REPORT

Managed Care Considerations and Economic Implications of Vaccination Practices

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ABSTRACT

Influenza is an acute viral respiratory disease caused by the influenza A and B viruses. The epidemiologic characteristics of influenza are in constant flux as the viruses mutate frequently, and the subsequent spread of illness depends on the affected population's susceptibility to the new antigens. These viral mutations necessitate frequent updates to the annual seasonal influenza vaccine. Those most at risk for serious complications of influenza are young children and elderly persons. Although influenza vaccination rates are highest among adults 65 years or older, vaccine effectiveness in this age group is often less than among younger persons. Thus, vigilance in efforts to increase vaccine uptake is warranted through a concerted effort across the entire healthcare and public health spectrum of providers and agencies, including clinicians, health systems, government, and community agencies. Managed care organizations are an excellent case study for implementing systemwide efforts to prevent influenza disease and its consequences.

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The Economic Burden of Influenza in the United States

The public health burden of influenza is enormous, with outbreaks creating significant morbidity and mortality annually. Attendant to the significant morbidity and mortality is a considerable economic burden. In a landmark 2007 study, Molinari et al undertook a systematic analysis of the total costs of influenza. Using data from health insurance claims, the investigators estimated the direct medical costs for outpatient visits, hospitalizations, and mortality, along with projections of either earnings or statistical life-values for indirect costs of illness-related work absenteeism or premature death. They then estimated healthcare resource usage associated with influenza. Results of the study showed that annual influenza epidemics led to approximately 610,660 life-years lost, along with 3.1 million patient-hospitalized days and 31.4 million outpatient visits. The economic burden of influenza across all age groups was $87.1 billion annually, including $10.4 billion in direct medical costs alone, and projected lost earnings due to illness and death were approximately $16.3 billion. Significantly, 64% of the total cost ($55.7 billion) was incurred by illnesses in older adults, due to their increased rates of hospitalizations and deaths associated with influenza, although older adults comprised only 13% of the US population at the time.[1]

Since the Molinari study, other research has explored the economic burden of influenza. In 2012, Mao et al assessed the annual economic costs of seasonal influenza for 3143 counties in the United States based on the 2010 US Census. The study researched spatial variations among counties regarding population size, age structure, income level, and influenza activity. Results showed that the annual economic costs of influenza varied from $13.9 thousand to $957.5 million across counties in the United States, with a median cost of $2.47 million. The authors suggested that prioritizing the distribution of influenza vaccines to counties with higher influenza rates may lead to fewer influenza cases and better net outcomes.[2]

A recently published study by Yan et al estimated the number of healthcare encounters and related costs attributable to influenza A and B in the United States during the 2001-2002 to 2008-2009 seasons. Over the 8 influenza seasons, 11.3 million to 25.6 million projected influenza-related healthcare encounters occurred. Related healthcare costs ranged from $2.0 billion to $5.8 billion.[3]

A new study by Young-Xu et al used electronic medical records (EMRs) from the Veterans Health Administration of the Department of Veterans Affairs (VA) and respiratory viral surveillance data from the CDC to estimate the disease and economic burdens of influenza among the US military veteran population from 2010 to 2014. An estimated 10,674 VA emergency department (ED) visits, 2538 VA hospitalizations, and 3793 underlying respiratory or circulatory deaths were attributed to influenza annually. Lost productivity during each year cost $27 million, with yearly costs for ED visits estimated at $6.2 million. Overall, the estimated annual economic burden related to seasonal influenza was $1.2 billion, with premature death being the largest cost driver, followed by hospitalization. The largest proportion of the burden of influenza affected those 65 years or older. Most of the lost productivity and hospitalization costs were incurred by older veterans.[4]

Cost-Effectiveness of Different Influenza Vaccines

The primary preventive strategy against the health and economic burden attributable to influenza is annual influenza vaccination. However, the reduction in influenza burden depends on vaccine coverage, effectiveness, and relative effectiveness of various vaccine formulations (eg, trivalent or quadrivalent; inactivated or live attenuated; standard-dose or high-dose; and cell-based, egg grown, or adjuvanted), as well as the relative uptake of the different vaccine types.

Over 5 recent influenza seasons, overall vaccine coverage has ranged from a low of 41.8% in 2011-2012 to a high of 47.1% in 2014-2015. In 2016-2017, coverage was 49.9% among those 6 months to 17 years, 33.6% among those 18 to 49 years, 45.4% among those 50 to 64 years, and 65.3% among those 65 years or older.[5,6] During these years, the US Influenza Vaccine Effectiveness (VE) Network reported that the overall influenza VE was 47% in 2011-2012, 49% in 2012-2013, 52% in 2013-2014, 19% in 2014-2015, and 48% in 2015-2016. These factors, including uptake, VE, costs of vaccine and administration, and costs of disease are essential components of analyses to determine whether and under what scenarios vaccination is cost-effective.[7] Ting et al recently reviewed 31 studies of influenza vaccination cost-effectiveness across diverse population subgroups. Vaccination was found to be cost-effective for children, adolescents, pregnant and postpartum women, and high-risk groups, such as those with comorbid conditions and the elderly, from both societal and health-system perspectives.[8]

A 2017 review by deBoer et al used medical databases to identify economic evaluations of trivalent influenza vaccine (IIV3) versus quadrivalent influenza vaccine (IIV4) formulations. They found that the comparative benefits of the IIV4 formulation can vary by influenza season, because the VE of IIV3 depends on how well the B virus contained in IIV3 matches with the circulating B virus, and on the level of cross-protection provided by IIV3 against the influenza B virus not included in the vaccine. Additionally, the price difference between IIV3 and IIV4 is a factor in the cost-effectiveness potential of IIV4. Results suggested that switching from a IIV3 to IIV4 formulation could be both clinically and economically beneficial; however, the authors recommended that the impact of the 2 formulations should be studied from multiple influenza seasons to better assess and reflect the circulation of the B strains from one season to another.[9]

Cost-effectiveness studies specific to adults 65 years or older have focused on use of the high-dose influenza vaccine versus the standard-dose influenza vaccine. One 2015 study based on US influenza-related health outcome data assessed the cost-effectiveness of high-dose inactivated influenza (IIV3-HD) versus standard-dose IIV3 and the standard-dose quadrivalent inactivated influenza (IIV4) vaccines. Results demonstrated that IIV3-HD vaccine compared with standard-dose influenza vaccine would avert 195,958 cases of influenza, 22,567 influenza-related hospitalizations, and 5423 influenza deaths among the US elderly. IIV3-HD generated 29,023 more quality-adjusted life-years (QALYs) and a net societal budget impact of $154 million, with an incremental cost-effectiveness ratio for this comparison of $5299 per QALY. The investigators concluded that the high-dose influenza vaccine is expected to achieve significant reductions in influenza-related morbidity and mortality and is a cost-effective alternative to the standard-dose influenza vaccines studied.[10]

Using Markov state transition decision analysis modeling, Raviotta et al compared vaccination strategies using the standard-dose influenza vaccine, IIV3-HD, and IIV4 vaccines in persons 65 years or older to assess their cost-effectiveness and public health benefits. Cost analyses showed that the cost of standard-dose inactivated, trivalent influenza vaccine was $3690 per QALY gained when compared with no vaccination at all. IIV4 cost $20,939 per QALY gained compared with standard-dose inactivated, trivalent influenza vaccine, and IIV3-HD cost $31,214 per QALY when compared with IIV4. Overall differences of 83,775 fewer influenza cases and 980 fewer deaths were projected with the IIV3-HD formulation compared with IIV4. The investigators concluded that IIV3-HD would be the favored vaccination strategy if the actual willingness to pay for the formulation is greater than or equal to $25,000 per QALY gained. This compares with standard willingness-to-pay thresholds of $50,000 to $100,000 per QALY gained used in US literature. This study also examined the cost-effectiveness of an adjuvanted influenza vaccine (aIIV3). The cost-effectiveness of aIIV3 would depend on its price and effectiveness, which are still under study, but this formulation might be considered more favorable if its relative effectiveness is at least 15% greater than that of the standard IIV3 vaccine.[11]

Increasing the Rate and Cost-Effectiveness of Adult Influenza Immunization: The 4 Pillars Practice Transformation Program

Despite variability in its effectiveness from year to year, the case for vaccination against seasonal influenza is well established. Yet, vaccination uptake remains suboptimal, even among those most vulnerable to its complications, such as elderly persons and those with chronic health conditions. The reasons for influenza vaccine hesitancy are myriad and have features that differ from other vaccines. A lack of confidence in the vaccine was found to be the most important barrier to receipt of seasonal influenza vaccine, exemplified by negative attitudes, misconceptions about the disease or the vaccine, and its low perceived effectiveness. In addition, for elderly persons living alone, low perceived risk of disease and access to vaccination were important barriers to vaccine uptake.[12]

Although vaccination rates among the elderly population are higher than among other adult age groups, there are disparities in uptake by race, with vaccination rates among older Caucasians at 67.7%, Hispanics at 66.8%, and African Americans at 56.1% in 2010.[13] A decision-analysis model has been examined to estimate the cost-effectiveness of a hypothetical national vaccination program aimed at eliminating the disparities in the vaccination rates among these populations. A proposed cost of $10 per targeted person per year was assumed, with all groups reaching 70% vaccination uptake within 10 years. The vaccination intervention program compared with no intervention program cost $48,617 per QALY saved. At willingness-to-pay thresholds of $50,000 and $100,000 per QALY saved, the likelihood of the vaccination program being cost-effective was shown to be 38% and 92%, respectively. Overall, the investigators concluded that such a hypothetical model would have a moderate to high likelihood of being cost-effective in resolving current disparities in vaccination rates among the different racial/ethnic populations studied.[14]

Although hypothetical models such as those highlighted above provide potentially promising data for establishing public policy to maximize influenza immunization's cost-effectiveness, every influenza season presents a renewed challenge to achieve the updated Healthy People 2020 goals to increase the number of adults aged 18 years and older vaccinated against seasonal influenza.[15] The Community Preventive Services Task Force has recommended multi-strategy, evidence-based interventions to increase vaccination rates in the United States through enhanced access to vaccination services, increased community demand for vaccinations, and improved provider- and system-based vaccine-related interventions. Moreover, the Task Force recommended that 1 or more strategies from each of the interventions be used in combination for the best outcomes.[16,17]

One such intervention is the 4 Pillars Practice Transformation Program (also called the 4 Pillars Immunization Toolkit or 4 Pillars Program), a compilation of evidence-based best practices for increasing immunization rates in the primary care setting.[17,18] This program addresses the Task Force's 3 primary interventions and adds motivation by an immunization champion to form the 4 pillars. Strategies within each pillar are derived from decades of research into the barriers and facilitators of adult immunizations from the perspective of providers and patients, along with trials of successful strategies to increase immunization rates.[17,19] The 4 Pillars Program allows primary care practices of all sizes and structures to customize the intervention to suit their unique, individual needs.

The intervention strategies used to increase adult vaccination are shown in **Table 1**, grouped by pillar and delineated specifically for influenza immunization.[17]

The 4 Pillars Program was tested for effectiveness in 25 primary care practices in Pittsburgh and Houston in a randomized, controlled cluster trial. The practices were randomized to intervention and control arms. A total of 70,549 adults was included, with baseline mean age of 55.1 years and a distribution that was 35% male, 21% nonwhite, and 35% Hispanic. After 1 year of follow-up, both the intervention and control cohorts significantly increased influenza vaccination, averaging increases of 2.7 to 6.5 percentage points. The likelihood of influenza vaccination was significantly higher in practices with lower percentages of patients with missed opportunities for immunization. In the second year intervention, the likelihood of vaccination again increased, especially in those sites that reduced missed opportunities for vaccination.[17] The 4 Pillars Program has been successfully used to raise vaccine uptake for other adult and adolescent vaccines.[19-21]

The cost-effectiveness of the 4 Pillars Program for improving vaccination rates in older adults has also been studied. Smith et al assessed the program by estimating cost-effectiveness to increase pneumococcal, influenza, and pertussis-containing vaccine uptake in adults 65 years and older seen in the primary care setting. The study was based on QALYs, public health outcomes, costs, and vaccination rates; intervention costs were obtained from the randomized controlled clinical trial referenced above. By using the 4 Pillars Program and extrapolating data over 10 years, results showed that there would be approximately 60,920 fewer influenza cases, along with 2031 fewer pertussis cases and 13,842 fewer pneumococcal illnesses in the older population studied. The per-person vaccination and illness costs would be higher using the program intervention (an increase of $23.93) but would have an increase in effectiveness of $7635 per QALY gained with the intervention (**Table 2**).[22] There was no individual parameter variation that caused the intervention to cost more than $50,000 per QALY gained.[22]

The Role of Standing Orders in Increasing Vaccination Rates

Among the strategies in the 4 Pillars Program, one of the most effective has been shown to be standing order programs (SOPs). SOPs allow clinicians to administer influenza and pneumonia vaccinations

TABLE 1. Intervention Strategies Used to Increase Adult Vaccination Rates From the 4 Pillars Practice Transformation Program[17]

Pillar 1: Convenient vaccination services
• Use every patient visit type as an opportunity to vaccinate • Offer open access/walk-in vaccination during office hours • Hold express vaccination clinics outside normal office hours where only influenza vaccine is offered and systems for check-in, screening, and record keeping are streamlined • Create a dedicated vaccination station • Extend the influenza vaccination season by vaccinating as soon as supplies arrive and continuing to vaccinate as long as flu is circulating in the community
Pillar 2: Communication with patients about the importance of vaccination and the availability of vaccines
• Train staff to discuss influenza vaccine during routine processes such as vital signs • Discuss the serious nature of influenza • Promote vaccination of staff to set a good example • Record telephone on-hold messages that advertise vaccine availability or promote vaccination • Use posters/fliers/electronic message board/website postings/social media promoting vaccination • Conduct outreach by email, phone, text, mail, health portal, etc, that vaccines are due and/or available
Pillar 3: Enhanced office systems to facilitate adult vaccination
• Assess vaccination eligibility for every scheduled patient at the beginning of the day and discuss in daily huddles • Assess immunizations as part of vital signs upon rooming patients and record outside vaccinations in EMR • Incorporate EMR prompts for vaccination into the workflow • Incorporate standing order programs for vaccination by nurses and/or medical assistants into the workflow • Ensure sufficient vaccine inventory to handle increased immunizations • Promote simultaneous vaccination (eg, offer other vaccines at the time of influenza vaccination)
Pillar 4: Motivation through an office immunization champion
• Create a chart to track progress. Set an improvement goal and regularly track progress (eg, daily or weekly). Post the graph of your progress in a prominent location and update it regularly • Provide ongoing feedback to staff on vaccination progress using email, posted notices, making announcements, or using a combination of these. Encourage, nudge, and cheer as needed to keep up the momentum • Report upon progress at staff or huddle meetings. Facilitate discussion at these meetings to identify which pillar activities are working, which are not working and why, and to identify changes that need to be made • Create a competitive challenge among your staff for the most vaccinations given • Provide rewards for successful results to create a fun-spirited environment that promotes vaccination across the practice. Ideas include: reward for highest vaccinator, team competitors, vaccination goal poster contest, etc

EMR indicates electronic medical record.
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according to a protocol approved by a physician or health system without an individual physician order or examination. Assessments have shown that such programs may be both a promising and an economically favorable investment in flu prevention.[23,24]

Zimmerman et al assessed the awareness of SOPs in the primary care setting using a nationwide survey of 1640 primary care physicians. Among the 67% who responded, 42% reported consistent SOP use, although they differed in awareness and recommendations surrounding its use, size and type of practice, number and level of training of in-practice clinical staff, and other staff attributes. Variables associated with the highest likelihood of using SOPs for influenza vaccination were awareness of recommendations to use SOPs and physician agreement with their effectiveness for use in practice.[25] In a related study using the same sample, Albert et al showed that only 23% of those surveyed used SOPs consistently for both influenza and pneumococcal vaccines, with only 20% using SOPs for influenza immunization. Critical practice-level factors that were associated with enhanced use of SOPs included perceived practice openness to change, a strong teamwork focus, EMR access, presence of an "immunization champion" within the practice to promote SOP use, and access to nurse/physician assistant staff as opposed to only medical assistants for SOP implementation. The investigators concluded that SOPs are underused overall but have the potential for substantial positive public health impact, and that more clinician and nonclinician education surrounding SOPs should be considered nationally, focusing on current vaccine recommendations and policies to better administer immunizations and facilitate adoption of SOPs.[26]

SOPs for influenza and pneumococcal vaccination among those 65 years or older have been shown to be cost-effective from a third-party payer perspective, costing $14,171 per QALY gained, compared with no SOP program. Lin et al used a Markov model and showed that SOPs are economically favorable in scenarios when SOPs increased vaccination rates by 4% or more and when costs to implement were less than $21 per person. Thus, SOPs have the potential to improve public health through increased immunization rates, and they allow physicians more time to address other health issues in the limited amount of time allotted per patient.[24]

A number of other evidence-based clinical strategies have been shown to increase adult vaccination rates and improve vaccine parity. These include enhanced documentation systems (eg, EMRs, health maintenance flow sheets in patient charts), routine screening of vaccination status, provider reminders, and recall systems.[23] One best-practice model used by the US Veterans Health Administration included development of performance measures and accountability standards for rates of preventive services, including immunizations. Multiple systems-based interventions were used to improve vaccination coverage rates in both hospitals and clinics, including clinical reminders, feedback, annual distribution of an

TABLE 2. Cost-Effectiveness Analysis Results: 4 Pillars Program to Increase Immunization Rates[22]

Strategy	Cost, $	Incremental Cost, $	Effectiveness (QALYs Lost)	Incremental Effectiveness (QALYs)	Incremental Cost-Effectiveness Ratio, $
No Program	2083.53	–	−0.1016	–	–
Program	2107.45	23.93	−0.0985	0.0031	7635

QALY indicates quality-adjusted life-year.
From Smith KJ, Zimmerman RK, Nowalk MP, Lin CJ. Cost-effectiveness of the 4 Pillars Practice Transformation Program to improve vaccination of adults aged 65 and older. *J Am Geriatr Soc*. 2017;65(4):763-768. Copyright 2017 by John Wiley Sons, Inc. Reprinted by permission of John Wiley & Sons, Inc.

influenza vaccination toolkit, and national coordination of vaccine distribution. This led to improvements across all geographic regions, types of hospitals, and sociodemographic groups.[27] Overall, health systems must establish better in-practice structures to track patient vaccination status, implement SOPs for appropriate vaccinations, and provide stronger and clearer recommendations to older adults to undergo influenza vaccination.[23]

An important factor in a practice's ability to increase uptake is its readiness to implement changes necessary to improve adult vaccination. Using qualitative research techniques, including observation and key informant interviews, Hawk et al identified 4 practice characteristics that were important to implementation of the 4 Pillars Program. They were degree of quality improvement history, communication and practice leadership style, effectiveness of the immunization champion, and organizational flexibility. Practices that scored high overall on these factors (high implementers) also implemented the most strategies to improve vaccination rates, such as SOPs, and demonstrated significant increases in influenza and tetanus–diphtheria–pertussis vaccination uptake.[28]

Patients and Influenza Vaccination Acceptance

Vaccine hesitancy remains an intractable barrier to increasing adult influenza vaccination rates. Reasons given by patients for not receiving the influenza vaccine are frequently examined in the context of the theory of reasoned action and the theory of planned behavior. These behavioral theories divide barriers and facilitators of vaccination into knowledge and attitudes, social norms, and perceived behavioral control, with the addition of habit in revised iterations.[29] Harris et al studied adults 18 years and older who were surveyed in November (mid-influenza vaccination season) about their intention to receive influenza vaccine and in March and April (after influenza vaccination season) about their actual vaccination behavior. Just over half of those who intended to receive influenza vaccine had received it by the end of the season. Of those who intended to receive the vaccine but failed to do so, 50% cited not getting around to being vaccinated as their primary reason. Twenty-two percent of those not intending to be vaccinated believed they did not need the vaccine. A strong recommendation from a healthcare provider would have improved receptivity to vaccination among 81% of those with intention and 44% of those without an intention.[30] Reviews of quantitative and qualitative studies to identify the barriers to influenza vaccination uptake and intention found that the most frequently reported deterrents to vaccination acceptance were negative attitudes toward the vaccine, including worries about its safety and belief that the vaccine causes influenza, decreased perceived effectiveness of the vaccine, and a lack of trust in health authorities. Social norms, such as a perception that influenza vaccination was not the norm among one's peers, were also found to be a barrier to influenza vaccination. However, physician recommendation was an important facilitator.[31] In addition, low perceived risk of influenza and of the severity of disease are frequent barriers to vaccination. A 2015 study found that unvaccinated patients seeking outpatient medical care for an acute respiratory illness with intent to receive future vaccination were 1.5 times as likely to have actual laboratory-confirmed influenza when compared with those who were already vaccinated and intended another vaccination in the following season. Yet a significant number of patients reported no intention to receive the influenza vaccine in the next season, despite requiring medical treatment for an acute respiratory illness.[32] Many unvaccinated adults report that they forgot to receive it, a measure of perceived behavioral control, while vaccine receipt has been highly associated with previous vaccination history.[33]

Conclusions

Underusage of influenza vaccine in adults 65 years or older remains a critical concern in medical practice in the United States. To successfully address the health and economic burden of influenza and benefits of immunization, change is needed at the health-system, provider, and patient levels. Strategies for health systems include recognition of the cost-effectiveness of influenza vaccination, of alternative vaccination strategies, and of interventions at the practice level to improve vaccination rates; facilitation and implementation of SOPs; programming the EMR rates for provider immunization reminders; and instituting feedback on rates to providers. Strategies for providers include support of vaccination assessment and administration by nonphysician staff, use of available toolkits for increasing vaccination rates, and providing release time for the immunization champion to foster motivation among staff. Patient-level strategies include efforts by providers, such as creating or procuring age-, language-, and health literacy-appropriate patient education materials; holding staff in-service sessions to prepare for influenza vaccination season; and recommendation of influenza vaccine by all members of the office staff so patients understand that it is a health priority. A concerted effort among providers and agencies, including clinicians, health systems, government agencies, community advocates, and families, can improve vaccination rates for older adults and reduce their annual morbidity and mortality from influenza.

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