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Perspective

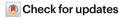
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Women's brain health and brain capital

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Brain capital, broadly defined as a form of capital that prioritizes brain skills and brain health, is urgently required. Integrating social, emotional and cognitive brain resources is a great asset for a wealthy and healthy society. Nevertheless, there is little investment in women's brain health on a global scale. Women, on average, spend nine additional years in poor health compared with men, which hinders their participation in education, the workforce and society at large. This Perspective highlights the crucial intersection between investing in women's brain health and the concept of 'brain capital.' Here we argue that addressing the women's health gap could potentially increase the global economy by US \$1 trillion in annual incremental gross domestic product. Furthermore, we hope this article will serve as a springboard to stimulate discussion and concrete stakeholder actions toward closing the women's brain health gap and will add to the growing discourse on sex- and gender-specific healthcare and its impact on global community well-being.

The world aspires to a future in which women can realize their cognitive, social and emotional potential and be their full selves at work, with their families and in the community, thriving with their brains and mental health. Investment in brain health remains critically underfunded despite its importance and potential. This shortfall is even more pronounced for women's health, for which the lack of resources and attention worsens health disparities. That potential can fall short without a comprehensive understanding of the female brain and equitable investments in women's brain health. Despite women living longer than men, they spend 25% more time in poor health on average. According to global data in 2019, a 60-year-old woman was expected to live 22.7 additional years, with only 73.1% of those years being in good health, compared with a man of the same age, who is expected to live 19.5 additional years, with 75.9% in good health¹. Female individuals also experience higher rates of neurological and psychiatric disorders² (Box 1) and are more likely to become caregivers^{3,4}.

At the time of writing, none of the targets of the gender equality goal (Sustainable Development Goal 5) of the United Nations 2030 Agenda for Sustainable Development have been attained 1.5-7. The gender equality goal entails achieving gender equality and empowering

all women and girls by addressing barriers such as gender-based discrimination, violence and unequal access to healthcare, education and socioeconomic decision-making processes, which are critical for improving health outcomes. Overcoming the gap in women's health would improve the quality of women's lives, increase their workforce participation and create positive ripple effects for families and communities. The economic impact resulting from expanded participation in the workforce, fewer early deaths, fewer health conditions and increases in productivity could generate at least US \$1 trillion annual incremental gross domestic product (GDP) by 2040. Of this opportunity, brain health, including neurological and psychiatric disorders (*International Classification of Diseases* Tenth Edition (ICD-10)), accounts for nearly 25%, or US \$250 billion (ref. 8).

Take, for example, depressive and anxiety disorders, largely prevalent among women of working age. Beyond direct and indirect medical costs, the associated reduced work engagement, absenteeism, presenteeism and high turnover suggest that individuals affected by depressive and anxiety disorders are not contributing effectively to the economy°. It has been estimated that reducing the burden of depressive disorders alone could contribute up to US \$100 billion in

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BOX 1

Definitions of brain health, mental health and brain capital

There are currently no consensus definitions for brain health and mental health. We use these terms following the definitions of the World Health Organization and mostly refer to research on psychiatric and neurological disorders as defined by the ICD⁸⁷.

Brain health can be described as a dynamic state encompassing the optimal functioning of cognitive, sensory, emotional, social, behavioral and motor systems supporting, across all stages of life, an individual's overall well-being and the ability to lead a meaningful and productive life regardless of the presence or absence of disorders^{7,88}.

Mental Health refers to a state of mental well-being that allows individuals to cope with life challenges, learn well, work productively and contribute to the community⁸⁷.

Brain and mental health are deeply interconnected, relying on shared mechanisms that contribute to the development of neurological and psychiatric disorders⁸⁹ and encompassing physiological and psychological variables related to these conditions on a spectrum⁹⁰.

Neurological disorders, or diseases of the nervous system, are a group of conditions characterized as being in or associated with the nervous system⁸⁷. Examples include migraine, Alzheimer disease, Parkinson disease, multiple sclerosis, epilepsy and stroke⁸⁷.

Psychiatric disorders, also known as behavioral and neurodevelopmental disorders, are conditions characterized by clinically significant disturbance in an individual's cognition, emotional regulation or behavior⁸⁷. Examples include depression, anxiety disorders, schizophrenia, bipolar disorders and eating disorders.

Brain capital is the cumulative cognitive abilities, knowledge and overall brain health of a population. This concept highlights the critical importance of investing in education, mental health care and neurological health to enhance intellectual capacities and creativity. Prioritizing brain capital enables societies to drive innovation, adaptability and sustainable growth. By incorporating brain capital into national metrics alongside traditional economic indicators, policymakers can better guide investments to improve societal well-being and resilience⁹¹.

GDP growth due to an increase in productivity, while improvement in anxiety disorders could add nearly US \$50 billion (ref. 8) (Fig. 1).

In this Perspective, building on the definition of 'brain capital,' ^{10,11} we propose the concept of women's brain capital, focusing on what is economically lost if we overlook women's brain health, including mental health and neurological disorders. Our aim is to provide evidence surrounding sex-specific and gender-specific health research and health-care investments, recognizing their profound impact on the well-being of communities globally. Beyond educating about this unmet medical need, we hope to stimulate discussions on the compelling business case for investing in women's brain health across the entire lifespan and mobilizing leaders to action.

Women's brains face unique challenges

While brain health is measured on a spectrum, diagnoses help communicate effectively about clusters of signs/symptoms that severely impact an individual's functioning. We focus on research about diagnoses of neurological and psychiatric disorders as these are clearly

defined by the ICD. More importantly, approximately half of the world's population will grapple with a psychiatric disorder at some point in their life¹². Similarly, neurological disorders have been reported to affect over 43% of the global population¹³.

Building evidence suggests sex differences in the prevalence and the signs/symptoms of psychiatric and neurological disorders. The definition of sex has been iterative over time, and it is typically a biological distinction between male and female individuals in humans and animals¹⁴. It is crucial to acknowledge the distinction between sex and gender definitions as they are not synonymous and are frequently misused¹⁵. Sex, typically determined by genetics (for example, females having XX chromosomes and males having XY chromosomes), and gender, a complex interplay of behavioral, social and personal identity factors, can serve as pivotal, independent or interacting determinants. In fact, as it is understood today, gender is multidimensional and includes cisgender and transgender identities, as well as non-binary identities. Cisgender refers to individuals whose gender identity aligns with their sex assigned at birth, whereas transgender describes individuals whose gender identity differs from their sex assigned at birth. Non-binary identities, which encompass a range of gender experiences beyond the male-female binary, include agender, bigender and gender fluid, among others. These distinctions emphasize the diversity and complexity of gender as a construct¹⁶.

Female individuals are more likely to experience migraines, multiple sclerosis, Alzheimer disease, eating disorders, depression and anxiety¹⁷. Furthermore, while autism spectrum disorders and attention deficit hyperactivity disorder are more prevalent among male individuals, female individuals present with different symptoms, which has historically led to underdiagnosis 18,19. It is only recently that researchers have begun to dissect the underlying sex differences in psychiatric and neurological disorders²⁰⁻²². Evidence has shown that fluctuations in sex hormones during menstruation are the major biological factors driving sex differences in anxiety and depression risk,²³ with further influence on many brain disorders^{24–28}. We argue that sex and gender are highly intertwined and can individually, in parallel or subsequently influence health outcomes, ^{29,30} although the implications are beyond the scope of this Perspective. To ensure clarity, we strive to incorporate definitions of sex and gender and their use in this paper (Box 2).

Studies have also found sex differences in brain regions such as the amygdala, hippocampus and insula, known to be implicated in neurological disorders ^{31,32}. Sex-biased gene expression ³³ has an impact on cortical brain development, potentially leading to novel sex-specific underlying mechanisms. In fact, one study has shown causal genes with sex-differentiated or sex-biased protein expression ³⁴. Sex-specific mechanistic studies are essential for understanding underlying mechanisms, and future advancements in brain health depend on successful sex-specific research.

The women's brain health gap is a multifaceted domain that extends beyond biological factors, with sex/gender having an essential role in shaping environments and experiences. For example, gender has a substantial role in children's educational attainment. Girls and women from the most disadvantaged rural areas tend to have the lowest levels of educational attainment¹. A low educational attainment increases the risk of neurological disorders such as Alzheimer disease and leads to a pervasive cycle of greater lifetime risk predisposition for dementia³⁵. Furthermore, this pervasive cycle can, in turn, lead to reduced access to health-care systems later in life and heightened chances of negative health outcomes³⁰, as well as reduced employment, lower income and increased caregiver burden^{3,4}.

Finding ways to advance women's brain health is crucial for a better future for everyone. By addressing women-specific health factors, we can reduce misdiagnosis or late diagnosis generated by biases permeating medicine and therefore enhance women's brain health, as well as life and career trajectories. This strengthens families, communities

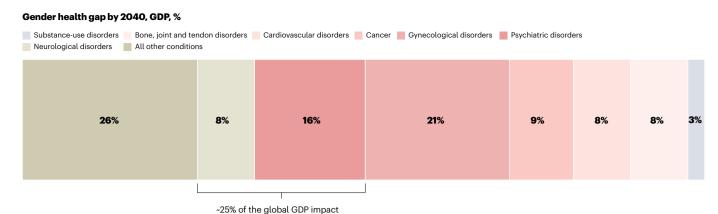


Fig. 1| **Breakdown of the global US \$1** trillion GDP opportunity of closing the women's health gap by conditions. The opportunity for brain health, encompassing psychiatric and neurological disorders, makes up nearly a quarter of the total GDP opportunity. Analysis made by building on the report published in 2024 by the World Economic Forum in collaboration with the McKinsey Health Institute. Analysis is based on an assessment of neurological disorders and psychiatric diseases burden, measured in disability adjusted life years in women in the USA, as estimated in the Global Burden of Disease dataset published by the Institute of Health Metrics and Evaluation (http://ghdx.healthdata.org/gbd-2021).

Conditions were chosen as part of the 64 conditions from the original report on the basis of a ranking of conditions contributing the most to the female health burden globally (as measured in disability adjusted life years). To size the economic gap, we estimated the benefits of having a larger, healthier and more productive female labor force, which was used to project the annual potential GDP contribution to 2040. Neurological disorders (8%) and psychiatric disorders (16%) are combined into brain health. Brain health, at 25%, is the largest segment of conditions impacting the gender health gap. Note: figures do not sum to 100% because of rounding.

and society by reducing health burdens and increasing economic participation, among other benefits.

However, one of the longstanding challenges is the persistent gap in data in which an individual's sex juxtaposes with their gender at birth or in which data regarding sex at birth have been altered to align with a gender identity and sex at birth is no longer disclosed. At the time of writing, there is limited evidence disentangling the individual or synergistic effects of sex and gender. This includes evaluating the intersection of gender and brain health, particularly for non-cisgender individuals, including transgender and non-binary identities.

Women's brain health gap

Although there is much to rejoice about regarding women's resilience (greater longevity, even in the face of disease, lower prevalence of cancer), the neglect of women's health has led to the current translational gap in women's brain health. Here we briefly highlight four core global reasons. First, there is a limited understanding of sex-based differences in brain health. Historically, the study of human biology used the male body,^{36,37} which created a gap in knowledge about mechanisms of disease development in the female body and, therefore, resulted in fewer and less effective treatments available for female individuals. For example, women make up 75% of the population affected by migraines, and evidence suggests differences attributed to sex or gender;³⁸ however, there has been a notable lack of research into understanding the nature of these differences and their clinical implications³⁹. Migraines are likely influenced by gonadal hormones specific to the female sex 38,40,41. In fact, migraines tend to appear around puberty, change during pregnancy, coincide with menstruation in more than 50% of women and worsen often during perimenopause 42,43. Findings of magnetic resonance imaging studies show that among individuals who suffer from migraines, structural and functional differences between the male and female brain exist, including differences in cortical thickness and connectivity of regions involved in pain perception, interoception and emotional processing. This evidence has been interpreted as indication of a greater association of migraines with pain and disability among women^{40,41,44}. Therapeutics such as combination therapy for migraines with triptan plus acetylsalicylic acid and non-steroidal anti-inflammatory drugs show 22% lower effectiveness in women than in men⁴⁵. Exploring sexand gender-specific solutions for migraines could potentially reduce or eliminate suffering, providing a profound advancement in precision medicine for brain health.

Second, data gaps can lead to the underestimation of women's health burden. In addition to the case of Alzheimer disease (for details, see refs. 46–50), two examples of such data gaps are the neglected investigations of hormonal transitioning phases and the X chromosome transcriptome in brain health studies. Although recent studies pointed out changes in whole-brain dynamics across the menstrual cycle and women's lifespan^{51–53} and sex steroid hormones as powerful modulators of learning and memory⁵⁴, less than 0.5% of the neuroimaging literature considers hormonal transition phases, such as the influence of hormonal contraceptives, pregnancy and menopause^{55,56}.

Another example of under-collected data is the X chromosome transcriptome, which makes up a meaningful part of the genome in both males and females but is frequently excluded from genome-wide association studies and DNA methylation arrays⁵⁷ because of the complex statistical analysis in bioinformatics pipelines⁵⁸. Less than half of the genes associated with human pathology on the X chromosome are currently known, and many more are yet to be clinically characterized⁵⁹. Therefore, limited understanding exists regarding the role of sex chromosomes in brain health and beyond³⁷. The under-collection of data on these variables that are crucial to women's health can lead to overlooking effective starting points for treatments tailored to women, for example, hormone replacement therapy for menopausal women experiencing migraines⁶⁰.

The third reason is the sex-/gender-based barriers to brain health-care delivery and equitable healthcare. Anyone seeking treatment for brain disorders may face discrimination, limited access or biased care. Women, however, historically encounter additional sex- and gender-specific obstacles. The outdated concept of hysteria, rooted in ancient misconceptions about a 'wandering uterus,' perpetuated stereotypes and dismissed women's signs/symptoms, labeling them as hysterical⁶¹. Post-partum depression remains stigmatized, often overshadowed by societal expectations of motherhood. Anxiety disorders, too, are subject to gendered stereotypes, with women unfairly labeled as naturally fearful, undermining the recognition of anxiety as a legitimate and treatable condition. Urgency in addressing these issues is reflected in reported statistics showing that 71% of worldwide anxiety disorders could be avoided with effective prevention and optimal treatment,

BOX 2

Definitions of sex and gender, intersectionality and brain health equity

This Perspective reflects women's health as a market segment. As many of the studies discussed here did not specify the method of collection, in case these data were unknown, we opted to use the terms 'sex.' 'male' and 'female' when describing biology and 'gender,' 'man' and 'woman' when we assume a prevailing effect of societal/behavioral factors. The term 'sex/gender' denotes sex 'and/or' gender. We acknowledge the importance of healthcare for the transgender, non-binary and gender-fluid communities and that not all people who identify as women are born biologically female. Therefore, as required, we often use the term 'sex/gender' to reflect inclusive language and recognize the need for future research into health issues that are inclusive of the transgender, non-binary and gender-fluid communities. We also acknowledge the profound differences for women due to factors such as race, ethnicity, socioeconomic status, disability, age and sexual orientation. Additional work and research should reflect how to tackle these barriers alongside the overall women's health gap.

To this end, the concept of intersectionality provides a framework for understanding how various aspects of a person's identity, such as the preceding factors, interact and contribute to unique experiences of discrimination or privilege⁹². Intersectionality is instrumental for brain health equity because it contributes to the understanding of factors that influence disparities in health outcomes, including brain health.

Brain health equity can be defined as ensuring that all individuals, regardless of their social, economic or cultural background, have equal opportunities to achieve optimal brain health⁹³. Brain health equity emphasizes removing barriers and addressing disparities that disproportionately affect historically marginalized populations, ensuring fair access to resources that promote neurological health and well-being.

underlining the need for urgent action^{13,17}. Furthermore, different dimensions of prenatal maternal distress potentially contribute in a cross-generational way, shaping infant brain and behavior^{62,63}. This underscores the critical need to confront bias to ensure equitable access to brain healthcare for women across the lifespan.

In addition, socioeconomic barriers such as limited finances, lack of insurance and caregiving duties can impede women's access to healthcare. Women may be especially affected during their childbearing years as many treatments for brain disorders are not fully compatible with pregnancy and breastfeeding^{64,65}. Reproductive psychiatrists, who focus on mental health of women during reproductive years, remain inaccessible to many. Last, sex bias in diagnostics may overlook women's signs/symptoms, frequently attributing them to hormones and therefore dismissing their seriousness. While hormones and hormonal fluctuations influence brain health and are, for example, a major biological driver for migraines⁶⁶, this should not justify ineffective treatment. Women in historically underrepresented or vulnerable populations may face an additional challenge in accessing the health-care system, demonstrating the intersectional nature of brain health equity. For example, studies indicate that Black women are less likely than their white counterparts to seek treatment for psychiatric disorders^{67,68}. Investing in women's brain capital requires developing the systems and foundation to support all women in getting access to equitable and comprehensive care.

Fourth, low investment in women's health limits the scale of innovation. For example, although women are two to three times more likely than men to be affected by migraines, just 37% of US National Institutes of Health (NIH) funding in migraine research in 2019 was directed toward understanding sex-specific differences⁶⁹. Moreover, research consistently highlights the profound impact of investing in brain health, revealing a remarkable return of US \$4 for every \$1 invested globally⁶⁹. Improved brain health not only enhances health and productivity but also alleviates burdens on both individuals and society. To capture brain health opportunities, we must re-evaluate our investment strategies, which involves not only allocating adequate resources but also incentivizing and de-risking investments specifically targeted toward women's brain health. The NIH mandates that sex must be considered as a biological variable in all research grants. While it is essential to recognize areas for improvement, we also commend the strides the NIH has made in addressing these inequalities. The next step is to create an incentive system to report sex- and gender-stratified results of such funded research.

By fostering partnerships among government entities, academia, non-profits and the private sector, we can leverage our collective expertise and resources to maximize the impact of brain health investments. Creating investment funds that are specifically designed to achieve measurable social and health outcomes related to women's brain health will help ensure accountability and allow us to track progress effectively. Standardized metrics will enable investors to assess the societal and health impacts of their investments, empowering them to make informed decisions and drive meaningful change. Most importantly, addressing the limited understanding of sex differences and the complex interplay of gender differences, as well as closing data gaps that undercount women's health burdens, combating bias in healthcare delivery and increasing investments, is essential to realizing the potential lost in the women's brain health gap.

Global actions

Understanding the importance of brain capital throughout a woman's life sheds light on the profound impact of sex-/gender-specific health factors. However, understanding and awareness are only the first steps to change. Every stakeholder in the health-care ecosystem has the opportunity to contribute to closing the gap and empowering women to optimize their brain health at all stages of life, reducing their burden of mental health and neurological disorders (Table 1). While it is essential to recognize areas for improvement, we acknowledge the needs of different countries, for which addressing educational inequalities and access to basic health-care rights is of monumental importance but also sits within an extremely complicated context of cultural norms and societal structures, which are usually highly gendered³⁰. Therefore, global actions should be iterative and adapted to regional settings.

To close the women's brain health gap, we propose four opportunity areas. The first is to destigmatize and raise awareness of psychiatric and neurological disorders across the lifespan. This involves increasing societal awareness of stigmas and women-specific challenges related to psychiatric and neurological disorders. This could include targeted education campaigns at schools and workplaces and among decision makers. It also means specifically destigmatizing the notion that women's hormonal changes throughout their lives are legitimate health risks. This can be tackled by promoting a holistic understanding of the impact of hormone cycles and hormone transitions on brain health. Furthermore, it is crucial to advocate the inclusion of sex-/gender-specific brain health topics in medical school curricula to ensure health-care providers are equipped to address the unique needs of women.

Table 1 | Global actions that stakeholders across industries can take to address the women's brain health gap, which has potential intergenerational effects

Reason for women's brain health gap	Proposed solutions	Proposed implementation		
Limited understanding of sex- based differences in brain health	De-bias the brain health-care delivery system at large and for women	-Provide bias-awareness training for health-care providers -Develop clinical guidelines considering sex and gender differences -Increase women's representation in clinical trials and research studies		
Low investment in women's health that limits the scale of innovation and precision medicine	Invest in women's brain capital	-Provide dedicated funding for sex-specific brain health research -Cultivate a network of public and private investors interested in funding women's brain health -Offer grants and accelerator programs for start-ups focusing on women's brain health		
Data gaps that result in women's health burdens being undercounted/ neglected/ underestimated	Destigmatize and raise awareness on brain health conditions	-Increase awareness of stigmas and female-specific challenges through targeted education campaigns -Promote understanding of the impact of hormone cycles on brain health -Advocate inclusion of female-specific brain health topics in medical school curricula		
Sex-/gender-based barriers to brain health-care delivery	Implement policies that advance women's brain health	-Advocate comprehensive health-care coverage for brain health conditions -Support workplace policies for affected individuals -Allocate government funds for gender-specific brain health research		

The second opportunity area is to de-bias the brain health-care delivery system at large and for women. This could be aided by implementing training for health-care providers to recognize and address gender biases in diagnosis, treatment and referral practices. It is also important to develop clinical guidelines that consider sex/gender differences in psychiatric and neurological disorders, ensuring equitable access to diagnosis and treatment for women. In addition, increasing the representation of women in clinical trials and research studies ensures that findings are applicable to diverse populations of women.

The third opportunity area is to implement policies that advance women's brain health. This could include advocating the integration of comprehensive coverage for brain disorders within health-care plans, encompassing regular screenings and interventions. It is important to emphasize the inclusion of treatments compatible with different stages of a woman's life, including pregnancy and breastfeeding. Employers should be encouraged to create workplace policies that support individuals impacted by psychiatric and neurological disorders or those caring for affected loved ones. Promoting flexible work arrangements can alleviate employees' psychological stress, which women have indicated is a top priority⁷⁰. Allocating government funds for sex-/gender-specific research on brain health and amplifying current academic policies that include sex as a biological variable in preclinical and clinical brain health studies is crucial.

The fourth opportunity area is to invest in women's brain health. This includes, but is not limited to, offering national and region-specific funding for understanding sex differences in preclinical research, emphasizing a lifespan approach. It is also beneficial to foster an ecosystem of public and private investors interested in funding

women's brain health to share knowledge, promote collaborations and provide information about the progress and return on investments in women's brain health. Providing specific grants and accelerator programs for start-ups focusing on developing diagnostic tools, protocols and therapies tailored to women's brain health is another important consideration.

How can investments in women's brain capital be implemented across the lifespan?

Building on the economic benefits gained from reducing the burden of psychiatric and neurological disorders among women, we encourage a broader perspective on women's brain health across the lifespan. We seek to place women's brain capital at the center of a new narrative that includes young and late-life brain capital 71,72 . We have laid out initial global recommendations on how investments in women's brain capital can be implemented across the life course (Table 2). Engaging with local communities to ensure that the proposed solutions and indicators are culturally sensitive and feasible within the local context is warranted.

Furthermore, we envision that women's brain capital over the course of a lifetime can be tailored for each psychiatric and neurological disorder. For example, given the high risk of depression associated with a family history of depression, it may be possible to determine which young girls are at elevated risk and study their psychobiological functioning⁷³. Thus, by identifying known sex-/gender-specific risks of depression, there is an opportunity to intervene earlier in the life course. Investing in a young girl's brain health through a multipronged strategy to prevent depression could improve brain capital in her life and in generations to follow. More concretely, this could include increasing depression screening during the pregnancy period and developing personalized detection, prevention and intervention programs for girls at higher risk of depression. In addition, brain capital emphasizes a focus on the brain in society, recognizing that brain health is not improved merely through clinical interventions. It is important to develop strategies to reduce depression in women through education and community systems.

Another brain disorder that will benefit from being considered from a lifespan perspective is dementia. While it contributes to a relatively small percentage of the calculated GDP women's health gap, in 2021, 64% of the 51.6 million people affected by dementia globally were women⁷⁴. Similar to other psychiatric and neurological disorders, sex accounts for notable heterogeneity of dementia signs/symptoms, and biological sex differences such as gonadal hormones, hormone cycles and sex chromosomes may be the underlying cause^{2,20,37,75}. Many have extensively examined the effects of menopausal hormone therapy and its implications for dementia⁷⁶. However, we recognize that the relationship between gonadal hormones, hormone cycles and dementia remains a topic of debate, with only weak evidence linking endogenous circulating estrogens to Alzheimer disease biomarkers, which is beyond the scope of this Perspective. Still, roughly 4% of the NIH budget dedicated to Alzheimer disease research was allocated to women-specific research in 2019 (ref. 77). Dementia is known for its strong impact on the affected individual's family: in the United States, nearly half (48%) of all informal caregivers of older adults care for someone with dementia, for an average of 31 hours per week. One out of four dementia caregivers is a 'sandwich generation' caregiver, caring for both an aging parent and at least one child, and 41% have a household income of US \$50,000 or less⁷⁴. A meta-analysis showed that dementia caregivers are at higher risk of depression and anxiety compared with non-caregivers⁷⁸ and experience more depressive signs/symptoms than non-dementia caregivers⁷⁹. Recent research suggests that the caregiver burden is further amplified for women 80-84, with additional variables (for example, sociodemographic variables, culture and ethnicity), requiring further study. Addressing the women's health gap for dementia would substantially influence the lives of patients and informal caregivers,

Table 2 | Initial recommendations, barriers or risk factors, potential solutions, initiatives, required tools, key performance indicators and potential road blocks for implementation of women's brain capital across different life stages

Life stage	Barriers/women's risk factors	Potential solutions	Initiatives	Required tools	Road blocks	Key performance indicators
Embryo/fetus -	Environmental toxins	Develop public health campaigns to reduce exposure to toxins	Prenatal care access programs and maternal wellness initiatives	Educational materials, mobile health clinics, training for health- care providers	Lack of funding, cultural barriers to health-care access, insufficient health- care infrastructure	Reduction in low birth weight, increased prenatal care visits, lower maternal cortisol levels
	Inadequate prenatal care	Expand access to prenatal care				
	Maternal stress	Implement stress- reduction programs for expectant mothers				
Childhood and adolescence	Poor nutrition	School-based nutrition programs	Targeted geographical nutritional campaigns and sex/gender workshops	Skilled personnel, educational grants, training materials for workshops	Socioeconomic disparities, gender discrimination and stigma, resistance to cultural change	Improved body mass index scores, higher school enrollment rates for girls, increased awareness of gender biases
	Limited access to education	Scholarships for girls, increase education technology initiatives such as open courses targeting girls				
	Societal gender norms	Sex/gender equality workshops, increase gender equality representation in films and entertainment				
Early adulthood (reproductive years)	Women hold the majority of caregiving roles	Telemedicine for reproductive health and women's health more broadly, corporate policies for flexible work hours, improved childcare support and policies, violence prevention and support networks	Flexible working programs, brain health and mental health targeted telehealth platforms	Resource allocation for the development of telehealth platforms, HR policy frameworks, support hotlines and shelters	Stigma around reproductive health, corporate resistance to policy change, lack of legal protection in some geographical regions	Decrease in reported reproductive health problems, improved job satisfaction, reduction in domestic violence cases, increased rates of males in caregiving roles
	Women are still a minority in the labor workforce					
	Gender-based violence					
Middle adulthood (post-menopause)	Menopause-related symptoms dismissed or underdiagnosed	Access to specialized clinics for women's health, financial support for professional caregiver services, normalized discussions about menopause	Health-care system improvements to recognize and treat menopausal symptoms, targeted work policies for menopausal women	Resource allocation for affordable healthcare and professional caregiver services	Insufficient funding for health-care infrastructure, inadequate public funding for elder care and childcare services, persistent societal taboos	Improved health, higher social and professional engagement, improved job satisfaction
	Menopause stigma causing reduced influence in social and professional settings					
	Increased caregiving role (elderly parents and adult children)					
Late adulthood (post- menopause)	Social isolation	Mental health awareness campaigns, community exercise programs, senior community centers	Dementia prevention programs for women, social prescribing initiatives to mitigate loneliness, innovations in elder-care models	Exercise equipment, public service announcement, community center facilities	Health-care affordability, psychiatric illness stigma, urban-rural divide in resource allocation	Increased access to long-term elder care, increased numbers of intergenerational communities
	Psychiatric and neurological disorders stigma hinders diagnosis and public policies					
	Lack of subsidized long- term elderly care					

This table is a starting point and should be adapted to the specific needs of the region or country in question. The key performance indicators are derived from ref. 1, which provides a framework for measuring the impact of these potential solutions. The road blocks consider the geographical and cultural challenges that may impede the implementation of these initiatives. It is important to engage with local communities and stakeholders to ensure that the solutions are culturally sensitive and feasible within the local context.

BOX 3

City-level interventions

With the global urban population expected to reach 70% by 2050, the significance of cities in shaping health outcomes is increasingly evident. The McKinsey Health Institute⁹⁰ highlights that focusing on health at the city level could unlock an additional 20 to 25 billion years of high-quality life globally⁹⁴. This focus is particularly crucial for addressing the women's brain health gap as urban environments offer unique opportunities and challenges that can influence women's mental health and well-being. By tailoring interventions to the dense and diverse urban contexts, cities can become pivotal arenas for pioneering and implementing health strategies that directly benefit women's brain health.

To effectively bridge the women's brain health gap, cities can adopt targeted, evidence-based interventions. Task sharing stands out as a highly effective approach^{95,96}. This strategy involves training both clinical and non-clinical personnel to deliver basic, evidence-based psychological treatments, such as cognitive behavioral therapy and interpersonal therapy. These interventions are particularly beneficial for treating psychiatric disorders such as anxiety and depression, which disproportionately affect women.

For example, the Common Elements Treatment Approach and the Friendship Bench project are innovative models that have been successfully implemented in various urban settings. The Common Elements Treatment Approach integrates multiple mental health services into a cohesive treatment plan, while Friendship Bench utilizes community volunteers, such as trained grandmothers, to deliver mental health support. These approaches not only increase the accessibility of mental health resources but also reduce the stigma associated with seeking help, a considerable barrier for many women.

of whom nearly two thirds are women, who are currently reducing their working hours or quitting work completely to be able to care for affected family members.

A holistic understanding of brain health goes beyond the absence of disease, including efforts to improve overall cognitive clarity, resilience to stress, social skills, a sense of direction and life satisfaction. A recent survey by the McKinsey Health Institute of over 30,000 employees across 30 countries revealed that women are more exhausted and experience poorer mental and spiritual health than men, putting them at higher risk of burnout. Globally, 46% of female and 38% of male participants reported symptoms of exhaustion. Slightly fewer female than male participants reported having good mental health (65% versus 70%, respectively) and good spiritual health (56% versus 61%, respectively)⁸⁵. Employers can play a crucial role in driving markers of positive health and reducing markers of negative health (for example, burnout). For example, women who have the flexibility to work from their preferred location have 15% better mental health, 19% better spiritual health and 19% less exhaustion⁸⁵. Employers are advised to view such workplace design changes as a fruitful investment. Employees who reported better overall health also tended to score higher in job performance and innovation85. One example of workplace investment is city-level interventions that take into account the diverse urban contexts to prioritize women's brain health (Box 3). Investing in women's brain capital and women's health is an essential perspective that weaves together both psychiatric and neurological disorders with broader brain health-including burnout and resilience. By investing in women's brain capital and women's health, we can holistically strengthen brain skills and well-being (Fig. 1).

BOX 4

Current vehicles for women's brain health funding

Currently, support for women's brain health initiatives is available through the public and private sector, including profit and nonprofit organizations. For example, agencies of the NIH, such as the National Institute on Aging and the Office of Research on Women's Health, prioritize funding for studies on women-specific neurological conditions. Other public funders include Horizon Europe (through its Health Cluster), the Swiss National Science Foundation and the Canadian Institutes of Health Research, who allocate resources to understand sex differences in brain aging, cognitive decline and mental health. Vehicles to foster women's brain health also include initiatives sponsored by the private sector, including pharmaceutical and health tech companies and philanthropic foundations. A notable example is the Melinda Gates Foundation, which recently launched the Action for Women's Health initiative, with the goal of addressing the gaps in funding and support for women's health issues, including brain health. Similarly, RH Capital and Go Red for Women Venture Fund are private investment funds that focus on women's health and health equity, and women's cardiovascular health, respectively. The Women's Brain Foundation has also undertaken a substantial effort in establishing public-private partnerships aimed at mobilizing resources expertise, and innovation from the private sector to address health disparities and promote sustainable progress in women's health globally. Moreover, the Women's Brain Foundation is currently leading a pioneering initiative to establish a venture studio dedicated to supporting start-ups and entrepreneurs in developing solutions, technologies and research that address critical gaps in women's brain and mental health.

Conclusion

For far too long, women's brain health has been totally neglected. The rising interest in sex- and gender-specific health factors of neurological and psychiatric disorders offers a great potential for improving women's physical and mental health, discovering tailored ways to diagnose and treat these disorders and enabling women worldwide to increase their participation in workforce and community with notably decreased health burden. By closing the gap in women's brain health, we unlock a brighter future for everyone. Furthermore, another compelling perspective is to frame women's brain health as an integral part of women's health as a whole. This approach not only underscores the holistic nature of health but also creates synergies that could potentially leverage greater investment opportunities. By integrating women's brain health into the broader context of women's health, stakeholders can address multiple health determinants simultaneously, thereby driving more comprehensive and impactful health interventions and funding initiatives. We encourage leaders across industries to tap into this potential with focused actions to increase understanding of and investment in women's brain health (Box 4).

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Author contributions

L.C.-A. conceived the paper. L.C.-A., M.G., L.P., E.S. and H.A.E. collected data for the article. L.C.-A. consolidated the first and final draft. L.C.-A., M.G., L.P. and E.S. contributed with substantial writing and discussion of all sections. M.B. contributed substantially to the finalization of the revised manuscript. H.A.E. and A.S.C. reviewed the

manuscript before submission. All authors approved the final version of the manuscript.

Competing interests

L.C.-A. was the scientific project manager of the Women's Brain Foundation. M.B. is the scientific lead of the Women's Brain Foundation. H.A.E. is an employee of Rice University's Baker Institute for Public Policy; receives consulting fees from Meadows Mental Health Policy Institute and Kooth; has received speaking fees from Novo Nordisk, Roche and Lundbeck; and has received consulting fees from Novo Nordisk and ALTOIDA. A.S.C. is the co-founder and pro bono CEO of the Women's Brain Foundation, and is also the pro bono Euresearch vice president.

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