Clinical Decision Support and Palivizumab

A Means to Protect from Respiratory Syncytial Virus

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Keywords

Respiratory syncytial virus, palivizumab, electronic health records, clinical decision support

Summary

Background and Objectives: Palivizumab can reduce hospitalizations due to respiratory syncytial virus (RSV), but many eligible infants fail to receive the full 5-dose series. The efficacy of clinical decision support (CDS) in fostering palivizumab receipt has not been studied. We sought a comprehensive solution for identifying eligible patients and addressing barriers to palivizumab administration.

Methods: We developed workflow and CDS tools targeting patient identification and palivizumab administration. We randomized 10 practices to receive palivizumab-focused CDS and 10 to receive comprehensive CDS for premature infants in a 3-year longitudinal cluster-randomized trial with 2 baseline and 1 intervention RSV seasons.

Results: There were 356 children eligible to receive palivizumab, with 194 in the palivizumab-focused group and 162 in the comprehensive CDS group. The proportion of doses administered to children in the palivizumab-focused intervention group increased from 68.4% and 65.5% in the two baseline seasons to 84.7% in the intervention season. In the comprehensive intervention group, proportions of doses administered declined during the baseline seasons (from 71.9% to 62.4%) with partial recovery to 67.9% during the intervention season. The palivizumab-focused group improved by 19.2 percentage points in the intervention season compared to the prior baseline season ($p < 0.001$), while the comprehensive intervention group only improved 5.5 percentage points ($p = 0.288$). The difference in change between study groups was significant ($p = 0.05$).

Conclusions: Workflow and CDS tools integrated in an EHR may increase the administration of palivizumab. The support focused on palivizumab, rather than comprehensive intervention, was more effective at improving palivizumab administration.

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1. Background

Respiratory syncytial virus (RSV) causes lower respiratory tract infections in infants and young children. In the United States, RSV causes 75,000 to 125,000 hospitalizations and 400 deaths annually [1–3]. Risk of hospitalization increases in premature infants and in infants and children with congenital heart disease, chronic lung disease of prematurity, immunodeficiency, and other immunocompromised states [3, 4]. The mainstay of management is prevention and supportive care. There is no licensed vaccine for RSV, but passive immunization with the monoclonal antibody palivizumab has demonstrated efficacy for decreasing hospitalization rates and emergency room visits due to RSV infection [5–9].

Palivizumab provides approximately one month of protection and is recommended for certain patients throughout the RSV season each year [3]. Given the expense of administering palivizumab – \$800 to \$3,000 per dose – universal prophylaxis is not considered feasible [10]. To support appropriate use of palivizumab, the American Academy of Pediatrics (AAP) has produced policy statements for its administration during peak RSV season [3, 11]. These eligibility criteria are complex as they change over time and weigh multiple factors, including degree of prematurity, the age at the start of the RSV season, and complicating factors like heart or lung disease. Proper delivery of palivizumab requires that healthcare providers carefully interpret these complex criteria, account for diverse insurance company approval procedures, order doses of palivizumab from suppliers and schedule timely visits to administer these doses [12]. With these difficult steps it is not surprising that compliance with palivizumab administration recommendations among pediatric practices varies with some practices as low as 25% [12, 13].

There are numerous barriers to palivizumab administration that are beyond the immediate control of the office. Previous studies have cited challenges such as limited access to care, insurance coverage, transportation problems, communication difficulties, inconvenience to parents, distance from the clinic, the cost of prophylaxis, and a lack of understanding of the severity or consequences of RSV [12, 13]. Interventions to overcome these barriers have included home-based programs for administration of palivizumab, patient reminder calls and parental education efforts [12, 14]. One study focused on provider education to develop expertise in determining eligibility for palivizumab [15]. Though this intervention was labor intensive it demonstrated greater success at reducing inappropriate palivizumab administrations rather than reducing the proportion of missed eligible patients. Additionally, as eligibility guidelines change over time these knowledge-based interventions can become outdated [16].

To date, although vaccine decision support has proven effective in other settings, there are no reports of EHR-embedded alerts or workflow-based clinical decision support (CDS) interventions to improve palivizumab administration rates [17–19]. The only identified CDS intervention describes an online web application to streamline the prior-authorization process and to send monthly dose prompts to pediatricians [20]. We hypothesized that CDS tools would be effective in improving palivizumab receipt.

2. Objectives

We sought a comprehensive solution for identifying eligible patients and addressing barriers to palivizumab administration. In this study, we examine an internally developed, EHR-embedded CDS module for facilitating palivizumab eligibility identification and streamlining palivizumab administration to eligible infants and children.

3. Methods

We performed a secondary analysis of a 3-year cluster-randomized active control trial to evaluate the effect of different CDS interventions on palivizumab prophylaxis rates among premature infants. The goal of the larger trial was to broadly improve preventive healthcare for premature infants. This cluster-randomized trial was concurrent with a network-wide initiative to improve palivizumab pro-

phylaxis rates. Our study team developed quality improvement tools to support this initiative. In this manuscript, we report the impact of the palivizumab interventions we developed.

3.1 Study location and population

All primary care practices affiliated with The Children's Hospital of Philadelphia (CHOP) were invited to participate. One practice declined due to the small number of premature infants receiving primary care at their location. Due to the differences in insurance payer-mix and socioeconomic status that were known to affect workflow and outcomes for premature infants, we stratified randomization by urban versus suburban practice location and sorted sites by size to achieve balance in the randomization.

Data were examined for children born before 35 weeks gestation who received preventive health-care before their second birthday from one of 20 practices owned by CHOP between 5/1/2009 and 4/30/2012. The first baseline RSV season was from 11/1/2009 to 4/30/2010, the second baseline season was from 11/1/2010 to 4/30/2011, and the intervention season was from 11/1/2011 to 4/30/2012. Analysis was restricted to children who were eligible to receive 5 doses of palivizumab based on the 2009 AAP policy statement during at least one of the three RSV seasons during the study period [7].

3.2 Intervention Development

We extracted the published AAP policy statement recommendations for palivizumab eligibility using the Guideline Elements Model, an ASTM standard for guideline representation, and formatted the recommendations using the JBoss Rules (Drools) programming language to create an algorithm for identifying these patients that was implementable within our EHR [21]. Additional details about this implementation are available online [22]. Although this was a policy statement rather than a clinical guideline, it was remarkably clear, actionable and able to be codified.

Our original study design conceived in 2008 was to cluster-randomize twenty practices from our primary care network into two groups: an intervention group receiving a comprehensive set of premature infant CDS tools integrated in the EHR (the "Premie Assistant"), and a control group using the standard EHR. All practices use the ambulatory EHR, EpicCare (Verona, WI). During the 2009–2010 RSV season – the first baseline study season – our primary care network identified palivizumab administration as a target for quality improvement. To support this initiative, we provided CDS for palivizumab to both the intervention and control groups in our study. This manuscript compares palivizumab administration rates between these two study arms (palivizumab-focused CDS vs. comprehensive CDS for premature infants).

3.3 Palivizumab-focused Intervention Group

The first two seasons were used to establish baseline rates. Study locations were randomly assigned to one of two groups for the third RSV season (11/1/2011 to 4/30/2012). The first group (palivizumab-focused) served as an "active control" group within the premature infant decision-support trial and received CDS and workflow tools for coordinating palivizumab administration efforts at each site visible only to nurses, not providers. This care management intervention included a list of patients and an interactive form embedded in the EHR that tracked eligibility information, insurance approval, delivery of palivizumab doses to the site, prior doses administered and upcoming appointments (► Figure 1 and ► Figure 2). Nurses received one-on-one training about how to use the decision support. It is important to note that the education provided to nurses did not include how to interpret palivizumab eligibility.

3.4 The "Premie Assistant" Comprehensive Intervention Group

In addition to the previously described palivizumab-focused CDS tool, practices in the comprehensive intervention group received additional decision support (► Figure 3). This CDS tool, called the

“Premie Assistant,” delivered clinician-directed alerts about palivizumab eligibility and supported five additional issues important to the care of premature infants:

1. growth assessment,
2. nutrition recommendations,
3. developmental milestones,
4. blood pressure screening,
5. documentation for retinopathy of prematurity.

The Premie Assistant applies a combination of CDS approaches including alerts, order support, guideline based CDS, forms, clinical context, and clinical pathways. For example, there was an alert to check blood pressure, but passively displayed reminders for nutrition recommendations. Clinician training was completed in an in-person group training session, and nurses responsible for the palivizumab administration workflow received one-on-one training that was identical in content to the training received by nurses in the palivizumab-focused intervention group.

3.5 Primary Outcome

The primary outcome of interest for this analysis was receipt of palivizumab during each month of eligibility. As an additional analysis, we categorized why doses were missed in each arm of the study. A priori we identified four categories of palivizumab administration disposition:

1. palivizumab was given;
2. palivizumab was not given due to non-office factors, which included insurance issues, failure to attend a scheduled appointment, or palivizumab refusal;
3. palivizumab was not given due to office workflow factors, which included missed opportunities while the child was in the office, or failure to schedule appointments; and
4. palivizumab was not given due to lack of recognition of child eligibility.

EHR data to determine palivizumab eligibility, doses administered, and the covariates were extracted in an automated process. Manual chart review was then performed independently by two authors (AH and RG) to confirm eligibility and determine reasons doses were not given and recorded in REDCap [23]. All disagreements were reconciled by consensus agreement in discussion with all authors.

3.6 Covariates

We controlled for covariates since randomization by cluster (treatment location) can leave imbalances between treatment groups by patient-level factors if the randomized locations have different characteristics. Children with lower socioeconomic status may have barriers to accessing healthcare that prevent receiving timely doses of palivizumab [12, 24]. Also, younger children who are significantly premature may be identified as eligible during the first year of life more reliably than older children during their second season of eligibility or children who are eligible due to cardiac or lung problems. Consequently, we examined race, ethnicity, insurance type (public, private or no insurance), urban versus suburban practice location, gestational age at birth, and age at start of the season for between-treatment-group imbalance in order to confirm the need to adjust for associations between these child characteristics and receipt of palivizumab.

3.7 Statistical Analysis

We performed a longitudinal analysis of the effect of the interventions over time in a two-step process. First, owing to imbalances in patient-level characteristics, we had to develop a model for treatment assignment as a function of patient-level factors. We did so using logistic regression in a model with the binary treatment indicator as the outcome and the patient-level factors as predictors. In this step, we calculated treatment assignment weights as a method of standardizing the two treatment groups to the characteristics of the children in the intervention group. This form of adjustment balances patient-level covariates to reduce any residual confounding after randomization. Second, in a

response model, we implemented a multinomial logit model, weighted by the treatment assignment weights for each person, in which outcomes were the four categories:

1. palivizumab given
2. not given due to family or insurance barrier
3. not given due to an office workflow problem, and
4. the office did not recognize that the child was eligible for palivizumab.

The model covariates in this response model were treatment assignment (palivizumab-focused versus comprehensive intervention), RSV season (the time of measurement), and their interaction, as well as a single practice-level covariate, a binary indicator of whether the practice was urban or suburban. To account for the cluster-level randomization we used robust variance estimates with the practice site as the clustering variable. Finally, we used predictive margins to calculate probabilities and their 95% confidence intervals (CI) for the four outcomes by season and by intervention group from the multinomial logit model. We chose this two-step method to achieve adjusted estimates of outcomes (predicted probabilities) that would be clinically meaningful but with careful attention to issue of bias and variance that can occur in cluster randomized designs. Analyses were done using Stata v 13.1 (Stata Corp, College Station, TX, 2013). Data management was performed using SAS v 9.3 (Cary, NC). The Institutional Review Board at CHOP approved the study and waived the requirement for consent from individual children/families.

4. Results

4.1 Study Population

Using our eligibility criteria, we identified 356 children who were eligible to receive 5 doses of palivizumab during at least one of the three RSV seasons (two baseline seasons and one intervention season) as summarized in ► Table 1. Of these children, 114 were eligible during the first baseline season and 115 were eligible during the second baseline season. During the intervention season, 146 children were eligible. Some children (n=19) were eligible for multiple seasons. The urban cohort (n=190) was predominantly Black or African American (86.8%) and publicly insured (84.7%). The suburban cohort was predominantly White (60.2%) and privately insured (64.8%). Randomization resulted in a similar distribution of demographic characteristics between the two study arms, with the exception that publicly insured children were more prevalent among the palivizumab-focused intervention sites compared to privately insured children ($p = 0.001$). Additional demographic characteristics are shown in ► Table 1 and ► Table 2.

4.2 Palivizumab Administration Rates

Rates of palivizumab administration during the three RSV seasons are summarized in ► Table 3 and shown visually in ► Figure 4. Within the palivizumab-focused intervention group, after adjusting for patient level characteristics and practice location, the proportion of palivizumab doses administered increased in the intervention season to 84.7% as compared to the two baseline seasons (68.4% in the first season and 65.5% in the second season). Among practices randomized to the comprehensive intervention group, the proportion of doses administered during the baseline seasons fell from 71.9% in the first baseline season to 62.4% in the second baseline season. There was partial recovery from this decline during the intervention season (67.9% of doses were administered). In comparison to the second baseline season, there was not a statistically significant difference in the comprehensive intervention sites' proportion of palivizumab doses administered (increase of 5.5 percentage points, $p = 0.288$, 95% CI [-4.6, 15.5]), but there was a statistically significant increase at the palivizumab-focused intervention sites (increase of 19.2 percentage points, $p < 0.001$, 95% CI [9.5, 28.9]). The difference in change between study groups (5.5 vs. 19.2 percentage points) was significant ($p = 0.05$).

4.3 Reasons for Missed Palivizumab Doses

The proportion of doses missed in each season by study group and reason are shown in ► Table 4. There was a statistically significant change in missed doses attributed to office workflow issues. Compared to the second baseline season, the proportion of doses missed attributed to workflow issues significantly decreased 5.8 percentage points ($p < 0.001$, 95% CI [-2.6, -9.0]) at the palivizumab-focused intervention sites. At the comprehensive intervention sites there was a trend towards an increased proportion of doses missed due to workflow issues (increased 7.7 percentage points, $p = 0.092$, 95% CI [-1.2, 16.7]). The difference between study groups (-5.8 vs 7.7 percentage points) was significant ($p=0.005$).

There were two distinct categories of office workflow issues that resulted in missed doses of palivizumab:

1. failure to schedule appointments, and
2. missed opportunities to give doses to eligible children while they were in the office.

At the palivizumab-focused intervention sites, the rate for both of these failure modes decreased (improved) during the intervention season while the rate increased (worsened) for both failure modes among the comprehensive intervention sites.

Recognition of eligibility to receive palivizumab significantly improved in both study groups from the second baseline season to the intervention season. At the palivizumab-focused intervention sites the proportion of patients recognized as eligible improved 11.4 percentage points ($p=0.006$, 95% CI [3.3, 19.6]) and at the comprehensive intervention sites by 15.2 percentage points ($p<0.001$, 95% CI [8.1, 22.3]). There were no significant changes in the rate of problems occurring beyond the immediate control of the office (e.g. insurance denial, family no show and family refusal). Of the 356 children in this 3-year study, 17 (4.7%) missed at least one dose due to an insurance-related problem and 3 (0.8%) due to family refusal. Of 17 children with insurance problems, 7 were denied palivizumab for all or part of a season, 4 had delays in the approval process resulting in missed doses, 4 children had a gap in insurance coverage resulting in missed doses, and for 2 children out of pocket expenses (i.e. co-pays) exceeded the family's ability or willingness to pay.

5. Discussion

Supporting a quality improvement initiative with the introduction of CDS and workflow tools, we improved recognition of palivizumab eligibility and may have improved the rate of appropriate palivizumab administration across a large, diverse care network. Regardless of the type of decision support (palivizumab-focused vs. comprehensive), the improved recognition of eligible patients proved to be the principal driver for the improvement in the rate of palivizumab administration. Both the palivizumab-focused and the comprehensive decision support led to improvements in palivizumab administration at rates comparable or better to those of published CDS interventions, but this improvement was only statistically significant in the palivizumab-focused intervention group [25]. When evaluating the impact of decision support, the comprehensive CDS was less effective than the palivizumab-focused intervention at improving palivizumab administration rates.

5.1 Targeting Decision Support

We expected that practices receiving the comprehensive intervention would have similar or improved palivizumab administration rates compared to the palivizumab-focused intervention group. Specifically, we anticipated a reduction in missed opportunities during office visits through the use of electronic reminders to providers at the time of patient interaction. We instead found that sites receiving the palivizumab-focused intervention had better administration rates than the comprehensive intervention sites. The palivizumab-focused sites had significantly fewer missed doses due to office workflow issues (i.e. missed opportunities during office visits and failure to schedule visits for administration of doses). In contrast, the comprehensive intervention sites had a trend toward more missed doses due to office workflow issues.

Within our network, nurses have been historically responsible for managing palivizumab administration. The nurses took ownership of reminding clinicians verbally that palivizumab was available should an eligible child present for an office visit. The comprehensive intervention broadened the targeted audience for this decision support tool to include clinicians at the time of office visits. With the introduction of clinician-directed alerts at the comprehensive intervention sites, the nurses may have assumed that the electronic reminder was sufficient and their verbal reminder was no longer necessary. However, since the comprehensive intervention advised clinicians about multiple tasks relevant to the primary care of premature infants, clinicians may not have noticed the palivizumab reminder. Such information overload could have contributed to “alert fatigue” with the result being missed reminders and failures to administer doses of palivizumab [26, 27]. Alert fatigue and potentially undesired workflow changes due to decision support remain challenging problems and are worthy of further study.

5.2 Recognizing Eligible Patients

Prior examinations of the reasons for failure to complete the palivizumab series have investigated factors impacting compliance [12, 13]. However, in our study the most common reason why eligible patients did not complete the series was the failure to recognize the patient as eligible for palivizumab. Without an automated process to screen a practice’s entire patient panel for risk factors and qualifying diagnoses, the task of screening for eligible patients can be substantial. In the review by Frogel et al, home-based delivery programs were associated with increased compliance with palivizumab administration compared to office-based programs [12]. However, even in home-based interventions, the identification of eligible children may be difficult. Our decision support tool, with the ability to utilize existing EHR data to “flag” potentially eligible patients based on established eligibility guidelines, directly addressed this challenge to the administration of palivizumab.

One of the paradoxical findings in our study was the increase in office workflow issues such as failure to schedule appointments and missed opportunities during office visits within the comprehensive intervention group. It is possible that since more patients were recognized as eligible to initiate the series, there was an increased opportunity for other failure modes to appear. However, there was also improved eligibility recognition at the palivizumab-focused sites but a decrease in office workflow issues. As noted before, the new clinician-directed alerts in the comprehensive intervention may have also led to a diffusion of responsibility over these tasks, with clinicians and nurses possibly assuming the other would ensure these tasks were completed. Further study is required to better understand the causes of this paradoxical finding.

5.3 Insurance Considerations

Insurance issues, although present, were an uncommon reason for missed doses of palivizumab. In our chart reviews, insurance issues proved to be more complex than simply denial of the palivizumab series. Since palivizumab is considered a specialty medication and not an immunization, some insurance plans have co-payment requirements for members [28]. Our chart reviews revealed that two children had high out of pocket costs for palivizumab. Documentation in the charts suggested these financial considerations were barriers for these families and resulted in incomplete administration of the series.

5.4 Limitations

This study had several limitations. Due to the system wide quality improvement initiative to improve palivizumab administration rates, there was no opportunity to have a control group receiving no intervention. Also, although this study was randomized, due to the small number of practices, there may have been other unmeasured characteristics of the sites that affected the results (e.g. site leadership support for the project or availability of nurses with appropriate skill and time to manage palivizumab scheduling). Another limitation was that the intervention period was only one year. It is unknown whether the observed results would have been sustained over additional seasons.

In addition, this trial was performed within a single healthcare system using a single EHR, which may limit its generalizability. However this network does cover a diverse geographic region of urban and suburban practice and both academic and non-academic practice cultures are present. The EHR features we used for this project (patient lists, point of care alerts, and structured data capture) should be available in any EHR that meets Stage 2 meaningful use requirements [29]. However, challenges including the difficulty of sharing decision support tools developed in one setting and the need for local technical expertise to customize the EHR remain for information technology teams to achieve the same degree of integration of complex decision support and workflow tools into the EHR.

The guidelines for palivizumab administration have recently changed [11]. With the new guidelines, fewer children will be eligible to receive palivizumab than in prior seasons [30]. This will make it difficult to compare future palivizumab administration rates to prior years since the denominators will be different. We anticipate maintaining a high level of patient identification through CDS version updates, as compared to more traditional methods of knowledge dissemination [16].

6. Conclusions

A quality improvement initiative supported by CDS and workflow tools integrated in the EHR improved recognition of eligibility and may have increased palivizumab administration rates. The palivizumab-focused intervention performed significantly better than a comprehensive intervention, although both resulted in improvement in palivizumab administration rates. Reasons for this difference are likely attributable to a diffusion of responsibility in office workflow and information overload resulting from the comprehensive intervention. CDS implementers are advised to thoughtfully consider project scope to maximize the impact of their interventions.

7. Abbreviations

- ASTM – American Society for Testing and Materials
- CDS – Clinical decision support
- EHR – Electronic health record
- RSV – Respiratory syncytial virus

Clinical Relevance Statement

Passive immunization with palivizumab helps reduce emergency department visits and hospitalization rates due to respiratory syncytial virus among high-risk children, yet there are numerous barriers to receipt of the 5 dose series. Our study revealed that a clinical decision support tool embedded in an electronic health record system may improve palivizumab receipt. These tools were more effective at improving workflow when focused on palivizumab delivery alone as compared to a more comprehensive intervention for premature infants.

Conflict Of Interest

Dr. Grundmeier and Dr. Fiks are co-inventors of the Care Assistant decision support framework, which was used to implement portions of the intervention evaluated in this manuscript. No patent or licensing agreement exists for this technology and the invention has generated no revenue. As co-inventors of the Care Assistant, Dr. Grundmeier and Dr. Fiks may have a perceived conflict of interest. However, statisticians on the study team who have no conflicts of interest reviewed all study data and analyses.

Acknowledgements

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network of primary care physicians and their patients and families for their contributions to clinical research through the Pediatric Research Consortium at CHOP.

Human Subjects Protection

The Institutional Review Board at CHOP approved the study and waived the requirement for consent from individual children/families.

Eligibility	Status ^Δ	Last Dose	Next Dose	Distributor	RSV Comment
Does not meet AAP criteria for Palivizumab	Appeal Denied				
Does not meet AAP criteria for Palivizumab	Approved	Given - [REDACTED]	No appointment due [REDACTED] (ordered)	Acro Pharmacy	
gestational age 29 weeks	Approved	Given - [REDACTED]	No appointment due [REDACTED] (ordered)	Acro	authorization number [REDACTED] for questions 484-494-8217
gestational age 29 weeks	Approved	Given - [REDACTED]	No appointment due [REDACTED] (ordered)	acro	
congenital heart disease on medications	Approved	Given - [REDACTED]	None in range [REDACTED] (ordered)	acro	acro 484-494-8217
congenital heart disease on medications	Approved	Given - [REDACTED]	No appointment due [REDACTED] (ordered)	Aetna Specialty Pharmacy	866-782-2779 aetna specialty pharmacy
chronic lung disease on	Approved	Given - [REDACTED]	Scheduled [REDACTED]	aetna specialty	

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Fig. 1 Patient list tracking doses of palivizumab for all eligible patients in the practice.

Premie Assistant

Chronological Age: 8 months
 Corrected Age: 5 months

Gestational Age: 30 weeks
 Birth Weight: 1.899 kg

RSV and Synagis Patient is candidate for 5 dose(s) Palivizumab (Synagis)

Criteria: chronic lung disease on treatment; gestational age 30 weeks
[View AAP Policy Statement...](#)
[Run Chart Review...](#)

Will submit for approval?
 Insurance Provider
 Synagis Distributor

Initial Submission Date
 Will submit for appeal?

Initial Submission Response
 Appeal Submission Date

Appeal Submission Response

Doses Approved

Dose	1	2	3	4	5
Date Range:	11/1/11 - 11/10/11	11/29/11 - 12/4/11	12/29/11 - 1/8/12	1/28/12 - 2/7/12	2/27/12 - 3/8/12
Status:	Given	No appointment	No appointment	No appointment	No appointment
Date:	11/4/11				
Weight Estimate:		4.152 kg	4.603 kg	4.972 kg	5.265 kg
Order:	<input type="text" value="Received"/>	<input type="text" value="Ordered"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

Comments:

Fig. 2 A report with information needed for insurance paperwork

Premie Assistant		Chronological Age: 5 months Corrected Age: 2 months	Gestational Age: 28 weeks Birth Weight: 1.400 kg																		
Summary <table border="1"> <thead> <tr> <th>Issue</th> <th>Status</th> <th>Resources</th> </tr> </thead> <tbody> <tr> <td> Growth Nutrition </td> <td>Low weight Continue preterm formula or breast milk. No purees or cereal until 4-6 months corrected age (approximately in 5 weeks)</td> <td> Growth & Nutrition Calculator... </td> </tr> <tr> <td> Development ROP </td> <td>Not documented, use 2 month checklist today Complete vascularization AAP: Conclude screening if no retinopathy in zone 3 and no prior retinopathy documented in zone 1 or 2 (or as directed by ophthalmology)</td> <td></td> </tr> <tr> <td>BP</td> <td>Check blood pressure Jul 2012</td> <td></td> </tr> <tr> <td> RSV </td> <td>Eligible for 5 doses of Palivizumab: gestational age 28 weeks</td> <td> RSV and Synagis... </td> </tr> <tr> <td>NICU History</td> <td>Abstracted</td> <td> Birth HX (use HXPRETERM)... </td> </tr> </tbody> </table>				Issue	Status	Resources	Growth Nutrition	Low weight Continue preterm formula or breast milk. No purees or cereal until 4-6 months corrected age (approximately in 5 weeks)	Growth & Nutrition Calculator...	Development ROP	Not documented, use 2 month checklist today Complete vascularization AAP: Conclude screening if no retinopathy in zone 3 and no prior retinopathy documented in zone 1 or 2 (or as directed by ophthalmology)		BP	Check blood pressure Jul 2012		RSV	Eligible for 5 doses of Palivizumab: gestational age 28 weeks	RSV and Synagis...	NICU History	Abstracted	Birth HX (use HXPRETERM)...
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NICU History	Abstracted	Birth HX (use HXPRETERM)...																			
Premie Education Materials Premie Epic Smart Tools																					

Fig. 3 Premie Assistant tool for physicians with information about palivizumab eligibility and other preventive health issues for premature infants.

Fig. 4 Palivizumab doses given by season and study group. Error bars represent 95% confidence intervals.

Table 1 Description of child characteristics by palivizumab-focused versus comprehensive CDS sites. Note that some patients may have been eligible to receive 5 doses of palivizumab in more than one season.

	Palivizumab-Focused (N=194)	Comprehensive CDS (N=162)	Total (N=356)
Race*			
White	63 (33%)	44 (27%)	107 (30%)
Black or African American	109 (56%)	95 (59%)	204 (57%)
Asian or Pacific Islander	8 (4%)	4 (2%)	12 (3%)
Other or Unknown	14 (7%)	19 (12%)	33 (9%)
Ethnicity			
Hispanic or Latino	9 (5%)	7 (4%)	16 (4%)
Non-Hispanic	185 (95%)	155 (96%)	340 (96%)
Female	102 (53%)	77 (48%)	179 (50%)
Insurance payer†			
Public	130 (67%)	89 (55%)	219 (62%)
Private	61 (31%)	72 (44%)	133 (37%)
Self-pay	3 (2%)	1 (<1%)	4 (1%)
Gestational Age			
< 29 weeks	127 (65%)	99 (61%)	226 (64%)
29 – 31 weeks	60 (31%)	58 (36%)	118 (33%)
32 – 34 weeks	7 (4%)	5 (3%)	12 (3%)
Co-morbidity			
Chronic Lung Disease	56 (28%)	51 (29%)	107 (26%)
Cardiac Disease	16 (8%)	12 (7%)	28 (7%)
Age at season start‡			
2009–2010	63	51	114
0–11 months old	45 (71%)	41 (80%)	86 (75%)
12–23 months old	18 (29%)	10 (20%)	28 (25%)
2010–2011	63	52	115
0–11 months old	49 (78%)	33 (63%)	92 (79%)
12–23 months old	14 (22%)	19 (37%)	25 (21%)
2011–2012	74	72	146
0–11 months old	63 (85%)	54 (75%)	117 (80%)
12–23 months old	11 (15%)	18 (25%)	29 (20%)

*There were no children with multiple races.

†Compared to privately insured children, publicly insured children were more prevalent among the palivizumab-focused intervention sites ($p = 0.001$).

‡Each child may have been eligible for 5 doses of palivizumab in either 1 or 2 seasons.

Table 2 Description of child characteristics by RSV season. Note that some patients may have been eligible to receive 5 doses of palivizumab in more than one season.

	Children eligible for 5 doses palivizumab		
	2009–2010 (N=114)	2010–2011 (N=115)	2011–2012 (N=146)
Race+			
White	40 (35%)	37 (32%)	34 (23%)
Black or African American	62 (54%)	66 (57%)	87 (60%)
Asian or Pacific Islander	2 (2%)	5 (4%)	8 (5%)
Other or Unknown	10 (9%)	7 (6%)	17 (12%)
Ethnicity			
Hispanic or Latino	8 (7%)	3 (3%)	6 (4%)
Non-Hispanic	106 (93%)	112 (97%)	140 (96%)
Female	60 (53%)	56 (49%)	74 (51%)
Insurance payer			
Public	67 (59%)	75 (65%)	88 (60%)
Private	47 (41%)	40 (35%)	54 (37%)
Self-pay	0 (0%)	0 (0%)	4 (3%)
Gestational Age			
< 29 weeks	70 (61%)	71 (62%)	97 (66%)
29 – 31 weeks	39 (34%)	40 (35%)	44 (30%)
32 – 34 weeks	5 (4%)	4 (3%)	5 (3%)
Co-morbidity			
Chronic Lung Disease	37 (32%)	29 (25%)	41 (28%)
Cardiac Disease	4 (4%)	6 (5%)	18 (12%)

*There were no children with multiple races

Table 3 Proportion of doses administered to eligible children by season and intervention group.

Season	Palivizumab-Focused group	Comprehensive CDS group
2009–10	68.4% [50.6, 86.2]	71.9% [66.7, 77.1]
2010–11	65.5% [53.4, 77.6]	62.4% [55.8, 69.0]
2011–12*	84.7% [77.3, 92.1]	67.9% [60.9, 74.8]

*Intervention season

Table 4 Proportion of doses not administered to eligible children grouped by reason.

Season	Palivizumab-focused group	Comprehensive CDS group
Doses not given because practice did not recognize that the child was eligible for palivizumab		
2009–10	18.0% [3.9, 32.1]	5.8% [0.0, 12.1]
2010–11	12.8% [3.1, 22.6]	17.8% [8.9, 26.8]
2011–12*	1.4% [0.0, 3.0]	2.6% [0.0, 5.5]
Doses not given due to office workflow issues (failure to schedule appointments, missed opportunity in office)		
2009–10	8.0% [3.3, 12.7]	10.7% [6.1, 15.2]
2010–11	10.4% [4.7, 16.1]	11.5% [6.8, 16.3]
2011–12*	4.6% [1.8, 7.4]	19.2% [14.2, 24.3]
Doses not given due to reasons external to the practice (family refusal, no show, or insurance denial)		
2009–10	5.5% [1.7, 9.4]	11.7% [6.6, 16.8]
2010–11	11.2% [5.3, 17.2]	8.3% [4.9, 11.7]
2011–12*	9.3% [4.3, 14.3]	10.3% [6.6, 14.0]

*Intervention season

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