A Two-Compartment Mixed-Effects Gamma Regression Model for Quantifying Between-Unit Variability in Length of Stay among Children Admitted to Intensive Care

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Objective. To quantify between-unit variability in mean length of stay (LoS) between intensive care units (ICUs) after adjusting for differences in case mix using a method that does not require arbitrary trimming of data.

Setting. An analysis of registry data from pediatric ICUs (PICUs) in Australia and New Zealand.

Study Design. The relationships between patient LoS and associated patient factors were modeled as a log-linear function of the covariates using two gamma distributions. The predicted distribution is estimated as a weighted average of the two distributions where the relative weighting is conditional on the patient's elective status.

Data Collection. Data for 12,763 admissions submitted to the Australian and New Zealand Paediatric Intensive Care Registry from the eight dedicated PICUs in Australia and New Zealand in 2007 and 2008.

Principal Findings. The two distributions of the mixture model accurately described the distribution of short- and long-stay patients in ICUs. After adjusting for patient case mix, several sites had a statistically significant effect on patient LoS.

Conclusion. The two-compartment model characterizes ICU LoS for short- and long-stay patients more effectively than a single-compartment model. There is significant site-level variation in the LoS among children admitted to ICUs in Australia and New Zealand. Differences in the site-level variation between short- and long-stay patients indicate differences in discharge practice.

Key Words. Quality indicators, pediatrics, length of stay, intensive care, risk adjustment

Previous research has shown that there is significant variation of mean patient length of stay (LoS) among intensive care units (ICUs). Robust methods for measuring site-level variation in LoS are desirable because LoS is commonly used as a marker of resource use in ICUs (Rothen and Takala 2008). Prolonged LoS in ICUs has important implications for unit efficiency and may also act as an indicator of quality of care (Straney et al. 2010a). Poor quality of care may result in infections and other complications that are associated with prolonged stay in an ICU. Conversely, effective care should lead to more rapid diagnosis, treatment, and recovery to the point of discharge.

A method for quantifying unit-level variation in mean ICU stay among pediatric ICUs (PICUs) using random effects has been previously described (Straney et al. 2010a). Patients staying in ICUs >28 days were excluded from the analysis and therefore not predicted by the model. While patients staying >28 days comprise a small proportion of the admissions, they comprise a significant proportion of the total care days provided and thus have important implications for efficiency of resource use (Marcin et al. 2001; Carmeli and Bursztein 2008).

Compartmental or mixture models have been shown to be useful in modeling LoS (Lee et al. 2007). These models use two or more distributions to model ICU LoS, with assignment to each distribution being probabilistically inferred from the data. Given the typically heavy right skew of LoS data, previous studies have often trimmed the data at arbitrary, although potentially clinically meaningful, cut points (Ruttimann and Pollack 1996; Marik and Hedman 2000; Straney et al. 2010a). Using this approach, a significant number of the total care days may be excluded from the analysis. A possible advantage of compartmental models is that two distributions may be used to describe the short- and long-stay components of the LoS distribution, providing a better fit to the long tail of the distribution and avoiding the need to trim the data arbitrarily.

The objective of this paper is to quantify between-ICU variability in mean LoS after adjusting for differences in case mix, using a method that negates the need to trim the data at an arbitrary cut-point. In doing so, we

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describe a two-compartment gamma mixed-effects model that provides a better fit than a single-compartment model and that may help to elucidate differences in ICU efficiency, discharge practices, and quality of care.

METHODS

The Data

The Australian and New Zealand Paediatric Intensive Care (ANZPIC) Registry collects data from the eight dedicated PICUs in Australia and New Zealand and pediatric data from multiple general ICUs that accept pediatric admissions. All data are subjected to quality checks before being approved as cleaned and uploaded into the registry. To improve data integrity further, and to reduce inter-rater discrepancy, ICUs have periodic external auditing of a random selection of source records, and data collectors participate in training sessions provided by the registry. Data from the general ICUs were excluded due to small sample sizes. The mean number of admissions in the PICUs ($n = 8$) was 1,595 (ranging 989–2,237). Among excluded general ICUs ($n = 15$), the mean number of admissions was 153 (ranging 2–518). The data in this study were collected in 2007 and 2008, providing a total of 16 institution years of data.

Inclusion Criteria

Cleaned data from all eight Australian and New Zealand PICUs participating in the Registry were included in this analysis. For inclusion in the study, patients must have been aged less than 16 years at time of admission.

Mean LoS in the ICU will be confounded by patients who die. Given short LoS is considered a marker of good efficiency, patients who die quickly within the ICU may contribute to a spuriously good estimate of efficiency. Patients who die in the ICU represent a distinct population that warrant separate investigation and modeling approaches (Straney et al. 2010a). For these reasons, patients who died in the ICU were excluded from this study.

Patients with a LoS less than 2 hours were excluded because it was considered that these did not represent true ICU stays ($n = 123$), and it is unlikely that their outcomes would be reflective of the quality or practice of care in ICU. In addition, those patients who were recorded as still in ICU or who were transferred to another ICU were excluded from this analysis as their LoS could not be reliably quantified ($n = 363$).

Variable Selection

The model covariates are described in Table 1. Univariate analyses were performed to identify risk factors associated with LoS, and risk factors with an associated p -value $< .2$ were included in the multivariate analyses. With the exception of physiologic measures, only variables present in at least 90 percent of patients were considered for inclusion in the model.

The patients' principal diagnosis at admission was assigned using the ANZPIC Registry diagnostic coding, which has been previously described (Slater, Shann, and McEniery 2003). The large number of unique diagnoses meant that many diagnoses often had small patient

Table 1: Description of Covariates in the Australian and New Zealand Paediatric Intensive Care Registry

<i>Variable</i>	<i>Variable Description</i>	<i>Variable Type</i>	<i>Missing Values (%)</i>
ICU length of stay	Patient length of stay in ICU measured in days	Continuous	0 (0.0)
Respiratory support in the first hour	Mechanical respiratory support given within the first hour of admission(0/1; no/yes)	Binary	0 (0.0)
Elective admission	Was the admission elective? (0/1; no/yes)	Binary	0 (0.0)
Retrieval	Patient required specialist retrieval team? (0/1; no/yes)	Binary	43 (0.1)
Systolic blood pressure	Systolic blood pressure at admission (mmHg)	Continuous	4,025 (31.5)
FiO ₂	Fraction of inspired oxygen	Continuous	7,798 (61.1)
PaO ₂	Partial arterial oxygen	Continuous	6,704 (52.5)
Age	Age in years at admission (e.g., 18-month old has age = 1.5)	Continuous	0 (0.0)
Pupils	Fixed and dilated pupils at admission? (0/1; no/yes)	Binary	0 (0.0)
Principal diagnosis	ANZPIC diagnostic coding	Categorical	5 (<0.1)
Recovery	Recovery from a procedure? (0) no; (1) Yes, recovery from a bypass procedure; (2) Yes, recovery from other procedure	Categorical	0 (0.0)
ICU admission source	(1) Direct ICU admission; (2) Operating theater or recovery; (3) Emergency department; (4) Ward; (5) other ICU or NICU (same hospital)	Categorical	0 (0.0)
Previous admission	(0) No; (1) Yes, readmitted <48 hours postdischarge; (2) Yes, readmitted >48 hours postdischarge	Categorical	43 (0.1)

numbers. This necessitated the creation of risk groupings based on a comparison of the mean LoS for each principal diagnosis with the overall mean. Those conditions with a mean LoS that was significantly higher or lower (at the 95 percent level) than the overall mean were assessed for inclusion in the multivariate model. Diagnostic groupings were formed by grouping the significant diagnoses into four categories based on the ratio of the condition-specific mean LoS to the overall mean LoS. Groupings were assigned using cut points at the ratios of ≤ 0.33 , ≤ 0.67 , ≥ 1.5 , and ≥ 3 . Diagnostic codes with a ratio of between 0.67 and 1.5 were assigned to the central reference group. Diagnostic codes that had a mean LoS that was not significantly different from the mean were assigned to the central reference group regardless of the ratios of mean LoS.

The $\text{FiO}_2/\text{PaO}_2$ ratio was modeled as a covariate in the model; in cases where either value was missing, the ratio was imputed as zero. Missing systolic blood pressure values were assumed to be normal ($\text{SBP} = 120$). This “normal” imputation method is consistent with the manner described in the Pediatric Index of Mortality (PIM) (Slater, Shann, and Pearson 2003). In addition, we tested the sensitivity of our estimates of site-level variation using mean imputation for missing biological predictors.

Model Development

The data were randomly split into two subsets to be used for model building (2/3) and validation (1/3). The final model used the combined dataset (12,763 observations).

The gamma distribution is a flexible continuous probability distribution that has been shown to be effective in modeling LoS (Marazzi et al. 1998; Lee, Ng, and Yau 2001; Lee et al. 2007). The Gamma distribution is a two-parameter probability distribution governed by a shape and scale parameter (Jambunathan 1954). For a gamma distributed variable with scale θ and shape σ , the mean is $\sigma\theta$, the variance is $\sigma\theta^2$, and the probability density function is given by

$$f(x) = \frac{x^{\sigma-1} e^{-x/\theta}}{\theta^\sigma \Gamma(\sigma)} \quad (1)$$

The probability density function of ICU LoS is assumed to be a two-component gamma mixture where y_{jk} represent the LoS for the j th patient in the k th ICU. In the current study, the relationships between patient LoS and

associated risk factors were modeled using a maximum likelihood method. The data were described as a log-linear function of two gamma distributions where the proportion of children assigned to either distribution was inferred from the data and also whether the admission to the ICU was elective:

$$f(y_{jk}) = pf_1(y_{jk}) + (1 - p)f_2(y_{jk}) \quad (2)$$

and the probability (p) (or weighting of the first distribution) is modeled as a logistic function the patient's elective status (χ_e) such that

$$p = e^{\theta_e} / 1 + e^{\theta_e} \quad (3)$$

and

$$\theta_e = \rho_0 + \rho_1(\chi_e) \quad (4)$$

To quantify between-institution variation, random effects (u) for each site were incorporated into each function of the model, where i represents the i th component and n represents the n th covariate. The random effect apportions residual variation attributable to the site after accounting for patient-level factors.

$$\log(\mu_{ijk}) = \beta_{0i} + \dots + \beta_{in}x_{jkm} + u_{ik} \quad (5)$$

All potential variables were included in the saturated predictive model. The complete data (including building and validation subsets) were used for the final model. Complete-case analysis used 12,763 admissions. To assess the predictive ability of the compartmental model, a single-compartment model was constructed using the same covariates, and the predictive performance of the two-compartment and single-compartment models was compared.

Validation

Out-of-sample validation was used to assess the model's predictive ability. The predicted value for a patient was equal to the weighted value of the predictions from each function. The model coefficients and random effects derived from the building subset were applied to the validation subset and the total predicted care days among ICUs and diagnostic groups were contrasted with the total observed. The concordance correlation coefficient was used to assess the relationship parametrically (Lin 1989).

The final model's ability to distinguish between short- and long-stay patients was assessed using a modified approach to the receiver operating characteristic (ROC) method (Tu and Mazer 1996). Observed LoS,

dichotomized at the median (1.17 days), was taken as the comparison variable, and area under the ROC curve (AUC) of >0.7 was considered to indicate acceptable discriminatory performance (Hosmer et al. 1997).

RESULTS

While patients staying more than 28 days made up only 0.98 percent of ICU patients discharged alive in this study, they were responsible for 18.0 percent of care days in the ICU (9,003 of 49,952 total care days). The overall mean LoS was 3.37 days, with a range from 2 hours to 605 days (median 1.17 days; interquartile range 0.79–3.13 days). Of the 349 unique conditions coded in this data, 77 diagnoses had a mean LoS that was significantly higher than the mean LoS, while 84 diagnoses had a mean LoS that was significantly shorter than the population mean. The diagnostic groupings 1 through 5 represent the shortest to longest mean LoS. The classification of these diagnoses has been provided as an appendix.

Application of the building model to the validation subset provided good estimates of the total care days at the PICU level and among different diagnostic conditions. The concordance correlation coefficient was 0.99 and 0.95 for diagnostic group and PICU-level estimates, respectively.

In the final model, the AUC was acceptable at 0.821 (95 percent CI: 0.814–0.828). The coefficients for the final model are presented in Table 2. The mean of the first compartment (F1) was 1.75 days, and the mean of the second compartment (F2) was 6.93 days. The probability (equation 4) for elective patients was 0.83, indicating that 83 percent of elective patients have their LoS predicted by the first function. The corresponding probabilities for nonelective patients were 0.63 and 0.37 for the first and second (short and long stay) compartments, respectively. The differences in the proportion of elective and nonelective patients assigned to the second distribution were significant at the 0.05 significance level ($p < .0001$).

The frequency distribution of the observed LoS, the weighted distribution of the two-compartment model, and the frequency distribution of the predictions from a single-compartment model are shown in Figures 1 and 2. Figures 1 and 2 show the LoS distributions for 0–10 days and 11–100 days, respectively. The two-compartment model better characterized the high initial peak associated with short-ICU stays and the long tail associated with the heterogeneity in ICU LoS.

Table 2: A Compartmental Mixed-Effects Gamma Regression Model of Patient Length of Stay in Intensive Care Units Receiving Pediatric Admissions in Australia and New Zealand, 1997–2006

	β_1	95% CI	p	β_2	95% CI	p
Intercept	0.186	−0.021 to 0.392	.070	1.398	1.100 to 1.697	<.0001
Respiratory support in the first hour (yes)	0.687	0.635 to 0.739	<.0001	0.534	0.433 to 0.635	<.0001
Diagnostic Group 1	−0.322	−0.399 to −0.246	<.0001	−1.665	−1.915 to −1.415	<.0001
Diagnostic Group 2	−0.300	−0.350 to −0.251	<.0001	−0.591	−0.701 to −0.480	<.0001
Diagnostic Group 3	Ref			Ref		
Diagnostic Group 4	0.554	0.476 to 0.632	<.0001	0.585	0.461 to 0.708	<.0001
Diagnostic Group 5	0.801	0.648 to 0.954	<.0001	1.546	1.310 to 1.782	<.0001
Age (in years at admission)	−0.016	−0.021 to −0.012	<.0001	0.003	−0.006 to 0.013	.429
Pupils (yes, fixed and dilated at admission)	0.846	0.093 to 1.599	.033	−0.162	−2.041 to 1.717	.840
Previous admission						
No	Ref			Ref		
Yes, readmitted ≤ 48 hours postdischarge	0.044	−0.111 to 0.199	.514	−0.175	−0.402 to 0.053	.110
Yes, readmitted >48 hours postdischarge	0.108	0.016 to 0.200	.028	0.495	0.308 to 0.682	.001
Retrieval	0.215	0.126 to 0.304	.001	−0.119	−0.264 to 0.025	.090
Recovery from a procedure?						
No	Ref			Ref		
Yes, recovery from a bypass procedure	−0.190	−0.310 to −0.069	.008	0.088	−0.173 to 0.349	.439
Yes, recovery from other procedure	−0.122	−0.230 to −0.013	.034	0.066	−0.147 to 0.279	.475
$100 \times \text{FiO}_2/\text{PaO}_2$, mmHg ^{−1}	0.376	0.308 to 0.443	<.0001	0.233	0.094 to 0.372	.006
ICU admission source						
Operating theater or recovery	Ref			Ref		
Emergency department	−0.127	−0.246 to −0.008	.040	−0.047	−0.274 to 0.179	.628
Ward	−0.054	−0.171 to 0.062	.298	0.331	0.110 to 0.551	.011
Other ICU or NICU (same hospital)	0.263	−0.092 to 0.618	.120	0.284	−0.327 to 0.894	.299
Direct ICU admission	−0.309	−0.439 to −0.178	.001	0.200	−0.037 to 0.437	.085

Figure 1: The Frequency Distribution 0–10 Days of Observed LoS, Predicted LoS from a Single-Compartment Model, and the Combined Distribution of Two Functions Predicted by a Two-Compartment Model

Observed and predicted distributions of LoS between 0 and 10 days

The coefficients for the final model are given in Table 2. Significant factors associated with prolonged LoS in the first compartment (F1) were a high $\text{FiO}_2/\text{PaO}_2$ ratio, retrieval, fixed dilated pupils, and respiratory support within the first hour of admission. Respiratory support and a high $\text{FiO}_2/\text{PaO}_2$ ratio were both also associated with prolonged LoS in the second compartment (F2). Some predictors were significant in the first compartment of the model and not in the second and vice versa. Age was associated with a decreased LoS in the first compartment of the model but not a significant predictor in the second component of the model.

The antilog of the site-specific random effects for each compartment is shown in Figure 3. The charts are arranged in ascending order of the antilog of the site RE for F1. After adjusting for patient characteristics at time of admission, three sites had significantly longer mean LoS than the population average for F1 (short-stay patients), while two sites had a mean LoS that was significant shorter than the population mean. Two sites had significantly longer mean LoS than the population average for F2 (long-stay patients), while two sites had a mean LoS that was significantly shorter than the population

Figure 2: The Frequency Distribution 10–100 Days of Observed LoS, Predicted LoS from a Single-Compartment Model, and the Combined Distribution of Two Functions Predicted by a Two-Compartment Model

Figure 3: Site Effect Values for F1 (A) and F2 (B) of a Two-Compartment Gamma Mixed-Effects Regression Model of ICU LoS in Australian and New Zealand PICUs 2007–2008

mean. The remaining sites had an average LoS that was not significantly different from the population mean at the 95 percent level. The site-specific random effects were not significantly different when missing biological predictors were imputed using mean imputation.

DISCUSSION

This study revealed significant differences in the risk-adjusted mean LoS between PICUs in Australia and New Zealand. Using the methods previously described by Lee, Ng, and Yau (2001) and Lee et al. (2007), we were able to quantify between-ICU variability in the entire patient population of the study ICUs, including extremely long-staying patients.

The separate components of the model are usefully contextualized as short- and long-stay components but are both assumed to follow gamma distributions with possible values ranging from zero to infinity. The distinction is useful and can be summarized by the mean of the respective distribution. The distribution of the first compartment peaks sharply and early, whereas the second compartment is flatter and peaks later and thus describes the majority of the long-stay patients.

Previous approaches using multicompartment mixture models have allowed the probability to be influenced solely by the distribution of the data. We added elective status as a covariate in calculating the probability such that the proportion of patients assigned to the long-stay subgroup is conditional on elective status. We reasoned that elective status defines distinct patient subpopulations, and in this sense, it is useful in differentiating the assignment to each distribution. The proportion of children in the long-stay component is higher for nonelective patients than elective patients (0.37 versus 0.17). Other patient-specific covariates were used to estimate the patient's LoS within each distribution.

The compartmental approach described offers advantages over the single-compartment model that has been previously described (Straney et al. 2010a). In particular, the ability to describe site-level variation among short- and long-stay patients may help to differentiate where there may be greatest opportunity to improve resource use. A statistically significant site effect >1 indicates that the site's adjusted mean LoS is higher than expected in that subpopulation. For an individual site, the random effect values for each function help to characterize the distribution of LoS in their units after adjusting for underlying differences in case mix. A F1 RE that is not significantly different from one and a F2 RE that is significantly lower than 1 (sites 1 and 10) suggests that the tail of the distribution may be shorter than expected after accounting for case mix. The reasons for this may relate to practice of care, such as discharge to step

down facilities, and thus have implications for resource use and patient management. Site-effect values >1 for both functions indicate prolonged LoS among both short- and long-stay patients and could be indicative of inefficient patient flow.

Despite using two compartments to predict LoS, it is likely that the site-level results may still be biased by significant LoS outliers (less than 25 percent of children have a LoS that is greater than the mean). There is a valid argument that robust regression methods may provide a truer picture of the relationships between the covariates and the typical ICU patients. However, given the purpose of the model is to attempt to measure resource use at the ICU level, it might be reasonable to consider that the site effect be influenced by those patients in ICU with very long stays, and therefore consuming considerable resources. Given that the objective of the model is not to assess the relationships between the covariates and LoS in a causal sense, we have used parametric regression methods; however, investigation using robust regression methods is warranted in future research.

While the implication of these results is that there is variation in efficiency of resource use, there is likely to be unmeasured patient factors associated with significantly shorter or longer LoS. If there are systematic differences in the factors among units, then this will influence our estimate of site-level effects. Risk-adjustment methods are not intended or able to adjust for all patient characteristics so should not be considered an absolute measure of unit performance. As with all risk-adjustment methods, this model is intended as a preliminary quality assessment tool and does not provide detailed insight into the causes for variation in LoS. Further modeling approaches in this study population have examined duration of respiratory support and LoS concurrently (Straney et al. 2010b), revealing that differences in LoS may be partly explained by unit-level variation in duration of respiratory support. This study provides further insight into the nature of variation in LoS among different subpopulations and may be useful for informing studies of discharge practice.

CONCLUSION

Compartmental modeling of ICU LoS permits analysis of the entire ICU population without requiring the exclusion of long-stay patients. The two-compartment model characterizes the distribution of ICU LoS more effectively than a single-compartment model. The site effect varied for sites between

distributions, suggesting that sites do not uniformly influence LoS. There was significant variation in patient LoS at the ICU level not accounted for by patient case mix.

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Appendix SA1: Author Matrix.

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