

ADDING URGENCY TO ACTION

# LAUSANNE XI

1 - 3 October 2024

**Opportunities for Action & Collaboration** 









### **Table of Contents**

The Frontlines of Care: Clinical Experiences in the New Era of Alzheimer's Treatments	4
Pathways to Precision: Revolutionizing Diagnostic and Care Pathways	5
Data in Action: Building Platforms for Real-World Evidence Generation	6
Catalyzing Transformative Patient Care	7
<b>Preventative Power:</b> Promoting Brain Health to Address the Alzheimer's Crisis	8
<b>Igniting the Future of Women's Health:</b> A Global Wakeup Call	9
Capital for the Cure: Investing in Alzheimer's Innovations	10
Advancing the Path toward Preclinical Prevention	11
The Next Frontier: The Big Ideas Redefining the Alzheimer's World	12

#### **Introductory Note**

The global burden of Alzheimer's and related cognitive disorders is escalating at an alarming rate, with over 400 million people currently living with or at risk of developing this debilitating condition. As populations age, the number of people affected is projected to soar, further straining healthcare systems, economies, and societies worldwide. The economic cost of dementia is expected to reach an astonishing \$20 trillion within this decade, encompassing direct healthcare expenditures, long-term care costs, and lost productivity.

Adding to this challenge is the growing loss of workforce participation, as an estimated 100 million people step away from jobs to provide essential caregiving for those living with dementia. This trend, if left unaddressed, will exacerbate labor shortages and place immense pressure on both caregivers and the broader economy.

To address this mounting crisis, there is an urgent need for enhanced collaboration, swift action, and coordinated efforts across sectors—governments, healthcare providers, businesses, and communities alike. The time to act is now, as the scale and complexity of the issue will only intensify with the aging of populations. Without immediate, comprehensive intervention, the impact on future generations will be devastating.

With this backdrop, experts from across all sectors convened in Lausanne again this year, from October 1-3, for the 11th annual Lausanne Workshop. Since the inception of the workshop, the organizers have strived to create a global platform for cross-sector Alzheimer's stakeholders to identify challenges, set solution paths, measure progress, and hold each other accountable to act. Moreover, each year, the dialogue at the conference guides CEOi's agenda for the following year. The following intends to summarize the conversation, guide collaborations in 2025, spur new ideas and inform the global Alzheimer's agenda.

## The Frontlines of Care: Clinical Experiences in the New Era of Alzheimer's Treatments

New treatments, blood tests, and other breakthroughs in the Alzheimer's field that have long been discussed are now arriving – albeit at uneven and often restricted paces across geographeis. Patients and physicians now have real-world clinical experiences that provide important lessons for how to address the "last-mile problem" and speed access for patients in countries around the world.

### **Opportunities for Action and Collaboration**

- Reinvigorate the fight against stigma: Stigma remains one of the biggest barriers to early
  detection and, consequently, more effective treatment. While the scale of the Alzheimer's
  challenge must be appreciated, sharing personal level stories of stories of patients who are
  seeing results with new treatments and diagnostics can be most compelling. Showcasing
  success stories of patients on therapy can help reduce the stigma that prevents patients
  from seeking a diagnosis or care until it may be too late to intervene.
- Build care pathways that include new detection tools and treatments: In the US, building a leading Alzheimer's care program currently requires a robust health system, working across departments from initial evaluation to imaging to infusions and the pharmacy. In China, health systems are navigating hurdles in the regulatory and reimbursement system, particularly province-by-province payer decisions.
- **Define the role of blood tests and scaling access:** The landscape for blood-based biomarker tests, CSF testing, and imaging is evolving in the US, with uptake of blood tests rapidly expanding. This presents opportunities to study, define, and standardize the role of blood tests for streamlined diagnosis and treatment. Educating primary care providers so these tests can be used earlier in the process may be especially important.
- Drive regulators and payers to embrace new innovations: To date, only eight countries
  have approved lecanamab. Fewer have approved donanemab as it is more recently
  approaching regulators. Where the treatments are approved, there are significant barriers to
  access ranging from data collection requirements on the provider to requiring self-pay.
  Where possible, groups should contribute to multi-stakeholder regulatory convenings to
  represent the patient voice and emphasize that patients deserve the opportunity to make the
  choice. Comparisons to oncology therapies with potentially shorter clinical benefit and more
  severe symptoms may be useful.

Clinicians, researchers, and advocates are working to chart a path forward, including with patient registries and more robust real-world data collection. While disease-modifying treatments and blood-based tests are often framed as "on the horizon," they are indeed in the clinic, here and now, with opportunities for learning, collaboration, and improvement.

### Pathways to Precision: Revolutionizing Diagnostic and Care Pathways

A wave of new biomarker tests and detection tools bring great promise, especially alongside new therapies. However, we need matching advancements in implementation research, health system resources, care protocols, and data collection to keep pace and make the most of these technologies.

### **Opportunities for Action and Collaboration**

- Drive consensus on how BBM's fit in the care pathway: More effort is needed to educate on how BBMs fit in primary and secondary care pathways. As one example, the CEOi Blood-Based Biomarkers (BBMs) Workgroup's recommendations on integration into clinical practice were published during the conference. Expanding the provider base who use BBMs (e.g., geriatricians) may help with capacity constraints, as will ensuring protections for patients whose records end up in an EMR. Highlighting the value of BBMs in the care pathway even if no DMTs are available will also be important.
- Promote Better Access & Reimbursement for BBMs: Payers play a large role in determining the utilization of BBMs. Generating better real-world experience and evidence along with leveraging possible FDA approval should help drive confidence and better coverage for BBMs. Advocating for formal coverage policies would help not only for reimbursement of BBMs but also help ensure their use is not seen as experimental in the eyes of payers considering new DMTs prescribed based on BBM amyloid confirmation.
- Expand Efforts for Increasing Diversity: The field must continue to increase the understanding of accuracy of these tools in minority populations. These populations may have different genetic, environment and health factors that influence both the progression of the disease and the biomarker used. Adding additional biomarkers that could be more relevant for diverse populations, including those with other forms of memory disorders or in earlier stages of the disease, would be beneficial.
- Address Other Friction Points: Several key unresolved friction points need to be addressed, including: educating the broader community about BBMs about evidence and access, building capacity for more specialists, exploring fast track models similar to other diseases (e.g., Danish cancer model) and investing in EU and global infrastructure.

Precise, cost-effective, easily available tests are essential to achieving well-characterized patient populations—a desirable goal for all stakeholders.

### **Data in Action: Building Platforms for Real-World Evidence Generation**

Stronger platforms for real-world evidence are critical to understanding both new disease-modifying treatments and Alzheimer's disease as a whole. This data can help to inform complex clinical decisions, support analysis of new treatments for heterogenous populations, and identify clinically and economically meaningful outcomes that may emerge only over the long term.

### **Opportunities for Action and Collaboration**

- Create harmonized global platforms for real-world data collection: The International Registry for Alzheimer's Disease and other Dementias (InRad) aims to provide an overarching "registry of registries" to inform treatment management and track long-term outcomes most important for patients, clinicians, and payers. In multiple sclerosis, the MSBase registry shows that a size of 5,000-10,000 patients is needed for effective data analysis. While efforts have advanced, 75+ countries are not represented in current registries.
- Design registries for the needs and priorities of different stakeholders: Demonstrating the (non-monetary) value of registries is critical for all groups, independent of the availability of DMTs.
  - Clinicians need a tool that is easy-to-use and provides insights, data, and support for decisions beyond what is available from their standard EHR.
  - Patients need a tool that empowers them to understand their data, reduce risk, and slow progression, potentially using wearables for passive data collection; they must have a simple way to enter data (possibly via reimbursement for data entry).
  - Regulators and payers need a tool that supplements trial data on safety and long-term benefits, especially economically meaningful outcomes like delay in need for care or shift to care facility.
- Take policy action in conjunction with registries: At the global level, the WHO is updating data collection for the Global Dementia Observatory; at the national level, governments can harness registry data to work towards diagnostic targets in their national plan. Registries also present an opportunity for more countries to participate in global science, even if they don't have the infrastructure for large clinical trials.

With the right design and participation, Alzheimer's disease registries could support analysis of thousands of patients for years or decades – providing a powerful tool to answer questions beyond those investigated in clinical trials.

### **Catalyzing Transformative Patient Care**

While the landscape for healthcare system preparedness varies widely across and within countries, every country has opportunities to deploy new strategies and tools that strengthen the continuum of care – from awareness and prevention, to early detection and accurate diagnosis, through access to medical care and social support. Inaction is itself taking an action, but one that will leave countries unprepared for the growing burden of disease.

### **Opportunities for Action and Collaboration**

- Share lessons globally, building preparedness locally: While capabilities will vary, effective strategies can be deployed or pioneered everywhere. Lower-resource settings such as Brazil and Ghana have shown better ability to drive connected and/or digital support services that can be a model across the globe. Much of this was built off the learnings of the COVID-19 experience (e.g., digital vaccination tracking). In geographies with access to new detection tools and treatments, changes in policy, society, and frontline care are still needed to realize the value of these tools.
- Continue the push to extend detection and other solutions to the primary care level:
   Achieving this long-standing goal requires incentives for cognitive screening, workforce training, access to and education on how best to use new blood and genetic tests, and support systems that enable physicians. This is important even in locations without access to DMTs as risk reduction and other strategies can be pursued. "
- **Promote team and navigator models:** Integrated team-based care is a critical model to highlight, with the role of navigators especially important to improving patient outcomes. Highlighting how these navigators can come form different backgrounds (e.g., nurses, community health worker, social workers, etc.) can make the model more scalable. Virtual navigator models should also be explored.
- Start now to drive policy change for secondary prevention in preclinical populations:

  This requires scalable solutions like widespread access to screening tests, ways to inform people about risk, and real-world evidence to confirm benefits in under-studied populations. Emphasizing the value of preventing or delaying onset of disease can help to win policymakers' support.

All aspects of Alzheimer's care are interconnected. This can lead to difficult challenges, but also cascading solutions. By thinking big, failing fast and fixing quickly, , governments and health systems can work towards a future with transformative care.

## Preventative Power: Promoting Brain Health to Address the Alzheimer's Crisis

Global surveys indicate that while people want to reduce their risk for Alzheimer's disease, a stubborn myth that "there's nothing you can do" still persists. New and evolved strategies are needed to change perceptions and equip people with actionable, accurate information.

### **Opportunities for Action and Collaboration**

- Embrace a life-course approach to brain health: National and international brain health plans should be renewed and / or developed. The recent UNGA EBC event and the Africa Alzheimer's conference show an interest in this concept. These plans should take a holistic view as it was noted that we will not end Alzheimer's by focusing on the end of the disease. For example, public health messaging might engage expectant parents to build their own brain health and that of their child; an employer campaign might start with older workers and then extend to the entire employee population. Focusing on the immediate benefits of lifestyle changes, with reduced Alzheimer's risk as an additional benefit, can help motivate people to take action.
- Expand efforts to reduce mid-life risk factors: Addressing cardiometabolic disease, improving access to hearing aids, addressing oral health and other interventions could significantly reduce the future prevalence of Alzheimer's disease but these efforts are underscaled and the importance of the interventions is under-recognized.
- Adapt prevention strategies for local context: Efforts like WW-FINGERS and the Lancet Commission recommendations provide a blueprint, which local initiatives and experts can then tailor. For example, a screening and brain health effort in Brunei incorporated physical activity into Muslim prayer movements to support participation.
- Engage policymakers with the concept of "brain capital": A positive framing will focus on investing in the brain health of future generations, helping older workers extend careers, enabling inclusive economic growth, and ensuring competitiveness in the knowledge sector. Advocates say this is more effective than messaging on burden and costs. What is needed next are actionable policy proposals to make these frameworks more appealing to policymakers who want immediate action. A goal should be to identify simple changes that can drive sustainable results: many people doing something small is better than a few people doing something big.

Overall, prevention initiatives and strategies are shifting to be more inclusive, positive, and overarching – with the broad concept of promoting brain health, across the entire lifespan, for more countries and communities than have been included in the past. Put simply, the goal is to build better brains for a better world.

### Igniting the Future of Women's Health: A Global Wake-up Call

It is well established that women represent roughly two thirds of all Alzheimer's cases, progress faster through the disease, and bear the disproportionate burden of caregiving for loved ones with Alzheimer's. And yet, there remains a lack of investment and urgency in researching and addressing the aspects uniquely faced by women living with or caring for Alzheimer's patients.

### **Opportunities for Action and Collaboration**

- **Define the Objectives for Investment:** There are many troubling statistics and discrepancies that should be addressed, including disparities in public research dollars, VC investment in women led startups, and more. Setting clear goals and objectives will focus advocacy efforts, for example, ensuring clinical trials are powered appropriately so researchers can conduct analyses to better understand biological differences. Accountability indexes could be one way to measure and track progress.
- Build the Business Case: Advocates should think about building the case for greater
  investment in understanding how this disease disproportionally affects women. Framing this
  as a vast economic opportunity may resonate with policymakers and funders (e.g., payers
  would be interested to know how to target treatments more efficiently and avoid ineffective
  spending).
- **Drive Education and Awareness:** While the disproportionate burden borne by women may be well established, it may not be well known. More can be done to raise visibility to the issue among providers, policymakers, investors and more.

It's time to prioritize the unique challenges women face in Alzheimer's, both as patients and caregivers, by increasing research investment, closing funding gaps, and driving accountability for progress. Together, we can build a case and raise awareness to ensure women's voices are heard and supported in the fight against Alzheimer's.

### **Capital for the Cure: Investing in Alzheimer's Innovations**

Venture capital organizations are focusing on drug development for novel mechanisms of action, though biomarkers, diagnostics, and digital assessments also represent important areas. VC firms bring a variety of processes and viewpoints to determine the most promising targets.

### **Opportunities for Action and Collaboration**

- Expand the understanding about the role of VC funding: While VC plays a critical role in the Alzheimer's ecosystem, not everyone understands their approach and model. Improving the understanding of their capabilities can accelerate expertise sharing and collaborative efforts.
- Innovate at the pre-clinical stage: While pharmacology models are well established, models designed to emulate human disease (e.g., transgenic mouse models) may not be reflective of the full complexity of the disease. VC firms are adapting with different approaches, such as research with naturally aged animals and targeting whole-body aging mechanisms.
- The opportunity to drive resilience: We should urgently add focus on brain resilience, informed by the science of brain plasticity, as it offers an actionable pathway to delay cognitive decline, promote recovery, and reduce the long-term societal and economic impacts of dementia.
- Increase investment in enabling technology like diagnostics and biomarkers: Diagnostic firms are known to face challenges in raising capital. VC funds face the same barriers in making the case for these tools with their donors. Advocating for their value and reimbursement and exploring risk sharing opportunities can help foster their development. Doing so can enable focus on new predictive and preventative markers, and promote precision medicine in neurodegeneration like the oncology field has seen.
- Address the Discrepancy in investment between EU and US companies: Structural barriers
  have promoted a difference in early stage investment between EU and US companies.
  Highlighting this issue and the compelling science from EU companies should be a priority.

VC firms are developing investment theses that consider ongoing developments in the preclinical space and look to the next generation of drug development, as the Alzheimer's treatment landscape continues to evolve.

### **Advancing the Path toward Preclinical Prevention**

There is growing optimism about the prospect of active and passive immunotherapies for prevention in pre-clinical patients within the next decade, but the field must align expectations between scientists, regulators, payers, and patients. With multiple active and passive immunotherapies now in Phase 2 trials, alignment is more urgent than ever.

#### **Opportunities for Action and Collaboration**

- **Better define the disease staging:** Alzheimer's progression is not as clearly defined as other disease areas. Definitions of "presymptomatic" or "pre-clinical" patient populations may require further definition or refinement as new detection methods such as voice analysis may push the window of "symptomatic" disease earlier.
- Build the case for biomarkers and harmonize their use: Biomarkers will be critical to
  defining who the right patients are, how they can be identified, and how impact should be
  measured. Regulators and sponsors should align on what the thresholds of benefit are.
  Analogs from other disease areas may be useful, such as Duchenne muscular dystrophy
  where dystrophin was used as a biomarker; and HPV where approval was granted based on
  infection prevention.
- Clearly and proactively define the path to development and approval: Trials that target preclinical stages face the challenge of a long lag time from drug administration to demonstration of benefit. Regulators and industry should work to align on what safety and clinical benefits need to be shown. Conditional approval pathways should be explored and leveraged.
- Explore Co-pathologies: Active and passive immunotherapies should consider the benefit of targeting Alzheimer's in patients with mixed dementias and/or targeting other mechanisms. As efforts pre-clincial populations are targeted it can be harder to be certain about the later course of disease. New biomarkers for vascular dementia and combination approaches may be particularly useful.
- **Build patient confidence:** The increase in vaccine hesitancy since COVID-19 raises questions about how to build confidence to support adoption of future immunotherapies. That said, a recent trial saw approximately ~5x faster recruitment than originally expected, suggesting potential enthusiasm among patients.

In addition, the field should consider how to fund early-stage research, establish biomarkers and link to clinical benefit, and consider whether a new generation of targets is needed beyond amyloid and tau.

### The Next Frontier: The Big Ideas Redefining the Alzheimer's World

The Alzheimer's field is entering an exciting period, with the opportunity to build on deepening understanding of the disease and pursue transformative new concepts.

### **Opportunities for Action and Collaboration**

- Deploy AI, imaging, and digital tools for greater precision in care: These tools could support both drug development and clinical pathways, including predicting risk (for example, AI-enabled analysis of MRI to identify brain age), making an early diagnosis, matching patients to new therapies, and monitoring safety. Leveraging continuous, passive measurement through connected apps and devices may be highly valuable for precision public health strategies. Promoting coverage and reimbursement of these technologies will be critical.
- Expand the focus beyond traditional amyloid and tau targets: In drug development, focus and investment have moved to a wider set of targets especially those associated with the holistic biology of aging. New endpoints (e.g., time to progression irrespective of amyloid levels) and new therapeutic approaches (e.g., GLP-1s) warrant exploration, especially for combination approaches.
- Take a global perspective: There is an opportunity for the next wave of Alzheimer's efforts to serve a more diverse set of people, countries, and communities in promoting brain health. While global conversations have advanced on Alzheimer's, global commitments have not expanded commensurate with the burden of disease. Learnings and insights from low resource settings (e.g., blood spot technology, saliva testing, voice recognition etc.) may provide models to also lower the cost of care administration in high resource settings.

In the next frontier for Alzheimer's disease, a wider set of tools, therapies, and technologies will unlock progress against some of the most stubborn challenges in medicine – ultimately providing more options and greater benefit to people at global scale.