

# The Vaccine Safety Datalink: A Model for Monitoring Immunization Safety

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## KEY WORDS

vaccine safety, immunization, Vaccine Safety Datalink, postmarketing evaluation, surveillance

## ABBREVIATIONS

AEFI—adverse event(s) following immunization  
 CDC—Centers for Disease Control and Prevention  
 VSD—Vaccine Safety Datalink  
 MCO—managed care organization  
 VAERS—Vaccine Adverse Event Reporting System  
 DDM—distributed-data model  
 DDF—dynamic data file  
 RCA—rapid cycle analysis  
 TIV—trivalent inactivated influenza vaccine  
 OR—odds ratio  
 CI—confidence interval  
 GBS—Guillain-Barré syndrome  
 RR—rate ratio

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## abstract

The Vaccine Safety Datalink (VSD) project is a collaborative project between the Centers for Disease Control and Prevention and 8 managed care organizations (MCOs) in the United States. Established in 1990 to conduct postmarketing evaluations of vaccine safety, the project has created an infrastructure that allows for high-quality research and surveillance. The 8 participating MCOs comprise a large population of 8.8 million members annually (3% of the US population), which enables researchers to conduct studies that assess adverse events after immunization. Each MCO prepares computerized data files by using a standardized data dictionary containing demographic and medical information on its members, such as age and gender, health plan enrollment, vaccinations, hospitalizations, outpatient clinic visits, emergency department visits, urgent care visits, and mortality data, as well as additional birth information (eg, birth weight) when available. Other information sources, such as medical chart review, member surveys, and pharmacy, laboratory, and radiology data, are often used in VSD studies to validate outcomes and vaccination data. Since 2000, the VSD has undergone significant changes including an increase in the number of participating MCOs and enrolled population, changes in data-collection procedures, the creation of near real-time data files, and the development of near real-time postmarketing surveillance for newly licensed vaccines or changes in vaccine recommendations. Recognized as an important resource in vaccine safety, the VSD is working toward increasing transparency through data-sharing and external input. With its recent enhancements, the VSD provides scientific expertise, continues to develop innovative approaches for vaccine-safety research, and may serve as a model for other patient safety collaborative research projects. *Pediatrics* 2011;127:S45–S53

High vaccination coverage has significantly reduced vaccine-preventable disease morbidity and mortality worldwide, especially among children.<sup>1,2</sup> Vaccines are generally regarded as safe and effective; however, serious adverse events following immunization (AEFI) can occur.<sup>3,4</sup> Although vaccine safety is rigorously assessed during prelicensing clinical trials, sample sizes are not adequate to detect rare adverse events, long-term adverse events are not examined, and populations are not heterogeneous.<sup>5</sup> In recent years, public concerns about the safety of vaccines have grown significantly.<sup>5</sup> Immunization-safety programs are an important component of maintaining the public trust in our national immunization program.<sup>5</sup> Close monitoring of vaccine safety also protects the public's health and contributes to safer vaccines and vaccination practices.

In 1990, the Centers for Disease Control and Prevention (CDC) National Immunization Program created the Vaccine Safety Datalink (VSD) project to conduct postmarketing evaluations of vaccine safety.<sup>6,7</sup> Initially, the project used medical event and demographic information from ~6 million children younger than 6 years for VSD research from 4 participating managed care organizations (MCOs): Group Health Cooperative of Puget Sound (GHC) (Seattle, WA); Kaiser Permanente Northwest (NWK) (Portland, OR); Kaiser Permanente of Northern California (KPNC) (Oakland, CA); and Kaiser Permanente of Southern California (Los Angeles, CA).<sup>6-9</sup> Later, vaccine-safety studies were conducted to include children younger than 18 years at all 4 sites and adults 18 years of age and older at GHC, KPNC, and NWK. In 2001, 4 additional MCOs joined the VSD, and during the last 7 years the VSD has made other changes to enhance its ability to serve as the primary mechanism for population-based evaluations of vac-

cine safety in the United States. The VSD is part of the CDC Immunization Safety Office. The Immunization Safety Office also includes the Vaccine Adverse Event Reporting System (VAERS), the Clinical Immunization Safety Assessment Network, and the Brighton Collaboration.

In this article we provide a review of the VSD and focus on the important modifications and enhancements the project has undertaken since 2001.

## THE VSD PROJECT SINCE 2001

### Population

The VSD population has increased substantially since 2001, when 4 new MCOs joined the project to provide data on members younger than 18 years: Kaiser Permanente of Colorado (Denver, CO); Marshfield Clinic Research Foundation (Marshfield, WI); Health Partners Research Foundation (Minneapolis, MN); and Harvard Pilgrim/Harvard Vanguard (Boston, MA). In 2007, the VSD population expanded again as all participating sites except 2 began providing data on members of all ages. Currently, data for >18 million persons spanning 16 years are available for VSD research.

### Data Sources, Collection, and Confidentiality

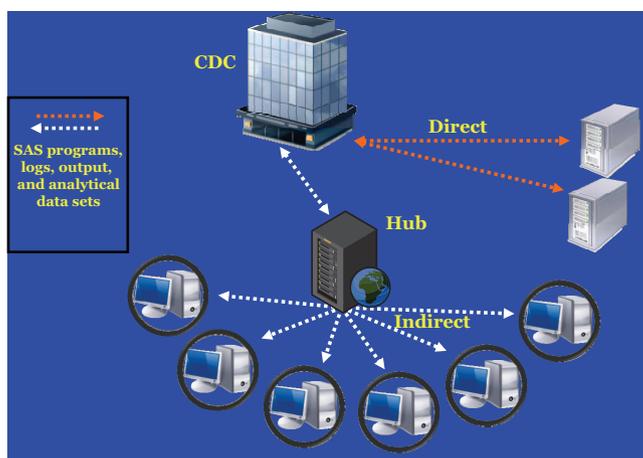
Since inception of the VSD, each MCO has prepared annual data files, called cycle files, that contain member information obtained from administrative files maintained by the individual MCOs. The cycle files include demographic and medical services information on their members, such as age and gender, health plan enrollment, vaccinations, hospitalizations, outpatient clinic visits, emergency department visits, urgent care visits, mortality data, and additional birth information (eg, birth weight) when available. To ensure confidentiality and comply with federal regulations, each

person within the VSD is assigned a unique, randomized VSD study identification number that is not linked to their MCO member identification number. VSD study identification numbers can be used to link data on demographics and medical services. A standardized data dictionary, which ensures data consistency across sites, is updated each year by the CDC and the VSD MCOs. Frequently, medical record data and, occasionally, participant survey or interview data are used to validate clinical diagnosis and vaccination data.

### Distributed Data Model

From 1991 through 2000, the VSD used a centralized-data model, which required each MCO to send its cycle files to the CDC annually for merging and analyses. When data were needed for a specific VSD study, the CDC would send a subset of cycle data to the MCO responsible for performing the study analysis. Because of heightened confidentiality concerns, the centralized-data model was replaced by a more secure distributed-data model (DDM) in 2001 (see Fig 1).

The DDM allows each MCO to assemble and maintain its computerized data files on a secure server at the site rather than transferring data to the CDC,<sup>10</sup> and ownership of the data is retained by the MCOs. Data required for specific VSD studies are transferred between the CDC and the VSD sites by using 2 secure methods known as the "indirect" and "direct" methods. With the indirect method, CDC and MCO computers share information through a secure server known as the "hub." CDC researchers send computer programs to the hub, which are retrieved at specified intervals by an MCO computer. All computer programs are written for a statistical computer program (SAS [SAS Institute, Inc, Cary, NC]); data files are also stored by using this plat-



**FIGURE 1**

Representation of the VSD DDM. Sites using the indirect method retrieve SAS programs at regular intervals from the hub. Output is then sent back to the hub where it is retrieved by analysts at the CDC. For sites that use the direct method, SAS programs and output are transferred through SAS Connect directly between the sites and the CDC. Both methods use encryption methods to secure data transfers.

form. Each MCO can retrieve and use its own SAS programs but cannot access programs or information that belongs to other MCOs. Each MCO sends its SAS logs, output, and analytical data subsets back to the hub for retrieval by CDC researchers. With the direct method, CDC researchers submit SAS programs interactively through a secure SAS remote session by using SAS Connect, an Internet communication protocol. Four SAS macros, which are a collection of SAS program statements that can be easily recalled, are used to facilitate access of the data and retrieval of SAS logs and output. All data transfers are conducted securely by using encrypted methods.

### Dynamic Data Files

Development of the DDM as a secure data-transfer system enabled the VSD to restructure the way data files are collected and used, which led to the creation of dynamic data files (DDFs) in 2005. DDFs permit the ongoing capture of near real-time event-based MCO administrative data, including data on vaccination, hospitalizations, emergency department visits, clinical visits, MCO enrollment, and certain demographic characteristics. Most files

are updated weekly with new data from each MCO, although some files are updated monthly or quarterly, depending on the capabilities of each site's data systems. Using the DDM, files are accessed by the CDC on an ongoing basis for analysis and/or extraction of necessary data for each ongoing study. The DDFs use the same standardized data dictionary as the cycle files and continue to provide the flexibility to conduct various types of studies. Additional tracking and data-quality measures were developed to monitor the new DDFs. The sample size of the DDF continuously increases as new data are added to the files, which date back to 1991. The combination of the DDM and DDFs enable the VSD to conduct near real-time postlicensure surveillance, enhance the timeliness of certain studies, and increase efficiency in the creation of cycle files.

### Research and Surveillance Process

The VSD continues to conduct numerous studies on a wide range of immunization-safety topics. Table 1 lists the specific strategic priorities for the VSD. For each study, a team of VSD investigators, comprised of mem-

**TABLE 1** VSD Strategic Priorities

Evaluate the safety of newly licensed vaccines
Evaluate the safety of new vaccine recommendations for existing vaccines
Evaluate clinical disorders after immunizations
Assess vaccine safety in special populations at high risk
Develop and evaluate methodologies for vaccine-safety assessment

bers from several of the participating MCOs and the CDC, develops a comprehensive study proposal that is presented and reviewed by the members of the project. This scientific proposal includes a detailed description of the hypothesis in question, study design, and analytical plan along with a rigorous review of the medical outcomes to be evaluated. All studies meet the necessary institutional review board and Health Insurance Portability and Accountability Act (HIPAA) requirements. Computerized data often supplemented with additional medical record or other data are used to create study-specific analytical data files that contain only an extremely small portion of the entire VSD data. Analyses and manuscript preparation are typically led by a single MCO or the CDC with input from participating investigators.

### Study Designs

The VSD uses several analytical methodologies to evaluate vaccine safety. The calculation of background rates allows the VSD to conduct multiple types of observational studies and to calculate disease incidence and vaccination coverage. Early VSD studies typically used observational study designs such as retrospective cohort studies or case-control studies. Several recent VSD studies have used self-control case-series designs, which involve an analysis based on a person's exposure and control time windows, because appropriate independent control groups may be unavailable or subject to confounding.<sup>11,12</sup> Because a large percentage of the VSD population is vacci-

nated, it is difficult to obtain data on unvaccinated persons to be used as a comparison or control group. Self-control case-series designs allow researchers to determine if the rate of AEFI is elevated in the hypothesized exposure window compared with the other time windows. Additional new case-only methods are being developed and refined to better control for seasonal differences in the uptake of vaccines relevant to studies that involve influenza vaccine and vaccines given seasonally in advance of school or college attendance.

### Postmarketing Surveillance: Rapid Cycle Analysis

Since 2005, several new vaccines have been licensed: live, oral, human-bovine reassortant rotavirus vaccine (RotaTeq [Merck & Co, Inc, Whitehouse Station, NJ]), the tetravalent meningococcal polysaccharide-protein conjugate vaccine (Menactra [Sanofi Pasteur, Inc, Swiftwater, PA]), 2 tetanus, diphtheria, and acellular pertussis vaccines (Boostrix [GlaxoSmithKline Biologicals, Rixensart, Belgium] and Adacel [Sanofi Pasteur, Toronto, Ontario, Canada]), the human papillomavirus vaccine (Gardasil [Merck & Co, Inc]), and a combination measles-mumps-rubella and varicella vaccine (ProQuad [Merck & Co, Inc]). Using DDFs, the VSD is conducting near real-time postmarketing surveillance for these 6 newly licensed vaccines. The studies, referred to as the rapid cycle analysis (RCA)<sup>13,14</sup> projects, are an active surveillance system that routinely assesses possible associations between vaccines and predefined potential adverse events.

In the RCA, the observed number of suspected adverse events is compared with the expected number of events. The expected number of events may be determined from a variety of sources including previously determined back-

ground rates from the VSD or published literature, background rates from other data sources, concurrent comparison control groups, or self-control methods. Because the comparisons are conducted weekly, the estimates are adjusted by sequential methods to control for repeated analysis of the data.<sup>13,14</sup> When conducting RCA, researchers are on alert for a “signal,” which is generated if the expected rate of adverse events is significantly greater than the control rate when adjusting for sequential methods and other factors. A VSD data-coordinating center was created to handle the increased demand for data management and analysis generated by these RCA studies.

### Postmarketing Surveillance: VSD Collaboration With the VAERS

VSD data are also used in conjunction with information from VAERS to examine AEFI. VAERS is a passive surveillance system that receives adverse-event reports from various sources, including vaccine manufacturers, health care providers, immunization programs, and vaccine recipients.<sup>15</sup> Possible associations are examined by comparing the number of adverse events reported to VAERS with background rates for these events from VSD data.<sup>16–18</sup> Summaries of 2 such analyses for the newly licensed RotaTeq and Menactra vaccines are included in this article to illustrate this collaboration (see “Postmarketing Monitoring Supplementing VAERS Data With VSD Background Rates”).

### Data-Sharing and Oversight

Recognized as an important resource in vaccine safety, the VSD is working toward increasing transparency. In 2002, the VSD established a data-sharing program that allows external researchers to analyze data sets from VSD studies published after August 2002 or to create novel analytical

data sets for analysis by using VSD data through December 31, 2000. This program is administered through the National Center for Health Statistics of the CDC. More information on this program can be found at [www.cdc.gov/vaccinesafety/Activities/VSD/Datasharing.html](http://www.cdc.gov/vaccinesafety/Activities/VSD/Datasharing.html).

On 2 occasions, the VSD has invited external experts from a number of scientific disciplines and community members to contribute to the design, implementation, and presentation of high-priority studies. These studies include the study entitled “Early Thimerosal Exposure and Neuropsychological Outcomes at 7 to 10 Years” and the ongoing thimerosal and autism case-control study.<sup>19</sup> A public-use data set from the thimerosal and neurodevelopmental outcomes study is available at [www.cdc.gov/vaccinesafety/Concerns/Thimerosal/neuropsychological\\_Outcomes.html](http://www.cdc.gov/vaccinesafety/Concerns/Thimerosal/neuropsychological_Outcomes.html).

### EXAMPLE STUDIES

The VSD conducts rigorous epidemiologic studies primarily on a wide range of vaccine-safety priorities as well as other immunization-related topics, including vaccine coverage, disease incidence, research methodology, cost-effectiveness, and medical informatics. Through its innovative approaches, the VSD has proven its ability to adapt and respond to the increasingly complex and controversial topics in immunization research. Below are a few examples that illustrate the capabilities of the VSD.

#### Hepatitis B Vaccine and Risk of Autoimmune Thyroid Disease<sup>20</sup>

A possible link between hepatitis B vaccine and autoimmune thyroid diseases such as Graves’ disease and Hashimoto thyroiditis had been suggested by a study conducted in Europe and by reports to the VAERS. Supplementing patient interviews and medical record data with routinely collected automated

data, the VSD was able to investigate this relationship through a multisite case-control study.<sup>20</sup> Cases were initially identified through VSD cycle data and validated through medical record review, and then telephone interviews were conducted to verify hepatitis B vaccination status. The study analyzed 355 cases of Graves' disease, 418 cases of Hashimoto thyroiditis, and 1102 frequency-matched controls and revealed that having ever received hepatitis B vaccine did not increase the risk of either Graves' disease or Hashimoto thyroiditis.<sup>20</sup> This study's results reveal the ability to collect comprehensive vaccine information and to accurately identify and confirm cases through alternative data-collection methods.

### Safety of Trivalent Inactivated Influenza Vaccine in Children Aged 6 to 23 Months<sup>21</sup>

As a result of the decision by the CDC's Advisory Committee on Immunization Practices to recommend routine vaccination of all children aged 6 to 23 months with trivalent inactivated influenza vaccine (TIV) in 2004, the VSD proved to be well suited to assess the safety of TIV in this population. In one of the largest population-based TIV studies to date, the VSD conducted a retrospective cohort study of 45 356 children who received a total of 69 359 influenza vaccinations between January 1, 1991, and May 31, 2003.<sup>21</sup> Self-control case-series methods were used for this analysis. Cycle files were analyzed to identify medically attended events seen in clinic, emergency department, or hospital settings after vaccination with TIV. Preliminary analyses revealed that gastritis/duodenitis was more likely to occur in the 14 days after TIV (matched odds ratios [ORs]: 5.50 [95% confidence interval (CI): 1.22–24.81] for control period 1 [0–3 days] and 4.33 [95% CI: 1.23–15.21] for control period 2 [1–14 days]). No other significant associations with medically

attended events were found. Further analysis including chart review and a subanalysis of 28 820 children with no underlying medical conditions that would put them at increased risk of complications of influenza vaccination revealed that children vaccinated with TIV were not at increased risk of gastritis/duodenitis compared with the entire study population.<sup>21</sup> This study supported the Advisory Committee on Immunization Practices vaccination recommendation by providing reassurance to support the safety of universally immunizing all children aged 6 to 23 months with influenza vaccination.

### Early Thimerosal Exposure and Neuropsychological Outcomes at 7 to 10 Years<sup>19</sup>

In 1999, the Public Health Service and the American Academy of Pediatrics called on vaccine manufacturers to remove thimerosal, a mercury-containing preservative, from vaccines. The decision to remove thimerosal was a precautionary measure,<sup>22</sup> and subsequent studies have found no significant association between thimerosal and neuropsychological deficits.<sup>19,23–31</sup> In an effort to better improve on previous studies, the VSD was able to rigorously assess the relationship between thimerosal exposure and neuropsychological functioning through a retrospective cohort study with extensive assessments and interviews among the study population and their mothers. The study population included 1047 children between the ages of 7 and 10 years who were enrolled in 4 of the VSD MCOs and had received vaccinations as infants when thimerosal was used as a preservative in many childhood vaccines. For the analysis, the children were grouped according to their level of mercury exposure (low, medium, and high), which was determined from VSD MCO immunization records, medical records, personal immunization records, and

parent interviews. Information on potential confounding factors was obtained from the interviews with mothers and from medical records. Standardized tests that assessed 42 neuropsychological outcomes, including speech and language measures, verbal memory, fine motor coordination, tics, and behavioral regulation, were administered to the children. Only 5% of the statistical tests (19 of 378) showed significant associations; 12 tests revealed a positive association, and 7 tests revealed a negative association. The vast majority of the tests revealed no association, and the 5% that showed associations could be explained by chance alone. The results added to accumulated evidence that thimerosal does not cause neuropsychological deficits in children.<sup>19</sup> This study's results further show the ability of the VSD to supplement administrative data with data from other sources to conduct rigorous studies and test vaccine-safety hypotheses.

### Postmarketing Monitoring Supplementing VAERS Data With VSD Background Rates

The VSD has collaborated with VAERS in conducting postmarketing surveillance of potential AEFI for newly licensed vaccines. The potential association between RotaTeq and intussusception was assessed by comparing the number of VAERS intussusception reports to the number of intussusception cases expected to occur by chance alone.<sup>16,32</sup> To determine the expected number of cases that would occur by chance alone, the VSD first determined the background rates of natural intussusception (*International Classification of Diseases, Ninth Revision* code: 560.0) by using VSD data files from 2000 to 2004, when no rotavirus vaccine was in use. The analysis was stratified into 3 age groups, because background rates of natural intussusception and the number of doses ad-

ministered varied substantially according to age. Using these data, the expected number of background cases was calculated by multiplying VSD background rates for each age group according to the estimated number of vaccine doses administered to that age group. The findings suggested that there is no association between RotaTeq vaccination and intussusception, because the number of cases of intussusception reported to the VAERS (32) was not elevated above the expected number of cases (52).<sup>16,32</sup> Similar analyses were conducted to compare the potential association between Menactra and Guillain-Barré syndrome (GBS). For the study time period, the background incidence rate of GBS was determined to be 0.11 per 100 000 person-months in the VSD. By dividing the VAERS reporting rate of GBS (0.20 per 100 000 person-months) by the background incidence rate of GBS (0.11 per 100 000 person-months), the VSD determined the reporting rate ratio (RR) to be 1.77 (95% CI: 0.96–3.07).<sup>17,18</sup> Although the data suggest a possible small increased risk of GBS in persons aged 11 to 19 who received Menactra vaccination, the findings should be viewed with caution.<sup>17,18</sup>

### Postmarketing Monitoring Using VSD RCA

In addition to providing background rates to supplement the VAERS, the VSD is also conducting RCA studies to monitor the safety of several vaccines including RotaTeq, Menactra, Gardasil, Adacel and Boostrix, ProQuad, and seasonal influenza vaccination. Between May 2006 and May 2008, >205 000 doses of RotaTeq were administered orally to infants at ages 2, 4, and 6 months in VSD-monitored MCOs. Only 5 cases of intussusception within 30 days of vaccination were reported among RotaTeq recipients; in contrast, on the basis of historical background rates, 6.75 cases were expected to oc-

cur by chance alone. Only 2 of the intussusception cases were confirmed by medical chart review. This analysis suggested that there was no evidence that RotaTeq vaccine is associated with an increased risk for intussusception or other prespecified events.<sup>32–34</sup> Between March 2005 and September 2008, >570 000 Menactra doses were delivered in participating MCOs, and no cases of GBS after medical record review were observed among vaccine recipients aged 11 to 19 years within 6 weeks of vaccination (0.9 cases would be expected during that period). During the same period, 5 unconfirmed cases of GBS were identified among an unvaccinated comparison group of >900 000 persons aged 11 to 19 years (Dr Lieu, update on Menactra RCA through September 2008, personal communication, October 20, 2008 and refs 14, 17, and 18). The results of neither study suggest an association of serious AEFI with these vaccines. In February 2008, VSD investigators presented the Advisory Committee on Immunization Practices with preliminary results from an analysis performed after a possible signal of seizure was observed in the VSD ProQuad RCA study.<sup>35</sup> On the basis of >43 000 administered doses of the combination measles-mumps-rubella and varicella vaccine (MMRV), the attributable risk for seizures on days 7 to 10 after MMRV was calculated as 1 per 2000 doses compared with the measles-mumps-rubella and varicella vaccines administered separately but at the same visit.<sup>35</sup> The VSD continues to investigate this association and continues to monitor the potential risk of GBS after Menactra. The VSD is now in the process of developing RCA studies for Kinrix (GlaxoSmithKline Biologicals, Rixensart, Belgium), Pentacel (Sanofi Pasteur Ltd, Toronto, Canada), Rotarix (GlaxoSmithKline Biologicals, Rixensart, Belgium), and pandemic H1N1 influenza vaccination.

### POWER CONSIDERATIONS

With the addition of 4 new MCOs in 2001, the size of the VSD cohort increased and, with it, the statistical power available to detect rare vaccine-associated adverse events. Two examples, which illustrate the capacity of the VSD to detect rare events, follow.

The intussusception background rate of infants 6 to 35 weeks old, the age during which RotaTeq vaccine is given, is 32.4 per 100 000 person-years, as estimated from VSD data. The number of infants aged 6 to 35 weeks in the VSD cohort is ~95 000. At 90% vaccination coverage and 80% power, it would require 4.3 years to detect an RR equivalent to 2.0, 1.4 years to detect an RR of 3.0, and 0.7 years to detect an RR of 4.0.

However, the VSD has limited capability to detect very rare AEFI in minimal time periods for minimal risk ratios. For example, the background rate of GBS among 11- to 19-year-olds is 1.3 to 1.4 per 100 000 person-years (unpublished data). The average monthly cohort of 11- to 19-year-olds in the VSD cohort is between 870 000 and 1 000 000 (average monthly 11- to 19-year-old cohort). At 70% vaccination coverage and 80% power, it would require ~13 years to detect an RR of 2.0, 4 years to detect an RR of 3, and 2 years to detect an RR of 4.

### CONCLUSIONS

The VSD has conducted important vaccine-safety research since its inception in 1990, and since 2001 it has made changes that have enhanced its ability to answer urgent questions about vaccine safety and other immunization-related issues and to inform US vaccination policy.

The ability of the VSD to adapt to a changing environment is exemplified by the development of the DDM, the creation of DDFs, and the implementation of RCA projects. The DDM, a system for securely and quickly trans-

ferring data within the VSD, was developed in response to heightened confidentiality concerns. The DDM enabled the development of the DDFs. Together, the DDM and DDFs enabled the implementation of RCA, which is allowing researchers to monitor events in near real-time after the introduction of new vaccines and new vaccine recommendations. The VSD continues to refine previously used methodologies and develop new methodologies, such as the maximized sequential probability ratio test (maxSPRT), which is applicable to the VSD's RCA.<sup>15,14,36</sup> With the recent expansion of the VSD, the project is well positioned to conduct RCA studies and traditional VSD analyses on new vaccines being introduced for teenagers and young adults. Although the majority of VSD studies focus on hypotheses related to vaccine safety, the VSD has also demonstrated its ability to conduct studies on vaccine coverage,<sup>37–41</sup> disease incidence,<sup>42–49</sup> methodology,<sup>14,36,50</sup> cost-effectiveness,<sup>51–53</sup> and medical informatics.<sup>10,54</sup>

As described previously, the computerized vaccination records have been shown to be of high quality,<sup>55</sup> whereas the accuracy of computerized records to determine medical outcomes varies.<sup>56</sup> The VSD recognizes this limitation and uses additional data sources, especially medical chart review, to validate administrative data. Although not

critical for the strategic priorities of the VSD (listed in Table 1), further studies that compare population characteristics and disease incidence rates to additional non-MCO sources characterizing the national population could be beneficial for VSD studies, especially those that describe estimates of vaccine coverage and disease incidence.

The VSD is one of several worldwide research programs that are able to conduct vaccine-safety studies by using large databases. Other established programs include the US Defense Medical Surveillance System,<sup>57–59</sup> the UK General Practice Research Database,<sup>60</sup> postlicensure epidemiology of childhood vaccinations in Denmark,<sup>61</sup> and the Vietnam Vaccine Data Link.<sup>62</sup> The VSD provides scientific expertise, continues to develop innovative approaches for vaccine safety, is the primary mechanism for population-based evaluations of vaccine safety in the United States, and may serve as a model for other patient-safety collaborative research projects.

Information about the VSD project can be obtained at [www.cdc.gov/vaccinesafety/Activities/VSD.html](http://www.cdc.gov/vaccinesafety/Activities/VSD.html).

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