RESEARCH LETTER

Where High-Risk Adults Receive Influenza Vaccine During a Shortage

The United States has recently experienced influenza vaccine shortages because of manufacturing problems and distribution delays.1 During the 2004-2005 season, only 61 of the expected 100 million influenza vaccine doses were available to the US market after 1 of the 2 licensed companies withdrew their product.1,2 The Centers for Disease Control and Prevention (CDC) recommended that available vaccine be reserved for persons at high risk for influenza-related complications and close contacts of high-risk persons.1 That year, vaccine coverage levels were lower among those prioritized for influenza vaccination, including older adults, long-term care residents, and health care workers.3,4 Only 63% of elderly persons and 46% of adults with chronic conditions who tried were able to obtain the influenza vaccine. Half of adults in high-risk groups did not attempt to get the vaccine, often citing vaccine shortage as an important reason.3 Ironically, when the influenza season ended, 4 million doses remained undistributed, highlighting the need to improve the supply and demand match.

To better understand where consumers obtain influenza vaccine in the setting of limited vaccine supply, we compared influenza vaccine coverage rates and place of vaccination for persons in different risk groups during the 2004-2005 influenza season with the 2003-2004 “non-shortage” baseline.

Methods. We used validated data from the Behavioral Risk Factor Surveillance System (BRFSS), a telephone survey conducted by state health agencies (in collaboration with the CDC) in all 50 states, the District of Columbia, Guam, Puerto Rico, and the US Virgin Islands. Noninstitutionalized adults 18 years and older were selected through random-digit dialing. Data were compiled year round and adjusted for the probability of selection of a telephone number, number of adults and telephones in a household, and age and sex to ensure that the distribution of this weighted sample mirrored population estimates by the US Census Bureau.6

The 2004 and 2005 BRFSS surveys included questions on demographic characteristics, including self-reported race and ethnicity, chronic diseases, and influenza vaccination information. Interviewers in all states and territories asked “A flu shot is an influenza vaccine injected into your arm. During the past 12 months, have you had a flu shot?” and “During the past 12 months, have you had a flu vaccine that was sprayed in your nose?” (FluMist; MedImmune Vaccines, Inc, Gaithersburg, Maryland). Those in California, Maine, Minnesota, New Hampshire, Ohio, Vermont, Wisconsin, and Wyoming were also asked “At what kind of place did you get your last flu shot/spray?” Response rates by these participating states ranged from 39.0% to 63.2% in 20047 and 38.7% to 61.3% in 2005.8

Data were restricted to responses from the first 6 months of 2004 and 2005 surveys to correspond with the 2003-2004 and 2004-2005 seasons, respectively. We then compared influenza vaccination rates and place of vaccination for persons in various risk groups by χ2 analysis using SUDAAN software (Research Triangle Park, North Carolina). This study was approved by the University of Washington institutional review board.

Table 1. Influenza Vaccination Rates by Influenza Season and Risk Groups

<table>
<thead>
<tr>
<th>Respondent Characteristics</th>
<th>Influenza Vaccination Rates by Season, %</th>
<th>2003-2004 Baseline</th>
<th>2004-2005 Shortage</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>All persons aged ≥65 y</td>
<td></td>
<td>75.9</td>
<td>66.6</td>
<td>.001</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td></td>
<td>78.0</td>
<td>69.4</td>
<td>.001</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td></td>
<td>42.4</td>
<td>70.8</td>
<td>.04</td>
</tr>
<tr>
<td>Hispanic</td>
<td></td>
<td>78.9</td>
<td>65.5</td>
<td>.18</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>69.5</td>
<td>58.9</td>
<td>.43</td>
</tr>
<tr>
<td>Veteran status and insurance coverage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonveteran with Medicare/HMOc</td>
<td></td>
<td>75.9</td>
<td>66.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Veterand</td>
<td></td>
<td>76.7</td>
<td>73.1</td>
<td>.39</td>
</tr>
<tr>
<td>High-risk conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With asthma</td>
<td></td>
<td>88.2</td>
<td>80.0</td>
<td>.13</td>
</tr>
<tr>
<td>With diabetes</td>
<td></td>
<td>78.0</td>
<td>78.6</td>
<td>.91</td>
</tr>
<tr>
<td>Persons aged 18-64 y</td>
<td></td>
<td>45.1</td>
<td>33.4</td>
<td>.02</td>
</tr>
<tr>
<td>with asthma or diabetes</td>
<td></td>
<td>44.5</td>
<td>31.1</td>
<td>.01</td>
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<tr>
<td>With asthma</td>
<td></td>
<td>50.8</td>
<td>39.6</td>
<td>.04</td>
</tr>
<tr>
<td>With diabetes</td>
<td></td>
<td>26.2</td>
<td>15.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Persons aged 18-64 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>without asthma or diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: HMO, health maintenance organization.

a Unweighted sample sizes.

bP values were determined using χ2 analysis, comparing the 2003-2004 with 2004-2005 influenza seasons.

cAnswered “yes” to “Do you have any kind of health care coverage, including health insurance, prepaid plans such as HMOS, or government plans such as Medicare?” and “no” to “Have you ever served on active duty in the US Armed Forces, whether in the regular military or in a National Guard or military reserve unit?”

dAnswered “yes” to “Have you ever served on active duty in the US Armed Forces, whether in the regular military or in a National Guard or military reserve unit?”
Results. In the 2004 and 2005 survey periods, 149,934 and 183,232, respectively, noninstitutionalized adults 18 years and older responded to the BRFSS surveys. Data from the 8 states that participated in the place of vaccination question provided 20,661 respondents (20.4%) to the 2004 survey and 23,255 respondents (22.1%) to the 2005 survey for this analysis. Vaccinated respondents specified place of vaccination in 94.7% of cases (n=7960) in 2004 and 94.2% (n=6472) in 2005.

For noninstitutionalized adults in all risk groups, influenza vaccination rates were statistically significantly lower in 2004-2005 compared with 2003-2004 (Table 1). This included older adults in all racial groups, except for non-Hispanic blacks, who had a significantly higher vaccination rate. Adults 65 years and older with asthma or diabetes did not experience a significant reduction in vaccination rates, and this group reported higher rates than elderly persons without these comorbidities. In contrast, younger adults aged 18 to 64 years with asthma or diabetes had almost a 12% absolute reduction in vaccine coverage during the vaccine shortage year.

The elderly persons and adults with high-risk conditions were primarily vaccinated in a physician’s office or health maintenance organization, locations that provided approximately half of all doses during both nonshortage and shortage seasons (Table 2). Vaccinated adults aged 18 to 64 years who had asthma or diabetes were more likely to receive vaccine in the physician’s office or health maintenance organization during the vaccine shortage. The elderly participants reported no significant change in their place of vaccination between the 2 seasons.

During the vaccine shortage season, the majority of vaccine recipients at most sites were elderly, who composed 74% of those who received vaccine in community centers, 50% of those who received doses in the physician’s offices or health departments, 40% of those who received vaccine in other clinics or health centers, and only 2% of those receiving vaccine in the workplace. Elderly non-Hispanic blacks were more likely to visit their physician’s office (54.2% vs 66.2%), community center (0.7% vs 2.0%), or store (1.5% vs 6.6%) during the shortage season (P=.50).

Comment. The 2004 US influenza vaccine shortage was associated with significantly lower vaccination rates among those belonging to priority groups, including younger high-risk adults and elderly persons. Vaccine shortages resulted in a greater proportion of younger high-risk patients seeking vaccinations at their physician’s office. Vaccine shortage did not alter the site for receiving vaccination among older adults, suggesting that those who were unable to receive vaccinations from their usual places did not seek or find vaccines elsewhere.

Our results differ from those reported by Santibanez and colleagues, who found that the delayed availability of the 2000-2001 influenza vaccine did not affect influenza vaccination rates in elderly persons but did alter the site of vaccination. More elderly persons in that study received vaccinations at community clinics or senior citizen centers if their physician’s supply of vaccine arrived late, compared with the elderly persons enrolled in a clinic that received vaccine on time. These differences in findings may be explained by the degree of vaccine delay and shortage and by temporal and regional variations. As future vaccine shortages could lead to other patterns in the ways patients obtain vaccines, it is important to develop mechanisms to rapidly identify and overcome barriers to vaccination.

A poll taken during the 2004 influenza vaccine shortage revealed that many did not seek vaccination for reasons such as concerns over its safety and effectiveness and underestimation of the severity of influenza illness and complications. Zimmerman and colleagues reported a change in elderly patients’ attitudes during the 2000-2001 influenza vaccine shortage, compared with the
previous nonshortage year. More elderly persons were concerned about the vaccine, and fewer understood its importance or reported receiving a recommendation from their medical providers to get vaccinated. A health care provider's recommendation to receive vaccination is highly effective and is important even if vaccines are not readily available at the time of patient encounter.

The main limitation of this study is that BRFSS summarizes aggregate patterns during the influenza season. Questions regarding place of vaccination were only posed in selected states, potentially obscuring local and regional variations that may have occurred. There may have been nonresponse bias, given an overall response rate of about 50%, and selection bias, since BRFSS is a landline telephone-based survey. Nevertheless, during vaccine shortage, efforts should be made to provide vaccines to physicians' offices and assist elderly patients in finding alternate vaccination locations.

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COMMENTS & OPINIONS

Phosphorus-Related Mechanisms of Vascular Calcification

Recently, Dhingra et al reported relations of increased serum phosphorus and calcium levels in the incidence of cardiovascular disease in individuals without chronic kidney disease. In chronic kidney disease, the relation between hyperphosphatemia and cardiovascular calcification was identified, and high mortality and morbidity due to cardiovascular calcification were reported. According to Dhingra et al, potential mechanisms of the proven relation between cardiovascular calcification and increased serum phosphorus level may include inhibition of 1,25-dihydroxyvitamin D synthesis, direct promotion of vascular injury by an increase in phosphorus level, increased osteopontin expression, increased calcium and phosphorus product, subclinical renal dysfunction, and increased parathyroid hormone level caused by a high serum phosphorus level.

We report other mechanisms of vascular calcification that were discovered. (1) Extracellular inorganic phosphate is considered to promote transformation of the vascular phenotype of human aortic smooth cells. (2) Inorganic phosphate increases the expression of the osteogenic markers osteocalcin and core-binding factor-1 gene. (3) The role of PIT-1 (GLVR-1) as a potent sodium-dependent phosphate cotransporter is another mechanism. Phosphate uptake through PIT-1 is essential for smooth muscle cell calcification. Serum calcium and phosphorus levels can act simultaneously in vascular matrix mineralization: elevated serum phosphate levels stimulate phosphate uptake via Pit-1, and elevated calcium levels induce expression of Pit-1 messenger RNA. (4) Platelet-derived growth factor, a potent atherogenic factor, plays a role in calcification in the presence of mineral imbalance even under normal phosphate level conditions.

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Analgesic Use and Risk of Hypertension: Concern About Bias

The study by Forman et al is a welcome addition to the literature exploring the association between hypertension and nonnarcotic analgesic use. However, I am concerned about bias as an