THE SCORCHED EARTH LANDSCAPE OF VACCINE SAFETY

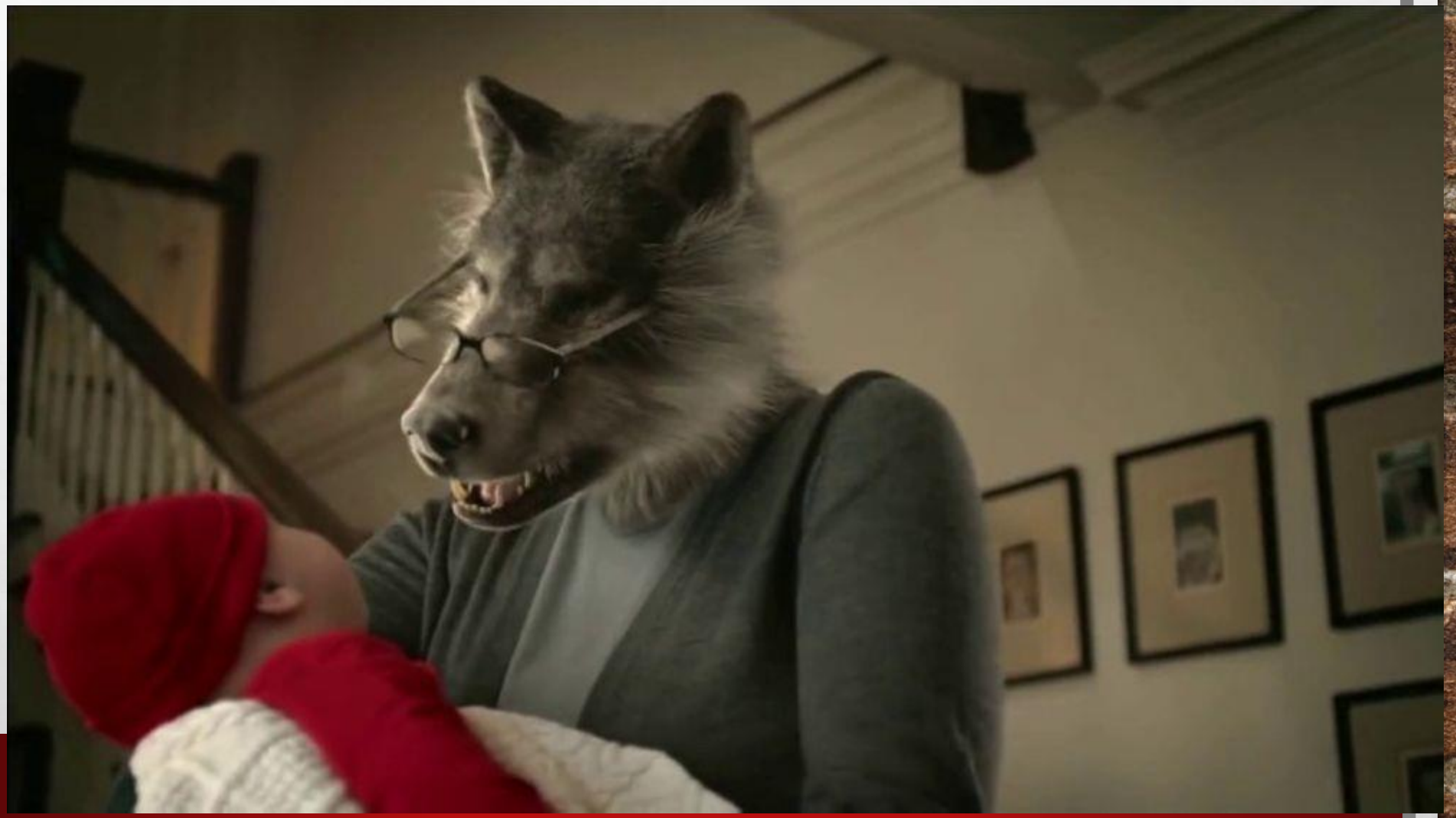
BRIAN S. HOOKER, PH.D., P.E.

SCIENCE ADVISOR

FOCUS FOR HEALTH

NOV. 16, 2019

THE FUROR



MEASLES OUTBREAK OF 2019

- STARTING IN EARLY 2019, THERE WERE THREE MAIN "CLUSTERS" OF MEASLES CASES IN THE U.S. IN ROCKLAND COUNTY, NY; CLARK COUNTY, WA AND BROOKLYN, NYC, NY.
- THE PHARMACEUTICAL INDUSTRIAL COMPLEX INCLUDING VACCINE MANUFACTURERS, THE HHS AND THE PRESS SOUGHT TO MAKE NON-VACCINATING AND EX-VACCINATING FAMILIES PUBLIC ENEMY #1
- THE FUROR REGARDING THESE MEASLES CASES HAS RESULTED IN MANY MANDATE BILLS, NEW MANDATES AND FINES FOR SIMPLY BEING UNVACCINATED WITH THE MMR VACCINE
- MERCK'S VACCINE SALES HAVE SOARED!
- CDC IS ACTIVELY OPPOSED TO STATE RELIGIOUS EXEMPTIONS AND PBES

THE DANGER OF MEASLES?

VIRAL IMMUNOLOGY

Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens

Michael J. Mina[1,2,3*†], Tomasz Kula[1,2], Yumei Leng[1], Mamie Li[2], Rory D. de Vries[4], Mikael Knip[5,6], Heli Siljander[5,6], Marian Rewers[7], David F. Choy[8], Mark S. Wilson[8], H. Benjamin Larman[9], Ashley N. Nelson[10‡], Diane E. Griffin[10], Rik L. de Swart[4], Stephen J. Elledge[1,2,11†]

Measles virus is directly responsible for more than 100,000 deaths yearly. Epidemiological studies have associated measles with increased morbidity and mortality for years after infection, but the reasons why are poorly understood. Measles virus infects immune cells, causing acute immune suppression. To identify and quantify long-term effects of measles on the immune system, we used VirScan, an assay that tracks antibodies to thousands of pathogen epitopes in blood. We studied 77 unvaccinated children before and 2 months after natural measles virus infection. Measles caused elimination of 11 to 73% of the antibody repertoire across individuals. Recovery of antibodies was detected after natural reexposure to pathogens. Notably, these immune system effects were not observed in infants vaccinated against MMR (measles, mumps, and rubella), but were confirmed in measles-infected macaques. The reduction

WHAT IS MINA ET AL. 2019 IMPLYING?

- UNVACCINATED INDIVIDUALS WHO CONTRACT MEASLES ARE UNPROTECTED AGAINST OTHER INFECTIOUS DISEASES
- MEASLES DISEASE CAUSES “IMMUNOLOGICAL AMNESIA”
- MEASLES VIRUS COULD HAVE CAUSED AS MUCH AS 50% OF ALL CHILDHOOD DEATHS DUE TO INFECTIOUS DISEASE IN THE “PRE-VACCINE ERA”

WHY DO MINA ET AL. 2019 MAKE CLAIMS REGARDING MEASLES VIRUS?

E. Shrock for assistance with assays. **Funding:** This work was supported by a grant from the Value of Vaccine Research Network to S.J.E. and M.J.M.; a grant from the Gates Foundation to S.J.E.; an NIH/NIAID U24 grant to H.B.L. and S.J.E.; a grant from the European Union Seventh Framework Program

Value of Vaccine Research Network is funded entirely by the Gates Foundation

COMPETING INTERESTS?

H.B.L., R.D.d.V., and R.L.d.S.; Writing: M.J.M., T.K., and S.J.E.; Supervision: S.J.E. **Competing interests:** M.S.W. and D.F.C. are employees of Genentech. S.J.E. is a founder of TSCAN Therapeutics, MAZE Therapeutics, and Mirimus. S.J.E. serves on the scientific advisory boards of CRISPR Therapeutics, Homology Medicines, TSCAN Therapeutics, and XChem and is an adviser for MPM Capital, none of which affect this work. M.J.M. has served as a member of Sanofi advisory board for RSV therapeutics. D.E.G. is a member of the GlaxoSmithKline Vaccine Research and Development Advisory Board. S.J.E., T.K., and H.B.L. are inventors on a patent application filed by The Brigham and Women's Hospital (US20160320406A) that covers the use of the VirScan library to identify pathogen antibodies in blood. All other authors declare no competing interests. **Data**

WHAT DOES MINA ET AL. 2019 ACTUALLY SAY?

- MEASLES VIRUS (MV) PATIENTS LOST 11 TO 73% OF THEIR ANTIBODY REPERTOIRE
- ANTIBODIES WERE RESTORED AFTER "NATURAL REEXPOSURE TO PATHOGENS"
- "FURTHERMORE, BECAUSE, IN THE PREVACCINE ERA, MV INFECTED NEARLY ALL CHILDREN WITHIN THE FIRST DECADE OF LIFE, THE VACCINE ***MAY HAVE*** CONTRIBUTED TO CONSIDERABLY GREATER BENEFITS BY PREVENTING MEASLES AND IMMUNE AMNESIA. BY PRESERVING IMMUNITY, MEASLES VACCINES ***MAY HAVE*** RESET OVERALL BASELINE MORBIDITY AND MORTALITY RATES TO LOWER LEVELS (15)."

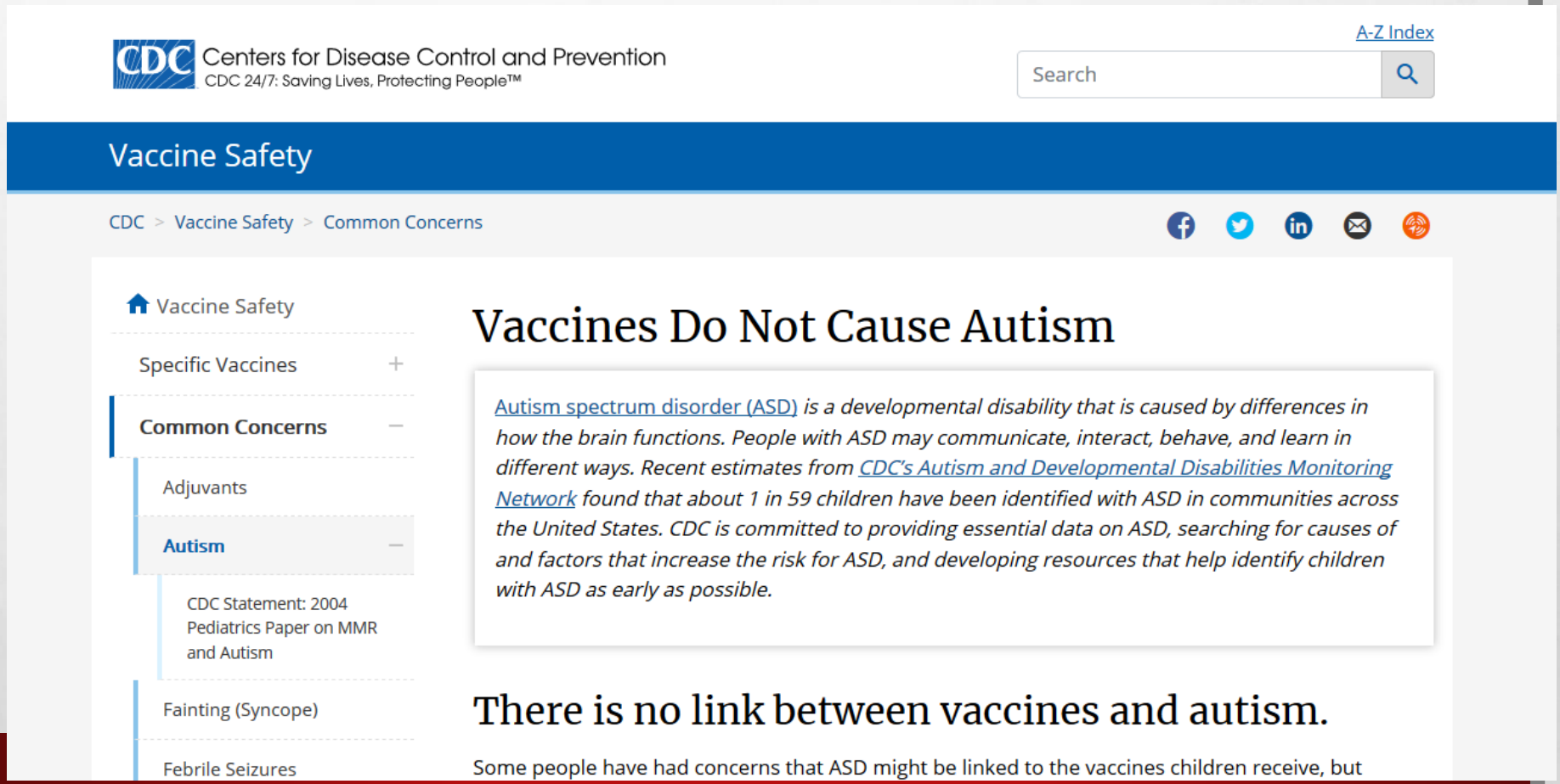
THE PRESENCE OF CIRCULATING ANTIBODIES DOES NOT CORRELATE TO IMMUNITY AGAINST INFECTIOUS DISEASE

- THE IMMUNE SYSTEM IS EXTREMELY COMPLEX WITH HUMORAL (BLOOD) AND CELLULAR (T-CELL) COMPONENTS ALL DESIGNED TO FIGHT INFECTIOUS DISEASE AND DEVELOP "IMMUNE MEMORY"
- IMMUNE MEMORY IS A COMPILATION OF BOTH B- AND T- MEMORY LYMPHOCYTES, NONE OF WHICH WERE MEASURED IN MINA ET AL. 2019
- NATURAL IMMUNE MEMORY INVOLVES BOTH TYPES OF CELLS WHERE VACCINATION STIMULATES B-CELLS ONLY
- VACCINATED PATIENTS WITH ANTIBODY "PROTECTION" HAVE CONTRACTED MV INFECTIONS (AMMARI ET AL. 1993)
- PATIENTS WITH A GENETIC CONDITION (AGAMMAGLOBULINEMIA) WHO PRODUCE NO ANTIBODIES RECOVERED FROM MEASLES NATURALLY (BURNET ET AL. 1940)
- NATURAL MV INFECTIONS IN SENEGAL AND BANGLADESH DID NOT RESULT IN INCREASED MORTALITY IN CHILDREN OR T-LYMPHOCYTE SUPPRESSION (AABY, ET AL. 2002, 2003)

"DOESN'T THE CDC MONITOR VACCINE SAFETY ON A 'POST-MARKET' BASIS?"

- CDC SPENDS $4.6 BILLION/YEAR PURCHASING, PROMOTING AND DISTRIBUTING VACCINES
- CDC SPENDS APPROXIMATELY $30 MILLION/YEAR ON VACCINE SAFETY
- ACIP MEMBERS WHO APPROVE THE "VACCINE SCHEDULES" VOTE THEMSELVES AND THEIR CORPORATIONS RICH VIA THE REVIEW PROCESS
- VACCINE SAFETY OFFICIALS ARE INCENTIVIZED *NOT* TO FIND VACCINE AE CAUSATION

DO VACCINES CAUSE AUTISM?



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A-Z Index

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Vaccines Do Not Cause Autism

Autism spectrum disorder (ASD) is a developmental disability that is caused by differences in how the brain functions. People with ASD may communicate, interact, behave, and learn in different ways. Recent estimates from CDC's Autism and Developmental Disabilities Monitoring Network found that about 1 in 59 children have been identified with ASD in communities across the United States. CDC is committed to providing essential data on ASD, searching for causes of and factors that increase the risk for ASD, and developing resources that help identify children with ASD as early as possible.

There is no link between vaccines and autism.

Some people have had concerns that ASD might be linked to the vaccines children receive, but

CASE STUDY: DOES THE MMR VACCINE CAUSE AUTISM?

- INSTITUTE OF MEDICINE COMMITTEES IN 2004 AND 2011 HAVE BOTH DENIED A LINK BETWEEN THE MMR VACCINE AND AUTISM
- THE NVICP FOUND NO LINK BETWEEN THE MMR VACCINE AND AUTISM IN THREE TEST CASES
- HOWEVER, THE NVICP CONCEDED A "MMR TABLE INJURY" (HANNAH POLING) WHERE THE CHILD HAD A DIAGNOSIS OF AUTISM

DESTEFANO ET AL. 2004 – THE TEXT SAYS ONE THING BUT THE DATA SAY SOMETHING ELSE

Age at First Measles-Mumps-Rubella Vaccination in Children With Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta

Frank DeStefano, Tanya Karapurkar Bhasin, William W. Thompson, Marshalyn Yeargin-Allsopp and Coleen Boyle

Pediatrics 2004;113;259
DOI: 10.1542/peds.113.2.259

STATISTICALLY SIGNIFICANT RELATIONSHIPS WERE SEEN BETWEEN MMR EXPOSURE AND AUTISM INCIDENCE

TABLE 3. Association Between Age at First MMR Vaccination and Autism Case Status for the Total Sample and the Birth Certificate Sample and According to Gender and Age

Sample	Case Subgroup	Cases	<18 Months, OR (95% CI)	<24 Months, OR (95% CI)	<36 Months, OR (95% CI)
Total sample	All cases	624	1.12 (0.91–1.38)	1.21 (0.93–1.57)	1.49 (1.04–2.14)
Unadjusted analyses*	Boys	500	1.22 (0.97–1.54)	1.29 (0.96–1.73)	1.67 (1.10–2.53)
	Girls	124	0.83 (0.52–1.30)	0.96 (0.55–1.68)	1.06 (0.51–2.20)
	Aged 3–5 y	214	1.08 (0.73–1.60)	1.66 (0.95–2.92)	2.34 (0.99–5.54)
	Aged 6–10 y	410	1.14 (0.90–1.46)	1.10 (0.82–1.49)	1.33 (0.89–1.98)
Birth certificate sample	All cases	311	0.93 (0.66–1.30)	0.99 (0.63–1.55)	1.23 (0.64–2.36)
Adjusted analyses†	Boys	243	0.94 (0.65–1.38)	1.01 (0.61–1.67)	1.64 (0.77–3.49)
	Girls	68	0.79 (0.33–1.86)	0.84 (0.26–2.77)	0.24 (0.04–1.47)
	Aged 3–5 y	112	0.77 (0.39–1.50)	1.67 (0.60–4.67)	2.63 (0.51–13.45)
	Aged 6–10 y	199	0.98 (0.65–1.47)	0.87 (0.51–1.46)	1.09 (0.52–2.30)

* Conditional logistic regression model stratified by the matching variables (age, gender, school)

STATISTICALLY SIGNIFICANT RELATIONSHIPS WERE SEEN BETWEEN MMR EXPOSURE AND AUTISM INCIDENCE

- ALL CHILDREN AND ESPECIALLY BOYS WERE MORE LIKELY TO RECEIVE AN AUTISM DIAGNOSIS IF THEY RECEIVED MMR PRIOR TO 36 MONTHS OF AGE
- THIS RESULT WAS STATISTICALLY SIGNIFICANT
- RELATIONSHIPS ARE BLAMED ON SPECIAL PRESCHOOL REQUIREMENTS FOR MMR VACCINE IN AUTISTIC "CASES"
- THIS IS FALSE – IF THAT WAS TRUE, YOU WOULD SEE THE EFFECT IN ALL DEMOGRAPHICS (BOTH BOYS AND GIRLS, AS WELL AS EACH RACE CATEGORY)

REANALYSIS OF DESTEFANO ET AL. 2004

Reanalysis of CDC Data on Autism Incidence and Time of First MMR Vaccination

Brian S. Hooker, Ph.D., P.E.

This study is a re-analysis of Centers for Disease Control and Prevention (CDC) data pertaining to the relationship of autism incidence and the age at which children got their first measles-mumps-rubella (MMR) vaccine. Statistically significant relationships were observed when African-American males were considered separately while looking at those individuals who were vaccinated prior to and after a 36-month age cut-

"birth-certificate" sample was to provide access to birth records on child's birth weight and gestational age as well as maternal race, parity, age, and education. In general, when significance was seen in the overall sample, it was not obtained in the birth-certificate sample. However, when considering race as a category, only the results for the "birth-certificate" sample were presented—even though the school records for all children in

DEMOGRAPHIC DATA

Table 1. Descriptive Statistics for the Sample

Category	Controls (n)	Controls (%)	Cases (n)	Cases (%)
Total*	1824	74.5	624	25.5
White and other males	901	75.3	296	24.7
1st MMR < 18 months	683	75.0	228	25.0
1st MMR 18 to 36 months	151	75.5	49	24.5
1st MMR > 36 months	67	77.9	19	22.1
Black males	480	72.2	185	27.8
1st MMR < 18 months	290	69.9	125	30.1
1st MMR 18 to 36 months	139	72.4	53	27.6
1st MMR > 36 months	51	87.9	7	12.1
White and other females	191	71.3	77	28.7
1st MMR < 18 months	145	72.9	54	27.1
1st MMR 18 to 36 months	36	66.7	18	33.3
1st MMR > 36 months	10	66.7	5	33.3
Black females	156	77.6	45	22.4
1st MMR < 18 months	96	78.7	26	21.3
1st MMR 18 to 36 months	41	75.9	13	24.1
1st MMR > 36 months	19	76.0	6	24.0

*96 controls and 21 cases were missing race information

AFRICAN AMERICAN MALES

Table 3. Odds ratio for receiving an autism diagnosis for African-American males receiving the first MMR vaccine before or after different age cutoffs

Age cut-off for first MMR vaccine	Odds Ratio	*p*-value	95% Confidence Interval	Number of Cases/Controls: Before
				After
18 months	1.49	0.066	0.98 – 2.26	125/290
				60/190
24 months	1.82	0.029	1.06 – 3.11	162/381
				23/99
36 months	3.86	0.005	1.49 – 10.0	178/429
				7/51

AUTISM WITHOUT MENTAL RETARDATION

Table 4. Odds ratio for receiving an autism diagnosis without mental retardation for all subjects receiving the first MMR at specific age cut-offs

Age cut-off for first MMR vaccine	Odds Ratio	*p*-value	95% Confidence Interval	Number of Cases/Controls Before
				Cases/Controls After
18 months	1.23	0.227	0.87 – 1.73	190/1275
				58/549
24 months	1.47	0.094	0.94 – 2.32	222/1535
				26/289
36 months	2.52	0.012	1.23 – 5.17	239/1659
				9/165

TAKE-HOME MESSAGES

- AFRICAN-AMERICAN MALES ARE MORE LIKELY TO GET AN AUTISM DIAGNOSIS IF THEY GET THE MMR ON TIME VERSUS AFTER 36 MONTHS OF AGE
- THIS EFFECT IS NOT SEEN IN OTHER RACE/GENDER CATEGORIES
- THERE APPEARS TO BE A RELATIONSHIP IN THOSE DIAGNOSED WITH AUTISM WITHOUT MENTAL RETARDATION (AMONG ALL RACE/GENDER CATEGORIES)

WHAT DID THE ORIGINAL CDC AUTHORS SEE?

			Matched Analyses											
Sample	Cases	Variable	All Subjects			White Model			Black Model			Other Model		
			OR	L95CI	U95CI	OR	L95CI	U95CI	OR	L95CI	U95CI	OR	L95CI	U95CI
Total	596	MMR<18	1.14	0.92	1.40	0.96	0.71	1.29	1.23	0.91	1.57	1.41	0.63	3.13
		MMR<36	**1.61**	**1.10**	**2.34**	0.89	0.52	1.52	**2.25**	**1.25**	**4.03**	1.97	0.64	6.09
		MMR Categories												
		0-11 mo	1.16	0.51	2.65	1.08	0.37	3.16	1.42	0.36	5.59	NA	NA	NA
		12-15 mo	1.74	1.18	2.55	0.99	0.58	1.70	**2.17**	**1.18**	**4.00**	2.33	0.72	7.57
		16-18 mo	1.42	0.94	2.15	0.69	0.39	1.24	**2.65**	**1.43**	**5.05**	1.71	0.46	6.35
		19-23 mo	1.55	0.96	2.49	0.83	0.41	1.67	2.02	1.00	4.10	3.00	0.63	14.17
		24-35 mo	1.61	0.97	2.68	0.96	0.45	2.08	2.03	0.99	4.14	1.11	0.11	11.43
		36+ mo	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Isolated	222	MMR<18	1.12	0.78	1.61	1.01	0.67	1.52	1.35	0.77	2.36	NA	NA	NA
		MMR<36	**2.48**	**1.16**	**5.31**	1.26	0.55	2.84	3.85	0.92	16.09	NA	NA	NA
		MMR Categories												
		0-11 mo	1.01	0.19	5.43	0.51	0.06	4.45	3.30	0.28	39.16	NA	NA	NA
		12-15 mo	**2.61**	**1.20**	**5.64**	1.31	0.58	2.96	4.12	0.96	17.65	NA	NA	NA
		16-18 mo	**2.34**	**1.05**	**5.25**	1.20	0.51	2.83	3.86	0.86	17.41	NA	NA	NA

HOW TO MAKE RESULTS DISAPPEAR

- SUBJECTS WERE ELIMINATED FROM THE RACE ANALYSIS IF THEY DID NOT HAVE VALID GEORGIA BIRTH CERTIFICATES
- THIS REDUCED THE "STATISTICAL POWER" OF THE ANALYSIS AND THE ASSOCIATION "WENT AWAY."
- ALL RESULTS SHOWING THE STATISTICALLY SIGNIFICANT EFFECT WERE THROWN AWAY IN LARGE GARBAGE BINS IN A MEETING IN SEPTEMBER, 2002

WHY DID CDC HIDE THESE RESULTS?

- THIS WAS THE ONLY MMR-AUTISM STUDY USING U.S. CHILDREN
- THESE RESULTS WERE TO BE PRESENTED AT THE 2004 INSTITUTE OF MEDICINE MEETING “VACCINES AND AUTISM”
- POSITIVE ASSOCIATIONS COULD BE USED IN THE OMNIBUS AUTISM PROCEEDINGS (OAP) OF THE NVICP TO JUSTIFY INJURIES TO AFRICAN AMERICAN MALES AND CHILDREN WITH “AUTISM WITHOUT MR”
- THE OAP COMPRISED OVER 5000 CLAIMS TO THE NVICP WHICH COULD HAVE BANKRUPTED THE PROGRAM MANY TIMES OVER

DR. WILLIAM THOMPSON

THOMPSON TRIED TO WARN CDC DIRECTOR DR. JULIE GERBERDING

February 2nd, 2004

Dear Dr. Gerberding,

We've not met yet to discuss these matters, but I'm sure you're aware of the Institute of Medicine Meeting regarding immunizations and autism that will take place on February 9th. I will be presenting the summary of our results from the Metropolitan Atlanta Autism Case-Control Study and I will have to present several problematic results relating to statistical associations between the receipt of the MMR vaccine and autism.

THOMPSON REPLACED BY DESTEFANO IN 2004 IOM MEETING

- THOMPSON WAS REPRIMANDED FOR SENDING THE LETTER TO GERBERDING
- HE WAS REPLACED BY DR. FRANK DESTEFANO TO PRESENT THE MMR-AUTISM RESULTS AT THE IOM MEETING
- DESTEFANO PRESENTED FRAUDULENT RESULTS SHOWING NO EFFECT
- IOM REPORTED NO “BIOLOGICAL MECHANISMS” FOR A RELATIONSHIP BETWEEN VACCINES AND AUTISM

CDC OFFICIALS WANTED TO FIRE THOMPSON

Frank DeStefano called me in the evening and told me that Bob Chen wanted to fire me. I asked why Bob would be able to fire me? Frank didn't give any clear reason why. He suggested my e-mails provided clear reasons to fire me.

THE 2004 IOM OUTCOMES WERE "FIXED" TO DENY CLAIMS IN THE NVICP

- THE OUTCOME OF THE 2004 IOM REPORT "VACCINES DON'T CAUSE AUTISM" WAS CITED IN EACH OF THE OAP TEST CASES
- THE CDC PRESENTED FRAUDULENT RESULTS REGARDING THE MMR VACCINE AT THE 2004 IOM
- THE CDC PRESENTED FRAUDULENT RESULTS REGARDING THIMEROSAL CONTAINING VACCINES AT THE 2004 IOM
- THE CDC SLANDERED DR. MARK AND DAVID GEIER TO DISCREDIT THEIR VERY SOUND RESULTS SHOWING THE RELATIONSHIP BETWEEN THIMEROSAL AND AUTISM

COMPLAINT WAS FILED TO HHS OFFICE OF RESEARCH INTEGRITY IN OCT. 2014

Re: Alleged Research Misconduct – falsification by omission of material results in the publication of: "Age at First Measles-Mumps-Rubella Vaccination in Children With Autism and School-Matched Control Subjects: A Population-Based Study in Metropolitan Atlanta. 2004;113:259-266 [The Paper; Exhibit 1]

Dear Drs. Jaffe and Wright,

We write to report apparent research misconduct by senior investigators within the National Immunization Program (NIP), Battelle Memorial Institute at the Centers for Public Health Evaluation (CPHE), and the National Center on Birth Defects and Developmental Disabilities (NCBDDD), and to request an immediate investigation.

ORI INITIAL RESPONSE TO COMPLAINT

The Office of Research Integrity (ORI) is in receipt of your February 2, 2015, letter and related documentation. Thank you for providing the revised and supplementary information noted in your letter.

ORI first became aware of this matter in late August 2014 and received your initial letter outlining your concerns on October 14, 2014. When allegations of possible research misconduct are received directly by ORI, the Division of Investigative Oversight (DIO) within ORI assesses the allegation to determine if this Office has jurisdiction. If we do, we refer the matter to the institution where the alleged misconduct occurred, as ORI lacks the authority to directly investigate research misconduct allegations. In this case, we determined that officials at the Centers for Disease Control and Prevention (CDC) were already taking appropriate steps to assess your concerns.

CDC Investigates Itself

CDC INVESTIGATES ITSELF

DATE: May 6, 2019

FROM: Dr. Joanne Cono, CDC Research Integrity Officer

TO: Dr. Brian Hooker

SUBJECT: CDC Research Misconduct Investigation: DIO 5732

This memo is to notify you that the CDC Deciding Official has affirmed the findings of the Investigation Committee in the case referred to above as DIO 5732 in accordance with the CDC Policy and the Public Health Service Regulations on Research Misconduct, 42 CFR Part 93. The findings are *no scientific (research) misconduct*.

As set out in the regulations and policy, the Investigation Report and its supporting case materials will be provided to the Department of Health and Human Services, Office of Research Integrity for their evaluation and oversight review.

"The findings are no scientific (research) misconduct"

FLU SHOTS DURING PREGNANCY AND MISCARRIAGE

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Inactivated influenza vaccine and spontaneous abortion in the Vaccine Safety Datalink in 2012–13, 2013–14, and 2014–15

James G. Donahue [a,*], Burney A. Kieke [a], Jennifer P. King [a], Maria A. Mascola [b], Tom T. Shimabukuro [c], Frank DeStefano [c], Kayla E. Hanson [a], David L. McClure [a], Oluwatosin Olaiya [a], Jason M. Glanz [d], Rulin C. Hechter [e], Stephanie A. Irving [f], Lisa A. Jackson [g], Nicola P. Klein [h], Allison L. Naleway [f], Eric S. Weintraub [c], Edward A. Belongia [a]

DONAHUE ET AL. 2019 – NO RELATIONSHIP BETWEEN FLU SHOT IN PREGNANCY AND SPONTANEOUS ABORTION

- A PREVIOUS STUDY BY CDC (DONAHUE ET AL. 2017) SHOWED AN INCREASE IN SPONTANEOUS ABORTION (SAB) IN PREGNANT WOMEN RECEIVING THE H1N1 (SWINE) FLU VACCINE
- THIS FOLLOW-UP STUDY WAS A POLICY EFFORT TO INDEMNIFY THE SEASONAL FLU VACCINE FROM ANY RELATIONSHIP WITH SAB
- INVESTIGATION OF SAB IN FLU-SHOT SEASONS 2012-13, 2013-14, 2014-15
- POOR STUDY DESIGN (LIMITED STATISTICAL POWER) MAKES IT IMPOSSIBLE TO DRAW ANY CONCLUSIONS FROM DONAHUE ET AL. 2019

LIMITED STATISTICAL POWER?

a given influenza season and stratum (vaccinated in the previous season or not). We determined that 250 matched pairs per stratum per season were required to detect an OR of 3.5 with a power of 0.82 in the primary risk window. Pooling stratum-specific data

- **"WE DETERMINED THAT 250 MATCHED PAIRS PER STRATUM PER SEASON WERE REQUIRED TO DETECT AN OR (ODDS RATIO) OF 3.5 WITH A POWER OF 0.82 IN THE PRIMARY RISK WINDOW"**
- **EARTH SPEAK: THEY COULD DETERMINE AN INCREASED ODDS OF SAB OF 3.5X OR HIGHER IN VACCINATED PATIENTS WITH AN 82% CERTAINTY**
- **THE STUDY WAS *INSUFFICIENTLY POWERED* TO PICK UP ANY RISK BELOW 3.5X**
- **IF THE RISK IS SOMEWHERE BETWEEN 1.0X AND 3.5X, THEY SIMPLE DON'T KNOW…**
- **INFERENCE: ANY INCREASES IN SAB DUE TO THE SEASONAL FLU SHOT *BELOW THIS THRESHOLD ARE ACCEPTABLE***

WHAT DO THE DATA SAY?

Table 5
Odds ratios for the association of SAB with influenza vaccination relative to conception[a], by influenza season and vaccination status in the previous season[b].

		Influenza season 2012–13			2013–14			2014–15			All seasons combined		
	Vaccination to reference date (days)	Disc. Pairs[c]	Crude OR[d]	aOR[e]	Disc. Pairs[c]	Crude OR[d]	aOR[e]	Disc. Pairs[c]	Crude OR[d]	aOR[e]	Disc. Pairs[c]	Crude OR[d]	aOR[e]
Vaccinated in previous season	>42 days before	18/25	0.6	0.6 (0.3, 1.0)	17/14	1.0	0.8 (0.4, 1.7)	12/20	0.6	0.5 (0.2, 1.0)	47/59	0.7	0.6 (0.4, 0.9)
	0–42 day before	8/9	0.7	0.8 (0.4, 1.7)	9/11	1.0	1.1 (0.5, 2.3)	8/16	0.7	0.6 (0.3, 1.2)	25/36	0.8	0.8 (0.5, 1.2)
	1–28 days after	3/14	0.3	0.3 (0.1, 0.7)	9/7	0.9	1.3 (0.6, 3.0)	7/4	1.6	2.1 (0.8, 5.2)	19/25	0.7	0.9 (0.5, 1.4)
	>28 days after	3/10	0.5	0.5 (0.2, 1.3)	5/12	0.7	0.8 (0.3, 1.8)	6/3	1.2	1.6 (0.5, 4.6)	14/25	0.7	0.8 (0.5, 1.4)
Not vaccinated in previous season	>42 days before	8/11	0.9	1.0 (0.4, 2.7)	10/10	0.8	0.9 (0.4, 2.3)	9/13	0.7	0.6 (0.3, 1.4)	27/34	0.8	0.8 (0.5, 1.3)
	0–42 day before	3/8	0.3	0.4 (0.1, 1.6)	4/6	1.0	1.6 (0.5, 5.2)	6/5	1.7	1.6 (0.5, 5.0)	13/19	0.9	1.1 (0.6, 2.2)
	1–28 days after	7/3	1.8	3.2 (0.9,11.9)	3/4	0.4	1.0 (0.2, 4.5)	6/6	0.8	0.4 (0.1, 1.4)	16/13	0.9	1.1 (0.5, 2.2)
	>28 days after	5/12	0.3	0.4 (0.1, 1.2)	6/18	0.4	0.4 (0.2, 1.0)	6/8	0.8	0.9 (0.3, 3.0)	17/38	0.4	0.5 (0.3, 0.9)

In the 2014-15 flu-shot season, an OR of 2.1 was seen for SAB in women receiving the vaccine between 1 and 28 days after conception

BURIED IN THE PAPER'S SUPPLEMENT…

Supplemental Table 5. Odds ratios for the association of influenza vaccination with SAB relative to conception,[a] by influenza season and by vaccination status in the previous season.[b] Cases include those with gestational age of 5-<20 weeks.

		Influenza season							
		2012-13		2013-14		2014-15		All seasons combined	
	Days between vaccination and conception	Crude OR[c]	aOR[d]	Crude OR[c]	aOR[d]	Crude OR[c]	aOR[d]	Crude OR[c]	aOR[d]
Vaccinated in previous season	>42 days before	0.8	0.7 (0.4, 1.3)	1.1	1.1 (0.6, 2.0)	0.7	0.6 (0.3, 1.1)	0.8	0.8 (0.6, 1.1)
	0-42 day before	0.8	0.9 (0.4, 1.7)	1.0	1.1 (0.5, 2.2)	0.8	0.6 (0.3, 1.3)	0.8	0.8 (0.6, 1.2)
	1-28 days after	0.4	0.3 (0.1, 0.8)	1.0	1.2 (0.6, 2.8)	1.8	2.3 (0.9, 5.5)	0.8	0.9 (0.6, 1.5)
	>28 days after	0.5	0.6 (0.2, 1.4)	0.7	0.8 (0.3, 1.8)	1.3	1.6 (0.5, 4.6)	0.8	0.8 (0.5, 1.4)
Not vaccinated in previous season	>42 days before	1.0	1.1 (0.5, 2.7)	0.9	1.1 (0.5, 2.5)	0.6	0.6 (0.3, 1.3)	0.8	0.8 (0.5, 1.3)
	0-42 day before	0.4	0.5 (0.1, 1.8)	0.7	1.1 (0.4, 3.3)	1.4	1.3 (0.4, 3.8)	0.7	0.9 (0.5, 1.8)
	1-28 days after	1.9	3.2 (0.9, 11.6)	0.4	1.0 (0.2, 4.3)	0.7	0.4 (0.1, 1.2)	0.8	1.0 (0.5, 2.0)
	>28 days after	0.3	0.4 (0.1, 1.2)	0.4	0.4 (0.2, 1.0)	0.8	0.9 (0.3, 2.9)	0.4	0.5 (0.3, 0.9)

[a]Conception is defined as the date of the last menstrual period plus 14 days

When the analyses are redone using the same parameters as the previous paper, the OR for the 2014-15 season increases to 2.3

BUT THESE RESULTS AREN'T STATISTICALLY SIGNIFICANT…

- TABLE 5 – OR = 2.1 (0.8, 5.2)
- SUPPLEMENTAL TABLE 5 – OR = 2.3 (0.9, 5.5)
- LOWER 95% CONFIDENCE INTERVAL MUST BE 1.0 OR GREATER
- HOWEVER, THIS STUDY DOES NOT HAVE SUFFICIENT POWER TO PICK UP AN OR BELOW 3.5
- THIS "MARGINALLY SIGNIFICANT" RESULT SHOULD RAISE A RED FLAG…

COULD A STUDY WITH SUFFICIENT POWER BE DONE?

- 302 CASES AND 285 CONTROLS WERE INVESTIGATED FOR 2014-15 FLU-SHOT SEASON
- SOURCE OF THE DATA WAS THE CDC'S VACCINE SAFETY DATALINK (VSD)
- VSD CONTAINS RECORDS FOR OVER 9 MILLION PATIENTS
- IT IS NOT CLEAR IN THE PAPER WHY THE SAMPLE SIZE IS SO SMALL
- HOWEVER, CASES AND CONTROLS FOR THE STUDY WERE "ADJUDICATED" BY STUDY AUTHORS DIRECTLY

THE GREAT UNKNOWN

- THE SAFETY OF VACCINATION SCHEDULE ALONG WITH THE INDIVIDUAL VACCINES IS WOEFULLY UNDERSTUDIED
- THE U.S. INSTITUTE OF MEDICINE IN 2011 LOOKED AT 154 ADVERSE REACTIONS FROM 8 DIFFERENT VACCINES AND HAD INSUFFICIENT DATA TO RULE OUT 138 OF THE REACTIONS
- THIS INCLUDED THE INABILITY TO RULE OUT A RELATIONSHIP BETWEEN THE DTAP VACCINE AND AUTISM
- ANOTHER REPORT BY THE U.S. INSTITUTE OF MEDICINE IN 2013 STATED, "NO STUDIES HAVE COMPARED THE DIFFERENCES IN HEALTH OUTCOMES THAT SOME STAKEHOLDERS QUESTIONED BETWEEN ENTIRELY UNIMMUNIZED POPULATIONS OF CHILDREN AND FULLY IMMUNIZED CHILDREN."

TAKE HOME MESSAGES

- VACCINES *ARE NOT* ADEQUATELY SAFETY TESTED DURING PRE-APPROVAL CLINICAL TRIALS
- PROGRAMS LIKE FAST TRACK IN THE FDA HAVE LED TO AGENCY CAPTURE AS UP TO 45% OF FDA'S REVENUES COME FROM PHARMA
- CDC CANNOT BE TRUSTED FOR RECOMMENDATIONS TO THE VACCINATION SCHEDULE NOR FOR POST-MARKET SAFETY SURVEILLANCE
- THE VACCINATION SCHEDULE IN LIGHT OF THE EPIDEMIC OF NEURODEVELOPMENTAL DISABILITIES IS WOEFULLY UNDERSTUDIED

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