

Quality Improvement Initiative to Increase Influenza Vaccination in Pediatric Cancer Patients

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abstract



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Dr Freedman conceptualized and designed the study, performed the data analysis and interpretation of the data, and drafted and revised the manuscript; Dr Reilly conceptualized and designed the study, participated in analysis and interpretation of the data, and critically reviewed and revised the manuscript; Mrs Powell conceptualized and designed the study, drafted key parts of the manuscript, was critical in implementing our process changes in the clinical setting, and critically reviewed and revised the manuscript; Dr Bailey conceptualized and designed the study, was critical in implementing the electronic medical record aspects of our study, participated in analysis and interpretation of the data, drafted key parts of the manuscript, and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-0943

DOI: 10.1542/peds.2014-0943

Accepted for publication Sep 8, 2014

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

BACKGROUND: Pediatric patients with cancer face more severe complications of influenza than healthy children. Although Centers for Disease Control and Prevention guidelines recommend yearly vaccination in these patients, in our large academic center, <60% of oncology patients receiving chemotherapy were immunized at baseline. Our objective was to increase this rate through a multifaceted quality improvement initiative.

METHODS: Eligible patients were >6 months old, within 1 year of receiving chemotherapy, >100 days from stem cell transplant, and had ≥ 1 outpatient oncology visit between September 1, 2012, and March 31, 2013. Five interventions were instituted concomitantly: (1) family education: influenza/vaccine handouts were provided to families in clinic waiting rooms; (2) health informatics: daily lists of outpatients due for immunization were generated from the electronic medical record and sent automatically to triage staff and nurses; (3) outpatient clinic: patients due for vaccination were given colored wristbands during triage to alert providers; (4) inpatient: vaccine order was built into admission order set; and (5) provider education: staff education was provided at conferences on screening of patients, vaccine ordering, and documentation of refusals/contraindications.

RESULTS: The complete influenza immunization rate increased by 20.1% to 64.5%, and the proportion of patients receiving ≥ 1 dose of vaccination increased by 22.9% to 77.7%. Similar changes were noted across all cancer types, with highest rates of immunization in leukemia/lymphoma patients (86.8%) and lowest in patients after stem cell transplant (66.7%).

CONCLUSIONS: Technology, education, and multidisciplinary clinical process changes increased influenza vaccination rates. Ongoing efforts are targeting subgroups with lowest rates of immunization.

Vaccinations are a critical component of preventive health services provided to all children. For pediatric patients with cancer, targeted vaccinations are even more important. Notably, this group of patients is immunosuppressed from cancer itself, anticancer therapies, and stem cell transplants (SCTs), all of which contribute to decreased ability to mount a humoral and cellular immune response to the influenza virus.¹

Children receiving chemotherapy are at heightened risk of severe influenza infection and resulting complications, including prolonged hospitalization, worse pulmonary complications, and a greater rate of concurrent bacteremia than children without cancer or chronic conditions.¹⁻³ Those who have undergone allogeneic SCT are at even higher risk.^{4,5} Furthermore, influenza in these children may cause delay in planned anticancer therapy and can

contribute to poorer overall and event-free survival.^{1,6} In addition, from an infection prevention standpoint, immunization may also reduce risk of transmission among high-risk patients with more outpatient visits and inpatient admissions.

The immune response to vaccination in immunosuppressed patients has been widely debated and remains controversial. Most studies to date demonstrate suboptimal immunogenicity in pediatric oncology patients compared with healthy children.^{1,2,6-8} Seroconversion rates after vaccination are slightly better when vaccination occurs earlier in the course of anticancer therapy.⁹ There is also a varied response depending on the immunosuppressive extent of a patient's antineoplastic regimen, with particularly marked effects in patients undergoing SCT.^{8,9} In transplant patients, a recent study in adults found no difference in increased T-cell-mediated immunity in patients given 1 versus 2 doses of the vaccine posttransplantation, arguing that attention to providing ≥ 1 dose of the immunization in patients with cancer can produce significant benefit.⁵ Conversely, 2 recent pediatric studies demonstrated better immunogenicity in children with cancer after repeated doses and with use of higher adult doses.^{10,11} Although the response to vaccination may be suboptimal and the influenza vaccine imperfect, studies to date do demonstrate seroconversion and protection for children with cancer.¹

Current Centers for Disease Control and Prevention (CDC) guidelines recommend routine yearly influenza vaccination for all people ≥ 6 months of age, with emphasis on those who are immunosuppressed or have chronic illness.^{1,12,13} Patients who are < 9 years of age who have never been immunized against influenza should receive 2 doses, 1 month apart, which is associated with a better

immunologic response.^{12,14} Because the vaccine is safe and poses no risk of viral transmission, routine vaccination of the pediatric cancer population is recommended.^{1,15} The vaccine formulations are well tolerated, and serious complications are rare; severe allergy to the vaccine or 1 of its components is among the few contraindications to receiving the inactivated vaccination.¹⁶

For children with cancer at the large children's hospital in this study, historical rates of influenza vaccination were 53% to 56%. While staff must receive the vaccine as part of infection prevention efforts at the hospital, vaccination of patients was done at the discretion of individual providers, despite a general acceptance that vaccination is desirable. These children are seen frequently in outpatient clinic, allowing ample opportunity for vaccination, but reducing the urgency for vaccination at any 1 visit. The workflow in busy outpatient practices, changing immunization recommendations, and evolving computer-ordering interfaces, make it a challenge to ensure vaccination becomes standard practice.¹⁷ Previous vaccination efforts, including chart review and follow-up with providers for targeted disease groups yielded some improvement in subsets of patients but did not generalize effectively.

In response to this need, a quality improvement project to increase the rates of influenza vaccination in pediatric patients with cancer was undertaken. Similar initiatives have been successful in improving vaccination status in children and adults with chronic conditions¹⁸⁻²⁰ and those who are immunocompromised.^{1,21,22} Furthermore, computerized clinical decision support systems have been shown to greatly improve physician performance, and their increasing use makes this well suited for quality improvement initiatives.²³ We

therefore implemented a multifaceted initiative with concurrent interventions in the areas of clinical informatics, education, and multidisciplinary clinical process interventions to increase the rate of vaccination in the pediatric cancer population.

METHODS

Intervention

The intervention was deployed in the oncology inpatient unit and 3 outpatient clinic sites at the Children's Hospital of Philadelphia (CHOP) from September 1, 2012, to March 31, 2013. Patients targeted by the program included those who were ≥ 6 months of age, had a cancer or SCT diagnosis, and had received chemotherapy in the 365 days before their scheduled outpatient clinic visit (for laboratory evaluation, physical examination, or consultation) and/or were ≥ 100 days from SCT. Patients who were contraindicated by age, allergy, medical contraindication (determined by primary treating team), or being too close to SCT were excluded. Five distinct interventions were instituted concomitantly:

1. Parent/family education: educational interventions in the outpatient oncology clinic included posters reminding families about the importance of vaccination. More detailed educational materials in English and Spanish were made available for families in the waiting room and via the patient/family nurse educator (see Supplemental Information).
2. Clinical informatics: scheduling information for oncology clinics was retrieved daily from the EpicCare electronic medical record. Oncology treatment plan records and problem list entries were automatically scanned for each patient to identify patients ≥ 6 months old who had chemotherapy prescribed within the preceding 365 days and were ≥ 100 days

from SCT; these patients were classified as high risk for complications of influenza. Previously recorded doses of influenza vaccine, both administered in the CHOP network and captured from patient/parent report, were retrieved, and each patient's immunization history was compared by the program to the CDC 2012 guidelines for influenza immunization to determine whether an individual was fully immunized (all required doses received since July 1, 2012), partially immunized (CDC guidelines recommend 2 doses in current year, and only 1 dose received since July 1, 2012), or unimmunized (no doses received since July 1, 2012, regardless of previous immunization). Finally, allergy data were automatically screened for evidence of previous adverse reaction to influenza immunization or severe egg allergy (ie, reactions including respiratory symptoms, hemodynamic instability, or nausea/vomiting), and problem lists were screened for recorded influenza vaccine refusals in the current year; these patients were marked as not eligible for immunization regardless of their immunization history. Data were aggregated into a report color-coding patients due for first or second doses. This daily report was e-mailed to the clinic triage team and clinic nursing leadership, reviewed in preclinic conferences, and used in triage as described subsequently.

3. Outpatient clinic interventions: an effort was made to improve training of clinic support associates (CSAs), who are responsible for triaging patients. Education also focused on the provider team to identify patients needing vaccines through standardized questions. CSAs would reference the daily report during patient triage. If a patient appeared on the list as due for a vaccine dose, the CSA would then use the standard

screening questions to confirm that the patient had not yet received the vaccine. If the lack of vaccination was confirmed, the CSA then placed a bright yellow wristband on the patient. These bands served as a cue to providers to order the vaccine, or discuss and document refusals, during the clinical encounter.

4. Inpatient intervention: orders for influenza vaccination were built into admission order sets to trigger vaccination at discharge. Clinicians reviewed these ordering prompts and the patient's immunization history at admission to determine whether the patient required additional doses of vaccine.
5. Provider educational intervention: tutorials and information about the quality improvement initiative were presented at divisional conferences, clinic meetings, staff nurse meetings, and via reference material circulated by e-mail. Information distributed described the process of patient screening, correct ordering and dosing of vaccines, documentation of vaccine refusals and doses received elsewhere, and contraindications precluding vaccination (eg, history of severe aplastic anemia). Influenza vaccination rates were reported monthly at the divisional Quality Improvement Committee meetings to maintain momentum and awareness.

Outcomes

Rates of immunization were measured at the patient level, as

proportion of all patients meeting high-risk criteria at their last clinic visit and receiving none, some, or all recommended doses of influenza vaccine between September 1, 2012, and March 31, 2013. Results were compared with the year before (September 1, 2011–March 31, 2012). Patients who refused vaccination were considered unvaccinated. A test of proportions (Z-test) in Stata 12.1 (College Station, TX) was used to determine if proportions differed significantly between years, and χ^2 tests were used to compare vaccination across demographic parameters. Because this study comprised quality improvement work, it was not subject to review by the CHOP Institutional Review Board, consistent with institutional practice.

RESULTS

Cohort

The patients included in this analysis are shown in Table 1. The average age in both years was 10.5 years. There were no significant differences between the study years in patients' age or gender. There were significantly more patients with leukemia/lymphoma in 2012–2013 and significantly fewer who underwent SCT. The majority of patients each year had either hematologic (leukemia/lymphoma) or non-central nervous system solid tumor malignancies. There were no substantial changes in clinic structure, scheduling, or physician/nursing staff between study years.

TABLE 1 Baseline Characteristics of the Patient Population (N = 1128)

	2011–2012 (n = 480)	2012–2013 (n = 648)	P
Age, mean	10.5 y	10.5 y	.94
Gender, n (%)			
Female	218 (45.4)	284 (43.8)	.59
Male	262 (54.6)	364 (56.2)	.59
Disease, n (%)			
Leukemia/lymphoma	142 (29.5)	258 (39.8)	<.001
Solid tumors	165 (34.4)	187 (28.9)	.048
Brain tumors	121 (25.2)	164 (25.3)	.97
SCT	52 (10.8)	39 (6.1)	.003

Vaccination Rates and Demographics

Figure 1 demonstrates the improvements achieved by vaccination status. Over the 2-year period, the proportion of patients receiving all required doses of the vaccine increased by 20.1% ($P < .001$), with a corresponding decrease in completely unimmunized patients. There was no significant change in those receiving some, but not all, required doses of the vaccination. There were also no differences in vaccination rates by gender in either year. As Table 2 demonstrates, partial vaccination in those <9 years old did not account for a significant fraction of our overall improvement.

Diagnosis Subtypes

The inpatient unit and primary outpatient clinic site are divided into 4 separate services, each with a distinct group of clinicians, according to patients' cancer diagnoses. Figure 2 demonstrates the proportion of patients receiving ≥ 1 dose of vaccination, separated by disease subtype. The proportion of

patients receiving ≥ 1 dose of vaccine in 2012–2013 increased 22.9% ($P < .001$). The vaccination rate in patients with leukemia/lymphoma, which started at a higher baseline than other disease groups, rose by only 16.4% ($P < .001$). Conversely, for patients with solid tumors, who had the lowest baseline rate, the increase was 26% ($P < .001$), with an intermediate rise of 21.7% ($P < .001$) for patients with brain tumors. Although immunization increased in patients who had undergone a SCT, the difference did not reach significance.

For patients with leukemia/lymphoma, who again had the highest baseline rate, the rise in the number of patients receiving all recommended doses of vaccine was 15.3% ($P < .001$). Rates for those with a solid tumor rose by 23% ($P < .001$), whereas for those with a brain tumor, rates increased by 16.3% ($P = .006$). Again, there was no statistically significant increase in complete vaccination in SCT patients.

Unvaccinated Patients

Vaccines were refused or deferred in 1.8% of patients in 2011–2012 and 2.9% of patients in 2012–2013 ($P = .2$). Parent refusal was the most common reason for nonvaccination, accounting for 70% of refusals in 2011–2012 and 85% in 2012–2013. Providers deferring vaccination was rare and typically reflected either a decision to avoid immune stimulation, a medical contraindication, or a known history of severe aplastic anemia, for which recurrence after influenza immunization has been documented.²⁴

Timing of Vaccination

Figure 3 describes the vaccination process over the study periods, with each time point reflecting the proportion of patients seen in the previous 2 weeks who were immunized. A more rapid rate of vaccination, and greater overall proportion of patients vaccinated, can be appreciated in the 2012–2013 intervention period compared with 2011–2012.

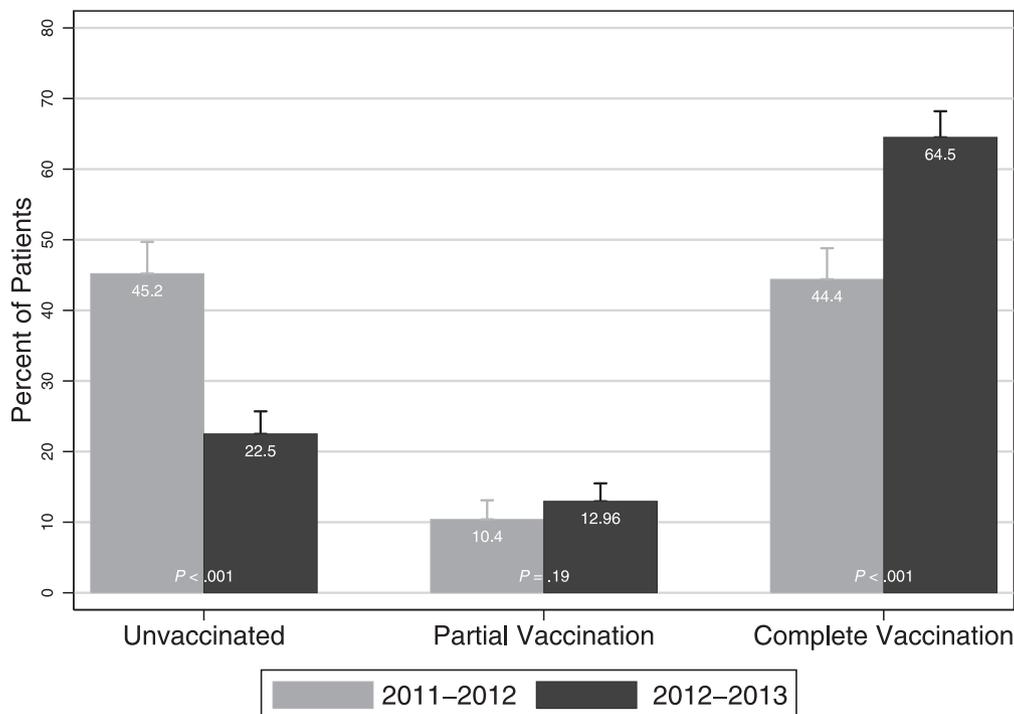


FIGURE 1

Influenza vaccination rates 2011–2012 versus 2012–2013 by immunization status.

TABLE 2 Change in Vaccination Rates by Age Group

Vaccination Status	Age ≤9 y				Age >9 y			
	2011–12	2012–13	% Change (95% CI)	P	2011–12	2012–13	% Change (95% CI)	P
Unvaccinated	47.2%	21.0%	−26.2% (−18.3 to −34.0)	<.001	43.4%	24.0%	−19.4% (−11.7 to −27.1)	<.001
Partial	21.8%	26.3%	+4.5% (2.7 to 11.7)	.23	—	—	—	—
Complete	31.0%	52.7%	+21.7% (13.5 to 29.8)	<.001	56.6%	76.0%	+19.4% (11.7 to 27.1)	<.001

CI, confidence interval; —, not applicable.

DISCUSSION

Many initiatives have aimed to close the gap in influenza vaccination in immunocompromised adults and children with chronic conditions, but to our knowledge, none have focused exclusively on the pediatric cancer population.^{19–22,25} This program, employing a multifaceted intervention, demonstrated that combining health information technology, education, and clinical process changes is feasible and can successfully lead to increased rates of influenza vaccination in pediatric patients with cancer. Given conflicting data on the number of influenza vaccines immunocompromised patients ought to receive, the primary end point chosen was proportion of patients receiving ≥1 dose of the

vaccine. Nonetheless, the increases in at least partially and completely vaccinated patients were similar. The improvement seen was largely due to the significant decrease in those patients remaining unvaccinated, which fell from 45.2% to 22.5%. Because significant improvements were seen across all tumor subtypes, higher baseline rates of vaccination in the leukemia/lymphoma patients cannot account for all of the changes we saw. It is not surprising that the strongest momentum of vaccination is within the first 2 months of vaccine availability. It is noteworthy, however, that the process improvements encouraged vaccination earlier in the season.

Each process change addressed a gap in the vaccination process. The

education of patients and families added to their understanding of why vaccination was crucial. Education of the triage team and providers improved the screening process and helped to identify those who needed vaccine, those who had already received it somewhere else, and how to document accordingly. Use of bright yellow wristbands provided a visual cue to the provider and nurse to spark a dialogue about the influenza vaccination with the patient and family. The daily computer-generated list of clinic patients in need of the vaccine served as a reference for triage staff and nurses to minimize missed opportunities to identify candidates for immunization and facilitated practitioners in ordering the vaccine when necessary.

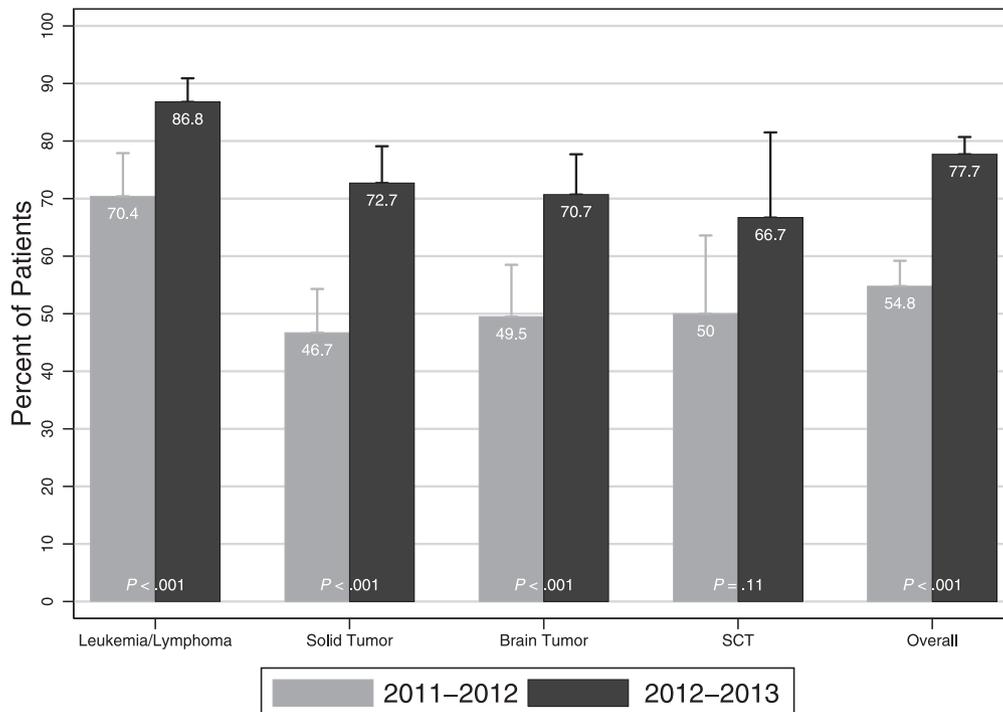


FIGURE 2 Proportion of patients receiving ≥1 influenza vaccination per year by disease group.

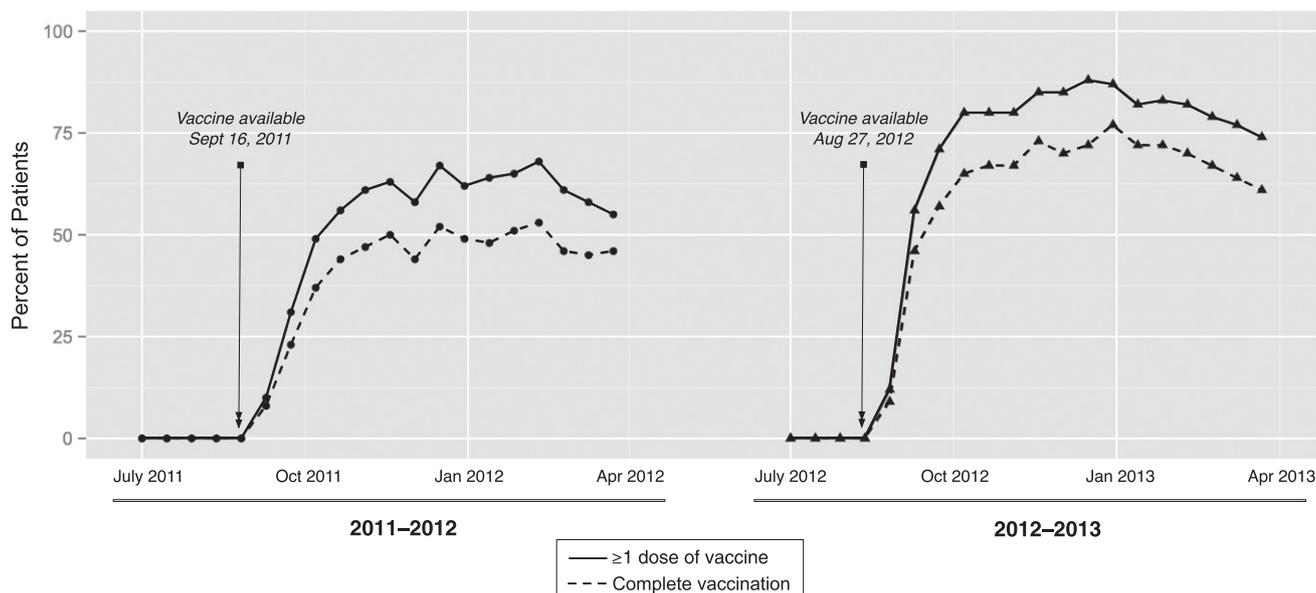


FIGURE 3 Influenza vaccination rates over time in 2011–2012 versus 2012–2013. Each point reflects the vaccination rates of all eligible patients in the preceding 2 weeks.

Use of a standardized set of orders when patients were being admitted to the hospital facilitated vaccination to those patients at some point before discharge. Interestingly, in both 2011–2012 and 2012–2013, 90% of all vaccines were delivered in the outpatient clinic. Therefore, our continued efforts should focus primarily on our outpatient setting, where the greatest number of opportunities for vaccination exists.

A major component of success here was based on involvement of a diverse care team and continuous involvement of physician and nursing champions in both inpatient and clinic settings, as well as the triage and nursing teams who facilitated communication about the flu and each child’s needs among patients, families, and the providers. This teamwork, with overlapping process improvements, aided the momentum of the initiative.

Given the low rates of severe clinical infection even in this at-risk population, determining the effect of vaccination status on rates of serious influenza illness, hospitalization, or postinfluenza outcomes would require follow-up of a larger

population than available to detect significant differences. Our study therefore used immunization rates as a surrogate measure to characterize the impact of the intervention. Additional work on a multiinstitutional scale will be necessary to assess the impact of increased vaccination on these outcomes.

Those patients who remained unvaccinated reflect a variety of clinical situations. Refusals by parents or providers constituted a minority of cases. Other likely contributors include fewer clinic visits in off-therapy patients, patients who became age eligible toward the end of the initiative, those nearing the end of life, and those who were seen as consults or second opinions in our clinic once, all of which reduced opportunities for immunization. Not surprisingly, our experience suggests that children who remained unimmunized had fewer clinic visits overall.

There are always substantial practical challenges inherent in quality improvement initiatives. Instituting several process changes at once may lead to greater success than a separate pilot of each measure but makes it more difficult to identify

specific changes with greatest impact. However, given the value of the influenza vaccine, a more rapid process improvement that instituted all modalities for change simultaneously was most appropriate. Each component targeted a workflow aspect critical to a successful vaccination program; these process changes are entwined and reliant on each other for successful screening and vaccination.

Keeping these limitations in mind, this project has several important implications. Such projects are clearly feasible and can be accomplished with moderate resources. Components of this work can be easily adapted for use by other subspecialty practices and institutions. This initiative also highlights the importance of standardization and repetition to ensure compliance with, and sustainability of, new process changes. Increasing demands and time constraints with limited clinical support make adding new processes challenging in any setting; interventions that reduce the need for clinicians to seek out relevant information for each patient

contribute to increased effectiveness. Continued reminders and education throughout the season were necessary to sustain the improvement, which also emphasizes the importance of encouraging immunization during early, eligible visits and not deferring vaccination to a later point.

CONCLUSIONS

A multifaceted intervention combining clinical informatics, education, and clinical process changes was feasible and led to a successful increase in the rate of influenza vaccination in at-risk pediatric patients with cancer at a large academic medical center. Efforts are ongoing to improve these rates further, targeting disease groups with the lowest overall vaccination rates (solid tumor and brain tumor).

ACKNOWLEDGMENTS

We thank the providers, triage staff, oncology nursing team, and patients at the Children's Hospital of Philadelphia for their hard work and collaboration on this project.

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DOI: 10.1542/peds.2014-0943 originally published online January 12, 2015;

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