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William J. Sacco, et al

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August 1975

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EDGEWOOD ARSENAL TECHNICAL REPORT

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RESEARCH ON TRAUMA INDICES

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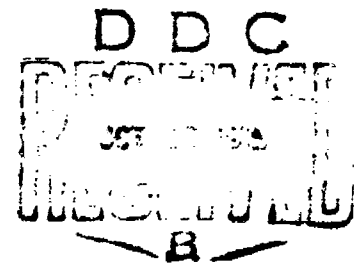
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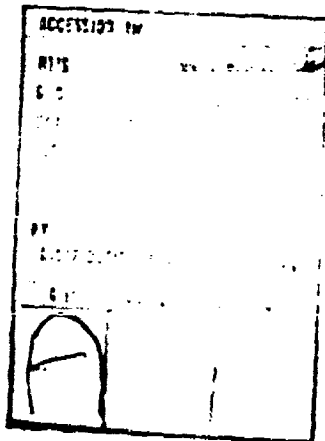
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20. ABSTRACT (Contd)

rates where the predictions were based on the curves derived in the retrospective study; construction of probability of death curves for combined retrospective and prospective data sets; analysis of sepsis variables and variables of hepatic dysfunction; and several characterizations of therapy. New rationales for *Patient Triage* and *Evaluation of Care* were introduced.

These indices are merely numbers which may be related to a probability of survival using current therapeutic techniques. They are not to be interpreted as a "death sentence;" but rather as a challenge to trauma specialists to extend the boundaries of efficacious therapy. Their purpose "at the bedside" is to augment, not to replace, the traditional precepts of history and clinical examinations.

PREFACE

The work described in this report was authorized under Project 3A162110A821, Combat Surgery. This work was started in April 1974 and completed in March 1975.

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RESEARCH ON TRAUMA INDICES

I. INTRODUCTION.

The effort to refine our objective assessment of the severity of a patient's illness is important for several reasons: (1) for epidemiological studies; (2) to compare incidence, management, and therapeutic results from center to center and within a center; and (3) to make more accurate prognoses for individual patients. In an effort supported by Army funding (1972 to 1974), a number of systems analyses and pattern recognition techniques were used to determine physiological and biochemical *profiles* which characterized post-traumatic states. Participating in the study were the Biophysics Division, Edgewood Arsenal, Maryland; the Maryland Institute for Emergency Medicine (MIEM), Baltimore, Maryland; and the US Army Materiel Systems Analysis Activity (AMSAA), Aberdeen Proving Ground, Maryland.

In April 1974, support was provided by the Office of the Surgeon General to validate the existing indices, using additional retrospective and prospective data, and to attempt to develop additional indices for characterizing the severity of acute trauma, sepsis, and the liver dysfunction. This paper gives the results of that study.

II. BACKGROUND.

The study of shock and trauma has both military and civilian applications. One of the foremost is to gain knowledge leading to improved therapy for severely injured patients. Studies of World War II, Korea, and Vietnam casualties have revealed that hemorrhagic shock was the primary cause of death in 36% to 68% of all battle fatalities. The establishment of a special trauma unit at William Beaumont Hospital, Fort Bliss, Texas, indicated the Army's special interest in the treatment of acute trauma. The organization of shock-trauma centers, such as the MIEM, reflects the civilian need to treat severely injured patients. The Maryland Institute for Emergency Medicine treats about 1000 patients each year. Similar units are being established throughout the country.

A systems study of quantitation of injury was undertaken early in 1972 by the Biophysics Division, the MIEM, and the AMSAA. The MIEM data bank contained clinical, cardiovascular, metabolic, and therapeutic information on more than 1500 patients. This data bank has been duplicated at the Biophysics Division, and a computer retrieval program for the UNIVAC 1108 was written to give easy access to the data.

The initial objectives of the study were: to specify profiles of physiological and biochemical measurements which would indicate the severity of a patient's illness by defining good and poor *prognosis regions* in the *profile space*; and to describe and evaluate the change in the patient's *state* with time.

Using medical guidance supplied by clinicians from the MIEM and the Biophysics Division, a pattern recognition analysis was done on a data set consisting of initial and final measurements of 60 physiological and biochemical variables from over 500 patients. Each of the variables and many combinations (profiles) of variables were correlated with mortality. Probabilities of survival were computed for regions of *profile space*, and the time courses of patients were followed in this space. The results of these initial studies were promising.¹

With the completion of the computer retrieval program, data from many time periods became available for each patient. The course of each patient is then characterized by a set of variables (profile) whose values may change rapidly with time as the patient's condition improves or deteriorates. In attempting to discriminate survivors from nonsurvivors, we were confronted with a *nonstationary* discrimination problem. In mathematical terms this means that the probability density functions which characterize the survivors and nonsurvivors are time varying because they depend on the patient's changing condition. At this time we chose, for most of our analyses, to characterize patients by the notion of derangement, or *distance from normality*,² which traditionally has been a qualitative guide for clinicians. Using data available on several hundred patients, four indices were evolved, three of which are distances: the CHOP index, the renal index, and the SHAP index. The CHOP index is based on serum creatinine, hematocrit, serum osmolality, and systolic blood pressure. The SHAP index is based on admission values

of serum sodium, hematocrit, arterial pH, and systolic blood pressure. These three indices, along with a respiratory index, have been correlated with patient mortality and are used, individually and in combination, to track the state of the patients.

III. ORGANIZATION OF THE RESULTS.

This paper has two parts: retrospective and prospective. In the retrospective study the values of the CHOP index, renal index, respiratory index, SHAP index, acute trauma index, and a combined CHOP and respiratory index are presented in tabular and graphic forms which relate the index values to mortality (expressed as probability of death). The probability curves are based on a mathematical model which permits the inclusion of other variables such as age, sex, and type of hospital admission. These are discussed at some length in section IV.B.

An analysis is made of *sepsis variables*, but no index is suggested by the data.

The results of the prospective study of 237 patients include:

1. A comparison of predicted average death rates and actual death rates. The predictions were based on the curves derived in the retrospective study.
2. Probability of death curves for combined retrospective and prospective data sets.
3. An analysis of sepsis variables and variables of hepatic dysfunction.
4. Several characterizations of therapy.

IV. RETROSPECTIVE STUDY.

A. Patient Material.

The patients discussed here were all treated at the MIEM. Most patients were trauma victims who were transported to the MIEM by helicopter from the scene of the accident between March 1971 and October 1972.

The patients studied for the CHOP index, renal index, and sepsis consisted of a heterogeneous group of 751 consecutive patients. These included 21 burned patients (of which 8 or more were third degree), 38 elective surgical patients, 98 patients with critical medical problems, and 594 patients with severe multiple system injuries. In the last group, 163 had central nervous system (CN) injury, 201 had thoracic injury, 141 had abdominal injury, 111 had musculoskeletal injury, and 80 had head injury; and many of course had combinations of these.

The acute trauma index was based on 360 consecutive direct admission patients from the above group of 151 patients.

The respiratory index was investigated in 177 consecutive intubated and ventilated patients from the group of 751 mentioned above.

For the CNS study, data from 944 patients were available. Of these patients, 321 sustained central nervous injuries which are specified in table 1. The diagnoses given are all the diagnoses for all of these patients; therefore, a patient may have more than one diagnosis.

Eighty-three of the 321 patients with CNS injury (25.8%) had sufficient data available for analysis. They are among the patients listed in table 1 in the column labeled "patients studied."

A diagnosis of brain stem contusion was assigned to a patient with a consciousness level of stupor or worse with decerebrate or decorticate posturing that was either spontaneous or in response to pain.

Table 1. Diagnoses and Mortality on 321 Patients Sustaining CNS Injury

Diagnosis	Number of patients		Mortality for group %
	Total	Studied	
Concussion (treatment)	101	-	2
Cerebral contusion			
Mild (24 hours or less)	39	-	5
Moderate (24 to 72 hours)	20	-	5
Severe (more than 72 hours)	49	43	55
Brain stem contusion	24	20	50
Cerebral laceration	12	9	33
Hematoma			
Intracerebral	8	7	50
Epidural, acute	8	8	50
Subdural, acute	26	21	67
Gunshot wound to brain	16	12	87
Spinal cord injury	32	-	25
Severe intracranial injury; brain dead on admission	31	-	100

NOTE: Duration of unconsciousness is shown in parentheses.

Severe cerebral contusion was defined as stupor or worse, for a period of 72 hours or more, with or without evidence of increased intracranial pressure. This diagnosis was also made frequently in association with intracranial hematomas at the time of surgery when the cortex was visualized to be severely contused. No patient who was "brain dead" on admission was included in the study.

B. Methods.

1. Indices.

The CHOP index is based on four variables: serum creatinine (C), hematocrit (H), serum osmolality (O), and systolic blood pressure (P). It is the square root of the sum of the squares of the deviations (measured in standard deviation units) from *normal* average values of the four variables; that is,

$$\text{CHOP index} = \sqrt{\left(\frac{C-1.0}{0.5}\right)^2 + \left(\frac{H-37.0}{6.0}\right)^2 + \left(\frac{O-292.0}{15.0}\right)^2 + \left(\frac{P-127.0}{21.0}\right)^2}$$

In mathematics, this quantity is called the *Euclidean distance* and reflects the difference between an *actual* patient's state and a *desired* patient's state. In each of the squared terms in the sum under the radical, the number in the numerator is the estimated normal average value of the variable; and the number in the denominator is the estimated standard deviation of that variable. For example, 37.0 is the average for hematocrit (H) and 6.0 is the standard deviation. These estimates of the averages and standard deviations were obtained from final recorded values from 350 survivors.

Admission and daily CHOP index values were obtained on each patient. The highest value was correlated with patient mortality.

The parameters for the study of renal function were the blood urea nitrogen (BUN), the serum creatinine, and the hourly urine volume. Admission and daily measurements were made of the serum creatinine and the BUN. Each patient's 12-hour urine volume was measured and converted to a normalized value called Urine Vol_N, as shown in table 2. The daily values of the above parameters were used to compute an index of renal function using the formula:

$$\text{Renal index} = 1/3 (\text{Cr}_N + \text{BUN}_N + \text{Uring Vol}_N)$$

Cr_N was calculated from the difference between the measured creatinine value and the mean value for survivors, and dividing this difference by the standard deviation of the creatinine level in the survivors. The BUN_N was calculated in the same way. (More details are given elsewhere.)^{3,4} The renal index was computed for each day, and the highest value was correlated with patient mortality.

A respiratory index was computed at least four times a day for each patient. It was computed by the formula:

$$\text{Respiratory index} = \frac{\left[(P_B - P_{\text{H}_2\text{O}^T}) F_{\text{I}\text{O}_2} - P_{\text{a}\text{CO}_2} \right] - P_{\text{a}\text{O}_2}}{P_{\text{a}\text{O}_2}}$$

where

P_B = barometric pressure

$P_{\text{H}_2\text{O}^T}$ = alveolar water vapor pressure at the patient's temperature T (approximately 47 mm Hg)

$F_{\text{I}\text{O}_2}$ = fractional concentration of O₂ in inspired gas

$P_{\text{a}\text{CO}_2}$ = arterial partial pressure of carbon dioxide. In this formula we assume it to be equal to the alveolar partial pressure of the carbon dioxide

$P_{\text{a}\text{O}_2}$ = arterial partial pressure of oxygen

(More details are given elsewhere.)⁵ For each patient the highest value of the respiratory index was correlated with mortality.

Table 2. Relation of Urine Vol_N to Urine Volume Produced by Patient

Average urine volume per hour over 12 hours	Urine Vol _N
ml	
> 50	0
31-50	1
21-30	2
16-20	3
11-15	4
0-10	5

On the basis of a previous study,⁶ two *decision rules* were derived for predicting mortality in patients with CNS injuries. The rules were based on measurements of consciousness level, serum osmolality, intracranial pressure, and the SHAP index which is composed, as earlier stated, of admission values of serum sodium (S), hematocrit (H), arterial pH (A), and systolic blood pressure (P). The SHAP index, like the CHOP index, is a *distance from normality*, computed by the formula:

$$\text{SHAP index} = \sqrt{\left(\frac{S-137}{6.21}\right)^2 + \left(\frac{H-36.9}{5.96}\right)^2 + \left(\frac{A-7.46}{0.065}\right)^2 + \left(\frac{P-127}{21.0}\right)^2}$$

For each patient the admission value was correlated to mortality. As in the CHOP index, the numbers in the numerators and denominators are averages and standard deviations.

The acute trauma index, like CHOP and SHAP, is a *Euclidean distance*. It is based on admission values of systolic blood pressure (P), hematocrit (H), arterial pH (A), and prothrombin time (T), all of which respond soon after trauma. It has the form

$$\text{Acute trauma index} = \sqrt{\left(\frac{P-127}{21.0}\right)^2 + \left(\frac{H-36.9}{5.96}\right)^2 + \left(\frac{A-7.46}{0.065}\right)^2 + \left(\frac{T-13.0}{2.0}\right)^2}$$

This index is used to provide a characterization of a patient at the time of admission.

For each patient the admission value was correlated to mortality. Each index was related to probability of death in two formats: tabular and graphic. The tabular format assigns a probability of death to each of several intervals of values of the index. The calculation takes into account the a priori probability of death associated with the respective patient group.

The graphical format consists of the probability of death curves obtained by fitting the data to a logistic model of the form

$$P_D(X|\beta) = \frac{1}{1 + e^{-A}}$$

where

$P_D(X|\beta)$ = the probability of death

$$A = \beta_1 + \beta_2 x_2 + \dots + \beta_n x_n$$

$X = (1, x_2, \dots, x_n)$ is a vector of measurement variables

and

$\beta = (\beta_1, \dots, \beta_n)$ is a vector of weights (coefficients) associated with the measurement variables

The measurement variables may be physiological or biochemical variables, various indices, age, and they may also include *indicator* variables for sex (say 1 for males and 2 for females), and type of hospital admission. The weights (β 's) are obtained here by the Walker-Duncan regression algorithm which produces approximate maximum likelihood estimates.⁷ In the regression calculation, the dependent variable $P_D(X|\beta)$ used in estimating the β 's is assigned a zero if the patient lives or a 1 if the patient dies.

The mathematical model chosen to represent the data is one of several closely related sigmoid curves frequently encountered in this context. A test of the significance of the fits, or appropriateness of the model, was made in the following manner. At each data vector X we presume that we have a binomial experiment in which we obtain a response ($y=1$) with probability (p) or no response ($y=0$) with probability ($1-p$). We then obtain an estimate

p^* of p by fitting the reduced model $p^* = \frac{1}{1 + e^{-\beta_1}}$. This is the same for all vectors X . We then obtain another estimate

\hat{p} of p by using the full model; that is

$$\hat{p} = \frac{1}{1 + e^{-(\beta_1 + \beta_2 x_2 + \dots + \beta_n x_n)}}$$

and compute the likelihood ratio

$$\lambda = \frac{\prod_{i=1}^N (p^*)^{y_i} (1-p^*)^{(1-y_i)}}{\prod_{i=1}^N (\hat{p}_i)^{y_i} (1-\hat{p}_i)^{(1-y_i)}}$$

where N is the number of datum values

If our estimates for the full model are, in fact, the maximum likelihood estimates, then the statistic $L^* = 2 \ln \lambda$ is distributed as $\chi^2(n-1)$ and is a test of the hypothesis H_A : some $\beta_i \neq 0$; $i=2, \dots, n$, versus the null hypothesis $H_0: \beta_2 = \dots = \beta_n = 0$. If the likelihood under the full model is less than the maximum likelihood estimate, we have a conservative test; that is, we will tend not to reject H_0 when we should. Each of the curves appearing in this paper were such that H_0 was resoundingly rejected ($p < .0001$), indicating that the model represents the data very well. Approximate 95% confidence bounds on each curve were also computed (see appendix); the maximum average width of the bands was about 0.12. The acid test of the model came in using it for prediction, and those results are indicated below.

In addition to computing probabilities of death for the indices, we also computed a quantity called *information gain*. Information gain is a number which measures the *predictive power* of an index and has a simple clinical interpretation. It is interpreted as the average amount by which one would alter the prognoses of a patient group based on given values of an index. Mathematically the information gain is written

$$\sum_{I=1}^n |P_D - P(D|I)| P(I)$$

where

P_D is the a priori probability of death

$P(D|I)$ is the probability that a patient will die given that the index takes on a value in the interval I

$P(I)$ is the probability that the index takes on a value in I

The range of values of the index is divided into n intervals for the calculation. The maximum value of the information gain, which is 0.50, would be obtained if an index were a *perfect* discriminator in a treatment facility where the death rate was 50%.

2. Sepsis Variables.

The sepsis variables selected for analysis were temperature and white blood count. Means and standard deviations were computed (for survivors and nonsurvivors) for peak (maximum) values and for least (minimum) values. Information gains and probability of death tables were computed for peak and least values.

C. Results.

1. Indices.

Probabilities of death for various indices are given in table 3 for peak values and in table 4 for admission values. Table 5 gives information gains for various indices. Probability of death curves for the peak (maximum) values of the CHOP index, renal index, respiratory index, and the admission value of the acute trauma index appear in figures 1 through 4. The logistic model for these calculations reduces to $P_D(X|\beta) = \frac{1}{1+e^{-(\beta_1+\beta_2x_2)}}$. It possesses two coefficients, a constant term β_1 , and β_2 , which is the coefficient of the index value, x_2 .

The coefficients for the curves of figures 1 through 4 appear in table 6 together with coefficients for models which account for age, sex, and type of hospital admission (direct or referral). Also in table 6 are the coefficients for a model which considers the CHOP index and the respiratory index simultaneously.

Table 3. Peak Values of Various Indices Related to Probability of Death (P_D) of Patients Studied

Renal index					
Direct admission patients		Referral patients		Total patient set	
235 Lived	28 Died	202 Lived	81 Died	437 Lived	109 Died
Index value	P_D	Index value	P_D	Index value	P_D
0-0.99	0.07	0-0.99	0.11	0-1.99	0.15
1.0-1.99	0.23	1.0-1.99	0.24	2.0-2.99	0.62
> 2.0	0.29	2.0-2.99	0.80	> 3.0	0.92

CHOP index					
Direct admission patients		Referral patients		Patient surviving at least 1 day	
333 Lived	49 Died	238 Lived	105 Died	528 Lived	106 Died
Index value	P_D	Index value	P_D	Index value	P_D
0-1.99	0.06	0-1.99	0.05	0-1.99	0.01
2.0-2.99	0.09	2.0-2.99	0.13	1.0-2.99	0.03
3.0-3.99	0.08	3.0-3.99	0.35	3.0-3.99	0.09
4.0-4.99	0.34	4.0-4.99	0.40	4.0-4.99	0.23
5.0-5.99	0.40	5.0-5.99	0.58	5.0-5.99	0.58
> 6.0	0.71	> 6.0	0.87	> 6.0	0.86

Respiratory index	
177 Consecutive intubated patients	
Index value	P_D
0-0.99	0.05
1.0-1.99	0.20
2.0-2.99	0.27
3.0-3.99	0.27
4.0-4.99	0.36
> 5.0	0.74
> 6.0	0.88

Table 4. Admission Values of Various Indices Related to Probability of Death (P_D) of Patients Studied

Probabilities of Death			
Renal index		CHOP index	
Referral patients		Referral patients	
197 Lived	77 Died	220 Lived	86 Died
Index value	P_D	Index value	P_D
0-0.99	0.24	0-1.99	0.15
1.0-1.99	0.23	2.0-2.99	0.27
≥ 2.0	0.75	≥ 3.0	0.51
SHAP index		Acute trauma index	
Serious CNS patients		Direct admission patients	
49 Lived	37 Died	310 Lived	50 Died
Index value	P_D	Index value	P_D
0-0.99	0.23	0-1.99	0.06
1.0-1.99	0.41	2.0-2.99	0.13
2.0-3.49	0.45	3.0-3.99	0.20
≥ 3.5	0.85	≥ 4.0	0.65

Table 5. Information Gains for Various Indices

Index	Information gain
<u>Renal index</u>	
Peak: direct admission	0.07
Peak: referrals	0.23
Peak: total patients	0.15
<u>CHOP index</u>	
Peak: direct admission	0.09
Peak: referrals	0.23
Peak: total patients	0.18
<u>Respiratory index</u>	
Peak: 177 consecutive intubated patients	0.20
<u>SHAP index</u>	
Admission: serious CNS patients	0.15
<u>Acute trauma index</u>	
Admission: direct admission	0.15

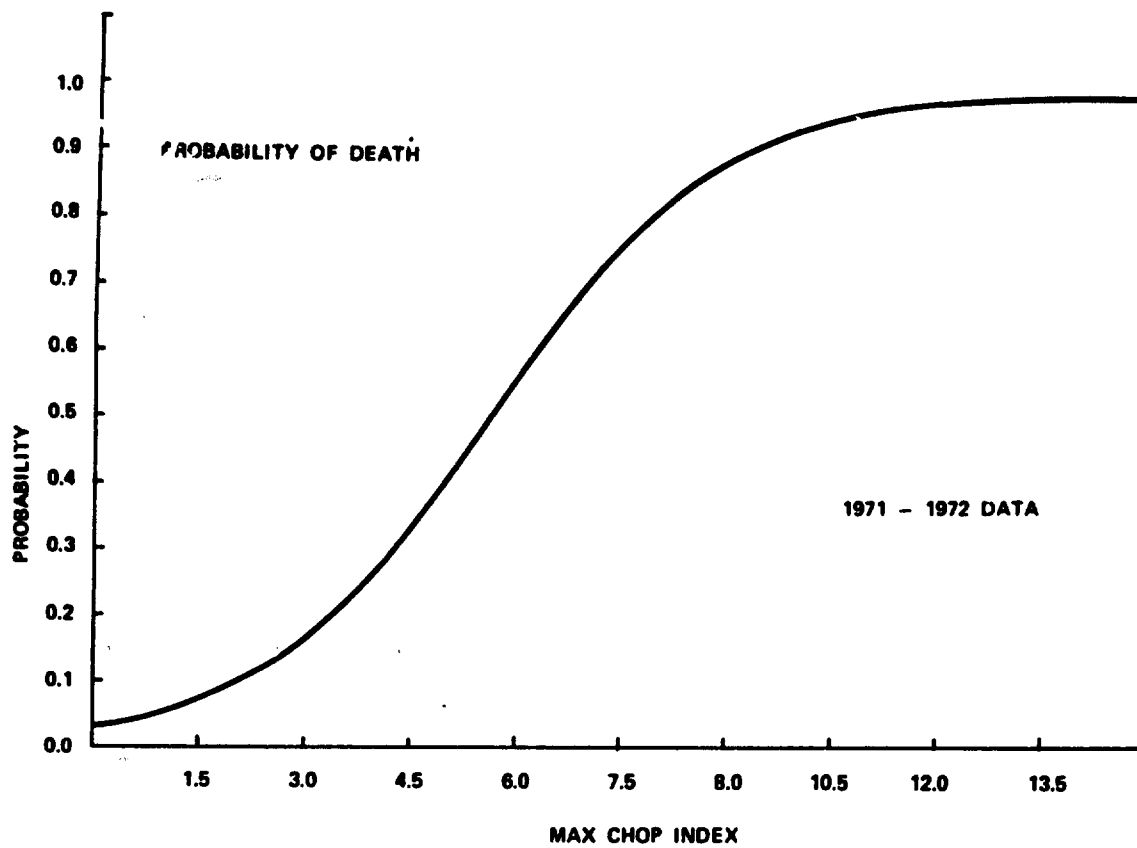


Figure 1. Probability of Death Curve for the CHOP Index

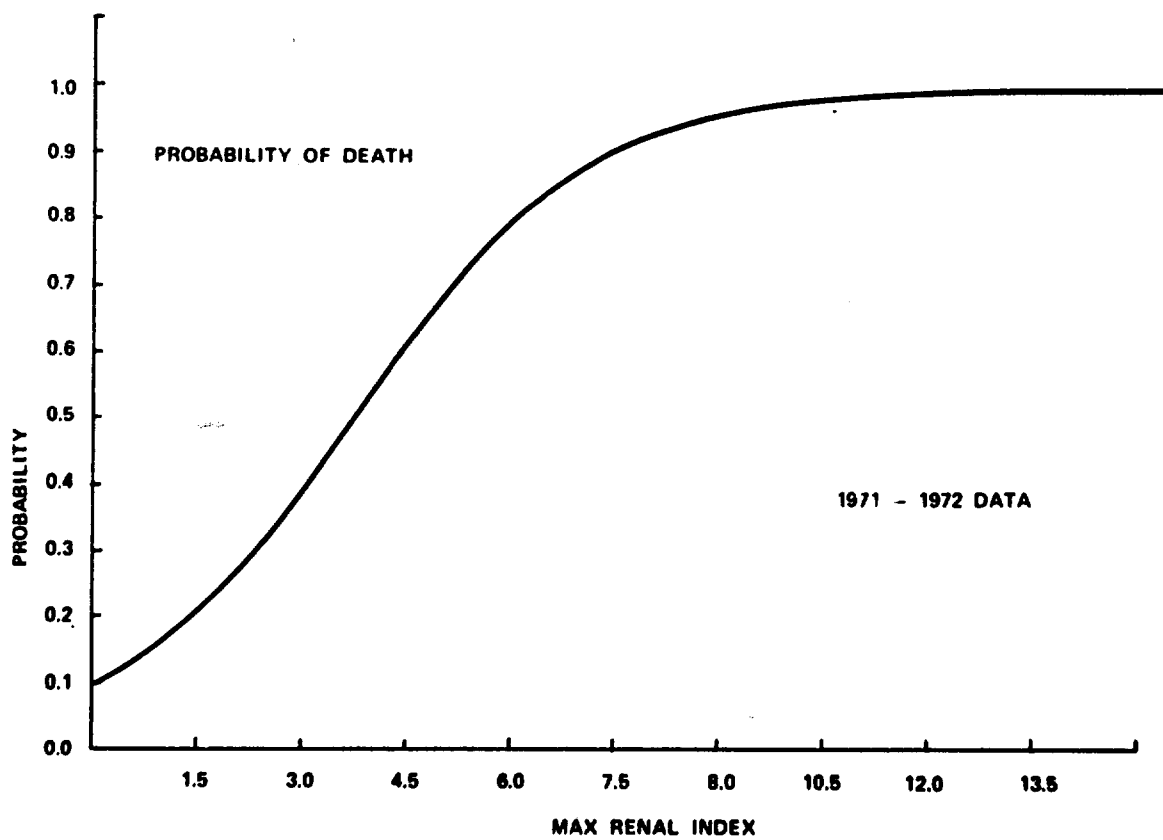


Figure 2. Probability of Death Curve for the Renal Index

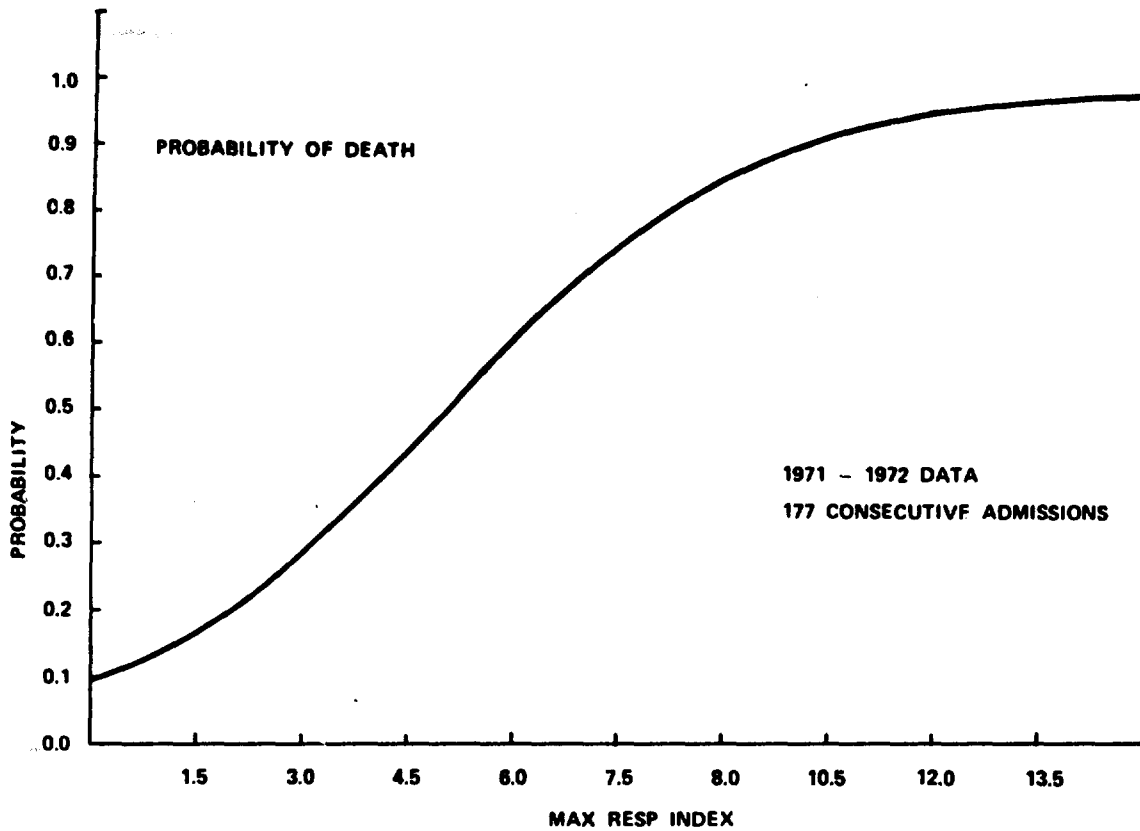


Figure 3. Probability of Death Curve for the Respiratory Index

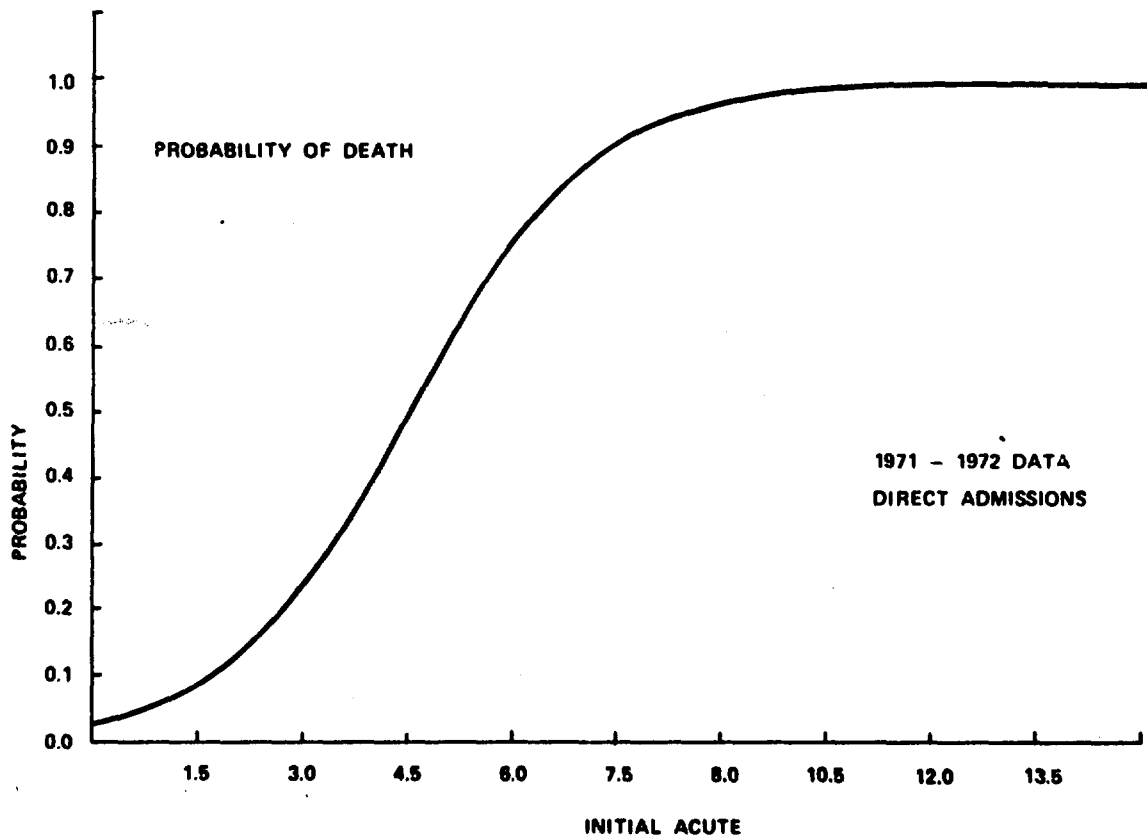


Figure 4. Probability of Death Curve for the Acute Trauma Index

Table 6. Logistic Model Coefficients for Various Indices and Parameters for 1971 and 1972 Data

Index	Constant term	Coefficients			
		Age	Sex	Admission	Index
	β_1				
Maximum CHOP	-3.43				0.607
Maximum CHOP	-4.42	0.009	0.030	0.387	0.613
Maximum renal	-2.25				0.594
Maximum renal	-3.30	0.017	-0.082	0.368	0.581
Maximum respiratory	-2.26				0.443
Maximum respiratory	-3.47	-0.0004	0.096	0.629	0.445
Maximum CHOP and maximum respiratory	-4.32				CHOP: 0.523 RESP: 0.361
Admission acute	-3.51				0.766
Admission acute	-3.51	0.009	-0.168		0.732

A *generalized probability curve* (figure 5) can be used with table 6 to compute probabilities of death for models involving more than two coefficients. The abscissa of the graph in figure 5 is $A = \beta \cdot X = \beta_1 + \beta_2 x_2 + \dots + \beta_n x_n$. Given the coefficients (β_i 's) for a specific example from table 6 and the patient's age, sex, type of admission, and index value, one may compute $\beta \cdot X$ and identify the corresponding probability of death from figure 5. In our application of the model

$$x_2 = \text{age in years}$$

$$x_3 = 1 \text{ for males; } 2 \text{ for females}$$

$$x_4 = 1 \text{ for direct admission; } 2 \text{ for referral}$$

$$x_5 = \text{value of the index}$$

As a specific example, for a 40-year old female referral patient whose maximum renal index is 4.0, we have $x_2 = 40$, $x_3 = 2$, $x_4 = 2$, $x_5 = 4.0$. From table 6 we take $\beta_1 = -3.30$, $\beta_2 = 0.017$, $\beta_3 = -0.082$, $\beta_4 = 0.368$, and $\beta_5 = 0.581$. We compute

$$\begin{aligned} A = \beta \cdot X &= \beta_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \beta_5 x_5 \\ &= -3.30 + (0.017)40 + (-0.082)2 + (0.368)2 + (0.581)4.0 \\ &= 0.272 \end{aligned}$$

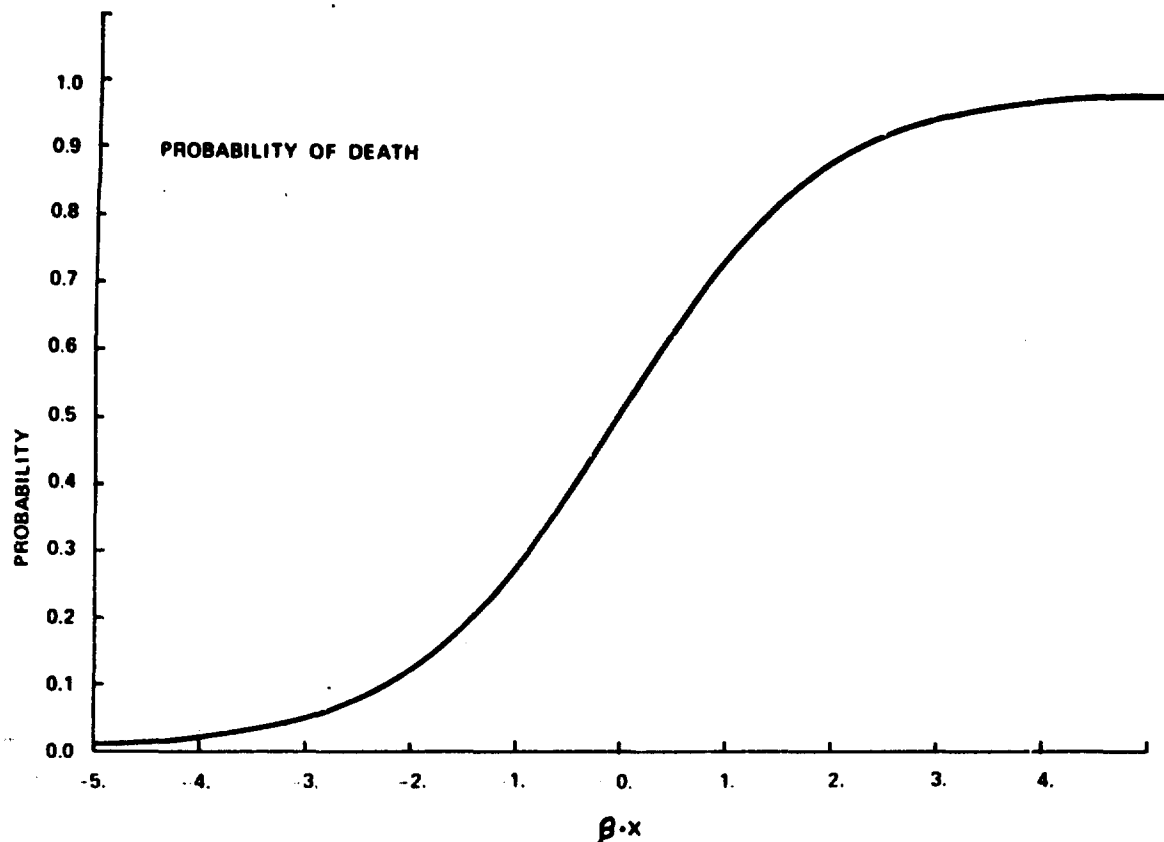


Figure 5. Generalized Probability of Death Curve

The corresponding probability of death read from figure 5 is approximately 0.55. For this example it is interesting to observe from figure 2 that a peak renal index value of 4.0 gives approximately the same probability of death of 0.55.

2. Combined Analysis of the CHOP Index and the Respiratory Index.

Prognosis regions were specified in the space determined by the CHOP index and the respiratory index for the same set of 177 consecutive intubated and ventilated patients used in the study of the respiratory index. More details of this study are given elsewhere.*

3. Analysis of Sepsis.

Temperature and white blood count statistics and probability tables were computed for the 751 patient data set. Means and standard deviations for peak (maximum) values and least (minimum) values appear in table 7 for survivors and nonsurvivors, together with tables of the probability of death.

*Sacco, W., Goldfarb, M., Weinstein, M., Ciurej, T., Cowley, R., Champlon, H., Long, W., Gill, W., and McAslan, T. Two Prognostic Indices for the Trauma Patient. Forthcoming Edgewood Arsenal Technical Report. (See figure 3.)

Table 7. Temperature and WBC Statistics for the 751 Patient Data Set

Statistic	Temperature		White blood count	
	Peak values	Least values	Peak values	Least values
Mean (live)	101.2	98.3	18,100	9,500
Mean (die)	101.8	96.1	22,100	10,200
Standard deviation (live)	1.7	1.5	7,825	4,060
Standard deviation (die)	2.8	2.3	8,510	6,540
Information gain	0.09	0.13	0.06	0.04

Probabilities of Death

Peak temperature		Least temperature	
Value	P _D	Value	P _D
<97.0	1.00	<97.0	0.52
97.1-103.0	0.10	97.1-101.0	0.10
103.1-105.0	0.30	>101.0	0.11
>105.0	0.54		

V. PROSPECTIVE STUDY.

A. Patient Material.

Data were collected on 237 patients (193 survivors, 44 nonsurvivors) treated at the MIEM during the period 1 May through 1 October 1974. In the remainder of this report this data set will be called the New Patient Data. Daily values were obtained of arterial pCO₂, pO₂, and pH, fractional concentration of inspired oxygen, systolic blood pressure, hematocrit, prothrombin time, serum creatinine, serum osmolality, blood urea nitrogen, serum sodium, temperature, white blood count, consciousness level, intracranial pressure, and hourly values of urine volume. For patients with liver injuries, daily values of bilirubin, LDH, SGOT, SGGT, and alkaline phosphatase were obtained.

B. Methods and Results.

1. Indices Other Than the SHAP Index.

Admission index values were computed for all of the indices and daily index values were computed for the CHOP index, the renal index, and the respiratory index. Expected death rates were computed for the new patient data using the probability of death curves based on the retrospective data (figures 1 through 4). These *predicted* outcomes are compared with actual death rates in table 8.

**Table 8. Predicted Expected Deaths (for Patients Studied Prospectively)
Compared with Actual Deaths for Various Indices**

Index	Number of patients (lived)	Number of patients (died)	Predicted expected number of deaths
Admission acute	178	39	46
Admission acute (age, sex)	170	39	44
Peak respiratory	196	41	43
Peak respiratory (age, sex, admission)	154	39	35
Peak CHOP	176	40	50
Peak CHOP (age, sex, admission)	156	39	51
Peak renal	161	41	41
Peak renal (age, sex, admission)	143	40	38

NOTE: The predictions were based on probability of death curves determined from 1971 and 1972 data.

Both data sets (new and retrospective) were combined to obtain new probability curves which appear in figures 6 through 9. The coefficients for these curves, together with coefficients for models which account for age, sex, and type of hospital admission, appear in table 9.

2. SHAP Index.

The patients in this study were selected by the same criteria as those in the retrospective CNS study. There were 34 such patients, 14 of whom survived. The admission values of the SHAP index were combined with the retrospective data to obtain probabilities of death (table 10).

3. Analysis of Sepsis Variables.

Temperature and white blood count statistics and probability tables were computed for the New Patient Data. Means and standard deviations for peak (maximum) values and least (minimum) values appear in table 11 for survivors and nonsurvivors. The probabilities of death correspond closely to the values computed from the retrospective data and hence are not included here.

4. Liver Study.

The patients in this study were those who experienced trauma involving the liver parenchyma and whose daily measurements of bilirubin subsequently exceeded a value of 3. Bilirubin, LDH, SGOT, SGGT, and alkaline phosphatase were measured daily. There were 52 such patients, 41 of whom survived. Means, standard deviations, and frequency of occurrence of measurements for different intervals appear in tables 12 and 13, for peak values of each of the parameters. We felt that the sample size was too small to warrant calculation of probabilities of death.

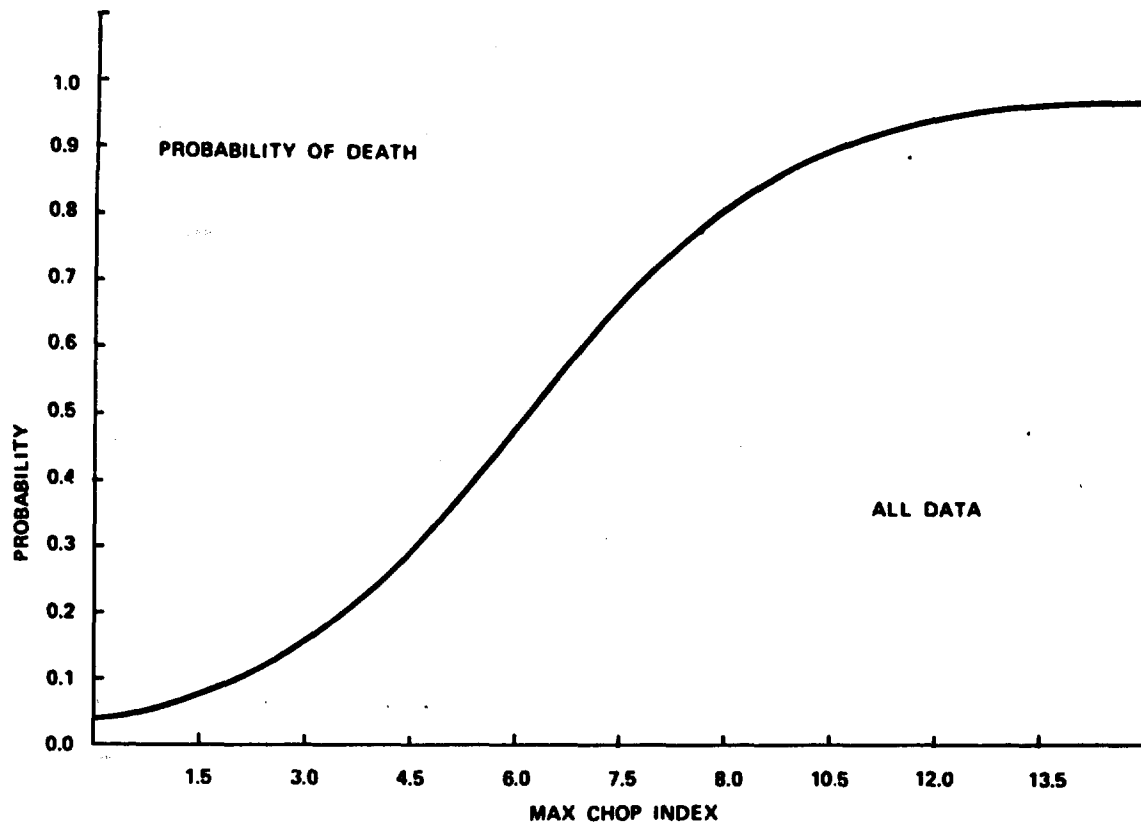


Figure 6. Probability of Death Curve for the CHOP Index

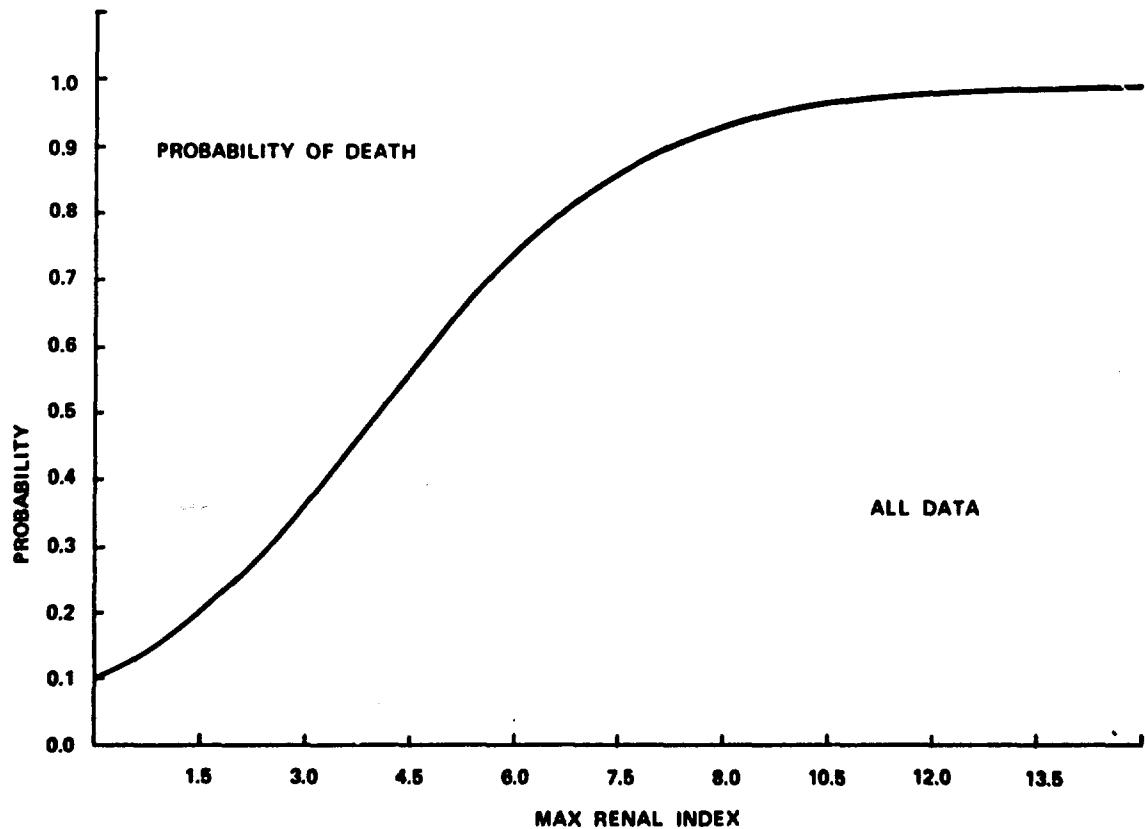


Figure 7. Probability of Death Curve for the Renal Index

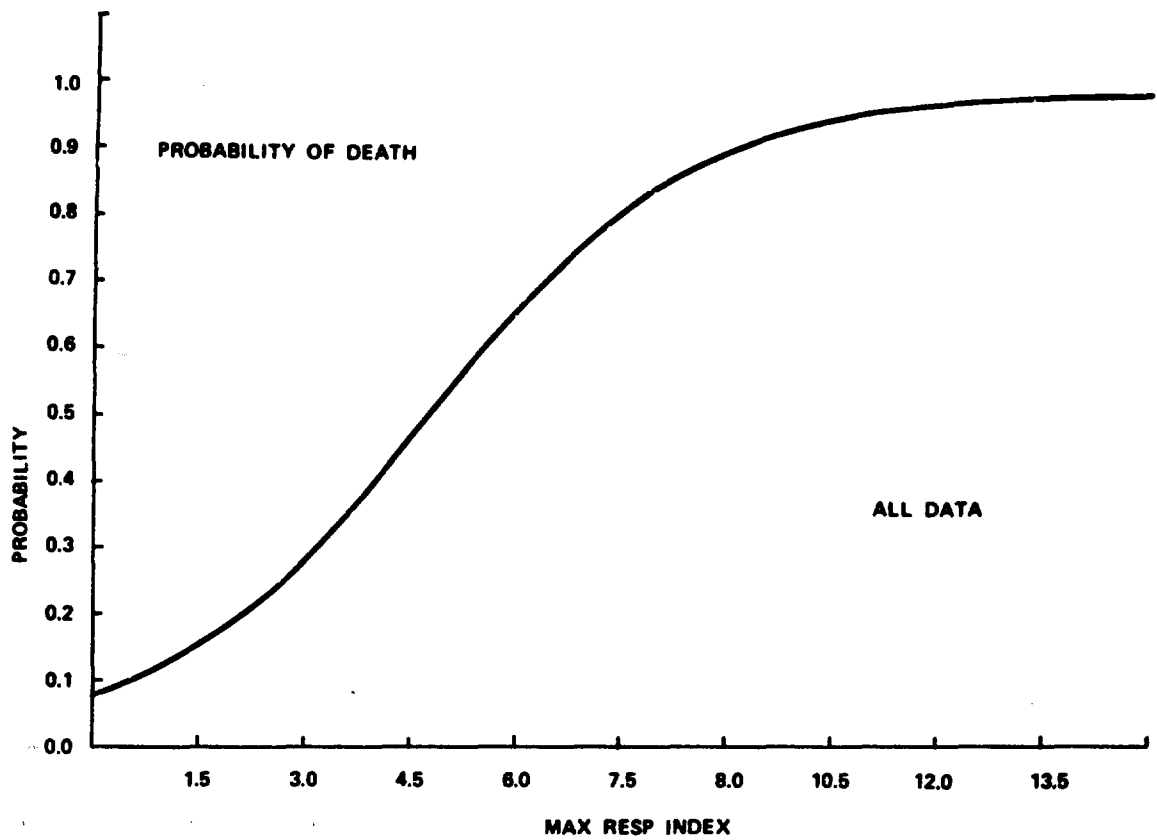


Figure 8. Probability of Death Curve for the Respiratory Index

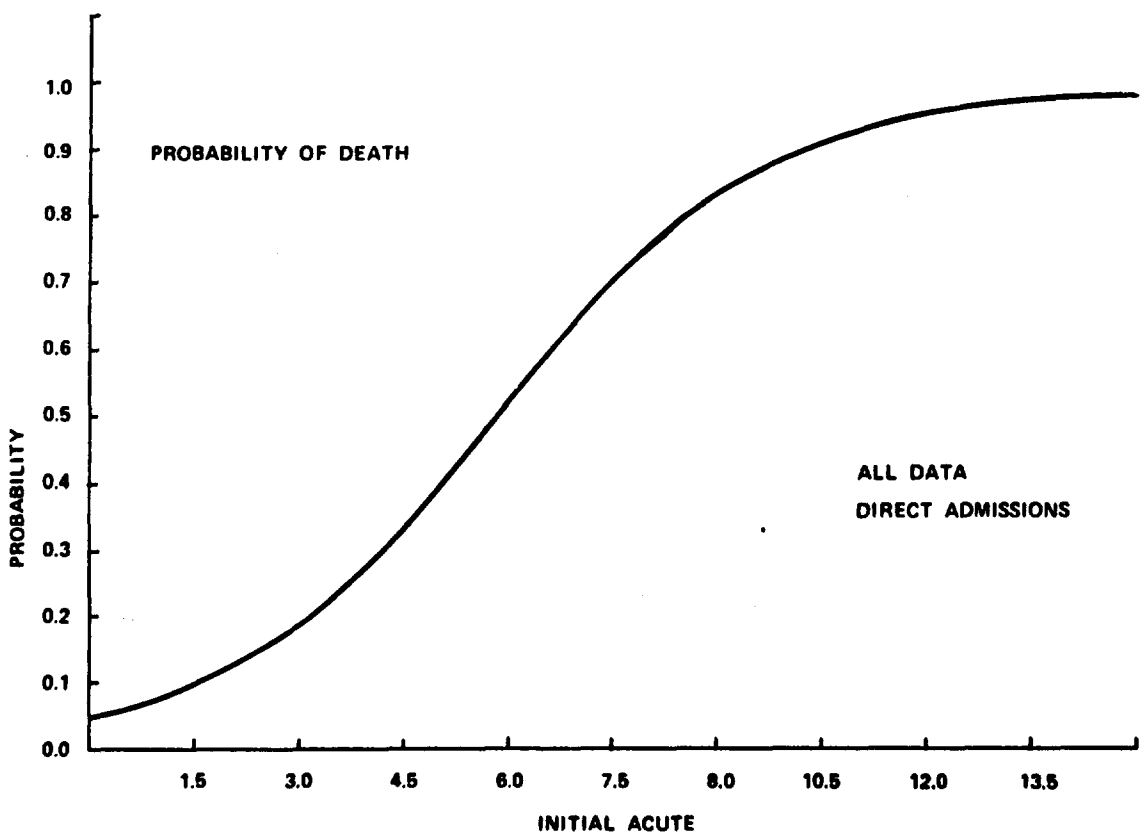


Figure 9. Probability of Death Curve for the Acute Trauma Index

Table 9. Logistic Model Coefficients for Various Indices and Parameters Based on the Total Data Set

Index	Constant term	Coefficients			
		Age	Sex	Admission	Index
	β_1				
Maximum CHOP	-3.25				0.524
Maximum CHOP	-4.43	0.0131	0.132	0.457	0.479
Maximum renal	-2.19				0.535
Maximum renal	-3.34	0.0157	0.000440	0.469	0.48P
Maximum respiratory	-2.48				0.514
Maximum respiratory	-3.44	0.00523	0.00590	0.551	0.479
Admission acute	-2.99				0.509
Admission acute	-3.18	0.0174	-0.251		0.474

Table 10. Probability of Death (P_D) for Admission Values of the SHAP Index Based on Combined Data from Retrospective and Prospective Studies

SHAP index	
Serious CNS Patients	
63 Lived	67 Died
Index value	P_D
0-0.99	0.36
1.0-1.99	0.44
2.0-3.49	0.47
≥ 3.5	0.74

Table 11. Temperature and WBC Statistics for the New Patient Data

Statistic	Temperature		White blood count	
	Peak values	Least values	Peak values	Least values
Mean (live)	100.6	98.8	17,800	9,200
Mean (die)	101.7	97.7	21,700	8,700
Standard deviation (live)	1.3	1.2	7,250	3,900
Standard deviation (die)	2.1	1.8	10,000	5,200

Table 12. Means and Standard Deviations for Peak Values of Various Measurements on a Set of 52 Patients with Liver Trauma (41 Survivors; 11 Deaths)

Statistic	Bilirubin	LDH	SGOT	SGGT	Alkaline phosphatase
Mean (survivors)	6.8	530	346	163	133
Mean (deaths)	13.6	762	477	210	120
Standard deviation (survivors)	5.7	276	298	165	101
Standard deviation (deaths)	9.9	489	696	213	100

Table 13. Frequencies of Occurrences for Measurement Intervals for Peak Values of Various Measurements from a Set of 52 Patients with Liver Trauma (41 Survivors; 11 Deaths)

Peak bilirubin			Peak LDH		
Value	Number of survivors	Number of deaths	Value	Number of survivors	Number of deaths
3.0-8.0	31	4	0-400.0	14	2
8.1-12.0	5	1	400.1-1200.0	24	6
12.1-16.0	2	1	1201.0-1600.0	2	1
>16.0	3	4	>1600.0	0	1

Peak SGOT			Peak SGGT		
Value	Number of survivors	Number of deaths	Value	Number of survivors	Number of deaths
0-400.0	27	8	0-200.0	13	2
400.1-800.0	10	0	201.0-400.0	4	1
>800.0	3	2	>400.0	1	0

Peak alkaline phosphatase		
Value	Number of survivors	Number of deaths
0-200.0	31	9
201.0-400.0	8	1
>400.0	1	0

5. Therapy Profiles.

Two therapy profiles were obtained. The first profile is a 13-component binary vector, $X = (x_1, \dots, x_{13})$. Each component x_i specifies the presence (denoted by a 1) or absence (denoted by a 0) of a given type of medication or therapeutic maneuver. The 13 components are as follows:

Component

x_1	Blood and components
x_2	Oxygen
x_3	Ventilator
x_4	Steroids
x_5	Antibiotics
x_6	Vasopressors
x_7	Vasodilators
x_8	Diuretics
x_9	Dialysis
x_{10}	Surgery
x_{11}	Anticoagulant
x_{12}	Insulin
x_{13}	Bicarbonate

Such daily vectors were recorded for 100 patients.

A more extensive profile evolved during the study and was recorded on 50 patients. It consists of daily recordings of therapies which were grouped into six major types; namely, respiratory, central nervous system, renal, cardiovascular, metabolic, surgery, and coagulation. It includes all of the information in the first profile plus surgical procedures; readings of FIO_2 and PEEP; amounts of mannitol, blood, packed cells, colloid, fresh frozen plasma, platelets, vitamin K, diuretics, and bicarbonate; and the presence or absence of therapies for dehydration, convulsions, and temperature regulation.

VI. DISCUSSION.

A large number of patients have illnesses attributable to many factors which we believe can be quantified by a *multi-index descriptor*. The indices provide the clinician with a precise *characterization of patient's state* which may help to pinpoint the time for the initiation of therapies and aid in assessing therapies. In this paper we have evaluated respiratory, renal, acute trauma, and CNS indices, and a general trauma index called the CHOP index. These indices, which are composed of measurements obtainable in most treatment centers, are simple to compute by hand, calculator, or by tables which we have constructed (for example, page 6 of the Champion *et al.* report).³ The indices are easily modified to include other measurements which appear to

complement existing ones. A concept called *Marginal Information Gain* can be used to test a parameter one may wish to incorporate to enhance the validity of prognoses. The indices also provide a useful baseline for comparing the effect of therapeutic maneuvers. Frequently, the indices yield surprising and significant clinical insights. For example, we have previously reported the use of a prognostic index,² which by combining commonly assessed clinical evaluations allows a downward trend to be identified several days before it becomes clinically recognizable.

At the MIEM, the CHOP index is used as a general predictor of survival for referral patients and for direct admission patients after the first 24 hours. A decision rule, based on the CHOP index, which predicts death or survival, resulted in a misclassification rate of less than 10% for 650 patients in the unit for more than 1 day. The misclassifications can be reduced by several percent by comparing the variables which contribute to a large index value to a table of "critical states."

Respiratory failure has in the past been responsible for as many as one-third of the deaths in surgical intensive care units. Respiratory distress syndrome of trauma will occur as an early complication in some 30% of the victims of major blunt trauma with a mortality of up to 50% if it is not recognized early and is aggressively managed. Without such sophisticated assessment as is available in major centers, many physicians find difficulty in assessing the severity of respiratory problems. In addition, there is the added problem of following the patient's progress. We believe that the respiratory index and its associated probability of death chart provide the physician with a simple and helpful guide. A respiratory index of 0.1 to 0.37 is normal. A value of 2 or greater is an indication for intubation, and a value above 6 is associated with a 12% probability of survival. The index reflects the presence of pulmonary shunting in a variety of circumstances including atelectasis, pulmonary contusion, or pulmonary emboli. A nomogram has been constructed which simplifies computation of the index and allows one to follow the course of the patient with respiratory problems.⁵

The *space* determined by the CHOP index and the respiratory index is also used to *track* patients. Prognosis regions have been specified in this space.*

The relationship between individual variables of renal function and the renal index and survival are shown in table 2 of the Champion *et al.* report.³ Creatinine levels above 4.0 mg per 100 ml, a BUN over 80.0 mg per 100 ml, and a renal index of 3 are all rare in survivors. Data for those patients who did have one of the criteria just mentioned were further analyzed to identify that variable which first reached the "critical level." (These details are given in table 3 of the Champion *et al.* report.) In most cases the most sensitive indicator was a renal index of 3.

Although acute renal failure after surgery or trauma is recognized as a grave complication, it too seldom provokes the urgent therapeutic response required. The therapeutic approach to acute renal failure in major trauma must be clearly distinguished from that in chronic renal failure, where the traditional approach is appropriate. Multiple major trauma is frequently accompanied by hemorrhagic shock, requiring massive blood transfusion under circumstances which sometimes do not allow time for complete cross-matching. Crushed muscle, hematoma formation, and jaundice are commonly components of the primary complicating clinical syndrome. Under aggressive resuscitation, with massive colloid infusion, and the early promotion of diuresis, many patients exhibit only slight or transient impairment of renal function. Once renal failure is established, however, the prognosis is poor, despite full supportive treatment. We believe this accounts for the higher mortality rate in referred patients with an index >2.0 (see table 3).

To reiterate, our results indicate that survival is unlikely when a patient's renal failure deteriorates to those levels earlier defined (e.g., renal index >3), and that aggressive therapy must be directed at preventing deterioration to this level. A trial of early dialysis is needed to assess the therapeutic effects of preventing the

*Sacco, W., Goldfarb, M., Weinstein, M., Ciurej, T., Cowley, R., Champion, H., Long, W., Gill, W., and McAslan, T. Two Prognostic Indices for the Trauma Patient. Forthcoming Edgewood Arsenal Technical Report.

BUN from reaching 80 mg/100 ml, or the serum creatinine from reaching 4 mg/100 ml, or the renal index from reaching a value of 3. This will frequently mean dialysis within 24 hours of the trauma or surgery because of the gross catabolism and hyperkalemia.

The renal index is but one example of organ-oriented indices based on calculated deviations from normal organ function. Such indices have considerable potential in intensive care because they give early warning of deterioration in the patient's condition.

The acute trauma index and the SHAP index (which is one factor in the decision rules for estimating prognoses of patients with serious head injuries) are both four-parameter indices. They have three factors in common: systolic blood pressure, hematocrit, and arterial pH. The non-common factors are prothrombin time in the acute trauma index and serum sodium in the SHAP index. The importance of the three common factors is emphasized by their roles as good prognostic indicators in two separate analyses.

In the sepsis study, neither the white blood count nor the temperature were powerful predictors of survival. However, the analysis of the data indicates that temperatures above 105° or below 97°F reduce a patient's probability of survival from the a priori 80% to about 50%. We have not attempted to construct a sepsis index.

Our first attempts to quantitate "therapy" have been modest. However, we believe that collection of therapy information is feasible, not expensive, and will lead to useful findings as the data base grows.

Although the sample size is small in the liver study, it appears that for survival prognoses, SGOT, SGGT, and alkaline phosphatase are not promising variables; the LDH may be of some value and the bilirubin has promise. At this time we plan to incorporate the bilirubin into a *multi-system profile* to consist of the respiratory index, serum creatinine, serum osmolality, prothrombin time, arterial pH, hematocrit, systolic blood pressure, consciousness level, temperature, and bilirubin.

Rationales for *patient triage* and *evaluation of care* have evolved during this study.

We believe the triage rationale could be useful in a mass casualty situation where the goal is to maximize the number of survivors. Triage is a two-step process which may be described as follows:

Step 1. Sort the casualties into three groups.

Group A. Those who will recover with little or no help.

Group B. Those who cannot be saved even with the best of care.

Group C. Those who will survive only if they are given medical care.

Step 2. Decide the order of treatment for patients in group C. In the proposed rationale, casualties in group C are ordered using the probability of survival, P_s , based (at this time) on the acute trauma index.

It can be shown (under certain assumptions) that the expected number of survivors will be maximized if patients having higher values of P_s are treated first. The best procedure of course includes the updating of survival probabilities for patients in the queue. This very difficult and sensitive question will be discussed at length in a future paper.

We now discuss a methodology for evaluating care in a trauma center. The indices and the associated probabilities of death appearing in this paper may not necessarily apply to patients in other centers for several reasons which include: (1) involved in the calculations of probabilities of death (appearing in the tables and in the figures) is the a priori probability of survival; these may differ among centers; (2) modes of therapy may

differ; (3) patient population may differ. Despite these reservations we have found that for multiple-trauma patients, other than those with head injuries only, the severity of injury of the direct admission patient is well reflected by the value of the acute trauma index.

A starting-up methodology by which a trauma center could evaluate itself is as follows:

An index such as the acute trauma index could be computed based on, say, 200 consecutive direct admissions, other than patients having head injury only. A probability curve (figure 9) based on these index values would become a baseline for comparing the care of future patients. For a "new" patient group, the expected survival rates may be computed by summing the probabilities of survival associated with each patient of the new group. If the actual survival rate exceeds the expected rate, the center can *assume* that care is improving. Probability of death curves can be computed for the new data set to serve as a new baseline. Admittedly, this type of evaluation is in its infancy, and it is not difficult to foresee instances where serious discrepancies will exist between the index characterization of a patient and a clinician's characterization. We believe that it will be possible to incorporate additional information in the indices to diminish these discrepancies.

VII. FOLLOW-ON WORK.

Follow-on studies suggested by the results of this paper are:

1. A comparison of the prognostic and therapeutic value of the respiratory index with more complex pulmonary indices including percent pulmonary shunting, compliance, end respiratory reserve volume, etc.
2. A clinical trial of early dialysis as dictated by the renal index.
3. The construction of a single multi-system index composed of the respiratory index, serum creatinine, serum sodium, serum osmolality, arterial pH, hematocrit, prothrombin time, systolic blood pressure, temperature, and bilirubin.
4. Continuation of the study of liver dysfunction.
5. A patient characterization which combines anatomical indices and physiological-biochemical indices.
6. The development of a stochastic model to improve evaluation and prognosis of the acute trauma patient.

LITERATURE CITED

1. Copes, W., Cowley, R. A., Masaitis, C., Sacco, W., Sperrazza, J., and Turney, S. Application of Pattern Recognition to Shock Trauma Studies. Symposium Proceedings, Computer Graphics in Medicine, Pittsburgh, Pennsylvania. March 1972.
2. Sacco, W., Cowley, R. A., Goldfarb, M., Champion, H., Gill, W., Long, W., and Copes, W. EATR 4777. A Prognostic Index in Critical Care Medicine. July 1973. (Also appears in Journal of Trauma, Vol 14, No. 12, December 1974.) UNCLASSIFIED Report.
3. Champion, H., Sacco, W., Nyikos, P., Long, W., Smith, H., Cowley, R., and Gill, W. Indications for Early Haemodialysis in Multiple Trauma. Lancet, June 8, 1974.
4. Sacco, W., Nyikos, P., Champion, H., Long, W., Smith, H., Cowley, R., and Gill, W. EB-TR-74038. A Renal Index for Multiple Trauma. August 1974. UNCLASSIFIED Report.
5. Goldfarb, M., Ciurej, T., McAslan, T., Sacco, W., Weinstein, M., and Cowley, R. Tracking Respiratory Therapy in the Trauma Patient. The American Journal of Surgery. Vol 129, No. 3, March 1975.
6. Dunn, J., Sacco, W., and Broome, P. A Multidimensional Statistical Analysis of 321 Consecutive Patients with Central Nervous System Injury. Congress of Neurological Surgeons, Hawaii. October 1973.
7. Walker, S., and Duncan, D. Estimation of the Probability of an Event as a Function of Several Independent Variables. Biometrika, Vol 54, No. 1, 1967.
8. Kendall, M., and Stuart, A. The Advanced Theory of Statistics. Vol 1, Hafner Publishing Company, New York, New York. 1969.

APPENDIX

CONFIDENCE BOUNDS FOR THE LOGISTIC FUNCTION

Approximate 95% confidence bounds can be found by methods discussed by Kendall and Stuart.⁸ The idea is to find the standard error (SE) at each point along the curve and then to add and subtract 2 SE from the actual curve value. Hence, the upper limit (UL_z) at $x = z$ is

$$UL_z = \min [1.0, P_D(z|\beta) + 2 SE_z]$$

Similarly, the lower limit is

$$LL_z = \max [0.0, P_D(z|\beta) - 2 SE_z]$$

Following their procedure one obtains for the two-parameter model,

$$P_D(X|\beta) = \frac{1}{1 + e^{-(\beta_1 + \beta_2 x)}}$$

$$(SE)^2(x) = K^2(x) [\sigma_1^2 + 2x\sigma_{12} + x^2\sigma_2^2]$$

where σ_1 is the estimate of the standard deviation of β_1 , σ_2 is the estimate of the standard deviation of β_2 , σ_{12} is the estimate of covariance of β_1 and β_2 , and

$$K(x) = \left[1 + e^{-(\beta_1 + \beta_2 x)} \right]^{-2} e^{-(\beta_1 + \beta_2 x)}$$

The values of σ_1 , σ_2 , and σ_{12} are given as part of the output of the computer program for the Walker-Duncan algorithm. Table 14 gives the values of σ_1^2 , σ_2^2 , and σ_{12} for the logistic model coefficients based on the total data sets (figures 6 through 9). For each of the indices, calculations of SE were made at index values of 1, 5, and 10. The standard errors of estimate increase from an average of .01 at an index value of 1 to an average of .03 at an index value of 5 to an average of .05 at an index value of 10.

Table 14. Variance and Covariance Estimates of the Logistic Model Coefficients Based on the Total Data Sets

Two coefficient model			
Index	Variance of β_1	Variance of β_2	Covariance (β_1, β_2)
Maximum CHOP	0.0363	0.00230	-0.00816
Maximum renal	0.0162	0.00439	-0.00538
Maximum respiratory	0.0469	0.00448	-0.0116
Admission acute	0.0686	0.00802	-0.0204