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Expanding the Influenza Vaccination Season: A New Paradigm for Increasing Immunization Rates

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Expanding the Influenza Vaccination Season: A New Paradigm for Increasing Immunization Rates

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Introduction: Expanding the Influenza Vaccination Season

Influenza immunization remains the best defense against the morbidity and mortality associated with influenza infection. National influenza immunization guidelines are in place and are updated annually to identify the groups of individuals that should be vaccinated each year and to provide counsel on how and when vaccine should be administered.¹ Despite this specific guidance to clinicians, community immunizers, and public health workers, there is broad-based evidence of influenza vaccine underutilization in all groups for whom vaccination is warranted,² resulting in potentially preventable illness and complications of influenza (pneumonia, hospitalization, and death).³ One of the contributions to immunization rates that fall far below target levels is a sizable number of missed opportunities throughout the vaccination season (i.e., healthcare visits during which at-risk patients are not vaccinated).

The Centers for Disease Control and Prevention (CDC) and other health experts have slightly differing definitions of the influenza vaccination season. Although administration of influenza vaccine in October and November is traditional, it has become clear that full implementation of CDC recommendations cannot be accomplished if vaccination occurs only in the fall, in advance of the influenza season. The CDC and others advocate broadening the influenza vaccination season, such that patients are immunized even after influenza activity has begun in a community. To maintain consistency throughout this supplement to *The American Journal of Medicine*, we are using terminology based on CDC influenza recommendations and defining the *influenza disease season* as October through May and the *influenza vaccination season* as October into January and beyond.¹ This shift in the vaccination timing paradigm requests all healthcare professionals to recognize the value and medical need of vaccines given throughout the season and to vaccinate at-risk patients at every opportunity. In meeting public health vaccination goals, healthcare professionals are also called upon to increase their own influenza immunization rates. Healthcare professionals should view annual influenza vaccine as a professional responsibility for

many reasons: it make us positive role models for our patients, it minimizes the likelihood that we will get influenza and be unable to work at a time when the healthcare system needs us most, and it will help us avoid doing harm by infecting patients in our care.

Given the emphasis on influenza immunization in US public health policy, a series of articles on the topic have been published together in this supplement. The subjects discussed in these articles are as follows: missed vaccination opportunities, practice-proven interventions that increase immunization rates, the delicate balance between vaccine supply and demand, and adult immunization barriers.

In the first article, Drs. Gregory A. Poland and David R. Johnson set the stage by discussing the substantial burden of influenza infection on affected individuals, the healthcare system, and society at large. Given the availability of an effective and safe vaccine, the authors then review in some detail the rationale for the current CDC recommendation that at-risk patients be vaccinated throughout the influenza season, beginning when vaccine first becomes available to the time when supply is exhausted. They develop the rationale that vaccination throughout the influenza season is medically relevant and feasible. The authors also present results from a newly released study in which patients at risk for influenza saw a healthcare provider on average 2.2 times between November and February, yet did not receive influenza vaccine. These findings underscore the frequency with which missed vaccination opportunities contribute to sub-optimal vaccination levels. With the supply of influenza vaccine now plentiful, efforts must be focused on reducing missed vaccination opportunities such that national target objectives are achieved. Healthcare providers are encouraged to use all opportunities to vaccinate, which now represents best practice.

In the second article, Nurse Practitioner Patricia K. Stinchfield presents a literature-based review of practice-proven interventions that increase influenza immunization rates and extend the vaccination season. In this regard, interventions that increase patient demand and vaccine access and overcome practice-related barriers (e.g., standing orders, reminder and recall efforts, vaccination-only clinics) are discussed. It is suggested that sites select and implement ≥ 1 intervention that addresses site-specific needs, with choices based on necessary resources and other factors to

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optimize the reach of vaccination. By way of example, the author provides case studies of practices that deliver influenza vaccine efficiently and effectively to a large proportion of their target patients.

The focus of the third article, coauthored by Dr. Walter A. Orenstein and me, is the delicate balance between vaccine supply and demand and its impact on the realization of influenza immunization goals. The complexities of vaccine production and distribution, and financing are reviewed, with a particular focus on the implications for the provider. With substantial growth in supply expected over the coming years, demand for the influenza vaccine should be increased. A number of strategies are discussed to promote improved vaccine uptake.

In the final article, Dr. Johnson and colleagues present the results of a structured telephone survey, which was conducted to determine the attitudes and knowledge of consumers and healthcare providers about adult vaccines (influenza, pneumococcal, and tetanus). Factors affecting vaccination decisions were assessed. According to the survey responses, immunization rates for adults are much lower than target rates established by national guidelines. Of note, the reasons consumers gave for not receiving vaccinations were not consistent with those given by healthcare providers. The researchers provide us with a sampling of these reasons, which can be used to inform and refine policies to increase immunization rates in adults.

It is the hope of the authors that these articles will help to shape new viewpoints and practices, culminating in the

vaccination of all persons at risk for influenza illness and transmission of influenza to others.

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Increasing Influenza Vaccination Rates: The Need to Vaccinate Throughout the Entire Influenza Season

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ABSTRACT

The burden of influenza on affected individuals and the healthcare system, as well as on society, is substantial. Although the supply of an effective and safe influenza vaccine was limited in previous years, advances in manufacture and distribution have alleviated such shortages. In most seasons, millions of doses go unused, and large numbers of unvaccinated, at-risk persons are left vulnerable to infection and its complications. According to insurance claims data, high-risk patients are seen by their healthcare providers on average 2.2 times between the peaks in vaccination (November) and in disease activity (February), yet they remain unvaccinated. The current 2- to 3-month time frame over which patients are traditionally immunized is too short to fully implement immunization recommendations and inconsistent with the duration of influenza activity. Both healthcare providers and patients should reevaluate their approach to influenza vaccination and recognize the need to extend the immunization time period into January and beyond. To increase influenza immunization rates, the Centers for Disease Control and Prevention (CDC) and other professional societies recommend an expanded immunization season, with vaccination offered at every opportunity between October and May.

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Annual influenza vaccination of persons at risk for either complications of influenza infection or for transmitting influenza virus is the most important component of the US public health strategy for preventing influenza-associated morbidity and mortality.¹ Historically, most healthcare practitioners have offered influenza vaccination to their at-risk patients each year from September to about November, and vaccination rates decrease precipitously before year's end. This approach to vaccination was conceived at a time when fewer individuals were in target groups for vaccination and when the vaccine supply was limited, necessitating prioritization of doses to the most vulnerable persons. The vaccine supply is now plentiful,² and target groups have expanded to include approximately 3 of every 4 Americans.³ The most recent expansion calls for universal vacci-

nation of all children through 18 years of age.⁴ Some have postulated that widespread pediatric vaccination may yield a herd immunity affect. Current evidence is modest, though, and herd immunity, though possible,^{5–7} needs further study.

Adoption of a new paradigm that includes a much longer vaccination period—starting in the autumn and continuing through the entire influenza season—is critical to protecting the large number of at-risk persons. According to the Centers for Disease Control and Prevention (CDC), vaccine administered after the influenza season has begun is beneficial. As a consequence, current CDC recommendations emphasize that immunization providers should offer influenza vaccine and even schedule immunization clinics throughout the entire influenza season, from October to May.

INFLUENZA: THE ILLNESS AND ITS IMPACT

Influenza is an acute and potentially serious viral infection that affects 1 or 2 of every 10 Americans annually.⁸ Classic influenza, generally an uncomplicated and self-limited illness, is characterized by respiratory as well as constitutional

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signs and symptoms (e.g., nonproductive cough, high fever, chills, headache, sore throat, myalgia, and malaise).⁹ Additional symptoms unique to children include abdominal pain, diarrhea, and vomiting. Influenza infection can lead to serious sequelae, including secondary bacterial pneumonia, sinusitis, bronchitis, and myocarditis, as well as croup, bronchiolitis, and acute otitis media in children.^{1,8,10} Influenza can also exacerbate underlying medical conditions; it can trigger acute myocardial infarction or stroke^{11,12} and increase the rate of death from coronary heart disease (odds ratio, 1.3).¹³ Complications of the acute infection are most common in young children, the elderly, and persons of any age with underlying medical conditions that place them "at risk" (e.g., diabetes mellitus, asthma, cardiovascular disease).¹⁴

Influenza has a substantial impact on both affected individuals and society. A typical case of influenza results in 3 to 4 days of bed rest and an additional 5 to 6 days of restricted activity.¹⁵ Absenteeism from work and school was attributed to influenza in a study of >12,000 US households with ≥ 1 school-aged child reporting influenza-like illness.¹⁶ Influenza-associated "presenteeism" (ill but still at work or school) has been shown to decrease job performance,^{17,18} and infection is associated with functional decline in older adults.¹⁹

An average of >200,000 hospitalizations and 36,000 deaths due to influenza occurred annually in the United States during the 1990s.^{20,21} The current hospitalization and mortality rates attributable to influenza are even higher owing to increased numbers of at-risk persons (e.g., individuals who are elderly, have diabetes, or are immunocompromised). To provide perspective, the number of influenza deaths in the United States is on the same order of magnitude as the number of deaths from colorectal cancer and breast cancer.²²

The economic impact of annual influenza epidemics is substantial. Based on 2003 data, which included >334,000 hospitalizations (3.1 million hospitalization days), 41,000 deaths, and 31.4 million outpatient visits, Molinari and colleagues²³ estimated direct medical costs (in 2003 US dollars) of \$10.4 billion (95% confidence interval [CI], \$4.1-\$22.2 billion) and projected lost earnings of \$16.3 billion (95% CI, \$8.7-\$31.0 billion). Adding indirect costs related to death (lost productivity and intrinsic value of human life), the total economic burden was \$87.1 billion (95% CI, \$47.2-\$149.5 billion). This exceeds the combined direct and indirect annual costs of arthritis in the United States (\$82 billion).²⁴

VACCINE SAFETY AND EFFICACY

Multiple studies, in multiple settings, have consistently demonstrated the safety and efficacy of both trivalent inactivated influenza vaccine (TIV) and live attenuated vaccine (LAIV) in mitigating clinical illness and decreasing the risk of associated complications. Influenza vaccines, like all vaccines, are not 100% effective. Efficacy varies based on

the antigenic match between circulating and vaccine strains and the age and immune status of vaccine recipients. Further, clinical study findings vary based on the outcome measured (e.g., culture-confirmed influenza infection, prevention of medically attended acute respiratory illness).

Estimates of TIV efficacy against laboratory-confirmed influenza in healthy adults <65 years range from 70% to 90% when the antigenic match is good²⁵⁻²⁸ to 50%-77% when the antigenic match is suboptimal.^{25,27,28-31} In this same population, LAIV provides significant reductions in days of illness, days of work lost, days with healthcare provider visits, and use of prescription antibiotics and over-the-counter medications.

Efficacy against laboratory-confirmed infection is lower in older persons (for whom only TIV is currently approved), but the true benefit of vaccination for this group is the reduction in risk of serious complications and death. Influenza vaccination (TIV) is 30% to 70% effective in preventing hospitalization for pneumonia and influenza in community-dwelling elderly persons^{32,33} and up to 80% effective in preventing death among elderly nursing home residents.³⁴⁻³⁷

Studies have also confirmed vaccine efficacy in children (TIV is approved for use in all children aged ≥ 6 months; LAIV is approved for use in children aged ≥ 24 months without asthma). In a 5-year study, TIV reduced laboratory-confirmed influenza A infection by 77% to 91% in children aged 1 to 15 years.³⁸ During a season marked by a suboptimal antigenic match, TIV was 51% effective in children 6 months to 8 years of age against medically-attended, clinically-diagnosed pneumonia or influenza.³⁹ Across 2 influenza seasons, 1 marked by a drifted influenza strain, LAIV was 92% effective against laboratory-confirmed influenza in children 60 to 71 months of age.^{40,41}

Both types of influenza vaccine are contraindicated in individuals with a history of hypersensitive reaction to eggs or egg proteins. The most frequent side effect associated with TIV is soreness at the vaccination site.⁴² For LAIV, the most frequent side effect is runny nose. Guillain-Barré syndrome (GBS) was associated with the 1976 swine influenza vaccine, but evidence of a connection between GBS and subsequent vaccines has been inconsistent.¹ The CDC advises that it is "prudent" to avoid vaccinating persons with a history of GBS who are not at high risk for severe influenza complications. However, the potential risk of infection may outweigh concerns about GBS for those at high risk.

VACCINATION RECOMMENDATIONS

Based on the available evidence, the CDC has recommended that certain groups of persons should receive annual influenza vaccination (Table 1).^{1,4} In sharp contrast to prior years in which only high-risk persons were targeted for vaccination, the most current CDC recommendations suggest influenza vaccination of any person wanting to reduce his or her risk of influenza or the potential of transmitting

Table 1 Recommendations for Influenza Vaccination

Annual influenza vaccination is recommended for:

- Any person, including a school-aged child, who wishes to reduce the likelihood of becoming ill or of transmitting the infection to others
- Any person at risk for influenza complications:
 - Children aged 6–59 mo*†
 - All persons aged ≥50 yr
 - Children and adolescents on long-term aspirin therapy
 - Pregnant women
 - All persons (adults and children) with a chronic disease (e.g., asthma, diabetes mellitus, cardiovascular disease) excluding hypertension
 - All persons (adults and children) who are immunosuppressed
 - All persons (adults and children) with a condition that can compromise respiratory function, handling of secretions, or increase the risk for aspiration (e.g., cognitive dysfunction, spinal cord injury, seizure disorder, other neuromuscular disorder)
 - Residents of nursing homes and other chronic-care facilities
- Any person at risk of transmitting influenza:
 - Healthcare personnel
 - Healthy household contacts (including children) and caregivers of:
 - Children aged ≤59 mo†
 - Adults aged ≥50 yr
 - Persons (adults and children) with a medical condition that increases their risk for severe complications of influenza

Adapted from Centers for Disease Control and Prevention.^{1,4}

*On February 27, 2008, the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices voted to expand its recommendations for annual influenza vaccination to include all children 6 months through 18 years.

†Children aged <6 months cannot be vaccinated and should be protected through vaccination of close contacts.

the illness. The current target groups for influenza vaccination include approximately 218 million Americans, or 73% of the US population.³ In 2006, the CDC's Advisory Committee on Immunization Practices signaled its intent to move toward a universal influenza immunization recommendation⁴³ and in early 2008 voted to recommend extending pediatric recommendations to all children from 6 months through 18 years.⁴

Despite these recommendations from the CDC and other professional organizations (eg, the American Academy of Family Physicians [AAFP], American Academy of Pediatrics [AAP], American College of Obstetricians and Gynecologists, American College of Physicians, American Medical Association [AMA]), influenza vaccination rates remain low (Figure 1).¹ Approximately 60% of adults ≥65 years and only 10% to 40% of other target groups were vaccinated in 2005.¹ The current level of vaccination falls far short of the Healthy People 2010 national health objectives of 90% for persons ≥65 years and 60% for younger

persons who have risk factors.⁴⁴ Worse, the majority of US healthcare workers themselves fail to get the influenza vaccine each year.⁴⁵

Most persons recommended for influenza vaccination should receive a single dose each year. The exception is children 6 months to 9 years of age who are receiving influenza vaccine for the first time. They should receive 2 doses administered ≥1 month apart.¹⁴ No influenza vaccine is currently licensed for children aged <6 months; these vulnerable infants should be protected indirectly through vaccination of close contacts.

In 2006, approximately 150 million Americans in target groups lacked the protection conferred by influenza vaccination. This was at a time when the supply was abundant, and millions of vaccine doses were ultimately discarded.² Vaccine doses left over after one influenza season cannot be used during the following season due to changes in circulating strains (i.e., antigenic drift) and vaccine expiration.¹⁴

STRATEGIES TO INCREASE INFLUENZA VACCINATION

As the number of people for whom influenza immunization is recommended has increased, so has the challenge of reaching them all. The US Public Health Service (USPHS) Healthy People 2010 influenza immunization goals will not be achieved without a change in the influenza immunization paradigm. This requires efforts on 3 fronts: (1) consumer demand for influenza immunization needs to be high and sustainable from season to season; (2) there must be an adequate vaccine supply; and (3) the healthcare system should use all opportunities to vaccinate (e.g., at routine healthcare visits, during hospitalizations) throughout the influenza season. Although the influenza season often peaks in February (Figure 2),¹ it can last for many months afterward in the United States. Therefore, vaccination into January and beyond is beneficial.

Consumer Demand

Surveys show that many Americans have misperceptions about their risk of influenza, whether they should get vaccinated, vaccine efficacy, and the safety of influenza vaccines. For instance, in a randomized, nationally representative sample of unvaccinated Medicare beneficiaries, the most common explanations were that they were “unaware of vaccination's need” and “concerned that the vaccine causes influenza” and “could cause side effects.”⁴⁶ Approximately half of adult respondents to a survey conducted before the 2006 to 2007 influenza season indicated they did not plan to be immunized. Their reasons included thinking that influenza is not serious enough to warrant immunization (43%), that they are not at risk for influenza/complications (37%), that the vaccine is not effective (19%), and that vaccination in a prior year makes revaccination unnecessary (15%).⁴⁷

Healthcare providers can influence their patients' decisions regarding vaccination. A first step is to set a good

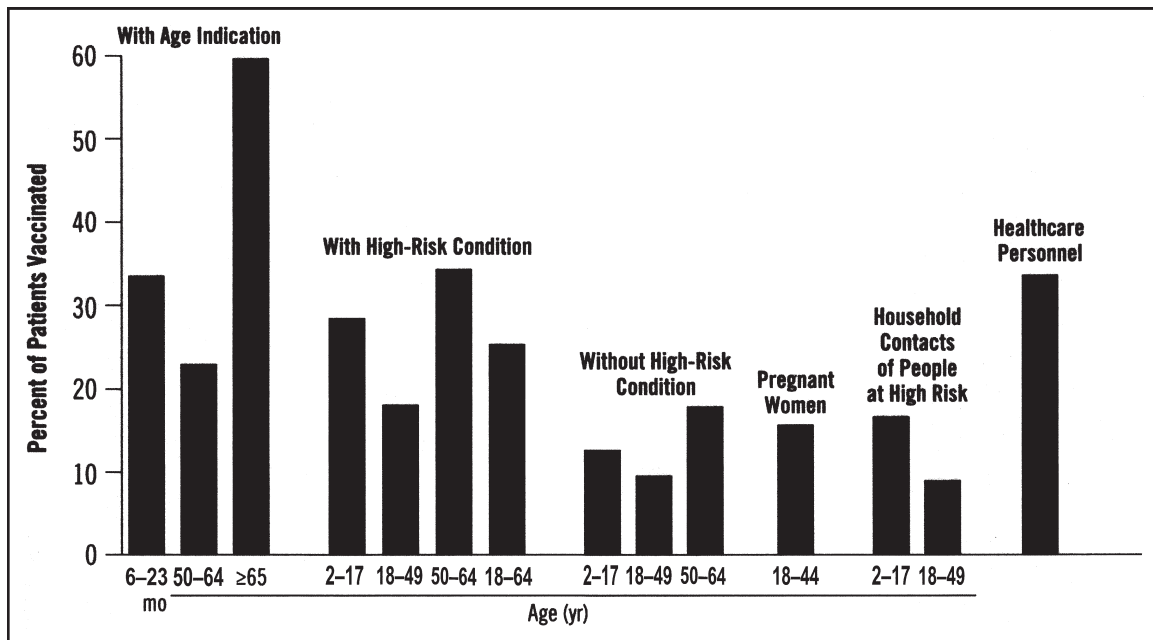


Figure 1 Self-reported influenza vaccination levels by target population. (Reprinted from *MMWR Recomm Rep.*¹)

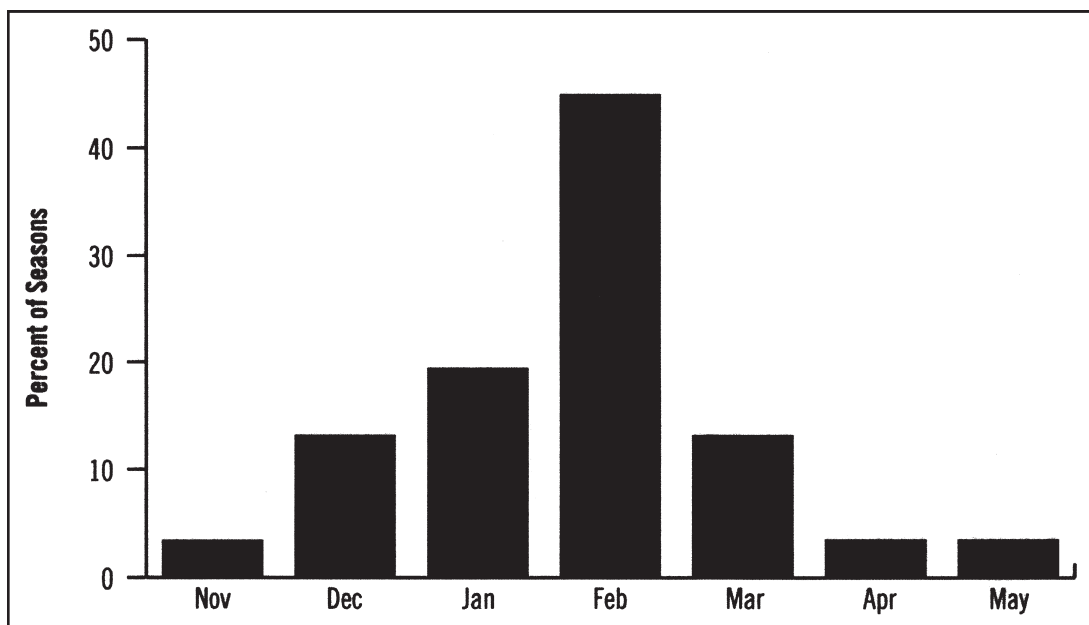


Figure 2 Peak influenza activity in the United States by month, 1976 to 2006. (Reprinted from *MMWR Recomm Rep.*¹)

example for their patients by vaccinating themselves and their staff.^{48,49} Getting an annual influenza vaccination should be viewed as a professional responsibility. Vaccination reduces the risk that healthcare workers will get influenza and be unable to work at a time when the healthcare system's needs are greatest. Even more importantly, it reduces the risk that healthcare workers will transmit a potentially deadly virus to the patients in their care. Once vaccinated, healthcare workers are in a better position to strongly recommend influenza vaccination to all at-risk pa-

tients.^{50,51} In this supplement to *The American Journal of Medicine*, Johnson and colleagues⁵² report that many unvaccinated persons (54%) have never discussed influenza vaccination with their healthcare provider. Yet most adults (79%) are likely to follow their physician's recommendation that they be vaccinated. As reviewed in detail by Stinchfield,⁵³ influenza vaccination rates also may be positively affected by other interventions that increase vaccine access, increase demand, and overcome practice-related barriers.

Communication between healthcare providers and at-risk patients may be especially important for influenza vaccination later in the season. Fishbein and associates⁵⁴ found that specific inquiries or discussion of vaccination status with patients led to vaccination rates in December and afterward that were comparable to rates earlier in the season, when patients tended to be self-motivated to seek vaccination. Physician-to-patient education about the importance of getting vaccinated throughout the season (October through May) is increasingly being supported by consumer awareness campaigns sponsored by the CDC and a variety of medical groups (e.g., American Lung Association [ALA], AMA, Childhood Influenza Immunization Coalition, National Foundation for Infectious Diseases, National Influenza Vaccine Summit). All of these groups' Web sites provide information about influenza vaccination to consumers and healthcare providers.⁵⁵⁻⁵⁷

Vaccine Supply

Ample influenza vaccine should be available now and for the foreseeable future in the United States. Although there have been fluctuations in supply (and 1 large disruption during the 2004 to 2005 season), shortages came at a time when there were fewer vaccine manufacturers. As a consequence, production problems involving a single manufacturer had a larger relative impact on overall supply than they would now that several additional companies are manufacturing and distributing influenza vaccine. A record 121 million influenza vaccine doses were available for the US market in 2006; 130 million doses were expected to be produced in 2007 and 150 million in 2008.²

While total vaccine supply continues to grow and manufacturers strive to deliver vaccine as early as possible, the realities of the production process prevent all doses from being delivered at once or before the start of the season. Healthcare providers should begin vaccinating as soon as vaccine is available and continue until no more vaccine is distributed for the season.

Inherent complexities in the manufacture of a biological product like influenza vaccine mean that many doses (~30%) are delivered in November and later.⁵⁸ Because protection is achieved very quickly (within 2 weeks) after immunization,^{59,60} it is medically relevant to continue vaccination into January and beyond. In fact, vaccination throughout the entire influenza season, not just in the early months as has been the practice in recent years, is the only way to fully utilize all available vaccine and to meet the recommendations of the CDC, AAFP, AAP, AMA, and other groups, as well as to meet the Healthy People 2010 goals.

Extending the Vaccination Season

One way to meet the challenge of protecting more Americans from influenza is to recognize the need for and the

value of vaccination throughout the influenza season.⁶¹ According to data gathered by the CDC, the peak in influenza activity between 1976 and 2006 occurred well after the start of the year (Figure 2).¹ Half of all cases (up to 30 million a year) occur after the peak, which usually occurs in February or later.

These findings are corroborated in the following study of influenza vaccination and diagnosis visits from 2004 to 2007. Data for the study were obtained from the electronic healthcare claims submitted by >240,000 physicians in practice across the United States to all types of third-party payers (i.e., Medicare, Medicaid, commercial). A longitudinally stable identifier was assigned to each patient to protect his or her anonymity and was used to track patients over time. The source data are geographically representative and well characterized, providing a high degree of precision and accuracy in projections to the entire US population. Data were monitored at the practitioner level to ensure completeness and consistency in reporting. Multiple outside sources were used to validate estimates from the model. The number of times CDC-defined high-risk patients¹ were seen in a physician's office between September 1 and March 31 was determined for 2004 to 2005 and 2005 to 2006, as was the number of patients immunized and the number of influenza diagnosis visits over the same months during the 3 years from 2004 to 2005 through 2006 to 2007. Taken together, these data provide insight into missed immunization opportunities for high-risk patients.

Data show an early surge in uptake of influenza vaccination with rates peaking around Thanksgiving, and then immunization rates decrease dramatically for the rest of the season (Figure 3). The early peak in immunization is likely driven by patients who seek out immunization and by media attention during the fall. Healthcare visits resulting in influenza diagnoses peak much later in the season. The gap between the 2 peaks—for vaccination and diagnosis—is a full 16 weeks.

Although many believe the drop off in immunization results from poor access to at-risk patients, such is not the case. Approximately 25 million unimmunized, high-risk patients visit their healthcare providers a total of 55 million times, or on average 2.2 times each, during the period between peaks in immunization and disease activity. If these opportunities to vaccinate were used throughout the influenza season, significant improvements in vaccination rates certainly could be made.

More recent data for the 2007 to 2008 influenza season show no deviation from the pattern of the previous several years. With record amounts of influenza vaccine distributed in the United States, an even greater surge in vaccination claims took place during October and most of November, followed by a very similar and precipitous decrease in those claims beginning in late November and running through December.

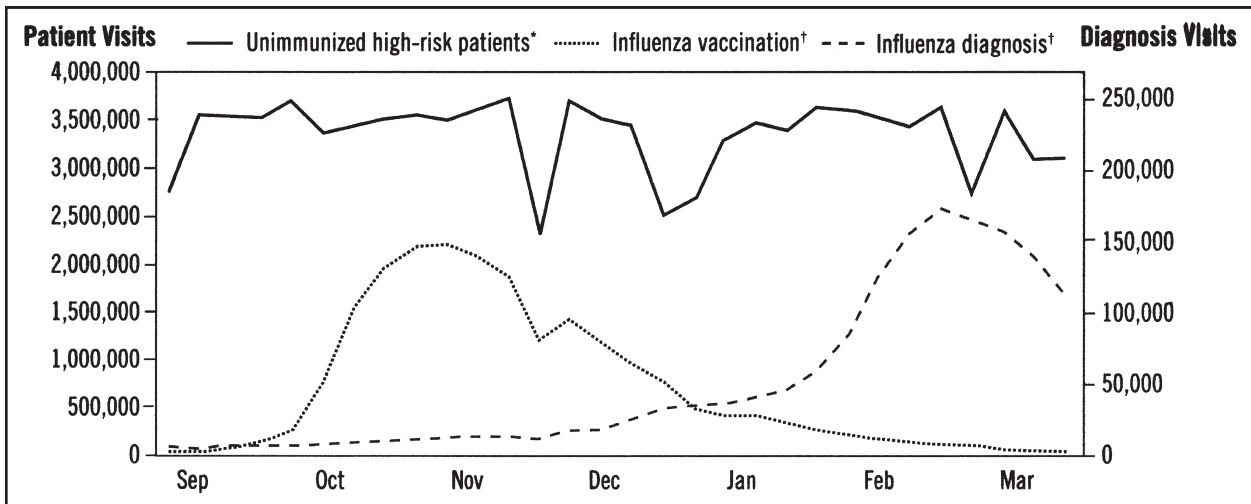


Figure 3 Influenza activity versus vaccination. “Patient Visits” is the scale for both unimmunized high-risk patients (solid curve) and influenza vaccination visits (dotted curve); “Diagnosis Visits” is the scale for influenza diagnosis visits (dashed curve). * = 2-Year average; † = 3-Year average.

SUMMARY

Although influenza vaccine is effective, safe, and simple to administer, vaccination rates remain substantially lower than target levels. Access to influenza vaccination is no longer constrained by problems in supply and distribution, as more manufacturers are providing more influenza vaccine to the US market than ever before. Vaccination throughout the entire influenza season, not just in the early months, is the only way to fully utilize the available vaccine and to meet the target vaccination levels established by the USPHS. High-risk patients make office visits on a regular basis throughout the influenza season but fail to receive the vaccine. Thus, healthcare providers are missing important opportunities to vaccinate millions of people, from October to May every year. To increase vaccination rates in at-risk patients, healthcare professionals should emphasize the need for vaccination throughout the influenza season.

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Practice-Proven Interventions to Increase Vaccination Rates and Broaden the Immunization Season

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ABSTRACT

The Centers for Disease Control and Prevention (CDC) recommends that most (73%) persons residing in the United States be vaccinated against influenza each year. The actual rate of influenza vaccination is substantially below target levels: about 60% of persons ≥ 65 years (target is 90%) and only 10% to 40% of other groups (target is 60% for younger persons who have risk factors and 60% for healthcare personnel). Vaccinating patients throughout the influenza vaccination season (from October into January and beyond)—providing access beyond the traditional “fall immunization season”—is an important step toward meeting the substantial need for influenza vaccination. Vaccination rates may also be increased by interventions that increase patient demand and access to vaccine and overcome practice-related barriers. Such interventions include vaccination-only clinics, standing orders, strong recommendations from healthcare providers, as well as reminder and recall efforts. For maximum impact on immunization rates, interventions should be combined into a multifaceted immunization program rather than used alone. Interventions that address site-specific needs, taking resources into account, should be implemented on a practice-by-practice basis. With supply of influenza vaccine now plentiful, efforts need to be focused on reducing missed vaccination opportunities and promoting vaccination beyond the traditional fall time frame to protect as many Americans as possible from serious and potentially deadly influenza infection. © 2008 Elsevier Inc. All rights reserved. • *The American Journal of Medicine* (2008) 121, S11–S21

KEYWORDS: Best practices; Influenza; Interventions; Vaccination; Immunization season

In the United States, most persons in need of annual influenza vaccination are seen, at least periodically, in the healthcare system.¹ Thus, those who remain unvaccinated do so, in part, because of missed opportunities (i.e., healthcare encounters in which persons who are eligible for vaccination are not completely vaccinated).

The magnitude of missed vaccination opportunities has been documented in diverse practice settings. In a prospective cohort study of 4 pediatric practices in Colorado (N = 926 children aged 6 to 72 months with ≥ 1 chronic condition), missed opportunities for influenza vaccination occurred at 68% of visits during October and November and at

86% of visits during the next 2 months.² Parents reported lack of a physician recommendation and low perceived susceptibility to influenza as the primary reasons for not immunizing their children, underscoring the need for strong healthcare provider recommendations and patient education. In another urban setting, in California, approximately 50% of opportunities to immunize were missed (Figure 1).³ In a health maintenance organization, Kramarz and coworkers determined that only 9% or 10% of >100,000 children with asthma were immunized against influenza during 2 consecutive years (1995 to 1997), and 61% of the unvaccinated children had made ≥ 1 outpatient clinic visit during the influenza season (October through May).⁴ Extrapolations from a large medical claims database indicated that millions of unimmunized patients visited their healthcare providers on average 2.2 times between the peak in immunization and the peak in disease activity.⁵ This underimmunization of high-risk groups was part of the rationale for approving a new policy for universal influenza vaccination annually for all children 6

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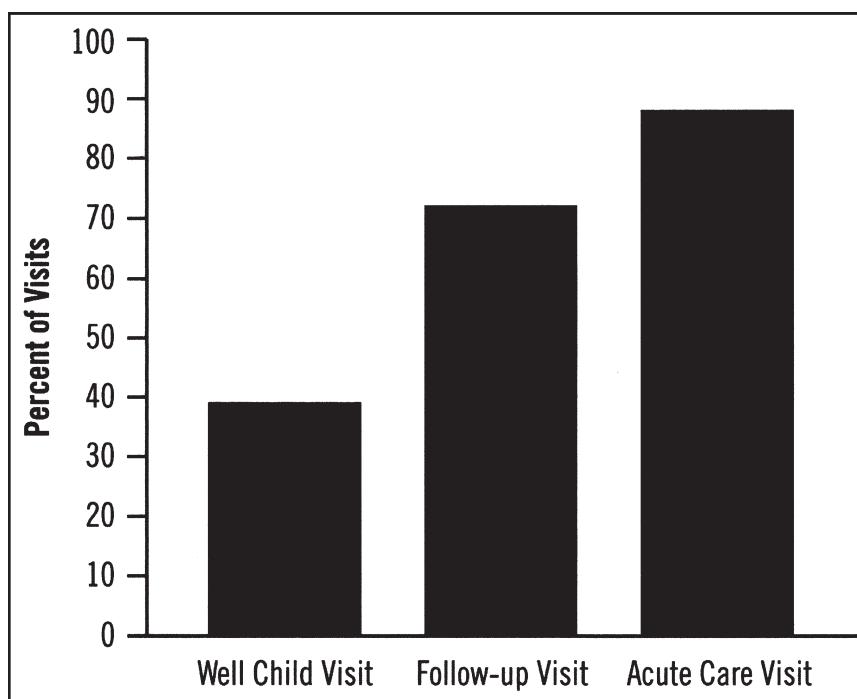


Figure 1 Missed vaccination opportunities are common. (Reprinted from *Am J Prev Med.*³)

months to 18 years.⁶ With a simple message, “All children need an influenza vaccine,” the hope is that morbidity and mortality will be prevented in all children.

Sustainable systems are needed that support high immunization rates of all at-risk persons targeted for immunization. This article describes various strategies designed to eliminate missed vaccination opportunities and increase immunization levels. These strategies, especially when used in combination, can result in an effective and long-lasting vaccine delivery program. The interventions that prove useful may differ from practice to practice and over time. Case studies, which differ in geography, population served, size of practice, and resources, showcase how these interventions have led to meaningful gains in influenza immunization coverage in day-to-day clinical practice.

SUCCESSFUL TYPES OF INTERVENTIONS

Influenza vaccination rates may be improved by interventions that increase vaccine access, increase demand, and overcome practice-related barriers (Table 1).^{7,8}

Stone and associates⁸ conducted a meta-analysis of high-quality studies designed to determine the relative effectiveness of diverse approaches for improving adherence to adult immunization. They found that interventions involving organizational changes in staffing and clinical procedures (e.g., vaccine-only clinic, use of a planned care visit for immunization, designation of a nurse or allied health staff member to administer vaccine) were the most effective (adjusted odds ratio [OR], 16.0 vs. usual care or control group). Other effective interventions were provider remind-

ers (adjusted OR, 3.8) and patient reminders (adjusted OR, 2.5). A physician recommendation to a patient in a high-priority target group (not assessed in the meta-analysis) has also been shown to dramatically increase influenza vaccination rates.^{9,10} These and other techniques are briefly discussed below.

Broaden the Influenza Vaccination

Beginning in 2007, the Centers for Disease Control and Prevention (CDC) emphasized the need to offer influenza vaccine and schedule immunization clinics throughout the influenza vaccination season (October into January and beyond). Thus, the period of vaccination now extends beyond the traditional fall immunization season of October through November.¹¹ This message needs to get out to practitioners, because it clearly differs from previous practice. A cross-sectional survey sent to a national, random sample of internists and general practitioners (N = 1,606) before this change in recommendation revealed that 43% of the respondents stopped vaccinating in December, and only 27% continued vaccinating into February and beyond. Furthermore, 43% of the physicians indicated that they were either neutral or hesitant to vaccinate after the onset of influenza activity in their community.¹²

Case Study. In a busy private practice in Clarks Summit, Pennsylvania, 1 physician and 2 nurses provide healthcare to about 5,000 children during 12,000 visits each year. A season-long approach achieves high vaccination rates. The providers communicate their strong recommendation for vaccination at all visits during the influenza vaccination

Table 1 Strategies to increase influenza vaccination coverage

Intervention	Description
● Increase vaccine access	
—Vaccinate in January and beyond	Deliver vaccine to patients throughout the influenza season rather than just in the early months of the season (October and November)
—Vaccinate at all visit types	Assess patient need for influenza vaccination at all types of healthcare visits, including routine visits, sick and follow-up visits, and during hospitalization
—Vaccine-only clinics	Reduce waiting time/need to make an appointment to obtain vaccination through vaccination-only services
—“Express-lane” vaccination service	
—Extend office hours	Increase or make more convenient the hours during which vaccination services are provided
—Provide vaccination services at alternative, nontraditional sites	Deliver vaccinations in settings in which they were not previously provided
● Increase demand	
—Clinic-based patient education	Provide information regarding vaccination to target patients served in a specific medical or public health clinical setting; techniques include mass mailings, workshops, posters, booklets, and televisions in the waiting room
—Community-wide education	Deliver information regarding vaccination to a target population in a geographic area; techniques include media campaign (television, radio, newspapers, posters, leaflets, booklets) and computer-based programs
—Patient reminder/recall systems	Send alerts that vaccinations are due (reminders) or late (recall) to patients; delivery techniques include telephone calls, letters, postcards, and e-mails
● Overcome practice-related barriers	
—Standing orders	Empower medical personnel to prescribe or deliver vaccinations to patient populations by protocol without direct physician involvement at each interaction
—Provider reminders/recall	Settings include clinics, hospitals, and nursing homes. Inform those who administer vaccinations that individual patients are due (reminder) or overdue (recall) for vaccination. Delivery techniques include flag patient charts, and computer or e-mail notifications.
—Assessment and feedback for vaccination provider	Perform a retrospective evaluation of provider performance (vaccination of at-risk patients) and report results to providers to motivate higher vaccination rates; can also involve other activities (e.g., benchmarking; comparing performance to a goal or standard)
—Addition of influenza vaccination to quality-care checklists	Formalize influenza vaccination into routine practices that form the basis of high-quality patient care
—Provider education and recommendation	Provide information to vaccination providers to increase their knowledge or change attitudes; techniques include written materials, videos, lectures, continuing medical education programs, and computer-based learning programs

Adapted from the Centers for Disease Control and Prevention (CDC)⁷ and *Ann Intern Med*.⁸

season. Educational posters placed in the waiting room urge annual vaccination. Vaccine-only clinics are offered weekly during the influenza vaccination season.¹³

Immunize at Every Opportunity/Extended Hours/Vaccine-Only Days

The CDC recommends that healthcare providers offer vaccine to their patients at every opportunity, including during routine healthcare visits and during hospitalization, whenever vaccine is available. Given the constraints of a busy practice and limited hours of operation, healthcare providers can use specific strategies to increase vaccine access for their patients. They can direct patients to clinics dedicated to vaccine delivery or provide vaccination services during extended office hours or

on days when the office is typically closed (e.g., vaccine-only weekends during the influenza season).

Vaccine clinics have become an integral component of the influenza vaccination program in many practices. Weekend, evening, or parallel-track daytime “flu vaccine only” sessions and walk-in or same-day appointments are useful.¹⁴ Eliminating the need for making an appointment in advance and avoiding excessive waiting time during a clinic or office visit are factors that encourage some people to seek vaccination.^{15,16} The immunization rate approximately doubled when a pharmacy team based out of a primary care clinic designed and implemented vaccine-only clinics for high-risk patients.¹⁷ Scheduling vaccine-only or walk-in clinics in January and beyond is 1 way that practices can broaden their influenza vaccination season.

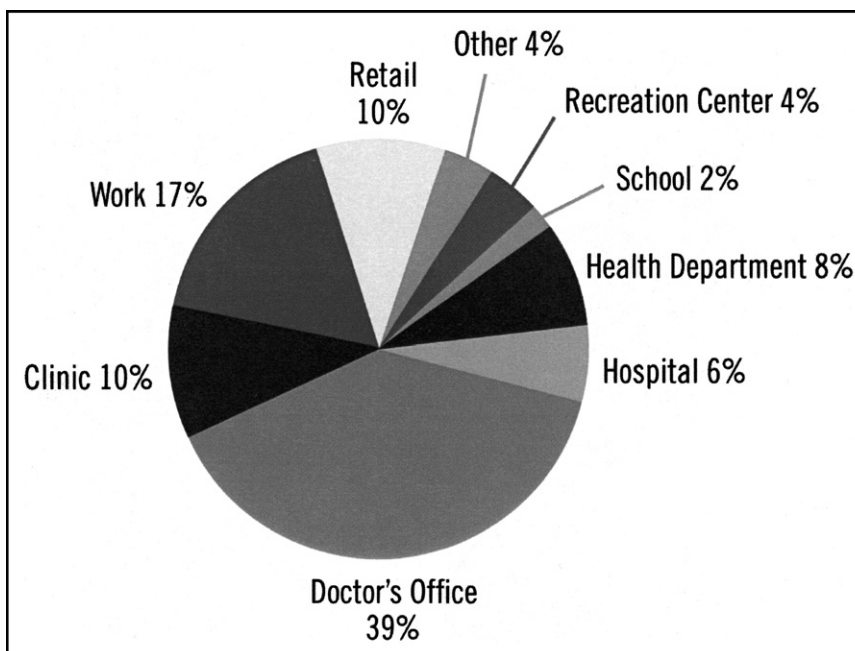


Figure 2 Locations at which patients receive their influenza vaccination. (Reprinted from *MMWR Recomm Rep*.¹⁹)

Case Study. Mountain Park Health Centers, a federally funded, full-service pediatric clinic with 4 satellite locations in and around Phoenix, Arizona, offers influenza vaccine during extended hours at “no appointment necessary” clinics. Children who received influenza vaccine in prior years are eligible to come to these clinics. The practice also holds mass influenza vaccine-only clinics on several Saturdays during the influenza season. The clinics are publicized by on-site fliers and posters and through postcard mailings.¹⁸

Vaccination in Nontraditional Settings

Vaccines, including influenza vaccines, have historically been administered in traditional medical settings (e.g., pediatric clinics and other offices, and health departments). But these traditional settings may not have sufficient infrastructure to handle increasing levels of vaccination. It will be necessary to use every opportunity and setting to deliver influenza vaccine. Delivery of the 130 million or more doses available during the influenza season requires additional sites and universal understanding that vaccine is beneficial when administered even after influenza activity has begun in a community. Development of alternative sites, such as schools, also establishes the infrastructure that will be necessary to address increased vaccine demand in the event of an influenza pandemic.

A substantial number of adults already receive influenza vaccine in alternative, nontraditional settings (Figure 2).¹⁹ According to a CDC-sponsored survey, the most common locations where patients received their influenza vaccine during the 2005-2006 season were physicians' offices (39%), the workplace (17%), and community health clinics

(10%). Providing influenza vaccination services at “nontraditional” sites that offer extended hours, are easily accessible, or are frequently visited (e.g., groceries and other stores, malls, pharmacies, senior centers, churches) can increase access for those who might otherwise go unvaccinated.¹⁹ Other nontraditional settings where vaccine might be provided include adult day-care centers, casinos, bingo halls, major transit points, airports, and polling stations on election days. Drive-through vaccination programs may also be a feasible alternative.²⁰

Emergency departments have not been a traditional location for immunization programs against vaccine-preventable diseases, but >10% of the population visits them each year. Rimple and coworkers²¹ from the University of New Mexico reported on the impact that such a program had at their inner-city trauma center. Over a 3-week period, 674 patients completed a survey that included demographic and medical history data, immunization history, and perceptions of their risk of influenza and need for immunization. Vaccine was offered to all high-risk patients who were not current with their immunizations. As a result, the rate of influenza vaccination increased from 16% to 83%.

Similar results were observed during a prospective, randomized, controlled study of an immunization program in a pediatric emergency department at the University of Rochester in New York.²² Eligible at-risk families (characterized as those in which someone living at the same address was in an at-risk category for influenza-related morbidity and mortality) were randomized to receive either influenza vaccine education alone or education with an offer of vaccination. At a follow-up assessment at the end of the influenza sea-

son, the immunization rate was higher among those offered vaccine in the emergency department for pediatric patients (57% vs. 36% for those provided education only) and their accompanying family members (75% vs. 34%, respectively). These experiences provide examples of a nontraditional setting in which a vaccination program was proved to be feasible and successful.

When developing immunization programs in nontraditional settings, healthcare providers should consider the potential role of all forms of influenza vaccine. The newer live attenuated vaccine formulation does not need to be frozen and the volume of the dose administered is smaller than the older formulation.

One issue of concern with widespread influenza vaccination in nontraditional settings is the resulting fractioning of healthcare services and generation of multiple charts that make it difficult to know which of several specialists or generalists has immunized the patient. Optimally, all vaccinations should be tracked in national immunization information systems (IIS). In fact, a national health objective for 2010 is for 95% of children aged <6 years to participate in a fully operational IIS.²³ Until optimal IIS use is achieved, however, providers will have to continue to do a verbal check of vaccination status by asking their patients if they have received influenza vaccine in the current season. Such immunization information systems, or registries, are especially important for newly vaccinated children under the age of 9 years who require 2 doses of influenza vaccine in the same season, particularly those who may get them from different providers.

Provider and Patient Education

Persons responsible for administering vaccine, including physicians, nurse practitioners, and their staff who interact with patients must be knowledgeable about influenza, the vaccines available, and vaccination scheduling. Although provider education is certainly important, in isolation it has little impact on immunization rates.²⁴ Yet, it stands to reason that when providers are up to date in their knowledge, they are more likely to establish appropriate standards within their practices, and medical and support staff are more likely to be immunized themselves, to communicate the need for vaccine, and to recommend it to patients.

Consistent evidence of provider shortcomings in the knowledge of persons at risk of influenza²⁵⁻²⁸ highlights the need for healthcare providers to take a proactive role in patient education. Survey responses show that many Americans have basic misperceptions about their risk of influenza and its complications, their need for vaccination, and the efficacy and safety of vaccine, and that these misunderstandings lead to low vaccination rates among those for whom vaccine is recommended. For instance, in a sample of persons obtained through random-digit dialing, 50% of those at high risk of complications from influenza based on CDC criteria did not know about their own high-risk status and, therefore, were not vaccinated.²⁶ In a national consumer survey conducted before the 2006-2007 influenza

season, 48% of respondents said they did not plan to be immunized and cited various reasons, many of which were based on misconceptions. Among the explanations was the belief that the vaccine can cause influenza (46%), that influenza was not a severe enough illness to justify vaccination (43%), that they were not at risk of infection (37%), and that vaccination does not prevent influenza (23%).²⁷ Patient education should focus on changing misconceptions that affect vaccination decisions.²⁹

In addition to direct recommendations from their healthcare provider, patients can receive education about influenza and the vaccine through other channels. Some examples are prominently displayed posters in waiting rooms, brochures, e-mails, and Web site resources. Public service educational programming delivered by mass media (television, radio) also has a place in the education of patients, as well as healthcare personnel. Direct communication by e-mail or letter to providers from recognized, local influenza vaccine experts is also helpful.

Recommendation by a Healthcare Professional

Direct recommendations from healthcare providers to patients increase vaccination rates.¹⁰ This is especially true later in the season.³⁰ Among patients with a negative attitude about vaccination, Nichol and associates³¹ noted that the influenza vaccination rate was 3-fold higher for those whose physician recommended vaccination than for those who did not receive a recommendation from their physician. The impact was even greater in a study by Brewer and Hallman,²⁶ who found a physician's recommendation to be a statistically significant predictor of influenza vaccination.

Children are more likely to be vaccinated if a healthcare professional recommends it to the parent or guardian. This has been demonstrated for healthy children aged 6 to 23 months (OR, 5.5)³² and children with chronic medical conditions (OR, 2.6 to 6.0).^{9,33}

Standing Orders

Healthcare providers should make operational changes to reduce barriers and to promote more efficient delivery of routine vaccination services.⁸ One operational change with substantial impact has been standing orders, or protocols, which allow nurses and other allied health personnel to vaccinate persons without direct physician supervision. In office settings where standing orders are in place, the front-office staff can initiate questions about vaccination status, and designated staff can deliver vaccine; medical intervention is necessary only for unvaccinated patients who decline vaccine or who need an assessment for a true medical contraindication.

Standing orders (Figure 3) have been implemented in various settings, such as clinics, hospitals, emergency rooms, and nursing homes. Based on their beneficial effect, the Advisory Committee on Immunization Practices recommends the use of standing order programs in outpatient and hospital settings to increase immunization levels.³⁴

Standing orders, whether used alone^{24,35} or combined with other targeted strategies,³⁶ have increased immuniza-

STANDING ORDER

Annual influenza immunization for all high-risk persons and other individuals who wish to reduce the likelihood of becoming ill with influenza is recommended by the Centers for Disease Control and Prevention and the Minnesota Coalition for Adult Immunization. A standing order to immunize high-risk patients, or patients not at high risk but requesting influenza immunization, and who are hospitalized or receiving services is provided below.

To Be Completed by Nurse/Pharmacist

RISK CATEGORY: _____

Patient is "High Risk" due to:

- Age 50 or older
- History of heart disease, lung disease, diabetes, or other chronic medical condition

Patient is not "High Risk"

COMPLETE IF PATIENT AT "HIGH RISK" or not high-risk but requests influenza immunization:

Influenza Vaccine not indicated for this patient due to:

- Previous immunization this influenza season
- Serious allergies to eggs
- Previous severe reaction to influenza vaccine
- Acute febrile illness
- Refusal of vaccine by patient because he/she:
 - Believes not at risk for disease
 - Believes immunization doesn't work
 - Fear of adverse effects
 - Wants further advice (e.g., physician, family)
 - Would rather receive elsewhere
 - Other reason: _____
- Not indicated for other reason (explain) _____

Influenza Vaccine Indicated. Give Influenza Vaccine Information Statement and Influenza Vaccine 0.5 ml IM if 13 years or older. (If patient is 12 years or younger, contact attending MD for order and refer to Pediatric Dosing Guidelines.)

Information Collected by _____ Date _____

INFLUENZA IMMUNIZATION ORDERS

Figure 3 Sample influenza vaccination standing order form. (Courtesy of Immunization Action Coalition.)

tion rates among adults. In a study of 6 community hospitals, standing order programs led to a 40% influenza vaccination rate, which was superior to both physician reminders (17%) and educational programs for physicians (10%).²⁴ The influence of standing orders on vaccine status was evaluated in a 14-month study conducted at an urban, public teaching hospital.³⁵ The hospital's computer system identified inpatients eligible for influenza vaccination, who were then randomized to 2 groups: vaccine standing order (directed to nurses at the time of patient discharge) and physician reminder. Standing orders resulted in significantly

more patients being vaccinated (42% vs. 30% with physician reminders, $P < 0.001$).

It appears that standing orders for influenza vaccination are used more commonly for inpatients than outpatients (76% vs. 9%) and in acute compared with nonacute care settings (prevalence ratio 1.7).³⁷ Few long-term care facilities (<10%) have used standing orders to improve vaccination rates of residents,³⁸ which is unfortunate given the sustained benefit realized by those facilities that have standing vaccination orders.³⁹ There are ample opportunities for increased use of standing order programs to improve influenza vaccination coverage.

Reminder/Recall Systems

Patient and provider reminder/recall systems increase vaccine coverage.⁴⁰ For instance, use of a computerized reminder/automatic telephone recall system in a pediatric clinic in Texas increased the frequency of influenza vaccination of children with asthma or reactive airway disease (cohort N = 925) by about 6-fold (from 5% to 32%).⁴¹

The effectiveness of patient reminder/recall systems in improving influenza immunization rates was assessed in a Cochrane Database systematic literature review.⁴² Reminders were effective for both childhood (OR, 2.87) and adult influenza vaccinations (OR, 1.66), increasing immunization rates by 1% to 20% across studies. Reminders were highly effective in a variety of settings, including academic institutions (OR, 3.33), private practice (OR, 1.79), and public health clinics (OR, 2.09).⁴³ All types of reminders were effective: telephone calls (OR, 4.25), patient/practitioner reminders (OR, 3.99), postcards (OR, 2.15), autodialer calls (OR, 1.51), and letters (OR, 1.50).⁴⁴

Healthcare professionals can implement their own reminder/recall systems to facilitate the identification of patients for whom immunization is due or past due (Figure 4). The form of the reminder will vary based on the needs and resources of the practice. For example, computer-generated lists can be run to notify a provider of patients to be seen that day who are in need of vaccination. Alternatively, a receptionist or nurse can stamp the charts of patients who need vaccination with a message such as “No Influenza Vaccine on Record” or clip an “Immunization Due” note to relevant charts.

By whatever method, reminder/recalls can decrease missed vaccination opportunities, especially when they are combined with other strategies with a similar objective. If used consistently by knowledgeable medical staff, a reminder system can be an aid in promoting immunization of at-risk patients.¹ Sending reminder/recalls in December and later to patients who have not already been vaccinated is a way for practices to broaden their influenza vaccination season, in accordance with CDC recommendations.

Audit and Feedback

Evaluation (audit) and feedback to vaccine providers is another intervention that can increase immunization rates. Provider performance (i.e., how many at-risk patients are/are not vaccinated) is retrospectively evaluated, and providers are told the results to motivate higher vaccination rates. Provider performance can also be benchmarked or compared with a goal or standard. In a systematic review of the literature, Bordley and colleagues⁴⁵ found that the results of 12 of 15 studies suggested audit and feedback, either alone or in combination, might improve vaccination rates.

Multifaceted Approach

Although each of the aforementioned interventions may decrease missed vaccination opportunities, a comprehensive program that uses multiple interventions is often the best

approach. For instance, in a 10-year study conducted at a Veterans Administration Medical Center in Minneapolis, Minnesota, Nichol³⁶ showed that standing orders combined with physician education, an annual mailing to patients, and other organizational strategies (walk-in clinics, use of standardized, preprinted documentation forms) led to a successful and durable influenza vaccination program (Figure 5). Combining any of the above interventions with an expanded vaccination season will likely have even greater impact on compliance with CDC recommendations.

Case Study: Private Pediatric Clinic. A private pediatric group practice in Nashville (12 pediatricians; 26,000 patients) combines many interventions, with a goal of immunizing all children in recommended categories and any other patient desiring the vaccine.⁴⁶ Parents are educated about vaccination for preventable diseases at all well and sick visits. A patient reminder is mailed in September. During the influenza season, the practice’s “on-hold” message includes information about influenza vaccination, which can also be found on the practice’s Web site. To streamline vaccine delivery, multiple vaccine clinic days are offered, with nurses administering vaccine according to a standing order; the clinics allow for 10 appointments per hour. The vaccination program is evaluated at the end of every season, potential areas for improvement are discussed, and adjustments are made.

Case Study: Large Healthcare System. The Geisinger Health System, with >40 clinics throughout Pennsylvania, uses a multifaceted approach to identify, remind, and vaccinate high-risk patients (e.g., those with diabetes, heart failure, or end-stage renal disease).⁴⁷ As part of Proven-Care,SM a program designed to change the way the medical system delivers care, at-risk patients in need of influenza vaccination are identified by searching the electronic medical database. These patients receive a reminder letter, which notes that they are due for their annual influenza vaccine and provides a telephone number to schedule a vaccination appointment. A medical staff member contacts all persons who do not schedule a visit. In addition, the medical information system initiates a warning flag each time unvaccinated, at-risk persons make a visit for a reason unrelated to influenza vaccine. Delivery of vaccine is made easier by a standing order, allowing nurses to administer vaccine to patients without a provider preorder. With this program in place, the majority of high-risk patients (75% of 16,000) were vaccinated during the 2006-2007 influenza season, including 69% of patients with diabetes (up from 57% in the previous year).

Case Study: University-Based Clinic. During the 2007-2008 influenza season, Arizona State University increased influenza vaccination among students, faculty, and staff by 41% (from 2,343 to 3,980 vaccine doses), compared with the previous year.⁴⁸ The improved vaccination rate occurred despite an increase in price from \$10 per vaccination in

**CHILDREN'S HOSPITAL'S AND CLINICS
INFLUENZA VACCINE REGISTRY NOTICE**

Patient Name:
MRN:
DOB:
Encounter location:
Encounter Reg-date-time:
Patient Account no.:

This patient may be an individual for whom influenza vaccine is indicated due to his or her age and/or medical condition(s).

1. Is the patient 6 months to 18 years of age? OR
2. Is the patient 6 months of age or older and has a high-risk diagnosis for influenza? Or is a sibling of a patient with a chronic condition?
3. Has the patient not been immunized yet this season?
4. If the patient is less than 9 years of age and has received influenza vaccine for the first time this year, has he or she only been immunized once this season?
5. This patient has no contraindications for influenza vaccine?

⇒If the answers are YES then providers, please consider vaccinating against influenza at this visit.

This notice has been written from computer-generated rules. The final decision to immunize against influenza is the clinical judgment of the provider.

This notice is NOT part of this patient's medical record and should be discarded securely after the visit. For questions about this notice, call Patsy Stinchfield, CPNP in Infectious Disease at 651-220-XXXX.

Figure 4 Sample provider reminder form. (Courtesy of Children's Hospitals and Clinics of Minnesota.)

2006 to \$18 for students and \$20 for employees in 2007. A multifaceted program included convenient access to vaccinations and increasing demand through education and giveaways. Vaccine was made available during 2 week-long events at the student union. In addition, nurses visited residence halls. Education and awareness were enhanced through signage, advertising in the student newspaper and radio station, and free T-shirts given to persons who were

vaccinated. Next season, a vaccination event is being planned during parents' weekend.

Case Study: Hospital-Based Ambulatory Pediatric Clinic. Children's Hospitals and Clinics of Minnesota–St. Paul (Children's–St. Paul) has a multispecialty ambulatory clinic associated with the 150-bed, tertiary care children's hospital. Approximately 29,000 outpatient visits are con-

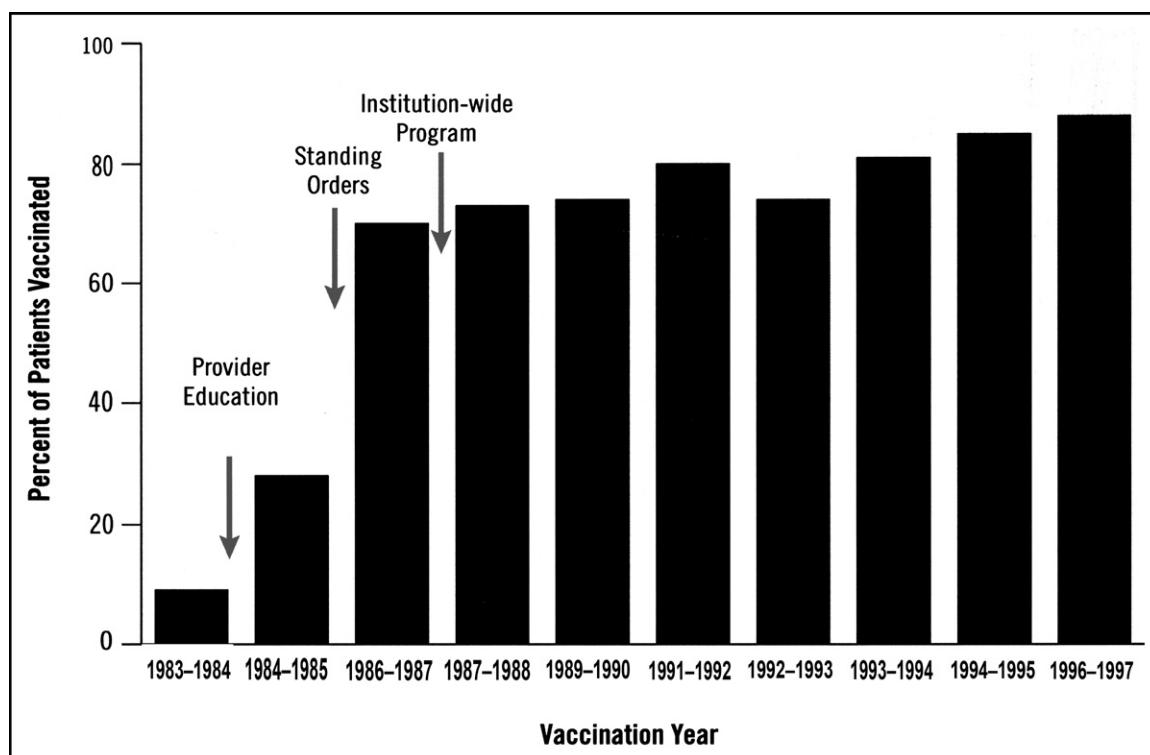


Figure 5 Standing orders as part of a multifaceted influenza vaccination program. $P = 0.03$ for 1983-1984 vs. 1984-1985; $P < 0.001$ for 1984-1985 vs. 1986-1987; $P < 0.001$ for 1986-1987 vs. 1996-1997. (Reprinted from *Am J Med.*³⁶)

ducted each year by a staff of 6 pediatricians, 4 pediatric nurse practitioners, 2 registered nurses, and 6 medical assistants, with the support of pediatric residents and pediatric nurse practitioner students who rotate through the clinic on a year-round basis. A multifaceted approach—including medical informatics, staff and parent education, reminder/recall postcards, dedicated immunization clinics, and a centralized influenza vaccine hotline—optimizes the level of influenza vaccination at Children’s–St. Paul.

A strong emphasis is placed organizationally on influenza vaccine for all employees and professional staff of the Minnesota Children’s hospital system. Usual interventions of onsite clinics for all shifts, roving influenza vaccine carts to units, use of a declination process, and extensive communication resulted in an employee influenza vaccine rate of 63% in 2006-2007. The rate increased to 74% when an electronic employee tracking system could report influenza vaccine rates in real time to department managers and medical directors. With provider-recommended influenza vaccine being correlated with high influenza vaccination rates among patients, those providers who are vaccinated themselves can encourage their patients with credibility.

A highly developed medical informatics system identifies influenza vaccine candidates defined by risk status (from the problem list of the electronic medical record) and demographic characteristics (e.g., age, diagnosis). The computer system creates the list to generate materials for both

provider and patient reminder/recall. Reminders are placed on the charts before regularly scheduled visits to general pediatric or specialty clinic visits, prompting the provider to administer influenza vaccine to children who are not fully vaccinated. The computer system collects billing data per patient, which assists in calculating the total influenza vaccination level across risk groups, allowing strategies to be developed for the next influenza season.

To keep the clinic staff up-to-date, the most current influenza vaccine recommendations are mailed to all professional staff members before the influenza season begins reviewing new recommendations on vaccination, treatment, etc. Providers are encouraged to educate and remind parents of the benefits of influenza vaccination for children with certain risk factors (e.g., asthma, diabetes mellitus) at all visits throughout the year. Each visit is considered a vaccine visit and future necessary vaccines are discussed, including influenza vaccine and the optimal time to receive it. To reinforce these educational efforts, brochures are available to parents in waiting areas and clinics all year long.

An integral component of the influenza vaccination program at Children’s–St. Paul is the reminder/recall postcards that are mailed to parents from both the Minneapolis and St. Paul clinics. During 2007, >11 000 postcards were sent in 3 mailings to the homes of children aged 6 to 59 months and to high-risk patients (identified through electronic medical records). The cost of postcards is considered an investment

in reaching the highest risk patients. For cost-effectiveness, postcards were mailed in the 2007 season late in December only to those high-risk patients who had not yet been vaccinated. Data are tracked based on high-risk patients who were sent postcards as identified through the data warehouse, compared with those billed for influenza vaccine. This does not take into account vaccine that may have been received elsewhere.

To increase the efficiency of administration and access to influenza vaccine, 4 half-day vaccination-only clinics were held on Saturdays in October and November of the 2006-2007 season. In 2007-2008, these "flu-vaccine-clinic-only visits" were integrated into the day and evening hours, with 2 medical assistants vaccinating up to 6 patients every 15 minutes (most had appointments, but walk-ins were accepted as well). All relevant paperwork and supplies were prepared in advance and placed in a room where the vaccinators remained and the patients were brought to them.

An influenza vaccine hotline complements direct professional-to-patient/parent education. Updated daily or as needed with new information, this centralized resource includes the latest influenza news, any alerts about supply changes, flu clinic details, and similar information.

The 2006-2007 influenza season in Minnesota started late with infections beginning in earnest in January. However, late in January there were 6 pediatric deaths in Minnesota in a 4-week period. This created huge public demand for vaccination later in the season. With 48 hours of planning, Children's-St. Paul collaborated with the Minnesota Department of Health and the county to vaccinate >1,000 individuals, mostly insured children from neighboring private clinics in a 4-hour Saturday clinic and another 1,100 the following Saturday morning. There were 30 rooms and vaccinators available, but the vaccinations were accomplished with 21 rooms and vaccinators active at the peak and another 10 support staff (working the front desk, crowd control, etc.).

The memory of the pediatric deaths remained fresh in parents' minds in 2007 and 2008, resulting in a high uptake of vaccine early in the season. Because vaccine uptake was high early in the season, there was barely a surge in demand late in the season when an influenza-related death of a 12-year-old with asthma and a staphylococcal pneumonia was well publicized. Data are being analyzed at this writing to compare rates from the 2006-2007 season with the 2007-2008 season.

Provider education, both formal and informal in 2008, has emphasized starting to vaccinate as soon as vaccine is available and through the influenza season. In 2007-2008, the late onset of the season was a good reminder that "it is not too late to vaccinate," and this was a constant message in the clinics, hospital, and in the media. Emphasis to keep immunizing well past the winter holidays through January and February will slowly be helpful in "unlearning" an old habit and learning a new practice.

SUMMARY

Despite the documented beneficial effects of several practice-proven interventions, meaningful proportions of primary care physicians (14%) and medical specialists (25%) fail to strongly recommend influenza vaccinations to their high-risk and elderly patients, according to a self-administered questionnaire.⁴⁹ Likewise, many physicians (>70%) do not use other effective strategies for promoting vaccine delivery (e.g., special clinics, standing orders, patient reminders). Taken together, these findings suggest areas for improvement if all vaccination opportunities are to be utilized and national immunization goals are to be reached. The case studies described above illustrate the techniques used in a range of practice settings to broaden the immunization season and increase influenza vaccination rates. By combining relevant aspects of these approaches with other interventions that are based on the particular needs and resources of the practice, healthcare providers should be able to extend the benefits of vaccination to all recommended patients.

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Lessons Learned: Role of Influenza Vaccine Production, Distribution, Supply, and Demand—What It Means for the Provider

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ABSTRACT

The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention (CDC) has been increasing the size of the population for whom influenza vaccine is recommended to reduce the substantial and persistent annual health burden of influenza. Realization of current and future public health influenza immunization goals requires assuring vaccine supply will be adequate to meet demand. This has posed distinct challenges for the many stakeholders in the influenza vaccine program—government agencies, federal, state, and local policymakers, vaccine manufacturers and distributors, and the medical community—each of whom must make critical decisions in a constantly shifting environment. Factors such as the yearly changes in influenza virus strains, the complicated vaccine production and distribution process, revisions in vaccination recommendations, and changing demographics can all affect the delicate balance between supply and demand. While vaccine shortages and delays have been well-publicized concerns in the recent past, there has been a marked increase in supply in the past several years, with substantial growth in supply expected in the future. The primary issue today is to strengthen the demand for the influenza vaccine, which would in turn help ensure the continued availability of the vaccine to reduce disease burden. A number of strategies are discussed, including increased efforts to publicize and fully implement current CDC recommendations and to offer influenza vaccine beyond the typical vaccination season of October and November, because in the great majority of years, vaccination into January and beyond will still provide health benefits.

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KEYWORDS: Demand; Influenza; Supply; Vaccine production

Influenza causes the greatest vaccine-preventable burden of disease in the United States, accounting for an estimated annual average of 36,000 deaths and 226,000 hospitalizations.^{1,2} To decrease this burden, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) gradually has increased the size of the population recommended for annual vaccination, which now covers about 73% of the US population, or 218 million people.³ This includes persons at high risk for complications from influenza and the individuals who

might transmit the virus to them, such as their household contacts and healthcare workers. Starting no later than the 2009-2010 influenza season, vaccination recommendations will be extended to include all children 5 to 18 years of age,⁴ which will add approximately 30 million children (~10% of the US population) to the group who should be vaccinated annually. In addition, the ACIP encourages anyone who wants to avoid influenza to obtain the vaccine. Thus, almost the entire US population is either recommended to be vaccinated annually or is covered by a permissive recommendation.

Influenza vaccine is different from all other vaccines because it is administered annually to persons for whom it is recommended. More doses of influenza vaccine are used annually than of any other vaccine.⁵ Nevertheless, the burdens of providing influenza vaccine have left many provid-

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ers frustrated. The purpose of this article is to explain the reasons why there may be problems in vaccine supply in a given season and to outline potential steps providers can take to help their patients avoid the burdens of influenza while at the same time enhancing production and distribution capacity to meet present and future demands.

In the United States, the major stakeholders in the influenza immunization program include government agencies, state, federal, and local policymakers, vaccine manufacturers, distributors, and clinicians, including community immunizers as well as those who provide influenza vaccine at the workplace.⁶ These participants must make decisions regarding the vaccine composition, the assessment of vaccine potency and purity, the amount of vaccine to produce, how many doses to order, how to distribute, how to finance, when to administer the vaccine and to whom, and how to reach patients. Numerous factors come into play, many of them subject to change. For example, influenza viruses undergo frequent mutations. Thus, the vaccine must be reformulated each year to include new strains experts think are likely to circulate the following season. In any given year, availability of vaccine may be affected by low production yields, higher-than-expected demand, and changes in vaccine recommendations. Longer-term factors (e.g., demographic), such as the increase in the elderly population, a group at high risk for influenza-related complications, may also influence future supply and demand.

There have been several influenza supply disruptions since the 2001-2002 season.^{7,8} Disruptions have occurred, for example, when manufacturers have exited the marketplace or when manufacturers' products became available after the traditional influenza vaccination season, which the CDC had previously defined as October through November (now considered to be October into January and beyond).^{3,9,10} A highly publicized shortage occurred in 2004-2005, when contamination forced the vaccine manufacturer Chiron to suspend production of its anticipated 46 million influenza doses at its facility in Liverpool, England. At the time, Chiron was 1 of only 3 companies providing the influenza vaccine to the US market, and these lost doses represented about half of the anticipated US vaccine supply for 2004-2005. Although federal agencies moved quickly to prioritize who should receive the vaccine, concern eventually focused on the country's inability to administer all doses of even this limited supply.^{11,12} With the subsequent entry of additional manufacturers into the marketplace, which now includes sanofi pasteur, Novartis, GlaxoSmith-Kline, MedImmune, and CSL Biotherapies, the vaccine production capacity appears to be less vulnerable. It is estimated that a record 130 million doses were produced for the 2007-2008 influenza season,¹³ and in the future, a steady and plentiful supply of vaccine is expected. Thus, the overriding issue today involves complying with ACIP recommendations to prevent the influenza burden each season. This requires increasing consumer demand and providing incentives to providers to ensure sufficient supply. For example, annual coverage for persons ≥ 65 years, 1 of the

priority groups for vaccination, is typically $<70\%$, when national targets call for $\geq 90\%$.¹⁴ This article discusses the current system of vaccine production, distribution, and financing in the context of supply and demand. It also highlights new developments and approaches that may help achieve immunization goals to the benefit of all influenza vaccine stakeholders.

PRODUCTION OF THE INFLUENZA VACCINE

Although a larger manufacturing base will help to avert vaccine supply shortages, some degree of uncertainty is inevitable, given the inherent complexities of the influenza vaccine production process. Unlike manufactured drugs, biologics are natural products and therefore are less predictable.¹⁵ The lack of predictability begins with influenza viruses themselves. One or more of 3 strains of influenza viruses are responsible for seasonal influenza epidemics—2 strains of type A influenza (A/H1N1 and A/H3N2) and influenza type B. These viruses undergo antigenic changes (antigenic drift), resulting in new strains that may not be recognized by the body's immune system.¹⁶ To keep up with these changes and remain effective, the influenza vaccine is reevaluated each year and reformulated when new variants appear to be emerging. Even if there is no reformulation, vaccine must be produced anew each year because it is not until March that the strains to be included in the following season's vaccine are decided upon. Thus, the previous year's vaccine expires and must be discarded before the next influenza vaccination season.

Vaccine production takes about 8 or 9 months, but is actually an ongoing process if one considers the importance of year-round global influenza surveillance.¹⁷ Based on global surveillance data collected by World Health Organization (WHO) Collaborating Centers, including the CDC, the US Food and Drug Administration (FDA) selects 3 influenza strains (type B, A/H1N1, and A/H3N2) thought to be the likely cause of influenza epidemics in the upcoming season. The efficacy of the vaccine depends in part upon a close match between the vaccine strains and circulating strains. However, even when the vaccine is not optimally matched to the predominant viruses, it usually still affords some protection, inasmuch as antibodies made in response to the vaccine can protect against related strains (cross-protection).¹⁸ In January, the CDC provides influenza "reference" viruses to the FDA, which distributes them, in turn, to the manufacturers.¹⁷ It should be noted that at this early point in the production process, well in advance of the upcoming influenza season, manufacturers must consider issues of both supply and demand. For example, they must estimate demand, taking into account "prebookings" from government, large public/private purchasers, and small private purchasers, as well as the previous year's demand.^{15,17} They must consider the "yield," or growth potential, of each strain, because this dictates the amount of vaccine that can be produced, while also estimating the number of doses that will be produced by other manufacturers.

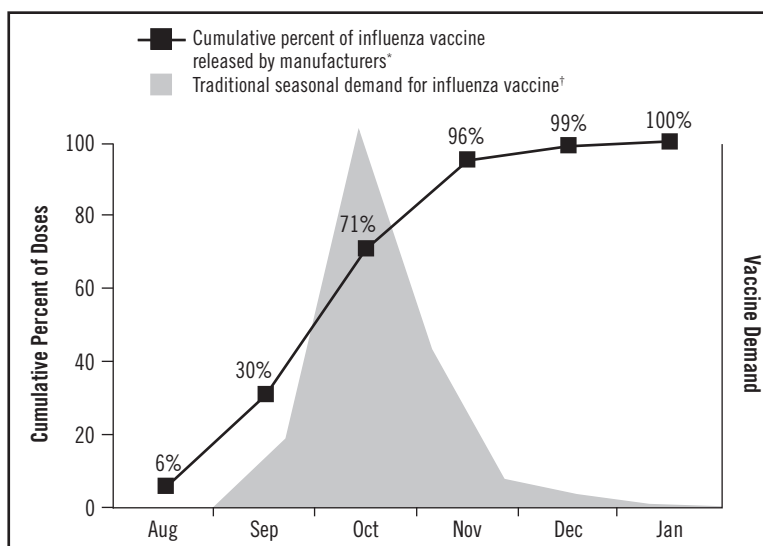


Figure 1 Influenza vaccine supply versus demand. *Composite data from 2004 to 2007; †Based on influenza vaccination pattern—Tennessee, 2003–2004 season. (Adapted from “Vaccine Supply Update & Programmatic Implications”²¹ and *Clin Infect Dis.*²²)

The vaccine production cycle extends through August, when completed lots become available.¹⁷ During this process, the FDA tests vaccines multiple times for purity and efficacy. Indeed, the testing and approval process accounts for a substantial proportion of production time. For both injectable and nasal vaccines, the 3 strains are produced separately in embryonic eggs. The monovalent concentrates are harvested and combined into the trivalent form, which is then used to fill vaccine delivery devices (vials, syringes, nasal sprayers).¹⁷ Injectable vaccines undergo additional steps after harvesting including inactivation and disruption of the lipid envelope of the virus resulting in split or subviral products.¹⁹ Live attenuated vaccines for intranasal administration are produced by reassortment of cold-adapted, temperature-sensitive parent virus strains with wild viruses to produce a virus containing the 6 internal genes of the parent attenuated strain and the hemagglutinin and neuraminidase of the wild virus.²⁰ Vaccines are packaged for distribution and kept at appropriate temperatures to guarantee potency. Each lot must be approved separately for release by the FDA before shipment. Thus, no matter how efficiently vaccine is produced, it will generally be distributed in stages over time.

DISTRIBUTION

Private practices, public clinics, and other small and large (e.g., pharmacy chains and supermarkets) immunization providers may order vaccine either directly from the manufacturers, or from a distributor. Orders are taken by manufacturers and distributors as early as January of the prior season. Distribution normally begins in September and continues for as long as vaccine supplies are available.

The timing of vaccine production as well as distribution issues generally results in vaccine supply reaching providers throughout the fall months. During the last 3 influenza seasons, about 70% of the vaccine supply was delivered by October.²¹ In previous seasons, when total supply was lower, early demand usually outpaced early supply. Given the recent increases in supply, this will hopefully no longer be the case. However, a substantial number of doses will continue to be delivered after the current peak in vaccination (Figure 1).^{21,22} Extending vaccination efforts into January and beyond will harmonize supply-demand discordance and provide protection for more at-risk individuals.

The existence of multiple vaccine producers coupled with numerous distribution channels also affects the timing of vaccine delivery, thereby creating real or perceived shortages and delays. Thus, there may be temporary shortages at the local level, even when the national supply is adequate. It is also possible that providers in the same local area who ordered from different manufacturers or distributors may receive their vaccine supply at different times. Indeed, these disparities in vaccine delivery at the local level, particularly early in the vaccination season, continue to be a substantial source of confusion and concern among physicians.

GROWING THE DEMAND TO ENSURE THE SUPPLY

Public (federal, state, and local) and private (health plans, insurers, providers) stakeholders have an important role to play in increasing the demand for the influenza vaccine to reach the >80% of the US population (which includes the 30 million children recommended to be vaccinated no later than the 2009–2010 season) who should be vaccinated an-

nually. Driving the demand up would not only ensure that individuals and populations who would benefit from the vaccine actually receive it, but would also help to mitigate some of the risks, thereby encouraging the continued participation of manufacturers, distributors, and providers in the system.⁷ The willingness of manufacturers and distributors to participate in the program depends, to a large degree, on demand for the vaccine and adequate returns from sales.^{10,15}

The financing of immunizations is 1 component of assuring vaccine availability. In the case of children, the government shares the burden for immunization coverage with the private insurance industry and private payers/parents.²³ Two sources of federal funds are the Section 317 program, administered by the CDC, and the Vaccines for Children program. Since 1993, Medicare has reimbursed the costs of the influenza (and pneumococcal) vaccine for those aged ≥ 65 years without applying a copay or deductible.²³ For other adults, the government has only a modest role, and influenza vaccines are purchased and administered in the private sector. Gaps and fragmentation of insurance coverage are areas of concern. Limited insurance coverage not only increases the stress placed on the public sector but also increases the burden on private providers. These financial barriers for patients and providers may lead to missed opportunities for immunization, depressing demand and ultimately supply.²⁴

Addressing financing issues is only part of the solution, however. Influenza vaccination rates have remained suboptimal even in vulnerable populations (e.g., Medicare beneficiaries ≥ 65 years old) that have coverage. According to 1 study, Medicare recipients cited lack of knowledge of the need for immunization and the belief that the vaccine itself might cause disease as reasons for avoiding influenza vaccine.²⁵ Demand may also wane when the influenza season is perceived to be of "mild" severity, while demand may increase in seasons where influenza is perceived to be severe or occurs early.⁷ This applies to healthcare workers as well. The CDC recommends that all healthcare providers obtain yearly vaccinations. By so doing, healthcare providers set an example for their patients, while protecting not only their own health but also that of their patients.

Efforts should also be directed at following the CDC's recommendations to make use of the entire vaccination season (October into January and beyond) and take advantage of all opportunities to vaccinate patients, which would further bolster demand and ensure supply.³ Typically, demand is high in the fall and then subsides. The reason influenza vaccine ideally is administered in the fall is to protect against potential early influenza seasons. However, influenza activity peaked in February for 45% of the seasons during the period 1976-2006.³ In only 16% of the seasons did influenza disease peak before January, and in some seasons disease activity peaked as late as April or May. Thus, in the great majority of years, influenza vaccination into January and beyond is beneficial. The CDC has urged that healthcare providers make the influenza vaccine avail-

able throughout the entire vaccination season.³ This should increase demand beyond the traditional fall immunization time frame, and ensure that vaccines do not remain unused when they can still confer benefit. To take advantage of every opportunity, healthcare workers are advised to offer the vaccine during routine healthcare visits or during hospitalization. Although physician offices and clinics will likely remain the primary sites of vaccination, the CDC also supports immunizing patients in nontraditional settings, including the workplace, retail stores, and senior citizen centers.³

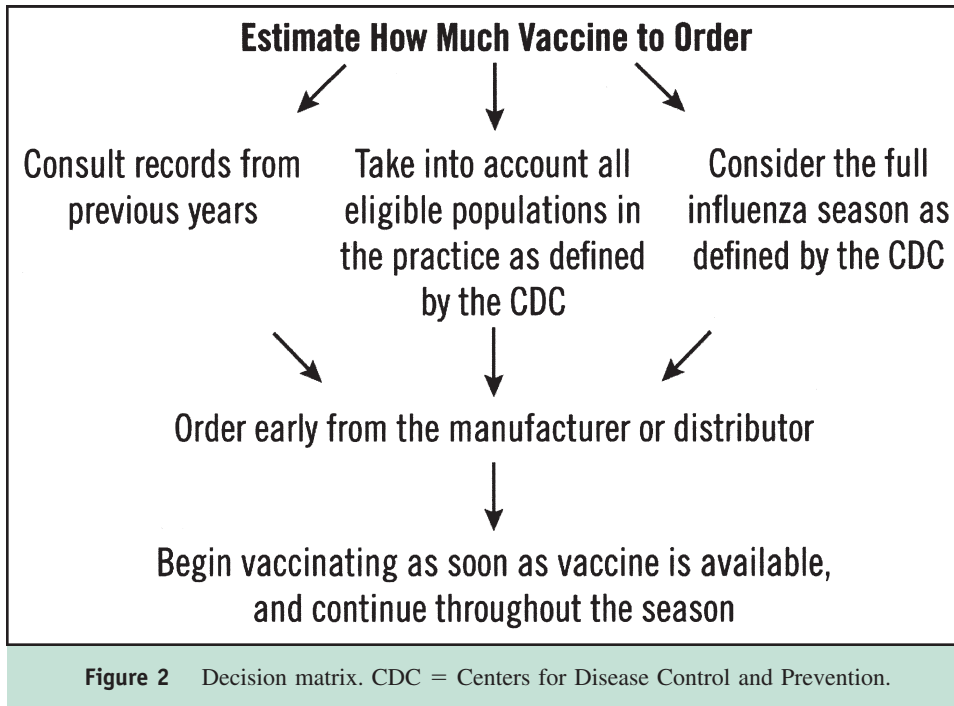
WHAT THIS MEANS FOR THE PROVIDER

Healthcare providers are in a unique position to strengthen demand by educating their patients about the serious consequences of influenza and the benefits of immunization, and by making the vaccine available from October into January and beyond. Providers can play a key role in encouraging and facilitating patients' receipt of routine annual influenza immunizations. In following this approach, providers will not only be providing an important service to their patients but also will be minimizing potential risks to themselves.²⁶

Healthcare providers must decide how much vaccine to order, when to administer, and to whom. At the same time, they must incur the costs (which have increased) of purchasing the vaccine, and of storage, insurance against loss, and administration. In estimating how many doses to order, physicians have traditionally reviewed their records from previous years to purchase a supply sufficient to cover their at-risk patients. They have been reluctant to purchase more vaccine than they can use, out of concern that they would be left with unused (and unreturnable) doses and the financial loss that this entails.⁷ When supplies run out, physicians often refer their patients to other locations.²⁷ However, patients may not always avail themselves of these opportunities, thus remaining exposed to infection and its complications.

A factor that should enter into providers' calculations (Figure 2) in the present context is the CDC's recommendation that vaccination take place throughout the entire influenza vaccination season, beginning in October and continuing into January and beyond. Taking advantage of the full season will give providers added flexibility, enabling them to better deal with the vagaries of the vaccine market. Thus, if vaccine doses are delayed or distributed over a longer period, providers will have more opportunities to use their entire supply over the course of a longer vaccination season.

Providers should continue to administer the vaccine early, to immunize as many persons as possible before influenza activity begins. Physicians should avail themselves of all opportunities to vaccinate in December, January, and later. Those working in other healthcare settings, such as public clinics, can schedule vaccine clinics throughout the season. In addition to providing a benefit to patients



in the great majority of years, this approach will minimize the chances of financial loss. Providers should also be aware that the Centers for Medicare and Medicaid Services raised vaccine-administration payments beginning in the 2005-2006 season.

FUTURE DEVELOPMENTS

New strategies and technologies that affect the influenza vaccine production system at various points are being explored. These may ultimately be beneficial in terms of reducing production time and ensuring a steady supply. As discussed, influenza vaccine preparation takes about 8 to 9 months; vaccine testing and approval at the FDA is an essential part of the process. The FDA is considering ways to accelerate the vaccine review and approval process as part of an effort to expedite the production process.²⁷

Numerous alternatives to egg-based vaccine manufacturing technology are also being developed.^{28,29} Although egg-based technology has been used since the 1950s, and has produced billions of safe, efficacious influenza vaccine doses, other newer technologies may prove to be beneficial in shortening the manufacturing process and perhaps easing delivery constraints by allowing the vaccine to be available sooner.³⁰ Just how beneficial remains to be determined. Two technologies in development are cell culture^{10,17} and reverse genetics.³⁰ In contrast to traditional manufacturing methods, cell culture offers the possibility of faster startup of vaccine production, although this may represent time savings of only a few weeks, perhaps even days, at the beginning of the process.¹⁷ Reverse genetic technology is used to prepare reference virus strains and is applicable to either egg-based or cell culture production.¹⁷ This approach

allows scientists to alter the virus in an effort to produce a vaccine that better matches the new strain of influenza and increases production yield.³⁰ It is worth noting that these new technologies may prove to be more expensive and consequently may increase vaccine costs.

SUMMARY

Influenza vaccination is the best defense against the morbidity and mortality associated with influenza, and meeting public health immunization goals is a top priority. To ensure that all those who would benefit actually receive the vaccine requires achieving a balance between supply and demand in the vaccine marketplace. In the past, the focus has been on the supply side, as persistent supply shortages and distribution delays dominated the news. Today there is ample supply, and those involved in the overall influenza vaccine system, including government agencies, federal, state, and local policymakers, vaccine manufacturers and distributors, and healthcare providers, have a role to play in making sure that demand is sufficient to make optimal use of the available supply to decrease the substantial health burden of influenza. It will also help to guarantee the continued availability of the influenza vaccine in the future and minimize the residual risks associated with vaccine production and distribution.

AUTHOR DISCLOSURES

The authors who contributed to this article have disclosed the following industry relationships:

Walter A. Orenstein, MD, has received grant support for clinical trials and research from Merck & Co., Novartis, and Sanofi Pasteur, Inc.; and serves on 2 data safety mon-

itoring boards for clinical vaccine trials, Encorium (formerly Dynport) for bioterrorism threats and GlaxoSmithKline for pneumococcal vaccine.

William Schaffner, MD, serves as a consultant to GlaxoSmithKline, MedImmune, Merck & Co., Novartis, Sanofi Pasteur, Inc, and Wyeth Pharmaceuticals; and is a member of a data safety evaluation committee for experimental vaccines for Merck & Co.

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Barriers to Adult Immunization

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ABSTRACT

Our aim was to provide a better understanding of why many adults fail to receive recommended immunizations. Consumers (N = 2,002) and healthcare providers (N = 200) completed structured telephone interviews concerning their attitudes and knowledge about adult vaccines and factors affecting their vaccination decisions. Self-reported immunization rates for tetanus, influenza, and pneumococcal vaccines (which were emphasized in the surveys) were lower than goal rates set by national guidelines. Among the most common reasons consumers gave for not receiving immunizations were lack of physician recommendations and mistaken assumptions (e.g., healthy people do not need immunizations). Healthcare providers tended to cite concerns such as side effects, fear of needles, and lack of insurance coverage as reasons consumers forego vaccination. Providers also cited practice issues, such as lack of an effective reminder system, as barriers to increasing adult immunization rates. We conclude that a better understanding of why adults do not get vaccinated is important for efforts to increase immunization rates in this broad age group.

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KEYWORDS: adult immunization; barriers; consumer; provider surveys

At the beginning of the new millennium, the Centers for Disease Control and Prevention (CDC) listed immunization as 1 of the top 10 public health achievements of the 20th century.¹ The Advisory Committee on Immunization Practices (ACIP) of the CDC, along with other professional organizations, recommends immunization schedules for children and adolescents² and for adults³ and updates them regularly. The recommendations are available to both healthcare professionals and the general public.

Although the US childhood immunization program has been very successful, the same level of success has not been achieved in adults. For example, annual influenza vaccination has long been recommended for everyone aged ≥ 65 years and for any adult with certain chronic conditions. Yet in a recent year in which vaccine availability was not an issue, only 65% of noninstitutionalized adults aged ≥ 65

years and 30% of younger high-risk adults reported receiving influenza vaccine.⁴ Pneumococcal vaccination also is recommended in these populations, but in the same year just 57% of noninstitutionalized men and women aged ≥ 65 years and 17% of younger high-risk adults received the pneumococcal vaccine.⁴ In 1999, the last year that the CDC reported rates for tetanus vaccination in adults, rates ranged from 36% in females aged ≥ 65 years to 71% in males aged 18 to 49 years.⁵

To learn why adults do not receive recommended immunizations, we conducted surveys of $>2,000$ adult consumers and 200 healthcare professionals in the United States. The surveys focused on general vaccination attitudes and knowledge of 3 specific vaccines recommended for routine use in adults: tetanus, influenza, and pneumococcal vaccines.

METHODS

The surveys were designed and conducted by Adelphi Research by Design, a healthcare marketing research firm. There were 2 distinct populations and survey instruments, 1 for healthcare professionals and 1 for other people (hereafter called “consumers”). Structured telephone interviews

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using these survey instruments took place between September 15, 2006 and October 15, 2006.

Consumers were contacted by random digit dialing. The caller asked to speak to the person aged ≥ 19 years with the most recent birthday. The respondent was given the option of conducting the interview in Spanish. The response rate, calculated as the percentage of those contacted who agreed to participate, was 3.1%, resulting in a population of 2,002 for the consumer study. The survey, which lasted approximately 25 minutes, solicited information about the respondent's personal immunization history, barriers or reasons why the respondent did not receive vaccines, the respondent's relationship with healthcare providers, and personal demographics. Questions about personal immunization emphasized 3 vaccines recommended for all adults or for those in particular age groups: tetanus vaccine, which should be administered routinely every 10 years; influenza vaccine, which is recommended annually for those ≥ 50 years or in certain high-risk groups; and pneumococcal vaccine, for people ≥ 65 years or in certain high-risk groups.³

In addition, 200 healthcare providers were randomly recruited from a national database of >16,000 primary care practices. They were contacted by e-mail or fax, and the response rate was 3.5%. This population consisted of 100 primary care physicians (50 internists, 50 family physicians/general practitioners), 34 registered nurses, 33 physician assistants, and 33 nurse practitioners. They completed a structured telephone interview lasting about 45 minutes that solicited information about their practice, their recommendations for adult patients regarding vaccines (again emphasizing tetanus, influenza, and pneumococcal vaccines), and barriers to vaccination.

To ensure that the consumer survey results reflected a nationally representative sample, iterative proportional fitting was used to weight the consumer data to match US Census Bureau data for 2000 on age, ethnicity, sex, income, education, and region of the continental United States. Because differences between weighted and unweighted data were minimal, unweighted consumer survey data are reported in this article. Data from healthcare providers were not weighted.

Statistical significance was determined by the independent *t*-test for means (assuming equal variances) and the independent *Z*-test for proportions. At the 95% confidence level, calculated using a standard formula, the margin of error for the consumer survey was $\pm 2.2\%$. The smaller healthcare provider sample had a margin of error of $\pm 9.8\%$. Significant differences are indicated at the 95% confidence level (2-tailed $P < 0.05$).

RESULTS

Consumer Survey

Population Characteristics. The consumer survey population was almost equally divided between men (48%) and women (52%). Age distribution was 17% aged 19 to 34, 16% aged 35 to 44, 20% aged 45 to 54, 20% aged 55 to 64,

15% aged 65 to 74, and 13% aged ≥ 75 . Of the 2,002 persons in the consumer survey, 74% were non-Hispanic white, 7% were non-Hispanic black, 9% were Hispanic and 10% were other or gave no report.

Most respondents (82%) rated their health as good-to-excellent, but 20% reported having a serious or chronic medical condition. The most common conditions mentioned were obesity (12%), diabetes mellitus (12%), heart disease (10%), and chronic lung disease (9%). In the 12 months before the survey, 20% of respondents had not seen a physician for a well-care visit and 29% had had a single routine care visit; 46% had not had a sick visit.

About half (48%) of respondents worked full-time or part-time, and 19% felt that their job put them at above-average risk of injury (e.g., construction, law enforcement). Approximately 1 of 4 consumers (24%) said their job increased their risk of acquiring a vaccine-preventable illness or brought them into contact with people who were extremely susceptible to illness.

Household income was $< \$35,000$ for 30% of respondents and $\geq \$75,000$ for 21%. Most consumers (84%) had some type of health insurance; 25% received their coverage through Medicare, 4% through Medicaid, and 4% through the military or the Veterans Administration.

Vaccine Awareness and Personal Vaccination History.

Most consumers were aware of the influenza (96%) and tetanus (90%) vaccines. Only 65% were aware of the pneumococcal vaccine, although awareness was higher in the groups for whom this vaccine is recommended. For example, 85% (95% confidence interval [CI], 82% to 88%) of respondents aged ≥ 65 years versus 50% (95% CI, 46% to 53%) of those < 50 years knew about the pneumococcal vaccine ($P < 0.001$). Awareness of this vaccine was 79% (95% CI, 75% to 83%) among people with chronic health conditions compared with 62% (95% CI, 59% to 64%) among those without chronic conditions ($P < 0.001$), and 67% (95% CI, 61% to 73%) among those with increased occupational risk compared with 53% (95% CI, 49% to 58%) among those without occupational risks ($P < 0.001$).

Although most consumers were aware of the tetanus vaccine, only 36% knew that adults should receive a booster every 10 years. Just 27% knew when they were next due for a tetanus immunization. Among the 533 consumers who had received a pneumococcal vaccination, 147 were aged ≤ 65 years and had a chronic condition, and 46% of these individuals were not aware they needed a booster.

Most consumers (82%) believed that it is important to keep up-to-date with immunizations, yet 34% said they were skeptical about receiving any type of vaccine. The skepticism may reflect misunderstandings about vaccination; for example, 26% of respondents who were aware of the influenza vaccine but did not receive it as recommended were concerned about getting the disease from the vaccine.

Of the 3 vaccines surveyed, the 1 that the most consumers (70%) recalled having received as an adult was the tetanus vaccine. In all, 62% of respondents reported having had an influenza vaccination as an adult. Rates for pneumococcal vaccination for those in recommended groups were low: 61% among people aged ≥ 65 years and 52% among those with chronic illness. For all 3 vaccines, the self-reported rates of vaccination were higher among at-risk groups for whom each vaccine is recommended (Figure 1).

Reasons for not Receiving Vaccines. Most consumers (79% to 85%, depending on the vaccine) indicated that they were likely to receive a vaccination if their healthcare provider recommended it. However, when given a list of possible reasons for not being immunized, 51% of consumers who were aware of the tetanus vaccine but had not received it, chose: "Doctor hasn't told me I need it." This explanation was selected by 38% with regard to the influenza vaccine and 57% with regard to the pneumococcal vaccine (Figure 2). Among consumers who knew of the vaccines, "Don't know when to get it" was cited as a reason for not having a vaccination by 37% of consumers for tetanus immunization, by 21% for influenza immunization, and by 26% for pneumococcal immunization.

The most consistent reason for not receiving a vaccine was the belief that a healthy person does not need it (60% or 61%, depending on the vaccine). Concern about side effects was cited by 22% of consumers as a reason for avoiding tetanus immunization, by 43% for influenza immunization, and by 40% for pneumococcal immunization.

Other frequently selected explanations for not receiving vaccinations were specific to the particular vaccine. The most common reason for not having a recent tetanus vaccine was the belief that it was necessary only when an injury occurred, an explanation chosen by 74% of respondents. For influenza vaccination, 59% cited a short supply which should be used by others who need it more—despite widely disseminated predictions of ample vaccine supply at the time of the survey.

Financial concerns were not a deterrent to immunization for most consumers. "No, this is not a reason" was the response to "Costs too much" by 80% to 82% of consumers as an explanation for not having each of the 3 immunizations. Only 14% to 17% of respondents stated that they failed to receive 1 of the 3 vaccines because their insurance did not cover it. When asked whether they would probably receive a vaccine if their out-of-pocket costs were \$25 to \$30, 72% of consumers said they were willing to pay that amount of money for the tetanus vaccine, 67% for the influenza vaccine, and 76% for the pneumococcal vaccine. An immunization costing \$25 to \$30 that could prevent missed days from work or hospitalization would be highly valuable, according to 83% of consumers.

Healthcare Providers Survey

Among the 100 physician practices included in the survey, 23% were urban, 57% suburban, and 20% rural. For the 100

nonphysician providers (a mix of physician assistants, nurse practitioners, and registered nurses [PA/NP/RN]), the practice locations were 25% urban, 38% suburban, and 37% rural.

Recommendations to Patients. Almost all healthcare providers (90% of physicians and 94% of the PA/NP/RN group) believed that all of their adult patients should be immunized. They also claimed to discuss recommended vaccinations with their adult patients, especially during annual exams or well-care office visits. Physicians in particular were less likely to discuss immunizations during acute-care or sick visits, with only 29% (95% CI, 20% to 38%) of physicians reporting this practice compared with 42% (95% CI, 32% to 52%) of the PA/NP/RN group ($P = 0.03$).

When asked about specific vaccines, 85% of physicians and 88% of the PA/NP/RN group said they recommend the tetanus vaccine to all adults. Recommendations were much less frequent for influenza and pneumococcal immunizations, as shown in Table 1. The responses in this table indicate that healthcare providers are not routinely following recommended immunization practices for adults. Some may not even be aware of the recommendations, as only 60% of physicians and 56% of the PA/NP/RN group stated that the official guidelines were their personal sources of information about adult immunizations.

Most healthcare professionals indicated that they have systems in place to ensure that patients receive recommended vaccines. These systems include an immunization sheet or reminder in patient charts and office protocols. Many practices post fliers in waiting rooms and exam rooms and instruct staff to remind patients about immunizations. Only ~33% of providers had ever conducted an objective evaluation, such as a chart review, of their adult immunization rates.

Perceived Barriers to Immunization. Healthcare professionals were presented reasons why patients might not receive tetanus, influenza, and pneumococcal immunizations (Table 2). According to healthcare providers, failure of patients to come for regular well-care visits and lack of an effective reminder system were among the more common reasons that adults do not receive recommended immunizations.

Healthcare providers also indicated that patients' dislike of needles, fear of adverse effects, and lack of knowledge about disease prevention were frequently responsible for missed immunizations. Yet >50% of the providers acknowledged that they do not always inform patients about the consequences of missing vaccinations. The PA/NP/RN providers were significantly more likely than physicians to always talk to patients about the consequences of not receiving recommended vaccines: 56% versus 34% ($P < 0.001$), 61% versus 47% ($P = 0.02$), and 59% versus 40% ($P = 0.004$) for tetanus, influenza, and pneumococcal vaccines, respectively.

Additionally, healthcare providers frequently cited inadequate insurance coverage and, to a lesser extent, con-

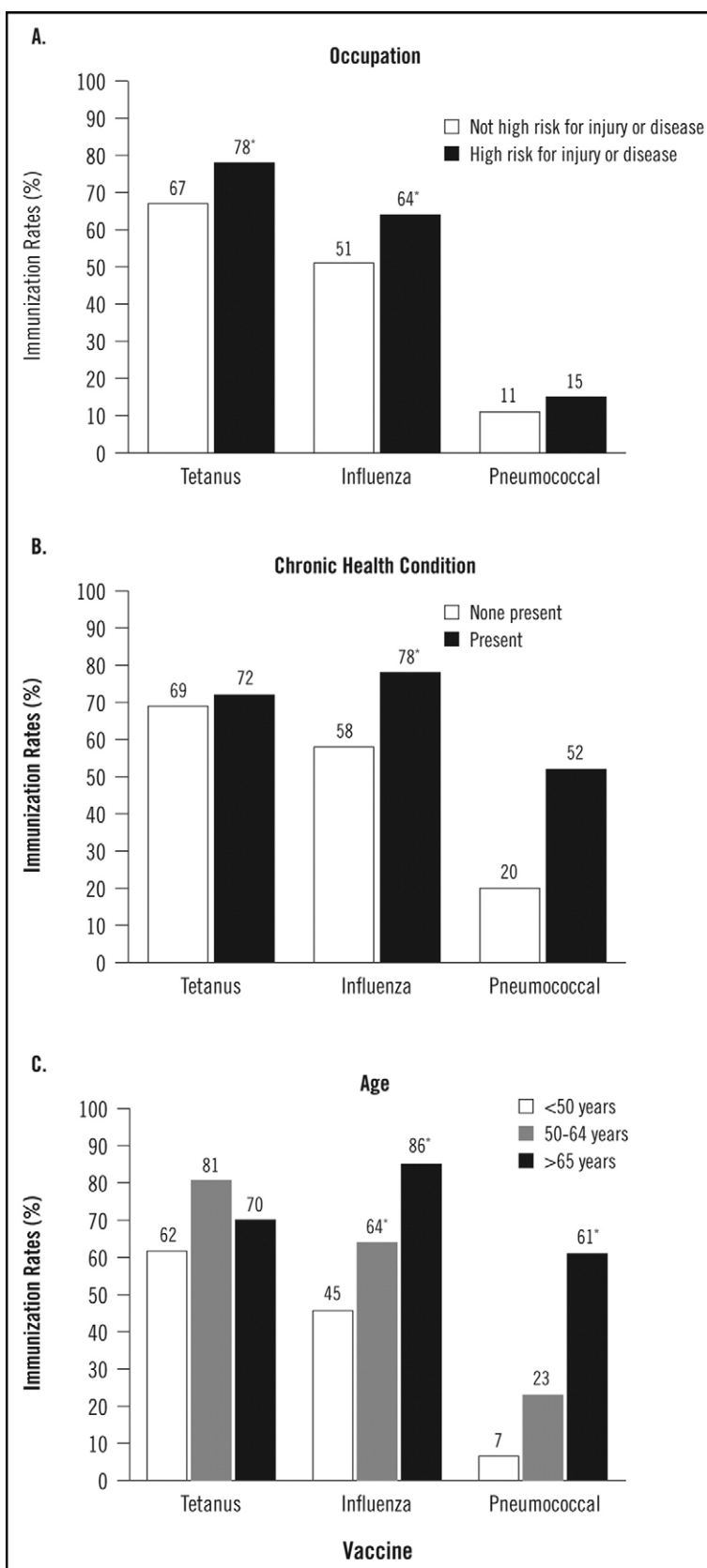


Figure 1 (A-C) Immunization rates reported in consumer survey, by risk factor (Vaccinations ever received as adults, as reported by 2,002 consumers). * $P < 0.05$ vs. nonrisk groups.

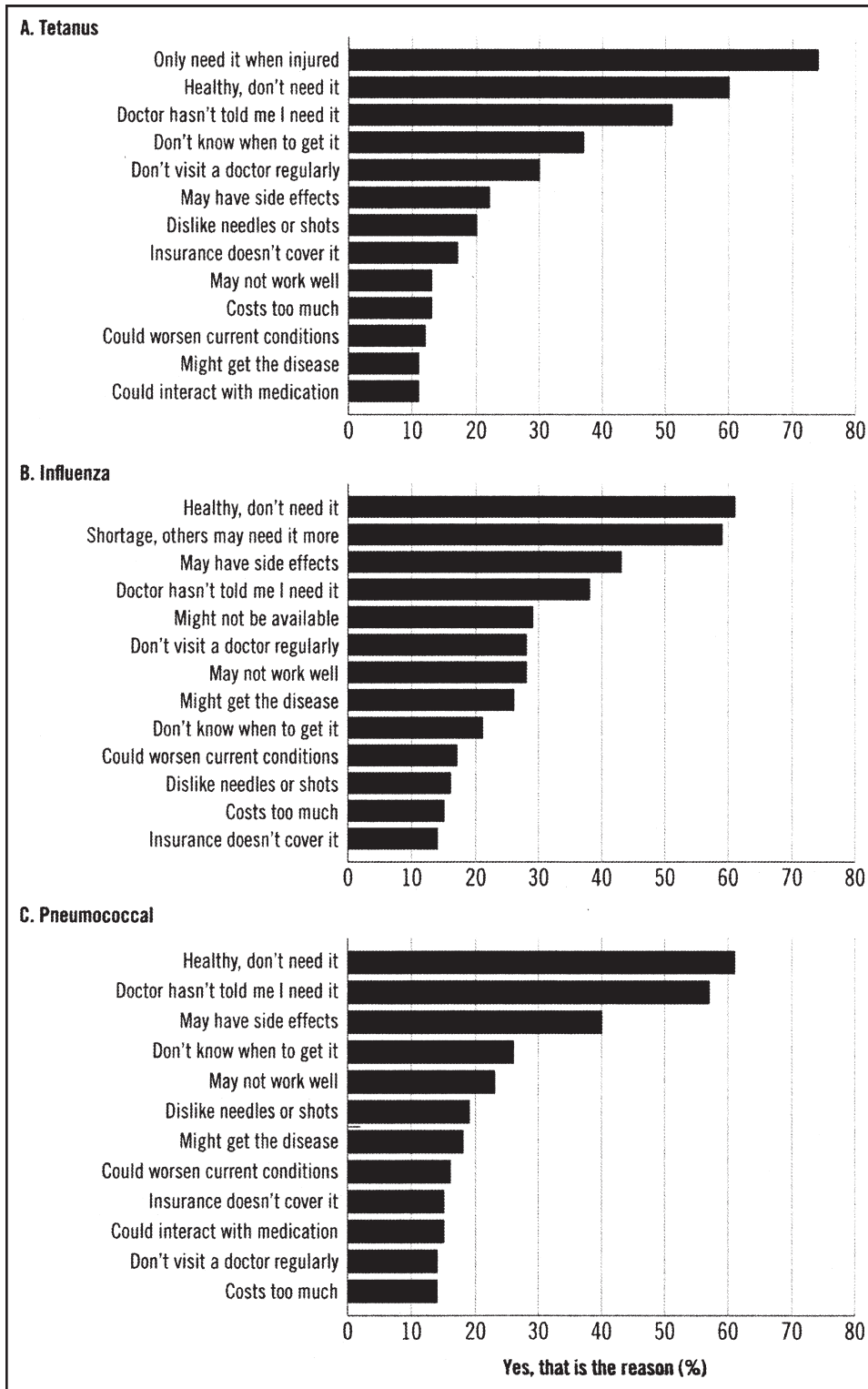


Figure 2 (A-C) Reasons consumers acknowledge for not receiving immunizations, by vaccine type. Scale shown is the percent of consumers who were aware of the immunization and who agreed that this is a reason they have not received it or will not receive it.

cern about the cost of vaccines as reasons adults might forgo immunizations. Depending on the vaccine and the professional group, between 61% and 79% of healthcare

professionals thought their adult patients would be likely to receive a vaccine if their out-of-pocket costs were \$25 to \$30.

Table 1 Healthcare provider recommendations for influenza and pneumococcal vaccinations by patient type

Patient Type	Influenza Vaccine		Pneumococcal Vaccine	
	Physicians (n = 100)	PA/NP/RNs (n = 100)	Physicians (n = 100)	PA/NP/RNs (n = 100)
All adults	39%	59%*	—	—
Aged ≥50 yr	28*	15	4%	18%*
Aged ≥65 yr	37	28	65	55
Chronic lung disease	45	40	68	55
Diabetes mellitus	31	25	44*	26
Heart disease	20	11	29*	12
Chronic liver disease	22	16	27	20
Chronic kidney disease	22	12	25	17
Weak immune system	17	20	24	29
Radiation/chemotherapy	14	9	17	10
Asplenia	—	—	27*	8
Complications or risk from other illness	25	17	28	23
Smoker	—	—	13	11
Close contact with someone at high risk	24	22	11	10

NP = nurse practitioner; PA = physician assistant; RN = registered nurse.

*Significantly greater ($P < 0.05$) than other provider group.

DISCUSSION

Our surveys confirmed that many adults do not receive immunizations as recommended. This is not the first time barriers to adult immunization have been examined. However, many studies are a decade old,⁶⁻⁸ and attitudes, beliefs, and knowledge about immunization may have changed. Some previous studies were limited to particular populations, such as the elderly^{6,9,10} or economically disadvantaged,¹¹ whereas the sample in our consumer survey covers people in all economic groups and the entire adult age span. In general, our study confirms findings from previous studies and adds to our understanding about why adults do not receive immunizations.

False assumptions, such as a belief that healthy people do not need immunizations, are important reasons that consumers fail to receive vaccinations. Efforts to inform and educate the public occasionally misfire. For example, publicity about past influenza vaccine shortages appears to have had a lasting negative effect. In our survey, consumers cited the desire to save a vaccine in short supply for others who needed it as a reason to skip influenza immunization, although there was no shortage at the time.

The Medicare Current Beneficiary Survey has consistently found that people fail to receive influenza vaccinations because they do not know they should be immunized.¹² Most of the consumers in our study said they were likely to follow their physician's recommendations for immunization, echoing earlier research.⁷ Both groups of healthcare providers in our study acknowledged that they were more likely to discuss immunization during well-care visits than during sick visits. Similarly, Szilagyi and associates¹³ found that the most significant practice barrier to immunization was other urgent concerns that dominated the office visit. However, a mild acute illness, even a febrile

illness, is not a contraindication for immunization.¹⁴ In recognition of this missed opportunity, hospitals have established standard operating procedures and protocols to offer vaccinations to inpatients and those treated in emergency rooms.^{15,16}

A comprehensive review of the literature found patient reminder/recall systems to be 1 of the strongest ways to increase community demand for immunizations.¹⁷ A review of 41 studies looking exclusively at patient reminder/recall interventions also found this to be an effective strategy.¹⁸ However, >70% of the providers in our survey noted the ineffectiveness of their reminder systems for tetanus and pneumococcal immunizations.

Although responses from our 2 different surveys should be compared with caution, it appears that healthcare providers and consumers do not always agree on reasons that adults go unvaccinated, especially those reasons related to consumer attitudes and beliefs. For example, >66% of providers thought that consumers avoid vaccinations because of concern about side effects, dislike of needles, or fear that the vaccine would make them ill. Consumers mentioned these concerns far less frequently as reasons that they did not receive immunizations.

Economic factors were another area where providers' perception of barriers differed from consumers' concerns. Most consumer respondents had insurance coverage for vaccinations, and only 13% to 15% stated that immunizations cost too much. But 50% to 66% of healthcare providers thought that monetary concerns were a major barrier to immunization. Some providers may not have been aware that immunizations are covered under Medicare. The program has been paying for pneumococcal immunization since 1981 and for influenza immunization since 1993.¹⁹

Table 2 Healthcare providers' explanations for why adults may not receive tetanus, influenza, and pneumococcal vaccines*

Explanation	Tetanus Vaccine		Influenza Vaccine		Pneumococcal Vaccine	
	Physicians (n = 100)	PA/NP/RN (n = 100)	Physicians (n = 100)	PA/NP/RN (n = 100)	Physicians (n = 100)	PA/NP/RN (n = 100)
Patient does not make regular well visits	85%	80%	83%	73%	88%†	77%
Concern about side effects, that it will cause illness	65	68	87	87	65	77
Lack of knowledge about illness prevention	73	76	62	75†	73	83
No effective reminder system	73	77	62	63	71	72
Fear of needles	71	68	71	68	69	67
Inadequate insurance coverage	66	71	61	67	68	79
Not going to same physician regularly	65	73	59	65	62	71
Unaware of vaccination schedule	64	70	50	56	70	68
Confused about recommended vaccination schedule	63	61	50	45	68	62
Think healthy people don't need it	49	55	66	63	68	68
Not receiving physician's recommendation	59	55	53	54	58	60
Vaccine too expensive	51	46	52	43	62	54
Think won't work if sick	38	33	58	58	46	52
Could worsen current conditions	31	28	58	53	37	43
Believe lifetime protection from childhood vaccines	49	45	28	29	35	31
Not enough time in office visit to discuss it	40	30	37	27	39	30
Think it's ineffective	24	22	48	46	31	30
Could interact with current medications	25	29	26	33	21	37†
Think only for elderly	—	—	56	57	68	73
Vaccine shortage	—	—	87	83	—	—
Need only when injury or open wound	80	82	—	—	—	—

NP = nurse practitioner; PA = physician assistant; RN = registered nurse.

*Percent of providers who agreed when presented a list of reasons adult patients might not receive the vaccine.

†Significantly greater ($P < 0.05$) than other provider group.

Lack of knowledge on the part of healthcare providers was a surprising finding in this study. Almost 50% of those surveyed did not rely on the CDC/ACIP guidelines, which are widely available in both print and electronic media.

Our surveys have several limitations. The response (willingness to participate) rates in both surveys were low, which could bias the findings. The healthcare provider sample was small. Although the consumer sample was large, it was mostly non-Hispanic whites. Studies have found differences in barriers to immunization among other ethnic groups.^{20,21} The immunization history in the consumer survey was based completely on patient recall. Finally, survey respondents often underreport behaviors that may be perceived negatively and overestimate behaviors perceived as good.

Although patient and provider education is needed to fill knowledge gaps and misunderstandings, knowledge by it-

self is not sufficient to improve immunization practices.²² Efforts should be made to make administration of recommended immunizations a routine part of all healthcare encounters. Based on the evidence in 118 studies involving 17 intervention strategies, the Task Force on Community Preventive Services recommended a variety of strategies to increase immunization rates in adults.²³

The National Vaccine Advisory Committee has called for identification and minimization of barriers to receiving vaccines.²⁴

SUMMARY

Findings from the consumer and provider surveys reported here may help distinguish the real reasons adults forego immunizations from the presumed barriers. This knowledge has the potential to further inform and refine policies established to increase adult immunization rates.

AUTHOR DISCLOSURES

The authors who contributed to this article have disclosed the following industry relationships:

David R. Johnson, MD, MPH, is a full-time employee of Sanofi Pasteur Inc.

Kim Lipczynski, PhD, has served as a consultant to Sanofi Pasteur Inc.; and is a full-time employee of Adelphi Research by Design.

Kristin L. Nichol, MD, MPH, has served as a consultant to CSL Biotherapies, GlaxoSmithKline, MedImmune, Novartis, and Sanofi Pasteur Inc; and has received research funding from GlaxoSmithKline and Sanofi Pasteur Inc.

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