Frequency and Cost of Vaccinations Administered Outside Minimum and Maximum Recommended Ages—2014 Data From 6 Sentinel Sites of Immunization Information Systems

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Objective To quantify vaccinations administered outside minimum and maximum recommended ages and to determine attendant costs of revaccination by analyzing immunization information system (IIS) records.

Study design We analyzed deidentified records of doses administered during 2014 to persons aged <18 years within 6 IIS sentinel sites (10% of the US population). We quantified doses administered outside of recommended ages according to the Advisory Committee on Immunization Practices childhood immunization schedule and prescribing information in package inserts, and calculated revaccination costs. To minimize misreporting bias, we analyzed publicly funded doses for which reported lot numbers and vaccine types were consistent.

Results Among 3 394 047 doses with maximum age recommendations, 9755 (0.3%) were given after the maximum age. One type of maximum age violation required revaccination: 1344 (0.7%) of 194 934 doses of the 0.25-mL prefilled syringe formulation of quadrivalent inactivated influenza vaccine (Fluzone Quadrivalent, Sanofi Pasteur, Swiftwater, PA) were administered at age ≥36 months (revaccination cost, $111 964). We identified a total of 7 529 165 childhood, adolescent, and lifespan doses with minimum age recommendations, 9542 of which (0.1%) were administered before the minimum age. The most common among these violations were quadrivalent injectable influenza vaccines (3835, or 0.7% of 526 110 doses administered before age 36 months) and Kinrix (GlaxoSmithKline Biologicals, Rixensart, Belgium; DTaP-IPV) (2509, or 1.2% of 208 218 doses administered before age 48 months). The cost of revaccination for minimum age violations (where recommended) was $179 179.

Conclusion Administration of vaccines outside recommended minimum and maximum ages is rare, reflecting a general adherence to recommendations. Error rates were higher for several vaccines, some requiring revaccination. Vaccine schedule complexity and confusion among similar products might contribute to errors. Minimization of errors reduces wastage, excess cost, and inconvenience for parents and patients. *(J Pediatr 2017;■■:■■-■■).*

The US Food and Drug Administration approves vaccines for defined indications and age ranges. The Advisory Committee on Immunization Practices (ACIP) issues recommendations to guide vaccination practices in the US.[1,2] These recommendations include minimum and maximum ages and intervals for vaccination, and which age-related errors require revaccination. Over the years, the US childhood immunization schedule has increased in complexity as new vaccines have been introduced and recommendations have expanded.[1,3,4]

For some vaccines, recommended dose volumes vary between age groups. For example, several products are available within the class of inactivated influenza vaccines. Before 2016, 1 of these products was licensed for 0.25-mL intramuscular injection in children aged 6-35 months (Fluzone Quadrivalent, Sanofi Pasteur Inc., Swiftwater, PA). This product (and other inactivated influenza vaccines) should be administered as a 0.5-mL dose to persons aged ≥36 months, and revaccination procedures are specified for scenarios in which administered vaccines or dose volumes are incorrect for a vaccinated patient.[5,6]

Introduction of new vaccines and increasing complexity of the immunization schedule increases the opportunity for vaccination errors, which potentially can leave patients less protected from vaccine-preventable diseases and generate additional costs, particularly in instances where revaccination is required. These errors waste vaccine, require additional clinical staff time and resources, and inconvenience patients and caregivers. Errors also have the potential to decrease patient confidence in the healthcare system.

Previous studies have sought to document age-related vaccination errors. During 1997, one clinic analyzed 6983 vaccine doses administered during a 3-month period to children aged <5 months and identified 4.1% of the doses as invalid, with 35.5% of patients receiving at least 1 invalid dose.[7] During 2000, it was estimated that

ACIP	Advisory Committee on Immunization Practices
CDSi	Clinical Decision Support for immunizations
IIS	Immunization information system

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10.5% of a nationally representative sample of 19- to 35-month-old US children received at least 1 dose before the minimum age or minimum interval, necessitating revaccination[8]; the national proportion of children receiving an invalid dose requiring revaccination was estimated as 8% during 2005.[9] A more recent study analyzed vaccination errors reported to the Vaccine Adverse Event Reporting System during 2000-2013[10] and identified 5947 errors (27% of the total error reports) classified as "inappropriate vaccine schedule," indicating that vaccines had been administered outside recommended ages or with improper spacing between doses.

To provide an estimate of errors among routinely recommended vaccines in persons aged <18 years, we used provider-reported vaccination records from 6 immunization information systems (IIS), quantifying the frequency of vaccination outside minimum and maximum recommended ages. IISs are confidential databases that record vaccine doses administered to persons residing within defined jurisdictions and perform a spectrum of functions that improve vaccination practices.[11] Fully functioning IISs serve providers at the time and location of clinical care by consolidating immunization histories submitted by multiple providers and supporting help to identify vaccinations that are due or that must be repeated owing to age or interval errors. Provider-reported, population-based IIS data are uniquely suited to provide comprehensive assessments of age-related vaccination errors across large populations.

Methods

During 2014, IIS sentinel sites were located in Michigan, Minnesota, North Dakota, 6 contiguous Oregon counties, Wisconsin, and New York City. Collectively, these geographic areas contain approximately 10% of the US population aged <18 years.[12] These sites receive competitive cooperative agreement funding through the Centers for Disease Control and Prevention (CDC), and all meet high IIS data quality standards, with at least 85% of persons aged <19 years and at least 85% of provider sites in these jurisdictions participating in their respective IIS. These sites transmit quarterly batches of deidentified IIS records to the CDC to enable public health studies. Data submissions are processed through the IIS Trends in Immunization Practices System, a SAS-based (version 9.3, SAS Institute, Cary, North Carolina) program that performs data quality processing functions, including removing suspected duplicate records[13] and conducting data cleaning to remove records with errors in critical date fields or product identifiers.

Each IIS sentinel site queried its respective IIS during January 2015 and transmitted the deidentified vaccination records to the CDC. We analyzed routinely recommended vaccines given to persons aged <18 years between January 1, 2014, and December 31, 2014. We used reported "CVX codes" to identify the type of vaccine that was administered. These numerical identifiers are defined by the CDC and are used by IIS and other information systems to identify the vaccines indicated for protection against the same disease and have the same formulation, concentration, and manufacturing process. Vaccines that share these aspects receive the same CVX code, even if trade names or manufacturers differ. CVX codes were grouped according to their indication for total counts of vaccines given for each disease,[14] and related CVX codes (eg, preservative-containing and preservative-free influenza vaccines that are reported as distinct CVX codes) are described as a single product type for instances in which age recommendations were identical for the grouped products.

To minimize the effects of misreporting, wherein the vaccine type reported differed from the vaccine type administered, we restricted the analysis to doses that were "verified." We verified doses by comparing the reported lot number to reference tables that linked known lot numbers of publicly purchased vaccines to corresponding CVX codes; this table contained all lot numbers for vaccines purchased or distributed through the CDC's centralized distribution system from July 2013 through December 2014 (personal communication with J. Santoli and L. Galloway, November 17, 2015). For instances where it was necessary to distinguish between products that shared a CVX code, we identified products by examining reported trade name and manufacturer codes.

Statistical Analyses

We performed all analyses using SAS version 9.3 and Excel 2010 (Microsoft, Redmond, Washington). For each vaccine type within a routinely recommended vaccine type grouping, we quantified doses administered outside the vaccine type's recommended ages, as defined by the "preferable vaccine type begin/end age," identified in Clinical Decision Support for Immunizations (CDSi) version 3.1,[15] with the exception of products for which recommendations changed between 2014 and the release of CDSi version 3.1. CDSi resources systematically document ACIP recommendations; where ACIP recommendations were not available, these tables rely on product labeling for determining recommended ages. Counts of doses outside recommended age limits were included regardless of dose number or intervals between doses. Narrative description of individual products was limited to vaccines with at least 100 doses administered outside recommended age limits; products with fewer errors were included in the tables. We were unable to exclude vaccinations deliberately administered off-schedule from dose counts, because the submitted data did not include information describing patient travel, local outbreaks, or other indications of deliberate off-label administration. Underlying health conditions and other indicators of increased risk were not available for individual vaccination records, which prevented allowances for recommendations specific to these groups. For doses administered from multidose vials, we were unable to determine dose volume, and in such instances, dose volumes were assumed to be correct for the patient's age.

Revaccination cost (c) was calculated as $c = n\,(p + a + w + t)$, where n is the number of verified doses requiring revaccination, p is the price per dose for vaccines purchased through 2014 CDC vaccine contracts,[16] a is administrative cost per vaccination for vaccines administered at a public clinic (set to $8.34

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