

An Event History Analysis of Childhood Immunization: The Changing Tempo of MMR Vaccination in the United States

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Wakefield et al's (1998) *Lancet* article, falsely linking the Measles-Mumps-Rubella (MMR) vaccine with autism, sparked a renewed culture of vaccine resistance in the United States. Although subsequently retracted, the article succeeded in feeding a fear of vaccines (evident since Jenner first developed the cowpox vaccine in 1796), a growing distrust of federal, medical, and corporate institutions (the CDC and FDA, western medicine, and "Big Pharma"), and a desire to minimize one's individual risk (often at the expense of community health).

This misinformation and resulting controversy has led many parents to refuse vaccines altogether or to choose an "alternate vaccination scheduling" (Blendell & Fehr, 2012): delaying one or more vaccine doses until children are older; splitting combination vaccines (MMR, DTaP) into components parts; or selecting only certain recommended childhood immunizations. Nearly half (45%) of the parents who reported intentionally delaying vaccinations made this choice out of concerns for "vaccine safety or efficacy" and, of all the US children whose parents intentionally delayed vaccines, only 35% received all their recommended vaccines by the recommended age (Smith et al, 2010). Ultimately, only half (51%) of US children born 2004-2008 were fully vaccinated by the age of 2 years (CDC, 2013a).

Leaving only a few children unvaccinated may not be cause for concern (and exemptions are available for children who choose not to get vaccinated for legitimate medical, religious, or philosophical reasons). However, delaying or refusing vaccinations extends the time during which clusters of unvaccinated children are susceptible to contracting and transmitting disease (Glanz et al, 2009). The dangers of vaccine resistance are evident in recent outbreaks of various vaccine-preventable diseases (including measles, mumps, Hib, and pertussis). As of August 2013 (less than eight months into the year), 159 cases of measles had been reported in 16 states across the country, more than double the median annual number of cases reported (60) over the previous twelve years. 131 of these measles cases (82%) occurred among people who were unvaccinated (CDC, 2013b).

The Advisory Committee on Immunization Practices (ACIP) recommends that children in the United States receive a total of 15 doses of six different vaccines (the 4:3:1:3:3:1 vaccine series) by the age of 19 months, including one dose of MMR vaccine between 12-15 months (360-540 days) of age. Using provider vaccination data from the National Immunization Survey (NIS), a nationally representative annual sample of 20,000 US children aged 19 to 35 months (Smith et al, 2001), this study conducts an event history analysis to examine whether vaccination delay has become more common in recent years. Specifically, between 1995 and 2011, was there a significant increase in the age (measured in days) at which "critical proportions" of US children were left unvaccinated against MMR?

Anderson & May (1991) estimated "critical proportions" of a population that need to be immunized to eradicate various infectious diseases. By their estimates, 90% to 95% of a community must be immunized to provide herd immunity against measles. Given the recent increase in measles cases across the US, this paper will focus on testing for delays in the age at

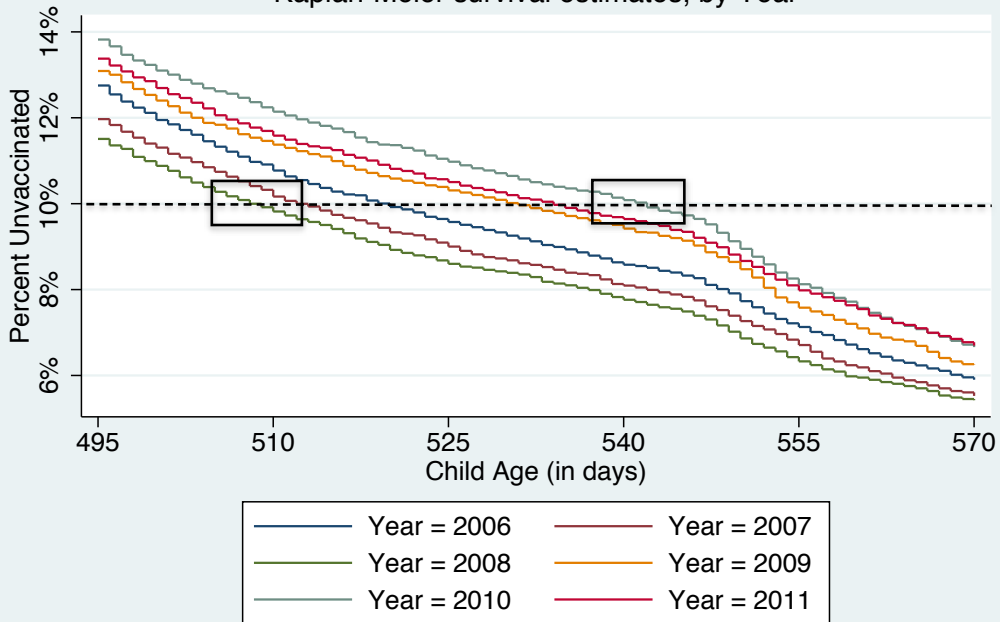
which 90% and 95% of children received the MMR vaccine (measured conversely by the age at which 10% and 5% of children are still unvaccinated against MMR).

This study will consist of a multivariate analysis using Cox, proportional hazard, and parametric regression models (the latter providing an accelerated failure time (AFT) model) to estimate the timing—rather than relative hazard—of MMR vaccination (Sethi & Gange, 2009). Additionally, the analysis will assess whether any vaccination delay varied significantly by socioeconomic status (SES). Given previous research showing higher rates of vaccine refusal among Whites, married mothers and college graduates (Smith, Chu & Barker, 2004), at least part of any delay may be explained by "alternate vaccination scheduling" among high-SES parents (defined by mother's level of education). This finding would provide evidence to contradict the SES-Health Gradient (which typically finds higher SES associated with better health outcomes).

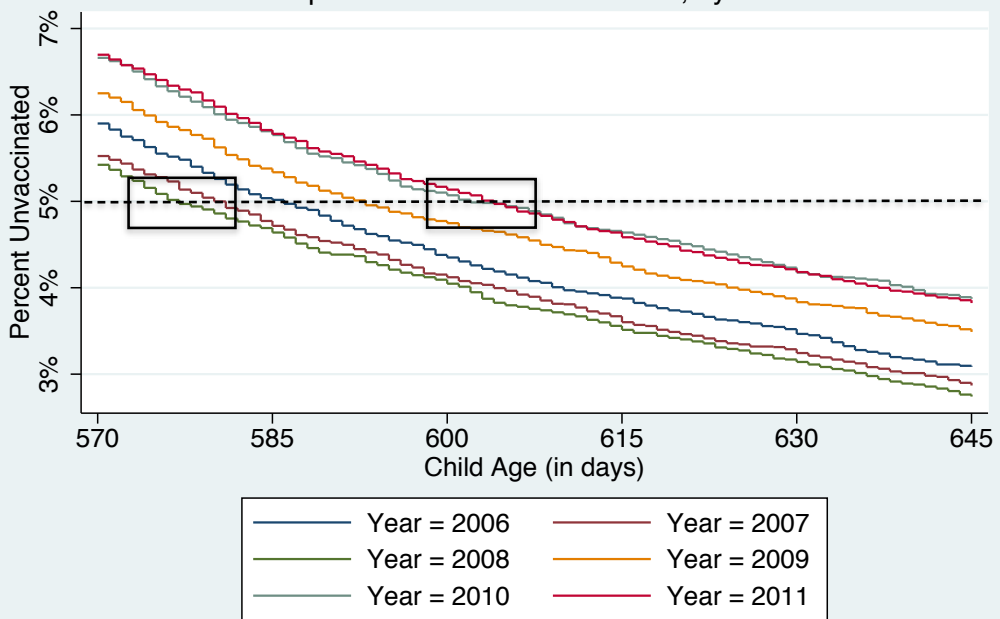
Preliminary results show that, while critical proportions of children were vaccinated at increasingly younger ages during the early years under consideration, recent years have seen a delay of about one month in the age at which 10% and 5% of children were still unvaccinated against MMR (as seen in the two Kaplan-Meier survival curves, below). Between 2008 (when 10% of children were unvaccinated at about 510 days of age) and 2010 (when the same proportion of children were still unvaccinated at 540 days of age), this critical proportion of children remained unvaccinated against MMR for an additional 30 days. Likewise, 5% of children were unvaccinated at 575 days of age in 2008, while the same proportion of children were still unvaccinated at 605 days of age in 2010, again leaving a critical proportion of children unvaccinated against MMR for another 30 days. So, over the course of just a couple of years, 10% and 5% of US children remained unvaccinated for an additional month (already beyond the recommended age of vaccination and approaching 18 to 20 months of age) extending even further the time during which a critical proportion of children (and their communities) were susceptible to measles outbreaks.

In the true nature of Type 2 Translational Research, immunization programs and policies need to understand and address the source of this delay in order to reduce outbreaks of vaccine-preventable disease and improve the health of individuals along with entire communities.

Ten Percent (10%) of Children Unvaccinated Kaplan-Meier survival estimates, by Year



Five Percent (5%) of Children Unvaccinated Kaplan-Meier survival estimates, by Year



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