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## Timeliness of childhood vaccination in the Federated States of Micronesia

Ashley Tippins<sup>a,\*</sup>, Andrew J. Leidner<sup>b</sup>, Mehreen Meghani<sup>c</sup>, Aja Griffin<sup>d</sup>, Louisa Helgenberger<sup>e</sup>, Mawuli Nyaku<sup>a</sup>, J. Michael Underwood<sup>a</sup>

<sup>a</sup> Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases, Immunization Services Division, Atlanta, GA, United States

<sup>b</sup> Berry Technology Solutions, Atlanta, GA, United States

<sup>c</sup> Leidos, Inc., Atlanta, GA, United States

<sup>d</sup> Association of Schools & Programs of Public Health, Atlanta, GA, United States

<sup>e</sup> Federated States of Micronesia Department of Health & Social Affairs, Pohnpei, Federated States of Micronesia

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### ABSTRACT

**Background:** Vaccination coverage is typically measured as the proportion of individuals who have received recommended vaccine doses by the date of assessment. This approach does not provide information about receipt of vaccines by the recommended age, which is critical for ensuring optimal protection from vaccine-preventable diseases (VPDs).

**Objective:** To assess vaccination timeliness in the Federated States of Micronesia (FSM), and the projected impact of suboptimal vaccination in the event of an outbreak.

**Methods:** Timeliness of the 4<sup>th</sup> dose of diphtheria, tetanus, and acellular pertussis vaccine (DTaP) and 1<sup>st</sup> dose of measles, mumps, and rubella vaccine (MMR) among children 24–35 months was assessed in FSM. Both doses are defined as on time if administered from 361 through 395 days in age. Timeliness was calculated by one-way frequency analysis, and dose delays, measured in months after recommended age, were described using inverse Kaplan-Meier analysis. A time-series susceptible-exposed-infected-recovery (TSEIR) model simulated measles outbreaks in populations with on time and late vaccination.

**Results:** Total coverage for the 4<sup>th</sup> dose of DTaP ranged from 36.6% to 98.8%, and for the 1<sup>st</sup> dose of MMR ranged from 80.9% to 100.0% across FSM states. On time coverage for the 4<sup>th</sup> dose of DTaP ranged from 3.2% to 52.3%, and for the 1<sup>st</sup> dose of MMR ranged from 21.1% to 66.9%. Maximum and median dose delays beyond the recommended age varied by state. TSEIR models predicted 10.8–13.7% increases in measles cases during an outbreak based on these delays.

**Conclusions:** In each of the FSM states, a substantial proportion of children received DTaP and MMR doses outside the recommended timeframe. Children who receive vaccinations later than recommended remain susceptible to VPDs during the period they remain unvaccinated, which may have a substantial impact on health systems during an outbreak. Immunization programs should consider vaccination timeliness in addition to coverage as a measure of susceptibility to VPDs in young children.

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### 1. Introduction

Childhood vaccination improves life expectancy, decreases healthcare costs, and reduces the spread of preventable diseases [1–4]. Routine vaccination averts an estimated 2–3 million deaths globally due to diphtheria, tetanus, pertussis, and measles every year [5]. In the United States alone, routine vaccinations prevented an estimated 322 million illnesses, 21 million hospitalizations, and 732,000 deaths, at a net savings of \$295 billion in direct costs and \$1.38 trillion in total societal costs, for children born during the period 1994–2013 [6]. International organizations such as the World Health Organization (WHO) implement programmatic

**Abbreviations:** WHO, World Health Organization; VPD, vaccine-preventable disease; ACIP, Advisory Committee on Immunization Practices; FSM, Federated States of Micronesia; DTaP, diphtheria and tetanus toxoids and acellular pertussis; MMR, measles, mumps, and rubella; TSEIR, time-series-susceptible-exposed-infected-removed.

\* Corresponding author at: Immunization Services Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd., MS-A19, Atlanta, GA 30329, United States.

E-mail address: [ikp9@cdc.gov](mailto:ikp9@cdc.gov) (A. Tippins).

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immunization programs to ensure high vaccination coverage around the world [7].

The Federated States of Micronesia (FSM) is an island nation spread nearly 2700 km across the Pacific Ocean just north of the equator. There are four island states, Chuuk, Kosrae, Pohnpei, and Yap, and all states except Kosrae are comprised of one main “high” island surrounded by lower lying outer islands. According to the 2010 census, there were 12,073 children under the age of 5 years throughout the FSM states [8]. Researchers from the Centers for Disease Control and Prevention (CDC) partner with local immunization programs to monitor vaccination coverage among children and adults in FSM and other U.S. Affiliated Pacific Island jurisdictions. Technical assistance provided by CDC based on vaccination coverage assessments aid the local programs in assessing the level of vulnerability to vaccine-preventable diseases (VPD) in their jurisdictions, evaluating their program interventions, and developing recommendations and technical support for key stakeholders [9].

Most childhood vaccines are administered in FSM according to the Advisory Committee on Immunization Practices (ACIP) recommendations, with a few exceptions based on the increased burden of some VPDs in the region. The ACIP recommendations include guidelines for vaccination timeliness, or adherence to the recommended timing and spacing of doses, ensuring protection from VPDs as early in life as possible. Late vaccine administration increases the length of time required to obtain adequate protection from VPDs [10]. Previous studies have shown low vaccination timeliness despite high vaccination coverage in many countries [11–17].

While prior CDC assessments found moderate to high vaccination coverage in FSM, they did not account for timing of vaccination in the assessment. In 2016, CDC researchers reassessed vaccination data for 1824 children born between 2007 and 2014. The objective of this study was to examine the traditional measure of total vaccine uptake compared to on time vaccination coverage for four doses of diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) and one dose of the measles, mumps, and rubella vaccine (MMR) among children 24–35 months. Additionally, a standard deterministic compartmental model was developed to represent transmission dynamics and estimate the potential impact of a hypothetical measles outbreak in each state based on measured levels of vaccine uptake and timeliness. The assessment of on time coverage in this study provides a more rigorous examination of the nuanced aspects of vaccination coverage than a traditional vaccination coverage assessment; typically vaccination coverage assessments only measure the number of vaccine doses administered by a certain age, regardless of timing and spacing [16]. This study highlights the importance of vaccination timeliness in the context of vaccination coverage assessments, local immunization program objectives, and community protection against the spread of VPDs, and provides information that can be used by the immunization program to improve planning and strategy of vaccination outreach activities.

## 2. Methods

### 2.1. Survey methods

Cross-sectional vaccination coverage assessments were conducted in the four FSM states from 2010–2016. Vaccination dates for children 24–35 months were collected from shot cards, hospital medical records, foreign medical records, public health immunization log books, or immunization information system records, where available.

In Pohnpei, a randomized household-based survey was conducted by the FSM Department of Health and the CDC from October 18, 2010 to December 30, 2010. On the Pohnpei main island, a population-based systematic random sampling survey

was conducted. Starting from a randomly chosen point in each enumeration district on the main island, every 4<sup>th</sup> household was selected to determine eligibility in the survey. Eligibility was determined by the presence of at least one child age 19–35 months living in the household. Enumeration districts in this survey are the same used by the FSM Census. Because the population on the outer islands was small (353 total households), a full census was conducted in those locations. If a respondent from any household on a neighboring island or any randomly selected household on the main island was not available, two follow-up attempts were made for that household.

In Chuuk (2016), Kosrae (2013), and Yap (2015), a census of administrative data and public health records was conducted as a cost- and time-efficient alternative to a household survey to estimate vaccination coverage. Children 24–35 months were identified using birth records and public health records, then all available vaccination records were collected for each child. Data from each available source were combined, compared, and de-duplicated to provide the most accurate vaccination history for each child.

Informed consent was obtained during survey interviews and all data collection protocols were approved by the CDC Institutional Review Board and the FSM Department of Health & Social Affairs review board.

### 2.2. Outcome measures

Vaccination doses recommended for this age group by the ACIP or FSM Department of Health included: 1 dose of Bacillus Calmette-Guerin vaccine, 4 doses of diphtheria and tetanus toxoids and acellular pertussis vaccine, 3 doses of inactivated poliovirus vaccine, 2 doses of measles, mumps and rubella vaccine, 3 doses of *Haemophilus influenzae* type B vaccine and 3 doses of Hepatitis B vaccine. For the purpose of this study, timeliness was assessed for two vaccines, DTaP, and MMR. These vaccines were of particular interest because FSM experienced outbreaks of pertussis and measles in recent years [18,19]. Only the first dose of MMR was included in this analysis because the open-ended definition of the recommended age for the second dose of MMR in FSM ( $\geq 13$  months) was not suitable for these types of analyses.

In addition to total coverage, or percentage of children up-to-date with the recommended number of vaccine doses by age 24–35 months, we analyzed receipt of vaccine doses according to the schedule approved by FSM Department of Health (Table 1). Because number of days in a month varies, an average of 30.4 days was used to calculate age at vaccine dose. Recommended age for routine administration of the four doses of DTaP according to ACIP are 2 months, 4 months, 6 months, and 15–18 months, respectively; ACIP states the 4<sup>th</sup> dose can be administered as early as age 12 months, provided a minimum interval of at least 6 months has elapsed since the third dose. Recommended age for routine administration of the 1<sup>st</sup> dose of MMR according to ACIP is 12–15 months. FSM recommends the 4<sup>th</sup> dose of DTaP and the 1<sup>st</sup> dose of MMR at the minimum age of 12 months. Measures of on time coverage for these doses follow the FSM recommendation. The recommended vaccine schedule describes minimum age and minimum intervals between doses of a vaccine series to confer optimal immunity. However, to avoid re-administration of early doses, the ACIP defines a dose as acceptably early if the dose occurs during a 4 day grace period before the minimum age or interval. Doses received within the grace period were included in the measure of on time coverage [10].

### 2.3. Statistical analysis

#### 2.3.1. Vaccine uptake and timeliness

Total vaccination coverage and on time coverage were calculated by one-way frequency analysis. Household survey results

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