A national examination of pharmacy-based immunization statutes and their association with influenza vaccinations and preventive health

Kevin W. McConeghy a, *, Coady Wing b

a Providence Veterans Affairs Medical Center, Department of Veterans Affairs, United States
b Indiana University, School of Public and Environmental Affairs, United States

ABSTRACT

Background: A series of state-level statute changes have allowed pharmacists to provide influenza vaccinations in community pharmacies. The study aim was to estimate the effects of pharmacy-based immunization statutes changes on per capita influenza vaccine prescriptions, adult vaccination rates, and the utilization of other preventive health services. Methods: A quasi-experimental study that compares vaccination outcomes over time before and after states allowed pharmacy-based immunization. Measures of per capita pharmacy prescriptions for influenza vaccines in each state came from a proprietary pharmacy prescription database. Data on adult vaccination rates and preventive health utilization were studied using multiple waves of the Behavioral Risk Factor Surveillance System (BRFSS). The primary outcomes were changes in per capita influenza vaccine pharmacy prescriptions, adult vaccination rates, and preventive health interventions following changes. Results: Between 2007 and 2013, the number of influenza vaccinations dispensed in community pharmacies increased from 3.2 to 20.9 million. After one year, adopting pharmacist immunization statutes increased per capita influenza vaccine prescriptions by an absolute difference (AD) of 2.6% (95% CI: 1.1–4.2). Adopting statutes did not lead to a significant absolute increase in adult vaccination rates (AD 0.9%, 95% CI: −0.3, 2.2). There was also no observed difference in adult vaccination rates among adults at high-risk of influenza complications (AD 0.8%, 95% CI: −0.2, 1.8) or among standard demographic subgroups. There was also no observed difference in the receipt of preventive health services, including routine physician office visits (AD −1.9%, 95% CI: −4.9, 1.1). Conclusions: Pharmacists are providing millions of influenza vaccines as a consequence of immunization statutes, but we do not observe significant differences in adult influenza vaccination rates. The main gains from pharmacy-based immunization may be in providing a more convenient way to obtain an important health service.

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1. Introduction

Increasing the rate of influenza vaccination is an important public health goal in the United States [1]. One way to promote access to basic health services is to expand the scope of practice afforded to non-physician health occupations which affect wages, prices, and utilization of health services [2–8]. Starting in the 1990s, state governments have expanded the pharmacist scope of practice laws to allow pharmacists to provide vaccinations [9]. By 2010, pharmacists were allowed to provide influenza vaccines to adults in every state, the District of Columbia, and Puerto Rico. Pharmacy associations, schools, and community practitioners have encouraged these changes and trained pharmacists to provide vaccines [9,10]. When pharmacist scope of practice is restricted, pharmacies can still offer vaccinations in a limited way by hosting clinics staffed by nurses or other providers [11]. However directly allowing pharmacists to vaccinate may be beneficial because pharmacies are located in rural and urban areas, provide vaccinations without appointment, accept insurance plans or cash, and operate on expanded hours relative to primary care clinics or other vaccinators [12]. This convenience...
could increase adult vaccination rates by reaching individuals not vaccinated in traditional settings. The CDC estimates that 20% of all influenza vaccinations in the 2010–2011 influenza season were administered by pharmacists [13].

The rise of pharmacy-based immunization could also come from a re-allocation of market share (i.e. some patients may go to a pharmacy rather than alternative vaccination providers). Re-allocation could occur without increasing the number of people who are vaccinated and may have unintended negative effects. If influenza vaccination gives patients a reason to schedule physician appointments and physicians tend to bundle vaccinations with other preventive health services, then pharmacy-based immunization may result in fewer physician office visits and preventive services. Despite the possible advantages and disadvantages offered by a pharmacy delivery model, there is no nationwide study evaluating the effects of pharmacy-based immunization regulations.

The main objectives of this study were to examine the effects of pharmacy-based immunization statutes on: (1) Per capita pharmacy influenza vaccine prescriptions, (2) adult influenza vaccination rates, (3) preventive health interventions.

2. Methods

2.1. Study design

This study employs a quasi-experimental difference-in-differences (DID) design that exploits the differential timing of pharmacy-based immunization adoption across states to study the pharmacy-based immunization effects [14]. In the simplest version of DID, treatment and comparison groups are observed at two time points. Between periods, the treatment group is exposed to treatment and the control group is not. In our analysis, control groups are states and years where pharmacy-based immunization was not allowed or allowed by individual physician prescription only.

Treatment effects are estimated by subtracting the change in the control group from the change in the treatment group. This “double-differencing” adjusts for biases from time varying confounders that affect both groups, and permanent pre-existing differences between the two groups. We apply this framework to include multiple states and time periods that adjusts for fixed pre-existing differences between the states, and from time-varying “trend” factors that affect all of the states.

2.2. Measures

2.2.1. Pharmacy-based Immunization statutes

Data on state level changes in pharmacy laws related to pharmacy-based immunization that occurred between 1996 and 2013 were compiled. The American Pharmacist Association’s reports, legislative databases, state boards of pharmacy, and other secondary sources were used to corroborate the timing of the policy changes [9,15,16]. Appendix A contains more detailed information about these resources. In this manuscript we evaluate all 50 U.S. states, Puerto Rico and the District of Columbia referred to collectively as states. States have used four approaches to allow pharmacy-based immunization: (i) physician prescription requirements, (ii) state-wide protocol agreements, (iii) independent pharmacist authority, or (iv) pharmacist-physician collaborative practice agreements. In the analysis, we defined flexible statutes as those that allow pharmacy-based immunization through state-wide protocol agreements, independent pharmacist authority, or pharmacist-physician collaborative practice agreements. In comparison, statutes that did not permit pharmacy-based immunization at all or that allowed pharmacy-based immunization only with an individual prescription from a physician were considered restrictive. We study the effects of adopting a flexible pharmacy-based immunization policy relative to a restrictive policy.

2.2.2. Per capita pharmacy prescriptions

We estimated the number of influenza vaccines dispensed in community pharmacies using a pharmaceutical prescription sales database called the Pharmaceutical Audit Monthly Suite (PHAST). The PHAST data includes ~82% of all prescriptions filled in community pharmacies [17,18]. Influenza vaccines administered in other settings are not routinely sent as prescriptions to pharmacies, therefore this was considered a reasonable measure of vaccinations occurring by pharmacists themselves. Prescriptions for influenza vaccinations were identified in the PHAST using Uniform System of Classification Code (USCC) 027210. The counts included both intranasal and injectable influenza vaccine forms, and both single- and multiple-dose vials (high-dose vaccines were not available in the time periods studied). Previous work suggests that influenza antiviral prescriptions follow trends in influenza-like illness [19]. Pharmacy-based immunization statute changes should not directly affect antivirals and if they do then it seems likely that the statutes are correlated with unmeasured state trends in influenza related illnesses. Using PHAST data, we computed the number of influenza antiviral prescriptions dispensed in community pharmacies in each state and year. The antiviral prescriptions were identified using USCC code 82230, which includes oseltamivir, zanamivir, rimantidine and amantadine. Adamantanes were then excluded by NDC code because they are used for other indications [2]. Raw prescription counts were changed to per capita rates using population data from the U.S. Census Bureau [19]. Data were only available from 2007 to 2013, and restricted to 2010 for models to match the vaccination rate timeframe.

2.2.3. Adult influenza vaccination rates

The Behavioral Risk Factor Surveillance System (BRFSS) was used to study the effects of pharmacy-based immunization statutes on the broader population [20]. The BRFSS is a large, annual, nationally representative cross-sectional survey that includes survey questions about influenza vaccination from all sources and receipt of a range of preventive health services. We pooled data from the 1996 to 2010 waves of BRFSS with all available states, D.C. and Puerto Rico. All of our analyses of the BRFSS data used sampling weights to account for the survey design. The BRFSS sampling design changed for the 2011 survey year so 2010 was the last year included. In addition, our main analysis is based on an unbalanced panel because some states did not fully participate in the survey in every year from 1996 to 2001. Appendix B presents estimates using only a balanced panel data from 2001 to 2010. We measured influenza vaccination status for the calendar year at the individual level in repeated cross sectional samples using the BRFSS. The survey items across years were combined to a binary variable indicating whether a person received an injection or nasal spray influenza vaccination in the previous 12 months.

We examined the effects of pharmacy-based immunization in sub-populations defined by gender, age, health insurance status, and employment status. To examine the effects of pharmacy-based immunization on people who are at increased risk of complications from influenza, we also examined a high risk sub-population consisting of pregnant women, American Indians/Alaskan Natives, people aged 65 or older, and/or people with a past medical history of asthma, stroke/myocardial infarction or angina, diabetes, or body mass index $\geq 40$ [21]. We also fit versions of the core regression models that included controls for basic demographic characteristics including: age, gender, education, health insurance status and racial/ethnic background.
2.2.4. Preventive health

To assess concerns that pharmacy-based immunization might reduce utilization of other preventive services by reducing contact with the core health care system, we also used the BRFSS to examine a panel of binary measures of preventive care utilization. This included whether a respondent had a routine physician office visit, cholesterol blood test, clinical breast exam, hemoglobin A1c test, and/or clinical foot exam for diabetics [19]. The items can be individually limited in scope (i.e. women for clinical breast exam, diabetics for clinical foot exam/A1c test). The cholesterol item questionnaire was not asked in survey years 2006, 2008 and 2010. The routine physician check-up item was not asked in survey years 2003 and 2004. In each case, the survey items refer to occurrence over the previous 12 months.

2.3. Statistical analysis

We estimated the DID treatment effects using two way fixed-effect regression models in which outcomes were regressed on an indicator variable set to 1 if a flexible pharmacy-based immunization statute was enacted in the previous year period, state fixed effects, and year fixed effects, as well as state-specific linear trends (included in Appendix B). The statute variable was lagged one year to ensure that pharmacy-based immunization was legal before the relevant influenza season. In each model, the coefficient on the statute variable represents the effect of changes in pharmacy-based immunization statutes on the outcome under analysis. Poisson models of per capita pharmacy prescriptions for vaccines and antivirals were estimated using state by year level data from PHAST. Models of influenza vaccination rates and the receipt of preventive care were estimated using individual level data from the BRFSS; some specifications of the individual level models also included individual level covariates. Statute effects were estimated and reported as absolute and relative percent differences. Standard errors were estimated with a Huber-White covariance matrix that allowed for heteroskedasticity and state level clustering with a two-tailed p-value < 0.05 to be considered statistically significant. Analyses were performed using STATA SE 12 (Statacorp, TX).

3. Results

3.1. Pharmacy practice statute changes

Table 1 shows that there were 14 states with statutory changes during the 2007 to 2010 period included in our analysis of community pharmacy vaccination prescriptions based on PHAST data. There were 41 states with statutory changes during the 1996 to 2010 period included in our adult vaccination rates and preventive health intervention analysis. Ten states allowed pharmacy-based immunization prior to 1996.

3.2. Trend and event studies

Between 2007 and 2013, the number of influenza vaccine prescriptions in community pharmacies increased from 3.2 to 20.9 million (Fig. 1 Top). In comparison, influenza antiviral prescriptions increased from 1.7 million in 2007 to 4.9 million in 2013. A simple event study graph of vaccine prescription counts shows increases after statutory changes (Fig. 1 Bottom). The graph plots prescription counts relative to the year of flexible pharmacy-based immunization adoption (year 0 being the enacted year). Per capita influenza vaccine prescriptions increase after enacted statutes.


Estimates from two way fixed effects regressions suggest that per capita pharmacy vaccine prescriptions increased by a mean...
Table 2
Pharmacy-based immunization statutory effects.

<table>
<thead>
<tr>
<th>Per capita pharmacy prescriptions, PHAST 2007–2010</th>
<th>N (State by year)</th>
<th>Statute effect (SE), 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RD (%)</td>
<td>AD (%)</td>
</tr>
<tr>
<td>All influenza vaccines</td>
<td>208</td>
<td>579 (207), 62–2736</td>
</tr>
<tr>
<td>Seasonal influenza vaccines only</td>
<td>208</td>
<td>653 (214), 69–3253</td>
</tr>
<tr>
<td>Antivirals</td>
<td>208</td>
<td>62 (115), 24–113</td>
</tr>
<tr>
<td>Adult vaccination rates, BRFSS survey 1996–2010</td>
<td>N (respondents)</td>
<td>Statute effect (SE), 95% CI</td>
</tr>
<tr>
<td></td>
<td>RD (%)</td>
<td>AD (%)</td>
</tr>
<tr>
<td>Population effect</td>
<td>3,825,963</td>
<td>2.9 (1.9), –0.8 to 6.6</td>
</tr>
<tr>
<td>Population effect adjusted for covariates(^4)</td>
<td>3,719,455</td>
<td>2.7 (1.7), 0.6 to 6.0</td>
</tr>
<tr>
<td>Not high-risk population effect(^5)</td>
<td>2,071,586</td>
<td>4.2 (2.8), 1.3 to 9.7</td>
</tr>
<tr>
<td>High-risk population effect(^6)</td>
<td>1,754,457</td>
<td>1.7 (1.1), –0.5 to 3.9</td>
</tr>
<tr>
<td>Adult vaccination rates, BRFSS survey 2007–2010</td>
<td>N (respondents)</td>
<td>Statute effect (SE), 95% CI</td>
</tr>
<tr>
<td></td>
<td>RD (%)</td>
<td>AD (%)</td>
</tr>
<tr>
<td>Population effect</td>
<td>1,690,636</td>
<td>–0.5 (1.2), –2.9 to 1.9</td>
</tr>
<tr>
<td>Population effect adjusted for covariates(^4)</td>
<td>1,639,307</td>
<td>–1.4 (1.2), –3.8 to 1.0</td>
</tr>
<tr>
<td>Not high-risk population effect(^5)</td>
<td>814,798</td>
<td>–1.9 (2.1), –6.0 to 2.2</td>
</tr>
<tr>
<td>High-risk population effect(^6)</td>
<td>875,838</td>
<td>0.8 (0.9), 1.0 to 2.6</td>
</tr>
</tbody>
</table>

Each row represents the estimated effect of adopting a flexible pharmacy-based immunization statute on the stated measure adjusting for state- and year-fixed effects. Flexible pharmacy-based immunization statutes are those that allow immunization under a collaborative practice agreement or written protocol versus no authority or physician prescription alone. Each observation is the per capita prescription rate in a given year, state. SE = Standard error, CI = Confidence Interval, RD = Relative percent difference, AD = absolute percentage point difference.

\(^4\) Includes: age, sex, highest education level achieved, race/ethnic background, smoking status, diabetes and body mass index.

\(^5\) High-risk defined as: individuals aged >65 years, Native American/Alaskan or presence of any of the following medical conditions: asthma, diabetes, smoker, currently pregnant, coronary artery disease. History of MI, or stroke.

absolute difference [AD] of 2.6% (95% CI: 1.1–4.2) and a relative difference [RD] of 579% (95% CI: 62–2736) after states adopted flexible statutes (Table 2). Excluding data on H1N1 vaccines that were given during the 2009–2010 influenza season did not materially alter the results (RD 653%, 95% CI: 69–3253). Changes in PBI regulations had a smaller but statistically significant effect on per capita antiviral prescriptions (RD 62%, 95% CI: 24–113).


Overall, adult influenza vaccination rates have increased from 1996 to 2010 (Fig. 2). In the non-elderly population, influenza vaccination rates grew from 19% to 35%. Vaccination rates among the elderly grew from 60% to 66% over the same period. The two way fixed effects models suggest that adopting flexible statutes led to a small non-statistically significant increase in adult vaccination rates (AD 0.9%, 95% CI: –0.3, 2.2) (Table 2). Including covariates in the regression model did not substantially change the estimated effect (AD 0.9%, 95% CI: –0.3, 2.0). The effects of pharmacy-based immunization were similar among the high-risk sub-population (AD 0.8%, 95% CI: –0.2, 1.8). Additionally, no statistically significant effects were observed when restricting the sample to the

Fig. 2. Influenza vaccination rates over time by age group. Description. Mean vaccination rates by age group in each BRFSS survey year from 1996 to 2010.

Table 3
Pharmacy-based immunization statutory effects on special populations.

<table>
<thead>
<tr>
<th>BRFSS survey 1996–2010</th>
<th>N</th>
<th>Statute effect, % change (SE), 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RD</td>
<td>AD</td>
</tr>
<tr>
<td>Men</td>
<td>1,476,695</td>
<td>1.6 (1.8), 1.9 to 5.1</td>
</tr>
<tr>
<td>Women</td>
<td>2,349,268</td>
<td>4.0 (2.1), 0.1 to 8.1</td>
</tr>
<tr>
<td>Under 65 years of age</td>
<td>2,799,361</td>
<td>4.2 (2.6), 0.9 to 9.3</td>
</tr>
<tr>
<td>65 years and older</td>
<td>996,787</td>
<td>1.8 (1.1), 0.4 to 4.0</td>
</tr>
<tr>
<td>Health insurance</td>
<td>3,373,611</td>
<td>2.8 (1.9), 0.9 to 5.5</td>
</tr>
<tr>
<td>No insurance</td>
<td>442,763</td>
<td>3.2 (2.8), 4.2 to 10.6</td>
</tr>
<tr>
<td>Currently employed</td>
<td>2,120,119</td>
<td>3.9 (2.5), 1.0 to 8.8</td>
</tr>
<tr>
<td>Unemployed</td>
<td>1,692,677</td>
<td>2.1 (1.5), 0.8 to 5.0</td>
</tr>
</tbody>
</table>

Each row represents the estimated effect of adopting a flexible pharmacy-based immunization statute on the stated subpopulation adjusting for state- and year-fixed effects. Flexible pharmacy-based immunization statutes are those that allow immunization under a collaborative practice agreement or written protocol versus no authority or physician prescription alone. SE = Standard error, CI = Confidence Interval, RD = Relative percent difference, AD = absolute percentage point difference.
same years as the prescription analysis (2007–2010). No particular sub-population had a statistically significant increase in adult vaccination rates (Table 3), women had the largest increase post-statute change observed in any group (AD 1.4, 95% CI: −0.0, 2.7). Overall, flexible pharmacy-based immunization does not significantly increase adult vaccination rates relative to what it they would have been in the absence of flexible statutes.


Routine physician office visits had a small non-statistically significant decrease in response to flexible pharmacy-based immunization statutes (AD −1.9, 95% CI: −4.9, 1.1). Pharmacy-based immunization had small non-statistically significant negative effects on the other measures of preventive health service utilisation as well: Cholesterol blood tests (AD −0.9, 95% CI: −2.2, 0.4), clinical breast exam (AD −0.5, 95% CI: −1.6, 0.6), hemoglobin A1c check (AD 0.2, 95% CI: −1.1, 1.4) or diabetic foot exam (AD −0.3, 95% CI: −2.4, 1.9). Results restricting the sample to 2007–2010 are included in Appendix B. The analysis of preventive health services suggests that flexible pharmacy-based immunization statutes do not lead to substantial decreases in the receipt of preventive health care services.

4. Discussion

Our study was designed to evaluate the effect of pharmacy based immunization statutes on adult vaccination rates and related measures of preventive health care services. We observed a large relative increase (57%) in per capita pharmacy influenza vaccine prescriptions after states adopt flexible pharmacy-based immunization statutes. However, we did not observe changes in adult influenza vaccination rates or for any particular subgroup.

The strong relationship between enacted pharmacist immunization statutes and per capita prescriptions further supports they are able to capture pharmacist-administered vaccinations. This large relative increase occurs because the per capita rate pre-statute is near zero for most states, but the absolute change is also high (2.6%). South Carolina has a prominent pre-statute per capita vaccine prescription rate in Fig. 1 (year −1). South Carolina’s initial statute changed occurred in the 1990s but was prescription only, and changed to a flexible statute in 2010 as a response to the influenza pandemic which may explain the relatively large number of pre-statute prescriptions [22].

One explanation for why prescriptions increase but not overall rates is that pharmacy-based immunization statutes may allow patients to shift from traditional vaccination providers (i.e. patients consider pharmacies more convenient). We hypothesized a potential downside of this re-allocation is that patients might end up receiving less preventive care. This could occur if physicians tend to bundle several preventive services into a single office visit and if demand for vaccinations is a key reason that people schedule well-care appointments. For each preventive health outcome the effect estimates are negative, but the confidence intervals suggest pharmacy-based immunization statutes may have no negative effect at all and rule out large reductions in preventive health care.

To our knowledge this is the most extensive evaluation of pharmacy-based immunization to date, and it is the first study to examine the possibility that pharmacy-based immunization has undesirable effects on the delivery of a broader set of preventive health services. One previous study, by Steyer et al., examined regulatory changes that occurred early in the pharmacy-based immunization movement and found that pharmacy-based immunization increased adult influenza vaccination rates among people over age 65 [15]. However, that study relied on data from a smaller subset of states over a short time period early in the pharmacy-based immunization movement (1990s) without adjustment for confounding by group or time-specific effects. Therefore, our estimates can be considered more robust to potential sources of bias and expansive relative to this early work.

The most important assumption in our DID design is that states which adopt flexible pharmacy-based immunization regulations in a given year would have otherwise been subject to the same secular trends as the states that did not make changes in that year. This is called the “parallel trends” assumption in the methodological literature on DID estimation. If late adopters of pharmacy-based immunization pursued other pro-vaccination strategies (funding for clinics, health education, advocacy) rather than pharmacy-based immunization the estimates could be biased towards a null hypothesis of no effect. In contrast, if states adopting flexible pharmacy-based immunization statutes adopted other pro-vaccination strategies then the estimates could be biased upwards. We have not found systematic evidence to support this interpretation especially considering the apparent increase in vaccine prescriptions that appears after the adoption of flexible pharmacy-based immunization statutes (Fig. 1).

Weak evidence that pharmacy-based immunization statutes coincide with increased demand for influenza treatment comes from our analysis of antiviral prescriptions. Although substantially smaller in magnitude than the effect on vaccinations, we unexpectedly observed a 62% increase in antiviral prescriptions relative to statute changes. In general, pharmacy-based immunization should not directly impact antiviral prescriptions. However, the advertising and community engagement effect of pharmacy-based immunization could have led to an increase in the demand for influenza treatment. This cause should not bias our main conclusions. It is also possible that pharmacy-based immunization regulatory changes coincided with other measures to improve access to healthcare or with short run demand for influenza treatment (e.g. 2009 H1N1 pandemic). The antiviral results could be picking up these other changes, suggesting upward bias in our main results. We separately analyzed seasonal influenza vaccines and still found significant increases post- pharmacy-based immunization statute change.

It should also be recognized that changing pharmacy-based immunization statutes are not sufficient to produce increased vaccinations by pharmacists. Other factors such as corporate participation by the large chain community stores (CVS, Walgreens etc.) may be as important as the statutory changes themselves in increasing the number of vaccines administered by pharmacists. The models here do not account for these post-regulatory steps. Additionally, our analysis did not evaluate the potential differences in cost between traditional or pharmacy-based immunization services. These cost differences due to physician co-pays or insurance coverage may play a significant role in the decision on where to receive influenza vaccination. In sum, our estimated effects adjust for many sources of bias but there remains some possibility that the true impact is somewhat larger or smaller than the actual average effect of the statute changes.

5. Conclusion

Pharmacy-based immunization is a prime example of the more general rise of a new retail model of health service delivery. We provide the strongest evidence to date that pharmacists are administering millions of influenza vaccinations as a direct consequence of changes in state statutes that expand their scope of practice. However we do not observe substantial increases in adult influenza vaccination rates or resultant decline in other preventive health services, which suggests that most of the people vaccinated by
pharmacists would have been vaccinated anyway. The main benefits from PBI regulations may accrue to patients, who now have a more convenient and flexible way to obtain an important health service.

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**Appendix A. Supplementary data**

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2016.04.076.

**References**


