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BRIEF REPORT

MMR Vaccine Adverse Drug Reactions Reports in the CDC WONDER System, 1989–2019

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From January 1 to December 31, 2019, 1282 individual cases of measles were confirmed in 28 states. Of these cases, 128 required hospitalization and 61 presented complications, including pneumonia and encephalitis. This is the greatest number of cases reported in the United States since measles was declared eliminated in 2000 [1, 2]. An important potential driving factor of this outbreak may be the increased number of unvaccinated children over recent years. In fact, during the various measles outbreaks in the United States since 2000, up to 80% of the confirmed measles cases in children age ≤18 were unvaccinated [2, 3].

Despite the evidence-based benefits of vaccines as a tool to provide immunity against preventable diseases, in recent years there has been growing opposition to the use of vaccines [3]. According to the 2015 National Immunization Survey, only 72.2% of children aged 19 to 35 months in the United States were fully vaccinated [4]. Concerns about vaccine safety are a common reason parents express for refusing vaccinations for their children [5].

The dissemination of false and misleading information online has led to negative consequences, including feeding parents' concerns about vaccine safety and not giving consent to having their children vaccinated. Health care providers are recommended to counter misinformation, explaining why misinformation is wrong and providing alternative evidence-based and up-to-date explanations [6]. The Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) is a system developed to promote information-driven decision-making and provide access to detailed public health information to health care providers, which can be a useful tool to counter misinformation about vaccine safety [7]. This brief report aims to support the simplicity and versatility of the CDC WONDER Web interface to obtain up-to-date information about vaccine safety evaluating the reports submitted to the Vaccine Adverse Event Reporting System (VAERS) of children exposed to the MMR vaccine from 1989 to 2019 to provide health care workers with another tool to counter vaccine safety misinformation.

METHODS

We retrieved data from the VAERS database, a national postlicensure vaccine safety surveillance system, through the CDC WONDER interface for reports of children aged 12 months to 6 years vaccinated with the MMR vaccine in the United States between January 1, 1989, and January 1, 2019. Specific adverse drug reactions (ADRs) evaluated in this analysis included anaphylaxis, febrile seizures, encephalitis, orchitis, and idiopathic thrombocytopenic purpura. Disproportionate reporting of ADRs was assessed using proportional reporting ratios (PRRs) to identify possible new vaccine safety signals. This is a statistical aid to signal generation based on the proportionate approach and the stability of a large database. It involves the calculation of the proportions of specified reactions or groups of reactions of drugs of interest where the comparator is all other drugs in the database [8]. The result is the PRR where the PRR is a/(a + c) divided by b/(b + d) in a 2×2 table [8]. The statistical analysis was performed using SPSS software, version 23.0 (IBM, Armonk, NY, USA).

RESULTS

A total of 158 602 ADR reports were identified for the MMR vaccine (all manufacturers), and 329 379 reports for all other vaccines (Table 1). ADR terms with disproportionately higher reporting after MMR vaccine compared with all other vaccines were assessed using the criteria of Evans et al. (PRR ≥2, χ^2 ≥4 with Yates correction, and number of individual cases ≥3) [8]. No disproportionate reporting of any AE was found, except for orchitis (Table 2), even though we might expect to see a higher proportion of these ADRs with the MMR vaccine than for all other vaccines. We further evaluated disproportionate

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Table 1. CDC WONDER Reports Retrieved

	MMR Vaccine	All Other Vaccines
Anaphylaxis	130	197
Febrile seizures	1390	2446
Encephalitis	86	123
Orchitis	25	16
Severe orchitis	1	2
ITP	60	83
All ADR	158 602	329 379
All severe ADR	22 002	41 344

Anaphylaxis included anaphylactic reaction (122 MMR vaccine reports, 187 all other vaccines) and anaphylactic shock (8 MMR vaccine reports, 10 all other vaccines).

Abbreviations: ADR, adverse drug reaction; CDC WONDER, Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research; ITP, idiopathic thrombocytopenic purpura.

reporting of severe orchitis (defined as orchitis that resulted in death, permanent disability, hospitalization, congenital anomaly or birth defect, life-threatening event, or prolongation of existing hospitalization, as specified by the CDC WONDER "Serious" tab selection), and no disproportionate reporting was found.

DISCUSSION

We found no disproportionate reporting of ADRs historically associated with the MMR vaccine as compared with all other vaccines over 30 years. The CDC WONDER interface allowed us to access a fairly large data set of 158 602 ADR reports and to calculate proportional reporting ratios utilizing a simple 2×2 contingency table to detect safety signals with the criteria by Evans et al. [8].

Vaccine hesitancy has been identified as 1 of the top 10 threats to global health and is a serious hurdle to the global elimination and eradication of measles and other vaccine-preventable diseases [3, 9]. Due to parental concerns about vaccine safety, fueled by vaccine adverse reaction misinformation and propagated through organized antivaccine groups, social media, and celebrity endorsements, many families choose to opt out their children from vaccinations by obtaining nonmedical exemptions based on religious or philosophical beliefs [4, 10]. All 50 states in the United States allow medical exemptions for certain patients, for instance, immunocompromised patients or patients allergic to various vaccine components. Moreover, 30 states allow exemptions for children whose parents cite religious reasons, and 18 states permit exemptions for parents expressing philosophical reasons [5]. This growing antivaccination movement, based heavily on nonmedical exemptions, poses a threat to public health, as shown in a study that found that states with higher overall nonmedical exemption rates do have significantly lower MMR vaccine coverage [4, 9].

Table 2. Proportional Reporting Ratio Analysis

	PRR (95% CI)	χ^2 With Yates Correction	No. of Individual Cases	Meets Evans et al. Criteria?
Anaphylaxis	1.372 (1.099–1.712)	7.550	130	No
Febrile seizures	1.182 (1.106–1.263)	24.401	1390	No
Encephalitis	1.441 (1.094–1.897)	6.459	86	No
Orchitis	3.375 (1.811–6.292)	15.240	26	Yes
Severe orchitis	0.940 (0.085–10.362)	0.000	1	No
ITP	1.501 (1.077–2.093)	5.407	60	No

Evans et al. criteria for signal detection: PRR ≥2, the χ^2 ≥4, and number of individual cases ≥3.4.

Abbreviations: ITP, idiopathic thrombocytopenic purpura; PRR, proportional reporting ratio.

The CDC WONDER interface, in conjunction with VAERS, is an important tool that health care workers can use to address parents' concerns about vaccine safety for currently available vaccines, such as the MMR vaccine, or following the introduction of new vaccines. Safety data can be rapidly collected, assessed in near real time, and used to counter misinformation. On the other hand, the CDC WONDER interface can also successfully detect real safety signals requiring further investigation. For instance, during the 2010–2011 influenza, disproportional reporting for febrile seizures in young children following an inactivated influenza vaccine was detected using VAERS and PRRs. Clinical review of these reports indicated that the cases were uncomplicated and all children fully recovered. The information was quickly communicated to the public, along with reassurances on the benefit–risk balance of vaccinating their children against influenza [11].

In conclusion, the CDC WONDER online interface allows health care workers to access the large-linked electronic health record database VAERS and perform a near real-time vaccine safety analysis to provide information-driven decision-making, either to counter vaccine adverse reaction misinformation or inform parents about true possible adverse reactions.

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