Science, Public Health Policy, and The Law
Volume 1:21-23
August 1, 2019

An Institute for Pure and Applied Knowledge (IPAK)
Public Health Policy Initiative (PHPI)

Excess Teen Suicide Risk Associated with Gardasil™ Exposure: Implications for Public Health Policy

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Abstract
There are likely but hitherto unreported safety signals for Gardasil™ vaccine in the form of increased risk of suicides and deaths from all causes in clinical trial group exposed to the Gardasil vaccine. Comparison of suicide rates in the two exposure clinical groups yielded relative risks of 3.53 and relative risk of death from all causes of 1.77 compared to CDC-reported baseline suicide rates. Since these are the only clinical trial data available on the question, public health policy on Gardasil recommendations should be updated and as soon as possible, new clinical studies focused on suicide rates utilizing inert placebo (i.e., truly saline-only) vs. vaccine clinical group comparisons must be undertaken.

Keywords
Gardasil™, suicide, drug overdose, clinical trials, adverse events, vaccine safety

Contents

1. Introduction

Suicide rates have been on the rise in the US since 2006 [1]. The Merck Quadrivalent vaccine Gardasil was designed to protect against four strains of human papillomavirus and was approved by the FDA in 2006. At that time, recommendation for use in young girls was implemented following limited clinical studies with admixed control groups [2].

2. False Equivalence Masking Suicide Risk Signal

Without explanaiton, Merck combined the outcome groups of 'drug overdose' and 'suicide'. Page seven of the FDA package insert for Gardasil™ presents data on deaths from all causes during the clinical trials, and death by suicide. There are three concerning details in the data that may warrant further investigation. One cause for concern is the fact that the document does not differentiate between death by drug overdose from death by suicide. The document creates a combined category defined as "drug overdose / suicide." Any single death in a

clinical trial is carefully documented and reviewed. The fact that Merck chose to merge these two categories of deaths together is irregular and outside the realm of normal protocol for Stage III clinical trials. A second cause for concern is the high relative risk for "drug overdose / suicide" in the clinical trial described. The Gardasil™ package insert states "drug overdose / suicide: (2 individuals who received GARDASIL and 6 individuals who received AAHS [amorphous aluminum hydroxyphosphate sulfate] control." Given that all participants in the trial were exposed to the vaccine, to AAHS, or both, it is important to note the risk of drug overdose/suicide should be assessed for all of the trial groups, and measured against a similar group *not* in the clinical trial. In the clinical trial, 15,706 participants received the Gardasil shot as it was then formulated, containing amorphous aluminum hydroxyphosphate sulfate as an adjuvant (as Gardasil-9 (Nonavalent) vaccine still contains today); 13,023 of the trial group received injections of AAHS. There was no inert placebo control group for this trial. Thus, the clinical trial group to be assessed is that of 28,729 trial participants all exposed to vaccine relevant doses of AAHS, compared to a similar cohort not exposed to AAHS. The outcomes to be assessed are death by "drug overdose / suicide" and death by all causes.

3. Over 300 Percent increased Risk

The eight "drug overdoses / suicides" in the 28,729 combined clinical trial participants equates to 27.2 per 100,000 study participants committing suicide. In same-age groups of females in the general population during that same time period, there were only 7.7 per 100,000 suicides, per official CDC death statistics. [2]. The apparent relative risk from suicide in the AAHS exposed groups is 3.53 or 353% of the expected number compared to non AAHS exposed general population. Study participants are carefully screened for psychological and physical issues before they are permitted to enroll in a research study, and they are carefully monitored during the study period. The rate of suicides in the study groups is a concerning result that should warrant further independent investigation. Further, the CDC suicide statistics are assessed over a full twelve-month period; the FDA package insert Gardasil clinical trial group was followed for seven months. If one extrapolates the numbers of "drug overdoses / suicides" over a full twelve-month period at the same rate as occurred over the seven-month clinical trial period, the twelve-month number would be 13.7 "drug overdoses / suicides." This equates to 47.7 / 100,000 "drug overdoses / suicides" over 12 months, or a relative risk of 6.19 compared to age, sex, time period adjusted cohort not exposed to AAHS. A third cause for concern highlighted by the FDA package insert concerns overall death rate in the clinical trial group. The overall death rate of participants in the clinical trial is also significantly higher than the death rate for same-age females in the general population, as recorded in CDC mortality tables for the same time period.

4. Higher Death Rate From Any Cause

The FDA Gardasil Package Insert discloses that "(a)cross the clinical studies, 40 deaths (GARDASIL N = 21 or 0.1were reported in 28,729 (GARDASIL N = 15,706; AAHS control N = 13,023)." Accordingly, 140 per 100,000 enrollees in the study died from any cause. CDC death statistics for the same time period adjusted for age and sex are 79 deaths per 100,000. The apparent relative risk for death from all causes is 1.77 or 177% higher than expected in similar non AAHS exposed populations. Since the initial study only involved females, the baseline suicide rate in the general US population is actually lower. The 70% is the crude CDC number for both sexes (79/100,000 expected) compared to the 140/ 100,000 in the study group. Therefore, the 1.77 relative risk number is conservative. [3] The statement in the package insert page 7 paragraph 4 reads "The events reported were consistent with events expected in healthy adolescent and adult populations" is contradicted given the rates implied by CDC mortality tables for this same time period. Further, the CDC death statistics are assessed over

a full twelve-month period[1]. The FDA package insert reports that the Gardasil clinical trial group was followed for seven months. If one extrapolates the numbers of "deaths" over a full twelve-month period at the same rate as occurred over the seven-month clinical trial period, the twelve-month number would be 68.57 "deaths." This equates to 238.6 per 100,000 "deaths" over 12 months, or a relative risk of 3.03 compared to age, sex, time period adjusted cohort not exposed to AAHS.

5. Boeing 737-800 Analogy

The Boeing 737-800 aircraft was fast tracked through Federal Aviation Administration approval. In a similar manner, the HPV vaccine was fast tracked through the Food and Drug Administration approval process. It was only after the loss of two of the Boeing aircraft, along with 346 souls, that the approval process and documentation was carefully, skeptically, and independently re-assessed. It was than learned that all the warning signs that the aircraft is potentially unsafe in some flight conditions is apparent in the approval documentation. In a similar vein, as the HPV vaccine has moved into mass distribution, the increase in reports of death by all causes, and death by suicide, in vaccine recipients has raised concerns. Careful review of the clinical data available in the VRBPAC [4] and FDA package insert [2] disclose that serious safety signals regarding excess suicides and excess deaths in trial participants are evident in the clinical trial data.

6. Conclusion

The CDC report notes that "Suicide rates increased from 1999 through 2014, with greater annual percent increases after 2006." Gardasil was approved in the United States in 2006; thus, temporal association is established, supporting (not negating) causality. Data from Merck's randomized prospective clinical trial on Gardasil lead to the conclusion that Gardasil and/or AAHS exposure appears to have a corresponding increase in the risk of suicide and deaths from all causes. Public health policies on recommended use of Gardasil should be updated accordingly. New, super-transparent trials conducted by independent research organizations not connected to Merck should be conducted immediately to confirm or refute the conclusions warranted by the initial clinical trial data.

References

[1] CDC. **CDC United States suicide statistics** . CDC .

[2] FDA. **FDA GARDASIL®. [Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant] Insert** . FDA .

[3] CDC. **About Underlying Cause of Death, 1999-2017** . *CDC WONDER*, 2018. CDC .

[4] VRBPAC. **VRBPAC Background Document Gardasil(TM) HPV Quadrivalent Vaccine** . *Fearless Parent*, May 2006. FearlessParent .