Improving Influenza Testing and Treatment in Hospitalized Children

Ashley Murphy, MD,a Mary Lou Lindegren, MD, MPH,b William Schaffner, MD, David Johnson, MD, Lindsay Riley, MSN, APRN,c James D. Chappell, MD, PhD,c Joshua D. Doyle, MD, Anna Kate Moen, MD, Grant P. Saxton, MD, Rahul P. Shah, MD,c Derek J. Williams, MD, MPHb

OBJECTIVES: National guidelines recommend influenza testing for children hospitalized with influenza-like illness (ILI) during influenza season and treatment of those with confirmed influenza. Using quality improvement methods, we sought to increase influenza testing and treatment of children admitted to our hospital medicine service with ILI from 65% to 90% during the 2014–2015 influenza season.

METHODS: We targeted several key drivers using multiple plan-do-study-act cycles. Interventions included awareness modules, biweekly flyers, and failure tracking. ILI admissions (fever plus respiratory symptoms) were reviewed weekly once surveillance data revealed elevated influenza activity. Appropriate testing and treatment of ILI was defined as influenza testing and/or treatment within 24 hours of admission unless a known cause other than influenza was present. We used statistical process control charts to track progress using established quality improvement methods. Appropriate testing and treatment was also assessed in the 2016–2017 influenza season by using similar methods, although no new interventions were introduced.

RESULTS: For the 2014–2015 season, appropriate testing and treatment increased from a baseline mean of 65% to 91% within 3 months. For the 2016–2017 season, appropriate testing and treatment remained at a mean of 80% throughout the influenza season.

CONCLUSIONS: Appropriate influenza testing and treatment increased to 90% in children with ILI during the 2014–2015 season. Improvements were sustained in a subsequent influenza season. Our initiative improved recognition of influenza and likely increased treatment opportunities. Future work should be focused on wider implementation and further reducing variation.
Acute respiratory illnesses account for more pediatric hospitalizations in the United States than any other condition in childhood.\(^1\)\(^,\)\(^2\) Viruses cause the vast majority of these illnesses. Among these, the influenza virus is notable both because of its associated morbidity\(^3\)\(^-\)\(^6\) and because it is the only respiratory virus with effective prevention and treatment options. Differentiating influenza from other respiratory viruses, however, is difficult on the basis of clinical features alone.\(^7\) Diagnostic tests for influenza are widely available, and their use is associated with reduced antibiotic use and increased use of influenza antiviral therapy.\(^8\)\(^,\)\(^9\) Positive influenza test results have also been shown to significantly decrease additional diagnostic testing such as blood cultures or chest radiographs.\(^7\) Unfortunately, testing is often underused among hospitalized children, and the diagnosis of influenza frequently goes undetected.\(^9\)

The use of influenza antiviral agents is associated with better outcomes in persons hospitalized with influenza.\(^9\)\(^-\)\(^11\) Guidelines from the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics recommend antiviral treatment as soon as possible for all children hospitalized with confirmed or suspected influenza.\(^11\)\(^-\)\(^12\) Despite these recommendations, antiviral use is variable even when influenza is confirmed. In 1 study, researchers found that antiviral use in children hospitalized with a diagnosis of influenza across 46 children’s hospitals between 2009 and 2014 ranged between 38% and 83% across hospitals.\(^13\) Another study conducted at our own institution and 2 others during the influenza season revealed that only one-third of children hospitalized with laboratory-confirmed influenza (tested per study protocol) had an influenza test performed for clinical care, and only 28% had a discharge diagnosis of influenza.\(^8\) This latter study, along with our collective clinical experience, identified an important gap in the management of children hospitalized with influenza-like illness (ILI) at our institution. To address this gap, we conducted a quality improvement (QI) initiative with which we sought to increase the identification and treatment of influenza among children hospitalized with ILI.

**METHODS**

**Setting**

Our institution is a 271-bed, freestanding children’s hospital in Nashville, Tennessee, with >50,000 emergency department (ED) visits and >15,000 hospitalizations annually. In 2015, the division of hospital medicine provided general pediatric care for >4000 hospitalized infants and children, representing 70% of all inpatient general pediatric care. The hospital medicine service is run by 2 teams; each is staffed by an attending physician from the division of hospital medicine (rotating weekly), 2 resident physicians from pediatrics or medicine-pediatrics, and 4 to 5 interns (rotating monthly). Influenza tests available include rapid antigen, polymerase chain reaction (PCR), and viral culture. For hospitalized children, all negative rapid antigen tests reflex to respiratory virus shell vial culture with direct immunofluorescence confirmation unless the clinician separately orders molecular respiratory viral testing or respiratory viral culture, in which case shell vial culture is deferred.

**Improvement Team**

Our multidisciplinary team included faculty and staff from hospital medicine, emergency medicine, infection control, pathology, microbiology and immunology, and the pediatric residency program. The team met weekly for the duration of the project and was responsible for all aspects of the work, including developing a specific, measurable, achievable, realistic, and timely (SMART) aim; identifying key drivers; organizing and implementing interventions; and collecting data.\(^14\)

Over the course of the 2014–2015 influenza season, we sought to increase appropriate influenza testing and treatment of children <18 years of age admitted to hospital medicine services with ILI from a baseline of 65% (October to November 2014) to 90% during the period that influenza was prevalent in the local community. ILI was defined as fever >38.0°C plus 1 or more respiratory symptoms (cough, sore throat, wheezing, rapid breathing, etc). Influenza was considered prevalent when weekly data revealed elevated influenza activity, defined as consecutive weeks with multiple positive influenza tests.

Appropriate testing and treatment was defined as (1) influenza testing (rapid antigen or PCR) or use of an influenza antiviral (oseltamivir) within 24 hours of admission for any child with ILI unless a known cause other than influenza (eg, positive detection of respiratory syncytial virus (RSV)) or a clear alternative diagnosis (eg, retropharyngeal abscess) was present and (2) use of an influenza antiviral for any child with a positive influenza test.

**Key Drivers and Interventions**

Key drivers targeted emergency department and hospital medicine providers and included knowledge of local influenza prevalence, consistent recognition of ILI, and knowledge and acceptance of CDC recommendations for influenza testing and treatment in hospitalized children (Fig 1). Interventions targeting each of the key drivers were tested in multiple plan-do-study-act cycles before final implementation.\(^14\)

**Biweekly ILI E-mail Alert and Flyers**

Our first intervention was an ILI e-mail alert that included information regarding local influenza prevalence and influenza testing and treatment recommendations as outlined by the CDC. Content was developed by members of the improvement team and revised in an iterative fashion on the basis of provider feedback. As the project progressed, our control chart was added. The alert was distributed to hospital medicine and emergency providers. Although most providers appreciated the communications, several noted that they do not check e-mail frequently and preferred other forms of communication.

This led to the development of a paper flyer that included content similar to the e-mail alert. These were posted in provider workrooms in the inpatient areas and in the ED. Additional plan-do-study-act cycles were focused on optimizing delivery of the flyer to providers. For example, in the ED, we reduced the size and content of the flyer.
such that it could be posted on provider workstations (Fig 2). Later, we added this information to the ED’s QI Data Corner, which was an initiative separate from the project to centralize reporting of QI activities in the ED.

**Awareness Modules**

Awareness modules were created to increase the visibility of our project, educate providers regarding guideline recommendations for influenza testing and treatment, and engage with providers face-to-face to identify and address challenges. We identified several areas for improvement, including identifying children with ILI and high-risk groups, knowledge regarding availability and test characteristics of influenza diagnostics at our institution, and addressing a perceived lack of efficacy of antiviral agents after 48 hours of symptoms. In these modules, we targeted hospital medicine and ED providers as well as the pediatric house staff, and modules were facilitated by a member of the improvement team during regularly scheduled conferences.

**Failure Feedback**

The final intervention centered on engaging providers when influenza testing or treatment was not ordered in children with ILI (failures). For this, the hospital medicine attending for the preceding week was contacted by e-mail and asked to review and comment on failures. Feedback received was discussed by the study team and mapped to 3 key drivers by group consensus: provider knowledge of local influenza prevalence, consistent recognition of ILI, and knowledge of testing and treatment guidelines (Table 1).

**Data Collection**

During the 2014–2015 season, all ILI admissions to the hospital medicine service were reviewed via the electronic medical record on a weekly basis. Data were...
among 374 eligible ILI admissions included, and the remaining 10 children who were influenza positive. Five children (2%) were prescribed antiviral therapy on the basis of clinical suspicion alone.

2016–2017 Season
Among 409 eligible ILI admissions, appropriate influenza testing and treatment was documented in 334 children (82%) overall, including 260 children with influenza testing performed, 72 children with a clear alternative diagnosis, and 2 children who received empirical treatment without testing. In addition, the mean percentage of children with appropriate testing and treatment remained at 80% throughout the influenza season (Fig 4).

Of the 260 children with testing performed, influenza was identified in 43 children (17%). Of these, 29 (67%) received influenza treatment within 24 hours of hospitalization. Of the remaining 14 children who did not receive treatment within 24 hours, 12 had an initial negative rapid antigen test with a subsequent positive influenza test after the first 24 hours, 1 had a positive rapid antigen test but had previously completed treatment, and 1 child had a positive rapid antigen test but had stopped treatment because of concern for drug allergy. Only 6 children (2%) received empirical antiviral therapy without documented influenza.

DISCUSSION
By using QI methods, appropriate influenza testing and treatment of children hospitalized with ILI at our institution increased from a baseline of 65% to 91% over a single influenza season and from a historical mean of ~33%. In a subsequent season when no new interventions were implemented, appropriate testing and treatment remained at a mean of 80% throughout the season. Antivirals were consistently prescribed in children with influenza detected but rarely prescribed empirically.

Similar to other studies, empirical treatment of suspected influenza in the absence of a positive confirmatory test was low; only 2% of children receiving antiviral treatment were treated on the basis of
clinical suspicion alone. Many respiratory illnesses in hospitalized children have similar presentations and there may be hesitation to provide antiviral agents empirically when the specific etiology is unknown. In addition, antiviral treatment is more likely to be given in those with a positive influenza test. Hence, our interventions primarily emphasized use of influenza testing, although it is likely that this also led to more frequent use of antiviral agents.

Our interventions targeted several key drivers. One of the primary reasons influenza testing was not performed was because of unawareness of local influenza prevalence. When reviewing failures, providers expressed a belief that the influenza season had already passed. Prevalence of other viruses also influenced testing for influenza; for example, when RSV was perceived to be highly prevalent, influenza was less often considered in the differential diagnosis. Additionally, although accurate influenza surveillance data at both the state and national levels were easily accessible, knowledge of influenza prevalence was low. Delivering this information directly to providers was useful and likely helped to reduce cognitive bias because we observed increases in testing after the implementation of interventions in which provider awareness was targeted. Future efforts should be focused on timely delivery of viral surveillance information to providers at the point of care and embedded within provider workflows as demonstrated by the Germ Watch study, whose researchers sought to increase provider awareness of common circulating respiratory pathogens.

Additional reasons for lack of influenza testing involved provider misconceptions regarding appropriateness of influenza testing or treatment and lack of awareness of guideline recommendations. Per CDC and American Academy of Pediatrics guidelines, influenza testing and treatment should be considered for high-risk patients with ILI. This includes all children requiring hospitalization regardless of duration of symptoms because several studies have revealed that antiviral use is associated with reduced complications and better outcomes. Many providers, however, were unaware that influenza treatment was recommended beyond 48 hours of symptom onset. Of particular concern is that providers may fail to consider influenza in high-risk populations admitted with ILI, such as children with asthma. In these children, management may center on treating the acute exacerbation of the chronic illness while failing to fully consider triggers such as influenza. Although education is a useful initial strategy to address these challenges,
future efforts will likely require more reliable interventions targeting consistent recognition of ILI, such as an alert embedded within the electronic health record to flag children with ILI and prompt providers regarding management. A perceived lack of efficacy of influenza antiviral agents and concerns regarding side effects may also contribute to low empirical antiviral use and apathy toward testing. Indeed, both of these were concerns raised during our study. Unfortunately, data from randomized controlled trials regarding the efficacy of influenza antiviral agents in hospitalized children are lacking. Observational studies in both adults and children, however, revealed that oseltamivir is well tolerated, associated with shorter hospitalizations, and may reduce mortality. These recommendations, while also acknowledging the need for additional studies in which the use of antiviral agents among hospitalized children is evaluated, likely facilitated provider buy-in for our improvement initiative.

Lack of access to rapid and highly sensitive diagnostics for influenza may also decrease adherence to testing and treatment recommendations. Although rapid antigen testing is widely available, low sensitivity is a problem. At our institution, negative rapid antigen tests reflex to shell vial culture with direct immunofluorescence for hospitalized patients. We discovered that provider knowledge of this practice was limited. In addition, although this combined approach improves sensitivity, reliance on culture-based methods means results are often not available for 24 to 48 hours. In contrast, influenza PCR testing of upper respiratory tract samples is highly sensitive and specific, and results are often available in 24 hours or less. At our institution, however, influenza PCR testing was most often coupled with multiplex panels, which substantially increases costs. Researchers examining the clinical usefulness of expanded viral molecular diagnostics for children hospitalized with acute respiratory illness have demonstrated varying results. Although some researchers suggest that these tests may reduce antibiotic use or otherwise improve patient care, others have demonstrated little impact. These conflicting results, coupled with the added costs for multiplex PCR testing, may have led some providers to forego influenza testing. Education regarding the institutional availability and reduced cost of influenza monoplex versus multiplex PCR testing, as well as interventions to couple diagnostic testing with decision-support strategies, are needed to further improve the management of children hospitalized with ILI.

FIGURE 4 Percent of children hospitalized with ILI with appropriate testing and treatment within 24 hours, 2016–2017 influenza season.

![Graph](https://example.com/graph.png)
An important limitation of our study is the possibility that increased testing of influenza was independent of our improvement efforts. For instance, there may be an inclination for increased influenza testing as the respiratory viral season progresses. Influenza testing did increase, however, with our weekly initiatives in January through March of the 2014–2015 season despite a relatively stable prevalence of influenza. The association of the centerline shifts with our interventions increases our confidence that the interventions were associated with the changes in provider behavior. In addition, in a subsequent influenza season when no new interventions were implemented, appropriate testing and treatment remained at a mean of 80%. This further supports the conclusion that our previous work led to sustained improvement. Nonetheless, although we reached our target of 90% appropriate testing and treatment in the first season, important variability remained as noted by the special cause variation observed in March and April 2015. Each of the deployed interventions required few resources, which allowed for rapid implementation and adaptation but also suffered from low reliability. Future plans include the development of an electronic decision support tool embedded within the electronic health record to deliver real-time influenza prevalence data along with recommendations for testing and treatment.

CONCLUSIONS

Our study reveals the capacity of QI strategies to increase appropriate testing and treatment of children hospitalized with ILI. Important key drivers included real-time knowledge of local influenza prevalence, consistent recognition of ILI, and knowledge of testing and treatment guidelines. We anticipate continuing these improvement efforts in future influenza seasons and spreading to other units at our institution to further improve care for children hospitalized with ILI.

REFERENCES


### Improving Influenza Testing and Treatment in Hospitalized Children

Ashley Murphy, Mary Lou Lindegren, William Schaffner, David Johnson, Lindsay Riley, James D. Chappell, Joshua D. Doyle, Anna Kate Moen, Grant P. Saxton, Rahul P. Shah and Derek J. Williams

*Hospital Pediatrics* 2018;8;570

DOI: 10.1542/hpeds.2017-0223 originally published online August 14, 2018;

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at: <a href="http://hosppeds.aappublications.org/content/8/9/570">http://hosppeds.aappublications.org/content/8/9/570</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplementary Material</td>
<td>Supplementary material can be found at: <a href="http://hosppeds.aappublications.org/content/8/9/570#BIBL">http://hosppeds.aappublications.org/content/8/9/570#BIBL</a></td>
</tr>
<tr>
<td>References</td>
<td>This article cites 22 articles, 5 of which you can access for free at: <a href="http://hosppeds.aappublications.org/content/8/9/570#BIBL">http://hosppeds.aappublications.org/content/8/9/570#BIBL</a></td>
</tr>
<tr>
<td>Subspecialty Collections</td>
<td>This article, along with others on similar topics, appears in the following collection(s):</td>
</tr>
<tr>
<td></td>
<td><strong>Infectious Disease</strong> <a href="http://www.hosppeds.aappublications.org/cgi/collection/infectious_diseases_sub">http://www.hosppeds.aappublications.org/cgi/collection/infectious_diseases_sub</a></td>
</tr>
<tr>
<td></td>
<td><strong>Influenza</strong> <a href="http://www.hosppeds.aappublications.org/cgi/collection/influenza_sub">http://www.hosppeds.aappublications.org/cgi/collection/influenza_sub</a></td>
</tr>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="http://www.hosppeds.aappublications.org/site/misc/Permissions.xhtml">http://www.hosppeds.aappublications.org/site/misc/Permissions.xhtml</a></td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online: <a href="http://www.hosppeds.aappublications.org/site/misc/reprints.xhtml">http://www.hosppeds.aappublications.org/site/misc/reprints.xhtml</a></td>
</tr>
</tbody>
</table>
Improving Influenza Testing and Treatment in Hospitalized Children
Ashley Murphy, Mary Lou Lindegren, William Schaffner, David Johnson, Lindsay Riley, James D. Chappell, Joshua D. Doyle, Anna Kate Moen, Grant P. Saxton, Rahul P. Shah and Derek J. Williams
Hospital Pediatrics 2018;8:570
DOI: 10.1542/hpeds.2017-0223 originally published online August 14, 2018;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hosppeds.aappublications.org/content/8/9/570