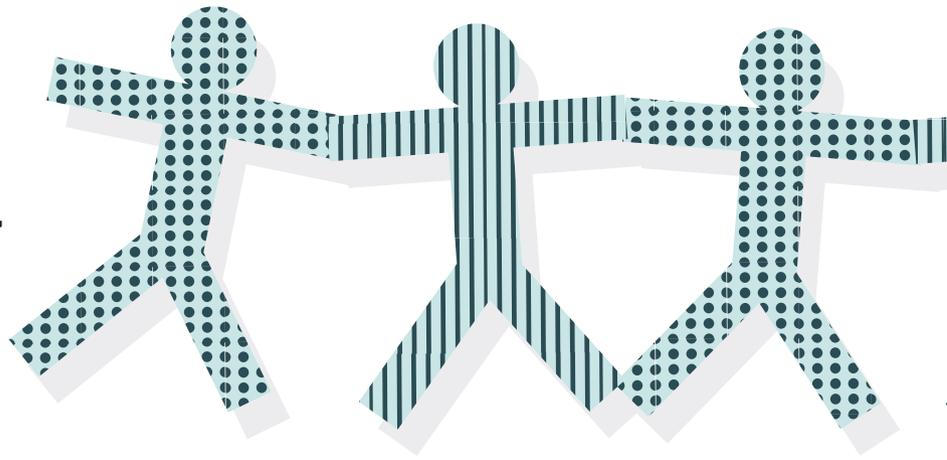


# Autism counts



Shifting diagnoses and heightened awareness explain only part of the apparent rise in autism. Scientists are struggling to explain the rest.

BY KAREN WEINTRAUB

**W**hen Leo Kanner first described autism in 1943, he based his observations on 11 children with severe communication problems, repetitive behaviours such as rocking and an acute lack of social interaction. The physician and psychiatrist at Johns Hopkins University in Baltimore, Maryland, predicted that there were probably many more cases than he or anyone else had noticed<sup>1</sup>. “These characteristics form a unique ‘syndrome’, not heretofore reported,” he wrote, “which seems to be rare enough, yet is probably more frequent than is indicated by the paucity of observed cases.”

Kanner’s prophecy has been more than fulfilled. An early study<sup>2</sup>, in 1966, examined eight- to ten-year-old schoolchildren in Middlesex, UK, and estimated a prevalence of 4.5 cases per 10,000 children. By 1992, 19 in every 10,000 six-year-old Americans were being diagnosed as autistic<sup>3</sup>.

Numbers skyrocketed in the first decade of the twenty-first century, according to data from the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. Surveying what is now known as autism spectrum disorder (ASD), the CDC found that by 2006, more than 90 in 10,000 eight-year-olds in the United States had autism<sup>4</sup>. Put another way, autism was now affecting 1 in every 110 children — a figure that strengthened public fears that an ‘epidemic’ was afoot (see ‘Diagnosis: rising’).

For the most part, research into autism’s prevalence had explained away the increase. Studies attributed it to greater awareness of

the condition, the wider diagnostic criteria for ASD, more frequent diagnosis of children with mental retardation as also having autism and diagnosis at younger ages. But by the mid-2000s, researchers started to note that these explanations were coming up short. “A true risk due to some, as yet to be identified, environmental risk factor cannot be ruled out”, read one study from 2005 (ref. 5).

That shift is important. If the rise in autism can be explained mainly by increased awareness, diagnosis and social factors, then the contributing environmental factors will always have been present — perhaps an ill-timed infection in pregnancy or some kind of nutritional deficit. If the increase can’t be explained away — and at least part of the rise is ‘real’ — then new factors must be causing it, and scientists urgently need to find them.

The subject is sensitive. Parents of children with autism agonize over whether they could have done something to prevent it. Researchers have been wary of invoking environmental triggers because that harkens back to a long-discarded idea that cold, unloving ‘refrigerator’ mothers were the source of their children’s problems. And the increase in prevalence has been used to support more recently debunked hypotheses such as the idea that vaccines cause autism.

Thomas Insel, director of the National Institute of Mental Health in Bethesda, Maryland, says it is time to get past these

legacies. “This whole idea of whether the prevalence is increasing is so contentious for autism, but not for asthma, type 1 diabetes, food allergies — lots of other areas where people kind of accept the fact that there are more kids affected.” To him, it is clear that there is a real increase in autism, and researchers need more funding and encouragement to look at possible environmental causes. During the past decade, the US federal government has spent about US\$1 billion researching the genetics of autism and only about \$40 million on studies of possible environmental factors.

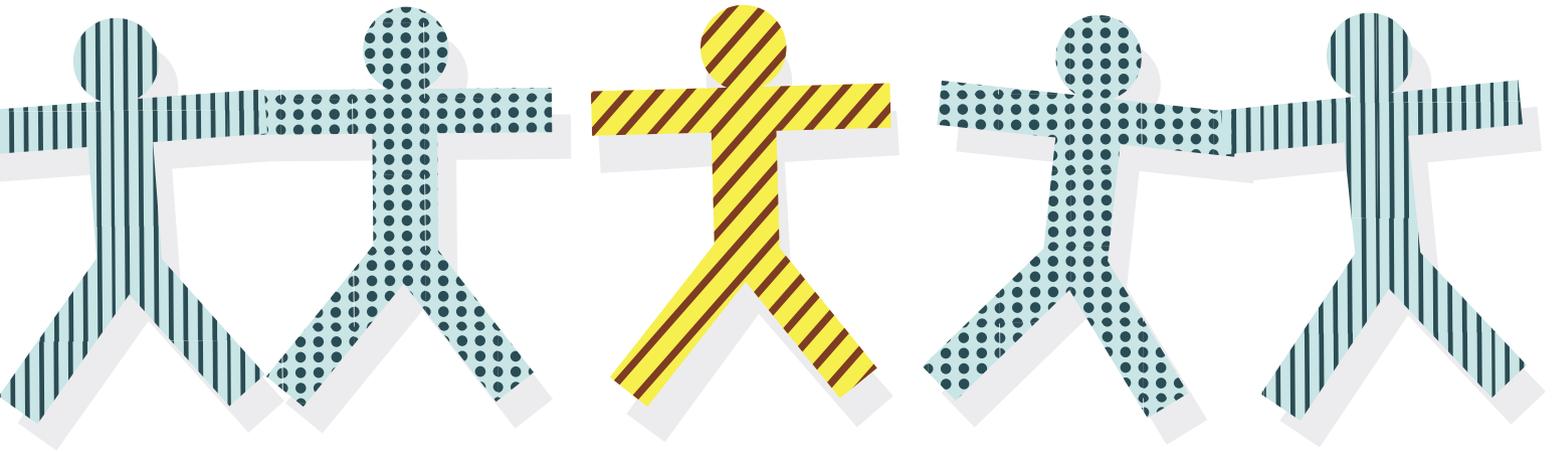
Not everyone agrees with Insel’s assessment. Some argue that the current data aren’t strong enough to say for certain that the increase in autism diagnoses represents a true change in its prevalence. “It feels like the numbers are going up. It really does,” says Richard Grinker, an anthropologist at George Washington University in Washington DC. But “when I look at the science, that doesn’t stand up”, he says. “You simply can’t take prevalence estimates of autism as if they are the kind of hard scientific evidence that you would get from mapping out the increase in a virus.”

## CHANGING CRITERIA

No one knows for sure what causes autism, although genes and environment both seem to be involved. The brain’s white matter may grow too fast in the first two years of life, leaving its networks jumbled. Synapses, the junctions between neurons, might not be functioning normally. Or other physiological processes could be involved: autism has



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been variously linked to epilepsy, digestive problems, immune or hormonal dysfunction, mitochondrial function and more.

The diagnostic criteria for autism have changed over time. In 1952, autism defined by Kanner's narrow description was diagnosed as 'early-onset schizophrenia'; it was renamed 'infantile autism' in 1980 and then 'autism disorder' in 1987. In the past decade, the common name autism has covered a wider range of behavioural, communication and social disorders also referred to by the umbrella term ASD, which includes autistic disorder, Asperger's syndrome and other related conditions.

Diagnoses of autism are also subjective. Social skills vary widely in the general population, as do other behaviours associated with autism. When does lack of spontaneity or an inability to make eye contact become a problem worthy of a medical label? And the frequency of diagnosis often reflects how eager parents are to receive one. When there's a stigma attached, diagnoses are likely to fall; when public support rises, so will cases.

A diagnosis is mutable, says Grinker. "It is a framework for a set of symptoms. And it's a framework that works at a particular point in time with a certain society and a certain health-care system and education system, and that will change as society changes."

Such considerations help to explain the startlingly high prevalence of autism that Grinker found in South Korea in a study published this year<sup>6</sup>. In the 1980s, he had found Korean families generally unwilling to admit that anything might be wrong with their children, because of the stigma attached<sup>7</sup>. But when he undertook the latest study, attitudes had changed. Families in Ilsan, a stable, residential community on the outskirts of Seoul, welcomed information about autism, which in this study was offered confidentially. His team screened more than 55,000 children born between 1993 and 1999, and came up with an estimated prevalence for ASD of 1 in 38 (ref. 6). Grinker says that this is perhaps an

overestimate, but it's the best his team could produce.

Current US prevalence figures for autism are likely to be too low, Grinker says, because they don't look at the entire population. Many US studies are based on diagnosed cases of autism, either in the California school district — the nation's largest — or in the CDC's Autism and Developmental Disabilities Monitoring Network. But the California data count only children old enough to be in school and disabled enough to get a diagnosis or need services. The CDC surveillance also only picks up children with a documented developmental disorder. These methods probably miss children at the milder end of the spectrum.

Some research suggests that the prevalence has always been high. In a study published this year<sup>8</sup>, a team led by Terry Brugha, a psychiatrist at the University of Leicester, UK,

counting cases of autism in the 1970s. He found a prevalence of autism of 0.7% among seven-year-old Swedish children in 1983 (ref. 9) and 1% in 1999 (ref. 10). "I've always felt that this hype about it being an epidemic is not really very likely," he says.

#### FILLING THE GAP

Nevertheless, with numbers rising fast, many expect to see some sort of smoking gun in the environment. Peter Bearman, a sociologist at Columbia University in New York, has been trying to figure out how much of the increase is driven by social forces. He analysed nearly 5 million California birth records and 20,000 records from the state's department of developmental services. By linking birth with detailed diagnostic data he was able to generate a rich picture of the demographics and life history of those with autism, which yielded clues to the social factors that influence diagnosis.

*"This whole idea of whether the prevalence is increasing is so contentious for autism."*

looked into autism's past by counting adults with the disorder. His team knocked on more than 7,000 doors across England. And although Brugha expected to uncover a very low prevalence of autism in adults, he and his colleagues calculated it as 9.8 in 1,000 — close to the frequency found in US children.

Brugha says that the research needs to be repeated in different groups, but the implication is that autism prevalence is stable. "If this is confirmed in other studies, it means we should also be looking for causes of autism that have always been there, and not just for causes that have developed in recent years or decades," he says.

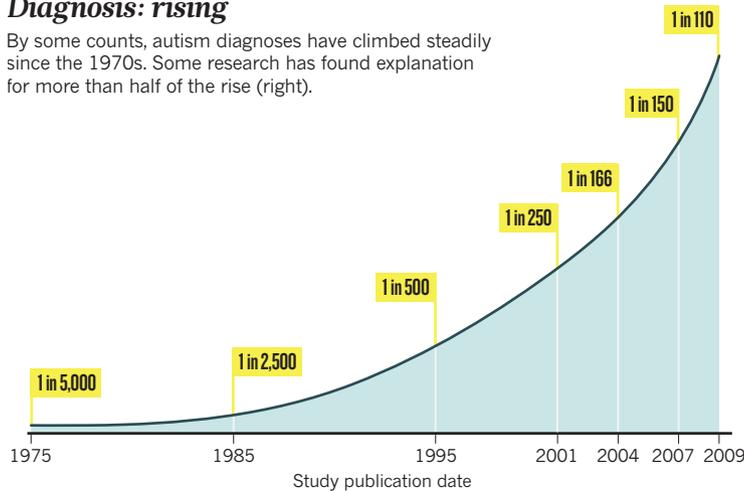
Christopher Gillberg, who studies child and adolescent psychiatry at the University of Gothenburg in Sweden, has been finding much the same thing since he first started

So far, Bearman says, he can account for just more than 50% of the observed increase (see 'Reasons: unclear'). Around 25% of the rise in autism over the past two decades can be attributed to what he calls "diagnostic accretion". He could see from the medical records that some children who would have been diagnosed as mentally retarded a decade ago are now given a diagnosis of both mental retardation and autism<sup>11</sup>. Another 15% can be accounted for by the growing awareness of autism — more parents and paediatricians know about it<sup>12</sup>.

Geographic clustering accounts for 4%, Bearman says. The most fascinating cluster lies in and around the hills of Hollywood, California. Children living in a 900-square-kilometre area centred on West Hollywood are four times more likely to be diagnosed with autism than are those living elsewhere

## Diagnosis: rising

By some counts, autism diagnoses have climbed steadily since the 1970s. Some research has found explanation for more than half of the rise (right).



in the state<sup>12</sup>. Some residents worried that something in the water was triggering autism — perhaps the legacy of a 1959 nuclear accident at the Santa Susana Field Laboratory in nearby Simi Valley — but Hollywood shares its water supply with Los Angeles, where autism rates are not uniformly high. Moreover, rates are high whether families have lived in Hollywood for years or have just moved there, Bearman says.

He suspects that the real reason for the cluster has to do with neighbourliness: a parent explains to a neighbour over the back fence where to find help and how to navigate the medical and educational systems. Once a cluster of informed, involved parents builds up, specialists are more likely to settle in that

**“If it is an environmental cause contributing to an increase, we certainly want to find it.”**

area, diagnosing and treating even more kids, Bearman says.

Another 10% of the increase may be explained by a social change with biological implications: people having children when they are older. Some research has found that children born to parents older than 35 have a higher risk of being diagnosed with autism. Studies are divided about whether the mother’s age or the father’s has the strongest influence, but Bearman’s work on parents older than 40 suggests that the mother’s age matters more<sup>13</sup>.

The fact that he still cannot explain 46% of the increase in autism doesn’t mean that this ‘extra’ must be caused by new environmental pollutants, Bearman says. He just hasn’t come up with a solid explanation yet. “There are lots of things that could be driving that in addition to the things we’ve identified,” he says.

But many researchers now say that at least part of the rise in autism is real and caused by

something in the environment. Rather than quibbling over recents they are focusing on finding the causes.

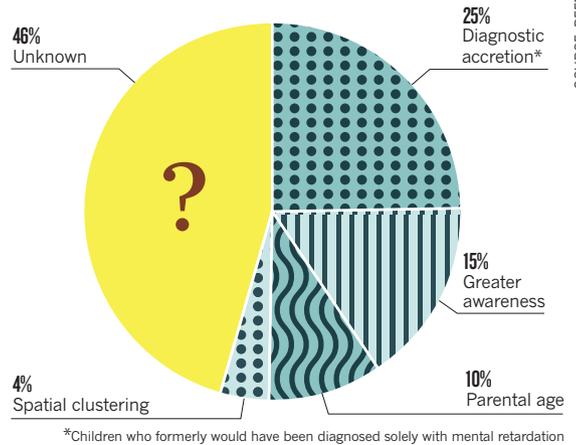
Since autism was first identified, ideas about its cause have swung to and fro between nature and nurture. The early focus on ‘refrigerator’ mothers resulted in a backlash and a stronger focus on genetics. The pendulum now seems to have settled somewhere in the middle, which is where many think it should be. “The bulk of the autism research that’s occurred has only looked at genetics,” says Lisa Croen, director of the autism research programme at the health-insurance provider Kaiser Permanente, in Oakland, California. “We’ve learned a lot but we haven’t found the magic bullet. I think that’s because part of the

picture has been missing.”

Several major federally funded trials, together with other smaller ones, are now under way in the United States and elsewhere to try to fish out what makes a child autistic. They are hoping to uncover unknown risk factors and markers for autism by monitoring environmental exposures and taking regular biological samples from children and their parents.

In 2007, for example, the Study to Explore Early Development (SEED), under the auspices of the CDC, began recruiting about 2,700 children aged two to five. The study includes developmental evaluations, questionnaires, a review of medical records and analysis of blood, cheek-cell and hair samples to examine genetic make-up and exposures to environmental chemicals. The Early Autism Risk Longitudinal Investigation (EARLI), funded by the National Institutes of Health, is enrolling up to 1,200 families that have a

## Reasons: unclear



child with autism and are preparing to have another baby. The study intends to look for any interplay between environmental factors and genetic susceptibility that might contribute to autism risk in their next child.

“These studies are really going to fundamentally change the landscape,” says Croen, who is a lead investigator on SEED. She and others expect a dramatic improvement in the understanding of autism and its prevalence over the next five to ten years.

Craig Newschaffer, an epidemiologist at Drexel University in Philadelphia, Pennsylvania and an investigator with EARLI, says that a focus on the rise in diagnoses may be less important than figuring out what is causing autism in the first place. “If it is an environmental cause that’s contributing to an increase,” he says, “we certainly want to find it.” It may be time to move on from the question of whether or not autism is truly rising, “I think it’s probably a nearly intractable question to answer.” ■

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