeline of new treatments in AD is made up of repurposed drugs. In light of the recent approval of the two anti-amyloid antibodies, Dag Aarsland (King's College London), leader of RADAR-AD and PREDICTOM, mentioned the importance of clinical studies for gathering real world evidence on these innovations, also considering patient eligibility for treatment, which is currently based on very narrow criteria.

Craig Ritchie noted that if EPAD were to be done again, he would put a repurposed medication into the platform as a proof-of-concept rather than starting off with an innovative compound. He suggested that we should not necessarily give up on the idea of an European platform.

Several participants made the point that there is a need for qualified and predictive biomarkers that can be deployed and used as endpoints, giving a readout in a short timeframe as enablers for innovation in trial design. The need to test the biomarkers in clinical trials was stressed – this is something that diagnostic companies cannot do on their own.

Raj Long gave the example of a regulatory safe space between the regulatory authorities from several countries that was created to develop common guidelines for Alzheimer's disease. She said that a similar approach could result in common principles for developing biomarkers for Alzheimer's disease.

"We will never get global standards. We will never get harmonised standards because regulators are individual jurisdictions. But we can agree on some common principles that can then be translated to implementation." she said.

A recommendation was made to bring the HTA into the conversation at an earlier point, to ensure that the generation of the necessary pharmaco-economic data and real world data is timely and correctly considered.

The workshop participants heard that rates of clinical trials being carried out in Europe were dropping, whereas they are accelerating in the US, Asia, the UK and Australia.

There are different dynamics for first-in-human and Phase III trials, European sites have to become more competitive compared to those in the rest of the world.

> *"We will never get global standards. But we can agree on some common principles."*
>
> – **RAJ LONG, GATES VENTURES**

Angela Bradshaw of Alzheimer Europe reminded the participants that patients in Europe want to be part of innovative trials, and called for more support for the clinical trial ecosystem in Europe.

The workshop participants heard that clinical site performance has to improve, and the training of raters was highlighted as a particular challenge to this end.

Two problems that were identified were: i) the need for a (digital) endpoint with early readout that is accepted by the whole R&I community; and ii) standardisation of rater training. Linus Jönnson (Karolinska Institute), leader of PROMINENT, pointed out that any endpoint must not only be read early but also be credibly linked to the final endpoints and benefits that are of concern to patients and payers. Cristina Sampaio referred to a common training platform for raters that is accepted by all the pharmaceutical companies that has been developed for Huntingdon's disease, and said that this could be an example to follow.

6 Data solutions and digital innovation

IHI's Executive Director, Niklas Blomberg, chaired the data solutions and digital innovation session. The discussions were kick-started by Anthony Brookes (University of Leicester) from the EPND project and Dag Aarsland (RADAR-AD and PREDICTOM projects).

Anthony Brookes started the discussion by presenting the data platform of EPND. "The needle we're focusing on is to enable this community to come together more and do more collaboration, more data sharing, more sample reuse and so on," he said.

The data platform developed by the EPND project is different from other data storage systems because is community designed. The user has control of both the data and the access that they grant to said data, per user. The data platform also goes beyond a simple data solution since it also includes samples. It is federated and based on the ADDI AD workbench. Most importantly, the platform is well on track to becoming sustainable.

"It's a place where you can describe your data, describe your samples, find samples, request access, process access requests, collaborate, analyse data and so on," said Brookes. The progress of the EPND hub has been strong with around 100 cohorts already included in the platform and progress made in its "multi-tenancy model", where the hub has already been re-used by new projects (e.g. AD-RIDDLE).

Brookes stressed the importance of boosting collaboration and diminishing competition. More work on data and metadata standards, as well as platform interoperability, is needed to enable the sharing and re-use of data. A common data structure is also vital to enable the use of AI.

> *"The needle we're focusing on is to enable this community to come together more and do more collaboration, more data sharing, more sample reuse and so on."*
>
> – **ANTHONY BROOKES,**
> **UNIVERSITY OF LEICESTER**

Cristina Sampaio urged participants to consider data management from the initial phases of project development. She stressed that it is also vital to educate the community on these topics.

"Make a proper data management plan beforehand. All of these things are not standard practice," she advised. She pointed to a website called ENROLL HD which has a wide range of resources and documents regarding data management and use.

Dag Aarsland spoke next about digital cognitive tests, highlighting examples from the RADAR-AD and PREDICTOM projects. RADAR-AD developed a digital platform that drew on information gathered via smartphone, wearable and home-based digital technologies to track subtle changes in the cognitive and functional abilities of people with Alzheimer’s disease. PREDICTOM used the learnings from RADAR-AD and is developing a platform that can identify people at risk of dementia, even before symptoms start. The project aims to move disease screening out of hospitals towards primary care settings. Patients could even start the screening process from their own homes, by collecting their own samples of bodily fluids and using digital technologies.

Ethics, regulatory aspects and integrating patient feedback into the digital tools are vital parts of the two projects. “We can have a fantastic digital tool, but if the patients with cognitive impairment are unable to use it, we can forget it,” said Aarsland.

Combining digital cognitive tools with biomarkers, biofluids, imaging and results from tests that measure electrical activity in the brain (EEGs) will be the way forwards, Aarsland said. He also said that moving from the hospital to GP clinics and ultimately to patients’ home will revolutionise Alzheimer’s care. He spoke about joining the dots between projects and making much-needed connections so that IMI and IHI projects complement each other rather than duplicating efforts. “We don’t need three different platforms. We need one platform in Europe where the data can flow and the users can access it,” he said.

On that point, Magali Haas of Cohen Veterans Bioscience asked whether IHI would organise and manage a central platform for all data that is generated through these programmes, and Niklas Blomberg answered that as a funder it was not IHI’s role to operate such a platform for the community. IHI’s role is to fund health projects generated from competitive calls for proposals, including those related to digital health and data. If such a platform were to be created, it should include a clear business case considering different potential income streams, and there must be a research community interested in it. Raj Long warned the workshop participants not to underestimate the work behind making a platform self-sustainable.

Paola Barbarino from Alzheimer’s Disease International made the point that the design of a research project is really critical and that engaging the end users, the patients, at the early stages is necessary to maximise the impact of the outputs.

The need for sustainability was highlighted and several participants said that establishing a legal entity to carry on the work of the project past the project’s end is necessary.

“Establishing a legal entity needs about 40-50% of the total budget and this is always underestimated,” said Andreas Ebneth of Johnson & Johnson Innovative Medicine Janssen Research and Development, who was speaking from his experience of starting a non-profit foundation to continue the work of the EBISC project. This experience was integrated in the early design of the sustainability model of EPND.

Martin Hoffman-Apitius of the Fraunhofer Institute for Algorithms and Scientific Computing also pointed out that there is the possibility to re-use legal texts and resources that are created for one project in other projects. He called for more standardisation of legal components.

The value of the public-private partnerships (PPPs) also featured strongly during this discussion. Miia Kivipelto outlined that PPPs are the perfect vehicle to standardise data and ensure that it is of high quality, that PPPs enable data sharing in a trustworthy way, and help navigate the regulatory landscape.

Brookes also emphasized the value of the PPP model, saying that building a high-quality platform and creating a viable solution for the longevity of the EPND technical hub would not have been possible if it were undertaken by academics alone.

“Academia could have designed and built this, we could have come up with these technologies, but it would have been academic-grade software. By having groups like Gates Ventures and ADDI and the private sector involved, we ended up producing bulletproof, very professional, sustainable software,” he said.

7 Filling the pipeline and improving translation

The afternoon session was kick-started with an introduction to AETIONOMY, an IMI project that ran from 2014 to 2018 and focused on generating a mechanism-based taxonomy of Alzheimer’s and Parkinson’s disease. When the project first started, the knowledge about biomarkers and the guidelines we have today were not yet available.

“It was starting out in the wild. AETIONOMY was special, it was one of the first big data projects in the IMI context, starting with a holistic approach and trying to escape the trap of over-analysis,” said Martin Hofmann-Apitius, who leads the bioinformatics department at the Fraunhofer Institute for Algorithms and Scientific Computing and was the academic lead for the AETIONOMY project.

The AETIONOMY project was a frontrunner as a big data project in neurodegenerative research, generating data landscapes and heavily focusing on data interoperability and standardisation. To this day, AETIONOMY has one of the largest and most comprehensive common data models for neurodegenerative diseases and the project led to the establishment of one of the first foundational models for Alzheimer’s disease.

Knowledge graphs to study neurodegenerative diseases were used for the first time in AETIONOMY, the participants heard, and the project was the first to carry out comparable progression modelling for neurodegenerative diseases.

Johannes Streffer, SVP Global Clinical Development of Lundbeck and member of the World Dementia Council, highlighted the importance of knowledge graphs and the development of disease progression modelling.

“It is critical because industry can’t do it. It fosters innovative trial designs, for instance those using Bayesian approaches. If we would come to a point where we would have a better understanding of progression modelling and could use it for clinical trials, then that will reduce sample numbers and trial duration significantly. Industry is ready to use these designs if the field is supportive of it,” he said.

> *“Industry is ready to use these designs as well if the field is supportive of it.”*
>
> – **JOHANNES STREFFER, LUNDBECK**

Entire inventories of pathophysiology mechanisms for Alzheimer’s were developed by the project and there are 124 of them now, recently updated. They are available within a new project called COMMUTE which builds on the work of AETIONOMY. The COMMUTE project is primarily focusing on the links between COVID-19 and neurodegenerative disease, and it is investigating whether people who were infected with COVID-19 might now be more prone to dementia. It also explores the links between the immune system, social and psychological conditions and the risks of developing a neurodegenerative condition.

The results and learnings from AETIONOMY are now also being used in a new precision medicine hospital, in the United Arab Emirates. In that hospital, the lessons learned from AETIONOMY are being used to promote healthy brain ageing.

AETIONOMY also profited from its interactions with the project EPAD and its work has also informed the ongoing work on risk modeling in PREDICTOM.

The workshop participants heard that, building on progression modelling and stratification, the experts expect to see more personalised risk models in the future when there is more information available regarding qualified biomarkers. The importance of comparing models with existing placebo arms of trials, both for the validation of the models and for increased understanding of the patient populations included in the trials, was mentioned.

Johannes Streffer reminded the workshop participants about the work spearheaded by the project EMIF that led to the definition of different clusters in Alzheimer’s disease. The next thing that needs to happen is that this outcome is linked to progression modeling. Precision medicine seemed to be a key route for future progress. The workshop participants heard that areas that need to be explored further include: how to use progression models for individual predictions for patients, how to group patients into clusters and finally how to treat them with a personalised approach. Emilio Merlo Pitch marked the potential of building on AETIONOMY’s work for the development of digital twins for optimisation of clinical trials – Holger Fröhlich, from the Fraunhofer Institute for Algorithms and Scientific Computing (SCAI), noted that AI modeling based on predictions of speed of progression of disease in enrichment trials can significantly reduce sample sizes.

The push for innovative trial designs, including enrichment trials, also should be appreciated by regulators, the workshop participants heard. The European Medicines Agency was criticised for being slow with relation to innovative trial designs and digital twins, especially in comparison with the American Food and Drugs Administration (FDA).

To that, the European Medicines Agency responded that they are always open for any early dialogue but that they can do no more than promote that fact. The EMA also highlighted that they operate under a different legal framework to the FDA, and as an example they pointed out that the FDA’s framework allows them to make decisions based on predictions of clinical benefit, whereas the EMA has to be provided with a risk/benefit analysis which is positive before they can make authorisations.

8 Management of disease and healthcare preparedness

Linus Jönnson, coordinator of the PROMINENT project, kicked off the session by emphasising that the European population is ageing and that the healthcare system needs to be prepared for the future. He outlined how the PROMINENT project in particular is taking on the challenge of implementation science, utilising a health economics approach to develop tools that will facilitate evidence-based and personalised decision-making for the treatment of Alzheimer's patients. Their tools take into account cost-effectiveness and societal impact as well as direct health outcomes for the patient. Speed is of the essence, since solutions must become available to enable the introduction of innovations in the healthcare system. PROMINENT took the approach of involving innovative companies that have already marketed solutions into their consortium. The project then built on these innovations, enabling them to move rapidly from discovery to delivery to patients. For example, they have developed two new solutions for automated imaging analysis which will allow clinicians to better integrate this diagnostic information with other patient data. PROMINENT's final goal is to develop a clinical decision-making support system, not only for the benefit of the clinicians but also for the patients and caregivers. PROMINENT's tools also integrate cost-effectiveness algorithms which are important for the healthcare system.

“This type of project could not be done outside of this type of vehicle that IHI represents,” he said, outlining how patient perspectives in particular are incorporated into PROMINENT's work, and how the stakeholders involved in the consortium are from a wide range of sectors.

“We have the direct involvement of patients and caregivers, we have health economists and people who are very knowledgeable about healthcare systems as well as clinicians, innovators and researchers,” he said. He also stressed the importance of the connections made between two other IHI projects, AD-RIDDLE and PROMINENT, the cross-fertilisation that happened between them and the value of their collaboration. “We see solutions that we did not see when we started the consortium,” he said.

He had a cautionary note on how the “pull” from the healthcare system is essential to drive implementation.

“We try to make it possible for the healthcare system to use these technologies, but that will not be enough. The healthcare system has to actually want to use them. How do we make healthcare systems feel that dementia diagnosis, treatment and prevention is part of their core business? It isn't, at the moment.”

> *“How do we make healthcare systems feel that dementia diagnosis, treatment and prevention is part of their core business?”*
>
> – **LINUS JÖNNSON, PROMINENT PROJECT COORDINATOR**

Martin Hofmann-Apitius added that the healthcare system is currently so stable, it is risk-averse and asked the workshop participants to consider how to convince politicians or payers to change the status quo and become more open towards the innovations.

Jönnson stressed that researchers need to consider what the payers and the politicians care about in order to have impact. He observed that politicians are usually elected for short terms and that that should be considered when presenting them with proposals. He also suggested new financial approaches so that the people who are responsible for the relevant budget are involved.

“For instance, healthcare decision-makers are usually not responsible for elderly care,” he told the workshop. “Even if we have a solution that reduces the risk of nursing home placements, they’re not going to care. If we consider a different funding vehicle, for instance health impact bonds, that enables you to separate budgets and sync up with financial incentives.”

Paola Barbarino from Alzheimer’s Disease International told the participants that healthcare systems are scared of the hidden costs of care. “There are so many moving parts, and healthcare systems differ greatly. They are like supertankers, slow to change course, wherever you are,” she said.

Matthias Müllenborn from Novo Nordisk emphasised the importance of doing research on new financial models. He gave the example of an upcoming IHI project on cardiovascular disease that will do exactly this, suggesting that the time is ripe for a similar initiative in Alzheimer’s disease.

Angela Bradshaw advised the workshop participants to focus on drivers and incentives.

“Healthcare practitioners were financially incentivised to offer vaccinations and preventive health programmes in the pandemic. If we look at drivers and incentives based on an understanding of barriers, then we might be able to move the needle a little bit more,” she said.

Annemie Ribbens of Icometrix, leader of the CLAIMS project, outlined how, for SMEs, the fragmentation of the healthcare systems was a significant hurdle representing a large work burden, especially for a smaller company. She mentioned how reimbursement of their solution helped them in the US, and it was a relatively smooth process, whereas in Europe the system fragmentation requires approaching each individual country’s authorities separately. A solution that

> *“There are so many moving parts, and healthcare systems differ greatly. They are like supertankers, slow to change course, wherever you are.”*
>
> – **PAOLA BARBARINO, ALZHEIMER’S DISEASE INTERNATIONAL**

could help to ease the way through the fragmented European regulatory landscape would benefit smaller companies greatly.

For George Vradenburg, the drivers of motivation within the health system will be the patients. “Consumer activation is going to be a huge driver of change inside health systems,” he said. “We have to raise awareness that there are new drugs and new blood tests and that will have an impact. Primary care is the entry point.”

Using disease progression modelling could prove convincing to healthcare systems because it can provide a coherent measure of treatment effect, Jönnson pointed out. “If we can show that a particular treatment has a certain delay consistently in clinical measures and biomarker measures, if we can show that this patient will live for a longer time in the disease state but with a better quality of life, then we will have a convincing story,” he said.

A core factor of Alzheimer’s disease is the care component. People with Alzheimer’s often need a high level of care, and that can be difficult to quantify. Raj Long noted that healthcare stakeholders and patients alike probably want to know that they can not only live longer, but live longer without being a burden.

“Without being a burden to the state, in the context of care, without being a burden to the payer, in the context of insurance. It’s that parameter that we struggle with,” she says. But in Europe, one size won’t fit all, she warned. “The systems in Europe are different, and how you translate that burden is also going to be different. Is there room to do a small pilot?”

Simon Lovestone said he disagreed with a lot of what was said in the session, but brought a note of hope. “As a field we are punch-drunk with failure and we should raise our standards and expectations and plan for success, not for failure,” he said.

“Five years ago, obesity wasn’t a treatable condition. Five years ago, pharma-economists would tell you there was no business model for it because the effects of obesity are long-lasting, they take decades before they affect your health, and as a consequence of this, healthcare services are not going to fund GLP agonists. What happened? The patients are demanding [the new obesity drug] because they know they get a benefit from it. They don’t need to be persuaded with ever more sophisticated data. We need a drug that works. If we had a drug that worked, then all of these things we are worrying about would disappear like spring snow. We should be brave and bold and open enough to find a drug that actually works really well in neurodegeneration.”

> *“We should raise our expectations and plan for success, not for failure. We should be brave and bold and open enough to find a drug that actually works well in neurodegeneration.”*
>
> – **SIMON LOVESTONE, JOHNSON & JOHNSON**

Cristina Sampaio also spoke about the key hurdles to implementation in healthcare system, mentioning the need for reimbursement models for new (and sufficiently efficacious) drugs and, most importantly, the need to change the way the care system works. This is a challenge because the healthcare systems are complex and different in the European member states.

She also reminded the participants of the existence of the new EU Health Technology Assessment (HTA) Regulation which aims to increase cross-border cooperation to support Europe's innovation ecosystem. A key part of that is the establishment of the Coordination Group on Health Technology Assessment (the 'HTACG'), composed of Member States' representatives, mainly from HTA authorities and bodies.

9 Working with people affected by dementia

Angela Bradshaw set the scene for the patients' session by painting a picture of how Alzheimer Europe has been involved with IHI and IMI's research projects since 2010.

"As our journey progressed, so has the type and scale of our involvement," said Bradshaw. She outlined how, initially, in the first projects they took part in, Alzheimer Europe did a lot of communications and outreach, connecting people with lived experience to the project. Then, their involvement progressed to include ethics, and with that came public involvement activities. Patient advisory groups set up as part of projects have since expanded to include not only patients but their carers as well, and older adults that are at risk of the disease.

"We see our role as bridging science to society but also, really importantly, bringing society into science," said Bradshaw. "It's important that both of these aspects of the patient contribution are valued."

She stressed the importance that the early dialogue with patients continues, and about how dementia care sits between healthcare and social care, and how vital it is to integrate those two aspects.

> *"We see our role as bridging science to society but also very importantly bringing society into science."*
>
> – **ANGELA BRADSHAW, ALZHEIMER EUROPE**

Ana Diaz, also from Alzheimer Europe, presented a case study of a project that had successfully integrated patient input from the get-go – RADAR-AD. She emphasised how the early dialogue with patients was so crucial to select the correct devices to carry out the studies of the project. Key concerns raised by the patients included how often the devices needed to be charged, were they waterproof, would they be discrete or would they be extremely obvious when they were wearing them.

Diaz noted that sometimes patients have concerns that highlight an issue that may be inconvenient for researchers – for instance, one question sometimes raised is why there is an age limit of 75 for clinical trials. She encouraged researchers to listen to these concerns and to properly consider whether improvements could be made. She also highlighted the fact that the PPP model was a necessary enabler for this dialogue.

She emphasised the need for more diversity in research, more voices and different views. One clear impact, she said, is that early discussions with patients makes it much easier for patients to use the fledgling innovation later on.

Bradshaw highlighted that a key legacy of their involvement in so many projects is that there is an increased awareness in the research community. Now, she noted that when a new project starts, the engagement with patients happens much earlier than before. There is also a large amount of supporting materials available which wasn't the case before (e.g. a paper on informed consent delivered via the EPND project).

As an example of how projects can use results and outputs from previous projects, Cathy Brem from King's College London outlined how PREDICTOM leveraged RADAR-AD materials in their project. She also told the participants that several IHI projects focusing on Alzheimer's projects – PROMINENT, PREDICTOM and AD-RIDDLE – will soon meet in Luxembourg to discuss how to leverage even more joint learnings on patient and public engagement.

Liz Tunbridge of Boehringer Ingelheim made the point that patients are often as concerned about alleviating symptoms as they are about eradicating the disease completely, and that focusing on solutions that reduce the symptoms that patients experience on a daily basis can have an important impact on quality of life.

Communication with patients regarding the benefits of research outputs can be challenging, and Bradshaw noted that patients are often receiving a vast horde of information, some of which is misinformation, and that clear, evidence-based messages about research benefits need to cut through the noise. The participants heard that understanding what patients want to know and carefully considering what language to use is important – one questions raised was should conversations centre around prevention, risk reduction or other elements for instance.

George Vradenburg shared his experience from the US of talking to patients about the benefits of a treatment. He emphasised how important it is to use the right language and to make the links with what really matters to patients: "if you tell them it is more years with their family they get that."

He also mentioned the importance of considering gender, ethnicity and socio-economical differences when communicating with patients. This should be fed back into the clinical design e.g. when considering endpoints.

Niranjan Bose from Gates Ventures pointed out to the participants that "involving patients should be a no-brainer, so why is it a problem in Alzheimer's research?"

Wendy Weidner of Alzheimer's Disease International posited that this may be due to a certain level of discomfort in talking about a neurodegenerative disease. She also flagged the importance of the involvement of researchers, patients and civil societies, especially for ensuring future implementation in healthcare systems.

The session closed with a reminder of the importance of public involvement and how patients should be engaged from the early stages of research as a standard practice. The workshop participants also reflected on the quote that Kevin Quaid said at the beginning of the day: "do not assume, ask".

10 Beyond Europe: creating global value

Given the current geopolitical climate, the participants reflected that creating global value has become more difficult as various countries become less interested in globalisation and in working collaboratively across borders. They heard that it is difficult to define the value of brain health, or to measure it concretely.

Cristina Sampaio made the point that we need to think about the return on the investment. She referred to a US National Institute of Health (NIH) calculation that for every $1 invested in health research, the benefits are worth $5. She called for a similar calculation to be done in Europe.

Within European public-private projects, infrastructure and data platforms are being developed but Sampaio warned that their use is not adequately tracked. Are data platforms being used sufficiently at European level? Are they being used outside Europe, and if so, by whom and how much?. Lastly, to increase the global impact of the many data lakes created it would be important to find mechanisms for cost sharing.

Magali Haas, the founder of Cohen Veterans Bioscience who was involved in the PRISM2 project, labeled IMI as an inspiration for public-private research partnerships in the US.

“I don’t think that the US engages industry as deeply as you do within the IMI/IHI programme,” she said. “A lot of progress has been made and it can be leveraged. IHI has done extraordinary things for the field and can do more.”

> *“IHI has done extraordinary things for the field and can do more.”*
>
> – **MAGALI HAAS**

The participants heard some contradicting views on governance. Sampaio stressed the need for more efficient governance structures within scientific projects. Do we evaluate how well they function? The right governance structure, she said, can ensure the proper ethics, transparency and fairness but it should not be so complicated that it becomes a barrier to use. However, other participants refuted this, saying that the governance structure outlined in the template for IMI and IHI projects has worked well across a variety of consortia.

Looking towards the future at strategic avenues that IHI could pursue, Haas recommended the formal development of a brain health index, which could help in the identification of common biomarkers for brain disease risk, as is already done for glucose, blood pressure and cholesterol for heart disease. It could also help bridge the divide between psychiatry and neurology. Another recommendation was the establishment of a single roadmap that could map all projects and against which progress could be assessed. This could include technical requirements and milestones to be achieved. A good start could be a critical “postmortem” of all the projects that were presented at the workshop and a technical gap analysis considering the critical challenges highlighted.

The participants also heard that a shift from focusing on brain disease to brain health is seeing traction on the global scale and that patients and other stakeholders appreciate that approach.

Some final suggestions included revisiting the process by which IHI requests proposals from the public partners, and reviewing the participation rules to ensure that there is more industry engagement.

11 Where to go next?

Elisabetta Vaudano summarised the key points from the previous sessions and then gave the floor to Niranjan Bose of Gates Ventures to hear his suggestions for the future.

Bose explained that Gates Ventures (GV) entered the AD research field rather recently, in 2018, and became part of its first IMI project in 2020. Five focus pillars have been identified so far: therapeutics, diagnostics, research to increase disease understanding to drive translation, data use, and clinical bottlenecks. The Gates Ventures' approach is pragmatic: "We just want to get it done. Whatever it takes, whatever the finish line is, we want to get there."

While in some areas (e.g. data use and diagnostics) there has been satisfactory progress, others are still fully open for future initiatives (e.g. clinical bottlenecks), while new ones are emerging, e.g. AI agent opportunities. Talking about key open questions, he stressed that we need to get data from more diverse patient populations, increase our understanding of sex and gender differences in neurodegenerative diseases, move disease progression models forwards, bring blood-based biomarkers into the clinic (adoption and scale up) and increase research on digital biomarkers (e.g. voice biomarkers). He also mentioned the need to make a reusable, low-cost, non-commercial data platform available to the community (beyond neurodegeneration), and pointed to the EPND hub as a first pilot of this. He emphasised the need to foster database interoperability. Regarding data initiatives the message was clear: we have data, the next chapter is to find the scientific questions to go after using them.

Bose stressed the importance of collaboration and partnership: "everything we have done is a partnership, without the partners we could not have done anything." He also mentioned that some overlap across initiatives has been done intentionally, to ensure the community comes together. "If you don't, if you create them in silos, then it's hard to break those silos down," he said. He also agreed with previous speakers about the importance for global consensus on a roadmap and urged the audience not to forget the key message given by Kevin Quaid at the start of the workshop. Finally, he urged this community to keep the momentum going forward.

A short brainstorming discussion followed. Paola Barbarino raised a question on "how to translate some of these advances into positive news for the outside world so that they can buy into positivity." She also emphasised the importance of keeping the community together, not to get stuck on labels and to always remember the importance of the job to get done, which responds to a very concrete need for many patients and their families.

George Vradenburg stressed that the research community must get better at communicating whether or not progress is made in ways that can be understood by the external world, avoid contradictions and communicate the sense of urgency. "But let's set some goals and get it done rather than just waiting for things to happen," he said.

Cristina Bescos of EIT Health followed, inviting the participants to engage with her organisation and contribute to the definition of the next EIT Health business plan 2026/2028. EIT Health is naturally positioned after IHI projects and might be able to help some innovations (those that are mature enough) to progress into the market and reach the patients.

Anna Chioti, chair of the IHI Science and Innovation Panel, said many of the points raised deserve further discussion by the panel. She then highlighted some points that could already be addressed by future PPPs: implementation science (including elements of education and training to develop more clinician scientists); opportunities for innovation in ATMPs; and combination treatments.

Magali Haas then intervened with a plea to not overlook traumatic brain injury (TBI), which often progresses to neurodegenerative disease. Sarah Bauermeister, of Dementia Platform UK, informed the workshop that TBI is already part of their initiative (as is amyotrophic lateral sclerosis- ALS). Bose Naranjan added that the ADDI platform is open for TBI as well as other neurodegenerative disorders data.

The conversation then moved again to the challenges of the healthcare system. Cristina Sampaio stated that there is a lack of all types of medical professionals in healthcare, and the situation is going to get worse. She said that it cannot be solved only by increasing education and training, or by new AI tools. What is needed is the reorganisation of medical care, in dementia and generally. It is a huge problem that needs new solutions.

While some participants agreed, still others flagged that it is a very challenging problem. Before it could ever be solved, if that is even possible, efforts to engage different types of medical professionals in thinking about the brain and its mechanisms of resilience and reserve should be intensified. Efforts should also be made to increase their awareness and skill sets.

IHI executive director Niklas Blomberg rounded up the workshop by thanking all the participants for their partnership and flagging three potential areas for future initiatives:

1. How to get to the next breakthrough treatment? Considering the elements flagged by the participants, this could be broken down into actionable steps (e.g. better understanding of disease, improved clinical trials, the right biomarkers and endpoints).

2. While waiting for that breakthrough, a lot of interesting areas mentioned during the day are addressable and actionable right now.

3. How can we scale those solutions and make sure that they reach more people, not only in Europe but also globally, including low and middle income countries? Niklas invited all participants to reflect further on these areas which can only be tackled successfully via partnerships and by setting high levels of ambitions.

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