

Better hygiene in wealthy nations may increase Alzheimer's risk

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New research has found a "very significant" relationship between a nation's wealth and hygiene and the Alzheimer's "burden" on its population. High-income, highly industrialised countries with large urban areas and better hygiene exhibit much higher rates of Alzheimer's.

Using 'age-standardised'* data - which predict Alzheimer's rates if all countries had the same population [birth rate](#), life expectancy and [age structure](#)—the study found strong correlations between national sanitation levels and Alzheimer's.

This latest study adds further weight to the "hygiene hypothesis" in relation to Alzheimer's: that sanitised environments in [developed nations](#) result in far less exposure to a diverse range of bacteria, viruses and other microorganisms—which might actually cause the immune system to develop poorly, exposing the brain to the [inflammation](#) associated with Alzheimer's disease, say the researchers.

"The 'hygiene hypothesis', which suggests a relationship between cleaner environments and a higher risk of certain allergies and [autoimmune diseases](#), is well— established. We believe we can now add Alzheimer's to this list of diseases," said Dr Molly Fox, lead author of the study and Gates Cambridge Alumna, who conducted the research at Cambridge's Biological Anthropology division.

"There are important implications for forecasting future [global disease burden](#), especially in developing countries as they increase in sanitation."

The researchers tested whether "pathogen prevalence" can explain the levels of variation in Alzheimer's rates across 192 countries.

After adjusting for differences in population age structures, the study found that countries with higher levels of sanitation had higher rates of Alzheimer's. For example, countries where all people have access to clean drinking water, such as the UK and France, have 9% higher Alzheimer's rates than countries where less than half have access, such as Kenya and Cambodia.

Countries that have much lower rates of infectious disease, such as Switzerland and Iceland, have 12% higher rates of Alzheimer's compared with countries with high rates of infectious disease, such as China and Ghana.

More urbanised countries exhibited higher rates of Alzheimer's, irrespective of life expectancy. Countries where more than three-quarters of the population are located in urban areas, such as the UK and Australia, exhibit 10% higher rates of Alzheimer's compared to countries where less than one-tenth of people inhabit urban areas, such as Bangladesh and Nepal.

Differences in levels of sanitation, infectious disease and urbanisation accounted respectively for 33%, 36% and 28% of the discrepancy in Alzheimer's rates between countries.

Researchers said that, although these trends had "overlapping effects", they are a good indication of a country's degree of hygiene which, when combined, account for 42.5% of the "variation" in countries' Alzheimer's disease rates—showing that countries with greater levels of hygiene have much higher Alzheimer's rates regardless of general life expectancy.

Previous research has shown that in the developed world, dementia rates

doubled every 5.8 years compared with 6.7 years in low income, developing countries; and that Alzheimer's prevalence in Latin America, China and India are all lower than in Europe, and, within those regions, lower in rural compared with urban settings—supporting the new study's findings.

The results of the study are newly published by the journal *Evolution, Medicine and Public Health*, with these latest results coming hard on the heels of previous research led by Fox on the benefits of breastfeeding for Alzheimer's prevention.

"Exposure to microorganisms is critical for the regulation of the immune system," write the researchers, who say that since increasing global urbanisation beginning at the turn of the 19th century—the populations of many of the world's wealthier nations have increasingly very little exposure to the so-called 'friendly' microbes which "stimulate" the immune system—due to "diminishing contact with animals, faeces and soil."

Aspects of modern life—antibiotics, sanitation, clean drinking water, paved roads and so on—lead to lower rates of exposure to these [microorganisms](#) that have been "omnipresent" for the "majority of human history", they say.

This lack of microbe and bacterial contact can lead to insufficient development of the white blood cells that defend the body against infection, particularly those called T-cells—the foot soldiers of the immune system that attack foreign invaders in the bloodstream.

Deficiency of anti-inflammatory ("regulatory") T-cells has links to the types of inflammation commonly found in the brain of those suffering with Alzheimer's disease, and the researchers' proposal that Alzheimer's risk is linked to the general hygiene levels of a nation's population is

reinforced by their analysis of global Alzheimer's rates.

"The increase in adult [life expectancy](#) and Alzheimer's prevalence in developing countries is perhaps one of the greatest challenges of our time. Today, more than 50% of people with Alzheimer's live in the developing world, and by 2025 it is expected that this figure will rise to more than 70%," said Fox.

"A better understanding of how environmental sanitation influences Alzheimer's risk could open up avenues for both lifestyle and pharmaceutical strategies to limit Alzheimer's prevalence. An awareness of this by-product of increasing wealth and development could encourage the innovation of new strategies to protect vulnerable populations from Alzheimer's."

While childhood—when the immune system is developing—is typically considered critical to the '[hygiene hypothesis](#)', the researchers say that regulatory T-cell numbers peak at various points in a person's life—adolescence and middle age for example—and that microorganism exposure across a lifetime may be related to Alzheimer's risk, citing previous research showing fluctuations in Alzheimer's risk in migrants.

The team used the disability-adjusted life year (DALY) rates to calculate the incidence of Alzheimer's across the countries studied. The DALY measurement is the sum of years lost due to premature mortality combined with years spent in disability – the World Health Organisation (WHO) says that one DALY can be thought of as "one lost year of 'healthy' life".

The researchers say this method is a much better measure than death rates as it "omits the effects of differential mortality rates" between developed and developing [countries](#). The study was based on the WHO's 'Global Burden of Disease' report, which presents world dementia data

for 2004.

More information: *Age-standardised data:

The process of age-standardisation presents a "single summary rate that reflects the number of events that would have been expected if the populations being compared had had identical age distribution" (WHO 2001)

The age-standardised data is calculated by adjusting the crude data for 5-year age groups by age-weights reflecting the age-distribution of the standard population. In the version of the WHO's Global Burden of Disease report we utilised, the terminal age category has been extended from the previous 85+ to 100+, which allows for better adjustment for differences in the proportion of population in older strata.

The age-adjusted and disability-adjusted life year (DALY) rates are calculated by "adjusting the crude estimates to an artificial population structure, the WHO Standard Population, that closely reflects the age and sex structure of most low and middle income countries" (WHO 2013).

The effort to construct a standard population for comparing data across populations with varied age-structures began in the 1840s, and progressed to an international scale in 1960 and was then adopted by the WHO. Statisticians have been researching and improving this process for the past five decades.

The new WHO World Standard was developed in 2000 to best reflect projections of world age-structures for the period 2000-2025. This new standard is based on the UN Population Division's assessments every two years and future projections for every five years of each country's population age-structure. This standardised procedure is widely accepted

across the world, and is the basis for all relevant WHO-sponsored analyses.

Provided by University of Cambridge

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