

Reducing Hospitalization Rates for Children With Anaphylaxis

Karen S. Farbman, MD, MPH,^a Kenneth A. Michelson, MD,^a Mark I. Neuman, MD, MPH,^a Timothy E. Dribin, MD,^a Lynda C. Schneider, MD,^b Anne M. Stack, MD^a

BACKGROUND AND OBJECTIVES: Most children with anaphylaxis in the emergency department (ED) are hospitalized. Opportunities exist to safely reduce the hospitalization rate for children with anaphylaxis by decreasing unnecessary hospitalizations. A quality improvement (QI) intervention was conducted to improve care and reduce hospitalization rates for children with anaphylaxis.

METHODS: We used the Model for Improvement and began with development and implementation in 2011 of a locally developed evidence-based guideline based on national recommendations for the management of anaphylaxis. Guideline adoption and adherence were supported by interval reminders and feedback to providers. Patients from 2008 to 2014 diagnosed with anaphylaxis were identified, and statistical process control methods were used to evaluate change in hospitalization rates over time. The balancing measure was any return visit to the ED within 72 hours. To control for secular trends, hospitalization rates for anaphylaxis at 34 US children's hospitals over the same time period were analyzed.

RESULTS: Over the study period, there were 1169 visits for children with anaphylaxis, of which 731 (62%) occurred after the QI implementation. The proportion of children hospitalized decreased from 54% to 36%, with no increase in the 72-hour ED revisit rate. The hospitalization rate across 34 other US pediatric hospitals remained static at 52% over the study period.

CONCLUSIONS: We safely reduced unnecessary hospitalizations for children with anaphylaxis and sustained the change over 3 years by using a QI initiative that included evidence-based guideline development and implementation, reinforced by provider reminders and structured feedback.

The prevalence of anaphylaxis is increasing in the United States.^{1,2} Guidelines exist to assist emergency department (ED) clinicians in deciding whether to hospitalize patients with anaphylaxis to monitor for biphasic reactions (ie, the recrudescence of symptoms after a period of resolution).³ However, despite these guidelines, national hospitalization rates vary widely, suggesting that opportunities exist to reduce unnecessary hospitalizations.⁴ This variation supports the need for

quality improvement (QI) initiatives to standardize disposition for patients with anaphylaxis in the ED setting. From 2000 to 2010, the hospitalization rate at our institution exceeded 50% for children with anaphylaxis. We hypothesized that hospitalization rates for children with anaphylaxis could be safely reduced by decreasing unnecessary hospitalizations. Local ED QI initiatives for other conditions have safely reduced hospitalization rates, congruent with the observation that

abstract



Divisions of ^aEmergency Medicine and ^bAllergy/Immunology, Department of Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts

Dr Farbman conceptualized and designed the study, assisted with analyses, and drafted the initial manuscript; Dr Michelson assisted with study design, conducted analyses, and provided input into the manuscript; Dr Neuman assisted with study design, assisted with analyses, and provided input into the manuscript; Dr Dribin assisted with analyses and provided input into the manuscript; Dr Schneider provided expert input into the design of the evidence-based guideline and the study; and Dr Stack supervised the design of the study, assisted with analyses, and provided input into the manuscript; and all authors approved the final manuscript as submitted.

DOI: <https://doi.org/10.1542/peds.2016-4114>

Accepted for publication Feb 21, 2017

Address correspondence to Karen S. Farbman, MD, MPH, Division of Emergency Medicine, BCH 3066, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115. E-mail: karen.farbman@childrens.harvard.edu

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

Copyright © 2017 by the American Academy of Pediatrics

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

FUNDING: Supported by grant T32HS000063 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality. Funded by the National Institutes of Health (NIH).

To cite: Farbman KS, Michelson KA, Neuman MI, et al. Reducing Hospitalization Rates for Children With Anaphylaxis. *Pediatrics*. 2017;139(6):e20164114

local guidelines are often more influential on local practice than national guidelines.⁵ In addition, in our setting, we have developed a culture of improvement by using local evidence-based guidelines (EBGs) to standardize care, and we sought to build upon that experience.^{6–10}

Hospitalization rates for anaphylaxis vary widely among hospitals, suggesting that opportunities exist to reduce unnecessary hospitalizations.⁴ A single-center study including 234 children with anaphylaxis reported a reduction in hospitalizations from 63% to 31% after implementation of an anaphylaxis management guideline.¹¹ We are not aware of other QI initiatives or proven methods to reduce anaphylaxis hospitalizations.

The goal of the present study was to reduce the proportion of patients with anaphylaxis who are hospitalized by 25% by December 2014 with the implementation of a QI initiative.

METHODS

Intervention

Using the Model for Improvement, a QI initiative was designed to standardize care and reduce hospitalization rates for children with anaphylaxis. The setting was an urban, tertiary care pediatric ED with an annual volume of ~60 000 visits. We assembled a multidisciplinary team consisting of pediatric emergency medicine physicians, a pediatric emergency nurse, a pharmacist, and a pediatric allergist.

First, to standardize care, an EBG was developed reflecting the 2010 to 2011 National Institute of Allergy and Infectious Diseases anaphylaxis guidelines.¹² The EBG underwent 3 rounds of revisions by all stakeholders over a 6-month period. This process included review by individual pediatric emergency

physicians in an iterative fashion for face validity and usability. Individuals considered to be leaders within our division and institution were recruited to enhance acceptability. A draft guideline was then presented to a large group of ~30 divisional faculty and fellows to enhance awareness and assess buy-in before we introduced a final version on October 1, 2011.

The EBG (Supplemental Information) recommended that children meeting criteria for anaphylaxis receive prompt intramuscular epinephrine. It was also recommended that patients receive diphenhydramine and a glucocorticoid. Those whose symptoms did not resolve were hospitalized, and those with resolution of symptoms were monitored for 4 hours. The EBG recommended that clinicians hospitalize patients requiring >1 dose of epinephrine, patients presenting with wheezing, and patients with any hypotension.

Several change strategies were implemented to promote acceptability and adherence. Key aspects of the EBG were e-mailed annually to division faculty after implementation. The division published a pocket-sized brochure, distributed to physicians and nurses that highlighted all divisional EBGs. There were 9 active EBGs in our division at the time of this pocket card production. Copies were easily available in print and online versions. The anaphylaxis EBG recommendations were integrated with electronic health record (EHR) order entry sets to facilitate adherence. With implementation of the anaphylaxis QI initiative, the anaphylaxis ED order set in the EHR included prepopulated intramuscular epinephrine, along with diphenhydramine and glucocorticoid, as standard weight-based medication choices to dispense to ED patients who present with anaphylaxis. Later in the implementation

phase, accessibility of discharge instructions was improved by linking the instructions to the discharge diagnosis codes.

To share successes of adoption and adherence, annual reports of hospitalization rates were shared with stakeholders with group e-mails and a review of EBG strides at a faculty conference. Over the year before the rollout of this EBG, there was an active culture of improvement in the ED centered around reducing variation and resource utilization in clinical care via a program of EBGs.

Measures

Our primary outcome was hospitalization rate. Secondary outcomes included ED length of stay (LOS) and receipt of instruction regarding epinephrine auto-injector (EAI) use. Patient characteristics were measured by using the EHR, including acuity (measured with the Emergency Severity Index, a score assigned during triage that rates the immediacy of the condition and projected amount of resource required to treat it), race, ethnicity, insurance status (public versus private), distance from home to hospital (using the center of the patient's home ZIP code), trigger (using diagnosis code), and co-diagnosis of asthma.¹³

The balancing measure was ED revisits, defined as any return to the ED within 72 hours among discharged patients.

Study of the Interventions

We included all children with *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes for anaphylaxis (995.0, 995.3, or 995.60–995.69) who received intramuscular epinephrine in the ED or before arrival to the hospital. All patients transferred from another hospital and those with prolonged ED observation (LOS >12 hours) were excluded because those patients had

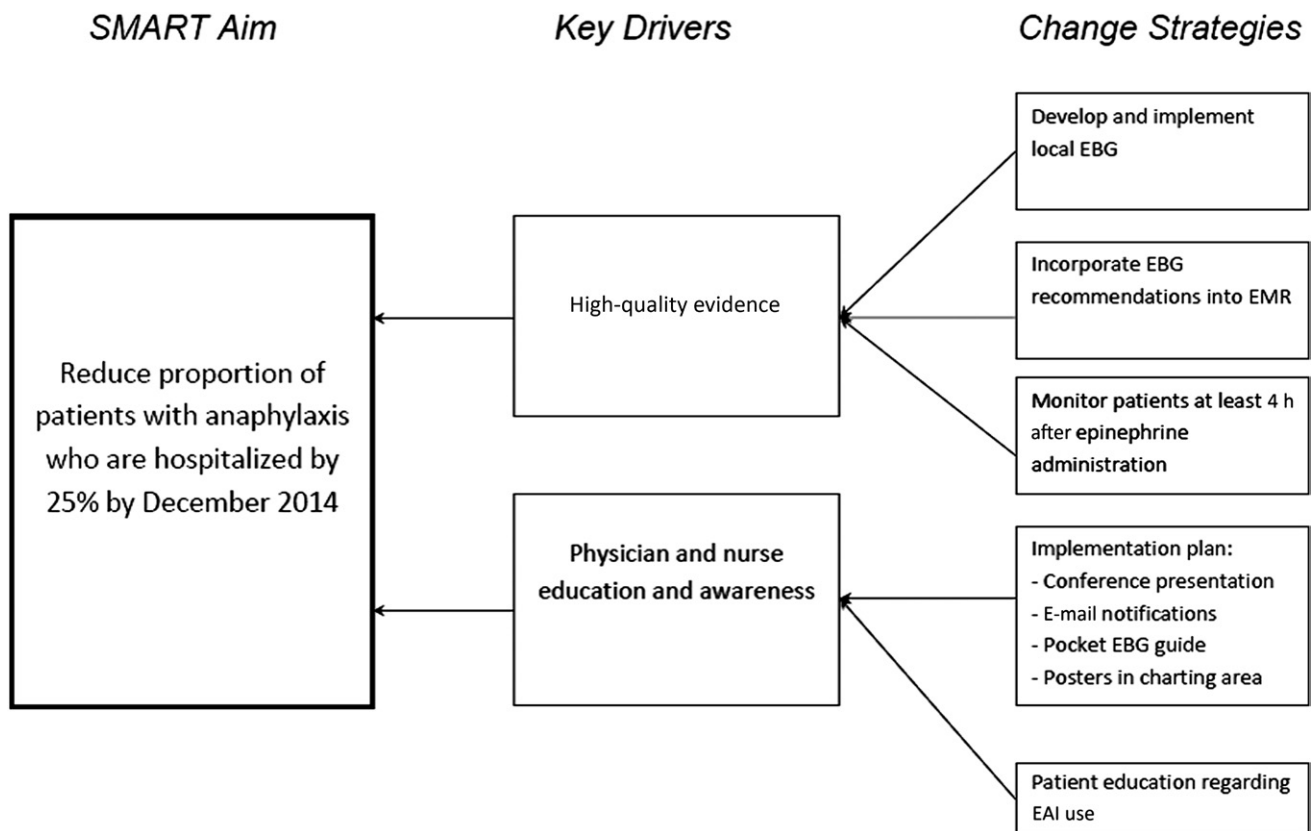


FIGURE 1
Key driver diagram for reduction of hospitalizations of patients with anaphylaxis.

attained an ED LOS approaching that of a typical hospitalization.

We queried the EHR database (Cerner Corporation, Kansas City, MO) to identify eligible patients. For those treated with epinephrine in the ED, EHR data were used to determine time of epinephrine administration. For those without ED-administered epinephrine, medical records were manually reviewed to assess for epinephrine administration before arrival to the hospital. Those children with missing epinephrine treatment data were categorized as not given and were therefore not included in the study. All other variables were collected from the EHR database.

Our aim was supported by 2 key drivers: (1) high-quality evidence designed to reduce practice variability; and (2) provider buy-in (Fig 1).

Analysis

The study compared the pre-implementation phase (January 1, 2008–September 30, 2011) with the implementation phase (October 1, 2011–December 31, 2014). Patient characteristics were compared by using descriptive statistics. Continuous data were compared by using a Wilcoxon rank-sum test, and categorical data were compared by using a χ^2 test in Stata (Stata Statistical Software Release 13.1; Stata Corp, College Station, TX).

Statistical process control methods were used to monitor changes in the hospitalization rate over time for children with anaphylaxis. Control limits were set at 3 SDs from the mean rate.^{14,15} Standard Western Electric Rules were used to determine centerline changes. The initial centerline occurred at the arithmetic mean of the preintervention measurements.

The centerline was moved after 7 consecutive points above or below the previous mean. If the centerline moved after a major intervention, the centerline was plotted backward to the intervention to improve readability. Statistical process control charts were created by using Chartrunner Lean version 3.0 (PQ Systems, Inc, Dayton, OH). A cumulative summation chart was used to examine the effect of our initiative on the total number of hospitalizations avoided.¹⁶ Trends in ED revisits were examined as a balancing measure.

To determine whether prevailing trends in academic pediatric EDs could explain the change in hospitalization rates for patients with anaphylaxis, hospitalization data were collected for patients with an *International Classification of Diseases, Ninth Revision, Clinical Modification* code for anaphylaxis

from the database of 34 children’s hospitals that participate in the Pediatric Health Information System (Children’s Hospital Association, Overland Park, KS); previously described methods were used.¹⁷ Our own hospital was excluded from analysis to assess trends outside our institution. We used negative binomial regression to determine whether anaphylaxis visits changed over the study period. Our model used anaphylaxis visit counts as the dependent variable and the quarter number (ie, first calendar quarter [January–March] of the first year of the study coded as a 1, the second quarter coded as a 2, and so on until the end of the study period) as the independent variable. The total number of ED visits to all 34 analyzed hospitals was used for the number of at-risk individuals in each quarter. To address clustering according to hospital, SEs were adjusted by using robust sandwich estimators according to hospital.

Ethical Consideration

According to the policy for activities that constitute research at Boston Children’s Hospital, this research met criteria for operational improvement activities exempt from ethics review. Specifically, this project was approved by the hospital’s Department of Medicine’s Performance Excellence Group as a QI initiative.

RESULTS

There were 1169 patients who met criteria for inclusion, 438 pre-implementation and 731 in the implementation period. Age, race, and history of asthma did not differ according to study phase, but patient acuity as measured by ESI increased over time (Table 1). There were some differences in the triggers for anaphylaxis. More patients in the pre-implementation

TABLE 1 Demographic Characteristics of Children With Anaphylaxis

Characteristic	Pre-implementation (1/2008–10/2011) (n = 438)	Implementation (10/2011– 12/2014) (n = 731)	P
Age, median (IQR), y	6.7 (3.2–14.0)	7.1 (2.7–14.7)	.97
Male sex	244 (56)	389 (53)	.41
Race			.29
White	184 (44)	268 (39)	
Black	108 (26)	197 (28)	
Asian	42 (10)	65 (9)	
Other/unknown	87 (21)	166 (24)	
Ethnicity			.89
Hispanic	73 (19)	127 (19)	
Non-Hispanic	314 (81)	559 (81)	
Insurance status			.03
Public	124 (28)	257 (36)	
Private	282 (65)	429 (59)	
Both	30 (7)	36 (5)	
Distance from home to hospital			.04
0–4.9 miles	278 (64)	455 (63)	
5–9.9 miles	70 (16)	142 (20)	
10–19.9 miles	51 (12)	54 (7)	
≥20 miles	36 (8)	74 (10)	
Trigger			.01
Peanuts	81 (24)	94 (15)	
Crustaceans	5 (1)	6 (1)	
Fruits/vegetables	9 (3)	8 (1)	
Tree nuts	42 (12)	71 (12)	
Fish	5 (1)	11 (2)	
Food additive	0	1 (0)	
Milk	18 (5)	23 (4)	
Eggs	5 (1)	21 (3)	
Other specified food	44 (13)	70 (11)	
Other unspecified food	26 (8)	71 (12)	
Multiple foods	5 (1)	21 (3)	
Other nonfood	100 (29)	215 (35)	
Asthma	132 (30)	190 (26)	.13
Emergency severity index ¹³			<.01
1	0	42 (6)	
2	154 (35)	394 (54)	
3	250 (57)	256 (35)	
4	29 (7)	34 (5)	
5	3 (1)	2 (0)	
Diagnosis code			.01
Allergic reaction	98 (22)	119 (16)	
Anaphylaxis	340 (78)	612 (84)	

Continuous data are presented as median (interquartile range), and categorical data are presented as N (%). The Wilcoxon rank-sum test was used for continuous data, and the χ^2 test was used for categorical data. Numbers do not add up to 100% due to missing data.

phase presented with peanut allergy and fewer presented with a nonfood allergy. A greater percentage of enrolled patients were coded as having an allergic reaction instead of anaphylaxis in the pre-implementation period.

The mean anaphylaxis hospitalization rate decreased from a baseline of 54% to 36% shortly after guideline introduction (Fig 2). This

improvement was sustained through the analysis period. Cumulative summation analysis revealed that anaphylaxis hospitalizations began to decline immediately after implementation of the EBG, and this trend continued over the study period, with 140 potential admissions avoided (Fig 3). Median ED LOS was 220 minutes in the pre-implementation phase and 244 minutes in the implementation phase ($P = .003$).

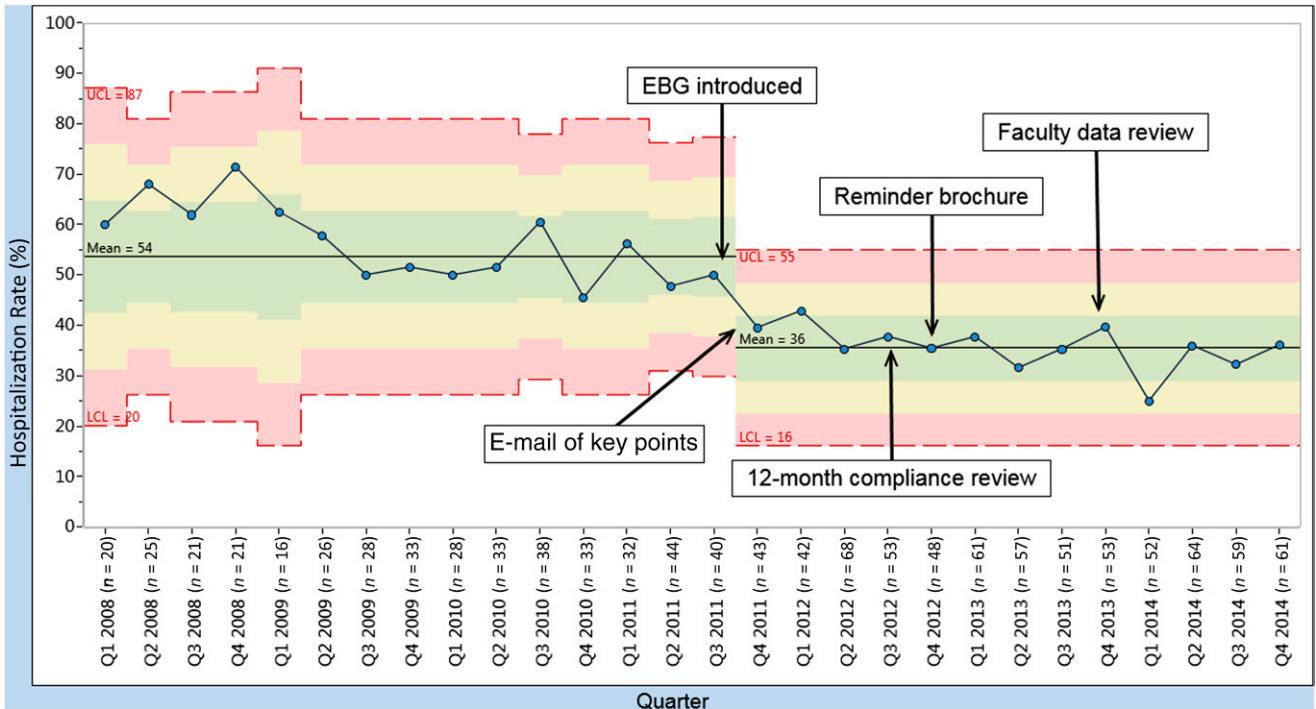


FIGURE 2 Statistical process control chart showing hospitalization rate over time with control limits set at 3σ and annotations (time of EBG introduction and interventions). LCL, lower control limit; UCL, upper control limit.

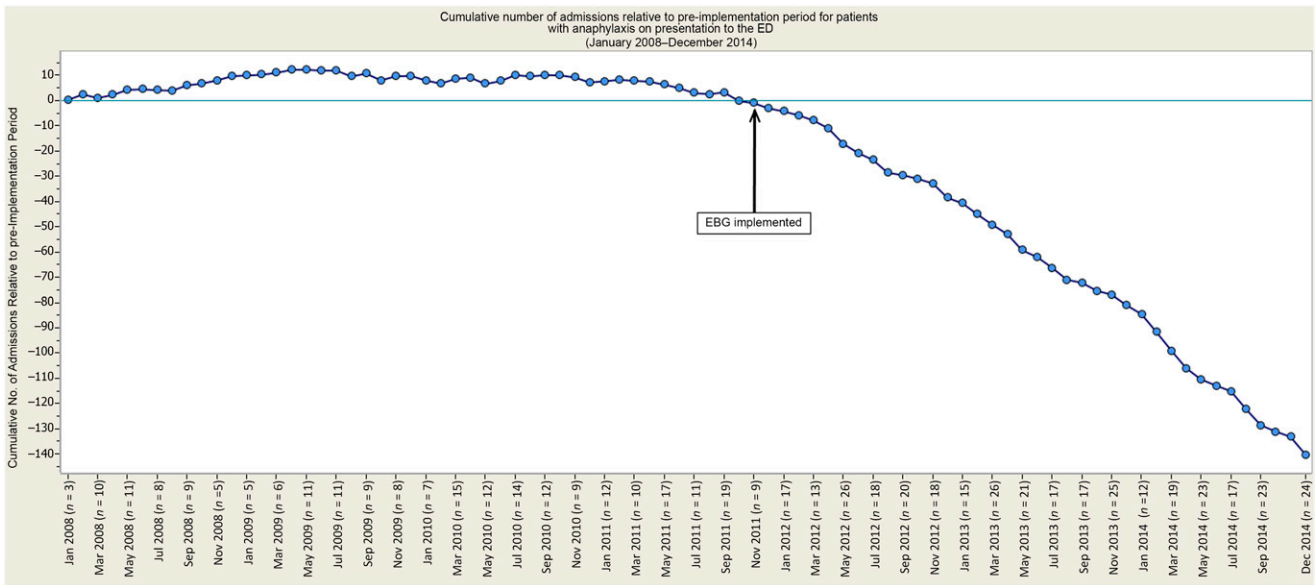


FIGURE 3 Cumulative summary chart of anaphylaxis admissions avoided since introduction of EBG.

The rate of EAI teaching and instruction increased from 21% to 80% over the implementation phase. When EAI teaching and instructions were added to the EHR as part of a discharge order

set, discharge teaching rates increased even further, to 92% (Supplemental Fig 5). The number of patients with anaphylaxis seen between each 72-hour revisit did not change after

implementation of the EBG (Supplemental Fig 6).

The hospitalization rate across 34 US pediatric hospitals decreased by 0.2% (95% confidence interval, -1.2

to 0.8; $P = .68$) per quarter over the study period (Fig 4).

DISCUSSION

The present study safely reduced hospitalization rates for children treated in the ED for anaphylaxis through a QI initiative that included development and implementation of a local anaphylaxis EBG and iterative engagement of stakeholders. ED LOS increased by a median of 24 minutes, reflecting greater adherence to a 4-hour observation period. EAI teaching increased from 21% to 92% of visits. Our balancing measure of time between revisits did not change after our QI intervention, suggesting that revisits did not increase as a result of the intervention.

In 2010, a local ED program of EBGs was launched at our institution. Over the course of the year before initiation of the anaphylaxis guideline, several guidelines were developed and implemented via a structured process.¹⁸ Performance data were provided to clinicians on a regular basis, and this approach served to support a culture of improvement. Divisional leadership approved the development of the anaphylaxis EBG and endorsed its specific recommendations. Both the established culture around guidelines and support by leadership fostered buy-in from ED staff. The rationale for choosing hospitalization rate as our primary outcome measure for this QI initiative was a dedication to reducing expensive, potentially unnecessary hospitalizations for patients with anaphylaxis who could be monitored at home after a period of ED observation. To safely discharge patients diagnosed with anaphylaxis, we wanted to ensure that all patients were observed for at least 4 hours, the time frame within which many biphasic reactions occur.¹⁹ Also, we sought to ensure that the discharged patients received EAI prescriptions and teaching on

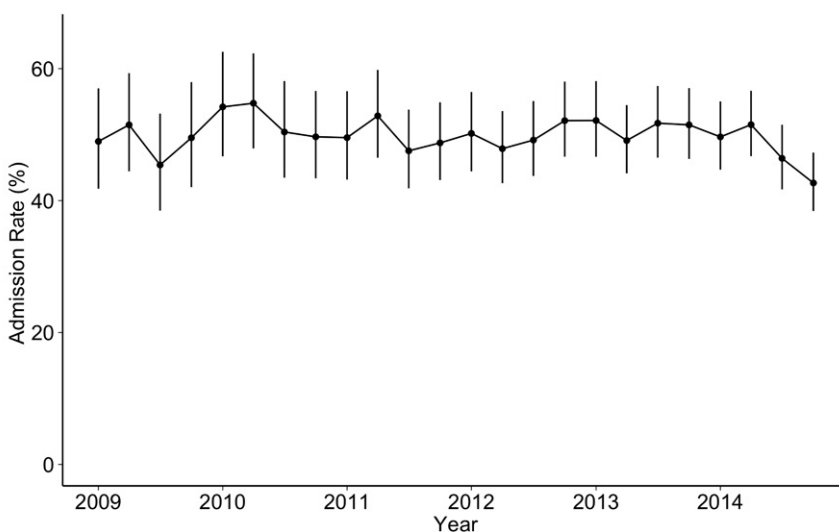


FIGURE 4

Mean hospitalization rate according to quarter for the 34 children's hospitals by using the Pediatric Health Information System database.

use and indications. Hence, the secondary outcomes of ED LOS and receipt of EAI teaching were trended. Monitoring patients for at least 4 hours and ensuring access to EAI at time of discharge are directives for discharged patients in line with the 2014 ED practice parameter of the American Academy of Allergy, Asthma & Immunology.³

Although treatment of most cases of anaphylaxis leads to complete and sustained symptom resolution, biphasic reactions are well described. Recent studies, including a meta-analysis with >4000 patients, found the risk of biphasic anaphylactic reactions to be ~5%.^{4,19} In a review of 2819 adult ED patients with anaphylaxis and allergic reaction, only 5 patients had clinically important biphasic reactions.²⁰ Of these, 2 experienced their recurrence of symptoms during the 4-hour ED monitoring period. These biphasic reactions were all treated with epinephrine, and the symptoms resolved.

Most patients respond quickly to epinephrine and are thus candidates for discharge with careful outpatient monitoring. One recent retrospective review found no cases of fatalities

associated with their series of biphasic reactions.²⁰ Low-risk patients who understand the signs and symptoms of anaphylaxis and have ready access to their EAI can be treated promptly should a biphasic reaction occur. As shown in our ED and nationally, the predominant practice pattern has been to hospitalize most patients after an anaphylactic reaction to observe for a biphasic reaction. Although patients with sustained symptoms are not safe for discharge, through use of this guideline with regular feedback on performance, providers became more comfortable discharging the majority of patients whose symptoms resolved with 1 dose of epinephrine.

Our QI team found that by consolidating high-quality evidence into a local EBG and making it easily accessible, we were able to influence provider practice. One strategy to gain buy-in initially included vetting of the draft guideline with 5 to 6 faculty members individually and incorporating suggestions iteratively before presentation to the larger faculty group. We specifically included local thought leaders in the preliminary review to gain public support. We then conducted the group review in an open and

frank faculty forum. This approach, along with the cultural context of improvement in the ED, likely influenced acceptance and adherence to recommendations. We observed an almost immediate reduction in admission rates, and we believe sharing the data with the group empowered peers to safely discharge patients.

There are some limitations to this research. First, the underlying reasons for a significant increase in anaphylaxis case numbers over the study are unclear, although the incidence of anaphylaxis nationally has risen significantly over the last decade.^{1,2} Second, rates of discharge may have trended downward independent of our QI initiative. However, the brisk reduction of the hospitalization rate soon after the QI initiative began suggests acceptance of our intervention. Moreover, the

data from comparator hospitals showed no secular downward trend in hospitalization rates. An additional limitation was that the comparator hospital data are from an administrative database, which lacks clinical detail. However, the hospitalization rates between our hospital and the comparator hospitals tracked together in the pre-implementation phase and diverged immediately at the time of implementation. Also, it is possible that patients may have revisited elsewhere, underestimating our revisit rate. Regarding the generalizability of this QI initiative, local contexts may differ, and adherence may be limited. Also, in remote areas, there may be legitimate reluctance to send patients far from the health care setting. Finally, our results may not generalize to settings in which there is not a culture of EBG utilization.

CONCLUSIONS

An anaphylaxis QI initiative was successfully introduced that included EBG development and implementation, reinforced by provider engagement and feedback in the context of a program of EBGs. We were able to safely reduce the hospitalization rate among children with anaphylaxis without increasing the frequency of revisits. The reduction in hospitalizations was not explained by secular trends.

ABBREVIATIONS

EAI: epinephrine auto-injector
EBG: evidence-based guideline
ED: emergency department
EHR: electronic health record
LOS: length of stay
QI: quality improvement

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

REFERENCES

1. Michelson KA, Monuteaux MC, Neuman MI. Variation and trends in anaphylaxis care in United States children's hospitals. *Acad Emerg Med*. 2016;23(5):623–627
2. Jackson KD, Howie LD, Akinbami LJ. Trends in allergic conditions among children: United States, 1997–2011. *NGHS Data Brief*. 2013;(121):1–8
3. Campbell RL, Li JT, Nicklas RA, Sadosty AT; Members of the Joint Task Force; Practice Parameter Workgroup. Emergency department diagnosis and treatment of anaphylaxis: a practice parameter. *Ann Allergy Asthma Immunol*. 2014;113(6):599–608
4. Rohacek M, Edenhofer H, Bircher A, Bingisser R. Biphasic anaphylactic reactions: occurrence and mortality. *Allergy*. 2014;69(6):791–797
5. Bekmezian A, Fee C, Weber E. Clinical pathway improves pediatrics asthma management in the emergency department and reduces admissions. *J Asthma*. 2015;52(8):806–814
6. Guse SE, Neuman MI, O'Brien M, et al. Implementing a guideline to improve management of syncope in the emergency department. *Pediatrics*. 2014;134(5). Available at: www.pediatrics.org/cgi/content/full/134/5/e1413
7. Lyons TW, Stack AM, Monuteaux MC, et al. A QI initiative to reduce hospitalization for children with isolated skull fractures. *Pediatrics*. 2016;137(6):e20153370
8. Paul R, Melendez E, Stack A, Capraro A, Monuteaux M, Neuman MI. Improving adherence to PALS septic shock guidelines. *Pediatrics*. 2014;133(5). Available at: www.pediatrics.org/cgi/content/full/133/5/e1358
9. Akenroye AT, Baskin MN, Samnaliev M, Stack AM. Impact of a bronchiolitis guideline on ED resource use and cost: a segmented time-series analysis. *Pediatrics*. 2014;133(1). Available at: www.pediatrics.org/cgi/content/full/133/1/e227
10. Schonfeld D, Fitz BM, Nigrovic LE. Effect of the duration of emergency department observation on computed tomography use in children with minor blunt head trauma. *Ann Emerg Med*. 2013;62(6):597–603
11. Desai SH, Jeong K, Kattan JD, Lieberman R, Wisniewski S, Green TD. Anaphylaxis management before and after implementation of guidelines in the pediatric emergency department. *J Allergy Clin Immunol Pract*. 2015;3(4):604–606.e2
12. Burks AW, Jones SM, Boyce JA, et al. NIAID-sponsored 2010 guidelines for managing food allergy: applications in the pediatric population. *Pediatrics*. 2011;128(5):955–965
13. Gilboy N, Tanabe P, Travers DA, Rosenau AM, Eitel DR. *Emergency Severity Index, Version 4: Implementation Handbook*. Rockville, MD: Agency for Healthcare Research and Quality; 2005
14. Benneyan JC, Lloyd RC, Plsek PE. Statistical process control as a

- tool for research and healthcare improvement. *Qual Saf Health Care*. 2003;12(6):458–464
15. Pimentel L, Barrueto F Jr. Statistical process control: separating signal from noise in emergency department operations. *J Emerg Med*. 2015;48(5):628–638
 16. Grigg OA, Farewell VT, Spiegelhalter DJ. Use of risk-adjusted CUSUM and RSPRT charts for monitoring in medical contexts. *Stat Methods Med Res*. 2003;12(2):147–170
 17. Michelson KA, Monuteaux MC, Neuman MI. Glucocorticoids and hospital length of stay for children with anaphylaxis: a retrospective study. *J Pediatr*. 2015;167(3):719–724. e1–3
 18. Akenroye AT, Stack AM. The development and evaluation of an evidence-based guideline programme to improve care in a paediatric emergency department. *Emerg Med J*. 2016; 33(2):109–117
 19. Lee S, Bellolio MF, Hess EP, Erwin P, Murad MH, Campbell RL. Time of onset and predictors of biphasic anaphylactic reactions: a systematic review and meta-analysis. *J Allergy Clin Immunol Pract*. 2015;3(3):408–416. e1–2
 20. Grunau BE, Li J, Yi TW, et al. Incidence of clinically important biphasic reactions in emergency department patients with allergic reactions or anaphylaxis. *Ann Emerg Med*. 2014;63(6):736–744.e2