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Ask people if Alzheimerâ??s can be prevented, and most will say no. This knowledge gap creates profound political obstacles.

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Dr Arcadi Navarro is a leading figure in modern Alzheimerâ??s research, heading efforts at the Pasqual Maragall Foundation in Barcelona and its university partners. His work spans genomics, bioinformatics, neurotropic viruses, and personalised brain organoids. Under his leadership, the foundation has doubled its research capacity and become a key player in global brain health and prevention-focused strategies. Equally committed to the social dimension of Alzheimerâ??s, Dr Navarro has positioned the Foundation as a national benchmark in advocacy, public engagement, and support for caregivers, making brain health not just a scientific challenge, but a societal one.

What would you highlight as the most significant advances in your Alzheimerâ??s research since our last conversation in early 2022?

Our progress operates across two distinct but interconnected dimensions: my research programme and our institutional strategic expansion. Within my research group, we have substantially deepened our genomic analysis capabilities, leveraging our ALFA cohort to unlock previously inaccessible insights into Alzheimerâ??s pathogenesis. Concurrently, we have developed ground-breaking initiatives in neurotropic virus research, securing substantial European Union funding for projects examining the intersection between viral pathogens and neurodegeneration.

Our most innovative work involves two parallel investigations: first, exploring the relationship between Epstein-Barr virus and multiple sclerosis; second, examining the potential connections between SARS-CoV-2 infection and Alzheimerâ??s disease progression. For this latter project, we have pioneered the use of personalised brain organoids â?? a revolutionary technology that enables us to model individual genetic risk profiles and their responses to specific environmental stressors, including viral infections.

From an institutional perspective, our foundation has experienced exponential growth, effectively doubling our research capacity. By year-end, we shall operate as an intermediate-scale institute rather than the boutique research facility we once were. This expansion has enabled us to launch comprehensive studies in digital biomarkers, sleep disorders, and nutritional neuroscience, whilst simultaneously advancing our involvement in large-scale international initiatives, including Brain Health Services.

Critically, our research strategy extends beyond traditional biomedical inquiry to encompass the societal dimensions of brain health advocacy. We recognise that addressing Alzheimerâ??s as an unsolved challenge requires not merely scientific innovation, but also strategic social science research to identify optimal methods for societal mobilisation and political engagement.

In a crowded public health and amid funding pressures, how do you position brain health strategically to ensure it remains a priority?

This represents a fascinating strategic challenge, though we fundamentally reject the zero-sum competitive framework that some stakeholders adopt. Rather than viewing ourselves as competing against cardiovascular disease, diabetes, or obesity initiatives, we recognise profound synergistic opportunities across these domains.

The Lancet Commission has identified 14 distinct risk factors for Alzheimerâ??s disease, the majority of which constitute independent public health challenges. Successful interventions targeting obesity, diabetes, or cardiovascular health generate cascading benefits for neurodegeneration prevention. When we successfully promote increased physical activity and improved nutritional choices across populations, we simultaneously reduce long-term Alzheimerâ??s prevalence â?? a realisation that positions us as natural collaborators rather than competitors.

We are already implementing strategic partnerships with organisations focused on childhood obesity prevention, recognising that early-life interventions yield substantial downstream benefits for brain health. This long-term strategic perspective differentiates our approach and creates multiple pathways for collaborative impact.

With political cycles lasting just four years and your research requiring long-term commitment, how do you navigate the disconnect, particularly considering frequent ministerial changes in Spain?

That is a fundamental tension in health policy implementation. However, whilst our prevention strategies certainly require long-term commitment, we simultaneously address immediate, politically actionable challenges that can generate measurable outcomes within standard political timeframes.

The critical strategic shift involves reframing Alzheimerâ??s from a purely clinical condition to a comprehensive societal challenge with immediate ripple effects across multiple domains: family

structures, workplace productivity, urban planning, and healthcare system capacity. These impacts manifest immediately, not decades hence.

We advocate for immediate policy interventions: enhanced awareness programmes, employer education initiatives, caregiver support systems, and public health official training. These measures can be implemented and demonstrably impact the lives of hundreds of thousands, potentially over one million, Spanish families within a single political term. This is not long-term speculation; it represents achievable, measurable improvement in quality of life for current constituents.

Whilst I maintain optimism about immediate intervention opportunities, we cannot ignore fundamental structural barriers to effective policy implementation. Alzheimerâ??s prevention represents a preventable condition, yet public awareness of this fact remains inadequate. Conduct a street survey: people understand that cardiovascular disease can be prevented through exercise, and that lung cancer can be prevented by avoiding tobacco use. However, when asked whether Alzheimerâ??s can be prevented, the majority will respond negatively.

This knowledge gap creates profound political obstacles. How can we generate public support for prevention programmes when citizens fundamentally believe prevention is impossible? This represents a critical communication challenge with direct political implications.

Nevertheless, demographic evidence demonstrates that prevention strategies are already working, even without explicit recognition. Current seventy-year-olds exhibit lower Alzheimerâ??s rates than their counterparts thirty to forty years ago. This improvement reflects enhanced lifestyle choices: increased physical activity, better social engagement, and improved nutritional habits. People are effectively implementing Alzheimerâ??s prevention strategies without conscious awareness.

The Lancet Commission estimates that approximately 40% of annual diagnoses could be delayed or avoided through lifestyle modifications. This represents an enormous prevention opportunity that remains largely untapped due to inadequate public education and fragmented policy implementation.

In Spain specifically, we face additional structural challenges: funding remains siloed across health, research, and social service departments, preventing the comprehensive, transversal approach that Alzheimerâ??s prevention requires. We are attempting to address this through coalition building â?? last year, we successfully coordinated thirty different institutions focused on elderly health and rights, producing a unified document proposing ten specific policy measures for implementation across central and autonomous government levels.

Could you give us an overview of the ALFA study and cohort, particularly what sets it apart from other Alzheimerâ??s research initiatives?

The Pasqual Maragall Foundation pioneered a ground-breaking research approach in 2012 â?? thirteen years ago â?? that has proven strategically prescient. We recognised that Alzheimerâ??s likely involved an extended, asymptomatic phase preceding clinical manifestation. This hypothesis has since been validated: we now understand that proteinopathy and neurodegeneration occur potentially fifteen to twenty years before symptom onset.

Given this extended preclinical period, the optimal research strategy requires a longitudinal study of at-risk populations before clinical symptoms develop. In 2012, genetic risk stratification was insufficiently developed for precise population selection. Our solution: recruit approximately 3,000 first-degree relatives of Alzheimerâ??s patients â?? typically offspring â?? who possess moderately elevated disease risk through familial exposure.

This population exhibits threefold higher rates of APOE4 â??carriershipâ?• compared to the general populations, providing natural enrichment for genetic risk factors. Through longitudinal blood sampling and comprehensive phenotyping, we can retrospectively analyse biomarker progression patterns. For instance, when we identify participants with elevated phosphorylated tau-217 levels â?? indicating elevated Alzheimerâ??s risk â?? we can examine historical samples to understand biomarker evolution over time.

This methodology has enabled us to validate blood biomarkers as reliable proxies for brain pathology, deepen understanding of lifestyle-genetics interactions, confirm that Alzheimerâ??s pathology begins decades before symptom onset, and obtain precise data regarding lifestyle modification impacts on disease probability.

After more than a decade of data collection from these extraordinarily committed participants, who literally donate their time and blood to scientific advancement, we are now implementing deeper phenotyping protocols and expanding our analytical capabilities with previously unavailable technological tools.

Your focus on healthy volunteers was innovative back in 2012. Have international groups sought to replicate this approach, and how transferable is the model across different regions and populations?

Two parallel developments have emerged. First, several international research groups independently developed similar cohort methodologies, and we now collaborate extensively across these complementary initiatives â?? a development that strengthens the entire field.

Second, and strategically crucial, the pharmaceutical industry has fundamentally shifted its clinical trial focus. Until 2019-2020, most industry trials targeted intermediate or late-stage disease phases. These approaches universally failed â?? over one hundred molecules were tested and subsequently abandoned. The industry has now pivoted toward early-phase or even preclinical interventions, making our longitudinal cohorts invaluable resources for participant recruitment and trial design.

This represents a fundamental paradigm shift that validates our decade-old strategic vision. Our participants are comprehensively phenotyped and ideally positioned for selection into prevention-focused clinical trials.

I must emphasise our ultimate strategic objective, shared with researchers globally: we envision a world without Alzheimerâ??s, achieved not through end-stage therapeutic intervention, but through early risk detection and prevention during the two-decade asymptomatic period. Our goal is a future where no individual receives a clinical Alzheimerâ??s diagnosis because we have successfully identified risk factors and implemented effective interventions â?? whether pharmacological or lifestyle-based â?? to prevent symptom development entirely.

Blood biomarkers are widely seen as a game-changer for early detection and intervention. Despite challenges around cost, access, and clinical use, how do you assess their strategic potential?

We must distinguish between short-term realities and medium-term possibilities. In the immediate term, these biomarker technologies are not yet optimised for general population screening. This parallels historical precedents: twenty years ago, faecal biomarker testing for colorectal cancer was

technically feasible, yet widespread population screening was not implemented.

Today, in Spain and Catalonia, citizens over fifty receive home-based colorectal cancer screening kits every two years. They complete testing, submit samples to pharmacies, and receive automated results â?? typically reassurance, but occasionally referrals for further evaluation. This represents a transformative public health intervention, but it required extensive system preparation: large-scale colonoscopy capacity, surgical capabilities, and pharmacological treatment options.

We currently face an identical scenario with Alzheimerâ??s biomarkers. General population screening is technically feasible, though some optimisation challenges remain. However, widespread implementation would be inappropriate because we cannot yet offer screened individuals anything beyond lifestyle counselling â?? advice we can provide universally without screening.

In the medium term, five to ten years, pending clinical trial outcomes, if current pharmaceutical pipeline drugs receive approval, these biomarkers will become invaluable tools for early detection and population triage. At that point, routine blood testing will likely include Alzheimerâ??s risk assessment alongside cholesterol and glucose monitoring, because the healthcare system will be prepared to offer meaningful interventions beyond lifestyle modification.

The potential is tremendous, but successful implementation requires coordinated development of both diagnostic capabilities and therapeutic responses.

How significant are recent regulatory decisions on new Alzheimerâ??s treatments in driving continued pharmaceutical investment and research, given their modest efficacy and ongoing challenges around cost and access?

These initial approvals represent a critical inflexion point, though not yet the paradigm transformation we ultimately require. They demonstrate that our advancing understanding of disease biology is translating into therapeutic utility, providing genuine cause for cautious optimism.

The current drugs are available and demonstrate efficacy, albeit modest. Associated risks require careful consideration, and healthcare systems require substantial preparation for administration protocols that they currently cannot support. However, the fieldâ??s narrative has fundamentally shifted from therapeutic nihilism to cautious optimism, and we can reasonably expect continued improvement.

The pharmaceutical pipeline is extraordinarily robust, with early-phase clinical trial results showing genuine promise. It would be highly unusual if this level of activity did not yield superior therapeutic options within the foreseeable future.

Nevertheless, I emphasise two critical caveats. First, timeline predictions remain inherently uncertain and require appropriate caution. Second, and essential: Pharmaceutical advances must not eclipse prevention strategies. We cannot allow a scenario analogous to certain responses to some medications, where individuals assume pharmaceutical intervention excuses poor lifestyle choices.

Just as some hypertension patients inappropriately increase salt consumption upon receiving antihypertensive medications, we must prevent the emergence of attitudes suggesting that Alzheimerâ??s drugs eliminate the need for prevention measures. Pharmaceutical interventions and prevention strategies must function as complementary, not substitute, approaches.

You have described the current outlook in Alzheimerâ??s research as one of â??cautious optimism.â?? Does this still reflect your view? Over the next five years, what developments give you the most reason for hope and concern?

Predicting the future remains inherently challenging. Rather than offering predictions, permit me to outline my strategic wishlist, clearly labelled as aspirational rather than prophetic.

My priorities operate across both societal and scientific dimensions. At the societal level, I wish for a fundamental transformation in public perception of Alzheimerâ??s: from viewing it as an inevitable curse to understanding it as a preventable disease that we will eventually control effectively. Current societal misperceptions represent a catastrophic barrier to progress, preventing individuals from taking meaningful action.

If we successfully shift public understanding, we would mobilise not only lifestyle changes but also substantially increased research investment, because people would recognise that research offers genuine solutions. This societal transformation could generate a profound impact within five years.

Scientifically, I hope that by 2030 we will have moved far beyond our current two approved drugs to possess multiple therapeutic options employing diverse strategic approaches. Combined therapeutic strategies â?? administering multiple complementary drugs simultaneously â?? offer particular promise. If by 2030 we can provide combined pharmaceutical interventions to individuals in preclinical phases, before symptom development, I will consider my professional aspirations substantially fulfilled.

This represents ambitious but achievable progress: societal recognition of prevention possibilities coupled with sophisticated, multi-modal therapeutic interventions implemented during the extended preclinical window. These developments would fundamentally transform the Alzheimerâ??s landscape and offer genuine hope for eliminating this devastating condition.

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