
Vaccine Safety Quarterly (VSQ) | Summer 2020

Brighton Collaboration 2.0

Frederick Varricchio, PhD, MD - *Editor in Chief*

Les Garber - *Style Editor*

Progress Toward a Global Vaccine Data Network.

Assessment of Adverse Events Following Immunization (AEFI) that have a delayed onset or diagnosis, occur beyond clinical trial study follow-up, are very rare or occur among subpopulations are often beyond the scope and statistical power of initial clinical programs and single country observational studies. The Global Vaccine Data Network (GVDN) was established in 2019 for the purpose of conducting international studies of vaccine safety, effectiveness, and risk-benefit through a network of over 16 sites in 14 countries encompassing five WHO regions for conducting international studies of vaccine safety, effectiveness, and risk-benefit. These sites have all previously demonstrated capacity in vaccine safety studies using clinical databases either independently or as collaborators. There is an estimated population of over 235 million under surveillance among these sites and potential new partners from low- and middle-income countries in Africa and South East Asia have been approached to join the consortium based on their potential to contribute through capacity building. The consortium is supported by a coordinating center based at the University of Auckland in New Zealand.

The Network aims to operate through a governance model that ensures full participation of sites on a voluntary basis from study conception through to study reporting. It is governed by a geographically diverse executive committee of seven site leaders and two (co) directors. Coordination of process, finance, secretariat and data management is provided by the

coordinating center. To protect privacy but allow collaborative agreements, the collaborators will use common data models (CDMs) for the participating sites that are flexible in terms of allowing for diverse data sources. This will also facilitate tiered participation dependent upon data availability, allowing for greater participation in the network as capacity is developed.

Today there is an urgent need to prepare for the deployment of COVID -19 vaccines. This includes determining the background rates for the potential Adverse Events of Special Interest and planning for Phase IV studies. Currently the capacity exists globally to assess vaccine safety across a network of geographically diverse sites. Further, developing this capacity further in mature sites as well as mentoring LMIC sites will be critical to the safe assessment of COVID-19 vaccines and other newly introduced vaccines in the future.



Helen Petousis Harris

University of Auckland
Member, Brighton Collaboration
Science Board

Collaborating sites are: Argentina, Australia, Canada, China, Denmark, Finland, France, Scotland, South Africa, Spain, New Zealand, Taiwan, UK, and USA

If you didn't receive this newsletter directly and wish to, [please enroll](#).

THE BRIGHTON WEBSITE

As part of our transition from BC1.0 to BC2.0, we have been working on a new and improved website! [The old website](#) will remain operational through December 2020 so that there is no disruption in members' access to the BC Academy feature. The initial version of the new website is already up and running at <http://brightoncollaboration.us> and <http://brightoncollaboration.info>, and contains all content from the old site except for some of the content contained solely within the Academy. Once we finalize the Academy portion of the new website (later this year), we will close the old site down and make the original URL the primary URL for the new site as well. We also plan to bring in further web development expertise to make the new website as professional and user friendly as possible. In the meantime, please feel free to provide feedback on content and structure of the new website by emailing the BC coordinator at bc-coordinator@taskforce.org, and keep an eye out for new content and features on the website as we go forward!

COVID-19

Covid-19 has dominated the news in recent months. The New York Times devotes 2-3 pages every day on subjects from viral proteins to vaccine trials. There are many excellent charts, graphs, and maps. PubMed has 25,000 entries coded COVID-19. This shows a monumental effort by the medical-scientific community to combat this new disease. Journals have accelerated publication. There were 30 publications in Am Med Assoc journals in one week. Articles have reported [experience with 72,300 patients in China](#) and [5700 in New York](#). Symptoms and sequelae are evolving rapidly. For the non-specialist, there are several sequential [short reviews by Del Rio](#). The New York Times has published [a 6 month summary of Covid-19 coverage](#). An unintended consequence is that well baby visits

and routine immunizations and other medical care have been disrupted. Will we see an uptick in vaccine preventable diseases? And amazingly anti-vaxers have used the occasion to increase their efforts coinciding with intense vaccine efforts to produce a safe and effective Covid-19 vaccine. Our colleague Lisa Chung has been a part of Emory COVID-19 Outbreak Response Team, providing testing services and community outreach programs to [predominantly Hispanic/Latinx migrant workers in rural Georgia, US](#).

BC has been involved along with CEPI in developing [a list of possible AEFIs](#) that may be associated with a COVID-19 vaccine. One concern is the potential for enhanced disease. This is theoretical for COVID-19 but has been seen with SARS and MERS-Cov vaccines in animal models. A Brighton case definition for enhanced disease is nearly complete. Also at least 6 different approaches are being used to develop the more than 100 vaccines reported to be under investigation on the WHO website. Many of these approaches have not been used in a commercially available vaccine to date.

JOURNAL CLUB

In collaboration with the International Society for Pharmacoepidemiology (ISPE) Special Interest Group (SIG) on Vaccines, the Brighton Collaboration is pleased to launch the Vaccine Safety Journal Club. Members of both organizations are invited to review and discuss the latest research on vaccine safety, from epidemiological methods to qualitative research. The journal club will take place quarterly during SIG meetings via Webex, and will be co-hosted by SIG Vice-Chair Cathy Panozzo, Harvard and BC member Nadja Vielot, U of No Carolina. The details of the first meeting will be announced in the next VSQ issue for Q4. To receive invitations to participate in or lead a journal club discussion, please complete this [Google Form](#).

VACCINE MISINFORMATION

Dudley and Offit have published [reviews of vaccine safety](#). They consider slightly different lists of AEs but both conclude vaccines are generally safe. A similar review by DeStefano was mentioned in the last VSQ. A 2018 survey found vaccine resistance 10-30% in the 20 countries surveyed. Dubé outlined approaches to improving communication to the public and reviewed materials available in Canada. They [made specific suggestions for improvement](#) such as: 1) targeting an audience and establishing trust, 2) providing balanced information, risks and benefits, 3) giving facts first before myths, 4) using visual aids, and 5) testing materials first. The CDC has [1 page "tipsheets"](#) on frequent vaccine questions and responses. These are available in bulk should physicians be encouraged to keep some in their literature rack. Probably there is still more to be done. I invite suggestions which will be included in the next VSQ. A New York Times article has already appeared addressing the question, "[what if 50% of people don't accept the COVID-19 vaccine?](#)". The journalist discusses the outsized influence of the relatively small number of anti-vaxers. He attributes this to their use of social media. He also makes suggestions about what we could do better. If you read this article as well, send your thoughts.

The UN has just [announced](#) an effort to make reliable covid'19 information available to everyone called "[Verified](#)". It enables volunteers from around the world to share information. The theory is to enable social organization, people providing information to friends, family, and social networks. Has anyone read about this already? I wonder how this has been publicized.

Another thought provoking article about information in Scientific American is entitled, "[Which Experts](#)

[Should You Listen To During The Pandemic?](#)" Is there more than one kind of expert? But the public has difficulty in differentiating.

NEGATIVE REPORTS

Two recent reports did not find evidence to support a vaccine related AE.

1. Investigating the association of receipt of seasonal influenza vaccine with occurrence of anesthesia/paresthesia and severe headaches, Canada 2012/13-2016/17, the Canadian Vaccine Safety Network. Ahmed MA¹, Vaccine Evaluation Center, BC Children's Hospital, University of British Columbia, Vancouver
2. Association Between Rotavirus Vaccination and Type 1 Diabetes in Children, Jason M. Glanz, PhD^{1,2}; Christina L. Clarke, MS¹; Stanley Xu, PhD¹; et al

DR. KAWASAKI

[Dr. Tomisaku Kawasaki](#), the physician who initially described Kawasaki Disease and bears his name, died on June 5. Interestingly he once attributed his observation of Kawasaki disease to the decrease in measles cases which made Kawasaki disease- more visible. What else is behind the shadows?

VSQ READERS

The spring VSQ was emailed to over 800 readers. An estimate from the returned reader survey shows 30% of readers are from the US followed by Canada and India. Occupations are varied from clinical research to statistics to fund raising.

LITERATURE

A PubMed search for Vaccine Safety yields about 21,000 entries. This is increasing by approximately 100 entries per month. I have selected a few recent articles which may be of general interest. Is anyone interested in leading a discussion or journal club on any of these or any other topic?

1. The State of Vaccine Safety Science: Systematic Reviews of the Evidence

[Lancet](#). 2020 May 1; 20(5), E80-899.
doi: 10.1016/S1413-3099(20)30130-4

Corresponding Author: Daniel A. Salmon (Institute for Vaccine Safety, Johns Hopkins Bloomberg School of Public Health)

This Review updates the scientific evidence assessing possible causal associations of adverse events following immunisation (AEFI) compiled in the 2012 report from the Institute of Medicine and the 2014 report from the Agency for Healthcare Research and Quality. For 12 of 46 AEFI examined, a causal relationship has been established with at least one vaccine currently routinely recommended to the general USA population: anaphylaxis, arthralgia or arthritis (mild, acute, and transient, not chronic), deltoid bursitis (when vaccine is administered improperly), disseminated varicella infection (in immune deficient individuals for whom the varicella vaccine is contraindicated), encephalitis, febrile seizures, Guillain-Barré syndrome, hepatitis (in immune deficient individuals for whom the varicella vaccine is contraindicated), herpes zoster, immune thrombocytopenic purpura, meningitis, and syncope. Other than mild acute and transient arthralgia or arthritis, which is very common in adult women after rubella vaccine, these adverse reactions are rare or very rare. Vaccines have an excellent safety profile overall and provide protection against infectious diseases to individuals and the general population.

2. An opportunity to incentivize innovation to increase vaccine safety in the United States by improving vaccine delivery using vaccine patches

[Vaccine](#). 2020 May 22;38(25):4060-4065.
doi:10.1010/j.vaccine.2020.04.044

Corresponding Author: Kimberly M. Thompson (Kid Risk, Inc., Orlando FL, USA)

Vaccines represent cost-effective and safe interventions that provide substantial health and economic benefits to individuals and populations. The US vaccine enterprise that supports all aspects of immunization continues to encourage innovation. Despite some limited historical recommendations to create a fund to support investments in vaccine safety, and recent legislation that supports innovation for new vaccines (the 21st Century Cures Act, Public Law 114-255), to date the US lacks financial incentives to fund innovation in vaccine delivery technologies.

3. Effect of the lay press on physicians and patients. Impact of media reports regarding influenza vaccine on obstetricians' vaccination practices.

Vaccine. 2020 Apr 16;38(18):3474-3479.
doi: 10.1016/j.vaccine.2020.02.051

Corresponding Author: Sean T. O'Leary (Adult and Child Consortium for Health Outcomes Research and Delivery Science, University of Colorado Anschutz Medical Campus and Children's Hospital Colorado, Aurora CO, USA)

In 2017, three media stories regarding influenza vaccine may have impacted obstetricians' (OB) influenza vaccination practices: reports of reduced influenza vaccine effectiveness, a severe influenza season, and a possible increased risk of miscarriage among pregnant women receiving 2009 H1N1 vaccine in the 1st trimester who had received H1N1 vaccine the previous season (later disproven).

A survey among a nationally representative sample of OBs April to June 2018: Response rate was 65% (302/468). 88% of OBs were "very aware" of the severe season, 74% of lower effectiveness, and 25% of the miscarriage study (47% "completely unaware" of miscarriage study). Among those aware, 58%, 57%, and 16% reported $\geq 10\%$ of pregnant patients initiated discussions about the severe season, lower effectiveness, and miscarriage study, respectively. Most (83%) agreed reports about increased severity increased their enthusiasm for recommending influenza vaccine; fewer agreed reports about the miscarriage study (18%) and lower vaccine effectiveness (12%) decreased their enthusiasm for recommending influenza vaccine. Providers were more likely to initiate discussion with patients about increased severity of the season than the other reports. However, 35% agreed the miscarriage study reports increased their concerns about influenza vaccine safety; 18% (n = 48) reported changing the way they recommended influenza vaccine. Of those, 17 (6% of all respondents) reported not recommending influenza vaccine to women during

the 1st trimester and 26 (10% of all respondents) recommended it but were willing to delay until the 2nd trimester.

During a season in which media stories could have influenced OB influenza vaccination behaviors in different directions, reports underscoring the importance of influenza vaccine may have had more impact on OBs' recommendations than reports questioning vaccine safety or effectiveness.

4. A view from another country and another health care system.

Title: A Cuban Perspective on the Anti-vaccination Movement.

[Intl J of Cuban Health and Med](#). 2019 Nov 25.

Corresponding Author: Beklys M. Galindo-Santana (Pedro Kourí Tropical Medicine Institute [IPK], Havana, Cuba)

Vaccination is one of the most cost-effective interventions for control of communicable diseases. This health achievement could flounder if measures are not taken by health systems to prioritize immunization, increase vaccination rates and educate health professionals to address public concerns about vaccine safety and efficacy. Parents' refusal to vaccinate their children directly affects public health, because it puts both individual and group immunity in danger; immunization coverage is effective only when high population coverage is attained. The growing number of anti vaccination (anti vaxxer) groups around the world is alarming, contributing to falling vaccination rates. Troubling consequences include disease outbreaks in several countries globally and in our hemisphere. This article looks at the history and features of anti vaxxer movements around the world and proposes ways the Cuban health system, through its National Immunization Program can address dangers for the population associated with potentially negative

influences of social-network anti vaxxer campaigns. The paper underscores the role of mass and social media, health professional training and sustained competence, and the importance of a vaccine-related adverse events surveillance system.

5. A Chinese review of 11 AE reporting systems

Title: A Scoping Review of Active Surveillance Systems for Vaccine Safety World-Wide [Chinese J of Prev Med](#). 2019 Jun 30, 53(7):724-730. doi: 10.3760/cma.j.issn.0253-9624.2019.07.013

Corresponding Author: Cai Ting (School of Public Health, Peking University, Beijing 100191, China)

Abstract: Post-marketing surveillance of vaccine safety is an important measure to detect adverse events following immunization and therefore reduce the harms to public health. The conventional method for safety surveillance is a passive way through spontaneous reporting, which suffer from under-reporting and incomplete. While active surveillance, a newly proposed surveillance method in developed countries, is capable to make up the deficiencies of passive surveillance. The surveillance system of vaccine safety in China is currently using passive surveillance, and facing many problems and challenges. This arouses a need to promote development of an active surveillance system for vaccine safety in China, learning from the experience world-wide. This commentary aims to throw out suggestions for establishing the active surveillance system, according to the specific situation in China and based on a scoping review of literature.

Objective: To identify post-marketing active surveillance systems for vaccine safety around the

world and understand their features and mechanisms, in order to provide guidance for vaccine administration activities in China.

Methods: Following the steps of scoping review, literature about active surveillance systems for vaccine safety and published by 30 June 2018 were identified by searching electronic databases, including PubMed, Scopus, and Cochrane Library. Grey literature was also sought by exploring relevant websites. Identified literature were screened according to eligibility criteria, and informative data from included literature were then charted. Framework Synthesis and Thematic Analysis were performed to integrate the charted data.

Results: 97 pieces of literature were included for review, and 11 active surveillance systems for vaccine safety were identified, mostly located in developed countries. These systems were constructed by 3 types of organizations: administration departments, academic or research institutions, and health care providers. Their data sources included immunization registries, electronic medical records, claims data, case reports of adverse events following immunization electronic questionnaires, and epidemiologic study data. According to their operation procedures, these systems were grouped into 4 modes of active surveillance: Data Linkage, Investigator Network, Automatic Follow-up System, Studies Consortium.

Conclusion: Practice of active surveillance for vaccine safety greatly varies across countries, with different conditions and advantages. It is suggested that developing countries should choose a suitable mode of active surveillance considering their local situations.

New Brighton Collaboration Publications

In the recently launched website, newly published Brighton Collaboration articles and tools will be posted in [English](#) and some in Chinese, Spanish, French or Portuguese.

A couple of notable recent publications are:

- [Standardized Template for Collection of Key Information for Benefit-Risk Assessment of Protein Vaccines](#)
- [Sensorineural Hearing Loss \(SNHL\) as an Adverse Event Following Immunization \(AEFI\): Case Definition & Guidelines for Data Collection, Analysis, and Presentation of Immunization Safety Data](#)

- [Don't rush to deploy COVID-19 vaccines and drugs without sufficient safety guarantees](#)
- [Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomized, first-in-human trial](#)
- [The potential danger of suboptimal antibody responses in COVID-19](#)
- [COVID-19 vaccine research must involve Black and Latinx participants](#)
- [Study raises concerns for pregnant women with the coronavirus](#)
- [Mitochondrial respiratory states and rates](#) (Gnaiger, E., Varrichio, F., et al, 2019)

NEW NEWS...

Articles and Comments to the VSQ are welcomed and invited.

The VSQ is produced by volunteers. But there are unavoidable expenses for office supplies etc. If you would like to help financially with the VSQ, [click here](#) and accept our thanks.

**We would like to have a series of groups that work on vaccines, vaccine safety.
What have you done? What are you doing? What would you like to do?**

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