GENERATION ZERO

Thomas Verstraeten's First Analyses of the Link Between Vaccine Mercury Exposure and the Risk of Diagnosis of Selected Neuro-Developmental Disorders Based on Data from the Vaccine Safety Datalink: November-December 1999

Safe Minds

November 2004

“THIMEROSAL ANALYSIS”

From: Verstraeten, Thomas

Sent: Monday, November 29, 1999 11:45 AM

To: ‘Robert Davis’

Cc: ‘Frank Destefano’

Subject: Thimerosal analysis

Hi Bob,

After running, re-thinking, re-running, re-thinking….for about two weeks now I should touch base with you, I think, to see whether you can agree with what I came up with so far. I’ll attach the SAS programs hoping you or one of your statisticians can detect major flaws before I jump to conclusions. I’ll try to structure my findings….

Thomas Verstraeten, M.D.

SUMMARY (I)

Between February 2000 and November 2003 Thomas Verstraeten and his supervisors at the National Immunization Program produced four separate generations of an analysis designed to assess the impact of vaccine mercury exposures on neuro-developmental disorders in children. With each generation, elevated and statistically significant risks were reduced and/or eliminated.

But before these four generations of report were produced, Verstraeten conducted an earlier analysis of these issues in November and December of 1999. He never prepared a formal report on this work, but statistical tables obtained by Safe Minds in a FOIA request (and not previously analyzed) demonstrate large and statistically significant mercury exposure effects that in many cases exceeded the findings of the later reports.

These "Generation Zero" analyses followed a straightforward methodology that was relatively unaffected by biases applied later and was considerably more sensitive with respect to detecting mercury exposure effects than the later reports.

- **Most notably, these initial analyses compared disease risk in the *highest exposure* population groups to disease risk in *zero exposure* population groups.**
- **In addition, the target study population had not yet been subject to numerous exclusions and adjustments applied later, the cumulative effect of which was to reduce the reported impact of mercury exposure on children's health outcomes.**

SUMMARY (II)

The results of the Generation Zero analyses are striking and more supportive of a causal relationship between vaccine mercury exposure and childhood developmental disorders (especially autism) than any of the results reported later

- **Relative risks of autism, ADD, sleep disorders and speech/language delay were consistently elevated relative to other disorders and frequently significant. Disease risk for the high exposure groups ranged from lows of 1.5X-2 times to as high as 11 times the disease risk of the zero exposure group.**
- **Many other outcomes showed no consistent effect, while a few appeared to show a protective effect from vaccine mercury exposure (most likely children with these diagnoses were immunized later).**
- **The strongest effect was for the highest levels of mercury exposure at the earliest time of exposure, consistent with the idea that infant brain development is most sensitive to the earliest exposures.**
- **The elevated risk of autism for the highest exposure levels at one month ranged from 7.6 to 11.4 times the zero exposure level. This increased risk level corresponds to the tenfold increase in autism rates seen since vaccine mercury exposures increase starting in 1990.**

The difference in these results from the later reports reveal a number of methodological choices that may have been powerful sources of bias in later publications, including

- **the exclusion of children with less than two polio vaccines: these children would have been most reliably in the zero exposure group, whereas children with two polio vaccines with low reported mercury exposure would be more likely to have exposure reporting errors.**
- **the elimination of zero exposure categories in general as the referent category for risk assessment as well as the reduction in the measured exposure in the highest category: the smaller the spread between high and low exposures, the more an exposure effect is diluted.**

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OVERVIEW OF THE GENERATION ZERO ANALYSES (I)

Verstaeten's specific findings revolved around an analysis of a set of distinct ICD 9 diagnosis codes, several with related subordinate codes. These codes covered a range of developmental disorders (presumably selected by Verstraeten) that might plausibly be connected to developmental mercury damage.

Verstraeten appeared to run two separate analyses, one reported in late November and another (with a more narrowly chosen subset of disorders) a few weeks later in mid December. The statistical outcomes were broadly similar in these two different data runs, but there are several inconsistencies that have no clear explanation (most notably in ADD/ADHD and "coordination disorders").

Each analysis provided a calculation of the relative risk of disease at one and three months of age. Using a referent exposure level of zero mcg of mercury, each set of calculations showed the relative risk of disease based on mercury exposures above the EPA limit and to three or four exposure levels as compared to zero exposure. The population groups spanned a range of exposure levels

- **at one month, from 0 mcg to exposures >25 mcg**
- **at three months, from 0 mcg to exposures >=75 mcg**

OVERVIEW OF THE GENERATION ZERO ANALYSES (II)

Diagnoses with elevated risks

399.0 Autism
307.0 Stammering
307.2 Tics
- ***307.20, tic disorder, unspecified***

307.4 Specific disorders of sleep of non-organic origin
- ***307.45, phase shift disruption of 24 hr. sleep-wake cycle***
- ***307.46, somnambulism or night terrors***

314.0 Attention deficit disorder
- ***314.00, ADD without mention of hyperactivity***
- ***314.01 ADD with hyperactivity***

315.3 Developmental speech or language disorder
- ***315.31, developmental language disorder***
- ***315.39, other developmental speech or language disorder***

315.4 Coordination disorder
583 Nephritis and nephropathy, not acute or chronic
- ***583.9 nephritis and nephropathy, with unspecified pathological lesion in kidney***

Diagnoses with no clear or reduced risks

307.5 Other and unspecified disorders of eating
- ***307.50, eating disorder, unspecified***

313 Disturbances of emotion specific to childhood
- ***313.1, misery and unhappiness disorder,***
- ***313.8, other or mixed emotional disturbances***
  - ***313.81 oppositional disorder***

315.8 Other specific delays in development
315.9 Unspecified delays in development
319 Unspecified mental retardation
331 Other cerebral degeneration
- ***331.4, obstructive hydrocephalus***

333 Other extrapyramidal disease
343 Infant cerebral palsy
345 Epilepsy
- ***345.1, generalized convulsive epilepsy***
- ***345.4, partial epilepsy, with impairment of consciousness***
- ***345.5, partial epilepsy, without mention of impairment of consciousness***
- ***345.9, epilepsy, unspecified***

348 Other conditions of brain
349.9 Unspecified disorders of nervous system

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KEY ATTRIBUTES OF THE NOVEMBER ANALYSIS

Compared relative risk of each diagnostic outcome due to multiple discrete levels of mercury exposure from vaccines, using the zero exposure level as the "referent", at one and three months of age

Not yet stratified for birth month, birth year, HMO site or "adjusted for gender"

Not yet restricted to exclude several large population groups, so groups later excluded from the study group remained in the sample, including

- **children receiving hepatitis B immunoglobulin**
- **children receiving less than 2 polio vaccines**
- **children outside the two primary HMOs**

NOVEMBER ANALYSIS: ONE MONTH FINDINGS

At the highest level of exposure, >25 mcg, the increased relative risk due to mercury exposure is strikingly high for several, but not all, disorders

High mercury exposure levels at one month required an unusual pattern of exposure, for example

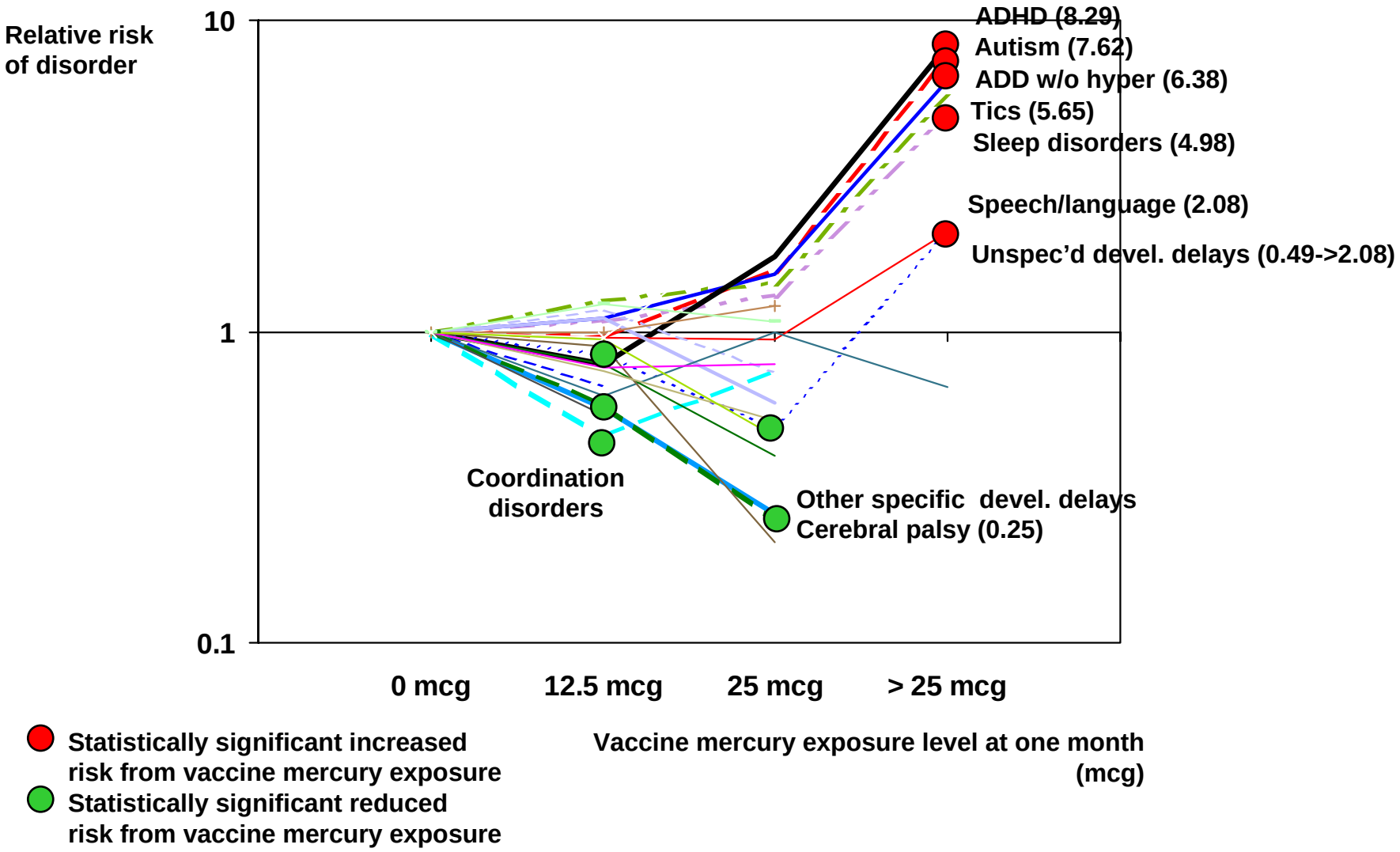
- **First DPT/DTaP or Hib given ahead of schedule**
- **Hepatitis b immunoglobulin exposure**

ADHD risks were the highest, with a reported relative risk for the group with >25 mcg exposure at 8 times the zero exposure group, followed by autism, ADD (without hyperactivity), tics, sleep disorders and speech language disorders

Cerebral palsy cases showed a reduced risk for mercury exposure, suggesting these cases were either less likely to receive vaccinations on schedule or (less probable) that the hepatitis B vaccine is protective against cerebral palsy

Most measured disorders displayed no association at all with vaccine mercury exposure. These results suggest there is no inherent bias in Verstraeten's method or sample that produced an elevated risk of disease.

AT ONE MONTH OF AGE, HIGH MERCURY EXPOSURES RESULTED IN ELEVATED RELATIVE RISKS FOR SEVERAL NEUROLOGICAL DISORDERS, INCLUDING AUTISM



NOVEMBER ANALYSIS: THREE MONTH FINDINGS

At the three month point, many risk levels remain elevated but only ADD and coordination disorders are significant

The strength of the result for coordination disorders is questionable, since the December analysis produced a sharply different and non-significant result for the same three month exposure gradient

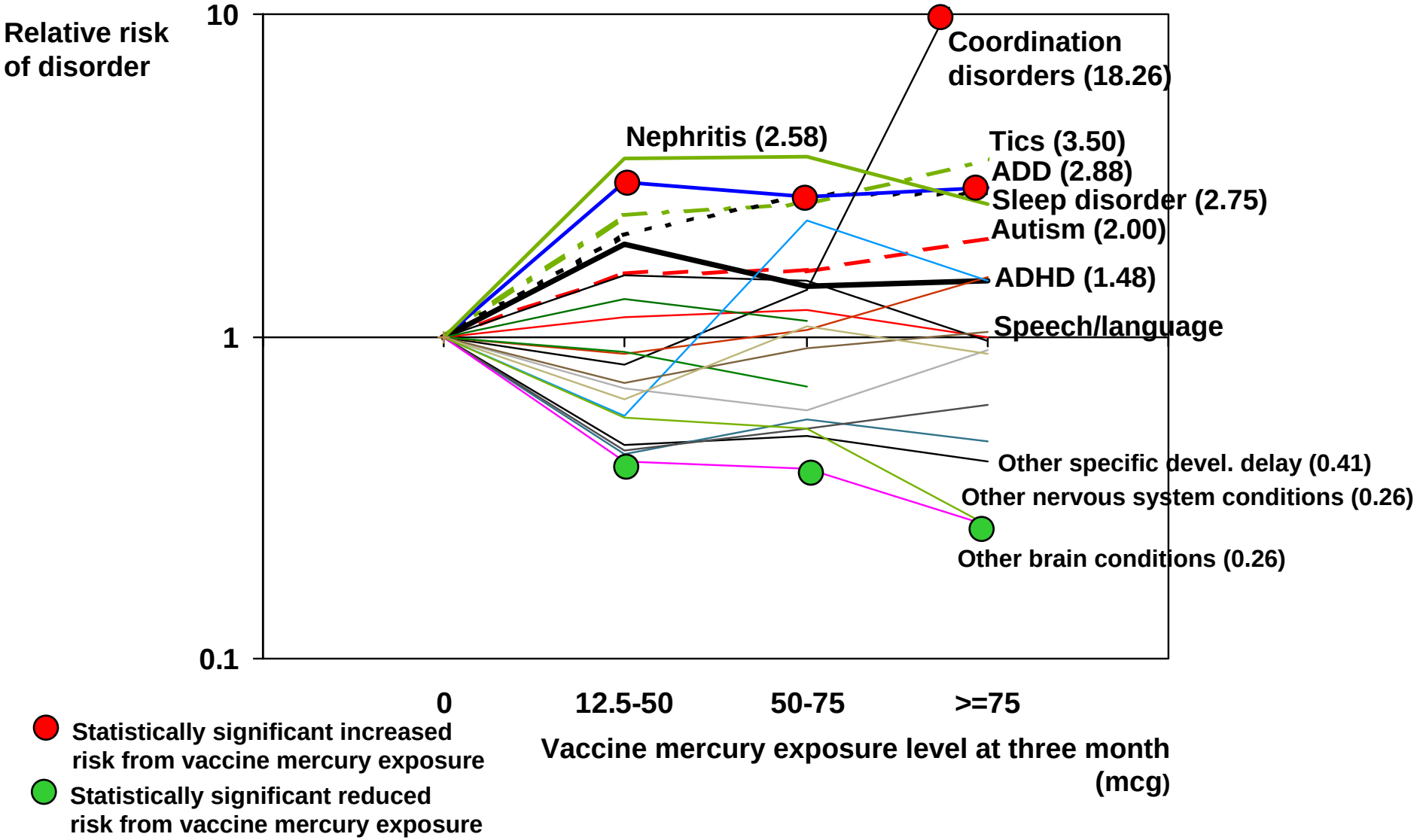
Nephritis and nephropathy, although not significant, showed elevated disease risk. Since kidney damage is a known primary effect of mercury exposure, this results is intuitive and potentially important.

Relative risks of autism, sleep disorders and tics all remain elevated, at over 2 times the risk in the zero exposure group.

Speech/language disorders (the most significant and durable of the Generations 1-4 findings) is not significant at all, raising an interesting question:

- **do the later study parameter on stop dates effectively shunt other diagnoses (e.g. autism) into this category?**

AT THREE MONTHS OF AGE, ELEVATED MERCURY EXPOSURE LEVELS WERE CORRELATED WITH INCREASED RISKS



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SUMMARY OF FINDINGS FROM THE DECEMBER SUMMARY REPORT

Verstraeten revised his analysis in unknown ways between his first run in November and his second in December. He focused his analysis on five specific disease categories. The general patterns remained the same with a few notable changes.

Autism risks were the highest of all the diagnostic codes, with a relative risk at one month of 11.35 between the high and zero exposure groups.

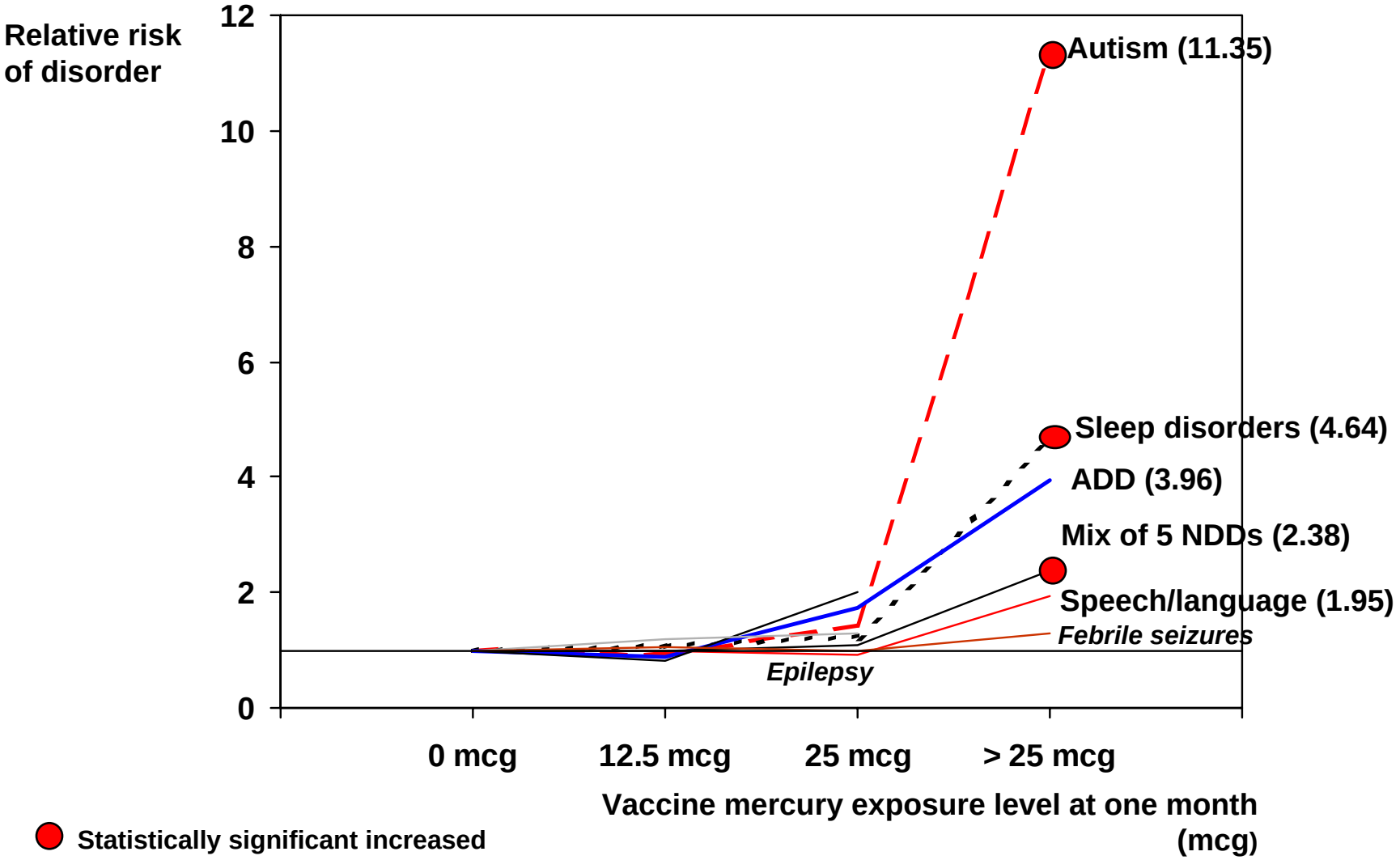
Sleep disorders remained significant at one month and ADD risks at three months, while both risks remained elevated in both periods at the highest exposure levels.

Speech language disorders were modestly elevated in both periods.

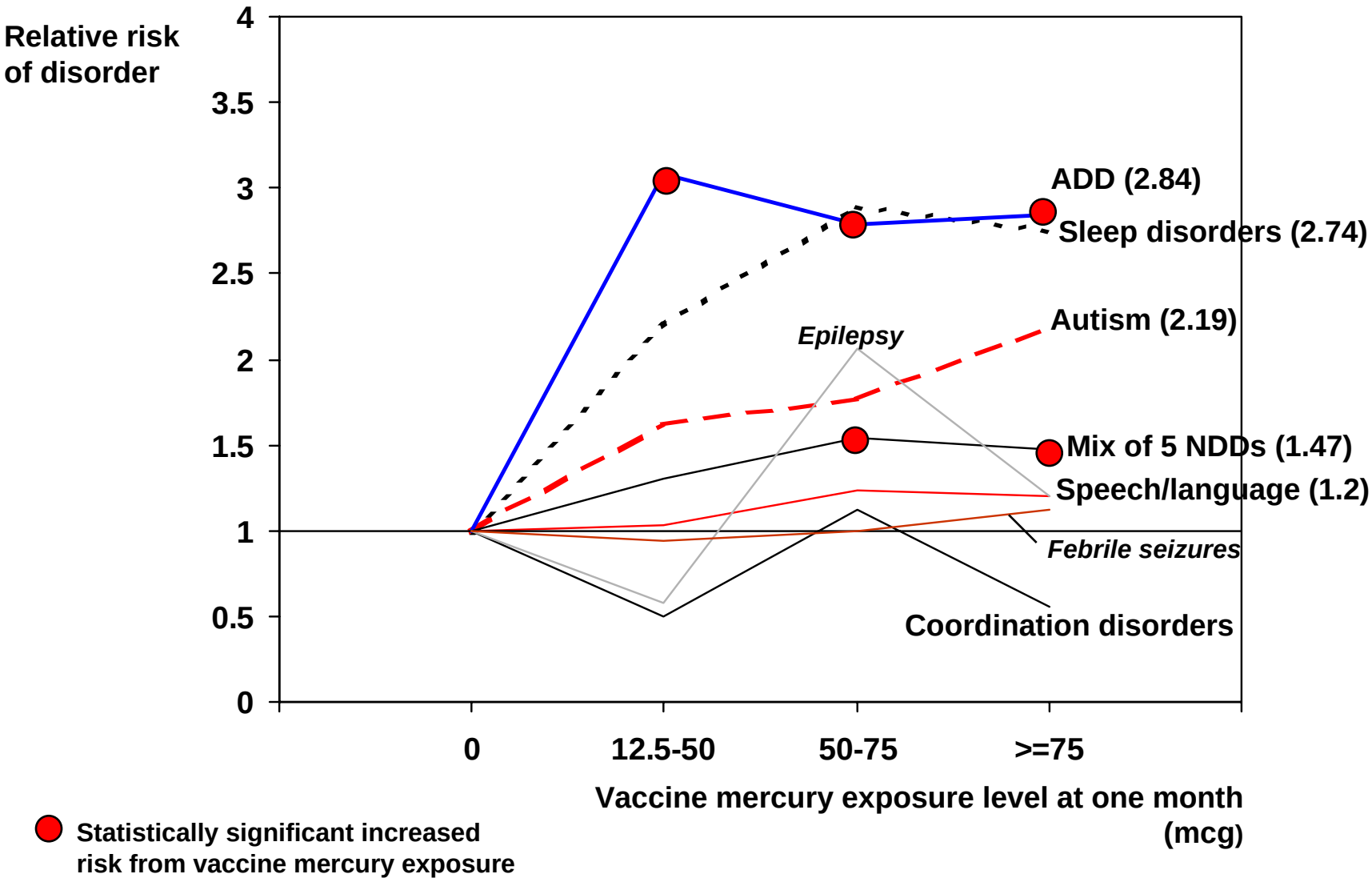
Two control diagnoses, epilepsy and febrile seizures, were not elevated in either period

Results for coordination disorders changed markedly from November (highly elevated and significant) to December (not significant, even reduced).

ONE MONTH EXPOSURE: SUMMARY ANALYSIS OF FIVE NDDs
Comparison to Control Diagnoses Epilepsy and Febrile Seizures



THREE MONTH EXPOSURE: SUMMARY ANALYSIS OF FIVE NDDs



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“IT JUST WON’T GO AWAY”

From: Verstraeten, Thomas

Sent: Friday, December 17, 1999 4:40 PM

To: ‘Robert Davis’

Cc: Destefano, Frank

Subject: It just won’t go away

Hi,

Attached please find four tables with RRs [relative risks] and three SAS programs…

As you’ll see, some of the RRs increase over the categories and I haven’t yet found an alternative explanation…Please let me know if you can think of one. Frank proposes we discuss this on a call after the New Year…

Happy Holidays!

Thomas Verstraeten, M.D.

RISING TO THE CHALLENGE AFTER THE HOLIDAYS: DAVIS ET AL DEVELOPED MANY WAYS TO MAKE IT GO AWAY

Eliminated assessments of risk in the highest exposure groups, lumping these populations in with lower exposure populations. This choice would mask the detection of any threshold effects that might kick in at the highest level.

Reduced the statistical power of the zero mercury exposure population in two ways

- **Fewer comparisons in the later analyses were based on a referent level of zero mercury exposure, many risk assessments bundled reported exposures up to 25 mcg with the true zero exposure group.**
- **All comparisons excluded children who did not receive 2 polio vaccines, thereby eliminating the children and families most likely to avoid vaccination on principle and increasing the likelihood that the recorded zero exposure group actually included children with missing records of other vaccinations (i.e. why would a child receive polio but not DTaP?)**

Introduced "stop dates", potentially diverting diagnoses like autism to earlier, less severe, diagnoses such as speech and language delays. Many children who receive an autism diagnosis receive other diagnoses along the way.

Reduce the size and diversity of the study population, eliminating all but two HMOs.

SELECTED DIAGNOSES COMPARING GENERATION ZERO TO GENERATION ONE RESULTS FROM FEBRUARY 2000

	Generation Zero 1999 analyses (relative risk)	Generation One 2/29/2000 report (relative risk)	Percent reduction
Autism (399.0)			
• 1 month	7.62/11.35	1.58	79-86%
• 3 month	2.00/2.19	2.48	12-19
Attention deficit disorder (314.0)			
• 1 month	3.76/3.96	2.14	43-46
• 3 month	2.88/2.84	2.45	14-15
Developmental speech delay (315.39)			
• 1 month	2.32	0.80	66
• 3 month	0.99	1.30	(31)
Sleep disorders (307.4)			
• 1 month	4.98/4.64	1.74	62-65
• 3 month	2.75/2.74	n.a.	n.a.
Low/high exposure level			
• 1 month	0 to >25 mcg	0 to >12.5 mcg	
• 3 month	0 to >=75 mcg	<37.6 to >62.5 mcg	

GENERATION ZERO FINDINGS REVEAL THE POTENTIAL FOR MANIPULATION OF COMPLEX EPIDEMIOLOGICAL ANALYSES

Any population based epidemiological analysis involves numerous subtle choices with respect to study design and reporting, including

- **inclusion criteria for the study population**
- **exposure measures and break points for reporting exposure**
- **criteria for identification of cases within separate diagnostic categories**
- **referent exposure levels for the purpose of relative risk calculations**
- **statistical models of risk (regression techniques, stratification and confounders, etc.), follow up time, quality of fit measures, etc.**

Supervisors of such population based studies therefore have wide discretion in the results they choose to report, depending on whether they are interested in reporting a positive or negative finding.

In their words and actions, Verstraeten and his supervisors demonstrated clear biases against reporting positive results and made numerous deliberate choices that took positive findings in a single direction, towards insignificance.

The pattern of behavior constitutes malfeasance and should not be permitted to stand. It is time to remove the parties involved from their role in vaccine safety assessment and to subject the VSD data base to open and independent review.