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## **Sex and gender research improves health outcomes and the economy for everyone**

The world's leading causes of death are cardiovascular disease, cancer and respiratory disease, with each of these conditions showing differences in mortality rates between men and women. Better health is correlated with economic prosperity. Women spend 25 percent more time in "poor health" compared to men; addressing this gap would not only improve the health and lives of millions around the world, but could increase the global economy by at least \$1 trillion annually by 2040.

These findings underscore the critical importance of understanding how sex and gender influence morbidity and mortality at all stages of life. Sex refers to factors including genetics (e.g., sex chromosome complement), physiology (e.g., gonadal hormone status), and anatomy (e.g., reproductive organs). Gender-related factors include self-perceived identity, as well as gender-associated roles and relations which can directly impact health outcomes. By studying sex- and gender-related factors across the lifespan, we can improve diagnoses, refine treatments, and better address the health needs of all individuals to optimize both quantity and quality of life.

Key examples include:

**Heart disease:** The leading cause of death in the world is heart disease. However, men develop heart disease a decade earlier than women, and heart disease is often missed in women, who commonly experience different heart attack symptoms than men, such as nausea and fatigue instead of chest pain. Individuals with more roles traditionally ascribed to women, irrespective of gender identity, have a greater risk of recurrent heart disease. Understanding factors that lead to these differences will save lives.

**Cancer:** Globally, men have a higher incidence of cancer compared to women. Although the causes of these differences in cancer incidence and mortality are not yet well understood, genetic, environmental, and behavioral factors likely play a role. Research is urgently needed to identify drivers of sex and gender differences in causes of cancer.

**Dementia:** Over 55 million people worldwide are living with dementia. By 2050, this number is projected to rise to 139 million. Alzheimer's disease is the most common cause of dementia, with women being at higher risk. Men and women with Alzheimer's disease show different cognitive and psychiatric symptoms, with women experiencing faster cognitive decline after diagnosis. Given the aging population, studying and reporting sex and gender differences in disease symptoms, biomarkers, progression, risk factors, and treatment responses is crucial for developing precision medicine in Alzheimer's disease.

**Infection:** Women have stronger immune responses but are more prone to autoimmune diseases, while men face higher risks of dying with severe infections due to less robust immune systems. Understanding these differences will lead to better treatments and health outcomes.

**Medications:** Over a 4 year period, 8 out of 10 drugs withdrawn by the US Food and Drug Administration posed greater health risks for women than for men. Accounting for important factors such as sex-based differences in body composition and drug metabolism is critical to avoid drug toxicity in all individuals.

The United States has seen a troubling decline in life expectancy over the last two decades, falling behind all other high-income nations, and US maternal mortality is the highest in the G7. We strongly support health research and studies of fundamental biology that incorporate sex- and/or gender-based factors and how they are affected by environmental exposures, behaviors and roles across a person's lifetime. This research is critical to advancing health care, improving health outcomes, and addressing key public health issues for all women, men, and gender-diverse people.