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Review Article

# The US Universal Varicella Vaccination Program: CDC Censorship of Adverse Public Health Consequences

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## Abstract

**Introduction:** A Research Analyst *insider* reports findings that the Universal Varicella Vaccination Program alters the epidemiology of herpes zoster (shingles); and details ways in which the CDC, in collusion with the Los Angeles Department of Health Services (LADHS)—the Acute Communicable Disease Control unit—apparently manipulated data to conceal unwanted outcomes that supported an immunologically-mediated link between varicella and herpes zoster (HZ) epidemiology.

**Methodology:** The Varicella Active Surveillance Project (VASP) was one of three CDC-funded projects in the US whose mission was to monitor the effects of the varicella vaccine on the population of 300,000 within the geographically isolated region of the Antelope Valley (consisting of principally two cities: Lancaster and Palmdale, California). Starting in 1995, prior to varicella vaccine licensure in March, under a cooperative agreement between CDC and the LADHS, the VASP collected baseline epidemiological data, which when considered with data from the other two surveillance projects (Travis County, Texas and West Philadelphia, Pennsylvania), would assist the CDC in recommending policies pertaining to the vaccine.

**Results:** Trends in vaccine efficacy were masked by averaging varicella vaccine efficacy over several years instead of stratifying efficacy by year. High HZ incidence rates among children that had had natural varicella were masked by reporting a single mean of a bimodal distribution that included children that were administered the varicella vaccine. While CDC researchers initially opposed and criticized the Research Analyst's methodology and calculation of childhood HZ incidence rates, eventually they used similar methodology and found similar outcomes. The CDC rates, however, represented only half the true rates in the population since two-source capture-recapture statistical methods revealed 50% reporting completeness.

**Conclusion:** The CDC mainly published selective studies and manipulated findings to support universal varicella vaccination and aggressively blocked the Research Analyst's attempt to publish deleterious trends or outcomes (e.g., declining vaccine efficacy, increasing HZ incidence rates, etc.), prompting his resignation in protest against what he perceived was research fraud. His letter of resignation stated, "When research data concerning a vaccine used in human populations is being suppressed and/or misrepresented, this is very disturbing and goes against all scientific norms and compromises professional ethics."

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- Varicella zoster virus
- Capture-recapture
- Exogenous boosting
- CDC obfuscation

## INTRODUCTION

The Research Analyst, Gary S. Goldman, PhD, was hired in January 1995 by Vestex Human Resource Systems in behalf of the Los Angeles County Department of Health Services (LADHS), Acute Communicative Disease Control (ACDC) Unit to conduct epidemiological studies under the CDC-funded Antelope Valley Varicella Active Surveillance Project (AV-VASP). This project's mission was to monitor the effects of the Universal Varicella Vaccination Program on the population within the Antelope Valley region (principally two cities Lancaster and Palmdale in California) beginning in 1995. Later, in 2000, herpes zoster (HZ) was added to the active surveillance.

AV-VASP managed to collect 100% of the biweekly varicella case logs from all 300 plus reporting units participating in the AV-VASP (e.g., daycares, preschools, public and private schools, physicians, health care clinics, etc.) during 1995 to 2000. Moreover, the surveillance was able to detect sensitive trends early in the Universal Varicella (chickenpox) Vaccination

Program because of four contributing factors: (1) the survey region was relatively isolated geographically with few residents seeking healthcare or attending schools outside the region, (2) the population was relatively stable, (3) there was no sampling (whereas, the other two CDC-funded sites did sampling), and (4) the existence of two ascertainment sources (schools and healthcare providers) allowed the use of capture–recapture statistical methods to determine reporting completeness and correct for under-ascertained counts of varicella and HZ case reports. The AV-VASP data collection was uninterrupted and surveillance activities remained relatively stable from 1995 through 2002, and after a non-reporting period of HZ (from 2004 through 2005), from 2006 through 2007.

The Research Analyst wrote various software programs (using Delphi Pascal) to allow input of all demographic and clinical variables, perform statistical calculations, provide analyses, and automate the Varicella Active Surveillance Project (VASP). Once each month, a tracking program sent a reminder fax to each reporting unit whose biweekly report of varicella (and later HZ) cases was delinquent. This is what characterized the surveillance as active. Later, under the direction of the VASP Co-Principal Investigators and Varicella Chief, the database of all clinical and demographic variables (collected from VASP staff who conducted structured interviews with parents of children reported as having chickenpox or shingles) were transferred to the CDC in a format agreed upon by both the CDC Health Scientist (John X. Zhang) and the Research Analyst. This allowed the CDC to access the VASP's raw data for independent analyses.

## Main text

The Research Analyst was encouraged by the Co-Principal Investigators to pursue any and all analyses and studies that might be suitable for publication. Selective studies that mainly supported the positive features of the varicella vaccination program were quickly approved by the CDC and VASP and subsequently presented and/or published [1-10]; studies suggesting negative findings or deleterious effects [11-20] were either suppressed or forbidden, prompting the VASP Research Analyst to resign after eight years in October 2002 in protest against what he perceived was research fraud. This would allow the opportunity to address VASP data that suggested impact of the Universal Varicella Vaccination Program on the closely related HZ epidemiology in the absence of sponsor (CDC and VASP) bias [11-20].

## Evidence of malfeasance/obfuscation by the CDC and LADHS

The evidence of obfuscation and malfeasance by the CDC and the AV-VASP include the various actions that are listed in Table 1.

## Active surveillance of varicella during 1995 through 1999 seemed promising

During the first five years of surveillance, universal single-dose varicella vaccination in the Antelope Valley appeared to be a success—with an 80% reduction in reported chickenpox cases from 2,934 in 1995 to 587 in 1999. When the varicella vaccine was licensed in March of 1995, healthcare insurance providers did not immediately cover its cost, and therefore relatively few doses were administered. In 1996, when vaccine costs were covered by healthcare insurance, healthcare providers consistently recommended and administered varicella vaccine to the majority of children aged 12 to 15 months.

## Early publication of positive VASP findings; publication delays or suppression of deleterious findings

Since 1995 happened to represent the peak of a naturally occurring 3- to 4-year interepidemic cycle in clinical varicella cases and the vaccine coverage among 19- to 35-month-old children was only 18% by the fourth quarter of 1996 [8], it was after 1997 that the observed decline in varicella cases could be attributed to the Universal Varicella Vaccination Program (Figure 1). Thus, even though a six-year study of varicella disease after the introduction of varicella vaccine during "1995 to 2000" was published by the *Journal of the American Medical Association*, the optimistic conclusions from VASP data actually reflected vaccination trends occurring only during the last three years. By contrast, the publication of a 3-year trend (2000 to 2002) of a high HZ incidence rate among children that had had natural varicella would not be considered by CDC/VASP authors until after a total of seven years of data had been collected (in 2006), with an additional three years to publication in 2009. Findings of increases in adult HZ case reports were never published.

## Varicella Chief has Research Analyst collaborate his findings on varicella transmission with CDC Modeler

Since the Antelope Valley is a region located in the upper (or high) desert, the unique opportunity existed to investigate how the transmission of varicella might be affected by high ambient air temperature in the community. In 1995, there were five consecutive months (March-July) that had an average temperature of 28.9°C (84°F) or higher. Concurrently, the Research Analyst investigated trends in varicella transmission due to population density which might be associated with the clustering of students in school. This required the determination of the number of days each student was home or off campus due to a holiday or simply being "off-track" based on each specific school's calendar and attendance schedule.

Using empirical methods, the Research Analyst found that varicella cases declined during months (a) with mean temperatures exceeding 28.9°C or (b) that contained lengthy school vacations and these two factors were independent. Figure 1 shows the seasonal variation in reported varicella cases by month in the Antelope Valley, 1995-1999. The CDC Varicella Chief had the Research Analyst collaborate with Dr. John Glasser, CDC disease modeler, who proceeded to fit the discrete air temperature data and person-day enrollments to continuous Fourier-series curves. This model confirmed the earlier conclusions of the Research Analyst and predicted the number of varicella cases each month to within an accuracy of 80% [1,2].

## All three VASPs participate in a CDC-sponsored seminar on capture-recapture methods

After attending a special multiple-day workshop at the CDC headquarters in Atlanta, GA on the use of two-source capture-recapture statistical methods, the Research Analyst employed this technique using two ascertainment sources (schools and

**Table 1:** Actions by the CDC and the AV-VASP contributing to obfuscation and malfeasance.

1) Published mainly positive findings related to decreases in varicella disease and related hospitalizations [8]—ignoring the impact on the closely-related HZ epidemiology [21].
2) Argued that active surveillance was not a proper way to gather HZ cases—yet ultimately added HZ (shingles) to the active surveillance project.
3) Reported an overall cumulative (1997–2001) vaccine efficacy of 87.4% (95% C.I., 83.0% to 90.6%) using household contacts aged <20 years and 78.9% (95% C.I., 69.7% to 85.3%) using contacts aged 1 to 14 Years [22]. These reported cumulative efficacy figures were artificially high due to confounding caused by the circulating wild-type varicella zoster virus (VZV)—especially during 1997 through 1999 [17].
4) Directed the Research Analyst not to pursue further analysis of trends in HZ cases.
5) Supported the improper use of a single mean for a bimodal distribution of HZ incidence among two widely different cohorts—those vaccinated and those with a prior history of natural varicella—masking the high HZ incidence among children with a history of natural or wild-type varicella [14].
6) Conducted a study of HZ incidence in a population where the varicella vaccination had not been widely administered [23] to misleadingly produce 'evidence' that the Universal Varicella Vaccination Program had no effect on the closely related epidemiology of HZ [24]. Thus, when other studies suggested a correlation between reduction in varicella and increasing HZ incidence, the CDC would counter those correlations that were reported by stating, "*studies are not conclusive on this issue*"—citing the misleading CDC study as "proof" of its assertion.
7) Referenced a poorly designed study [23] and another study by the Massachusetts Department of Public Health that had insufficient statistical power to conclude that there was "no increase in shingles" attributable to universal varicella vaccination.
8) Attempted to discredit the Research Analyst whose objective, in an act of transparency, was to publish preliminary data [12,14] supporting the Hope-Simpson hypothesis of 1965 that the different HZ incidence rates by age are due to that age group's frequency of exposure to children with "wild" (or natural) chickenpox.
9) Justified adding varicella vaccination to the "Immunization" schedule based on societal (not medical) considerations. Specifically, the Universal Varicella Vaccination Program's main benefit was the attributed value associated with a parent's loss of work to take care of a child with chickenpox [25].
10) Made three false assumptions to justify universal varicella vaccination: **(1)** the vaccine would cost $35/dose; **(2)** a single dose would provide life-long immunity; and **(3)** there would be no immunologically-mediated link to HZ epidemiology [25].
11) Served notice to the Research Analyst to "cease and desist" publication in a medical journal when he sought to objectively publish all of the data and results—both positive and deleterious.
12) Claimed that confidence intervals on HZ incidence calculations were too wide and not sufficiently longitudinal.
13) Suggested that the 16-year HZ incidence study by Hope-Simpson produced more reliable rates than those derived from the AV-VASP data [26].
14) Claimed HZ might have always been unusually high in the Antelope Valley population relative to other US populations.
15) Deemed that use of capture-recapture methods was inappropriate for ascertainment correction of HZ cases, while embracing its use to show consistent reporting completeness each year for varicella cases [3,8,27].
16) Prevented investigation as to why the recurrent HZ incidence rate was three-fold higher than expected based on 10 adults who experienced onset of HZ twice within a 12-month period.
17) Featured commercials for varicella vaccine that portrayed a child dying—even though chickenpox is generally benign.
18) Suggested that, if the relevant immune systems of adults were previously boosted by the annual varicella epidemics in their communities, the immune systems of those adults could alternatively be boosted by adding a 'shingles' vaccine.
19) Started the monitoring of shingles cases five (5) years after the start of the monitoring of cases of chickenpox. [Thus, active-surveillance-program baseline data for HZ (shingles) cases did not exist.]
20) Claimed that an Adolescent Survey could be used to study varicella susceptibility [10], but was not designed to assess historical cumulative HZ incidence rates—even though the Research Analyst received prior authorization from the Co-Principal Investigators to expand the survey to obtain the necessary additional information [11].
21) Claimed that trends of increasing HZ incidence rates had already begun prior to the start of universal varicella vaccination, but these increases were of a lower magnitude than those in communities where varicella vaccination was widespread. [These annual percentage increases in the pre-vaccine era were low, generally 2% to 4% or a somewhat higher percentage when adults aged 65 years and older, whose age-related decline in immune system function, were included.]
22) Promoted and distributed the varicella vaccine having a financial conflict of interest and lack of objectivity concerning the reporting of individual and population harmful effects of the varicella vaccination program.
23) Potentially could use threats of "defunding" other LADHS projects to ensure that its Acute Communicable Disease Control (ACDC) Unit published only those "findings" in support of the CDC's Universal Varicella Vaccination Program.

healthcare providers) to determine that the VASP was annually capturing about 45% of the varicella cases during 1995-2000. With cases from other reporting units included (other than schools and healthcare providers), VASP was capturing 65% of varicella cases and the consistent annual percentage of missed cases demonstrated that the surveillance units were reporting consistently and not losing interest in the project [3,8].

## Early years of HZ active surveillance ignite controversy

In 1999, for the first time, school nurses began reporting to VASP having observed an unexplainable increase in the number of cases of HZ (shingles) among school-aged children. In view of these observations and the imminent five-year (2000 through 2004) grant renewal, the Research Analyst proposed that HZ cases be added as a new data point to the already existing VASP. Beginning January 2000, the CDC formally added the active surveillance of shingles to VASP. It would have been logical to start collecting HZ case reports in 1995 along with varicella case reports since the Summary Base Agreement between the FDA and Merck included the apprehension that "There is additional concern that universal vaccination might result in increased rates of herpes zoster in vaccinated and unvaccinated individuals" [28]. Was the VASP negligent for failing to collect baseline HZ data starting in 1995?

Near the end of the first year of HZ active surveillance, initial

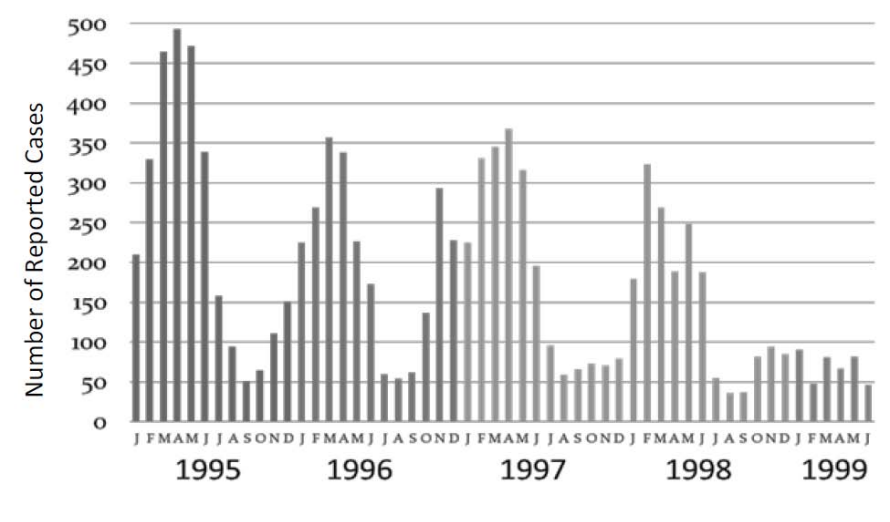



**Figure 1** Seasonal variation in reported varicella cases, Antelope Valley 1995-1999 [16].

COUNTY OF LOS ANGELES
OFFICE OF THE COUNTY COUNSEL
648 KENNETH MANN HALL OF ADMINISTRATION
500 WEST TEMPLE STREET
LOS ANGELES, CALIFORNIA 90012-2712
APRIL 10, 2003
**VIA CERTIFIED MAIL – RETURN RECEIPT REQUESTED**

**Re: Varicella Active Surveillance Project**

Dear Mr. Goldman:

…

This letter is notice to you to cease and desist in your efforts to publish or disseminate any information gathered as part of your participation on the VASP.

…

**Figure 2** Notice to Research Analyst to "cease and desist" publication].

quantitative evidence emerged of extremely high HZ incidence rates among children with a prior history of natural or wild-type varicella. Notably, such high HZ incidence rates were previously associated with older adults, not children. This new HZ active surveillance data corroborated the qualitative observations of the school nurses who had earlier anecdotally reported unexpected childhood cases of shingles. The CDC Varicella Chief and VASP Co-Principal Investigators offered several hypotheses as to what might have caused the high HZ incidence rate other than mass varicella vaccination:

• HZ incidence rates based on one-year of data were not sufficiently longitudinal;

• There was no baseline incidence data for HZ in the Antelope Valley;

• Such an immediate effect of the varicella vaccination program on HZ epidemiology was not expected—and if there was an effect, it would likely not be seen for some 20 years;

• Perhaps children in the Antelope Valley region experienced higher HZ incidence rates than children located in other regions of the US; and

• Perhaps active surveillance resulted in more complete collection of HZ cases than was typical of other studies.

Furthermore, VASP Co-Principal Investigators directly told the Research Analyst that to validate findings (no matter how robust), such as increasing adult HZ cases or the unusually high HZ incidence rate among children who had had natural chickenpox, would require duplication in other communities among other populations and in studies using different methodologies.

The Research Analyst agreed with these sound epidemiologi-

cal principles and scientific methods, but additionally explained to his colleagues the biological mechanism accounting for why the VASP HZ incidence rate in children who had had natural chickenpox was now higher than rates published in any historical study. The Co-Principal Investigators agreed that the association between increased HZ reactivation and reduction in circulating wild-type varicella-zoster virus (VZV) due to mass varicella vaccination was indeed plausible. However, in an apparent last ditch effort to proffer a justification to bury the findings, the Co-Principal Investigators simply and spuriously argued that the VASP did not provide a suitable platform for which to study HZ incidence rates.

Unfortunately, there were no baseline HZ incidence rates in the Antelope Valley for which to compare this first post-licensure rate which was nearly four-fold higher than rates in the same age group in two surrogate studies that used different methodology [11,26]. Moreover, the observed low HZ incidence rate among vaccinated children served as a control—indicating that physicians were not misdiagnosing cases of HZ in children. Thus, it was unlikely that over diagnosing could have inflated the number of HZ cases and biased the HZ incidence rate high.

By the end of 2001, the second year of HZ active surveillance, there was a statistically significant 28.5% increase ($p<0.042$, $t=2.95$, $df=4$) in HZ cases among adults 20 to 69 years of age, from 158 cases reported in 2000 to 203 reported in 2001. The number of reported HZ cases maintained or increased in every 10-year adult age category except elderly adults (70 years and older).

Despite all the objections by the CDC and Co-Principal Investigators, evidence continued to mount following 1999 which demonstrated that the epidemiology of HZ in both children and adults (who had had natural chickenpox in the pre-licensure era) was being adversely influenced [19]. Preliminarily, the unusually high HZ incidence rates being reported by VASP demonstrated that exogenous exposures to the wild-type VZV being shed by those infected with natural chickenpox in the community played a significant role in boosting cell-mediated immunity (CMI) to VZV. The lack of robust exogenous boosting by the less contagious vaccinated children (1) accelerated the recurrence of shingles in children who had had natural chickenpox and (2) increased the likelihood of shingles recurrence in adults.

To convey the VASP finding of unusually high HZ incidence among children, a meeting was arranged in Los Angeles that was attended by the Research Analyst, Project Director and part-time Co-Principal Investigators (Dr. Laurene Mascola and Dr. Carol Peterson) along with two of their assistant epidemiologists. The Co-Principal Investigators presented a very basic point—that HZ incidence in children is usually computed by taking the total number of childhood HZ cases aged <10 years and dividing by the total number of children aged <10 years in the population [26,28,29]. This calculation yields an HZ incidence rate that is referred to as the crude or population HZ incidence rate. Since 50% of children aged <10 years have not had chickenpox and therefore cannot reactivate HZ [11], the true HZ incidence rate (only pertaining to those children with a history of varicella) is approximately twice the population rate. In the older age groups, the population rate and true rates begin to coincide because these older cohorts consist almost entirely of individuals who have had a history of chickenpox, with only very few individuals that remain susceptible to varicella disease.

The Research Analyst explained that the basic HZ incidence rate calculation was no longer applicable in a community with moderate to widespread varicella vaccination. Instead, scientific study of HZ incidence rates presently required that two separate true rates be calculated—one for each of the two vastly different cohorts of children present in the community with differing exposure histories to varicella: (1) for varicella vaccinated children who were reactivating at a low HZ incidence rate and (2) for children who did not receive varicella vaccine because they experienced a prior case of natural or wild-type varicella who were reactivating at a relatively high HZ incidence rate. He emphasized that it would be statistically invalid to combine these two cohorts and compute a single mean HZ incidence rate for this obviously bimodal distribution of HZ cases.

As the meeting concluded, Dr. Mascola, ignoring the issues of cost effectiveness and the incomplete disease suppression by the vaccine, suggested that if exogenous boosting were significant among children—the situation of high HZ incidence could perhaps be ameliorated by vaccinating not only those who never had chickenpox, but all children—including those with a prior history of natural chickenpox. But vaccinating children who have had natural chickenpox would result in them harboring not one but two strains of varicella zoster virus (VZV). As cell-mediated immunity to VZV diminished over time, this could result in an increased incidence of reactivation of HZ [30] by one or both strains (the wild-type and attenuated Oka-strains). Moreover, the potential existed for virulent mutations and reversions of VZV to emerge.

In what appeared to be an attempt to quash the unwanted outcomes in the years following 2000, the CDC and VASP began to manipulate vaccine efficacy data. Also, by failing to properly stratify the HZ incidence rates by varicella exposure history into (1) the rate for those vaccinated and (2) the rate for those who had had the natural disease, they sought to conceal: (a) the importance of exogenous boosting, (b) the increasing HZ incidence rates, and (c) the other unwanted outcomes that supported an immunologically-mediated link between varicella shedding and the incidence of HZ.

**Table 2:** Comparison of cumulative HZ incidence rates (in cases/100,000 person-years) determined by CDC/VASP authors [36] and Research Analyst [17].

| Varicellaexposure History Age in years | Cumulative 2000-2006 HZ incidence rate[36] (95% C.I.) | Cumulative 2000-2003 HZ incidence rate[17] | |
|---|---|---|---|
| | | Uncorrected (95% C.I.) | Ascertainment-Corrected |
| Vaccinated, 1-9 | **19** ( 15 - 25) | **14** ( 9 - 21) | 28 |
| Natural Disease, 1-9 | **239** (193 - 295) | **223** (180 - 273) | 446 |
| Natural Disease, 10-19 | **69** ( 61 - 77) | **61** ( 51 - 72) | 122 |

**Table 3:** Annual efficacy of single-dose varicella vaccine in households, VASP 1997-2002 [17].

| Year of Study | Vaccine efficacy percentage (95% C.I.) |
|---|---|
| 1997[a] | **87** (75-93) |
| 1998 | **94** (83-98) |
| 1999 | **96** (83-99) |
| 2000[b] | **86** (74-92) |
| 2001 | **74** (58-84) |
| 2002 | **59** (14-80) |

[a]37.9% varicella vaccination coverage among children aged 19 – 35 months
[b]82.1% varicella vaccination coverage among children aged 19 – 35 months

## CDC finds dramatic increase in HZ incidence rates among adults outside VASP and subsequently reports "inconsistent" findings from inherently confounded studies

Ironically, after initial years of declaring "no increase in HZ incidence," on June 16, 2005, Varicella Chief Seward and other CDC authors utilized the Massachusetts Department of Health survey data and reported, "age-standardized estimates of overall herpes zoster occurrence increased from 2.77/1,000 to 5.25/1,000 (90%) in the period 1999-2003" [31]. Regarding this average 18% annual increase during each of five years, the authors concluded, in part, "As varicella vaccine coverage in children increased the incidence of varicella decreased and the occurrence of herpes zoster increased. If the observed increase in herpes zoster incidence is real, widespread vaccination of children is only one of several possible explanations" [31]. This finding was similar to that reported earlier by VASP: HZ among adults (aged >20 years) increased 56.1%--from 237 reported cases in 2000 to 370 cases in 2002, also an average of approximately 18% annual increase during each of three years [16]. Later, additional surveillance for HZ demonstrated a statistically significant increase of 27.5% in reported HZ cases among adults aged >50 years, from 316 cases in 2006 to 404 cases in 2007 [16]. These are raw case reports that were not ascertainment corrected.

Some years later in 2010, CDC authors presented a new study that included adults aged 65 years and older [32] whose age-related decline in immunity placed them at higher risk of HZ reactivation and only served to confound the study of increasing HZ incidence solely due to the effects of exogenous boosting. Seemingly, this was done such that the obvious immunologically-mediated link between varicella and HZ could later be (1) touted as "inconclusive" and (2) peddled as "elusive" [33].

For nearly 15 years after varicella licensure, (with the exception of VASP and the Massachusetts Department of Health), the CDC neglected to conduct HZ incidence rate studies in adults. Was this intentionally done to mask the double-digit annual increases in HZ incidence rates within communities where varicella vaccination was widespread?

Finally, the CDC claimed that both prior- and post-varicella vaccine licensures, HZ incidence rates demonstrated a similar increasing trend. However, the increases were on the order of 2% to 4% annually and most of the children and adults in the study populations chosen by the CDC in the vaccine era were still receiving sufficient natural exogenous boosts to their immunity. In the pre-licensure period, studies such as Ragozzino et al., which reported a 35% increase in HZ incidence during 1944-1959 (16 years) [34], actually corresponds to an average annual HZ increase of 2.2% (35%/16 years)—substantially lower than the 18% annual increase in the HZ incidence rate reported in communities with widespread varicella vaccination.

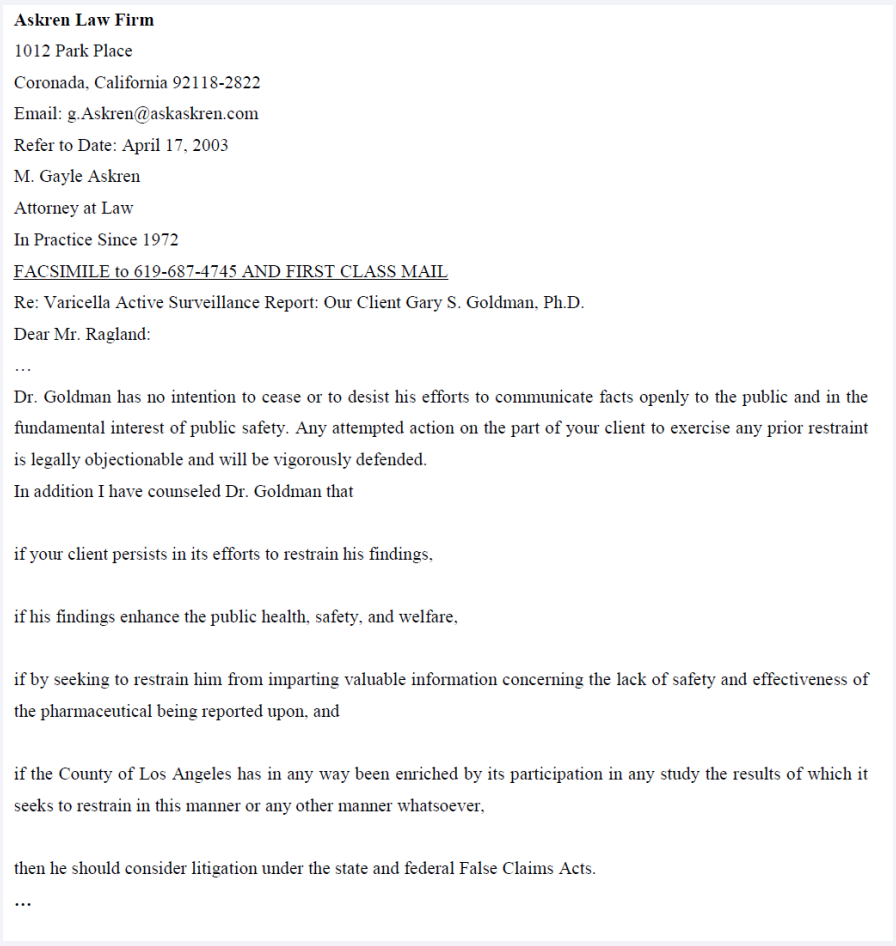
Based on the confounders present due to poor methodology and the results of inappropriate studies, CDC-funded researchers were reporting relatively low percentages of annual increases in HZ incidence rates that were more likely the result of (1) an aging population whose immune system was steadily declining, (2) the societal trend toward fewer adults and elderly living in the same household with children who provided exogenous boosting, and/or (3) a population with improved ease of access to healthcare that simply identified more HZ cases over time.

## CDC Varicella Chief cites two bogus studies to prove "no increase in shingles"

On several occasions, the Varicella Chief at the CDC made reference to a "Massachusetts Department of Public Health" (MDPH) study to justify her conclusion that "no increase in shingles incidence has occurred" during the Universal Varicella Vaccination Program. This study consisted of a phone survey with only a total sample size of 7,319 in the cohort of individuals aged 1- to 19-years during a two-year period, 1999 and 2000. It had insufficient statistical power to detect an increase in HZ incidence. By comparison, the AV-VASP was conducting HZ surveillance annually among some 100,000 individuals aged 1- to 19-years. Despite the MDPH study's obvious insufficiencies, its conclusion (and not the VASP's findings) was shared (1) at the September 2002 42nd ICAAC (Interscience Conference on Antimicrobial Agents and Chemotherapy) sponsored by The American Society for Microbiology during the question phase of the symposium on Varicella Zoster Virus (from 8:30 am to 11:00 am) with Dr. John Edmunds presenting *Potential Changes in Zoster Epidemiology with Childhood Immunization* and (2) with the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) in Australia.

Another CDC study, referred to as the Group Health Cooperative (GHC) and cited by the Varicella Chief in support of "no increase in HZ incidence", found no increase in HZ incidence [23], and was severely criticized because it was conducted in a population with low varicella vaccine uptake [24]. Since wild-type VZV was still circulating among the study population providing exogenous boosts, the HZ incidence rates had not yet been affected.

The vaccination rates in the Seattle, Washington population cohort comprising the GHC study were lower than the national average such that "few children (aged 1-9 years) had been vaccinated during 1996 and 1997" [23]. Thus, by 2002, the slow uptake of varicella vaccination was below the threshold necessary to impact HZ incidence. In a discussion of study limitations, the CDC authors acknowledged, "The study may



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In Practice Since 1972
FACSIMILE to 619-687-4745 AND FIRST CLASS MAIL
Re: Varicella Active Surveillance Report: Our Client Gary S. Goldman, Ph.D.
Dear Mr. Ragland:
…
Dr. Goldman has no intention to cease or to desist his efforts to communicate facts openly to the public and in the fundamental interest of public safety. Any attempted action on the part of your client to exercise any prior restraint is legally objectionable and will be vigorously defended.
In addition I have counseled Dr. Goldman that

if your client persists in its efforts to restrain his findings,

if his findings enhance the public health, safety, and welfare,

if by seeking to restrain him from imparting valuable information concerning the lack of safety and effectiveness of the pharmaceutical being reported upon, and

if the County of Los Angeles has in any way been enriched by its participation in any study the results of which it seeks to restrain in this manner or any other manner whatsoever,

then he should consider litigation under the state and federal False Claims Acts.
…

**Figure 3** Attorney for Research Analyst replies to notice to "cease and desist".

have been conducted too early to detect an increase attributed to decrease in exposure to varicella" [23]. By contrast, vaccination coverage of children between the ages of 19 and 35 months in the VASP region increased earlier and more rapidly following licensure, from 37.9% in 1997 to 82.1% in 2000.

The serious population-sample limitation of the GHC study was confirmed by the reported 1992-1996 varicella incidence rates of 14.54, 8.2, and 1.9 cases/1000 among children aged 1- to 4-years, 5- to 9- years, and 10- to 19 years, respectively, which were only 14.5%, 9.9%, and 15.6% of the respective "gold standard" 1990-1994 rates reported by The National Health Interview Survey (NHIS) in these same age categories. By contrast, the corresponding 1995 ascertainment-corrected incidence rates from the AV-VASP data were 91.5%, 99.8%, and 89.3% of the reported NHIS incidence rates, respectively [13,19].

## Capture-recapture estimates produce results that compare with a gold standard

Meaningful capture–recapture results require that a population is closed and that duplicate individuals can be matched. However, if the samples are not independent, the ascertainment sources can display dependence and heterogeneity of capture probabilities that can lead to inaccurate and sometimes misleading results [27].

The accuracy and robustness of the assumptions inherent to two-source capture-recapture estimates can only be determined if a "gold standard" exists to which the estimates can be compared. Capture-recapture methods applied to varicella cases reported via active surveillance during 1995 among those 1- to 19-years of age indicated under-reporting in excess of 50%. However, the ascertainment-corrected incidence of 50.9 cases per 1000 in VASP differed from the 1990-1994 National Health Interview Survey (NHIS)—the "gold standard"—by -4.2% [13]. The close agreement between this incidence rate and other stratified varicella incidence rates suggested the assumption of uniform reporting probabilities was plausible. Also, since the same surveillance units reported both varicella and HZ, it was logical to conclude that reporting completeness of both varicella and HZ might be similar.

Using only the raw number of HZ case reports to VASP, the cumulative 2000 to 2003 true HZ incidence rate was 14 (95% C.I. 9-21) cases/100,000 person-years among vaccinated children aged 1- to 9-years based on 21 cases reported during an observation time of 152,250 person-years. During this same period, the HZ incidence rate was 223 (95% C.I. 180-273) cases/100,000 person-years among children aged 1- to 9-years with a prior history of varicella based on 94 cases reported during an observation time of 42,096 person-years.

Thus, without the application of any statistical methods such as capture-recapture, the HZ incidence rate among children with a history of varicella was high [11,26] and near the pre-licensure rate usually associated with adults. These figures are shown in the 2nd column of Table 2.

Applying capture-recapture to VASP reports of HZ yielded 50% (as was expected) under-reporting of HZ cases. Thus, the last column of Table 2 shows the ascertainment-corrected incidence rate of 28 cases/100,000 person-years among vaccinated children aged 1- to 9-years. This closely compares to the HZ incidence rate among children aged 12 years and younger of 27.4 (95% C.I. 22.1 to 32.7) cases/100,000 person-years reported in the Tseng et al. study with a nearly 3-fold longer observation time of 446,027 person-years [35]. Likewise, applying capture-recapture to VASP reports of HZ among children with a prior history of varicella yields an ascertainment-corrected HZ incidence rate of 446 cases/100,000 person-years (Table 2).

## CDC Varicella Chief asks VASP Co-principal Investigators if Research Analyst has sufficient proof of deleterious effects

**Dr. Michael Oxman—Researcher heading Merck-funded Shingles Prevention Study:** In 2000 and 2001, the first two years of HZ surveillance, there was a statistically significant increase in reported HZ cases-from 189 to 235 or 24%, with increases in each 10-year age group (under 70 years of age) [16]. Knowing that Dr. Oxman was involved in a study of HZ incidence rates among adults and having noted an increasing trend in HZ incidence in the VASP, the Research Analyst phoned Dr. Oxman to share results and see if he was also seeing similar increases. Dr. Oxman was interested in learning more about the VASP findings but was travelling and would get back to the Research Analyst later.

After a few months, on December 26, 2000, Dr. Oxman contacted Dr. Jane Seward, the CDC Varicella Chief, via email to make an inquiry concerning who it was that had contacted him by telephone about shingles some months earlier and what VASP had found regarding the unexpectedly high HZ incidence rates among children. On January 2, 2001, Dr. Jane Seward, evidently realizing that the Research Analyst was the caller, asked Dr. Carol Peterson if they might confer as soon as possible over their response to Dr. Oxman. Later, that same morning, Dr. Peterson forwarded Dr. Seward's email to VASP Project Director Teresa Maupin who supervised the project from an office at High Desert Hospital in Lancaster, CA where two other assistants and the Research Analyst worked daily on the VASP. Dr. Peterson asked Teresa Maupin, "Did you know that Goldman had called Dr. Oxman?" She, however, did not know about this matter. Dr. Peterson explained, "Dr. Seward wished to call Dr. Oxman to explain thoroughly the reasons why the VASP investigators did not believe Goldman had data from the VASP that supported deleterious effects of the Universal Varicella Vaccination Program at this early date."

Dr. Seward emailed Dr. Oxman citing the deficient Massachusetts study indicating that declines in chickenpox following vaccination have yielded "no increases in shingles incidence rates." She also described several other current CDC-sponsored explorations of shingles-related issues. She concluded, "The data reported by Gary Goldman is highly preliminary and inconclusive since no baseline data exist to which Goldman's findings might be compared." She also further claimed that shingles diagnoses in Antelope Valley were too small in number to yield significant results. Interestingly, she shared with Dr. Oxman, "(Gary Goldman) was totally untrained in epidemiology and did not understand the severe limitation of the data issues involved." This was in contrast to a previous comment the Research Analyst had received from CDC modeler, Dr. John Glasser, "Your (Goldman's) work, while not mainstream epidemiology (not a criticism, why should it be?) is rather extraordinary. I believe that we can do some truly great work together, and communicate it to the folks who need to learn about it." Nevertheless, Dr. Seward stressed authoritatively that she "did not think it was appropriate for VASP to conclude anything definitive at this time from their shingles data collected through active surveillance by the AV-VASP."

The inadvertent discovery of the thread of emails regarding Dr. Oxman, in a notebook on the open shelf next to VASP surveillance data, did not deter the Research Analyst's continued probing into the issue of the extraordinarily high HZ incidence rates. Subsequently, the Research Analyst wrote an independent draft paper highlighting and discussing the findings of increasing HZ incidence rates among unvaccinated children with a prior history of chickenpox. He made a formal request to the Project Director to have the Co-Principal Investigators and appropriate individuals at the CDC review the manuscript and provide feedback so that any issues could be addressed prior to the VASP's submittal to a journal for publication.

The VASP annual report to the CDC for the year 2000 did not include additional discussion of the HZ case incidence rates nor did it differentiate between the HZ cases in varicella-vaccinated children and those children who had had natural (wild-type) varicella. The final report only included the number of raw shingles cases reported to the project [16]. Also omitted from the annual report were the results of the Adolescent Study from which the cumulative pre-licensure HZ incidence rate among children was derived. The adolescent study on varicella susceptibility that the Research Analyst had drafted was accepted word-for-word and eventually presented to the 36th National Immunization Conference in May 2002 [10]. However, the data and analysis of the HZ incidence rate among adolescents in that study was entirely deleted without any discussion on the matter [16]. This adolescent study consisted of a survey of 4,216 middle-school students in the AV-VASP surveillance region that measured varicella susceptibility and the cumulative HZ incidence rate among children [11]. Could it be that the HZ analyses were deleted because they (1) served as a surrogate for the pre-licensure baseline HZ incidence rate of children in the Antelope Valley and (2) demonstrated that the cumulative HZ incidence rate in the pre-licensure period was not abnormally high (as CDC and VASP had postulated), but typical of children elsewhere in the US [11]?

The Project Director provided no explanation as to why the analysis of the HZ incidence rate from the adolescent study was deleted in its entirety from the VASP annual report to the CDC.

**Dr. Philip R. Krause—FDA Lead Research Investigator:**

The Research Analyst reached out in February 2001 to Dr. Philip R. Krause, Lead Research Investigator at the Food and Drug Administration (FDA) Centers for Biologic Evaluation and Research (at that time). In a February 28, 2001 email, Dr. Krause thought that "the most intriguing shingles-related issue is the one that (Goldman) was working on—which is the question of how continuous re-exposure influences shingles rates." Dr. Krause concluded, "If exogenous (outside) exposures did contribute heavily to maintenance of immunity, the potential certainly existed that as a result of universal varicella vaccination, increases in wild-type shingles in the unimmunized and potentially also the immunized population might ensue."

Meanwhile, the VASP Co-Principal Investigators seemed content to not deal with this issue at all. In fact, Dr. Seward, the Varicella Chief, had previously stated to the Co-Principal Investigators, "Questions related to the effects of the varicella vaccination program on HZ were not designed to be answered by the AV-VASP."

**Dr. John Glasser, CDC Disease Modeler:** On May 4, 2001, Dr. John Glasser, with whom the Research Analyst had collaborated on the modeling of varicella cases in terms of high ambient air temperature and clustering of students in schools, indicated he would initially review the methods section of the HZ paper. Dr. Glasser had previously expressed his interest in modeling HZ disease and suggested that such a model could be confirmed through data collected by the AV-VASP.

However, the next day his response was "the conclusions were premature and that neither the Co-Principal Investigators nor CDC Chief will clear any manuscript on shingles for years." Dr. Glasser also shared, "I tell my Boy Scouts to lead by example, but I don't seem to be having much impact on you (Dr. Goldman)." He further admonished the Research Analyst to follow his example which involved "(a) clearing an abstract with superiors, (b) submitting this cleared abstract for presentation at a scientific meeting, and (c) then preparing a manuscript for publication in a peer-reviewed medical journal."

Was going through all those procedures, which Dr. Glasser had outlined before pursuing publication, really required? Were his multistep "routing" suggestions merely more excuses designed to discourage the Research Analyst from pursuing the entire shingles results issue, much less publishing his findings?

**Additional feedback from Dr. Krause:** Dr. Krause, likewise, considered the multi-step procedures outrageous, reasoning "Would CDC argue that Dr. Hope-Simpson or Harry Guess should never have published their study of shingles incidence rates? Unless scientific findings are publicized, the very foundation on which further results can be based is never built." Krause continued, "While some speculations on shingles may not be answered definitively for some number of years, this did not mean people wouldn't be interested in the most current data. Publication of the results might cause other investigators to look at the same question in different ways, making it unnecessary for the CDC to bear the full burden of future work on this issue."

Since VASP results were somewhat different from those previously published by others, an inquiring scientific mind should want to understand why. Dr. Krause concluded, "Even if the hypothesis that the unexpectedly high incidence rate of shingles is due to vaccination is wrong, the results raise interesting questions about variability of shingles rates and these could be very important in interpreting past and future studies."

## Research analyst prevented from conducting objective research

On May 9, 2002 during a VASP conference call with CDC Varicella Chief—Dr. Seward, the Co-Principal Investigators, Project Director, and Research Analyst, it was stated that the HZ papers were "in the process" of being reviewed. For months, the Research Analyst never heard anything concerning the review. It was now October, 2002, nearly 3 years of HZ incidence data had been collected, and it seemed that Dr. Glasser was correct as he intimated that no manuscript that contained deleterious effects of varicella vaccination would ever be approved for publication. The Research Analyst was denied permission to contact (via phone interview) ten individuals who had reported a second recurrence of shingles 12 months following their first reported case. Such interviews would have helped to resolve whether the high incidence rate in this cohort was due to rare exogenous exposures or alternatively, due to the higher risk of HZ reactivation associated with immunocompromised adults?

The Research Analyst was further directed not to pursue the analysis of the HZ incidence data. Given these severe restrictions on his conducting objective research and desiring not to have a part in what he perceived was research fraud, he resigned October 18, 2002, stating, "When research data concerning a vaccine used in human populations is being suppressed and/or misrepresented, this is very disturbing and goes against all scientific norms and compromises professional ethics."

Now, free from CDC/VASP sponsor bias, the Research Analyst could follow through and independently publish all the varicella and HZ data he had analyzed [11-15,17-20]. Since VASP is a publicly funded project by the CDC, the VASP data collected is available to any citizen through the Freedom of Information Act [16].

## CDC/VASP attempts to suppress publication of HZ data

**Notice to "cease and desist" publication:** Sometime after the Research Analyst's resignation, he notified VASP and CDC that he had planned to submit several papers that had been finalized for publication in a medical journal. He inquired as to whether VASP and/or the CDC wanted to be included in the authorship credits. As a response to this deferential solicitation, the Research Analyst received a notice from the County of Los Angeles Legal Department to "cease and desist" publication in a medical journal (Figure 2).

The Research Analyst phoned the attorney who had sent the notice, Lloyd Pellman, Esq., to discuss the reason for such notice. The Research Analyst asked Mr. Pellman, "Why does Dr. Mascola wish to prevent publication of my manuscripts? I've waited patiently for up to two years for her to review them and provide me with any comments or criticisms she might have had."

Pellman bluntly said, "She doesn't agree with your

conclusions."

The Research Analyst tried reasoning with Pellman, "I am sorry to hear that. However, it is not unusual for researchers to disagree about the meaning of research data. What specific points in my conclusion did she disagree with? Another renowned FDA scientist, Dr. Philip R. Krause, supported publication of my research findings."

Pellman responded, "I'm afraid you don't understand: She—or they—don't want your manuscripts published. Now, how can we resolve this matter?"

The Research Analyst suggested, "… I am willing to let the expert peer-reviewers and medical journal editors to whom I've submitted my manuscripts state their opinions and decide the issue."

Pellman said, "I don't think VASP will find this compromise acceptable."

The Research Analyst subsequently retained an attorney, Mr. Gayle Askren, whose reply (Figure 3) seemed to resolve any legal issues. Subsequently three of the Research Analyst's papers were published in 18 consecutive pages (pp. 4238-4255) in the October 1, 2003 issue of *Vaccine*, a well-respected European medical journal [11-13].

## CDC is critical of Research Analyst's three published studies

The CDC responded by writing a "Scientific Commentary" that was critical of the Research Analyst's methodology, results, and conclusions in all three *Vaccine* papers [11-13]. However, since no specific criticism was leveled against the study that assessed varicella incidence using capture-recapture methods [13], the National Library of Medicine linked only two of the three Research Analyst's studies with the "Scientific Commentary" at www.PubMed.gov [11-12]. Moreover, the CDC authors had denigrated the Research Analyst and his contributions to VASP in the initial version of their commentary. The Research Analyst's attorney responded to the CDC with a list of the defamatory, libelous, and inaccurate characterizations that CDC authors subsequently removed in the final proof version of the " Scientific Commentary".

The "Scientific Commentary" advocated the statistically invalid calculation of a single mean from a clearly bimodal distribution of HZ incidence rates among children with differing varicella exposures. The combined mean was neither well representative of the HZ rate among varicella vaccinated children nor the rate among children who had had natural varicela. The *Vaccine* journal editors published the Research Analyst's rebuttal response that included the warning, "Public policies that are based on invalid assumptions and conclusions may ultimately be damaging to public health" [14].

In 2004, the Research Analyst submitted a fourth paper that concerned a cost/benefit analysis of the varicella vaccination program taking into account the closely-related HZ epidemiology [15]. Although the editors of *Vaccine* accepted the paper for publication, a single phone call from the CDC to the Life Science Editor of *Elsevier* (who oversees publication of *Vaccine*) resulted in a one-year postponement of the print edition of the paper.

## In 2009, CDC authors publish VASP HZ incidence rates similar to those of the Research Analyst

Ironically, six years after publishing the "Scientific Commentary" critical of the Research Analyst's cumulative 2000–2003 HZ incidence rates, CDC and VASP authors in 2009 published cumulative 2000–2006 HZ incidence rates [36] that were not statistically different [17]. This time, CDC correctly stratified the children into two separate cohorts—those administered the varicella vaccine and those with a prior history of varicella (Table 2). CDC's additional years of "verified" HZ data produced only marginal improvements in the narrowing of the confidence intervals since the Research Analyst had used both the number of verified (i.e., interview was conducted with the case parent/gaurdian by phone) and probable (i.e., case was reported only by healthcare professional with no parent/guardian interview) shingles case reports [36]. Moreover, CDC authors incorrectly assumed 100% reporting completeness by not adjusting for under-reporting of HZ cases to VASP, producing incidence figures that were roughly one-half the true rates (Table 2).

## VASP findings support 1965 Hope-Simpson hypothesis

VASP staff had suggested that the 16-year study by Hope-Simpson presented a more robust calculation of HZ incidence rates compared to rates derived from VASP data. However, Hope-Simpson's HZ incidence rates for children <10 years old were based on a mean annual population of 510 children in Cirencester, England followed for 16 years, during which time there were only six reported cases of childhood HZ [26]. By comparison, the AV had over 100-fold more children (58,000), such that each year of observation time in the AV equated to approximately 114 years (58,000/510) of observation time in Hope-Simpson's small community [12,16,19]. Thus, confidence intervals produced by the quantity of HZ cases reported to VASP and length of observation time were much narrower than those of Hope-Simpson and reasonable compared to other studies reporting HZ incidence rates [26,28,29].

The analysis of VASP data trends in a population with widespread varicella vaccination was neither unusual nor unexpected. These outcomes had been anticipated decades earlier and now, for the first time, VASP was providing evidence in support of Dr. Hope-Simpson's 1965 hypothesis: "The peculiar age distribution of zoster may in part reflect the frequency with which the different age groups encounter cases of varicella and because of the ensuing boost to their antibody protection have their attacks of zoster postponed" [12,17,19,26].

## CDC masks declining varicella vaccine efficacy by failing to stratify results by year

Vaccine efficacy refers to the effectiveness of a vaccine to prevent disease. The increase in vaccine efficacy from 87% in 1997 to 96% in 1999 [17], demonstrated the "honeymoon" effect (Table 3) when the efficacy of the vaccine was enhanced or being boosted by the circulation of wild-type VZV concomitantly when reported cases of varicella still demonstrated the characteristic seasonality (Figure 1). Seward et al., in a study of contagiousness of varicella within households, reported only

the mean accumulative efficacy during 1997-2001 of 78.9% (95% C.I., 69.7% to 85.3%), stating that there was no statistically significant difference in efficacy at the 95% confidence level when the analysis was stratified by year [22]. This mean efficacy over five years, masked the fact that efficacy declined 22% (96%-74%) from 1999 to 2001—which while not significant at the 95% confidence level (z = 1.96), was significant at the 94% confidence level (z = 1.88) (Table 3).

### Shingles vaccine costs and failings

To prevent (1) a single case of shingles, (2) a single case of mild post-herpetic neuralgia (PHN), and (3) a single case of moderate to severe PHN, required the treatment of (or vaccine administered to) 59, 360, and 1000 adults, respectively, at a cost of US $11,800, $72,000, and $200,000 [37], based on the current cost of US $200 per dose for Zostavax®.

The relatively weakened immune systems of older adults (compared to young adults), when presented with a VZV challenge "may underlie their inability to contain VZV reactivation and prevent the development of HZ" [38]. One study conducted during 2009 to 2016 among a large cohort of adults aged 50 years and older demonstrated a shingles vaccine effectiveness of 50% the first year, decreasing to no effect by the fifth year [39].

## CONCLUSION

The Universal Varicella Vaccination Program was adopted based on three assumptions that all proved false [25]. Instead of a single varicella vaccine at a cost of US $35 providing lifelong immunity with no influence on the closely related HZ epidemiology, a booster vaccine is now required, yielding a cost of over US$230 for the two vaccines at current CDC pricing. Worse, a shingles vaccine for adults at US $200 per dose purportedly provides the protection from shingles they normally received at no cost from exogenous exposures to the children with chickenpox during its annual epidemics (prior to licensure of the varicella vaccine and initiation of the Universal Varicella Vaccination Program).

Varicella disease in the pre-vaccine era accounted for only 25% of the VZV medical costs. The other 75% of the VZV medical costs were attributed to HZ disease. In the post-vaccine period, universal varicella vaccination has created a disproportional increase in HZ costs associated with increasing HZ incidence especially among adults with a history of wild-type varicella [18].

As cell-mediated immunity to VZV wanes in vaccinated children following the administration of their final 4- to 5-year recommended booster dose, they too will begin reactivating HZ at increasing rates unless serially vaccinated for the rest of their lives. It is unfortunate that after 20 years of research, VASP and CDC authors have published relatively few studies on HZ incidence and recently stated in a 2016 publication that a 63% increasing trend in HZ incidence from 2000 to 2006 was documented among 10- to 19-year olds; however, the reason for "the increased incidence could not be confidently explained" [33]. Of course, the reported incidence rate in this cohort was not stratified by vaccination status—likely because such a proper analysis would have revealed (1) a low incidence rate among the majority of varicella vaccinated individuals and (2) an extraordinarily high rate among the pre-vaccination-era individuals with a history of wild-type varicella infection. Had those widely differing HZ incidence rates been reported separately, their difference would have provided a definitive answer to the question that the Research Analyst first asked back in 2000: Does universal varicella vaccination affect the epidemiology of HZ? Clearly, that answer was the Universal Varicella Vaccination Program increased the HZ incidence among those who had a case of "wild-type" VZV. Interestingly, the authors conceded, "the possibility persists that children infected by wild-type VZV experienced increased rates of HZ because they were having fewer opportunities to be exposed to exogenous VZV, leading to reduced immune control of HZ" [33].

Presently, two studies conducted in two different U.S. populations with widespread varicella vaccination, using different methods, found nearly the same 18% increase per year in HZ incidence reports: (1) VASP reported an HZ incidence rate increase of 56.1% over 3 years (2000-2002) [16,17] and (2) Massachusetts Public Health BRFSS reported an HZ incidence rate increase of 90% over 5 years (1999-2003) [31]. Additional analyses and studies conducted in communities with widespread varicella vaccination have supported both the increases in HZ incidence among adults [40,41] and the Hope-Simpson hypothesis [42-44].

Sentinel data from a Melbourne-based (Australia) medical deputizing service in the 15 years from 1998 to 2012 demonstrated a 50% decrease in the age-standardized varicella incidence risk, while the age-standardized incidence risk of HZ almost doubled [45]. However, vaccine uptake progressed much slower in Australia (compared to the US) and only during the last seven of 15 years was varicella vaccination funded under the National Immunisation Program (NIP) for all children at age 18 months.

How many more studies will be required before CDC or FDA recognize that universal varicella vaccination has adversely altered the closely-related HZ epidemiology [15,16], such that there is a negative cost/benefit and adverse outcomes to those vaccinated and even to those to whom the vaccines were not administered?

Defying all logic, in an attempt to counter both the VASP findings [16,17], and now, their own findings in Massachusetts [31], CDC continued to fund/sponsor studies lacking widespread vaccination coverage [23], seemingly to support its false claim that universal varicella vaccination has not led to increasing HZ incidence [24].

Prior to the Universal Varicella Vaccination Program, 95% of adults experienced natural chickenpox (usually as school age children)—these cases were usually benign and resulted in long-term immunity.

In the US, adults who had long-term, natural immunity in the pre-licensure era, are now compromised by waning cell-mediated immunity to VZV concomitant with mass varicella vaccination of children, which provides, at best, 70 to 90% immunity that is temporary and of unknown duration [46]. Moreover, increased risk of shingles aside, the Universal Varicella Vaccination Program will shift chickenpox to a more vulnerable adult population (especially among those who remain

unvaccinated, never acquired chickenpox, or initially received a single dose when vaccine efficacy was low) where chickenpox carries 25 times more risk of death compared to children aged one to four years [47], and 13 times more risk of hospitalization compared to children aged five to nine years [48]. Add to this the adverse effects and corresponding healthcare costs associated with the chickenpox and shingles vaccines as well as the long-term potential of excruciating pain caused by shingles events due to increased HZ incidence among adults. Therefore, unless it is ended, the Universal Varicella (Chickenpox) Vaccination Program now requires and will continue to require a lifetime-series of costly booster vaccines. In 2006, a costly HZ vaccine for adults was introduced to keep in check the otherwise increasing HZ incidence in that adult cohort. The adult shingles vaccine provides immunologic boosting (albeit limited) that was previously accomplished naturally, for free, and for a lifetime by an adult's exposure to circulating wild-type VZV.

Additionally, Canniff et al., report an association between those individuals with clinical or laboratory evidence of VZV infection and lower risk of glioma [49], suggesting a protective effect of VZV against glioma [49-51]. The authors explain, "The protective effect of prior VZV infection against the incidence of glioma may be mediated by cytotoxic T lymphocytes (CTL) that recognize epitopes shared by VZV and glioma cells" [49]. Additional research will be required to elucidate whether the vaccine-strain VZV offers this same protection as the wild-type strain against gliomas. Also, will vaccinated mothers have sufficient protective antibodies to VZV such that the incidence of infants born with congenital varicella syndrome remains rare?

Routine universal varicella vaccination against chickenpox has produced complex, continual cycles of treatment and disease [18-20]. While epidemics of wild-type varicella are rare after five or more years of widespread varicella vaccination, concomitant with a loss of the seasonal variation (Figure 1), lack of exogenous boosting has increased recurrence of HZ among those with natural varicella. VZV has not been eliminated. Both vaccinated and unvaccinated individuals are experiencing onset of chickenpox and/or reactivation as shingles due to (1) reversions of the attenuated (or Oka) vaccine strain VZV that cause wild-type virus pathogenicity [52] or (2) various heterologous (genetically different) strains of VZV, some strains of which have been shown to be antiviral resistant. Hence this fabricated cycle of disease and treatment has a substantial cost burden to the healthcare system and has caused distress even to those to whom the vaccine has not been administered. In 2018, Marchetti et al., suggest, "given current knowledge of HZ pathogenesis and exogenous boosting, targeted varicella vaccination of adolescents was the only [modeling] strategy that was not predicted to impact the epidemiology of HZ…." [53].

CDC and pharmaceutical industry-sponsored public relations campaigns, target the public and continue to promote that "vaccines are the safest of all medicines", "vaccines save lives", and "vaccination relies on science- or evidenced-based medicine", fostering an increasing demand for vaccine mandates. Based on the actions by the CDC to suppress deleterious outcomes, could it be that varicella vaccine policy and research was being unduly influenced by Dr. Julie Gerberding—who after serving as Director of CDC from 2002 to 2009, headed Merck's Vaccine Division which manufactures the varicella vaccine? Likely, a combination of financial conflicts of interests, lack of proper controls, and poor methodology in varicella studies commissioned by the CDC often yielded improper or confounded results and conclusions—producing research based on pseudoscience that should more appropriately be relegated to a faith-based belief system rather than the realm of science.

## AVAILABILITY OF DATA AND MATERIALS

The datasets supporting the conclusions of this article, collected via the Antelope Valley Varicella Active Surveillance Project, are available through the Freedom of Information Act (FOIA) request to Centers for Disease Control and Prevention (CDC, Atlanta, GA) through a request for the Antelope Valley Varicella Active Surveillance Project (VASP) Summary Reports provided by the Los Angeles County Department of Health Services; Cooperative Agreement No. U66/CCU911165-10.

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The study was conceived by the sole author, GSG who was involved in the planning, design, conduct, analyses, and reporting of the study.

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