

The pediatric risk of mortality III— Acute physiology score (PRISM III-APS): A method of assessing physiologic instability for pediatric intensive care unit patients

Murray M. Pollack, MD, Kantilal M. Patel, PhD, and Urs E. Ruttimann, PhD

Objective: To develop a physiology-based measure of physiologic instability for use in pediatric patients that has an expanded scale compared with the Pediatric Risk of Mortality (PRISM) III score.

Study design: Data were collected from consecutive admissions to 32 pediatric ICUs (11,165 admission, 543 deaths). Patient-level data included physiologic data, outcomes, descriptive information, and diagnoses. Physiologic data included the most abnormal values in the first 24 hours of pediatric ICU stay from 27 variables. Initially, ranges of each physiologic variable were evaluated for their association with mortality. A multivariate logistic regression analysis was used to determine the final variables and their ranges. Integer scores reflecting the relative contribution to mortality risk were assigned to the variable ranges.

Results: A total of 59 ranges of 21 physiologic variables were selected. This score is called the Pediatric Risk of Mortality III—Acute Physiology Score (PRISM III-APS). Mortality increased as the PRISM III-APS score increased. Most patients have PRISM III-APS scores less than 10, and these patients have a mortality risk of less than 1%. At the other extreme, the mortality rate of the 137 patients with a PRISM III-APS score of greater than 80 was greater than 97%.

Conclusion: The PRISM III-APS score is an expanded measure of physiologic instability that has been validated against mortality. Compared with PRISM III, PRISM III-APS should be more sensitive to small changes in physiologic status. (J Pediatr 1997;131:575-81)

Accurate and reliable prognostications are important for decision making. In most circumstances, subjective prognostic estimates (clinical judgments) use clinical and laboratory data that have not been objectively calibrated to maximize prediction performance. When objective prognostic estimates are available, they most commonly derive

From the The George Washington University School of Medicine, Children's National Medical Center, Center for Health Services and Clinical Research, Children's Research Institute, and the National Institute on Alcohol Abuse and Alcoholism, the National Institutes of Health, Washington, DC.

PRISM III algorithms are copyrighted and may be the subject of one or more patents held by Children's Research Institute. The equations are available with out charge for research uses including the independent verififcation of their accuracy and reliability. Children's National Medical Center may receive compensation resulting from non-research uses of PRISM III and PRISM algorithms.

Submitted Aug. 19, 1996; accepted Jan. 3, 1997.

Reprint requests: Murray M. Pollack, MD, Children's National Medical Center, 111 Michigan Ave., NW, Washington, DC 20010. 9/21/80257 from relatively simple data. For example, survival information for many tumors can be made by considering the tumor type, its stage of disease, and recent experience with available therapies.¹ Objective risk estimates may also use clinical and laboratory data that are statistically manipulated to maximize outcome prediction. A multivariate statistical approach is essential when a large number of variables that are related to each other in complex ways are involved.

22.2 M	60 M M				A. Commercial											211/01/2									
	CT 1993		CIPII.		1144441						- Se										100C A				
		12211-226	1.1.2.1.1	11111				1.12011	MC In		28.0									11.1711	1.25				
	201 H N	2.00 C - 100	****		102001	91 CC 27		244.0.1	10001157	r: 1140 r						- 19	C-04	211104							
		120 - 5	1.0			Ethern"	9 C. C. S		120105	1.0005	- CO	- NY 11	6 - CI	11+8.571	1110411					N 151					
	CO 1953	1.5	200		1 Particular		12.2012	14100	Sec. 2.	0.436	12 A 10				2007	244.4		1.1.1.1.1.1							
1.040	0010 KH 6				1+4627112	112211			1.1.1.1.1	10.00		~	19 E. 3		- COL				1222						
102	2623		23.45		5					~		- N - C		200-R.S	2427			12111							
1000	61855	10512323			1411146					- 1 C C				-		··· 89 ·				C 1914					
	1.164.4	10000-000			C-96-112	101091								100000000000											
		14201-530			CONTRACT OF		50	1227022	ad . the							11101-0			: Ci.						
11.14	21013	5011202	-		COLUMN S	111111				6 C 12 1			12,007	1.156511											
1000	жан		CH 2 M			11 - Marcell					221			 Annual A 	- 10 mail						1 Mar				
122.66	1.1	80. AC 8	10.0			1.184.4	C6	.					<i>.</i>	1.2	THE	1		A. 17		12.12			51°		
1.170	292.0			101111			1.1			80	7 .11 - 9			110010-0	1.000						100.000			: yr	
1556	61 E N	131.20.2			. 720 til (3					11.00	Sec. 1.2	1 12012				2 N T						C 311			
		- DO 10000				10.04210				10110			1 B 7 L M						12,113			1 10 11 11		110.0	
	-12x C	Margaret .				1.562.7	10.0										1 March 10								
		100	100.0	2012012			1.00	1.111		1.1.1				100,000			10.000	Se				12-9111	111.5		
111-10			- 37 C			** 24640	- 1 - 1 - 1	11010	10 C 10 C 10 C		10000			- -											
15.5	(122111		12313	110.241		1242942			L				- 10 -		1.00				1.111						
11170	3,905	100.00		- 10- A			100.00			1.5			-			10.11		L	1.1.1.1.1						
i a tr	10000	Her, 1120		201-1221		1515/22	12 12	1.21									-3212			= 1n -					
1.000	122611		2212				print [# 4] ;		the second second					1 TANKA 1 TA	•			1.1.1							
1.5	100.20	18017PC PC			1000		7.7.1.1	1.000	C										100.000						
	108.00	-1.0		INCOM		392 (h)	1.00	10000	COLUMN T			20 C 1			1,0903		= (G. 4								
11000	125.74	1000	199.8	- -	10 11 1 I.		1215.005	1244	1.00		11 M B		2 X X	10000-000		10414	10000								
	2100224	10.00	C 20 12			1.1000			P.4 1993		200 - 1 - 2							Design of the second se	*******						
	1365	10.0				a Miler	2012		2124	1.1	- 12 M	2.34	14. C. Mar												
											11.16							1.1111							
C 201	10.000					122112																			
1 1211	11215	100		× 0		110100																			

Mortality risk predictors are available for pediatric, adult, and neonatal ICUs.²⁻⁷ Disease-specific outcome predictors are also available for conditions such as sepsis.⁸ In pediatric intensive care, the Pediatric Risk of Mortality (PRISM) III score is a thirdgeneration, physiology-based score for quantifying physiologic status.³ PRISM III may be used for a variety of purposes, including estimating PICU care trait mortality risk based on the first 12 hours (PRISM III-12) or 24 hours (PRISM III-24) of PICU stay, estimating risk-adjusted length of PICU stay,9 and quantifying severity of illness for other purposes. The strength of PRISM III is that it was developed using a parsimonious model to predict ICU survival or death. That is, statistical criteria determined the fewest variables that would maximize the prediction performance of the model. This resulted in a score with only 17 physiologic variables broken down into 26 ranges. The main benefits of a parsimonious

approach are the protection against "overfitting" the model and the brevity of data collection. Although this approach is most applicable to the assessment of groups of patients (e.g., to assess institutional performance), the small number of variables and variable ranges makes it less desirable for quantifying small differences or changes in an individual patient's physiologic status. Quantification of overall physiologic instability is relevant to many issues, such as investigating the effects of various therapeutic interventions.

Therefore our goal in this investigation was to develop a model for assessing physiology-based severity of illness that would include more variables and more ranges of these variables than our previous PRISM III models. The premise is that such a model will be better suited to detect or track subtle changes in physiologic status in individual patients than PRISM III, which has been optimized to estimate mortality risk. The new score will be termed the PRISM III-Acute Physiology Score (PRISM III-APS). It was designed to have a broad severity scale from 0 to 356, with the higher values indicating higher instability.

METHODS

Site Selection

Details of the site selection procedures for the 32 study sites, data collection issues, and other analyses on this data set have been previously published.^{3,10,11} Sixteen of the PICUs were selected using a stratified random selection process and 16 were volunteer units. Data collection occurred from December 1989 through January 1992 and from January 1992 through December 1994 in the random and volunteer units, respectively.

Patients

Consecutive admissions to each unit were included. Readmissions to the PICU during the same hospitalization were analyzed as separate patients because each admission presented a separate opportunity for an outcome. Excluded from the study were (a) admissions for recovery from procedures normally cared for in other hospital locations, (b) patients staying in the unit less than 2 hours, (3) pa-

tients transferred from the study PICU to another ICU because their outcome could not be clearly credited to either ICU, and (d) patients admitted in a state of continuous cardiopulmonary resuscitation who did not achieve stable vital signs for at least 2 hours. Operating room deaths were included as an ICU death if the operation occurred during the unit stay and was a therapy for the illness requiring intensive care. Terminally ill patients who were transferred from the PICU for "comfort care" after discontinuation of an intensive care technology (e.g., mechanical ventilation) were included as PICU patients for the 24 hours after ICU discharge because 24 hours is a routine observational time after technology is discontinued. Terminally ill patients transferred from the PICU for comfort care while technologic support was maintained were included as ICU patients until 24 hours after the technologic support was discontinued. Patients transferred out of the PICU with technologic support, who were not considered terminal (e.g., chronic mechanical ventilation), were classified as intensive care survivors.

Each site collected data on consecutive admissions. When the last death in each site's sample occurred, all patients admitted before that death remained in the study. All units submitted patient logs. These logs were assessed to ensure data completeness: at least 97% of patients were included, and none of the missing patients died.

Data

Patient-level data included the following information: age, sex, PICU and hospital outcomes (survival, death), diagnosis based on data available in the first 24 hours, elective/emergency status, operative status, clinical service of primary responsibility, admission source (same hospital nursing unit, referral hospital nursing unit, home, physician office/clinic), transportation to the hospital by an organized transport system (helicopter, fixed wing, ambulance, none), previous PICU admission during the current hospitalization, cardiac massage before the ICU or hospital admission, and selected critical care modalities used in the first 24 hours of the PICU stay. Admission diagnoses were determined from admission day information.

Physiologic data included the most abnormal values in the first 24 hours of PICU stay. The variables included in the initial data set were either significant or approached statistical significance in previous studies.^{2,12} The data consisted of systolic and diastolic blood pressure, heart rate, respiratory rate, temperature (oral, axillary, or core), coma status, pupillary reactions, pupillary size and equality, sodium, potassium, total CO₂, total and direct bilirubin, total and ionized calcium, glucose, blood urea nitrogen, creatinine, albumin, hemoglobin, leukocyte count, platelet count, prothrombin and partial thromboplastin times, pH and PCO2 (arterial, venous, or capillary), and arterial PO₂ with a simultaneous FiO₂. Whole blood and serum/plasma measurements of sodium, potassium, and glucose were also collected. For variables where both high and low abnormalities may reflect increased mortality risk, we collected both the high and the low values; thus both high and low values of the same physiologic variable could contribute to severity of illness. Heart rate, respiratory rate, and blood pressure were not included at times that crying or iatrogenic agitation was noted. Mental status was included only for children with known acute central nervous system disease, or when acute central nervous system disease resulting from an acute, systemic event (e.g., hypoxia, hypotension) was a possibility. We did not include mental status assessments for the 2 hours after sedatives, paralyzing agents, or anesthetic agents were administered. If patients were sedated or paralyzed during the entire assessment period, the mental status assessment most proximate to PICU admission without sedation, paralysis, or anesthesia was used (usually in the emergency department). Altered mental status was defined as a Glasgow Coma Scale score of less than 8 or a clinical classification of stupor or coma.

We did not include physician-controlled variables such as oxygenation index because variability in care practices can alter the values. Similarly, we excluded variables such as PaO_2/FiO_2 because tracheal FiO₂ is often difficult to determine accurately in patients who are not tracheally intubated.

For patients dying within the first 24 hours of PICU care, physiologic data accumulated during the preterminal period when death was obvious were not included (usually, the last 2 to 4 hours of life). Routinely, at least the last 2 hours of data for these deaths were not considered.

The reliability of the data collection, entry, and verification processes was formally checked by reabstracting a random selection of more than 23 cases from each institution after completion of the initial data collection. The reabstractions were subjected to the identical processes of data entry and verification, and PRISM scores were recalculated. Institutions were included if the intraclass correlation coefficient of reliability¹³ for their abstraction/reabstraction of PRISM scores was more than 0.80. All the initial set of 16 sites met these criteria. The 16 volunteer sites were selected from 18 sites, 2 of which did not meet these criteria and were eliminated.

Statistical Methods

Initially, each of the possible explanatory physiologic variables was independently evaluated for its association with PICU mortality and for determination of clinical and statistical significance of its ranges. This univariate assessment was identical to that used in the first stage of developing the PRISM III-12 and the PRISM III-24 scores.³ First, 11 ranges for each of the continuous physiologic variables (e.g., blood pressure) were determined from the observed percentiles in the survivors (<5%, 5% to 10%, 10% to 20%, 20% to 30%, 30% to 40%, 40% to 60%, 60% to 70%, 70% to 80%, 80% to 90%, 90% to 95%, >95%). Unmeasured variables were assumed to fall in the survivor's 40th to 60th range. Most variables are routinely measured and are all routinely available. In addition, measuring frequencies of these physiologic variables are little affected by institutional practices.¹⁴ The resulting range limits were sometimes adjusted to reflect a similar but more clinically relevant value. For categorical or nominal variables (e.g., pupillary reactivity), categories of abnormality were compared with the normal category.

When normal ranges varied substantially by age, they were adjusted for the following age ranges: 0 to 1 month, 1 to 12 months, 12 to 144 months, and more than 144 months. Age-adjusted variables included systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, blood urea nitrogen, creatinine, albumin, bilirubin, hemoglobin, prothrombin time, partial thromboplastin time, and PaO2. These ranges were used to calculate odds ratios for mortality (mortality odds ratio) by univariate logistic regression analysis. The mid-range of the survivors (40th to 60th percentile) for each of the continuous variables constituted the baseline reference group. That is, the odds ratios were expressed with respect to the mid-range of each variable observed in the survivors.

Second, the odds ratios of neighboring ranges were compared to determine whether the ranges could be combined. Ranges were combined when the coefficient's ρ value was greater than 0.25, when the coefficient was negative, and when coefficient values were similar. Ranges adjacent to the survivor's 40th to 60th percentlies were pooled with the survivors' mid-range, if indicated, and included in the mid-range in subsequent analyses. This process yielded 22 physiologic variables partitioned into 78 ranges, with the importance of each range quantified by the MOR. In this analysis, the MOR reflects a patient' s mortality risk when only the data of a single variable are considered and the risk is referenced to the survivors mid-range.

Third, a multivariate logistic regression analysis was used to reweigh the MORs determined in the univariate analysis.¹⁵ The data set was randomly partitioned into a training sample comprised of 90% of the database from which the predictor was developed and a validation sample of 10%. Stepwise forward and backward variables selection procedures with a variable inclusion criterion ($p \le 0.25$) was applied, and both methods resulted in the same variable selections. The regression coefficients from the final multivariate model were multiplied by 10 times the MOR and rounded to the nearest integer to yield the score for the corresponding physiologic range. The sum of these scores for 59 ranges of 21 physiologic variables is called PRISM III-APS. The overall performance of the model was evaluated by Flora's method of z scores, the calibration of the model performance was evaluated by the Hosmer-Lemeshow χ^2 goodness-of-fit, and the discrimination of the model was evaluated by the area under the receiver operating characteristic curve.¹⁶⁻¹⁸ Goodness-of-fit tests were also performed by age and diagnosis.

RESULTS

Data were collected on 11,165 admissions (543 deaths) in the 32 PICUs. In the first set of 16 randomly selected PICUs, there were 5415 admissions, and in the second set of 16 volunteer PICUs, there were 5750. Data on the characteristics of the sites and patient samples are shown in Table I. The types of PICUs and patient characteristics in each of the ICUs varied widely; mortality rates ranged from 2.2% to 16.4%. Table II shows the descriptive characteristics of survivors and deaths. Deaths were more likely in emergency admissions, nonoperative patients, and in patients who had a previous ICU admission during their current hospitalization.

Initially, univariate analyses identified those physiologic variables and their ranges that significantly contributed to mortality. This resulted in 22 physiologic variables with 78 significant ranges (Table III). The MOR are shown for those variable ranges with statistically significant results in the univariate analysis. Thus MOR reflects severity of illness when the only data known pertain to the specific variable. The variables with the highest MOR (e.g., MOR > 30) included bilateral fixed pupils (MOR = 112.6), lowest systolic blood pressure range (MOR = 60.4), lowest temperature range (MOR = 30.9), and lowest pH range (MOR = 30.1). The variables with the lowest MOR (e.g., MOR < 5) included the highest respiratory rate (MOR = 2.5), highest systolic blood pressure (MOR = 2.8), lowest heart rate (MOR = 3.5), highest total CO₂, (MOR = 2.5), highest hemoglobin (MOR = 2.9), highest leukocyte count (MOR = 4.2), and lowest sodium (MOR = 3.0). Extreme deviations from normal that are



Figure. The Pediatric Risk of Mortality III-Acute Physiology Score (PRISM III-APS).

Table I. Study sites and patient characteristics

Site characteristics		
n	52	
PICU beds (n)	4-40	
Hospital pediatric beds (n)	20-325	
Volume (patients/mo)	. 13-151	
Intensivists (n)	- 25	
Residency programs (n)	28	
Pediatric critical care training programs (n)	8	
Patient characteristics	Total sample	PICUs
Sample size (n)	11,165	110-674
Deaths (n)	543	11-28
Mortality rates (%)	49	2.2-16.4
	a ta i suga na sa ina kan bar 🖓 🖬 🗤 na san dar b	
Age in months (mean)	63.8	44.6-94.3
Age in months (mean) Emergency admissions (%)	63.8 70.3	44.6-94.3 43.4-90.8
Age in months (mean) Emergency admissions (%) Postoperative admissions (%)	63.8 70.3 35.3	44.6-94.3 43.4-90.8 15.9-58.1

Table II. Patient characteristics by outcome

Variable	Survivors	Deaths	Significance level
${f n}$. A subscription of the second sec	10,622	543	
Age in months (mean [SEM])	64.3 (0.7)	53.1 (2.8)	0.0001*
Emergency admissions (n [%])	7,371 (69.4)	481 (88.6)	<0.0001 [†]
Postoperative (n [%])	3,832 (36.1)	113 (20.8)	<0.0001 [†]
Admission from inpatient unit (n [%])	5,414 (51.0)	274 (50.5)	0.826†
Previous PICU admission (n [%])	512 (4.8)	45 (8.3)	0.0008†
⁹ / test. ¹ Fischer's exact test.			

known to indicate severely ill states were not included because the rarity of their occurrence prevents their inclusion in the statistical models.

Multivariate logistic regression analysis using the variables and their ranges selected in the univariate procedure resulted in the PRISM III-APS score with 21 physiologic variables and 59 ranges of these variables (Table IV). The Figure illustrates the relationship of the PRISM III-APS score to mortality. The PRISM III-APS divisions are in increments of at least 5, and each division includes at least 100 admissions. Mortality increases as the PRISM III-APS score increases. Most patients have PRISM III-APS scores less than 10, and these patients have a mortality risk of less than 1%. At the other extreme, the mortality rate of the 137 patients with a PRISM III-APS score of more than 80 was greater than 97%.

Table V summarizes the performance of the PRISM III-APS score for the prediction of death in the training and validation samples. Overall in the total sample. 540.21 deaths were predicted and 543 were observed (p = 0.885). Tables VI and VII show goodness-of-fit tests in the total sample for age and diagnostic groups. For age, the goodness-of-fit test indicates that the overall results are not statistically different than expected. The number of predicted and observed deaths were quite close in all age groups except the 1 month to 12 month group in which 153.47 deaths were predicted and 172 were observed. The number of predicted deaths in the diagnostic groups were statistically different than observed primarily because the nonoperative and operative cardiovascular patients were not accurately calibrated.

The ability to discriminate between survivors and deaths is estimated by the area under the receiver operating characteristic curve and indicates excellent discrimination in the training sample (0.950 \pm 0.007) and very good discrimination in the validation sample (0.902 \pm 0.027).

DISCUSSION

The purpose of this analysis was to develop a measure of physiologic status that might be more sensitive to small changes

Table III. Results of the univariate analysis

Respiratory	rate (br <i>Hiab</i>	eaths/minute)		Blood pressure	systol Low	lic, (mm Hg)	Hiab		Blood press	ure, diastolic <i>Hiab</i>	(mm Hg)
MOR	2.501			MOR 5	.205	14.010	60.407	2.789	MOR	4.915	
N	>100			N 5	1-55	40-50	<40	>125	Ν	>80	
I	>100			1 5	6-65	45-55	<45	>135	1	>95	
C Ā	>80 >60			C 6 A 7	6-75 6-85	55-65 65-75	<55 <65	>150 >190	C A	>100 >110	
Heart rate (beats/mi	inute)	Hiah			Creatinine	(mg/dl) <i>Hiab</i>		BUN (n	ıg/dl) Hiab	
MOR	3.493	2.915	5.214	10,306		MOR	5.644	14.585	MOR	5.768	11.324
N	<75	195-214	215-225	>225		N	0.70-0.85	>0.85	N	12-15	>15
l I	<75	195-214	215-225	>225		1	0.75-0.90	>0.90	L	15-20	>20
C	<55	165-184	185-205	>205		C	0.75-0.90	>0.90	ç	15-20	>20
A	<55	135-144	145-155	>155		A	1.00~1.30	>1.30	A	15-20	>20
Total CO ₂ (i	mmol/L)		Low				High			
MOR		2.421	7.406	15.885		18.594	21.304	2.544			
All ages		17-20	16-14	13-8		7-5	<5	>34			
pH			La) φ				High			
MOR		5.040	9.055	19.979		30.090	4.348	7.633	12.327		
All ages	7	.2-7.28	7.19-7.10	7.09-7.00		<7.00	7.48-7.55	>7.56-7.6	>7.6		
PCO ₂ (mm I	łg)	Higb						PaO ₂ (mm Hg)	Low		
MOR		2.650	4.209	7.766				MOR	4.195	6.261	9.241
All ages		50-60	61-75	>75				All ages	50-60	49-42	<42
Hemoglobin	(gm/L)	an a				Hiab		Platelet count ((cells/mm ³)		
MOR		2.345	3.119	6.869		2.948		MOR	2.604	7.190	11.487
All ages	6	8.0-9.5	7.9-6.0	<6.0		>14		All ages	100-200	99-50	<50
Leukocytes	(cells/m	m ³) Law				Hiab					
MOR		2.282	5.083	13.098		1.711	2.862	4.157			
All ages	4	í.5-6.0	4.4-3.0	<3.0		25-30	>30-40	>40			
Prothrombin	1 time (s	seconds)						Partial thromb	oplastin time (s	econds)	
MOR		нцр 10.453	19.771					MOR	5.259	14.478	
All ages	1	6.5-22	>22					All ages	45-55	>55	
Potassium (mmol/L) ////////////////////////////////////									
MOR		3.646	6.404	10.882		2.263	6.166	8.253			
All ages	4	2.8-3.1	<2.8-2.5	<2.5		5.7-6.3	6.4-6.9	>6.9			
Total calciur	n (mg/d	ll) Zani				Tial					
MOR		3.619	6.923	5.555		5.464	6.109				
All ages	1	7.5-8.0	7.4-6.5	<6.5		10.5-12,0	>12.0				
Glucose (mg	g/dl)	T out									
MOR		3.332	11,928	12.630		17.445	2.312	4.497	8.894	12.787	
All ages		59-50	49-40	39-30		<30	160-200	201-250	251-400	>400	
Sodium (mr	nol/L)							Temperature (i	rectal, oral, blo	od, axillary) (Celsius)
MOD		Low 2 961	High G A10	17.966		년 월 12년 1일 11일 - 11일 - 11일		MOB	Low 20.040	Higb z onr	
		2.701 2130	0.419	17.296 160				Allagaa	00.940 ∠7,7°	0.805 _40°	
n 11 / 1				~100				···· 8803			
rupiis (size	and rea	ctivity) Worst						Coma	Worst		
MOR		3.859	112.550					MOR	19.114		
All ages	ο	ne fixed	Both fixed	an an ann an t-an an an Na t-ann an t-an t-an Na t-ann an t-an t-an t-an				All ages	Stupor/coma		
		>3 mm	<3 mm	renteri				요리에 가지 말했다.	GCS <8	uget (filter fil	

The Mortality Odds Ratios (MORs) indicate the mortality risk relative to the mid-range of survivors when each is considered separately without any additional clinical or laboratory data. Thus the MORs represent the relative importance in outcome determination if that were the only data considered. N, Neonate (0-<1 mo), I, infant (1-<12 mo), C, child (12-144 mo), A, adolescent >144 mo). Table IV. Performance characteristics of PRISM III-APS

No.	of patients (death:	s) AUC (SE)	Flora's z (p)	Log likelihood ratio (df) AIC
PRISM III-APS training	9997 (483)	0.950 (0.007)	0.0 (1.0)	2072.85 (1)	1800.43
PRISM III-APS validation	1168 (60)	0.902 (0.027)	0.507 (0.6122)		

H, Degrees of freedom; SE, standard error; AUC, area under the receiver operating characteristic curve; AIC, Akaike information criterion; log, natural logarithm.

Table V. Goodness-of-fit test for the PRISM III-APS (10,622 survivors, 543 deaths).

	Sury	ivors	Deaths			
Age (mo)	Predicted	Observed	Predicted	Observed		
0-<1	545,74	551	57.26	52		
1-<12	2632.53	2614	153.47	172		
12-<36	2194.73	2203	102.27	94		
36-<72	1491.18	1489	66.82	69		
72-144	1918.66	1915	81.34	85		
>144	1841.95	1850	79.05	71		

Table VI. Goodness-of-fit test for the diagnostic groups using the total sample (10,622 survivors, 543 deaths).

	Surv	ivors	Deaths		
Diagnosis	Predicted	Observed	Predicted	Observed	
Nonoperative cerebro- vascular disease	586.93	561	46.07	72	
Operative cerebro- vascular disease	1002.02	1016	66.98	53	
Central nervous system infections	338.01	340	16.99	15	
Head trauma	1054.26	1050	114.74	119	
Pneumonia	987.25	981	25.75	32	
HIE	62.68	61	17.32	19	
Sepsis	199.99	196	48.01	52	
Miscellaneous	6393.64	6417	204.36		
<i>HIE</i> , Hypoxic ischemic encepha	lopathy.				

Hosmer-Lemeshow χ^2 goodness of fit, 6 degrees of freedom = 24.196, p = 0.0005; Flora's z test: z = 0.145, $\rho = 0.885$.

in physiology, even changes that may not contribute significantly to mortality risk. We anticipate that patient assessments in future studies for issues such as effectiveness of drugs or for other purposes might be more concerned with the changes in physiologic status, even if they are not necessarily related to changes in mortality risk.

Because the development of a score such as this one needs an outcome on

which to calibrate it, we chose mortality because it is clearly related to physiologic status, and the classification of outcome in terms of survival or death is clear. However, in developing this model, we were not concerned with maximizing overall prediction performance for mortality, only in providing sufficient validation data to show that higher scores indicate higher physiologic instability (increased mortality risk). Because we incorporated age in the score by providing ageadjusted variables, we investigated the score's performance for mortality prediction in the various age groups.

Other mortality prediction models have used a variety of other case-mix variables to adjust for nonphysiologic issues, such as diagnosis, chronic health status, and lead-time bias. The PRISM III-12 and the PRISM III-24 models included adjustments for specified diagnosis that reflect both acute diseases and chronic health status, as well as other case-mix variables related to outcome. These adjustments provide additional information that is not accounted for by physiologic status. PRISM III-APS performed worse for nonoperative cardiovascular patients. In our previous PRISM III models, we specifically adjusted for nonoperative cardiovascular patients and also added other adjustments for items such as chromosomal anomalies, also common in this group of patients. Thus it was not surprising that the number of observed and predicted outcomes in the diagnostic distribution did not fit as well as the other PRISM III models. Therefore a PRISM III-APS score in one patient should not be taken to represent the identical mortality risk in another patient with the same score but with different case-mix variables.

Our data do indicate that higher scores indicate more severe physiologic instability. The data also indicate that no age bias is present. However, the current score should not be used in applications such as quality assessment or calculating the mortality risk for individual patients. We recommend other PRISM III models for these calculations because they were developed and calibrated specifically for that purpose and they perform exceptionally well at providing this information.

A by-product of this analysis was the provision of MORs for individual variables. Table III provides odds of dying

THE JOURNAL OF PEDIATRICS Volume 131, Number 4

compared with patients within a "normal" range (the mid-range of survivors). In clinical medicine, we often consider the impact of certain data elements on our estimation of severity of illness. For example, specific components of the neurologic examination have greater prognostic significance than other aspects in the context of head injury, coma, and a variety of antenatal and perinatal conditions.¹⁹⁻²⁵ We have provided relative risks when one variable at a time is considered and within the context of diseases and conditions in our database that were treated. Although this does not directly give clinical risks, it does compare the relative importance of various physiologic derangements and our ability to treat them. Future analysis will attempt to create more clinically relevant clusters of physiologic variables for the estimation of morality risk.

REFERENCES

- Pollack IF. Brain tumors in children. N Engl J Med 1994;331:1500-7.
- Pollack MM, Ruttimann UE, Getson PR. The Pediatric RISk of Mortality (PRISM) Score. Crit Care Med 1988;16:1110-6.
- Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated pediatric risk of mortality score. Crit Care Med 1996;24:743-52.
- Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system: risk prediction of hospital mortality for critically ill hospitalized adults. Chest 1991;100:1619-36.

- Richardson DK, Gray JE, McCormick MC, Workman K, Goldmann DA. Score for neonatal physiology: a physiologic severity index for neonatal intensive care. Pediatrics 1993;91:617-23.
- Tarnow-Mordi W, Ogston S, Wilkinson AR, et al. Predicting death from initial disease severity in very low birth weight infants: a method for comparing the performance of neonatal units. BMJ 1990;300:1611-4.
- Lemeshow S, Teres D, Klar J, Avrunin JS, Gehlbach SH, Rapoport J. Mortality probability models (MPM II) based on an international cohort of intensive care unit patients. JAMA 1993;270:2478-86.
- Le Gall JR, Lemeshow S, Leleu G, et al. Customized probability models for early severe sepsis in adult intensive care patients: intensive care unit scoring group. JAMA 1995;22:644-50.
- Ruttimann UE, Pollack MM. Severity of illness adjusted length of stay. J Pediatrics 1996;128:35-44.
- Pollack MM, Cuerdon TC, Patel KM, Ruttimann UE, Geston PR, Levetown M. Impact of quality-of-care factors on pediatric intensive care unit mortality. JAMA 1994; 272:941-6.
- Pollack MM, Cuerdon TC, Getson PR. Pediatric intensive care units: results of a national study. Crit Care Med 1993;21:607-14.
- Pollack MM, Ruttimann UE, Getson PR, et al. Accurate prediction of pediatric intensive care outcome: a new quantitative method. N Engl J Med 1987;316:134-9.
- Fleiss JL. The design and analysis of clinical experiments. New York: John Wiley; 1986. p 2-3.
- Pollack MM, Patel KM, Ruttimann UE, Cuerdon T. Frequency of variable measurement in 16 pediatric ICUs: influence on ac-

curacy and the potential for bias in severity of illness assessment. Crit Care Med 1996; 24:74-7.

- SAS/STAT users guide, Version 6. 4th ed., Vol. 2. Cary, NC: SAS Institute; 1995. p. 1071-126.
- Hosmer DW, Lemeshow S. Applied logistic regression. New York: John Wiley; 1989. p. 14-15, 141.
- Flora JD. A method for comparing survival of a burn patient to a standard survival curve. J Trauma 1978;18:701-5.
- Ruttimann UE. Statistical approaches to development and validation of predictive instruments. Crit Care Clin 1994;10:19-35.
- Hahn YS, Chyung C, Barthel MJ, et al. Head injuries in children under 36 months of age: demography and outcome. Child Nerv Syst 1988;4:34-40.
- Kalff R, Kocks W, Pospiech J, Grote W. Clinical outcome after head injury in children. Child Nerv Syst 1989;5:156-9.
- Seshia SS, Johnson B, Kasian G. Non-traumatic coma. Dev Med Child Neurol 1983; 25:493-501.
- Margolis LH, Shaywitz BA. The outcome of prolonged coma in childhood. Pediatrics 1980;65:477-81.
- Luerssen TG, Klauber MR, Marshall LF. Outcome from head injury related to patient's age. J Neurosurg 1988;68:409-16.
- Holst K, Andersen E, Philip J, Henningsen I. Antenatal and perinatal conditions correlated to handicap among 4-year-old children. Am J Perinatol 1989;6:258-67.
- 25. van de Bor M, van Zeben-van der Aa TM, Verloove-Vanhorick SP, Brand R, Ruys JH. Hyperbilirubinemia in preterm infants and neurodevelopmental outcome at 2 years of age. Pediatrics 1989;83:915-20.