Critical care outcome prediction equation (COPE) for adult intensive care

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ABSTRACT

Objective: Development and validation of a critical care outcome prediction equation (COPE) using data that are collected routinely for administrative purposes.

Design: Retrospective observational study using multivariate logistic regression modelling. Calibration and discrimination were assessed by standardised mortality ratio (SMR), area under the receiver operating characteristic plot (ROC AUC), and Hosmer–Lemeshow contingency tables.

Setting: All intensive care units in the state of Victoria, Australia.

Participants: Consecutive adult hospital episodes between 1 July 2004 and 30 June 2006.

Results: 17 880 records (1 July 2004 – 30 June 2005) were used to derive the COPE model, which incorporated five variables (age, unplanned admission, mechanical ventilation, hospital category and admission diagnosis) and was validated on the 17 848 records from the following year (1 July 2005 – 30 June 2006). The 95% confidence interval of the SMR in the validation sample was 1.00–1.01, and for the ROC AUC was 0.83–0.84. The COPE model was validated in three major hospital categories (tertiary, metropolitan, and regional) and in five individual ICUs, and compared favourably to the APACHE III model (SMR = 0.83–0.86; ROC AUC = 0.87–0.88).

Conclusion: The COPE model is a simple, robust, risk-adjusted outcome prediction tool based on five fields from data that are routinely collected for administrative purposes.

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Risk-adjusted outcome prediction models have many applications in critical care medicine, including research, benchmarking, performance monitoring and accreditation. The Acute Physiology and Chronic Health Evaluation (APACHE version III[1]) methodology has been adopted for use by the Australian and New Zealand Intensive Care Society[2] (ANZICS) and by the Australian Council of Healthcare Standards[3] as the preferred model and benchmark. It has a strong research foundation and is widely used as an international benchmark. A number of other models (eg, SAPS-3[4] and MPM-II[5]) have also been validated and published overseas, but data for these models are not routinely collected by ANZICS. Why then should we attempt to "reinvent the wheel" by developing yet another outcome prediction model?

The APACHE models have a number of limitations,[6] particularly when used to monitor clinical performance (Table 1), and not all hospitals in Australia collect this information. While some of these limitations may be overcome given sufficient time and resources, and may be partially addressed by the more recent APACHE IV model,[7] an alternative approach is to address them in a more timely and less costly fashion by developing a new model.

A valid outcome prediction model should include all patients and accurately predict outcomes in large and heterogeneous populations, and must therefore take into account the complexity and diversity of casemix and illness severity.[6] The dependent variable (outcome) should be clinically important and reflect the quality of care,[8] such as unexpected death or major morbidity. Its definition should be simple and unambiguous to avoid subjects being incorrectly classified. The input variables should be independent of therapy to avoid bias, otherwise the model cannot assess the quality of that care.

New Zealand and all states in Australia collect patient data pertaining to hospital admissions for epidemiological, administrative and financial purposes. The Victorian Admitted Episode Dataset (VAED)[9] is one such data repository, and has a number of features that render it suitable for investigation as a data source for an outcome prediction model. The data are extracted and coded in a timely manner by qualified and trained health information managers in all Victorian public hospitals, and the data quality is regularly audited, both internally and externally.[10] In addition, patient episodes associated with admission to an intensive care unit are readily identifiable using the field "ICU hours".

Administrative datasets may be comparable to clinical datasets for outcome prediction,[11] but have a number of important limitations.[12] The primary purpose of the VAED, for example, is administrative and financial (for casemix-based funding) — not clinical. More specifically, the VAED contains only limited clinical and no physiological data.[9] We therefore investigated whether selected VAED fields could

Table 1. Advantages and limitations of the APACHE III model for Australian intensive care[6]

Advantages	Limitations
Internationally validated	Historical bias (last calibrated 2003)
Multiple variables: 7 chronic disease, 4 demographic, 8 physiological, 10 pathological, and 78 diagnostic variables	Resource-intensive Data coding error
Acute physiological and pathological data	Therapeutic bias Lead-time bias
Data from any period during first 24 ICU hours	Therapeutic bias Mathematical coupling
Multiple (78) diagnostic categories	Model-specific, non-standard Diagnostic error Exclusions (eg, burns, transplant)

be used to derive a clinically and statistically valid critical care outcome prediction equation (COPE) for in-hospital mortality in critically ill adult patients.

Methods

Source data

The original concept and pilot model of the COPE model was developed at a single site (the Northern Hospital, Melbourne, Victoria) using fields from the VAED, and the results were used as "proof of concept" to develop the statewide model presented here. Two authors (GJD and JS) received approval from the Victorian Health Information Reporting System, Department of Human Services Victoria, for access to preselected VAED fields for all adult public hospital separations over two financial years (2004–06) that were associated with an admission to an ICU. The de-identified data fields provided, and their derived variables, are listed in Table 2. The 2004–05 population was used to derive the COPE model, and this model was then validated by testing it on the 2005–06 population and its subsets (see Appendix 1 and Appendix 2).

Grouped data were expressed as median (interquartile range) and compared using the Mann–Whitney U test ($P<0.05$). Multivariate logistic regression modelling, using SPSS version 12 statistical software (SPSS, Chicago, Ill, USA), was used to analyse and validate the models. All variables except age were entered as dichotomous variables. The cut-off for the inclusion of variables was set at $P<0.05$. The dependent variable was hospital outcome (in-hospital death).

The VAED field "Primary diagnosis" is defined as "the [single] diagnosis established after study to be chiefly responsible for occasioning the patient's episode of care in hospital or attendance at the health care facility",[9] and is based on the International Classification of Diseases (10th revision, Australian modification; ICD-10AM[13]). The primary diagnosis is the ICD-10AM code that best explains the clinical reason for admission to hospital, and may or may not be the reason for the subsequent transfer to the intensive care ward. To simplify their inclusion in the model, the diagnosis codes were grouped according to the first three (of the five) characters in each ICD-10AM code. This reduced several thousand separate diagnostic codes to 165 distinct clinical groups (see Appendix 3).

Model performance

There are a several recommended methods for assessing the performance of outcome prediction models.[14,15] Calibration of the models was assessed using the standardised mortality ratio (SMR), and the Hosmer–Lemeshow goodness of fit χ^2 statistic based on deciles of risk.[16] Calibration is displayed in two formats — the Hosmer–Lemeshow contingency tables based on deciles of risk (with equal numbers; H_{10} statistic), and a calibration chart based on deciles of risk (with equal intervals; C_{10} statistic). Calibration describes how closely the predicted values are to the actual outcomes, and a well-calibrated model will have an SMR close to unity, a low χ^2 value (<15.5; $df=8$), and a high P value (>0.05).

Model discrimination — that is, how well the model distinguishes survivors from non-survivors — was assessed using the area under the receiver operating characteristic plot (ROC AUC).[14] The ROC plot is a method for analysing

Table 2. Variables from VAED included in the derivation model

Variable	VAED field source	Surrogate for
ICU admission*	ICU hours (> 0)	(Study population)
Sex	Sex (male)	Sex-related risk
Age (years)†	Date of birth	Pre-admission function
Admission from residential aged-care facility	Admission source	Pre-admission function
Unplanned admission†	Admission type	Illness severity
Interhospital transfer	Admission source	Illness severity
Mechanical ventilation†	Mechanical ventilation hours (>0)	Illness severity
Principal diagnosis†	Diagnosis (first of)	Casemix
Hospital category†	(Hospital name)	Casemix
Outcome‡	Discharge destination	(Outcome)

VAED = Victorian Admitted Episode Dataset.
* VAED field used to identify ICU population.
† Independent variables selected in the COPE model.
‡ Dependent variable in the COPE model.

Table 3. Demographic data for the derivation and validation datasets

Dataset	Development	Validation	*P*
Date range	1 Jul 2004 – 30 Jun 2005	1 Jul 2005 – 30 Jun 2006	
Number of episodes	17 880	17 848	
Age (years)*†	65 (51–75)	65 (50–75)	0.32
Sex: male	10 675 (59.7%)	10 641(59.6%)	0.87
Unplanned admission to hospital†	12 361 (69.1%)	12 366 (69.3%)	0.76
Interhospital transfer	2424 (13.6%)	2507 (14.0%)	0.18
Admit from RACF	136 (0.76%)	132 (0.74%)	0.82
Mechanical ventilation†	8546 (47.8%)	8772 (49.1%)	0.75
In-hospital mortality	2186 (12.1%)	2231 (12.5%)	0.43

RACF = residential aged-care facility.
* Data expressed as median (interquartile range).
† Independent variables selected in the COPE model.

both the sensitivity and specificity of the model. A value of 1.0 indicates that the model accurately predicts the outcome in all patients, whereas a value of 0.5 indicates that the model is no better than chance. An ROC AUC value above 0.80 is desirable.

Several models were constructed (by adding or deleting individual variables), and their calibration and discrimination characteristics were compared. The model that displayed the best discrimination (ROC AUC) with the least difference between observed and predicted outcomes (using Hosmer–Lemeshow contingency tables and χ^2 statistic) was selected as the final model.

Validation

The final COPE model (derived from the entire 2004–05 cohort) was then validated in four ways. First, it was externally validated using the entire 2005–06 cohort. Secondly, the model was tested in the three hospital categories — tertiary referral, metropolitan and regional — from the 2005–06 dataset. Thirdly, the model was validated using the 2005–06 data from five individual ICUs (two tertiary referral, two metropolitan and one regional hospital).

Each validation procedure was undertaken in a standard manner. The relevant variables were extracted for each patient, the associated model coefficients were summed for each variable present, and finally the logit of this sum was calculated (see Appendix 1). The resultant fraction (range, 0–1) equates to the observed mortality rate of a group of similar patients from the development dataset and is referred to as the "predicted outcome". By comparing the observed and predicted outcomes in the selected population (SMR), it is possible to determine the accuracy of the prediction model.

Finally, the COPE model was compared with the APACHE III model for the same year (hospital separation date between 1 July 2005 and 30 June 2006). The ANZICS Adult Patient Database (APD) kindly provided the APACHE IIIJ predicted "risk of death" values for all adult admissions from the 21 ICUs that routinely submit APACHE III data. There are 23 adult ICUs in Victoria. Records for patients readmitted to the ICU (during the same hospital admission) were excluded from the analysis.

All datasets were de-identified for both hospital and patient by providing hospital category rather than hospital name, and patient age (to the nearest year) rather than date of birth. As the analysis was based on data extracted

Table 4. Validation and comparison test results for COPE

Dataset	Number	Mortality	SMR (95% CI)	Hosmer–Lemeshow χ^2*	*P**	ROC AUC (95% CI)†
2004–05	17 880	12.20%	1.00	23.1	0.003	0.83–0.84
2005–06	17 848	12.50%	1.00–1.01	26.9	0.001	0.83–0.84
APACHE III	16 346	13.10%	0.83–0.86	28.9	< 0.001	0.87–0.88
Tertiary	9 002	13.30%	1.00–1.04	25.1	0.002	0.78–0.81
Metropolitan	4 280	15.50%	0.91–0.96	14.6	0.067	0.80–0.83
Regional	4 566	8.10%	0.97–1.05	22.1	0.005	0.85–0.88
Hospital A	1 903	16.30%	1.01–1.14	9.6	0.29	0.77–0.82
Hospital B	1 010	14.60%	0.96–1.10	10.9	0.21	0.77–0.84
Hospital C	1 400	9.60%	0.86–0.97	8.7	0.36	0.80–0.87
Hospital D	734	12.80%	0.90–1.07	4.3	0.83	0.75–0.84
Hospital E	624	22.30%	0.91–1.04	4.1	0.85	0.76–0.84

SMR = standardised mortality ratio. * Hosmer–Lemeshow tests ($df = 8$). † Area under receiver operating characteristic curve (95% confidence interval).

retrospectively from the VAED, the hospitals' health information managers (who coded and submitted the data) were not aware of this project. The Department Of Human Services Victoria and the Northern Hospital Ethics and Research Committee each gave their approval for this research.

Results

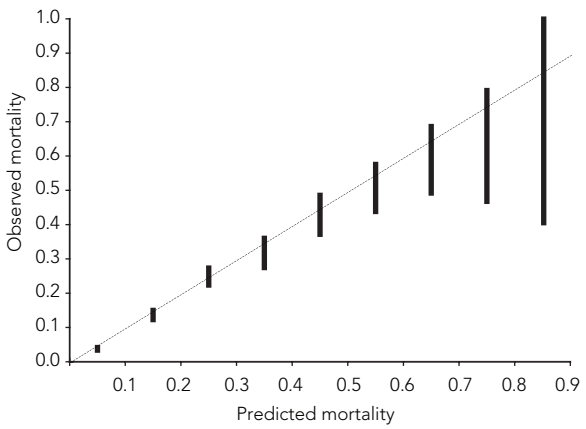
The demographic data for both patient groups are summarised in Table 3. There was no significant difference in the explanatory variables between the two populations. There were no missing data fields in the VAED. A total of 16 346 APACHE III records (92% of the number of VAED records for the same time period) were available in the APD dataset.

The five variables selected for inclusion in the final COPE model included three demographic variables (age, unplanned admission to hospital and hospital category), one therapeutic variable (mechanical ventilation), and one diagnostic category. Although 42 of the original 165 diagnostic categories were selected for inclusion in the model, only one was used for each patient. The Hosmer–Lemeshow χ^2, the SMR and the ROC AUC values for the COPE model are listed in Table 4. The Hosmer–Lemeshow contingency table for the validation (2005–06) dataset is presented in Table 5, and the calibration chart in Figure 1. The variables and their coefficients are detailed in Appendix 3.

Table 5. Contingency table for Hosmer–Lemeshow test

	Survivors		Non-survivors		
Decile	Observed	Expected	Observed	Expected	Total
1	1777	1774	8	11	1785
2	1770	1761	15	24	1785
3	1751	1744	34	41	1785
4	1735	1723	50	62	1785
5	1685	1692	100	93	1785
6	1610	1650	175	135	1785
7	1572	1589	213	196	1785
8	1459	1477	326	308	1785
9	1331	1300	454	485	1785
10	926	911	856	871	1782

Figure 1. COPE model calibration curve



Graph shows 95% confidence intervals of the observed mortality versus predicted mortality for each decile of risk. Note: no patient had predicted mortality > 0.9. The dotted line shows line of perfect fit.

Discussion

The COPE model is a novel and potentially useful outcome prediction tool for adult intensive care that has been derived from a readily accessible administrative dataset. It provides a locally derived model that is complementary to the international benchmark (APACHE III) model. Given the simplicity of the five variables in the COPE model, the absence of physiological markers, and the fact that all variables are determined before ICU admission, it is surprising that it performs as well as it does. Its calibration and discrimination appear to be comparable to those of the APACHE III model and thus worthy of further investigation.

The COPE model complements our current "gold standard" model (APACHE III) by addressing many of its limitations (Table 1).[6] The variables are simple, and all except age are categorical. The model is independent of therapy, except possibly where mechanical ventilation is initiated after ICU admission. The data collectors are trained and qualified, and they are independent of the ICU (and other hospital) staff whose quality of care the model may be used to assess. The resources and logistics required to collect the required dataset already exist. Its variables are derived from a comprehensive, all-inclusive, and regularly audited dataset (VAED), that is available in a timely manner. The COPE model is designed so that it can easily be recalibrated, perhaps annually, to allow for shifts in casemix and coding patterns, and to maintain its validity as a monitor of performance. As the VAED is updated within 2–4 weeks of hospital separation, there is the potential to use the COPE model as a performance monitoring tool (clinical indicator) for real-time monitoring of the quality of care in adult ICUs.[6,8]

There are several limitations to the COPE methodology. The model has been derived from a non-clinical administrative dataset[9,12] that is not specific to ICU or critically ill patients, and it has thus far only been validated in a small

number of ICUs (Table 4). The data are not collected, nor audited, by clinicians. There is a risk of coding variations or errors, although this is minimised by regular internal and external quality audits. The method used to collapse the ICD-10AM codes into a smaller number of diagnostic groups (see Appendix 3) was developed by one author (G J D) in a single centre and may be criticised as arbitrary; this requires further refinement.

The Hosmer–Lemeshow χ^2 statistic suggests that the calibration of the model is no better than that of the APACHE III model (Table 4). This parameter is less useful for large populations,[16,17] where small (non-clinical) differences between observed and predicted outcomes are more likely to be statistically different (high Lemeshow χ^2 and low *P* value), erroneously suggesting poor calibration of the prediction model. This may be observed in Table 4 by comparing the values for the small and large populations.

There are inherent limitations in any risk-modelling methodology. Regression models are limited to the variables available, and select only variables that are statistically significant, irrespective of their clinical significance. For example, the COPE model was restricted to variables already available within the VAED. The finding of a statistical association between a variable and an adverse outcome does not prove a causal link. The variables included in the COPE model are likely to be surrogates for true causal factors, such as severity of illness and premorbid functional status (Table 2).

Outcome prediction models, such as the COPE and the APACHE models, should only be applied to groups, not individuals. The predicted "mortality risk" calculated for each individual patient may be considered a "severity of illness" score, but is not a predictor of outcome in that individual, and thus should not be used to guide clinical management or resource allocation.

Further investigation is required to assess whether the addition of comorbidity and procedural variables improves the performance of the COPE model. Validation in other hospitals and in larger populations is also planned.

Conclusions

Administrative data, such as those contained in the VAED, can be used to derive a risk-adjusted critical care outcome prediction equation (COPE) that addresses many of the limitations of other models. The COPE model is a better predictor of overall mortality in ICUs in Victoria than the APACHE III model (SMR, 1.00–1.01 versus 0.83–0.86), although the later discriminates between death and survival slightly better than the COPE model (ROC area, 0.87–0.88 versus 0.83–0.84). Some ICUs do not collect APACHE III data, the data are not available for many months, and the quality of those data is not yet validated. On the other hand, the information needed to calculate the COPE is available for every ICU admission within 2–4 weeks of hospital discharge and is regularly validated. Inclusion of other variables from the VAED may improve the model's performance, and further validation is required to ascertain its utility in other hospitals within and beyond the state of Victoria.

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Appendix 1. Calculation of critical care outcome prediction equation (COPE)

Predicted mortality risk, $p = e^y/(e^y + 1)$,

where y = A(age) + B + C + D + E + constant;

A = age coefficient;

B = coefficient for unplanned admission to hospital;

C = hospital category coefficient;

D = diagnostic coefficient from Appendix 3 (for all other diagnoses, D = 0);

E = mechanical ventilation in ICU coefficient; if variable not applicable then coefficient = 0.

For example, a 60-year-old (A) patient is urgently admitted (B) to a metropolitan hospital (C) with penetrating trauma (D) and requiring mechanical ventilation (E).

$$Y = (0.04 \times 60) + (0.8 \times 1) + (0.28 \times 1) + (2.12 \times 1) + (1.65 \times 1) - 6.80$$
$$= 0.45.$$

Predicted risk of mortality, $p = e^{0.45}/(e^{0.45} + 1)$

$$= 1.5683/(1.5683 + 1) = 0.61.$$

Appendix 2. Definitions of variables

Variable		Definition	Format
A	Age	Patient age	Years
B	Unplanned admission	Admission to hospital that was not planned, booked or elective	Yes = 1 No = 0
C	Hospital category	Peer group	Metropolitan = 1 Tertiary or regional = 0
D	Primary diagnosis	Diagnosis on admission to hospital (not ICU)	See Appendix 3 All other diagnoses = 0
E	Mechanical ventilation	Mechanical ventilation anytime during ICU admission	Yes = 1 No = 0

Appendix 3. The variable coefficients in the critical care outcome prediction equation (COPE) model

Variable		B	SE	Wald	*P*	Exp(B)	Exp(B) 95% CLs	
Age (years)		0.04	0	523.9	<0.001	1.04	1.04	1.05
Mechanical ventilation		1.65	0.06	788.3	<0.001	5.18	4.62	5.81
Unplanned admission		0.8	0.07	120	<0.001	2.23	1.93	2.57
Hospital category*		0.28	0.06	21.9	<0.001	1.32	1.17	1.48
Constant		–6.8	0.16	1840	<0.001			
Diagnostic category	ICD-10†							
Haemopoietic malignancy	C80–99	2.34	0.19	146.9	<0.001	10.4	7.12	15.19
Penetrating trauma	T15–19	2.12	0.61	11.9	<0.001	8.32	2.5	27.67
Other CNS disease	G9	2.06	0.33	38.6	<0.001	7.85	4.1	15.03
Cardiac arrest	I46	1.96	0.22	76.1	<0.001	7.06	4.55	10.96
Aplastic anaemia	D6	1.94	0.35	31.2	<0.001	6.98	3.53	13.81
Protozoal sepsis	B50–64	1.84	0.59	9.7	<0.001	6.32	1.98	20.13
Haemorrhagic shock	R57–58	1.74	0.42	17.2	<0.001	5.72	2.51	13.04
Secondary malignancy	C76–79	1.62	0.22	56.9	<0.001	5.06	3.32	7.7
Stroke or CVA	I63–64	1.6	0.19	71.6	<0.001	4.94	3.41	7.15
Interstitial lung disease	J8	1.54	0.27	31.7	<0.001	4.64	2.72	7.93
Liver disease	K7	1.52	0.19	66.7	<0.001	4.59	3.18	6.61
Bacterial sepsis	A4	1.47	0.13	137.9	<0.001	4.36	3.41	5.58
Lung malignancy	C3	1.43	0.23	37.5	<0.001	4.17	2.64	6.59
Intracranial haemorrhage	I60–62	1.4	0.13	122.2	<0.001	4.07	3.17	5.22
Anaemia	D5	1.4	0.72	3.8	0.05	4.06	0.99	16.58
CNS malignancy	C69–72	1.35	0.64	4.4	0.04	3.85	1.1	13.5
Pulmonary vascular	I26–28	1.31	0.3	19.4	<0.001	3.69	2.06	6.6
Fungal sepsis	B30–49	1.27	0.49	6.8	0.01	3.56	1.37	9.22
Renal failure	N1	1.25	0.21	34.6	<0.001	3.5	2.31	5.32
Ischaemic bowel	K55	1.24	0.23	29.9	<0.001	3.45	2.21	5.38
GIT investigation	R1	1.2	0.5	5.7	0.02	3.3	1.24	8.81
Environmental disease	T66–79	1.17	0.34	11.7	<0.001	3.22	1.65	6.31
Breast cancer	C5	1.08	0.48	5.1	0.02	2.94	1.15	7.48
Malignancy — other	D37–49	1.06	0.46	5.2	0.02	2.87	1.16	7.1
Pneumonia	J1	1.03	0.12	76.6	<0.001	2.8	2.23	3.53
Pneumoconiosis	J60–79	0.95	0.29	10.8	<0.001	2.57	1.46	4.52
Head injury	S0	0.94	0.14	47.2	<0.001	2.57	1.96	3.36
Pancreatic cancer	C22–26	0.91	0.37	6	0.01	2.49	1.2	5.17
Type 2 diabetes	E11	0.84	0.18	21.8	<0.001	2.3	1.62	3.27
Cardiac arrhythmias	I49	0.84	0.2	17.3	<0.001	2.3	1.55	3.42
Fluid and electrolyte disorders	E86–88	0.82	0.35	5.5	0.02	2.28	1.15	4.53
Enteritis or colitis	K50–52	0.82	0.42	3.8	0.05	2.28	1	5.21
Other intestinal disease	K63	0.81	0.34	5.7	0.02	2.25	1.15	4.38
Respiratory failure	J95–99	0.75	0.18	17	<0.001	2.12	1.48	3.03
Lower limb trauma	S7	0.72	0.2	12.8	<0.001	2.05	1.38	3.04
Other cerebrovascular disease	I65–69	0.72	0.35	4.3	0.04	2.05	1.04	4.05
COPD	J40–44	0.65	0.14	22.4	<0.001	1.91	1.46	2.49
Malabsorption	K9	0.58	0.26	4.9	0.03	1.79	1.07	2.99
Drug poisoning	T36–50	–0.66	0.24	7.6	0.01	0.52	0.32	0.83
Epilepsy	G4	–1.38	0.52	7.2	0.01	0.25	0.09	0.69
Cardiac failure	I22–25	–1.7	0.34	24.6	<0.001	0.18	0.09	0.36
Myocardial ischaemia	I20	–2.04	0.23	77.7	<0.001	0.13	0.08	0.21
All other diagnoses		0						

CL = confidence limit. CVA = cerebrovascular accident. CNS = central nervous system. GIT = gastrointestinal.
COPD = chronic obstructive pulmonary disease. * Hospital category = metropolitan. † First two or three characters of ICD-10AM code.[13]