

Original article

Meningococcal Conjugate Vaccine Uptake, Measured by Michigan's Immunization Registry

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Abstract

Purpose: To describe the uptake of meningococcal conjugate vaccine (MCV4) in Michigan adolescents following its approval in January 2005, and compare it to the use of meningococcal polysaccharide vaccine (MPSV4) in 2004.

Methods: All available records of meningococcal immunizations given between February 1986 and March 2006 were obtained from the Michigan Childhood Immunization Registry (MCIR), which is used by about 95% of Michigan immunization providers. During late 2005 and early 2006, these records were analyzed by immunization type, administration date, recipient age, and health care provider type (public or private).

Results: The MCIR contained 63,253 meningococcal immunizations. A total of 15.2% were given in 2004, 68.8% in 2005, and 10.8% in 2006. In those years, most immunizations occurred in June, July, and August. In 2005, 85.2% were MCV4. In 2004, 17 to 18-year olds received nearly all meningococcal immunizations; in 2005, 11 to 16-year olds received 58.0% of them. Estimates of immunization coverage were 4.0% for 11 to 12-year olds, 3.4% for 13 to 16-year olds, 5.9% for 17 to 19-year olds, and 19% for freshmen entering college.

Conclusions: Compared to 2004, in 2005 there was a large increase in the number of doses administered, with more MCV4 than MPSV4. Patterns of immunization were consistent with the Advisory Committee on Immunization Practices (ACIP) recommendations. Coverage of Michigan adolescents is low, but increased in 2005 compared with 2004. © 2007 Society for Adolescent Medicine. All rights reserved.

Meningococcal (*Neisseria meningitidis*) infection is rare, but it can cause severe meningitis or sepsis. It infects about .5 to 1 person per 100,000 population per year in the United States, with a case-fatality ratio of 10% to 14% despite treatment [1]. From 10% to 20% of survivors have long-term sequelae such as limb loss, hearing loss, or mental retardation [2]. There were 44 confirmed or probable cases of invasive meningococcal disease reported in Michigan in 2005, corresponding to an incidence of .4 cases per 100,000 population; the previous 3 years were similar (J. Beggs,

Michigan Department of Community Health, personal communication, June 28, 2006).

Tetravalent meningococcal polysaccharide vaccine (MPSV4) has been used to prevent meningococcal disease in the United States since 1981, although it was only recommended by the Advisory Committee on Immunization Practices (ACIP) for certain high-risk groups (such as certain international travelers, asplenic persons, or persons with terminal complement component deficiencies) [3]. ACIP has not routinely recommended MPSV4 for college students, although it has recommended that colleges, health care providers, and public health authorities inform college students about the disease and the vaccine [4]. Although a Michigan law was enacted in 2001 directing the Michigan Department of Community Health (MDCH) to support such informational efforts for college and high school students

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[5], meningococcal immunization of any specific group is not required by law.

On January 14, 2005, tetravalent meningococcal conjugate vaccine (MCV4) was approved for use in the United States by the U.S. Food and Drug Administration (FDA) [6]. In May 2005, the ACIP recommended routine MCV4 immunization of 11 to 12-year olds, of persons aged about 15 years prior to high school entry, of incoming college freshmen living in dormitories, and of certain other persons at increased risk of meningococcal disease [1]. Demand for MCV4 outstripped available supply in the United States in 2005, such that the manufacturer limited ordering of MCV4 in July [7]. However, the ACIP recommendations did not change to address the shortage until May 2006, when the Centers for Disease Control (CDC) recommended deferring MCV4 for 11 to 12-year olds [8]. This deferral was rescinded in November 2006 [9]. ACIP recommends that MPSV4 be considered an “acceptable alternative” if MCV4 is unavailable [1].

Once a vaccine is recommended by ACIP, it is important to monitor the implementation of the recommendation. Traditionally, the National Immunization Survey (NIS) has been used for monitoring uptake of new vaccines as well as vaccination coverage at the national and state level. Until recently, the NIS was conducted for children aged 19–35 months [10]. During the fourth quarter of 2006, the NIS will begin collecting data for adolescents 13 to 17 years of age. However, there is usually a lag time between when a recommendation is made and when a national survey will have sufficient data to evaluate implementation, limiting an immunization program’s ability to adjust implementation strategies if needed.

In contrast to a national survey mechanism, state or local immunization information systems (IISs), also referred to as immunization registries, contain immunization information on a diverse population (including adolescents and adults in some states) and can receive updates in a more timely manner. IISs are therefore useful for monitoring implementation of vaccine recommendations soon after they are made. The Michigan Childhood Immunization Registry (MCIR) has been operational since 1998. Its primary purpose is to furnish accurate, complete information on patients’ immunizations to health care providers, thereby improving immunization coverage and preventing unnecessary immunizations. The MCIR also receives funding from the CDC as an Immunization Information System Sentinel Site [11], which helps support research activities using MCIR data. We analyzed information from the MCIR to: estimate the amount of meningococcal immunizations given in Michigan, determine whether their use is consistent with ACIP recommendations, compare meningococcal vaccination patterns pre- and post-recommendation, and determine if vaccination patterns differ between public and private health care providers.

Methods

Michigan Childhood Immunization Registry (MCIR)

As of March 23, 2006, there were 3,290,797 persons under the age of 20 years having 43,343,704 immunizations recorded in the MCIR. Of those persons, 47.6% were aged 11 years or older. At the time of this study, state law required deletion of persons’ information in MCIR once they had reached 20 years of age; this restriction was later removed [12]. It was therefore impractical to examine meningococcal immunization trends before 2004, because older teenagers at that time would have reached 20 years of age by the time of the study.

At the end of 2005, there were 2082 private sites providing immunizations in Michigan, 95% of which had reported one or more immunizations to the MCIR from July to December 2005; in addition, all of Michigan’s 262 public immunization sites reported immunizations during that time frame. All Michigan health care providers are required to report vaccinations to the Michigan Department of Community Health using the MCIR unless the patient or his/her guardian has chosen to be removed from it; as of March 23, 2006, 2386 (<1%) persons have done so. Additional characteristics of the MCIR are available online [13].

Meningococcal immunization data

All records containing a date of vaccination with meningococcal vaccine were abstracted from the MCIR on October 27, 2005. A second abstraction was performed on March 23, 2006 to obtain additional data for vaccines administered after October 27, 2005. The two datasets were merged to create a single dataset that included: date of birth, type of meningococcal vaccine received (MCV4 or MPSV4), date of vaccination, and whether the vaccine was administered by a public or private provider.

Analysis included determining the total number of meningococcal doses administered over time, determining the distribution of vaccine among various age groups, and comparing provider type with type of vaccine administered, age at vaccination, and year of immunization.

Other data sources

Immunization coverage estimates were calculated by age group, as well as for college freshmen. To obtain a denominator for estimation of the proportion of entering freshmen who were immunized, the 2004 Integrated Postsecondary Education Data System (IPEDS) [14] (maintained by the National Center for Education Statistics [NCES]) was used. This database provided the number of full-time, first-time degree/certificate-seeking undergraduates enrolled for credit in Michigan postsecondary educational institutions. Information on the capacity of institution-supplied housing was used to eliminate institutions without housing from the denominator. In addition, state of residence at admission of

first-time degree/certificate-seeking undergraduates, as well as the state where their colleges were located, were used to estimate in-migration and out-migration by college freshmen, because students might be immunized in their home state before going out-of-state to college.

U.S. census data were used to determine denominators for immunization coverage by age group. This was necessary because the MCIR is not notified when a child moves out of Michigan; therefore, the MCIR overestimates population size, and would therefore underestimate immunization coverage if MCIR child records were used as the denominator. The MCIR contained records on 359,321 11 to 12-year olds (135% of the census estimate), 727,788 13 to 16-year olds (130% of the census estimate), and 474,018 17 to 19-year olds (104% of the census estimate). A dataset containing population estimates on July 1, 2004 for persons of any given age in Michigan (<http://www.census.gov/popest/datasets.html>) was used to estimate the number of persons who were 11 to 12 years old, 13 to 16 years old, and 17 to 19 years old on April 1, 2005.

Statistical analysis was performed during late 2005 and early 2006, using SAS 9.1 (SAS Institute, Inc., Cary, NC). This study was approved by the Michigan Department of Community Health (MDCH) Institutional Review Board.

Results

The MCIR yielded records of 63,253 meningococcal immunizations given to 61,798 persons from February 1986

to March 2006. Of these persons, 1312 (2.1%) had 2 or more meningococcal immunizations, and 702 (1.1%) persons had received both MPSV4 and MCV4. Of the 63,253 meningococcal immunizations, 6800 (10.8%) were given in 2006; 43,513 (68.8%) were given in 2005; 9612 (15.2%) were given in 2004; and 801(1.3%) were given in 2003. The remaining 2527 (4.0%) immunizations were given between 1986 and 2002. Of the immunizations given in 2005, 37,090 (85.2%) were MCV4 and the remainder were MPSV4. Overall, there were 43,469 records of MCV4 immunizations in the MCIR and 304 (.5%) were administered prior to 2005; these are probably due to data entry errors.

In 2004 and 2005, most recorded meningococcal immunizations were given in June, July, and August, with August being the peak month (Figure 1). The number of immunizations dropped sharply in September of both years.

Figure 2 shows the distribution of meningococcal immunization by age. In 2004, almost all recorded meningococcal immunizations were given to persons 17 or 18 years of age, with 18-year olds predominating. In 2005, the most common age at which meningococcal immunization was received remained 18 years. However, 58.0% of meningococcal immunizations were given to persons aged 11 to 16 years. Only 1.1% of meningococcal immunizations in 2005 were given at age 10 years or less.

Administration of meningococcal immunizations differed depending on whether they were given by a public or private provider (Table 1). Private providers were significantly more likely than public providers to report immuni-

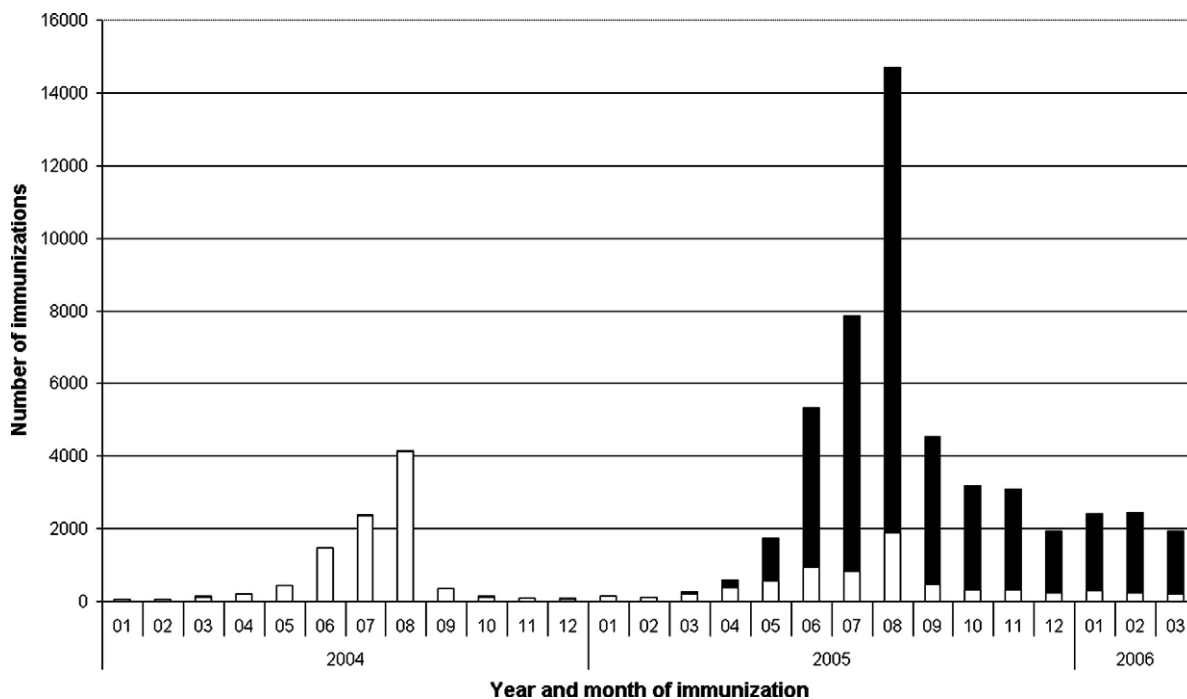


Figure 1. Number of meningococcal immunizations administered monthly from January 1, 2004 to March 23, 2006, by immunization type, Michigan Childhood Immunization Registry (MCIR). White columns signify meningococcal polysaccharide vaccine (MPSV4); black columns signify meningococcal conjugate vaccine (MCV4).

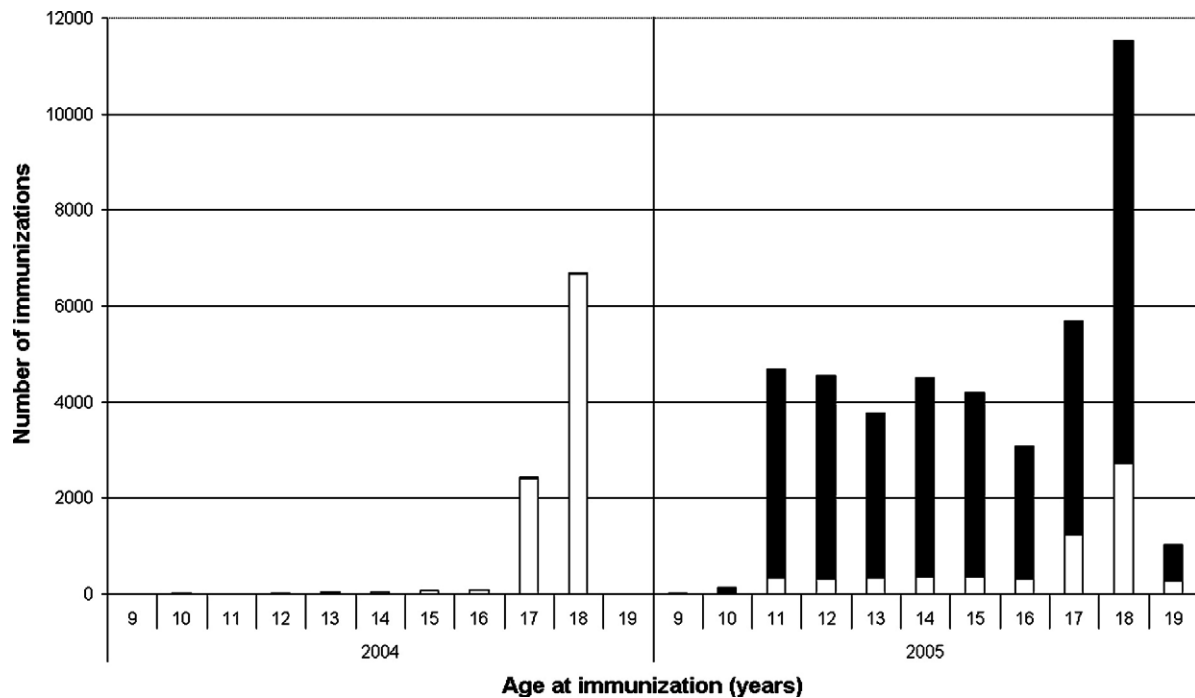


Figure 2. Number of meningococcal immunizations administered in 2004 and 2005 by age at immunization, Michigan Childhood Immunization Registry (MCIR). White columns signify meningococcal polysaccharide vaccine (MPSV4); black columns signify meningococcal conjugate vaccine (MCV4).

zations in persons aged 11–16 years and to report immunizations in 2005 compared with 2004. Although private providers were significantly more likely to report MPSV4 instead of MCV4 when compared to public providers, the difference between the two groups was less than two percentage points.

An estimate of the proportion of incoming college freshmen immunized against meningococcal disease was made. The MCIR contained 14,543 records of meningococcal immunizations given from May 1, 2005 through September 30, 2005 to persons aged at least 18 years by December 1, 2005 (corresponding to Michigan's statutory starting age for kindergarten [15]). There were 77,822 full-time, first-time

degree/certificate-seeking undergraduates enrolled for credit in Michigan in the fall of 2004. Assuming that enrollment was similar in fall 2005, and that all of these immunizations were given to full-time, first-time degree/certificate-seeking undergraduates, an estimated 19% received a meningococcal immunization near the start of the academic year. Further assuming that all of these immunizations were given to students attending institutions that provide housing (49,428 persons), an estimated 29% were immunized. These proportions do not appear to be affected by migration, because 8271 first-time degree/certificate seeking undergraduates (full-time or part-time) entered Michigan from other areas in 2004, while 8587 left Michigan to study elsewhere

Table 1

Association of public/private provider status with other aspects of meningococcal immunization delivery

Association of private provider with:	Distribution of immunizations		OR	95% CI	p-value
	Private	Public			
	(n = 30401)	(n = 13112)			
Age 17–19 at immunization in 2005	29.6%	70.6%	Reference		
Age 11–16 at immunization in 2005	70.4%	29.4%	5.7	5.5–6.0	<.0001
MCV4 given in 2005	84.7%	86.5%	Reference		
MPSV4 given in 2005	15.3%	13.5%	1.2	1.1–1.2	<.0001
	(n = 34924)	(n = 18201)			
Immunization in 2004	13.0%	28.0%	Reference		
Immunization in 2005	87.0%	72.0%	2.6	2.5–2.7	<.0001

MCV4 = meningococcal conjugate vaccine; MPSV4 = meningococcal polysaccharide vaccine; OR = odds ratio; CI = confidence interval.

(79,810 remained in Michigan to study). This amounts to 1.03 students leaving for each student entering. Assuming that meningococcal immunization coverage is similar among students entering and leaving Michigan, migration would have little effect on the proportion of students immunized.

Estimated immunization levels for the total population in various age groups are much lower than estimated immunization levels for incoming college freshmen. U.S. Census Bureau estimates for July 1, 2004 indicate that there were 265,865 Michigan residents who would be aged 11–12 years on April 1, 2006, as well as 558,269 aged 13–16 years, and 455,325 aged 17–19 years. There were 9059 meningococcal immunizations given to such 11–12-year olds, 20,294 to 13–16-year olds, and 27,283 to all 17–19-year olds (regardless of whether they entered college). Thus, assuming that the population of these groups was essentially unchanged since July 1, 2004, the estimated vaccination coverage levels on March 23, 2006 for these age groups are 3.4%, 3.6%, and 6.0%, respectively; coverage for the group as a whole (aged 11–19 years) is estimated to be 4.4%.

The effect of a Food and Drug Administration (FDA) alert that was released on September 30, 2005 regarding a possible association between MCV4 administration and Guillain-Barré syndrome (GBS) [16] was investigated. Examining MCIR records of MCV4 by week of administration showed a decrease of roughly 30% in the number of immunizations administered in the week of October 2–8, which recovered over the next 3 weeks, but this may be due to chance (data not shown).

Discussion

Principal findings

Our results indicate that there was a clear shift from MPSV4 to MCV4 in Michigan in 2005. In addition, meningococcal immunization increased in 2005, and health care providers began to immunize children aged 11 to 16 years. Persons aged 17 and 18 years were most likely to have immunizations reported in both years. Private providers were much more likely than public providers to report meningococcal immunizations to children aged 11–16 years in 2005; private providers were also more likely to report immunizations in 2005 compared to 2004. Generally, immunization providers in Michigan appear to have followed ACIP recommendations on the use of meningococcal vaccines in persons under 20 years of age. However, overall coverage among the 11 to 19-year old age group remained low (4.4%). A trend of increased immunization in June, July, and August was seen in both 2004 and 2005, consistent with students getting immunized prior to a new academic year.

Limitations

There are several limitations to this study. The deletion of data at age 20 years hindered examination of past trends, because many immunized persons were older than age 20 by the time the data were obtained. For example, the immunization status of most 19-year olds in 2004 could not be determined because they had aged past 20 years when the data were first abstracted on October 27, 2005. In addition, continual improvement in provider participation in the MCIR confounds trend interpretation; there are apparent increases in immunization coverage from year to year, as more immunizations are reported. It is also possible that some MCV4 immunizations were mistakenly recorded as MPSV4 by MCIR users, biasing downward the proportion of MCV4 in 2005. Furthermore, because not all immunization providers fully participate in the MCIR, the data must be incomplete. Although approximately 95% of Michigan immunization providers participated to some degree during the last 6 months of 2005 [13], MCIR users might enter adolescent immunizations less commonly than childhood immunizations. These combined factors bias downward the number of meningococcal immunizations recorded, possibly by a large amount.

The MCIR contains substantially more records of adolescents than census data would suggest. This is mainly because persons who move into Michigan and are immunized get added to the MCIR, but the MCIR is not notified when a person moves out of Michigan. Therefore, the MCIR can be viewed as a registry of persons who received at least one immunization in Michigan, but do not necessarily live in Michigan currently. For this reason, U.S. Census Bureau population estimates were used as the denominator for the coverage estimates, preventing further downward bias in the coverage estimates.

There are also potential problems with comparing immunization patterns between public and private providers. Public providers have tended to provide better quality data than private providers, and to adopt the MCIR earlier. Therefore, there has been more growth in private provider reporting from 2004 to 2005 than there has been in public provider reporting. This would tend to inflate the association of private provider status with immunization in 2005, and might also explain the slight association of private providers with MPSV4 administration (private providers might be more likely to mistakenly record MPSV4).

Relationship to other studies

These data yield the rough estimate that 19% or more of incoming Michigan college freshmen were immunized against meningococcal disease just prior to the start of the 2005–2006 academic year. Considering that Michigan law does not require college freshmen to be immunized against meningitis, our estimate is higher than we expected. Only one other attempt to quantify meningococcal immunization

in this group was found in the literature. In 1999, 2000, and 2001, 13%, 46%, and 60%, respectively, of incoming Brown University (Providence, RI) freshmen had received MPSV4 (an educational intervention occurred prior to students' arrival in 2000 and 2001) [17]. Other researchers have found that mass immunization campaigns on college campuses following real or perceived meningitis outbreaks have immunized 51% to 87% of the targeted population [18]. In this context, the magnitude of the estimate provided here seems reasonable, recognizing that it is an underestimate. It will be possible to calculate a more reliable estimate for 2006.

Timeliness, flexibility, low cost, and the ability to capture great detail are important advantages to the use of immunization information systems (IISs) for determining immunization coverage and uptake, compared to national surveys. For example, the pneumococcal conjugate vaccine (PCV7) was first recommended by ACIP in October 2000 [19]; the first PCV7 coverage estimates that the National Immunization Survey (NIS) produced were for 2002, and were published in August 2003 [20], almost 3 years after the recommendation. The NIS can only monitor immunization coverage on a yearly basis, and must limit the amount of information requested from respondents to attain high response rates. In contrast, IISs can provide any subset of their information at any particular time, and contain far more detail than the NIS can capture. At this time, studies of IIS data cannot replace the NIS, which provides representative and comparable immunization coverage estimates for urban areas, states, and the United States as a whole. IISs cannot currently provide rigorous statewide population-based estimates due to incomplete or varying coverage of the population, although they can provide detailed information for public health workers at the state and local levels for the relatively low cost of employing an epidemiologist or data analyst. IISs are continuing to improve and expand, however, and the usefulness of their data will continue to increase.

Interpretation of the study

It is likely that some people who wanted MCV4 were unable to get it due to demand outstripping supply in 2005 [7]. This may have caused more administration of MPSV4 than would have been seen in the absence of an MCV4 shortage, as well as causing people to delay immunization. Unfortunately, little information was available regarding the impact of the shortage in Michigan. Although Michigan did not experience a shortage of publicly purchased MCV4 vaccine (D. Wildt, Michigan Department of Community Health, personal communication, May 8, 2006), there is anecdotal evidence that some Michigan health care providers had difficulty obtaining MCV4 privately, and Sanofi Pasteur released a statement addressing the shortage in July 2005 [7]. Almost a year later (May 19, 2006), the CDC

recommended that administration of MCV4 to persons aged 11 to 12 years be deferred, while stating that Sanofi Pasteur expected the demand for MCV4 to continue outpacing the supply through the summer of 2006 [8]. The CDC declared the shortage over in November 2006 [9]. The MCIR may prove useful in the future for studying the effects of such incidents on immunization, and has already been used to examine PCV7 shortages [21].

The FDA released an alert on September 30, 2005 regarding a possible association between MCV4 administration and Guillain-Barré syndrome (GBS) [16]. Preliminary evidence of such an association was reported on October 6, 2005 [22]. The MCIR did not show a large or sustained decrease in MCV4 administration following those events. Further information was published by the CDC in October 2006, indicating that the risk of GBS might be slightly higher in the 6-week window following MCV4 immunization, although investigation is continuing [23].

In addition to MCV4, other new immunizations are being targeted to adolescents (human papillomavirus vaccine [HPV]; tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine [Tdap]). It can be difficult to reach adolescents for immunizations, but this study shows that Michigan is having some success with MCV4. As the MCIR continues to improve, it will become more useful for monitoring immunization uptake in adolescents.

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