

Does size really matter in post-licensure vaccine safety monitoring?

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Post-licensure surveillance for vaccine adverse events (VAEs) is important as clinical trials may have limited power or are not designed to detect rare adverse events, health outcomes with delayed onset, or safety issues that are specific to subpopulations not included in clinical trials. Passive surveillance of VAEs is used in many countries typically for the purposes of generating hypotheses or “signals” that may require further investigation. These signals can be evaluated using large-linked databases, such as the Vaccine Safety Datalink (VSD) in the United States, that provide information on vaccine exposures, health outcomes, and demographic information necessary for testing hypothesis regarding vaccines and adverse health outcomes. The VSD has also been used to conduct active surveillance where pre-specified outcomes are monitored in near real time for newly introduced vaccines and mass vaccination programs (H1N1).

Recently, the United States has developed several other systems modeled after the VSD, including the Post-licensure Rapid Immunization Safety Monitoring (PRISM) Network and medical databases from the Centers for Medicare & Medicaid Services (CMS), the Indian Health Service (IHS), the Department of Defense (DoD), and the Department of Veteran Affairs (VA). Most recently, in response to the FDA Amendments Act of 2007, FDA created the Sentinel Initiative which aims to achieve, by July 2012, active post-market adverse event surveillance of drugs covering a population of 100 million people, utilizing electronic health care data.

The optimal size for such active surveillance systems is not clear, as there may be a point of diminishing returns if and when the cost of including larger numbers of persons is not offset by the advantages of greater study power. When evaluating size requirements for these systems, several issues are worth considering, including that the incremental cost of adding more persons from a site is often minimal once that site is already participating in an active surveillance system, different databases may be particularly useful for certain subpopulations, and the public health value of timeliness and the rarity of the adverse health outcome being evaluated. Moreover, building a scalable system with entities capable of contributing data in special situations (e.g. pandemics) may be a policy option for optimizing cost and efficiency of obtaining safety data. However, such scalable systems will require pre-signal planning involving compatibility in data systems and *a priori* consideration of legal and ethical issues. This paper discusses building national post-licensure surveillance systems and outlines considerations for how to optimize size with logistical and cost-constraints, and tradeoffs between the size of the databases and ready access to medical records.