Mortality and length-of-stay outcomes, 1993–2003, in the binational Australian and New Zealand intensive care adult patient database*

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Objective: **Intensive care unit (ICU) outcomes have been the subject of controversy. The objective was to model hospital mortality and ICU length-of-stay time-change of patients recorded in the Australian and New Zealand Intensive Care Society adult patient database.**

Design: **Retrospective, cohort study of prospectively collected data on index patient admissions.**

Setting: **Australian and New Zealand ICUs, 1993–2003.**

Patients: **The Australian and New Zealand Intensive Care Society adult patient database, which contains data for 223,129 patients.**

Interventions: **None.**

Measurements and Main Results: **Hospital mortality and ICU length of stay were modeled using logistic and linear regression, respectively, with determination (80%) and validation (20%) data sets. Model adequacy was assessed by discrimination (receiver operating characteristic curve area, A_z) and calibration (Hosmer-Lemeshow $\hat{C}$) for mortality and R^2 for length of stay. Predictor variables included patient demographics, severity score, surgical and ventilation status, ICU categories, and geographical locality. The data set comprised 223,129 patients: Their mean (SD) age was 59.2 (18.9) yrs, 41.7% were female, their mean (SD) Acute Physiology and Chronic Health Evaluation (APACHE) III score was 53 (31), they had 16.1% overall mortality rate, and 45.7% were mechanically ventilated. ICU length of stay was 3.6 (5.6) days. A_z, $\hat{C}$ statistic, and R^2 for developmental and validation model data sets were 0.88, 17.64 ($p = .02$), and 0.18; and 0.88, 12.32 ($p = .26$), and 0.18, respectively. Variables with mortality impact ($p \leq .001$) were age (odds ratio [OR] 1.023), gender (OR 1.16; males vs. females), APACHE III score (OR 1.06), mechanical ventilation (OR 1.66), and surgical status (elective, OR 0.17; emergency, OR 0.47; compared with nonsurgical). ICU level and locality had significant mortality-time effects. Similar variables were found to predict length of stay. Risk-adjusted mortality declined, during 1993–2003, from 0.19 (95% confidence interval 0.17–0.21) to 0.15 (0.13–0.16) and similarly for ventilated patients: 0.26 (0.24–0.29) to 0.23 (0.21–0.25). Predicted mean ICU length of stay (days) demonstrated minimal overall time-change: 3.4 (2.2) in 1993 to 3.5 (2.7) in 2003, peaking at 3.7 (2.4) in 2000.**

Conclusions: **Overall hospital mortality rate in patients admitted to Australian and New Zealand ICUs decreased 4% over 11 yrs. A similar trend occurred for mechanically ventilated patients. Length of stay changed minimally over this period. (Crit Care Med 2008; 36:46–61)**

KEY WORDS: intensive care; database; hospital mortality; length of stay; longitudinal study; generalized linear model; random effects

Intensive care unit (ICU) outcomes, such as mortality and length of stay, have been a subject of interest and controversy (1–4) as well as a focus of critical care professional organizations (5–7) and commercial organizations interested in purchasing health care (8, 9). By far, the majority of articles looking at such outcomes have not unreasonably used the individual ICU as the prime descriptor. A national database, such as that maintained by the Database Management Committee of the Australian and New Zealand Intensive Care Society (ANZICS) (10), permits analysis of aggregate outcome measures over time.

Raw mortality rates are influenced by differences in severity of illness, case mix, discharge practices, geographical location, and the allocation of human and material resources (11–14). The majority of studies addressing mortality outcome from ICUs have situated analysis within established prediction algorithms (15–17), using a relatively small set of predictor variables. ICU length of stay has also been the subject of detailed analysis (18–20), but few studies have evaluated change over a prolonged time period (21), the majority presenting cross-sectional analyses over a relatively short

***See also p. 336.**

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periods of months (22) to 1–2 yrs (23). Studies of ICU length of stay have focused mainly on responsible patient factors (2, 20) rather than on organizational/geographical factors (18, 23–25).

We wanted to expand this paradigm by extending the potential predictors (26) to more fully account for those multiple factors, as just described, which may have influenced the time course of both mortality and ICU length of stay of patients recorded in the ANZICS Adult Patient Database Management Committee database over the period 1993–2003. Thus, a focus of interest was the influence of available ICU descriptors, for example, ICU level and geographical location, although such changes may have been specific to the national database. As the objective of the current study was to explain variation as fully as possible (27), we were less concerned with principles such as transportability and overfitting (28), which are apposite predictive concerns.

METHODS

The ANZICS Adult Patient Database is a binational (Australia and New Zealand) voluntary data collection of individual ICU admissions, commencing in 1990. This database was interrogated to define an appropriate patient set, over the time period 1993–2003, the earliest comprehensive data being for calendar year 1993. The data set requirements are specified in a data dictionary (29). Data were collected at the individual ICU and uploaded to the central repository (ANZICS adult patient database) for processing and quality assurance, consisting of a cycle of error and exception checks, site feedback, resubmission, and incorporation into a final reporting data set. Physiologic variables collected were the worst in the first 24 hrs after ICU admission. All first ICU admissions to a particular hospital for the period 1993–2003 were selected. Access to the data was granted by the ANZICS Database Management Committee in accordance with standing protocols; local hospital (The Queen Elizabeth Hospital) Ethics of Research Committee approval was waived.

Exclusions were patients with unknown hospital vital outcome and date of discharge; patients with an ICU length of stay ≤4 hrs; and patients <16 yrs of age. Specific attention was directed to the fidelity of severity of illness records, in particular the scoring of the Glasgow Coma Scale. Records were used only when all three components of the Glasgow Coma Scale were provided. Records for which all physiologic variables were missing were excluded, and for the remaining records, missing variables were replaced with the normal range and weighted accordingly. ICU and hospital length of stay, initially recorded in hours, was transformed to fractional days. Patients with an ICU length of stay >60 days and hospital length of stay >365 days were not considered in formal analysis. No established trimming methods were employed (30). The Simplified Acute Physiology (SAPS) II score (17) was back-calculated for the calendar year 1993. Descriptors of ICU admission primary organ system dysfunction were generated by consolidating the diagnostic categories of the Acute Physiology and Chronic Health Evaluation (APACHE) algorithms to yield the following descriptors: cardiovascular, gastrointestinal, metabolic, neurologic, respiratory, trauma, and renal/genitourinary.

Statistical Methods

Variables were reported using mean (SD), except where otherwise indicated. For summarizing raw variable time-change, simple nonparametric trend tests were used, with statistical significance ascribed at $p < .05$. Categorical variables were analyzed using the chi-square test. Stata (version 9.2 MP, 2006, College Station, TX) statistical software was used.

Hospital mortality was modeled using logistic regression with standard errors adjusted by 1) clustering on ICU-year units, formed by ICU-site × calendar-year interaction, on the basis that within-cluster observations were not independent (e.g., subject to serial correlation); and 2) using robust variance estimates to allow for any within-cluster heteroscedasticity (nonconstant variance) (31). For the units created by this site × year interaction, minimum patient number was set at 150, to ensure estimation stability. Choice of severity-of-illness score was determined by discrimination of the score, assessed by receiver operating characteristic (ROC) curve area, when entered into the logistic model as the sole covariate. The continuous variables were age, severity-of-illness scores, and calendar year; candidate categorical predictors were parameterized as simple indicator variables. Clinically meaningful combinations of variables and their two-way interactions were assessed for effect in the logistic model; higher order interactions were not entertained in the final model. The potential for multiple colinearity was tested using the variance inflation factor (VIF) and condition number (CN), where VIF <10 and CN <30 (32) are desirable. Model adequacy was gauged by the traditional criteria of discrimination (ROC area) and calibration, and Hosmer-Lemeshow (H-L) $\hat{C}$ statistic and model chi-squared were calculated for each parameter (33) to adjudge its relative importance. The final model was developed on a training (80% of data) and determination set (20% of data), the random samples being stratified by calendar year. Mortality probabilities and 95% confidence intervals (CIs) were generated from the final model with continuous covariates centered and categorical covariates held at the reference category. Predicted probabilities with 95% CI were collapsed and averaged over patient categories and calendar year to yield appropriate graphical display. Details of the approach to modeling and graphical display are given in Appendix 2. To further investigate potential heterogeneity of mortality effect (34), the final model was re-estimated using a two-level, patients within ICU-year units, random effects logistic regression model (the gllamm Stata module) (35). Parameter estimates and performance were compared with those of the logistic model.

Log ICU length of stay was modeled using ordinary least squares (OLS) regression, with the same covariate set and standard error adjustment to allow comparability of variable effects, and back-transformation to the day scale using Duan's smearing estimate (36). The applicability of this covariate set was tested using the split sample technique, as previously described. Model performance was assessed by the coefficient of determination (R^2), on the day scale (37), computed as the square of the correlation between predicted and observed length of stay (38), and residual analysis by assessment of residual normality and heteroscedasticity.

RESULTS

Demographics

The database, exclusive of ICU readmissions for both the same and separate hospital admissions (n = 6,001) and patients having ICU length of stay <4 hrs (n = 5,762, hospital mortality = 50.6%), contained records of 253,163 patients for the period 1993–2003. Incomplete Glasgow Coma Scale scores were recorded for 14,644 patients, there being no calendar-year time trend of this incompleteness (percent exclusion, 1.3% to 11%; $p = .34$). Missing hospital mortality outcome that constituted >10% of monthly admission totals occurred in 587 of 6,084 site-month units (9.65%). After exclusion of ICU-year units with n < 150, the final data set comprised 223,129 patients from 99 ICUs over the 11-yr period. Mean (SD) age was 59.2 (18.9) years, 41.7% were female, and the mortality rate was 16.1%. Overall, 45.7% were mechanically ventilated, and of these 60.6% were male. Mean severity-of-illness scores across the whole database (n = 223,129) were APACHE II 15.4 (8.5), APACHE III 52.7 (30.6), and SAPS II 31.6 (17.6). Severity score discrimination as ROC curve area with respect to hospital mortality was

Table 1. Patient demographics and Acute Physiology and Chronic Health Evaluation (APACHE) III score by intensive care unit (ICU) geographical location and mechanical ventilation status

Locality	ICU Mortality, %		Hospital Mortality, %		ICU LOS, Days		Age, Yrs		Gender, % Males		APACHE III Score	
	NV	V	NV	V	NV	V	NV	V	NV	V	NV	V
Northern territory (n = 5222)	3.8	24.9	7.7	24.9	2.1 (3.4)	5.8 (7.2)	49.7 (17.0)	47.0 (17.0)	57	64	41.4 (24.7)	73.4 (34.9)
New South Wales (n = 72670)	4.2	20.1	9.0	27.3	2.5 (3.5)	5.5 (7.3)	59.7 (19.2)	59.6 (18.9)	55	61	41.4 (23.1)	69.9 (34.2)
Australian capital territory (n = 5995)	3.2	17.0	6.4	22.1	2.0 (4.1)	5.3 (7.0)	58.3 (18.4)	56.6 (19.1)	57	59	38.6 (20.3)	54.8 (29.0)
South Australia (n = 22480)	6.9	20.6	14.1	29.4	2.4 (3.3)	5.2 (7.7)	62.8 (18.1)	58.7 (19.3)	56	61	48.1 (24.7)	71.0 (34.2)
Victoria (n = 63377)	3.4	17.4	7.8	24.8	2.3 (3.3)	5.6 (7.2)	62.2 (17.8)	58.9 (19.0)	58	61	41.7 (21.7)	66.2 (32.4)
New Zealand (n = 11393)	5.0	18.9	9.0	25.7	1.9 (3.1)	4.0 (6.0)	56.5 (20.5)	57.4 (19.6)	55	60	41.2 (23.6)	65.2 (31.7)
Queensland (n = 39970)	3.2	14.2	7.1	18.2	2.0 (3.1)	4.4 (6.6)	57.5 (19.2)	58.3 (18.6)	55	60	38.8 (21.8)	59.4 (31.1)
Tasmania (n = 6130)	5.5	20.9	10.0	27.9	2.4 (3.3)	6.2 (7.3)	58.9 (18.0)	57.7 (18.7)	58	61	39.2 (24.1)	71.1 (32.4)
Western Australia (n = 369)	4.4	18.3	6.6	25.0	2.1 (1.7)	4.2 (3.4)	65.4 (16.5)	66.4 (15.5)	56	41	37.3 (18.2)	57.5 (24.2)

NV, not ventilated; V, ventilated; LOS, length of stay.

Table 2. Demographics of intensive care unit (ICU) hospital level, ventilation, and surgical status: mean (SD)

ICU Hospital Level	Overall	Not Ventilated			Ventilated		
		Nonsurgical	Elective Surgical	Emergency Surgical	Nonsurgical	Elective Surgical	Emergency Surgical
Rural							
ICU length of stay, days	3.1 (5.0)	2.4 (3.5)	1.9 (2.4)	2.3 (3.4)	5.7 (8.2)	5.2 (6.4)	6.4 (8.2)
APACHE III score	44.8 (29.1)	37.6 (23.5)	34.7 (16.0)	39.5 (20.7)	76.5 (35.5)	58.6 (27.5)	69.3 (32.0)
Age, yrs	59.2 (19.1)	56.8 (19.5)	65.6 (15.2)	63.0 (19.5)	55.9 (19.5)	67.0 (14.3)	64.6 (18.3)
% males	57	57	59	52	57	67	59
ICU mortality, %	8.2	5.0	1.1	3.2	28.8	10.4	15.9
Hospital mortality, %	12.2	8.5	3.7	7.3	34.6	16.8	23.6
Metropolitan							
ICU length of stay, days	3.9 (6.7)	2.8 (4.4)	1.9 (3.02)	2.2 (3.1)	6.3 (9.3)	4.9 (7.3)	7.1 (9.5)
APACHE III score	54.5 (31.9)	44.5 (25.5)	38.6 (17.1)	43.3 (22.1)	77.9 (35.5)	56.9 (25.5)	70.6 (32.0)
Age, yrs	59.4 (19.2)	56.9 (19.8)	66.2 (14.6)	62.0 (19.7)	55.6 (19.6)	67.4 (13.9)	62.9 (19.1)
% males	56	53	59	54	57	62	60
ICU mortality, %	10.4	5.7	0.7	2.5	25.3	5.8	15.9
Hospital mortality, %	15.9	11.1	3.6	7.0	32.6	10.6	23.2
Tertiary							
ICU length of stay, days	4.0 (6.9)	2.9 (5.2)	1.5 (2.2)	2.1 (3.7)	6.1 (8.9)	2.8 (5.1)	5.9 (8.0)
APACHE III score	55.7 (31.1)	48.0 (26.2)	36.1 (16.5)	40.8 (21.2)	72.7 (35.3)	47.9 (20.8)	62.9 (29.7)
Age, yrs	57.6 (19.1)	55.1 (20.0)	62.3 (16.1)	58.2 (20.3)	55.2 (19.5)	62.8 (15.5)	57.4 (20.3)
% males	60	55	60	57	60	63	63
ICU mortality (%)	12.2	7.5	0.7	2.5	25.7	3.0	14.6
Hospital mortality (%)	18.7	14.5	3.6	8.2	33.7	6.5	22.7
Private							
ICU length of stay, days	3.0 (5.2)	2.8 (4.1)	1.6 (2.1)	2.0 (3.0)	6.9 (8.6)	3.2 (4.6)	5.6 (7.4)
APACHE III score	46.1 (25.4)	46.2 (23.6)	34.2 (14.8)	41.5 (19.5)	77.8 (34.3)	48.9 (19.7)	64.8 (29.9)
Age, yrs	65.5 (16.0)	64.9 (17.9)	65.0 (15.4)	66.7 (16.3)	64.4 (17.4)	67.0 (13.5)	66.8 (16.6)
% males	57	52	59	53	55	63	54
ICU mortality, %	5.6	5.9	0.4	2.4	28.7	2.2	12.8
Hospital mortality, %	9.5	12.0	2.1	6.7	36.1	4.7	21.0

APACHE, Acute Physiology and Chronic Health Evaluation.

APACHE II 0.85 (SE 0.001), APACHE III 0.87 (0.001), and SAPS II 0.86 (0.001), suggesting better discrimination for the APACHE III score, which was selected as the severity-of-illness score for this study. Demographics, by geographical locality and hospital level and surgical status, are shown in Tables 1 and 2. No time-change of fraction of first day post-ICU admission mechanically ventilated patients was evident by nonparametric trend test ($p = .18$).

We found the following with respect to categorization of ICU admission physiologic system derangement by ICU level and surgical status: For nonsurgical cases, the primary physiologic system derangements were cardiovascular and respiratory; for elective surgical, cardiovascular and gastrointestinal; and for emergency surgical, gastrointestinal, cardiovascular, and trauma. Within and between each ICU level, there were significant ($p = .0001$) distributional differences of primary physiologic system derangement and surgical status. The current database did not incorporate records from coronary care units, and the percentage of cases with an ICU admission diagnosis of acute myocardial infarction was 1.7%.

ICU length of stay was 3.6 (5.6) (median 1.8, interquartile range 2.9 [0.9–3.8]) days, and hospital length of stay was 16.4 (19.5) (median 10.1, interquartile range 14.6 [5.1–19.7]) days. The overall

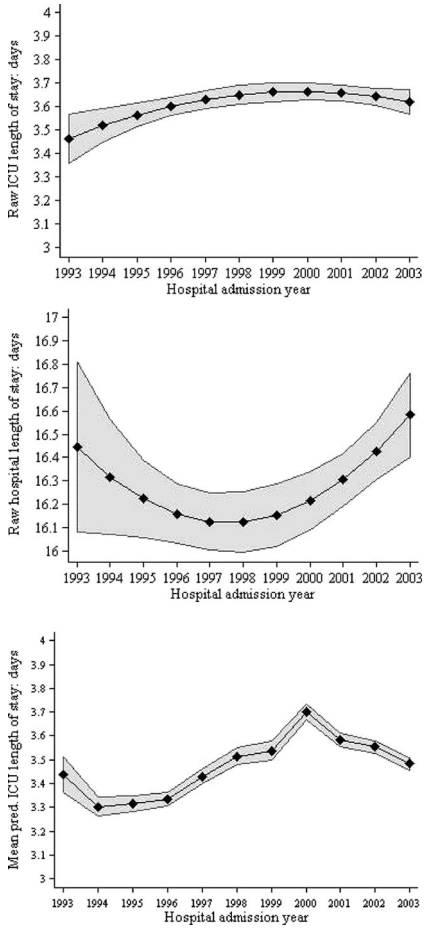

Figure 1. *Top*, raw intensive care unit length of stay in days (vertical axis), with 95% confidence intervals, plotted against calendar year (horizontal axis); *middle*, raw hospital length of stay in days (vertical axis), with 95% confidence intervals, plotted against calendar year. *Bottom*, mean predicted intensive care unit length of stay in days (vertical axis), with 95% confidence intervals, plotted against calendar year. *pred.*, predicted; *connected triangle symbol line*, point estimate; *shaded area*, 95% confidence intervals.

percentage of patients with ICU length of stay >60 days was 0.16%, varying over calendar years from 0.09% to 0.25%, with no significant time trend ($p = .18$). Raw ICU, but not hospital, length of stay demonstrated an increment over time, 1993–2003 ($p = .04$ and .60, respectively). The increase of raw ICU length of stay over calendar years was significant as a quadratic effect (time, $p = .05$; time^2, $p = .02$), visualized, with hospital length of stay, in Figure 1, *top* and *middle panels*, respectively.

Raw Mortality and Length of Stay

ICU and hospital mortality and APACHE III scores by calendar year and ICU type are shown in Table 3. Over the whole database, 1993–2003, raw (mean) ICU and hospital mortality showed a decline between 1993 and 2003 (nonparametric trend, $p = .008$ and .02, respectively). For private and tertiary ICUs, there were significant decreases in raw ICU and hospital mortality over time. No trend was discernible for metropolitan ICUs ($p = .42$ and .79, respectively), and for rural ICUs there were significant increases over time for both ICU and hospital mortality. Time-change of raw ICU length of stay, by outcome and ventilation status, stratified by APACHE III tertiles, is shown in Figure 2, *left*. For ICU survivors, the length of stay demonstrated an increase across the APACHE III tertiles, APACHE III scores 0–36, 37–60, and 61–216, respectively, with a mild time increase in length of stay in ventilated patients in the uppermost APACHE III tertile. However, for non-ICU survivors, length of stay across the tertiles of APACHE III was reversed, suggesting a substantive qualitative interaction. No time trend of ICU mortality was evident across any of the six APACHE III tertile-ventilation strata ($p \geq .34$).

Hospital survivors were discharged to home (83.4%), a rehabilitation facility (5.4%), or another hospital (11.2%). The percentage of survivors discharged to a rehabilitation facility increased from 2.4% (1993) to 6.7% (2003) ($p = .01$, nonparametric trend); beyond 1994, no time trend was evident ($p \geq .08$). The percentage of patients discharged to another hospital demonstrated no time trend ($p = .43$).

Hospital Mortality Model

With such a large database and number of events, 28,641 deaths in the development set, the potential number of predictors that could properly be incorporated into a logistic model was substantial (39), as was the potential for multicollinearity. Calendar year was modeled as a continuous centered variable, including a simple quadratic effect, and referenced to 1999–2000, after Milberg et al (40). This also reduced the number of parameters occasioned by interactions.

The development set (n = 178,506) had an ROC area of 0.88, with p values for Windmeijer's goodness-of-fit test and H-L $\hat{C}$ of 0.77 and 0.02, respectively; for the validation set (n = 44,623), ROC area was 0.88 and H-L $\hat{C}$ 12.32 ($p = .26$). Reported estimates were therefore generated on the whole data set with an ROC area of 0.88, Windmeijer's goodness-of-fit test ($p = .26$), and H-L $\hat{C} = 23.59$ ($p = .003$). The parameters of the final model, point estimates as odds ratios (ORs) with p val-

Table 3. Raw intensive care unit (ICU) and hospital mortality and Acute Physiology and Chronic Health Evaluation (APACHE) III score (mean, SD): ICU type by calendar year

Hospital Admission Year	Overall[a] ICU Mortality	Overall[b] Hospital Mortality	Rural[a] ICU Mortality	Rural[b] Hospital Mortality	Rural APACHE III	Metro ICU Mortality	Metro Hospital Mortality	Metro APACHE III	Tertiary[b] ICU Mortality	Tertiary[b] Hospital Mortality	Tertiary APACHE III	Private[a] ICU Mortality	Private[a] Hospital Mortality	Private APACHE III
1993	0.12	0.183	0.06	0.11	47.8 (32.1)	0.10	0.17	62.4 (34.5)	0.13	0.19	58.4 (40.0)	NR	NR	NR
1994	0.12	0.171	0.07	0.09	40.7 (26.0)	0.11	0.19	61.0 (34.0)	0.15	0.2	58.1 (32.7)	0.09	0.14	46.7 (26.7)
1995	0.11	0.163	0.07	0.10	42.1 (28.2)	0.09	0.14	48.7 (32.6)	0.14	0.2	58.1 (33.1)	0.09	0.14	49.7 (29.1)
1996	0.11	0.164	0.07	0.11	41.8 (28.1)	0.09	0.14	48.9 (31.2)	0.14	0.21	56.3 (31.7)	0.07	0.11	47.5 (26.8)
1997	0.11	0.159	0.08	0.12	42.3 (28.8)	0.10	0.14	52.0 (31.4)	0.13	0.19	56.1 (31.8)	0.07	0.11	48.5 (27.0)
1998	0.11	0.164	0.07	0.11	43.0 (29.5)	0.11	0.16	57.1 (33.2)	0.11	0.18	53.8 (30.7)	0.08	0.11	50.0 (28.0)
1999	0.10	0.158	0.10	0.13	45.0 (31.1)	0.10	0.15	55.4 (31.6)	0.11	0.17	52.2 (30.3)	0.06	0.11	51.5 (29.8)
2000	0.11	0.174	0.11	0.15	47.5 (29.0)	0.12	0.18	57.3 (32.3)	0.12	0.19	55.5 (31.2)	0.04	0.09	45.9 (23.8)
2001	0.10	0.161	0.11	0.16	49.4 (30.7)	0.11	0.16	56.7 (31.8)	0.11	0.18	54.5 (30.8)	0.04	0.08	45.4 (23.6)
2002	0.10	0.156	0.10	0.14	49.1 (29.5)	0.10	0.16	56.1 (31.2)	0.12	0.18	55.7 (30.5)	0.05	0.09	44.4 (24.5)
2003	0.09	0.148	0.08	0.12	46.4 (29.0)	0.11	0.17	54.4 (29.9)	0.11	0.18	56.0 (30.0)	0.04	0.07	43.9 (23.3)

Metro, metropolitan; NR, not recorded in the database.
[a]$p < .01$ for linear trend; [b]$p < .05$ for linear trend.

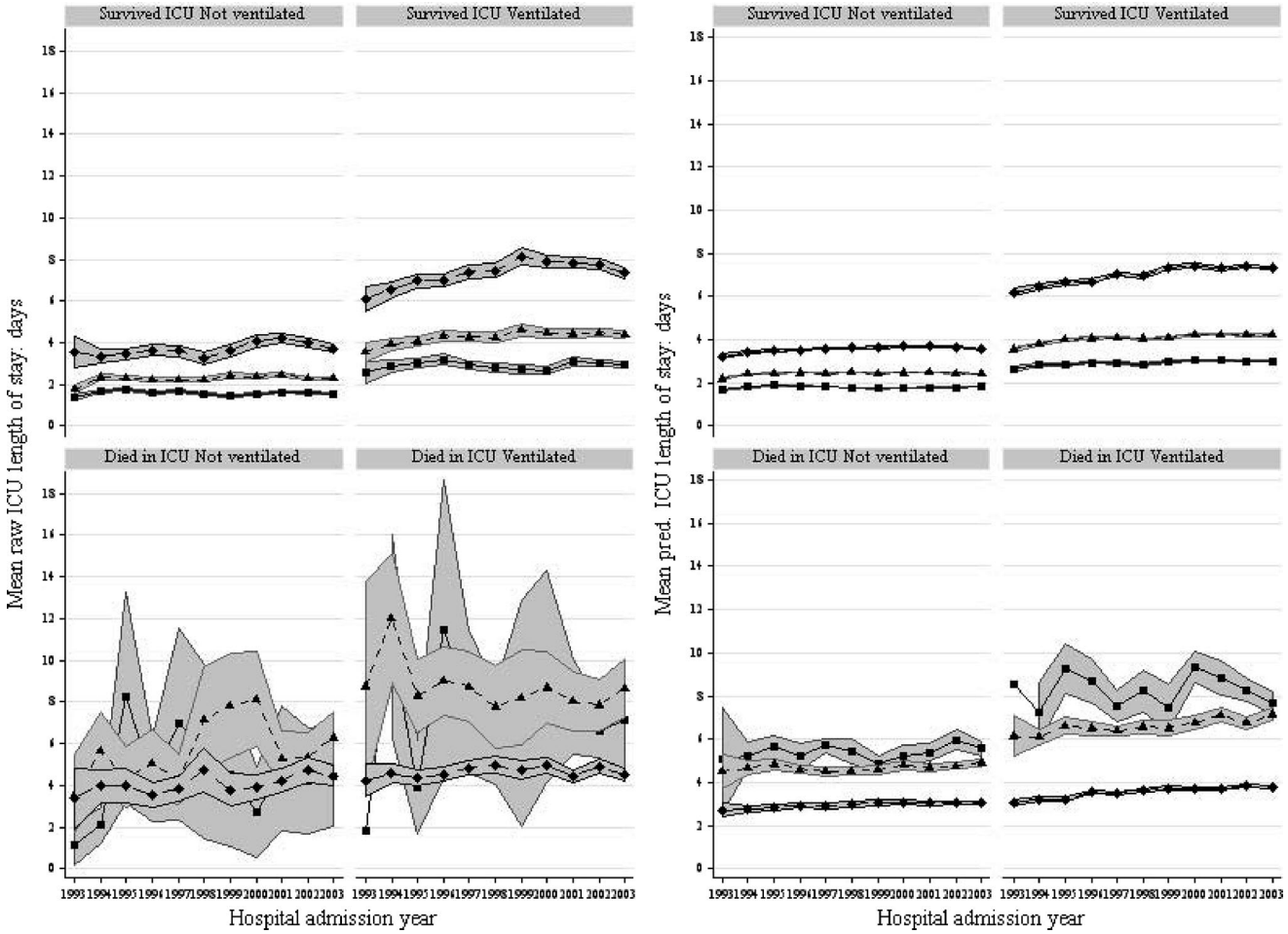

Figure 2. *Left*, mean raw intensive care unit (*ICU*) length of stay for (intensive care unit) survivors/nonsurvivors, by ventilation status, stratified by Acute Physiology and Chronic Health Evaluation (APACHE) III tertiles plotted against calendar year (horizontal axis). *Squares*, APACHE III scores 0–36; *triangles*, APACHE III scores 37–60; *diamonds*, APACHE III scores 61–216; *pred.*, predicted; *connected line*, point estimate; *shaded area*, 95% confidence intervals. *Right*, mean predicted intensive care unit length of stay for (intensive care unit) survivors/nonsurvivors, by ventilation status, stratified by APACHE III tertiles plotted against calendar year (horizontal axis). *Squares*, APACHE III scores 0–36; *triangles*, APACHE III scores 37–60; *diamonds*, APACHE III scores 61–216; *pred.*, predicted; *connected line*, point estimate; *shaded area*, 95% confidence intervals. No consistent 95% confidence intervals were obtained for calendar year 1993 for the patient category *died in ICU ventilated* for APACHE III scores 0–36 (for both mean raw intensive care unit length of stay and mean predicted intensive care unit length of stay); point estimates only are given.

ues and 95% CIs, are displayed in Appendix 1, *columns 2–5*. The VIF and CN for the final model, with only age and APACHE III score centered, were 8.53 and 68.1, respectively, indicating modest multicollinearity. With calendar year also centered, VIF and CN fell to acceptable values of 4.2 and 23.7, respectively.

The most important model variables, indexed by the magnitude of the model chi-squared (Appendix 1, *column 6*), were patient variables: APACHE III score and its quadratic form, age and interaction with APACHE III score, ICU admission primary organ system dysfunction and interactions with APACHE III score, patient surgical status and interaction with primary organ system dysfunction, and mechanical ventilation and interactions. ICU hospital level, year-site admission number, and geographic-demographic variables, as main effects, had lesser impact. Other noteworthy components of the model were as follows:

There was decline in overall adjusted mortality from 0.19 (95% CI 0.17–0.21) in 1993 to 0.15 (95% CI 0.13–0.16) in 2003, as seen in Figure 3, *left*, the rate of decline decreasing and tending to reverse between the years 1996 and 2000. With no time interactions, mortality showed a significant, albeit modest decrease over time as a simple quadratic (likelihood ratio test, $p = .0001$; calendar year, 0.987 [95% CI 0.982, 0.992]; calendar year squared, 0.997 [95% CI 0.995, 0.999]). This main-effect estimate was subsequently modified, by interactions developed within the final model (Appendix 1, calendar year effects, and time effect of geographical determinants, respectively).

Adverse mechanical-ventilation mortality outcomes showed a distinct trend for improvement, as shown in Figure 3, *right*: 1993, 0.26 (95% CI 0.24–0.29) to 2003, 0.23 (95% CI 0.21–0.25). This was not evident for those not initially ventilated. A similar time-decrease of overall raw mortality occurred in ventilated but not in nonventilated patients ($p = .01$ and $p = .1$, respectively).

Surgical patients fared better than nonsurgical patients (Fig. 4). Although the main effects, emergency vs. elective surgery (OR 2.86, 95% CI 2.44–3.34, $p = .0001$), suggested a worse outcome for emergency surgery, this

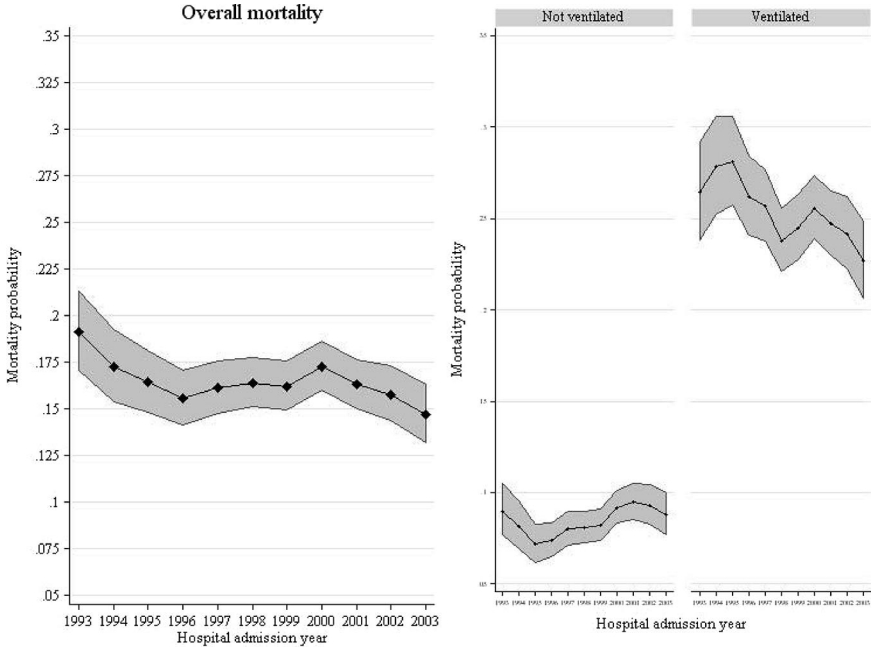

Figure 3. Adjusted mortality (*connected line*, point estimate; *shaded area*, 95% confidence intervals) at hospital discharge (y-axis) plotted against calendar year (x-axis) for overall mortality (*left*) and ventilation status (*right*). *Connected triangle symbol line*, point estimate; *shaded area*, 95% confidence intervals.

was modified by interactions with ICU primary organ system dysfunction, in this case, gastrointestinal and yearly admission number. Generalized time-decreases in mortality occurred for these patient-surgical and diagnostic categories, as seen in Figures 4 and 5.

There was an impact of yearly admission number. Admission of <711 patients per year was associated with a favorable OR of 0.84 (95% CI 0.76–0.92). No temporal trend or interaction with mechanical ventilation or APACHE III score was evident ($p = .13$, $p = .96$, and $p = .71$, respectively).

The OR of rural and metropolitan ICUs was advantageous compared with tertiary ICUs (Appendix 3). These main effects were modified by statistically significant interactions with APACHE III score and with both the effect of admitting <711 patients per year and calendar year, although the clinical importance, in terms of the OR estimate, was variable.

An overall adverse effect for ventilated males compared with females was evident, the OR for the combination of ventilation, gender, and ventilation × gender being 1.74 (95% CI, 1.57–1.93; $p = .0001$). There was no evident interaction with age or with APACHE III score ($p = .39$ and $p = .26$, respectively).

As a sensitivity analysis, the full model was re-estimated with omission of the 587 site-month-units with >10% missing hospital outcome. Parameter estimates were materially unchanged, and the model was adequately specified (ROC area = 0.88; Windmeijer's goodness-of-fit test = 0.33, and H-L $\hat{C} = 24.6$, $p = .002$).

Random Effects Model

The random effects model demonstrated a significant variance component compared with the conventional pooled logistic regression model, although the intraclass correlation coefficient was modest at .019 (95% CI 0.015–0.023, $p = .0001$). The ROC curve area was 0.89, this being statistically different at ($p = .09$) from the final model, and the H-L $\hat{C}$ was 19.4 ($p = .01$). Comparing the parameter estimates between the two models (Appendix 1, *columns 7–10*), revealed the following:

Little substantive change was found in the patient-specific variable ORs or p values.

The impact of ventilation was maintained.

For ICU site-specific and geographical variables, a lessening of statistical significance as parameter estimates moved toward the null (OR ≡ 1) was found. Of note, the variable *yearly site admissions <711* retained clinical and statistical significance.

ICU Length-of-Stay Model

For ICU length of stay modeled as a function of various covariates, the determination and validation data sets had R^2 of .18; final coefficients and predicted length of stay were therefore produced from a full data set ($R^2 = .18$). Residuals were normally distributed, and there was no evidence of heteroscedasticity.

Parameter and effect estimates, the latter as percentage change (41), are seen in Appendix 1, *columns 11–15*. Time-change of overall predicted length of stay is seen in Figure 1, *bottom left*, demonstrating a mild sigmoid convexity. Patient variable effect changes (Appendix 1, *patient variables, % change*) were relatively small; however, over the APACHE III tertiles, substantial changes in length of stay occurred for both ICU survivors and those who died, as seen in Figure 2, *right*. Main-effect changes associated with ICU admission primary organ system dysfunction ranged from −27% to 8% compared with cardiovascular organ system dysfunction. Large length-of-stay increments were associated with mechanical ventilation, compared with no ventilation, and its specific interaction with trauma and respiratory organ system dysfunction. The effect of hospital/ICU level and geographical locality on length of stay was again variable.

As noted in the display of time-change of raw ICU length of stay (Fig. 2), a qualitative interaction was suggested between outcome and ventilation status, stratified by APACHE III tertiles. Accordingly, *death in ICU* and the two appropriate interactions were incorporated into the final model, with no material increase in colinearity (VIF = 4.3, CN = 24.2). All three parameters were associated with large effects, in concordance with the raw mortality effects, with a decrease of length of stay in non-ICU survivors across increments in APACHE III score.

DISCUSSION

The current study addressed a number of factors determining mortality outcome and length of stay: patient and demographic/geographic factors, time trends, and their interactions, although they reflected a particular national database. The analysis also emphasized 1) the necessarily multivariable nature of any explana-

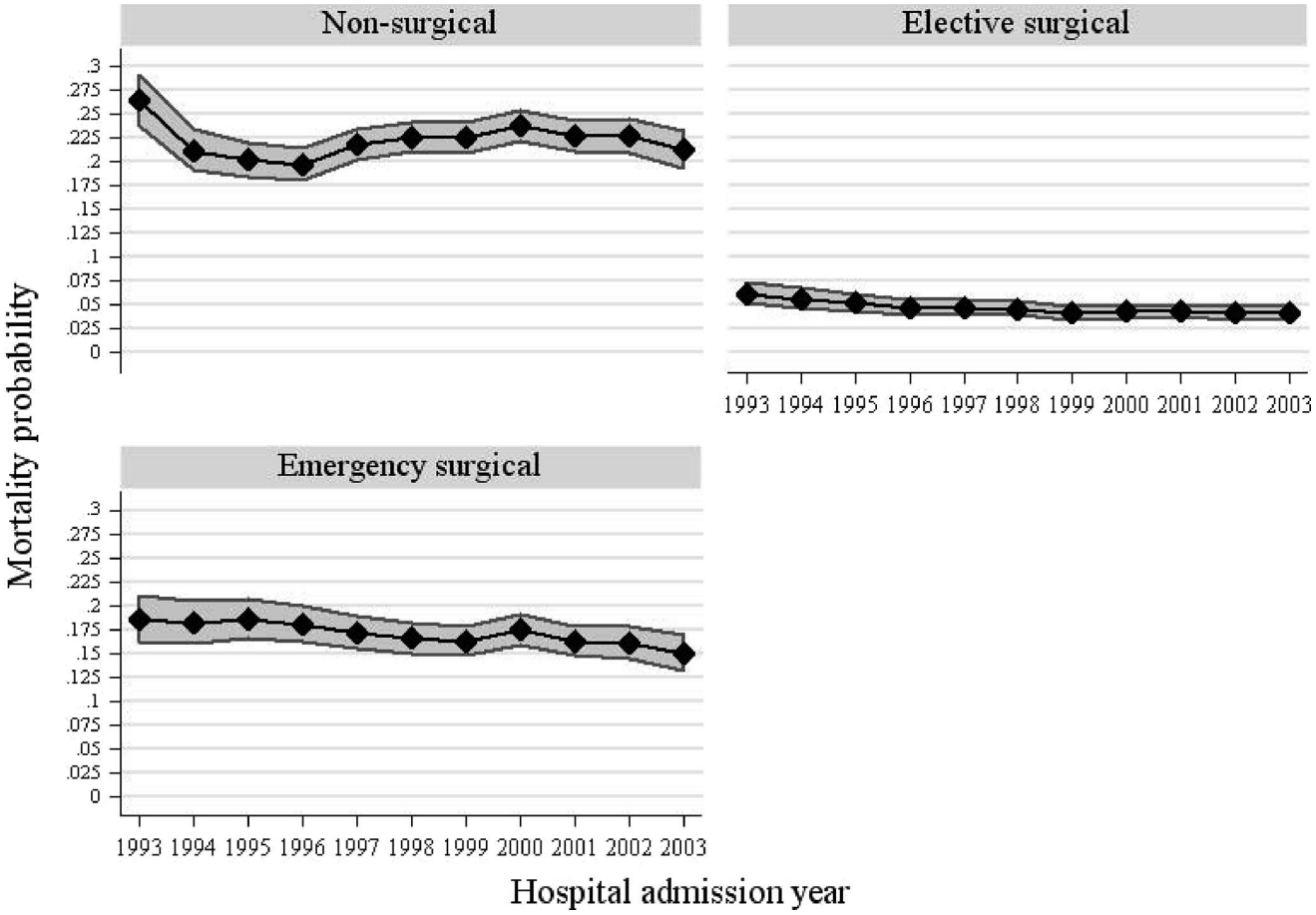

Figure 4. Adjusted mortality (point estimate and 95% confidence intervals) at hospital discharge (y-axis) plotted against calendar year (x-axis) for patient surgical classification. *Connected triangle symbol line*, point estimate; *shaded area*; 95% confidence intervals.

tory model that presumes to adequately address mortality over time in a large national database (the explanatory structure of such a model cannot be reduced to the familiar core set of variables that populate the standard predictive algorithms); and 2) the requirement for the full explication of interactions, as reflecting plausible model mechanisms (42). This being said, these model mechanisms were entirely transparent, standard continuous variable transformations as quadratic effects and simple two-way interactions.

Mortality Outcome

Patient Factors. Not surprisingly, the APACHE III score and age were confirmed as important mortality determinants, consistent with reports in the literature (16, 43, 44). The overall adverse effect for males highlights the diverse reports in previous, smaller studies: increased risk for both males (45) and females (46) and no difference (47–49).

An attempt was made to characterize the mortality effect of acute disease as an independent factor (50); the potential number of diagnostic categories from the APACHE algorithms (15, 16) was limited to seven by grouping, with cardiovascular dysfunction as the comparator. Such a strategy had the obvious potential for misclassification but was deemed necessary to constrain the model parameters to an interpretable number. The relatively favorable outcome for trauma and metabolic dysfunction compared with cardiovascular was understandable as was the adverse outcome of gastrointestinal and neurologic. These effects were modified by interaction with severity of illness and patient surgical status. The effect of *emergency surgery* and *no surgery before admission*, compared with elective surgery, has been variously incorporated into predictive algorithms: the weighting of these surgical factors in the SAPS II score (17) and the Mortality Probability Model II (51), where the variable *no elective surgery* had an OR of 3.3.

Treatment Factors. The adverse survival effect of mechanical ventilation has also been previously documented, for instance, in the Mortality Probability Model II study (51), where OR for ventilation was 2.2 (95% CI 2.0–2.5). As expected, ventilation had a variable impact on primary admission physiologic dysfunctions compared with cardiovascular dysfunction. The reversal of mortality trend in ventilated patients between 1999 and 2000 (Fig. 3, *right*) is unexplained. The beginning of the decline in mortality from year 2000 to 2003 was temporally coincident with the publication of the pivotal ARDS Network trial of low tidal volumes (52), but a similar pattern was also observed in nonventilated patients. *Yearly site admission <711 per year* was associated with a favorable OR of 0.84 (95% CI 0.76–0.92) resonating with the volume-outcome debate (53) but suggests, paradoxically, that performance may be constrained by high input. The point estimates

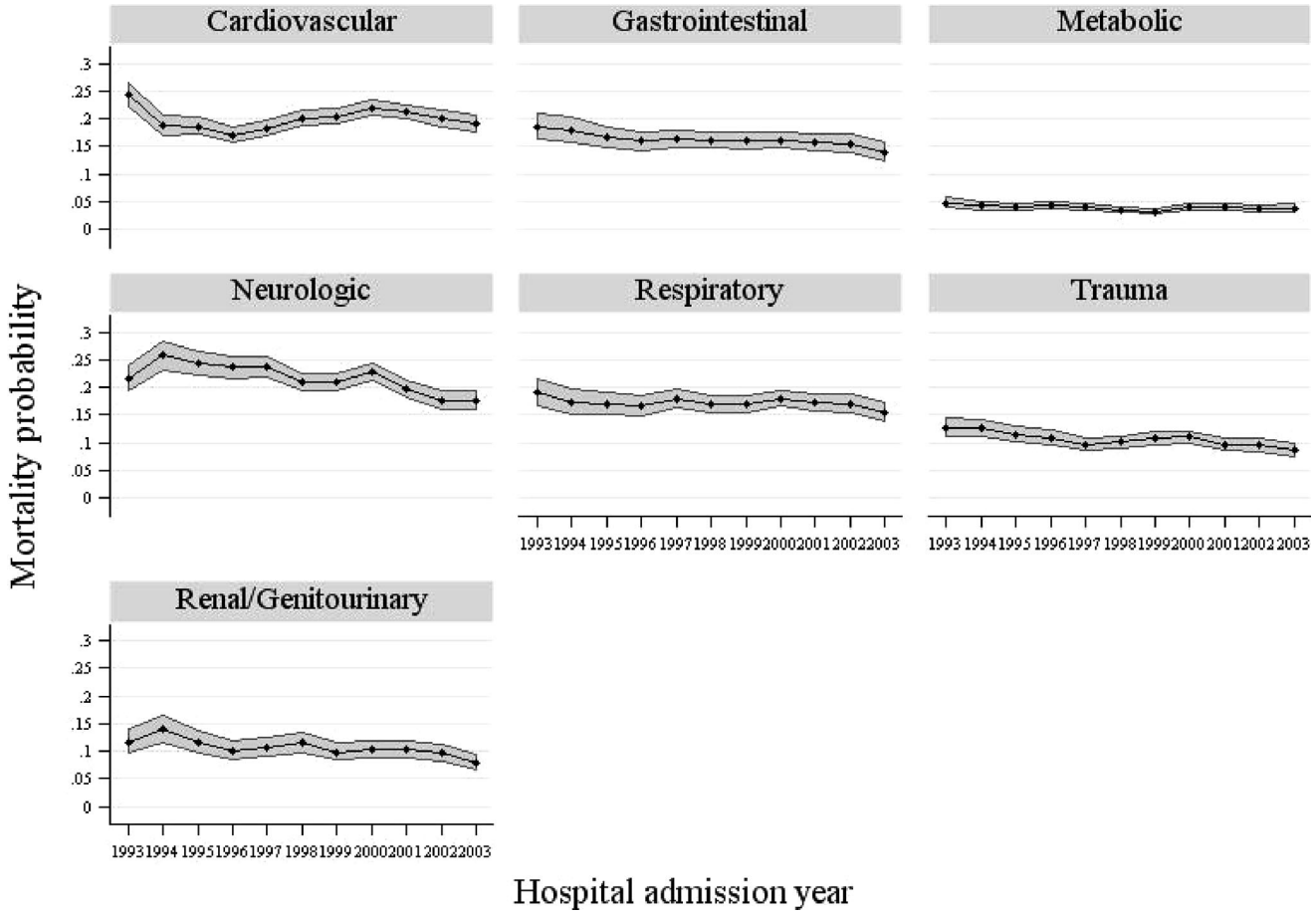

Figure 5. Adjusted mortality (point estimate and 95% confidence intervals) at hospital discharge (y-axis) plotted against calendar year (x-axis) for intensive care unit admission primary organ system dysfunction. *Connected triangle symbol line*, point estimate; *shaded area*; 95% confidence intervals

of the interactions of median yearly ICU admission number with both ICU level and surgical status, and the model chi-squared of these interactions (Appendix 1, *column 6*), suggested considerable determinacy (54), although there were no interactions with age and APACHE III score. *Yearly site admission <711 per year* was presumably a surrogate for factors like the adverse effects of excessive staff workload (55) or patient transfer (56).

Geographic Determinants. Mortality variations by geographical areas (13, 57) and hospital category (12) (Appendix 3) have been reported from different countries. Again, these geographical factor variables are presumably surrogates for determinants such as allocation of resources, human and nonhuman factors (11, 58, 59), and socioeconomic factors (60) that were not captured in the database.

ICU Length of Stay

The performance of the length-of-stay model (R^2 = .18) was modest but consistent with previously reports, R^2 = .13 (21) to R^2 = .21 (24), although in the latter study, ICU length of stay was truncated to 23 days (99th percentile). Obviously, the degree of explained variation of length of stay was limited but again consistent with the performance of other regression models using skewed data, for instance, costs (61). For linear regression models with log transformation, Rapoport et al. (20) found a "somewhat higher R^2 (. . . 0.26 . . .) than the equation using the untransformed variable," and Render et al. (24) found similar results. In the current study, estimation with log ICU length of stay resulted in substantive increments in R^2 from .18 to .28, consistent with standard precepts (37).

The magnitude of time-variation of mean predicted ICU length of stay was ≤0.4 days, with no overall clinically significant change, 1993 vs. 2003. The recorded time-changes in ICU length of stay in the literature have been relatively small, less than one calendar day (14, 19, 21), and also of questionable clinical significance. It was also unclear from these studies how length of stay was initially recorded, that is, in whole days or hours (22). Both Rosenberg et al. (21) and Sirio et al. (14), over 4- to 6-yr periods in the 1990s, reported fractional day decreases in ICU length of stay of 0.11 and 0.2, respectively, in the context of significant and varying percentages of coronary care admissions (6.2% to 20.8%). Both studies recorded concomitant decreases in hospital length of stay, 3 and 1.9 days, respectively, but the increased rate of patient discharge over time to skilled nursing facilities confounded the time-decrease of hospital length of stay and standardized mortality ratio found in the Sirio et al. study (14). In contradistinction to these studies, the current database recorded only a small percentage of myocardial infarction patients (1.7%), and no substantive change in discharge practice/destination appeared to have occurred over the whole study period.

Patient Variables. ICU length of stay has usually been characterized within a

developed algorithm (2, 14, 21, 23), in particular APACHE III (16), which incorporated predictive equations for length of stay (2). The contribution of particular factors to ICU length of stay, as percentage of chi-squared, reported by Knaus et al. (2) in 16,622 patients were predominately physiology (48.7%) and disease (34.1%), with relatively little by age (3.4%), chronic health (0.9%), region (3.2%), and hospital bed size (0.8%). The current model suggested considerable determinacy of disease, patient surgical status, and mechanical ventilation plus interactions, although the length-of-stay effect across APACHE III score deciles was substantive (Fig. 2; Appendix 1, *% change*). These parameter changes were consistent with those studies where there was independent modeling of length of stay (18, 20).

Effect of ICU Death on Length of Stay

APACHE III score increments in survivors were associated with increases in ICU length of stay, raw and predicted, in ventilated and nonventilated patients in the absence of significant changes in ICU mortality across the strata. The general effect of nonsurvival was to increase ICU length of stay, more so in ventilated patients, but length of stay was noted to decrease across the APACHE III tertiles (Fig. 2; Appendix 1, *ICU mortality status*). This trend for sicker patients to die earlier would appear intuitively reasonable and finds support in the studies of 1) Rapaport et al. (20), who described a β coefficient for *Died* of 0.68 as a main effect in the context of an interaction: SAPS II (43) *mortality probability* × *Died* (β coefficient −2.22); and 2) Woods et al. (23), who, using APACHE III-generated mortality probabilities, noted severity-of-illness-dependent increases in length of stay that plateaued at a predicted mortality of 59% for survivors and for nonsurvivors a decrease in length of stay when predicted mortality was >30%. As ICU length of stay of survivors and nonsurvivors presumably reflects an interaction, at some level, between patient severity of illness and the treating health professionals, it was of interest to note that the relationship, length-of-stay/survival status, was relatively consistent over a decade (Fig. 2), except for a mild increase in ICU length of stay in ventilated survivors. This may reflect the particular structure of critical care practice in Australia and New Zealand being that of a uniform training scheme of relatively long history (62) and the almost exclusive predominance of closed ICUs (59).

Time Trends

The unique feature of the current analysis was the ability to assess change of outcomes in a national database over a relatively long period of time (11 yrs), although not every ICU was a contributor for each calendar year. Analysis using a restricted model with continuously contributing ICUs year by year could have been performed, but this would have addressed a quite different question and, for nonbiased estimation, would have required the specific modeling of missingness or selection for the database as applied to ICU participation. However, the focus of the current article was to report a binational experience in terms of the aggregate outcome of all assessable database patients.

The problems associated with time-limited cross-sectional league tables were thus avoided, although the focus was not on individual ICU performance (63). The precise relationship between the overall mortality decrements and specific therapeutic innovations, such as noninvasive (64) and low-volume ventilation (52), activated protein C (65), low-dose corticosteroids (66), and intensive insulin therapy (67), was not evident from this aggregate analysis. Generalized mild mortality decreases occurred over various ICU categorical descriptors, although a modest overall mortality decrease occurred beyond calendar-year 2000, from when it could be surmised that such innovations may have been introduced (Fig. 3). Temporal improvements in outcomes, over prolonged periods, have been noted for general medical patients (57, 68) and in the critically ill for specific conditions (40, 64, 69), although this was not the case in a recent study (49) for ventilated patients over the period 1992–2000. It is perhaps more likely that observed overall mortality decreases were a function of general improvements in ICU care, as been argued (64), rather than the impact of specific innovations, which may not have been widely implemented or fulfilled initial promise (70). This would be consistent with the cautions regarding "regression artifacts" in causal inference from Campbell's landmark study on interventions and longitudinal data (71).

Critique of Methodology

The data used in the study were collected over a long period of time, and issues like on-site data collection quality control could not be optimally addressed. Furthermore, criteria for patient admission were not standardized among the contributing ICUs over this period. Although the mortality model demonstrated excellent calibration and discrimination, the random effects analysis demonstrated, perhaps not surprisingly, residual heterogeneity and was preferred on formal statistical testing. As was expected, random effects parameter estimates moved toward the null. The statistical and clinical significance of patient variables was generally preserved; the ICU level and geographical variables, which were likely to be surrogates for more specific nonmodeled variables, tended to lose significance. To this extent, the analysis concurred with that of Silber et al. (26), who, in a large study of 73,174 patients in 137 hospitals, addressed "which outcomes vary with hospital rather than patient characteristics" and located "most of the predictable variation" in patient characteristics. More complex hierarchical models incorporating patients within ICU-year-units, within ICU levels, and within localities could potentially address these issues (34). Similarly, potential inferential problems in the length-of-stay model associated with an outcome measure (*death in ICU*) as an independent variable could also be addressed using a treatment-effects approach, in which the effect of an endogenous binary treatment variable (*death in ICU*) on a continuous variable is estimated (72). This being said, observational studies, however analyzed, are not "natural experiments" (the illusion of statistical control) (73), and the tendency to think of all regression coefficients as causal effects cannot be sustained (74).

CONCLUSIONS

Overall risk-adjusted mortality in critically ill patients in a large national database declined over an 11-yr period, as did that for ventilated patients. This time-change of mortality was variably reflected in patient and organizational factors. No overall decline in risk-adjusted ICU length of stay was demonstrated over the same period. Although the analytic models that were employed demonstrated good performance, the relationship of the

observed changes in outcomes over time to therapeutic innovations was uncertain.

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APPENDIX 1

Models for hospital mortality and intensive care unit (ICU) length of stay

Variable	LR	*p*	95% CIL	95% CIU	Model χ^2	gllamm	*p*	95% CIL	95% CIU	OLS Log	*p*	95% CIL	95% CIU	% Change
Patient variables														
Age	1.0226	.000	1.0207	1.0245	6527.1	1.0227	.000	1.0209	1.0246	−0.0047	0.0000	−0.0052	−0.0042	−0.47
Age squared	1.0001	.002	1.0000	1.0001	543.5	1.0001	.001	1.0000	1.0001	−0.0002	0.0000	−0.0002	−0.0002	−0.019
APACHE III score	1.0585	.000	1.0555	1.0614	59688.2	1.0590	.000	1.0561	1.0620	0.0136	0.0000	0.0126	0.0145	1.37
APACHE III score squared	0.9999	.000	0.9999	0.9999	29299.6	0.9999	.000	0.9999	0.9999	−0.0001	0.0000	−0.0001	0.0000	−0.005
Age × APACHE III score	0.9998	.000	0.9997	0.9998	1385.4	0.9998	.000	0.9998	0.9998	0.0000	0.4840	0.0000	0.0000	−0.001
Gender	1.1623	.000	1.1095	1.2176	2.8	1.1575	.000	1.1060	1.2113	0.0141	0.0070	0.0038	0.0243	1.41
ICU admission primary organ system dysfunction														
Gastrointestinal	1.1439	.003	1.0480	1.2487	2.3	1.1224	.009	1.0294	1.2238	0.0663	0.0010	0.0271	0.1054	6.832
Metabolic	0.2300	.000	0.1901	0.2781	2618	0.2248	.000	0.1860	0.2717	−0.3241	0.0000	−0.3608	−0.2874	−27.69
Neurologic	1.4505	.000	1.2935	1.6264	390.5	1.4427	.000	1.2875	1.6166	−0.1639	0.0000	−0.2075	−0.1202	−15.1
Respiratory	1.3104	.000	1.2177	1.4102	31.5	1.3051	.000	1.2131	1.4042	0.0811	0.0000	0.0480	0.1143	8.44
Trauma	0.6553	.000	0.5657	0.7592	726.5	0.6474	.000	0.5577	0.7515	0.0401	0.1060	−0.0085	0.0887	4.06
Renal/genitourinary	0.7461	.000	0.6469	0.8605	280.3	0.7350	.000	0.6367	0.8485	−0.0497	0.0460	−0.0985	−0.0009	−4.88
Gastrointestinal × APACHE III score	0.9932	.000	0.9914	0.9951	6976	0.9934	.000	0.9916	0.9952	0.0010	0.0120	0.0002	0.0017	0.096
Neurologic × APACHE III score	0.9959	.001	0.9934	0.9983	7839.8	0.9962	.002	0.9938	0.9986	−0.0065	0.0000	−0.0075	−0.0056	−0.65
Respiratory × APACHE III score	0.9905	.000	0.9888	0.9922	8293.5	0.9908	.000	0.9891	0.9925	0.0008	0.0190	0.0001	0.0015	0.08
Metabolic × APACHE III score	1.0017	.373	0.9980	1.0053	1636.5	1.0015	.419	0.9979	1.0051	0.0005	0.2200	−0.0003	0.0014	0.05
Trauma × APACHE III score	1.0003	.802	0.9976	1.0031	4235.4	1.0006	.648	0.9980	1.0033	−0.0030	0.0000	−0.0041	−0.0019	−0.3
Renal/genitourinary × APACHE III score	0.9919	.000	0.9882	0.9956	1039.1	0.9918	.000	0.9881	0.9955	0.0032	0.0000	0.0022	0.0043	0.32
Patient surgical status														
Elective surgery	0.1649	.000	0.1433	0.1897	10886.3	0.1829	.000	0.1603	0.2087	−0.3542	0.0000	−0.4078	−0.3006	−29.85
Emergency surgery	0.4709	.000	0.4244	0.5226	12.6	0.4704	.000	0.4236	0.5224	0.0151	0.6230	−0.0453	0.0756	1.476
Elective surgery × APACHE III score	1.0018	.135	0.9994	1.0042	6710.7	1.0018	.140	0.9994	1.0042	0.0009	0.0140	0.0002	0.0016	0.089
Emergency surgery × APACHE III score	1.0017	.039	1.0001	1.0034	7062.4	1.0016	.052	1.0000	1.0033	0.0028	0.0000	0.0022	0.0034	0.28
Gastrointestinal × elective surgery	2.6700	.000	2.3180	3.0754	1029.5	2.5755	.000	2.2400	2.9612	0.0430	0.1120	−0.0101	0.0961	4.35
Respiratory × elective surgery	2.3458	.000	1.9965	2.7563	1356	2.1932	.000	1.8660	2.5778	−0.0897	0.0010	−0.1428	−0.0365	−8.58
Neurologic × elective surgery	1.9203	.000	1.5942	2.3130	1099.1	1.8142	.000	1.5135	2.1747	0.0821	0.0030	0.0274	0.1367	8.51
Trauma × elective surgery	2.2282	.000	1.7173	2.8913	525.4	2.1550	.000	1.6607	2.7965	−0.2664	0.0000	−0.3294	−0.2035	−23.43
Renal/genitourinary × elective surgery	2.0418	.000	1.5541	2.6825	750.3	1.9501	.000	1.4856	2.5598	0.0077	0.8380	−0.0664	0.0819	0.704
Gastrointestinal × emergency surgery	1.4079	.000	1.2500	1.5858	101.8	1.4123	.000	1.2528	1.5921	−0.2035	0.0000	−0.2597	−0.1474	−18.45
Respiratory × emergency surgery	1.2511	.009	1.0587	1.4784	127	1.2330	.014	1.0427	1.4581	−0.3712	0.0000	−0.4276	−0.3148	−31.04
Neurologic × emergency surgery	1.9549	.000	1.6868	2.2657	219.5	1.9244	.000	1.6620	2.2283	0.1202	0.0000	0.0610	0.1793	12.74
Trauma × emergency surgery	1.6820	.000	1.4571	1.9417	127	1.6602	.000	1.4370	1.9181	−0.0029	0.9270	−0.0646	0.0588	−0.337
Renal/genitourinary × emergency surgery	1.4759	.006	1.1174	1.9494	121.9	1.4607	.008	1.1045	1.9318	−0.2170	0.0000	−0.2886	−0.1453	−19.55
Mechanical ventilation impact														
Ventilation	1.6585	.000	1.4990	1.8349	11326.7	1.5825	.000	1.4341	1.7464	0.4277	0.0000	0.3969	0.4585	53.36
Ventilation × APACHE III score	0.9916	.000	0.9897	0.9934	42157.9	0.9920	.000	0.9902	0.9939	0.0017	0.0000	0.0010	0.0024	0.17

Continued

Variable	LR	*p*	95% CIL	95% CIU	Model χ^2	gllamm	*p*	95% CIL	95% CIU	OLS Log	*p*	95% CIL	95% CIU	% Change
Ventilation × age	0.9959	.000	0.9937	0.9982	4887.5	0.9958	.000	0.9936	0.9980	0.0000	0.9190	−0.0006	0.0007	0.003
Ventilation × calendar year	0.9718	.000	0.9570	0.9868	189.1	0.9774	.004	0.9625	0.9925	0.0043	0.2080	−0.0024	0.0109	0.428
Ventilation × male gender	0.9010	.000	0.8520	0.9529	4243	0.9015	.000	0.8525	0.9534	−0.0104	0.2290	−0.0274	0.0066	−1.04
Ventilation × gastrointestinal	0.8961	.033	0.8100	0.9913	926.1	0.8943	.026	0.8103	0.9870	0.0700	0.0000	0.0316	0.1083	7.23
Ventilation × metabolic	0.8189	.056	0.6672	1.0052	592.5	0.8352	.088	0.6793	1.0268	−0.2215	0.0000	−0.2651	−0.1779	−19.88
Ventilation × neurological	1.2186	.002	1.0755	1.3807	2479.7	1.2102	.002	1.0702	1.3685	0.1137	0.0000	0.0639	0.1636	12.01
Ventilation × respiratory	0.7872	.000	0.7148	0.8670	1127.7	0.7804	.000	0.7095	0.8585	0.2610	0.0000	0.2256	0.2964	29.81
Ventilation × trauma	1.0786	.390	0.9078	1.2816	0.5	1.0613	.495	0.8946	1.2590	0.3977	0.0000	0.3417	0.4536	48.78
Ventilation × renal/ genitourinary	0.8301	.086	0.6712	1.0265	1.2	0.8404	.108	0.6800	1.0387	−0.1218	0.0000	−0.1809	−0.0627	−11.51
Impact of yearly admission number														
Yearly site admissions <711	0.8367	.000	0.7595	0.9217	1.8	0.8780	.000	0.8184	0.9420	0.0119	0.6050	−0.0332	0.0570	1.17
Rural year × site admissions <711	1.4858	.000	1.2345	1.7884	273.7	1.4411	.000	1.2275	1.6919	−0.0634	0.3430	−0.1944	0.0677	−6.35
Metropolitan × year-site admissions <711	0.8051	.026	0.6649	0.9749	17.6	0.7916	.011	0.6609	0.9481	−0.0294	0.5980	−0.1389	0.0802	−3.05
Private year-site × admissions <711	0.6371	.000	0.4977	0.8155	1204	0.5782	.000	0.4807	0.6955	−0.0209	0.8060	−0.1875	0.1457	−2.42
Elective surgical × year-site admissions <711	1.2262	.003	1.0731	1.4012	6354.6	1.1517	.029	1.0146	1.3073	0.1212	0.0000	0.0663	0.1761	12.84
Emergency surgical × year-site admissions <711	0.9723	.502	0.8957	1.0554	1.7	0.9859	.722	0.9116	1.0662	−0.0195	0.4750	−0.0732	0.0342	−1.97
Calendar year effects														
Calendar year	1.0171	.141	0.9944	1.0402	40.2	1.0099	.453	0.9842	1.0364	0.0280	0.0000	0.0169	0.0390	2.84
Calendar year squared	0.9973	.154	0.9935	1.0010	0	0.9981	.308	0.9943	1.0018	−0.0010	0.3300	−0.0029	0.0010	−0.1
Geographical determinants														
Rural	0.6027	.000	0.5143	0.7064	389	0.6140	.000	0.5364	0.7029	0.2240	0.0000	0.1038	0.3443	24.88
Metropolitan	1.0038	.965	0.8510	1.1840	0.5	0.9864	.867	0.8401	1.1582	0.1689	0.0010	0.0708	0.2669	18.25
Private	1.1427	.245	0.9128	1.4307	1216	1.1717	.034	1.0119	1.3568	0.1430	0.0820	−0.0183	0.3043	14.98
Rural × APACHE III score	1.0055	.000	1.0026	1.0084	7010	1.0053	.000	1.0024	1.0081	−0.0021	0.0000	−0.0028	−0.0013	−0.21
Metropolitan × APACHE III score	1.0013	.184	0.9994	1.0033	10611.8	1.0014	.141	0.9995	1.0034	−0.0010	0.0030	−0.0016	−0.0003	−0.1
Private × APACHE III score	1.0046	.004	1.0015	1.0078	4985	1.0047	.001	1.0019	1.0075	−0.0002	0.6310	−0.0012	0.0007	−0.02
Northern territory	1.0719	.444	0.8974	1.2802	7.5	1.0746	.428	0.8993	1.2842	−0.3023	0.0000	−0.3786	−0.2260	−26.15
Australian capital territory	1.1445	.035	1.0096	1.2973	29.3	1.1128	.173	0.9543	1.2975	−0.0403	0.1610	−0.0967	0.0161	−3.99
South Australia	1.0619	.383	0.9279	1.2154	983.2	1.0436	.408	0.9433	1.1545	−0.1531	0.0000	−0.2115	−0.0947	−14.24
Victoria	0.9728	.463	0.9038	1.0471	73.4	0.9770	.470	0.9174	1.0406	−0.0636	0.0010	−0.1013	−0.0260	−6.18
New Zealand	1.1949	.005	1.0546	1.3537	2.2	1.1514	.031	1.0128	1.3090	−0.3009	0.0000	−0.3997	−0.2020	−26.08
Queensland	0.9499	.228	0.8738	1.0327	536.1	0.9704	.438	0.8993	1.0470	−0.1454	0.0000	−0.1826	−0.1083	−13.55
Tasmania	1.2011	.038	1.0100	1.1428	0.3	1.2063	.016	1.0361	1.4046	−0.0165	0.7590	−0.1218	0.0889	−1.78
Western Australia	0.3410	.000	0.2985	0.3896	19.2	0.3519	.000	0.3107	0.3985	0.2247	0.0000	0.1662	0.2832	20.88
Time effect of geographical determinants														
Northern territory × calendar year	0.8963	.000	0.8469	0.9485	20.5	0.9125	.003	0.8599	0.9685	−0.0332593	0.0190	−0.061125	−0.0053936	−3.28
Australian capital territory × calendar year	0.9311	.001	0.8936	0.9702	0.7	0.9367	.006	0.8937	0.9818	−0.0859797	0.0000	−0.1011271	−0.0708324	−8.24
South Australia × calendar year	1.0051	.819	0.9620	1.0502	0.8	1.0082	.676	0.9703	1.0477	−0.0252163	0.0050	−0.0428152	−0.0076174	−2.49
Victoria × calendar year	0.9666	.008	0.9424	0.9913	30	0.9798	.118	0.9550	1.0052	−0.0263602	0.0000	−0.040344	−0.0123763	−2.6
New Zealand × calendar year	0.9895	.503	0.9592	1.0206	0.1	0.9998	.993	0.9661	1.0348	−0.0125932	0.3190	−0.0373879	0.0122015	−1.26

Continued

Variable	LR	*p*	95% CIL	95% CIU	Model χ^2	gllamm	*p*	95% CIL	95% CIU	OLS Log	*p*	95% CIL	95% CIU	% Change
Queensland × calendar year	0.9876	.436	0.9571	1.0191	241.1	0.9999	.997	0.9686	1.0323	−0.0257742	0.0000	−0.0392762	−0.0122723	−2.55
Tasmania × calendar year	0.9365	.017	0.8875	0.9881	30.7	0.9396	.036	0.8863	0.9960	−0.0565279	0.0010	−0.0907262	−0.0223296	−5.51
Western Australia × calendar year	0.6414	.000	0.6109	0.6734	17	0.6451	.000	0.6128	0.6792	0.044592	0.0000	0.0240113	0.0651727	4.55
Rural × calendar year	1.0193	.139	0.9938	1.0456	98.3	1.0167	.177	0.9926	1.0414	−0.0038837	0.6090	−0.0187907	0.0110233	−0.39
Metropolitan × calendar year	1.0319	.010	1.0077	1.0568	11	1.0286	.020	1.0045	1.0533	−0.0062275	0.3820	−0.0202213	0.0077663	−0.62
Private × calendar year	0.9742	.193	0.9366	1.0133	270.6	0.9696	.090	0.9356	1.0048	−0.0017852	0.8370	−0.0188474	0.0152769	−0.18
SD of random effect (year × site)	N/A				N/A	0.2570				N/A				N/A
ICU mortality status														
Death in ICU	N/A					N/A				0.4563	0.0000	0.3800	0.5325	57.7
Death × ventilation	N/A					N/A				−0.1995	0.0000	−0.2750	−0.1241	−18.15
Death × APACHE III score	N/A					N/A				−0.0218	0.0000	−0.0229	−0.0207	−2.155

LR, logistic regression model for hospital mortality; 95% CIL, lower limit of 95% confidence interval of parameter; 95% CIU, upper limit of 95% confidence interval of parameter; model χ^2, comparison of the log-likelihood of the model containing only the intercept with that of the model having the single predictor; gllamm, random intercept logistic regression as estimated by Stata module "gllamm"(35); OLS log, ordinary least squares regression with log (ICU days) as the dependent variable; APACHE, Acute Physiology and Chronic Health Evaluation; N/A, not applicable; % change, percentage change in the untransformed dependent variable (ICU length of stay, in days) as calculated by the Stata module "logdummy"(41); ×, interaction.

Comparators are Female for Male and interactions; Cardiovascular for Gastrointestinal, Metabolic, Neurologic, Respiratory, Trauma and Renal/Genitourinary and interactions; Nonsurgical for Elective surgery and Emergency surgery and interactions; Tertiary for Rural, Metropolitan and Private ICUs and interactions; Yearly site admissions >711 for Yearly site admissions <711 and interactions. New South Wales for geographical areas (Northern Territory, Australian Capital Territory, South Australia, Victoria, New Zealand and Western Australia).

APPENDIX 2

Statistical Analysis

Modeling Mortality by Logistic Regression. The continuous variables used were age, severity-of-illness scores, and calendar year; the predictive effect of these variables was entered initially as both linear and simple quadratic; more complex nonlinear forms were not formally developed. Candidate categorical predictors were parameterized as simple indicator variables with the reference level (≡0) indicated in parentheses in the following list:

Gender (female)
Mechanical ventilation (not ventilated)
ICU level, as defined in the ANZICS database, as rural, metropolitan, tertiary and private (tertiary)
State of origin, that is, New Zealand and the States of the Commonwealth of Australia (New South Wales [NSW], the largest contributor)
Patient surgical status as postelective surgery, postemergency surgery, and nonsurgical (nonsurgical)
Descriptors of ICU admission primary organ system dysfunction, these being a consolidation of the "diagnostic categories" of the APACHE algorithms: cardiovascular, gastrointestinal, metabolic, neurologic, respiratory, trauma, renal/genitourinary (cardiovascular)
Calendar year, also considered as a categorical variable using indicator variables (1993 as the reference), and forward adjacent differences: each level vs. the previous level (2003 as reference year)
Annual patient admission number (n), created by the ICU site × calendar-year interaction, was empirically tested by categorizing total n into quartiles, tertiles, and median, the reference category being that denoting the highest number of yearly admissions (e.g., for the median difference, as a binary variable, the variables denoted *<711* and *>711* yearly admissions, scored 1 and 0, respectively, with *>711* being the reference category).

Model adequacy was gauged by the following:

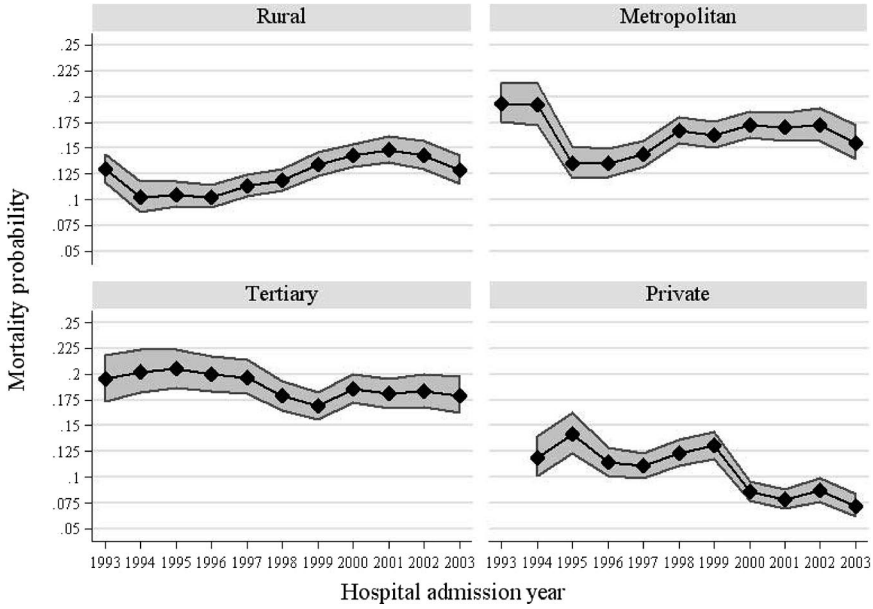
a. Progressive reduction in Akaike information criterion and Bayesian information criterion (75), both of which are penalized (with respect to number of observations and model parameters) likelihood methods for model determination.
b. The traditional criteria of discrimination (ROC area) (76) and calibration: Windmeijer's goodness-of-fit test (77) and the Hosmer-Lemeshow (H-L) $\hat{C}$ statistic (78). The latter test was interpreted with some caution, given the size of the database (>200,000 patients), as the *p* value will invariably be significant ($p \ll 0.1$; H-L statistic $\gg$ 15.99) under these conditions (3, 79).
c. The model chi-squared was calculated for each parameter (33) to adjudge the relative importance of the parameter, after Knaus et al. (2), although the final model, using cluster/robust variance adjustments, did not strictly support such likelihood ratio tests. At best, these chi-square values are to be interpreted heuristically.

Modeling ICU Length of Stay by Ordinary Least Squares. For logarithmic transformation of the dependent variable (i.e., log-ICU-length of stay), the interpretation of the independent (predictor) variables was 1) for continuous variables, that they demonstrate the percentage change in the untransformed dependent variable per one-unit change of predictor; and 2) for categorical (dummy) variables, such an interpretation is biased (it provides the estimated median of the distribution rather than the mean). Consistent estimates of dummy variable (fixed) effects were therefore computed after Hal-

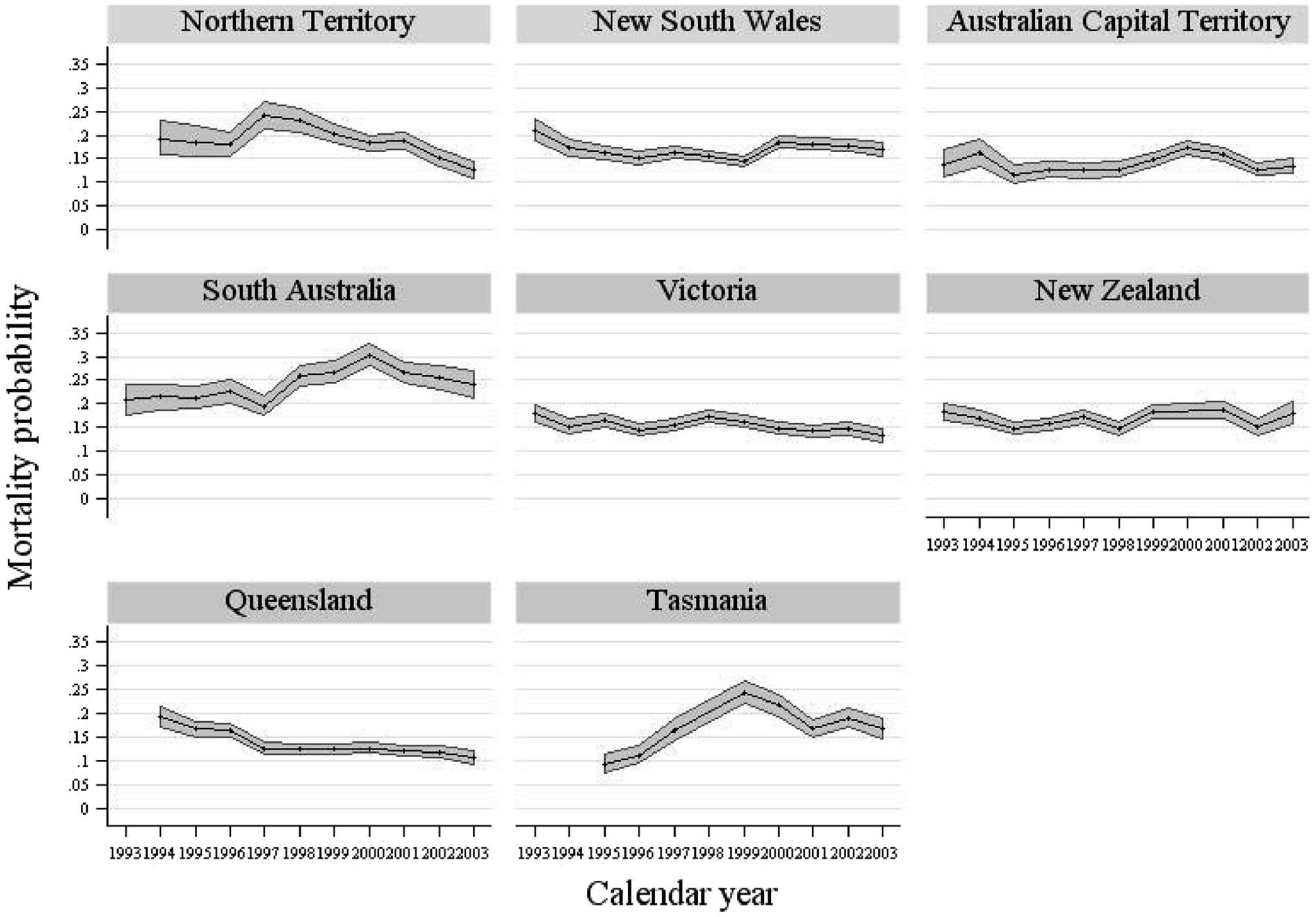
vorsen and Palmquist (80) using the Stata module *logdummy* (41).

Presentation and Interpretation of Graphic Display of Predicted Mortalities. Given the potential number of covariates and interactions, the appropriate graphic display of predicted mortalities for various patient categories was a nontrivial matter: 1) predicted probabilities with 95% CI were collapsed and averaged over patient categories and calendar year to yield appropriate graphic display, although the "average" covariate method may be problematic (81); 2) the interpretation or a simple summary measure of the interaction effect ($\beta_{12}x_1x_2$, where β_{12} is the regression coefficient of the interaction of two predictor variables, x_1 and x_2) in nonlinear models (such as logistic and Cox regression) is also not facile. As demonstrated by Ai and Norton (82), the interaction effect is conditional on *all* the independent variables (unlike the interaction effect in linear models); the sign of the regression coefficient (β_{12}) does not necessarily indicate the sign of the interaction effect across *all* the variables, and the effect could be nonzero, even if $\beta_{12} = 0$ (exponentiated, as OR $\equiv$ 1). Thus, understanding the transformation of parameter estimates and their multiple interactions onto the probability scale must take into account these implicit constraints. For predicted ICU length of stay, mean values and 95% CI were computed and displayed graphically using the methods of Rabe-Hesketh and Everitt (83).

APPENDIX 3



Adjusted mortality (point estimate and 95% confidence intervals) at hospital discharge (y-axis) plotted against calendar year (x-axis) for intensive care unit classification. *Connected triangle symbol line*, point estimate; *shaded area*, 95% confidence intervals.



Adjusted mortality (point estimate and 95% confidence intervals) at hospital discharge (y-axis) plotted against calendar year (x-axis) for geographic location. *Connected triangle symbol line*, point estimate; *shaded area*, 95% confidence intervals.