Real-world Effectiveness of the Influenza Vaccine in Young Children

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Influenza causes substantial illness and healthcare utilization among children. Randomized clinical trials (RCTs) demonstrate that the influenza vaccine reduces influenza illness detectable via active surveillance, but RCTs typically have insufficient samples to examine economically meaningful outcomes such as healthcare provider visits. In this study we document that children aged two through five whose well-child visits occur when the seasonal influenza vaccine is broadly available are 23.4 percentage points more likely to be vaccinated than those whose visits do not. Using large administrative healthcare datasets, we leverage this variation in vaccination rates to show that the influenza vaccine reduces outpatient and emergency department visits significantly. The results imply that making pediatric influenza vaccinations more convenient could substantially increase vaccination rates and reduce healthcare expenditures.

Though public health authorities prioritize influenza vaccination of young children, approximately half of US children go unvaccinated (CDC, 2023). Despite this policy focus, the benefits of increasing vaccination rates in this age group are poorly quantified. There is scarce real-world evidence on the effectiveness of the influenza vaccine in chil-

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dren and, given inherent limitations in large-scale testing, considerable uncertainty about the overall burden of disease caused by influenza (Sullivan, Monto and Longini Jr, 1993; Tokars, Olsen and Reed, 2018). Nevertheless, several patterns suggest that there may be high returns to vaccinating children against influenza. For example, infants and young children experience sharp increases in outpatient visits, antibiotic prescriptions, acute ear infections, emergency department (ED) visits, and hospitalizations during influenza season (Izurieta et al., 2000; Neuzil et al., 2000; Chiu et al., 2002; Neuzil et al., 2002; Heikkinen et al., 2004; Ruf and Knuf, 2014), suggesting a high burden of influenza disease. ED visit rates for influenza and pneumonia are also higher for children under five than any other age group except adults over 85 (Santo, Schappert and Ashman, 2021). Furthermore, 61% of parents report having a child with influenza-like illness (ILI) during influenza season, and parents whose children experience ILI report missing twice as many workdays over the season as those whose children experience other respiratory illnesses or no illness (Palmer et al., 2010). Taken together these statistics imply that, in addition to straining scarce health care resources during winter months, childhood influenza could account for up to 32 million missed days of work per year.

Randomized clinical trials (RCTs) with children have demonstrated the efficacy of the influenza vaccine in reducing influenza cases. Clinical trials, however, lack statistical power to credibly estimate effects on healthcare utilization measures. Knowledge of the vaccine's effectiveness in reducing healthcare utilization is essential for benefit-cost analyses. Of four RCTs estimating effects on healthcare utilization, one finds no effect (Hoberman et al., 2003), and the three that find statistically significant effects implement a research design that interacts the outcome of interest with an endogenous variable (a positive influenza test) (Claeys et al., 2018; Jain et al., 2013; Pepin et al., 2019*b*). As we describe in Appendix A.A1, interacting the outcome with a positive test result biases estimates of the vaccine's effect on healthcare outcomes. Furthermore, the testing protocol and placebo-controlled design likely alter the distribution of healthcare utilization relative to real-world settings. For example, parents may choose to seek care for their child because medical professionals have tested the child for influenza or have confirmed

that the child has influenza. Alternatively, uncertainty about whether their child received a real vaccine (versus a placebo) may make parents more likely to seek medical care for a child's respiratory illness. These factors limit the external validity of estimates of the effect of the vaccine on healthcare provider visits.

The remaining evidence on effectiveness for healthcare outcomes is limited to observational studies. These studies generally implement cohort or case-control designs that compare influenza visit rates between vaccinated and unvaccinated children (Ritzwoller et al., 2005; Allison et al., 2006; Eisenberg et al., 2008; Joshi et al., 2009; Blyth et al., 2014; Chung et al., 2016; McLean et al., 2017). A key limitation of these studies is the nonrandom selection of patients into vaccination. Furthermore, many studies focus only on laboratory-confirmed influenza cases, potentially missing the majority of influenza-related visits.

In this study we combine a quasi-experimental research design with data sets containing hundreds of thousands of children between the ages of two and five (inclusive) across eight influenza seasons in California. Instead of estimating effectiveness by directly comparing vaccinated and unvaccinated children, we exploit variation in vaccine receipt based on the child's week of birth and the week in which the vaccine became available each season. Well-child visits typically coincide with birthdays so, for example, children born in August tend to have wellness visits in August. These children are less likely to receive the influenza vaccine than children who are born and have wellness visits in September, as the vaccine generally becomes available in September. We leverage this variation to estimate effectiveness against outpatient visits, ED visits, and inpatient stays. We focus on children between the ages of two and five because this age range incurs higher per-capita costs of influenza-related healthcare visits than any group other than seniors (Putri et al., 2018) and because our research design isolates the most variation in vaccination rates for them.

Our study makes three contributions to the literature. First, we document that the influenza vaccine substantially reduces healthcare visits for respiratory illness. Our study fills an existing void in the literature: RCTs lack the precision to detect effects on health-

care visits, while case-control studies are vulnerable to confounding. Second, we find evidence that although influenza is only coded as the cause of 1.7 doctors' office visits per 100 children annually in our data, it is likely the underlying cause of at least 11 visits for general respiratory illness per 100 children annually. This finding suggests that RCT estimates lack external validity and that estimates from the literature of the public health burden of influenza are substantially downward biased. Third, we document that, despite ACIP recommendations, vaccine uptake depends strongly on convenience. The effect on vaccine uptake of having a child wellness visit when the vaccine is available is several times larger than observed responses among adults to monetary incentives for vaccine uptake in other contexts. Making pediatric influenza vaccines more convenient — by, for example, distributing them in pharmacies — could thus increase vaccinations and reduce outpatient and ED visits.

I. Background and data

RCTs have established the influenza vaccine's efficacy in reducing laboratory-confirmed influenza among children, and ACIP recommends the vaccine for everyone six months or older. Continual mutation of the influenza virus, however, necessitates regular updates to the vaccine. Each year there is a tight window for forecasting circulating strains, producing and distributing the vaccine, and inoculating people. Thus the seasonal influenza vaccine only becomes widely available shortly before the start of the influenza season, typically around September in the US.[1] In our data, the majority of children were vaccinated between September and November, with only 0.4 percent receiving an influenza vaccine in August.

While adult influenza vaccination occurs in a variety of locations, including pharmacies, supermarkets, workplaces, and community centers, child influenza vaccination typically occurs only in a healthcare setting. Appendix Table A2 presents data on vaccination locations for children taken from the California Health Interview Survey (CHIS). Approximately 95% of vaccinated children aged 2 to 5 received their vaccinations at a

[1] Appendix Table A1 presents vaccine availability dates.

doctor's office or clinic, and less than 1% received their vaccinations at a retail location (e.g. supermarket or pharmacy). This limited availability imposes a high time cost on parents unless they link the child's influenza vaccination to another pediatric office visit. Since well-child visits typically occur around birthdays, the implicit cost of influenza vaccination is lower for a parent whose child's month of birth aligns with the influenza vaccine's availability.[2]

Our vaccination and doctor's office visits data come from a major health maintenance organization's (HMO) administrative records of doctors' office and clinic visits in California. This sample includes all children between the ages of 2 and 5 inclusive who were enrolled in the HMO at any time between 1 September 2008 and 31 August 2016. In a typical year there were 148,639 children between the ages of 2 and 5 observed in the data.

We code children that received an influenza vaccine at any time between September 1 and August 31 as vaccinated for the corresponding season. For example, a child vaccinated on October 1, 2010 would be vaccinated for the 2010-11 influenza season. A single child in a single influenza season thus constitutes one observation. We define September 1 as the cutoff because over 99% of vaccinated children receive the vaccine for a given season after August 31. Appendix Table A2 presents survey evidence on the location at which children are receiving the influenza vaccine. This table suggests that only about 1.3 percent of children ages 2 to 5 in the HMO receive the vaccine in a location where it may not get captured in the HMO's electronic medical records. This behavior will bias our estimates downwards if it is disproportionately children whose well-child visits fall outside the vaccine availability window that get vaccinated in retail locations. However, the bias is likely minimal given the small fraction of children vaccinated at retail locations.

We combine our data on doctors' office vaccinations and visits with data on ED visits and inpatient stays for children ages 2 to 5 in all of California during the 2008-09 to

[2]Administering vaccines during sick-child visits is uncommon, as the vaccine is contraindicated for symptomatic children.

2015-16 influenza seasons. Outcomes of interest include visits for specific diagnostic categories. We code a child as having a visit for a specific illness if she visited a doctor, ED, or hospital for that illness between September 1 and August 31 during the relevant influenza season.

We categorize diseases based on the International Classification of Diseases (ICD) codes from visit records. We first drop well-child visits from the outcomes analysis, as these visits are mechanically related to the source of variation we exploit. We generate three categories of doctors' office visits: influenza, influenza or influenza-like illness (ILI), and respiratory illness.[3] We use the same categories for ED visits and hospitalizations and add a category for influenza, ILI, or pneumonia.[4]

II. Empirical design and results

A. *Empirical specification*

Most childhood vaccinations occur during well-child visits. For children six months or older in our sample, well-child visits are recommended at 6, 12, 18, and 24 months of age, and annually thereafter. The interaction of the timing of the well-child visit and the availability of the influenza vaccine results in children born during different times of the year displaying substantial differences in vaccination rates. For example, children turning two in October, when the influenza vaccine is typically available, are about 20 percentage points (50 percent) more likely to receive the vaccine than children turning two a few months earlier, when the vaccine is less likely to be available.

In concurrent and related work Worsham, Woo and Jena (2020) analyzed insurance claims data and found that children with fall birthdays were 10 to 15 percentage points more likely to be vaccinated than other children. This finding validates that our first stage applies nationally as well. It also found evidence of modest decreases in influenza diagnoses for children with fall birthdays (relative to other children), but it did not estimate

[3] Influenza visits are those with ICD9 codes in the 487.xx-488.xx range or ICD10 codes in the J09.xx-J11.xx range. ILI adds any visits with ICD9 codes 780.60 or 780.61 and 786.2 or 784.1 or ICD10 codes R50.9 or R50.81 and R05 or R07.0. Respiratory visits are those with ICD9 codes in the 460.xx-519.xx range or ICD10 codes in the J00.xx-J99.xx range.

[4] Pneumonia visits are those with ICD9 codes in the 480.xx-486.xx range or ICD10 codes in the J12.xx-J18.xx range.

vaccine effectiveness or effects on any outcomes beyond confirmed influenza diagnoses. In comparison we find that confirmed influenza diagnoses comprise only around 10% of vaccination's total impact on doctors' office visits, implying that the estimates in Worsham, Woo and Jena (2020) miss the majority of the vaccine's effects.

To exploit this distinctive source of variation in vaccine receipt, we construct an instrument that interacts the expected timing of well-child visits with vaccine availability. For each influenza season y (running from September 1 to August 31), our data consist of observations at the birth week (w) by week-of-year (v) level; e.g. one observation would be the number of visits in the fifth week of 2013 by children born in the second week of 2010. For each week-of-year v within a season y, we define a binary variable A_{yv} that indicates whether the vaccine was broadly available. To code A_{yv} we examine vaccinations in an out-of-sample population of 6 to 10 year old children and define the vaccine as available if over 1% of this population receives vaccines during week v in year y.[5] We estimate the proportion of children born in week w with a well-child visit in week-of-year v of season y to get an estimate of the probability a child has a well-child visit in a given week of the year ($p_{wyv}^{well\ visit}$). We then interact the probability of a well-child visit in a given week ($p_{wyv}^{well\ visit}$) with the availability of the vaccine (A_{yv}) in that week and sum over weeks-of-year :

$$Z_{wy} = \sum_{v=1}^{52} p_{wyv}^{well\ visit} A_{yv} \tag{1}$$

The resulting measure Z_{wy}, which varies at the birth-week-by-season level, is our instrument. Intuitively, for a child born in week w, it represents the expected number of well-child visits that occur during the time period the influenza vaccine for season y is available.

The instrument eliminates individual variation in vaccination choices, as these choices

[5]Our results are qualitatively similar if we use other thresholds (e.g. 0.5% or 2%) to define vaccine availability or assume the vaccine was available as of September 1 each year (see Appendix Tables A3, A4, and A5). Appendix Figure A1 plots the timing of vaccinations for each influenza season in our sample.

are inherently endogenous. The instrument may only be conditionally exogenous, however, for two reasons. First, as we demonstrate in Section II.B, there is an age gradient in well-child visit rates ($p_{wyv}^{well\ visit}$), and thus in the instrument. Since we also expect the outcomes to have a strong age gradient, we flexibly control for age using a quadratic spline. Second, there is a season-of-birth component to the instrument due to the interaction between the birthday timing of well-child visits and the unavailability of the influenza vaccine prior to early fall — the correlation between $p_{wyv}^{well\ visit}$ and A_{yv} is highest for children born in fall. If outcomes also vary by season of birth, irrespective of vaccination, this seasonality could introduce bias. This bias, if present, would likely attenuate our estimates as children born in fall and winter (i.e. those with the highest instrumented vaccination rates) tend to have higher rates of allergies and illness.[6] Nevertheless, we address this possibility by estimating specifications that include birth-month fixed effects and by performing placebo tests for older children.

To implement our instrumental variables strategy we estimate the following first-stage regression:

$$Vaccinated_{wy} = \pi\, Z_{wy} + \sum_{y=2008}^{2015} \Big(\alpha_{0y} + \alpha_{1y} Age_{wy} + \alpha_{2y} Age_{wy}^2 + \alpha_{3y} \mathbb{1}(Age_{wy} > 3)(Age_{wy} - 3)^2 + \alpha_{4y} \mathbb{1}(Age_{wy} > 4)(Age_{wy} - 4)^2 \Big) + u_{wy} \tag{2}$$

In this regression, $Vaccinated_{wy}$ represents the vaccination rate in influenza season y for children born in week w, and Z_{wy} is the instrument as defined in Equation (1). Age_{wy} represents a cell's age on October 1, and the quadratic spline coefficients, α, vary by influenza season y. The spline includes knots at ages 3 and 4. π is the first-stage coefficient of interest, i.e. the effect of the instrument on vaccination rates.

Using the predicted vaccination rate from Equation (2) we estimate the following specification:

[6]Children born in winter have higher rates of allergies (Nilsson et al., 1997; Vassallo et al., 2010; Susanto et al., 2017), illnesses (Atchison, Tam and Lopman, 2009), and obesity (Hemati et al., 2021).

$$Y_{wy} = \tau \widehat{Vaccinated}_{wy} + \sum_{y=2008}^{2015} \Big(\beta_{0y} + \beta_{1y} Age_{wy} + \beta_{2y} Age_{wy}^2 + \beta_{3y} \mathbb{1}(Age_{wy} > 3)(Age_{wy} - 3)^2 + \beta_{4y} \mathbb{1}(Age_{wy} > 4)(Age_{wy} - 4)^2 \Big) + \varepsilon_{wy} \tag{3}$$

In this regression, Y_{wy} represents the outcome (e.g. the rate of outpatient influenza visits) in influenza season y for children born in week w, and $\widehat{Vaccinated}_{wy}$ represents the predicted vaccination rate in influenza season y for children born in week w. The quadratic spline is specified as described for Equation (2). τ is the coefficient of interest, i.e. the effect of vaccination on outcome Y. We estimate Equation (3) using two-stage least squares (2SLS). The estimation sample includes children aged from 24 to 72 months as of October 1 in the influenza season of interest, and we compute heteroskedasticity-robust standard errors.

B. Graphical results

Figure 1a plots what percent of children have a doctor's office or clinic visit at a given age. The figure separates well-child visits (solid blue line) from illness or injury visits (dashed black line). Vertical lines indicate ages at which well-child visits are recommended. Clear spikes appear in the number of well-child visits immediately following the recommended ages for these visits. In contrast there is little change in the number of illness or injury visits that are not attached to a wellness visit at the recommended ages for well-child visits.

Figure 1b plots actual and predicted influenza vaccination rates by age on October 1 (a date by which the vaccine begins to be widely available). Vaccination rates (black triangles) fall sharply after each of the recommended well-child visit ages, since children who are slightly older than these ages often have their well-child visits shortly before the vaccine becomes available. For example, a child who is 2.2 years old on October 1 likely had a well-child visit in August, prior to vaccine availability. The first-stage fitted values (blue circles) closely track actual vaccination rates from ages two to five, validating the

theory underlying our instrument. The first-stage F-statistic is 793, suggesting no weak-instrument problems. Appendix Figures A2 through A9 plot similar series by influenza season. In all seasons there is strong visual evidence of a first-stage relationship.

Figure A10 plots, by age on October 1, the percentage of children who were unvaccinated (black triangles) and the average number of medically-attended influenza visits (green triangles). The percentage of children unvaccinated demonstrates a cyclical pattern with troughs at the recommended well-child visit ages: 2, 3, 4, and 5.[7] The number of medically attended influenza visits follows the same cyclical pattern, with troughs shortly before ages 3, 4, and 5. This pattern suggests a negative relationship between influenza vaccination receipt and the outcome.

Figure 2a, presents a residualized version of Figure A10. We create this figure by fitting Equation (2) without Z_{wy} included, keeping the quadratic splines in age. The quadratic splines, which vary across seasons, absorb age effects, making the cyclical patterns in the outcomes easier to discern. We plot the resulting residuals for both vaccinations and influenza-coded doctors' office visits. The residuals for the doctors' office visits, and all the other outcomes, are noisier than the first-stage residuals because the rates are substantially lower. For this reason we also include a kernel-smoothed version (green line in the figure). Panel (a) reveals that, as seen previously in Figure A10, cohorts with low vaccination rates have higher rates of office visits for influenza. Figures 2b and 2c present results for influenza combined with ILI and visits for all respiratory causes. These panels also reveal patterns of doctors' office visits that line up with the pattern in vaccination rates.

Figure 3 and Appendix Figure A11 present the profiles of residualized outcomes for emergency department visits and inpatient stays respectively. ED visits and inpatient stays are much less common than doctors' office visits, so the profiles are much noisier than the ones in Figure 2. The four panels of Figure 3 reveal that ED visits due to influenza and visits due to either influenza or ILI have patterns similar to the pattern in

[7] Recall that we now plot the unvaccinated rate, rather than the vaccinated rate, so the figure should be a mirror image of Figure 1, panel b.

vaccination rates. However, neither pneumonia or respiratory visits show substantial evidence of being affected by vaccination. The profiles of inpatient admissions in Appendix Figure A11 do not reveal any striking patterns. This is not surprising, as the figures are much noisier than the comparable figures for doctors' office visits; for this age group, doctors' office visits are approximately 100 times more common than hospitalizations.

C. *Regression results*

Table 1 reports results from estimating Equation (3) using outpatient visits as the outcome. On average, 1.2% of children experienced an influenza-related visit each year, and 1.7% experienced an ILI-related visit. Each column in Table 1 corresponds to a different visit category: influenza, influenza or ILI, and respiratory illness. Vaccination reduced influenza visits by approximately 2.1 (per 100 children) and ILI visits by approximately 1.9 (per 100 children). Both results are statistically significant, with magnitudes close to or above the average rates of these visits, suggesting a high degree of vaccine effectiveness (the percentage reduction in an outcome that the vaccine induces). Implied effectiveness against influenza visits and influenza or ILI visits is 100% and 74% respectively.[8] Vaccination reduced overall respiratory illness visits by approximately 25 (per 100 children), or 31% of the mean visit rate. This suggests that the majority of doctors' office visits caused by influenza are not coded as influenza visits, substantially biasing downward estimates of the public health burden of influenza.

The top rows of Table 2 report results from estimating Equation (3) using ED visits as the outcome. On average, each year 0.3% of children experienced an influenza-related ED visit and 0.7% of children experienced an influenza or ILI-related ED visit. Vaccination reduced influenza visits by approximately 0.1 (per 100 children) and influenza or ILI visits by approximately 0.2 (per 100 children). Both results are statistically signifi-

[8]Vaccine effectiveness is given by $e = \frac{100(-\tau)}{\bar{y}_0}$, where τ represents the vaccine's effect on the outcome and $\bar{y}_0$ is the "attack rate" for the outcome (i.e. the percentage of unvaccinated individuals that experience the outcome). Let v be the proportion vaccinated, u be the proportion unvaccinated, and $\bar{y}$ be the average rate of the outcome in the relevant sample. If the attack rate is similar for the vaccinated and unvaccinated, then $\bar{y} = u\bar{y}_0 + v(\bar{y}_0 + \tau)$. Thus $\bar{y}_0 = \bar{y} - v\tau$, and $e = \frac{100(-\tau)}{\bar{y} - v\tau}$. In our context, τ and $\bar{y}$ correspond to the coefficients and sample means reported in Table 1, and $v = 43.6\%$. Thus, effectiveness against influenza is $e = \frac{100(2.106)}{1.181 - .436(-2.106)} \approx 100\%$.

cant, with magnitudes approximately one-third to one-half of the average rates of these visits. Vaccination had no statistically significant effect on broader respiratory-related ED visits.

The bottom rows of Table 2 report results from estimating Equation (3) using hospitalizations as the outcome. On average, each year 0.02% of children experienced an influenza-related hospitalization and 0.8% of children experienced a respiratory illness-related hospitalization. Vaccination had no statistically significant effects on influenza or ILI-related hospitalizations, but it reduced respiratory illness-related hospitalizations by a marginally significant 0.2 (per 100 children), or approximately one-quarter the average rates of these visits.

Appendix Table A3 presents a rich set of robustness checks for doctor's office visit results (Table 1). Briefly, we consider different thresholds for coding vaccination availability (0.5% or 2% of the eligible population receiving vaccines in a given week, instead of 1%), a cubic spline (instead of quadratic), birth-month fixed effects, different age ranges, different knot placements, and the interaction of different knot placements with a cubic spline. While the point estimates vary across specifications, in all cases the results remain statistically significant.

One important concern is that seasonality in health endowments might bias the estimates. The first row of Appendix Table A6 presents coefficients from versions of Equation (3) in which the dependent variable is a measure of health endowment at birth (birthweight, gestational age, or Apgar score). While the relationships are statistically significant, the coefficient magnitudes are small relative to the measures' standard deviations. Furthermore, for birthweight the relationship with vaccination status is negative, which would likely bias us against finding any positive effects of vaccination since lower birthweights are associated with worse health outcomes (Black, Devereux and Salvanes, 2007). The second row of Appendix Table A6 reveals that when month of birth fixed effects are included, the relationships between instrumented vaccination and the three measures of health endowment become trivial in size and statistically insignificant, with magnitudes that are less than 1 percent of their respective standard deviations. Since the

inclusion of month of birth fixed effects only strengthens the results (Appendix Table A3), we conclude that the effect on doctors' office visits is highly robust to specification choice.

Appendix Tables A4 and A5 present analogous robustness checks for ED and inpatient results (Table 2). In general the effects of vaccination on influenza or ILI-related ED visits remain negative and statistically significant across different specifications, losing significance only when expanding the age range to include one year old children. The effects of vaccination on respiratory illness-related hospitalizations, which were only marginally significant in Table 2, are not robust across different specifications.

Appendix Tables A7, A8, and A9 report "placebo" results for two different age groups (ages six through nine and ages ten through thirteen, inclusive) for doctors' office visits, ED visits, and inpatient stays respectively. The motivation for this test is that the relationship between week of birth and vaccination status is substantially attenuated for children six and older (Appendix Figure A12). The estimates are from Equation (3) with the knots in the splines at 7 and 8 for the analysis of six through nine year olds and knots at 11 and 12 for ten through thirteen year olds. The predicted vaccination status ($\widehat{Vaccinated}_{wy}$) of children two through five is used for the analysis of both age groups examined in the placebo tests.[9] In general, results that are statistically significant in the analytic sample are not significant for the placebo age groups, lending credence to the research design.[10]

III. Discussion

We find statistically significant effects of vaccination on outpatient and ED visits. The coefficients imply vaccine effectiveness against influenza or ILI outpatient visits in the range of 70% to 100%, consistent with RCTs using active surveillance (Vesikari et al.,

[9]To maintain any seasonal structure in the data the vaccination status of two through five year olds is merged onto children exactly 4 years older for the six through nine year old group and 8 years older for the ten through thirteen year old group. Using the predicted vaccination for two to five year olds is a way of checking if the first stage is correlated with the reduced form due to characteristics of the cohort other than vaccination — for example, if vaccination rates correlate with underlying health due to season of birth.

[10]One exception is the effect of vaccination on influenza-related doctors' visits for six to nine year olds; we suspect this relationship is significant because as can be seen in Appendix Figure A12 there is a significant, though attenuated, first-stage relationship for six to nine year olds (i.e. they are not a pure placebo group). This group qualifies as partially treated because of their small contemporaneous first stage and the substantial first stage in vaccination they experienced at younger ages, which may cumulatively boost their immunity for several years.

2006). The pattern of significance, however, varies across outcomes. For outpatient visits, statistical significance appears across all three types of diagnoses (influenza, ILI, and respiratory illness). For ED visits, significance concentrates in influenza and ILI diagnoses.

The magnitude of the vaccine's effect on respiratory illness-related outpatient visits is notable: the vaccine reduces respiratory illness visits by 24.6 (per 100 children) and has implied effectiveness of approximately 27% against these visits. This effect is five to ten times larger than RCT estimates (Claeys et al., 2018; Jain et al., 2013; Pepin et al., 2019*b*), which measure PCR-confirmed influenza visits, and suggests that influenza underlies a substantial fraction of respiratory illness cases during influenza season that warrant medical attention. The one order of magnitude difference between the respiratory illness visit coefficient (24.6) and the influenza visit coefficient (2.11) implies that most influenza cases are not detected. There are multiple reasons for undercounting influenza-related visits: most respiratory visits do not trigger influenza tests; rapid influenza tests have low sensitivity; and even polymerase chain reaction (PCR) tests may fail to detect influenza based on timing.[11]

In recent pre-COVID years, the share of pediatric visits that are for ILI in the CDC influenza surveillance network (6.5%) is of similar magnitude to the share of total visits averted by influenza vaccination in our data (5.3%). This result suggests either that most ILI visits should be due influenza, which is inconsistent with test-positive rates, or that influenza induces visits beyond ILI visits. In fact, the definition of ILI likely undercounts the number of influenza-induced healthcare visits. CDC defines ILI as "fever (temperature of 100°F [37.8°C] or greater) and a cough and/or a sore throat" (Centers for Disease Control and Prevention, 2024). Thus, any visit for a cough or sore throat that is not accompanied by fever is *not* classified as ILI, regardless of the cough's etiology. Suzuki, Ichihara and Johnson (2007) found that most fevers in pediatric influenza cases fall below 37.8°C within 48 hours of onset. In contrast, approximately three-quarters of

[11]The COVID-19 pandemic has demonstrated that even with highly-sensitive PCR tests, successfully detecting a virus depends on the exact timing of the test (Liang et al., 2020).

patients who see a medical provider for a cough related to upper-respiratory-tract infection (URTI) wait over 48 hours after symptom onset (Jones and Stewart, 2002). Thus a supermajority of coughs caused by influenza likely are not classified as ILI, which reconciles our estimated magnitudes with reported ILI incidence rates.

We combine our respiratory estimates in Tables 1 and 2 with estimated costs of outpatient, ED visits, and hospitalizations to compute potential benefits of vaccination. Putri et al. (2018) reports average costs of $134 for a pediatric influenza visit, $1,011 for a child influenza ED visit, and $8,596 for a child influenza inpatient stay.[12] Our estimates thus imply that vaccination reduces outpatient, ED, and inpatient costs by $3,298, −$234, and $1,624 respectively per 100 vaccinated children.[13] The combined cost reduction across all three visit categories is $4,688, with a standard error of $1,362 ($p < 0.001$). There are approximately 20 million children between the ages of 2 and 5 inclusive in the United States. Thus, at full (50%) vaccination rates, the annual cost savings of influenza vaccination for this age group are $938 ($469) million. The implied benefit of approximately $50 per vaccination is more than double the cost of purchasing and administering the influenza vaccine.[14] Both the benefits and costs are underestimates, however, since they do not include the value of lost school days or parental leave, both when avoiding illness and vaccinating children. To the degree that influenza vaccinations are administered at well-child visits or in convenient locations like local pharmacies, parental time costs can be minimized on the vaccination side of this calculation.

Our findings also highlight the critical role of nonpecuniary costs in determining influenza vaccination rates among children. Our first-stage regression has a partial R^2 of 0.58, implying that the interaction between well-child visits and vaccine availability (i.e. our instrument) explains the majority of the variation in the early age profile of vaccination. Furthermore, our first-stage results reveal that children with the highest vaccination rates (i.e. those born in early October) are over 11 percentage points more likely to be

[12] We inflate all costs to 2021 dollars using the Medical Care CPI.

[13] We use average point estimates of −24.61, 0.231, and −0.189 for outpatient, ED and, inpatient effects respectively.

[14] The CDC contract for influenza vaccines through 2023 pays approximately $14 per dose (Centers for Disease Control and Prevention, 2022). Rothberg and Rose (2005) report an average cost of $6.92 (2021 dollars) of healthcare worker time for administering the vaccine.

vaccinated at three years old than children with the lowest vaccination rates (i.e. those born in spring). The magnitude of this difference exceeds the differential in vaccination rates associated with having a usual place of care, insurance type, poverty level, ethnicity, or race (Appendix Table A10); the only factor that predicts a larger gap in vaccination rates is having no insurance at all.

That timing of well-child visits impacts vaccination rates to the observed degree raises the possibility of substantial welfare gains from increasing the distribution points for pediatric influenza vaccines. For example, in recent years a number of states, including California, have moved to allow pharmacies to administer influenza vaccinations to children as young as three years old. Our results suggest that convenience and time costs play a large role in parents' decisions to vaccinate their children against influenza.

To understand the economic magnitude of our first-stage results, we compare the estimates in our study to the established effects of financial incentives on vaccine uptake. To the best of our knowledge, no recent experiments have measured the price elasticity of demand for child influenza vaccines in the general population.[15] Nevertheless, two benchmarks may be informative regarding the magnitude of our estimates. One study, Bronchetti, Huffman and Magenheim (2015), implemented a field experiment estimating the effects of financial incentives on influenza vaccination uptake among college students. It found that a $35 incentive (in 2021 dollars) increased influenza vaccination rates by 10.7 percentage points. Another study, Campos-Mercade et al. (2021), offered a monetary incentive to Swedish adults for COVID-19 vaccination. It found that a $24 (SEK 200) incentive increased vaccine uptake by 4.2 percentage points. While neither

[15] Yokley and Glenwick (1984) offered cash lottery incentives combined with prompts to randomly selected parents of children who were not up to date with measles-mumps-rubella (MMR), diphtheria-tetanus-pertussis (DTP), or polio vaccinations. Compared to children that received only a prompt, the lottery incentive — which had an expected value of $2.61 (in 2021 dollars) — increased vaccination rates by a statistically insignificant five percentage points at three months. Minkovitz et al. (1999) randomly assigned a potential $46 per month (in 2021 dollars) loss of Aid to Families With Dependent Children (AFDC) benefits to families whose children were not up to date with MMR, DTP, and polio vaccinations; after two years the experimental group had vaccination rates that were one to four percentage points *lower* than the control group (the differences were not statistically significant). Kerpelman, Connell and Gunn (2000) randomly assigned potential loss of AFDC benefits for children who were not up to date on MMR, DTP, and polio vaccinations; treated children were 12 percentage points more likely to be up to date on vaccinations than control children (a statistically significant difference). While Kerpelman et al. did not report average AFDC benefits in their sample, the average Georgia AFDC recipient received a monthly benefit of $154 (in 2021 dollars) during the relevant time period (Office of the Assistant Secretary for Planning and Evaluation, 1998), implying that increasing vaccination rates by 10 percentage points requires an annual payment on the order of $1,500.

study is directly analogous to our context, together they suggest that raising vaccine uptake by 10 percentage points in a developed country requires payments on the order of $33 (first study) to $57 (second study). Our first-stage coefficient implies that making the influenza vaccine available during a well-child visit increases the probability of vaccination by 23.4 percentage points. Thus, the added convenience of this option corresponds to an economic incentive in the range of $77 to $133 (e.g. $\frac{33 \cdot 23.4}{10} = 77$), which we interpret as being of economically significant magnitude.

IV. Conclusion

Using novel variation in vaccine receipt tied to timing of birth and administrative data from a major California HMO, we estimate the effectiveness of the influenza vaccine in reducing pediatric healthcare visits. We find robust effects on doctors' office visits that are economically and statistically significant. Using ED visit data for all of California, we also find significant effects on ED visits. The value of these avoided healthcare visit costs represents a lower bound on the benefits of vaccination, but it is nevertheless several times larger than the cost of the vaccine. Including the value of avoided school absences and parental sick days, as well as the spillover effects of vaccination in reducing influenza transmission, would further increase the benefit-cost ratio.

Our results also highlight the central role of convenience in determining pediatric influenza vaccine uptake. Historically, influenza vaccines for young children have only been administered in pediatric offices, and the cost of scheduling and completing a pediatric visit can be high for many parents. Reducing the nonpecuniary cost of vaccination by making pediatric influenza vaccines available in pharmacies and other locations, as some states have recently done, seems likely to yield positive net benefits.

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Acknowledgement is now located at the first page.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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Table 1: Doctors' Office Visits

	Influenza	Influenza or ILI	Respiratory Illness
Vaccination	-2.106***	-1.892***	-24.61***
	(0.379)	(0.683)	(6.617)
Visits per 100	1.181	1.745	78.70
Underlying Pop.	1,189,111	1,189,111	1,189,111

Notes: The reduction in the rate of doctors' office visits from the IV estimation of Equation (3) is presented with robust standard errors clustered by age in October directly below in parenthesis. Analysis is restricted to children ages 2-5 inclusive on October 1st and influenza seasons 2008-2015. Visits are counted over a 12 month period starting in September 1st. We examine visits that are not coded as wellness visits. In the earlier seasons the cause of the visits were coded using ICD 9 codes. In the later seasons there was a switch to ICD10 codes. Influenza includes: ICD9 codes in 487.xx-488.xx and ICD10 codes in J09.xx-J11.xx. Influenza Like Illness includes: ICD9 codes (780.60 or 780.61) and (786.2 or 784.1), ICD10 codes (R50.9 or R50.81) and (R05 or R07.0). Respiratory illness includes: ICD9 codes in 460.xx-519.xx, ICD10 codes in J00.xx-J99.xx.

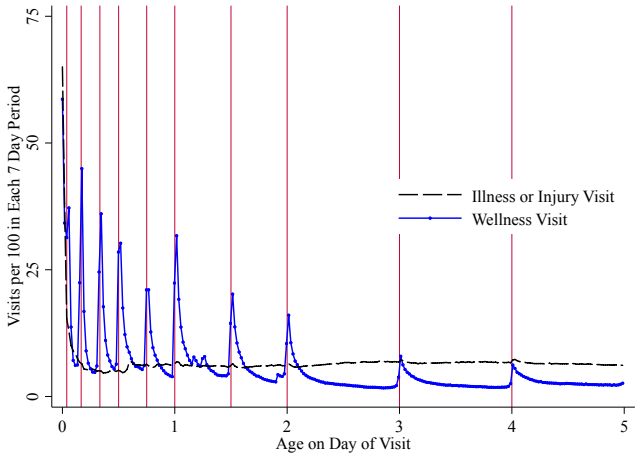
Table 2: Emergency Department Visits and Inpatient Admissions

	Influenza	Influenza or ILI	Influenza, ILI, or Pneumonia	Respiratory Illness
ED Visits				
Vaccination	-0.130***	-0.246***	-0.0524	0.231
	(0.0426)	(0.0726)	(0.135)	(0.567)
Visits per 100	0.266	0.666	1.581	10.86
Inpatient Admissions				
Vaccination	-0.0171	-0.0151	-0.0477	-0.189*
	(0.0137)	(0.0157)	(0.0487)	(0.100)
Visits per 100	0.0241	0.0289	0.275	0.798
Underlying Pop.	16,812,012	16,812,012	16,812,012	16,812,012

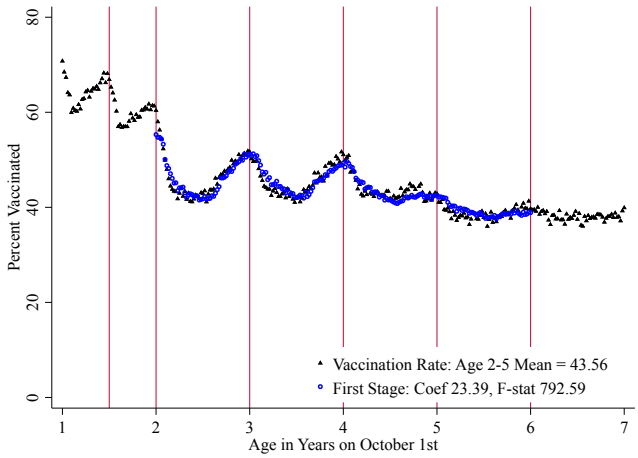
Notes: The reduction in the rate of emergency department visits and hospitalizations from the IV estimation of Equation (3) is presented with robust standard errors clustered by age in October directly below in parenthesis. Analysis is restricted to children ages 2-5 inclusive on October 1st and influenza seasons 2008-2015. Rates are computed over a 12 month period starting in September 1st. In the earlier seasons the cause of the visits were coded using ICD 9 codes. In the later seasons there was a switch to ICD10 codes. Influenza includes: ICD9 codes in 487.xx-488.xx and ICD10 codes in J09.xx-J11.xx. Influenza Like Illness includes: ICD9 codes (780.60 or 780.61) and (786.2 or 784.1), ICD10 codes (R50.9 or R50.81) and (R05 or R07.0). Influenza or Pneumonia includes: ICD9 codes 480.xx-486.xx and ICD10 codes J12.xx-J18.xx. Respiratory illness includes: ICD9 codes in 460.xx-519.xx, ICD10 codes in J00.xx-J99.xx.

Figure 1: Effect of Wellness Visit Timing on Vaccinations

(a) Age Profiles of Doctor's Office Visits



(b) Age Profiles of Vaccinations and Fitted First Stage



(c) First Stage: Residual of Instrument and Vaccination

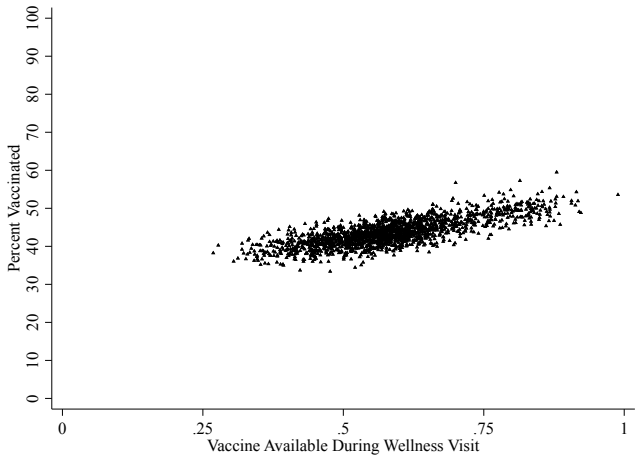
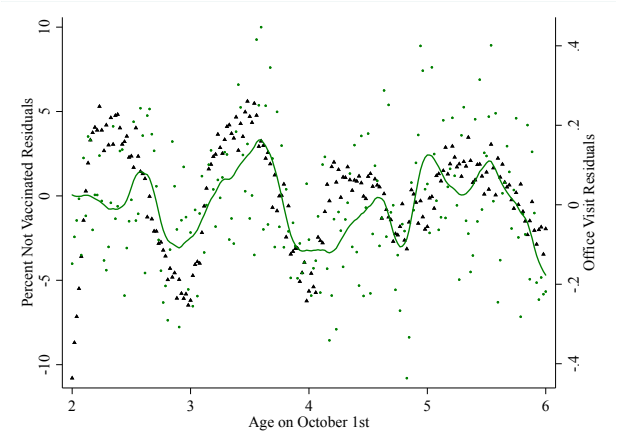


Figure 2: Doctors' Office Residual Figures for All Outcomes

(a) Influenza

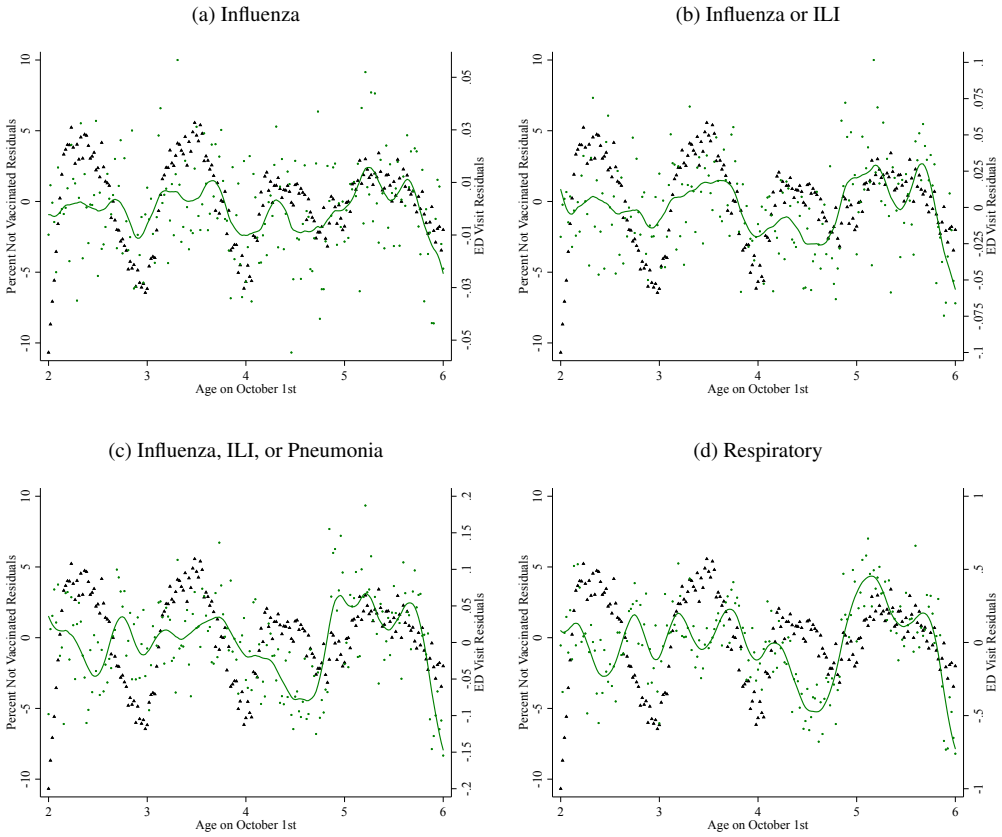


(b) Influenza and ILI

(c) Respiratory

Notes: Residual vaccination rates and doctor's office visit rates for each of the 2008-2015 influenza seasons are calculated based on age on October 1. The black triangles are residuals for the percent not vaccinated. The green dots are the residual doctor's office visits per 100 for the listed outcomes. The solid green line is a smoothed estimate of the doctor's office residuals from a kernel regression.

Figure 3: ED Residual Figures for All Outcomes



Notes: Residual vaccination rates and ED visit rates for each of the 2008-2015 influenza seasons are calculated based on age on October 1. The black triangles are residuals for the percent not vaccinated. The small green dots are the residual ED visits per 100 for the listed outcomes. The solid green line is a smoothed estimate of the ED residual visit rates from a kernel regression.

APPENDIX

A1. Clinical trial design

Randomized clinical trials with children have consistently demonstrated the efficacy of the influenza vaccine in reducing influenza cases detected via active surveillance (i.e. rigorous monitoring and testing of study participants). Fifteen placebo-controlled RCTs including children have been published since 1998 (Belshe et al., 1998, 2000; Hoberman et al., 2003; Vesikari et al., 2006; Tam et al., 2007; Neto et al., 2009; Lum et al., 2010; Jain et al., 2013; Rolfes et al., 2017; Claeys et al., 2018; Mallory et al., 2018; Pepin et al., 2019*a*,*b*; Wang et al., 2020; Nolan et al., 2021). Of these, fourteen found significant effects on influenza cases detected via active surveillance, as the enhanced detection rate greatly increases statistical power. Four of the studies also estimated the effects on healthcare utilization measures such as healthcare provider visits, antibiotic use, emergency room visits, and inpatient hospitalizations.

Appendix Figure A13 presents efficacy estimates from the four studies that examined healthcare utilization (Hoberman et al., 2003; Claeys et al., 2018; Jain et al., 2013; Pepin et al., 2019*b*).[16] The red circles represent estimates of the efficacy of the vaccine against influenza detected via active surveillance. All four studies found that the vaccine reduced influenza cases, with efficacy estimates ranging from 40 to 75 percent. The black triangles represent estimates of the efficacy for healthcare utilization. A sharp dichotomy emerges between one study and the rest regarding healthcare utilization. The first study, Hoberman et al. (2003), found no evidence of effects for any type of healthcare utilization outcome, with point estimates all clustered around zero. In contrast, Claeys et al. (2018), Jain et al. (2013), and Pepin et al. (2019*b*) (hereafter CJP) found statistically and clinically significant results for most outcomes, with efficacy estimates clustered around the estimated efficacy of the vaccine against influenza.

This striking difference in findings between Hoberman et al. (2003) and CJP may arise from the research design used in CJP. Hoberman et al. (2003) estimated differences in

[16]There are five columns in Appendix Figure A13 because one study, Jain et al. (2013), presented estimates for two subsamples.

healthcare outcomes between the treatment group and the control group, as is convention in RCTs. By contrast CJP estimated differences between treatment and control groups in healthcare visits (and other outcomes) that occurred within a 15-day period after testing positive for influenza while under active surveillance; i.e. they interacted the outcome with an endogenous variable. Since the vaccine has efficacy against influenza detected via the active surveillance protocol, the vaccine will also demonstrate efficacy against *any* outcome, even if it is unaffected by vaccination, as long as the outcome occurs sufficiently frequently to provide statistical precision. For example, children who visit the ED for sutures within the 15-day window after testing positive for influenza will be coded as having an ED visit. Since children with the vaccine are less likely to test positive for influenza, they will also be less likely to test positive for influenza and then visit the ED for sutures within 15 days after testing positive, establishing (spurious) vaccine-effectiveness against visits for sutures.

To better characterize the source of the bias, consider a vaccine with 75% efficacy against influenza under the active surveillance protocol. By definition, the rate of influenza cases detected in the control group will be four times higher than in the treated group on average. Consider an outcome that is not affected by the vaccine, such as external injuries. In expectation there will be four times as many "influenza injuries" in the control group as in the treatment group if we interact injuries with a positive influenza test. As a result the estimate of the efficacy of the vaccine against injuries will, on average, be the same as the efficacy against influenza.

Below we formally derive the bias resulting from interacting with a positive influenza test. If the majority of healthcare utilization observed in the study population is not caused by influenza, the RCT estimand of the vaccine's efficacy for an outcome when interacting with a positive test will be close to

$$1 - \frac{P(S_i = 1 \,|\, V_i = 1)}{P(S_i = 1 \,|\, V_i = 0)} \tag{A1}$$

where V_i represents vaccination status and S_i equals unity if individual i tests positive

in the active surveillance protocol and zero otherwise. This quantity is the efficacy of the vaccine against a positive influenza test. More generally, the efficacy of the vaccine will be exaggerated for healthcare outcomes that are not largely driven by influenza.

In addition to this "mechanical" bias, the active surveillance protocol may induce additional bias for the case of doctors' office visits, even if a substantial fraction are due to influenza. If informing a parent that their child has tested positive for influenza significantly increases the probability of a doctor's office visit, then the point estimates for doctors' office visits will also be biased towards the effect on detected influenza cases.

The patterns in Appendix Figure A13 are consistent with the bias described in Equation (A1) driving the estimates of Claeys et al. (2018), Jain et al. (2013), and Pepin et al. (2019*b*). Hoberman et al. (2003), which presents the unconditional effects of vaccination, has efficacy estimates clustered near zero, but the confidence intervals (not shown) cannot rule out clinically significant effects.

Formal derivation of bias:

Consider a RCT that interacts all outcomes with testing positive for influenza under a protocol of active surveillance. Treatment V_i is randomly assigned. Let S_i equal unity if i tests positive in the active surveillance protocol and zero otherwise. For convenience assume the outcome Y_i is binary (e.g. it corresponds to any healthcare visits).

The target parameter is the efficacy of vaccination on Y_i:

$$
\begin{aligned}
& 1-\frac{E[Y_i(1)]}{E[Y_i(0)]} \\
&= 1-\frac{E[Y_i(1)\,|\,V_i=1]}{E[Y_i(0)\,|\,V_i=0]} \\
&\overset{OR}{=} 1-\frac{E[Y_i\,|\,V_i=1]}{E[Y_i\,|\,V_i=0]} \\
&\overset{IE}{=} 1-\frac{E[Y_i\,|\,V_i=1,S_i=1]P(S_i=1\,|\,V_i=1)+E[Y_i\,|\,V_i=1,S_i=0]P(S_i=0\,|\,V_i=1)}{E[Y_i\,|\,V_i=0,S_i=1]P(S_i=1\,|\,V_i=0)+E[Y_i\,|\,V_i=0,S_i=0]P(S_i=0\,|\,V_i=0)} \\
&= 1-\frac{P(Y_i=1\,|\,V_i=1,S_i=1)P(S_i=1\,|\,V_i=1)+P(Y_i=1\,|\,V_i=1,S_i=0)P(S_i=0\,|\,V_i=1)}{P(Y_i=1\,|\,V_i=0,S_i=1)P(S_i=1\,|\,V_i=0)+P(Y_i=1\,|\,V_i=0,S_i=0)P(S_i=0\,|\,V_i=0)}
\end{aligned}
$$

The RCT estimand of efficacy when interacting Y_i with testing positive is:

$$\begin{aligned} & 1 - \frac{P(Y_i = 1 \;\&\; S_i = 1 \,|\, V_i = 1)}{P(Y_i = 1 \;\&\; S_i = 1 \,|\, V_i = 0)} \\ = \quad & 1 - \frac{P(Y_i = 1 \,|\, V_i = 1, S_i = 1) P(S_i = 1 \,|\, V_i = 1)}{P(Y_i = 1 \,|\, V_i = 0, S_i = 1) P(S_i = 1 \,|\, V_i = 0)} \end{aligned}$$

Thus the RCT estimand is biased unless

$$P(Y_i = 1 \,|\, V_i = 1, S_i = 0) P(S_i = 0 \,|\, V_i = 1)$$

and

$$P(Y_i = 1 \,|\, V_i = 0, S_i = 0) P(S_i = 0 \,|\, V_i = 0)$$

both equal zero. Since not everyone tests positive for influenza ($P(S_i = 0) \neq 0$) this implies that the RCT estimate will be biased unless the outcome in question never occurs absent a detected influenza case (i.e. $P(Y_i = 1 \,|\, S_i = 0) = 0$). Ignoring the $P(Y_i = 1 \,|\, V_i = 1, S_i = 0) P(S_i = 0 \,|\, V_i = 1)$ and $P(Y_i = 1 \,|\, V_i = 0, S_i = 0) P(S_i = 0 \,|\, V_i = 0)$ terms will generally exaggerate the efficacy of the vaccine for outcome Y, as $P(S_i = 0 \,|\, V_i = 1) > P(S_i = 0 \,|\, V_i = 0)$ (i.e. the vaccinated are more likely to test negative) and $P(Y_i = 1 \,|\, V_i = 1, S_i = 0) \approx P(Y_i = 1 \,|\, V_i = 0, S_i = 0)$ (i.e. vaccination has little impact on Y conditional on not getting influenza).

In Claeys et al. (2018), Jain et al. (2013), and Pepin et al. (2019*b*) healthcare outcomes, such as an emergency department visits, are coded as due to influenza ($Y_i = 1$) if they occurred within 15 days of a the onset of influenza, regardless of what the child was treated for.[17] Consider the case where the outcome in question is unaffected by influenza and independent of treatment assignment (e.g. Y_i corresponds to external injuries, so that $P(Y_i = 1 \,|\, V_i, S_i) = P(Y_i = 1)$). In this case the efficacy of vaccination is clearly zero but

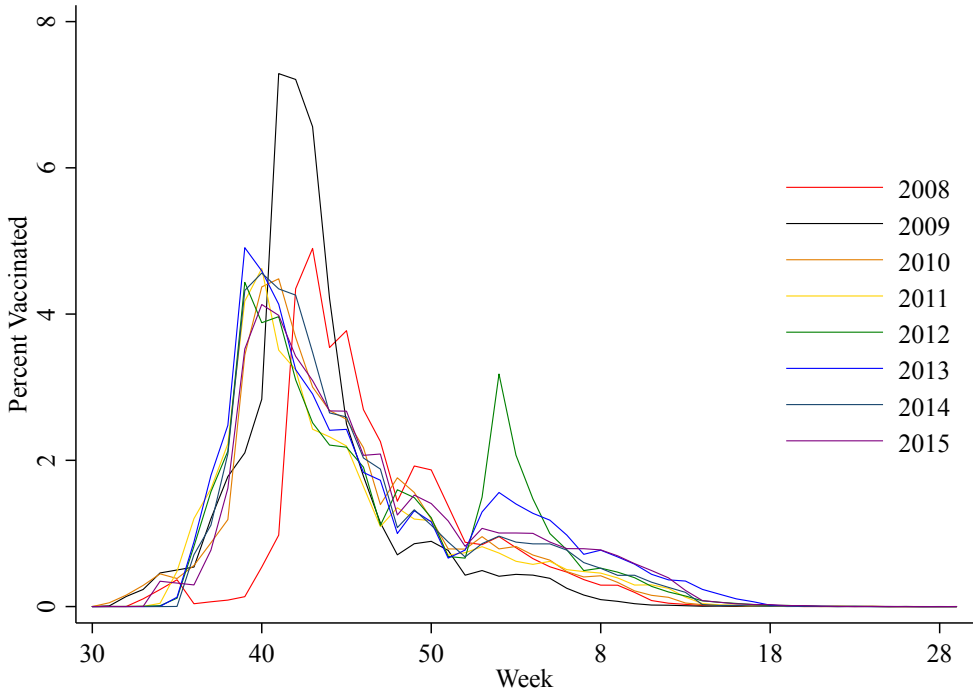
[17] For a example, a child that goes to the emergency department with a broken arm 12 days after the start of an influenza episode would be coded as having an influenza related emergency department visit.

the RCT estimand of efficacy when interacting with testing positive is:

$$\begin{aligned} & 1 - \frac{P(Y_i = 1 \;\&\; S_i = 1 \,|\, V_i = 1)}{P(Y_i = 1 \;\&\; S_i = 1 \,|\, V_i = 0)} \\ = \;& 1 - \frac{P(Y_i = 1 \,|\, V_i = 1, S_i = 1) P(S_i = 1 \,|\, V_i = 1)}{P(Y_i = 1 \,|\, V_i = 0, S_i = 1) P(S_i = 1 \,|\, V_i = 0)} \\ = \;& 1 - \frac{P(Y_i = 1) P(S_i = 1 \,|\, V_i = 1)}{P(Y_i = 1) P(S_i = 1 \,|\, V_i = 0)} \\ = \;& 1 - \frac{P(S_i = 1 \,|\, V_i = 1)}{P(S_i = 1 \,|\, V_i = 0)}. \end{aligned}$$

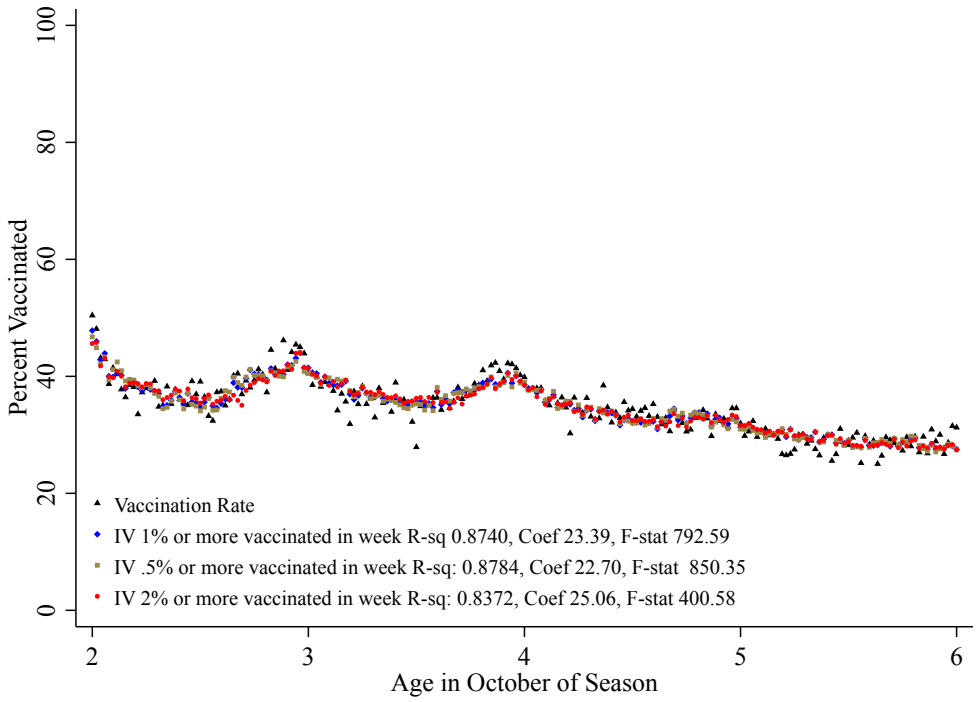
This reveals that in this extreme case where the actual efficacy of the vaccine against the outcome is zero, the RCT estimate of the efficacy for a healthcare outcome converges to the efficacy of the vaccine against testing positive for influenza while under active surveillance.

Figure A1: Timing of Vaccinations Over the Season



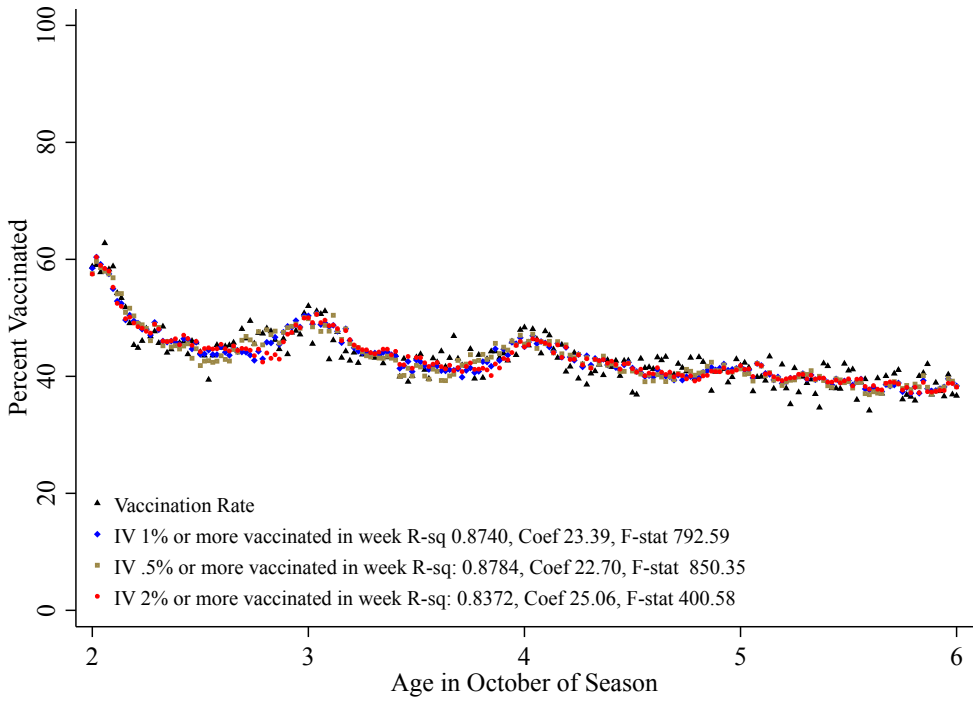
Notes: The time series are the fraction of the eligible population that is vaccinated in a given week.

Figure A2: Vaccination Rate by Age 2008-2009 Season



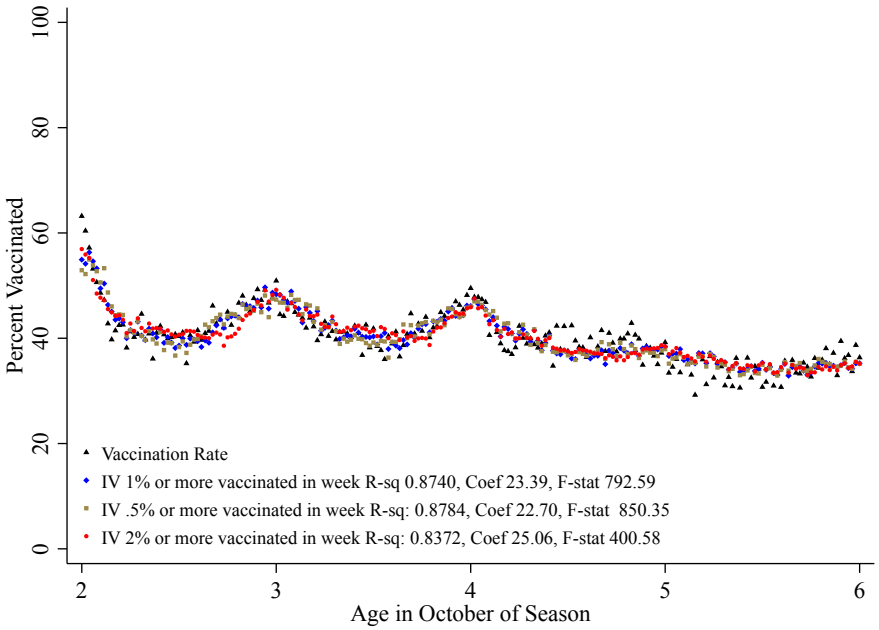
Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

Figure A3: Vaccination Rate by Age 2009-2010 Season



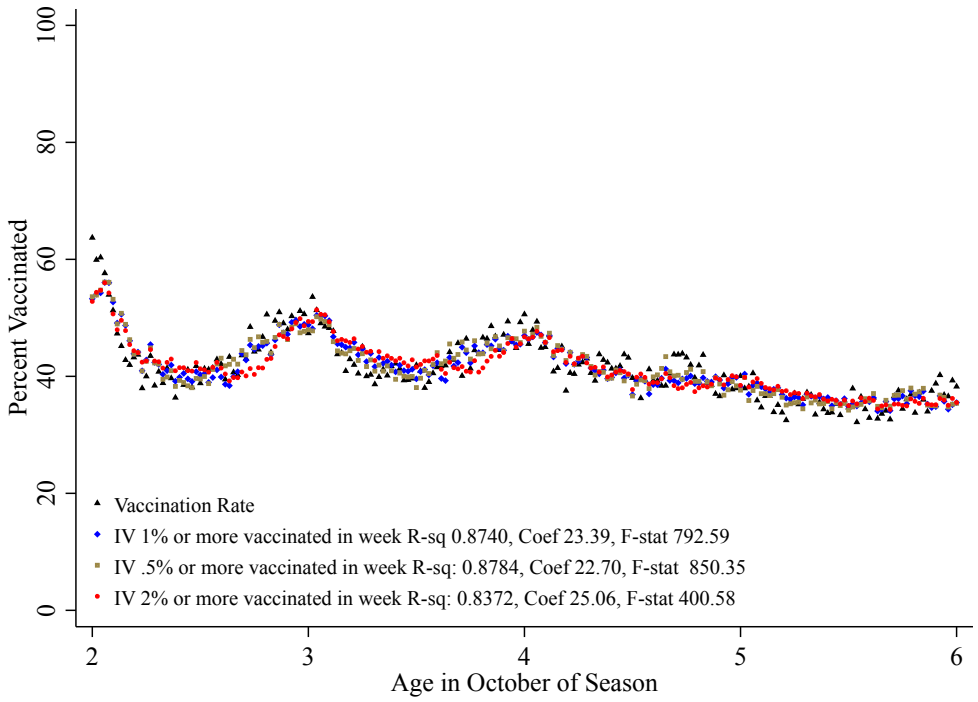
Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

Figure A4: Vaccination Rate by Age 2010-2011 Season



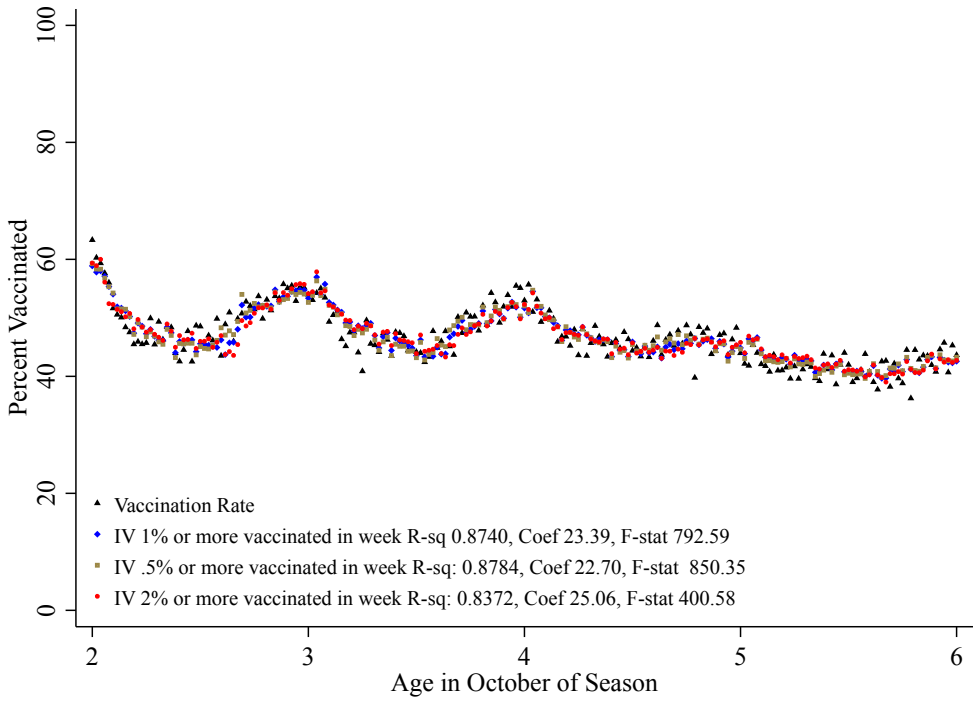
Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

Figure A5: Vaccination Rate by Age 2011-2012 Season



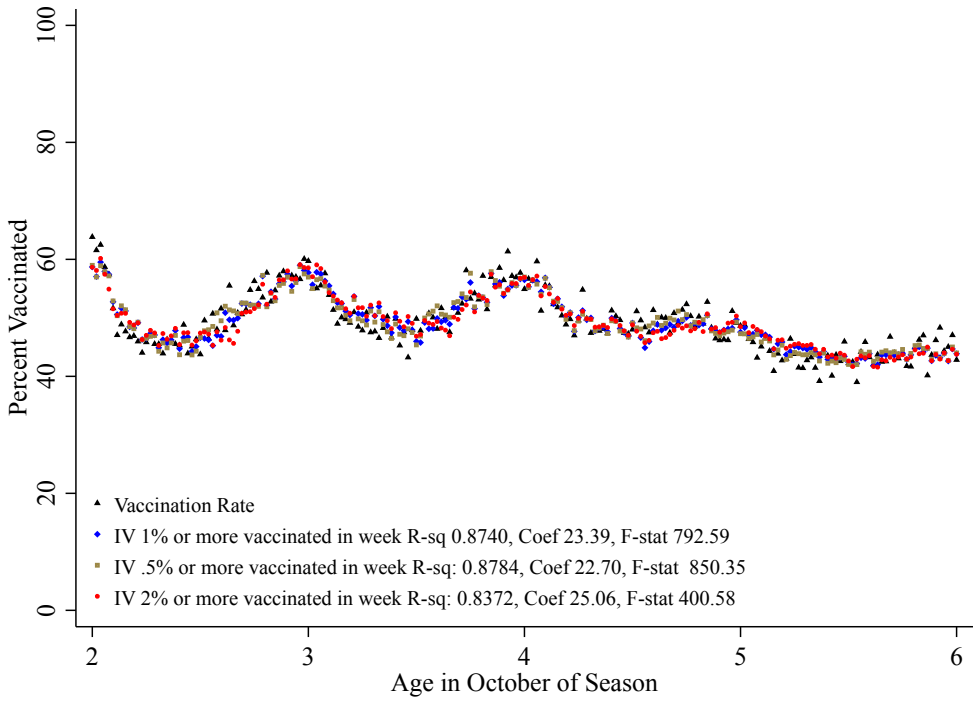
Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

Figure A6: Vaccination Rate by Age 2012-2013 Season



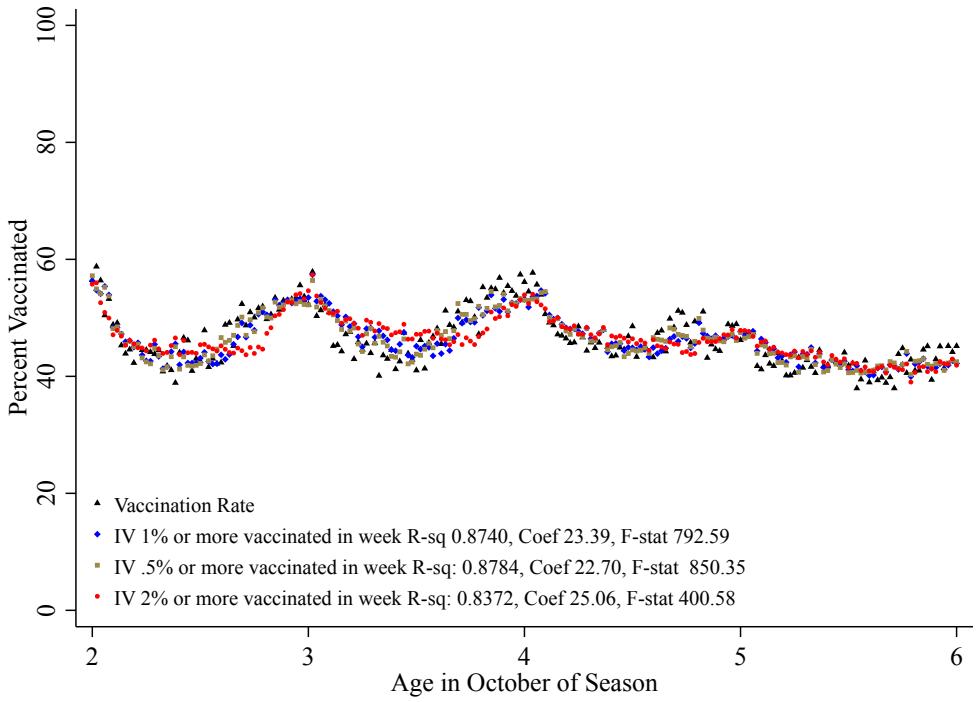
Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

Figure A7: Vaccination Rate by Age 2013-2014 Season



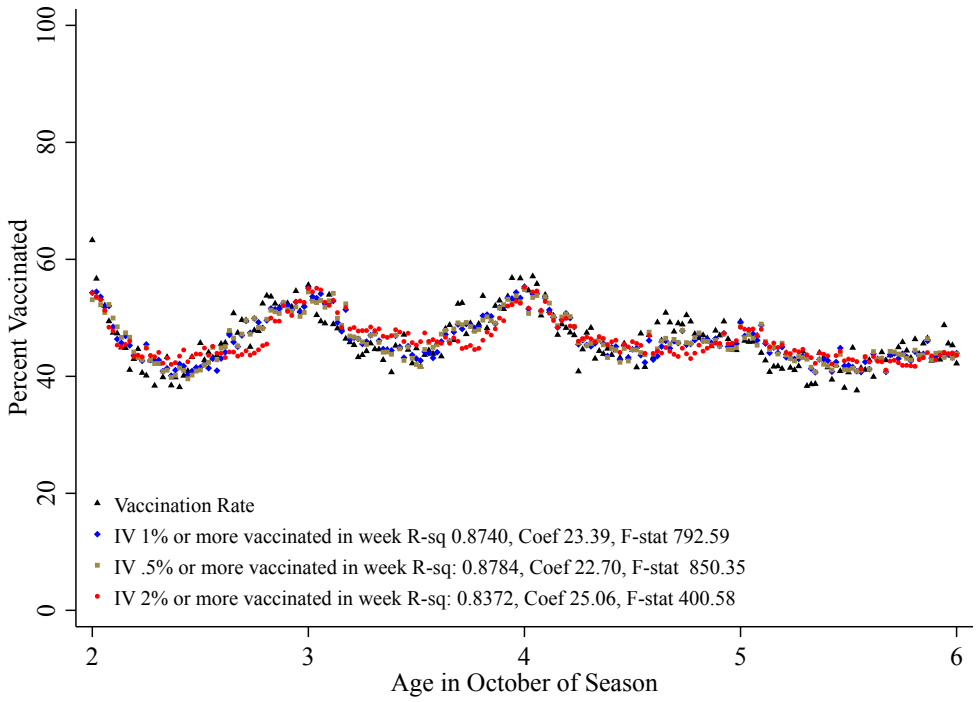
Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

Figure A8: Vaccination Rate by Age 2014-2015 Season



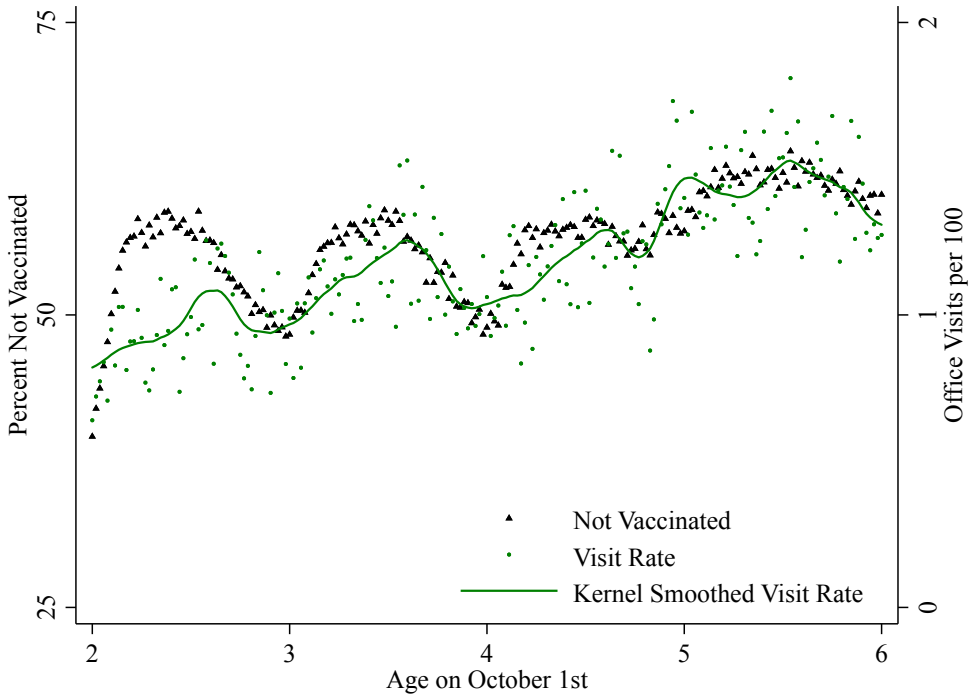
Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

Figure A9: Vaccination Rate by Age 2015-2016 Season



Notes: The black dots are the vaccination rates for one week birth cohorts. The three other profiles are fitted first stages from an instrument that is the interaction of vaccine availability and well-child visit timing for each one week birth cohort.

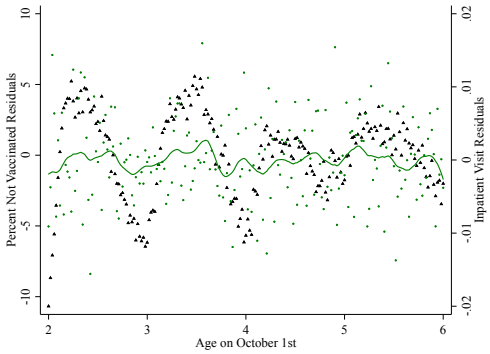
Figure A10: Doctors' Office Visits for Influenza



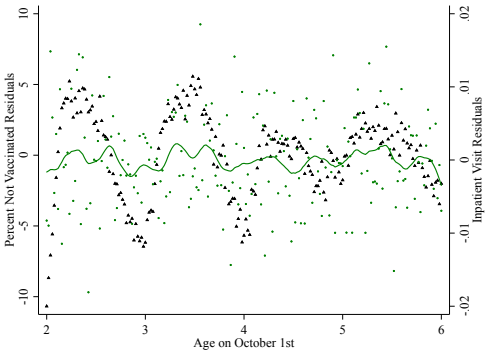
Notes: Vaccination rates and illness rates for each of the 2008-2015 influenza seasons are calculated based on age on October 1. The small green dots are the percent with a doctor's office visit for influenza (ICD9 codes in 487.xx-488.xx or ICD10 codes in J09.xx-J11.xx) at some point in the year. The solid green line is a smoothed estimate of the doctor's office visit rate from a kernel regression.

Figure A11: Inpatient Residual Figures for All Outcomes

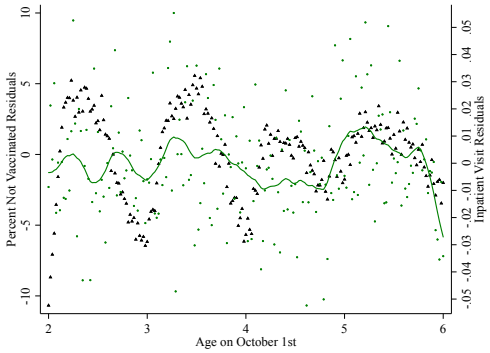
(a) Influenza



(b) Influenza or ILI



(c) Influenza, ILI, or Pneumonia

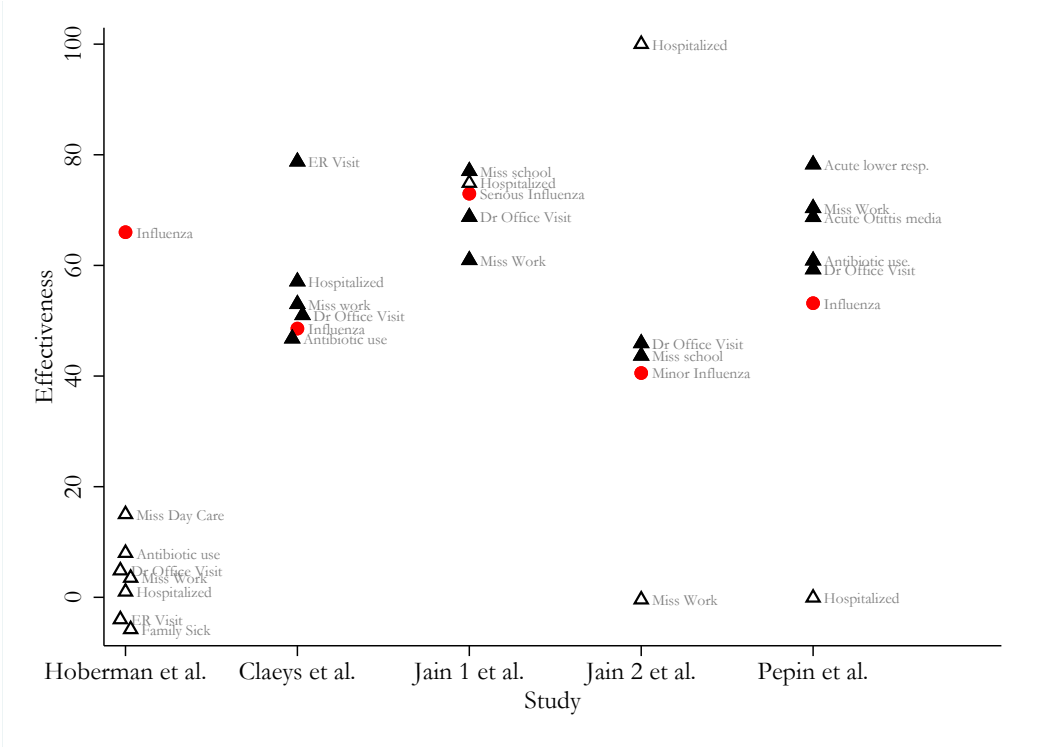


(d) Respiratory

Figure A12: Age Profiles of Vaccinations

Notes: The vertical lines denote the wellness visit schedule.The black dots are average vaccination rates for the 2008-2015 influenza seasons.

Figure A13: Efficacy of Influenza Vaccine



Notes: Hoberman et al. (2003) estimates a treated versus control difference. The three other studies interact the outcome with a positive test before estimating the treated versus control difference. Jain et al. (2013) have two subsamples with separate estimates. Solid shapes denote statistically significant effects and hollow shapes denote insignificant effects.

Table A1: Vaccine Availability Dates

Season	First Week of Availability	Last Week of Availability
2008-09	02-Oct-2008	12-Feb-2009
2009-10	10-Sep-2009	24-Dec-2009
2010-11	09-Sep-2010	03-Feb-2011
2011-12	01-Sep-2011	09-Feb-2012
2012-13	06-Sep-2012	14-Feb-2013
2013-14	05-Sep-2013	27-Feb-2014
2014-15	04-Sep-2014	12-Feb-2015
2015-16	10-Sep-2015	03-Mar-2016

Table A2: Child Vaccination Rates and Location of Vaccine

	Ages 0-11	Ages 2-5	Ages 2-5 in HMO
Vaccination Rate (%)	51.76	56.69	64.85
Location of Vaccination			
Doctor's Office	64.61	66.93	78.9
Health Clinic	26.19	27.97	14.94
Hospital or ER	1.97	2.09	4.87
Store (Market, Drugstore, Pharmacy)	1.57	0.56	0
School	4.5	1.86	0.65
Other	1.18	0.59	0.64
Observations	7980	3060	308

Notes: Vaccination rates are from California Health Interview Survey (CHIS), years 2009 and 2011-2015. Location data are from CHIS survey years 2009, 2011 and 2012.

Table A3: Doctors' Office Visits Robustness

	Influenza	Influenza or ILI	Respiratory Illness	First Stage F-Stat
Baseline IV	-2.106***	-1.892***	-24.61***	792.6
	(0.379)	(0.683)	(6.617)	
Availability (0.5%)	-1.961***	-1.946***	-29.72***	850.3
	(0.356)	(0.643)	(6.527)	
Availability (2%)	-2.158***	-1.793**	-19.22**	400.6
	(0.417)	(0.771)	(7.501)	
Availability (Sept-Feb)	-2.056***	-1.950***	-26.76***	783.3
	(0.378)	(0.662)	(6.682)	
Cubic	-2.362***	-1.987***	-26.31***	1014
	(0.432)	(0.770)	(8.022)	
Birth Month x Birth Year Controls	-1.887**	-3.497**	-52.44***	338.3
	(0.852)	(1.501)	(13.46)	
Ages 1-5 (Knots at 2&3)	-1.726***	-1.675***	-17.29***	823.2
	(0.320)	(0.568)	(5.864)	
Ages 1-6 (Knots at 2&3)	-1.852***	-1.810***	-17.75***	869.9
	(0.307)	(0.531)	(5.488)	
Knots at 3&5	-1.882***	-1.601**	-17.89**	716.7
	(0.386)	(0.696)	(7.234)	
Knots at 4&5	-1.853***	-1.813***	-18.01***	558.1
	(0.358)	(0.619)	(6.199)	
Knots at 3&5, Cubic	-2.152***	-1.709**	-21.71***	927.2
	(0.431)	(0.784)	(7.876)	
Knots at 4&5, Cubic	-1.858***	-1.497**	-17.58**	676.5
	(0.389)	(0.716)	(6.993)	
Visits per 100	1.181	1.745	78.70	
Underlying Pop.	1,189,111	1,189,111	1,189,111	

Notes: See Table 1 notes for the baseline specification. "Availability" specifications alter the thresholds used to define A_v^y. "Cubic" specifications use a cubic polynomial instead of quadratic in Equations (2) and (3). The "Birthmonth Controls" specification includes dummies for month of birth in Equations (2) and (3). Ages for all specifications are 2-5 inclusive unless otherwise specified. Knots for the splines are set at ages 3 and 4 unless otherwise specified.

Table A4: Emergency Department Visits Robustness

	Influenza	Influenza or ILI	Influenza, ILI, or Pneumonia	Respiratory Illness
Baseline IV	-0.130***	-0.246***	-0.0524	0.231
	(0.0426)	(0.0726)	(0.135)	(0.567)
Availability (0.5%)	-0.0996**	-0.236***	-0.0421	0.133
	(0.0440)	(0.0718)	(0.136)	(0.559)
Availability (2%)	-0.163***	-0.268***	-0.185	-0.301
	(0.0471)	(0.0795)	(0.144)	(0.641)
Availability (Sept-Feb)	-0.109**	-0.227***	0.0224	0.493
	(0.0442)	(0.0718)	(0.138)	(0.582)
Cubic	-0.143***	-0.271***	-0.158	-0.319
	(0.0480)	(0.0773)	(0.148)	(0.653)
Birth Month x	-0.156*	-0.451***	-0.686**	-2.394**
Birth Year Controls	(0.0938)	(0.162)	(0.284)	(1.159)
Ages 1-5	-0.0753*	-0.105	0.0177	-0.0265
(Knots at 2&3)	(0.0422)	(0.0748)	(0.153)	(0.570)
Ages 1-6	-0.103**	-0.156**	-0.100	-0.629
(Knots at 2&3)	(0.0404)	(0.0713)	(0.142)	(0.547)
Knots at 3&5	-0.110**	-0.186**	0.128	1.245*
	(0.0449)	(0.0768)	(0.149)	(0.640)
Knots at 4&5	-0.100**	-0.154**	0.322**	2.474***
	(0.0447)	(0.0768)	(0.159)	(0.667)
Knots at 3&5, Cubic	-0.125***	-0.226***	-0.0418	0.285
	(0.0479)	(0.0782)	(0.145)	(0.645)
Knots at 4&5, Cubic	-0.110**	-0.182**	0.129	1.238*
	(0.0451)	(0.0786)	(0.147)	(0.634)
Visits per 100	0.266	0.666	1.581	10.86
Underlying Pop.	16,812,012	16,812,012	16,812,012	16,812,012

Notes: See Table 2 notes for the baseline specification. "Availability" specifications alter the thresholds used to define A_v^y. "Cubic" specifications use a cubic polynomial instead of quadratic in Equations (2) and (3). The "Birthmonth Controls" specification includes dummies for month of birth in Equations (2) and (3). Ages for all specifications are 2-5 inclusive unless otherwise specified. Knots for the splines are set at ages 3 and 4 unless otherwise specified.

Table A5: Inpatient Hospital Stays Robustness

	Influenza	Influenza or ILI	Influenza, ILI, or Pneumonia	Respiratory Illness
Baseline IV	-0.0171	-0.0151	-0.0477	-0.189*
	(0.0137)	(0.0157)	(0.0487)	(0.100)
Availability (0.5%)	-0.00883	-0.00487	-0.0379	-0.139
	(0.0136)	(0.0156)	(0.0499)	(0.0992)
Availability (2%)	-0.0194	-0.0249	-0.0508	-0.244**
	(0.0148)	(0.0171)	(0.0520)	(0.114)
Availability (Sept-Feb)	-0.0152	-0.0109	-0.0351	-0.163
	(0.0146)	(0.0167)	(0.0499)	(0.0994)
Cubic	-0.0230	-0.0184	-0.0979*	-0.279**
	(0.0145)	(0.0167)	(0.0569)	(0.117)
Birth Month x	-0.0232	-0.00279	-0.155	-0.0885
Birth Year Controls	(0.0287)	(0.0332)	(0.126)	(0.237)
Ages 1-5	-0.0165	-0.00980	-0.00893	-0.258**
(Knots at 2&3)	(0.0135)	(0.0151)	(0.0547)	(0.110)
Ages 1-6	-0.0146	-0.0106	-0.00897	-0.253**
(Knots at 2&3)	(0.0126)	(0.0141)	(0.0504)	(0.103)
Knots at 3&5	-0.0148	-0.0116	-0.0121	-0.143
	(0.0144)	(0.0164)	(0.0513)	(0.103)
Knots at 4&5	-0.00317	0.000942	0.0759	0.0333
	(0.0159)	(0.0178)	(0.0542)	(0.111)
Knots at 3&5, Cubic	-0.0222	-0.0178	-0.0827	-0.268**
	(0.0146)	(0.0168)	(0.0564)	(0.116)
Knots at 4&5, Cubic	-0.0135	-0.0116	-0.0133	-0.152
	(0.0147)	(0.0167)	(0.0516)	(0.102)
Visits per 100	0.0241	0.0289	0.275	0.798
Underlying Pop.	16,812,012	16,812,012	16,812,012	16,812,012

Notes: See Table 2 notes for the baseline specification. "Availability" specifications alter the thresholds used to define A_v^y. "Cubic" specifications use a cubic polynomial instead of quadratic in Equations (2) and (3). The "Birthmonth Controls" specification includes dummies for month of birth in Equations (2) and (3). Ages for all specifications are 2-5 inclusive unless otherwise specified. Knots for the splines are set at ages 3 and 4 unless otherwise specified.

Table A6: IV Regressions on Birth Outcomes

	Birthweight	Gestation	Apgar
Vaccination	-90.41***	2.263***	0.0247***
(Baseline Specification)	(12.09)	(0.713)	(0.00867)
Vaccination	-3.998	-0.0550	0.00137
(Month of birth Controls)	(11.99)	(0.652)	(0.0143)
Mean	3298	274.4	8.9
St. Dev.	593.7	23.2	0.62
Observations	1,632	1,632	1,063

Notes: Data come from OSHPD. Equation (3) is estimated using 2SLS with birth outcomes. The coefficients on vaccination are presented with standard errors directly below in parenthesis. Analysis is restricted to children ages 2-5 inclusive and influenza seasons 2008-2015. 2-2.75 year olds are missing in the 2015 season. Observations with an Apgar score are limited to individuals born from December 2006 to 2012. The control function is a quadratic spline with knots set at ages 3 and 4. Birthmonth by birthyear dummies are also included as controls.

Table A7: Doctors' Office Visits Placebo Tests

	Influenza	Influenza or ILI	Respiratory Illness
Baseline	-2.106***	-1.892***	-24.61***
	(0.379)	(0.683)	(6.617)
Visits per 100	1.181	1.745	78.70
Underlying Pop.	1,189,111	1,189,111	1,189,111
Ages 6-9	-0.280***	-0.194*	0.762
Reduced Form	(0.0847)	(0.113)	(1.163)
Ages 6-9 IV	-1.221***	-0.846*	3.327
	(0.365)	(0.489)	(5.003)
Visits per 100	1.349	1.592	60.07
Underlying Pop.	1,295,605	1,295,605	1,295,605
Ages 10-13	0.00244	-0.0533	-1.918*
Reduced Form	(0.0760)	(0.0819)	(1.061)
Ages 10-13 IV	0.0111	-0.232	-8.368*
	(0.327)	(0.352)	(4.529)
Visits per 100	1.205	1.293	48.02
Underlying Pop.	1,433,800	1,433,800	1,433,800

Notes: The reduction in the rate of doctors' office visits is presented with robust standard errors directly below in parenthesis. Analysis is restricted to the 2008-2015 influenza seasons. Visits are counted over a 12 month period starting on September 1st. We examine visits that are not coded as wellness visits. In the earlier seasons the cause of the visits were coded using ICD 9 codes. In the later seasons there was a switch to ICD10 codes. Influenza includes: ICD9 codes in 487.xx-488.xx and ICD10 codes in J09.xx-J11.xx. Influenza Like Illness includes: ICD9 codes (780.60 or 780.61) and (786.2 or 784.1), ICD10 codes (R50.9 or R50.81) and (R05 or R07.0). Respiratory illness includes: ICD9 codes in 460.xx-519.xx, ICD10 codes in J00.xx-J99.xx. The baseline specification includes children ages 2-5. Ages for the other specifications are indicated.

Table A8: Emergency Department Visits Placebo Tests

	Influenza	Influenza or ILI	Influenza, ILI, or Pneumonia	Respiratory Illness
Baseline	-0.130***	-0.246***	-0.0524	0.231
	(0.0426)	(0.0726)	(0.135)	(0.567)
Visits per 100	0.266	0.666	1.581	10.86
Underlying Pop.	16,812,012	16,812,012	16,812,012	16,812,012
Ages 6-9	-0.0143	-0.0144	-0.000406	-0.123
Reduced Form	(0.00904)	(0.0138)	(0.0229)	(0.0908)
Ages 6-9 IV	-0.0626	-0.0630	-0.00178	-0.537
	(0.0394)	(0.0599)	(0.0983)	(0.392)
Visits per 100	0.204	0.352	0.675	5.359
Underlying Pop.	16,949,885	16,949,885	16,949,885	16,949,885
Ages 10-13	-0.00375	-0.00463	0.000213	0.145**
Reduced Form	(0.00839)	(0.0106)	(0.0151)	(0.0618)
Ages 10-13 IV	-0.0162	-0.0200	0.000782	0.633**
	(0.0361)	(0.0455)	(0.0651)	(0.268)
Visits per 100	0.156	0.225	0.402	3.725
Underlying Pop.	16,550,683	16,550,683	16,550,683	16,550,683

Notes: The reduction in the rate of emergency department visits is presented with robust standard errors directly below in parenthesis. Analysis is restricted to the 2008-2015 influenza seasons. Visits are counted over a 12 month period starting on September 1st. In the earlier seasons the cause of the visits were coded using ICD 9 codes. In the later seasons there was a switch to ICD10 codes. Influenza includes: ICD9 codes in 487.xx-488.xx and ICD10 codes in J09.xx-J11.xx. Influenza Like Illness includes: ICD9 codes (780.60 or 780.61) and (786.2 or 784.1), ICD10 codes (R50.9 or R50.81) and (R05 or R07.0). Influenza or Pneumonia includes: ICD9 codes 480.xx-486.xx and ICD10 codes J12.xx-J18.xx. Respiratory illness includes: ICD9 codes in 460.xx-519.xx, ICD10 codes in J00.xx-J99.xx. The baseline specification includes children ages 2-5. Ages for the other specifications are indicated.

Table A9: Inpatient Hospital Stays Placebo Tests

	Influenza	Influenza or ILI	Influenza, ILI, or Pneumonia	Respiratory Illness
Baseline	-0.0171	-0.0151	-0.0477	-0.189*
	(0.0137)	(0.0157)	(0.0487)	(0.100)
Visits per 100	0.0241	0.0289	0.275	0.798
Underlying Pop.	16,812,012	16,812,012	16,812,012	16,812,012
Ages 6-9	0.000981	0.000284	0.00810	0.0221
Reduced Form	(0.00276)	(0.00307)	(0.00943)	(0.0200)
Ages 6-9 IV	0.00428	0.00124	0.0353	0.0964
	(0.0119)	(0.0132)	(0.0405)	(0.0855)
Visits per 100	0.0147	0.0170	0.120	0.431
Underlying Pop.	16,949,885	16,949,885	16,949,885	16,949,885
Ages 10-13	-0.00268	-0.00325	0.00609	0.0297*
Reduced Form	(0.00203)	(0.00226)	(0.00645)	(0.0157)
Ages 10-13 IV	-0.0117	-0.0142	0.0265	0.130*
	(0.00874)	(0.00970)	(0.0278)	(0.0670)
Visits per 100	0.00992	0.0116	0.0742	0.410
Underlying Pop.	16,550,683	16,550,683	16,550,683	16,550,683

Notes: The reduction in the rate of hospital stays is presented with robust standard errors directly below in parenthesis. Analysis is restricted to the 2008-2015 influenza seasons. Stays are counted over a 12 month period starting on September 1st. In the earlier seasons the cause of the visits were coded using ICD 9 codes. In the later seasons there was a switch to ICD10 codes. Influenza includes: ICD9 codes in 487.xx-488.xx and ICD10 codes in J09.xx-J11.xx. Influenza Like Illness includes: ICD9 codes (780.60 or 780.61) and (786.2 or 784.1), ICD10 codes (R50.9 or R50.81) and (R05 or R07.0). Influenza or Pneumonia includes: ICD9 codes 480.xx-486.xx and ICD10 codes J12.xx-J18.xx. Respiratory illness includes: ICD9 codes in 460.xx-519.xx, ICD10 codes in J00.xx-J99.xx. The baseline specification includes children ages 2-5. Ages for the other specifications are indicated.

Table A10: Correlates of Influenza Vaccination

	All (ages 0-11)	Ages 2-5	Ages 2-5 (Emp or Priv Ins)
No Usual Place of Care	-9.191***	-7.332**	-13.17**
	(1.931)	(3.678)	(6.432)
No Insurance	-14.05***	-21.67***	
	(1.751)	(3.240)	
Medicaid	0.181	-0.187	
	(0.992)	(1.735)	
Private Insurance	-4.386***	-5.368**	-6.237**
	(1.457)	(2.726)	(2.743)
0-99% Federal Poverty Line	-1.491	-4.205**	-2.813
	(1.188)	(2.075)	(4.269)
100-199% Federal Poverty Line	-4.081***	-6.843***	-9.789***
	(0.988)	(1.773)	(2.408)
200-299% Federal Poverty Line	-8.882***	-11.19***	-10.44***
	(1.006)	(1.783)	(1.966)
AFDC/TANF/Calworks	-0.0368	-0.716	-6.561
	(1.405)	(2.246)	(23.25)
Hispanic	4.301***	3.637***	-1.041
	(0.730)	(1.263)	(1.628)
African American	8.439***	7.113***	6.070**
	(1.218)	(2.104)	(2.565)
Observations	25,228	8,172	5,274

Notes: Data come from California Health Interview Survey. Age fixed effects included.