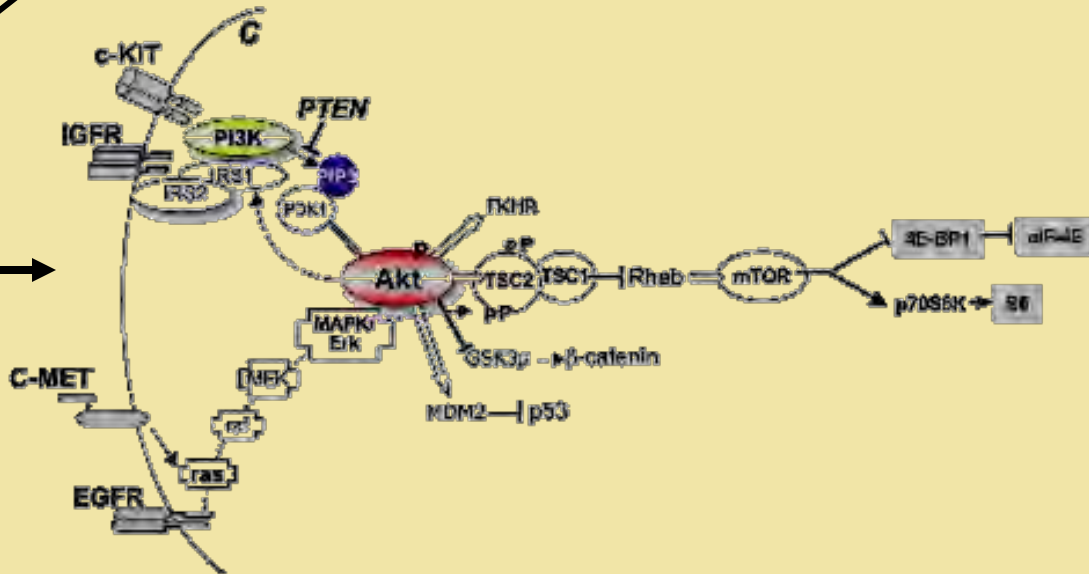


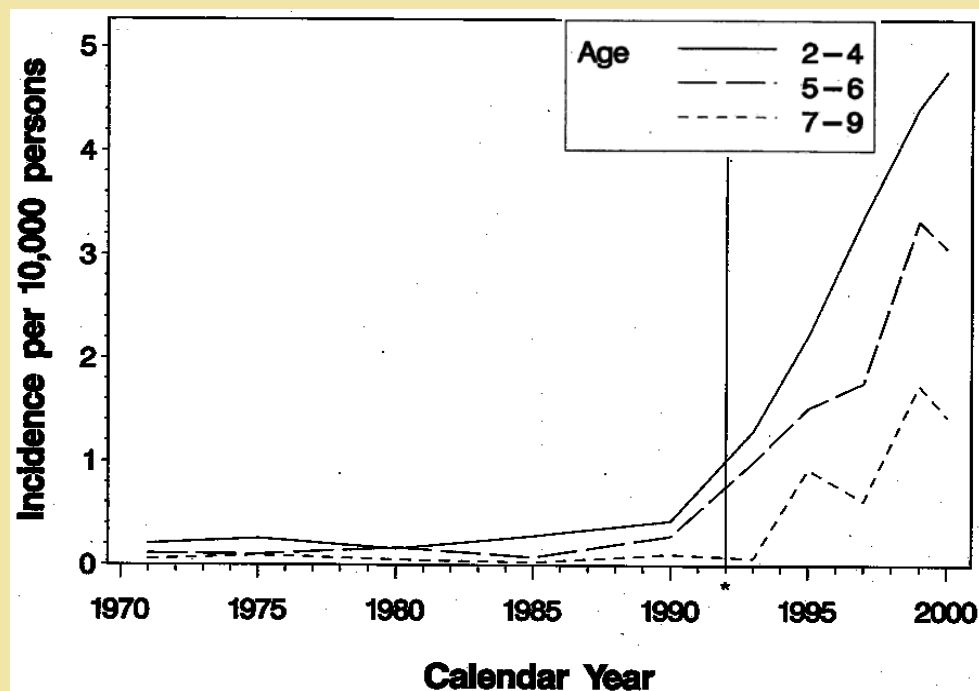
Is there a case for extending the analysis of vaccine additives as risk factors for autism spectrum disorders?

Developmental regulation
Cell-extrinsic signaling molecules
Genetics
Toxicants
Physiological Stressors

Redox/Fyn
/c-Cbl
pathway



Madsen *et al.*: There “was no trend toward an increase in the incidence of autism during that period when thimerosal was used in Denmark, up through 1990. From 1991 until 2000 the incidence increased and continued to rise after the removal of thimerosal from vaccines, including increases among children born after the discontinuation of thimerosal.”

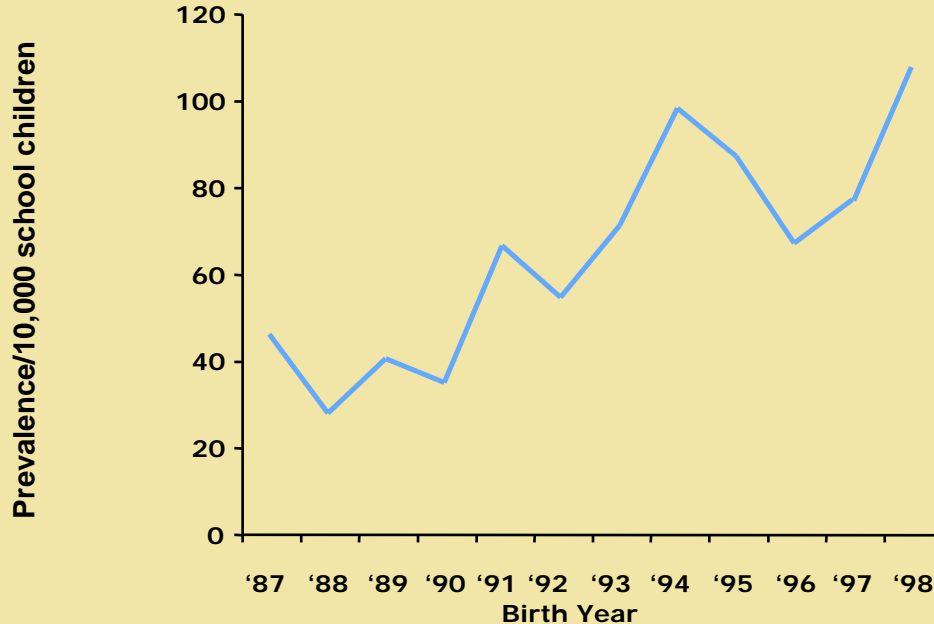


There have been major changes in diagnosis of ASD, increased public awareness of ASD, increased social services for children with ASD and earlier ages of diagnosis for these children.

Fombonne et al:

“On average, the prevalence rate increased by 10% annually over the 12 years of the study”

“A statistically significant linear increase in pervasive developmental disorder prevalence was noted during the study period”.



Calculating the contribution of non-biological factors to increases in ASD prevalence

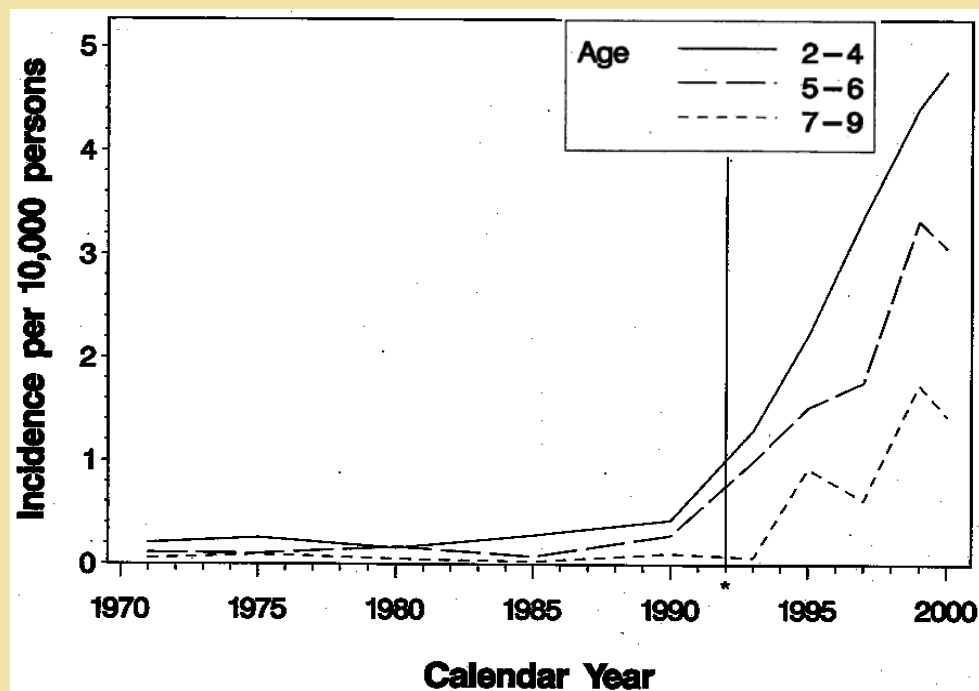
Method 1: Assume it's not biological. Value = 3.4

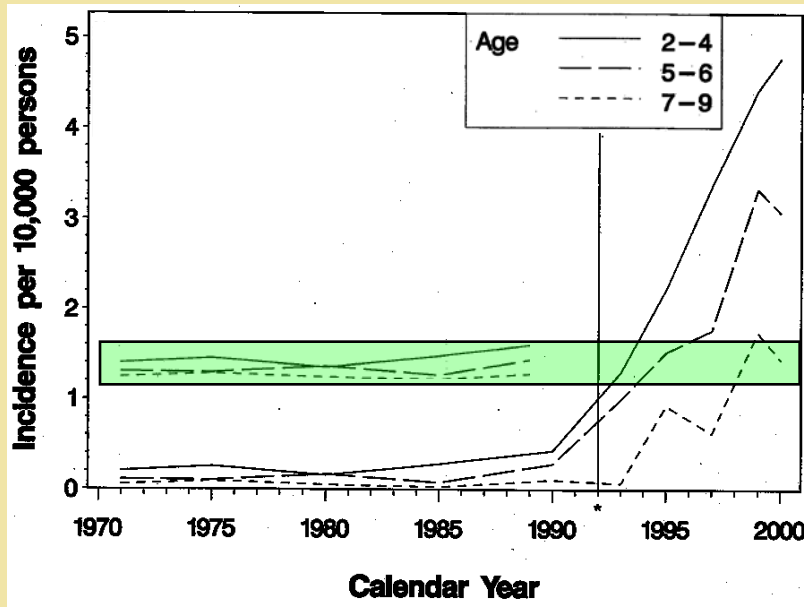
Method 2: See if mental retardation and language disorders went down while ASD went up. Value = 5.2

Method 3: Re-analyze medical records from earlier cohorts to ask how many children who were diagnosed with something else would now be diagnosed with ASD. Value = 8.4

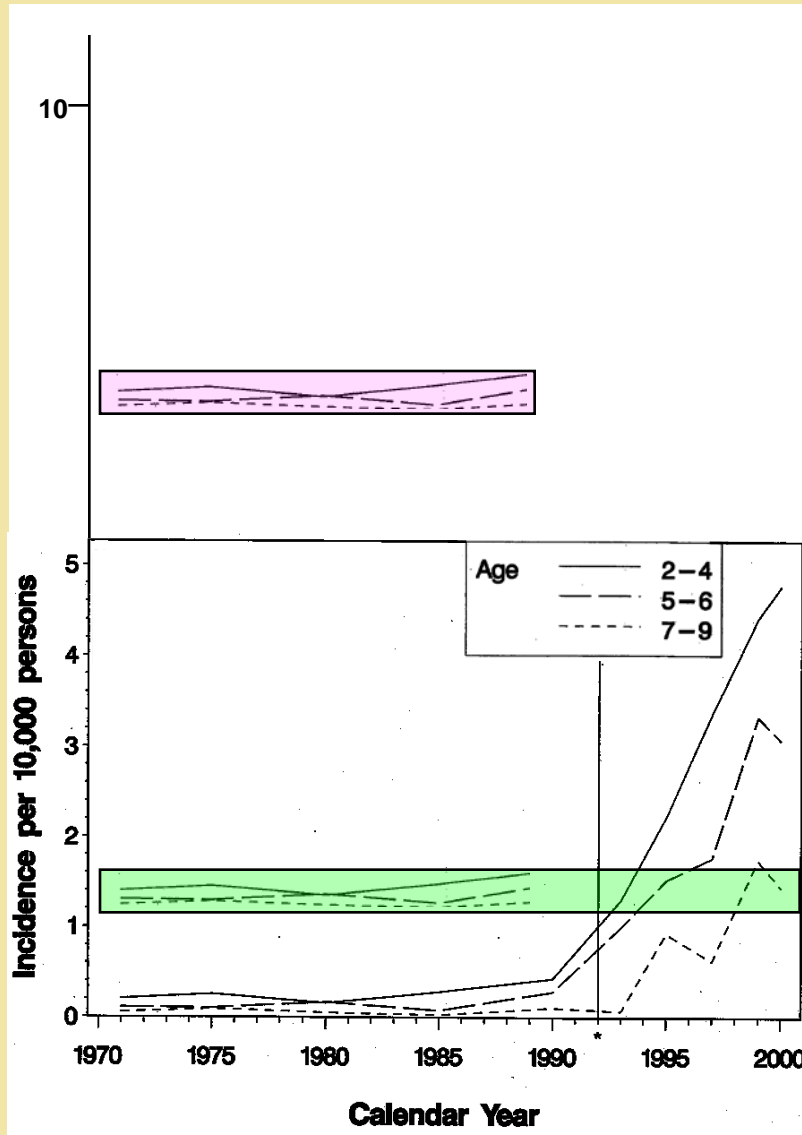
Method 4: Do a meta-analysis of the studies of others. Range = 2.1 - 28.8, with different values for different age groups

Madsen *et al.*: There “was no trend toward an increase in the incidence of autism during that period when thimerosal was used in Denmark, up through 1990. From 1991 until 2000 the incidence increased and continued to rise after the removal of thimerosal from vaccines, including increases among children born after the discontinuation of thimerosal.”





Values corrected for effect of changes in diagnostic criteria; correction factor = 5.2



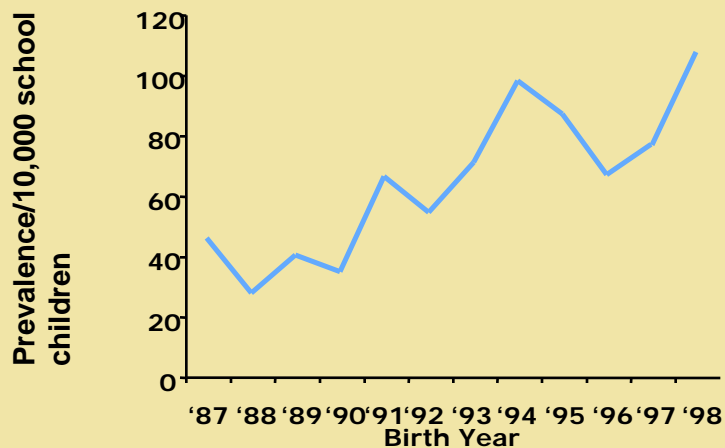
Values corrected for addition of outpatients to total data sample beginning in 1995

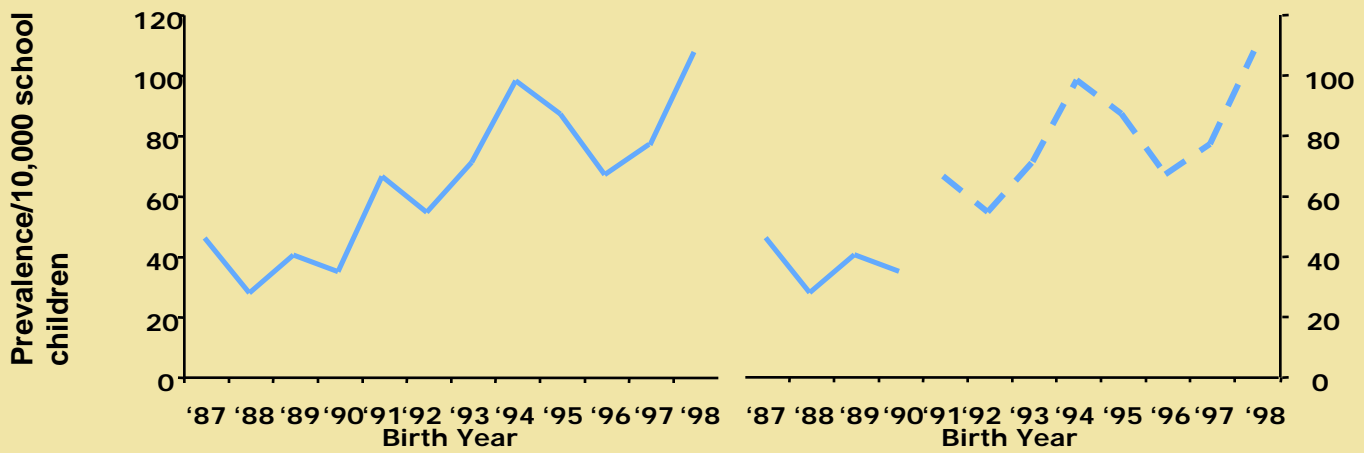
Values corrected for effect of changes in diagnostic criteria; correction factor = 5.2

Fombonne et al:

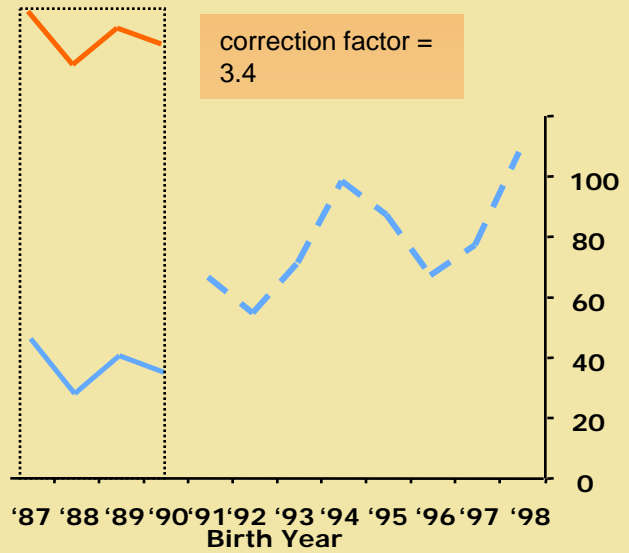
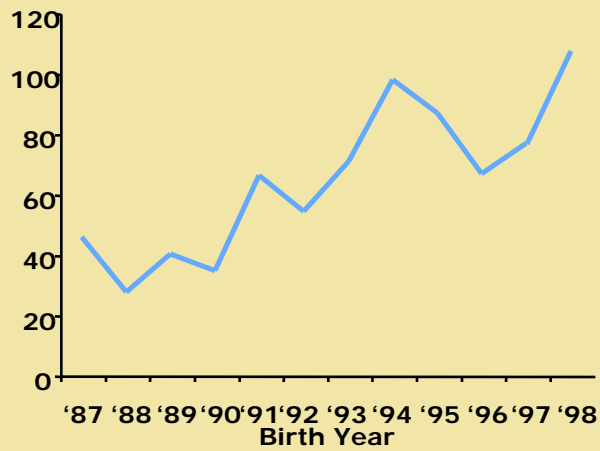
“On average, the prevalence rate increased by 10% annually over the 12 years of the study”

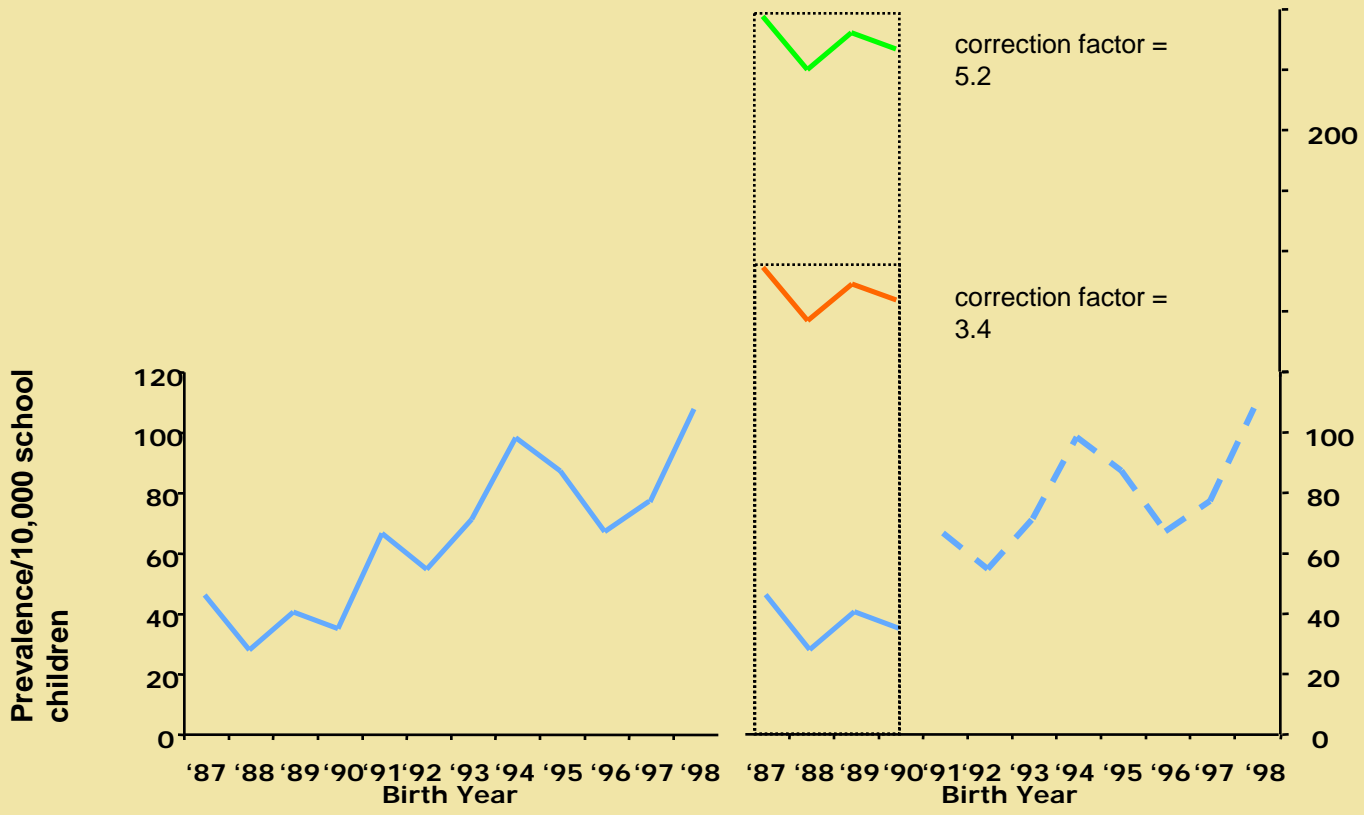
“A statistically significant linear increase in pervasive developmental disorder prevalence was noted during the study period”.

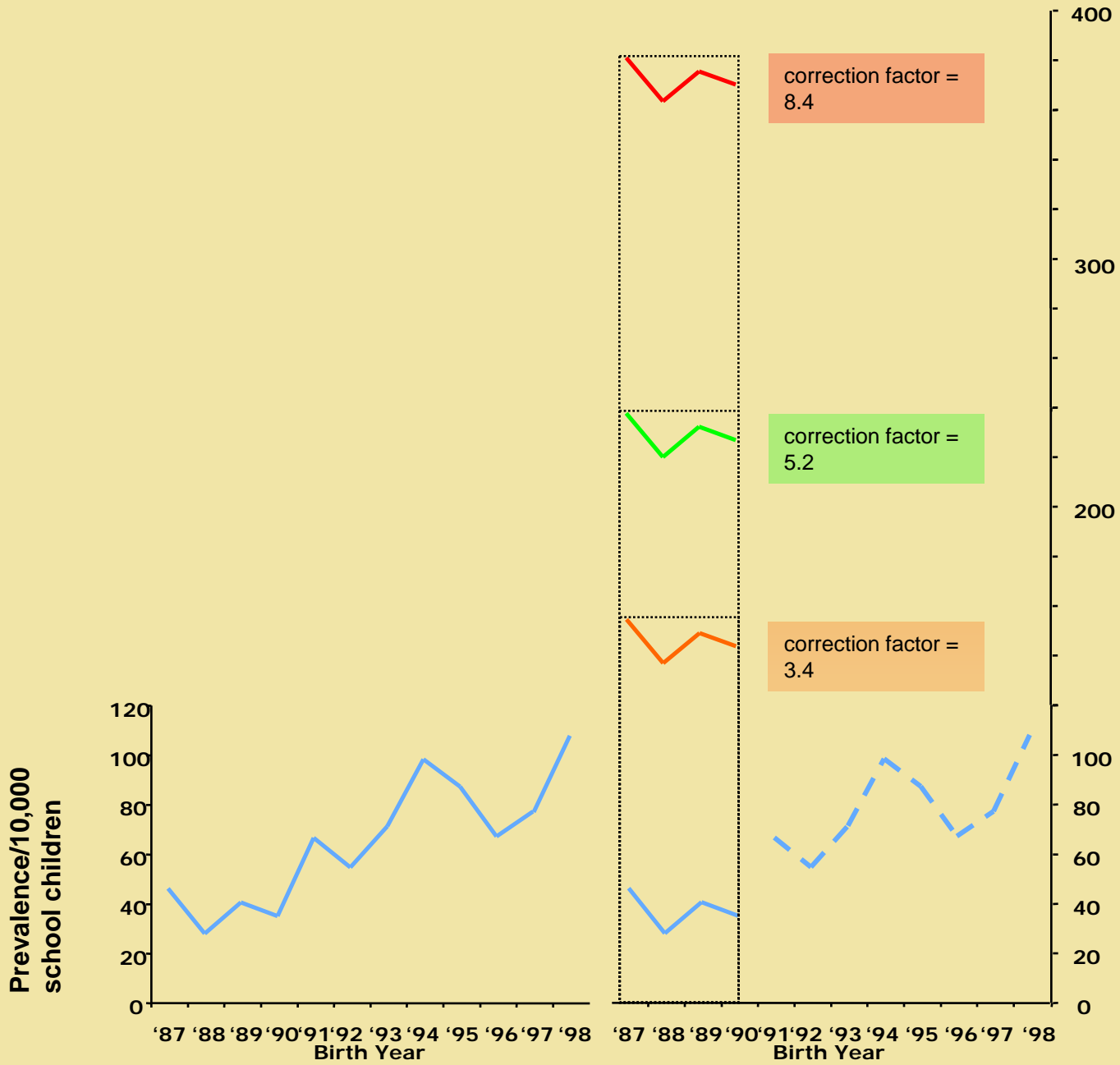


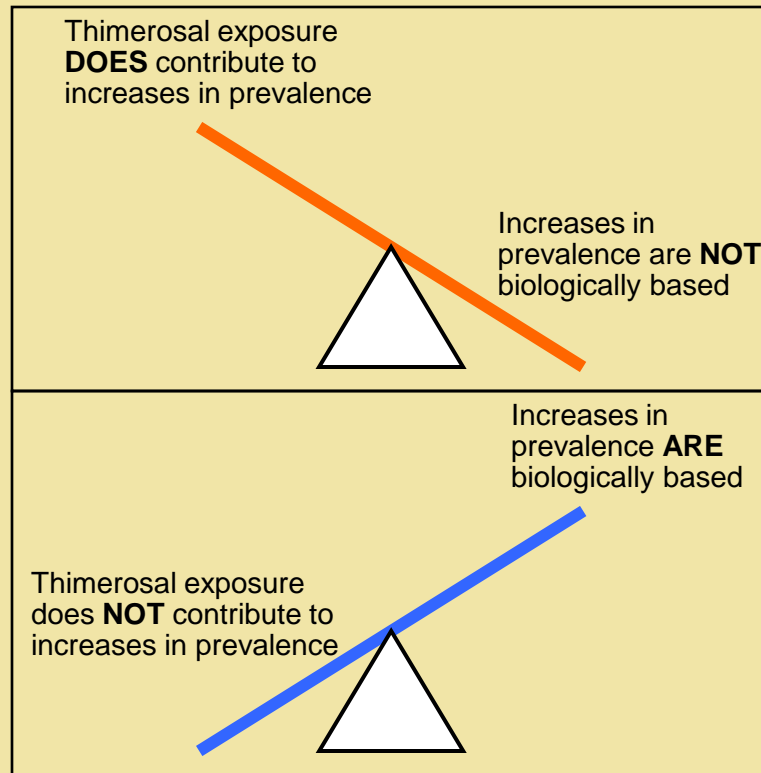


Prevalence/10,000 school children









Arguments that the primary causes for increases in ASD prevalence are not biological in nature and that thimerosal is safe are quantitatively incompatible. Arguments that increases in autism/ASD prevalence do not represent a true biological increase requires application of correction factors to data analysis that increase the magnitude of the contributions of thimerosal exposure to ASD pathogenesis. Conversely, if the increases in ASD prevalence are claimed to be primarily biological in origin, then support for the hypothesis that thimerosal exposure is relevant to understanding pathogenesis of these syndromes becomes weaker.

Andrews et al: General Practice Research Database in the UK from the years 1988-1997, and using the number of vaccinations with diphtheria-tetanus-whole-cell pertussis (DTP) vaccine or diphtheria-tetanus (DT) vaccine as an indicator of thimerosal exposure.

Conclusions: "With the possible exception of tics, there was no evidence of an increased risk of various neurodevelopmental disorders with increasing thimerosal exposure at a young age via DTP/DT vaccination in the United Kingdom. For general developmental disorders, unspecified developmental delay, and ADD, there was an apparent protective effect from increasing thimerosal exposure."

Validation for the data analyzed: 162 of 166 cases queried, and 19% of diagnoses could not be confirmed.

For those with a confirmed diagnosis, 39% were considered to be transient problems (which is not a description that would normally be applied to autism) and the duration of the problem could not be determined for an additional 35% of cases.

Only 26% of the validation attempts established that problems were long-term in children with a confirmed diagnosis (i.e., 100% of the confirmed diagnoses - [39% + 35%]). As the group of children with a confirmed diagnosis only represented 79% of the attempted validation sample, this would mean that only 20.5% of children in the attempted validation sample were confirmed as having long-term problems (i.e., $.79 \times .26$).

The authors provide no information that allows the reader to determine the specific subgroups to which this 20.5% figure pertains (with the sole exception of tics).

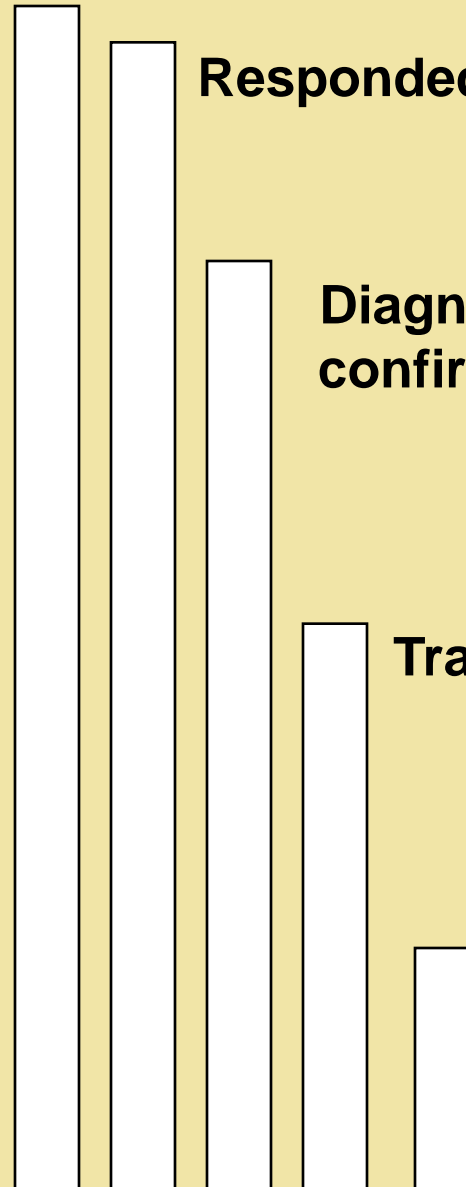
Queried

Responded

Diagnosis confirmed

Transient problems removed

Confirmed continued problems



Conclusions

The safety of thimerosal has not been proven.

As we know more about thimerosal than about, e.g., aluminum salts, we should not draw conclusions that exceed the data about other vaccine-related questions.