CDC suppression of deleterious data associated with the US universal varicella vaccination program: the effect of declining exogenous exposures on herpes zoster incidence rates

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**Abstract:**

**Background:** A Research Analyst provides evidence that the Universal Varicella Vaccination Program dramatically altered the epidemiology of herpes zoster (HZ, or shingles) in the first decade following varicella vaccine licensure in March 1995, and describes how CDC misrepresented data to conceal the significance of exogenous (external) exposures in (1) augmenting varicella vaccine efficacy, and (2) helping to prevent or postpone reactivation of HZ. **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 Antelope Valley (Los Angeles, California) population of 300,000 residents. In 1995, VASP started collecting baseline epidemiological data pertaining to varicella disease (excluding herpes zoster). Active surveilliance for HZ began in 2000 in residents of all ages. Since reporting sites consisted of schools and medical providers, two-source capture-recapture statistics were applied to determine reporting completeness of varicella and HZ cases among children and adolescents, and compute ascertainment-corrected incidence rates. **Results:** Deleterious trends in vaccine efficacy due to declines in exogenous exposures were masked by averaging varicella vaccine efficacy over several years instead of stratifying efficacy by year. High HZ incidence rates among children who previously had varicella were initially masked by reporting a crude HZ incidence rate that included varicella-vaccinated children. In 2009, CDC first published unadjusted HZ incidence rates for 2000-2006 among children and adolescents; true rates in the population were approximately two-fold higher since capture-recapture estimated a reporting-completeness of 50%. VASP had a statistically significant increase of 56.1% in adult HZ case reports from 2000-2002. **Conclusions:** CDC mainly published selective studies with misrepresented data to support universal varicella vaccination and aggressively blocked the Research Analyst’s attempt to publish deleterious trends or outcomes, prompting his resignation in protest against what he perceived was research fraud.

**Keywords:**  Universal varicella vaccination program; varicella vaccine; varicella vaccine efficacy; herpes zoster incidence rates; varicella zoster virus; CDC suppression; research fraud

**Strengths and limitations of this study**

• Population-based active surveillance of varicella (since 1995) and herpes zoster (since 2000) in a community of 300,000 residents.

• Capture-recapture methods were used to determine reporting-completeness of varicella and herpes zoster case reports to derive estimates of population incidence rates instead of project-specific incidence rates.

• The assumptions inherent to two-source capture-recapture methods were tested by comparing ascertainment-corrected rates with rates from studies considered to be criterion standards.

• CDC confirmed unadjusted HZ incidence rates over longitudinal period of seven years (2000-2006)

• No baseline herpes zoster incidence data were available from 1995 to 1999. **1. 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 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 300,000 residents comprising the study population within the Antelope Valley region (principally two cities, Lancaster and Palmdale in California) beginning in 1995. In 2000, herpes zoster (HZ) was added to the active surveillance.

AV-VASP collected 100% of the biweekly varicella (chickenpox) case logs from all 300 plus reporting units (e.g., daycares, preschools, public and private schools, physicians, health care clinics, etc.) from 1995 to 2000. Moreover, the surveillance was able to detect sensitive trends early in the Universal Varicella Vaccination Program because of four contributing factors: (1) the survey region was relatively isolated geographically with few residents seeking medical providers 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 medical 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 2000 for varicella and 2000 through 2002 for herpes zoster. After the Research Analyst’s resignation at the end of 2002, the project continued through 2010.

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 VASP Co-Principal Investigators and the CDC 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 CDC in a format adopted by both CDC Health Scientist, John X. Zhang, and the Research Analyst. This allowed CDC to access VASP’s raw data for independent analyses.

From the project onset, the Research Analyst was encouraged by the Co-Principal Investigators to pursue any and all analyses and studies that might be suitable for publication. In fulfillment of this directive, the Research Analyst authored and co-authored studies that highlighted positive aspects of the varicella vaccination program. These studies were quickly approved by the CDC and VASP and subsequently presented and/or published [1-11]; other studies suggesting negative or deleterious findings [12-20] were either suppressed or disallowed, 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 him to publish all VASP data, in the absence of CDC and VASP sponsor bias, including evidence of the deleterious impact of the US universal varicella vaccination program on the closely related HZ epidemiology. [12, 13, 15- 20]

This review provides evidence of multiple actions taken by CDC that had the effect of masking undesirable findings and suppressing publication of deleterious data associated with the US universal varicella vaccination program. VASP data provides evidence that (1) single-dose varicella vaccine efficacy declined, and (2) significant increases in HZ incidence rates occurred within the first decade following widespread varicella vaccination due to diminished exogenous exposures to the circulating varicella virus. These findings are sufficiently robust to challenge other CDC and CDC-sponsored study conclusions that suggest the universal varicella vaccination program has had *no* impact on HZ incidence rates.

**2. Methodology**

When the Los Angeles County Department of Health Services, Acute Communicable Disease Control Unit, entered into a cooperative agreement with the CDC, no provision existed for VASP to initiate HZ active surveillance. Thus, no baseline HZ incidence data existed from 1995 through 1999 in the Antelope Valley study region.

Initially (from 2000-2002), the CDC/VASP advocated the calculation of a single crude HZ incidence rate among children aged <10 years [15]. This had the effect of masking the true HZ incidence rates among two distinct cohorts in that age category: (1) those who were administered the varicella vaccine, and (2) those with a history of varicella. [13,15-20] Moreover, due to incomplete case ascertainment, the percentage of completeness of HZ cases reported to VASP was unknown, producing HZ incidence rates that could be misleading. Thus, use of raw numbers of HZ cases reported to VASP produced only *unadjusted* HZ incidence rates that were VASP-specific, *not* population rates. Comparisons of such rates with rates published in other studies were problematic—especially if these other studies used different methodologies that involved more complete case ascertainment.

To scientifically study effects of universal varicella vaccination and concomitant loss of exogenous exposures (boosts) on the closely-related HZ epidemiology, the two significant confounders—use of *crude* and *unadjusted* HZ incidence rates—needed to be overcome.

**2.1 Using *true* versus *crude* childhood HZ incidence rates overcomes confounding**

Most studies in the pre-varicella licensure era computed *crude* HZ incidence rates using a denominator consisting of the number of *all* the age-specific individuals in the population—including individuals who were still susceptible to varicella and therefore incapable of developing HZ. [21-23] By contrast, *true* HZ incidence rates are computed using a denominator consisting of only those age-specific individuals with a history of varicella and therefore are capable of developing HZ. The difference between crude and true HZ incidence rates is greatest among children. Crude and true rates converge to the same value in older age categories since few individuals in these categories remain susceptible to varicella. It is commonly presumed that HZ incidence rates are low in children, then increase with age among adolescents and adults due to a decline in cell-mediated immunity (CMI) due to aging. This observation, however, is an artifact of using crude versus true rates.

Consider, for example, the 1960 to 1981 study by Guess et al. [22] This pre-licensure era study reported crude HZ incidence rates strictly increasing from 20 cases per 100,000 person-years (p-y) among children aged <5 years to 63 cases per 100,000 p-y among adolescents aged 15 to 19 years. [22] However, since an estimated 70% of children aged <5 years remained susceptible to varicella zoster virus (VZV) [12], the true rate is estimated at 67 cases per 100,000 p-y (among only children with a history of varicella) or very nearly the same rate found in the 15-19 age category. [22]

As another example, consider the 1947-1962 study by Hope-Simpson that reports a crude HZ incidence rate of 74 cases per 100,000 p-y among children aged <10 years and a higher rate of 138 cases per 100,000 p-y among adolescents aged 10-19 years. [21] Taking into account that an estimated 50% of children aged <10 years remain susceptible to VZV [12], the true rate is double, or 148 cases per 100,000 p-y—again similar to the rate found in the 10-19 category. [21]

Thus, using Hope-Simpson HZ rates as a reference, *true* HZ incidence rates in the pre-licensure era were more accurately represented by a step-wise function with a relatively constant HZ incidence rate (using rounded figures) of 140 cases per 100,000 p-y among individuals aged 1-19, then nearly doubling to 260 cases per 100,000 p-y among adults aged 20-49, then nearly doubling again to 500 cases per 100,000 p-y among adults aged 50-59. [21] The age category of elderly adults, aged 60 years and older, is excluded from analysis since this cohort includes sedentary individuals not under the influence of exogenous exposures—either before or after varicella licensure. Unlike younger adults, the elderly experience sharply rising HZ incidence rates due to diminished immunologic functions that are most pronounced in this cohort. This qualitative analysis of HZ incidence rates puts into better perspective 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.”* [21] Aging adults experience progressively fewer exogenous exposures to children shedding VZV, resulting in higher HZ incidence rates due to loss of subclinical immune boosts that help to prevent or postpone the onset of HZ. The commonly accepted belief that HZ incidence is low in children, then increases due to a decline in CMI caused by aging is erroneous. More correctly, the aging adults are more susceptible to HZ because they receive fewer exogenous exposures (boosts) to contagious children shedding VZV.

Some authors have argued that higher HZ incidence rates reported among adult women versus men seemingly contradicts the “exogenous boosting theory” since women have greater contact with children, and therefore the opposite correlation should be expected. However, women may simply exhibit different innate and adaptive immune system responses to VZV than men. [24]

Age-specific HZ incidence rates were calculated for children aged <10 years and adolescents aged 10 to 19 years. The cohort aged <10 years was further stratified by type of varicella exposure: (a) those who were administered the varicella vaccine and (b) those with a history of varicella. This allowed calculation of the risk ratio of HZ incidence rate among children with a history of varicella to the rate among varicella-vaccinated children.

**2.2 Capture-recapture statistics using two-source ascertainment**

It would be scientifically invalid to compare VASP unadjusted HZ incidence rates to rates reported in other studies that have high levels of case ascertainment. However, capture-recapture methods can report ascertainment-corrected HZ incidence rates that are (a) representative of the AV study population and (b) suitable for comparisons.

After attending a workshop sponsored by CDC, the Research Analyst implemented capture-recapture statistics using two-source ascertainment—schools and medical providers—to adjust for the under-reporting of case reports to VASP. This allowed the number of raw cases reported to VASP to be ascertainment-corrected. Instead of simply reporting incidence rates of HZ that were specific to VASP, capture-recapture methods considered the number of duplicate cases found in both ascertainment sources to determine the number of cases that VASP missed. The percentage reporting-completeness is calculated and the ascertainment-corrected number of case reports is used to estimate true HZ incidence rates in the AV study population. [13,14]

Use of capture-recapture statistical methods to compute ascertainment-corrected rates can produce misleading estimates that are either over- or under-estimates of the true population rates. [25] Therefore, determining the accuracy and robustness of the assumptions inherent to two-source capture-recapture estimates requires use of a gold standard (i.e., a reliable study) to which the capture-recapture estimates can be compared. Such “gold standard” study results were available for comparison with the ascertainment-corrected HZ and varicella incidence rates. The close agreement between these figures confirm reasonable accuracy and indicate that assumptions of source independence and homogeneity of capture probabilities are plausible.

***2.2.1 The “gold standard” study for varicella incidence***

In 1995, VASP case reports of varicella among those 1- to 19-years of age indicated under-reporting of approximately 46% using schools and medical providers as the two ascertainment sources. However, the ascertainment-corrected incidence of 50.9 cases per 1000 in VASP closely agreed with the 53.2 cases per 1000 reported by the 1990-1994 National Health Interview Survey (NHIS)—the “gold standard”—differing by less than 5%. [14]

***2.2.2 The “gold standard” study for HZ incidence***

Since the same VASP surveillance units (i.e., schools and medical providers) that reported varicella cases also reported HZ cases, it would be logical to expect to find the same or similar reporting completeness of HZ cases to VASP. Indeed, capture-recapture methods found a similar 50% reporting completeness of HZ cases. The Research Analyst reported an unadjusted, cumulative 2000-2003 HZ incidence rate of 14 cases/100,000 p-y (95% C.I. 9-21) among varicella-vaccinated children aged <10 years based on 21 cases during an observation time of approximately 150,000 p-y. [17] The ascertainment-corrected HZ incidence rate of 28/100,000 p-y among vaccinated children aged <10 years differed 2.2% from the cumulative 2002-2008 HZ incidence rateof 27.4/100,000 p-y (95% C.I. 22.7–32.7) among children aged ≤12 years based 122 cases during an observation time of 446,027 p-y reported by Tseng et al. [26]

**2.3 Surrogate for missing baseline HZ incidence rate among children**

CDC had VASP conduct a separate study among adolescents in the AV population. This study reported the cumulative 1987-1995 crude and true HZ incidence rates among children aged <10 years in the AV population which could serve as a surrogate in the absence of baseline HZ incidence data. [12] The *crude* (or population) age-specific HZ incidence rate reported in the adolescent study, 71 cases/100,000 p-y (95% C.I. 42-112) among children aged <10 years, was nearly the same as the 74 cases/100,000 p-y reported in the same age category by Hope-Simpson. [12,21] The *true* HZ incidence rate (among only those children aged <10 years with a history of varicella) confirmed our expectations from the discussion in Section 2.1 by being nearly double the crude rate at 145 cases/100,000 p-y (95% C.I. 86-228)—similar to Hope-Simpson’s 138 cases/100,000 p-y among adolescents in the next age category (aged 10-19 years). [12,21]

**2.4 VASP ascertainment-corrected, age-specific, HZ incidence rates are compared with pre-licensure era rates reported by Hope-Simpson**

Since Hope-Simpson’s HZ incidence rates [21] (a) closely agree with pre-licensure era HZ incidence rates reported in the AV adolescent study [12] and (b) are nearly double the rates reported by Guess et al, [22], comparing Hope-Simpson pre-licensure rates with VASP post-licensure rates is more appropriate and conservative.

Hope-Simpson, through rigorous efforts, likely achieved complete or nearly complete ascertainment of cases in Cirencester, England. Despite the wide confidence intervals associated with his small sample and observation times, Hope-Simpson’s rates have been confirmed by larger datasets from the Royal College of General Practitioners (RCGP), likely because his sample demonstrated societal mixing and homogenous properties that were representative of the larger population.

**3. Results**

Each of the three established VASPs (Antelope Valley, CA; West Philadelphia, PA; and Travis County, TX) reported dramatic decreases in annual varicella cases from 1995 to 2000. Results were published in the February 6, 2002 *Journal of the American Medical Association*. [8] This paper concluded: “Continued implementation of existing vaccine policies should lead to further reduction of varicella disease . . . throughout the United States.” [8] (The Research Analyst, a co-author of this study, initially opposed the study’s conclusion because it was premature—effectively based on only three years of varicella data and minimal HZ data—but acquiesced based on the good-faith expectation and promise from the VASP Project Director that VASP’s HZ findings would soon be published.)

In 1999, for the first time, school nurses began reporting to VASP their observations of an unexplainable increase in the number of cases of HZ (shingles) among school-aged children. In view of the imminent five-year (2000 through 2004) grant renewal, the Research Analyst proposed that HZ cases be reported to the already existing VASP. Beginning January 2000, CDC formally added the active surveillance of HZ. 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 (the vaccine manufacturer) included the apprehension that “There is additional concern that universal vaccination might result in increased rates of herpes zoster in vaccinated and unvaccinated individuals.” [27]

**3.1 CDC and VASP are slow to publish deleterious HZ incidence rates among children and ignore statistically significant increases in HZ case reports among adults**

The peak of a naturally occurring 3- to 4-year inter-epidemic cycle in clinical varicella cases happened to occur in 1995. In addition, vaccine coverage among 19- to 35-month-old children was only 18% and 37.9% by the fourth quarters of 1996 and 1997, respectively (Figure 1). [8] Thus, only from 1998 onward could the observed decline in varicella cases be attributed to the Universal Varicella Vaccination Program. Thus, the optimistic conclusions from CDC/VASP study [8] actually reflected vaccination trends occurring only during the last three years.

Increases in unadjusted HZ incidence among children would first be published in 2009. Statistically significant increases in HZ case reports among adults were never published.

**3.2 Analysis of varicella vaccine efficacy: first evidence of the significant effect of exogenous exposures on varicella zoster virus (VZV)**

Vaccine efficacy refers to the effectiveness of a vaccine to prevent disease. CDC published a study (Seward et al.), on the contagiousness of varicella within households, but reported only the mean accumulative varicella vaccine 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 [28]. This mean efficacy over five years, masked the fact that efficacy declined 22%, from 96% in 1999 to 74% in 2001—which while not significant at the 95% confidence level (z = 1.96), was significant at the 94% confidence level (z = 1.88) (Table 1). Further double-digit declines in vaccine efficacy in 2002 and thereafter were statistically significant.

**3.3 Increases in HZ incidence among children: second evidence of the significant effect of exogenous exposures on VZV**

          During the first five years of surveillance, universal single-dose varicella vaccination in the Antelope Valley appeared to be successful, with an 80% reduction in reported varicella cases, from 2,934 in 1995 to 587 in 1999 (Figure 1) [8].However, AV-VASP experienced a notable change following active surveillance of HZ starting in 2000. Tensions seemed to mount, first among CDC representatives, then among VASP Co-Principal Investigators, as VASP’s active surveillance for HZ in 2000 yielded an unexpectedly high HZ incidence rate among children with a history of varicella and then statistically significant increases in HZ case reports among adults in 2001 and 2002. (See Appendix I)

Using only raw numbers of HZ case reports to VASP, the cumulative 2000 to 2003 unadjusted HZ incidence rate was 14 (95% C.I. 9-21) cases/100,000 p-y among vaccinated children aged 1- to 9-years based on 21 cases reported during an observation time of 152,250 person-years (Table 2, column 3). [17] During this same period, the unadjusted HZ incidence rate was 223 (95% C.I. 180-273) cases/100,000 p-y among children aged 1- to 9-years with a history of varicella based on 94 cases reported during an observation time of 42,096 person-years (Table 2, column 3). [17] 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 [17,21-23] and near the pre-licensure rate usually associated with adults. [21,23]

Applying capture-recapture to VASP case reports of HZ yielded 50% reporting completeness that was relatively stable for various combinations of age groups <20 and years 2000 through 2003. (A sample capture-recapture calculation is shown in Table 3.)

Thus, the last column of Table 2 shows the ascertainment-corrected incidence rate of 28 cases/100,000 p-y among vaccinated children aged 1- to 9-years. This low HZ incidence rate among vaccinated children was as expected [26] and served as a control that physicians were not likely misdiagnosing HZ disease in children.

Likewise, applying capture-recapture to VASP reports of HZ among children with a history of varicella yields an ascertainment-corrected HZ incidence rate of 446 cases/100,000 p-y (Table 2). This HZ incidence rate among children aged <10 years was (a) nearly four-fold higher than the cumulative 2000-2003 ascertainment-corrected HZ incidence rate of 122 cases/100,000 p-y among adolescents, aged 10-19 years (Table 2), and (b) three-fold higher than the VASP surrogate cumulative 1987-1005 HZ incidence rate of 145 cases/100,000 p-y among children aged <10 years [12] (Table 2). *This high HZ incidence rate among children with a history of varicella seemingly added support to Dr. Hope-Simpson’s 1965 hypothesis [21] and VASP was the first post-licensure study to quantitatively report the rate in a population with widespread varicella vaccination.* The fact that the cumulative 2000-2003 ascertainment-corrected HZ incidence rate was similar to the pre-licensure era rate reported by Hope-Simpson [21] could be due to the fact that adolescents have more mature immune systems than children, not as sensitive to the near loss of exogenous boosting. However, the VASP HZ incidence rate among adolescents would experience a 63% increase between 2000 and 2006. [29] (See Section 3.4)

In 2009, CDC reported, “The estimated risk of herpes zoster among vaccinated children <10 years of age was 4 to 12 times lower than among children of similar age with a history of varicella.” [29] However, CDC neglected to mention that the Universal Varicella Vaccination Program, with concomitant loss in exogenous exposures, was responsible for this unprecedented increase in the cumulative 2000-2006 ascertainment-corrected HZ incidence rate of 478 cases/100,000 p-y (or 2 times the unadjusted rate of 239 cases/100,000 p-y reported by CDC in Table 2, column 2) among children aged <10 years with a history of varicella—dramatically higher than any historical HZ incidence rate reported for that age category.

Ironically, six years after publishing a “scientific commentary” critical of the Research Analyst’s cumulative 2000–2003 HZ incidence rates [15], CDC and VASP authors in 2009 published cumulative 2000–2006 HZ incidence rates [29] that were not statistically different. (Tables 2, 4). CDC correctly stratified the children into two separate cohorts—those administered the varicella vaccine and those with a history of varicella (Tables 2, 4). 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/guardian by phone) and probable (i.e., case was reported only by medical professional with no parent/guardian interview) HZ case reports [17,29]. CDC authors’ comparison of VASP unadjusted HZ incidence rates with rates in other studies having more complete case ascertainment was misleading. [29]

The VASP annual report to CDC for the year 2000 did not include additional discussion of the HZ incidence rates nor did it differentiate between the HZ cases in varicella-vaccinated children and those children with a history of varicella. The final report only included the number of raw HZ cases reported to the project [11].

**3.4 Statistically significant annual increases in HZ incidence among adolescents reported by CDC: third evidence of the significant effect of exogenous exposures on VZV**

During the first two decades post-licensure, VASP and CDC authors published relatively few studies on HZ incidence. A recent 2016 CDC study [30] sought to update a previous VASP study’s finding of a 63% increasing trend in unadjusted HZ incidence rates—from 59.5 cases/100,000 p-y (95% C.I. 42.7-82.9) in 2000 to 96.7 cases/100,000 p-y (95% C.I. 75.7-123.6) in 2006 among adolescents aged 10 to 19 years. No prior pre-licensure HZ study had ever reported an 8% (63%/7 years) annual increase in HZ incidence among adolescents. CDC and VASP authors conceded, the reason for “the increased incidence could not be confidently explained,” and “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.” [29, 30]

In 2000, adolescents aged 10-19 years had not been affected by the loss of exogenous exposures since their age-specific, ascertainment-corrected HZ incidence rate was 120 cases/100,000 p-y—similar to the 138 cases/100,000 p-y reported by Hope-Simpson in the pre-licensure era (Table 5). However, by 2006 the ascertainment-corrected HZ incidence rate was double, or 193 (or 2•96.7) cases/100,000 p-y—approaching the pre-licensure era incidence rate expected among adults (aged 20-49 years). [21]

**3.5 Statistically significant annual increases in HZ incidence among adults reported by VASP: fourth evidence of the significant effect of exogenous exposures on VZV**

By the end of 2001, the second year of HZ active surveillance, there was a statistically significant difference in the number of reported HZ cases among adults aged 20 to 69 years, from 158 cases reported in 2000 to 203 reported in 2001 (p<0.042, t=2.95, df=4)—an increase of 28.5% [11]. The number of reported HZ cases maintained or increased in every 10-year adult age category except elderly adults (70 years and older) (Figure 2). HZ case reports among adults continued to experience double-digit increases in subsequent years (2002 and 2003). [11]

CDC/VASP authors misrepresented that HZ surveillance was restricted to residents aged <20 years and chose not to publish statistically significant increases in adult HZ reports that occurred during 2000-2003. [29] The CDC Varicella Chief had expressed that the 300,000 residents (in 1995) of the AV was inadequate for the study of HZ. Yet, when responding to the question whether universal varicella vaccination was having an impact on increasing HZ incidence, the Varicella Chief stated, “no increase in shingles” based on a 1999-2000 study (discussed in Section 4.2) of HZ incidence *among individuals aged 1- to 19-years-old* with a mean annual observation time of 4,020 p-y or 30-fold less than that of VASP in that same age category (Figure 3).

**3.6 Statistically significant annual increases in HZ incidence among adults reported in a population outside VASP: fifth evidence of the significant effect of exogenous exposures on VZV**

Ironically, after initial years of declaring “no increase in HZ incidence,” on June 16, 2005, Dr. Jane Seward (CDC Varicella Chief) and other CDC authors utilized survey data from the Massachusetts Department of Public Health (MDPH) 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 90% increase in 5 years, or average annual increase of 18% (90%/5 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, or an average annual increase of approximately 18.7% (56.1%/3 years) [11]. 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 [11,17]. These are raw case reports that were not ascertainment corrected.

During 15 years post-varicella vaccine licensure, (with the exception of VASP and the Massachusetts Department of Health), the CDC conducted no population-based adult HZ incidence rate studies in communities with widespread varicella vaccination. This had the effect of masking double-digit annual increases in HZ incidence rates within such communities.

**4. Evidence of CDC obfuscation**

**4.1 VASP deletes separate study reporting HZ incidence rate among AV children**

In 2000, CDC had VASP conduct a separate study among adolescents with the purpose of investigating varicella susceptibility in the AV population. This study consisted of a survey to be completed by parents of high school students. The Research Analyst obtained authorization from VASP Co-principal Investigators to add several questions to the survey that would help determine HZ incidence rates. Upon collection of the survey data, the Research Analyst wrote a paper discussing the findings regarding varicella susceptibility and incidence of HZ. CDC/VASP accepted the paper precisely as the Research Analyst prepared it [10]; however, the section on incidence of HZ was deleted with no explanation. Moreover, the Annual Report to CDC only made mention of the varicella susceptibility findings and nothing regarding HZ incidence rate findings. [11] Following the Research Analyst’s resignation, he submitted the entire study to *Vaccine*. The paper was subsequently peer-reviewed and published. [12]

**4.2 CDC Varicella Chief cites two inadequate studies to prove “no increase in shingles”**

On several occasions, the CDC Varicella Chief made reference to the 1999-2000 MDPH survey to justify her conclusion that “no increase in shingles incidence has occurred” during the Universal Varicella Vaccination Program. This paper consisted of a phone survey with an inadequate sample size of 8,039 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 changes in age-specific HZ incidence. By comparison, according to the Antelope Valley 2000 census figure, the AV-VASP was conducting HZ surveillance among 118,685 individuals aged 1- to 19-years (Figure 3). Using a typical HZ incidence rate (characteristic of the pre-licensure era) of 140 cases/100,000 p-y in this cohort and 100% reporting completeness, the MDPH study would ascertain an estimated 6 HZ cases annually compared to VASP’s 166. Despite the MDPH study’s obvious insufficiencies, its conclusion—and not VASP’s findings—was shared by the CDC Varicella Chief at the September 2002 42nd Interscience Conference on Antimicrobial Agents and Chemotherapy and with the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases in Australia.

Another CDC study,the Group Health Cooperative (GHC) study, was cited by the Varicella Chief as having found “no increase in HZ incidence.” [32] This study was severely criticized because it was conducted in a population with low varicella vaccine uptake [33]. Since wild-type VZV was still circulating among the study population providing exogenous boosts, the HZ incidence rates had not yet been affected. 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.” [32] 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 have been conducted too early to detect an increase attributed to decrease in exposure to varicella” [32]. 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 [32]. 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 [14,19].

Finally, the CDC claimed that both prior- and post-varicella vaccine licensure, HZ incidence rates demonstrated a similar increasing trend. However, most of the children and adults in the early post-licensure study populations chosen by the CDC were still receiving sufficient natural exogenous boosts to their immunity. Several long-term studies in the pre-licensure era, such as by Ragozzino et al. reported a 35% increase in HZ incidence from 1944-1959 (16 years) [34], or average annual HZ increase of 2.2% (35%/16 years). However, this increase was substantially lower than the 18% annual increase in the HZ incidence rate reported in communities with widespread varicella vaccination. [11,31]

**4.3 Research Analyst prevented from (a) publishing papers on HZ incidence and (b) 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. Months passed without any reviews forthcoming. It was now October, 2002, nearly 3 years of HZ incidence data had been collected, and Dr. Glasser (CDC Modeler) was correct as he intimated that no manuscript that discussed preliminary deleterious effects of varicella vaccination would ever be approved for publication.

Finally, the Research Analyst was directed not to pursue further analysis of HZ data, including rates of HZ recurrence. Since “research” outcomes were now being driven by the CDC sponsors and the Research Analyst desired no 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 [12-20]. 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 [11].

**4.4 Research Analyst receives 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 5).

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 [Chief of the Acute Communicable Disease Control (ACD) unit for the Los Angeles County Department of Health's Public Health Programs & Services] 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 [Dr. Mascola] 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? A 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 6) 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 [12-14].

**4.5 VASP findings have substantially more observation time than Hope-Simpson and support the 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. [21] By comparison, the AV had over 100-fold more children (58,000), such that each year of observation time in the AV would require approximately 114 years (58,000/510) of observation time in Hope-Simpson’s small community. [15,19,22] Thus, confidence intervals produced by the quantity of HZ cases reported to VASP and length of observation time were (a) much narrower than those of Hope-Simpson and (b) reasonable compared to other studies reporting HZ incidence rates (Figure 4). [12,21-23]

**5. Recent studies continue to mask the effect of the Universal Varicella Vaccination Program on the closely related herpes zoster epidemiology**

A major limitation in the study of HZ incidence rate trends is the failure of all three CDC-commissioned varicella active surveillance projects (in Antelope Valley, CA, West Philadelphia, PA and Travis County, TX) to acquire baseline HZ incidence data during 1995-1999. Several recent studies attempt to retrospectively analyze such early trends in an attempt to fill in gaps in baseline HZ incidence data.

**5.1 Merck study shows consistent annual increases in the HZ incidence rate**

Now more than twenty years post-varicella vaccination, authors sponsored by Merck & Co. (the varicella vaccine manufacturer) produced a retroactive study of HZ incidence rates. [35] This study is an update to an earlier study of HZ incidence by CDC authors covering the period 1993-2006 using MarketScan data. [36] The Merck study by Wolfson et al covering the expanded period from 1991 to 2016 concluded “… that the annual incidence of HZ in adults increased at approximately the same rate … in the years before and after childhood varicella vaccination took effect.” [35] Yet, how robust of a conclusion can this be when authors commenting on the pre-varicella period conceded, “Significantly, health plan enrollment was not captured in MarketScan data sets for years 1991–1995, necessitating the imputation of the denominator for incidence rate calculations in this period; this could mean that rates in 1991–1995 were either overestimated or underestimated.” [35] Thus, 1991-1995 represents extrapolated—not actual—data. Further anomalies in the reporting of HZ incidence rates in the post-licensure period are considered below.

Quantitative analysis of the adults aged >65 years shows that HZ incidence increased 250% from 400 cases/100,000 population in 1991 to 1400 in 2012. [35] This 11.4% (250%/22 years) average annual increase was greater than that of any other age category. With the exception of the effects of aging, annual increases in HZ incidence should be lowest among elderly adults in comparison to other younger adults, since the elderly cohort includes those with sedentary lifestyles who simply do not have many opportunities for exogenous exposures (boosts) both prior to and post-varicella vaccine licensure. Moreover, the mean incidence rate in the >65 age group is subject to wide variations that reflect differences in age distribution, especially as higher proportions of septua-, octo-, and nona-genarians enroll in healthcare programs reporting data to MarketScan. Thus, use of this age group is a confounder when investigating HZ incidence rate trends.

Finally, it should be recognized that utilization of MarketScan databases may not reflect the true varicella and HZ incidence rates of the population. For example, the annual incidence rates of varicella in 1995 for children aged 1-4, 5-9, and 10-14 should approach those of the 1990-1994 National Health Interview Survey (NHIS) criterion standard which reported approximately 10000, 9300, and 1900 cases/100,000, respectively. Yet, the study by Wolfson et al reports approximately 1400, 900, and 200 cases/100,000, respectively [35]—only 7% to 10% of the NHIS 1990-1994 US population rates.

The Wolfson et al study describes “annual incidence of HZ increasing steadily from 1991 to about 2012 in the age categories >18 years.” [35] This translates quantitatively into a greater than 100% increase in HZ incidence over 18 years (1995-2012), or 5.6% annually. Certainly, this annual HZ increase reported in the post-varicella licensure period does not reflect the same order of magnitude increase reported in pre-licensure HZ studies such as by Ragozzino et al that found a 35% increase in HZ incidence over 16 years (1944-1959), or 2.2% annual increase. [34]

The authors conclude, “… no definitive conclusion about the contribution of exogenous boosting is possible,” and that is true due to the limitations inherent to the methodology used in this study. [35]

**5.2 CDC/Vaccine Manufacturer retrospective studies claim “no impact of Universal Varicella Vaccination on herpes zoster incidence”**

Several recent studies published in 2018 and 2019—all sponsored by the CDC—show a consistent increase in adult HZ incidence that is unchanged in the periods before and after varicella licensure, with annual increases of less than 6%. Additionally, the HZ incidence rate among younger, varicella-vaccinated age groups is shown to level off. [39-42] Of course, decreases in HZ incidence in the <10 and 10-19 year-old age categories would be expected as the proportion of varicella-vaccinated individuals (recently boosted by the vaccine) to those with natural disease increased. However, the vaccinees, with the near loss of exogenous exposures, would be candidates for later reactivation of VZV as HZ as adults.

Regardless of how these retroactive studies may be maneuvered to conclude that annual HZ incidence rates have “always been steadily increasing” and are not caused by the Universal Varicella Vaccination Program, VASP quantified dramatic increases in HZ incidence rates that had already occurred within the first decade following 2000, when exogenous exposures became rare. Logically, the HZ incidence rates of adults (aged <60 years) should level off at approximately 500 cases/100,000 p-y, the rate found in adults aged 50-59 years (Table 5), based on the Hope-Simpson hypothesis that these adults receive the least exogenous exposures relative to the other younger age groups. [12]

**6. Discussion**

The validity of the exogenous boosting hypothesis of Hope-Simpson [21] has been demonstrated in numerous studies with different methodologies and in different populations. [17,26,29,37,38] Two US studies demonstrated average annual adult HZ rate increases of 18%. [17, 31] This increasing HZ incidence rate among adults in communities with widespread varicella vaccination coverage is of greater magnitude compared to the relatively small annual HZ increases reported in the pre-licensure era that were attributed to aging and gradual changes in age-specific contact patterns. [34]

Five years post- licensure, in 2000 when exogenous exposures became rare and varicella no longer displayed its characteristic seasonality, the HZ incidence among children with a history of varicella approached 500 cases/100,000 p-y—a rate typically found among older adults (aged 50-59 years). [12, 21] This quantitative result is robustly reinforced by the fact that the HZ incidence rate among varicella-vaccinated children was at its expected low rate of 28 cases/100,000 p-y which served as a control. The HZ incidence rate among adolescents aged 10-19 years HZ incidence rate of 120 cases/100,000 p-y had maintained the same pre-licensure rate—likely due to the fact that adolescents have more mature immune systems than children. However, by 2006, the HZ incidence rate among adolescents with a history of varicella had increased 63% (or an 8% increase per year)—approaching 200 cases/100,000 p-y, the rate typical of younger adults (aged 20-49 years). [12, 21] Statistically significant increases occurred among adults during 2000-2003. Unfortunately, other than AV-VASP and the 1999-2003 MDPH studies that showed an average 18% annual increase in HZ incidence, no further population-based studies of HZ incidence were conducted in communities with widespread varicella vaccination during the first (or second) decade of the post licensure period.

Presently, other various theories that claim “no impact” of universal varicella vaccination have surfaced that are based on retrospective studies having far less robust data than that collected by VASP. Retrospective analysis of MarketScan and other health plan data have obscured double-digit increases in adult HZ incidence rates that occurred during the first decade following varicella licensure, by introducing numerous confounders that likely are the result of one or more of the following health plan study limitations: (1) use of a convenience sample rather than a random population sample, (2) changes in patterns of insurance enrollments and utilization, (3) preference toward large employers creating a homogenous study population that is not fully representative of the U.S. population, and (4) changing size of enrollments.

The CDC and VASP’s primary focus was to promote positive findings associated with varicella vaccination and encourage its uptake. There seemed to be a concerted effort by the CDC to deny and conceal a causative association between the Universal Varicella Vaccination Program and dramatic increases in adult HZ incidence rates as exogenous exposures became rare. While CDC and VASP disapproved of the Research Analyst’s investigation of deleterious trends in HZ data, he received support on less-controversial findings. For example, the Research Analyst’s model that quantified the number of varicella cases reported monthly to VASP garnered the attention of the CDC Varicella Chief. She had the Research Analyst collaborate with Dr. John Glasser, CDC Disease Modeler. Dr. Glasser confirmed the Research Analyst’s estimates of monthly cases of varicella reported to VASP (to an accuracy of 80%) based solely on population density (clustering of children in schools) and ambient air temperature (Figure 1). [1, 2]

Several actions that provide evidence of obfuscation and malfeasance by the CDC and AV-VASP are summarized in Table 6.

Two doses of a varicella vaccine for children and two doses of a herpes zoster vaccine for adults are likely to remain standard recommendations for years to come.

**7. Conclusion**

Some early opponents to the adoption of a US Universal Varicella Vaccination Program suggested that only those children who attained the age of 12 years without contracting natural varicella should be candidates for the varicella vaccine. This scenario would avoid increasing HZ incidence caused by the near absence of exogenous (outside) exposures (boosts) since the attenuated Oka-strain VZV comprising the varicella vaccine was much less contagious than wild-type or natural varicella. Exogenous boosts to cell-mediated immunity from circulating wild-type VZV were understood to be significant in postponing or preventing the reactivation of HZ. This concern was included in the *Summary Base Agreement* between the FDA and Merck (the vaccine manufacturer): “There is additional concern that universal vaccination might result in increased rates of herpes zoster in vaccinated and unvaccinated individuals” [27].

Although health authorities were uncertain of the impact that universal varicella vaccination of all children would have on the closely-related HZ epidemiology, such a program was adopted in the US based on three assumptions that all proved false [43]:

*Assumption 1*—A single varicella vaccine would be sufficient to confer long-term immunity. *Reality:* Currently two doses are required since efficacy induced by the single-dose protocol declines rapidly each year following vaccination, in the near absence of exogenous boosting that previously occurred from periodic exposures to cases of wild-type varicella. (Table 1).

*Assumption 2***—**The US Universal Varicella Vaccination Program would be cost-effectiveat $35 per dose, one dose required.*Reality:* A booster vaccine is now required, yielding a cost of over US $230 for the two vaccines at current CDC pricing.

*Assumption 3*—Universal Varicella Vaccination would have no impact on the closely related HZ epidemiology. *Reality:* Rates of HZ significantly increased following universal vaccination. 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 HZ 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.

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-licensure 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 recommended booster dose at 4 to 6 years of age, they too will begin reactivating HZ at increasing rates unless serially vaccinated for the rest of their lives. After twenty years and two recent studies [30,35], the question is still being asked: Does universal varicella vaccination affect the epidemiology of HZ? The answer is Yes, based on considerable population-based data collected by VASP and other studies.

There seems to be a double standard when it comes to publication of vaccine data: positive trends are readily published while deleterious trends are censored. Some studies are essentially propaganda rather than science. While appearing to present robust data, often vaccine studies utilize invalid statistical methods or selective data that mislead and promote inaccurate results and conclusions. In reality, the question appears to be not about the science, but more about greed and conflicts of interest that have influenced, dominated, and ultimately corrupted use of the scientific method.

The Research Analyst asked the following questions, and others should reflect on them as well:

• Why did all three CDC-funded VASPs fail to initially include surveillance of HZ? The extent to which the US Universal Varicella Vaccination Program would potentially impact HZ incidence rates was a fundamental issue and concern prior to initiation of the Program. The CDC's failure to obtain baseline HZ data would postpone early detection of HZ trends.

• Why did CDC approve the adding of active surveillance of HZ to VASP, but then illogically, the CDC Varicella Chief expressed that VASP was inadequate for the study of HZ?

• If the size of the AV study population (300,000 in 1995) was considered insufficient to conduct studies of HZ incidence, why did the CDC Varicella Chief rely on a 1999-2000 MDPH study whose observation time was 30-fold smaller than that of VASP to conclude “no increase in shingles had occurred during universal varicella vaccination.”

• Why did CDC reject VASP as a platform for HZ study when acertainment-corrected counts of HZ reports among vaccinated children confirmed their expected low incidence rate? Given this control, why was the ascertainment-corrected HZ incidence rate among children with a history of varicella censored?

• Why did CDC commission a study on the impact of universal varicella vaccination on HZ in a community where varicella vaccination was not yet widespread [32,33]? This had the effect of masking increases in HZ incidence.

• Why did CDC/VASP report a single mean varicella vaccine efficacy for 1997-2001 rather than stratify the efficacy by year to demonstrate the significant role of exogenous exposures in augmenting varicella vaccine efficacy?

• Why did CDC/VASP fail to stratify HZ cases by varicella exposure, instead, they reported a single mean of a bimodal distribution by combining both varicella-vaccinated individuals and those with a prior history of varicella into a single cohort? Again, this had the effect of masking increasing HZ incidence rates among children with a history of varicella.

• Why were the Research Analyst’s studies that demonstrated positive effects of varicella vaccination readily accepted by CDC/VASP for presentation and publication while studies concerning deleterious effects were disregarded, never reviewed , and/or suppressed for years?

• Why did the CDC provide an on-site workshop on the use of capture-recapture methods specifically to those involved in VASP, then illogically discourage their use?

• Following the Research Analyst’s resignation, why did Laurene Mascola, Co-principal Investigator of VASP, representing the County of Los Angeles Acute Communicable Disease Control Unit, issue a *Notice to Cease and Desist Publication* in a medical journal?

Presently, two studies conducted in two different U.S. populations with widespread varicella vaccination, using different methods, found similar 18% annual increases in HZ incidence rates: (1) VASP reported an HZ incidence rate increase of 56.1% over 3 years (2000-2002) [11,17] 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 confirmed both (a) the increases in HZ incidence among adults [44,45] and (b) the Hope-Simpson hypothesis that as exogenous exposures decrease, HZ incidence rates increase [37,38,46].

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 [47]. 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. Varicella in adults carries 25 times more risk of death compared to children aged one to four years [48], and 13 times more risk of hospitalization compared to children aged five to nine years [49]. Add to this the adverse effects and corresponding medical 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.

Routine universal varicella vaccination against chickenpox has produced complex, continual cycles of treatment and disease [18-20]. It has contributed to increased reactivation of VZV as 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 [50] or (2) various heterologous (genetically different) strains of VZV, some strains of which have been shown to be antiviral resistant. Hence, this manmade cycle of disease and treatment has a substantial cost burden to the healthcare system and has caused distress even to those in whom the vaccine has not been administered. In 2018, Marchetti et al., suggested, “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….” [51].

CDC and pharmaceutical industry-sponsored public relations campaigns target the public and continue to claim that “vaccines save lives” and “vaccination relies on evidenced-based medicine”, fostering an increasing demand for vaccine mandates. However, based on actions by the CDC to suppress deleterious scientific outcomes, it appears that the CDC as a regulatory agency may have been captured by the industry it is commissioned to regulate. A combination of financial conflicts of interest, lack of proper controls, and poor methodology in varicella studies sponsored by the CDC often yielded improper or confounded results and conclusions, producing research seemingly based on predetermined desired outcomes more similar to propaganda and promotional marketing than 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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**Table 1:** Efficacy of single-dose varicella vaccine in households, VASP 1997-2001 stratified by year [17] and CDC-reported mean efficacy [28].

|  |  |  |
| --- | --- | --- |
| **Year of Study** | **Vaccine efficacy percentage**a  **(95% C.I.)** | **CDC Reported Mean Efficacyb**  **(95% Confidence Limits)** |
| 1997c | 87 (75-93) | 78.9 (69.7-85.3) |
| 1998 | 94 (83-98) |
| 1999 | 96e (83-99) |
| 2000d | 86e (74-92) |
| 2001 | 74e (58-84) |

abased on household contacts aged <20 years

bbased on household contacts aged 1-14 years; but neglected transmission resulting from vaccinated (breakthrough) primary cases which increased in proportion from 3.4% in 1997 to 32.9% in 2001.

c37.9% varicella vaccination coverage among children aged 19 – 35 months

d82.1% varicella vaccination coverage among children aged 19 – 35 months

eCDC’s single mean efficacy masked the fact that vaccine efficacy declined more10% or more per year after 1999 when 50% of children aged <10 years had been vaccinated. The 20% decline in vaccine efficacy from 1999 to 2001is not statistically significant at the 95% confidence level (*z* = 1.96), but is significant at the 94% confidence level (*z* = 1.88).

**Table 2:** Comparison of cumulative HZ incidence rates (in cases/100,000 person-years) determined by CDC/VASP [29] and Research Analyst [17].

|  |  |  |  |
| --- | --- | --- | --- |
| **Varicella exposure History Age in year**s | **Cumulative 2000-2006 HZ incidence rate [29]**  **(95% C.I.)a** | **Cumulative 2000-2003**  **HZ incidence rate [17]** | |
| **Un**adjusted **rate**  **(95% C.I.)a** | **Ascertainment-**  **corrected rateb** |
| Vaccinated, 1-9 | **19** ( 15 - 25) | **14** ( 9 - 21) | 28c |
| Natural Disease, 1-9 | **239** (193 - 295) | **223** (180 - 273) | 446d |
| Natural Disease, 10-19 | **69**f( 61 - 77) | **61**f ( 51 - 72) | 122e,f |

**a**CDC/VASP authors confirm HZ incidence rates (with only slight narrowing of 95% confidence intervals) initially derived by Research Analyst using unadjusted, raw counts of reported HZ cases.

bThe ascertainment-corrected rates were approximately double when capture-recapture methods were applied which indicated 50% reporting completeness of HZ cases (the same reporting completeness found in the reporting of varicella cases).

cThis HZ incidence rate agrees with the rate reported in a larger study. [26]

dThis HZ incidence rate is more than 3-fold higher than the expected true HZ incidence rate in the pre-licensure era. [12, 21]

eThis HZ incidence rate among those aged 10-19 years is similar to the expected pre-licensure rate and so unlike the younger category aged <10 years, those in the next category aged 10-19 years with more mature immune systems that are not as sensitive to the early decrease in exogenous exposures during 2000-2003. [21]

fThe table shows the mean or cumulative HZ incidence during the indicated range of years. The raw or unadjusted annual HZ incidence rates among adolescents aged 10-19 years with a history of varicella increased 63%--from 59.5 cases/100,000 person-years (95% C.I. 42.7-82.9) in 2000 to 96.7 cases/100,000 p-y (95% C.I. 75.7-123.6) in 2006 [29]—with an ascertainment-corrected rate of 193 cases/100,000 p-y in 2006.

**Table 3.** Two-source **c**apture-recapture methods for ascertainment-corrected HZ cases reported to VASP among individuals aged 5 to 19 years with a history of natural varicella during 2000 and 2001,

|  |  |
| --- | --- |
| **Capture-Recapture Inputs** | **Raw number of HZ case reports** |
| *c* Cases reported only by Medical Providers | 72 |
| *b* Cases reported only by Schools: | 35 |
| *a* Duplicates reported by both Medical Providers and Schools | 19 |
| *a + b + c* Total different HZ Case Reports enumerated | 126 |

|  |
| --- |
| **Capture-Recapture Results (using Lincoln-Peterson Estimate)** |
| No. of HZ cases missed: *d* = *b* • c/(*a* +1) = 126 |
| Ascertainment-corrected no. of HZ cases: *p* = (*a*+*b*+1)(*a*+*c*+1)/(*a*+1) - 1 = 252 |
| Percentage Reporting completeness: 50% (95% C.I. 34-65%)1 |

1Goodness-of-fit confidence intervals [14]; reporting-completeness was stable using various combinations of age groups <20-years-old and years (2000-2003)

**Table 4.** Comparison of CDC [29] and Research Analyst [17] derivations of *unadjusted* HZ incidence rates (per 100,000 person-years) among varicella-vaccinated children and children with a history of varicella aged <10 years, 2000-2003 and cumulative.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Year | Varicella-vaccinated children | | | | Children with a prior history of varicella | | | |
| CDC | | Research Analyst | | CDC | | Research Analyst | |
| No. of Casesa | HZ incidence ratec  (95% C.I.) | No. of Casesb | HZ incidence ratec  (95% C.I.) | No. of Casesa | HZ incidence ratec  (95% C.I.) | No. of Casesb | HZ incidence ratec  (95% C.I.) |
| 2000 | 4 | 17 (6-45) | 4 | 15 (4-38) | 35 | 316 (227-441) | 38 | 236 (167-323) |
| 2001 | 5 | 16 (7-39) | 5 | 14 (5-33) | 20 | 234 (151-362) | 27 | 251 (169-371) |
| 2002 | 7 | 20 (9-41 | 6 | 14 (21-53) | 8 | 135 (67-269) | 13 | 156 (83-267) |
| 2003 | 9 | 23 (12-43) | 6 | 12 (5-27) | 10 | 227 (122-423) | 16 | 232 (133-295) |
| Cumulatived | 51 | 19 (15-25) | 21 | 14 (9-21) | 84 | 239 (193-295) | 94 | 223 (180-273) |

aCDC made adjustments in number of cases sometime after the actual year of surveillance.

bResearch Analyst included probable HZ cases; whereas, CDC did not.

cHZ incidence rates are similar between CDC and Research Analyst despite differences in methodology of determining the at-risk population.

d CDC cumulative years 2000-2006 (CDC data not shown for 2004 through 2006); Research Analyst cumulative years 2000-2003.

Abbreviations: CDC – Centers for Disease Control and Prevention;

**Table 5**. Comparison of HZ incidence rates (cases/100,000 person-years) reported by Hope-Simpson [21], VASP Adolescent Study [12], and Research Analyst [17] among individuals with a history of natural (wild-type) varicella

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Hope-Simpson  1947-1962 cumulative  crude HZ  incidence rate [21] | VASP Adolescent Study [12] 1987-1995 (pre-licensure) | | Research Analyst in 2000 [17]  (5-years post-varicella licensure) | |
| Age category  (years) | *crude* HZ  incidence rate | *true* HZ incidence rate | unadjusted HZ  incidence  rate | Ascertainment-  corrected HZ  Incidence rate |
| <10 | 74a | 71 (42-112) | 145 (86-228) | 236 (167-323) | 472 |
| 10-19 | 138 | --- | --- | 60c (43-83) | 120c |
| 20-49 | 260b | --- | --- | --- | --- |
| 50-59 | 509 | --- | --- | --- | --- |

a74 cases/100,000 p-y is the crude or population rate among all children aged <10 years; since approximately 50% of children in this cohort have never had varicella and herpes zoster is not possible, the true rate is approximately double (or 148 cases/100,000 p-y) among only those children with a prior history of varicella and similar to the rate in the next 10-19 age category. The crude rate approaches the true rate in the other age categories since those categories contain few individuals still susceptible to varicella.

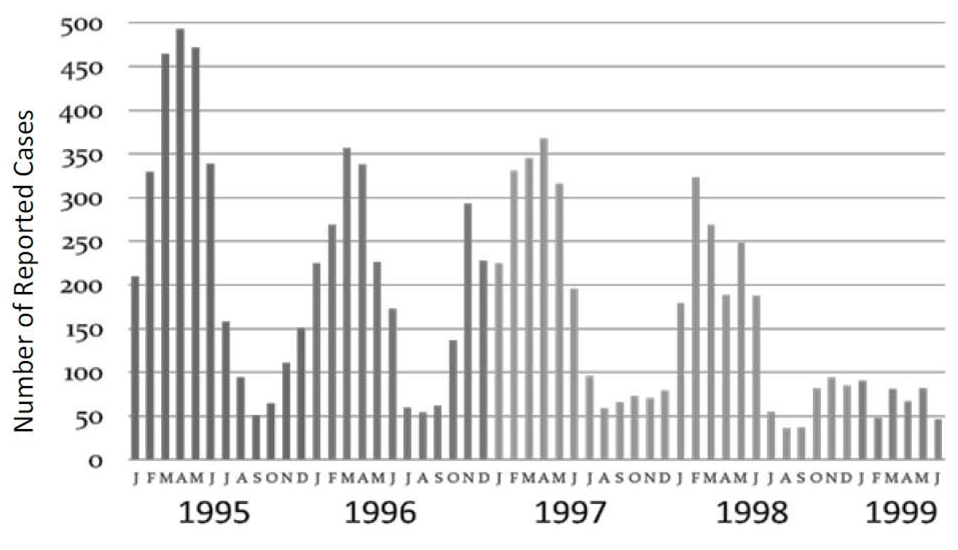
bThis is the mean of age categories 20-29, 30-39, and 40-49 which reported HZ incidence rates of 258, 229, and 292 cases/100,000 p-y, respectively.

cBy 2006, the unadjusted rate had increased 63% to 96.7 cases/100,000 p-y (95% C.I. 75.7-123.6); or an ascertainment-corrected rate of 193 cases/100,000 p-y. [29]

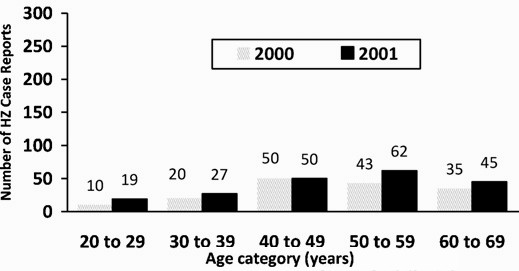
**Table 6:** Actions by the CDC and AV-VASP contributing to obfuscation and malfeasance.

|  |
| --- |
| • Started monitoring cases of chickenpox immediately when the Program began but waited five years before monitoring HZ (shingles) cases. Thus, active-surveillance baseline data for HZ cases did not exist.  • Published mainly positive findings related to decreases in varicella disease and related hospitalizations while disregarding and/or suppressing publication of the deleterious impact on the closely-related HZ epidemiology.  • Improperly calculated the crude HZ incidence rate among children aged <10 years by averaging two distinct cohorts—those who were vaccinated and those with a prior history of varicella—masking the high HZ incidence among children with a history of varicella.  • Reported a single mean for varicella vaccine efficacy 1997-2001. Failure to stratify efficacy by year masked the important role of exogenous exposures in augmenting vaccine efficacy (Table 1).  • After 7 years (2000-2006) of data collection and 3 additional years to publication, the CDC published VASP unadjusted HZ incidence rates; the true population rates were double based on 50% reporting completeness (Table 2).  • Never utilized capture-recapture methods to adjust for under-reporting of HZ cases to VASP (Table 3).  • Did not show concern that HZ incidence among children aged <10 years with a history of varicella was approaching the HZ incidence rate reported in older adults (Tables 4 and 5).  •Utilized active surveillance to monitor a decrease in varicella cases (Figure 1), but when VASP data provided evidence of a statistically significant increase in HZ cases, the CDC argued that active surveillance should not be utilized.  • CDC/VASP authors falsely claimed that HZ data was restricted to collection in residents aged <20 years. However, VASP collected HZ case reports in residents of *all* ages that demonstrated statistically significant increase from 2000 to 2001 with reported cases maintaining or increasing in each adult age category (<70 years). (Figure 2).  • Cited a study that had insufficient statistical power to conclude that there was "no increase in shingles" attributable to universal varicella vaccination (Figure 2).  • Claimed that confidence intervals on HZ incidence calculations were too wide and not sufficiently longitudinal when the number of HZ cases reported to VASP and observation time were either similar to or exceeded that of other published studies (Figure 3).  • 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 (Figures 4 and 5).  • Suggested that the 16-year HZ incidence study by Hope-Simpson produced more reliable rates than those derived from the AV-VASP data, when VASP, in a single year, demonstrated an observation time in children and adolescents more than 100-fold.  • Directed the Research Analyst not to pursue further analysis of HZ trends.  • Attempted to discredit the Research Analyst whose objective, in an act of transparency, was to publish preliminary data 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 natural (or wild) chickenpox.  • Justified adding varicella vaccination to the Immunization Schedule based on societal (not medical) considerations.  • 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.  • Conducted a study of HZ incidence in a population where the varicella vaccination had not been widely administered which had the effect of producing false evidence that the Universal Varicella Vaccination Program had no effect on the closely related epidemiology of HZ.  • Claimed that trends of increasing HZ incidence rates had already begun prior to the start of universal varicella vaccination, but these pre-licensure HZ incidence rates were of lower magnitude than those in communities where varicella vaccination was widespread.  • Promoted and distributed the varicella vaccine while having a bias concerning the reporting of individual and population-level harmful effects of the varicella vaccination program. |

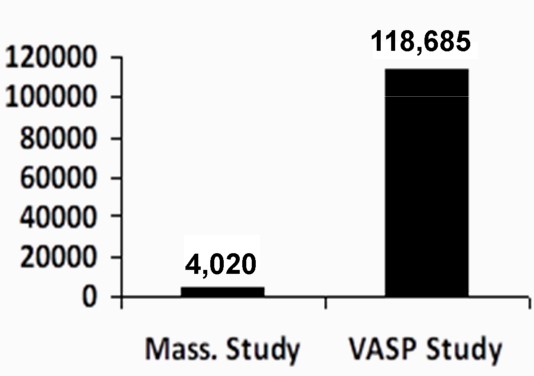
**Figure 1.** Seasonal variation in reported varicella cases, Antelope Valley VASP 1995-1999 [19].

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**Figure 2.** Herpes Zoster case reports among adults aged 20 to 69 years, Antelope Valley VASP 2000-2001 [11]



**Figure 3.** Comparison of mean annual observation time (in person-years) of the 1999-2000 Massachusetts Department of Public Health (MDPH) and 2000 VASP studies among individuals aged 1-19 years.



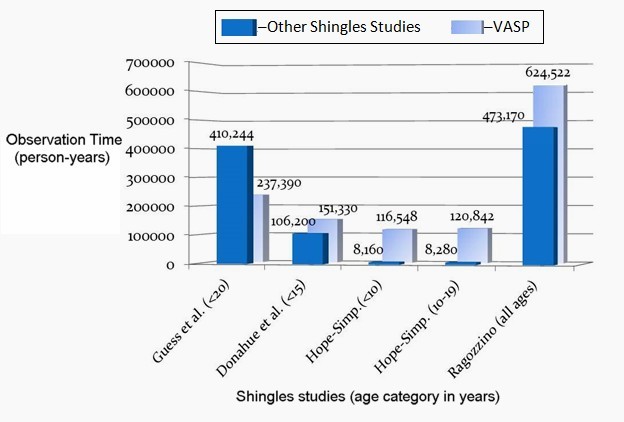
**Observation Time\***

**(person-years)**

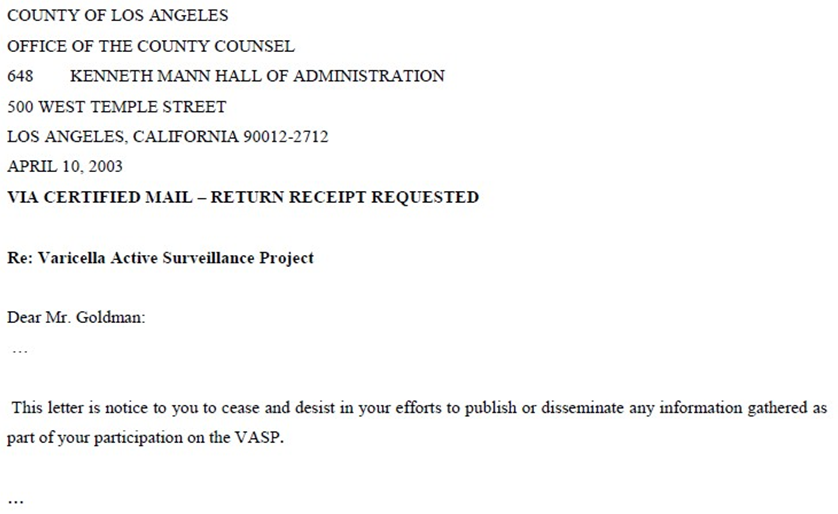
\*4020 is the mean of 4,916 and 3,123 individuals enrolled in the Behavioral Risk Factors Surveillance Systems (BRFSS) study during 1999 and 2000, respectively; 118,685 is the 2000 Antelope Valley population census figure for those aged 1-19 years. CDC Varicella Chief cited the MDPH study to conclude “no increase in shingles incidence” while declining to share true HZ incidence rates among vaccinated and unvaccinated individuals aged 1 to 19 years during 2000 from VASP that were based on a 30-fold greater observation time.

**Figure 4.** Comparison of 2000-2001 VASP observation times with other shingles studies

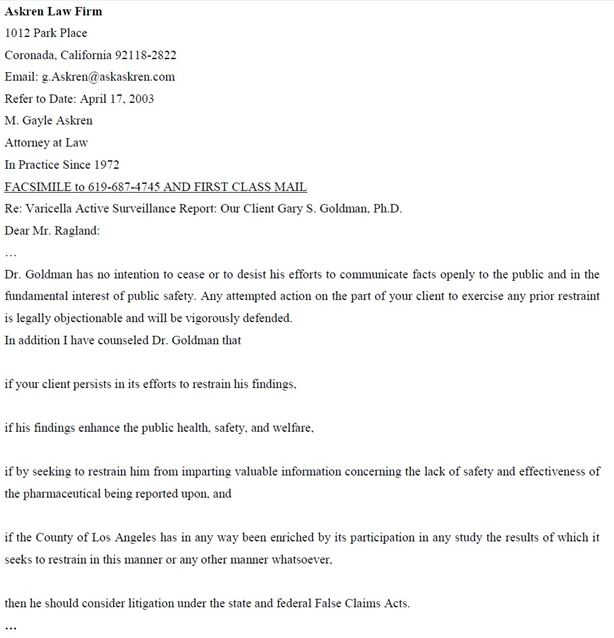
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**Figure 5.** Notice to Research Analyst to “cease and desist” publication

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**Figure 6.** Attorney for Research Analyst replies to “cease and desist” notice

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**Appendix I. CDC Varicella Chief explains the reasons why VASP investigators did not believe that the Research Analyst had data from the VASP that supported deleterious effects of the Universal Varicella Vaccination Program**

Learning that Dr. Michael N. Oxman headed the Merck-funded Shingles Prevention Study Group, the Research Analyst phoned him in October, 2000 to ask if he was observing notable increases in adult HZ incidence rates—perhaps augmenting the VASP finding of high HZ incidence among children and adults having a history of natural varicella. (Merck & Co. manufactures the varicella vaccine.) 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 had made the initial contact, asked VASP Co-principal Investigator, 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 VASP. Dr. Peterson explained to the VASP Project Director, “Dr. Seward wished to call Dr. Oxman to explain thoroughly the reasons why 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 1999-2000 MDPH survey (reporting HZ incidence among individuals aged 1- to 19-years-old) indicating that declines in chickenpox following vaccination have yielded “no increases in shingles incidence rates.” (Figure 3) 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 (incorrectly) claimed that shingles diagnoses in Antelope Valley were too small in number to yield significant results (Figure 4). 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 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.

***Comments from the 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) Center for Biologics Evaluation and Research. 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 AV-VASP.”

***Comments from the CDC Disease Modeler***

On May 4, 2001, Dr. John Glasser, the CDC Disease Modeler 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 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 instructed 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.”

***Additional comments from the FDA Lead Research Investigator***

The Research Analyst requested additional feedback from Dr. Krause who considered that the multi-step procedures were outrageous. He reasoned, “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 the reason 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.” Dr. Krause continued, *“However, even if they have full legal control of the data, I would hope the CDC does not want to be in a position where they are preventing publication without even reading the manuscript. Some pharmaceutical companies have been severely criticized for over-enforcing these types of agreements. This would create the impression that they are trying to manipulate the scientific data to prevent publication of data that could adversely influence immunization rates, regardless of the potential public health consequences.”*