Letter to The Editor

Journal of INDEPENDENT MEDICINE

Epidemiological Clues to Etiology of Autism Spectrum Disorder

Matthew Halma[1]

Dear Editor of the *Journal of Independent Medicine*,

Autism rates have risen in the United States of America by 24.1% between 1990 and 2019, according to a recent survey. (1) This rise has not been experienced by many other countries in the world. As autism presents a large and rising source of disease burden in the USA, (2) it is important to examine the driving factors behind the increase, occurring almost solely in the United States.

Autism Spectrum Disorder (ASD) is marked by poor social development, sensory anomalies, and repetitive behaviour. (3) As a spectrum disorder, it varies from its more minor form, Aspergers, to Autism in various grades. (4) At the more severe grades, those with ASD are nonverbal and require constant care to perform regular activities of life. (5)

Autism rates in the USA have risen precipitously since the seminal publication of Kanner in 1943 describing the condition in a cohort of 11 children. (6) Hans Asperger described a more mild form of the condition among a cohort of students in a 1944 report. (7) The condition Asperger described is now known as Asperger's syndrome. (8) Since then, the reported rate of autism has climbed from 5 cases per 10,000 children in the 1960s (9) to 1 in 36 children aged 8 years old in 2020. (10) The condition is four times more common in boys than girls, and 1 in 23 school-aged boys have an ASD diagnosis. (10)

While some of this is due to changes in diagnostic patterns, with estimates of the contribution to the increase in ASD ranging from 25% (11) to 60%. (12) Changes in diagnosing alone cannot explain the increase in ASD. Interestingly, examination of the changes between 1990 and 2019 from a recent burden of disease survey reveal that the United States saw the largest increase (24.1%) in age-adjusted ASD prevalence of any country worldwide. (1) For comparison, neighboring Canada only saw an increase in age-standardized ASD prevalence of 1.6% in this period.

The geographic restriction of the USA for the rise in ASD raises questions about what is unique to the USA that is leading to the rise in ASD, but not in other countries. Questions of ASD's causation have been highly contentious, especially since the controversy over Dr. Andrew Wakefield's study on enterocolitis in Measles, Mumps, and Rubella (MMR) vaccination recipients. (13) First, concerns were raised over an interpretation that it linked MMR vaccination with the development of ASD, leading to the partial retraction of this interpretation by 10 of the 13 original authors, (14) despite the original article explicitly stating "[W]e did not prove an association between measles, mumps, and rubella vaccine and the syndrome described." (13)

Further concerns over patient recruitment potentially being biased, undisclosed financial interests, and samples being outside of ethics council approval led to the full retraction of the article in 2010. (15) This episode remains salient in the debate around vaccination, about 6% of NYT articles using the phrase "vaccine hesitancy" also use the terms "Wakefield" OR "autism," suggesting that they are talking about the alleged link*.

[1] Independent Medical Alliance, Washington, DC, USA

Corresponding author:
Matthew Halma
Director of Scientific Research, Independent Medical Alliance
2001 L St. NW Suite 500, Washington, DC 20036, USA

This controversy has cast a shadow over environmental aetiologies for autism. Several epidemiological studies have investigated the link between MMR vaccination and autism, observing no significant increase in ASD rates in the MMR vaccinated. (16,17) Another study found a link between state level vaccination rate and autism diagnoses. (18) Other studies have found an association between vaccination rate, developmental delays, (19) and neurodevelopmental disorders. (20)

Vaccination is by no means widely accepted as an etiological factor in vaccination within the scientific community; 88.8% of US primary care physicians either strongly or somewhat agree with the statement "vaccines are safe," (21) and no scientists in a survey of 60 believed that there was any link between vaccination and autism. (22) Scientists predominantly endorse genetic explanations for autism, (22) and two-thirds believe the link between vaccination and autism should not be investigated further. (22) Among the public, approximately 1 in 4 American adults believe that MMR vaccination is linked to autism, (23) signaling a divergence between public opinion and the scientific community.

Other environmental effects have a strong evidentiary basis for their impact on ASD, including age of the parents, fetal environment (including drug exposures), exposure to high concentrations of sex steroids *in utero,* and infections. (24) Nutritional deficiencies, including vitamin D, iron, zinc, and copper in the mother during pregnancy, may also contribute to ASD risk. (24) Notably, epidemiological studies have revealed a role of toxic exposures in ASD aetiology, including air pollutants, heavy metals, pesticides and organic pollutants. (24)

Given that there is a significant difference in the growth of autism in the United States and not in other countries to nearly the same degree (1) (**Figure 1**), an investigation to the environmental factors leading to a rise in ASD in the USA can possibly bear clues for the etiology of ASD, and help to mitigate the environmental contribution to the increase in ASD.

It is difficult to fully capture the differences between countries with a minimal set of parameters. However, we can begin by studying the factors already identified through epidemiological or mechanistic studies as contributors to ASD, such as air pollutants, heavy metals, pesticides, and organic pollutants. (24) National and state comparisons using these factors may provide insight into the factors driving the rise in ASD in the United States and will be an important factor in averting an increase in ASD burden in the USA.

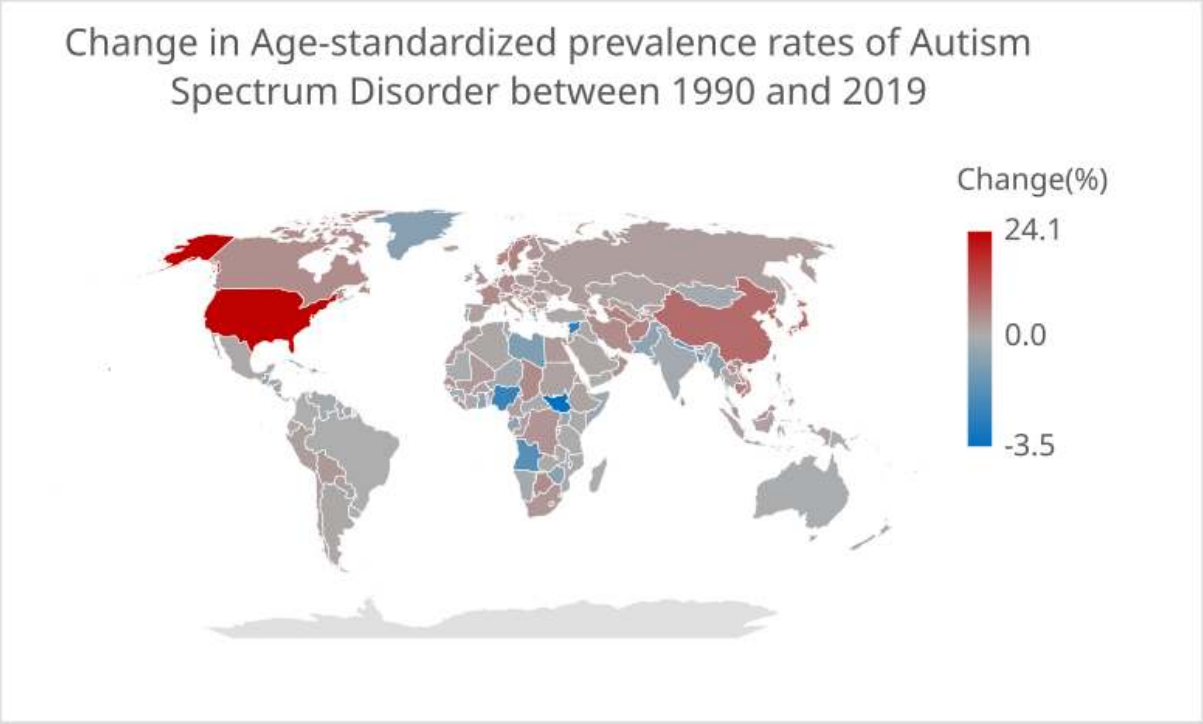
ASD has a large effect on both the affected and their families, with ASD resulting in higher healthcare costs (25,26) and school costs. (26) Discovering the environmental contributors to ASD will help to improve childhood health and decrease the burden of ASD.

Conflicts of Interest

The author declares no conflicts of interest.

*We performed the following search in the New York Times website (https://www.nytimes.com) for articles with the below keywords, published in the entire history of the newspaper.
"vaccine hesitancy": 623 results
"vaccine hesitancy" AND "Wakefield": 6 results
"vaccine hesitancy" AND "autism": 36 results
"vaccine hesitancy" AND ("autism" OR "Wakefield"): 36 results

Figure 1. Change in Age-standardized prevalence rates of ASD between 1990 and 2019



Legend: Data source (1).

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