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End-of-life decisions: a cohort study of the withdrawal of all active treatment in intensive care units in the United Kingdom

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Abstract *Objective:* To describe the epidemiology of active treatment withdrawal in a nationally representative cohort of intensive care units (ICUs) focusing on between-unit differences. *Design and setting:* Cohort study in 127 adult general ICUs in England, Wales and Northern Ireland, 1995 to 2001. *Patients:* 118,199 adult admissions to ICUs. *Measurements and results:* The decision to withdraw all active treatment was made for 11,694 of 118,199 patients (9.9%). There were a total of 36,397 deaths (30.8%) before discharge from hospital, and 11,586 (31.8%) of these occurred after the decision to withdraw active treatment, with no change over time (p=0.54). Considerable variation existed between units regarding the percentage of ICU deaths that occurred after the decision to withdraw active treatment (1.7–96.1%). Median time to death after the decision to withdraw active treatment was 2.4 h; 8% survived more than 24 h. After multilevel modelling, the factors independently associated with the decision to withdraw active treatment were: older age, pre-existing severe medical conditions, emergency surgery or medical admission, cardiopulmonary resuscitation in the 24 h prior to admission, and ventilation or sedation/paralysis in the first 24 h after admission. Substantial between unit variability remained after accounting for case-mix differences in admissions. *Conclusions:* Although we were unable to examine partial withdrawal or withholding of care in this study, we found that the withdrawal of all active treatment is widespread in ICUs in the United Kingdom. There was little change in this practice over the period examined. However, there was considerable variation by unit, even after accounting for patient factors and differences in size and type of ICU, suggesting improved guidelines may be useful to facilitate uniform decision making.

Keywords Critical care · Epidemiology · Intensive care units · Life support care

Introduction

The end-of-life experience frequently occurs in the intensive care unit (ICU); a recent study in the United States estimated that one in five of all deaths now occur in the ICU [1]. Overall 20% (range 6–41%) of patients admitted to adult general ICUs in the United Kingdom (UK) die before discharge from the unit and another 10% (4–20%) before leaving hospital [2]. As technology, particularly in ICUs, has improved, life can often be prolonged indefinitely. Because of this fact, withholding and withdrawing active treatment has become accepted practice in many countries, including the UK [3, 4, 5]. For patients in the ICU it is known that they are often not in a state to be making decisions regarding their care [6]. The decision to finally withdraw active treatment on a patient is often

made by the health care team in consultation with the family [7, 8]. The decision is difficult, and physicians are often called upon to provide information to the family both on prognosis and on the patient's course following withdrawal of active treatment to guide decision making. Having accurate data regarding the practice of and outcome following active treatment withdrawal is helpful to inform these discussions and to allow for improved decision making.

Many studies in ICUs have described the decision-making process and the issues of communication surrounding the decision to withdraw active treatment [8, 9, 10, 11, 12, 13, 14]. With regard to the practice of withholding and withdrawing treatment, studies reporting practice in individual ICUs have been reported [15, 16, 17, 18]. Practice has also been reported for groups of ICUs in individual countries, and wide variation has been reported in Spain [19], France [20], and the United States [21]. Unfortunately, no similar study exists for the UK. Recently comparisons across countries have been made, but these studies have involved either only a few ICUs in each country [3] or pooled results from the ICUs across the different countries [14]. One study examined and reported all (ICU and non-ICU) end-of-life decisions [22].

Few studies have comprehensively and prospectively examined practice across an entire country, and few data exist regarding practice in the UK. We used a high-quality clinical database to provide information from nationally collected data regarding the epidemiology of active treatment withdrawal in the UK. Some of these findings were presented at the European Society of Intensive Care Medicine Annual Congress 2003 [23].

Materials and methods

Data

Relevant data were extracted on 127,484 admissions to 127 adult general ICUs in England, Wales and Northern Ireland in the Intensive Care National Audit & Research Centre's (ICNARC) Case Mix Programme Database (CMPD), from the period December 1995 to August 2001 (approx. 54% of all adult general ICUs). These data were collected prospectively and abstracted according to precise rules and definitions using trained data collectors. Data were extensively validated, both locally and centrally, before pooling. Explicit steps are taken to ensure the accuracy (completeness, validity and reliability) of the data including use of a data dictionary, 2-monthly initial and refresher data collection training courses and manual and electronic validation of incomplete, illogical and inconsistent data, and reliability studies [24]. All patients were followed until ultimate discharge from an acute hospital.

Only data from the final stay in ICU were counted for patients admitted to ICU more than once in the same acute hospital stay (n=5,971, 4.7%). Admissions missing vital status at discharge from either ICU (n=13, 0.01%) or hospital (n=3,301, 2.6%) were also excluded. After exclusions, data on 118,199 patient admissions to 127 ICUs were analysed.

Active treatment withdrawal is defined in the CMPD as the decision to withdraw all active treatment, other than comfort measures; this does not include placing an upper limit on treatment (withholding treatment) and does not include changing the aims of treatment (for example, the decision to leave a patient ventilator dependent rather than to wean them from the ventilator). The date and time recorded represent when the decision was made to withdraw all active treatment. Prior decisions to withhold certain treatments may already have been made for some of these patients. Any patients recorded as having had active treatment withdrawn after confirmation of brainstem death were re-categorised as not having had active treatment withdrawn.

Statistical methods

Available individual and unit-level factors that may be associated with the decision to withdraw active treatment were identified a priori with reference to the literature: age, sex, Acute Physiology and Chronic Health Evaluation (APACHE) II Acute Physiology Score, severe conditions in the medical history, length of stay in hospital prior to ICU admission, readmission in the same acute hospital stay, location immediately prior to ICU admission, surgical status, cardiopulmonary resuscitation (CPR) in 24 h prior to ICU admission, mechanical ventilation in first 24 h after ICU admission, sedated/paralysed in first 24 h after ICU admission, organ failure, size of ICU, and type of acute hospital. A severe condition in the medical history was indicated by the presence of one or more of 16 defined, severe chronic conditions: biopsy-confirmed cirrhosis, portal hypertension, hepatic encephalopathy, severe cardiovascular disease, severe respiratory disease, home ventilation, chronic renal replacement therapy, AIDS, steroid treatment, radiotherapy, chemotherapy, metastatic disease, acute leukaemia, chronic leukaemia, lymphoma, congenital immune deficiency state. All factors were investigated for association with the decision to withdraw active treatment in patients dying in ICU using multilevel logistic regression modelling. Data were excluded from this analysis in patients aged less than 16 years or staying less than 8 h in the ICU (APACHE II exclusions) and in those with missing data for any of the factors investigated. Variation among ICUs was modelled by including the unit as a random effect in the model. The model was also adjusted for the mean value of all individual level covariates at the unit level [25]. The proportion of variance among the units explained by the covariates was explored by comparing the estimate of between unit variance from the full model with that from a multilevel model with no predictor variables.

Kaplan-Meier estimates of survival following the decision to withdraw active treatment were carried out by censoring patients that survived to ICU discharge, since time of death was not available for patients after ICU discharge. Multilevel analyses were performed in MLwiN 1.10 (Centre for Multilevel Modelling, Institute of Education, London, UK); all other analyses were performed using Stata 8.0 (Stata LP, College Station, Tex., USA).

Results

A decision to withdraw all active treatment was made for 11,694 (9.9%) patients. Median time from admission to ICU to the decision to withdraw active treatment was 2.0 days (interquartile range 0.7–6.3 days; range 0–103 days). This median time varied by ICU (range 0.9–8.5 days) but was not correlated with the percentage of patients in whom the decision to withdraw active treat-

ment was made (Spearman correlation coefficient 0.06, p=0.54).

Characteristics of patients who had the decision to withdraw active treatment made

The characteristics of patients in whom a decision to withdraw active treatment was made are described in Table 1. On average the patients in whom a decision to withdraw active treatment was made were: older (mean age 64.7 vs. 57.5 years), more severely ill in their first 24 h in ICU (mean APACHE II Acute Physiology Score 18.0 vs. 11.9), and more likely to have one or more serious conditions in their medical history prior to admission to ICU (20.3% vs. 13.5%) than other patients. When patients were categorised by surgical status (elective surgical, emergency surgical, non-surgical), a higher percentage of patients in whom a decision to withdraw active treatment was made were admitted for non-surgical (medical) reasons (75.3% vs. 53.3%). A much higher percentage had received CPR within the 24 h prior to admission (22.6% vs. 6.9%), and the majority were mechanically ventilated either on admission to or during the first 24 h in ICU (90.2% vs. 60.8%). A higher percentage were also sedated or sedated and paralysed for the whole of the first 24 h in ICU (sedated only 46.7% vs. 22.7%; paralysed and sedated 9.1% vs. 4.6%).

The most frequently recorded primary reason for admission to ICU for patients in whom a decision to withdraw active treatment was made was pneumonia (n=1,328; Table 2). This represented 17.7% of all patients with this diagnosis and 11.4% of admissions patients in whom a decision to withdraw all active treatment was made. Patients with anoxic or ischaemic coma or encephalopathy represented a smaller percentage of all admissions to ICU (2.6%), but many more had the decision made to withdraw all active treatment (37.6%).

Table 1 Characteristics of admissions by the decision to withdraw active treatment (*IQR* interquartile range; n=118,199)

	Decision to withdraw active treatment	
	Yes (n=11,694)	No (n=106,505)
Age (years)	64.7±15.7	57.5±20.1
Sex, male	6,737 (57.6%)	62,528 (58.7%)
APACHE II Acute Physiology Score	18.0±7.1	11.9±6.5
APACHE II score	23.0±7.4	15.8±7.2
Number with one or more severe conditions in medical history[a]	2,305 (20.3%)	13,930 (13.5%)
Length of stay in acute hospital prior to ICU admission (days), median (IQR)	1 (0–4)	1 (0–3)
Previously admitted to ICU within same acute hospital stay	589 (5.0%)	4,538 (4.3%)
Surgical status		
Elective surgical	579 (5.0%)	30,188 (28.4%)
Emergency surgical	2,291 (19.8%)	19,516 (18.4%)
Non-surgical	8,724 (75.3%)	56,652 (53.3%)
CPR in 24 h prior to admission to ICU	2,636 (22.6%)	7,281 (6.9%)
Mechanically ventilated in first 24 h in ICU	10,477 (90.2%)	64,314 (60.8%)
Sedated/paralysed in first 24 h		
No	1,337 (11.5%)	28,838 (27.5%)
For some of the time	3,798 (32.7%)	47,505 (45.3%)
Sedated	5,420 (46.7%)	23,837 (22.7%)
Paralysed and sedated	1,052 (9.1%)	4,800 (4.6%)

[a] Biopsy-confirmed cirrhosis, portal hypertension, hepatic encephalopathy, very severe cardiovascular disease, severe respiratory disease, chronic renal insufficiency, immuno-compromised

Table 2 Most frequently reported primary reasons for admission to ICU for patients in whom the decision to withdraw active treatment was made: proportion of total patients in whom the decision to withdraw active treatment was made (overall) and proportion of total patients admitted to ICU with this primary reason for admission (primary reason)

	Overall (%)	Primary reason (%)
Pneumonia (bacterial or no organism isolated) (n=1328)	11.4	17.7
Septic shock (n=693)	5.9	25.3
Acute myocardial infarction (n=474)	4.1	16.2
Aortic or iliac dissection or aneurysm (n=471)	4.0	6.7
Cardiogenic shock (n=415)	3.5	31.3
Intracerebral bleeding (n=320)	2.7	23.1
Subarachnoid bleeding (n=316)	2.7	18.1
Anoxic or ischaemic coma or encephalopathy (n=309)	2.6	37.6
Ventricular tachycardia or fibrillation (n=287)	2.5	20.1
Non-traumatic large bowel perforation (n=286)	2.5	16.2

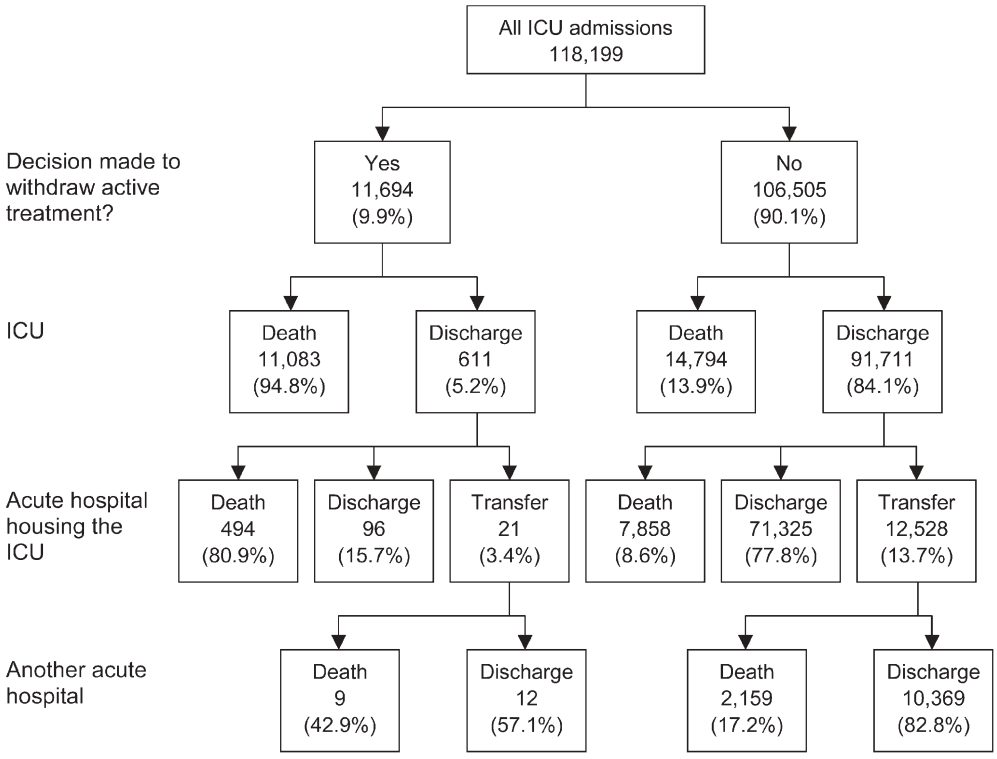

Fig. 1 Flow chart of ICU admissions, characterised by the decision to withdraw active treatment

Deaths after decision to withdraw all active treatment

Overall a total of 36,397 patients (30.8%) died before ultimate discharge from an acute hospital (Fig. 1). In total 11,586 deaths (99.1% of withdrawals and 31.8% of all deaths) occurred after the decision to withdraw all active treatment. Most of these deaths occurred in ICU (n=11,083, 94.8%). The remaining deaths occurred after discharge from ICU, but while in the same (n=494) or another acute hospital (n=9). There were 108 patients who survived to acute hospital discharge (presumably having had treatment reinstated). The patients who survived were slightly younger (mean age 61.8 vs. 64.7 years), had a lower mean APACHE II score (16.8 vs. 23.4), and had a slightly shorter ICU stay before the decision to withdraw all active treatment (1.8 vs. 2.0 days) than those who died after the decision to withdraw all active treatment.

There was considerable variation across units in the percentage of patients in whom a decision to withdraw all active treatment was made (range 0.6–31.8%). Across units, between 1.7% and 96.1% of ICU deaths occurred after a decision to withdraw active treatment; units were evenly distributed between these two extremes (Fig. 2). Median time to death following the decision to withdraw active treatment was 2.4 h. However, a quarter of patients survived longer than 7 h and 8% survived longer than 24 h (Fig. 3).

Changes over time in active treatment withdrawal

For each year (1996–2000) we calculated the percentage of total admissions to ICU resulting in a decision to withdraw all active treatment (range 9.1–10.7%), the percentage of deaths in ICU that occurred after a decision to withdraw active treatment (41.5–44.7%) and the percentage of all (ICU and hospital) deaths before acute hospital discharge that occurred after a decision to withdraw all active treatment (30.1–33.3%; Fig. 4). There were no statistically significant changes over the time examined in the use of active treatment withdrawal (p=0.20, p=0.54, and p=0.22, respectively, χ^2 for trend).

Factors associated with the decision o withdraw active treatment

We examined factors that might be associated with the decision to withdraw active treatment among patients who died while in the ICU (Table 3). For this analysis only admissions resulting in ICU death were included. Following exclusions (age less than 16 years, ICU stay less than 8 h, or missing data), 19,920 admissions (77% of ICU deaths) were included in the analysis. Increasing age, having one or more severe conditions in the medical history, admission following emergency surgery or as a non-surgical case, CPR within the 24 h prior to admission to ICU, mechanical ventilation in the first 24 h in ICU,

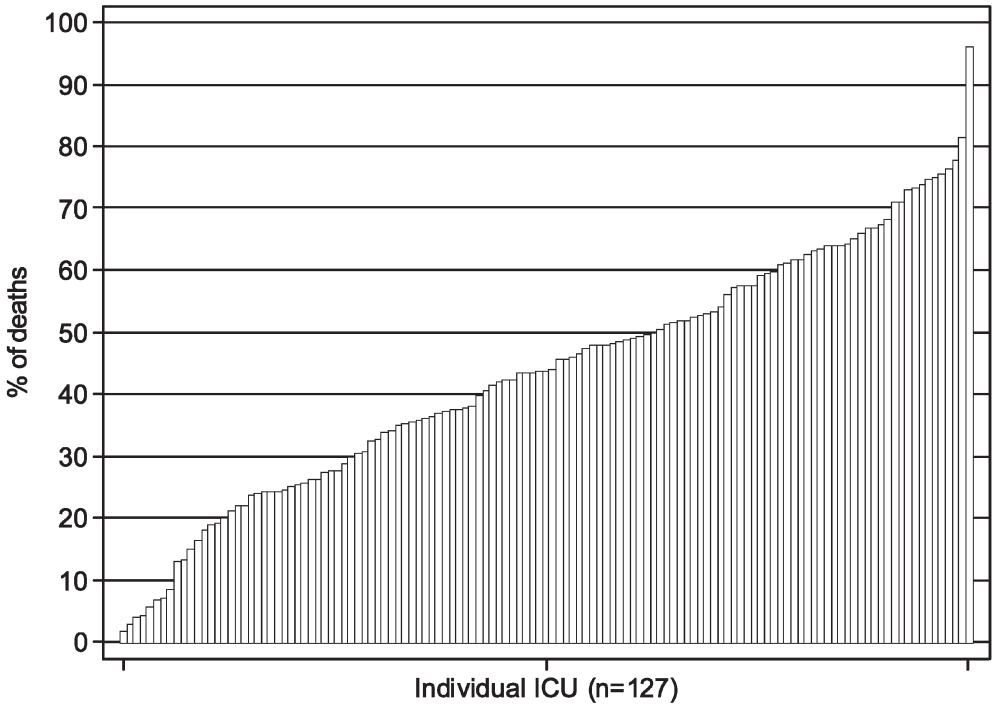

Fig. 2 By individual ICU, the percentage of ICU deaths that occurred following the decision to withdraw active treatment

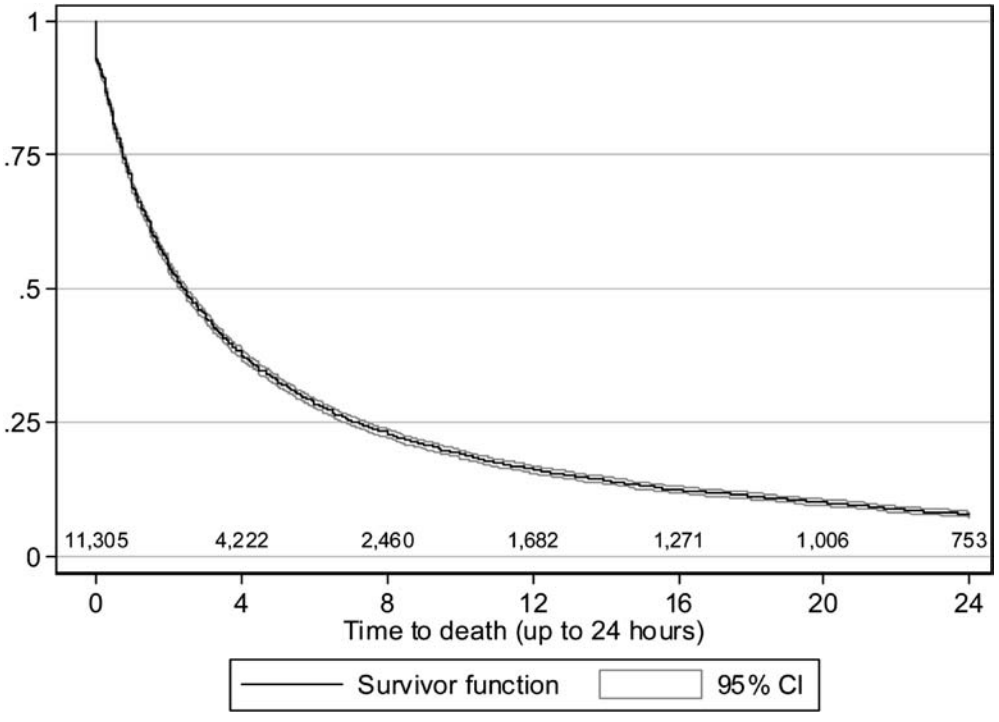

Fig. 3 Kaplan-Meier estimate of survival following decision to withdraw active treatment. Date and/or time of the decision or date and/or time of death/discharge from ICU were missing for 389 patients (3.3%) excluded from this analysis. Of those included in the analysis 573 were censored at time of discharge from ICU (470 died in hospital, 103 survived to hospital discharge). *Numerals at foot of figure* Numbers at risk

and sedation and/or paralysis in the first 24 h in ICU were all independently and significantly associated with the decision to withdraw active treatment. The model was additionally adjusted at the individual level for all possible combinations of organ system failures, assessed physiologically during the first 24 h in ICU according to the definitions of Knaus et al. [26]. The overall effect of adjusting for organ failures was significant (p=0.007).

At the unit level neither the type of hospital within which the ICU was located (university, university affiliated, or non-university) nor size of the ICU was significantly associated with the decision to withdraw active

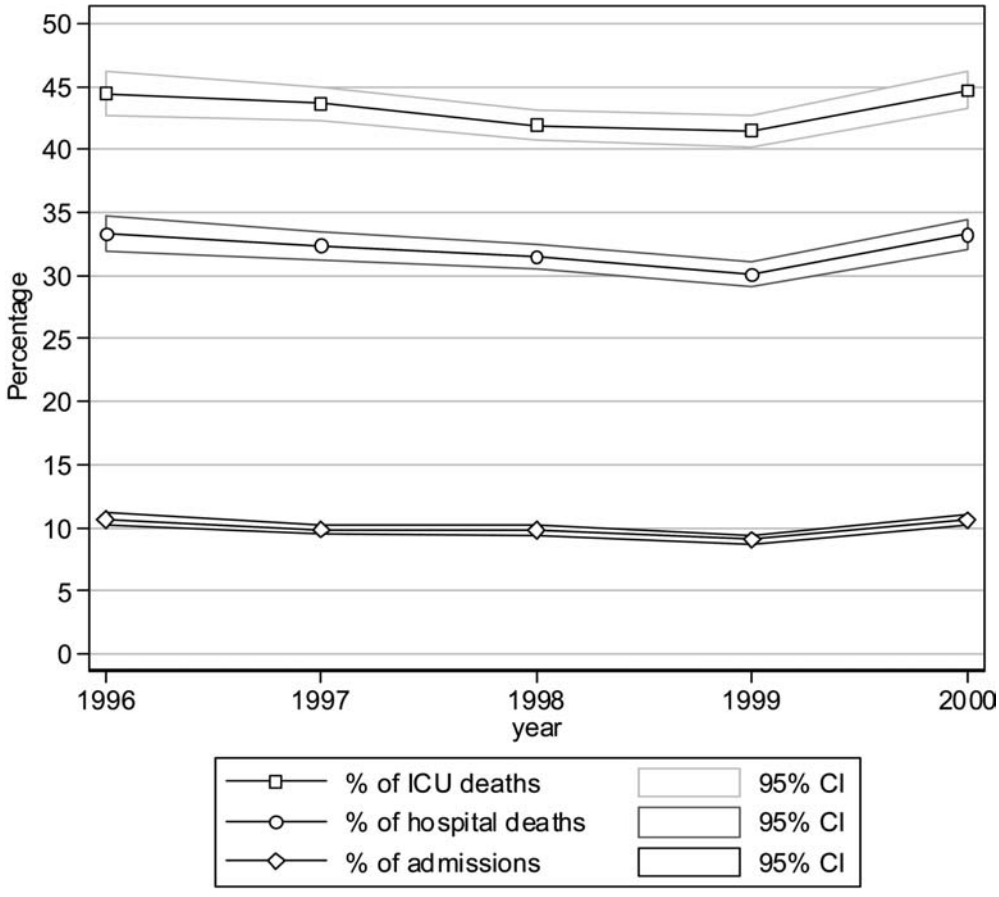

Fig. 4 Practice of deciding to withdraw active treatment over time (1996–2000)

treatment, after taking into account all of the individual covariates. The between-unit variance in the log odds of treatment withdrawal was 1.08 (95% CI 0.79–1.36) before and 1.23 (0.89–1.56) after adjustment for individual and unit level covariates, suggesting that these factors do not explain the variation between individual ICUs.

Discussion

This study confirms the general acceptance of withdrawing all active treatment in ICUs in the UK. Our study found a generally higher percentage of patients admitted to ICU had all active treatment withdrawn (9.9%) than reports in other studies (which unlike our study also included partial treatment withdrawal), ranging from 3% in a United States survey to 6.4% in a study in France [3, 19, 20, 21].

There remains very wide variation between UK ICUs in the use of active treatment withdrawal; some units almost never decided to withdraw all active treatment, while others used it routinely. The variation between units remained even after taking into account both differences in patient case mix and known characteristics of the individual ICUs. Some of the variation may be due to different interpretation of the definition for this variable; however, this is unlikely as all data collectors are trained by ICNARC, and the definition for this variable is used as a specific, practical example in the training course, as well as being clearly defined and stated in the manual provided to all data collectors.

The recent statement from the 5th International Consensus Conference in Critical Care (Brussels, Belgium, 2003) described differences between and within countries with regard to end-of-life decision making [6]. However, the main data regarding these decisions in Europe come from findings from a few ICUs in each country rather than nationally representative data [3]. Our results are unique due to the volume of admissions from such a large percentage of ICUs in one country in combination with the prospective collection of the data. This has allowed us to accurately describe the overall use of all active treatment withdrawal and also the widespread variation in practice across units, as opposed to having to extrapolate from practices reported from a single unit or small subset of units. These data are also minimally biased by response rate, as they were collected as part of a national audit of consecutive admissions to ICU rather than by selective survey or reliance on questionnaires regarding practice. Unfortunately, we were limited to examining only the withdrawal of all active treatment, as these are the only

Table 3 Predictors from multilevel logistic regression associated with the decision to withdraw active treatment (in ICU deaths only) The model is adjusted for the mean value of all individual covariates at the unit level, for length of time from ICU admission to treatment withdrawal or death, and for all combinations of organ system failures (Knaus definitions) occurring during the first 24 h in ICU (*parentheses* 95% confidence interval; *n*=19,920)

	Adjusted odds ratio	*p*
Individual level covariates		
Age (years)		<0.0001
16-44	1.00	
45-64	1.50 (1.34-1.67)	
65-84	1.80 (1.61-2.01)	
85+	2.01 (1.65-2.44)	
Sex		0.082
Male	1.00	
Female	1.06 (0.99-1.13)	
APACHE II Acute Physiology Score (per 10 point increase)	1.05 (0.99-1.12)	0.12
One or more severe conditions in medical history	1.24 (1.14-1.35)	<0.0001
Length of stay in hospital prior to ICU admission (per 7 days)	1.01 (0.99-1.04)	0.24
Readmission in same hospital stay	1.05 (0.91-1.23)	0.50
Location immediately prior to ICU admission		0.46
A&E	1.00	
Clinic or home	0.64 (0.34-1.19)	
High-dependency unit, same hospital	0.93 (0.80-1.08)	
ICU, same hospital	1.15 (0.83-1.58)	
Other hospital, not ICU	1.05 (0.91-1.22)	
Theatre and recovery	1.06 (0.75-1.49)	
ICU, other hospital	1.12 (0.92-1.35)	
Ward	1.02 (0.91-1.13)	
Radiography, endoscopy suite, computed tomography or similar	0.91 (0.74-1.11)	
Surgical status		<0.0001
Elective surgery	1.00	
Emergency surgery	1.51 (1.30-1.76)	
Medical	1.53 (1.07-2.18)	
CPR within 24 h prior to admission	1.18 (1.08-1.30)	0.0002
Mechanically ventilated in first 24 h in ICU	1.38 (1.21-1.58)	<0.0001
Sedated/paralysed in first 24h		<0.0001
No	1.00	
For some of first 24 h	1.19 (1.05-1.35)	
Sedated for all of first 24 h[a]	1.54 (1.35-1.77)	
Paralysed and sedated for all of first 24h[a]	1.29 (1.09-1.52)	
Unit level covariates		
Type of hospital		0.48
University	1.00	
University affiliated	1.43 (0.50-4.07)	
Non-university	1.37 (0.49-3.78)	
Size of ICU (per 5 bed increase)	0.94 (0.84-1.05)	0.26

[a] If stay was less than 24 h, then sedated/paralysed for entire time in ICU

data available within the CMPD. Withholding or placing an upper limit on treatment and partial withdrawal of treatment, which other studies have demonstrated are common practice in ICUs, are also important to consider when describing and assessing end-of-life care [19, 20, 21]. This means that our results are likely to be an underestimate of the overall use of limitation of therapy in end-of-life care in ICUs in the UK.

Time to death after active treatment withdrawal was on average 2 h. This is a little shorter than the findings of the recent ETHICUS study, which reported a median of 4.0 h for patients who had withdrawal of treatment [3]. Individual variation in time to death may be at least partially explained by the type of treatments being withdrawn (i.e. ventilatory support or antibiotics) or the time between the decision to withdraw treatment and the action. The relatively short average time to death suggests that this decision is generally a late point in the process of end-of-life decision making; many of these patients may have had care limited prior to the decision to withdraw all active treatment, which would be in keeping with current models of the dying process [14]. Unfortunately, we are not able to report on patient characteristics and treatment decisions during the period immediately prior to the decision to withdraw all active treatment, as we are limited by the variables available. A new version of the CMPD dataset in 2005 includes questions regarding CPR, withholding and withdrawing treatment.

Due to the retrospective analysis of our data physician characteristics and views, family perceptions and other influences on ICU care were not available. These have been shown to strongly influence decision making at the

end of life [8, 13, 14, 18]. A recent study in Canada showed that physician predictions regarding outcome, as well as perceptions regarding patient preferences, are strongly associated with the decision to withdraw mechanical ventilation in ICUs [14]. Having more data regarding the process of decision making in ICUs in the UK would be informative, especially given the major differences in attitude and laws internationally regarding end-of-life care highlighted recently by the 5th International Consensus Conference in Critical Care [6] and the wide variation reported in this study. Unlike in the United States, where respect for patient autonomy drives much of the decision making, professional medical organizations in the UK focus emphasis on the role of the clinician in making ultimate decisions regarding care [6]. However, this may begin to change as new laws and rulings are introduced to clarify the role of living wills and health care proxies in end-of-life decision making. Updates on the most recent rulings are available on the British Medical Association website (http://web.bma.org.uk/homepage.nsf).

A number of studies in the 1980s and 1990s showed that the use of withholding and withdrawing care was increasing dramatically in the United States and Canada [7, 27, 28]. Our data show relatively little fluctuation in withdrawal of active treatment between 1996 and 2000 in the UK. It is unclear whether there was a rapid increase in this type of decision making at an earlier time, which has now reached a plateau, or whether the UK, with its more limited number of intensive care beds and generally lower expenditure on health care has always implemented withdrawal of active treatment more frequently [29, 30].

A continuing scarcity of beds and pressure for admission is still reported as being felt by all ICUs in the National Health Service in the UK [31]. These differences in decision making regarding the use of active treatment withdrawal across units are all the more striking for occurring in such a national network of ICU beds. This study highlights an area where further information regarding the decision-making process in ICUs is needed, and implementation of common protocols for addressing end-of-life decisions may be appropriate.

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