

FOCUS: VACCINES

Improving Influenza Vaccination Coverage in the Pediatric Asthma Population: The Case for Combined Methodologies

Elizabeth V. Murphy, MD, MPH

Medical Informatics, Portland VA Medical Center, Portland, Oregon, and Department of Medical Epidemiology and Clinical Informatics, Oregon Health Sciences University, Portland, Oregon

The Advisory Committee on Immunization Practices recommends annual influenza vaccine for pediatric asthma patients. Despite considerable risk for influenza complications in pediatric asthma patients, including hospitalization and death, influenza vaccination among children with asthma remains low, especially among low-income pediatric asthma patients. Multiple interventions have been attempted to increase immunization in the pediatric asthma population, including recall and reminders, parent/patient education, and physician education. More recently, information technology methods have been employed, including electronic alerts and computerized physician order entry/clinical decision support interventions. Each of these interventions, as well as a recent legislative intervention, has evidence of effectiveness, but none achieved the Healthy People 2020 vaccination goals of 80 percent for this population. This goal may be achievable with a combination of these methodologies and strategies that increase access to care for underserved patients.

To whom all correspondence should be addressed: Elizabeth V. Murphy, Oregon Health Sciences University, Department of Medical Informatics and Clinical Epidemiology, Mail Code BICC 526, 3181 SW Sam Jackson Park Rd., Portland, OR 97239-3098; Email: murphel@OHSU.edu.

†Abbreviations: ACIP, Advisory Committee on Immunization Practices; CPOE, computerized physician order entry; EHR, electronic health record; CDSS, Clinical Decision Support System; NHIS, National Health Interview Survey; CDC, Centers for Disease Control and Prevention.

Keywords: pediatric asthma patients, influenza vaccination, underserved patients, low-income pediatric patients, immunization rates, randomized controlled trials, computerized physician order entry, clinical decision support, legislation, recall and reminders, pediatric asthma hospitalizations for influenza, influenza prevention

INTRODUCTION

Asthma is a leading cause of hospitalization, morbidity, and mortality in the pediatric population [1]. Although the prevalence of asthma in U.S. children is close to 8 percent, asthmatics represent over one-third of pediatric patients who are hospitalized for influenza complications and are at increased risk for influenza-associated pneumonia and death [1]. The Advisory Committee on Immunization Practices (ACIP†) has recommended annual influenza vaccination in asthmatics over 6 months of age since 1964 [2]. In 2010, the ACIP expanded influenza vaccine recommendations to include all children over 6 months of age, with an increased focus on vaccinating children with asthma [2].

Prior to the 2009 H1N1 influenza pandemic, vaccination rates for children with asthma were reported to be as low as 9 percent to 25 percent [3]. Following the 2010-11 influenza season, the Centers for Disease Control and Prevention (CDC) evaluated National Health Interview Survey (NHIS) data [2]. Despite the broadened recommendations for influenza vaccine in all children in 2010 and the seriousness of the 2009 H1N1 pandemic, only 50 percent of NHIS respondents reported that their asthmatic child had received an influenza vaccine in the past year [2], with self-reporting often overestimating vaccination rates. Of greater concern is that the rate of flu vaccination among asthmatic children without health insurance was only 26 percent and the vaccination rate for asthmatic children who did not have a usual place for receiving health care was only 19 percent [2]. There was also evidence of ethnic disparities, with only 44 percent of African-American asthmatic children receiving the vaccine [2].

Multiple strategies have been employed in order to increase the influenza vaccination rates in children with asthma, and several of these strategies have demonstrated moderate success. Common strategies have included recall and reminders, which often combine computer-generated reminders with phone calls, patient and provider education, and standing orders for vaccines

[4,5,6,7]. Some of these methods combine electronic alerts to physicians during office visits and parent and provider education on the risks and benefits of flu vaccine [3]. More recently, influenza vaccination provider alerts have become integrated into computerized physician order entry (CPOE) systems using a clinical decision support alert that reminds the provider about the need for vaccination at the point of care and facilitates immediate order entry [8,9,10]. At least one study of asthmatic high-risk adult patients has found increased influenza vaccination rates in clinics using patient-centered medical home and care management models [11], and there is evidence in studies with pediatric asthmatics that having a single source for medical care may contribute to increased vaccination rates [2,3]. Two states have instituted legislative interventions to increase vaccination rates in younger children, requiring influenza vaccination as a condition for enrollment in licensed child care or preschool in the 6 month to 59 month age group [12]. It appears unlikely, however, that any single strategy can achieve the near universal influenza vaccination in asthmatic children that is required in order to significantly decrease hospitalizations and influenza-related complications in the pediatric asthma population.

RECALL AND REMINDERS

Although the number of scientific studies of influenza vaccine interventions in asthmatic children is small, recall and reminder methods have demonstrated effectiveness in increasing vaccination rates (Table 1). Reminders are used to share knowledge about the importance of the vaccine with parents and providers. Recalls ask patients to come to a clinic for vaccination. In a 1992 randomized controlled trial, Szilagyi et al. combined computer-generated vaccination reminder letters sent to parents of asthma patients, with provider education, achieving an odds ratio of receiving the influenza vaccine of 6.15 in the intervention group compared with controls [6]. Szilagyi's study subjects

Table 1. Recall/Reminder Intervention Studies.

Study Author/Year	Intervention	Study Design	Population	Study Results
Szilagyi 1992 [6]	Computer-generated reminder letters sent to parents and providers/provider education.	Randomized Controlled Trial	N = 124; 1-18 years old; Mod/severe asthma	OR for vaccine =6.15; 95% CI (1.95,19.39); 30% in study group v. 7% in controls
Kemper 1993 [7]	Providers in control and intervention educated. Intervention parents sent letter offering vaccine at drop-in clinic for free. Standing order for vaccine.	Randomized Controlled Trial	N = 98; 6 months to 18 years old; mod/severe asthma; inner-city clinic	OR for vaccine = 3.32; 95% CI (1.36,8.12); 47% in intervention v. 21% in controls
Daly 2004 [13]	Parents sent two computer-generated reminder letters and then follow-up post-card.	Randomized Controlled Trial	N = 2007; 6 months to 6 years old; all high risk; 87% asthmatics	42% treatment group v. 25% control immunized, $p < .001$
Gagliani 2001 [14]	Parents sent letter and then auto-dial phone messages; comparison groups = two consecutive flu seasons.	Quasi-Experimental	N = 995; 6 months to 18 years; asthmatics	Vaccination increased from 5.4% to 32.1%, $p < .001$

were mostly Medicaid patients in a low-income community and were selected as having moderate to severe asthma with chronic medication use and prescription of a bronchodilator within the past year. All providers and nurses in the clinic were educated and re-informed about a clinic policy to vaccinate all moderate to severe pediatric asthma patients. Patients were randomized to control and intervention groups with intervention group patients receiving a personalized letter written at a sixth-grade level and controls receiving no letter [6]. The letter included the patient's name in the salutation and explained the risks of non-vaccination and effectiveness of the influenza vaccine in preventing these risks and the more minimal side effects of the vaccine. Parents were

asked to make a clinic appointment for vaccination [6]. In another randomized controlled trial, Kemper et al. combined computer-generated reminders with standing orders for influenza vaccine and no-appointment-needed drop-in clinics in an intervention directed toward inner-city pediatric asthma patients [7]. Patients were eligible if they had more than two visits in clinic or ER for asthma in the past year. Eligibility was determined, and the patients were randomized by computer. Intervention patients were sent a personalized letter and asked to bring the letter to clinic at any time for free vaccination without an appointment [7]. Control group patients were not sent a letter. The odds ratio for vaccination in the intervention group was 3.32 vs. the control group [7]. In

Table 2. CPOE/Clinical Decision Support/Combined Methodology Studies.

Study Author/Year	Intervention	Study Design	Population	Study Results
Martin 2006 [8]	Roster function of the EHR to identify asthmatics. Clinical decision support to educate providers, letters and postcards to parents, in-person parent education.	Quasi-Experimental. Before and after 2001-2003 flu seasons.	N = 1072; ages 0-18 years old; moderate to severe asthmatics	Vaccination increased from 8.7% to 42.7%; 95% CI, OR (2.8,4.8); hospitalizations decreased 50% in intervention group
Zimmerman 2006 [3]	Tailored approach at each clinic, patient reminders, provider decision support, CPOE, provider/patient education.	Quasi-Experimental. Before and after.	N = 2438; ages 2-17 years; high-risk medical, including asthma; inner-city clinics	OR vaccination = 2.8; 95% CI (2.3, 3.4); vaccination increased from 10.4% to 18.7%-31% at faith-based clinics
Fiks 2009 [9]	Provider alert at beginning of visit; no reason required for ignoring recommendation; no ascertainment of denominator data; patients already immunized elsewhere, allergic, refused.	Cluster-Randomized; Decision-Support Trial.	N = 10,667; ages 5-18 years old; all asthmatics, private insurance	Control sites: vaccination from 44.2% to 48.2%; study sites from 45.0% to 53.0%; not statistically significant
Venkat 2010 [10]	Ineligible patients determined by decision support tool. CPOE CDS, standing order, required "opt out," directly integrated into nursing order.	Quasi-Experimental; before and after 2007-2009.	N = 3091; age >6 months; emergency department visit, not vaccinated	Vaccination increased from 2.3% to 19.8%, p <.001
Hadler 2014 [12]	Legislative mandate for children to receive influenza vaccine prior to licensed child care or pre-school. Use of public health informatics tools to compare hospitalization rates in same age group across states.	Quasi-Experimental; before and after 2009-10, 2012-13.	N = 55,640; age 6-59 months; community-based	Vaccination increased from 67.8% to 84.1% (95% CI, 78.2%-90%). Hospitalizations decreased 12%, while hospitalizations increased in 9 of 11 EIP (control) states

another well-designed, randomized controlled trial conducted by Daly et al., intervention parents were sent two reminder letters and a postcard resulting in an increase

to 42 percent of patients vaccinated in the intervention group compared with 25 percent of patients in the control group [13]. Gagliani and colleagues conducted a quasi-experi-

mental design experiment to evaluate flu vaccination rates in the years prior to and after their intervention [14]. This study used the computer to identify pediatric asthma patients, send a reminder letter, and then an automated phone call 6 weeks later. The computer recorded patients' receipt of the vaccine from multiple sources so that phone calls were made only to patients who had not received the vaccine following the letter. The intervention increased influenza vaccination rates from 5.4 percent in prior years to 34.1 percent in the study year [14].

The main limitation of recall/reminder methods is that even the most successful interventions led to less than a 50 percent influenza vaccination rate in pediatric asthma patients. Moreover, vaccination rates in asthmatic children from economically underprivileged backgrounds were much lower, often averaging around 30 percent. Although several of these interventions generated computerized reminders, more recent interventions have captured more comprehensive capabilities of electronic health record systems.

CPOE WITH CLINICAL DECISION SUPPORT SYSTEMS

Clinical Decision Support System (CDSS) strategies include integrating provider reminders for vaccination into the computerized physician order entry system to educate providers and facilitate ordering; providing standing orders; retrieving data on vaccination status and the presence of contraindications to vaccine from the medical record; and generating decision support recommendations for patients (Table 2). In a quasi-experimental study design, evaluating vaccination rates in the year prior to and after an intervention, Martin et al. used the electronic health record system (EHR) to create a roster of asthmatic patients within several pediatric office practices, and clinical decision support was used to educate intervention providers on influenza practice guidelines [8]. Patients received computer-generated reminder letters and in-person education from providers. This study also used

an asthma care management team and patient educational tools developed by the author [8]. The intervention improved influenza vaccine rates by 80 percent, but the more significant outcome was a decrease in hospitalizations of pediatric asthma patients by 50 percent [8]. Zimmerman et al. used a "tailored" approach, letting several inner-city pediatric clinics choose from a menu of reminder and clinical decision support options in a quasi-experimental study that evaluated the year prior to intervention versus the year following intervention [3]. Interventions included telephone reminders, computer-generated reminders, parent and provider education, standing orders, clinical decision support alerts, and integration of alerts into a CPOE system for direct ordering. Although the odds ratio for receiving vaccination was 2.8 in the intervention year compared with the prior year, the highest rate of vaccination in any of the clinics was 31 percent, again highlighting the challenges in increasing influenza vaccination rates in high-risk children from underserved communities [3]. In another quasi-experimental study design, Venkat used standing orders with a clinical decision support tool to determine eligibility for influenza vaccine in an emergency department setting [10]. Patients were screened for prior vaccination and contraindications for vaccine, and the system automatically transmitted orders for all eligible patients to the nurse's task list for the patient. The study was limited by a vaccine shortage and other factors, but was still able to demonstrate effectiveness in delivering vaccine to patients presenting to the ER during flu season [10].

In contrast to successful studies, Fiks et al. [9] conducted a cluster-randomized decision support trial with increases in vaccination rates in the intervention clinics that were not statistically significant, although vaccination rates were higher in all intervention clinics compared with control clinics. Groups were randomized by clinic, rather than patient, and vaccination rates were compared for the previous year in each clinic and the intervention year. An educational intervention was given to providers in

the control and intervention clinics with the only difference being a one-time alert at the top of the electronic health record patient visit screen for the intervention group reminding providers that influenza vaccine was due [9].

The study was not well designed, since there was no requirement to respond to the alert or to list a reason for non-vaccination, so many non-eligible patients were likely included in the analysis. The authors conceded that there were known problems with parents refusing vaccination in their private clinics, yet they did not ascertain whether a parent had refused the vaccine [9]. The authors also acknowledged that they could not determine if a patient had already been vaccinated outside of their clinic unless, by chance, there was a text entry regarding outside vaccination that was detectable by a search program [9]. Patients who refused vaccination and patients who were already vaccinated at another clinic, urgent care, or at school or a local pharmacy were not excluded from analysis as ineligible. This incorrectly assigns ineligible patients to the denominator, thereby underestimating the effect of the intervention [9]. There were also several other flaws with this study, including unfavorable demographics for vaccination in the current year of the intervention clinics compared with the previous year since the study compared clinics rather than patients.

Clinical Decision Support (CDS) often includes computer-generated printouts or alerts that provide knowledge and technical support to patients and/or to providers in order to facilitate an action or decision (such as physician ordering of mammography or patient scheduling of a mammogram). Lobach et al. have recently published a comprehensive review of factors that aid in making clinical decision support more effective. Effectiveness factors include requiring providers to give reasons for failing to comply with CDS recommendations and giving decision support recommendations directly to patients [15]. These factors may be integrated into CDS interventions in order to increase effectiveness. Indeed, computer-generated re-

mindings providing decision support to parents/patients were successful in targeting low-income families in both the Szilagyi and Kemper studies [6,7].

LEGISLATIVE STRATEGIES

In 2010, Connecticut enacted legislation mandating influenza vaccination for children between 6 and 59 months old in order to enroll in licensed child care or preschool [12]. The intervention resulted in an 84 percent influenza vaccination rate among children in this age group and, more importantly, a 12 percent decrease in influenza-related hospitalizations. One of 11 control states had a much smaller decrease in hospitalizations (5 percent) and nine out of 11 control states had increased influenza-related hospitalization rates in this age group during the study period. There is also lower strength evidence from ecological studies following legislative interventions in Japan and Ontario, Canada, that legislative strategies are effective in decreasing influenza-related morbidity and mortality in the pediatric and adult population [16,17].

CONCLUSION

Asthma is the most common chronic disease in children and disproportionately affects poor children [3]. Although asthma patients are at higher risk for influenza-related hospitalizations and death, influenza vaccination rates in asthmatic children are disappointingly low, especially for children in underserved communities. Consistent with evidence from prior reviews [18], providing clinical decision support directly to patients/parents in the form of clinical reminders and education increased effectiveness of vaccine interventions, and at least two programs were able to increase vaccination in low-income communities to almost 50 percent through this approach [7,8]. Offering parents drop-in flu vaccine clinics at no charge [7] is another strategy that proved particularly effective, and recent studies have demonstrated effectiveness in using local pharmacies or schools for vaccination [19,20], particularly in rural or underserved areas. Fur-

thermore, many underserved patients will not have a regular source for care, so interventions should integrate screening and vaccination into all health care settings, including emergency departments [4] or urgent care.

Educational and decision support interventions can help address barriers in both the provider and parent communities that may have contributed to lower vaccination rates [21,22]. Recent influenza vaccines, including a live attenuated virus vaccine (LAIV) and a quadrivalent inactivated influenza vaccine (IIV4), have improved influenza vaccine effectiveness, and specific recommendations for the use of these vaccines may be included in provider education and as decision support in the order entry screens of the patient's medical record [23]. Provider recommendation of influenza vaccine and brief education of parents is an effective approach in overcoming parental barriers to vaccination and in allaying parents' fears about the safety of influenza vaccine for their asthmatic child [22].

A "model program" for increasing influenza vaccination in asthmatics would include several components. A state or local vaccine registry could be formed so that schools, clinics, hospitals, and pharmacies would report vaccinations to the registry, and vaccination status could be retrieved during office visits. Reminders would be sent to parents in the months before flu season with information on the effectiveness of influenza vaccine in preventing influenza-related complications and assurances regarding vaccine safety. Parents would be informed of drop-in, expanded hours, no cost clinics, or advised that their health plan will cover pharmacy, school-based, or urgent care vaccination costs. Physicians would be educated on the safety and efficacy of vaccines and coached on discussing these issues with patients. Clinical decision support alerts can inform providers that a patient is not vaccinated and present a check box for instant ordering based on the most recent vaccine recommendations. Health care centers can design CDS alerts so that providers must provide a reason for not ordering vaccine. Parents of high-risk children

could be offered influenza vaccine in the pediatric clinic [24]. Standing orders would be available in emergency departments and urgent care centers with automated entry of vaccine orders onto the nurse's task list.

Effective interventions will likely require a comprehensive program that includes multiple evidence-based methods delivered in a variety of health care and non-health care settings while addressing barriers to vaccination. Using a state-wide influenza vaccine registry may be useful in determining vaccination status [25], and patient-centered medical home care management models that have been successful in increasing influenza vaccination in adults with chronic disease [11] may also be useful in this effort. Incentives for providers, including Meaningful Use or pay for performance, and incentives for patients that may include legislative mandates for vaccination of preschool children will also be helpful. If a comprehensive approach is taken, it is likely that we will be able to achieve the Healthy People 2020 goals of vaccine coverage in 80 percent of the pediatric asthma population. Since low-income children are disproportionately burdened by asthma [26], effective interventions will also help alleviate health care disparities and may serve as a model for improving care for other diseases in underserved communities.

Acknowledgments: The author would like to acknowledge Dr. David Dorr for advice and encouragement in the preparation of this manuscript and for offering important insights into quality improvement concepts and methodologies.

REFERENCES

1. Dawood FS, Kamimoto L, D'Mello TA, Reingold A, Gershman K, Meek J, et al. Children With Asthma Hospitalized With Seasonal or Pandemic Influenza, 2003-2009. *Pediatrics*. 2011;128(1);e27-32.
2. Centers for Disease Control and Prevention (CDC). Vaccination coverage among persons with asthma — United States, 2010-2011 influenza season. *MMWR Morb Mortal Wkly Rep*. 2013;62(48):973-8.
3. Zimmerman RK, Hoberman A, Nowalk MP, Lin CJ, Greenberg DP, Weinberg ST, et al. Improving influenza vaccination rates of high-risk inner-city children over 2 intervention years. *Ann Fam Med*. 2006;4(6):534-40.

4. Jones Cooper SN, Walton-Moss B. Using reminder/recall systems to improve influenza immunization rates in children with asthma. *J Pediatr Health Care*. 2013;27(5):327-33.
5. Szilagyi P, Vann J, Bordley C, Chelminski A, Kraus R, Margolis P, et al. Interventions aimed at improving immunization rates. *Cochrane Database Syst Rev*. 2002;(4):CD003941.
6. Szilagyi PG, Rodewald LE, Savageau J, Yoos L, Doane C. Improving influenza vaccination rates in children with asthma: a test of a computerized reminder system and an analysis of factors predicting vaccination compliance. *Pediatrics*. 1992;90(6):871-5.
7. Kemper KJ, Goldberg H. Do Computer-Generated Reminder Letters Improve the Rate of Immunization in an Urban Pediatric Population? *Am J Dis Child*. 1993;147(7):717-8.
8. Martin E. Improving influenza vaccination rates in a pediatric asthma management program by utilization of an electronic medical record. *Clin Pediatr (Phila)*. 2006;45(3):221-7.
9. Fiks AG, Hunter KF, Localio AR, Grundmeier RW, Bryant-Stephens T, Luberti AA, et al. Impact of electronic health record-based alerts on influenza vaccination for children with asthma. *Pediatrics*. 2009;124(1):159-69.
10. Venkat A, Chan-Tompkins NH, Hegde GG, Chuirazzi DM, Hunter R, Szczesiul JM. Feasibility of integrating a clinical decision support tool into an existing computerized physician order entry system to increase seasonal influenza vaccination in the emergency department. *Vaccine*. 2010;28(37):6058-64.
11. Pourat N, Lavarreda SA, Snyder S. Patient-centered medical homes improve care for adults with chronic conditions. *Policy Brief UCLA Cent Health Policy Res*. 2013;(PB2013-3):1-8.
12. Hadler JL, Yousey-Hindes K, Kudish K, Kennedy ED, Sacco V, Cartter ML, et al. Impact of requiring influenza vaccination for children in licensed child care or preschool programs—Connecticut, 2012-13 influenza season. *MMWR Morb Mortal Wkly Rep*. 2014;63(9):181-5.
13. Daley MF, Barrow J, Pearson K, Crane LA, Gao D, Stevenson JM, et al. Identification and recall of children with chronic medical conditions for influenza vaccination. *Pediatrics*. 2004;113(1 Pt 1):e26-33.
14. Gaglani M, Riggs M, Kamenicky C, Glezen WP. A computerized reminder strategy is effective for annual influenza immunization of children with asthma or reactive airway disease. *Pediatr Infect Dis J*. 2001;20(12):1155-60.
15. Lobach D, Sanders GD, Bright TJ, Wong A, Dhurjati R, Bristow E, et al. Enabling health care decision making through clinical decision support and knowledge management. *Evid Rep Technol Assess (Full Rep)*. 2012;(203):1-784.
16. Reichert TA, Sugaya N, Fedson DS, Glezen WP, Simonsen L, Tashiro M. The Japanese experience with vaccinating schoolchildren against influenza. *N Engl J Med*. 2001;344(12):889-96.
17. Kwong JC, Stukel TA, Lim J, McGeer AJ, Upshur REG, Johansen H, et al. The effect of universal influenza immunization on mortality and health care use. *PLoS Med*. 2008;5(10):e211.
18. Murphy EV. Clinical Decision Support: Effectiveness in Improving Quality Processes and Clinical Outcomes and Factors that May Influence Success. *Yale J Biol Med*. 2014;87(2):187-97.
19. Murphy PA, Frazee SG, Cantlin JP, Cohen E, Rosan JR, Harshburger DE. Pharmacy provision of influenza vaccinations in medically underserved communities. *J Am Pharm Assoc (2003)*. 2012;52:67-70.
20. Grijalva CG, Zhu Y, Simonsen L, Mitchel E, Griffin MR. The population impact of a large school-based influenza vaccination campaign. *PLoS ONE*. 2010;5(11):e15097.
21. Joshi AY, Iyer VN, Hartz MF, Patel AM, Li JT. Effectiveness of trivalent inactivated influenza vaccine in influenza-related hospitalization in children: a case-control study. *Allergy Asthma Proc*. 2012;33(2):e23-7.
22. Buyukiryaki B, Soyer OU, Erkokoglu M, Dogan A, Azkur D, Kocabas CN, et al. What a pandemic teaches us about vaccination attitudes of parents of children with asthma. *Vaccine*. 2014;32(20):2275-80.
23. Grohskopf LA, Olsen SJ, Sokolow LZ, Breesee JS, Cox NJ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP) -- United States, 2014-15 influenza season. *MMWR Morb Mortal Wkly Rep*. 2014;63(32):691-7.
24. Cooper White P, Baum DL, Ross H, Falletta L, Reed MD. Cocooning: influenza vaccine for parents and caregivers in an urban, pediatric medical home. *Clin Pediatr (Phila)*. 2010;49(12):1123-8.
25. Clark SJ, Lamarand K, Dombkowski KJ. Identifying children with chronic conditions for influenza vaccination using a statewide immunization registry: initial experiences of primary care providers. *J Public Health Manag Pract*. 2012;18(3):204-8.
26. Goodman DC, Stukel TA, Chang CH. Trends in pediatric asthma hospitalization rates: regional and socioeconomic differences. *Pediatrics*. 1998;101(2):208-13.