

# International evaluation of GBS following pandemic influenza vaccine – an example of global collaboration

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In recent years, an increasing number of vaccines have become available both in developed and developing countries. The manufacturing base for vaccines used globally has expanded from Europe and North America to countries in other regions. In addition, over the last decade several vaccines have been introduced first or very early after their global introduction into low and middle income countries. These trends suggest that it is no longer optimal to rely on existing infrastructure in Europe and the US to assure the safety of the global vaccine supply and that thought must be given to development of a new global vaccine safety and evaluation infrastructure. Such infrastructure could both expand the safety net of comprehensive vaccine safety assessment to more countries and through collaborative effort, allow performance of studies with increased scope and statistical power, enabling more rapid resolution of vaccine safety questions.

Computerized clinical databases have been used in the UK, USA, Denmark, Vietnam and other countries to assess vaccine safety. These systems offer distinct advantages over passive reporting systems in that they do not rely on selected reporting to identify events but rather upon clinical datasets. This avoids the reporting and other biases associated with passive systems. In many instances computerized clinical databases also allow calculation of person-time denominators for estimation of incidence rates and attributable risk. In addition, Farrington has outlined a self controlled case series methodology which only requires unbiased case ascertainment and the ability to review case records rather than information on an entire cohort. Fewer resources are required for this methodology than for a cohort study because only the cases are reviewed and contribute information. This facilitates an increase in the number of sites, particularly among middle and low income countries, who can effectively participate in vaccine safety assessments based upon clinical data sets. However, there are minimal requirements for this method to yield accurate information, primarily the requirement that cases are identified in an unbiased uniform manner.

The H1N1 influenza pandemic that began in Mexico in the spring of 2009 and the consequent global effort to vaccinate with pandemic influenza vaccines provided an opportunity to test the feasibility of a collaborative effort to evaluate the risk of Guillain-Barré Syndrome following receipt of these vaccines. Beginning in 2010 with the help of WHO, the US FDA and NVPO, the HPA in the UK, the European CDC, the Brighton Collaboration, as well as a global network of investigators in 14 countries, a protocol was developed to identify cases of GBS through clinical data sets, classify such cases using a GBS case definition developed by the Brighton collaboration, and to utilize the self controlled case series methodology to perform analyses of the risk of GBS following pandemic vaccine, stratified as to whether the vaccine received was adjuvanted or adjuvant free.

The purpose of this collaborative effort is to both perform the scientific assessment of the risk of GBS following vaccine as well as to demonstrate the feasibility of developing and adhering to collaborative protocols, pooling data and performing a conjoint analysis. Work on this effort is ongoing. An international team is performing data simulations to select the most appropriate self controlled methodology, and information is being gathered at WHO from participating countries to develop the analysis dataset.