Supplementary Online Content

Guidet B, Leblanc G, Simon T, et al; ICE-CUB 2 Study Network. Effect of systematic intensive care unit triage on long-term mortality among critically ill elderly patients in France: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2017.13889

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Supplementary Methods

Study Oversight

- Members of the steering committee: Bertrand Guidet, Maité Garrouste-Orgeas, Caroline Thomas, Dominique Pateron, Tabassome Simon, Ariane Boumendil.
- The study was approved by the Comité de Protection des Personnes d'Ile-de-France 9.
- The Department of Clinical Research and Development of Ile-de-France (*Département de la Recherche Clinique et du Développement* –DRCD- Ile-de-France), served as independent oversight committee, had full access to the mortality data and could stop the trial in case of important disparity in mortality rates between groups.
- The conduct of the study was monitored by the clinical research assistants of the sponsor.
- There was no interim analysis.

Inclusion Criteria

1. Patients 75 years of age or over.
2. Admitted to the emergency department.
3. A diagnosis among a pre-established list of critical conditions (Table S1).
4. A preserved functional status, as assessed by an Index of Independence in Activities of Daily Living[1] ≥ 4 (0 = totally dependent, 6 = independent) or not evaluable.
5. A preserved nutritional status, defined as the absence of cachexia, subjectively assessed by physicians at bedside.
6. Free of active cancer.

Exclusion Criteria

1. An emergency department stay over 24 hours.
2. A secondary referral to the emergency department.
3. Patient's or surrogate decision-makers' refusal to participate.
4. No social security coverage.

Patient Follow-up

Three thousand and thirty-seven patients (N=3,037) were included in the trial and randomized to either intervention of control group. One patients withdrew consent to use of his data and was excluded from analysis, leaving 3,036 patients in the analysis. In the systematic-strategy group, 17 patients were alive at hospital discharge and were lost to follow-up at 6 months. In the standard-strategy group, 27 patients were alive at hospital discharge and were lost to follow-up at 6 months. Primary outcome data from patients who were lost to follow-up before 6 months were censored at their last follow-up assessment. The primary outcome was analysed in the intention-to-treat population (N=3,036 patients).

Electronic Database Search Strategy

The electronic search strategy was used to search for available randomized clinical trial of intensive care unit admission in critically ill elderly patients in the literature. This search strategy was peer-reviewed and approved by experts in literature review.

Medline

#1 Search "Critical Illness"[Mesh]
#2 Search "Critical Care"[Mesh:noexp]
#3 Search "Intensive Care Units"[Mesh]
#4 Search "Critical Care Outcomes"[Mesh]
#5 Search #1 OR #2 OR #3 OR #4
#6 Search "Triage"[Mesh]
#7 Search "Patient Admission"[Mesh]
#8 Search #6 OR #7
#9 Search "Aged"[Mesh]
#10 Search Clinical Trial[ptyp]
#11 Search #5 AND #8 AND #9 AND #10
#12 Search "critically ill"[tw]
#13 Search "critical illness"[tw] OR "critical illnesses"[tw]
#14 Search "critical care"[tw]
#15 Search "intensive care"[tw]
#16 Search "critical care outcome"[tw] OR "critical care outcomes"[tw]
#17 Search ICU[tw]
#18 Search #12 OR #13 OR #14 OR #15 OR #16 OR #17
#19 Search "old age"[tw] OR "old ages"[tw]
#20 Search senior*[tw]
#21 Search aged[tw]
#22 Search "advanced age"[tw] OR "advanced ages"[tw]
#23 Search "old patient"[tw] OR "old patients"[tw]
#24 Search elder*[tw]
#25 Search #19 OR #20 OR #21 OR #22 OR #23 OR #24
#26 Search triage*[tw]
#27 Search admission*[tw]
#28 Search admitted[tw]
#29 Search #26 OR #27 OR #28

#30 Search “randomized clinical trial”[tw] OR “randomized clinical trials”[tw] OR “randomised clinical trial”[tw] OR “randomised clinical trials”[tw]

#31 Search “randomized controlled trial”[tw] OR “randomized controlled trials”[tw] OR “randomised controlled trial”[tw] OR “randomised controlled trials”[tw]

#32 Search #30 OR # 31

#33 Search #18 and #25 and #29 and #32

#34 Search #11 OR #33

Date of last search: June 27th 2016

Number of references: 1175

Embase

#1 Search “critical illness”/exp

#2 Search “intensive care”/exp

#3 Search “intensive care unit”/exp

#4 Search “critical care outcome”/exp

#5 Search #1 OR #2 OR #3 OR #4

#6 Search “hospital admission”/exp

#7 Search #5 AND #6

#8 Search #7 AND ‘randomized controlled trial’/de AND ([aged]/lim or [very elderly]/lim)

#9 Search “critically ill”

#10 Search “critical illness” or “critical illnesses”

#11 Search “critical care”

#12 Search “intensive care”

#13 Search “critical care outcome” or “critical care outcomes”

#14 Search ICU*

#15 Search #9 OR #10 OR #11 OR #12 OR #13 OR #14

#16 Search “old age” OR “old ages”

#17 Search senior*

#18 Search aged

#19 Search “advanced age” or “advanced ages”

#20 Search “old patient” or “old patients”

#21 Search elder*

#22 Search #16 OR #17 OR #18 OR #19 OR #20 OR #21

#23 Search admission*

#24 Search triage*

#25 Search admitted

#26 Search #23 OR #24 OR #25

#27 Search “randomized clinical trial” OR “randomized clinical trials” OR “randomised clinical trial” OR “randomised clinical trials”

#28 Search “randomized controlled trial” OR “randomized controlled trials” OR “randomised controlled trial” OR “randomised controlled trials”

#29 Search #27 OR #28

#30 Search #15 AND #22 AND #26 AND #29

#31 Search #8 OR #30

#32 Search #31 AND [embase]/lim NOT [medline]/lim)

Date of last search: June 27th 2016

Number of references: 212

eTable 1. List of the Critical Conditions for Inclusion*

Cardiac disorder	Cardiogenic shock
	Congestive heart failure requiring NIV
	Arrhythmia
Surgery	Neurosurgery
	Multiple traumatic injuries
	Cardiac
	Gastrointestinal
	Others
Coma	Metabolic
	Toxic
	Stroke
	Status epilepticus
	Traumatism
	Anoxic
	Intracranial hypertension
Respiratory disorder	Chronic obstructive pulmonary disease
	Pulmonary embolism
	Severe pneumonia
	Acute respiratory failure requiring tracheal intubation
	Acute respiratory failure requiring NIV
	Acute respiratory failure requiring physiotherapy
Gastrointestinal disorder	Gastrointestinal tract hemorrhage
	Pancreatitis
	Acute liver insufficiency
	Abdominal emergency
Shock	Septic
	Hemorrhagic
	Hypovolemic
	Others
Renal	Acute kidney failure
Multiple traumatic injuries without surgery	
Others	

* The list of critical conditions for inclusion was retrieved from the ICE-CUB 1 study[1]. This list of critical conditions adapted to the elderly patient was established by a Delphi consensus method among emergency department physicians and adapted from the *Guidelines for Intensive Care Unit Admission, Discharge, and Triage*[2] and restricted to critical conditions that potentially require an organ support. NIV: Non-Invasive Ventilation.

eTable 2. Detailed list of Initial Clinical Diagnoses of Included Patients*

	Systematic strategy (N=1,518)	Standard strategy (N=1,518)
Cardiac disorder		
Congestive heart failure requiring NIV	87 (6)	131 (9)
Arrhythmia	45 (3)	54 (4)
Cardiogenic shock	45 (3)	46 (3)
Surgery		
Gastrointestinal	15 (1)	22 (1)
Neurosurgery	3 (0.2)	6 (0.4)
Cardiac	3 (0.2)	2 (0.1)
Multiple traumatic injuries	1 (0.1)	2 (0.1)
Others	4 (0.3)	4 (0.3)
Coma		
Stroke	65 (4)	64 (4)
Metabolic	32 (2)	15 (1)
Status epilepticus	27 (2)	13 (1)
Toxic	16 (1)	14 (1)
Intracranial hypertension	11 (1)	18 (1)
Anoxic	24 (2)	1 (0.1)
Trauma	12 (1)	7 (0.5)
Respiratory disorder		
Chronic obstructive pulmonary disease	71 (5)	109 (7)
Pulmonary embolism	26 (2)	48 (3)
Severe pneumonia requiring high oxygen supply	105 (7)	145 (10)
Acute respiratory failure requiring mechanical ventilation	57 (4)	32 (2)
Acute respiratory failure requiring NIV	209 (14)	138 (9)
Acute respiratory failure requiring physiotherapy	20 (1)	19 (1)

eTable 2. Detailed list of Initial Clinical Diagnoses of Included Patients* (continued)

	Systematic strategy (N=1,518)	Standard strategy (N=1,518)
Gastrointestinal tract hemorrhage	40 (3)	57 (4)
Pancreatitis	3 (0.2)	14 (1)
Acute liver insufficiency	0 (0)	5 (0.3)
Abdominal emergency	14 (1)	41 (3)
Renal		
Acute kidney failure	86 (6)	61 (4)
Shock		
Septic	244 (16)	169 (11)
Hemorrhagic	35 (2)	21 (1)
Hypovolemic	30 (2)	32 (2)
Others	11 (1)	16 (1)
Multiple traumatic injuries without surgery	10 (1)	9 (1)
Others	165 (11)	202 (13)

* Data are provided as numbers and percentages. NIV: Non-Invasive Ventilation.

eTable 3. Characteristics of the Triage Process*

	Systematic strategy (N=1,518)	Standard strategy (N=1,518)	P Value
Time of hospital admission - no. (%)			
8am-11pm	1,297 (85)	1,320 (87)	0.22
Midnight-7am	221 (15)	198 (13)	
Seniority of ED physicians - no./no. total (%)			
≥ 2 years	871/1,505 (58)	1,095/1,482 (74)	<0.001
< 2 years	343/1,505 (23)	102/1,482 (7)	
Resident	291/1,505 (19)	285/1,482 (19)	
Seniority of ICU physicians - no./no. total (%)			
≥ 2 years	1106/1,345 (82)	514/660 (78)	0.003
< 2 years	170/1,345 (13)	86/660 (13)	
Resident	69/1,346 (5)	60/660 (9)	
Primary referent** - no./no. total (%)			
Child	656/1,445 (45)	690/1,392 (50)	<0.001
Spouse / living partner	401/1,445 (28)	281/1,392 (20)	
Other family member	195/1,445 (13)	216/1,392 (15)	
General practitioner / nurse	55/1,445 (4)	62/1,392 (4)	
Friend	44/1,445 (3)	35/1,392 (3)	
Neighbor	17/1,445 (1)	22/1,392 (2)	
None	77/1,445 (5)	86/1,392 (6)	
Identified general practitioner - no./no. total (%)			
Yes	1,046/1,518 (69)	1,053/1,483 (71)	0.22
No	472/1,518 (31)	430/1,483 (29)	
Perceived burden for family - no./no. total (%)			
Average	477/644 (74)	148/180 (82)	0.07
Heavy but bearable	156/644 (24)	30/180 (17)	
Unbearable	11/644 (2)	2/180 (0.1)	

eTable 3. Characteristics of the Triage Process (Continued)*

	Systematic strategy (N=1,518)	Standard strategy (N=1,518)	P Value
ED physicians: opinion about ICU admission - no./no. total (%)			
Favorable	1,327/1,513 (88)	875/1,425 (61)	<0.001
Unfavorable	186/1,513 (12)	550/1,425 (39)	
ED physicians: reason for not proposing ICU admission- no./no. total (%)			
Patient is too well	66/179 (37)	209/390 (54)	0.001
No expected benefit due to underlying disease	69/179 (39)	113/390 (29)	
Patient is too sick	44/179 (25)	68/390 (17)	
ICU physicians: opinion about ICU admission - no./no. total (%)			
Favorable	1,110/1,473 (75)	623/938 (66)	<0.001
Unfavorable	363/1,473 (25)	315/938 (34)	
ICU physicians: reason for not proposing ICU admission- no./no. total (%)			
Patient is too well	148/355 (42)	105/292 (36)	0.25
No expected benefit due to underlying disease	115/355 (32)	116/292 (40)	
Patient is too sick	49/355 (14)	40/292 (14)	
Few available beds	43/355 (12)	31/292 (11)	
Opinion about ICU admission - no./no. total (%)			
Patients favorable			
and relatives favorable	207/1,515 (14)	53/1,517 (3)	<0.001
and relatives unfavorable	1/1,515 (0.1)	0/1,517 (0)	
and relatives have no opinion	206/1,515 (14)	92/1,517 (6)	
Patients unfavorable			
and relatives favorable	0/1,515 (0)	2/1,517 (0.1)	
and relatives unfavorable	11/1,515 (1)	14/1,517 (1)	
and relatives have no opinion	10/1,515 (1)	16/1,517 (1)	
Patients have no or unknown opinion			
and relatives favorable	214/1,515 (14)	77/1,517 (5)	
and relatives unfavorable	57/1,515 (4)	57/1,517 (4)	
and relatives have no opinion	809/1,515 (53)	1206/1,517 (79)	

* Data are reported as numbers and percentages. ED: Emergency Department, ICU: Intensive Care Unit

** Primary referent is the person who could take responsibility in the decision-making process

eTable 4. Number and Characteristics of Protocol Violations*

Protocol violations	Systematic strategy (N=1,518)	Standard strategy (N=1,518)
Index of ADL** < 4	5	16
Age < 75 years	1	5
Presence of cachexia	5	2
Absence of a pre-established critical condition	4	4
No social security coverage	1	3
Patient with known active cancer	1	4
	16***	33***

*There were a total of 49 protocol violation (49/3,036, 1.6%).

** Index of Independence in Activities of Daily Living[1].

***Two patients did not meet two inclusion criteria.

eTable 5. Number of Decisions for ICU Admission and Number of Patients Actually Admitted*

Decisions for ICU admission	Patients Admitted to the ICU		
	No	Yes	Total
Systematic-strategy			
No	572	1	573
Yes	0	931	931
Total	572	932	
Standard-strategy			
No	986	0	986
Yes	0	516	516
Total	986	516	

***** The number of decisions for ICU admission is not significantly different than the number of patients actually admitted to the ICU. In the systematic-strategy group, one patient was admitted to the ICU while a decision for no ICU admission had been made.

eTable 6. Characteristics of Patients Admitted to the Intensive Care Unit

	Systematic strategy (N=932)	Standard strategy (N=516)	Difference in medians or proportions (95%CI)	P Value
Age (years) - median (IQR)	84 (80-88)	84 (80-88)	0 (-0.5-1)	0.28
SAPS 3* - median (IQR)	65 (57-72)	62 (56-68)	3 (2-5)	<0.001
ICU length of stay (days)** - median (IQR)	4 (2-7)	3 (1-6.3)	–1 (-0.5-1)	0.32
Hospital length of stay (days)*** - median (IQR)	12 (4-22)	11 (5-19.8)	–1 (-1-3)	0.98
Male sex - no. (%)	448 (48)	236 (46)	2 (-3 - 8)	0.43
Mechanical ventilation - no. (%)	374/884 (42)	147/470 (31)	11 (6 - 16)	<0.001
Non-invasive ventilation - no. (%)	251/884 (28)	170/470 (36)	-8 (-13 - -3)	0.004
Vasopressors - no. (%)	346/884 (39)	166/469 (35)	4 (-2 - 9)	0.20
Kidney replacement therapy - no. (%)	117/884 (13)	49/469 (10)	3 (-1 - 6)	0.16
Fluid resuscitation - no. (%)	177/835 (21)	151/469 (32)	-11 (-16 - -6)	<0.001
Number of interventions - no. (%)				
At least one****	711/873 (81)	402/470 (86)		0.07
None*****	162/873 (19)	68/470 (14)		

* The Simplified Acute Physiology Score (SAPS) 3[4] ranges from 0 to 146, with higher scores indicating a more severe disease and a higher risk of death; data available for 897 patients in the systematic-strategy group and 482 patients in the standard-strategy group.
** Data available for 906 patients in the systematic-strategy group and 511 patients in the standard-strategy group.
*** Data available for 913 patients in the systematic-strategy group and 512 patients in the standard strategy group.
**** Number of patients who received at least one of the following interventions: invasive or non-invasive ventilation, vasopressors, renal replacement therapy or fluid resuscitation.
ICU: Intensive Care Unit, IQR: Interquartile Range

eTable 7. Baseline Index of Independence in Activities of Daily Living*

Index of ADL	Systematic strategy (N=1,330)	Standard strategy (N=1,200)
< 4.0	5 (0.4)	16 (1)
4.0	109 (8)	106 (9)
4.5	106 (8)	63 (5)
5.0	134 (10)	103 (9)
5.5	140 (11)	121 (10)
6.0	836 (63)	791 (66)

***** The Index of Independence in Activities of Daily Living (Index of ADL)[1] is based on an evaluation of the functional independence or dependence of patients in bathing, dressing, going the toilet, transferring, continence and feeding and ranges from 0, totally dependent to 6, independent; 188 missing values in the systematic-strategy group and 318 missing values in the standard-strategy group

eTable 8. Index of Activities in Daily Living Scale at 6 months*

Index of ADL**	**Systematic strategy (N=750)**	**Standard strategy (N=778)**	**P Value**
0.0	18 (2)	21 (3)	0.09
0.5	25 (3)	17 (2)	
1.0	25 (3)	34 (4)	
1.5	15 (2)	5 (1)	
2.0	24 (3)	27 (3)	
2.5	27 (4)	20 (3)	
3.0	31 (4)	28 (4)	
3.5	45 (6)	36 (5)	
4.0	47 (6)	40 (5)	
4.5	55 (7)	52 (7)	
5.0	77 (10)	98 (13)	
5.5	139 (19)	126 (16)	
6.0	222 (30)	274 (35)	

* The Index of Independence in Activities of Daily Living[1] (Index of ADL) is based on an evaluation of the functional independence or dependence of patients in bathing, dressing, going the toilet, transferring, continence and feeding and ranges from 0, totally dependent to 6, independent.

** Data on Index of ADL at 6 months were available for 750 patients in the systematic-strategy group and for 777 patients in the standard-strategy group.

eTable 9. Additional data at 6-month follow-up.

	Systematic strategy (N=1,067)	Standard strategy (N=1,192)	P Value
Median duration of follow-up - months (IQR)	6.0 (6.0-6.1)	6.0 (6.0-6.1)	
Deaths during follow-up*	234	262	
Contact for follow-up - no./total no. (%)			
Primary referent** / relatives	524/1,065 (49)	651/1,191 (55)	0.02
Patient	456/1,065 (43)	445/1,191 (37)	
General Practitioner	69/1,065 (6)	68/1,191 (6)	
Lost to follow-up	16/1,065 (2)	27/1,191 (2)	
Living place - no./total no. (%)			
Home	346/800 (43)	394/854 (46)	0.60
Home with assistance	270/800 (34)	272/854 (32)	
Long-term care	108/800 (14)	106/854 (12)	
Hospital	46/800 (6)	57/854 (7)	
Nursing home	29/800 (4)	25/854 (3)	
Homeless	1/800 (0.1)	0/854 (0)	
Home support - no./total no. (%)			
Alone	361/747 (48)	390/780 (50)	0.002
Spouse/partner	292/747 (39)	250/780 (32)	
Family	94/747 (13)	140/780 (18)	

*After hospital discharge

IQR : Interquartile Range

** Person who could take responsibility in the decision-making process

eReferences

1. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. Jama 1963;185:914-9.

2. Garrouste-Orgeas M, Boumendil A, Pateron D, et al. Selection of intensive care unit admission criteria for patients aged 80 years and over and compliance of emergency and intensive care unit physicians with the selected criteria: An observational, multicenter, prospective study. Critical care medicine 2009;37:2919-28.

3. Guidelines for intensive care unit admission, discharge, and triage. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Critical care medicine 1999;27:633-8.

4. Moreno RP, Metnitz PG, Almeida E, et al. SAPS 3--From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. Intensive care medicine 2005;31:1345-55.