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Impact of Parental Presence at Infants’ Bedside on Neonatal Abstinence Syndrome

Mary Beth Howard, MD, MSc,a Davida M. Schiff, MD,b Nicole Penwill, BA, Wendy Si, MD,c Anjali Rai, MD,d Tahlia Wolfgang, MPH,d James M. Moses, MD, MPH,d Elisha M. Wachman, MD,b

ABSTRACT

BACKGROUND: Despite increased incidence of neonatal abstinence syndrome (NAS) over the past decade, minimal data exist on benefits of parental presence at the bedside on NAS outcomes.

OBJECTIVE: To examine the association between rates of parental presence and NAS outcomes.

METHODS: This was a retrospective, single-center cohort study of infants treated pharmacologically for NAS using a rooming-in model of care. Parental presence was documented every 4 hours with nursing cares. We obtained demographic data for mothers and infants and assessed covariates confounding NAS severity and time spent at the bedside. Outcomes included length of stay (LOS) at the hospital, extent of pharmacotherapy, and mean Finnegan withdrawal score. Multiple linear regression modeling assessed the association of parental presence with outcomes.

RESULTS: For the 86 mother–infant dyads, the mean parental presence during scoring was on average 54.4% (95% confidence interval [CI], 48.8%–60.7%) of the infant’s hospitalization. Maximum (100%) parental presence was associated with a 9 day shorter LOS ($r = –0.31; 95\% CI, –0.48 to –0.10; P < .01$), 8 fewer days of infant opioid therapy ($r = –0.34; 95\% CI, –0.52 to –0.15; P < .001$), and 1 point lower mean Finnegan score ($r = –0.35; 95\% CI, –0.52 to –0.15; P < .01$). After adjusting for breastfeeding, parental presence remained significantly associated with reduced NAS score and opioid treatment days.

CONCLUSIONS: More parental time spent at the infant’s bedside was associated with decreased NAS severity. This has important implications for clinical practice guidelines for NAS.

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Dr Howard conceptualized and designed the study and drafted the initial manuscript; Dr Schiff drafted the initial manuscript and reviewed and revised the manuscript; Ms Penwill assisted with data collection and drafted the initial manuscript; Drs Si and Rai and Ms Wolfgang assisted with data collection; Dr Moses supervised data collection and critically reviewed the manuscript; Dr Wachman supervised study design, designed data collection instruments, coordinated and supervised data collection and analysis, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.
Between 2000 and 2012, in utero opioid exposure increased from 1.19 to 5.63 per 1000 live births in the United States.\textsuperscript{12} Parallel with this increase, the incidence of neonatal abstinence syndrome (NAS) increased five-fold.\textsuperscript{12} NAS is characterized by gastrointestinal, respiratory, autonomic, and central nervous system disturbances due to opioid withdrawal.\textsuperscript{3} Between 50% to 80% of opioid-exposed infants require pharmacologic treatment of NAS. Infants are typically treated with replacement opioids and then weaned over days to weeks.\textsuperscript{3,5} Pharmacologic management of NAS results in prolonged and costly hospital stays. On average, infants are admitted for 3 weeks, with estimated costs per admission ranging from $20,000 for inpatient pediatric ward care to $63,000 for neonatal intensive care.\textsuperscript{1,4,7} Despite the increased incidence of NAS and associated resource use, great variability exists in the management of opioid-exposed infants.\textsuperscript{6} Although pharmacologic therapy remains the mainstay of treatment, previous evidence suggests nonpharmacologic therapy decreases the severity of NAS and reduces the need for medication.\textsuperscript{8} Rooming-in, defined as allowing parent cohabitation with their hospitalized infants, has been shown to be independently associated with improved outcomes in NAS. Previous studies have demonstrated a decreased length of stay (LOS) by 5 to 12 days, decreased need for pharmacologic therapy by 19%, decreased duration of therapy by 8 to 12 days, and reduced cost of hospitalization by about 35%.\textsuperscript{13–17} Although previous studies have assessed the effect of a rooming-in model of care across various models of care or at different points in time, the amount of parental presence spent at the bedside has not been studied independently. Therefore, the objective of this study was to examine the effect of the amount of parental presence at the bedside on NAS severity; specifically, the association with 3 main outcomes: (1) hospital LOS, (2) extent of pharmacologic therapy required, and (3) mean Finnegan withdrawal scores.

**METHODS**

We performed retrospective chart review to identify all infants born at Boston Medical Center (BMC) between March 2015 and April 2016 with in utero opioid exposure. Eligibility criteria included maternal opioid agonist treatment with methadone or buprenorphine during the third trimester of pregnancy and infants with a gestational age $\geq$36 weeks treated with opioid replacement therapy for opioid withdrawal on a pediatric inpatient unit. Infants were excluded from the study if they were transferred from BMC to another hospital before being medically ready for discharge, or if they required a NICU admission for $>48$ hours or a prolonged hospital stay for reasons other than NAS (for example, respiratory distress, hypoglycemia requiring intravenous dextrose fluids, or birth weight $<1800$ g). Infants were also excluded if they did not require pharmacologic treatment of NAS given that these infants are cared for in the postpartum maternity unit for the majority of their hospitalization where their mothers are admitted as patients (Fig 1).

**Model of Care**

At BMC, each mother–infant pair room together for the duration of maternal hospital admission postdelivery, unless the infant is admitted to the NICU. BMC has practiced this rooming-in model of care of infants with NAS for $>15$ years. After the mother’s discharge (2 days for a vaginal delivery, 4 days for a cesarean delivery), the infant is transferred to the inpatient pediatric unit and monitored for at least 5 to 7 days for signs of withdrawal that would warrant medication treatment. This model of care encourages parents to stay at their infants’ bedside and there are no daytime visiting hour restrictions. One caregiver is allowed to stay overnight at the bedside.

During the study time period, infants were scored using the original Finnegan scale every 4 hours.\textsuperscript{17} Infants who scored 2 consecutive scores $\geq 8$ or 1 score $\geq 12$ were initiated on first-line treatment with oral morphine (starting at 0.3 to a maximum dose of 0.9 mg/kg per day divided every 4 hours) or oral methadone solution (starting at 0.3 to a maximum dose of 0.9 mg/kg per day divided every 8 hours). During the study period, 80% of infants were pharmacologically treated. Oral morphine solution was routine care at BMC during the study period. Some of the infants were concurrently participating in a randomized double-blinded clinical trial comparing methadone versus morphine (grant ID R01DA032889-03). The infants who participated in the randomized trial received the same Finnegan assessments every 4 hours, with criteria to initiate and escalate medication identical to routine care guidelines and identical total daily dosing of replacement opioids. For all infants with NAS, second-line therapy consisted of clonidine (6 mcg/kg per day) or phenobarbital (5–6.6 mg/kg per day) if the infant reached maximum doses of morphine or methadone with continued elevated Finnegan scores. All infants were weaned off opioids and clonidine as inpatients and completed phenobarbital weans in the outpatient setting. Infants were monitored for 24 to 48 hours off opioids before discharge from the hospital.

**Data Collection**

For all eligible mother–infant pairs, 2 investigators extracted data from the electronic medical record. Maternal baseline characteristics included age, smoking status, medications, illicit substance use during the pregnancy, and urine toxicology results. Infant data included birth demographics, LOS, total days of postnatal opioid therapy, total opioid dosage, and use of additional pharmacological agents in the treatment of more severe neonatal withdrawal. Additionally, investigators determined breastfeeding status (defined as any amount of breast milk consumed by the infant during the hospitalization) and infant custody status through the infant’s hospitalization.

NAS Finnegan scores with a documented corresponding status of parental presence at bedside were extracted from the medical record. Parental presence (biological mother or father) at time of NAS scoring was documented by nursing staff in the patient’s 24-hour flow sheet as part of routine care.

**Statistical Methods**

Descriptive statistics included baseline demographic characteristics of the mother–infant pairs. Independent sample
tests assessed whether parental presence differed across subgroups. We calculated a mean NAS score for each infant using NAS scores abstracted from the medical record with simultaneous documented parental presence. Listwise deletion was performed with missing data such that only scores with documentation of parental presence were included in analyses. Spearman or Pearson's correlation coefficients measured the correlation between parental presence and mean NAS score, LOS, total opioid days, and total opioid dose, in morphine equivalents. Coefficients of determination were calculated from the correlation coefficients to describe the proportion of the variance in the dependent variable that is predictable from the independent variable. We calculated morphine equivalents for the clinical trial participants using a 1:1 conversion for morphine and methadone total daily dosing. A list of potential covariates was selected on theoretical grounds at the onset of the study and examined in relation to parental presence and NAS outcomes. To maximize the ability to identify the effect of parental presence, only clinically relevant variables that were significantly associated with parental presence and/or a specific outcome at the $P < .05$ level in bivariate analyses were also included in regression models. Multiple linear regression models examined the association between parental presence and the outcome variables, adjusting for the significant covariate of breastfeeding. Clinical trial participation was included as an effect modifier in the models. The difference in NAS outcomes that could be attributed to by maximum (parent present all of the time) versus minimal (parent never present) parental presence was determined. For all analyses, $\alpha$ was set at $P < .05$, and all hypothesis tests were two-tailed. Statistical analyses were performed using SAS statistical analysis software (SAS Institute, Inc, Cary, NC). The study received Boston University Medical Center Institutional Review Board approval.

RESULTS

A total of 86 mother–infant pairs were identified. Table 1 provides the maternal and infant characteristics for the study population. Methadone was prescribed to 55.8% ($n = 48$) of the mothers and 44.2% were maintained on buprenorphine ($n = 38$). Rates of maternal smoking and concurrent pharmacologic exposures are described in Table 1. The average gestational age of the infants was 38.9 weeks (95% confidence interval [CI], 38.5–39.3) and almost half were breastfed (47.7%) during hospitalization. Twenty-three percent ($n = 20$) of infants were discharged from the hospital with their...
biological family, and 27.1% \((n = 25)\) were included in the concurrent randomized control trial. Across the entire cohort, the average LOS was 18.9 days \((95\% \text{ CI, 17.3–20.5})\). The average duration of opioid therapy was 15.1 days \((95\% \text{ CI, 13.7–16.5})\) and the total morphine equivalent dose was 15.9 mg \((95\% \text{ CI, 13.7–17.9})\). Thirty infants \((34.9\%)\) required a secondary pharmacologic agent for control of their withdrawal symptoms \( Table 1\). Parents were present on average 54.4% \((95\% \text{ CI, 48.8–60.7})\) of the infant’s total hospitalization.

In unadjusted analyses, any amount of breastfeeding was associated with a decreased LOS \((16.5 \text{ vs } 21.1 \text{ days}, P < .01)\) as was clinical trial participation \((15.8 \text{ vs } 20.0 \text{ days}, P < .01)\). Similarly, breastfeeding and clinical trial participation were also significantly associated with decreased duration of opioid therapy and a decreased total morphine equivalent dose \( Table 2\). The mean NAS score was significantly lower for infants who were breastfed \((5.3 \text{ vs } 5.7, P < .01)\) and participated in the clinical trial \((5.1 \text{ vs } 5.7, P < .01)\); however, these differences in scores were not clinically significant. Parental presence was higher for infants who were breastfed \((65.2\% \text{ vs } 44.5\%, P < .0001)\) and infants who were enrolled in the clinical trial \((65.0\% \text{ vs } 50.9\%, P < .01)\). Conversely, parental presence was significantly lower for infants in Department of Children and Families \((DCF)\) custody \((36.6\% \text{ vs } 59.7\%, P < .0001)\) \( Table 2\).

In bivariate analyses, 100% parental presence was significantly associated with a 1 point decrease in the mean NAS score \((r = –0.35; 95\% \text{ CI, } –0.52 \text{ to } –0.15; P < .01)\), a 9 day decrease in LOS \((r = –0.31; 95\% \text{ CI, } –0.48 \text{ to } –0.10; P < .01)\), and 8 fewer days of opioid therapy \((r = –0.34; 95\% \text{ CI, } –0.52 \text{ to } –0.15; P < .001)\). Additionally, although nonsignificant, there was a 5.3 mg decrease in the total morphine equivalent dose with increased parental presence \((r = –0.20; 95\% \text{ CI, } –0.39 \text{ to } 0.02; \text{ not significant})\) \( Fig \text{ 2}\).

Across the entire cohort, the mean NAS score when a parent was present was significantly lower compared with when a parent was not present \((6.1 \text{ [95\% CI, 4.9–5.5]} \text{ versus } 6.0 \text{ [95\% CI, 5.8–6.2]; } P < .0001)\).

In the multiple linear regression analysis, adjusting for the confounding variable of breastfeeding, parental presence remained significantly associated with a lower mean NAS score by 0.8 points \((\beta = –0.81; P = .02)\) and 5.7 fewer days of opioid therapy \((\beta = –5.68; P = .03)\) with a trend toward shorter LOS by >5 days \((\beta = –5.46, P = .09)\). After adding in the effect modifier of clinical trial participation, results were attenuated and were no longer statistically significant. DCF custody was not included in the final regression models because it did not significantly influence \(\beta\) values.

DISCUSSION

This is the first study to examine the impact of parental presence at the bedside on the treatment course for substance-exposed newborns on an inpatient pediatric unit encouraging rooming-in. Greater parental presence during the hospitalization was significantly correlated with a decreased mean NAS score, decreased LOS, and decreased total days of opioid pharmacotherapy.

The American Academy of Pediatrics recommends nonpharmacologic care as first-line treatment of infants with NAS, however, few previous studies have evaluated the impact of various nonpharmacologic interventions on NAS outcomes.\(^6\) Rooming-in represents one component of nonpharmacologic care. Compared with previous studies that have focused on a comparison of rooming-in on a

---

**TABLE 1** Baseline Characteristics of 86 Mother–Infant Pairs

<table>
<thead>
<tr>
<th>No. (%)</th>
<th>Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mothers</strong></td>
<td></td>
</tr>
<tr>
<td>Mean maternal age, y</td>
<td>29.4 (28.3–30.3)</td>
</tr>
<tr>
<td>Maternal opioid</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>48 (55.8)</td>
</tr>
<tr>
<td>Mean dose at delivery (mg/d)</td>
<td>100.1 (89.2–111.1)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>38 (44.2)</td>
</tr>
<tr>
<td>Mean dose at delivery (mg/d)</td>
<td>14.5 (12.9–16.1)</td>
</tr>
<tr>
<td>Maternal smoking in third trimester</td>
<td>62 (72.1)</td>
</tr>
<tr>
<td>Benzodiazepine use</td>
<td>19 (22.1)</td>
</tr>
<tr>
<td>Clinical trial participation</td>
<td>23 (27.1)</td>
</tr>
<tr>
<td>DCF custody</td>
<td>20 (23.3)</td>
</tr>
<tr>
<td>Breastfed</td>
<td>41 (47.7)</td>
</tr>
<tr>
<td>SSRI use</td>
<td>10 (11.6)</td>
</tr>
<tr>
<td>Polysubstance use</td>
<td>6 (21.4)</td>
</tr>
</tbody>
</table>

| **Infants** | | |
| Gestational age | 38.9 (38.5–39.5) |
| Male | 45 (53.2) |
| Breastfed | 41 (47.7) |
| DCF custody | 20 (23.3) |
| Clinical trial participation | 25 (27.1) |
| LOS, d | 18.9 ± 7.7 (17.3–20.5) |
| Days of opioid therapy | 15.1 ± 6.5 (13.7–16.5) |
| Total morphine equivalents, mg | 15.9 ± 10.0 (13.7–17.9) |
| Secondary agent | 30 (34.9) |

SSRI, selective serotonin reuptake inhibitor.

\(^6\) Heroin + cocaine, \(n = 3\); heroin + Percocet, \(n = 1\); benzodiazepine + Percocet, \(n = 1\); heroin + benzodiazepine, \(n = 1\).
hospital ward versus an intensive care setting. A strength of this study is the evaluation of a cohort of infants who all had the opportunity for rooming-in with their parents. This is also important because many hospitals care for infants with NAS in NICUs, where rooming-in is not possible. Alternatives to caring for these infants on the pediatric inpatient ward or level 2 nurseries, where 24-hour rooming-in is possible, even nonpatient residential settings could be investigated as possible standards of care. As shown in previously published cohorts of infants in Canada, breastfeeding was associated with a significantly decreased LOS in our study. Beyond rooming-in, this study suggests that a focus on parental presence to promote nonpharmacologic care through breastfeeding, skin-to-skin time, and parental–infant bonding is significantly associated with a decreased LOS for infants with NAS.

On average, in this ward-based model of care encouraging rooming-in for infants with NAS, parents were present just over half of the time. Several barriers to parental presence that have been identified through discussions with families at our institution include: transportation, additional child care responsibilities, off-site methadone dosing, residential substance use disorder treatment program requirements, and stigma and guilt experienced by women with substance use disorders watching their infants go through withdrawal. Previously published research supports these barriers in experiences of families with infants hospitalized for NAS. Additional research is needed to explore support programs to help eliminate these barriers.

Infants who were placed in DCF custody were found to have a decreased rate of parental presence compared with infants whose parents retained custody. For the majority of the infants at our institution, a decision about custody is deferred until the end of the hospitalization, so all parents have the opportunity to be present at the bedside with their infants. The differences in parental presence observed between those families that did not retain custody and those who were discharged from the hospital with their infants may highlight families who had additional barriers to being at the bedside, or who were actively using illicit substances. This difference is highlighted by a previous study demonstrating an inverse relationship between rooming-in and foster care placement. The percentage of parental presence could be an additional factor to consider in determining custody status or designing specialized programs to support the unique needs of each mother–infant dyad.

During the time period of this retrospective study, BMC participated in a multicenter randomized control trial (R01DA032889-03) assessing the pharmacologic treatment of NAS with methadone compared with morphine. The medication these infants received remains blinded. The infants participating in the trial were more likely to have a decreased LOS and decreased total treatment days compared with infants not participating in the trial. Trial participants were also more likely to have higher amounts of parental presence, although this is unrelated to any requirements of the clinical trial protocol. We included trial participation as an effect modifier in all of our regression models because it is not possible to separate the influence of clinical trial participation versus the impact of receiving methadone versus morphine on NAS outcomes. Previous studies have indicated that clinical trial participation is an independent predictor of improved outcomes, likely due to increased staff vigilance and patient engagement.

One previous randomized control trial comparing methadone versus morphine showed a decreased LOS for infants in the methadone group. Conversely, a retrospective chart review showed decreased LOS for infants treated with morphine when compared with methadone. At this point, it is unclear if some of the improvement in the infants enrolled in the trial may be secondary to methadone treatment.

### TABLE 2: Association of Covariates With LOS and Parental Presence at Bedside

<table>
<thead>
<tr>
<th>Covariate</th>
<th>% Parent Present (95% CI)</th>
<th>P</th>
<th>Average LOS, d (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal opioid</td>
<td>.12</td>
<td>.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>50.3 (43.1–57.0)</td>
<td>.20</td>
<td>20.0 (17.9–22.2)</td>
<td>.13</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>59.4 (50.3–68.1)</td>
<td>.17</td>
<td>17.5 (15.1–19.9)</td>
<td>.04</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>44.5 (38.3–52.4)</td>
<td>.07</td>
<td>21.1 (18.7–23.5)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>65.2 (59.8–71.2)</td>
<td>.15</td>
<td>16.5 (14.5–18.5)</td>
<td>.20</td>
</tr>
<tr>
<td>Benzoazepine use</td>
<td>50.8 (39.4–61.8)</td>
<td>.09</td>
<td>17.2 (14.0–20.4)</td>
<td></td>
</tr>
<tr>
<td>SSRI use</td>
<td>55.7 (50.2–64.4)</td>
<td>.03</td>
<td>19.6 (14.1–17.3)</td>
<td></td>
</tr>
<tr>
<td>Illicit drug use</td>
<td>54.9 (48.5–60.2)</td>
<td>.08</td>
<td>18.8 (16.8–20.8)</td>
<td></td>
</tr>
<tr>
<td>Clinical trial participant</td>
<td>52.2 (40.1–65.3)</td>
<td>.17</td>
<td>19.2 (16.4–22.0)</td>
<td></td>
</tr>
<tr>
<td>DCF custody</td>
<td>53.8 (47.5–59.8)</td>
<td></td>
<td>19.2 (17.3–20.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>58.9 (59.1–77.2)</td>
<td></td>
<td>17.2 (12.2–22.0)</td>
<td></td>
</tr>
</tbody>
</table>

SSRI, selective serotonin reuptake inhibitor.
There are important limitations to this research study. This was a retrospective chart review of clinical data, with parental presence being a new metric for nurses to document after transitioning to a new electronic medical record. As a result, for each infant, parental presence was documented an average of only 68.0% (95% CI, 64%–72%) of the time. Additionally, the way parental presence was documented does not allow us to assess the amount of time spent or the level of parental involvement, only that they were present at the time the scoring took place. Data on which caregiver was present were not available. Infants who did not receive pharmacologic treatment were excluded, because their hospital stays are inherently shorter, and the number of untreated infants in this cohort was too small to separate in a subgroup analysis.

Additionally, our institution has a number of unique factors in caring for infants with NAS that may limit the generalizability of the study. First, our model of care for infants with NAS on the inpatient pediatric ward was developed to maximize parental inclusion and involvement. Second, during the study period, >85% of infants required pharmacologic treatment, which is significantly higher than the national average and may have been secondary to a strict protocol aimed at early capture of symptoms to attempt to reduce LOS. Based on recent research, we have since modified our model of care to focus on the functioning of the infant (and ability to eat, sleep, and be consoled), with a 50% drop in our medication treatment rates. Despite these limitations, this study supports the growing body of literature that promoting rooming-in encourages breastfeeding and that the percentage of time parents are present in the hospital contributes to a reduction in LOS for pharmacologically treated infants.

**CONCLUSIONS**

In summary, this study supports the role of rooming-in and parental engagement in infant care for decreasing withdrawal severity, LOS, and pharmacologic treatment of infants with NAS. Additionally, the strong association of breastfeeding with parental presence suggests that breastfeeding should be encouraged to improve outcomes for infants with NAS. Clinical practice guidelines for the management of NAS should encourage parental presence in the model of care. Future research into the barriers that prevent parental presence at the bedside and interventions to increase parental presence at the bedside are warranted.

**Acknowledgments**

We thank the patients and families who made this research possible. We acknowledge the Boston Medical Center Department of Pediatrics, Inpatient Pediatric and Newborn Nursery Care Teams for their involvement as well as the Boston Medical Center Neonatal Abstinence Syndrome Quality Improvement and Research working groups. We also acknowledge Howard Cabral, PhD, MPH, for his assistance with statistical analyses. We also thank the Boston Combined Residency Program for their support of this research project.

**REFERENCES**


RESEARCH ARTICLE

Costs of Care for Hospitalized Children Associated With Preferred Language and Insurance Type

K. Casey Lion, MD, MPH,a,b Davene R. Wright, PhD,a,b Arti D. Desai, MD, MSPH,a,b Rita Mangione-Smith, MD, MPHa,b

ABSTRACT

OBJECTIVE: The study goal was to determine whether preferred language for care and insurance type are associated with cost among hospitalized children.

METHODS: A retrospective cohort study was conducted of inpatients at a freestanding children’s hospital from January 2011 to December 2012. Patient information and hospital costs were obtained from administrative data. Cost differences according to language and insurance were calculated using multivariate generalized linear model estimates, allowing for language/insurance interaction effects. Models were also stratified according to medical complexity and length of stay (LOS) ≥3 days.

RESULTS: Of 19,249 admissions, 8% of caregivers preferred Spanish and 6% preferred another language; 47% of admissions were covered by public insurance. Models controlled for LOS, medical complexity, home-to-hospital distance, age, asthma diagnosis, and race/ethnicity. Total hospital costs were significantly higher for publicly insured Spanish speakers ($20,211 [95% confidence interval (CI), 7781 to 32,641]) and lower for privately insured Spanish speakers ($16,730 [95% CI, −28,265 to −5195]) and publicly insured English speakers ($48,41 [95% CI, −67,81 to −29,02]) compared with privately insured English speakers. Differences were most pronounced among children with medical complexity and LOS ≥3 days.

CONCLUSIONS: Hospital costs varied significantly according to preferred language and insurance type, even adjusting for LOS and medical complexity. These differences in the amount of billable care provided to medically similar patients may represent either underprovision or overprovision of care on the basis of sociodemographic factors and communication, suggesting problems with care efficiency and equity. Further investigation may inform development of effective interventions.

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Dr Lion participated in study conceptualization and design, performed the data analysis, drafted the initial manuscript, and revised it critically; Dr Wright participated in study conceptualization and design, assisted with data analysis, and critically reviewed and revised the manuscript; Dr Desai participated in study conceptualization, assisted with data analysis, and critically reviewed and revised the manuscript; and Dr Mangione-Smith oversaw all aspects of the study, participated in study conceptualization and design, and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.
In 2011, 15% of US children lived at least 1 parent who had limited English proficiency (LEP), defined as speaking English less than "very well." Language barriers in health care have been associated with decreased adherence, comprehension, and satisfaction with care, and increased risk for serious adverse events. Language barriers often co-occur with other potential barriers to high-quality care, including poverty, low health literacy, and public insurance. However, the degree to which these factors interact with LEP to influence utilization and outcomes is poorly understood. Understanding these interactions may help target interventions to the patient population most likely to benefit.

Health care costs may be used to identify disparities in the provision of health care by revealing differences in care patterns at the clinic, hospital, or population level. Cost serves as a proxy for the amount of billable care provided to a given patient, which should be similar for medically similar patients. Examining differences in costs on the basis of demographic factors can facilitate identification of disparities in care, which in turn facilitates investigation and intervention.

The primary objective of the present study was to examine the association between costs of hospitalization and the interaction between patient language and insurance type at a freestanding children's hospital. We used insurance type (private versus public) as a proxy for income level because it is highly correlated with family income and was available for all patients. Secondary objectives included determining if cost variation was consistent across subpopulations defined according to level of medical complexity and length of stay (LOS).

METHODS

Study Population and Setting

Patients aged ≤21 years discharged from the inpatient medical or surgical unit of a freestanding children's hospital from January 1, 2011, through December 31, 2012, were eligible for this study. Patients admitted to observation status, bone marrow transplant, rehabilitation, or inpatient psychiatry were excluded because these admission types have unique patterns of resource utilization. Both medical and surgical inpatient (but not observation) admissions were included, as we expected family language, culture, and social or financial constraints to be interfacing with care delivery in similar ways for both groups. All eligible admissions were included for a given patient, clustering according to individual in the analysis. We also restricted assessments to first hospitalization in the study period in a sensitivity analysis.

The study hospital has comprehensive professional interpreter services (in-person, telephone, and video). However, the present study was unable to track the type and amount of interpreter services provided.

Predictors and Covariates

Primary Independent Variables

Caregiver-reported preferred language for medical communication was recorded in the electronic medical record at hospital registration. Patient caregivers were classified as preferring English (hereafter referred to as “English speakers”), Spanish (hereafter referred to as “Spanish speakers”), or another language. Insurance type was obtained from hospital administrative data and categorized as private or public (ie, Medicaid). Because <1% of children hospitalized at our institution are uninsured, they were included with the publicly insured patients.

Covariates

Patient race and ethnicity were collected at registration according to caregiver report. The following mutually exclusive categories were used for analysis: non-Hispanic white (“white”), non-Hispanic black (“black”), Hispanic of any race (“Hispanic”), Asian or Pacific Islander, other or mixed, and refused or unknown. Patient medical complexity was categorized according to the Pediatric Medical Complexity Algorithm, which classifies children as having no chronic illness, noncomplex chronic illness, or complex chronic illness by using retrospective International Classification of Diseases, Ninth Revision, codes. The Pediatric Medical Complexity Algorithm accounts for both diagnoses and intensity of utilization, and it does not require a minimum amount of retrospective data; however, it only uses data from the previous 3 years, beginning with the date of admission.

Patient LOS was obtained from hospital administrative data. Given its skewed distribution, the variable was winsorized at the 99th percentile. Accordingly, 192 admissions with LOS >60.7 days were assigned an LOS of 60.7 days.

Patient address and geographic information systems software were used to determine distance between home address and the hospital. Distances from the hospital were classified as <30 miles, 30 to 60 miles, 61 to 120 miles, >120 miles, or missing. Distance provided information about potential barriers to discharge and severity of illness, as children who reside long distances from this hospital are typically those who require tertiary and quaternary care.

We controlled for having an asthma diagnosis according to International Classification of Diseases, Ninth Revision, codes for several reasons. First, asthma is a common reason for admission that disproportionately affects lower income and minority children. Second, asthma admissions have shorter LOS and lower costs compared with other admissions, which might confound our analysis. Hospital administrative data were also used to identify the primary treating service (eg, hematology-oncology) for each admission.

Outcomes

Hospital charges were obtained from administrative data, including total charges and those designated as laboratory, pharmacy, and radiology. Charges for interpreter services were not included because these are not billed to families.
Charges were converted to costs by using the hospital-specific cost-to-charge-ratio, then inflation-adjusted to 2012 US dollars according to the medical care component of the Consumer Price Index.23,24 Because cost data have a skewed distribution, costs within each category were winsorized at the 99th percentile, affecting 193 encounters with total cost values from $362 661 to $3 455 981.

**Primary Analysis**

Descriptive statistics were generated for all predictors and outcomes. Multivariate analyses used generalized linear models with a log link and \( \gamma \) family.25 A separate multivariate model was constructed for each cost outcome: total, pharmacy, laboratory, and radiology. The relationships between the predictors of interest (language and insurance type) and each outcome were assessed, adjusting for race/ethnicity, LOS, age, medical complexity, distance from the hospital, and asthma diagnosis; they were clustered on individual. Given the potential for collinearity between language, race/ethnicity, and insurance status, multicollinearity diagnostic analyses were performed. All variance inflation factors were <5, indicating no problematic multicollinearity within the data set.26

Interaction terms between language, insurance type, and race/ethnicity were introduced into the multivariate models. Interactions associated with the outcomes at \( P < .05 \) were retained. Marginal differences in costs, according to language and insurance type, were then predicted from the generalized linear models.

**Secondary Analysis**

To investigate whether observed variation in costs differed according to patient medical complexity, the primary analysis of total costs was repeated after stratifying by medical complexity level: nonchronic, noncomplex chronic, and complex chronic. We also repeated the primary analysis after stratifying by LOS \( >5 \) days. In both cases, all covariates listed in the main analysis were controlled for, excluding the stratification variable.

**Sensitivity Analyses**

To assess whether cost patterns according to demographic characteristics were due to different types of illnesses requiring hospitalization, each of 26 admitting services was assessed for association with language, insurance type, and language/insurance combinations. The 12 services that were significantly associated with any of the predictors were included as additional covariates in a sensitivity analysis, which otherwise included the variables described previously. We also ran the models looking at total costs without controlling for LOS and after restricting inclusion to each patient’s first hospitalization during the study period. Finally, we reran the analyses after Winsorizing total costs and LOS at the 95th percentile (rather than the 99th percentile) to assess the influence of the most extreme values on our outcomes.

**RESULTS**

There were 19 249 hospital admissions that met study inclusion criteria, of which 47% were covered by public insurance and 14% involved caregivers preferring a non-English language for medical care (Table 1). Among admissions from Spanish-speaking families, 96% had public insurance. Overall median LOS was 2.6 days (interquartile range [IQR], 1.2 to 5.1 days; 95th percentile, 19.5 days; mean \( \pm \) SD, 5.8 \( \pm \) 13.5 days), and overall median hospital costs were $12 842 (IQR, $6 550 to $27 011; 95th percentile, $106 195; mean, $32 542 \( \pm \) $89 830).

**Total Costs**

In multivariate analysis, the interaction term between language and insurance type was statistically significant and was thus retained in the model. Because of the interaction term, the reference group for all language and insurance combinations was privately insured English speakers. In adjusted analyses, publicly insured English speakers had hospital stays that were $48 441 less expensive (95% confidence interval [CI], $6 781 to $29 092; \( P < .001 \)) (Fig 1) than the referent. Similarly, privately insured Spanish speakers had hospital stays that were $16 730 less expensive (95% CI, $28 265 to $5 195; \( P = .004 \)).

Publicly insured Spanish speakers, in contrast, had hospital stays that were $20 211 more expensive (95% CI, $7 781 to 32 641; \( P = .001 \)) than the referent. There were no significant differences in total cost among either privately or publicly insured children from families preferring other languages compared with the referent.

**Pharmacy, Laboratory, and Radiology Costs**

In the multivariate analysis of pharmacy costs \( (n = 18 973) \), a similar pattern to overall costs was found (Fig 2). Pharmacy costs were lower for publicly insured English speakers \( ($3 463 [95\% CI, $5 228 to $1 697]; P < .001; \) and privately insured Spanish speakers \( ($1 1485 [95\% CI, $2 285 to $3 14]; P = .056 \) and higher for publicly insured Spanish speakers \( ($15 560 [95\% CI, $2 529 to 28 592]; P = .01 \) compared with privately insured English speakers.

Among families preferring other languages for care, pharmacy costs were lower for those with public insurance \( ($6 317 [95\% CI, $1 2 038 to $5 41]; P = .03).\)

Adjusted analysis of laboratory costs \( (n = 16 240) \) revealed lower average costs for publicly insured English speakers \( ($4 29 [95\% CI, $7 78 to $7 9]; P = .02) \) and higher costs for publicly insured children preferring other languages \( ($13 51 [95\% CI, 174 to 252]; P = .02).\)

Analysis of radiology costs \( (n = 11 911) \) revealed lower costs for publicly insured English speakers only \( ($2 89 [95\% CI, $3 99 to $139]).\)

**Secondary Analyses**

Stratification according to medical complexity revealed no variation in cost by insurance or language among children with no chronic illness \( (n = 4826) \). Among children with noncomplex chronic illness \( (n = 4754) \), publicly insured English speakers had significantly less expensive hospital stays \( ($6 240 [95\% CI, $12 275 to $205]; P = .01) \), but there were no differences detected among non-English speakers. Among children with complex chronic illness \( (n = 9669) \), results mirrored those of our primary analysis, with less expensive
DISCUSSION

In this study of 19,249 hospital admissions, patterns of hospital costs varied significantly according to insurance type and preferred language for medical communication, even after controlling for potential confounders (including medical complexity, LOS, hospital service, and distance between the child’s home and hospital). Compared with privately insured English speakers, publicly insured English speakers and privately insured Spanish speakers had less costly hospital stays, whereas publicly insured Spanish speakers had more expensive stays. These patterns were most pronounced among children with hospital stays ≥3 days in length and those with complex chronic illness. Pharmacy and laboratory costs generally mirrored total cost patterns, with less variation in radiology costs. These results suggest there were differences in the amount of billable care provided to hospitalized children on the basis of demographic, rather than clinical, characteristics.

Sensitivity Analyses

Results for the total cost model were unchanged after controlling for 12 clinical service lines or restricting to the first admission per patient during the study time period (data not shown). Results were similar, with similar to slightly attenuated effect sizes, when costs and LOS were winsorized at the 95th percentile rather than the 99th percentile (Supplemental Information). When not controlling for LOS, the total cost findings for both publicly and privately insured Spanish speakers were more pronounced, whereas the findings for publicly insured English speakers became nonsignificant (Table 2).

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For publicly insured English speakers, we found lower hospital costs compared with their privately insured counterparts in all cost categories. However, the cost differences were not significant when we stratified costs according to LOS or did not adjust for LOS. Because LOS is the largest contributor to hospital costs, this finding suggests that publicly insured English speakers may have been staying longer but using fewer resources per day. This lower intensity of resource utilization may be due to several factors. For example, perceived barriers to discharge (eg, lack of transportation and/or access to follow-up care for publicly insured patients) may lead to keeping a child in the hospital longer than might be strictly medically necessary. Previous studies have found longer LOS among children with Medicaid in populations hospitalized for spinal fusion, infections, and asthma. For example, Glick et al reported longer LOS and similar costs (adjusted for LOS) among Medicaid-insured children with asthma; however, they found low-income patients to have longer LOS but lower LOS-adjusted costs, similar to our findings. Another mediating factor may be lower parent engagement among publicly insured families, leading to less parental advocacy for additional clinical diagnostics and intervention. Previous studies have found that minority and/or low-income children were less likely to receive potentially inappropriate antibiotic prescriptions, suggesting less parental demand for unnecessary treatment. However, the present analysis cannot determine whether there was underutilization for publicly insured patients, overutilization for privately insured patients, or some combination of both.

Hospital stays among privately insured Spanish speakers were less expensive. Although their caregivers registered as preferring Spanish for medical communication, the fact that these children had private insurance suggests that at least 1 parent may have been English-proficient, as the majority of private insurance at the time was employer based, and most jobs offering insurance likely required some English proficiency. The language barrier for these families may have been lower than for publicly insured Spanish speakers, but their hospital costs still significantly differed from their privately insured English-speaking counterparts. This finding highlights a central difficulty in identifying LEP families in pediatrics. Whose English proficiency matters? Even if we know that caregivers’ English proficiencies differ, how can we know which caregiver was at the bedside, and when? Controlling for LOS attenuated but did not adjust away the difference, suggesting a shorter stay contributed to but did not entirely explain the cost findings. These results could be accounted for by less parental advocacy, perhaps informed by the cultural value among Latino subjects of respect for authority figures, but without the delays to discharge that are associated with public insurance. These lower cost findings were primarily driven by children with medical complexity and longer LOS. Because many of the children without medical complexity at our institution receive medical care that is

![Figure 1](image-url)
standardized according to diagnosis,33 there may have been fewer opportunities to provide unequal care based on family characteristics or provider biases for those children.

Publicly insured Spanish speakers had more expensive hospital stays, likely reflecting the impact of language barriers. As seen in previous studies, parental LEP may result in providers performing more tests, trying more treatments, or observing patients for longer periods to compensate for incomplete information and poor communication.4,5,7,34 These more expensive stays may also reflect poorer access to outpatient care or delayed presentation,10 although controlling for distance from home to hospital likely attenuated those associations. As we found among privately insured Spanish-speakers, these cost differences were driven by children with medical complexity and prolonged LOS, suggesting that language barriers, cultural factors, and provider biases are most likely to affect care in visible ways when that care is more complicated or less evidence-based and standardized.

We found no associations between total cost, insurance type, and preferring a non-English, non-Spanish language, likely because the “other” group was a mix of many smaller languages and cultures, each too small to evaluate individually. Consolidation of these groups for analysis, while presently unavoidable, may be obscuring associations. Evaluation with larger samples is needed.

Previous studies examining language and hospital utilization have reported mixed results, with some finding increased LOS5,7 or resource utilization6,35 generally within more narrowly defined diagnosis groups, and some finding none.36 Public insurance and/or other markers for socioeconomic status have also been linked to increased LOS and, in some cases, increased resource utilization (including costs).27–31 In the present study, because we included children with many conditions, we chose cost as our outcome (rather than utilization of specific resources) because it provides a measure of all billable medical care that was provided during a hospitalization. We are unaware of other studies successfully able to examine the joint impact of language and insurance type on cost or utilization. Levas et al.7 in their study of children hospitalized with infections, found increased LOS associated with both parental LEP and public insurance but failed to find statistical interaction between the 2 factors; however, they were likely underpowered for such an analysis, with only 39 LEP families, of whom only 3 were privately insured. Failure to consider interactions between the multiple barriers to full engagement with the health care system that a family faces may mask the effects of factors that are exerting simultaneous, opposing pressures. For example, because the privately and publicly insured Spanish speakers had different cost patterns, assessment of cost according to language alone might miss important differences that deserve evaluation. Aside from language and insurance, other factors may create barriers to receiving equitable care, such as low health literacy, limited self-efficacy, and lack of trust in the system; these factors should also be

![Figure 2](https://example.com/figure2.png)
considered when targeting interventions to improve equity.

This study had several limitations. It was conducted at a single institution, and thus the results may not be generalizable. However, preferred language is generally not available in multi-institution data sets, as few institutions routinely collect or report this information. We were unable to account for the amount and type of professional interpreter services provided in our analysis; costs may have differed by the degree to which the language barrier was effectively bridged. Another limitation was our use of insurance type as a proxy for family income. We used insurance, rather than census tract income data, because we had this information for all participants but were missing home address data for nearly 20% of subjects (mostly post office box addresses). Although insurance type provides some idea of family income for many families, it may misclassify children with public insurance due to medical complexity, and it fails to account for additional elements of socioeconomic status such as parental education. It is also possible that the identified cost differences were driven by medical needs, or the continuation of expensive home medications, rather than demographic characteristics; however, our findings were robust to adjustment for a variety of markers of complexity and illness type. It should also be noted that LOS is central to overall costs, pharmacy costs (as most medications are given daily), and, to a lesser extent, laboratory costs; although all of our analyses controlled for LOS, differences in LOS likely remained an important driver of those outcomes. Finally, it is unclear whether the observed cost differences in this study reflect overutilization or underutilization.

### TABLE 2

<table>
<thead>
<tr>
<th>Preferred Language</th>
<th>Insurance Type</th>
<th>Main Analysisa</th>
<th>Stratified Analysisb</th>
<th>Sensitivity Analysis c</th>
</tr>
</thead>
<tbody>
<tr>
<td>English</td>
<td>Public</td>
<td>0.93 (0.91–0.96)*</td>
<td>0.97 (0.94–1.01)</td>
<td>0.98 (0.93–1.04)</td>
</tr>
<tr>
<td></td>
<td>Spanish</td>
<td>0.79 (0.67–0.93)*</td>
<td>0.84 (0.80–1.12)</td>
<td>0.58 (0.34–1.00)*</td>
</tr>
<tr>
<td>Other</td>
<td>Private</td>
<td>1.34 (1.12–1.59)*</td>
<td>1.08 (0.91–1.30)</td>
<td>1.75 (1.01–3.02)*</td>
</tr>
<tr>
<td></td>
<td>English</td>
<td>1.05 (0.95–1.17)*</td>
<td>1.01 (0.87–1.18)</td>
<td>1.11 (0.91–1.37)</td>
</tr>
<tr>
<td></td>
<td>Public</td>
<td>0.95 (0.84–1.07)*</td>
<td>0.94 (0.80–1.11)</td>
<td>1.01 (0.80–1.28)</td>
</tr>
</tbody>
</table>

* Based on a generalized linear model with log link, y family, and clustered on individual, controlling for LOS, race/ethnicity, distance from hospital, medical complexity, asthma diagnosis, age category, insurance type, preferred language, and the interaction between insurance and language.

* Adjusting for same potential covariates as main analysis and stratified according to LOS ≥3 days.

* Identical to main analysis but not controlling for LOS.

* P < .05.

* P < .05.
CONCLUSIONS

We found that costs of pediatric hospitalizations varied significantly based on the child’s insurance type and the family’s preferred language for care, even after controlling for LOS and medical complexity. This finding suggests that disparities may exist in the provision of medical care on the basis of demographic characteristics. Poor access to outpatient care may lead to requiring more services when children are inpatients; however, lower LOS-adjusted costs were found for publicly insured English speakers and privately insured Spanish speakers, and only publicly insured Spanish speakers had more expensive stays. These differences between language and insurance groups in the amount of billable care being provided require additional investigation to determine whether they reflect overutilization, underutilization, or both. In addition, the relative contributions of language barriers, health literacy, parental activation and advocacy, and provider bias should be explored. Identifying patterns of disparate care and their causes is essential for development of interventions to improve the equity and efficiency of inpatient pediatric care.

REFERENCES


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A Critical Asthma Standardized Clinical and Management Plan Reduces Duration of Critical Asthma Therapy

Jackson Wong, MD, Michael S.D. Agus, MD, Dionne A. Graham, PhD, Elliot Melendez, MD

ABSTRACT

BACKGROUND AND OBJECTIVE: Reduction of critical asthma management time can reduce intensive care utilization. The goal of this study was to determine whether a Critical Asthma Standardized Clinical Assessment and Management Plan (SCAMP) can decrease length of critical asthma management time.

METHODS: This retrospective study compared critical asthma management times in children managed before and after implementation of a Critical Asthma SCAMP. The SCAMP used an asthma severity score management scheme to guide stepwise escalation and weaning of therapies. The SCAMP guided therapy until continuous albuterol nebulization (CAN) was weaned to intermittent albuterol every 2 hours (q2h). Because the SCAMP was part of a quality improvement initiative in which all patients received a standardized therapy, informed consent was waived. The study was conducted in Medicine ICU and Intermediate Care Units in a tertiary care freestanding children’s hospital. Children ≥2 years of age who had CAN initiated in the emergency department and were admitted to the Division of Medicine Critical Care with status asthmaticus were included. The time to q2h dosing from initiation of CAN was compared between the baseline and SCAMP cohorts. Adverse events were compared. The Mann-Whitney test was used for analysis; P values <.05 were considered statistically significant.

RESULTS: There were 150 baseline and 123 SCAMP patients eligible for analysis. There was a decrease in median time to q2h dosing after the SCAMP (baseline, 21.6 hours [interquartile range, 3.2–32.3 hours]; SCAMP, 14.2 hours [interquartile range, 9.0–23.1 hours]; P < .01). There were no differences in adverse events or readmissions.

CONCLUSIONS: A Critical Asthma SCAMP was effective in decreasing time on continuous albuterol.

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Drs Wong, Agus, and Melendez conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, conducted initial analysis, drafted the initial manuscript, and reviewed and revised the manuscript; and Dr Graham designed the data collection instruments, coordinated and supervised data collection, conducted the initial analysis, and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.
Asthma continues to be a national and international health priority. A pediatric study in 2011 showed that although the rate of admission for asthma decreased by one-half during a 15-year period, the rate of critical asthma care tripled and hospital costs increased from $6.6 million to $9.5 million for a single state. Two reviews of the Pediatric Health Information System found marked regional variations in the choice of critical asthma medical interventions when children did not improve with standard therapy (inhalation of β-agonists and steroids). These investigators suggested that a clinical asthma score which directs asthma interventions may decrease clinical variation in care and improve cost of care. Critical asthma is considered to be present when a patient requires continuous albuterol nebulization or more advanced therapies for respiratory distress after standard asthma treatment in the emergency department (ED) has failed to result in improvement. Ten thousand children per year will require critical asthma care, with estimates of the average length of stay (LOS) ranging from 66.2 ± 8.7 hours to 116 ± 125 hours. LOS can be decreased with the use of “standard” pediatric inpatient asthma pathways (LOS, 4.2–2.7 days), but there are still concerns regarding the total cost of care and readmission rates. Despite these concerns, there are no “standard” asthma therapies for life-threatening asthma. Standardized Clinical Assessment and Management Plans (SCAMPs) have been shown to be effective in decreasing variation in clinical practice in children. They are iterative, data-backed, consensus-based care pathways aimed at improving patient care, reducing unnecessary resource utilization, and lessening clinician practice variability. In contrast to the implementation of traditional clinical practice guidelines, the SCAMP process involves data collection on pathway compliance and measures specific outcomes. This process thus allows for evaluation of the pathway and uses these data to improve upon the pathway in subsequent iterations. In addition, if an area in the algorithm is consistently associated with nonadherence, this pathway is compared with those with adherence to understand if the alternative pathway leads to improved outcomes. Oversight of the production of SCAMPs is provided by the Institute for Relevant Clinical Data Analytics, which is a nonprofit, tax-exempt organization that provides the education and resources for the development, implementation, and analysis of SCAMPs at its member institutions.

The Critical Asthma SCAMP was constructed as a quality improvement project to standardize asthma therapy in children who had continuous albuterol nebulization (CAN) initiated, with helium-oxygen–driven CAN (Heliox-CAN) as the adjunct therapy if the patient clinically did not improve or worsened. The hospital-wide asthma severity score (HASS) was used to direct the step-wise escalation or de-escalation of therapy until intermittent albuterol every 2 hours (q2h) occurred, which is the time point at which a patient can be transitioned to the inpatient floor at our institution. This particular SCAMP was designed to foster autonomy of the nursing and respiratory therapists by instituting conditional orders for management.

The primary aim of the present study was to determine whether the implementation of a SCAMP that used an HASS to trigger escalation and weaning of asthma therapies resulted in a decreased time of critical care management. A secondary aim was to determine whether the Critical Asthma SCAMP could be implemented without leading to worse patient outcomes or increased adverse events.

METHODS

Study Design

This single-site retrospective study included all patients (≥2 years of age) with a diagnosis of status asthmaticus in whom CAN was initiated in the ED and were admitted to the Boston Children’s Hospital (BCH) Intermediate Care Unit (InCU) or Medicine ICU (MICU) before any other ICU asthma therapies (intravenous terbutaline and noninvasive or invasive positive pressure ventilation (NIPPV and intermittent mechanical ventilation, respectively)). The InCU and MICU are subdivisions of the Division of Medicine Critical Care but geographically located adjacent to each other. The InCU is staffed 60% of the time by pediatric hospitalists, but an intensivist is immediately available if needed. The remainder of the InCU staffing, the entire MICU staffing, and all times from 5:00 PM to 8:00 AM are staffed by pediatric intensivists.

The Critical Asthma SCAMP (Fig 1) standardized the administration of CAN, intravenous steroids, intermittent ipratropium inhalation, and Heliox-CAN as an adjunct therapy in children with critical status asthmatics. The initiation of CAN occurred independently of the SCAMP per the clinical discretion of the ED attending physician. Before initiation of the SCAMP, all children ≥2 years of age admitted to the InCU or MICU on CAN were treated per the discretion of the Division of Medicine Critical Care attending physician. After implementation of the SCAMP, all children >2 years of age on CAN were managed via the SCAMP. There was no change in the physician, nursing, or respiratory therapy staffing ratio between the baseline and SCAMP periods, and no other algorithms were used to manage children with critical status asthmatics.

HASS was used to direct the escalation and de-escalation of critical asthma therapies until albuterol was weaned to intermittent dosing q2h. The HASS is currently a nonvalidated asthma severity score created for local use (S. McBride, MD, K. McCarthy, CPN, J. Wong, MD, V Chiang, MD, unpublished observations) (Table 1). The primary end point was defined as the time from initiation of CAN to the time when the patient reached q2h albuterol. In children who may have reverted to more frequent albuterol dosing than q2h or back to CAN due to worsening course, the final time that the child successfully achieved q2h dosing was used to assess the primary outcome. The time to q2h dosing was compared between baseline and SCAMP patients.

The study time periods for the baseline period ranged from May 2011 to March 2012 and from June 2012 to March...
FIGURE 1 Critical Asthma Standardized Clinical Assessment and Management Plan (SCAMP). BCH, Boston Children's Hospital; CXR, Chest x-ray; FiO2, fraction of inspired oxygen; OSH, outside hospital; SpO2, oxygen saturation by pulse oximetry; tcCO2, transcutaneous carbon dioxide.
1. If you did not continue on continuous albuterol, why?

2. If you did not order a CXR, why?

3. If you did not space to Q1 Albuterol when HASS < 8, why?
   - Patient not ready
   - Family-patient request
   - Lack of resources: MD RN RT
   - Spacing would be more successful in the morning
   - Other

4. If you did not proceed to ICU specific therapy when HASS > 12 as indicated in the decision tree, why?
   - Patient was improving but slowly
   - Patient did not require ICU specific therapy
   - Patient required more time on current treatment to assess the need of ICU therapies
   - Concerns of potential of ICU specific therapies toxicity
   - Other

5. If you did not initiate Heliox when HASS > 12 at hours 1-3 or when HASS ≥ 8 at hour 4, why?
   - Patient has pneumonia
   - Patient did not require escalation of care
   - Patient needed ICU specific therapies
   - Heliox would not be effective in this patient because (see E)
   - Other

6. If HASS is not obtained every hour, why?

7. If trial of Q1 Albuterol nebulization not done every 24 hours, why?

8. If Heliox not continued when HASS 8-12, why?

9. If you did not restart continuous Albuterol when HASS ≥ 8 after Q1 Albuterol, why?
   - Patient clinically improving
   - Patient HASS increased because he was asleep
   - Patient did not tolerate continuous albuterol
   - Insufficient time to evaluate the need to restart continuous albuterol
   - Other

FIGURE 1 Continued. Critical Asthma Standardized Clinical Assessment and Management Plan (SCAMP) Continued. BCH, Boston Children's Hospital; CXR, Chest x-ray; FiO2, fraction of inspired oxygen; OSH, outside hospital; SpO2, oxygen saturation by pulse oximetry; tcCO2, transcutaneous carbon dioxide.

2013 for the SCAMP cohort. The time period between March 2012 and June 2012 was a pilot period to correct logistical issues of implementation, but the SCAMP was not modified during this time period. All patients meeting inclusion criteria during the time periods were eligible for analysis. Patients were excluded if CAN was initiated outside BCH because the ED treatment at BCH for asthma is also standard, and we could not account for variation in treatment at referring facilities. Information from the medical record pertinent to medical therapy for critical asthma was extracted, compiled, and de-identified for analysis. Informed consent was waived because this study was a retrospective medical
10. If you did not continue Q1 Albuterol when HASS < 8, why?

11. If you did not space to Q2 Albuterol when HASS < 8, why?

**Best Clinical Judgment**

12. At Best Clinical Judgment after 8 hours of Heliox, what was your course of action? Please provide a reason for course of action.

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<tbody>
<tr>
<td>A</td>
<td>Q1</td>
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<td></td>
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<td>Patient was able to be spaced</td>
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<td></td>
<td></td>
<td>Other</td>
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<tr>
<td>B</td>
<td>Continuous Albuterol</td>
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<td></td>
<td></td>
<td>Patient improving but not ready to space</td>
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<td>Patient did not improve on Heliox</td>
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<td></td>
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<td>Other</td>
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<td>C</td>
<td>Continue Heliox</td>
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<td></td>
<td></td>
<td>Patient improving but not ready to space</td>
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<td>Patient not clinically indicated for ICU specific therapy</td>
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<td>D</td>
<td>ICU</td>
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<td></td>
<td></td>
<td>Patient condition worsening</td>
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<td>Patient not maintaining face mask</td>
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<td>Other</td>
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</tbody>
</table>

13. At Best Clinical Judgment at HASS > 12 or clinically indicated, what was your course of action after restarting continuous Albuterol? Please provide a reason for course of action.

<p>| | | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Heliox</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Patient may benefit from a late trial of Heliox</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Patient not clinically indicated for ICU specific therapy</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Other</td>
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<tr>
<td>B</td>
<td>ICU</td>
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<tr>
<td></td>
<td></td>
<td>Patient condition worsening</td>
<td></td>
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<td></td>
<td></td>
<td>Heliox would not be effective in this patient because (see 3)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Other</td>
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</tr>
</tbody>
</table>

**FIGURE 1** Continued.
weaning was recorded. Escalation to any other ICU asthma therapies (terbutaline, NIPPV, or intubation) beyond CAN or Heliox-CAN was also recorded.

To assess whether implementation of the SCAMP was associated with any adverse events, we recorded results of chest radiograph and electrocardiograph (ECG) testing. ST-segment elevation was defined if formal cardiology interpretation of the ECG was of ST-segment elevation. The incidence of adverse effects such as intubation, respiratory or cardiac arrest, and pneumothorax and pneumomediastinum were recorded. Readmissions to the InCU or MICU after discharge to the inpatient floor within 24 hours, readmission to the hospital within 7 days, and any ED visits within 72 hours of discharge were recorded as markers of failure of rapid weaning.

**Data Analysis**

A planned analysis was performed at 9 months from SCAMP initiation to assess outcomes and balancing measures. Demographic and ED presentation characteristics were compared between the baseline and SCAMP cohorts with \( \chi^2 \) tests for categorical variables and Wilcoxon rank sum tests for continuous variables. Similarly, time to q2h and LOS (hours) was compared between the 2 groups by using the Mann-Whitney test.

The following comparisons were made between the 2 groups by using Fisher’s exact test: the rates of escalation to Heliox-CAN; restart of CAN after weaning to intermittent albuterol; and escalation to IV terbutaline, NIPPV (continuous positive airway pressure or bilevel positive airway pressure), or intermittent mechanical ventilation. Rates of ancillary testing were compared with \( \chi^2 \) tests, and rates of adverse events and readmission were compared by using Fisher’s exact tests.

Medical record data were extracted and entered into a Microsoft Excel 2007 spreadsheet (Microsoft Inc, Redmond, WA). Statistical analysis was performed by using SAS version 9.3 (SAS Institute, Inc, Cary, NC). In all tests, statistical significance was achieved if a 2-sided \( P \) value was \( <.05 \).

**RESULTS**

In total, 150 baseline and 123 SCAMP patients with a diagnosis of asthma who were initiated on CAN before any ICU therapy were available for analysis. There was no statistical difference between the groups in terms of demographic characteristics except for race (\( P = .04 \)) (Table 2). The median ages of patients in the baseline and SCAMP groups were 6.2 years and 7.8 years, respectively (\( P = .29 \)). There were no clinically significant differences in initial vital signs, HASS, or venous blood gas results on clinical presentation between the 2 groups. The first HASS in the ED and the initial HASS before the start of CAN were not statistically different, with a median score of 9 in both cohorts.

There was a significant increase in the use of Heliox-CAN after SCAMP implementation (14.6% baseline vs 46.4% SCAMP; \( P < .001 \)). There was a 34% decrease in median time to q2h dosing (21.6 hours [interquartile range (IQR), 13.5 to 32.3 hours] vs 14.2 hours [IQR, 9.0 to 23.1 hours]; \( P < .01 \)), but there was no difference in LOS between the baseline and SCAMP groups (Table 3).

In the patients who received Heliox-CAN, there was a significant decrease in median time to q2h dosing: 40.3 hours (IQR, 30.5 to 75.5 hours) for baseline and 20.2 hours (IQR, 15.8 to 33.5) for SCAMP; \( P < .01 \). There was no difference in patients requiring restart of CAN after weaning to q2h dosing (14.8% vs 8.8%; \( P = .14 \)). Similarly, there was no increase in the need for ICU therapy or individual subtype of ICU therapy between the 2 groups (16.0% vs 12.0%; \( P = .34 \)) (Table 4).

The SCAMP algorithm was adhered to in full by the treating team in 84 (68.3%) of 123 patients. In 39 (31.7%) patients, there was at least 1 diversion from the recommended pathway. In review of patients with diversions, there was no obvious commonality among diversions to allow separate analysis. Patients with SCAMP full adherence were older than those with diversions (median age, 8.3 vs 6.5 years; \( P = .04 \)). There was no difference in adherence according to median initial HASS (9 in both groups; \( P = .51 \)). There was no difference in median time to q2h dosing between SCAMP full compliance patients versus diversion patients (16.2 vs 13.6 hours;
documented reason for diversion.

Four patients did not have a care team felt the patients did not require SCAMP recommended escalation because the 4 (10.3%) did not escalate therapy when the SCAMP recommended no change due to concerns regarding worsening, and when the SCAMP recommended weaning because the care team believed patients still required CAN, 6 (15.4%) escalated therapy because the care team believed that patients were weaned from therapy when the SCAMP algorithm recommended continuing therapy.

$P = .89$). In diversions, 17 patients (43.6%) were weaned from therapy when the SCAMP algorithm recommended continuing therapy because the care team believed that patients were improved, 8 (20.5%) were not weaned when the SCAMP recommended weaning because the care team believed patients still required CAN, 6 (15.4%) escalated therapy when the SCAMP recommended no change due to concerns regarding worsening, and 4 (10.3%) did not escalate therapy when the SCAMP recommended escalation because the care team felt the patients did not require escalation. Four patients did not have a documented reason for diversion.

**TABLE 2** Patient Demographic and Clinical Characteristics at Presentation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline ($n = 150$)</th>
<th>SCAMP ($n = 123$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at initial visit, y</td>
<td>6.3 (2.1–21.9)</td>
<td>7.8 (2.0–24.6)</td>
<td>.29</td>
</tr>
<tr>
<td>Male sex</td>
<td>86 (57.3)</td>
<td>73 (58.4)</td>
<td>.86</td>
</tr>
<tr>
<td>BMI</td>
<td>18.3 (12.5–48.3)</td>
<td>20.1 (13.0–49.0)</td>
<td>.22</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>48 (32.0)</td>
<td>54 (43.2)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>45 (30.0)</td>
<td>32 (25.6)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>43 (28.7)</td>
<td>22 (17.6)</td>
<td>.04</td>
</tr>
<tr>
<td>Asian</td>
<td>4 (2.7)</td>
<td>8 (6.4)</td>
<td></td>
</tr>
<tr>
<td>Not recorded*</td>
<td>10 (6.7)</td>
<td>9 (7.2)</td>
<td></td>
</tr>
<tr>
<td>First recorded in ED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate, beats per min</td>
<td>136 (76–188)</td>
<td>131 (65–188)</td>
<td>.48</td>
</tr>
<tr>
<td>Respiratory rate, breaths per min</td>
<td>36 (16–80)</td>
<td>35 (16–88)</td>
<td>.80</td>
</tr>
<tr>
<td>ED laboratory tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous pH</td>
<td>7.4 (7.2–7.4)</td>
<td>7.4 (7.2–7.4)</td>
<td>.76</td>
</tr>
<tr>
<td>Venous PO2 (mmHg)</td>
<td>39.8 (25.0–71.8)</td>
<td>41.6 (22.7–62.6)</td>
<td>.24</td>
</tr>
<tr>
<td>Venous bicarbonate (mmol/L)</td>
<td>23.0 (12.0–29.0)</td>
<td>23.0 (13.0–30.0)</td>
<td>.52</td>
</tr>
<tr>
<td>HASS</td>
<td></td>
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</tr>
<tr>
<td>First recorded in ED</td>
<td>9.0 (5.0–14.0)</td>
<td>9.0 (6.0–13.0)</td>
<td>.50</td>
</tr>
<tr>
<td>At start of CAN</td>
<td>9.0 (5.0–14.0)</td>
<td>9.0 (6.0–14.0)</td>
<td>.22</td>
</tr>
</tbody>
</table>

Data are presented as median (IQR) or N (%). *Includes patients who declined to answer, for whom race is unknown, or for whom data were unable to be collected.

$P = .001$).

**Ancillary Testing**

There was no difference in the initial utilization of chest radiographs between the groups (87.3% baseline vs 85.6% SCAMP; $P = .67$). Similarly, among those patients with an initial chest radiograph, there was no difference in the number of follow-up chest radiographs between the groups (29.0% baseline and 29.9% SCAMP; $P = .88$). Fewer initial ECGs were obtained in the SCAMP group (30.7% baseline and 19.2% SCAMP; $P = .03$). However, there was no difference in the use of follow-up ECGs between the groups (18.0% baseline and 10.4% SCAMP; $P = .61$).

**TABLE 3** Comparison of Time to Wean Off CAN, qh2 Albuterol, and Hospital LOS Between Baseline and SCAMP Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline ($n = 150$)</th>
<th>SCAMP ($n = 123$)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heliox-CAN utilization</td>
<td>22 (14.8)</td>
<td>58 (46.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total time to q2h, h</td>
<td>21.6 (15.5–32.5)</td>
<td>14.2 (8.0–23.1)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Patients receiving CAN only</td>
<td>19.3 (12.7–26.7)</td>
<td>9.6 (6.9–13.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Patients receiving Heliox-CAN</td>
<td>40.3 (30.5–75.5)</td>
<td>20.2 (15.8–33.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospital LOS, h</td>
<td>63.8 (45.6–87.8)</td>
<td>56.5 (38.6–83.1)</td>
<td>.09</td>
</tr>
</tbody>
</table>

Data are presented as N (%) or median (IQR).

**Adverse Events**

Only 1 patient required intubation, and this patient was part of the SCAMP group ($P = .45$). No patient experienced respiratory arrest or cardiac arrest, needed extracorporeal membrane oxygenation, or required isoflurane inhalation. There were no deaths. One patient developed a pneumothorax, and this patient was in the SCAMP group ($P = .45$); 4 patients developed pneumomediastinum (2 baseline and 2 SCAMP; $P = .99$). No patients required a chest tube placement. There were no differences in ST-segment changes found on the initial ECG (19 [41.3%] of 46 baseline and 7 [29.2%] of 24 SCAMP; $P = .44$) or subsequent ECGs (7 [17.5%] of 42 baseline and 1 [2.4%] of 47 SCAMP; $P = .99$) between the groups. There were also no differences in prolonged QTc found on the initial ECG (6 [13.0%] of 46 baseline and 3 [12.5%] of 24 SCAMP; $P = .99$) or subsequent ECGs (3 [7.5%] of 40 baseline and 1 [4.8%] of 21 SCAMP; $P = .99$) between the groups. Use of Heliox-CAN did not affect these findings (all, $P > .05$), and there were no findings of ST changes or prolonged QTc in patients who received Heliox-CAN in either group.

One patient developed supraventricular tachycardia in the baseline group ($P = .61$), and 1 patient with a history of ectopic atrial tachycardia developed this condition in the SCAMP group. No patient required electrical cardioversion.

There was no difference in the number of patients who required readmission to either the inCU or MICU within 24 hours of transfer to the inpatient floor (1 baseline vs 3 SCAMP; $P = .33$). Only 1 patient required an ED visit within 1 week of discharge (0 baseline vs 1 SCAMP; $P = .45$), and no patient required readmission to the hospital within 7 days.

**DISCUSSION**

This study showed that the SCAMP significantly decreased by 34% the time it took to wean patients to intermittent albuterol from the start of continuous albuterol. The SCAMP improved clinical outcomes, and it was also safe. Despite the SCAMP having parameters for escalation of care to ICU therapies if the HASS increased despite use of CAN or Heliox-CAN, there was...
no increase in the need for ICU therapy compared with the baseline group. Similarly, despite the SCAMP dictating weaning to intermittent nebulization from CAN when the HASS decreased, there was no increase in the need for restarting CAN after the initial weaning to q2h dosing.

The 2007 National Asthma Education and Expert Panel provided extensive recommendations for standardization of outpatient asthma and management of acute exacerbation. However, the panel had limited evidence and guidance for adjunct therapies for critical asthma, including Heliox-CAN, which was categorized as Level B evidence. In addition, indications for Heliox-CAN, which was categorized as Level B evidence. In addition, indications for initiation of Heliox-CAN were not detailed. Heliox-CAN is a controversial therapy that has been shown to be effective and ineffective in the treatment of status asthmaticus. In this SCAMP, Heliox-CAN was standardized to both severity and time of application. The SCAMP did increase the use of Heliox-CAN compared with previous research, indicating that compliance to the SCAMP occurred by the treating teams. Although the methods of the SCAMP and this study do not prove that Heliox-CAN is an effective stand-alone therapy, it does show that when Heliox-CAN is part of a bundle of care for critical asthma, this bundle is effective in decreasing time on continuous albuterol.

The present study had several limitations. The SCAMP algorithm was followed fully in only 68.3% of patients. It is possible that the diversions themselves were appropriate clinical decisions, which drove improvement in the other patients, and that the algorithm had not had similar outcomes as those who did not deviate. There was no pattern in the deviations, but the majority occurred with decision to wean, and this approach may have further improved the entire cohort’s time to q2hs dosing. In addition, the HASS was developed at BCH and has not been formally validated in children with critical asthma as with other asthma scores. Despite this limitation, the scoring system did trend the clinical condition of the patient and was used in all patients. In addition, due to the SCAMP being a bundle of care, it is unclear which part of the bundle was the most efficacious in improving outcomes. Seasonality differences before and after the study period could have affected the results; however, we elected to use data that immediately preceded the implemented protocol so as to not have a full season gap between before and after groups. Finally, the SCAMP was implemented as a quality improvement project and, as a result, was not a blinded study; thus, confounders (eg, treatment biases, quality improvement oversight) could have driven the observed improvement. Despite decreasing time on continuous albuterol, it did not decrease hospital LOS. Lack of statistical significance for LOS is most likely due to a power issue because of smaller relative changes and more variance around LOS. In addition, with reaching 2 hours, the quality improvement oversight ended and asthma management reverted to standard clinical management by clinical examination (predominantly auscultation) rather than by HASS. Perhaps an extension of the SCAMP to hospital discharge would affect hospital LOS.

Based on SCAMP methods, a revision of the SCAMP is ongoing and will be implemented to assess if patients who had incomplete compliance with the critical asthma bundle had an impact on outcomes and to consider if themes on diversions should be adopted in a new iteration. Lessons learned from further analysis of the data from this SCAMP can lead to future modification of the SCAMP algorithm to further improve outcomes.

REFERENCES

CONCLUSIONS
A Critical Asthma SCAMP that provided a structured bundle of care, with a HASS-guided management plan for escalation and weaning of CAN and Heliox-CAN, reduced time on continuous albuterol. The approach of bundled standardized care can be a model for improving outcomes and may lead to earlier results when double-blind, randomized controlled trials might not be feasible.

Acknowledgments
The authors express their gratitude to the nursing and respiratory staff in the ICUs and MICUs, Medicine Critical Care Division SCAMPs Committee, and the Institute for Relevant Clinical Data Analytics. They specifically thank Patricia Mantell, RN, Jason M. Thorton, RN, Daria Donelly, RTT, Danielle Dwyer, MD, Denise Anderson, RN, Heather Kennedy, RN, Melissa Whalen, MPH, Jessica Sang, MPH, Joshua Barlett, BA, Estella Kanevsky, MPH, Dorothy Miller, MPH, Caitlyn McCarthy, MPH, and Suvidha Dabas, MPH.


RESEARCH ARTICLE

Improving Pediatric Rapid Response Team Performance Through Crew Resource Management Training of Team Leaders

Ashley Siems, MD, Alexander Cartron, BS, Anne Watson, MSc, PhD, BSN, RN, Robert McCarter Jr, ScD, Amanda Levin, MD

ABSTRACT

BACKGROUND: Rapid response teams (RRTs) improve the detection of and response to deteriorating patients. Professional hierarchies and the multidisciplinary nature of RRTs hinder team performance. This study assessed whether an intervention involving crew resource management training of team leaders could improve team performance.

METHODS: In situ observations of RRT activations were performed pre– and post–training intervention. Team performance and dynamics were measured by observed adherence to an ideal task list and by the Team Emergency Assessment Measure tool, respectively. Multiple quartile (median) and logistic regression models were developed to evaluate change in performance scores or completion of specific tasks.

RESULTS: Team leader and team introductions (40% to 90%, \(P = .004\); 7% to 45%, \(P = .03\)), floor team presentations in Situation Background Assessment Recommendation format (20% to 65%, \(P = .01\), and confirmation of the plan (7% to 70%, \(P = .002\)) improved after training in patients transferred to the ICU (\(n = 35\)). The Team Emergency Assessment Measure metric was improved in all 4 categories: leadership (2.5 to 3.5, \(P < .001\)), teamwork (2.7 to 3.7, \(P < .001\)), task management (2.9 to 3.8, \(P < .001\)), and global scores (6.0 to 9.0, \(P < .001\)) for teams caring for patients who required transfer to the ICU.

CONCLUSIONS: Targeted crew resource management training of the team leader resulted in improved team performance and dynamics for patients requiring transfer to the ICU. The intervention demonstrated that training the team leader improved behavior in RRT members who were not trained.
In 2006, the Institute for Healthcare Improvement published their “100,000 Lives Campaign” and included rapid response teams (RRTs) as a modality to improve patient safety. The adoption of RRTs has prevented cardiac and respiratory arrest, improved survival after these events, reduced the need for ICU-level treatments soon after transfer, and lessened the time between deterioration and treatments. In spite of these successes, RRTs, like other complex medical teams, are challenged by difficulties with communication and collaborative problem-solving. Barriers to RRT performance include varying levels of confidence with one’s own skills, challenges overcoming professional hierarchies, and expectations of adverse interpersonal conflict. Recently, the 2016 Joint Commission National Patient Safety Goal to “improve the effectiveness of communication among caregivers” signaled the growing recognition that improvement in the “nontechnical” social interaction skills of health care providers is critical for the delivery of safe and effective patient care. Adverse events can often be attributed to poor interpersonal interactions and coordination rather than insufficient clinical knowledge. Communication errors have been reported to be responsible for nearly 60% of all medical errors. Thus, approaches to improving RRT performance are necessary and should focus on interpersonal interactions and communication.

One such approach is crew resource management (CRM), which is a strategy of training with a focus on nontechnical skills that complement a provider’s clinical knowledge and promote the delivery of safe care. CRM training of high-performance teams in other high-risk industries, including the military, aviation, and nuclear power fields, includes adoption of standardized tools and behaviors to improve teamwork and reduce risk. CRM focuses on leadership, problem-solving, situational awareness, communication skills, and resource management to enhance team performance. Careful consideration of one’s own fatigue coupled with verbal and nonverbal communication are paramount. CRM training is most effective when structured around simulation exercises, in which providers have the opportunity to safely practice vital nontechnical skills and receive real-time feedback in an environment uncoupled from adverse events. Although nontechnical skills have not historically been taught in clinical medical education, implementation of CRM training in the ICU and other medical settings has been shown to reduce complications and lower mortality in critically ill patients. Due to its previous successful application in high-risk industry and preliminary data suggesting it can be applied to medical teams, we hypothesized that CRM training can help improve RRT performance. The purpose of the current study was to evaluate CRM nontechnical skills training as an improvement technique for RRT performance.

In designing this study, we recognized that training and maintaining the skills of every potential responder to an RRT (nurses, trainees, rotating trainees, and respiratory therapists) was expensive and impractical to sustain. We targeted the team leaders of our RRT to have a high impact and minimize the cost and time barriers associated with comprehensive CRM training programs. We hypothesized that training the team leader would improve the overall team performance as well as completion of ideal tasks during RRT activation.

**METHODS**

**Setting and Design**

This study was conducted on the acute care floors of a single, urban, tertiary 313-bed pediatric medical center from March 2015 to December 2015. This institution averages 50 RRT activations per month. The RRT consists of personnel from critical care medicine (CCM) including a critical care fellow or nurse practitioner (NP), an ICU charge nurse, and an ICU respiratory therapist (RT) who joins the acute care floor team consisting of the bedside nurse, floor charge nurse, primary team physician or physician extender, and floor RT at the patient’s bedside. A pre- and postintervention design was used to assess leadership and team performance during RRT activations. Observations of RRT activations occurred before and after team leader training in CRM. Observations were conducted in situ to assess the impact of our training in real-life hospital environments with challenges of stress, time-pressure, and coordination of personnel unfamiliar with one another.

**Team Leader Training**

Our team leader training consisted of 2 sessions that were conducted by physician champions with knowledge of CRM principles. The first 90-minute training session was built on adult learning theory. The learners engaged in active learning and were introduced to evidence that rapid response systems reduce patient morbidity while being instructed on the ideal RRT task list and CRM principles. First-year CCM fellows and NPs attended the first session because it was designed to target junior practitioners. The second 60-minute session used simulation training to reinforce CRM principles and apply them to common RRT scenarios. All CCM fellows and NPs attended the second session. We defined junior practitioners as NPs and first-year fellows because these providers were new to both our ICU and to the team leader role on the RRT.

**Observations**

Members of the research team (A.C., A.W.) conducted all in situ observations based on the observer’s availability when the RRT system was activated. RRTs at our institution are activated via pagers. The observers carried pagers and would go directly to the patient room when an RRT was activated. The ICU team has 15 minutes to respond to the page allowing for the observer to be in place before the ICU team arrival. All observations were during the day and represent a convenience sampling.

The RRT observations were conducted in 3 phases. Ten RRTs were observed in the project development phase to validate and test the data collection instrument. These observations were not included in the final analysis. During this phase, both observers were present at each RRT observed. The second phase was the preintervention stage, where 36 RRT activations were observed during the spring and early summer of 2015. The intervention, team
leader training, occurred during the midsummer of 2015 with 37 postintervention observations occurring in the late summer and fall. During the second and third phase, only 1 observer was required to be present, although 20% of observations in these phases had both observers present. Interrater reliability was assessed using the observations that both researchers attended.

The observers used a paper data collection tool and recorded patient demographics and characteristics of the RRT events (eg, patient age, sex, mean duration of the event, and who called the RRT). The disposition status was also recorded to determine which patients were transferred to the ICU. The observers are not members of the RRT and although they may be identified by RRT members as researchers, the nature and purpose of their observations were not disclosed until the end of the study.

Measures of Leadership and Team Performance
Two metrics were used to assess team performance: 1 to observe the completion of tasks essential to RRT activations and a second to assess the nontechnical skills of the RRT. A focus group of key stakeholders in RRTs at our institution, including ICU physicians, nurses, RTs, acute care nurses, nurse educators, and acute care physicians, identified 12 ideal tasks essential to RRT function. The task list was developed from consensus opinion and previously published research. Elements previously shown to enhance team performance and patient outcomes, including using standard safety language such as Situation Background Assessment Recommendation (SBAR) to enhance shared mental models, formulating and stating a clear plan if the patient is going to remain on the acute care floor, and using cross-check techniques to identify concerns with the plan key elements of the task list.\(^{36-38}\) The 12 ideal tasks were: (1) measuring patient vital signs; (2) ICU team introduces themselves; (3) ICU team leads team introductions; (4) acute care team presents using SBAR; (5) team leader asks for additional input from the acute care team; (6) ICU team assesses patient; (7) ICU team formulates a clear plan with disposition; the plan delineates a time frame for (8) interventions, (9) task delegation, and (10) an escalation plan given with expectations of outcome; (11) acute care team repeats back plan; and (12) the ICU team asks for final concerns and questions.

The nontechnical skills of the team were scored using the Team Emergency Assessment Measure (TEAM), a 12-item tool validated to measure the performance of medical emergency teams.\(^{39-41}\) The TEAM tool includes 12 statements and offers subscore composites in leadership, team work, and task management measured on a 0 to 4 Likert scale, ranging from “never/hardly ever” (0) to “about as often as not” (2) to “always/nearly always” (4). Overall global team nontechnical performance was measured using a Likert scale ranging from 0 to 10.

Adherence to each item on the RRT ideal task list was recorded during the event. Within 15 minutes after the event, the observer rated the nontechnical skills of the team using the TEAM tool. Study data were managed using REDCap (Research Electronic Data Capture, Vanderbilt University, Nashville, TN) tools hosted at Children’s National Medical Center.\(^{42}\)

Data Analysis
Sample size calculation was powered to detect a 15% improvement in the global rating of the TEAM score, resulting in an \(N = 35\) per observation group. Descriptive statistics are presented as percentages for dichotomous variables, averages, and SDs. Pre and postintervention comparisons were presented as adherence frequencies ±95% confidence intervals (CI) for elements of the ideal RRT task list and as medians with 95% CIs for the overall and component TEAM scores. \(P\) values < .05 were regarded as statistically significant. We performed a quantile (median) regression model based on quantile regression in Stata (Stata Corp, College Station, TX) for the analysis of scores. This regression enabled us to evaluate interaction effects of patient severity defined by the need for ICU transfer. The distributions of study outcomes was not normal (parametric) and could not be transformed to meet the parametric assumption required for linear regression modeling. Estimating the median provided a nonbiased estimate of the central tendency of the sample distribution and by inference

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pre (n = 36)</th>
<th>Post (n = 37)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average patient age, mo (mean ± SD)</td>
<td>91 ± 77</td>
<td>73 ± 68</td>
<td>.30</td>
</tr>
<tr>
<td>Patient sex</td>
<td></td>
<td></td>
<td>.35</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>21 (58)</td>
<td>17 (46)</td>
<td></td>
</tr>
<tr>
<td>Patient insurance type (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Medicaid</td>
<td>9 (25)</td>
<td>10 (27)</td>
<td>.84</td>
</tr>
<tr>
<td>Medicaid</td>
<td>25 (75)</td>
<td>27 (73)</td>
<td></td>
</tr>
<tr>
<td>English speaking (%)</td>
<td>32 (89)</td>
<td>28 (76)</td>
<td>.12</td>
</tr>
<tr>
<td>Transferred to ICU (%)</td>
<td>15 (42)</td>
<td>20 (54)</td>
<td>.35</td>
</tr>
<tr>
<td>Time of call (%)</td>
<td></td>
<td></td>
<td>.48</td>
</tr>
<tr>
<td>Morning</td>
<td>22 (61)</td>
<td>19 (51)</td>
<td></td>
</tr>
<tr>
<td>Afternoon</td>
<td>14 (39)</td>
<td>18 (49)</td>
<td></td>
</tr>
<tr>
<td>Mean time to arrival, min (mean ± SD)</td>
<td>9.5 ± 4.16</td>
<td>10.0 ± 4.08</td>
<td>.57</td>
</tr>
<tr>
<td>Mean duration of call, min (mean ± SD)</td>
<td>11.0 ± 4.26</td>
<td>12.8 ± 7.93</td>
<td>.26</td>
</tr>
<tr>
<td>Who called RRT (%)</td>
<td></td>
<td></td>
<td>.94</td>
</tr>
<tr>
<td>Primary provider</td>
<td>17 (47)</td>
<td>19 (51)</td>
<td></td>
</tr>
<tr>
<td>Nurse</td>
<td>16 (44)</td>
<td>15 (41)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3 (8)</td>
<td>3 (8)</td>
<td></td>
</tr>
<tr>
<td>Parent/family present, n (%)</td>
<td>25 (69)</td>
<td>28 (76)</td>
<td>.61</td>
</tr>
</tbody>
</table>
of the population from which the sample was drawn. When we evaluated discreet (categorical) outcomes, we relied on logistic regression, which allowed us to estimate the change in odds of the outcome associated with a unit change in the independent variable (predictor) of interest. All statistics were performed on Stata 2013 software.

RESULTS

Interrater reliability was determined to be high in all categories, including adherence to ideal RRT tasks (intraclass correlation coefficient [ICC] = 0.97), TEAM rating in leadership (ICC = 0.98), team work (ICC = 0.99), task management (ICC = 0.96), and global rating (ICC = 0.97).

Patient demographics and characteristics of the RRT events are listed Table 1. Leader demographics pre- and postintervention were uniform with 56% of the RRT activations led by junior practitioners preintervention and 51% postintervention ($P = .81$).

The regression model showed a significant interaction effect when grouping the events in terms of disposition: transfer versus no transfer to the ICU. Due to this interaction, adherence rates for items on the ideal task list pre- and postintervention are presented in Table 2 by transferred versus nontransferred. After the team leader training, the team leader introduced themselves (40% preintervention vs 90% postintervention, $P = .004$) and led introductions of the team more often (7% preintervention and 45% postintervention, $P = .03$) for patients who required ICU transfer as highlighted in Fig 1. Although no member of the floor team participated in CRM training or had been trained with the task list, floor team members presented their patient concerns using SBAR more often in both the ICU (20% preintervention to 65% postintervention, $P = .01$) and nontransfer (28% preintervention to 64% postintervention, $P = .03$) groups postintervention. For patients who were transferred to the ICU, the occurrence of cross-check behavior improved 10-fold, from 7% preintervention to 70% postintervention ($P = .002$).

Evaluation of nontechnical skills and team dynamics using the TEAM tool is displayed in Table 3. All 3 composite measures (leadership, 2.5 [95% CI, 2.1–2.9] to 3.5 [95% CI, 3.1–3.9]; teamwork, 2.7 [95% CI, 2.3–3.1] to 3.7 [95% CI, 3.4–4.1]; task completion, 2.9 [95% CI, 2.5–3.2] to 3.8 [95% CI, 3.5–4.1]) and the global rating (6.0 [95% CI, 4.9–7.1] to 9.0 [95% CI, 8.0–10.0]) increased for the events with patient transfer to the ICU. In addition, the task management composite score for the events with no transfer to the ICU (3.3 [95% CI, 3.0–3.6] to 3.8 [95% CI, 3.5–4.2]) improved significantly after the CRM intervention. The results for the events with an ICU transfer are highlighted in Fig 2.

### TABLE 2 Percentage Adherence to Ideal RRT Tasks Pre- and Post-CRM Training

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Pre (n = 21)</th>
<th>Post (n = 17)</th>
<th>$P$</th>
<th>Pre (n = 15)</th>
<th>Post (n = 20)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICU fellow/NP introduces self, % (95% CI)</td>
<td>62 (41–82)</td>
<td>88 (72–100)</td>
<td>.08</td>
<td>40 (15–65)</td>
<td>90 (77–100)</td>
<td>.004</td>
</tr>
<tr>
<td>PICU fellow/NP leads introduction of team, % (95% CI)</td>
<td>14 (0–29)</td>
<td>41 (17–64)</td>
<td>.07</td>
<td>7 (0–19)</td>
<td>45 (23–67)</td>
<td>.03</td>
</tr>
<tr>
<td>Primary RN or LIP presents SBAR, % (95% CI)</td>
<td>28 (5–48)</td>
<td>64 (42–87)</td>
<td>.03</td>
<td>20 (0–40)</td>
<td>65 (44–86)</td>
<td>.01</td>
</tr>
<tr>
<td>Robust plan stated (patient remained on floor), % (95% CI)</td>
<td>62 (41–83)</td>
<td>70 (48–92)</td>
<td>.57</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Primary resident repeats the plan (patient remained on floor), % (95% CI)</td>
<td>38 (17–59)</td>
<td>53 (29–77)</td>
<td>.36</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Cross-check, % (95% CI)</td>
<td>38 (17–59)</td>
<td>65 (42–87)</td>
<td>.11</td>
<td>7 (0–19)</td>
<td>70 (50–90)</td>
<td>.002</td>
</tr>
<tr>
<td>Update family, % (95% CI)</td>
<td>52 (31–74)</td>
<td>59 (35–82)</td>
<td>.89</td>
<td>67 (45–91)</td>
<td>80 (62–98)</td>
<td>.38</td>
</tr>
</tbody>
</table>

LIP is a licensed individual provider and may be a resident, NP, or attending physician.

Figure 1: Improvement in RRT ideal tasks adhered to pre- and post-CRM training in patients transferred to the ICU. Error bars represent 95% CIs.
DISCUSSION

In this pre- and postintervention direct observational study of team dynamics, we implemented a short, pragmatic, and cost-efficient CRM training session for the team leaders. We were able to demonstrate improved leadership and overall team performance of our RRT in the real hospital environment with the use of skills learned at the simulation center to crises in real clinical settings.43

Significant effects of this training were found primarily for RRTs caring for patients who were transferred to the ICU, with poorer performance scores before the intervention compared with events where the patient was not transferred. In other words, postintervention scores in patients transferred to the ICU reached levels similar to the preintervention, non-ICU transfer group. Higher acuity patients may increase the stress of a situation, create more chaos, and lead to team breakdown.44,45 We believe that focusing education on nontechnical skills allowed team leaders to gain insight into the impact of their tone and leadership style during events, especially when the outcome was transfer to the ICU. Concrete steps, such as leading introductions and facilitating an SBAR presentation, may have diffused the stress and chaos of a team trying to care for a rapidly deteriorating patient. The leaders may have also learned how to create a safe environment and reduce the burden of hierarchies on team performance.

Interestingly, we would have postulated that RRTs caring for patients who remain on the floor after RRT involvement might have had poorer team performance based on previous research.46–50 ICU team members often perceive that floor patients do not require ICU expertise, transfer occurs primarily due to nurse staffing issues on the acute care floor, and leaving the ICU for a RRT call compromises the care of patients in the ICU. Floor team members often perceive that they have difficulty accessing the resources they need on the floor, have received punitive responses from the ICU team for activating the RRT, and experience stress involved in having to justify a transfer. More research that specifically examines the flow of the 2 types of events is needed to additionally refine nontechnical skill development interventions.

RRTs are fast-start, multidisciplinary teams composed of members from different professions and specialties who need to quickly establish trust and good communication in high pressure situations. Most implementations of CRM training occur in small fixed teams and include all team members. We adapted CRM to unfixed teams and trained only 1 vital team member, the leader. Although full-staff training in CRM principles has clear benefits for patient safety, the start-up costs balanced by concerns over efficacy make comprehensive implementation unfeasible at most institutions.31–33,51–53 We were able to incorporate a reproducible, short, and sustainable training program into an existing yearly critical care medicine education structure. This also helps to address concerns for training new staff and accounts for turnover. Finally, this strategy helps to reinforce the training before the skills expire.

By training the team leader in CRM principles, our data suggest that the entire

| TABLE 3 Median TEAM Composite Subscores Pre- and Post-CRM Training |
|---------------------------------|----------------|----------------|----------------|
| Remained on Floor (n = 38)      | Transferred to ICU (n = 35) |
|---------------------------------|----------------|----------------|----------------|
| Leadership composite, median (95% CI) | Pre (n = 21) | Post (n = 17) | P |
| 3.5 (3.2–3.8)                   | 3.5 (3.1–3.9) | 1.0            | 2.5 (2.1–2.9) | 3.5 (3.1–3.9) | <.001 |
| Teamwork composite, median (95% CI) | 3.4 (3.1–3.8) | 3.7 (3.3–4.1) | .28          | 2.7 (2.3–3.1) | 3.7 (3.4–4.1) | <.001 |
| Task management composite, median (95% CI) | 3.3 (3.0–3.6) | 3.8 (3.5–4.2) | .03          | 2.9 (2.5–3.2) | 3.8 (3.5–4.1) | <.001 |
| Global rating, median (95% CI)  | 8 (7.0–9.0)   | 8 (6.9–9.1)   | 1.0          | 6 (4.9–7.1)   | 9 (8.0–10.0)  | <.001 |

**FIGURE 2** Bar and whisker plot for median TEAM composite subscores pre- and post-CRM training in patients transferred to the ICU.
team performance improved. Targeting a high impact person and affecting team behavior have also been studied in cardiac arrest teams with similar results. The task management composite subscore of the TEAM instrument was higher posttraining for both the patients who were transferred and those who were not. In addition, one of the ideal tasks, presentation of the event in SBAR format, improved after training of the leader without any training of the frontline providers for both groups. It may be that the leader provided prompts for this type of complete report, especially the “recommendation” component of SBAR, which may be difficult in hierarchical environments, such as a standard RRT activation. This finding suggests that training communication skills, including how to create a shared mental model, resulted in a safer environment for nurses and trainees to speak up and express their perspective.

There are certain limitations to this study. The Hawthorne effect, the potential change in behavior of the team leader due to awareness that their behavior was being observed, especially after the intervention, was a limitation that we anticipated. We aimed to minimize this by blinding RRT members to the aims of the study and specific metrics used in observation. Furthermore, it is common for our RRT leaders to have experience with a varied number of team members with other types of observers, such as trainees, new staff, or administrative personnel, depending on the time of day. Another limitation we anticipated was the lack of independence of the ideal task list and TEAM metric, because both were assessed by the same observer. If the team completed the expected tasks on the list, it is plausible that the observers rated the TEAM metric higher. We attempted to limit this bias by using a strict data dictionary a priori for the TEAM metric Likert scores. Finally, the observations were conducted during normal business hours as part of a convenience sample due to research staff availability. Future research that observes RRT activations at night, when fatigue and decreased provider availability are likely, may give additional insight into team dynamics and performance.

Ultimately, we observed an improvement in objective task completion as well as in a validated metric for team performance. Our findings support the evidence that CRM improves nontechnical skills and add that CRM can be applied to RRTs. These findings help highlight the benefit of nontechnical skill education in the trainee curriculum.

CONCLUSIONS

Two short, successive simulation-based CRM trainings of RRT team leaders effectively improved team dynamics during RRTs for patients who were transferred to the ICU. The training also improved completion of ideal tasks during RRT activations and affected the behavior of those trained and untrained. Targeting high impact team members and training them in CRM principles improved the performance of the entire team.

Acknowledgments

We thank Abdullah Al Shammarri, who worked on the manuscript, provided valuable background research, and contributed to the creation of the observation tool.

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Impact of Enterovirus Testing on Resource Use in Febrile Young Infants: A Systematic Review

Sowdhamini S. Wallace, DO,a Michelle A. Lopez, MD,a A. Chantal Caviness, MD, MPH, PhDb

ABSTRACT

CONTEXT: Enterovirus infection commonly causes fever in infants aged 0 to 90 days and, without testing, is difficult to differentiate from serious bacterial infection.

OBJECTIVE: To determine the cost savings of routine enterovirus testing and identify subgroups of infants with greater potential impact from testing among infants 0 to 90 days old with fever.

DATA SOURCES: Studies were identified systematically from published and unpublished literature by using Embase, Medline, the Cochrane database, and conference proceedings.

STUDY SELECTION: Inclusion criteria were original studies, in any language, of enterovirus infection including the outcomes of interest in infants aged 0 to 90 days.

DATA EXTRACTION: Standardized instruments were used to appraise each study. The evidence quality was evaluated using Grading of Recommendations Assessment, Development, and Evaluation criteria. Two investigators independently searched the literature, screened and critically appraised the studies, extracted the data, and applied the Grading of Recommendations Assessment, Development, and Evaluation criteria.

RESULTS: Of the 257 unique studies identified and screened, 32 were completely reviewed and 8 were included. Routine enterovirus testing was associated with reduced hospital length of stay and cost savings during peak enterovirus season. Cerebrospinal fluid pleocytosis was a poor predictor of enterovirus meningitis. The studies were all observational and the evidence was of low quality.

CONCLUSIONS: Enterovirus polymerase chain reaction testing, independent of cerebrospinal fluid pleocytosis, can reduce length of stay and achieve cost savings, especially during times of high enterovirus prevalence. Additional study is needed to identify subgroups that may achieve greater cost savings from testing to additionally enhance the efficiency of testing.
Infants in the first couple months of life often present to the emergency department with febrile illnesses. Given their young age, immature immune systems, and recent exposure to birth canal flora, most infants in this age group will undergo evaluation for serious bacterial illnesses (SBIs), including bacteremia, urinary tract infection, and meningitis. After initial evaluation, infants are typically hospitalized for empirical antibiotic therapy while awaiting bacterial culture results. Despite the focus on SBIs, fever in febrile young infants is more often viral than bacterial in etiology. Krober et al. identified viral pathogens 41% of the time as compared with 15% for bacterial pathogens in febrile infants <90 days of age. The most common viral pathogen isolated in this series of 182 febrile infants was enterovirus.

Enterovirus is a common cause of fever occurring in 26% to 60% of cases of hospitalized young infants in various communities. Young infants with enterovirus infection generally have a benign course with resolution of fever within 3 days. However, the clinical symptoms and signs of enterovirus can be difficult to distinguish from SBIs at the time of presentation, and many infants undergo SBI testing and hospitalization for this reason. The objective of this systematic review was to determine whether routine enterovirus testing for all infants 0 to 90 days of age presenting with fever could result in a reduction in resource use. The study also aimed to identify specific patient subgroups with the potential for the greatest benefit from enterovirus testing through reductions in resource use.

METHODS
Search Strategy and Study Selection
We performed a systematic review of the published and unpublished medical literature. Two independent investigators and an experienced medical librarian searched Medline, Embase, and the Cochrane database for studies related to enterovirus infection or testing. The initial search strategy included the search terms “enterovirus testing” AND “neonates” in PubMed. We also searched the related articles column in PubMed and the reference lists of articles to identify additional articles. We searched for unpublished studies in published abstracts from national conference proceedings in the previous 3 years, in trial registries, and from national experts. The last search was performed in December 2015.

Two investigators screened the title and abstract of potentially eligible studies independently to identify articles related to enterovirus infection and/or testing. The investigators then met to determine the studies eligible for inclusion and any disagreements were resolved through discussion and consensus. Studies were included if they involved infants 0 to 90 days old within the population and if the outcomes of our study questions were assessed in this population. The outcomes included resource use (defined as hospital length of stay [LOS], cost, or charges) and patient subgroups for optimal resource use. We sought to include only systematic reviews, randomized controlled trials, and prospective cohort studies, but included retrospective cohort studies if they were the only study type used to address any of our study questions. We excluded case reports and case series with <20 infants 0 to 90 days old, 32 studies that underwent full-text review, 257 were from unique studies (Fig 1). Of the 32 studies that underwent full-text review, 7 were prospective cohort studies, 9 were retrospective cohort studies, 2 were retrospective cross-sectional studies, 5 were diagnostic studies, 1 was an economic evaluation, 1 was a case-control study, and 7 were case series. Twenty-four of these studies were excluded: 18 because they did not measure any of the outcomes of interest, 5 because they had <20 patients <60 days old with larger studies available to evaluate the same outcomes, and 1 because of the concern for biased methodology (Supplemental Table 5). The 1 study excluded due to major bias was excluded because of concern for selection bias. Enterovirus polymerase chain reaction (PCR) testing of the cerebrospinal fluid also served as a template for extracting the key elements of each study for the systematic review.

Quality of Evidence
Two investigators independently used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to evaluate the quality of evidence for each systematic review question. This system takes into account findings from multiple studies and grades the quality of evidence for each question as either high, moderate, low, or very low. The initial quality of evidence is high for results from randomized controlled trials and is low for results from observational studies. Ratings can be downgraded due to risk of bias, inconsistency, indirectness, imprecision, or publication bias. Ratings can be upgraded due to the presence of a large effect or a dose-response gradient or if attempts to control for confounding would not change the observed effect.

Risk of Bias Assessment for Individual Studies
Two investigators independently critically appraised the articles using study design–specific Critical Appraisal Skills Program (CASP) tools. The investigators used a CASP instrument for each study to assess the risk of bias by evaluating whether the study question was clearly defined, appropriately designed, methodologically valid, and had meaningful results and generalizable conclusions. The instrument also served as a template for extracting the key elements of each study for the systematic review.
fluid (CSF) was performed on only ill-appearing infants or infants <15 days of age, which comprised 29% of the population.4 The majority of the population was not tested.

After screening, assessment of eligibility, and full-text review, 8 studies were included in the systematic review (Fig 1, Table 1). The 8 studies included 1 prospective cohort study, 3 retrospective cohort studies, 2 diagnostic studies, 1 cross-sectional study, and 1 cost minimization analysis.

**Primary Outcome: Resource Use**

Of the 8 included studies, 4 included data pertaining to the impact of enterovirus PCR testing on hospital cost and LOS. 3 retrospective cohort studies7–9 and 1 retrospective cost minimization study (Table 1).10 The 3 retrospective cohort studies focused on the impact on hospital LOS whereas the cost minimization study identified the prevalence of enterovirus needed to achieve cost savings with empirical testing (Table 2).7,8,10 In Stellrecht et al,7 the faster turnaround time for the PCR was correlated with a reduction in LOS by nearly half. This study, however, was limited by a small sample of infants <3 months of age (n = 31), missing laboratory data, and potential for selection bias because all patients with CSF were not tested for enterovirus.7 Dewan et al8 had similar findings, but with a much larger sample size and higher degree of precision. They found that the LOS was reduced by 15% to 45% (10–33 hours) for patients who had a positive enterovirus test.8 Ramers et al9 focused on a subgroup of neonates with pleocytosis and also found similar reductions in LOS (Table 2). In the cost minimization analysis, the investigators found that enterovirus PCR testing can lead to cost savings when the prevalence of enterovirus is >5.9% with the assumption of discharge after 24 hours of hospitalization and a negative CSF culture.10 The greatest limitation of this study is that the comparison of outcomes in the “standard” practice group as compared with enterovirus PCR testing of all samples was based on decision tree modeling with assumptions of the outcomes in each arm rather than observed patient outcomes. In addition, one of the assumptions of all patients being discharged by 24 hours if they tested positive for an enterovirus was based on a population of infants 28 days to 12 months old and may not be generalizable to infants <28 days old. The authors, however, report that if only 50% are discharged within 24 hours, cost savings could be achieved with an enterovirus prevalence of 13%.10 Additional cost savings were seen as the prevalence was increased within their model. Overall, all 4 studies found reductions in LOS and potential cost savings with routine enterovirus testing; the magnitude of benefit was greater with faster turnaround times of enterovirus testing and with higher prevalences of enterovirus.7,8,10

**Secondary Outcomes: Patient Subgroups**

We found 5 studies that assessed whether enterovirus testing should be tailored to certain subgroups of young infants: 1 large prospective cohort study,11 3 retrospective cross-sectional studies,12–14 and 1 retrospective cohort study.1 In the prospective cohort study by Byington et al,11 the investigators found that there was no difference in clinical characteristics, such as age, sex, duration of symptoms, and temperature, between enterovirus-positive and enterovirus-negative patients (Table 2). These patient characteristics were not evaluated further in other studies, but the frequency of pleocytosis in young infants with enterovirus infection was additionally assessed. Three retrospective studies assessed the frequency of CSF pleocytosis in young infants with enterovirus infection.12,13,15 In these studies, infants <3 months of age with enterovirus infection had pleocytosis 44% to 90% of the time (Table 2).12,13,15 Younger infants with enterovirus infection had a lower frequency of pleocytosis, especially in the first month of life.12,15 Lower peripheral white blood cell count and lumbar puncture within 24 hours of onset of

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**FIGURE 1** Search strategy.
testing for enterovirus should not be pleocytosis to predict enterovirus infection, of young infants and the poor sensitivity for absence of pleocytosis in a large percentage all infants with CSF available. Given the enterovirus testing was not performed on was a potential for selection bias because retrospective nature of the 4 studies, there infants, pleocytosis due to the small sample of poor precision for the estimates of infection in patients # showed that CSF pleocytosis has poor pleocytosis.12 In addition, Mulford et al14 symptoms were associated with this lack of pleocytosis.15 In addition, Mulford et al14 showed that CSF pleocytosis has poor sensitivity for prediction of enterovirus infection in patients ≤2 months of age.

The study by Stellrecht et al7 was limited by poor precision for the estimates of pleocytosis due to the small sample of infants ≤90 days of age (Table 2). Due to the retrospective nature of the 4 studies, there was a potential for selection bias because enterovirus testing was not performed on all infants with CSF available. Given the absence of pleocytosis in a large percentage of young infants and the poor sensitivity for pleocytosis to predict enterovirus infection, testing for enterovirus should not be restricted to infants with CSF pleocytosis. No other patient characteristics have been identified to promote selective testing of patients.

### Study and Evidence Quality

#### Risk of Bias of Individual Studies

The cohort studies included in this review had several limitations (Table 3). Precision of the outcomes for several studies was low due to small sample size,7 and there was incomplete reporting of outcome data.8 Two studies, Ramers et al9 and Seiden et al,13 had the potential for selection bias based on their population definitions. Ramers et al9 only included patients who were tested for enterovirus, and the criteria for enterovirus testing was unclear in this retrospective study. Selection bias may have also been present in Seiden et al13 because lumbar puncture was not performed on every patient and the factors that influenced the decision to perform a lumbar puncture were unclear. We did not report the data for pleocytosis for 1 study because high age-based cutoff points were used, which could have biased the results toward an underestimation of the frequency of pleocytosis.9 Cross-sectional studies and cohort studies with limited follow-up after hospitalization were marked as “not applicable” for the concern for attrition bias because longer follow-up was not needed to measure the outcomes of interest.

For the 1 diagnostic study included in this review, CIs were not reported for the test.

<table>
<thead>
<tr>
<th>Study7</th>
<th>Study Design and Aim</th>
<th>Sample Size</th>
<th>Population</th>
<th>Type of EV Test</th>
<th>Prevalence of EV</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stellrecht et al7</td>
<td>Retrospective cohort; assess the clinical impact of EV PCR testing</td>
<td>N = 1056</td>
<td>Pediatric and adult patients with CSF EV PCR</td>
<td>CSF EV real-time PCR</td>
<td>20% (n = 20/100) in infants ≤1 mo old</td>
<td>Not clearly defined, LOS</td>
</tr>
<tr>
<td>Dew et al8</td>
<td>Retrospective cohort; evaluate the impact of EV testing on LOS</td>
<td>N = 1231</td>
<td>Febrile infants &lt;36 d old</td>
<td>CSF EV PCR</td>
<td>25% (n = 308/1251)</td>
<td>LOS</td>
</tr>
<tr>
<td>Ramers et al9</td>
<td>Retrospective cohort; to determine the impact of EV-PCR testing on diagnosis and clinical management of suspected aseptic meningitis cases</td>
<td>N = 276</td>
<td>Pediatric patients 0–18 y old with EV PCR sent</td>
<td>CSF EV PCR</td>
<td>49% (n = 137/276)</td>
<td>LOS, time from PCR result to discharge, intravenous antibiotic use, and use of ancillary tests. CSF pleocytosis also reported</td>
</tr>
<tr>
<td>Nigrovic et al10</td>
<td>Cost minimization analysis using a decision tree, assess whether empirical EV PCR testing as compared with usual practice would lead to cost savings and identify the prevalence of EV needed to result in cost savings</td>
<td>N = 126</td>
<td>Infants 28 d to 12 mo old with fever and CSF pleocytosis</td>
<td>CSF EV PCR</td>
<td>NA; prevalence varied within the decision tree to assess which prevalence led to cost savings</td>
<td>Total cost for usual care group and total cost for empirical EV testing group. Cost was defined using a cost-to-charge ratio of 0.65 and included hospital bed, nursing services, physician fee, and antibiotic</td>
</tr>
<tr>
<td>Byington et al11</td>
<td>Prospective cohort epidemiologic study; describe the epidemiology of EV infection through PCR testing of infants &lt;90 d of age with and without fever</td>
<td>N = 345</td>
<td>Infants &lt;90 d old with and without fever</td>
<td>Blood, urine, CSF, throat EV PCRs</td>
<td>26% (n = 89/345)</td>
<td>Characteristics of infants with and without EV infection</td>
</tr>
<tr>
<td>Yun et al12</td>
<td>Retrospective cross-sectional; describe characteristics of EV meningitis in absence of pleocytosis</td>
<td>N = 390</td>
<td>Children with +CSF EV PCR</td>
<td>CSF EV PCR</td>
<td>NA; only patients with EV included</td>
<td>CSF pleocytosis</td>
</tr>
<tr>
<td>Seiden et al13</td>
<td>Retrospective cross-sectional; to identify factors associated with CSF pleocytosis</td>
<td>N = 154</td>
<td>Infants &lt;90 d old with +CSF EV PCR</td>
<td>CSF EV PCR</td>
<td>NA; only patients with EV included</td>
<td>CSF pleocytosis</td>
</tr>
<tr>
<td>Mulford et al14</td>
<td>Cross-sectional study of diagnostic test; to determine if pleocytosis and/or elevated protein levels were predictive of positive EV PCR.</td>
<td>N = 728</td>
<td>Pediatric and adult patients</td>
<td>CSF EV PCR</td>
<td>38.1% (n = 277/728); reference standard was CSF EV PCR</td>
<td>Test properties for pleocytosis and CSF protein to diagnose EV infection</td>
</tr>
</tbody>
</table>

EV, enterovirus. NA, not applicable.

* Studies are listed by order of citation in the text.
properties. By calculating CIs from the raw data, we found that Mulford et al had precise estimates for the test properties for pleocytosis when used to diagnose patients with enterovirus infection. Additionally, the study by Mulford et al did not describe the disease severity of the population and, thus, spectrum bias cannot be excluded. Little information was provided to describe the study population aside from the age of the participants.

One economic analysis by Nigrovic et al was included in this review. Overall, this study was limited because the comparison between the cost of empirical enterovirus testing versus “standard practice” was based on decision tree modeling with assumptions for the LOS in each arm. The enterovirus PCR testing group was assumed to be discharged at 24 hours and the standard therapy group was assumed to stay in the hospital for 48 hours before discharge. It is possible that LOS from actual patient observations, if measured, may have differed from these assumptions. Another major weakness of the study was the lack of measurement of effectiveness of the intervention, which was routine enterovirus testing. There is evidence that CSF enterovirus PCR has good sensitivity and specificity and that enterovirus PCR testing leads to shorter LOS. However, there is no evidence about the effectiveness of diagnosing bacterial meningitis and the decision tree includes the assumption that the CSF culture would be negative at 24 hours and remain negative. Given the small number of patients (N = 126), the investigators did not have a large enough sample to give precise estimates of bacterial meningitis in the population studied. It is also unclear whether all important costs were measured. The investigators evaluated cost savings for inpatient hospitalization, antibiotics, and inpatient attending fee. They did not measure any costs from the parent or societal perspectives.

**Quality of Evidence**

When assessing the quality of the body of evidence to determine whether enterovirus testing led to a reduction in resource use, the overall quality of the evidence was low (Table 4). The quality of the evidence was downgraded by 1 point due to concern for bias in Nigrovic et al because there was a lack of evidence to show equal effectiveness in both arms for this cost minimization study. The quality of the evidence was upgraded by 1 point for dose response because Stelbrecht et al showed that a decrease in turnaround time for enterovirus PCR led to a shorter LOS and Ramers et al showed a shorter time to discharge after the PCR result was available for neonates with pleocytosis and a positive test. The evidence for testing in the absence of pleocytosis was of low quality (Table 4). The evidence was downgraded by 1 point because there could have been some selection bias involved in patient recruitment because all patients were not
tested for enterovirus. The evidence was upgraded by 1 point for large effect because a large percentage of infants <90 days with enterovirus meningitis had no pleocytosis.

**DISCUSSION**

In this systematic review of the literature, we found that empirical enterovirus testing can reduce hospital costs and LOS. No subgroups, including patients with pleocytosis, were identified to support a more selective approach for testing. Within the evidence, several factors were reported to affect the likelihood of cost savings through routine testing. The local prevalence and seasonality of enterovirus infection in the community determines the degree of potential cost savings through routine testing. The turnaround time of the enterovirus PCR test should also be considered.7,10

In addition to community prevalence and test characteristics, physicians must also be willing to discharge these young infants from the hospital sooner when enterovirus testing is positive. Shorter discharge times may be justified given the lower frequency of SBI in infants with enterovirus infection. Three prospective studies have reported the frequency of total SBI to be 1.6%, 6.6%, and 6.7% in infants that tested positive for enterovirus.11,13,16 Of the infants with enterovirus infection and SBI, urinary tract infection was the most common, bacteremia occurred in ≤1% of the population, and none of the infants had concurrent bacterial meningitis.11,13,16 Rittichier et al16 found that all patients with bacteremia were <28 days old. Given previous studies that have reported that 91% of blood cultures will be positive by 24 hours if the patient has true bacteremia,17 a 24 hour length of observation may be reasonable for a well-appearing neonate with enterovirus infection and even shorter observation times or discharge from the emergency department could be considered for well-appearing infants >28 days old.

These shorter observation times can increase cost savings and decrease hospital exposure for these young infants.

This systematic review has several limitations. The quality of the evidence to address the benefit of enterovirus testing was low given the observational nature of the studies included in this review. However, the findings of these studies appear to be consistent. Studies consistently report a shorter LOS for enterovirus-positive infants as compared with enterovirus-negative infants. The absence of pleocytosis in enterovirus-positive infants has also been consistently reported to occur more frequently in younger infants. Another limitation is that several studies included older infants and children within the population, and the subgroups reported had varying definitions for the upper age limit. Due to this limitation, quantitative analysis was not performed.

Additional studies are needed to evaluate the impact of empirical enterovirus testing.
on specific subgroups of infants with and without pleocytosis. The majority of studies in this review reported the frequency of pleocytosis in young infants, but none of the studies directly compared LOS, antibiotic use, and ancillary testing in infants with and without pleocytosis. Ramers et al\textsuperscript{9} reported great potential for cost savings in neonates with pleocytosis, but data on the potential for cost savings in neonates without pleocytosis were lacking. The age of the infant may also affect cost savings because many physicians manage neonates more conservatively than infants 1 to 2 months of age.

**CONCLUSIONS**

Routine enterovirus testing of febrile young infants 0 to 90 days of age has the potential to result in cost savings through a reduction in hospital LOS. Testing during times of higher enterovirus prevalence and with the use of a PCR test with faster turnaround time may yield higher cost savings. Additional studies are needed to evaluate the impact of enterovirus testing on resource use in specific subgroups of young infants based on age and pleocytosis.

**Acknowledgments**

We thank Ms Nha Huynh, medical librarian, for her assistance with the literature search. We also thank Dr Kathleen Kennedy for her review and editing of this manuscript.

**REFERENCES**


BRIEF REPORT

The Effect of Family Presence on Rounding Duration in the PICU

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BACKGROUND AND OBJECTIVE: The incorporation of family-centered rounds has become standard in PICUs across the United States. We compared rounding times in our institution, with and without family members present, to determine the effect on total rounding time and workflow.

METHODS: This observational study of a convenience sample was conducted over a 17-month period (May 2014–October 2015), accounting for typical seasonal variation in the PICU. The individual patient rounding times for 2657 encounters were recorded. The presence of family members, intubation status, physician assistant participation, interruptions during rounds, attending physician’s full- or part-time status, and patient census were documented. The effect of family presence on per-patient rounding time was analyzed, while controlling for influential variables.

RESULTS: Family members were present during 1743 of 2657 (66%) rounding encounters. The average per-patient rounding time with and without family members present was 8.6 minutes and 7.3 minutes, respectively, a difference of 1.3 minutes per patient. In statistical models that accounted for other influential variables, the presence of family members was associated with a highly significant (20.4%, P < .001) increase in the per-patient rounding time.

CONCLUSIONS: The presence of family members increases per-patient rounding times in the PICU. Family presence on rounds may have benefits that outweigh the additional time required to complete each patient interaction.
Family-centered rounds (FCR) are a multidisciplinary approach to rounding that partners with patients and their families, facilitating their inclusion in medical decision-making. FCR have been shown to increase family satisfaction during inpatient pediatric admissions because families have a positive view of the experience in that it allows them to be contributing members of the care team. Additional benefits of FCR have been widely documented, including improved staff satisfaction, better family communication, more efficient coordination of care, and improved educational opportunities. FCR have also been shown to reduce length of stay because family members become more knowledgeable of their child’s clinical condition and understand how to better manage symptoms at home. Beginning in pediatrics, FCR were originally implemented as a result of the unique roles of families during periods of illness in children; in 2003, the American Academy of Pediatrics issued a policy statement recommending that attending physician bedside rounds should include families.

Despite its many advantages, one of the barriers to conducting FCR is the perception by surveyed clinicians that it increases rounding times, thereby negatively affecting team efficiency and productivity. Studies including between 75 and 250 patient rounding encounters have shown family presence to significantly increase rounding times by up to 4 minutes per patient. This review of the literature is somewhat limited in that the environments in which the studies were conducted may be vastly different; for example, the NICU provides an entirely different set of care needs compared with inpatient pediatric wards. Nevertheless, the Society for Critical Care Medicine has strongly advocated the presence of family during rounds in the PICU.

We aimed to determine whether the observed trend of increased rounding times during FCR was substantiated by our large cohort of 2657 rounding encounters, which to our knowledge is the largest reported to date. Furthermore, we hypothesized that certain factors (patient- or provider-related) may be associated with observed differences in rounding times and may potentially impact efficiency for providers.

METHODS

Rounding Structure

Randall Children's Hospital (RCH) is a 165-bed children’s hospital with departmental academic affiliations with Oregon Health and Science University (Portland, OR). The RCH PICU is a 24-bed regional referral unit staffed continuously by pediatric critical care board-certified attending physicians, admitting >1000 patients yearly. A full complement of subspecialty support is available and the PICU provides extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy services. Outcome data are submitted to the Virtual Pediatric Systems Database and a vigorous quality improvement program is maintained. Although we do not provide a pediatric critical care fellowship or resident rotations, pediatric emergency medicine and surgery fellows have the opportunity to participate in clinical electives within the PICU. Multidisciplinary rounds have been conducted at the RCH PICU for the past 20 years. FCR begin at 9:00 AM on weekdays (Monday through Friday) and conclude between 10:00 AM and 12:00 PM, depending on the census. In general, rounds start at 1 end of the ward and progress from room to room; this routine may be altered depending on subspecialty availability. For each patient encounter, the attending physician presents the case in front of family members and input for the daily plan is obtained from the rounding team. Because our rounding team is sizeable (attending physician, bedside nurse, charge nurse, respiratory therapist, pharmacist, dietician, case manager, social worker, physician assistant [PA], medical scribe, subspecialists, family members, and patient, if appropriate), we instituted hallway rounds to ensure that there was sufficient space for the entire team as well as family members to be present. Hallway rounds allow the team to overcome the issue of isolation precautions, directly protecting patient safety by decreasing the number of individuals entering and exiting the room of an isolated patient. At the time of admission, families receive information regarding our PICU’s use of FCR and how patient confidentiality is maintained, primarily by performing FCR during designated hours.

Study Design

This was a prospective, observational study of a convenience sample of patient-centered work rounds conducted in a tertiary care PICU. Before rounds begin, the PICU attending physician reviewed the patient electronic medical record and updated patient charts with the help of a medical scribe. Scribes also timed rounding interactions with a stopwatch. The stopwatch was started when discussion was initiated by the PICU attending physician, and was stopped at the conclusion of the discussion for that patient. The total time of each encounter included all discussion of patient care, such as reviewing the history of present illness, case presentation, educational points, and daily plan review. Transit time between patient rooms was included in the rounding time for the next patient. A paper spreadsheet was used to record the following information: date of rounds, patient room number, per-patient rounding time, intubation status, family presence, ECMO status, and rounding interruptions (eg, phone calls or pages, requests for new admissions, computer malfunction, emergent procedures, off-topic conversations that delayed an encounter, and waiting for staff).

Although the team was aware that data collection was taking place, the results were not shared or discussed with team members during the study period. Of note, data for non-English speaking families where an interpreter was required were eliminated from the analysis because these rounding encounters often occurred outside of the scheduled rounding period. The data were transferred to an electronic database for analysis.
analyses were performed in the R package attending physicians having faster average physician were likely correlated, with some clustered in some other manner. In our repeated measures over time or are unmeasured dependence, or correlation, in epidemiology because they can handle generalized linear models used commonly equation (GEE) model.15 GEEs are a form of clustering by using a generalized estimating others), and we accounted for this physicians tended to round faster than clustered by attending physician (some decided to consider rounding data to be by attending physician (some physicians tended to round faster than others), and we accounted for this clustering by using a generalized estimating equation (GEE) model. GEEs are a form of generalized linear models used commonly in epidemiology because they can handle unmeasured dependence, or correlation, between the outcome data; they consist of repeated measures over time or are clustered in some other manner. In our case, rounding times for each attending physician were likely correlated, with some attending physicians having faster average rounding times than others. All statistical analyses were performed in the R package for statistical computing.16 This study was conducted in an ethically adherent manner and did not involve patients or subjects other than observation of normal clinical operations. Clinical data points (date of rounds, patient room number, intubation status, family presence, ECMO status) were not associated with identifiable protected health information. The Legacy Health Institutional Review Board found this study to be exempt from review.

RESULTS

A total of 2657 patient rounding encounters were observed over a 17-month period (May 2014–October 2015), accounting for the seasonal variation typically encountered in the PICU. Family members were present during 1743 (65.8%) and absent from 914 (34.4%) rounding encounters. The mean per-patient rounding time for the entire group was 487 s (median = 417, first quartile = 272, third quartile = 619). The mean per-patient rounding durations for encounters with family members present or absent were 513 s (median = 451, first quartile = 297, third quartile = 649) and 438 s (median = 370, first quartile = 238, third quartile = 563), respectively. In a univariate GEE model, the presence of family was significantly associated (P < .001) with a 22.1% increase in per-patient rounding time (Fig 1, Table 1).

In addition univariate analyses, we found that per-patient rounding time was also significantly associated with intubation status, the presence of a PA, and the total number of patients rounded on (all P < .001; Table 1). Although employment status of the attending physician (part-time or full-time) had only a borderline association with rounding time in the univariate analysis (P = .080; Table 1), it was included in the multivariable model.

In the final GEE multivariable model (Table 2), the presence of family resulted in a significant increase in per-patient rounding time (20.4%, P < .001). The effect of having family present was observed while controlling for patient intubation status (62.8% longer per-patient rounding time when intubated; P < .001), whether a PA was present or not (6.8% shorter per-patient rounding time when PA was present; P = .006), the total number of patients rounded on (2.2% shorter per-patient rounding time for each additional patient rounded on; P < .001), and employment status of the attending physician (17.4% longer per-patient rounding time for part-time attending physicians; P < .001).

To place these percentage changes in perspective, it is worth examining the predicted rounding times for different patient–family–physician scenarios. For example, the model would predict that rounding by a part-time attending physician on an intubated patient with family present but without a PA on a fairly light day (7-patient census) would take 12 minutes and 42 seconds per patient. On the other hand, the model would predict that rounding by a full-time attending on a nonintubated patient without family present, but with a PA on a heavier day (12-patient census) would take 4 minutes and 36 seconds per patient.

DISCUSSION

To our knowledge, this is the largest study to evaluate the duration of FCR in the PICU based on the presence or absence of family during rounds. Specifically, we found that our multidisciplinary rounding times were significantly longer when family was present. Intubation status and the total number of patients rounded on were significantly associated with increased rounding duration in the univariate analysis.
TABLE 1  Results of Univariate Analyses From GEE Regression Models That Also Account for Attending Physician as a Source of Clustering

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Effect</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family present</td>
<td>0.087</td>
<td>+22.1%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intubated</td>
<td>0.217</td>
<td>+64.4%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PA present</td>
<td>-0.039</td>
<td>-8.6%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of rounded patients</td>
<td>-0.012</td>
<td>-2.7%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Attending physician employment status</td>
<td>0.047</td>
<td>+11.3%</td>
<td>.080</td>
</tr>
</tbody>
</table>

The analyses were conducted using log_{10}-transformed rounding times and the “Coefficient” column shows the regression coefficients from these models. The “Effect” column shows the results back-transformed to show percentage changes in the original units (seconds) associated with each of the variables. For the first 3 rows, the results show the effect of these variables being “true.” For “No. of rounded patients,” the results show the effect of each additional patient rounded. For “Attending physician employment status,” the results show the effect of part-time (versus full-time) employment status.

as well as part-time employment status of attending physicians in the multivariate analysis.

Previous publications have shown that rounding times are increased when family is present, with 1 author reporting FCR to take ~20% longer than traditional rounds. In our institution, the presence of family on rounds led to a 1.3 minute increase in per-patient rounding times, less than what is currently reported in the literature. However, we believe that there are many benefits associated with having family present during rounds. Family presence has been shown to increase family satisfaction because they become more knowledgeable about physician medical decision-making and can have their concerns addressed and questions answered immediately by the care team. Family presence on rounds is also beneficial to the care team itself because they can communicate with parents at a designated time and do not routinely need to meet with them later in the day. Furthermore, medical staff may also be able to encourage families to maintain a degree of autonomy; FCR thus provide an educational opportunity for both staff and families. The multidisciplinary nature of FCR also encourages teaching and knowledge sharing among providers from several fields and levels of experience. We have found that keeping the patient at the center of the rounding discussion, maintaining open lines of communication, and answering questions can be accomplished efficiently despite the complexity of a modern PICU.

Using results from multivariable regression analysis, it is possible to better plan resources for the hospital system. Due to census variability (anywhere from 1–24 patients), the ability to anticipate expected rounding times would allow the team to better plan their activities, such as rounding on other floors and administrative meetings. Efficient scheduling can reduce bottlenecks throughout the organization and increase overall throughput. Standardization of our rounding technique may have contributed to our efficiency; however, the emphasis on family communication and satisfaction remains a priority, despite the complexities of a labile PICU environment.

There were several limitations to our study. First, although the number of rounding encounters are the largest reported to date, this was a single-center study and therefore may not be generalizable to every PICU. Second, we included transit time within the rounding time, which may have increased rounding times by 5 to 10 seconds per encounter. Nevertheless, we believe that our transit times are minimal, primarily because we begin rounds at 1 end of the unit and proceed in numerical order of patient rooms. Third, interruptions during rounds occurred in ~15% of all patient interactions, resulting in slightly increased average rounding times. These interruptions consisted mainly of phone calls from subspecialists concerning other patients, contributing to inconsistencies in per-patient rounding times. Fourth, significant differences in rounding times were observed between physicians. These inconsistencies suggest that rounding styles, including communication techniques, may differ from physician to physician. We did, however, account for these differences in our analysis where all of the data for a physician were considered to be clustered. Fifth, although our findings were highly statistically significant, additional studies are required to determine whether there is a clinical impact of increased rounding times. For example, it would be expected that the longer a patient has been in the PICU, the less time would be required to round on that patient. In addition, it might also be less likely that family would be present during rounds for a “long-term” patient. If true, this would cause these 2 factors to be associated, but there would not be a causal relationship. However, the number of PICU days for a patient was not tracked during this study, and therefore this issue could not be accounted for in the analyses. Finally, for non-English speaking

TABLE 2  Results of Multivariable Analyses From GEE Regression Models That Also Account for Attending Physician as a Source of Clustering

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Effect</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family present</td>
<td>0.081</td>
<td>+20.4%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intubated</td>
<td>0.212</td>
<td>+62.8%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PA present</td>
<td>-0.031</td>
<td>-8.8%</td>
<td>.006</td>
</tr>
<tr>
<td>No. of rounded patients</td>
<td>-0.010</td>
<td>-2.2%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Attending physician employment status</td>
<td>0.070</td>
<td>+17.4%</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

The analyses were conducted using log_{10}-transformed rounding times and the “Coefficient” column shows the regression coefficients from these models. The “Effect” column shows the results back-transformed to show percentage changes in the original units (seconds) associated with each of the variables. For the first 3 rows, the results show the effect of these variables being “true.” For “No. of rounded patients,” the results show the effect of each additional patient rounded. For “Attending physician employment status,” the results show the effect of part-time (versus full-time) employment status.
families, an interpreter was required and these discussions often occurred outside of the scheduled rounding period. This factor needs to be accounted for when planning workflow to maximize efficiency.

CONCLUSIONS
Family presence is associated with slightly longer rounding time, although qualitatively, we believe that the benefits outweigh the costs.

REFERENCES
Putting the Pieces Together: Clinically Relevant Genetic and Genomic Resources for Hospitalists and Neonatologists

Rebecca Miller, MS, CGC,a Alina Khromykh, MD,a Holly Babcock, MS, CGC,a Callie Jenevein, MS, CGC,a Benjamin D. Solomon, MDa,b,d

ABSTRACT

Genetic conditions are individually rare but are common in aggregate, and they often present in the neonatal and early pediatric periods. These conditions are often severe, can be difficult to diagnose and manage, and may heavily affect patients, families, health care systems, and society. Because of recent technological advances, the availability and uptake of genetic and genomic testing are increasing rapidly. However, there is a dearth of trained geneticists and genetic counselors to help guide and explain these conditions and relevant tests. To help hospitalists, neonatologists, and related practitioners navigate this complex and evolving field, we have compiled a list of free (mostly Web-based) resources relevant to the diagnosis and management of genetic conditions and related disorders. These resources, which we describe individually, can be useful for nongeneticist clinicians, and some also include material that can be used to explain concepts and conditions to patients or families. The resources presented are divided into the following categories (which overlap): general information, databases of genetic conditions, resources that can help generate differential diagnoses, databases of genetic testing laboratories (to help with logistics of ordering tests), information on newborn screening, and other resources. We also include a separate list of helpful textbooks and manuals. We conclude with 2 examples describing how some of these resources would be used by a pediatric hospitalist or neonatologist during the inpatient management of a child with a suspected genetic condition.
 Genetic and genomic disorders are individually rare but are common in aggregate. Approximately 3% to 5% of infants are born with a congenital anomaly or genetic disorder.\(^8,9\) By age 25, an older study estimated that \(\sim\)8% of individuals in the overall population are recognized as being affected with these types of diseases.\(^1\) The National Institutes of Health and rare disease advocacy groups generally concur with this estimates, citing 10% of the population as affected with a rare disease, 80% of ascribed to genetic causes (see https://rarediseases.info.nih.gov/; https://globalgenes.org/; https://rarediseases.org/). These conditions are often severe, can be difficult to diagnose and manage, and can heavily affect patients, families, the health care system, and society.\(^\ddagger,\ddagger\)

There are thousands of disorders with known genetic causes. More than 3000 individual genes are known to cause monogenic or Mendelian genetic diseases; this number does not represent genetic diseases caused by other mechanisms such as large deletions involving multiple genes, whole chromosome aneuploidy, or somatic mutations (as seen in some cancers and congenital disorders).\(^7\) It is important to also note that this number does not represent genetic diseases caused by processes such as epigenetics, a complex phenomenon involving modification of gene expression or activity rather than alteration of the genetic code. Recent technological breakthroughs have allowed the identification of previously unknown causes of genetic conditions at an unprecedented rate, with \(>14\) new “disease genes” currently published each month.\(^8,9\) These advances in technology create a genetic testing atmosphere with a dizzying number of options that is also in a constant state of growth and change. In addition, there is a shortage of clinical geneticists and genetic counselors to provide guidance, interpretation, and support for both patients and clinicians.\(^9\)

There is growing evidence that early molecular diagnosis (ie, finding the exact cause of the condition) for patients with genetic disorders is both medically and financially beneficial.\(^11,12\) In addition to avoiding costly “diagnostic odysseys” and possible related iatrogenic complications, finding the cause of a condition can allow the possibility for direct interventions, more tailored patient care, and informed counseling and decision-making.\(^8\)

Because many genetic disorders present in the early pediatric period and direct input from genetic specialists is not always immediately available, our specific aim was to prepare a list of mostly free, Web-based resources (those with mobile apps currently available are also mentioned) that can be helpful for clinicians (and researchers) who may encounter and treat these patients.

**METHODS**

This list of resources was compiled through a survey of clinical genetic counselors and geneticists in different specialty areas (prenatal, neonatal, pediatric, and adult medicine) and in both outpatient and inpatient clinical settings to determine which resources they and their nongeneticist colleagues found the most useful in areas related to patient care. We also reached out to bioinformaticians and laboratory genetic counselors and personnel for additional recommendations. All of the Web sites were used by \(\approx 1\) medical professional who was surveyed. This list is not meant to supplant formal genetic consultation and counseling but rather to provide reliable, readily accessible information that may help educate clinicians and provide navigation through this complex field.

We have divided the resources into sections based on the primary type of use. However, some assignments are challenging because many of the resources might have multiple types of uses. Finally, although there are many other such resources available, we have intentionally excluded those that, based on feedback from our internal group and from nongeneticist clinicians, are judged to be more appropriate for genetic specialists, are focused only on specific conditions or disorders, or are free to.

We have included links to each site and literature citations where available. It is important to note that some links to the provided resources might have changed since this article was initially written, but search engines may be used to identify the current address.

Included at the end of the online resource section is a list of relevant textbooks, manuals, and related written references. Table 1 lists free, Web-based resources. Table 2 lists recommended textbooks and additional resources. Although the main focus of this article is to enumerate free, Web-based resources, we thought it was important to include some essential textbooks that incorporate clinically relevant information about various genetic conditions.

**General Information**

Centers for Disease Control and Prevention http://www.cdc.gov/genomics/

The Centers for Disease Control and Prevention Web site contains areas dedicated to many relevant issues, including basic descriptions of genetics and genomics and related concepts, resources related to family history, condition-specific information, newborn screening, and highlights pertaining to particular current events involving genetics and genomics. Users can also subscribe to a weekly e-mail that includes topics of their choosing (http://www.cdc.gov/Other/emailupdates/).


Genetics Home Reference (GHR), which has recently undergone large-scale retooling, contains a great deal of information about genetic and genomic terminology and user-friendly descriptions of many common genetic conditions. Drop-down sections include information on the prevalence, genetic changes, inheritance pattern, diagnosis, and management associated with each condition. Numerous links to additional information and resources for both medical professionals and families are provided, including a section titled “Help Me Understand Genetics” (https://ghr.nlm.nih.gov/primer).

**National Coalition for Health Professional Education in Genetics:**

http://www.nchpeg.org/

The National Coalition for Health Professional Education in Genetics (NCHPEG) Web site includes several types of formal
education on genetics and genomics and fact sheets on current issues, such as noninvasive prenatal testing (a recent method of prenatal screening for chromosomal and related disorders) and the Genetic Information Nondiscrimination Act (a law created to protect patients from genetic discrimination by health insurance companies and employers). The “Point of Care” pages (under the Products and Programs heading: http://www.nchpeg.org/index.php?option=com_content&view=article&id=26&Itemid=64) also mention a number of useful resources, including “genetic red flags,” family history information and tools, and patient-friendly terminology for discussing genetics with patients.

**National Human Genome Research Institute:** https://www.genome.gov/

The National Human Genome Research Institute (NHGRI), part of the National Institutes of Health, hosts a Web site that includes information aimed at scientists, patients, and clinicians. Among other resources (such as explanations of the Genetic Information Nondiscrimination Act), the “Issues in Genetics” section (https://www.genome.gov/issues/) covers hot topics that frequently come up in discussions of the field, and there is a section (https://www.genome.gov/27527599/genetics-and-genomics-for-health-professionals/) specifically designed for clinicians.

**Condition Databases**

**Clinical Genomic Database:** http://research.nhgri.nih.gov/CGD/

The Clinical Genomic Database (CGD) contains a list of all single-gene disorders resulting from germline mutations. The CGD

### Table 1: Brief Description of Resources

<table>
<thead>
<tr>
<th>Resource</th>
<th>Web Site URL</th>
<th>Brief Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centers for Disease Control and Prevention</td>
<td><a href="http://www.cdc.gov/genomics/">http://www.cdc.gov/genomics/</a></td>
<td>General resource for genetic and genomic information</td>
</tr>
<tr>
<td>GHR</td>
<td><a href="http://ghr.nlm.nih.gov/">http://ghr.nlm.nih.gov/</a></td>
<td>General resource for genetic and genomic information</td>
</tr>
<tr>
<td>NCHPEG</td>
<td><a href="http://www.nchpeg.org/">http://www.nchpeg.org/</a></td>
<td>General resource for genetic and genomic information</td>
</tr>
<tr>
<td>NHGRI</td>
<td><a href="https://www.genome.gov/">https://www.genome.gov/</a></td>
<td>General resource for genetic and genomic information</td>
</tr>
<tr>
<td>CGD</td>
<td><a href="http://research.nhgri.nih.gov/CGD/">http://research.nhgri.nih.gov/CGD/</a></td>
<td>Gene-specific database related to management of conditions with known genetic causes</td>
</tr>
<tr>
<td>GeneReviews</td>
<td><a href="http://www.ncbi.nlm.nih.gov/gtr/">http://www.ncbi.nlm.nih.gov/gtr/</a></td>
<td>Compendium of review articles on genetic conditions, also includes testing and laboratory database</td>
</tr>
<tr>
<td>OMIM</td>
<td><a href="http://www.ncbi.nlm.nih.gov/omim">http://www.ncbi.nlm.nih.gov/omim</a></td>
<td>Database including conditions with and without known etiologies; can be used to generate differential diagnosis</td>
</tr>
<tr>
<td>Phenomizer</td>
<td><a href="http://compbio.charite.de/phenomizer/">http://compbio.charite.de/phenomizer/</a></td>
<td>Differential diagnosis generator based on standardized clinical features</td>
</tr>
<tr>
<td>Face2Gene</td>
<td><a href="http://www.fdma.com/face2gene/">http://www.fdma.com/face2gene/</a></td>
<td>Differential diagnosis generator based on facial photographs with or without clinical features</td>
</tr>
<tr>
<td>SimulConsult</td>
<td><a href="http://www.simulconsult.com/index.html">http://www.simulconsult.com/index.html</a></td>
<td>Differential diagnosis generator based on clinical features</td>
</tr>
<tr>
<td>Gene Tests</td>
<td><a href="https://www.genetests.org/">https://www.genetests.org/</a></td>
<td>Clinical testing, laboratory, and clinic database</td>
</tr>
<tr>
<td>NextGxDx</td>
<td><a href="https://www.nextgdx.com/">https://www.nextgdx.com/</a></td>
<td>Clinical testing and laboratory database</td>
</tr>
<tr>
<td>ACMG</td>
<td><a href="https://www.acmg.net/">https://www.acmg.net/</a></td>
<td>Includes newborn screening recommendations and related material, as well as other information related to genetics and genomics</td>
</tr>
<tr>
<td>NNSGRC</td>
<td><a href="http://genes-r-us-uthscsa.edu/">http://genes-r-us-uthscsa.edu/</a></td>
<td>Newborn screening recommendations and related material</td>
</tr>
<tr>
<td>MotherToBaby</td>
<td><a href="http://mothertobaby.org/">http://mothertobaby.org/</a></td>
<td>Database on pregnancy and breastfeeding-related exposures</td>
</tr>
<tr>
<td>PharmGKB</td>
<td><a href="https://www.pharmgkb.org/">https://www.pharmgkb.org/</a></td>
<td>Database on pharmacogenomics</td>
</tr>
</tbody>
</table>

### Table 2: Textbook Resources

<table>
<thead>
<tr>
<th>Textbook</th>
<th>Brief Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Significance and GC for Common Ultrasound Findings</td>
<td>Prenatal resource regarding ultrasound anomalies and genetic testing</td>
</tr>
<tr>
<td>Emery and Rimoin's Principles and Practice of Medical Genetics</td>
<td>Textbook (now fully online) on diverse aspects of genetics in clinical practice</td>
</tr>
<tr>
<td>The Encyclopedia of Genetic Disorders and Birth Defects</td>
<td>Reference for congenital disorders and birth defects</td>
</tr>
<tr>
<td>Gorlin's Syndromes of the Head and Neck</td>
<td>Compendium of genetic syndromes that involve the head and neck</td>
</tr>
<tr>
<td>Human Malformations and Related Anomalies</td>
<td>Reference for malformations organized by organ system</td>
</tr>
<tr>
<td>Management of Genetic Syndromes</td>
<td>Textbook on the diagnosis and management of selected genetic conditions</td>
</tr>
<tr>
<td>Signs and Symptoms of Genetic Conditions</td>
<td>Textbook on the diagnosis and management of selected genetic conditions</td>
</tr>
<tr>
<td>Smith's Recognizable Patterns of Human Malformations</td>
<td>Compendium of genetic syndromes involving malformations</td>
</tr>
<tr>
<td>Vademecum Metabolicum; Manual of Metabolic Pediatrics</td>
<td>Small manual on the diagnosis and management of various metabolic conditions</td>
</tr>
</tbody>
</table>
focuses on briefly describing medical interventions that would be indicated from finding a mutation in a disease-related gene.

**GeneReviews:** http://www.ncbi.nlm.nih.gov/books/NBK1116/

GeneReviews includes individual, periodically updated articles on clinical, diagnostic, and molecular aspects of many genetic disorders (usually written by a world expert on the particular condition). The individual articles can be found through the “GeneReviews” tab on the Genetic Testing Registry (GTR) homepage or through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/books/NBK1116/). Importantly, each of these articles includes information about diagnosis (both clinical and molecular), surveillance, ongoing management, genetic counseling, and support resources. Other information is available through the other GTR tabs, such as laboratories where testing is available (see details below, in the Laboratory and Testing Databases section).

**Online Mendelian Inheritance in Man:** http://www.ncbi.nlm.nih.gov/omim

Online Mendelian Inheritance in Man (OMIM), 1 of the longest-standing genetic databases, evolved from a printed resource. It contains overlapping information on genes and genetic conditions and may be searched based on either. OMIM may also be used to generate differential diagnoses from a list of symptoms or features. For patients with known or suspected genetic conditions, OMIM can be helpful for learning about historical aspects of a condition and characteristic clinical findings.

**Differential Diagnosis Generators (see also OMIM)**

**Phenomizer:** http://combio.charite.de/phenomizer/

The Phenomizer can be used to generate differential diagnoses for patients with suspected genetic disorders. The output differential, which is statistically calculated, includes both conditions with known genetic causes and syndromes without identified etiologies. To use the Phenomizer, clinicians input observed clinical features and can also use the inheritance pattern. The clinical features that can be selected are standardized and based on human phenotype ontology terms (see http://www.human-phenotype-ontology.org). An app-based version is also available. Note that the free software version is available only for academic instruction and research use, and commercial licenses are available.

**Face2Gene:** http://www.fdna.com/face2gene/

Face2Gene uses facial recognition algorithms to create differential diagnoses by using patient facial photos that can be uploaded via computer or through their apps (with patient consent). In addition to photos, the presence or absence of other features can be used to inform the differential diagnosis. Cases with unknown diagnoses can also be submitted to an electronic mailing list where participating dysmorphologists and geneticists can comment and make testing recommendations. An app-based version is also available, and the company has produced a small booklet focusing on dysmorphology.

**SimulConsult:** http://www.simulconsult.com/index.html

Individual clinicians can use a free version to input pertinent positives and negatives; output includes a ranked differential diagnosis, a list of applicable tests for definitive diagnosis, and a note generator. Other versions are available for reference laboratories and through accounts for health systems to integrate electronic health record data.

**Laboratory and Testing Databases (see also GeneReviews)**

**GeneTests:** https://www.genetests.org/

GeneTests is a medical genetics resource that includes a national and international laboratory directory, clinic directory, and links to other resources such as GeneReviews, OMIM, and GHR (see above for descriptions). Tests can be searched by gene, condition, or test name; output includes laboratories that do testing, test method, and turnaround time and price (when available).


GTR includes links to genetic test information as submitted by both US-based and international laboratory providers. As part of the National Center for Biotechnology Information, GTR provides links (see http://www.ncbi.nlm.nih.gov/gtr/docs/resources/) to other resources such as ClinVar (http://www.ncbi.nlm.nih.gov/clinvar/), a database of genetic variants and the evidence about whether they are related to disease, and MedGen (http://www.ncbi.nlm.nih.gov/medgen), a database on attributes of genetic conditions.

**NextGxDx:** https://www.nextgxdx.com

NextGxDx offers a service that finds all clinical laboratories that offer genetic testing, including enzyme studies and biochemical tests. The site allows searches by gene, condition, or test (such as for whole-exome sequencing), and displays prices, turnaround times, and links to the individual laboratory Web sites. The Web site also offers a fee-for-service option for direct testing.

**Newborn Screening**

American College of Medical Genetics and Genomics: https://www.acmg.net/

As expected for the official college site, there are many relevant resources available at the American College of Medical Genetics and Genomics (ACMG) Web site. One especially helpful resource involves newborn screening (https://www.acmg.net/ACMG/Publications/ACT_Sheets_and_Confirmatory_Algorithms/ACMG/Publications/ACT_Sheets_and_Confirmatory_Algorithms/ACT_sheets_Homepage.aspx?hkey=6d43e5d3-71fd-49f4-88d5-7197238f53). The ACMG “ACT Sheets and Confirmatory Algorithms” contain specific instructions for handling positive results for every condition tested for in newborn screening.

**National Newborn Screening & Global Resource Center** http://genes-r-us.uhscc.edu/

The National Newborn Screening & Global Resource Center (NNSGRC) is an independent national resource center for
newborn screening. Among other helpful resources, there are links to each state’s newborn screening contact person for the newborn screening laboratory and for the follow-up program.

Other Resources
MotherToBaby: http://mothertobaby.org/

Previously called Organization of Teratology Information Specialists (OTIS), this Web site includes information for patients and clinicians on medications and other exposures during pregnancy or breastfeeding. In addition to items such as fact sheets on FAQs and links to studies, the Web site includes mechanisms (phone, e-mail, and live chat) to get in touch with experts to help answer questions.

The Pharmacogenomics Knowledgebase: https://www.pharmgkb.org/
The Pharmacogenomics Knowledgebase (PharmGKB) is a knowledge resource that includes clinically relevant information related to pharmacogenetics and pharmacogenomics. Resources on PharmGKB include dosing guidelines, drug labels, and actionable gene–drug associations. For the most clinically relevant drug–gene interactions, Clinical Pharmacogenetic Implementation Consortium guidelines are available through the Web site (https://cpicpgx.org/guidelines/).

Textbook Resources
Clinical Significance and Genetic Counseling for Common Ultrasound Findings: http://nscg.org/p/cn/id/fid=232

The latest edition of this book provides updates on the significance of ultrasound findings, including those suggesting the presence of a genetic condition, and information to help determine whether and what type of additional prenatal or postnatal testing, follow-up, and counseling should be offered.

Emery and Rimoin’s Principles and Practice of Medical Genetics
This multivolume (the latest edition is fully available online) book includes sections on diverse aspects of genetics in clinical practice, including related to concepts, research approaches, and individual conditions.17

The Encyclopedia of Genetic Disorders and Birth Defects
This text offers lay readers and professionals a reference to congenital disorders and birth defects. This volume contains more than >1000 entries, appendices providing tables of statistics, directories of service and support groups, and an introductory history of human genetics.18

Gorlin’s Syndromes of the Head and Neck
This dysmorphology-focused text describes several hundred genetic syndromes involving structural defects affecting the head and neck. Additional sections include information on teratogens, deformation sequences, physical measurements and growth curves, and useful resources.19

Human Malformations and Related Anomalies
This reference book on malformations is organized by body system and provides pertinent information on each anomaly, including clinical variability, known and hypothesized causes, associated anomalies and syndromes, and management and prognosis.20

Management of Genetic Syndromes
This book includes individual chapters focusing on the diagnosis and management of 50 different genetic conditions and is written to be useful to both geneticists and nongeneticist clinicians.21

Signs and Symptoms of Genetic Conditions
Comprising 31 clinical protocols from leading clinical geneticists, this book provides a practical manual for the diagnosis and management of common human genetic conditions based on their presenting signs and symptoms. Each chapter examines a specific clinical finding and leads the user through a step-by-step approach to a differential diagnosis.22

Smith’s Recognizable Patterns of Human Malformation
Smith’s Recognizable Patterns of Human Malformation is a long-standing resource for malformation syndromes of environmental and genetic etiology and recognizable disorders of unknown cause. This book provides concise yet accessible guidance to help diagnose these disorders, establish prognoses, and provide appropriate management and genetic counseling. As the title suggests, the descriptions also include multiple patient photographs to aid in recognizing the patterns of physical features.23


This pocket-sized manual (with a recognizable yellow cover) includes compact reviews of inborn errors of metabolism from a clinically oriented perspective. The manual includes a section on evaluating signs and symptoms of metabolic disorders in the context of various clinical situations, including neonatal-onset disease, and can be helpful in interpreting metabolic and biochemical laboratory results.

CASE EXAMPLES
To emphasize the utility and importance of such resources in a clinical setting, 2 representative case scenarios are provided.

Case 1
A male term infant (39 weeks’ gestational age) with a history of intrauterine growth restriction and failure to thrive is transferred to the NICU shortly after delivery because of respiratory insufficiency. His immediate birth measurements are notable for microcephaly (head circumference <3rd centile for gestational age). His respiratory insufficiency improves, and after spending 5 days in the NICU, the infant is discharged from the hospital. Two weeks later, however, the patient is readmitted to the inpatient pediatric ward for feeding difficulties and poor weight gain. Upon physical examination of the infant by the pediatric hospitalist
team, dysmorphic features are noticed, including large ears. There is no obvious syndromic explanation, and family history is noncontributory. On careful examination based on feeding difficulties, the child is also noted to have a posterior cleft palate. An echocardiogram, performed because of a suspected pathologic murmur, shows aortic coarctation.

With this constellation of findings, it would be important to have a geneticist or genetic counselor perform a full consultation. If a genetic specialist is not immediately available (which is often the case), a clinician might start with a differential diagnosis generator Web site such as Phenomizer (which uses clinical features) or Face2Gene (which uses photographs of the patient, with appropriate consent, and clinical features) to help assess the child. These Web sites use clinical information to assist in forming a differential diagnosis.

On the third day of readmission, the infant undergoes a formal genetic consultation, and dysmorphology examination reveals long palpebral fissures with eversion of the lateral portion of the lower eyelid, tented upper lip, and prominent fingertip pads. The genetics team raises concern for the possibility of Kabuki syndrome and suggests testing for mutations in genes associated with this condition. To learn more about this condition to optimize patient care and facilitate family counseling at this point, the hospitalist team turns to GHR, OMIM, and GeneReviews. These various resources explain complex genetic information in both physician-friendly (nongeneticist) and patient-friendly text. The pediatric hospitalist also uses the NexGxOx Web site to check specimen requirements and turnaround times for the commercial genetic testing laboratory suggested by the geneticist.

Approximately 1 month later, after the child has been discharged from the hospital, the test result comes back positive for a mutation in the gene KMT2D, 1 of the genes related to Kabuki syndrome. The hospitalist team sends the result to the child’s outpatient pediatrician. The hospitalist, anticipating that this child may be readmitted, and the outpatient pediatrician review the condition and management recommendations in GeneReviews and the CGD.

Case 2
An 18-month-old boy of Caucasian ancestry was healthy until a recent illness after an upper respiratory infection, which had also been present in multiple household members. His parents brought him to the emergency department after ~1 week of worsening respiratory symptoms. He was admitted to the hospital for signs of heart failure, and a dilated cardiomyopathy was noted via echocardiogram. Incidentally, his blood work showed neutropenia. Family history is notable for a maternal uncle with a history of dilated cardiomyopathy diagnosed in his teens because of exercise intolerance. No additional family members have obvious signs or symptoms of dilated cardiomyopathy by report. Because of the family history, multiple family members, including the patient’s mother, have undergone echocardiograms, which have been negative by report. The patient has a healthy and asymptomatic 4-year-old sister.

With this strong history of dilated cardiomyopathy in male family members, it would be important to have a geneticist or genetic counselor perform a full consultation. While awaiting a formal genetics consultation, a clinician might start with a differential diagnosis generator Web site such as Phenomizer, which allows key clinical findings to be used to generate a list of potential syndromes and conditions.

On the second day of admission, the patient undergoes a formal genetics consultation, and the dysmorphology examination indicates a round face, full cheeks, prominent pointed chin, large ears, and deep-set eyes. The geneticist and the genetic counselor bring up the possibility of Barth syndrome and recommend preliminary plasma amino acids and urine organic acids to be ordered. As a hospitalist you look at GeneReviews before ordering the samples to be collected and see that a preliminary diagnosis of Barth syndrome can be made through genetic testing of the involved gene if the initial tests appear positive. This information helps in discussion with the family during evening rounds.

The urine and blood test results come back and show significantly elevated urine 3-methylglutaconic acid (3-MGC), which indicates Barth syndrome. As a hospitalist you are aware that every state has different recommendations and requirements for newborn screening, and you wonder whether elevated 3-MGC would have been seen when this patient was born. You check the patient’s chart and see that this baby was born in Louisiana. Consulting a Web site such as the NNSGRC, you confirm that 3-MGC is not currently on the state’s newborn screening panel.

The geneticist and genetic counselor recommend for additional confirmation of Barth syndrome to order genetic testing of the TAZ gene. You use OMIM to investigate the TAZ gene and find out that it is the only gene known to be associated with Barth syndrome.

Given the significantly elevated risk of heart failure in patients with Barth syndrome, the hospitalist, anticipating that this child may be readmitted, reviews the condition and management recommendations in GeneReviews and the CGD. Upon the boy’s eventual hospital discharge, with close cardiology, genetics, and immunology follow-up arranged for the child, the patient’s mother asks you whether her 4-year-old daughter should undergo genetic testing also. She has talked with the genetics team about this question but wants to review the information. First, you review inheritance with the patient’s mother and father by providing pictures downloaded from a patient-friendly Web site such as GHR. You then review the literature on the NHGRI Web site, which has various articles referencing the need for autonomy for testing asymptomatic family members who would at most be carriers of genetic conditions.

CONCLUSIONS
The resources described in this article may be used to aid in diagnosis, education, and patient communication. This information is especially important because of the frequent discoveries that are transforming
the field of genetics and many related areas of medicine, including inpatient pediatric care.

REFERENCES


The opioid abuse problem in the United States has grown into an epidemic, with an estimated 2.5 million Americans currently dependent on heroin or prescription pain medications. One of the many consequences of this growing public health crisis has been a marked increase in the number of infants born to mothers who used opioids during pregnancy. The rate of neonatal abstinence syndrome (NAS), the syndrome of withdrawal these infants may suffer after birth, quintupled from 2000 to 2012. Often, these infants occupy NICU beds for weeks or even months. Despite these skyrocketing numbers, long lengths of stay, and an enormous strain on the medical system, our standard management of these infants has remained largely unchanged for decades. With a critical reappraisal of our current approach and an eye toward innovation, we can alter our entire paradigm for managing infants with NAS and create opportunities for significant improvements in both patient outcomes and health care expenditures.

The current approach used by many institutions for the management of NAS has its roots in a study published 40 years ago. In 1975, the Finnegan Neonatal Abstinence Scoring System (FNASS) was developed and is now widely accepted as the primary tool to assess infants with NAS. The FNASS is a 21-item tool that lists signs of withdrawal and assigns a point value to each sign. Finnegan and her team developed this score to guide management of infants with NAS and decided, based on their own observations, that infants with scores of ≥8 generally needed pharmacologic treatment. Most institutions have developed protocols that use FNASS scores of ≥8 to trigger the initiation of pharmacologic therapy.

This FNASS-guided approach, though never validated, has gone largely unchallenged since its inception, and it is time to reconsider whether management should be driven by a system that is based so heavily on cataloguing specific signs of withdrawal, many of which may be unrelated to the infant’s function or comfort. Is it truly best to give morphine to an infant who yawned 4 times instead of 3, as the FNASS guides us to do? Almost all infants born to mothers dependent on opioids will have some signs of withdrawal, such as hypertonicity or tremors. The FNASS can list the specific signs of withdrawal, but should we not be more concerned with how we manage the infant to allow him or her to function well rather than measuring our success by whether we can reduce the number of sneezes in a given time period?

This reliance on the FNASS to guide our decisions about when to administer medications has also made it difficult to assess the effectiveness of nonpharmacologic interventions, which the 2012 American Academy of Pediatrics policy statement on neonatal drug withdrawal cites as first-line treatment. There is growing evidence that these
nonpharmacologic interventions, such as creating a low-stimulation environment, swaddling, and feeding on demand, can have a significant impact on clinical outcomes of infants with NAS. Institutions with parental rooming-in models have consistently reported decreases in length of stay and use of medication.6

Despite this evidence, most studies of NAS include only infants who receive medications for treatment of withdrawal. This is largely because we are using the FNASS both to diagnose NAS and to guide treatment. If a score of 8 is both the diagnostic cutoff for defining withdrawal and the threshold at which pharmacologic therapy should be administered, how can we ever assess the impact of nonpharmacologic interventions? Looked at another way, if we use intensive nonpharmacologic interventions to reduce the severity of withdrawal signs just enough to decrease the amount of time an infant receives medication, then we can demonstrate a benefit to nonpharmacologic interventions. However, if the effect of nonpharmacologic interventions is strong enough to prevent an infant from receiving medications, then that infant would not be given a diagnosis of NAS, and thus no benefit would be recorded. Although there is some logic in standardizing our assessment of withdrawal severity to allow a better comparison of treatment efficacies and outcomes, we must uncouple this assessment of severity from an automatic initiation of medications if we want to assess the effectiveness of nonpharmacologic interventions.

If we define infants with NAS as only those who receive medication for amelioration of withdrawal signs, only infants who do not benefit from or do not receive first-line, nonpharmacologic interventions actually receive a diagnosis of NAS. This is an unusual approach. Imagine if children with pus behind their tympanic membranes were diagnosed with acute otitis media only after treatment with amoxicillin failed and they were given amoxicillin/clavulanic acid as second-line treatment. That would be ridiculous, yet that is the current approach for infants with evidence of withdrawal. Clearly, nonpharmacologic interventions are not considered to be on the same therapeutic plane as pharmacologic therapy; put simply, it is not thought of as a “real” treatment. In fact, none of the published articles on NAS comparing different drug therapies control for nonpharmacologic interventions, nor are these interventions routinely documented. When a child has a score of ≥8, we do not make sure that the mother is at the bedside or review other nonpharmacologic interventions to ensure that they are maximized. We just give morphine.

If we change our definition of NAS back to something closer to the original definition, an infant with prenatal exposure to opioids who develops signs of withdrawal, we may be able to change our perspective on management. Instead of considering only opioid-treated infants as “treated,” we can initiate intensive nonpharmacologic interventions for opioid-exposed infants at birth. Thus, all exposed infants can be “treated,” although probably only a minority will receive second-line pharmacologic therapy. Once we fully understand the impact of nonpharmacologic interventions on this population, we can create protocols that take full advantage of the power of the maternal–infant dyad. For example, most infants with NAS are managed in NICUs, units that often cannot permit rooming in and have limitations in providing a low-stimulation environment. If we accept that nonpharmacologic interventions are the first-line treatment of NAS, how can we possibly continue to tolerate this practice? Would we ever send a child with asthma to a unit that could not provide albuterol?

There is substantial room for improvement in the care of infants with NAS, and we must start to look at our current approach with a critical eye. Using the FNASS to guide diagnosis and treatment encourages us to treat a number and not the patient. We need to move away from the FNASS to assess these infants and begin to prioritize assessment of the infant’s basic ability to function, such as eating, sleeping, and consolability. This change will also uncouple the use of medication from the diagnosis of NAS. Infants with exposure to opioids in utero who develop clear signs of withdrawal, such as hypertonicity or tremors, should be given a diagnosis of NAS. By returning to this definition, we can begin to assess the effectiveness of nonpharmacologic interventions, which can be a powerful therapy and should truly be regarded as first-line treatment. We need innovative approaches to these infants that will help minimize their exposure to additional opioids, reduce hospital stays, decrease costs, and ensure better long-term outcomes.

Acknowledgments
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ILLUSTRATIVE CASE

Timing Is Everything: Recurrent Infections and Failure to Thrive in an Infant

Amy M. DeLaroche, MBBS, Nirupama Kannikeswaran, MD, Helene Tigchelaar, MD

CASE

A 6-month-old African American boy presented to the emergency department (ED) with a rash first noted on his face, spreading to his torso and extremities over 2 days. He had no history of fever or new exposures, and the rash appeared to be pruritic. A review of systems was positive for a slight cough and increased work of breathing but was otherwise negative. Born full term via normal spontaneous vaginal delivery at 2466 g (2nd percentile), he was exclusively breastfed and immunized, with no allergies. His past medical history was significant for “episodes of wheezing,” without a formal diagnosis of asthma. A circumcision was his only surgical history. He had oral candidiasis and diaper dermatitis at 2 weeks of age, with no chronic illnesses; however, review of his electronic medical record revealed 3 hospitalizations and several ED and outpatient clinic visits. Hospitalized twice at 4 weeks of age for projectile vomiting associated with apnea, cyanosis, and seizure-like activity, he was then readmitted at 5 months of age for multifocal pneumonia with dehydration secondary to enteritis. After these 3 inpatient stays and outpatient evaluations by the neurology, pulmonology, and gastroenterology services for emesis, paroxysmal upper and lower extremity movements, and apnea, he received a diagnosis of gastroesophageal reflux disease, for which he received trials of 2 antireflux therapies. Throughout these encounters, his weight remained in the second percentile.

Vital signs in the ED were as follows: temperature of 38.0°C rectally, heart rate of 120 to 148 beats per minute, respiratory rate of 36 to 60 breaths per minute, blood pressure 114/63 mm Hg, and oxygen saturation 88% on room air, which improved to 100% on 2 L of oxygen through a nasal cannula. His weight was 6.3 kg (<2nd percentile). A complete physical examination was notable for clear rhinorrhea, tachypnea, bilateral intercostal retractions with accessory muscle use and a prolonged expiratory phase, a diaper rash, and a generalized maculopapular eruption. Intravenous access was established, and he was started on maintenance intravenous fluids. He was given 1 dose of acetaminophen for his fever. A capillary blood gas showed mild lactic acidosis with a pH of 7.392, pCO2 of 35.8 mm Hg, HCO3 of 21.3 mEq/L, base excess of −2.6 mEq/L, and a lactate of 2.5 mmol/L. His complete blood cell count showed a white blood cell count of 7.2/mm3, hemoglobin 10.2 g/dL, hematocrit 33.1%, and a platelet count of 239/mm3. The differential on his complete

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blood cell count was normal except for lymphocytopenia (3.2/mm³). Electrolytes, glucose, and creatinine were within reference range, whereas the blood urea nitrogen, calcium, albumin, and total protein were low at 2 mg/dL, 8.0 mg/dL, 3.8 g/dL, and 7.5 g/dL, respectively. A chest radiograph was obtained (Fig 1), which demonstrated multifocal parenchymal airspace disease consistent with pneumonia. He was started on azithromycin and clindamycin for coverage of both atypical and aspiration pneumonia and admitted to the pediatric floor. Upon admission, an immunodeficiency disorder was considered in the differential diagnosis because of the history of recurrent pneumonia and failure to thrive. Thus, as part of the initial evaluation, an HIV test was ordered.

**Question:** Why should HIV be included in the initial evaluation of children with clinical concern for an immunodeficiency disorder?

**Discussion**

Human immunity results from a complex interplay between the innate and adaptive immune systems, in combination with protection afforded by both anatomic and physical barriers. Disruption of these processes and structures leads to an immune deficiency, categorized as either primary or secondary. A primary immunodeficiency, which broadly includes antibody, T-cell, phagocytic, and complement disorders, stems from a genetic defect. Conversely, a secondary immunodeficiency is commonly attributed to barrier defects (e.g., burns), underlying systemic disease (e.g., HIV), or immune-mediating medications (e.g., corticosteroids). Primary and secondary immune deficiencies can present similarly; however, secondary immune deficiencies are more common in children. Thus, HIV should always be excluded as part of the initial evaluation for primary immunodeficiency.

**CASE CONTINUATION**

The HIV antigen/antibody combination test was reactive, and a subsequent HIV Western blot was positive. The initial ultrasensitive HIV viral load was 1 017 379 RNA copies per milliliter. A bronchoscopy with bronchoalveolar lavage led to a diagnosis of Pneumocystis jiroveci and a respiratory culture demonstrating rare Pseudomonas aeruginosa.

**Question:** What is the epidemiology of mother-to-child transmission (MTCT) of HIV in the United States, and why does this clinical problem persist?

**Discussion**

HIV is the most common severe acquired immunodeficiency in the United States, affecting ~1.2 million adolescents and adults. In 2010, the incidence of HIV was 4 times higher in men than in women; however, 20% of new infections occur in women, with 84% of women contracting HIV through heterosexual contact. Because women often contract HIV during their childbearing years, 91% of pediatric HIV results from perinatal transmission. Perinatal transmission of HIV, which peaked in 1991 at 1650 cases in that year, occurs during pregnancy, during labor and delivery, and in the postpartum period via breastfeeding. Various policies centered on the prevention of MTCT of HIV, recognized as a significant public health issue, were implemented in the 1990s. These policies, which included early diagnosis and provision of antiretroviral therapy combined with cesarean delivery when indicated and breastfeeding abstinence, resulted in a 95% reduction in the incidence of perinatal HIV in the United States. Although this is a remarkable public health achievement, ~164 infants were born with HIV in the United States in 2010. As with HIV among adolescents and adults, African American children are overrepresented, accounting for 65% of these diagnoses. Elimination of perinatal HIV in the United States is defined by the following 2 goals: an MTCT rate of <1% among HIV-exposed infants and an incidence of <1 infection per 100,000 live births. To achieve these goals, prevention in the United States centers around the Perinatal HIV Prevention Cascade, which includes primary prevention, preconception and prenatal care, universal prenatal HIV testing, antiretroviral prophylaxis, cesarean delivery as indicated, breastfeeding avoidance, and comprehensive clinical care for the mother and child. Unfortunately, missed opportunities are identified in 74% of infected infants. The majority stem from incomplete adherence to the prevention cascade secondary to various social and systemic barriers, such as poverty, maternal mental health problems, and underresourced health departments. However, continued MTCT of HIV may also result from events occurring outside the cascade, such as seroconversion during pregnancy or breastfeeding, which accounted for 8% of cases reported between 2005 and 2010. Thus, although elimination of MTCT of HIV is an achievable goal, prevention efforts continue to be undermined by complex problems related to delayed maternal diagnosis and insufficient antiretroviral prophylaxis.

To facilitate timely maternal diagnosis, the current standard of care includes routine opt-out HIV testing for all women in early pregnancy. Consequently, ~93% of women are tested at least once during pregnancy. Repeat testing in the third trimester, performed in less than one-quarter of patients, is recommended only in certain high-risk jurisdictions and circumstances. Reliance on risk-based HIV testing in the third trimester is
problematic, however, because 25% of new HIV infections are found in patients with no clear risk factors.11,15 As highlighted by our case, timely assessment and clear documentation of maternal HIV status in the newborn’s medical record is imperative because early initiation of antiretroviral therapy, within 6 to 12 hours after birth, is recommended for effective prevention of perinatal transmission.12 Given that 27% of mothers of HIV-infected infants receive their diagnosis after delivery,13 repeat testing in the third trimester should be considered for all women and can easily be performed at delivery or in the immediate postpartum period.12

**Question:** How do infants with HIV present, and what is the recommended initial diagnostic test for infants and children?

**Discussion**

Largely contracted in the perinatal period, pediatric HIV may have an acute or gradual presentation followed by an accelerated course compared with adults.16,17 The majority of infants with perinatal HIV present within the first year of life, commonly by 5 months of age.18 Although ∼20% remain asymptomatic in this period, the same is true for only 6% of children by 5 years of age.18 HIV is a multisystemic disease16 whose clinical manifestations can be variable, including fevers, lymphadenopathy, organomegaly, respiratory tract infections, recurrent otitis and sinusitis, hypotonia, and developmental delay.17 Although the acute retroviral syndrome is rare in infancy, there is typically an asymptomatic or mildly symptomatic period lasting months.19 This period is noted in our case, with a history of failure to thrive, enteritis, and recurrent mucocutaneous findings, all of which are common clinical features of children with HIV.17 This mildly symptomatic period typically ends as it did for our patient: AIDS, with *Pneumocystis jiroveci* being the most common AIDS-defining illness.18,17 To render a diagnosis of HIV in children <24 months of age, antibody assays are generally not recommended because children in this age group may have persistent maternal antibodies.12 Rather, direct virologic tests, including HIV DNA and HIV RNA polymerase chain reaction, are preferred.12 The specificity of both of these tests is 100% by 1 month of age, with an equivalent sensitivity at 3 months of age.12 Two positive virologic tests are considered diagnostic.12 In children >24 months of age, diagnosis rests on an HIV-1/2 antigen/antibody combination immunoassay confirmed by an HIV-1/HIV-2 antibody differentiation immunoassay.18 Upon diagnosis, infants should immediately be referred to a multidisciplinary clinic because early initiation of combination antiretroviral therapy hinders disease progression and improves growth, neurocognitive development, and mortality.12,21

**CASE RESOLUTION**

Additional history revealed that although the patient’s mother had received prenatal care, she had switched health care providers during her pregnancy. She was reported to be HIV negative based on testing conducted in early pregnancy, but these records could not be obtained. Third trimester HIV testing was not performed. This patient had a prolonged 25-day hospital stay during which he gained 220 g yet remained below the first percentile for weight. He completed therapy for *Pneumocystis jiroveci* and *Pseudomonas aeruginosa* pneumonia complicated by rhinoviral, entero viral, and adenoviral infections. He was also started on antiretroviral therapy including zidovudine, lamivudine, and lopinavir/ritonavir, with improvement in his viral load to 14,172 RNA copies per milliliter at the time of discharge.

**Question:** Had a secondary immunodeficiency disorder been excluded, is there a framework to aid clinicians with the initial approach to primary immunodeficiency disorders?

**Discussion**

A primary immunodeficiency, which encompasses >180 specific diagnoses,1 affects ∼1 of every 2000 children in the United States.22 However, the exact prevalence varies with the specific diagnosis: Milder disease, such as immunoglobulin A deficiency, occurs in 1 in 500 children, whereas serious forms such as severe combined immunodeficiency are seen in >1 in 100,000 children.2 Often diagnosed in childhood,23 the overall incidence of primary immunodeficiency is greatest in children <5 years of age.24 Thus, although certain specific diagnoses may be rare, collectively, primary immunodeficiencies are not an uncommon pediatric problem.2

Unfortunately, rendering a diagnosis of primary immunodeficiency in children is difficult, and diagnostic delay is well documented.24 Primary immunodeficiencies tend to present as 1 of 8 clinical presentations: recurrent ear, nose, and throat infections; failure to thrive from infancy; recurrent pyogenic infections; unusual or unusually severe infections; recurrent infection with the same type of pathogen; autoimmune or chronic inflammatory disease; characteristic combinations of clinical features suggestive of an eponymous syndrome, such as Chediak–Higashi syndrome; and angioedema.25 Although pattern recognition is the preferred approach to making a diagnosis of primary immunodeficiency,12 variable clinical presentation and disease severity complicates this process.25 Furthermore, the most common clinical presentation of primary immunodeficiency, recurrent respiratory infections, is also the hallmark of early childhood.1 In fact, after evaluation, only 10% of children with a history of recurrent infection are diagnosed with primary immunodeficiency.1 To aid clinicians, the “10 Warning Signs of Primary Immunodeficiency” were developed through expert opinion and published by the Jeffrey Modell Foundation.26 The presence of ≥2 “warning signs” should trigger diagnostic evaluation.27 Unfortunately, the “warning signs” have been shown to have low sensitivity (23%) and specificity (63%) and failed to identify more than one-third of patients who ultimately receive a diagnosis of primary immunodeficiency.28 If the diagnosis is called into question, a preferred starting point is to identify a history of serious, persistent, unusual, or recurrent infections.1 This history, in combination with a family history of
primary immunodeficiency, use of intravenous antibiotics for sepsis, and failure to thrive, identified ~90% of T-lymphocyte, complement, and neutrophil or mononuclear primary immunodeficiency in 1 cohort.29 Family history is the most robust identifier of primary immunodeficiency.29 This schema is particularly relevant to the pediatric hospitalist because careful review of growth parameters and specific inquiry into the family history when admitting a patient for intravenous antibiotics may help identify patients in need of additional investigation. Although various diagnostic approaches have been published,1,3,10 a reasonable approach is to first obtain a complete blood cell count with differential, immunoglobulins, a lymphocyte subset, and complement levels.1,3

CONCLUSIONS
Primary and secondary immune deficiencies can present similarly; however, secondary immune deficiencies, specifically HIV, are more common in children. Resulting from perinatal transmission, pediatric HIV persists in the United States because of complex issues resulting in delayed maternal diagnosis and insufficient antiretroviral prophylaxis. Although our case underscores the need for hard copies of maternal HIV laboratory results in the newborn’s medical record, it also highlights the fact that third trimester HIV testing at delivery or in the immediate postpartum period can be a life-saving approach to identifying children not identified through standard preventive interventions. Thus, routine third trimester HIV testing should be considered in all women but is rarely performed. Pediatric hospitalists, in collaboration with their obstetric colleagues, can help address this gap in care by developing systems to ensure routine rapid HIV testing at the time of labor and delivery, with documentation of these results in the newborn’s medical record. As perinatal HIV continues to largely affect a more challenging patient population, this systemic change in practice would serve to bring us a step closer toward eliminating MTCT of HIV in the United States.

LEARNING POINTS
• HIV should always be excluded as part of the initial evaluation for an immunodeficiency.
• Third trimester HIV testing should be considered for all women in labor or in the immediate postpartum period as a step toward eliminating MTCT of HIV in the United States.
• Immunodeficiency should be considered when a history of serious, persistent, unusual, or recurrent infections is elicited.

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Imagine in the not too distant future, you are rounding on a child who was admitted with gastroenteritis. You want to know whether he is ready for discharge, so you ask your hospital for an update:

*Hospitalist, talking aloud: “Hospital computer, when was Johnny’s last bowel movement?”*

*Overhead voice: “Patient Jonathan Smith had a bowel movement at 0538. It was yellow and seedy in appearance. He had 5 bowel movements in the last 24 hours, decreased from 10 the day prior. Would you like other vital information?”*

*Hospitalist: “No, thank you, hospital computer.”*

Although this scenario may seem straight out of an episode of *Star Trek*, is it really that far off? Everywhere we look these days, smart technology has infiltrated our lives. From Siri reminding me I am on call, or wearables that track our every biologic function, it seems you cannot make a move without generating measurable data.

But what about hospitals? Why am I still faxing discharge summaries while my friends in the tech sector make fun of me for using the word *fax*? Why have our work environments not kept pace with the rest of the world?

When I started working after my pediatric hospital medicine fellowship, the first quality improvement project assigned to me was to lead a group to improve hand hygiene on the wards. Over time, as our efforts evolved, a unique opportunity came my way. I learned that scientists at our university working in the field of artificial intelligence were interested in partnering with us.

Initially, the only way we monitored compliance was with physical audit cards done by hand, mainly by nursing staff. Consequently, we had little data on every other role. How could we recreate a fly on the wall to monitor compliance in real time, all the time, for anyone? With “computer vision” I was told.

The group was interested in placing depth sensors throughout the ward that could monitor movement and track whether the gel dispensers were being used at entry and exit of patient rooms. They could even be placed inside patient rooms to monitor whether, for example, someone washed their hands appropriately but then touched something they should not, and then interacted with the patient environment. They had previously used these sensors to track movement through subway stations in Europe and in other real-world applications but never anything in health care. Now, about 2 years after our initial meeting, we are collecting data, and I am excited about the future.

What if, in place of monitors and their wires, our patients could wear bracelets that transmitted biometric data directly to the electronic medical record (EMR)? This would save documentation time, free up staff for other activities, and allow more robust data collection (no more “missed” diapers). What if, combined with intelligent sensors analyzing patients’ movements, false alarms on monitors could be silenced automatically, alleviating alarm fatigue? What if, when I walked into a patient’s room, my badge was connected to a system that could let the patient...
know who I am, eliminating the confusion often felt by families about who their care team is? In some places, this technology is being used to provide cutting-edge care. Through a collaboration with IBM, the University of Pittsburgh has been able to create their own “smart room” that uses real-time location tracking information to bring patient information from the EMR to screens in the patient’s room.1,2

As hospitalists, we are poised to be on the forefront of appropriate innovation. There are plenty of times when technology fails us. It is usually when the technology was designed without the end user in mind. Pairing technological advances with someone who knows the hospital inside and out (that’s us!) could unlock huge potential that our hospital administrators may not realize. Getting from our first meeting in an office to depth sensors on the ceilings of a ward was no easy task. Along the way, I learned (sometimes the hard way) how best to try to bring a new technology to the hospital. Here are some ideas that can be helpful in driving successful collaboration if you too are interested in making your hospital smarter with technology:

LITERATURE SEARCH
Reading outside your usual journals can often bring new perspectives. Checking out casual technology news outlets such as Wired magazine or techcrunch.com can expose you to technology companies you may never have heard of in your traditional medical reading. Moreover, there are a myriad of health care information technology (IT) outlets to explore, such as the health care section of Information Week or Healthcare IT News3,4 or blogs such as Chilmark Research and KevinMD,5,6 that can be great sources.

RIGHT PROBLEM, RIGHT SOLUTION
When the computer vision team first contacted us, they broadly wanted to work on “hand hygiene.” Finding out exactly what our problem was and what their technology could realistically do helped us determine whether it would be better than our current state. This is probably one of the most important lessons from my experience. The world has been full of promises about new technology that will “revolutionize” how something is done. Consider the Segway7 or, even more recently, the rise and fall of Theranos.8 The time spent making sure the technology really solves a problem that exists, rather than being a solution to a problem that does not, is crucial. Moreover, in our field the proof of concept is paramount. It has to not only make sense but have proven efficacy if it is going to be adopted for improving clinical care.

TAKE THEM FOR A RIDE
Workflow integration with minimal disruption, especially in relation to brand new technology, is crucial. This has been noted in instances of large change such as a brand-new EMR rollout.9,10 At the beginning of our project, we invited the computer vision team to join rounds, tour the hospital, observe nursing staff workflow, and witness how many people go in and out of patient rooms. If for example, our sensors required people to change how they cleaned their hands or where they stood, it would have been impossible to move the project forward. This “field trip” is vital to making sure that a company truly understands what patient care looks like and is essential for success. No matter the technology, if it is designed without the end users’ workflow in mind, it is doomed to fail.

INVOKE ALL STAKEHOLDERS EARLY
Research has shown that with any large implementation, finding the “special” people is crucial to success.11 Your hospital’s leaders may be the first point of contact to green-light any project you propose. It is worthwhile to get their buy-in, perhaps with a short presentation and written proposal, to help push the project forward. In our case, we presented with our computer vision colleagues at a monthly chief executive meeting to answer questions and prove our case to get approval. Afterward, we focused on involving a variety of stakeholders including facility staff, engineering, occupational health and safety, nursing staff leaders, and so on. In any big project, it is also important to hold regular meetings with the stakeholders to maintain transparency and keep momentum. It also will make any hiccups along the way easier to swallow because people are not surprised by your project and have been aware of it all along.

COMMUNICATE, COMMUNICATE, COMMUNICATE

New technology can often bring skeptics and disbelief. Addressing these problems requires developing clear and direct messaging about what you are doing to the people who will be most affected and repeating this information regularly. For example, we created multiple staff notices via e-mail and in-person discussions until everyone had a good understanding of the technology and the project. We also created a notice to hand out to patients on that unit describing the project and inviting questions. Additionally, communicating your endeavor to your colleagues is just as important. You may never know who else might be interested in collaborating with you or might have similar interests in bringing technology to the hospital setting.

I have learned now that it is our responsibility not to wait on innovation to find us but the opposite. I never thought for a second when I decided to be a hospitalist that I would have such an opportunity to bring cutting-edge technology to the hospital in such a creative way, but I was fortunate that it happened by chance and found its way to me. This experience has encouraged me to not leave things to chance but rather to start thinking outside the hospital box. What this means is thinking about how technology might be able to solve problems I encounter on a daily basis and then find out whether they exist. It means leaving the confines of the academic hospital system and seeking out companies developing technology that could be helpful and reaching out to them. What is wrong with connecting with industry if the result is better, more efficient, and safer patient care? I would not mind disclosing that at all.

However, it is necessary to reach out to your hospital’s IT leaders to discuss your ideas first. Making technology improvements is their responsibility, and many welcome the
unique view of a clinician but may not seek it out. Given our time on the “front lines,” our experience is valuable so do not be afraid to seek opportunities to share it. However, if that is daunting, asking your division chief or department chair to facilitate a meeting may be a helpful first step.

So, while I listen to the unmistakable melody of another discharge summary being transmitted via fax, I look forward to the day when I can treat my hospital like the bridge of the starship Enterprise. The day when I can ask aloud what happened with Johnny’s bowel movements, and Johnny’s mother or father can ask aloud who their doctor is today and what time the cafeteria closes. I just hope I can wheel around in Captain Kirk’s chair on family-centered rounds when I am too old to walk the wards.

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