Long-term mortality of critically ill patients with diabetes who survive admission to the intensive care unit

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ABSTRACT

Objective: Long-term outcomes of critically ill patients with diabetes are unknown. Our objectives were to evaluate the effect of diabetes on both long-term survival rates and the average number of years of life lost for patients admitted to an intensive care unit who survived to hospital discharge.

Design and participants: A data linkage study evaluating all adult patients in South Australia between 2004 and 2011 who survived hospitalisation that required admission to a public hospital ICU.

Main outcome measures: All patients were evaluated using hospital coding for diabetes, which was cross-referenced with registration with the Australian National Diabetes Services Scheme for a diagnosis of diabetes. This dataset was then linked to the Australian National Death Index. Longitudinal survival was assessed using Cox proportional hazards regression. Life-years lost were calculated using age- and sex-specific life-tables from the Australian Bureau of Statistics.

Results: 5450 patients with diabetes and 17 023 patients without diabetes were included. Crude mortality rates were 105.5 per 1000 person-years (95% CI, 101.6–109.6 per 1000 person-years) for patients with diabetes, and 67.6 per 1000 person-years (95% CI, 65.9-69.3 per 1000 person-years) for patients without diabetes. Patients with diabetes were older and had higher illness severity scores on admission to the ICU, were more likely to die after hospital discharge (unadjusted hazard ratio [HR], 1.52 [95% CI, 1.45–1.59]; adjusted HR, 1.16 [95% CI, 1.10–1.21]; $P < 0.0001$) and suffered a greater number of average life-years lost.

Conclusions: Our study indicates that crude mortality for ICU survivors with pre-existing diabetes is considerable after hospital discharge, and the risk of mortality is greater than for survivors without diabetes.

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Mortality for ambulant patients with diabetes is two to four times greater than for the general population, with life expectancy considerably reduced.[1-4] The presence of diabetes also appears to be associated with reduced life expectancy for non-critically ill patients who survive an episode of hospitalisation, particularly for patients presenting due to ischaemic heart disease.[5-8] Interestingly, however, despite diabetes being a risk factor for the development and severity of critical illness due to any precipitant, the presence of diabetes does not appear to confer a greater risk of death within the index hospital admission for patients admitted to an intensive care unit, once adjusted for severity of acute illness.[9,10]

Acute mortality has decreased substantially for all critically ill patients admitted to ICU,[11] but longer-term outcomes for patients who survive to hospital discharge remain poor, with up to 40% of patients dying in the subsequent 5 years.[12] In patients with a chronic illness, such as diabetes, it is uncertain whether an episode of critical illness and ICU admission results in a pivotal change to their health, or just identifies those on a trajectory of worsening health.[13] The impact of diabetes on survival after critical illness may, therefore, be more or less substantial than its impact in the ambulant, non-critically ill population.

Given that the prevalence of diabetes in ICU patients is reported to be as high as 25%,[14] understanding the prognosis for this group of patients is clinically important. However, data about the long-term prognostic impact of diabetes on ICU patients are conflicting and limited, with study follow-up periods having been restricted to 1 year.[15,16]

Our objectives were to evaluate the effect of diabetes on long-term survival rates and on average years of life lost for patients admitted to the ICU who survived to hospital discharge.

Methods

We performed a retrospective, multicentre observational study across all public hospital ICUs in South Australia (SA). Public intensive care services in SA (population 1.7 million) are exclusively provided by four tertiary hospitals. Patient demographic, hospital episode and ICU admission data were collected prospectively at each contributing hospital for ongoing submission to the Australia and New Zealand Intensive Care Society (ANZICS) Adult Patient Database. Data from each ICU from 1 January 2004 to 31 December 2011, inclusive, were combined and linked to population-based datasets to match:

- International Classification of Diseases (ICD-10) coding for diabetes through a composite SA hospital dataset
- registration with the Australian National Diabetes Services Scheme (NDSS) with a diagnosis of diabetes
- mortality through the Australian National Death Index, up to 1 July 2015.

The NDSS is a national register, with more than 80% of Australians who have diabetes and have been hospitalised registered.[17] Patients were deemed to have "known diabetes" if ICD-10 codes from the diabetes chapter (E10-E14) were present in the current or any previous hospital separation, and/or if the patient was registered with the NDSS as having diabetes before, or within 30 days of hospital separation. Average life-years lost were calculated from the Australian Bureau of Statistics (ABS) life-tables for SA residents, 2015,[18] categorised by sex, and referenced to age at ICU admission.

The protocol was approved by the Research Ethics Committee of the Royal Adelaide Hospital with the need for informed consent waived. Access to data for the purpose of performing this research was approved by the NDSS, which is maintained by Diabetes Australia, and by the SA Department of Health, with third-party data-matching performed by the Australian Institute of Health and Welfare.

Statistical analysis

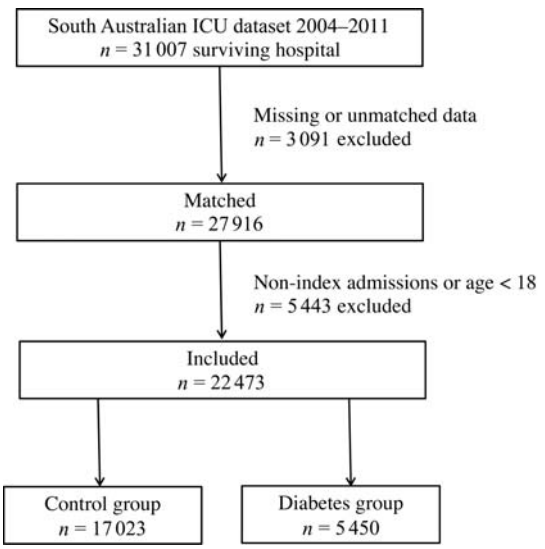
Data are presented as frequencies with proportions for categorical variables, and means with standard deviations (SDs) or medians with interquartile ranges (IQRs) for continuous variables. Between-group comparisons were performed by *t*, Wilcoxon rank-sum or χ^2 tests, as indicated. Patient survival was analysed using Cox proportional hazards regression with between-group effects shown as hazard ratios (HRs) with 95% confidence intervals (CIs). Between-group comparisons were considered statistically significant at $P < 0.05$. Inclusion of covariates in multivariate models was set at $P < 0.1$. All analyses were performed using Stata/MP, version 14.1 (StatCorp).

Results

Baseline characteristics

During the 8-year capture period, there were 22 473 separations from ICU of patients who survived to hospital discharge and fulfilled study eligibility criteria; 5450 separations were for patients (24%) who had diabetes, and 17 023 (76%) were for patients who constituted the control group (Figure 1). Non-index (repeat) ICU admissions were excluded. The group baseline characteristics are outlined in Table 1. Both groups contained

Figure 1. Derivation of the study sample



ICU = intensive care unit.

Table 1. Demographic data, by study group

Characteristic	Control group	Diabetes group	Total	*P**
Separations, *n* (%)	17 023 (76%)	5450 (24%)	22 473	–
Men, *n* (%)	10 122 (59%)	3174 (58%)	13 296 (59%)	0.11
Indigenous Australian, *n* (%)	798 (4.7%)	416 (7.6%)	1214 (5.4%)	< 0.0001
Mean age, years (SD)	57.6 (19.7)	64.7 (14.9)	59.3 (18.9)	< 0.0001
Median APACHE III score (IQR)	54 (38–72)	62 (48–80)	56 (41–74)	< 0.0001
Median length of stay, days (IQR)				
Intensive care unit	2.0 (1.0–4.1)	2.2 (1.1–4.5)	2.0 (1.0–4.2)	< 0.0001
Hospital	11.4 (6.1–21.7)	12.8 (7.3–23.8)	11.8 (6.4–22.1)	< 0.0001
Acute renal failure, *n* (%)	413 (2.4%)	339 (6.2%)	752 (3.4%)	< 0.0001
Median blood glucose level, (IQR)				
Maximum	8.2 (6.9–9.9)	11.1 (8.6–14.8)	8.7 (7.1–10.9)	< 0.0001
Minimum	5.9 (5.1–6.8)	6.5 (5.2–8.0)	6.0 (5.1–7.0)	< 0.0001
Hypoglycaemic,† *n* (%)	855 (5.0%)	430 (7.9%)	1285 (5.7%)	< 0.0001
APACHE-IIIj diagnostic group, *n* (%)				
Medical	10 370 (60.9%)	3440 (63.1%)	13 810 (61.4%)	0.004
Surgical	6653 (39.1%)	2010 (36.9%)	8663 (38.6%)	
Elective surgical	558 (8.4%)	152 (7.6%)	710 (8.2%)	0.24
Emergency surgical	6095 (91.6%)	1858 (92.4%)	7953 (91.8%)	
Cardiothoracic	1480 (8.7%)	664 (12.2%)	2144 (9.5%)	< 0.0001
Trauma	1719 (10.1%)	124 (2.3%)	1843 (8.2%)	< 0.0001

SD = standard deviation. IQR = interquartile range. APACHE = Acute Physiology and Chronic Health Evaluation. * Determined by χ^2, *t* or rank-sum tests, as indicated. † Defined as blood glucose < 4.0 mmol/L.

more men than women (59%). However, patients with diabetes were older, had higher illness severity scores, were more likely to be Indigenous Australians, were more likely to have a medical rather than surgical diagnosis, and were less likely to have suffered trauma, but more likely to have undergone cardiothoracic surgery. Patients with diabetes also had increased peak blood glucose concentrations but were more likely to have hypoglycaemic episodes within the first 24 hours and were more likely to have acute renal failure.

Table 2. Data analysis for covariates in the multivariable Cox proportional hazards model

Covariate	HR	SE	*Z**	Pr > *Z**	95% CI
Diabetes	1.16	0.0275	6.09	0.0000	1.1033–1.2113
Hospital B	0.92	0.0313	–2.36	0.0180	0.8636–0.9865
Hospital C	0.90	0.0292	–3.11	0.0020	0.8489–0.9635
Hospital D	0.87	0.0321	–3.78	0.0000	0.8090–0.9351
Age (years)	1.05	0.0009	53.96	0.0000	1.0449–1.0484
Male	1.17	0.0260	7.08	0.0000	1.1205–1.2226
Indigenous	1.87	0.1049	11.20	0.0000	1.6779–2.0899
APACHE-III score	1.00	0.0004	8.65	0.0000	1.0030–1.0047
APACHE-III diagnostic group†					
Cardiothoracic surgical	0.36	0.0207	–17.80	0.0000	0.3243–0.4055
Trauma	0.43	0.0314	–11.56	0.0000	0.3715–0.4950
Surgical	0.84	0.0519	–2.90	0.0040	0.7395–0.9433
Emergency	0.76	0.0689	–3.03	0.0020	0.6359–0.9074
Emergency surgical	1.38	0.1534	2.93	0.0030	1.1136–1.7198
Chronic health condition					
Respiratory	1.58	0.0552	13.16	0.0000	1.4781–1.6946
Cardiovascular	0.98	0.0069	–2.81	0.0050	0.9670–0.9940
HIV-positive	1.00	0.1470	–0.02	0.9810	0.7463–1.3306
AIDS	1.10	0.1620	0.63	0.5270	0.8222–1.4662
Immune suppressed, disease	1.49	0.1525	3.90	0.0000	1.2191–1.8210
Immune suppressed, treatment	0.94	0.0134	–4.23	0.0000	0.9157–0.9682
Cirrhosis	2.26	0.1436	12.82	0.0000	1.9950–2.5595
Metastatic cancer	2.82	0.1494	19.63	0.0000	2.5464–3.1330
Haematological malignancy	2.06	0.1848	8.02	0.0000	1.7239–2.4521
Acute hepatic failure	1.43	0.2289	2.25	0.0240	1.0479–1.9597
Cardiac arrest	0.87	0.1049	–1.15	0.2480	0.6871–1.1020

HR = hazard ratio. SE = standard error. CI = confidence interval. APACHE = Acute Physiology and Chronic Health Evaluation. HIV = human immunodeficiency virus. AIDS = acquired immune deficiency syndrome. * Z-statistic and probability for HR = 0. † APACHE-IIIj diagnostic groups, as per the Australian and New Zealand Intensive Care Society Adult Patient Database.

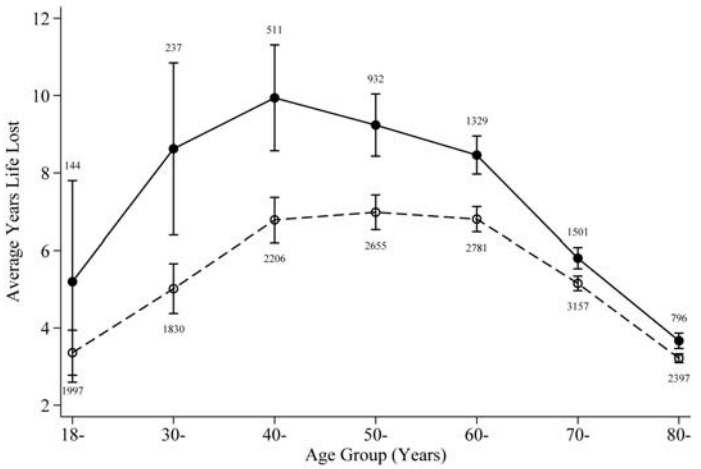
Mortality

Patients were followed for a median of 5.1 years (IQR, 3.1–7.3 years) after hospital discharge. A total of 2672 patients with diabetes (49%) and 5972 control patients (35%) died during the observation period. Crude mortality rates were therefore 105.5 per 1000 person-years (95% CI, 101.6–109.6 per 1000 person-years) and 67.6 per 1000 person-years (95% CI, 65.9–69.3 per 1000 person-years), respectively. The unadjusted HR was 1.52 (95% CI, 1.45–1.59; $P < 0.0001$). Diabetes remained an independent risk factor for death when adjusted for admitting hospital, age, sex, Aboriginal or Torres Strait Islander status, Acute Physiology and Chronic Health Evaluation (APACHE) III score, cardiothoracic surgery status, trauma status, and a medical *v* surgical admission diagnosis interacted with emergency admission status (HR, 1.16 [95% CI, 1.10–1.21]; $P < 0.0001$). We performed a sensitivity analysis including chronic disease (as per APACHE III) in the multivariate model, but this did not significantly alter the result (HR, 1.15 [95% CI, 1.10–1.20]) (Table 2).

Life-years lost

Average life-years lost showed a non-linear relationship with age (Figure 2), increasing to a peak in the fourth and fifth decades and decreasing thereafter. Below the age of 50 years, patients with diabetes had an average

Figure 2. Average life-years lost



Shown are means with 95% CI; number of patients in each age group (adjacent to CI). Solid line + black circles = diabetes group. Dashed line + white circles = control group.

reduction in life expectancy of 9.84 years (SD, 1.82 years) compared with controls, who lost an average of 5.95 years (SD, 1.53 years), losing an additional 3.89 years (95% CI, 3.65–4.14 years; $P < 0.0001$).

Causes of death

Table 3 outlines the most frequent primary causes of death during the follow-up period, as defined by the World Health Organization ICD-10 codes. Ischaemic heart disease was the most common primary cause of death in both the diabetes and control groups. Diabetes was identified by the responsible practitioner reporting the death as the primary cause of death in 11.4% of patients in the diabetes group.

Discussion

Our state-wide data linkage study indicates that crude mortality for ICU survivors with pre-existing diabetes is considerable after hospital discharge, and the risk of mortality is greater than for survivors without diabetes. Patients with diabetes represent an older cohort with increased illness severity on admission to ICU, but the number of life-years lost associated with admission to ICU is greater than for patients without diabetes.

Table 3. Top 20 primary causes of death within the follow-up period, based on WHO classification

WHO ICD-10 causes of death	Control group	Diabetes group	Total (%)
Ischaemic heart diseases	649 (10.9%)	367 (13.7%)	1016 (11.8%)
Chronic lower respiratory diseases	507 (8.5%)	156 (5.8%)	663 (7.7%)
Other heart diseases	322 (5.4%)	144 (5.4%)	466 (5.4%)
Remainder of malignant neoplasms	321 (5.4%)	116 (4.3%)	437 (5.1%)
Cerebrovascular diseases	226 (3.8%)	112 (4.2%)	338 (3.9%)
Diabetes mellitus	25 (0.4%)	304 (11.4%)	329 (3.8%)
Malignant neoplasm, trachea/bronchus	251 (4.2%)	56 (2.1%)	307 (3.6%)
Malignant neoplasm, colon/rectum/anus	220 (3.7%)	86 (3.2%)	306 (3.5%)
Other disease, genitourinary system	160 (2.7%)	107 (4.0%)	267 (3.1%)
Other disease, digestive system	147 (2.5%)	58 (2.2%)	205 (2.4%)
Other disease, respiratory system	142 (2.4%)	50 (1.9%)	192 (2.2%)
Diseases of liver	112 (1.9%)	67 (2.5%)	179 (2.1%)
Other disease, nervous system	138 (2.3%)	31 (1.2%)	169 (2.0%)
Malignant neoplasm, pancreas	90 (1.5%)	56 (2.1%)	146 (1.7%)
Malignant neoplasm, lip/oral cavity	104 (1.7%)	20 (0.7%)	124 (1.4%)
Other disease, circulatory system	100 (1.7%)	23 (0.9%)	123 (1.4%)
Malignant neoplasm, liver/intrahepatic	84 (1.4%)	28 (1.0%)	112 (1.3%)
Pneumonia	68 (1.1%)	40 (1.5%)	108 (1.2%)
Leukaemia	78 (1.3%)	23 (0.9%)	101 (1.2%)
Other external causes	76 (1.3%)	20 (0.7%)	96 (1.1%)
Total deaths (all causes)	*5972*	*2672*	*8644*

WHO = World Health Organization. ICD = International Classification of Disease.

Diabetes is associated with a large number of comorbidities and complications, including renal failure, neuropathy, cardiovascular disease and infection,[19-22] all of which may lead to ICU admission and may theoretically contribute to worse outcomes after critical illness. Several studies in multiple settings have reported increased mortality and worse outcomes in patients with diabetes after hospital discharge, including studies of ischaemic heart disease,[6,7] out of hospital cardiac arrest,[23] cardiac surgery[9] and diabetic ketoacidosis.[24,25] However, studies examining mortality in patients with diabetes after ICU admission have yielded conflicting results.

Most studies to date have evaluated in-hospital or short-term (up to 90-day) mortality and, surprisingly, have reported that mortality is comparable or slightly lower in patients with diabetes than in control patients, despite diabetes being identified as a risk factor for both the development and the severity of critical illness.[9,26-28] Consistent with this signal, several observational studies have reported that patients with diabetes seem to be somewhat protected from developing acute respiratory distress syndrome.[29,30] Various mechanisms have been proposed to explain the similar short-term outcomes of patients with and without diabetes. These include the anti-inflammatory effects of insulin, the potential protective effect of a higher body mass index, and chronic adaptation to hyperglycaemia and associated oxidative stress.[31]

Unlike previous studies, our study had a much longer period of follow-up (a minimum of 4 years) after hospital discharge. Our findings are in keeping with three previous studies which examined 1-year mortality in patients with diabetes after ICU admission.[15,16,32] In the largest of these studies, a Danish, population-based, cohort study of 45 018 patients, Christiansen and colleagues reported that ICU patients with type 2 diabetes had a higher 1-year mortality rate than control patients (HR, 1.19 [95% CI, 1.10–1.28]); and mortality was especially high in patients with diabetes and pre-existing kidney disease.[15] Smaller single-centre studies in Australia[16] and The Netherlands[32] also reported increased 1-year mortality in patients with diabetes after critical illness. In contrast, diabetes was not

associated with increased mortality after ICU admission in a single-centre study in Germany with a longer mean follow-up time of 490 days.[33] However, important limitations in this study included enrolment of only medical ICU patients and the identification of diabetes solely from medical records and medication charts.

Similarly to previous short-term observational and interventional studies, in this study we observed that patients with diabetes had a higher incidence of hypoglycaemia.[34-36] Such observations provide a persuasive rationale for further study of liberal glucose control in patients with type 2 diabetes, which may reduce this risk,[37,38] and we are currently enrolling patients into an ANZICS Clinical Trials Group-endorsed trial (www.anzctr.org.au ACTRN12616001135404) to address this issue.

Our study has a number of strengths. We identified patients with diabetes using both hospital coding and Australian NDSS data, so we are confident that our approach was sensitive in capturing patients with "known" diabetes. Any undiagnosed cases of diabetes would also have biased our results towards a null association. We were able to measure the longitudinal impact using Australian National Death Index data and, by including all patients admitted to a public hospital in SA, we believe our data are generalisable to other regions with similar standards of living and hospital systems. In addition, our cohort included patients admitted with a variety of medical and surgical diagnoses. The observed raw signal persisted when adjusted for measured potential confounders, and was not altered when we performed sensitivity analysis. Furthermore, because patients with diabetes were older, we estimated average life-years lost calculated from ABS life-tables for SA residents. Therefore, we believe the signal we observed is likely to represent a true association.

There are also certain limitations to our study. As with all observational studies, there may be measured or unmeasured confounding factors for which we were not able to adequately adjust. Specifically, there may have been an imbalance between the groups, in terms of acute-on-chronic diagnoses, that we were unable to account for in the analysis. We also have not provided information on the type of diabetes nor on glycaemic control before hospitalisation. Because there are no specific ABS life-tables for ICU survivors, we used common population sex-adjusted and age-adjusted life-tables to calculate average life-years lost. It should also be recognised that we focused on post-hospital mortality and only patients who survived initial hospitalisation were included. However, over the study period of 2004–2011 in SA public hospitals, the observed ICU mortality decreased from 15.2% to 9.3% and the hospital mortality for ICU survivors from 23.8% to 14.3%. These rates were similar to those of other ICUs across Australia and New Zealand.[11] Such dramatic reductions in hospital mortality underlie approaches to quantifying post-hospital morbidity and mortality. Finally, because our study was retrospective in design and used data linkage, we are unable to provide mechanistic explanations for the signal observed.

The effect of diabetes on mortality after critical illness that we observed in our study was less than that described in the ambulant population, but our epidemiological data suggest that survivors of ICU with diabetes are at considerable risk of death. Based on our findings, patients with diabetes who survive the ICU appear to be a vulnerable group, and further evaluation of novel approaches to improve outcomes for these patients is warranted. The evidence base for specific interventions that improve outcomes after critical illness is limited,[39] but patients with diabetes are known to benefit from specific rehabilitation programs after myocardial infarction[40] and studies of specialised ICU follow-up clinics and tailored rehabilitation programs for high-risk patients are ongoing.[41,42]

Conclusions

Evaluating long-term outcomes in a state-wide cohort of over 20 000 survivors of critical illness, our data suggest that patients with diabetes are more likely to die, and suffer a greater loss in life-years, than survivors of critical illness without diabetes.

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Competing interests

None declared.

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References

1 Brown LJ, Scott RS, Moir CL. All-cause mortality in the Canterbury (New Zealand) insulin-treated Diabetic Registry population. *Diabetes Care* 2001; 24: 56-63.
2 Morgan CL, Currie CJ, Peters JR. Relationship between diabetes and mortality: a population study using record linkage. *Diabetes Care* 2000; 23: 1103-07.
3 Franco OH, Steyerberg EW, Hu FB, et al. Associations of diabetes mellitus with total life expectancy and life expectancy with and without cardiovascular disease. *Arch Intern Med* 2007; 167: 1145-51.
4 Staff M, Chen JS, March L. Using computer modelled life expectancy to evaluate the impact of Australian Primary Care Incentive programs for patients with type 2 diabetes. *Diabetes Res Clin Pract* 2015; 109: 319-25.
5 Wu MC, Lee WJ, Tschen SM, et al. Predictors of mortality in hospitalized diabetic patients: A 7-year prospective study. *Diabetes Res Clin Pract* 2008; 80: 449-54.
6 Malmberg K, Yusuf S, Gerstein HC, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Q-wave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. *Circulation* 2000; 102: 1014-9.
7 Miettinen H, Lehto S, Salomaa V, et al. Impact of diabetes on mortality after the first myocardial infarction. The FINMONICA Myocardial Infarction Register Study Group. *Diabetes Care* 1998; 21: 69-75.
8 Jansson SP, Andersson DK, Svardsudd K. Mortality trends in subjects with and without diabetes during 33 years of follow-up. *Diabetes Care* 2010; 33: 551-6.
9 Siegelaar SE, Hickmann M, Hoekstra JB, et al. The effect of diabetes on mortality in critically ill patients: a systematic review and meta-analysis. *Crit Care* 2011; 15: R205.
10 Venkatesh B, Pilcher D, Prins J, et al Incidence and outcome of adults with diabetic ketoacidosis admitted to ICUs in Australia and New Zealand. *Crit Care* 2015; 19: 451.
11 Kaukonen KM, Bailey M, Suzuki S, et al. Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. *JAMA* 2014; 311: 1308-16.
12 Williams TA, Dobb GJ, Finn JC, et al. Determinants of long-term survival after intensive care. *Crit Care Med* 2008; 36: 1523-30.
13 Iwashyna TJ, Prescott HC. When is critical illness not like an asteroid strike? *Am J Respir Crit Care Med* 2013; 188: 525-7.
14 Plummer MP, Bellomo R, Cousins CE, et al. Dysglycaemia in the critically ill and the interaction of chronic and acute glycaemia with mortality. *Intensive Care Med* 2014; 40: 973-80.
15 Christiansen CF, Johansen MB, Christensen S, et al. Type 2 diabetes and 1-year mortality in intensive care unit patients. *Eur J Clin Invest* 2013; 43: 238-47.
16 Plummer MP, Finnis ME, Horsfall M, et al. Prior exposure to hyperglycaemia attenuates the relationship between glycaemic variability during critical illness and mortality. *Crit Care Resusc* 2016; 18: 189-97.
17 Plummer MP, Finnis ME, Phillips LK, et al. Stress induced hyperglycemia and the subsequent risk of type 2 diabetes in survivors of critical illness. *PloS One* 2016; 11: e0165923.
18 Australian Bureau of Statistics. Life Tables, States, Territories and Australia, 2013–2015. Canberra: ABS, 2015. ABS Cat. No. 3302.0.55.001. http://www.abs.gov.au/ausstats/abs@.nsf/mf/3302.0.55.001 (accessed Aug 2017).
19 Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000; 321: 405-12.
20 Fox CS, Coady S, Sorlie PD, et al. Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study. *Circulation* 2007; 115: 1544-50.
21 Shah BR, Hux JE. Quantifying the risk of infectious diseases for people with diabetes. *Diabetes Care* 2003; 26: 510-3.
22 Michalia M, Kompoti M, Koutsikou A, et al. Diabetes mellitus is an independent risk factor for ICU-acquired bloodstream infections. *Intensive Care Med* 2009; 35: 448-54.
23 Nehme Z, Nair R, Andrew E, et al. Effect of diabetes and pre-hospital blood glucose level on survival and recovery after out-of-hospital cardiac arrest. *Crit Care Resusc* 2016; 18: 69-77.
24 Henriksen OM, Roder ME, Prahl JB, Svendsen OL. Diabetic ketoacidosis in Denmark Incidence and mortality estimated from public health registries. *Diabetes Res Clin Pract* 2007; 76: 51-6.
25 Mårtensson J, Bailey M, Venkatesh B, et al. Intensity of early correction of hyperglycaemia and outcome of critically ill patients with diabetic ketoacidosis. *Crit Care Resusc* 2017; 19: 266-73.
26 Stegenga ME, Vincent JL, Vail GM, et al. Diabetes does not alter mortality or hemostatic and inflammatory responses in patients with severe sepsis. *Crit Care Med* 2010; 38: 539-45.
27 Graham BB, Keniston A, Gajic O, et al. Diabetes mellitus does not adversely affect outcomes from a critical illness. *Crit Car Med* 2010; 38: 16-24.
28 Vincent JL, Preiser JC, Sprung CL, et al. Insulin-treated diabetes is not associated with increased mortality in critically ill patients. *Crit Care* 2010; 14: R12.

29 Iscimen R, Cartin-Ceba R, Yilmaz M, et al. Risk factors for the development of acute lung injury in patients with septic shock: an observational cohort study. *Crit Care Med* 2008; 36: 1518-22.

30 Yu S, Christiani DC, Thompson BT, et al. Role of diabetes in the development of acute respiratory distress syndrome. *Crit Care Med* 2013; 41: 2720-32.

31 Siegelaar SE, Devries JH, Hoekstra JB. Patients with diabetes in the intensive care unit; not served by treatment, yet protected? *Crit Care* 2010; 14: 126.

32 Koh GC, Vlaar AP, Hofstra JJ, et al. In the critically ill patient, diabetes predicts mortality independent of statin therapy but is not associated with acute lung injury: a cohort study. *Crit Care Med* 2012; 40: 1835-43.

33 Bannier K, Lichtenauer M, Franz M, et al. Impact of diabetes mellitus and its complications: survival and quality-of-life in critically ill patients. *J Diabetes Complications* 2015; 29: 1130-5.

34 Egi M, Bellomo R, Stachowski E, et al. Hypoglycemia and outcome in critically ill patients. *Mayo Clin Proc* 2010; 85: 217-24.

35 The NICE SUGAR Investigators. Hypoglycemia and risk of death in critically ill patients. *N Engl J Med* 2012; 367: 1108-18.

36 Egi M, Krinsley JS, Maurer P, et al. Pre-morbid glycemic control modifies the interaction between acute hypoglycemia and mortality. *Intensive Care Med* 2016; 42: 562-71.

37 Kar P, Plummer MP, Bellomo R, et al. Liberal glycemic control in critically ill patients with type 2 diabetes: an exploratory study. *Crit Care Med* 2016; 44: 1695-703.

38 Di Muzio F, Presello B, Glassford NJ, et al. Liberal versus conventional glucose targets in critically ill diabetic patients: an exploratory safety cohort assessment. *Crit Care Med* 2016; 44: 1683-91.

39 Hodgson C, Cuthbertson BH. Improving outcomes after critical illness: harder than we thought! *Intensive Care Med* 2016; 42: 1772-4.

40 Soja AM, Zwisler AD, Frederiksen M, et al. Use of intensified comprehensive cardiac rehabilitation to improve risk factor control in patients with type 2 diabetes mellitus or impaired glucose tolerance — the randomized Danish Study of Impaired Glucose Metabolism in the Settings of Cardiac Rehabilitation (DANSUK) study. *Am Heart J* 2007; 153: 621-8.

41 Ali Abdelhamid Y, Phillips L, Horowitz M, Deane A. Survivors of intensive care with type 2 diabetes and the effect of shared care follow-up clinics: study protocol for the SWEET-AS randomised controlled feasibility study. *Pilot Feasibility Stud* 2016; 2: 62.

42 Herridge MS, Chu LM, Matte A, et al. The RECOVER program: disability risk groups and 1-year outcome after 7 or more days of mechanical ventilation. *Am J Respir Crit Care Med* 2016; 194: 831-44. ❑