Development and Impact of a Computerized Pediatric Antiinfective Decision Support Program

Charles J. Mullett, MD, PhD*‡; R. Scott Evans, PhD*§; John C. Christenson, MD‡; and J. Michael Dean, MD, MBA‡

ABSTRACT. Objective. Computerized medical decision support tools have been shown to improve the quality of care and have been cited by the Institute of Medicine as one method to reduce pharmaceutical errors. We evaluated the impact of an antiinfective decision support tool in a pediatric intensive care unit (PICU).

Methods. We enhanced an existing adult antiinfective management tool by adding and changing medical logic to make it appropriate for pediatric patients. Process and outcomes measures were monitored prospectively during a 6-month control and a 6-month intervention period. Mandatory use of the decision support tool was initiated for all antiinfective orders in a 26-bed PICU during the intervention period. Clinician opinions of the decision support tool were surveyed via questionnaire.

Results. The rate of pharmacy interventions for erroneous drug orders declined by 59%. The rate of antiinfective subtherapeutic patient days decreased by 36%, and the rate of excessive-dose days declined by 28%. The number of orders placed per antiinfective course decreased 11.5%, and the robust estimate of the antiinfective costs per patient decreased 9%. The type of antiinfective agents, decision support systems, drug therapy, medication errors, child, infant.

Errors in prescription, distribution, and administration of pharmaceutical therapy are a significant cause of injury to hospitalized patients. Almost 2% of admissions in an adult, tertiary care university facility experienced preventable adverse drug events, costing an average of $4700 per episode.1 Other investigators have published medication prescription error rates of 3.99 errors per 1000 orders in an adult hospital.2 Factors associated with errors included a decline in renal or hepatic function (13.9%); a history of allergy to the same medication class (12.1%); the use of the wrong drug name, dosage form, or abbreviation (11.4%); incorrect dosage calculation (11.1%); and atypical or unusual dosage frequency (10.8%). Studies in children show similar findings.3,4 Folli et al3 found that pediatric patients who are younger than 2 years or require treatment in a pediatric intensive care unit (PICU) were at the greatest risk. In their study, dosage errors were the most common medication error, with overdosage exceeding underdosage in frequency. Antibiotics were the most common class of pharmacotherapeutics with errant orders.

Technological solutions have been shown to have an impact on error rates. Computerized physician order entry systems for prescription of medications enable the presentation of standard dosages, automated dosage calculations, and presentation of clinically important drug–drug, drug–allergy, and drug–laboratory interactions at the time of the physician’s decisions.5–7 In addition, these systems eliminate the inherent problems associated with handwriting interpretations and retranscription of orders. Not surprising, the rate of serious medication errors dropped 55% in one analysis of the impact of the implementation of a physician order entry system in a large tertiary care center.8 Crude estimates by those authors suggested that the net savings to the hospital through fewer adverse events and their sequelae amount to $5 million to $10 million per year.

Clinicians must strike a balance when choosing the initial antimicrobial care. Appropriate empiric antiinfective therapy improves outcomes, whereas unnecessarily broad therapy puts the patient at risk for the development of resistant organisms, adverse drug events, and increased cost. Investigators have sought to develop computer-based tools to facilitate the clinician’s decision-making process. The first work in this field was by Shortliffe and colleagues9–11 with the MYCIN rule-based infectious

ABBREVIATIONS. PICU, pediatric intensive care unit; IHC, Intermountain Health Care; PCMC, Primary Children’s Medical Center; HELP, Health Evaluations through Logical Processing; STICU, shock-trauma intensive care unit; LOS, length of stay.

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used a statistical approach to publish a monthly list of most likely organisms and effective therapies by culture site. Evans et al at Intermountain Health Care (IHC) developed the first tool that automated the data-gathering process and calculated the most probable effective therapy at the time the physician was choosing the antibiotic. Later enhancements to this tool included drug dosage selection assistance, renal function and microbiology results monitoring, and reviews of antibiotic costs and bacterial sensitivity patterns. In adult patients, this computerized antiinfective decision support program reduced antibiotic/bacterial susceptibility mismatches, orders for drugs to which the patient had reported allergies, and alerts of excessive dosage of antiinfective agents. Benefits to the patients were noted in fewer adverse drug reactions, fewer total antiinfective doses, and lower antiinfective costs for the hospital. Other, more recent empiric antibiotic decision support systems have been associated with potential improvements in clinical care. Given this experience with an adult decision support tool, we anticipated a similar benefit in pediatrics. We hypothesized that a clinical decision support system designed to account for the therapeutic indication, the age and weight of the patient, the renal function, and the level of prematurity would improve antiinfective choices and dosage selections, reduce the rate of adverse drug events, and reduce the cost of antiinfectives used in the care of critically ill infants and children. This article describes the development and clinical evaluation of a pediatric antiinfective decision support tool founded on the adult antiinfective management program developed at IHC.

**METHODS**

**Setting**

Primary Children’s Medical Center (PCMC) is a 232-bed facility set on the University of Utah medical campus and owned and operated by IHC. It is the primary pediatric teaching facility for the University of Utah School of Medicine. The hospital serves as the tertiary referral center for all of Utah and significant portions of Nevada, Arizona, Montana, Wyoming, and Idaho. PCMC houses a PICU comprising 26 beds and averaging 1700 admissions per year of a broad array of critically ill medical and surgical patients. Pediatric critical care specialists, working together with critical care fellows-in-training, pediatric residents, and nurse practitioners, staff the unit. This team is responsible primarily for the medical patients and co-manages the surgical admissions.

Bedside computer terminals that run the Health Evaluations through Logical Processing (HELP) hospital information system facilitate patient care. HELP is a fully integrated hospital information system that provides data collection and reporting for a broad range of clinical areas, including laboratory results, pharmacy, radiology, and pathology. The PICU physicians and nurse practitioners use the HELP system primarily for laboratory results review and the generation of a morning summary report of patient vital signs, labs, pharmacology, radiology, and ventilator data. Before the implementation of the pediatric antiinfective decision support tool, all patient care orders from the physicians were handwritten. Antibiotic and other medication orders typically were interpreted by the clerk and rewritten by a pharmacist, who entered the order via the keyboard into the HELP system’s pharmacy module.

**Study Design**

A study to measure the impact of the pediatric antiinfectives decision support tool was planned, using 6-month pre- versus postimplementation comparison periods. With an average of 1700 admissions per year and an estimation that 75% would be treated with antibiotics, we anticipated capturing more than 600 patients in each study period. The time periods chosen for the study placed approximately one half of the summer season (with many bronchitis patients) and one half of the winter season (with many bronchitis patients) in each phase of the evaluation. The institutional review boards of the University of Utah and PCMC approved the study protocol.

For the PICU team of physicians and nurse practitioners, mandatory use of the pediatric antiinfective management tool for ordering antiinfectives was initiated on January 22, 1999. All pediatric residents, subspecialties (who are obligatory, clinicians chose whether to accept its recommendations on antiinfective agents and/or doses. During the last week of each 4-week resident rotation, resident physicians were surveyed using a questionnaire composed of 5-point Likert-type scales. The PICU pediatric nurse practitioners were surveyed once, at the end of the 6-month experimental period.

**Analysis**

The pharmacy staff monitored and recorded adverse drug events and kept a log of their interventions on drugs and drug dosages. A computer alerting program reported mismatches of bacterial culture sensitivities and patient antibiotic therapy. These mismatches were recorded and investigated as appropriate. A computer program was developed to review the PCMC patient
files comparing all administered antinfective agents to published therapeutic ranges with modifications for age and renal function. This program identified all doses that fell outside the therapeutic ranges and generated a file that contained subtherapeutic and excessive-dosage risk days.

Statistical Methods

Study data were stored and manipulated in Microsoft Access (Microsoft Corp, Redmond, WA). Between-group comparisons were performed using Fisher’s exact test for equality of proportions, χ² test for independence, and 2-tailed t tests for comparisons of means. During the latter analyses (t tests), consideration was given to logarithmic transformations and the use of Tukey’s biweight estimator for skewed variances when appropriate for non-normally distributed data. All χ² analyses were performed using Microsoft Excel. The regression analyses were performed using Statit Custom QC (Statware Inc, Corvallis, OR). Statistical significance levels were set at P values of .05 a priori.

RESULTS

During the 12-month study period, the PICU admitted 1758 patients: 809 patients during the preintervention period and 949 during the intervention period. The intervention group was more likely to be treated with antimicrobials while in the PICU (66.5% vs 60.2%; P < .05), but the rate of antimicrobial use during the total hospital stay did not differ significantly.

Additional comparisons are limited to “study patients,” defined as those patients with antinfectives ordered while hospitalized in the intensive care unit during the 2 periods. The intervention group was significantly younger (Table 1). However, the 2 groups were similar with respect to gender, PICU LOS, All Patient Refined Severity of Illness, and All Patient Refined Risk of Mortality, and percentage mortality, and total hospital costs.

Per-patient antinfective use measurements also were similar between the 2 groups, despite the implementation of the new management tool (Table 2). Specifically, there were no differences in the PICU or total hospital count of antinfectives or antinfective doses used per patient. There also was no difference in the PICU or total hospital costs of antinfectives.

However, the number of orders placed per antinfective course decreased 11.5% from an average of 1.56 to 1.38 orders/patient-antinfective (P < .01). In addition, application of Tukey’s biweight estimator, which downweights extreme values in non-normal distributions, revealed an underlying 9% decrease in the costs of antinfectives used for the average intervention group PICU patient (Table 2). Logarithmic transformations of non-normal data and application of Tukey’s biweight estimator did not change the interpretations of the other baseline population or antinfective use measurements between the 2 groups. Total antinfective use, by a comparison of the count of patients treated with each antinfective, also was similar between the 2 groups by χ² analysis.

Therapeutic mismatches between pathogens cultured in the microbiology laboratory and the antimicrobials being used to treat the patients were assessed by a time-driven computer alerting program at 1:00 PM on the day of published sensitivities. There was no difference in the incidence of mismatches between the 2 groups. Only 1 event was noted during the control period: a Staphylococcus epidermidis blood culture that initially was perceived as a contaminant and therefore was not being treated. During the intervention period, only 1 event was noted as well: an Enterococcus species urinary tract infection that was being treated with but ultimately found to be resistant to amoxicillin.

The total number of adverse drug reactions recorded in the PICU for the 12-month study period was 119, with 24 of those secondary to antinfectives. Twelve events were recorded in each of the 2 study periods. A breakdown of the reactions into the categories of mild (requiring no therapy change), moderate (requiring a change in therapy), and severe (potentially life-threatening) found no significant difference. In each group, only 1 of the 12 potentially was preventable secondary to known allergic sensitivities. During the intervention period, the potentially preventative allergic reaction occurred when a surgery resident, not using the antinfectives man-

### TABLE 1. Population Statistics for Patients With a PICU Antiinfective Order

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention (±SEM)</th>
<th>Intervention (±SEM)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>41.5</td>
<td>43.5</td>
<td>NS*</td>
</tr>
<tr>
<td>Age (y)</td>
<td>6.2 (±0.302)</td>
<td>5.3 (±0.244)</td>
<td>P &lt; .05†</td>
</tr>
<tr>
<td>PICU LOS (d)</td>
<td>4.93 (±0.490)</td>
<td>4.90 (±0.313)</td>
<td>NS‡</td>
</tr>
<tr>
<td>Hospital LOS (d)</td>
<td>10.76 (±0.778)</td>
<td>10.76 (±0.521)</td>
<td>NS‡</td>
</tr>
<tr>
<td>APR-DRG Severity of Illness (count)</td>
<td>1:98</td>
<td>1:120</td>
<td>NS‡</td>
</tr>
<tr>
<td></td>
<td>2:128</td>
<td>2:153</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3:142</td>
<td>3:177</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4:124</td>
<td>4:178</td>
<td></td>
</tr>
<tr>
<td>APR-DRG Risk of Mortality (count)</td>
<td>1:228</td>
<td>1:280</td>
<td>NS‡</td>
</tr>
<tr>
<td></td>
<td>2:84</td>
<td>2:135</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3:119</td>
<td>3:139</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4:56</td>
<td>4:74</td>
<td></td>
</tr>
<tr>
<td>Mortality (count)</td>
<td>18</td>
<td>20</td>
<td>NS*</td>
</tr>
<tr>
<td>Hospital costs (1999 dollars)</td>
<td>$28 257.67 (±2375.66)</td>
<td>$25 032.11 (±1210.70)</td>
<td>NS‡</td>
</tr>
</tbody>
</table>

APR-DRG indicates All Patient Refined–Diagnosis Related Groups; SEM, standard error of the mean; NS, not significant.
* Fisher’s exact test for equality of proportions.
† Two-tailed independent t test.
‡ χ² test.
management program, ordered a cephalosporin on a PICU patient who was known to be allergic to penicillins. (Note: Unlike pediatric residents in the PICU, the surgery residents were not involved in the study and were not required to use the pediatric antiinfectives management program.) Had the decision support tool been used, it would have alerted the physician to the allergy history.

The pharmacists in the PICU serve as a human “safety net” for ordered pharmaceuticals, making interventions on erroneous drug doses and other therapeutic improvement opportunities. In this capacity, they routinely keep a log of their interventions on the drugs ordered by the clinicians. During the study period, the interventions for all pharmaceuticals numbered approximately 1800, with antiinfectives comprising approximately 30%. Analysis of patient antiinfective doses compared with published minimum and maximum recommendations for age, weight, and renal function of the pediatric patient. Days of antiinfective therapy that fell outside the minimum and maximum recommendations were called subtherapeutic and excessive-dosage risk days. The combined effect is a 32% decrease in the rate of subtherapeutic risk days was found for the intervention group when compared with the control group (Table 3). Likewise, a significant 28% decrease was noted in the excessive-dosage risk days. The combined effect is a 32% decrease in the rate of antiinfective days that fall outside published recommended parameters.

Two post hoc analyses were performed to answer questions raised by the initial analyses. Was the younger age of the intervention patients responsible for the 5% increase in antimicrobial usage? The answer seems to be “no.” Multiple linear regression showed that age did not explain PICU antiinfective usage variability either alone or when controlled for study group. The second question was whether the decrease in PICU antiinfective costs found when analyzed using Tukey’s biweight estimator also was secondary to the younger age and presumably size of the intervention patients. Again, multiple linear regression did not find age to be a significant predictor of PICU antiinfective costs when controlled by study group or by the combination of study group, severity of illness, and risk of mortality.

**DISCUSSION**

This study found that implementation of computerized antiinfective decision support, provided at the time antiinfectives are ordered, increased the likelihood that the dose was on target for the given age, weight, and renal function of the pediatric patient. The tool provided support to the clinician in a num-

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**TABLE 2. Average Per-Patient Antiinfective Use Measurements**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention (±SEM)</th>
<th>Intervention (±SEM)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total antiinfective costs ($)</td>
<td>274.79 (±28.57)</td>
<td>289.60 (±23.47)</td>
<td>NS*</td>
</tr>
<tr>
<td>Total number of antiinfectives used</td>
<td>2.18 (±0.066)</td>
<td>2.22 (±0.063)</td>
<td>NS*</td>
</tr>
<tr>
<td>Total doses used</td>
<td>19.8 (±1.35)</td>
<td>22.0 (±1.33)</td>
<td>NS*</td>
</tr>
<tr>
<td>PICU antiinfective costs ($)</td>
<td>177.03 (±18.02)</td>
<td>183.53 (±14.75)</td>
<td>NS*</td>
</tr>
<tr>
<td>Robust estimate PICU antiinfective costs ($)</td>
<td>86.60 (±2.98)</td>
<td>78.43 (±2.29)</td>
<td>$P &lt; .05$†</td>
</tr>
<tr>
<td>PICU antiinfective doses</td>
<td>12.8 (±0.985)</td>
<td>13.4 (±0.777)</td>
<td>NS*</td>
</tr>
<tr>
<td>PICU number of antiinfectives</td>
<td>1.85 (±0.056)</td>
<td>1.97 (0.052)</td>
<td>NS*</td>
</tr>
<tr>
<td>PICU antiinfective orders per patient-antiinfective course</td>
<td>1.56 (±0.060)</td>
<td>1.38 (±0.032)</td>
<td>$P &lt; .01$*</td>
</tr>
</tbody>
</table>

SEM indicates standard error of the mean; NS, not significant.
* Two-tailed independent t test.
† Two-tailed modified t test using Tukey’s biweight estimator to downweight extreme observations.
outside recommended therapeutic ranges. The decreased number of days of therapy that fall pharmacy interventions for erroneous doses and also nonissue. These mechanisms explain the decrease in matic errors. Order legibility also was rendered a matically daily, and suggested doses were calculated without arith-

matically and prematurity considerations were factored auto-

matically, and doses were calculated without arithmetic errors. Order legibility also was rendered a nonissue. These mechanisms explain the decrease in pharmacy interventions for erroneous doses and also the decreased number of days of therapy that fall outside recommended therapeutic ranges.

The last step in the system’s antiinfective recommendations algorithm is to consider costs. The antiinfective management program recommends the less expensive agent when 2 or more drugs are found to be therapeutically equal. We therefore anticipated a cost benefit, as was seen in the adult study. In this pediatric study, the average cost of antiinfectives was no different between the 2 groups. However, application of Tukey’s biweight estimator, which down-weights extreme observations in non-normal distributions, identified a 9% decrease in the robust estimate of the cost of antiinfectives used in the intervention group. Therefore, a longer study may have documented cost savings using more conventional analytical methods. Moreover, given that one of the tool’s beneficial effects is to increase the doses administered when clinically indicated and 1 of its documented effects is to minimize the number of

TABLE 3. Subtherapeutic and Excessive-Dosage Risk Days

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention (±SEM)</th>
<th>Intervention (±SEM)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtherapeutic antiinfective days per 100 patient days</td>
<td>7.350 (±0.610)</td>
<td>4.702 (±0.441)</td>
<td>P &lt; .001*</td>
</tr>
<tr>
<td>Excessive-dosage antiinfective days per 100 patient days</td>
<td>8.454 (±0.460)</td>
<td>6.063 (±0.490)</td>
<td>P &lt; .001*</td>
</tr>
<tr>
<td>Total risk days per 100 patient days</td>
<td>15.80 (±0.734)</td>
<td>10.766 (±0.733)</td>
<td>P &lt; .0001*</td>
</tr>
</tbody>
</table>

SEM indicates standard error of the mean.

* Two-tailed independent t test.

TABLE 4. User Survey Results

<table>
<thead>
<tr>
<th>Question Topic</th>
<th>% Positive Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved overall antibiotic choices</td>
<td>81</td>
</tr>
<tr>
<td>Increased awareness of renal function</td>
<td>79</td>
</tr>
<tr>
<td>Beneficial dosage calculation assistance</td>
<td>96</td>
</tr>
<tr>
<td>Associated with fewer adverse drug events</td>
<td>89</td>
</tr>
<tr>
<td>Improved quality of care</td>
<td>81</td>
</tr>
</tbody>
</table>

TABLE 5. Comparison of Antiinfective Management Program Impact in Adult and Pediatric Studies

<table>
<thead>
<tr>
<th>Measurement</th>
<th>PICU Impact</th>
<th>STICU Impact</th>
<th>Baseline Rates Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptibility-mismatch alerts</td>
<td>No change</td>
<td>Large reduction</td>
<td>18/100 admissions in STICU vs 0.2/100 admissions in PICU</td>
</tr>
<tr>
<td>Drug allergy alerts</td>
<td>No change</td>
<td>Large reduction</td>
<td>12/100 admissions in STICU vs 0.4/100 admissions in PICU</td>
</tr>
<tr>
<td>Excessive days of antiinfective dose</td>
<td>Reduction</td>
<td>Reduction</td>
<td>2.4/100 admission in both STICU and PICU</td>
</tr>
<tr>
<td>Adverse drug events attributable to antiinfectives</td>
<td>No change</td>
<td>Large reduction</td>
<td></td>
</tr>
<tr>
<td>Pharmacists’ interventions</td>
<td>Large reduction</td>
<td>Not measured</td>
<td>$412/patient STICU vs $177/patient in PICU</td>
</tr>
<tr>
<td>Antiinfective costs</td>
<td>9% reduction</td>
<td>20% reduction</td>
<td></td>
</tr>
<tr>
<td>Length of stay</td>
<td>No change</td>
<td>No change</td>
<td>6.3 d in STICU vs 4.9 d in PICU</td>
</tr>
<tr>
<td>Mortality</td>
<td>No change</td>
<td>No change</td>
<td>22% in STICU vs 3.7% in PICU</td>
</tr>
</tbody>
</table>
interesting that the baseline rate of events per 100 admissions was similar in both units. One would surmise that fewer of the events in children are preventable, as they are less likely to be secondary to failing drug metabolism due to hepatic or renal dysfunction. The study data support this notion as only 1 of the 12 pediatric events at baseline could be judged as preventable by retrospective evaluation and none of these events could be attributed to failed organs or otherwise poor drug metabolism.

A 20% reduction in the costs of antiinfectives used at baseline was found in the study, whereas the pediatric drug costs are, at best, 9% improved. The baseline analysis shows that antiinfective costs averaged $412 (1995 dollars) per patient in the adult study and only $177 (1999 dollars) per patient in the pediatric evaluation. Once again, it should be noted that there was less opportunity for improvement in the pediatric case. Last, although the measures of severity of illness used in the 2 studies are different and are not comparable directly, it is instructive to note the 5-fold difference in incidence of death between the 2 units. The adult patients were far more likely to have terminal disease. One may conclude that the adults have more end-organ dysfunction affecting their responses to and internal metabolism of the antiinfective therapy used in the study. Therefore, it should not be a surprise that the impact of the antiinfective management program differs between the 2 units in the process and outcome measures evaluated.

With the improvements in the rate of pharmacy interventions and the number of days outside therapeutic ranges, one could anticipate a patient benefit in outcomes. Unfortunately, we were not able to document this, given the insensitivity of our patient outcome measures: adverse drug events, LOS, and mortality. However, one can conclude that although the incidence of adverse sequelae from medical errors is low, it is not 0, and minimization of outright errors and improvements in therapeutic dosing targets should affect both adverse events and the quality of care, given enough time. It is through considerations such as these that a majority of pediatric residents and nurse practitioners reported that they believed that the use of this clinical decision support tool should have a beneficial impact on adverse drug events and the quality of care. This is consistent with the adage that humans and computers working in tandem are better than either one alone.

The findings of this study are likely to be a conservative assessment of the benefit that would be anticipated from wide-scale implementation of this computerized decision support tool throughout the children’s hospital. A significant portion of the antimicrobial therapy measured in this study was ordered without the use of the tool—either by pediatric residents on the floor before transfer of the patient to the PICU or by surgery and surgery subspecialty residents transferring patients from either the floor or the operating room. Therefore, once these groups become users of the system, the doses ordered also would have the benefit of the elimination of calculation errors, plus the careful consideration of the indication, age, weight, and renal function rendered by the antiinfective management program.

After the completion of the study, by joint decision of the members of the medical, pharmacy, and nursing staffs, use of the pediatric antiinfectives management program remained mandatory for ordering antiinfectives within the PICU. Usage also spread to other areas of the children’s hospital. Although the pediatric antiinfectives management program is not transferrable without the HELP hospital information system, the implementation of a clinical computerized physician order entry system combined with a comprehensive system of antiinfective decision support rules likely would provide similar benefit in other pediatric institutions.

CONCLUSION

Implementation of a pediatric antiinfective decision support tool had a positive impact on the antiinfective therapeutic milieu of a PICU through better dosage selection, as documented by fewer pharmacy interventions on antiinfective orders and fewer antiinfective subtherapeutic and excessive-dosage risk days. These findings are supported by the survey of users who reported that use of the tool would result in fewer adverse drug events and improved quality of care.

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