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Redefining the concept of the elderly burn patient: Analysis of a multicentre international dataset

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ABSTRACT

Background: The elderly are highly vulnerable to major burn injuries. Typically, 'elderly' is accepted as ≥ 65 years of age. This cut-off is arbitrary, lacks a robust evidence base and is potentially damaging from a clinical-decision-making perspective. The study objective was to utilise a large international dataset of major burns to stratify mortality risk by age and objectively define 'elderly' patients with significantly higher risk of poor outcome.

Methods: We performed a sub-analysis of the RE-ENERGIZE clinical trial dataset. RE-ENERGIZE included 1200 patients admitted to 54 burn centres worldwide with 2nd and/or 3rd degree burns, who were expected to require skin grafting. In a first-of-its-kind age stratification study, we stratified major burns patients by five-year age intervals. Logistic regression and Cox proportional hazards analyses were performed with three-month mortality and time-to-discharge-alive (TTDA) as the primary and secondary outcomes.

Results: Three-month mortality was 15.41 %. Age was associated with three-month mortality upon multivariable logistic regression analysis (p = 0.000, OR=1.06, CI=1.05–1.08), independently of total burn surface area burned (TBSA%), Acute Physiology and Chronic Health Evaluation II (APACHE II) and Charlson Comorbidity Index (CCI). Age 80 + was independently associated with increased mortality and TTDA, when compared to all referent 5-year age groups ($p \leq 0.000$–0.043). The Lethal Dose 50 (LD50) for the 80 + group was 20.5 %.

Conclusions: We present a new threshold of risk stratification in patients with major burns; Patients ≥ 80 years have a significantly poorer outcome, irrespective of injury severity, resultant critical illness severity, and variables including comorbidities, which has implications for prognostication and management decisions.

1. Background

Outcomes in paediatric and adult major burns have significantly improved over recent decades due to advances in management practices. These improvements have not extended to the elderly [1]. This is concerning as the elderly are highly vulnerable to burn injuries and the elderly continues to grow as a demographic. The disparity in outcome has resulted in a specific focus on the elderly in many prognostic studies [2–5].

Several factors contribute to the elderly's greater susceptibility to burn injury including poor coordination, impaired vision, pre-existing medical conditions and the effects of medications [6,7]. Furthermore, their limited physiological reserves and higher incidence of malnutrition complicate recovery [6,8,9]. Differences in skin composition lead to deeper burns which is problematic when autografting, since the healing of donor sites is impaired [10,11]. These factors make the elderly susceptible to many in-hospital complications [1,12,13].

Although age is well recognised as a significant predictor of burn outcome and a key variable in pseudo-linear prognostic indices such as the Baux score, the definition of 'elderly' remains unclear. This is because the definition requires a conceptual simplification whereby the established inverse relationship between age and prognosis is simply

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represented by a discrete age cut-off. Various age cut-offs have been proposed (from as low as ≥45 to ≥90 years) but are arbitrary, outdated and unjustified [2,5–7,10,14–21,22–25]. This vagueness in defining 'elderly' hampers accurate comparisons between studies, complicates guideline modifications, confuses mortality reviews (when defining 'expected' versus 'unexpected' deaths) and maybe most importantly, misguides trauma teams assessing mortality risks.

The objective of this study was to utilise a large international data set of major burns to stratify mortality risk by age and objectively define 'elderly' patients with significantly higher risk of poor outcome. We hypothesised that there would be a clear age cut-off, independently associated with increased risk of mortality. Major burn injuries are relatively infrequent. For meaningful, sufficiently-powered analysis, a national or international dataset collected over many years is required, yet difficult to achieve. The original RE-ENERGIZE trial was a double-blind randomised nutritional trial, designed to evaluate the effect of supplemental enteral glutamine on the time-to-discharge-alive (TTDA) in patients with severe burn injuries. The negative outcome of the trial, (supplemental glutamine did not reduce TTDA from hospital) thereby produced a once-in-a-generation prospective dataset and likely the only opportunity, for a decade or so, to investigate certain important questions in burn care and provide meaningful insights that could shape future burn care guidelines.

2. Methods

2.1. Study design and patient population

This was a post-hoc analysis of the RandomizEd trial of ENtERal Glutamine to minimIZE Thermal injury (RE-ENERGIZE Clinical Trial (ClinicalTrials.gov number, NCT00985205) dataset [26]. RE-ENERGIZE prospectively recruited 1200 patients from 54 Burn Units worldwide, between 2011 and 2021. Ethical approval for the current sub-study was granted by the Health Research Authority (HRA) (IRAS ID: 300761).

RE-ENERGIZE recruited adult patients who had 2nd and/or 3rd degree burns, who were expected to require skin grafting and had the following size of burn injury based on age:

- Patients aged 18–39 years required a TBSA% ≥20%, or ≥15% when concomitant inhalation injury was present.
- Patients aged 40–59 years required a TBSA ≥15%.
- Patients aged 60 years or older required a TBSA ≥10%.

Detailed exclusion criteria can be seen in the Supplementary Methods, Supplementary Material.

2.2. Data collection

For the present nested study, data from the Research Electronic Data Capture (REDCap) system, used during RE-ENERGIZE, were sorted to remove patients lost to follow up at three-months (90 days), and those with incomplete data sets (Figure S1, Supplementary Material). Remaining patient baseline data, including demographics, TBSA%, Baux score, APACHE II and Charlson Comorbidity Index (CCI) were collated.

Primary outcome was three-month mortality (all causes). Secondary outcome was TTDA.

2.3. Statistical analyses

All statistical analyses were performed using STATA 18.5 (StataCorp, Lakeway Drive, College Station, Texas 77845 USA). Data are presented as medians (with interquartile range, IQR) or n (with percentage) as appropriate.

To identify significant factors associated with three-month mortality, univariable and multivariable (stepwise) logistic regression analyses were performed. Univariable association filtering was utilised (purposeful selection process involving univariable analysis of each variable, with any variable having significant predictive power ($p < 0.25$) being included in subsequent multivariable models). We base this on the Wald test from logistic regression, as is a commonly performed methodology [27,28]. Age was stratified into 5-year intervals and a series of univariable logistic regression models were constructed with three-month mortality as the dependent variable. In such analyses, age was an independent multilevel categorical variable. For this analysis, patients aged 18–24 were grouped together as one group to provide a 'reference group' of a similar size to the 'test' age categories.

A separate multivariable model was constructed using each age group at 5-year intervals between 50 and 95 years of age as the referent group, to identify differences in odds of three-month mortality between each reference group and the other age categories. The relative odds ratios (OR) between each level of the multilevel predictor remain the same in such models. However, the use of a separate model for each different referent age group allows for calculation of confidence intervals and P values for each level as compared to that model's particular referent value [29].

Cox proportional hazards logistic model identified differences in hazards ratio (HR) for TTDA between each referent group and the other age categories. An HR of < 1 indicates that the probability of hospital discharge was reduced, thus the LOS was longer. The Cox proportional hazards logistic model was adjusted for the following pre-specified baseline covariates: TBSA%, APACHE II score and CCI. The TTDA analyses treated death as a competing risk precluding discharge and censored patients at the earlier of 91 days. This was the same approach used in the very first publication of the RE-ENERGIZE clinical trial outcome [30].

Probit curving, performed in MedCalc, version 22.016, was used to estimate the burn size that was lethal for 50 % of the study population (LD50). For this, the data were subcategorised into different age groups prior to probit curve construction. Firstly, we calculated the LD50 for our study population overall (age 18–93 years). We then calculated the LD50 for the three age groups, defined by us as distinct in terms of their burn outcome; 18–49 years (which we define as "young adult"), 50–79 years (which we define as "older adult") and 80 + years (which we define as elderly).

3. Results

3.1. Patient characteristics

Table 1 shows participating RE-ENERGIZE trial countries and their recruitment as well as patients' characteristics. Following removal of patients who were lost to follow-up or withdrew consent, the study included a total of 1116 patients.

Major burn injury due to fire was the most frequent (90 % of the study population). There was a male and Caucasian predominance (73.8 % and 76.0 % respectively). Median age was 50 (Inter-quartile range 34–64), median APACHE II on admission was 13 (IQR 8–20). Median CCI was 0 (IQR 0–1, range 0–13), and 74.6 % of the patient cohort had no comorbidities deemed relevant to the CCI calculation. When considering a wider array of comorbidities as collected in the RE-ENERGIZE trial, 57.8 % of patients presented with at least one comorbidity. The highest SOFA score recorded during each patient's stay was available in the dataset. Median SOFA score was 3 (IQR 1–6). Three-month mortality was 15.41 % (n = 172), median TTDA was 40 days. Three-month mortality appeared slightly lower in males (14.6 %) versus females (17.8 %). Patient ages and outcomes were also stratified by geographical region (Table S1, Supplementary Material). Median ages across the regions were fairly consistent with the lowest median age (45 years) seen in Latin America and the highest median age (54.5 years) seen in Europe. Three-month mortality was found to be markedly higher in the developing regions of Asia (29.2 %) and Latin America (46.8 %) compared with that in Canada (10.4 %), USA (13.6 %), Europe (16.4 %)

Table 1
Characteristics of the study population.

Patient Characteristics and Outcomes ***(total cohort, n = 1116)***						
Age (years), median (IQR)				Full cohort: 50 (34–64) Male: 49 (33–63) Female: 52 (38–65)		
Number of subjects per age category, n (%)						
18–24 years	96 (8.6)	**45–49 years**	95 (8.5)		**70–74 years**	72 (6.5)
25–29 years	101 (9.1)	**50–54 years**	101 (9.1)		**75–79 years**	48 (4.3)
30–34 years	88 (7.9)	**55–59 years**	102 (9.1)		**80–84 years**	33 (3.0)
35–39 years	82 (7.4)	**60–64 years**	102 (9.1)		**85–89 years**	12 (1.1)
40–44 years	85 (7.6)	**65–69 years**	93 (8.3)		**90 + years**	6 (0.5)
Male:Female sex, n (%)				824:292 (73.8:26.2)		
Ethnicity, n (%)						
Caucasian	848 (76.0)			Native	30 (2.7)	
Hispanic	87 (7.8)			East Indian	3 (0.3)	
Black or African American	86 (7.7)			Other	12 (1.1)	
Asian or Pacific Islander	50 (4.5)					
Nature of Burn, n (%)						
Fire				1006 (90.1)		
Scald				77 (6.9)		
Chemical				27 (2.4)		
Other				6 (0.5)		
TBSA (%), median (IQR)				Full cohort: 29 (20.3–41.0) Male: 30 (21–41) Female: 26.3 (20–40)		
Baux score, median (IQR)				Full cohort: 82 (68–95) Male: 147 (110.5–176) Female: 152.2 (117–181)		
APACHE II on admission, median (IQR)				Full cohort: 13 (8–20) Male: 13 (8–19) Female: 13 (8–20)		
Charlson Comorbidity Index CCI, median (range)				Full cohort: 0 (0–13) Male: 0 (0–0) Female: 0 (0–1)		
Highest SOFA recorded during patient's stay, median (IQR)				Full cohort: 3 (1–6) Male: 3 (1–6) Female: 3 (1–5)		
Three-month mortality rate, n (%)				Full cohort: 172 (15.4) Male: 120 (14.6) Female: 52 (17.8)		
TTDA, median (IQR)				Full cohort: 40 (23–86.5) Male: 30 (21–41) Female: 26.3 (20–40)		
RE-ENERGIZE Trial Participating Country (percentage of enrolled patients per country).						
USA (56.3 %)		Belgium (2.7 %)			Spain (0.8 %)	
Canada (16.9 %)		Thailand (1.9 %)			Brazil (0.6 %)	
UK (8.6 %)		Sweden (1.8 %)			Singapore (0.3 %)	
Germany (4.4 %)		Italy (1.6 %)			Dominican Republic (0.2 %)	
Paraguay (3.3 %)		Austria (0.9 %)				

and UK (17.5 %). TTDA was also notably longer in Asia (64 days) and Latin America (72 days) compared with Canada (39 days), USA (36 days), Europe (41 days) and UK (56 days).

Stratifying TBSA% and APACHE II by age (Figure S2, Supplementary Material), demonstrated a trend in declining TBSA%, yet a fairly constant APACHE II across the age categories, hence smaller burns in the elderly invoke a similar level of critical illness to that seen following larger burns in younger populations. Overall mortality was approximately 8 % at the youngest age ranges and fell slightly to approximately 6 % at 30–34 and 40–44 years (Figure S3, Supplementary Material). There was an inexplicable peak in mortality in the 50–54 age group (25 %). There was a sharp increase in mortality at age 80 + years, with the 80–84, 85–89 and 90 + categories showing mortality rates of 50 %, 45.5 % and 80 % respectively. TTDA, remained relatively similar between the ages of 18–49, while at age 50–54, TTDA sharply increased to 46 days. TTDA then remained consistent up to the 75–79 age group. At age 80 + , there was another significant rise.

In line with the literature, increased age was strongly associated with three-month mortality at univariable logistic regression analysis (Table S2, Supplementary Material): For every incremental increase in age, there is a 6 % increase in the risk of death. Despite a slightly lower three-month mortality rate in males, sex was found to have no impact on patient outcome. TBSA% and Baux score both showed strong associations with mortality, as did the APACHE II, CCI and highest SOFA score recorded. Geographical region was not predictive of mortality despite the earlier observation of higher mortality rates in Asia and Latin America. In the multivariable model, age ($p = 0.000$, Odds Ratio [OR]= 1.04, 95 % Confidence Interval [CI]=1.03–1.05), TBSA% ($p = 0.000$, OR=1.04, CI=1.03–1.05), Baux score ($p = 0.000$, OR=1.07, CI=1.06–1.08), APACHE II ($p = 0.000$, OR=1.07, CI=1.05–1.09),CCI ($p = 0.000$, OR=1.34, CI=1.18–1.51) and highest SOFA score ($p = 0.000$, OR=1.23, CI=1.15–1.31) all retained significant predictive capacity for three-month mortality (Table S2, Supplementary Material).

Logistic regression models were also constructed with age as a categorical variable stratified into 5-year intervals, allowing potential age cut-offs to be tested against a 'reference' age group of 18–24 (Table 2). Median TBSAs across the age groups from 18 to 59 years remained consistent at approximately 30 %. At age 60–64 the median TBSA decreased to 24.8 % and continued to decline with increasing age. The multivariable model, adjusting for TBSA%, APACHE II, CCI and highest SOFA score showed that risk of mortality was significantly higher from age 50 + ; Risk of mortality for those patients aged 50–54 was 8.31 times

Table 2
Logistic regression model with three-month mortality as the dependent variable and age categorized into 5-year groups, as the independent variable, reported using the age group 18–24 as the referent. Significant differences are highlighted by shading.

Age Group	n	TBSA Median, (IQR)	Deaths (n, %)	Univariable model			Multivariable model (Adjusted for TBSA%, APACHEII and CCI)		
				OR	95% CI	p	OR	95% CI	p
18-24	96	32.4 (25-49.5)	8, 8.3	**1.0**	-	-	1.0	-	-
25-29	101	31.5 (25.0-45.0)	8, 8.6	0.95	0.34 - 2.63	0.916	1.20	0.38 - 3.80	0.758
30-34	88	32.8 (23-44.5)	5, 5.7	0.66	0.20 - 2.11	0.486	1.10	0.30 - 3.94	0. 890
35-39	82	33.5 (26.5-46.0)	7, 8.5	1.03	0.36 - 2.97	0.961	1.45	0.44 - 4.76	0.543
40-44	85	31.0 (24.0–41.0)	5, 5.9	0.69	0.22 - 2.19	0.526	1.22	0.34 - 4.31	0.762
45-49	95	32.5 (22.0-45.0)	11, 11.6	1.44	0.55 - 3.76	0.455	2.91	0.98 - 8.63	0.054
50-54	101	30.0 (22.0-45.0)	25, 24.8	3.62	1.54 - 8.49	0.003	8.31	3.04 - 22.68	0. 000
55-59	102	29.6 (21.0-42.0)	16, 15.7	2.05	0.83 - 5.03	0.119	4.84	1.70 - 13.79	0.003
60-64	102	24.8 (19.0-39.0)	18, 17.6	2.36	0.97 - 5.71	0.058	6.04	2.11 - 17.25	0.001
65-69	93	22.0 (16.0-30.0)	18, 19.4	2.64	1.09 - 6.42	0.032	11.11	3.77 - 32.73	0.000
70-74	72	20.0 (13.8-27.0)	16, 22.2	3.14	1.26 - 7.83	0.014	13.66	4.41 - 42.30	0.000
75-79	48	17.0 (12.0-33.0)	10, 20.8	2.89	1.06 - 7.90	0.038	13.44	4.03 - 44.82	0.000
80-84	33	20.0 (13.0-30.0)	16, 48.5	10.35	3.82 - 28.00	0.000	65.42	19.34 - 221.34	0.000
85-89	12	17.5 (14.5-22.5)	5, 41.7	7.86	2.02 - 30.52	0.003	42.32	8.30 - 215.69	0.000
90+	6	16.0 (16.0-18.0)	4, 33.3	22.0	3.48 - 139.25	0.001	183.90	25.02 - 1351.58	0.000

OR, Odds Ratio; CI, Confidence Interval; p, Probability.

as high as the risk of those aged 18–24 ($p = 0.000$, OR=8.31, CI=1.70–13.79). Considering the ORs, a major inflection point in the data was observed at age 80 +, with the risk of three-month mortality for those patients aged 80–84 at 65.4 times that of patients aged 18–24 ($p = 0.000$, OR=65.42, CI=19.34–221.34).

Next, we sought to use different age groups (≥50 years) as the reference group, when conducting logistic regression analysis. There was a peak in mortality risk for those patients aged 70 + when the 55–59 age group was used as the reference group (Table S3, Supplementary Material). Most strikingly, patients 80 + years had a statistically significant increased risk of three-month mortality when compared with every other referent age group, confirming that patients 80 + represent a distinct group with significantly greater risk of mortality. When grouping the data into age < 50, 50–79 and ≥ 80 years, patients aged 80 + are > 40 times more likely to have died three-months post burn ($p < 0.0001$), irrespective of burn size, severity and existing comorbidities (Figure S4, Supplementary Material). Using probit curves, the LD50 burn size associated with these three age categories was 89.7 %, 54.4 % and 20.5 % respectively (Fig. 1). To summarise, and for effective comparison, the key features of the survivors and non-survivors are presented in Table S4, Supplementary Material.

A multivariate Cox proportional hazards regression, adjusting for TBSA%, APACHE II, CCI and highest SOFA, revealed that TTDA was significantly longer for both the 50–79 and the 80 + age category when compared with the 18–49 age group (Table 3) ($p = 0.000$, HR=0.58, CI=0.50–0.67 and $p = 0.000$, HR=0.13, CI=0.08–0.21 respectively) (and depicted in Figure S5, Supplementary Material).

We propose a re-classification of adult major burn injuries encompassing three distinct prognostic sub-categories: 18–49 years, 50–79 years and > 80 years (Figure S6, Supplementary Material).

4. Discussion

The LD50 burn size and mortality in the "elderly" has remained the same over the past three decades, despite advances in burn management

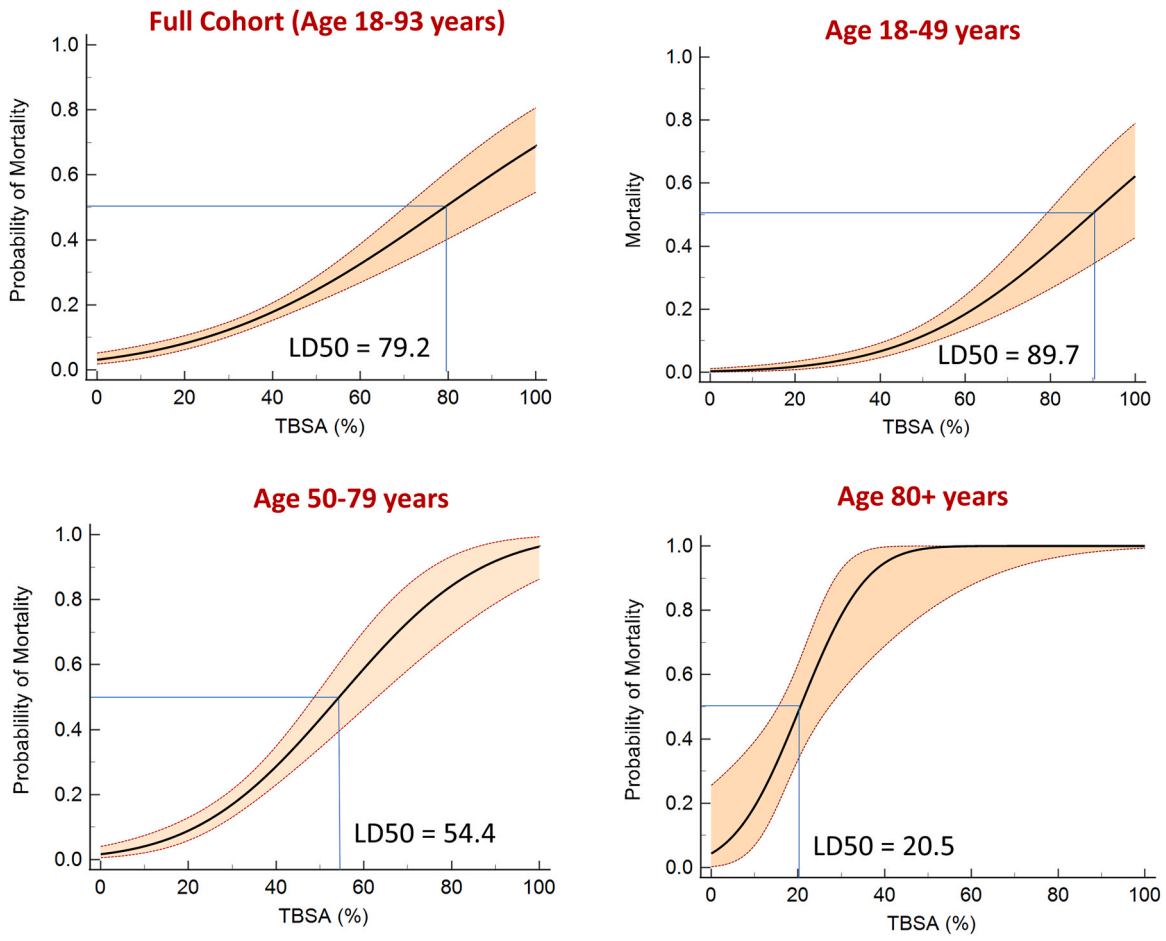

Fig. 1. Probit curves for Age vs LD50 burn size constructed for different age groups.

Table 3
Cox proportional hazards model with TTDA as the dependent variable and age categorized into 3 groups as the independent variable, reported using the age group 18–49 as the referent. Significant differences are highlighted by shading.

Age Group	n	Multivariable model (Adjusted for TBSA%, APACHEII and CCI)		
		Hazard Ratio (HR)	95% Confidence Interval (CI)	Probability (p)
18-49	547	**1.0**	-	-
50-79	518	0.58	0.50 - 0.67	0.000
80+	51	0.13	0.08 - 0.21	0.000

[1,31]. This highlights a need for more specialised burn care to be targeted towards a properly defined demographic.

Attempts to define a threshold age for poor burn outcome are severely limited, and yet there are numerous studies that discuss burn outcomes in the "elderly" without this clear definition [2,6,10,15,16,21]. Presumably the commonly-used cut-off of $\geq$ 65 years is used due to its historic association with retirement age and hence its use in numerous other clinical and non-clinical datasets. The approach of selecting a single cut-off age and examining the variable in a dichotomised manner has its flaws, since mortality rates at the extremes of age may overshadow any marginal changes in mortality that occur around the cut-off. A study by Jeschke *et al.* failed to establish a definitive age threshold for burn survival prediction, but did re-confirm the independent predictive power of age for mortality and demonstrated that the LD50 decreases from 45 % TBSA% to 25 % from the ages of 55–70 years [32]. Nevertheless, it is imperative that the threshold age cut-off at which burn outcomes are significantly poorer is identified so that it can be used for formulating triage criteria and directing more specialised burn care. This is also true at the lower end of the patient age spectrum; Standard practice uses three categories (paediatric, adult, elderly) but a more scientific approach would be to look at the objective evidence for inflection points in the data.

In line with the approach for defining the elderly population in major trauma, our study divided patient ages into 5-year intervals and used different reference groups for comparison in logistic regression analyses [33]. We observed decreasing TBSA% and fairly consistent APACHE II with age, indicating that smaller burns in the elderly invoke a similar change in APACHE II (state of critical illness) to that seen following

larger burns in younger populations (Figure S2, Supplementary Material). This is captured adequately through the APACHE II score which acknowledges the effect of age, even where the acute physiological derangement component of the score may not be as markedly raised. A statistically significant increase in mortality was evident in the 50–54 age group (Figure S3, Supplementary Material), affirmed by logistic regression analysis, adjusting for TBSA%, APACHE II, CCI and highest SOFA score (Table S3, Supplementary Material).

Interestingly, parameters such as male:female ratios, APACHE II scores, SOFA scores and TBSA% did not differ significantly between the 50–54 age group and adjacent age groups. Unmeasured factors during the trial seemingly contribute to this mortality pattern, unexplained despite multiple logistic regression analyses. Nevertheless, the data emphasise the vulnerability of over 50 s in major burn cases (Table 2). Detailed analyses using eight reference groups highlighted an increased mortality risk for patients aged 80 + (Table S3, Supplementary Material). These patients were 40 times more likely to have died three-months post burn, irrespective of burn size, severity and comorbidities (Figure S4, Supplementary Material). This highlights that even small burns in the elderly lead to poor outcomes, consistent with the literature and anecdotal evidence amongst burn surgeons [32].

In the 80 + age group, TTDA significantly differed from other age groups (Table 3). It is worth noting however, that although TTDA is heavily reliant on medical factors such as illness severity and comorbidities, there are also a variety of non-medical factors that can prevent discharge; Hospital stays may be lengthened for patients who require additional rehabilitation or support services while such services are arranged and implemented. Patients with lower socioeconomic status may face greater barriers to accessing home care, transportation, or support services. This is an especially important consideration in the present study, given the wide geographic distribution of the RE-ENERGIZE trial sites and the participation of burn centres in low- or middle-income countries. Indeed, we found that median TTDAs were significantly longer in Asia and Latin America when compared with high-income regions. However, with regard to elderly patients, this data must be interpreted with caution since only 2 % of the patients > 80 years of age in this dataset were from these regions. Considering all geographical regions together, a probit curve revealed a LD50 burn size in the 80 + age group to be 20.5 % (Fig. 1), highlighting the need for tailored management and a deeper understanding of factors contributing to poor outcomes in this vulnerable demographic. These results align with studies in trauma patients reporting that those aged 80 + represent a distinct group with heightened mortality risk and prolonged hospital stays [34,35].

Alpert *et al.* investigated mortality in octogenarians with burn injuries, comparing outcomes between those aged 65–79 and 80–89 [36]. Their study, with a smaller sample size (n = 282) from the Trauma Quality Improvement Program (TQIP) database, found no significant differences in mortality, hospital stay or complications. However, the authors recognized that focusing on both traumatic and burn injuries might limit generalization to isolated burn injuries. They emphasized in-hospital mortality and noted more octogenarians discharged to skilled nursing facilities. Acknowledging post-discharge mortality risks in older trauma patients, they cautioned about potential under-recognition of true mortality within three months post-injury.

Our study has several strengths and significant power. Data were gathered from a large international cohort allowing for the inclusion of, and therefore adjustment for, a diverse range of patient demographics, burn injury types and management approaches. The RE-ENERGIZE cohort is highly representative of the general major burn population admitted to hospital. The representativeness of the study population is assessed in the very first publication of the RE-ENERGIZE clinical trial outcome [30]. Thus, the results presented here can be widely generalised.

This is the first age stratification study of this nature. Our study focuses specifically on severe burns, rather than simply on burn injuries requiring hospital treatment. Median TBSA% was 29 (IQR, 20.3–41), significantly greater than many others reporting on burn outcomes in the elderly with median TBSA%s of 3–10 % [2,6,16]. Understanding the true impact of those burns that are resource intensive and clinically challenging is imperative for improving geriatric burn survival rates. It is also essential that those patients currently categorised as having a poor prognosis (e.g. a patient aged 66) are not prognosticated inaccurately for the purposes of clinical care, palliation decisions or mortality review process.

The study has some weaknesses. Data on inhalation injury were not available in this dataset, therefore the modified/adjusted Baux score could not be calculated. Data on invasive mechanical ventilation requirements were available, and this is arguably a more refined surrogate marker for true lung injury. This did not affect the independent predictive capacity of age when adjusted for in a multivariable model (data not presented).

Although this is the largest international dataset on major burn patients and was able to provide sizable numbers when the patients were stratified into age groups, it is worth noting that the number of patients in the 80 + group (n = 51) represented just under 5 % of the total cohort (n = 1116). This could cause a higher degree in uncertainty in estimations, and this is reflected in the wider confidence intervals in the logistic regression models. However, this number is similar to that included in the study by Alpert *et al.* when investigating mortality from traumatic as well as burn injuries specifically in octogenarians [36].

Frailty score data were also not available, which some would argue may play a large role in determining burn outcome; it has previously been shown (in smaller cohorts with smaller median TBSA%s) that frailty scores are useful predictors of outcome [2,3,37]. However, the present study adjusted for CCI which considers the presence of comorbidities that would affect the patient's level of independence and risk of mortality. In patients aged 80 +, risk of mortality was 4.87 times greater than the 75–79 age group (p = 0.000) (Table S3, Supplementary Material), highlighting the independent prognostic importance of age. We acknowledge that as health inequalities continue to increase the disparity between physiological and chronological age, it is likely that the young elderly or patients at risk of early senescence could potentially be considered as distinctive cohorts whose association between age, frailty and outcome require further investigation.

The dataset was generated by a clinical trial that recruited only adult patients admitted to participating hospitals who had 2nd and/or 3rd degree burns and who were expected to require skin grafting. This did, however, mean that superficial dermal burns that did not end up requiring grafting as well as deep dermal and full thickness burns requiring grafting were included, and so a further limitation of the present study is the lack of information available regarding burn depth given that the size of deep burns has been shown to be an important factor for mortality in many studies. These inclusion criteria also meant that only patients that were fit enough to be viewed as candidates for surgery were recruited. This could introduce a level of bias into the analysis, although the direction of any potential bias would be in the same direction as clinical decision to pursue curative care (vs. palliation) in patients with severe burn injury. The 72-hour recruitment window for the RE-ENERGIZE trial may have led to survivor bias, since patients had to survive long enough to enrol, potentially excluding more severely injured patients. The potential to skew the dataset would be in the direction of our conclusions. Hence removing any survivor bias would almost certainly make our results even more significant.

It is also worth noting that the RE-ENERGIZE trial excluded patients with specific renal dysfunctions/failure or liver cirrhosis, which are co-existing diagnoses and have a known association with mortality among burns [38–40]. Further, they are quite often seen in the general burn population. The exclusion of such prognostically important comorbidities is likely to have selected a sample of the population of burns with arguably better outcomes. This may also explain the LD50 reported in the present study being higher than those reported by comparable

studies [41].

In our study population, risk of death increases with increasing age, with notable mortality and TTDA inflection points observed at 50 and 80 years, regardless of burn size, illness severity and comorbidities. For patients 80 + , burns > 20.5 % TBSA% are associated with 50 % chance of mortality. But, at the same time, this also means that 50 % of the patients aged 80 + years are likely to survive a large burn. The findings are important in relation to the interpretation of current prognostic models; Since age is a crucial factor in the Baux score (Age + TBSA%), changes to the definition of elderly to account for more up-to-date mortality risks from major burns in this population, could lead to misinterpretation of this model. The findings suggest that consideration of the relevance and accuracy of the Baux score for mortality prediction may be required; A re-calibration of the Baux score may be needed to ensure that, as life expectancy increases and burn care improves, there is not an underestimation of the resilience of older adults to major burn injuries.

Although data regarding the highest SOFA score recorded during a patient's stay were available to us, data regarding diagnosis of sepsis were not. Sepsis is a significant factor affecting mortality and TTDA, particularly in elderly patients who face higher susceptibility due to reduced immune reserves, comorbidities, and prolonged hospitalisations. In a study of 175 patients with ≥ 20 % TBSA, 17 % developed complicated sepsis, and 22 % died [42]. Our work showed that the highest SOFA score recorded during a patient's stay was a strong predictor of patient outcome, but it also showed that the importance of patient age in determining the outcome is independent of this SOFA score. Further studies are needed to determine the precise relationship between age and susceptibility to sepsis in major burn injuries.

There is no clearer example of the relevance of this work than reflecting on the fact that the UK National Burn Mortality Audit caters for children, adults and 'elderly'. The previous definition of 'elderly' as age > 65 clearly lies in between two prognostic subgroups, and we have demonstrated that this incorrectly attributes poorer prognosis to the 65–79 years age group. We believe the new stratification has clear advantages in burn care prognostication, research and audit, and whilst no cut-off will be perfect, demonstrates significantly improved accuracy.

CRediT authorship contribution statement

Daren K. Heyland and Nina C. Dempsey had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Daren K. Heyland was the custodian of the data from the RE-ENERGIZE clinical trial. All the authors contributed to the revision of the intellectual content of the manuscript. Daren K. Heyland, Nina C. Dempsey and Kayvan Shokrollahi had substantial contribution to the design of the study. Nina C. Dempsey, Laura Cappuyns and Ascanio Tridente performed data cleaning, devised the analysis plan, and conducted all statistical data analyses, data interpretation, contributed to initial drafting, version control and revising of manuscript. All the authors gave their approval to the final version of the manuscript.

Consent for publication

Not Applicable.

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Declaration of Competing Interest

No conflicts of interest to declare.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.burns.2025.107468.

Availability of data and materials

The datasets used and/or analysed during the current study are available from Dr Daren Heyland on reasonable request.

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