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The Womenâ??s Brain Foundation, formerly the Womenâ??s Brain Project, has evolved into a fully-fledged foundation dedicated to advancing research in gender precision medicine with a strong focus on brain health. CEO pro-bono Dr Antonella Santuccione Chadha comments on the organisationâ??s newly extended global reach, progress in understanding the link between gender and Alzheimerâ??s disease, and how the foundation is leveraging data-driven insights to address gender disparities. Santuccione Chadha also weighs in on the impact of new Alzheimerâ??s therapies and achieving gender equity in Alzheimerâ??s clinical trials.

We last spoke almost four years ago, in which time the Womenâ??s Brain Project has become the Womenâ??s Brain Foundation. What have been the major milestones for your organisation over the past few years?

The transition from the Womenâ??s Brain Project, initially established as an association, to the Womenâ??s Brain Foundation marked a strategic evolution in response to both internal aspirations and stakeholder feedback. As an association, the organisation faced limitations, particularly in its recognition as an independent research institute within Switzerland. This status constrained its ability to act as a primary applicant for public funding, restricting it to a secondary role in collaborative applications. Transforming into a foundation not only overcame these barriers but also provided a robust framework to safeguard its mission and vision, ensuring they remain autonomous and

sustainable, irrespective of changes in leadership. Under the oversight of a regulatory authority, the foundation is now structured to carry its objectives forward, independent of individual contributions, securing a legacy of impact and innovation.

The foundationâ??s mission, while rooted in its original focus, has been polished and expanded to reflect its growing ambitions. At its core, the Womenâ??s Brain Foundation remains dedicated to advancing research in sex and gender precision medicine, with a strong emphasis on brain and mental health. However, it has also embraced new dimensions, including incubating startups through expert guidance and establishing a dedicated research centre to pioneer advancements in sex and gender-focused precision medicine. A key initiative is the launch of a venture studio, designed to nurture innovation by supporting startups that align with its mission in womenâ??s health and brain health.

To enhance its reach and influence, the foundation is strategically expanding its global presence. A physical location is being established in Switzerland, accompanied by plans to replicate its model through a sister foundation in Italy. This move ensures alignment with European Union frameworks, facilitating access to public funding. Beyond Europe, the foundation has cultivated affiliations with globally renowned institutions, including Weill Cornell Medicine, the University of Chicago, and the University of Melbourne. Additional partnerships with the University of Barcelona and the Barcelona Supercomputing Center further underscore its commitment to fostering collaborative research and innovation on an international scale. Through these initiatives, the Womenâ??s Brain Foundation continues to bridge expertise across borders, solidifying its role as a leader in precision medicine and gender-focused health research.

What advancements have been made in understanding the influence of sex and gender on Alzheimerâ??s disease, and what challenges persist in addressing these disparities?

Advances in research have underscored the profound impact of sex and gender on Alzheimerâ??s disease, revealing significant disparities in its trajectory, diagnosis, and treatment. Women not only represent the majority of patients but also the largest proportion of caregivers, placing them at the centre of this public health challenge. The diseaseâ??s progression in women is distinct, marked by faster cognitive decline and higher levels of toxic tau protein at comparable amyloid levels. Their advanced verbal abilities often allow them to mask symptoms effectively, which, while initially compensatory, leads to delays in diagnosis. Compounding this is a persistent bias in the healthcare system, where symptoms in women are frequently misattributed to depression or life events such as bereavement or empty-nest syndrome. This results in misdiagnoses and the inappropriate prescription of antidepressants as a first-line treatment.

A patient survey conducted across the United States and Germany with 120 participants provided qualitative insights into these issues. The survey revealed that women were more likely than men to be prescribed antidepressants throughout the course of the disease, often delaying appropriate treatment. Women also accessed specialized care later, frequently starting with general practitioners before eventually seeing neurologists or other experts. Strikingly, women demonstrated a lower awareness of Alzheimerâ??s, and its implications compared to men, highlighting an educational gap that must be addressed to empower patients and caregivers alike.

Institutional care data further illustrates systemic inequalities. Women, who live longer and are more likely to develop dementia, are disproportionately institutionalized in nursing homes or eldercare facilities. Once institutionalized, they receive significantly higher prescriptions of antipsychotic medications compared to men. These medications, often used as a means to manage behavioural

symptoms rather than treat the underlying disease, reflect suboptimal care practices. The reliance on antipsychotics underscores a troubling standard of care where calming symptoms takes precedence over providing meaningful therapeutic interventions. This aligns with findings from the Organisation for Economic Co-operation and Development (OECD), which consistently reports that women dominate dementia statistics across member countries and face greater institutionalization and medication disparities.

While these findings provide crucial insights into the gendered dynamics of Alzheimerâ??s disease, much of the data remains qualitative and localized. Expanding research to include larger, more diverse cohorts across different geographies is vital to developing a comprehensive understanding of these issues. Achieving this requires greater investment and collaboration to ensure that future care models are equitable and tailored to the unique needs of all affected populations.

How can the healthcare ecosystem effectively address gender disparities in Alzheimerâ??s and other neurodegenerative diseases, and what strategies does your organisation propose?

Addressing the pronounced gender disparities in Alzheimerâ??s and other neurodegenerative diseases necessitates a multidimensional, collaborative approach that engages all facets of the healthcare ecosystem. At the core of our strategy is evidence generation through robust scientific research. Data-driven insights provide a powerful basis for action, as facts are indisputable and enable targeted interventions. By presenting clear findings, we aim to educate and mobilize policymakers, healthcare professionals, patient organisations, and the pharmaceutical industry to integrate sex and gender considerations into both research and clinical practice.

A compelling example of this is a study we recently published in *Nature Aging*, which uncovered how biases related to the gender and relationship of assessors could impact Alzheimerâ??s disease evaluations. The study revealed that women conducting assessments using the Clinical Dementia Rating (CDR) Sum of Boxes (SOB) score tended to report higher levels of dementia, whereas men reported lower scores. Additionally, the nature of the assessor-patient relationship played a significant role, with close relatives like daughters or spouses identifying more cognitive impairment compared to healthcare professionals or distant caregivers. These findings underscore a critical issue: biases and inconsistencies in assessment methods may inadvertently influence clinical trial endpoints, potentially skewing the evaluation of treatment efficacy. Such insights demand immediate attention to standardize and refine assessment protocols, ensuring fairness and accuracy in research and care delivery.

Beyond Alzheimerâ??s, our research extends to other neurodegenerative diseases, including Parkinsonâ??s. In a forthcoming article in *Nature Medicine*, we explore the increasing prevalence of Parkinsonâ??s among younger women, a trend that may be influenced by environmental factors, though the precise causes remain unclear. This highlights the urgent need for further investigation and a more nuanced understanding of how sex and gender intersect with disease progression across various conditions.

To drive meaningful change, we advocate for a system-wide educational effort. This includes informing healthcare professionals about the implications of sex and gender in neurodegenerative diseases, empowering patients and caregivers through targeted awareness campaigns, and influencing policymakers to adopt evidence-based frameworks that address these disparities. Collaboration is central to this mission. By partnering with organisations such as Kearney, McKinsey, pharmaceutical companies, and advocacy groups, we aim to create solutions that are inclusive, actionable, and far-reaching.

Ultimately, the goal is to reshape the healthcare landscape into one that recognizes and responds to the unique challenges faced by women in neurodegenerative care. Through a combination of rigorous research, comprehensive education, and cross-sector collaboration, we strive to ensure that disparities are not only acknowledged but systematically eliminated.

What do recent advancements in Alzheimerâ??s therapies signify, and how should healthcare systems adapt to support these innovations effectively?

The introduction of new therapies for Alzheimerâ??s disease, such as Aducanumab, marks a pivotal advancement in the field of neurodegenerative disorders. These treatments challenge long-held assumptions about the brainâ??s inaccessibility, demonstrating that even complex barriers like the blood-brain barrier can be overcome to deliver targeted interventions. As someone who contributed to the discovery of Aducanumab, I view this breakthrough as transformative, showing that antibody-based therapies can successfully remove amyloid plaques and slow disease progression. However, these advances also expose the need for a fundamental shift in how healthcare systems and professionals approach such innovations.

Historically, neurology and psychiatry have relied heavily on oral medications, leaving many clinicians unprepared for the adoption of infusion-based therapies. This gap highlights the urgent need for systemic changes, including restructuring neurology units to incorporate infusion facilities and specialized nursing staff. Furthermore, the delays in approvals and reimbursement for these therapies, particularly in Europe and the United Kingdom, reflect a broader reluctance within medicine to embrace disruptive innovation. Medicine, as a field, has often been slow to adopt new paradigms, constrained by regulatory hurdles, budget limitations, and entrenched practices.

Beyond these practical barriers lies a more troubling issue: the intersection of ageism and sexism within the Alzheimerâ??s landscape. The disease disproportionately affects older adults, the majority of whom are women, and caregiving responsibilities often fall to women, many of whom work unpaid or are underpaid. These demographic realities contribute to the marginalization of Alzheimerâ??s within healthcare priorities, as both patients and caregivers are undervalued in societal and economic terms. For example, other therapeutic areas like oncology regularly secure significant funding for drugs that offer marginal survival benefits, yet similar investments in Alzheimerâ??s treatments are often deemed unsustainable. This disparity reflects a bias that devalues the lives and contributions of those affected by Alzheimerâ??s and related diseases.

To overcome these challenges, healthcare systems must adopt a multi-dimensional approach. Negotiations between payers and pharmaceutical companies must ensure fair pricing that balances accessibility with sustainability. Policymakers must recognize the broader societal and economic impacts of untreated Alzheimerâ??s, particularly the burden placed on caregivers. Structural reforms in healthcare delivery, including the integration of infusion therapies and the training of specialists, are essential. Equally important is addressing societal biases to elevate the prioritization of Alzheimerâ??s and other neurodegenerative conditions to align with their true significance. These therapies represent more than a medical breakthroughâ??they are an opportunity to redefine how we approach the treatment of neurodegenerative diseases. By addressing systemic barriers and fostering a culture of innovation and equity, we can ensure that the patient care paradigm is shifted for the better.

What are the persistent challenges in achieving gender equity in Alzheimerâ??s clinical trials, and how can future strategies address these gaps effectively?

Achieving true gender equity in Alzheimerâ??s clinical trials requires a systemic shift, addressing biases that permeate every stage of the research process. Although phase 3 trials today approach parity with approximately 50 percent female participation, this progress is paradoxical when compared to earlier studies of treatments like acetylcholinesterase inhibitors (AChEIs), where women represented over 60 percent of participants. This decline may be attributed to the increasing duration and complexity of modern trials, which demand extended patient retentionâ??a significant barrier for women, who often face additional responsibilities as caregivers.

The issue, however, begins long before phase 3. Biases in preclinical and early-phase research lay the groundwork for inequities that ripple through the entire drug development pipeline. For instance, female neuronal cell lines are still underrepresented in laboratory experiments, perpetuating a gender imbalance that limits our understanding of how treatments might uniquely benefit or affect women. This oversight risks missing critical insights, such as the potential need for women to receive different dosages, alternate administration routes, or combination therapies due to higher levels of tau protein. These nuances remain unexplored, leading to therapies that may inadequately address sex-specific differences.

The broader implications of this challenge extend beyond Alzheimerâ??s research. The COVID-19 pandemic provided a stark example of the consequences of failing to incorporate sex-disaggregated data into clinical trials. Women experienced disproportionately severe side effects from vaccines and treatmentsâ??issues that could likely have been mitigated with adjusted dosages tailored to biological differences. This example underscores how simple yet impactful changes, such as sex-based data analysis and dosage adjustments, could significantly improve outcomes across medical fields.

Emerging technologies, such as machine learning and artificial intelligence, offer promising tools to overcome these challenges. In one study, an algorithm trained to detect cognitive impairment outperformed clinicians in identifying early cognitive decline among women, particularly in cases where traditional methods failed to recognize subtle symptoms. These technologies demonstrate the potential to enhance diagnostic precision, reducing biases and improving patient outcomes.

Addressing these systemic gaps requires a multi-faceted approach. Research institutions and pharmaceutical companies must integrate sex and gender considerations at every stage of the process, from preclinical studies to trial design and execution. Equally important is the need for robust sex-disaggregated data to guide evidence-based decision-making. By fostering inclusivity and leveraging advanced technologies, the healthcare ecosystem can develop therapies that are not only scientifically sound but also equitable, ensuring that all patients benefit from the full potential of medical innovation.

How can artificial intelligence address biases in healthcare, and what ensures its effectiveness?

Artificial intelligence (AI) has emerged as a critical tool for addressing biases in healthcare, offering a way to mitigate the limitations of human judgment. A 2016 analysis of digital assistants like Siri highlighted significant disparities in how health inquiries were handledâ??straightforward issues such as headaches prompted referrals to specialists, while concerns like menstrual pain or suicidal thoughts often received inadequate responses. This revelation underscored the extent of embedded biases in systems designed to support healthcare decisions.

The strength of AI lies in its ability to analyze large datasets and detect patterns objectively. However, its effectiveness depends on the quality of the data used to train it. Robust, diverse

datasets are essential to ensure AI models produce equitable insights and avoid perpetuating existing biases. When built and trained with precision, AI can provide healthcare professionals with reliable, data-driven recommendations that enhance patient care. Ultimately, the success of AI in healthcare relies on inclusive and rigorous development. By addressing biases in its design and implementation, AI has the potential to transform decision-making, ensuring fairer and more effective outcomes for all patients.

What innovative approaches in biotech and startups could redefine womenâ??s health and neurodegenerative disease treatments?

Biotech and startup innovations are poised to revolutionize womenâ??s health and neurodegenerative disease care by embracing tailored approaches that consider gender-specific nuances from the outset. In my advisory roles, I encourage companies to move beyond the traditional one-size-fits-all framework and design therapies that directly address the unique needs of specific patient groups. This shift not only ensures better clinical outcomes but also makes these solutions commercially viable. For example, in Alzheimerâ??s treatment, therapies tailored to narrow yet well-defined patient subsets can deliver significant benefits, proving that personalization is both effective and profitable.

The economic case for investing in womenâ??s health is compelling. According to the 2024 World Economic Forum report, these investments could yield a return of USD 1 trillion by 2040, a figure comparable to the GDP of Switzerland. Intriguingly, a quarter of this potential return is linked to advancements in brain and mental health for womenâ??a stark indicator of the underinvestment in this area. The brain, despite being one of the most critical organs, remains underserved in female healthcare, receiving less attention than even reproductive health.

Driving meaningful change in this space requires collaboration and accountability from all stakeholders. Women and men alike must advocate for equitable solutions while recognizing and addressing inherent biases. It is a natural tendency for individuals to prioritize issues most familiar to themâ??women often champion womenâ??s issues, and men, menâ??sâ??but acknowledging this bias is the first step toward developing inclusive, equitable healthcare innovations. By combining cutting-edge science with a commitment to inclusivity, the biotech and healthcare sectors can make groundbreaking advancements, particularly in addressing the significant unmet needs in womenâ??s brain and mental health.

What is the key message for stakeholders regarding sex and gender considerations in Alzheimerâ??s care and healthcare innovation?

A fundamental message for stakeholders is the pressing need to redesign healthcare systems to accommodate innovation while embedding sex and gender considerations into diagnostic and treatment pathways. While the development of groundbreaking treatments is crucial, their success ultimately depends on systems capable of addressing the nuanced needs of diverse patient populations. This requires close collaboration with governments to create infrastructures that are responsive, inclusive, and equipped to implement these advancements effectively.

Equally critical is the importance of tailoring approaches to specific audiences. Just as marketing strategies adapt to the preferences of different demographics, healthcare must refine its language, outreach, and support mechanisms. For example, targeting women requires an understanding of the unique challenges they face, such as caregiving responsibilities, limited transportation options, or

even concerns as simple as maintaining their hairstyle. While these factors may seem peripheral, they can significantly influence womenâ??s willingness and ability to participate in clinical trials or access care. Addressing these obstacles through practical solutionsâ??such as providing childcare, transportation, or flexible schedulingâ??can greatly enhance inclusivity and engagement.

This tailored approach should extend to the design of clinical trials, which often rely on neutral methodologies that fail to account for gender-specific needs. A more inclusive framework not only increases participation but also ensures that innovations reflect and serve the diversity of the patient population. Ultimately, achieving meaningful progress in healthcare innovation requires moving beyond generalized solutions to embrace tailored strategies that prioritize inclusivity and equity. By recognizing and addressing these differences proactively, stakeholders can help drive transformative change, ensuring that the full potential of healthcare advancements is realized for all.

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