

Paediatric Index of Mortality 3: An Updated Model for Predicting Mortality in Pediatric Intensive Care*

Lahn Straney, PhD¹; Archie Clements, PhD²; Roger C. Parslow, BSc, MSc, PhD³; Gale Pearson, MBBS, MRCP, FRCPCH, Dip Math⁴; Frank Shann, MD, FRACP, FCICM⁵; Jan Alexander⁶; Anthony Slater, FRACP, FCICM^{6,7}; for the ANZICS Paediatric Study Group and the Paediatric Intensive Care Audit Network

Objectives: To provide an updated version of the Paediatric Index of Mortality 2 for assessing the risk of mortality among children admitted to an ICU.

Design: International, multicenter, prospective cohort study.

Setting: Sixty ICUs that accept pediatric admissions in Australia, New Zealand, Ireland, and the United Kingdom.

Patients: All children admitted in 2010 and 2011 younger than 18 years old at the time of admission and either died in ICU or were discharged. Patients who were transferred to another ICU were not included. Fifty-three thousand one hundred twelve patient admissions were included in the analysis.

Interventions: None.

Measurement and Main Results: A revised prediction model was built using logistic regression. Variable selection was based on

significance at the 95% level and overall improvement of the model's discriminatory performance and goodness of fit. The final model discriminated well (area under the curve, 0.88, 0.88–0.89); however, the model performed better in Australia and New Zealand than in the United Kingdom and Ireland (area under the curve was 0.91, 0.90–0.93 and 0.85, 0.84–0.86, respectively).

Conclusions: Paediatric Index of Mortality 3 provides an international standard based on a large contemporary dataset for the comparison of risk-adjusted mortality among children admitted to intensive care. (*Pediatr Crit Care Med* 2013; 14:673–681)

Key Words: healthcare; intensive care; mortality; pediatrics; quality indicators; risk adjustment

*See also p. 718.

¹School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia.

²School of Population Health, The University of Queensland, Brisbane, QLD, Australia.

³Centre for Epidemiology and Biostatistics, University of Leeds, Leeds, United Kingdom.

⁴Birmingham Children's Hospital, Birmingham, United Kingdom.

⁵Royal Children's Hospital, Melbourne, VIC, Australia.

⁶Australian and New Zealand Intensive Care Society, Brisbane, QLD, Australia.

⁷Royal Children's Hospital, Brisbane, QLD, Australia.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (<http://journals.lww.com/pccmjjournal>).

Dr. Parslow received grant support from the Department of Health (government grant - funds for data collection and analysis). Dr. Pearson served as the specialist advisor to the Care Quality Commission, is employed by the Birmingham Children's Hospital, provided expert testimony for Episodic and various sources, lectured for various entities, and received royalties from Elsevier. Dr. Alexander is employed by ANZPIC (registry manager). Dr. Slater is employed by the Royal Children's Hospital, Brisbane. The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: lahn.straney@monash.edu

Copyright © 2013 by the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies

DOI: 10.1097/PCC.0b013e31829760cf

Mortality prediction models have become an important tool for monitoring the quality of intensive care (1, 2). Various factors not related to quality of care influence an individual patient's risk of death, such as their diagnosis, baseline health status, and the severity of illness. Multivariable statistical approaches are commonly employed to adjust for case-mix and permit objective comparisons among ICUs and over time (3). These models are not intended for prognostic use on individual patients; however, they have been used to assess the risk of mortality when enrolling patients to clinical trials (4) although this application is contentious (5).

The first version of the Paediatric Index of Mortality (PIM) was developed using data collected from 5,695 admissions from seven PICUs in Australia and one from the United Kingdom (6). The second generation model, PIM2, was developed using data collected from 20,787 pediatric patients treated in intensive care between 1997 and 1999 in Australia, New Zealand, and the United Kingdom (7). Since the development of the PIM2 model, it is likely that the relationships between mortality and the predictors have changed (8). Recent applications of PIM2 to other study populations have shown mixed results (9–13). The degree to which these models accurately predict their intended outcome in patients over time depends on the

consistency of case-mix and clinical practice (7, 14–16). Thus, to ensure continued applicability of the models, recalibration using new data should be performed regularly.

Previous research has shown that the PIM2 model has drifted in calibration in the United Kingdom and Australia and New Zealand (17, 18). The aim of this study was to update PIM2 using recent data from two large international outcome registries of pediatric admissions to intensive care. The revised model is referred to as “PIM3.”

MATERIALS AND METHODS

Data were accessed from the Paediatric Intensive Care Audit Network (PICANet) in the United Kingdom and Ireland and the Australian and New Zealand Paediatric Intensive Care (ANZPIC) registry. Since 2002, the PICANet registry has collected data from 36 PICUs and ICUs which accept pediatric admissions from Ireland and 25 National Health Service trusts in England, Wales, and Scotland. Collection of personally identifiable data has been approved by the National Information Governance Board and ethical approval granted by the Trent Medical Research Ethics Committee. The ANZPIC registry was established in 1997 and contains data contributed from all nine specialist PICUs in Australia and New Zealand as well as 15 general ICUs that admit children. Ethical approval for maintaining the registry and using the data for research has been granted by the Human Research Ethics Committee, Royal Children’s Hospital, Brisbane.

The ANZPIC diagnostic codes were used to assign primary and associated diagnoses to children admitted in Australian and New Zealand PICUs (19). Children admitted to ICU in the United Kingdom and Ireland had a primary diagnostic code assigned using Clinical Terms 3 (The Read Codes) (20). The Read Codes were mapped to the ANZPIC diagnostic codes to permit exploratory analysis of diagnostic information. To assess the accuracy of the mapping, an independent auditor familiar with the ANZPIC registry system applied diagnostic codes to 100 random PICANet cases and the level of agreement assessed.

All analyses were conducted using Stata 10 (Stata Statistical Software: Release 10, 2007, StataCorp, College Station, TX).

Data Collection

Data for consecutive admissions to ICUs participating in the PICANet and ANZPIC registries were collected between January 1, 2010, and December 31, 2011. Only variables available in both registries could be considered for inclusion in the final model. Detailed information on sites participating in the registries can be found in the annual reports published by the registries (17, 18). **Table 1** lists the variables available for risk adjustment.

Inclusion and Exclusion Criteria

Children included in the study were younger than 16 years old at the time of ICU admission. During the study period, there were 35,701 admissions to the 36 units in the United Kingdom and Ireland, and 17,411 admissions to 24 units in Australia and New Zealand that met the inclusion criteria. Children transferred to other ICUs were not classified as ICU survivors

and were therefore excluded from the study ($n = 2,780, 4.9\%$). Readmissions were treated as new admissions, and probability of death was estimated based on characteristics at the time of the new admission.

Model Development

We constructed an interim model using the same predictor variables as those used in PIM2. Diagnoses that were previously categorized as high- or low-risk conditions in the PIM2 model were parsed out and entered into the model as dummy variables to assess whether they should still be included based on significance at the 95% level. Individual patient risk predictions using this interim model were summed by 377 unique principal diagnoses and contrasted with observed deaths to identify conditions that were poorly predicted by the model. Diagnoses with standardized mortality ratios (SMRs) significantly different to one at the 95% level were assessed for inclusion in the conditions for low- or high-risk weighting.

We collapsed diagnoses influencing the risk of mortality into three categories: very high-, high-, and low-risk groups. Diagnoses classified as very high had odds ratios greater than 5 in the interim multivariable model. High-risk diagnoses were those with statistically significant odds ratios greater than 1 but less than 5, whereas low-risk diagnoses were considered as those with statistically significant odds ratio below 1. The association between a diagnosis and risk of death may be confounded in instances where a child has multiple weighted conditions. In contrast to PIM2, these groups were assigned using a categorical variable and patients with multiple weighted diagnoses were assigned to only one group, with precedence of assignment in the order: very high-risk diagnosis, high-risk diagnosis, and low-risk diagnosis. Thus a patient with hypoplastic left heart syndrome (a high-risk diagnosis) who is admitted with acute bronchiolitis (a low-risk diagnosis) would be coded only as having a high-risk diagnosis.

Next, we considered alternate transformations of continuous predictors. Systolic blood pressure (SBP) is known to have a nonlinear relationship with the risk of mortality; both very high and very low SBP are indicative of poor health status. We considered three transformations of SBP for inclusion: the PIM2 approach, in which the variable $|\text{SBP} - 120|$ was included as a predictor, and alternative approaches in which a quadratic or third-degree polynomial was used. Where SBP was missing, a value of 120 was used.

We considered two transformations for the value of base excess: the absolute value of base excess and base excess as a quadratic function. Where base excess was missing, a value of zero was used.

We considered four approaches for incorporating PaO_2 and FiO_2 in the model. First, we calculated $([\text{FiO}_2 \times 100]/\text{PaO}_2)$ in the same manner as PIM2 replacing the ratio with zero if PaO_2 or FiO_2 was missing; second, replacing the ratio with 0.23 if PaO_2 or FiO_2 missing, derived from the normal value of PaO_2 in air $([0.21 \times 100]/90)$; third, the natural logarithm of $([\text{PaO}_2/\text{FiO}_2] \times 100)$ replacing the ratio with 430 if PaO_2 or FiO_2 missing; fourth, the absolute value of the difference between the calculated ratio $([\text{FiO}_2 \times 100]/\text{PaO}_2)$ and the normal value (0.23).

TABLE 1. Variables Available for Risk Adjustment

Variable ^a	Variable Description	Variable Type	Missing or Not Recorded (%)
ICU outcome	Patient was discharged to ward or home [0] Patient died in ICU [1]	Binary	0 (0.0)
Mechanical ventilation 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)
Systolic blood pressure	Systolic blood pressure (mmHg)	Continuous	2,485 (4.7)
Pao ₂	Partial pressure of arterial oxygen	Continuous	29,640 (55.8)
Fio ₂	Fraction of inspired oxygen	Continuous	21,821 (41.1)
Pupils fixed to light	Pupillary reaction to light fixed? [0/1; no/yes]	Binary	409 (0.8)
Base excess	Base excess in arterial or capillary blood (mmol/L)	Continuous	10,470 (19.7)
Principal or primary reason for admission	Australian and New Zealand Paediatric Intensive Care diagnostic coding or Read clinical codes	Categorical	46 (< 0.1)
Recovery	Primary reason for admission is recovery from a procedure [0/1; no/yes]	Binary	0 (0.0)
Bypass	Primary reason for admission is recovery from cardiac surgery where bypass was used [0/1; no/yes]	Binary	0 (0.0)

^aAs defined in Paediatric Index of Mortality 2 (7).

We examined whether running recovery from a procedure as a categorical variable ([0] No; [1] Yes, recovery from a bypass procedure; [2] Yes, recovery from non-bypass cardiac procedure; [3] recovery from noncardiac procedure) gave better model performance than binary variables for recovery and bypass procedure as in PIM2. Each combination of transformations was considered, giving a total of 48 different model forms (**supplemental data**, Supplemental Digital Content 1, <http://links.lww.com/PCC/A68>).

Model Selection

There were a total of 117 unit-years of data (57 units contributed both years, two units contributed only 2010 data and one unit contributed 2011 data). Each unit-year was treated as an observation and randomly allocated into two subsets to be used for model building (2/3) and validation (1/3). We assessed the out-of-sample performance using 20 random splits of the data for each of the 48 model forms (a total of 960 models were ran). The coefficients estimated by the model derived from the building subset were applied to the validation set to estimate mortality risk. We compared the predicted mortality to the observed mortality using the area under the curve (AUC) of the receiver operating characteristic (ROC) plot of sensitivity versus 1-specificity, to assess discrimination between death and survival (21). We used the Hosmer-Lemeshow goodness-of-fit test to evaluate calibration across the deciles of risk (22).

We selected the final model form with regard to the highest mean AUC, a nonsignificant goodness-of-fit test (based on the median X^2 value), and overall model complexity.

After considering alternate transformations, we also considered the addition of an interaction term to distinguish elective patients who received respiratory support from those who did not. Inclusion in the model was based on improvements to the model discrimination.

Final Model

To account for clustering within ICUs and countries, we ran random effects on the unit nested within the region. The final PIM3 coefficient and SE estimates were calculated by bootstrapping with 200 repetitions using the entire dataset. The expected probability of death was defined only by the fixed portion of the model. The discriminatory performance of the final model was assessed using the ROC-AUC for the entire population and for different subpopulations. We compared estimates of mortality obtained using the revised model with estimates derived from the existing PIM2 model.

RESULTS

During the study period 2010 and 2011, the unadjusted crude mortality was higher in the United Kingdom and Ireland than in Australasia (Australia and New Zealand combined) with 41.3 and 28.0 deaths per 1,000 admissions, respectively. Among patients receiving mechanical ventilation in the first hour, the mortality rates were 59.1 and 48.1 per 1,000 admissions for the United Kingdom/Ireland and Australasia, respectively. Elective admissions accounted for 41.0% of all admissions, and 39.7% of children were admitted for recovery following a procedure. Descriptive data on the units contributing data to the analysis are provided in **Table 2**. Five PIM2 variables remained

TABLE 2. Admission Characteristics of ICUs by ICU Type

ICU Type	United Kingdom and Ireland	Australia and New Zealand
General PICU		
No. of ICUs	20 ^a	3 ^a
Admissions per annum: mean (range)	385 (73–795)	452 (206–652)
Ventilated admissions per annum: mean (range)	191 (3–620)	147 (97–202)
General and cardiac PICU		
No. of ICUs	9	6
Admissions per annum: mean (range)	848 (232–1,182)	1,027 (731–1,239)
Ventilated admissions per annum: mean (range)	591 (181–911)	564 (306–853)
Cardiac PICU		
No. of ICUs	4 ^b	0
Admissions per annum: mean (range)	494 (272–691)	–
Ventilated admissions per annum: mean (range)	359 (191–508)	–
Surgical PICU		
No. of ICUs	2 ^c	0
Admissions per annum: mean (range)	267 (88–447)	–
Ventilated admissions per annum: mean (range)	95 (9–182)	–
Mixed adult ICU and PICU		
No. of ICUs	1	15
Admissions per annum: mean (range)	14	82 (9–398)
Ventilated admissions per annum: mean (range)	12	32 (0–149)

Dashes indicate no data.

^aIncludes one combined neonatal ICU/PICU.

^bIncludes one combined cardiac and respiratory PICU and one combined cardiac, ear, nose, and throat, and orthopedic ICU.

^cIncludes one neonatal surgical ICU.

significant, in their original form, in the updated PIM3 model. However, HIV infection and admission for recovery following elective liver transplant were not associated with an increased risk of death in ICU. HIV infection was removed from the high-risk conditions, and admission following an elective liver transplant was not included in the definition of liver failure.

The risk of mortality for bone marrow transplant (BMT) recipients and children admitted with necrotizing enterocolitis (NEC) was underpredicted by the interim model. Conversely, mortality among children admitted with a primary diagnosis that could be classified as a seizure disorder was overpredicted by the interim model. The level of agreement between the mapped diagnoses and those audited for the 100 U.K. cases was moderate (57%). There was better agreement for diagnosis classified by diagnostic group (95%), while the level of agreement for new diagnoses that were weighted in the model was high, 99%, 100%, and 99% for seizures, BMT, and NEC, respectively.

A full list of the models has been provided as supplemental data (Supplemental Digital Content 1, <http://links.lww.com/PCC/A68>). There was little difference in the out-of-sample performance among the top performing models. We

selected model 18 (using SBP as a quadratic, $100 \times \text{FiO}_2/\text{PaO}_2$ imputing 0.23 if missing, absolute base excess, and recovery as a categorical variable) as our final model as it has the highest ROC-AUC and was the least complex among the top performing models. The mean AUC across the splits for our selected model was 0.89 (range = 0.88–0.90) indicating good discriminatory performance. The median value for the goodness-of-fit test was not significant at the 95% level ($X^2 = 9.43$, $p = 0.31$).

An interaction term for elective patients with respiratory support in the first hour was significant in the model but did not improve overall model discrimination.

Table 3 shows the final PIM3 model coefficients derived from 53,112 consecutive admissions of children admitted to ICUs in Australia, New Zealand, Ireland, and U.K. ICUs in 2010 and 2011. Abnormal physiological values, fixed dilated pupils, and weighted high-risk diagnosis and mechanical ventilation in the first hour were all associated with an increased risk of death. Elective status, recovery from a procedure, along with weighted low-risk diagnoses were all associated with a decreased risk of death. The final model discriminated well

(AUC, 0.88, 0.88–0.89); however, in the combined dataset, the model performed better in Australasia than in the United Kingdom/Ireland (AUC, 0.92, 0.91–0.93 and 0.87, 0.86–0.88, respectively). Concordance between the observed and predicted deaths at the unit level was 0.94. The discrimination of PIM2 in the same data was similar to the revised model (AUC = 0.88; 95% CI = 0.87–0.88); however, the median SMR among units was 0.93—indicating that PIM2 overpredicted mortality in most units.

Figure 1 presents the calibration of the model across deciles of risk and shows the model performed well across different risk strata. **Table 4** shows the model performance across different diagnostic groups and unit volume. The model predicted well in the different groups with most groups showing no significant difference between observed and expected at the 95% level. However, the neurological conditions were underpredicted by the model (SMR, 1.32, 1.16–1.50). Instructions for coding PIM3 have been provided in **Appendix 1**.

DISCUSSION

The PIM model was developed as a simple method for assessing a child's risk of death in ICU based on data collected within the first hour of contact. PIM3 is an updated model

built using a larger dataset with more ICUs and greater representation across four countries. This may improve the generalizability of the model to populations outside this study group; however, population differences in admission thresholds, case-mix, resourcing, and the process of care should be considered when assessing model performance in different populations. The inclusion of patient data from children admitted to general ICUs may help to improve the performance of the model among children admitted to nonpediatric ICUs. Data for PIM are collected within the first hour of admission, which avoids potential bias from the effects of treatment after admission, and offers practical utility in assigning children to clinical trials soon after admission to intensive care.

The addition of NEC reflects the significant risk of death associated with this diagnosis as well as differences in clinical practice between European and Australasian ICUs. In the United Kingdom and Ireland, there were 207 children admitted to PICU with a primary diagnosis of NEC. It is likely that these babies were transferred to a children's hospital for surgery and admitted to PICU perioperatively. The crude mortality for patients admitted with this diagnosis was 17.5% (more than four times the overall crude mortality). In Australia and New

TABLE 3. Final Paediatric Index of Mortality 3 Model Coefficients Derived From 53,112 Consecutive Admissions of Children Admitted to Australian, New Zealand, and United Kingdom ICUs in 2010 and 2011

Variable	Paediatric Index of Mortality 3 Model Derived From Entire Sample (<i>n</i> = 53,112)		
	Coefficients	Odds Ratio	<i>p</i>
Pupils fixed to light? (Yes/No)	3.8233 (3.4581–4.1885)	45.7554 (31.7561–65.926)	< 0.001
Elective admission (Yes/No)	−0.5378 (−0.7234 to −0.3522)	0.584 (0.4851–0.7031)	< 0.001
Mechanical ventilation in the first hour (Yes/No)	0.9763 (0.8234–1.1293)	2.6547 (2.2783–3.0934)	< 0.001
Absolute value of base excess (mmol/L)	0.0671 (0.0576–0.0766)	1.0694 (1.0593–1.0797)	< 0.001
SBP at admission (mm Hg)	−0.0431 (−0.0524 to −0.0338)	0.9578 (0.949–0.9668)	< 0.001
SBP ² /1,000	0.1716 (0.1248–0.2183)	1.1872 (1.1329–1.244)	< 0.001
100 × FiO ₂ /Pao ₂ (mm Hg)	0.4214 (0.3313–0.5115)	1.5241 (1.3928–1.6678)	< 0.001
Recovery post procedure?			
Yes, recovery from a bypass cardiac procedure	−1.2246 (−1.4915 to −0.9576)	0.2939 (0.225–0.3838)	< 0.001
Yes, recovery from a non-bypass cardiac procedure	−0.8762 (−1.2418 to −0.5106)	0.4164 (0.2889–0.6001)	< 0.001
Yes, recovery from a noncardiac procedure	−1.5164 (−1.7998 to −1.233)	0.2195 (0.1653–0.2914)	< 0.001
Very high-risk diagnosis (Yes/No)	1.6225 (1.4706–1.7744)	5.0657 (4.3517–5.8968)	< 0.001
High-risk diagnosis (Yes/No)	1.0725 (0.9071–1.238)	2.9228 (2.4771–3.4487)	< 0.001
Low-risk diagnosis (Yes/No)	−2.1766 (−2.4825 to −1.8708)	0.1134 (0.0835–0.154)	< 0.001
Constant	−1.7928 (−2.2763 to −1.3093)	0.1665 (0.1027–0.27)	< 0.001

SBP = systolic blood pressure.

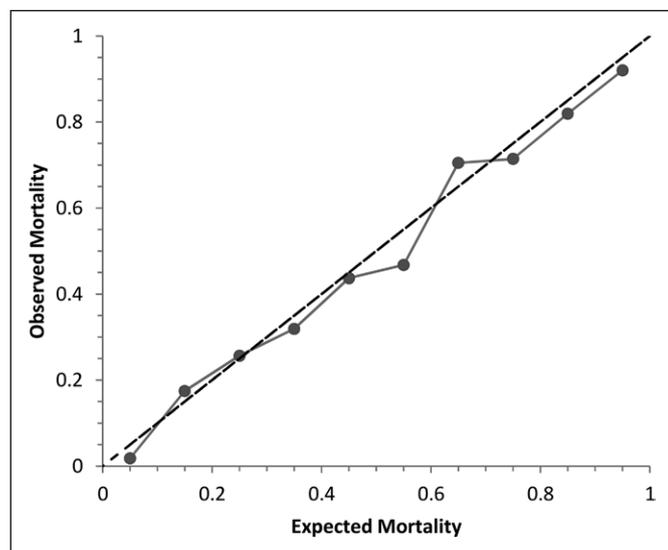


Figure 1. Calibration of model across deciles of risk, observed versus expected mortality.

Zealand, babies with NEC typically remain in neonatal ICUs even if surgery is required and therefore are rarely admitted to PICUs (only 10 patients were admitted to Australasian PICUs during 2010 and 2011). Bone marrow transplant recipients had a higher mortality than predicted. Patients in whom the primary reason for admission was a seizure disorder, including status epilepticus or prolonged febrile convulsion, had a lower mortality than predicted. The addition of these diagnoses to the high- and low-risk groupings improved overall model performance and the SMR across diagnostic groups.

The overall discriminatory ability for the final PIM3 model was similar to that reported for PIM2 (0.88 vs 0.90). On average, Irish and U.K. units admitted sicker patients: the mean PIM3 mortality risk for children in these units was 3.9% while in Australia and New Zealand it was 2.9%. This could possibly reflect differences in admission thresholds, in baseline population health status, or differences in patient management. It is possible that such differences are not adequately accounted for by the model and this will affect the overall measure of performance. Using PIM3, the SMR for the entire PICANet data during the period was 1.07, while in Australia and New Zealand it was 0.96. When monitoring PICU outcomes it is desirable to monitor performance using both the international standard (PIM3) as well as a locally calibrated version of the model, where the overall SMR for the local population is equal to 1. A locally calibrated model will allow ICUs to compare their performance with the local standard of care. If performed regularly, for example, at intervals of 1 or 2 years, local calibration also overcomes the issue of calibration drift due to improvements in quality of care and changes in case-mix. To standardize nomenclature, we recommend that the region and the final year of data be added to PIM3; PIM3-ANZ11 would denote a model calibrated using data from Australia and New Zealand corresponding to the study period reported here. Assessment against an international standard is also important as there may be factors in the healthcare system that are affecting the outcomes of children in the region more generally. These factors will not be appreciated if the only assessment that is made is local comparison. The use of a larger and more geographically diverse patient population in the future may help to improve the generalizability of the model to other settings.

TABLE 4. Standardized Mortality Ratio by Diagnostic Group and Unit Volume

Strata	n	Observed Survivors	Expected Survivors	Observed Deaths	Expected Deaths	Standardized Mortality Ratio	95% CI
Diagnostic group							
Cardiac (including postoperative)	13,838	13,413	13,407.6	425	430.4	0.99	0.90–1.09
Gastrointestinal/renal	1,797	1,669	1,678.1	128	118.9	1.08	0.90–1.28
Miscellaneous (including injury)	8,222	7,496	7,545.9	726	676.1	1.07	1.00–1.15
Neurologic	4,760	4,520	4,578.0	240	182.0	1.32	1.16–1.50
Noncardiac postoperative	11,178	11,101	11,093.0	77	85.0	0.91	0.71–1.13
Respiratory	13,317	12,951	12,920.4	366	396.6	0.92	0.83–1.02
Unit volume (2010–2011) Units							
0–600 admissions	26	5,833	5,848.8	213	197.2	1.08	0.94–1.24
601–1,200	15	12,526	12,496.5	415	444.5	0.93	0.85–1.03
1,201–1,800	11	15,763	15,805.5	592	549.5	1.08	0.99–1.17
1,801–24,77	8	17,028	17,072.0	742	698.0	1.06	0.99–1.14
Total	53,112	51,150	51,223	1,962	1,889	1	0.99–1.01

Physiologic variables used in PIM are not collected for all children admitted to ICU. The most common reason for missing physiologic data is that a clinical decision is made that significant abnormality in the variable is unlikely and that measurement of a variable is not required for patient management. In this situation, invasive procedures, such as arterial blood sampling, are not performed. As a result, PIM predictors such as base excess, FiO_2 , and PaO_2 have a high proportion of missing data which need to be imputed. Most common imputation methods assume the data are missing at random; however, the physiologic variables in PIM are not missing at random. Therefore, like PIM2, PIM3 relies on default imputation in which missing observations are given a value considered “normal” for that variable. Recent studies have shown that SpO_2 may be a suitable noninvasive replacement for PaO_2 (23–25). There is also preliminary evidence that prediction may be improved if blood lactate concentration is substituted for base excess (26). To facilitate further investigation, these variables have recently been added to the data collected for the ANZPIC and PICANet registries.

CONCLUSION

PIM2 overpredicted the risk of mortality in children admitted to ICU in 2010 and 2011. Recalibrating the coefficients improved the performance, but cardiac bypass no longer predicted mortality, and prediction was poor among low-risk patients. A PIM3 model based on more recent data, together with reclassification of diagnostic information, and modeling SBP as a quadratic, provides better estimates of mortality risk among children admitted to intensive care in the United Kingdom, Ireland, Australia, and New Zealand.

REFERENCES

- Slater A, Shann F; ANZICS Paediatric Study Group: The suitability of the Pediatric Index of Mortality (PIM), PIM2, the Pediatric Risk of Mortality (PRISM), and PRISM III for monitoring the quality of pediatric intensive care in Australia and New Zealand. *Pediatr Crit Care Med* 2004; 5:447–454
- Zimmerman JE, Kramer AA, McNair DS, et al: Acute Physiology and Chronic Health Evaluation (APACHE) IV: Hospital mortality assessment for today's critically ill patients. *Crit Care Med* 2006; 34:1297–1310
- Rothen HU, Takala J: Can outcome prediction data change patient outcomes and organizational outcomes? *Curr Opin Crit Care* 2008; 14:513–519
- Qureshi AU, Ali AS, Ahmad TM: Comparison of three prognostic scores (PRISM, PELOD and PIM 2) at pediatric intensive care unit under Pakistani circumstances. *J Ayub Med Coll Abbottabad* 2007; 19:49–53
- Vincent JL, Opal SM, Marshall JC: Ten reasons why we should NOT use severity scores as entry criteria for clinical trials or in our treatment decisions. *Crit Care Med* 2010; 38:283–287
- Shann F, Pearson G, Slater A, et al: Paediatric index of mortality (PIM): A mortality prediction model for children in intensive care. *Intensive Care Med* 1997; 23:201–207
- Slater A, Shann F, Pearson G; Paediatric Index of Mortality (PIM) Study Group: PIM2: A revised version of the Paediatric Index of Mortality. *Intensive Care Med* 2003; 29:278–285
- Pearson GA, Stickley J, Shann F: Calibration of the paediatric index of mortality in UK paediatric intensive care units. *Arch Dis Child* 2001; 84:125–128
- Eulmesekian PG, Pérez A, Minces PG, et al: Validation of pediatric index of mortality 2 (PIM2) in a single pediatric intensive care unit of Argentina. *Pediatr Crit Care Med* 2007; 8:54–57
- Ng DK, Miu TY, Chiu WK, et al: Validation of Pediatric Index of Mortality 2 in three pediatric intensive care units in Hong Kong. *Indian J Pediatr* 2011; 78:1491–1494
- Imamura T, Nakagawa S, Goldman RD, et al: Validation of pediatric index of mortality 2 (PIM2) in a single pediatric intensive care unit in Japan. *Intensive Care Med* 2012; 38:649–654
- Taori RN, Lahiri KR, Tullu MS: Performance of PRISM (Pediatric Risk of Mortality) score and PIM (Pediatric Index of Mortality) score in a tertiary care pediatric ICU. *Indian J Pediatr* 2010; 77:267–271
- Czaja AS, Scanlon MC, Kuhn EM, et al: Performance of the Pediatric Index of Mortality 2 for pediatric cardiac surgery patients. *Pediatr Crit Care Med* 2011; 12:184–189
- Pollack MM, Patel KM, Ruttimann UE: PRISM III: An updated Pediatric Risk of Mortality score. *Crit Care Med* 1996; 24:743–752
- Tibby SM, Holton F, Durward A, et al: Is Paediatric Index of Mortality 2 already out of date? *Crit Care* 2004; 8:P329
- Moreno RP: Outcome prediction in intensive care: Why we need to reinvent the wheel. *Curr Opin Crit Care* 2008; 14:483–484
- Alexander J, Tregear S, Slater A: Report of the Australian and New Zealand Paediatric Intensive Care Registry, 2010. Melbourne, Australian and New Zealand Intensive Care Society, 2012
- Universities of Leeds and Leicester: Paediatric Intensive Care Audit Network National Report 2009–2011. Leeds, Leicester, Universities of Leeds and Leicester, 2012
- Slater A, Shann F, McEniery J; ANZICS Study Group: The ANZPIC registry diagnostic codes: A system for coding reasons for admitting children to intensive care. *Intensive Care Med* 2003; 29:271–277
- Chisholm J: The Read clinical classification. *BMJ* 1990; 300:1092–1092
- Hanley JA, McNeil BJ: A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983; 148:839–843
- Hosmer DW, Hosmer T, Le Cessie S, et al: A comparison of goodness-of-fit tests for the logistic regression model. *Stat Med* 1997; 16:965–980
- Khemani RG, Thomas NJ, Venkatachalam V, et al; Pediatric Acute Lung Injury and Sepsis Network Investigators (PALISI): Comparison of SpO_2 to PaO_2 based markers of lung disease severity for children with acute lung injury. *Crit Care Med* 2012; 40:1309–1316
- Thomas NJ, Shaffer ML, Willson DF, et al: Defining acute lung disease in children with the oxygenation saturation index. *Pediatr Crit Care Med* 2010; 11:12–17
- Leteurtre S, Dupré M, Dorkenoo A, et al: Assessment of the Pediatric Index of Mortality 2 with the $\text{PaO}_2/\text{FiO}_2$ ratio derived from the $\text{SpO}_2/\text{FiO}_2$ ratio: A prospective pilot study in a French pediatric intensive care unit. *Pediatr Crit Care Med* 2011; 12:e184–e186
- Morris KP, McShane P, Stickley J, et al: The relationship between blood lactate concentration, the Paediatric Index of Mortality 2 (PIM2) and mortality in paediatric intensive care. *Intensive Care Med* 2012; 38:2042–2046

APPENDIX 1: PIM3 GENERAL INSTRUCTIONS

PIM3 is calculated from the information collected at the time a child is admitted to your ICU.

- Record the observations at or about the time of first face-to-face (not telephone) contact between the patient and a doctor from your ICU (or a doctor from a specialist pediatric transport team).
- Use the first value of each variable measured within the period from the time of first contact to 1 hour after arrival in your ICU. The first contact may be in your ICU, or your

emergency department, or a ward in your own hospital, or in another hospital (e.g., on a retrieval).

1. Systolic blood pressure, mm Hg (unknown = 120)^a
2. Pupillary reactions to bright light (> 3 mm and both fixed = 1, other or unknown = 0)^b
3. $([F_{iO_2} \times 100]/P_{aO_2})$. P_{aO_2} mm Hg, F_{iO_2} at the time of P_{aO_2} if oxygen via endotracheal tube or headbox (F_{iO_2} or P_{aO_2} unknown, $[(F_{iO_2} \times 100)/P_{aO_2}] = 0.23$)
4. Base excess in arterial or capillary blood, mmol/L (unknown = 0)
5. Mechanical ventilation at any time during the first hour in ICU (no = 0, yes = 1)^c
6. Elective admission to ICU (no = 0, yes = 1)^d
7. Recovery from surgery or a procedure is the main reason for ICU admission^e
 - [0] No
 - [1] Yes, recovery from a bypass cardiac procedure
 - [2] Yes, recovery from a non-bypass cardiac procedure
 - [3] Yes, recovery from a noncardiac procedure
8. Low-risk diagnosis. Record the number in brackets. If in doubt record 0.
 - [0] None
 - [1] Asthma is the main reason for ICU admission
 - [2] Bronchiolitis is the main reason for ICU admission^f
 - [3] Croup is the main reason for ICU admission
 - [4] Obstructive sleep apnea is the main reason for ICU admission^g
 - [5] Diabetic ketoacidosis is the main reason for ICU admission
 - [6] Seizure disorder is the main reason for ICU admission^h
9. High-risk diagnosis. Record the number in brackets. If in doubt record 0.
 - [0] None
 - [1] Spontaneous cerebral hemorrhageⁱ
 - [2] Cardiomyopathy or myocarditis
 - [3] Hypoplastic left heart syndrome^j
 - [4] Neurodegenerative disorder^k
 - [5] Necrotizing enterocolitis is the main reason for ICU admission
10. Very high-risk diagnosis. Record the number in brackets. If in doubt record 0.
 - [0] None
 - [1] Cardiac arrest preceding ICU admission^l
 - [2] Severe combined immune deficiency
 - [3] Leukemia or lymphoma after first induction^m
 - [4] Bone marrow transplant recipient
 - [5] Liver failure is the main reason for ICU admissionⁿ

Coding rules. These rules must be followed carefully for PIM3 to perform reliably:

- a. Record SBP as 0 if the patient is in cardiac arrest; record 30 if the patient is shocked and the blood pressure is so low that it cannot be measured.

- b. Pupillary reactions to bright light are used as an index of brain function. Do not record an abnormal finding if this is due to drugs, toxins, or local eye injury.
- c. Mechanical ventilation includes invasive ventilation, mask or nasal continuous positive airway pressure, or bilevel positive airway pressure, or negative pressure ventilation.
- d. Elective admission. Include admission (planned or foreseeable) after elective surgery or admission for an elective procedure (e.g., insertion of a central catheter), or elective monitoring, or review of home ventilation. An ICU admission or an operation is considered elective if it could be postponed for more than 6 hours without adverse effect.
- e. Recovery from surgery or procedure (includes a radiology procedure or cardiac catheter). Do not include patients admitted from the operating theater where recovery from surgery is not the main reason for ICU admission (e.g., a patient with a head injury who is admitted from the theater after insertion of an intracranial pressure monitor; in this patient the main reason for ICU admission is the head injury).
- f. Bronchiolitis. Include children who present either with respiratory distress or central apnea where the clinical diagnosis is bronchiolitis.
- g. Obstructive sleep apnea. Include patients admitted following adenoidectomy and/or tonsillectomy in whom obstructive sleep apnea is the main reason for ICU admission (and code as recovery from surgery).
- h. Seizure disorder. Include patients who require admission primarily due to status epilepticus, epilepsy, febrile convulsion, or other epileptic syndrome where admission is required either to control seizures or to recover from the effects of seizures or treatment.
- i. Cerebral hemorrhage must be spontaneous (e.g., from aneurysm or AV malformation). Do not include traumatic cerebral hemorrhage or intracranial hemorrhage that is not intracerebral (e.g., subdural hemorrhage).
- j. Hypoplastic left heart syndrome. Any age, but include only cases where a Norwood procedure or equivalent is required in the neonatal period to sustain life.
- k. Neurodegenerative disorder. Requires a history of progressive loss of milestones (even if no specific condition has been diagnosed), or a diagnosis where this will inevitably occur.
 - l. Cardiac arrest preceding ICU admission includes both in-hospital and out-of-hospital arrest. Requires either documented absent pulse or the requirement for external cardiac compression. Do not include past history of cardiac arrest.
- m. Leukemia or lymphoma. Include only cases where admission is related to leukemia or lymphoma or the therapy for these conditions.
- n. Liver failure, acute or chronic. Must be the main reason for ICU admission. Do not include patients admitted following an elective liver transplant.

Example of PIM3 Calculation

A 6-year-old girl receiving chemotherapy for relapsed leukemia presents to the emergency department of your hospital with febrile neutropenia. She is known to have chemotherapy-induced cardiomyopathy. A doctor from your ICU assesses her before admission and at the time the SBP is 70 mmHg, and she has reactive pupils. She is admitted to ICU, intubated and ventilated, and an arterial blood gas is performed within the first hour. The PaO_2 is 65 mmHg in FiO_2 of 0.7, the base excess is -12 mmol/L.

Interpretation: The admission is not elective or for recovery from a procedure. She is ventilated within the first hour of admission. The first SBP recorded after first contact with the

ICU doctor in the emergency department was 70 mmHg. She has both a very high-risk condition (leukemia after first induction) and a high-risk condition (cardiomyopathy). Only one risk diagnosis is considered with the very high-risk condition given precedence over the high-risk condition.

$$\begin{aligned} \text{PIM3} = & (3.8233*0) + (-0.5378*0) + \\ & (0.9763*1) + (0.0671*12) + (-0.0431*70) \\ & + (0.1716*(70^2/1000)) + (0.4214*(0.7/65)*100) \\ & + (-1.2246*0) + (-0.8762*0) + (-1.5164*0) \\ & + (1.6225*1) + (1.0725*0) + (-2.1766*0) \\ & - 1.7928 = -0.11114 \end{aligned}$$

$$\begin{aligned} \text{Probability of Death} = & \exp(-0.11114)/(1+\exp(-0.11114)) \\ = & 0.4722 \text{ or } 47.22\% \end{aligned}$$