

Effects of an Ongoing Epidemic on the Annual Influenza Vaccination Rate and Vaccination Timing Among the Medicare Elderly: 2000-2005

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Seasonal influenza disproportionately affects the population aged 65 years and older. Approximately 90% of the 36 000 influenza-related deaths and 63% of the 226 000 influenza-related hospitalizations per year in the United States occur among the elderly.^{1,2} Despite the significant disease burden of influenza disease and the benefits of influenza vaccination,^{3,4} influenza vaccination coverage levels among the noninstitutionalized elderly population have fluctuated between 60% and 67% since 1997.⁵

Influenza vaccine coverage rates tend to be lower when vaccine supply delays or shortages occur as observed in several seasons since 2000 (Table 1).^{6–8} Fortunately, vaccine production capacity has improved, in part because the number of influenza vaccine manufacturers supplying vaccine to the US market has increased from 3 in 2004 to 5 in 2007.⁹ During this period, the vaccine supply has increased from 57 million to 130 million doses. However, problems with vaccine supply remain as evidenced by the suspension of 46 million doses from one manufacturer during the 2004–2005 season (Centers for Disease Control and Prevention [CDC], unpublished data, 2006),⁹ and a problem with regulation compliance by manufacturers.¹⁰

Despite progress in vaccine production capacity, supply and demand for influenza vaccine remains a “chicken and egg” problem⁷ in which fluctuating or sporadically low demand for the vaccine leads vaccine manufacturers to reduce their supply or exit the market.^{7,9} To address this problem, several policy options have been proposed to motivate vaccine manufacturers, distributors, and providers to remain in the system.⁹ These options include extending vaccination efforts into January and beyond, reducing the financial burden for patients and providers,⁹ and instituting a public “buy back

program” for unused doses to reduce financial risk for manufacturers.¹¹

These options could also include improvement in the distribution of influenza vaccine, because often a large number of doses remain unused even during seasons with vaccine supply problems.⁹ It is difficult to predict vaccine demand, particularly late-season demand, for 2 reasons. First, manufacturers and distributors take vaccine orders as early as January of the prior season, because the vaccine production takes 8 or 9 months.⁹ Second, demand may decrease when influenza epidemic activity is perceived to be mild, whereas demand may increase when an influenza epidemic is perceived to be severe or occur early.⁷ Epidemic activity usually affects late-season demand because influenza activity peaks after January in most seasons (84% of the seasons from 1976 to 2006).¹²

Although the effect of ongoing influenza epidemics on vaccine demand was suggested

qualitatively by Layton et al.,⁷ to the best of our knowledge it has not been measured quantitatively in the literature. Previous studies have noted long-term responsiveness of influenza vaccine demand to epidemic activity with a 1-year lag, e.g., past year’s epidemic level.^{13–15}

We sought to measure short-term responsiveness of influenza vaccine demand to ongoing influenza epidemic levels and timing. We tested the hypothesis that weekly influenza epidemic change is positively associated with overall annual influenza vaccine receipt as well as daily vaccine receipt. We analyzed a 5-year period since 2000 during which influenza seasons varied with respect to the timing and severity of the epidemics, and vaccine supply.

This information could improve efficiency in distribution of influenza vaccine, particularly after the onset of an epidemic. Knowledge of this association might also help predict short-term, late-season vaccine demand in different geographic areas, thereby enabling better vaccine

Objectives. We assessed short-term responsiveness of influenza vaccine demand to variation in timing and severity of influenza epidemics since 2000. We tested the hypothesis that weekly influenza epidemic activity is associated with annual and daily influenza vaccine receipt.

Methods. We conducted cross-sectional survival analyses from the 2000–2001 to 2004–2005 influenza seasons among community-dwelling elderly using the Medicare Current Beneficiary Survey (unweighted $n=2280$ – 2822 per season; weighted $n=7.7$ – 9.7 million per season). The outcome variable was daily vaccine receipt. Covariates included the biweekly changes of epidemic and vaccine supply at 9 census-region levels.

Results. In all 5 seasons, biweekly epidemic change was positively associated with overall annual vaccination (e.g., 2.7% increase in 2003–2004 season) as well as earlier vaccination timing ($P<.01$). For example, unvaccinated individuals were 5%–29% more likely to receive vaccination after a 100% biweekly epidemic increase.

Conclusions. Accounting for short-term epidemic responsiveness in predicting demand for influenza vaccination may improve vaccine distribution and the annual vaccination rate, and might assist pandemic preparedness planning. (*Am J Public Health.* 2009;99:S383–S388. doi:10.2105/AJPH.2009.172411)

TABLE 1—Influenza Vaccination Rates Prior to and During an Influenza Epidemic Period Among the US Community-Dwelling Medicare Elderly Population: 2000–2005

| Influenza Season | Epidemic Start Date ^a | Vaccine Supply Problem | Vaccination Rate Based on Claims Data | | | Vaccination Rate Based on Survey Data |
|------------------|----------------------------------|------------------------|--|-------------------------------------|-----------------------|---------------------------------------|
| | | | From Sept 1 to Epidemic Start ^b | During Epidemic Period ^b | From Sept 1 to May 20 | |
| 2000–2001 | Dec 3 | Severe delay | 37.2% | 9.81% | 47.0% | 69.7% |
| 2001–2002 | Dec 16 | Moderate delay | 45.8% | 2.66% | 48.5% | 71.5% |
| 2002–2003 | Dec 15 | None | 50.4% | 0.54% | 50.9% | 72.9% |
| 2003–2004 | Oct 12 | Relative shortage | 34.5% | 18.3% | 52.8% | 73.7% |
| 2004–2005 | Dec 5 | Severe shortage | 35.5% | 7.93% | 43.4% | 67.1% |

^aStart date defined at the national level (influenza survey laboratory data percent positive $\geq 5\%$).

^bStart date defined at 9 census region level (influenza survey laboratory data percent positive $\geq 5\%$).

distribution and redistribution and thus improving the overall vaccine coverage level. Furthermore, measurement of short-term responsiveness to epidemic activity might be helpful in pandemic planning because of the possibility of insufficient vaccine supply compared with the demand for vaccine.¹⁶ There is also the potential for policies that target younger populations who may experience higher attack rates during a pandemic than in seasonal influenza epidemics.¹⁷

METHODS

We conducted a cross-sectional survival analyses of the Medicare Current Beneficiary Survey (MCBS) and associated claims data to examine the association between influenza epidemic levels and influenza vaccine receipt in subsequent weeks among the Medicare elderly population.⁶ We focused on 5 vaccination seasons between September 2000 and May 2005. The 2000–2001 season was chosen as the starting season because it was marked by a severe nationwide vaccine supply delay (CDC, unpublished data, 2006).¹⁸ The 2001–2002 season included a moderate vaccine supply delay, the 2003–2004 season had a moderate relative supply shortage later in the season because of unusually high demand, and the 2004–2005 season was marked by a severe supply delay and shortage (CDC, unpublished data, 2006).^{18–20}

Study Population

We defined 2 study populations: the “entire population” and an “unvaccinated subpopulation prior to the start of the epidemic.

The entire population sample was defined as individuals aged 65 years or older and continuously enrolled in Medicare Part B from September 1 to May 20, including those who were alive on September 1 but died between September 1 and May 20, in any given season. Medicare managed care enrollees were excluded because dates of vaccination were not available. We also excluded enrollees who resided in a skilled nursing facility because they presumably have less control over vaccination receipt or timing than community dwelling elderly. The effect on the annual vaccination rate was calculated using the entire population sample as a denominator.

The second study population was created for a survival analysis by additionally excluding the individuals who were either vaccinated or deceased prior to the start of an influenza epidemic. For individuals who died after the start of the epidemic, we excluded their observations after their date of death, keeping them in the analyses until their death. The sample size of these unvaccinated subpopulations ranged between 2280 and 2822 (unweighted), and 7.69 million and 9.74 million (weighted; Table 2). The epidemic start date, which varied at the 9 census region level (the 9 geographic regions defined by the US Census Bureau), was determined as the first date of a week when the percent positive in the regional influenza viral surveillance laboratory data reached 5% (CDC, unpublished data, 2008).²¹ These data indicate the percentage of specimens testing positive for influenza type A and B that were collected by state or county public health laboratories and some large medical centers.²¹ We used epidemic data at the 9 census region

level and not those at the state level because state level weekly epidemic data showed larger variance and were less accurate in capturing epidemic activity trends in some states with smaller populations.

Statistical Analyses

Our survival model's outcome variable was the number of days from an influenza epidemic start date until vaccination in each season. To measure this outcome, we used Medicare physician supplier and outpatient claims up to May 20 when the latest regional epidemic ended among 5 seasons.

The key independent variable was the bi-weekly epidemic activity change, i.e., the change rate in the past 2 weeks, compared with the prior 2 weeks. Epidemic activity was measured by weekly viral surveillance data (% positive for influenza) at the 9 census region level. We examined the association between vaccination and the epidemic activity change, applying a 2-week lag because the waiting time for elderly adults on Medicare to see their primary care provider for a checkup was 12.4 days on average in 2001 and 2003.²²

Another weekly varying covariate was the change of vaccine supply, measured by the number of vaccine doses distributed in the previous 4 weeks at the 9 census region level (CDC, unpublished data, 2006). This covariate was created using original monthly national data with the assumption of a linear increase over time and equal vaccine distribution proportional to the regional populations of all ages (CDC, unpublished data, 2006). Because of the difference in the epidemic start date across 9 census regions, estimated effects of vaccine supply in survival models reflected vaccine supply variations across regions as well as across different time periods. In other words, “day 1” in a survival model varied across the 9 regions. Other covariates were individual factors suggested by the literature,^{13–15,23} and are listed in Table 2.

A Weibull survival model was used to analyze time to vaccination because it fit with the data better than other parametric survival models. It accommodated decreasing baseline hazards, thus reducing the potential confounding effect of a seasonal trend of vaccination patterns, e.g., a decreasing trend after the start of an epidemic.

TABLE 2—Population Size, Outcome, and Explanatory Variables (Weighted Average of All 5 Seasons): United States, 2000–2005

| Influenza Season | Entire Community-Dwelling Elderly Population | Unvaccinated Subpopulation at an Epidemic Start |
|---|--|---|
| Population size, unweighted no. (weighted no.) | | |
| 2000–2001 | 4675 (14.9 million) | 2597 (8.31 million) |
| 2001–2002 | 4795 (15.8 million) | 2503 (8.29 million) |
| 2002–2003 | 4834 (16.1 million) | 2280 (7.69 million) |
| 2003–2004 | 4672 (16.1 million) | 2822 (9.74 million) |
| 2004–2005 | 4565 (16.4 million) | 2621 (9.60 million) |
| Influenza vaccine receipt, ^a % | 48.5% | 8.77% |
| Explanatory variables | | |
| Regional factors | | |
| Influenza epidemic level ^b (% of specimens testing positive for influenza) | 8.56 (0.120) | 16.2 (0.220) |
| Vaccine dose distributed in past 4 wk ^b (in millions) | 7.33 (7.19E-3) | 2.37 (0.141) |
| Individual factors, % | | |
| Female | 0.580 | 0.571 |
| Age ≥ 75 y | 0.515 | 0.489 |
| Race: other than White | 0.131 | 0.167 |
| Education: high school diploma | 0.696 | 0.666 |
| Income: ≥ \$20 000 per y | 0.542 | 0.505 |
| Subjective general health status: fair/poor | 0.218 | 0.222 |
| High-risk chronic conditions for flu | 0.513 | 0.473 |
| Private supplemental health insurance: Medigap | 0.741 | 0.680 |
| Medicaid enrollment | 0.119 | 0.149 |
| Household number ≥ 2 | 0.680 | 0.676 |
| Metropolitan residence | 0.721 | 0.723 |
| Current smoking | 0.105 | 0.120 |
| Avoid medical care when sick | 0.267 | 0.291 |
| See physician soon when sick | 0.343 | 0.339 |
| Presence of physician one regularly consults with | 0.807 | 0.775 |

^aOutcome variable.

^bWeekly, at the 9 census region level.

Hypothesized associations between a covariate and daily vaccination, i.e., earlier vaccination timing, were tested with an estimated hazard ratio. The possible positive association between a covariate and daily vaccination does not necessarily address the question of whether the covariate contributes to improvement in the overall annual vaccination rate throughout an entire epidemic period. This question was addressed by measuring the effect on the annual vaccination rate in 2 ways: (1) the effect of all observed changes in a covariate, and (2) the effect of 1 unit of change, i.e., a 100% biweekly increase in epidemic and a 1 million dose increase in the regional vaccine supply.

The effect of all observed changes in a covariate was estimated based on the difference in the annual vaccination rate (i.e., the cumulative hazard) between 2 cases predicted by an estimated Weibull model: a case reflecting all observed changes in the covariate, and a hypothetical case in which this covariate did not change throughout an epidemic period. It should be noted that a hypothesized positive hazard ratio of biweekly epidemic change indicated both positive and negative effects on daily vaccination during 1 season, i.e., the increasing epidemic changes increased daily vaccination up to an epidemic peak but the declining epidemic changes

decreased daily vaccination after an epidemic peak. The cumulative former positive effect is likely to be greater than the cumulative latter negative effect during 1 season, because the vaccination time trends generally decrease after the onset of an epidemic. Therefore, accounting for the offsetting negative effects after an epidemic peak, the cumulative effect of epidemic changes on the annual vaccination was likely to be positive but could be very small in magnitude.

Sensitivity analyses included the various measures of ongoing epidemic activity and definitions of an epidemic period. Epidemic measures included: (1) change rates and (2) the absolute levels of the epidemic with 1–4 week lags. The epidemic was measured in 2 ways: (1) percentage positive in laboratory data, and (2) mortality rates due to pneumonia and influenza (CDC, unpublished data, 2008).²¹

RESULTS

Table 1 presents influenza vaccination rates prior to and during an influenza epidemic period among the entire US entire community-dwelling elderly population. Among this population, approximately 70% of total influenza vaccinations, based on survey responses, were noted on Medicare claims records. The majority of vaccinations occurred prior to the start of an epidemic.

Among this entire population, the vaccination rate during an epidemic period ranged from 0.54% to 18.3%. This rate and its proportion among the annual vaccination rate tended to be higher when an epidemic started early or a vaccine supply problem occurred, such as in the 2000–2001, the 2003–2004, and the 2004–2005 seasons.

Association Between Epidemic, Vaccine Supply, and Daily Vaccinations

Table 3 shows the effects of biweekly influenza epidemic activity change and weekly incremental influenza vaccine supply on daily influenza vaccination during an influenza epidemic period. For instance, in the 2000–2001 season, a hazard ratio (HR) of 1.21 indicates that a Medicare beneficiary was 21% ($P < .001$) more likely to receive an influenza vaccine during the day, conditional on not being vaccinated up to that day, when influenza activity

TABLE 3—Effects of Biweekly Influenza Epidemic Activity Change and Weekly Incremental Influenza Vaccine Supply on Daily Influenza Vaccine Receipt During an Influenza Epidemic Period Among the US Community-Dwelling Elderly Medicare Population: 2000–2005

| Influenza Season | Epidemic Start Date ^a | Vaccine Supply Problem | Biweekly Epidemic Activity Change, ^b HR (95% CI) | Regional Vaccine Supply, ^c HR (95% CI) |
|------------------|----------------------------------|------------------------|---|---|
| 2000–2001 | Dec 3 | Severe delay | 1.21** (1.09, 1.34) | 2.59** (2.13, 3.15) |
| 2001–2002 | Dec 16 | Moderate delay | 1.20** (1.10, 1.31) | 1.93** (1.56, 2.38) |
| 2002–2003 | Dec 15 | None | 1.29** (1.19, 1.39) | NA |
| 2003–2004 | Oct 12 | Relative shortage | 1.07** (1.04, 1.10) | 1.70** (1.41, 2.05) |
| 2004–2005 | Dec 5 | Severe shortage | 1.05* (1.02, 1.09) | 2.36** (1.73, 3.22) |

Note. HR=hazard ratio; CI=confidence interval; NA=not available due to no variation of the variable. An influenza epidemic period as defined at the 9 census region level (influenza survey laboratory data percent positive $\geq 5\%$).

^aStart date defined at the national level (influenza survey laboratory data percent positive $\geq 5\%$).

^bEpidemic activity change in the past 2 weeks, compared with the prior 2 weeks where epidemic level was measured by (influenza survey laboratory data percent positive).

^cThe number of vaccine doses distributed at the 9 census region level in the past 4 weeks (million doses).

* $P < .01$; ** $P < .001$.

increased by 100% in the past 2 weeks, compared with the prior 2 weeks.

Despite the large variations in the vaccination rates during an epidemic period across 5 seasons (Table 3), the association between an epidemic activity change and daily vaccination was comparable and robust in all seasons in terms of the HR magnitude and its statistical significance level ($P < .01$).

An addition of 1 million vaccine doses within 4 weeks in a beneficiary's residence region was associated with a 70%–160% (HR=1.70–2.59) increase in the likelihood of daily vaccination in all 4 seasons estimated ($P < .001$). Because there was no increase in vaccine supply after an epidemic starting in mid-December in the 2002–2003 flu season, an HR could not be estimated for this season.

The magnitude of the HR for vaccine supply effect was larger during the 2000–2001 and 2004–2005 seasons when there was a severe supply delay and shortage, respectively, compared with the other 2 seasons ($P < .05$). These results could be interpreted to mean that distributed vaccines were more likely to be used during a season with a severe vaccine supply problem.

Association Between Epidemics, Vaccine Supply, and Annual Vaccination Rates

Table 4 shows the effects of biweekly influenza epidemic change and weekly

incremental influenza vaccine supply on annual influenza vaccination rates. The results of the increased daily vaccination presented in Table 3 suggest that, when the epidemic level increased rapidly or additional vaccine supply was available, vaccination occurred earlier during an epidemic period.

The effects on the annual vaccination rate were calculated, using the entire population as a denominator, to be comparable with the annual vaccination rates in Table 4, while Table 3 presents the effects on the daily vaccine receipt where a denominator is the subpopulation unvaccinated prior to an epidemic start.

Effects of all observed changes were listed in Table 4. For instance, in the 2000–2001 season, if there was no epidemic increase (i.e., constant epidemic activity level throughout), the annual vaccination rate would have declined by 2.42 percentage points ($P < .001$), which accounted for approximately a quarter of the observed vaccinations administered during the same epidemic period (9.81%).

Effects of the observed epidemic changes ranged in magnitude from 0.19% in the 2002–2003 season, when an epidemic started late with a low activity level, to 2.72% in the 2003–2004 season when an epidemic started early with a high activity level. The effect of the observed vaccine supply changes was a 7.31% increase in the annual vaccination rate in the

2000–2001 season, a season characterized by a severe supply delay.

The effect of a 1-unit increase in a covariate on the annual vaccination rate is presented in Table 4. For example, in the 2000–2001 season, if the epidemic activity kept increasing by 100% every 2 weeks throughout the epidemic period, the annual vaccination rate would have increased by 1.69%. In reality, because the epidemic level increased by more than 100%, the effect of observed epidemic changes (2.42%) was greater than the hypothetical case of 1.69%.

The effect of a 1-unit increase in vaccine supply on the annual vaccination rate was smaller in the 2000–2001 season (a 5.11% increase) characterized with a severe vaccine supply delay compared with the effect in the 2004–2005 season, which was marked by a severe vaccine shortage (a 7.79% increase). On the other hand, the effects of all observed vaccine supply changes in the former season were greater (a 7.31% increase) than that in the latter season (a 2.50% increase) because of the relatively larger amount of vaccine available in the former season.

Sensitivity analyses generally yielded comparable results.

DISCUSSION

Our results are consistent with prior studies.^{13–15} Specifically, the results confirmed our hypothesis that short-term influenza epidemic activity change was positively and strongly associated with: (1) overall annual influenza vaccination, and (2) earlier vaccination timing, i.e., vaccine receipt within 2 weeks of increases in the epidemic. These findings were seen across all 5 seasons, which differed considerably in epidemic levels, timing, and vaccine supply. All prior studies, using different measures of severity of influenza epidemics, have reported moderate associations between epidemic levels and vaccination in the subsequent year.

Interpretations of the Epidemic Effects

Three additional points should be noted in interpreting these findings. First, our estimates of the effect of epidemics and vaccine supply on vaccine receipt were likely conservative because of our use of claims data, which underestimate vaccination rates relative to patient survey data

TABLE 4—Effects of Biweekly Influenza Epidemic Activity Change and Weekly Incremental Influenza Vaccine Supply on Annual Influenza Vaccination Rates Among the US Community-Dwelling Elderly Medicare Population: 2000–2005

| Influenza Season | Epidemic Start Date ^a | Vaccine Supply Problem | Annual Vaccination Rate | | Vaccination Rate During an Epidemic Period ^b | Change in Vaccination Rate During an Epidemic Period ^c | | | |
|------------------|----------------------------------|------------------------|-------------------------|-------------|---|---|-----------------|--------------------------------------|-----------------|
| | | | Survey Data | Claims Data | | Biweekly Influenza Epidemic Activity Change ^d | | Regional Vaccine Supply ^e | |
| | | | | | | Observed Changes | 1-Unit Increase | Observed Changes | 1-Unit Increase |
| 2000–2001 | Dec 3 | Severe delay | 69.7% | 47.0% | 9.81% | 2.42%** | 1.69%** | 7.31%** | 5.11%** |
| 2001–2002 | Dec 16 | Moderate delay | 71.5% | 48.5% | 2.66% | 0.309%** | 0.443%** | 0.836%** | 1.59%** |
| 2002–2003 | Dec 15 | None | 72.9% | 50.9% | 0.540% | 0.193%** | 0.106%** | NA | NA |
| 2003–2004 | Oct 12 | Relative shortage | 73.7% | 52.8% | 18.3% | 2.72%** | 0.890%** | 3.97%** | 8.06%** |
| 2004–2005 | Dec 5 | Severe shortage | 67.1% | 43.4% | 7.93% | 0.382%** | 0.413%** | 2.50%** | 7.79%** |

Note. NA = not available due to no variation of the variable.

^aStart date defined at the national level (influenza survey laboratory data percent positive $\geq 5\%$).

^bBased on claims data. Vaccination rate increases among the entire elderly population during an epidemic period was defined at the 9 census region level (influenza survey laboratory data percent positive $\geq 5\%$).

^cBased on claims data.

^dEpidemic activity change in the past 2 weeks, compared with the prior 2 weeks where epidemic level was measured by influenza survey laboratory data percent positive (%). 1-unit change means the 100% increase in epidemic activity throughout an epidemic period.

^eThe number of vaccine doses distributed at the 9 census region level in the past 4 weeks (million doses). 1-unit change means the 1 million dose increase throughout an epidemic period. * $P < .01$; ** $P < .001$.

(as shown in Table 4). Vaccination rates based on survey data are not generally thought to be very accurate, because they tend to have higher sensitivity but relatively low specificity.^{24,25} Nevertheless, assuming that survey data were valid and that vaccination timing was similar between survey data and claims data, our estimated effects would increase by 40%–55%.

Second, although the effect sizes for the pattern of the epidemic were moderate, it is likely that an earlier and more severe epidemic would yield even greater effects. For instance, an ongoing epidemic was associated with an increase as large as 2.72% in the annual vaccination rate during the 2003–2004 season, when the epidemic started early and the resulting unusually high demand caused a moderate relative vaccine supply shortage later in the season (CDC, unpublished data, 2006).^{18–20} Had there been no incremental vaccine supply during the epidemic period in that season, the annual vaccination rate would have decreased by as much as 3.97% among the entire community-dwelling Medicare elderly population (Table 4).

Third, our study estimated the epidemic effects on vaccination only among a subpopulation of persons who were unvaccinated prior to an epidemic start, accounting for one third to one half of the entire community-dwelling

elderly population. Prior studies have examined the past year's epidemic effects among the entire population. The subpopulation we examined tended to have a lower propensity for influenza vaccination, as suggested by their delayed vaccination timing and lower rates of past season's influenza vaccination receipt, compared with those vaccinated earlier and excluded from our survival analyses. We analyzed this subpopulation to assess ways to improve the vaccination rate among this at-risk (and potentially less-motivated) population.

Limitations

Our study has several limitations. First, we assumed that vaccine supply at regional and local levels was proportional to the regional populations. The estimated effect of vaccine supply might differ if more detailed regional and local supply data were available. However, any random measurement error in vaccine supply would bias the vaccine supply effect toward the null.

Second, we were unable to evaluate other potential contributing factors on vaccination behavior such as vaccination recipient knowledge of either epidemics or vaccine (through mass media, health care providers or social networks), and experience from prior influenza

seasons in terms of vaccine shortages or surpluses and disease severity.

Policy Implications

Our results have policy relevance for estimating both short-term and long-term vaccine demand for seasonal influenza and may have implications as well for pandemic influenza preparedness. These findings could improve efficiency in redistributing influenza vaccine doses after the onset of an epidemic through improved estimates of immediate demand in different geographic areas. Consequently this might improve overall annual vaccine coverage levels, reducing influenza disease burden. More efficient geographic redistribution of vaccine doses would also decrease vaccine wastage, which would reduce the financial loss for manufacturers or public expenditures for vaccine “buy back programs.”¹¹ Also, because the vaccine supply is fixed in the very short run, a policy to stimulate short-run demand, e.g., by more aggressive outreach programs, would be useful, particularly in a lower epidemic activity region. Multiple studies have demonstrated the benefit of patient reminder and recall or outreach for improving influenza vaccination rates.^{26,27}

Our models could also improve demand predictions for the subsequent season. If the

previous year's demand could be separated into a "baseline-demand component" and an "unusual-demand component" caused by unusual epidemic severity or timing, manufacturers' predicted production amounts might better meet the subsequent season's demand. This would minimize financial risks of both manufacturers and public buy-back programs, caused by excessive production, and help ensure the survival of the manufacturers (and vaccine production capacity) in the market over the long run.

Caution is needed in extrapolating our estimates of demand responsiveness to seasonal influenza to pandemic influenza. Uncertainty in many factors, such as the risk of infection, disease severity, vaccine effectiveness, vaccine availability, and guidelines to prioritize target populations, may influence the demand for vaccination to a great extent.

Conclusions

Influenza vaccination is positively associated with weekly changes in influenza epidemics and vaccine supply. Accounting for short-term demand for vaccination based on these changes in an epidemic might improve the distribution of influenza vaccine, increase the annual vaccination rate, help stabilize vaccine supply, and could assist preparedness planning for pandemic influenza. ■

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Contributors

B.-K. Yoo conceived and supervised the study, conducted analyses, and led the writing. M. Kasajima assisted with the study and analyses. K. Fiscella assisted with the study and analyses. N.M. Bennett assisted with

the study and analyses. C.E. Phelps assisted with the study and analyses. P.G. Szilagyi conceived and supervised the study.

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Human Participant Protection

This study was approved by University of Rochester Research Subject Review (RSRB00015882; principal investigator: Byung-Kwang Yoo).

References

1. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA*. 2003;289(2):179–186.
2. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *JAMA*. 2004;292(11):1333–1340.
3. Nichol KL. Influenza vaccination in the elderly: impact on hospitalisation and mortality. *Drugs Aging*. 2005;22(6):495–515.
4. Fiore AE, Shay DK, Broder K, et al. Prevention and control of influenza, recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2008;57(RR07):1–60.
5. Gorina Y, Kelly T, Lubitz J, Hines Z. Trends in influenza and pneumonia among older persons in the United States. *Ageing Trends*. 2008;8:1–12. Available at: <http://www.cdc.gov/nchs/data/ahcd/agingtrends/08influenza.pdf>. Accessed December 25, 2008.
6. Centers for Medicare and Medicaid Services. *Medicare Current Beneficiary Survey: CY 2000-2006*. Baltimore, MD: US Dept of Health and Human Services; 2006.
7. Layton C, Robinson T, Honeycutt A. *Influenza Vaccine Demand: The Chicken and the Egg*. Research Triangle Park, NC: RTI International; 2005. RTI Project No. 0208665.001.
8. Rodewald LE, Orenstein WA, Mason DD, Cochi SL. Vaccine supply problems: a perspective of the Centers for Disease Control and Prevention. *Clin Infect Dis*. 2006; 42(Suppl 3):S104–S110.
9. Orenstein WA, Schaffner W. Lessons learned: role of influenza vaccine production, distribution, supply, and demand—what it means for the provider. *Am J Med*. 2008;121(7, Suppl 2):S22–S27.
10. Danzon PM, Pereira NS, Tejwani SS. Vaccine supply: a cross-national perspective. *Health Aff (Millwood)*. 2005;24(3):706–717.
11. Hinman AR, Orenstein WA, Santoli JM, Rodewald LE, Cochi SL. Vaccine shortages: history, impact, and prospects for the future. *Annu Rev Public Health*. 2006;27:235–259.
12. Fiore AE, Shay DK, Broder K, et al. Prevention and control of influenza: recommendations of the Advisory

Committee on Immunization Practices (ACIP), 2007. *MMWR Recomm Rep*. 2007;56(RR06):1–54.

13. Mullahy J. It'll only hurt a second? Microeconomic determinants of who gets flu shots. *Health Econ*. 1999; 8(1):9–24.
14. Li YC, Norton EC, Dow WH. Influenza and pneumococcal vaccination demand responses to changes in infectious disease mortality. *Health Serv Res*. 2004; 39(4 Pt 1):905–925.
15. Yoo BK, Frick K. Determinants of influenza vaccination timing. *Health Econ*. 2005;14(8):777–791.
16. Schuchat A. US passes million swine flu cases, officials say. *The New York Times*. June 27, 2009;Health.
17. Fraser C, Donnelly CA, Cauchemez S, et al. Pandemic potential of a strain of influenza A (H1N1): early findings. *Science*. 2009;324(5934):1557–1561.
18. Wallace GS. Influenza vaccine distribution 2006–07. Paper presented at: the 14th National Immunization Conference, March 5–8, 2007. Available at: <http://cdc.confex.com/cdc/nic2007/techprogram/P13052.HTM>. Accessed February 2, 2009.
19. Charatan F. Widespread flu in United States exposes shortage of vaccine. *BMJ*. 2004;328(7430):8.
20. Nelson R. Influenza vaccine shortage hits the USA. *Lancet*. 2003;362(9401):2075.
21. Centers for Disease Control and Prevention. Flu activity and surveillance. 2008; Available at: <http://www.cdc.gov/flu/weekly/fluactivity.htm>. Accessed December 24, 2008.
22. Trude S, Ginsburg PB. An update on Medicare beneficiary access to physician services. *Issue Brief Cent Stud Health Syst Change*. 2005;93:1–4.
23. Schneider EC, Cleary PD, Zaslavsky AM, Epstein AM. Racial disparity in influenza vaccination: does managed care narrow the gap between African Americans and whites? *JAMA*. 2001;286(12):1455–1460.
24. Zimmerman RK, Raymund M, Janosky JE, Nowalk MP, Fine MJ. Sensitivity and specificity of patient self-report of influenza and pneumococcal polysaccharide vaccinations among elderly outpatients in diverse patient care strata. *Vaccine*. 2003;21:1486–1491.
25. Mac Donald R, Baken L, Nelson A, Nichol KL. Validation of self-report of influenza and pneumococcal vaccination status in elderly outpatients. *Am J Prev Med*. 1999;16:173–177.
26. Szilagyi PG, Schaffer S, Shone L, et al. Reducing geographic, racial, and ethnic disparities in childhood immunization rates by using reminder and recall interventions in urban primary care practices. *Pediatrics*. 2002; 110(5):e58.
27. Jacobson VJ, Szilagyi P. Patient reminder and patient recall systems to improve immunization rates. *Cochrane Database Syst Rev*. 2005; (3):CD003941.