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## Original Article

## Prevalence and long-term outcomes of patients with life-limiting illness admitted to intensive care units in Australia and New Zealand

Kate Wagner, MBBS, M Bioeth<sup>a,\*</sup>, Neil Orford, MBBS, FCICM, FANZCA, PGDipEcho, PhD<sup>b,c,d,e</sup>, Sharyn Milnes, RN, PGCertCCN, PGDipEd, MBioeth, PhD<sup>b,c</sup>, Paul Secombe, BMBS(Hons), MClinSc, FCICM<sup>f,g</sup>, Steve Philpot, MBBS (Hons), FANZCA, FCICM, PGDipEcho, MHealth&MedLaw, GChPOM<sup>a,g,h</sup>, David Pilcher, MBBS, FCICM, FRACP<sup>d,h,i</sup>

<sup>a</sup> Cabrini Hospital, Malvern, VIC, Australia; <sup>b</sup> University Hospital Geelong, Barwon Health, Geelong, VIC, Australia; <sup>c</sup> School of Medicine, Deakin University, Geelong, VIC, Australia; <sup>d</sup> Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventative Medicine (SPHPM), Monash University, Melbourne, VIC, Australia; <sup>e</sup> Department of Critical Care, University of Melbourne, Melbourne, VIC, Australia; <sup>f</sup> Alice Springs Hospital, Alice Springs, NT, Australia; <sup>g</sup> Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, VIC, Australia; <sup>h</sup> Department of Intensive Care, Alfred Health, Commercial Road, Prahran 3004, VIC, Australia; <sup>i</sup> Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcomes and Resources Evaluation, 101 High Street, Prahran, VIC 3004, Australia

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## ABSTRACT

**Objective:** Determine the prevalence and outcomes of patients with life-limiting illness (LLI) admitted to Australian and New Zealand Intensive Care Units (ICUs).

**Design, setting, participants:** Retrospective registry-linked observational cohort study of all adults admitted to Australian and New Zealand ICUs from 1st January 2018 until 31st December 2020 (New Zealand) and 31st March 2022 (Australia), recorded in the Australian and New Zealand Intensive Care Society Adult Patient Database.

**Main outcome measures:** The primary outcome was 1-year mortality. Secondary outcomes included ICU and hospital mortality, ICU and hospital length of stay, and 4-year survival.

**Results:** A total of 566,260 patients were included, of whom 129,613 (22.9%) had one or more LLI. Mortality at one year was 28.1% in those with LLI and 10.4% in those without LLI ( $p < 0.001$ ). Mortality in intensive care (6.8% v 3.4%,  $p < 0.001$ ), hospital (11.8% v 5.0%,  $p < 0.001$ ), and at two (36.6% v 14.1%,  $p < 0.001$ ), three (43.7% v 17.7%,  $p < 0.001$ ) and four (55.6% v 24.5%,  $p < 0.001$ ) years were all higher in the cohort of patients with LLI. Patients with LLI had a longer ICU (1.9 [0.9, 3.7] v 1.6 [0.9, 2.9] days,  $p < 0.001$ ) and hospital length of stay (8.8 [49,16.0] v 7.2 [3.9, 12.9] days,  $p < 0.001$ ), and were more commonly readmitted to ICU during the same hospitalisation than patients without LLI (5.2% v 3.7%,  $p < 0.001$ ). After multivariate analysis the LLI with the strongest adverse effect on survival was frailty (HR 2.08, 95% CI 2.03 to 2.12,  $p < 0.001$ ), followed by the presence of metastatic cancer (HR 1.97, 95% CI 1.92 to 2.02,  $p < 0.001$ ), and chronic liver disease (HR 1.65, 95% CI 1.65 to 1.71,  $p < 0.001$ ).

**Conclusion:** Patients with LLI account for almost a quarter of ICU admissions in Australia and New Zealand, require prolonged ICU and hospital care, and have high mortality in subsequent years. This knowledge should be used to identify this vulnerable cohort of patients, and to ensure that treatment is aligned to each patient's values and realistic goals.

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\* Corresponding author at: Tel.: +61 408 294 212.

E-mail address: [katie.wagner1@health.nsw.gov.au](mailto:katie.wagner1@health.nsw.gov.au) (K. Wagner).

## 1. Introduction

Patients admitted to intensive care units (ICUs) require complex and invasive treatments, with associated physical, psychological and emotional burden for both patients and their families. For survivors of critical illness this burden extends into the recovery period and is clearly recognised as a post-intensive care syndrome (PICS).<sup>1–4</sup> Families of patients who die in ICU have both a burden of grief and post-traumatic stress.<sup>5</sup> The likelihood of these adverse consequences of ICU treatment may be higher in patients with significant co-morbidities prior to the onset of critical illness. Identifying patient characteristics linked to poorer outcomes would assist clinicians engaging in shared decision-making discussions with patients or their relatives about options for treatment, and help align treatment with patients' goals and values.

Objective clinical tools to identify patients with life-limiting illness (LLI), such as the Gold Standard Framework (GSF) and the Supportive and Palliative Care Indicators Tool (SPICT), are validated in community and hospital settings.<sup>6–10</sup> A range of variables including age, diagnosis, comorbidities, acute illness severity and frailty have been used to identify increased mortality in ICU patients.<sup>11–14</sup> However, these often mix acute and chronic components of disease, and do not separate the pre-critical illness trajectory using validated community-based tools. A single-centre Australian study reported a high prevalence of patients with LLI in ICU with high mortality.<sup>15</sup> This has not been validated on a larger scale. The aim of this project was to identify the prevalence and outcomes of patients with LLI admitted to ICUs across Australia and New Zealand.

## 2. Methods

### 2.1. Setting and participants

We conducted a retrospective registry-based observational cohort study of adults admitted to Australian and New Zealand adult ICUs between 1st January 2018 and 31st March 2022, reported to the Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database (APD). Exclusion criteria included readmission to ICU during the same or future hospitalisation, age 16 years or younger, and admission to ICU for the purposes of organ donation or palliative care.

### 2.2. Data source

The ANZICS APD is a bi-national quality registry dataset collected by the ANZICS Centre for Outcome and Resources Evaluation which contains information on all admissions to 98% of adult ICUs in Australia, and 67% of ICUs in New Zealand. Admission records were matched to the date of death recorded in the national death registers of each country using an encoded linkage key. Registry information was obtained from 1st January 2018 through to 31st December 2020 in New Zealand, and 1st January 2018 through to 31st March 2022 in Australia. This provided a maximum follow-up period of 36 months for New Zealand ICU patients and 51 months for Australian ICU patients.

### 2.3. Data collection

Data collected included patient demographics; clinical information; admission diagnosis, comorbidity and biochemical and physiological variables collected for the calculation of the Acute Physiology and Chronic Health Evaluation (APACHE) II and III/IV scoring systems; treatment limitations on admission to ICU; and interventions including invasive and non-invasive mechanical ventilation, tracheostomy, vasopressors, and renal replacement therapy.

LLI was defined as the presence of one or more APACHE II or III chronic organ insufficiency, frailty, or metastatic cancer (supplement Table 1). Frailty was measured using a modified version of the Canadian Study of Health and Aging Clinical Frailty Scale (CFS).<sup>16</sup> Patients were categorised as not-frail (CFS 1 to 3), pre-frail (CFS 4 or 5) or moderate to severely frail (CFS 6 to 8). The CFS 9 (terminally ill) category is not included in the APD and was not included for the purpose of this study. The CFS was assigned by clinicians working in ICU based on the patient's level of function in the two months preceding admission. In addition, patients were classified into a clinical trajectory group of cancer, organ system failure, frailty, or cancer with frailty.

### 2.4. Outcomes

The primary outcome was mortality at 1 year after ICU admission. Secondary outcomes included ICU and hospital length of stay, mortality at ICU and hospital discharge, and mortality at two, three and four years after ICU admission.

### 2.5. Statistical analysis

All data were assessed for normality. Categorical data were reported as frequency (%) and continuous data as mean (standard deviation) or median (interquartile range). Comparisons between patients with and without one or more LLI were made using Chi-square, student's t, Wilcoxon or Log-rank tests as appropriate depending on the type and distribution of data. Overall survival estimates are displayed using Kaplan–Meier plots. After assessing proportionality and co-linearity, the effect of an increasing number of LLIs on time to death was assessed using a Cox proportional hazards model, initially without adjustment and then adjusting for age, sex, hospital type, ICU admission source, ICU admission diagnosis, treatment limitations on admission, COVID-19 status and acute illness severity at ICU admission (using the sequential organ failure assessment (SOFA) score), with results reported as hazard ratios (HR, 95%CI). High levels of completeness were present for all variables with the exception of frailty. In the multi-variable analysis, this was handled by the creation of a category for missing frailty data which allowed inclusion of all patients. A further sensitivity analysis was undertaken which examined the effect of each individual LLI (as opposed to the overall number of LLIs). A two-sided p-value of <0.05 was used to indicate statistical significance. Analyses were undertaken using Stata 16.1, College Station, Texas.

### 2.6. Ethics approval

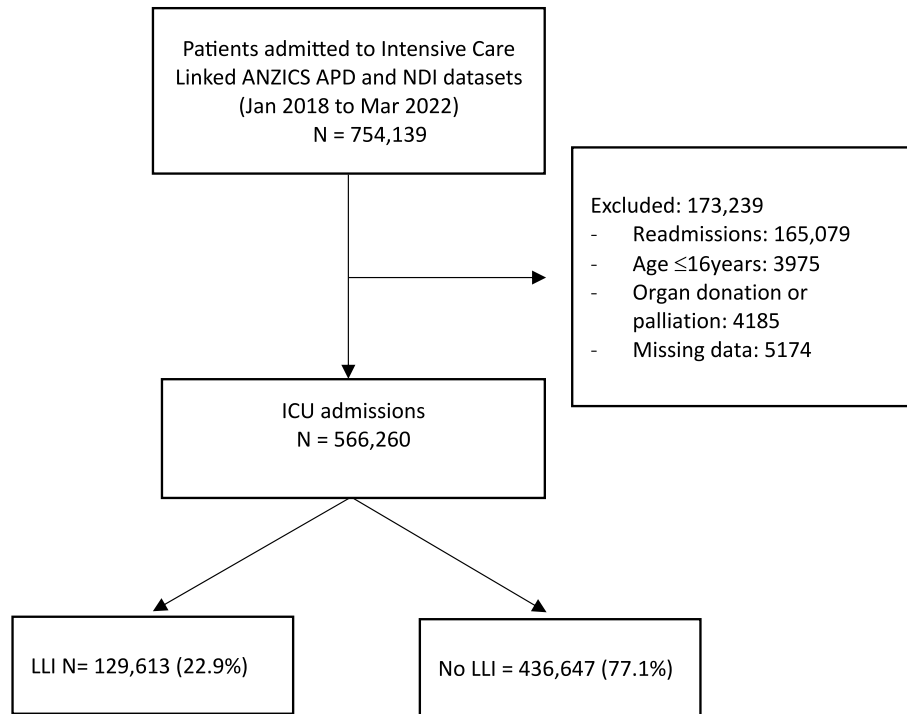
The study was approved by the Alfred Hospital Ethics Committee and conforms with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.<sup>17</sup>

## 3. Results

A total of 754,139 ICU admissions were recorded in the ANZICS Adult Patient Database during the study period. After exclusion, there were 566,260 patients included in the study, of whom 129,613 (22.9%) had one or more LLI (Fig. 1).

### 3.1. Characteristics of LLI

The most common LLI in patients admitted to intensive care was chronic cardiovascular disease (37%), followed by chronic respiratory disease (29%) and frailty (28.5%) (Table 1). Chronic liver disease (defined as proven cirrhosis or portal hypertension) was the least



**Fig. 1.** Selection of patient cohort for the study through linkage of ANZICS CORE APD and NDI. Abbreviations: ANZICS CORE = Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation Adult Patient Database; NDI = National Death Index; LLI = life limiting illness.

prevalent LLI (6%). Overall, 75.9% of the LLI group had only one type of LLI present at admission, with the remainder (24.1%) having 2 or more LLIs present.

### 3.2. Characteristics of patients with LLI

Demographics, referral source, admission diagnosis, LLI trajectory and pre-hospital treatment limitation order are presented

**Table 1**  
Characteristics of life limiting illness in adult patients admitted to Intensive Care.

| LLI Characteristics               | LLI present   |
|-----------------------------------|---------------|
| Number                            | 129,613       |
| Chronic organ insufficiency       |               |
| Cardiovascular                    | 47,944 (37.0) |
| Respiratory                       | 37,620 (29.0) |
| Dialysis dependent                | 16,074 (12.4) |
| Liver disease (cirrhosis)         | 7720 (6.0)    |
| Frailty category                  |               |
| Not frail (CFS1–5)                | 68,367 (52.7) |
| Frail (CFS 6–8)                   | 36,968 (28.5) |
| Unknown                           | 24,278 (18.7) |
| Metastatic cancer                 | 21,355 (16.5) |
| LLI category (mutually exclusive) |               |
| No LLI                            | 0 (0)         |
| Organ failure                     | 73,784 (56.9) |
| One organ failure                 | 61,585 (47.5) |
| Two or more organ failures        | 12,199 (9.4)  |
| Frailty present                   | 34,474 (26.6) |
| Metastatic cancer                 | 18,861 (14.6) |
| Frailty and metastatic cancer     | 2494 (1.9)    |
| Number of LLI                     |               |
| 0                                 | 0 (0.0)       |
| 1                                 | 98,405 (75.9) |
| 2                                 | 25,138 (19.4) |
| 3                                 | 5342 (4.1)    |
| 4                                 | 728 (0.6)     |

Abbreviations: LLI = life limiting illness; CFS = Clinical Frailty Scale.  
Data are show as mean ( $\pm$  standard deviation), or number (percentage).

for patients overall and by study period in [Table 2](#). Compared to patients without LLI, patients with LLI were older, (69.3 vs 60.3 years,  $p < 0.001$ ), more commonly admitted to a regional or rural ICU (18% vs 12%,  $p < 0.001$ ), more commonly admitted as a medical admission (47.9% vs 40.2%,  $p < 0.001$ ), with sepsis as an admission diagnosis (14.3 vs 9.4%,  $p < 0.001$ ), and with higher mean APACHE II ( $18.6 \pm 7.2$  vs  $13.5 \pm 6.7$ ,  $p < 0.001$ ) and SOFA ( $3.9 \pm 2.9$  vs  $3.2 \pm 2.7$ ,  $p < 0.001$ ) scores. Less common admission diagnoses for LLI patients compared to non-LLI patients included neurological conditions and neurosurgery, cardiac surgery, orthopaedic surgery and trauma ( $p < 0.001$ ). Patients with LLI were more likely to have a treatment limitation present at the time of ICU admission (17.3% v 3.7%,  $p < 0.001$ ). With regards to interventions received, patients with LLI admitted to intensive care less commonly received mechanical ventilation (26.9% vs 34.7%,  $p < 0.001$ ), more commonly received renal replacement therapy (5.7% vs 2.9%,  $p < 0.001$ ) or inotropes (38.6% vs 35.2%,  $p < 0.001$ ), and less commonly received mechanical circulatory support than patients without LLI (0.2% vs 0.3%,  $p < 0.001$ ) ([Table 3](#)).

### 3.3. Primary outcome

The primary outcome of 1-year mortality was greater in patients with LLI compared to patients without LLI (28.1% vs 10.4%,  $p < 0.001$ ) ([Table 3](#)).

### 3.4. Multivariate analysis

After adjusting for confounders including age, sex, hospital type, source of ICU admission, ICU admission diagnosis, treatment limitation on admission to ICU, and acute illness severity (SOFA score), the presence of an increasing number of LLI (one LLI: HR 1.74 (95%CI 1.71 to 1.76), two LLIs: HR 1.98 (95%CI 1.94 to 2.02), three LLIs: 2.10 (95%CI 2.03 to 2.19), four LLIs: 2.22 (95%CI 2.02 to 2.43)) was associated with progressively shorter survival times ([supplementary Table 2](#)). Each individual LLI was

**Table 2**

Baseline characteristics of adult patients admitted to Intensive Care with and without LLI.

|                                       | No LLI         | LLI present   |
|---------------------------------------|----------------|---------------|
| Number                                | 436,647        | 129,613       |
| Age (years)                           | 60.3 (±18.1)   | 69.3 (±14.4)  |
| Men                                   | 245,459 (56.2) | 72,936 (56.3) |
| Hospital Type                         |                |               |
| Public rural/regional                 | 51,149 (12)    | 22,736 (18)   |
| Public metropolitan                   | 58,719 (13)    | 24,297 (19)   |
| Public tertiary                       | 175,974 (40)   | 41,497 (32)   |
| Private                               | 150,805 (35)   | 41,083 (32)   |
| ICU admission source                  |                |               |
| Operating theatre                     | 259,621 (59.5) | 67,095 (51.8) |
| Emergency department                  | 109,224 (25.0) | 34,040 (26.3) |
| Hospital ward                         | 47,392 (10.9)  | 22,575 (17.4) |
| Other hospital                        | 19,247 (4.4)   | 5456 (4.2)    |
| Other/unknown                         | 1163 (0.3)     | 447 (0.3)     |
| Admission category                    |                |               |
| Emergency surgical                    | 72,636 (16.6)  | 21,811 (16.8) |
| Medical                               | 175,563 (40.2) | 62,034 (47.9) |
| Elective surgery                      | 188,448 (43.2) | 45,768 (35.3) |
| Admission diagnosis                   |                |               |
| Cardiac surgery                       | 52,793 (12.1)  | 10,483 (8.1)  |
| CT/vascular surgery - other           | 47,542 (10.9)  | 13,150 (10.1) |
| GI surgery                            | 56,404 (12.9)  | 17,669 (13.6) |
| Medical – other                       | 48,385 (11.1)  | 12,209 (9.4)  |
| Medical - cardiac                     | 30,078 (6.9)   | 12,705 (9.8)  |
| Medical - respiratory                 | 18,766 (4.3)   | 12,648 (9.8)  |
| Neuro/neurosurgical                   | 40,334 (9.2)   | 7790 (6.0)    |
| Orthopaedic surgery                   | 42,050 (9.6)   | 11,046 (8.5)  |
| Sepsis/infection                      | 41,047 (9.4)   | 18,586 (14.3) |
| Surgery - other                       | 33,982 (7.8)   | 9957 (7.7)    |
| Trauma                                | 25,266 (5.8)   | 3370 (2.6)    |
| Cancer related                        |                |               |
| With metastases                       | 0 (0)          | 21,355 (16.5) |
| Without metastases                    | 50,674 (11.6)  | 8388 (6.5)    |
| Treatment limitation at ICU admission | 16,143 (3.7)   | 22,474 (17.3) |
| SOFA score                            | 3.2 (±2.7)     | 3.9 (±2.9)    |
| APACHE II score                       | 13.5 (±6.7)    | 18.6 (±7.2)   |
| APACHE III score                      | 46.8 (±22.5)   | 57.6 (±23.5)  |
| ANZROD percent                        | 5.5 (13.5)     | 11.8 (19.1)   |

Abbreviations: SOFA = Sequential Organ Failure Assessment; APACHE = Acute Physiology and Chronic Health Evaluation; ANZROD = Australia and New Zealand Risk of Death; LLI = life limiting illness; GIT = gastrointestinal; CT = cardiothoracic. Data are shown as mean (± standard deviation), or number (percentage). P values for all characteristics <0.001, except male sex (p = 0.71).

independently associated with a shorter time to death, except for chronic cardiovascular disease. However, this was not significant (HR 0.98, 95%CI 0.97 to 1.0, p < 0.13). Frailty had the strongest negative association with survival (HR 2.08, 95%CI 2.03 to 2.12), followed by the presence of metastatic cancer (HR 1.97, 95%CI 1.92 to 2.02), chronic liver disease (HR 1.65, 95%CI 1.60 to 1.71), chronic respiratory disease 1.27 (95%CI 1.24 to 1.29) and chronic renal disease 1.23 (95%CI 1.20 to 1.26) (Table 4). The full analyses with unadjusted and adjusted hazard ratios are provided in Supplemental Tables 2 and 3

### 3.5. Secondary outcomes

All secondary outcomes were higher in patients with LLI compared to patients without LLI, including the incidence of delirium and pressure injuries, hospital length of stay, intensive care readmission rate, and all mortality endpoints (Table 3). Intensive care length of stay was longer for survivors with LLI than survivors without LLI (1.9 vs 1.6 days). In contrast, of those who died in ICU, ICU LOS was shorter for patients with LLI compared to patients without LLI (2.2 vs 2.7 days). The differences in survival according to individual LLI categories and LLI trajectory are shown in Fig. 2. There were significant differences in survival trajectories,

with lowest survival rates in patients with frailty, metastatic cancer, and frailty and metastatic cancer combined.

## 4. Discussion

This study aimed to identify the prevalence and outcomes of patients with LLI admitted to Australian and New Zealand ICUs. Patients with LLI made up almost a quarter (22.9%) of the 566,260 patients studied. They required longer ICU and hospital stays and had worse short and long-term outcomes. Frailty, metastatic cancer, chronic renal, respiratory, liver disease, and multiple chronic organ failures were all independently and cumulatively associated with an increased likelihood of death. This is the first large-scale, bi-national study examining the prevalence and outcomes of patients with LLI admitted to ICU. Our study adds to the growing literature around the validity and importance of objective indicators of LLI in healthcare settings.

### 4.1. Relationship to previous studies

The prevalence and long-term outcomes of patients with LLI reported in this study are an important addition to the existing literature and reinforce the need for validated LLI criteria in the intensive care setting. Firstly, the high proportion of patients with LLI admitted to intensive care observed in this study is consistent with recent literature and reflects variation in definitions used. In 2013, a single-centre Australian tertiary ICU reported 63% of patients referred to intensive care had a LLI, and this cohort accounted for approximately 45% of ICU admissions.<sup>15</sup> In a subsequent study using modified LLI criteria, the same group reported patients with LLI accounted for 21% of ICU admissions,<sup>18</sup> compared to 22.9% in this study. Similarly, the pattern of survival for this patient cohort in this study is consistent with existing literature.

**Table 3**

Intervention and outcomes for adult patients admitted to Intensive Care.

|                                    | No LLI                | LLI present           |
|------------------------------------|-----------------------|-----------------------|
| Number                             | 436,647               | 129,613               |
| Intensive care interventions       |                       |                       |
| Mechanical ventilation             | 151,366 (34.7)        | 34,851 (26.9)         |
| Renal Replacement Therapy          | 10,210 (2.9)          | 6394 (5.7)            |
| Inotropes                          | 129,482 (35.2)        | 44,246 (38.6)         |
| ECMO                               | 917 (0.3)             | 227 (0.2)             |
| Primary outcome                    |                       |                       |
| One year mortality                 | 36,311/350,275 (10.4) | 29,258/104,170 (28.1) |
| Secondary outcomes, ....           |                       |                       |
| Delirium                           | 11,983 (4.2)          | 6545 (7.0)            |
| Pressure injury                    | 3191 (1.1)            | 1465 (1.5)            |
| ICU LOS - all patients (days)      | 1.6 [0.9, 2.9]        | 1.9 [0.9, 3.7]        |
| Survived to ICU discharge          | 1.6 [0.9, 2.9]        | 1.9 [1.0, 3.6]        |
| Died in ICU                        | 2.7 [1.0, 6.2]        | 2.2 [0.8, 5.2]        |
| Hospital LOS - all patients (days) | 7.2 [3.9, 12.9]       | 8.8 [4.9, 16.0]       |
| Survived to hospital discharge     | 7.2 [4.0, 12.9]       | 8.9 [5.1, 6.0]        |
| Died in hospital                   | 6.2 [2.4, 14.4]       | 7.5 [3.0, 16.4]       |
| ICU readmission <sup>a</sup>       | 15,661 (3.7)          | 6229 (5.2)            |
| ICU mortality                      | 14,965 (3.4)          | 8795 (6.8)            |
| Hospital mortality                 | 21,764 (5.0)          | 15,302 (11.8)         |
| Two-year mortality                 | 33,560/238,340 (14.1) | 25,826/70,629 (36.6)  |
| Three-year mortality               | 22,108/125,038 (17.7) | 15,974/36,575 (43.7)  |
| Four-year mortality                | 55.6% (3186/5728)     | 3186/5728 (55.6%)     |

Denominators for annual mortality proportions exclude survivors who have not yet reached this time point (censored).

Data are shown as median [interquartile range] or number (percentage).

Abbreviations: LLI = life limiting illness; ECMO = Extra Corporeal Membrane Oxygenation; LOS = Length of Stay.

All p values for comparisons between groups <0.001.

<sup>a</sup> Denominator represents survivors at discharge from first ICU stay (420,562 with no LLI and 120,348 with one or more LLI).

**Table 4**  
Multivariable Cox proportional hazards model examining the individual effect of each LLI on time to death.

|                                                | Adjusted HR<br>(95% CI) | P value |
|------------------------------------------------|-------------------------|---------|
| Individual life-limiting illnesses             |                         |         |
| Chronic respiratory                            | 1.27 (1.24–1.29)        | <0.001  |
| Chronic cardiovascular                         | 0.98 (0.97–1.00)        | 0.13    |
| Chronic renal (dialysis dependent)             | 1.23 (1.20–1.26)        | <0.001  |
| Chronic liver (cirrhosis)                      | 1.65 (1.60–1.71)        | <0.001  |
| Metastatic cancer                              | 1.97 (1.92–2.02)        | <0.001  |
| Frailty                                        |                         |         |
| No frailty (CFS 1–3)                           | Reference value         |         |
| Pre-frail (CFS 4,5)                            | 1.51 (1.49–1.54)        | <0.001  |
| Frailty present (CFS 6–8)                      | 2.08 (2.03–2.12)        | <0.001  |
| Unknown                                        | 1.43 (1.41–1.45)        | <0.001  |
| Age (years)                                    | 1.029 (1.028–1.029)     | <0.001  |
| Male                                           | 1.13 (1.11–1.14)        | <0.001  |
| Hospital Type                                  |                         |         |
| Tertiary                                       | Reference value         |         |
| Rural/regional                                 | 0.89 (0.87–0.91)        | <0.001  |
| Metropolitan                                   | 0.9 (0.89–0.92)         | <0.001  |
| Private                                        | 0.8 (0.79–0.82)         | <0.001  |
| ICU admission source                           |                         |         |
| Operating theatre                              | Reference value         |         |
| Emergency department                           | 0.99 (0.96–1.02)        | 0.34    |
| General ward                                   | 1.15 (1.11–1.18)        | <0.001  |
| Other hospital                                 | 1.00 (0.97–1.04)        | 0.98    |
| Other sources of admission                     | 0.95 (0.84–1.06)        | 0.34    |
| ICU admission diagnosis                        |                         |         |
| CABG and valve surgery                         | Reference value         |         |
| Other cardiovascular surgery                   | 3.35 (3.21–3.49)        | <0.001  |
| Gastrointestinal surgery                       | 3.11 (2.98–3.24)        | <0.001  |
| Orthopaedic surgery                            | 2.35 (2.25–2.46)        | <0.001  |
| Surgery (other)                                | 2.41 (2.30–2.53)        | <0.001  |
| Trauma                                         | 3.37 (3.20–3.54)        | <0.001  |
| Neuro/neurosurgical                            | 5.38 (5.14–5.62)        | <0.001  |
| Medical (cardiac)                              | 5.63 (5.36–5.91)        | <0.001  |
| Medical (respiratory)                          | 5.02 (4.77–5.28)        | <0.001  |
| Associated COVID-19                            | 1.09 (1.05–1.14)        | <0.001  |
| Sepsis & other infections<br>(incl. pneumonia) | 3.88 (3.69–4.07)        | <0.001  |
| Medical (other)                                | 3.97 (3.77–4.17)        | <0.001  |
| Cancer related admission diagnosis             | 1.87 (1.83–1.91)        | <0.001  |
| Elective surgical ICU admission                | 0.74 (0.72–0.75)        | <0.001  |
| Treatment limitation on admission              | 2.05 (2.01–2.08)        | <0.001  |
| SOFA score                                     | 1.18 (1.18–1.19)        | <0.001  |

Abbreviations: LLI = Life Limiting Illness; CFS = Clinical Frailty Scale.

Secondly, the high observed mortality in patients with LLI reinforces the importance of objective criteria as a tool to identify patients at high risk of dying in the subsequent year. The purpose of this in a shared decision-making framework is not to deny access to care. Rather, it is to trigger goals of care discussions using prognostic information to help patients choose care options aligned to their values and goals. Time-limited trials (TLT) of intensive care have been proposed as a practical approach to establish appropriate goals of care, especially when long-term outcomes and benefits of aggressive interventions are uncertain<sup>19</sup>. Patients with LLI may particularly benefit from such TLTs.

After adjusting for confounders, frailty and metastatic cancer were the LLIs found to be associated with the shortest time to death. Additionally, frailty was the third most prevalent LLI in our cohort. The importance of frailty as a predictor of poor outcome within and post-ICU admission is well known.<sup>14,20</sup> With an

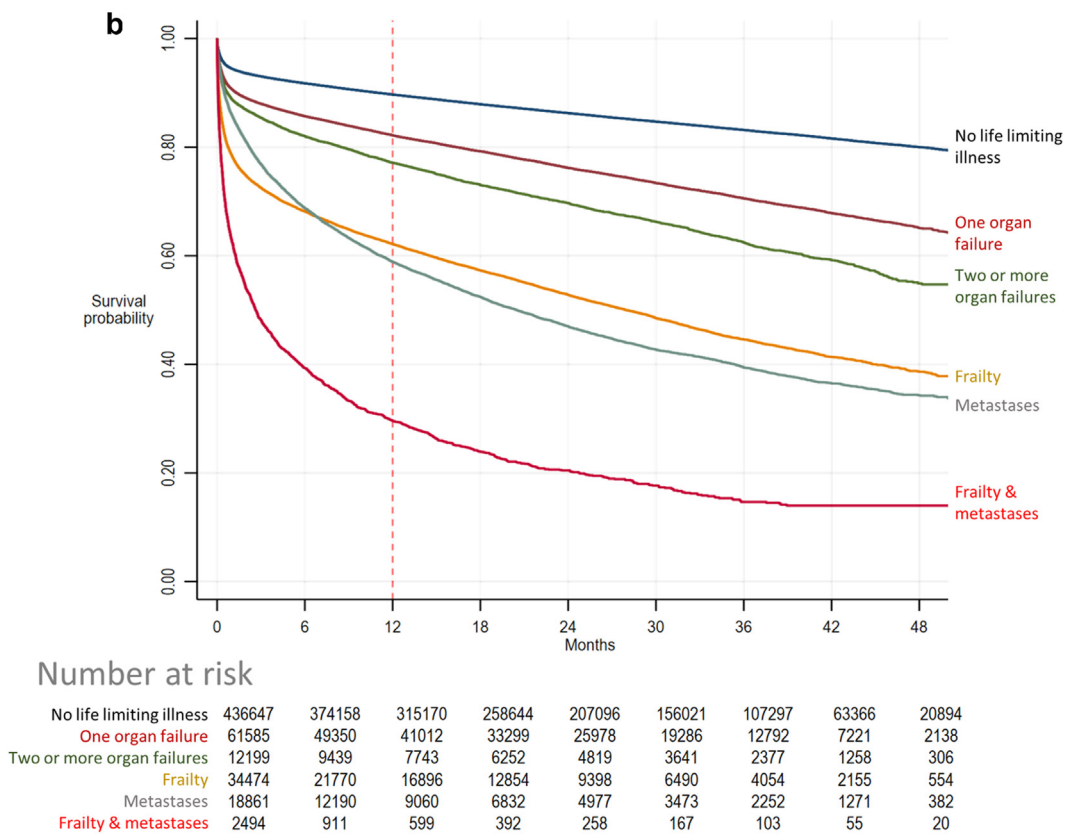
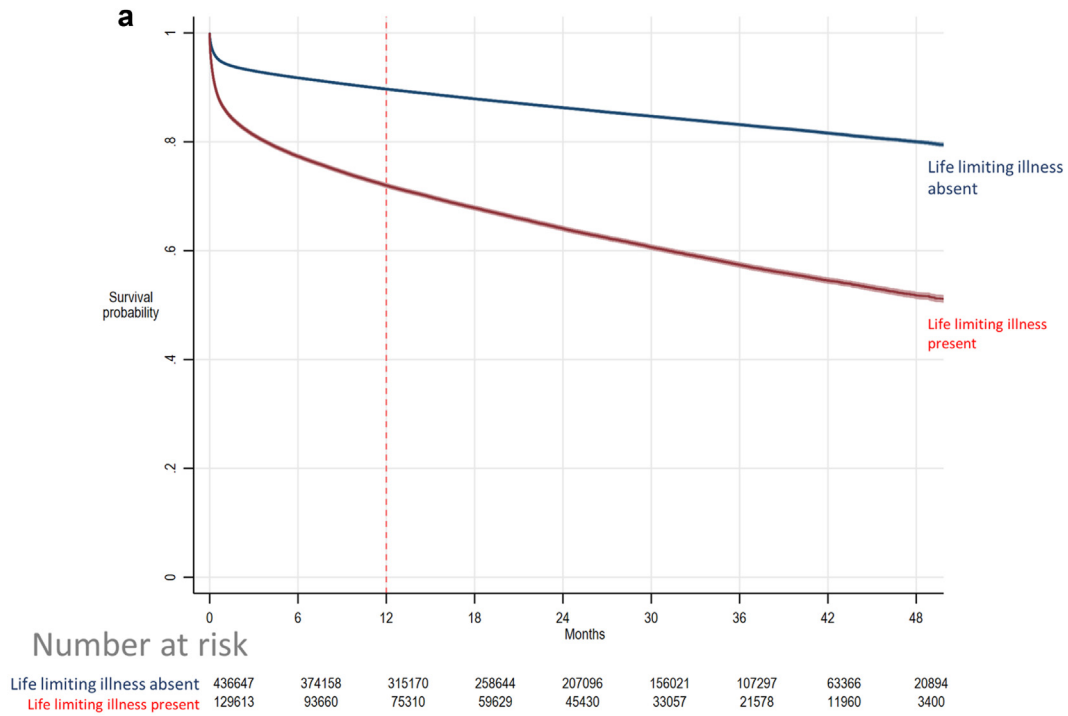
increasingly aging and comorbid population, patients with frailty will continue to account for a significant proportion of hospital and ICU admissions. Metastatic cancer was also found to be associated with poor outcomes, having the second shortest survival time following frailty. A combination of both frailty and metastatic cancer had an additive effect on mortality, with only one-third of these patients alive at one year post-ICU discharge, reflecting prior research findings.<sup>21</sup> By comparison, patients with organ failure LLIs, with the exception of chronic liver disease, were found to have more favourable survival trajectories than those without LLI, again reflecting recent literature.<sup>15</sup>

Finally, we found patients admitted to ICU with a LLI present were more likely to have a treatment limitation order at the time of their admission. In a 2013 study by Godfrey et al. only 3.2% of patients admitted to Australian and New Zealand ICUs within a 3-year period had treatment limitation orders present.<sup>22</sup> More recent research suggests that there is a trend toward an increase in the prevalence of treatment limitation orders present at the time of ICU admission,<sup>23</sup> especially amongst those patients identified as frail, elderly or comorbid.<sup>24</sup> The determination of treatment limitations has historically been influenced by well-recognised patient factors such as age and diagnoses. Our findings highlight the role that an objective indicator of the presence of LLI can play in predicting post-ICU outcomes. By identifying patients with LLI and recognising the associated outcomes, we hope to encourage clinicians to continue to apply goals of care discussions and personalise patient care as appropriate.

#### 4.2. Strengths and limitations

A major strength of this study was the ability to capture most public and private ICU admissions in Australia and New Zealand with the use of the ANZICS APD database. Our large sample size provides good external validity and limits the selection bias that may be present in smaller, single-centre studies.

There are some limitations of our study. Due to the retrospective nature of the study, we were not able to align our LLI criteria with the broadly used SPIC and GSF-PIG definitions. However, the association between LLI as defined in this study using indicators already routinely measured bi-nationally and poor long-term survival provides validated, scalable screening criteria for LLI in this population. Secondly, the data collected for the APD relies on individuals collecting patient information accurately. Whilst objective measures of chronic organ insufficiency, metastatic cancer and frailty are used in the APD definitions (see [supplementary Table 1](#)), this data collection nevertheless relies on accurate history taking and examination at the time of admission and may be subject to errors by the reporting individual. Thirdly, data on frailty status was missing for approximately 30% of the whole study cohort. It is possible that there were some patients in the non-LLI group who would have been classified differently if we had had frailty data for them. However, it is likely to be a small proportion given that the mortality of these patients is similar to those in the non-LLI group where frailty status was known. Fourthly, the time period of our study coincided with a two-year period on either side of the COVID-19 pandemic outbreak. It is unclear how this affected the prevalence of patients with LLI admitted to ICU, including cancellation of elective surgery and decisions regarding access to ICU during periods of peak COVID-19 workload. Finally, only patients admitted to



**Fig. 2.** (a) Kaplan–Meier survival curve for patients with LLI compared to without LLI admitted to Intensive Care. (b) Kaplan–Meier survival curve for presence and type of LLI in patients admitted to Intensive Care.

the ICU were analysed, preventing assessment of the cohort of patients with LLI referred to ICU but not admitted. A prospective study would be needed to further examine this cohort.

#### 4.3. Conclusion

A large proportion of patients admitted to Australian and New Zealand ICUs were found to have one or more LLI. These patients had significantly worse short and long-term outcomes, most notably those with frailty and metastatic cancer. Using objective indicators of LLI will help clinicians identify patients that may have worse in hospital and post-hospital outcomes. This may further assist appropriate goals of care discussions and planning. Our findings support the need for a consensus definition of validated, broadly applicable LLI criteria that can be applied to ICU patients.

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#### Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Credit authorship contribution statement

**Kate Wagner:** conceptualization, methodology, writing – original draft, writing – review and editing. **Neil Orford:** conceptualization, methodology, writing – review and editing. **Sharyn Milnes:** conceptualization, writing – review and editing. **Paul Secombe:** conceptualization, visualization. **Steve Philpot:** conceptualization, writing – review and editing. **David Pilcher:** formal analysis, data curation, software, supervision.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ccrj.2024.02.001>.

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