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A Quality Improvement Approach to Influence Value-based Mucolytic Use in the PICU

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Abstract

Introduction: High-cost medication administration, despite lacking evidence for use, results in poor healthcare value. This work aimed to reduce dornase-alfa utilization in critically ill mechanically ventilated children. **Methods:** The project employed an observational pre-post design to develop a value-based clinical pathway to guide provider choice in mucolytic utilization in a quaternary pediatric intensive care unit. This pathway was designed to continue using low-cost mucolytic aerosols (hypertonic saline, N-acetylcysteine) but decrease new starts and total doses per 100 patient days (P100PD) dornase-alfa among patients for whom there is little to no supporting evidence. Interventions included a departmental journal club for fellow and attending physicians and a rolling introduction of the pathway to residents and respiratory therapists. Control charts serially tracked ordering changes and location-specific dornase alfa orders. **Results:** New dornase-alfa starts P100PD decreased by 53% (1.17–0.55), and total doses P100PD decreased by 75% (16–4). N-acetylcysteine ordering more than doubled; however, total doses of P100PD remained unchanged after the intervention. The use of 3% sodium chloride increased significantly from 0.28 to 4.15 new starts and 4.37 to 38.84 total doses P100PD. Mechanical ventilation days P100PD decreased, suggesting there were no measured adverse effects of pathway implementation. The reduction in dornase-alfa utilization resulted in a cumulative and sustained 59% mucolytic cost reduction ($2183.08–$885.77 P100PD). **Conclusion:** A clinical pathway prioritizing pharmacoeconomics when evidence for use is lacking can improve health care value without adversely affecting patient outcomes. *(Pediatr Qual Saf 2021;6:e438; doi: 10.1097/pq9.0000000000000438; Published online July 28, 2021.)*

INTRODUCTION

Mucolytic aerosols, including hypertonic (3%) saline, N-acetylcysteine, and dornase alfa, are used in the pediatric intensive care unit (PICU) to optimize mucociliary clearance in intubated and noninvasively mechanically ventilated patients. Providers may choose to order these medications based on suctioned mucus characteristics, worsening oxygenation, increased atelectasis on standard radiography, or due to other patient-specific factors.[1] There are no specific guidelines for their use in the PICU, nor are there clear superiority metrics.[2,3] However, significant variability in cost creates the potential for excessive resource utilization in the face of limited efficacy data.

Dornase alfa can be effective in mucociliary clearance and decreasing mechanical ventilation duration in children.[4] Many patients with CF use dornase alfa as a cornerstone for pulmonary toilet daily. Limited reports also describe the use of dornase alfa in patients with plastic bronchitis, a lymphatic flow disorder, following cardiac surgery,[5] and in the setting of sickle-cell-disease–mediated acute chest syndrome compared with other mucolytics.[6–8] Others have demonstrated efficacy when dornase alfa is used during and immediately before extracorporeal membrane oxygenation (ECMO) decannulation as a means of lung recruitment.[9]

In comparison studies of critically ill newborns with radiographic atelectasis, hypertonic saline led to chest radiograph improvement after each treatment of hypertonic saline. At the same time, dornase-alfa required a full 3-day treatment before radiographic findings improved.[10] In this same study, oxygen saturations improved significantly in the hypertonic saline group compared to the dornase alfa group. Intubated critically ill adults have not demonstrated chest radiograph improvement with the use of dornase alfa compared with normal and hypertonic

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saline; they show no significant difference in P/F ratios extubation and airway pressures while requiring mechanical ventilation.[11]

In our unit, bronchiolitis, complicated and uncomplicated bacterial and viral pneumonia, and atelectasis secondary to mucus plugging have a far greater incidence than CF, plastic bronchitis, and ECMO cannulation. High resource expenditure is associated with the frequent use of dornase alfa in this population. This project aimed to reduce dornase alfa use outside of specific patient populations for which data exist to support its use. We hypothesized dornase alfa utilization, as measured by new starts and total doses per 100 patient days (P100PD), would be reduced by 40% after clinical pathway implementation while not increasing patient ventilator days.

MATERIALS AND METHODS

Needs Assessment and Pathway Development

Annual evaluation of medication cost in their contribution to care in our unit highlights high expenditure therapeutics. Dornase alfa has been a perpetually high expenditure drug. When comparing the 3 most commonly used mucolytics in our unit (hypertonic saline (3%), N-acetylcysteine, dornase alfa), there is a nearly logarithmic increase in their cost. Additionally, the cost of dornase alfa has risen by 426% to our hospital in the last 20 years.

The literature review described in the introduction suggested the exclusion of specific patient populations from pathway utilization. These included patients with cystic fibrosis (CF) or patients with plastic bronchitis in the context of sickle cell disease, in addition to patients with severe hypoxemia with an oxygenation index > 15 and/or undergoing recruitment maneuvers while supported by ECMO. Given the low frequency of these populations in our unit, we hypothesized there would be a significant opportunity for cost savings with decreased use of dornase alfa, even if this is associated with a concurrent increase in other mucolytics.

A multidisciplinary team consisting of an attending physician, a fellow physician, and 2 pharmacists, reviewed the evidence and developed a clinical pathway to reduce dornase alfa use in our unit with the plan to disseminate the information in various educational settings. The inclusion of the lead respiratory therapy in pathway preparation before unit rollout insured buy-in. Our key driver diagram targeted our specific aims (Fig. 1).

Ethical Considerations

This quality improvement project focused on improving mucolytic value in the PICU. Guidelines were evidence-based, and no comparative effectiveness analyses were undertaken. The project did not involve randomization of patients, and mucolytic prescription remained at the attending provider's discretion. Access to protected health information was limited to clinical and quality improvement staff and undertaken as part of their respective roles and scope of practice. For these reasons, the project does not meet the definition of human subjects research; therefore, institutional review board approval was not required.

Ordering

Implementation of a specific electronic medical record order improved tracking of dornase alfa ordering. The order "timed out" after 24 hours and defaulted to twice-daily dosing. However, this order could change at a provider's discretion. For the second PDSA cycle, the clinical algorithm recommended a maximum of twice-daily dosing.

Education

PICU attendings and fellows: A single-subject journal club reviewed the use of mucolytics in non-CF intubated and noninvasively mechanically ventilated patients, including continuous and bilevel positive airway pressure (CPAP and BiPAP, respectively) and high flow nasal cannula. Description of the economic implications of using these medications on a unit-wide level demonstrated their strain and misuse. Subsequent clinical pathway postings encouraged all ICU practitioners to utilize the pathway as able.

Residents: Residents rotate through our unit every 4 weeks. At the start of each rotation, clinical pharmacists provided an orientation lecture that included a description of the mucolytic pathway and guidance on implementation.

Pharmacists and respiratory therapists: During patient care rounds, pharmacists inquired about the utilization of dornase alfa. They provided a review of the pathway, and they discussed cost with providers during order review as appropriate.

Respiratory Therapists: Often, respiratory therapists and nurses are the first to notice a significant change in secretions and are usually the first to suggest a mucolytic to a patient's regimen. PICU respiratory therapy leadership was included in the pathway's development and received ongoing encouragement for its use with the posting of the pathway in their workroom.

PDSA Cycle #1

Plan-do-study-act (PDSA) cycle 1 included the review of high-cost drugs in the unit and selection of dornase alfa as a target for intervention, literature review of mucolytics to assess alternatives and indications, and development and implementation of the clinical pathway (Fig. 2) and electronic medical record order followed by post-intervention mucolytic utilization assessment and associated cost compared with the baseline period.

PDSA Cycle #2

After reviewing the data from PDSA cycle 1, we observed dornase alfa prescription at dosing above the FDA labeling twice daily.[12] Initial dornase alfa ordering for longer

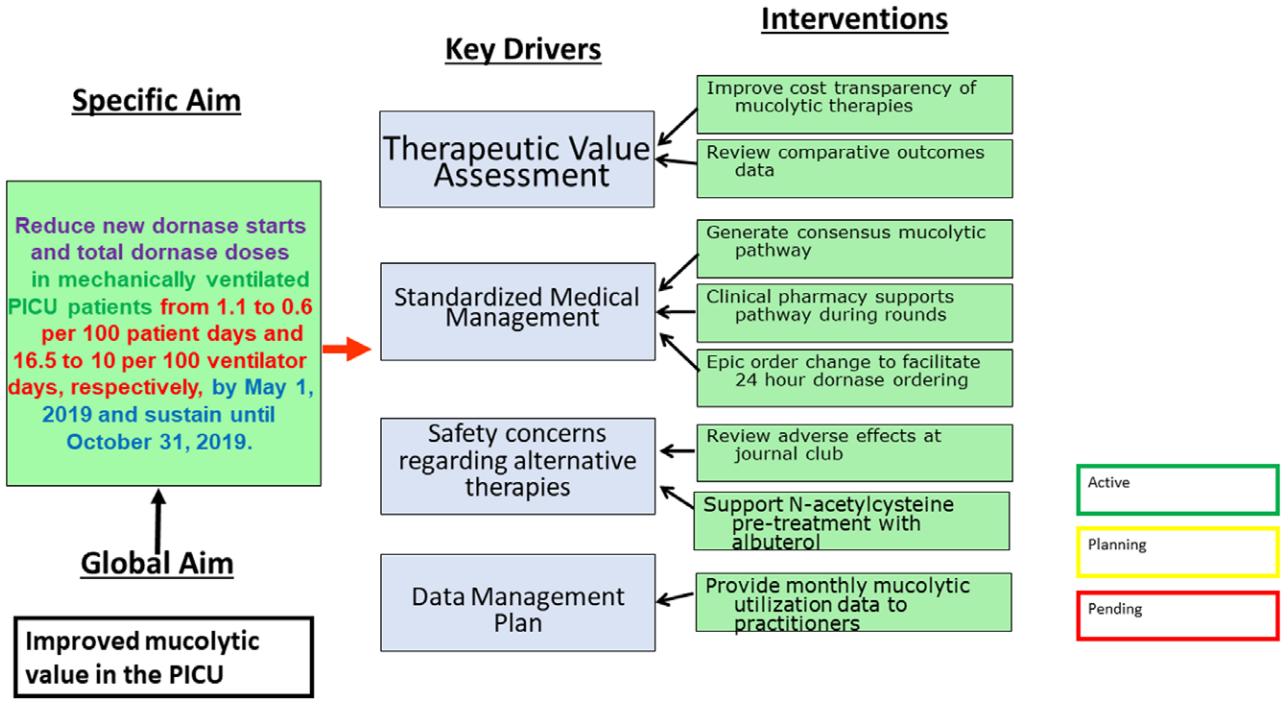


Fig. 1. Key Driver Diagram.

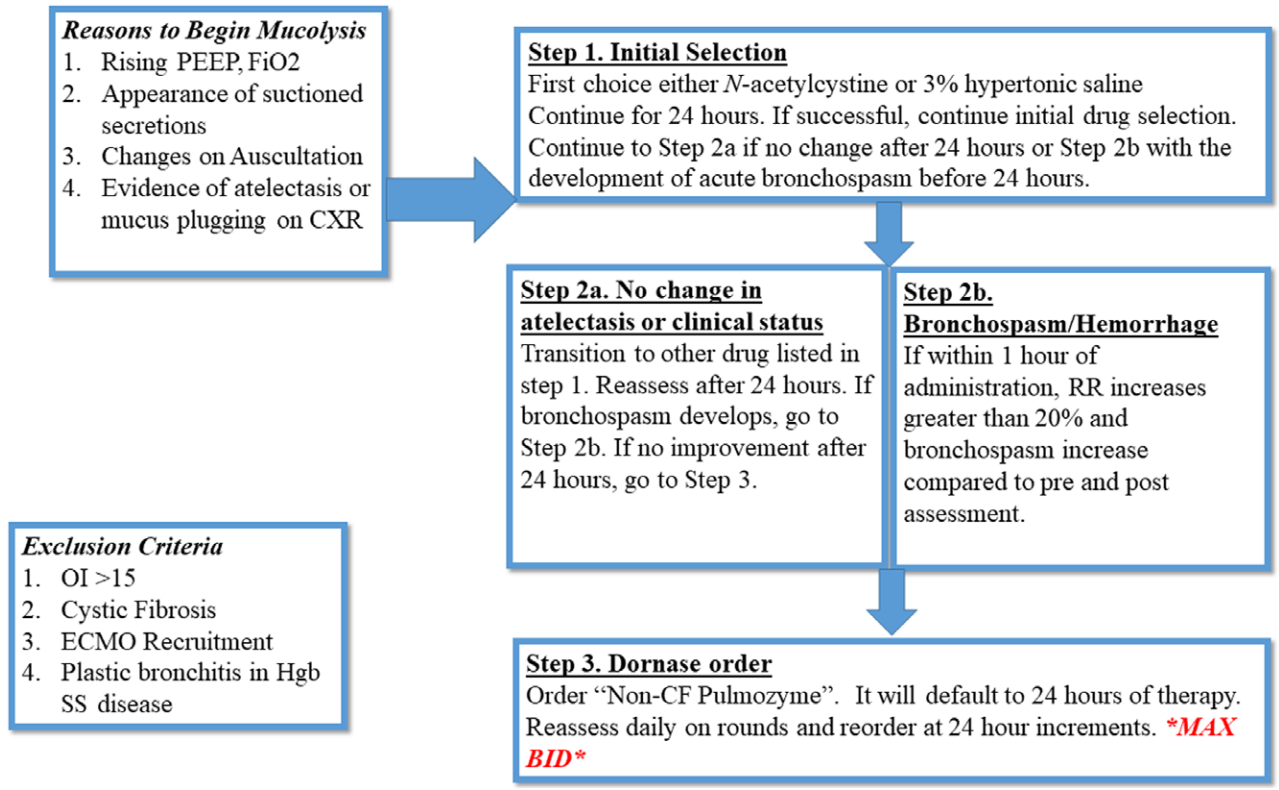


Fig. 2. Clinical pathway for mucolytic therapy for the first and second PDSA cycles. The bolded and starred portion shows a small change for PDSA cycle #2.

than the intended 24 hours stop time also occurred. In our second cycle, we limited dosing to twice daily (Fig. 2 bolded portion). The electronic medical record order and posted pathways were appropriately updated. Repeat education was completed with clinical staff to ensure updates could be implemented.

Outcomes and Statistical Analysis

Tabulation of medication new starts and total doses, ventilator days, and patient days occurred monthly. The definition of new starts includes any first course for the specific medication, or any new medication starts for the same patient following discontinuation for >48 hours. Ventilator days P100PD were chosen as the balancing measure, assuming any aggregate adverse effects of the mucolytic pathway would become evident by an increase in mechanical ventilation. Distributions are displayed on statistical process control charts incorporating rules for determining special cause variation.

RESULTS

New dornase alfa starts per P100PD decreased by 53% (1.17–0.55), and total doses of P100PD decreased by 75% (16–4) after the first PDSA Cycle. Following the second PDSA cycle, new starts of P100PD decreased further to 0.25. Total doses remained sustained through December 2019 at 4 P100PD (Figs. 3, 4). Concurrently, new uses of N-acetylcysteine occurred more than twice as often following pathway implementation; however, total doses P100PD ultimately remained unchanged after the intervention. Hypertonic saline use increased significantly from 0.28 to 4.15 new starts P100PD and was sustained through the second PDSA cycle. In regard to total doses, hypertonic saline use increased from 4.37 to 38.84 doses P100PD. Mechanical ventilation days P100PD decreased following pathway implementation, suggesting no measured negative effects of pathway implementation (Fig. 5).

Despite the increase in alternative mucolytic use, the reduction in dornase alfa utilization resulted in a cumulative and sustained 59% mucolytic cost reduction ($2183.08–$885.77 P100PD) (Fig. 6). Ordering practice changes for all medications resulted in a sustained centerline shift. The summation of these cost savings resulted in pharmacy cost savings of >$101,600 in 2019 compared with that in the previous year.

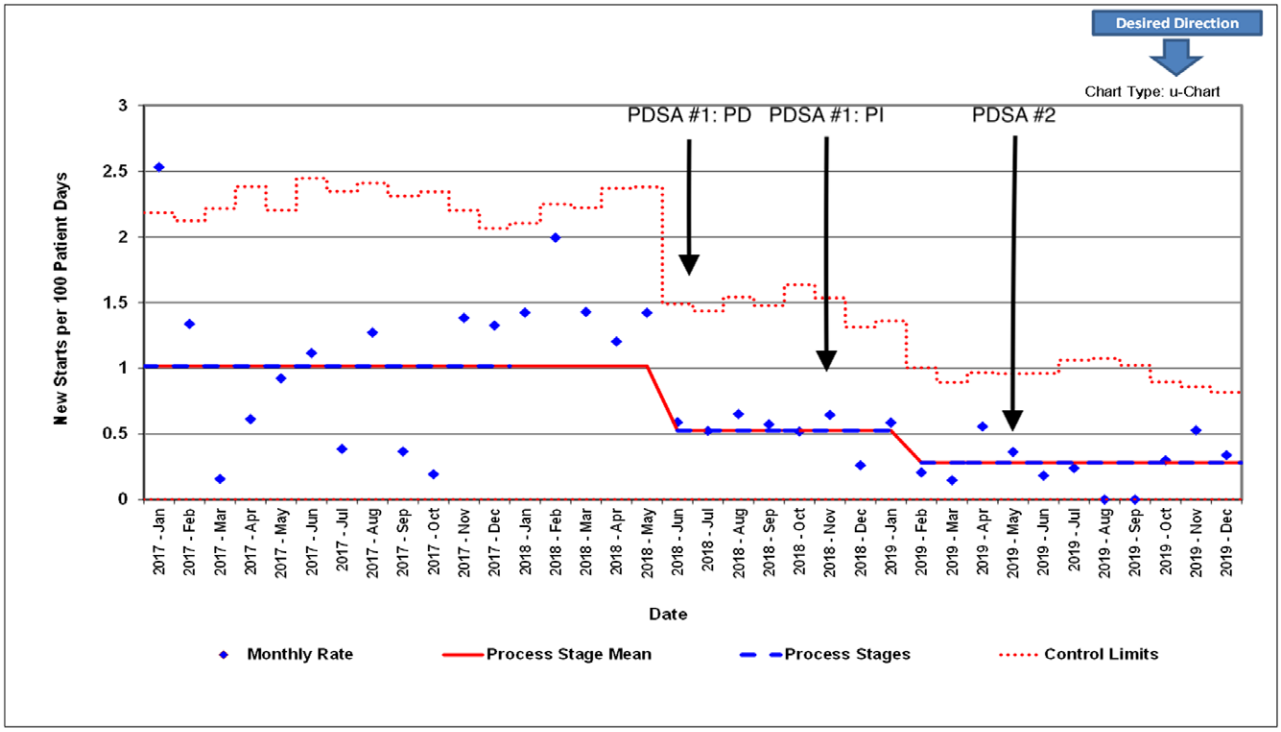
DISCUSSION

Health care value, defined as patient outcomes relative to care costs,[13] increases when costs decrease as patient outcomes improve or remain unchanged. Controlling costs by limiting the overuse and inappropriate use of medications is essential for maximizing healthcare value in the modern era, where aging populations, unexpected new infectious diseases, and new technology can increase overall resource utilization.[14] Respiratory illness in children remains one of the highest burdens on the pediatric healthcare system in United States, with much of the care given to critically ill patients with respiratory failure being supportive and lacking clear recommendations for use.[15,16] In addition to mucolytic therapies, another controversial therapy is chest physiotherapy.[17] Practitioners do not have clear evidence to support or refute the utilization of chest physiotherapy, which of the different techniques to employ, or their frequency. Like mucolytic therapies, given the contradictory evidence, it is easy to understand how a lack of straightforward evidence-based practice could result in individual or localized practice bias that may reduce health care value.

Our study sought to improve health care value by standardizing the utilization of mucolytic therapy. We found the financial disparity and lack of published evidence between available mucolytic pharmacotherapy was an ideal opportunity to utilize a pharmacoeconomic driven pathway to reduce medication use costs and improve the overall health care value. Our pathway's development led to a shift in mucolytic utilization with significant reductions in the use of the more expensive medication, dornase alfa, along with concomitant increases in the less expensive N-acetylcysteine and hypertonic saline nebulizations. This shift alone is thought to contribute toward a medication savings of over $100,000 for 2019, which adds to our ICU's health care value.

Of course, health care value cannot increase if decreasing the cost of care leads to worse patient outcomes. One of the more interesting findings was the balancing measure of invasive and noninvasive ventilator days was not merely maintained but was decreased. Although our protocol does not allow us to assume any causality in observing this outcome, we suspect that this is likely multifactorial. Greater intention to mucolytic ordering may have improved attention to other aspects of the pulmonary toilet. The PICU team has observed that since the advent of the pathway, mucolytic initiation appears to occur earlier and its effects followed more intensely. Additionally, a specific detailed discussion related to pulmonary toilet and any perceived benefits, deterioration, and need to modify therapy seemingly occurred more often during rounds. At face value, replacement with hypertonic saline may account for the decrease in dornase alfa use. However, while shifting mucolytic ordering practice, providers may have been more attentive to measures critical for assessing pulmonary mechanics relative to treatment (ie, lung compliance), leading to decreased overall mechanical ventilation duration and perhaps even increased compliance with ventilator weaning protocols. Our results suggest that higher cost medications alone do not equate to a higher quality of care.[18]

Active educational interventions, as opposed to passive ones, were likely what made our project successful. More likely, the steady and daily presence of pharmacists on rounds to cull orders, presenting the pathway to residents at the start of their rotation to ensure their active involvement, and working with nurses and RTs who are on the front lines of mucociliary clearance were the features of this project that made it an effective one. Project implementation occurred in a unit with a robust quality improvement culture and support structure. This infrastructure's importance cannot be underestimated.



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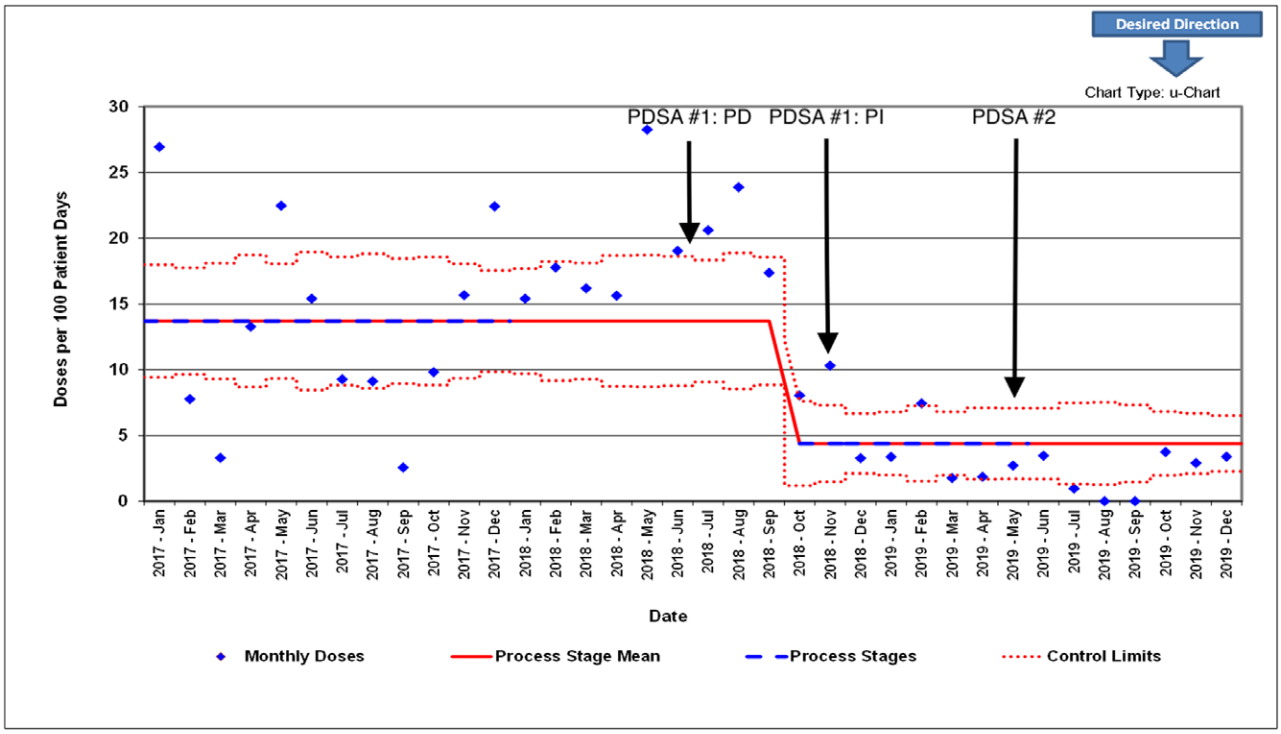
New Starts	17	10	1	3	6	5	2	6	2	1	9	11	11	12	9	6	7	3	3	3	3	2	3	2	4	1	1	3	2	1	1	0	0	2	4	3
Patient Days	672	748	636	490	650	448	518	472	546	520	651	830	773	602	630	499	492	510	573	461	524	386	466	764	683	485	678	539	552	548	416	402	461	669	759	887

Fig. 3. New dornase alfa starts P100PD decreased following the implementation of the clinical pathway.



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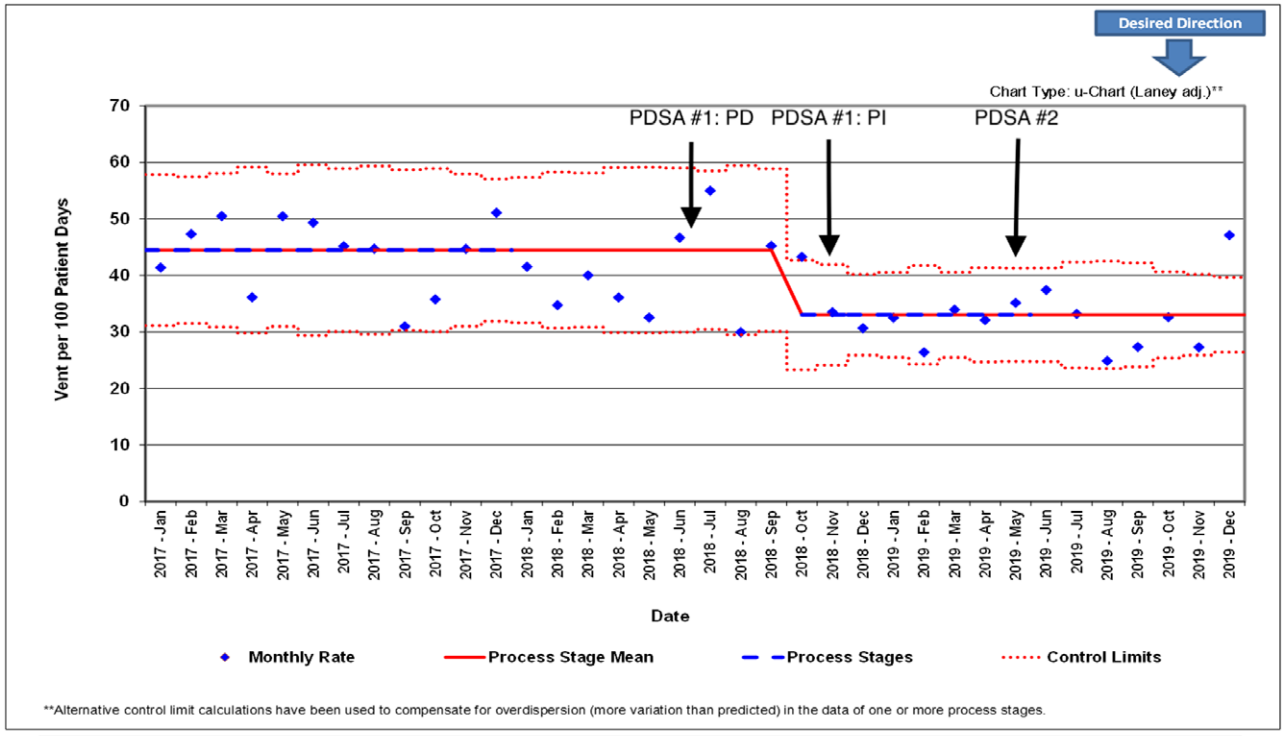
Doses	181	58	21	65	146	69	48	43	14	51	102	186	119	107	102	78	139	97	118	110	91	31	48	25	23	36	12	10	15	19	4	0	0	25	22	30
Patient Days	672	748	636	490	650	448	518	472	546	520	651	830	773	602	630	499	492	510	573	461	524	386	466	764	683	485	678	539	552	548	416	402	461	669	759	887

Fig. 4. Total dornase alfa doses P100PD decreased following the implementation of the clinical pathway.



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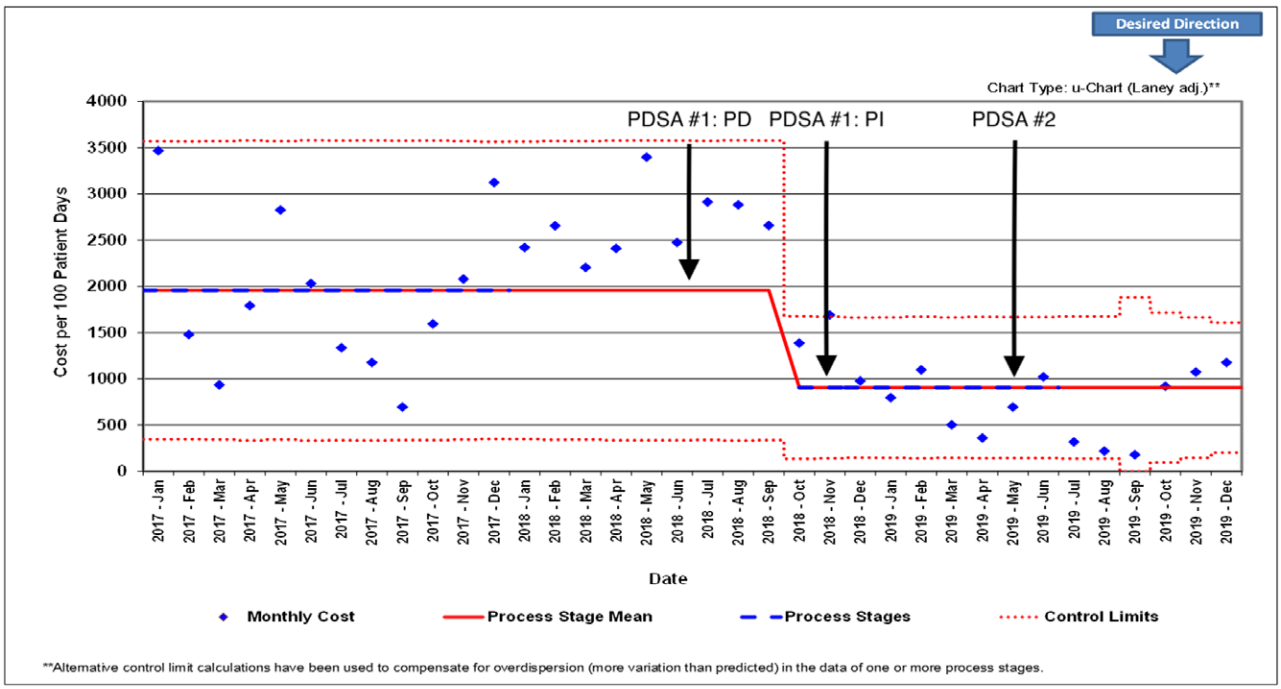
Vent Days	278	354	321	177	328	221	234	211	169	186	291	424	321	209	252	180	160	238	315	138	237	167	156	234	222	128	230	173	194	205	138	100	126	218	207	418
Patient Days	672	748	636	490	650	448	518	472	546	520	651	830	773	602	630	499	492	510	573	461	524	386	466	764	683	485	678	539	552	548	416	402	461	669	759	887

Fig. 5. Ventilator days P100PD did not increase due to implementing the mucolytic ordering pathway (balancing measure).



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Cost	23,292.56	11,059.88	5946	8,777.56	18,368.23	9,095.13	6,912.21	5,552.78	3,791.2	8,291.61	13,533.18	25,921.5	18,711.13	15,984.76	13,880.28	12,023.76	16,711.01	12,618.98	16,687.88	13,279.45	13,926.11	5,346.8	7,875.06	7,463.93	5,434.18	5,323.65	3,403.05	1,938.71	3,836.19	5,592.98	1,321.01	877.02	830.04	6,156.38	8,148.29	10,428.78
Patient Days	672	748	636	490	650	448	518	472	546	520	651	830	773	602	630	499	492	510	573	461	524	386	466	764	683	485	678	539	552	548	416	402	461	669	759	887

Fig. 6. Overall mucolytic cost P100PD decreased following implementation of the mucolytic ordering pathway.

Coordination among physicians, respiratory therapists, pharmacists, finance experts, and quality improvement specialists is essential for translating clinical practice changes into valued-based results.

Tester et al have recently published their use of a unit-specific guideline to reduce dornase alfa use. They found via a retrospective review following the implementation of their guideline a similar cost-saving and a reduced length of stay. However, our work is unique in that it used a QI methodology performed in real-time over the study period and not a pre-test post-test comparison.[19] This allowed for a more robust analysis of concomitant ordering practices, specifically hypertonic saline and N-acetylcysteine. Contrary to their findings in which N-acetylcysteine use decreased along with dornase alfa, we observed a significant increase in both alternative mucolytics. By including all patients receiving alternative mucolytics and not just those also receiving dornase alfa, we performed a more comprehensive analysis of the effects a clinical pathway targeting a single drug may have on the overall prescriber behavior.

With this in mind, the next stage of this project will reduce unnecessary mucolytic use by understanding the rationale for which they are used. These medications are often ordered for subjective findings, including provider perceived mucus viscosity and chest radiograph findings, while previous literature demonstrates little change in the length of stay with their use.[20,21] Administration of mucolytics requires additional respiratory therapy or nursing time. It potentially exposes these providers to additional risk of contamination and subsequent infection of healthcare workers[22,23] without the benefit of decreasing length of stay for our patients,[24] changes in patients' chest radiographs,[10] or other clinical outcomes.[25]

There are several limitations to our study. First, compliance with the clinical pathway was not explicitly measured; however, given substantial reductions from baseline data, it is presumed that there was relatively universal adoption of the pathway. The study opted to forgo attending provider-level analysis, given the multidisciplinary care provided, but this may have resulted in a further reduction in mucolytic use. Such analysis would help identify providers whose management may be biased by individual beliefs of clinical experience despite little evidence to support its use. Regardless, we anticipate as a result of the pathway, providers initially reluctant will have exposure to similar severely ill patients for whom dornase alfa is not ordered (eg, during night calls), and they will become late adopters. Our second centerline shift in dornase alfa utilization may highlight this hypothesis. Late adopters are a known barrier of implementation for procedure protocols and safety bundles previously.[26]

Recent literature has highlighted potential ways to measure concordance on a population level; however, more work is necessary to highlight adherence on a unit level.[27] The implementation of a unit-specific order attempted to curb the utilization of dornase alfa without a defined therapy duration. However, providers could still use dornase alfa outside this protocol-specific order. This safety measure ensured patients admitted to the PICU with a history of CF or other documented chronic use of dornase alfa did not unintentionally have their order expire but may have also led to inappropriate order selection for patients who were eligible for our pathway.

As a quality improvement initiative, our study is not one of clinical effectiveness or superiority where patient-level metrics are required. These are requirements for randomization, but not for quality improvement methodology. Although mucolytic therapy for bronchiolitis in the past has highlighted their lack of efficacy, the historical exclusion of critically ill patients remains a limiting factor.[28] As mechanical ventilation days remained unchanged in our population despite observed mucolytic practice changes, there is equipoise to investigate additional outcomes data associated with mucolytic use.

Our project can serve as a model for other groups considering value-based pharmacoeconomic projects. While recent publications promote a similar dornase alfa reduction workaround,[19] we feel it is essential to highlight the benefits of using a prospective QI-based approach instead of a pre/post design. The ability to track balancing measures (eg, ventilator days) and other unintended consequences, including a significant increase in alternative mucolytics in our case, allows for further contextualization of results and an additional layer of safety when performing this work.[29]

Lastly, understanding that cost-effectiveness training typically lags behind clinical training priorities in academic medical centers, we hope that this fellow-led project highlights the value of incorporating trainees in value-based improvement work. For example, while high-value care should be a tenet of intentional practice for all medical providers, only 22% of pediatric hospitalists reported any formal training in cost-effectiveness. In comparison, 91% of them believed they should participate in a cost-effectiveness curriculum.[29] These results likely also apply to pediatric critical care medicine training programs. They suggest that pediatric critical care medicine faculty and trainees could mutually benefit from incorporating value-based pharmacoeconomic improvement projects into their practice. Being new to their respective medical fields and spared from the bias ingrained from years of clinical practice, trainees are in a unique position to help drive improvements in value-based pharmacoeconomic practice.

CONCLUDING SUMMARY

A clinical pathway prioritizing pharmacoeconomics can improve health care value without adversely affecting patient outcomes. Promoting cost transparency and evidence-based prescribing behavior can result in significant cost savings.

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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