

# Development and validation of the critical care outcome prediction equation, version 4

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The critical care outcome prediction equation (COPE) model is designed to provide an estimate of the likelihood of inhospital death for adults admitted to an intensive care unit. The model is used to calculate how many hospital fatalities are likely to occur based on patient admission characteristics.

Risk-adjustment models such as COPE and the more widely used APACHE III-j (Acute Physiology and Chronic Health Evaluation)<sup>1</sup> have practical applications in epidemiology, clinical research, and monitoring of outcomes and patient safety. The COPE model provides a contemporary and local (state) benchmark that complements the current gold standard APACHE III-j model derived from a historical international cohort. The Victorian Intensive Care Data Review Committee employs both for monitoring intensive care services.<sup>2</sup>

The COPE model has undergone several modifications since the original version.<sup>3</sup> Given its routine and formal use in monitoring ICU mortality,<sup>2</sup> it is important for clinicians and administrators to have a degree of comfort and reassurance with regard to its performance and reliability. The objective of this article is to describe the development and validation of the fourth version of the COPE model (COPE-4).

## Method

Consecutive hospital records from 1 July 1999 to 30 June 2011 were extracted from the Victorian Admitted Episode Data Set (VAED), a statewide administrative database of all public hospital admissions.<sup>4</sup> Eligible records were for adults admitted to an accredited ICU<sup>5</sup> during their hospital stay. Paediatric admissions (defined for logistical reasons as < 15 years) were excluded. There were no exclusions according to diagnosis or length of stay.

Development of the prototype COPE model has been described previously.<sup>3</sup> The model is based on the VAED and applied logistic regression methods. The diagnostic classification system employed is based on the World Health Organization mortality classification system<sup>6</sup> and the *International statistical classification of diseases and related health problems, 10th revision, Australian modification* (ICD-10-AM).<sup>7</sup> ICD-10-AM was introduced into the Victorian casemix dataset in 1998. Good to excellent coding

## ABSTRACT

**Objective:** To revise and validate the accuracy of the critical care outcome prediction equation (COPE) model, version 4.

**Design, participants and setting:** Observational cohort analysis of 214 616 adult consecutive intensive care unit admissions recorded from 23 ICUs over 12 years. Data derived from the Victorian Admitted Episode Database (VAED) were used to identify treatment-independent risk factors consistently associated with hospital mortality. A revised version of the COPE-4 model using a random-intercept hierarchical logistic regression model was developed in a sample of 35 878 (16.7%) consecutive ICU separations.

**Main outcome measures:** Accuracy was tested by comparing observed and predicted mortality in the remaining 178 741 (83.3%) records and in 23 institutional cohorts. Stability was assessed using the standardised mortality ratio, Hosmer–Lemeshow H10 statistic, calibration plot and Brier score.

**Results:** The COPE-4 model had satisfactory overall discrimination with an area under receiver operating characteristic curve of 0.82 for both datasets. The development and validation datasets demonstrated good overall calibration with H10 statistics of 13.38 ( $P=0.10$ ) and 14.84 ( $P=0.06$ ) and calibration plot slopes of 0.99 and 1.034, respectively. Discrimination was satisfactory in all 23 hospitals and one or more calibration criteria were achieved in 19 hospitals (83%).

**Conclusions:** COPE-4 model prediction of hospital mortality for ICU admissions has satisfactory performance for use as a risk-adjustment tool in Victoria. Model refinement may further improve its performance.

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quality of ICD-10-AM has been demonstrated for procedure<sup>8,9</sup> and diagnosis codes.<sup>10</sup>

Candidate variables included age, sex, admission type, admission sources, hospital peer group (College of Intensive Care Medicine classification),<sup>5</sup> cardiac surgical interventions,

**Table 1. Development and validation demographics**

Variable*	Development	Validation
Time period, dates	1 July 2004 – 30 June 2006	1 July 1999 – 30 June 2004; 1 July 2006 – 30 June 2011
Population	35 878 (16.7%)	178 741 (83.3%)
Fatalities	4415 (12.3%)	22 306 (12.5%)
Age, years (95% CI)	61.6 (61.5–62.0)	61.2 (61.1–61.3)
Mechanical ventilation	17 384 (48.5%)	86 719 (48.5%)
Cardiac surgical	4931 (13.7%)	25 514 (14.3%)
Male	21 467 (59.6%)	116 053 (65.0%)

\* Number and percentage of patients unless otherwise indicated.

mechanical ventilation (MV), comorbid diagnoses, and 53 principal (admission) diagnoses. All variables except age were entered as categorical variables. The dependent variable was inhospital death. The definition of model variables is presented in Appendix 1.

Candidate variables were included in the final model only if they (a) included more than 25 subjects per annum; (b) were significantly ( $P < 0.05$ ) associated with mortality in both univariate and multivariate analysis (logistic regression using a forward stepwise method); (c) were orthogonal to all other fitted variables; and (d) the above criteria were met in at least 10 of the 12 yearly cohorts.

Collinearity was assessed through construction of a two-way correlation matrix and multiple collinearity by investigation of the tolerance and variance inflation factors. Correlations of greater than 0.40 identified collinear variables, and the one with a greater McFadden pseudo  $R^2$  value was retained in the model and the other discarded.

Following selection of variables, a parsimonious COPE model was estimated on (the central) 2 years of consecutive records from 1 July 2004 to 30 June 2006: the development dataset. This method of case record selection was chosen in preference to the standard method (of random selection of a proportion of records) to ensure proportional representation from all institutions and minimise seasonal influences, and to facilitate assessment of calibration drift over several ( $\pm 5$ ) years. This method also more closely reflects the practical application of the model.

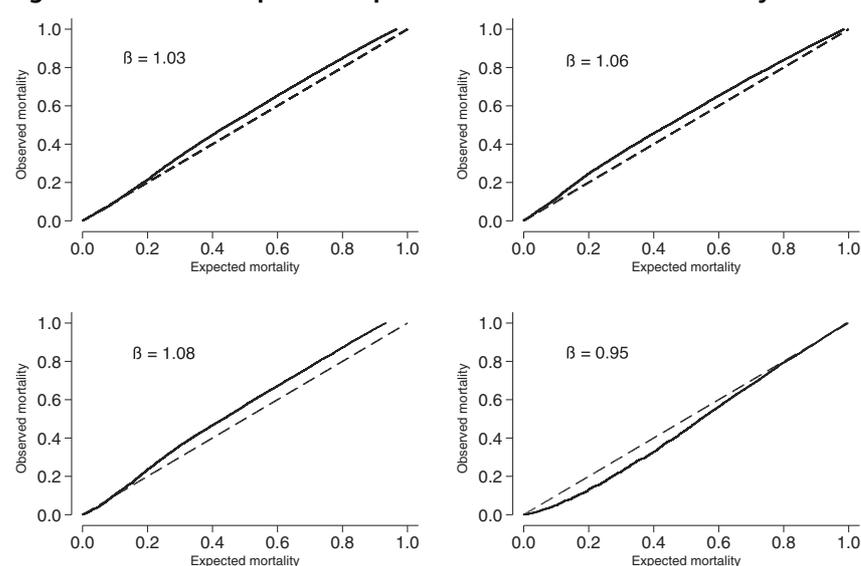
The development model was validated on each of the records for the

remaining 10 years, and separately for each of the 23 hospitals. A random-intercept hierarchical logistic regression model was employed to adjust for clustering at hospital level. Patient identifiers, to adjust for hospital readmission, were not available. Both fixed and random effects models<sup>11</sup> were tested without substantial difference, and the results of the more robust latter method are reported here.

Calibration (the ability to separate survivors and non-survivors) was assessed using standard parameters:<sup>12</sup> the Hosmer–Lemeshow  $\chi^2$  statistic (H10), the Brier score, the standardised mortality ratio (SMR) and the calibration plot.

By definition, the H10 index is collapsed on deciles of estimated probabilities, but because of its inherent sensitivity to small deviations in a large sample size ( $> 5000$ ),<sup>13</sup> it is potentially misleading. Where possible, one solution is to simply increase the number of groups ( $> 200$  if sample size  $> 5000$ ).<sup>14</sup> Another is to estimate the mean H10 statistic, for example, from 30 consecutive but random samples ( $n = 5000$ ), as presented here. An ideal model will have a  $P > 0.05$  for the H10 statistic, indicating substantial agreement between observed and predicted outcomes.

The Brier score<sup>12</sup> is a summary measure of the accuracy of the predictions and is calculated by the mean square of the error between observed and predicted outcomes. An ideal

**Figure 1. Calibration plot of expected versus observed mortality**

Critical care outcome prediction equation, version 4 (solid line) and ideal model (dashed line) for state (top left), tertiary (top right), metropolitan (bottom left) and regional (bottom right) validation datasets.  $\beta$  = calibration plot slope.

**Table 2. Calibration and discrimination characteristics of the critical care outcome prediction equation model in the validation and 23 hospital datasets**

Dataset	No. of patients	Mortality	AROC	SMR	$\beta$	$\alpha$	$R^2$	H10	$P$
Ideal			$\geq 0.75$	$1.0 \pm 0.05$	$1 \pm 0.1$	$0 \pm 5$	$1 \pm 0.05$	$< 18.4$	$> 0.05$
Validation	178 741	0.125	0.82–0.83	1.02–1.05	1.034	– 0.83	0.989	14.84	0.06
Tertiary 1	23 575	0.127	0.80–0.81	0.94–1.01	1.057	– 0.427	0.992	5.56	0.85
Tertiary 2	22 441	0.140	0.74–0.77	0.98–1.05	1.049	– 0.912	0.986	13.26	0.21
Tertiary 3	22 126	0.120	0.79–0.80	0.88–0.95	1.169	– 0.972	0.993	10.74	0.38
Tertiary 4	13 848	0.106	0.75–0.77	0.92–1.01	1.077	– 0.505	0.991	7.41	0.69
Tertiary 5	13 130	0.146	0.77–0.80	0.94–1.03	1.064	– 0.791	0.987	7.29	0.70
Tertiary 6	13 015	0.141	0.80–0.81	0.98–1.07	1.081	– 1.529	0.983	18.47	0.05
Metropolitan 1	9988	0.196	0.83–0.85	1.11–1.20	0.875	– 0.281	0.971	55.24	$< 0.001$
Metropolitan 2	9261	0.136	0.78–0.80	0.90–1.00	1.078	– 0.449	0.981	11.16	0.35
Metropolitan 3	8308	0.167	0.84–0.86	0.98–1.08	0.917	0.804	0.991	15.74	0.11
Metropolitan 4	8174	0.139	0.83–0.85	1.04–1.16	0.888	0.223	0.975	31.50	$< 0.001$
Metropolitan 5	6790	0.196	0.81–0.83	0.93–1.03	1.118	– 1.970	0.961	16.92	0.08
Metropolitan 6	5120	0.123	0.78–0.81	0.85–0.99	1.033	0.576	0.973	6.87	0.74
Metropolitan 7	2008	0.102	0.84–0.86	1.21–1.58	0.761	– 0.407	0.884	55.56	$< 0.001$
Regional 1	2731	0.218	0.81–0.82	1.21–1.39	0.862	– 2.041	0.945	70.15	$< 0.001$
Regional 2	9091	0.069	0.82–0.83	0.80–0.93	0.908	1.711	0.990	26.83	0.003
Regional 3	8622	0.090	0.81–0.83	0.95–1.09	0.815	1.418	0.995	18.59	0.05
Regional 4	7799	0.103	0.80–0.82	0.96–1.09	0.786	1.931	0.987	27.98	0.002
Regional 5	6859	0.040	0.78–0.81	0.72–0.86	1.193	1.974	0.961	51.88	$< 0.001$
Regional 6	5025	0.082	0.80–0.82	1.00–1.21	0.847	0.489	0.964	29.54	0.001
Regional 7	4801	0.054	0.83–0.84	0.65–0.83	0.996	1.880	0.978	44.15	$< 0.001$
Regional 8	4168	0.057	0.81–0.82	0.80–1.03	0.826	1.544	0.971	15.03	0.13
Regional 9	4075	0.111	0.78–0.81	0.94–1.12	0.831	1.504	0.984	27.38	0.002
Regional 10	3664	0.090	0.83–0.85	0.99–1.22	0.619	2.550	0.979	43.88	$< 0.001$

AROC = 95% confidence interval of the area under receiver operating characteristic curve. SMR = standardised mortality ratio (95% CI).  $\beta$  = calibration plot slope.  $\alpha$  = calibration plot intercept.  $R^2$  = correlation of calibration plot. H10 = Hosmer–Lemeshow statistic.  $P$  = probability of H10.

model will have small residuals and a low Brier score, whereas a model that is no better than chance will have a Brier score of 0.25. A Brier score of less than 0.1 is desirable.

The SMR is the ratio of observed to predicted outcomes and is another overall measure of model accuracy. It is sensitive to the frequency of the outcome of interest (death) rather than sample size (admissions). For the SMR to be clinically meaningful, the number of events (deaths) should exceed 100, preferably 200, so that its error range is within  $\pm 10\%$ . In this regard, we note that two metropolitan and all regional hospitals have less than 100 deaths per annum and therefore interpretation of the annual SMR parameter is not possible.

The calibration plot describes a simple linear relationship between observed and predicted outcomes over the entire range of prediction. The slope ( $\beta$ ) and intercept ( $\alpha$ ) describe

this relationship. An ideal model will produce  $\beta = 1$  and  $\alpha = 0$ . A model that overestimates risk (death) will have  $\beta > 1 \pm \alpha > 1$ , whereas a model that underestimates risk will have a  $\beta < 1 \pm \alpha < 1$ .

Comparing the annual SMR, H10 index and Brier scores for each hospital over 12 years provided an assessment of the stability of the model.

Discrimination (the ability to correctly order survivors and non-survivors) was tested using the area under a receiver operating characteristic curve (AROC). A perfect model will produce an AROC of unity, whereas a model that is no better than chance will have an AROC of 0.5. An AROC  $> 0.8$  is desirable, and  $> 0.7$  is acceptable.

Data analysis was undertaken using Stata/MP, version 11 software (StataCorp, College Station, Texas, USA). The Victorian Department of Health provided the dataset and approved this publication.

**Table 3. Stability of the critical care outcome prediction equation model showing the annual standardised mortality ratio (SMR), Brier score, and H10 (Hosmer–Lemeshow statistic) for peer-group hospitals**

Financial year	Tertiary			Metropolitan			Regional		
	SMR (95% CI)	Brier	H10	SMR (95% CI)	Brier	H10	SMR (95% CI)	Brier	H10
Ideal	1.0±0.05	<0.10	<18.4	1.0±0.05	<0.10	<18.4	1.0±0.05	<0.10	<18.4
1999–00	0.93–1.04	0.09	84.57	0.96–1.12	0.11	58.97	0.89–1.09	0.07	75.24
2000–01	0.96–1.07	0.09	41.56	0.91–1.06	0.11	27.26	0.89–1.08	0.06	66.07
2001–02	0.94–1.05	0.10	46.60	0.96–1.13	0.12	68.00	0.87–1.04	0.06	38.96
2002–03	0.92–1.03	0.09	19.81	0.99–1.15	0.12	35.85	0.90–1.07	0.07	46.54
2003–04	0.90–1.01	0.09	14.59	1.03–1.18	0.12	43.59	0.89–1.07	0.06	26.83
2004–05	0.90–1.01	0.09	17.05	1.00–1.15	0.11	23.95	0.92–1.10	0.06	16.29
2005–06	0.94–1.05	0.09	13.25	0.95–1.09	0.11	20.00	0.90–1.10	0.06	19.76
2006–07	0.94–1.04	0.09	14.74	0.93–1.08	0.11	21.30	0.91–1.10	0.07	19.22
2007–08	0.93–1.04	0.10	11.41	0.98–1.12	0.12	33.19	0.87–1.05	0.07	12.01
2008–09	0.93–1.04	0.09	18.43	0.99–1.13	0.11	25.33	0.85–1.04	0.07	20.47
2009–10	0.92–1.03	0.09	43.02	0.99–1.13	0.10	17.22	0.87–1.06	0.06	17.91
2010–11	0.92–1.02	0.09	68.21	1.00–1.15	0.10	12.98	0.83–1.02	0.06	44.23

## Results

### Study population

Victoria has 23 hospitals with onsite adult intensive care services. Over 12 years, there were 214 616 hospital separations that received intensive care (study population). Of these, 104 047 (48.5%) received MV in the ICU and 26 721 (12.5%) died. The characteristics of the development and validation datasets are summarised in Table 1. There were no missing data fields.

There were significant differences in the caseload and mortality between the 23 hospital populations (Table 2). One hospital did not commence ICU services until 2003. The respective proportions of the study population (214 616) and the MV subgroup (104 047) admitted to tertiary referral hospitals were 50.4% and 71.4%; to metropolitan hospitals, 23.1% and 20.2%; and to regional hospitals, 26.5% and 8.3%.

### Model variables

Six variables were selected for the final COPE-4 model: age, emergency admission, use of MV, elective postcardiac surgery admission, hospital peer group, and 15 primary diagnosis groups. See Appendix 1 for definition of selected variables and Appendix 2 for the table of coefficients.

### Model validation

The development model was estimated on 35 878 (16.7%) consecutive ICU separations (2004–2006) and the derived model was then applied to the validation dataset of 178 741 records (1999–2004 and 2006–2011). Dataset characteristics are summarised in Table 1.

Calibration and discrimination characteristics of the COPE-4 model for each campus are presented in Table 2 and Figure 1. The discrimination remained satisfactory in the validation sample and across all hospitals. The development and validation datasets demonstrated H10 statistics of 13.38 ( $P=0.10$ ) and 14.84 ( $P=0.06$ ) and calibration plot slopes of 0.99 and 1.034, respectively.

### Peer-group predictions

The COPE-4 model fulfilled one or more of the calibration criteria (SMR, H10 < 18.4, and calibration slope) in all of the tertiary hospitals, in five of the seven metropolitan hospitals, and in eight of the 10 regional hospitals. The prediction model had a tendency to underestimate risk (SMR > 1 and/or  $\beta > 1$ ) in the tertiary and metropolitan hospitals while overestimating risk (SMR < 1 and/or  $\beta < 1$ ) in the regional hospitals (see Figure 1 and Table 2).

### Annual predictions

Over the 12 years, there was a total of 271 separate yearly point estimates for hospital AROCs, SMRs, H10 indices and Brier scores. The discriminatory function of the COPE-4 model remained satisfactory (AROC > 0.75) in all hospitals across this time period. There was no significant trend in Brier scores ( $P > 0.10$ ; Table 3).

There appeared to be a trend for the COPE-4 model calibration to decline over 5 years, but this did not reach statistical significance ( $P > 0.15$ ). The model fulfilled the calibration criteria in 215 of 271 (79.3%) hospital-years, and compliance rates in the tertiary, metropolitan and regional hospitals were 89%, 81% and 72%, respectively

(Table 3). Comparative results for the APACHE III-j model, based on reported SMR figures for the same hospitals during the same time period, were 33%, 32% and 75%, respectively.<sup>2</sup>

## Discussion

The COPE model is a simple mortality prediction tool derived from an administrative database (the VAED) and contains six variables present on admission. The COPE-4 model provides an estimate of the risk of in-hospital death for adult patients admitted to the ICU and performs consistently and satisfactorily in the majority of hospitals across a diverse population.

The method employed had several unique features, such as the a priori restriction on candidate variables and the inclusion of all ICU admissions and hospitals. This ensured that the prediction variables were not influenced by clinical care and that the model was applicable to all (adult) intensive care services.

The resulting model has several strengths compared with other prediction models,<sup>15</sup> thus providing a complementary option to the current gold standard, the APACHE III-j model. With no exclusion criteria and based on a comprehensive timely data source, the COPE-4 model is a practical screening tool. The results indicate that it is a reliable tool for its current purpose — screening and monitoring intensive care services.

The COPE-4 model was derived from a large comprehensive and domestic dataset of nearly 36 000 consecutive adult ICU admissions from all hospitals with adult ICU services in Victoria, and validated in nearly 180 000 admissions in 23 hospitals over 12 years. By comparison, APACHE III was developed using only 17 440 (and APACHE IV using 66 270)<sup>16</sup> patients from selected hospitals in North America.

There were few exclusion criteria. The COPE-4 model includes all diagnostic groups and only excludes ICU readmissions and paediatric admissions. The COPE-4 model was restricted to variables that displayed a consistent association with mortality over at least 10 years. While this may be criticised as a technique for forcing the model to fit the (validation) data, the benefits are a parsimonious model that is stable over time.

The COPE-4 model has similar discrimination and improved calibration compared with the APACHE III-j model in Victoria.<sup>2,3</sup> Although the COPE-4 model failed to maintain any calibration criteria in four hospitals (17%), a degree of calibration variation between different clinical services and calibration drift over time are not unexpected.<sup>17</sup> Further refinement of the model may address these shortcomings.

There are several important limitations to the COPE methodology. Some of these are inherent to all prediction models, such as the reliance on surrogate variables (eg, age)

and the inability to predict outcome in small subgroups and in individuals.

The model was derived from an administrative database (the VAED) that is not specific to intensive care services. To date, the COPE-4 model has only been validated in two states of Australia.<sup>18</sup> The data are collected and audited by clerical staff independent of the ICU, which is a potential strength (independence) and weakness (ignorance).

The COPE-4 model is also limited by the variables available within the VAED and does not contain, for example, physiological data for the estimation of severity of illness, as is the case in APACHE III-j. Comorbidity variables have not yet been found to improve the predictive accuracy of the COPE-4 model.

The COPE-4 model appeared to underestimate risk in tertiary and metropolitan hospitals and overestimate risk in regional hospitals. In the majority, these deviations were small and much less than those currently observed for the APACHE III-j model.<sup>2,3</sup> Recalibration and refinement of the two models may address some of these limitations.

## Conclusion

The COPE-4 model was developed from a large state population and found to perform well as a predictor of hospital mortality for adult ICU admissions. It comprises six simple categorical (except age) variables and its overall performance is sufficient for its use as a screening tool for monitoring intensive care services. Further refinement, and validation in other jurisdictions, may improve its performance and utility.

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## Competing interests

None declared.

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### Appendix 1. Definition of critical care outcome prediction equation, version 4 variables\*

Variable	Definition	Score
A	Age	Age in 5-year increments 15-19.9 years = 4; 20-24.9 years = 5; 25-29.9 years = 6; etc
B	Emergency	Admission to hospital that was not planned, booked or elective Yes = 1; No = 0
C	Cardiac surgery	Elective postcardiac surgery admission Yes = 1; No = 0
D	Primary diagnosis <sup>†</sup>	Diagnosis on admission to hospital (not ICU) Other diagnoses = 0
E	Mechanical ventilation	Mechanical ventilation any time during ICU admission Yes = 1; No = 0
F	Peer group	CICM classification level 1, 2 or 3

CICM = College of Intensive Care Medicine. ICU = intensive care unit. \* See Appendix 2 for constants. † See Appendix 2 for primary diagnosis.

#### Calculation example:

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

where  $y = A + B + C + D + E + F + \text{constant}$  (see Appendix 2).

For example, a 61-year-old (A) patient is urgently admitted (B) to a level 3 hospital (F) with septic shock (D), requiring mechanical ventilation (E):

$y = (A \times 12) + (B \times 1) + (C \times 0) + (D \times 1) + (E \times 1) + (F \times 3) + \text{constant} = -1.021$ .

Predicted risk of mortality,  $p = e^{-1.021} / (e^{-1.021} + 1) = 0.73$ .

**Appendix 2. Critical care outcome prediction equation, version 4 model variables and coefficients**

Variable	ICD-10-AM prefix	Odds ratio	Coefficient	95% CI
Age group		1.225	0.203	0.191, 0.215
Cardiac surgery		0.074	- 2.583	- 2.815, - 2.402
Emergency		2.090	0.741	0.636, 0.839
Mechanical ventilation		5.878	1.749	1.687, 1.856
Peer group		1.159	0.166	0.079, 0.216
Constant			- 6.887	- 7.130, - 6.581
Primary diagnosis*				
Septicaemia	A3, A4	3.303	1.183	1.027, 1.362
Secondary malignancy	C76–C80	3.088	1.123	0.818, 1.437
Haematopoietic malignancy	C81–C96	7.987	2.031	1.804, 2.352
Type 2 diabetes mellitus	E11	2.105	0.738	0.498, 0.991
Intracranial haemorrhage	G7, G9	4.294	1.452	1.018, 1.897
Acute coronary syndromes	I21	1.726	0.544	0.407, 0.684
Cardiac disease (excluding acute coronary syndromes)	I26–I52	1.819	0.594	0.455, 0.742
Cerebrovascular diseases	I6	3.494	1.262	1.113, 1.389
Pneumonia	J12–J18	2.282	0.815	0.658, 0.992
Chronic lung disease (excluding COPD)	J6–J9	1.877	0.625	0.443, 0.816
Gastrointestinal and peritoneal disease	K2–K27, K55, K56, K63, K65, K67, K9	1.234	0.203	0.057, 0.363
Liver disease	K7	3.348	1.221	0.954, 1.462
Circulatory shock	R57, R58	5.229	1.634	1.036, 2.273
Head injury	S0	1.624	0.486	0.298, 0.672
Drug ingestion	T36–T40, T50	0.283	- 1.277	- 1.630, - 0.893

ICD-10-AM = *International statistical classification of diseases and related health problems, 10th revision, Australian modification.*<sup>7</sup> \* Select one per patient.

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