To cite: Leclaire C. Georges A.

de Stampa M. et al. 1-vear

medical patients treated

with a conservative or an

invasive approach (OCTO-

bmjopen-2024-089835

Prepublication history

and additional supplemental

available online. To view these

online (https://doi.org/10.1136/

files, please visit the journal

bmjopen-2024-089835).

Received 10 June 2024

Accepted 28 April 2025

© Author(s) (or their

material for this paper are

REVERSE study): a nationwide

observational study. BMJ Open

2025;15:e089835. doi:10.1136/

survival in critically ill elderly

# **BMJ Open** 1-year survival in critically ill elderly medical patients treated with a conservative or an invasive approach (OCTO-REVERSE study): a nationwide observational study

Clement Leclaire ,<sup>1</sup> Alexandre Georges,<sup>1</sup> Matthieu de Stampa ,<sup>2,3</sup> Philippe Aegerter <sup>2</sup>

ABSTRACT

**Objective** To determine whether an invasive approach is associated with favourable long-term outcomes among elderly medical patients in the intensive care unit (ICU), compared with a conservative approach.

**Design** Nationwide observational study (OCTO-REVERSE study) using data prospectively collected in the National French Healthcare Database (covering 99% of the population, 66 million people).

**Setting** Comprehensive multicentre study through the linkage of large-scale national registries (including all public or private facilities) from 2013 to 2018 to avoid ambiguities related to the COVID-19 pandemic.

**Participants** All non-surgical patients aged 80 years or older admitted to an ICU in France during the period (n=107 014 patients at 822 hospitals).

**Outcome measures** The main outcome was the 1-year survival rate. The association of the two approaches with 1-year survival was estimated using a time-dependent Cox model and a propensity score (PS) adapted to time-to-event analysis, yielding the average treatment effect in the treated and extended weighted Kaplan–Meier curves.

**Results** 107 014 patients were categorised into two groups based on the type of care received: invasive (n=51 680 (48%) received invasive ventilation and/or vasopressor support) or conservative (n=55 334 (52%) received neither). 1-year survival rate was significantly lower in the invasive group than in the conservative group (27% vs 59% estimated with extended time-dependent Kaplan–Meier method). The risk of death in the invasive group remained significantly higher after time-dependent PS weighting (HR 1.64; 95% Cl 1.60 to 1.69; p<0.001). The loss in restricted mean survival time was 67.7 days (95% Cl 65.7 to 69.8) in this group and 31% of deaths occurred the day of initiation of the procedure, or the following day.

**Conclusion** Among the whole population of critically ill elderly medical patients in France, the invasive approach was unknowingly associated with end-of-life care in nearly three quarters of cases. Further research is needed to align intensive care with compassionate goals.

# STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study uses the National French Healthcare Database, which records all medical procedures coded for reimbursement, ensuring exhaustiveness and real-world representativeness.
- ⇒ This study employs a robust time-dependent analysis using the extended Kaplan–Meier method, which accounts for variations in treatment exposure over time and improves survival estimates.
- ⇒ The simplified acute physiology score II, used in the propensity score model as the main severity adjustment factor, proved to be the primary determinant in balancing patient characteristics between groups.
- ⇒ The main limitation is the presence of potential unmeasured confounding factors, including key clinical parameters that could influence both treatment decisions and patient outcomes.
- ⇒ Information on whether care was withheld or withdrawn is not available, making it difficult to assess the impact of end-of-life decisions on mortality differences.

# **INTRODUCTION**

The proportion of older patients in the intensive care unit (ICU) has been steadily increasing over the past two decades, although the overall benefit to patient outcomes remains unclear.<sup>1</sup> Many studies have explored this topic, but variations in patient selection **Q** (age 65-90, surgical vs medical and invasive B vs conservative care) and outcome measures **g** (mortality vs functional status and early vs delayed assessment) have led to uncertain conclusions.<sup>2</sup> Additional research is needed to address the care consequences of this growing population. However, a randomised trial has been deemed infeasible on ethical grounds.<sup>3</sup> The ensuing uncertainty may have led to a decision-making process based solely on clinical judgement, while triage systems

employer(s)) 2025. Re-use permitted under CC BY-NC. No

Check for updates

commercial re-use. See rights and permissions. Published by BMJ Group. <sup>1</sup>Paris Public Hospital at Home (HAD AP-HP), Greater Paris

University Hospitals, Assistance Publique—Hopitaux de Paris, Paris, France <sup>2</sup>Inserm U1018, Center for Research in Epidemiology and Population Health (CESP), University of Versailles Saint-Quentin-en-Yvelines (UVSQ), CESP, Villejuif, France <sup>3</sup>Departmental Gerontological Center, Marseille, France

Correspondence to Dr Clement Leclaire; clement.leclaire@aphp.fr based on even limited evidence would have been preferable.<sup>4</sup> In addition, overoptimistic expectations<sup>5</sup> of outcomes could have favoured the expansion of timelimited trials,<sup>6</sup> some of which turned out to be disproportionate. Previous studies on this issue7-9 have identified older age ( $\geq 80$  years),<sup>10</sup> non-operative condition<sup>11</sup> and exposure to invasive procedures (primarily invasive mechanical ventilation and vasopressor therapy) $^{12-14}$  as prognostic factors that should be considered especially as to long-term outcomes. By conducting a nationwide study that combines these three factors, we aimed to assess the characteristics, management and 1-year survival of the entire target population of elderly patients admitted to the ICU for medical reasons in France.

### **METHODS**

#### Study design and data sources

We performed a nationwide retrospective analysis (OCTO-REVERSE study) using data prospectively collected in the Système National des Données de Santé (SNDS), the national French healthcare database that covers 99% of the population regardless of socioeconomic status (66 million). The SNDS was created for hospital payment and government purposes, and regular audits are conducted to ensure reliability and completeness. The SNDS also facilitates epidemiological research, with a specific interest in ageing by an extended follow-up. Formal methods have been developed to assess the strengths and limitations of databases, and populationlevel data have enhanced our understanding of the use and outcomes of mechanical ventilation,<sup>12</sup> particularly for elderly patients hospitalised in ICUs in France.<sup>15–17</sup> The SNDS links the national hospital discharge database of diagnosis-related groups (DRGs) 'PMSI (Programme de Médicalisation des Systèmes d'Information (French national hospital discharge database))' with the national death registry 'CépiDC', enabling the tracking of individual patient trajectories from any hospital stay through to death. This allows for the identification of the date and place of death, whether it occurs in hospital or in the community. It contains comprehensive medical and administrative data for all patients in the country. This linkage of large-scale French national registry populations contributes to guiding public decisions. Each patient is assigned a unique identification number with pseudonymised information, allowing individuals to be followed over time by linking inpatient and outpatient data from each hospitalisation in all public or private facilities in France. Procedures, including surgery or lifesustaining treatments, are time stamped and coded using a national classification system called CCAM (Classification Commune des Actes Médicaux (Common Classification of Medical Procedures)) (online supplemental appendix 1).

The study was submitted to and approved by the independent national data protection authority (CNIL (Commission Nationale de l'Informatique et des Libertés

(French Data Protection Authority)) Registration: Solution of the protection Authority)) Registration: Solution of the following invasive procedures during the for a single patient, only the first hospital stay, including a medical admission to an ICU during the study period, was considered for each patient, and readmission stays were sculuded. Finally, we considered the invasive condition for a single patient, only the first hospital stay, including a medical admission to an ICU during the study period, was considered for each patient, and readmission stays were sculuded. Finally, we considered the invasive condition (CCAM codes GLLD004, GLLD008 and GLLD015) or vasopressor support (CCAM codes EQLF001 and EQLF003) (online supplemental table 2, appendix 1).

benefit for the oldest patients. This choice was also driven by their coding reliability, as there is a clear-cut bedside decision without delay, marking a turning point in the ≥ patient's trajectory. We did not include non-invasive ventilation (NIV) because its use as a palliative treatment for dyspnoea has become increasingly common. We also ğ did not include renal replacement therapy (RRT) due to the large grey area in coding between acute and chronic situations, and because its initiation can often be delayed without threatening the prognosis.<sup>18</sup> We addressed potential confounding resulting from variation in the case mix by controlling for age, severity of illness, pre-existing medical conditions expressed by the Charlson comorbidity index, primary diagnosis at admission, preadmission location and academic status of the ICU. These confounders were  $\mathbf{\hat{G}}$ specified a priori to develop a risk adjustment model for **\$** mortality. Patients were followed until death or the end of the year 2019, whichever occurred sooner. The invasive and non-invasive cohorts were mutually exclusive.

### **Outcomes**

The primary objective of our analysis was to describe the 1-year mortality of two populations of elderly medical ICU patients based on the treatment intensity (invasive vs conservative care). Additionally, we analysed intermediate mortality rates and lengths of stay, both in ICU and in hospital.

#### **Statistical analysis**

Characteristics of patients according to the use of invasive procedures were described using mean and SD for age and median and IQR for other continuous variables. Categorical variables were presented as counts and percentages. Comparisons between the two groups were performed using the Wilcoxon test for continuous variables and the  $\chi^2$  test for categorical variables. Crude mortality rates were calculated at ICU and hospital discharge, along with 1-year readmission rates and the duration of procedures and hospital stays, for both groups and for each invasive procedure (online supplemental appendix 2, pp. 11-12).

Survival was measured from the date of ICU admission to the date of death or censored at the last follow-up. To limit immortal time bias, the occurrence of any invasive procedure was considered as a time-dependent covariate. Time precision was day, and the time of death was shifted by 0.1 day to avoid ties with the time of the procedure. Multivariate analysis of survival was performed by a Cox proportional hazards (PHs) model producing HRs. The handling of ties used the Efron approximation. The PH assumption was verified by scaled Schoenfeld residuals. The time-varying effect of a procedure was modelled by adding an interaction term between the corresponding covariate and some transformation of time. The restricted mean survival time (RMST) method was selected because it is not dependent on the number of events and on the assumption of PHs, as is the case in time-to-event analyses. RMST reflects the life expectancy of patients up to a specified time. Details regarding the statistical methods are provided in online supplemental appendix 1. As patients receiving invasive procedures may differ from the conservative ones, a propensity score (PS) was used to minimise the effects of confounding. Assumed confounders included age, sex, pre-existing comorbidities (Charlson comorbidity index), SAPS II score, year, reason for admission, availability of a palliative or geriatric care team in the hospital, preadmission location, ICU level and hospital characteristics (online supplemental figure S2 and table S1, appendix 1). However, the population at risk changes over time due to attrition (death or discharge). Therefore, we used an inverse probability of treatment weighting (IPTW) method adapted to the timedependent context.<sup>19</sup> IPTW usually estimates the average effect of treatment when the entire sample is moved from control to treated. But this seemed unrealistic for invasive support in the elderly population, so here IPTW targeted the average treatment effect in the treated (ATT). We divided the time span into strata within which a distinct PS could be calculated. These strata were each day until day 14, then periods 14-20, 20-30, every 15 days until 120 and then every 30 days until 365 (case base). This timestratified PS was built using a Cox model that predicted the use of invasive procedures by variables available at admission. The influence of continuous variables (age

and SAPS II) was modelled by fractional polynomials. Variable balance was assessed by examining the standardised mean differences before and after weighting. Weights were trimmed at the 1st and 99th percentiles. To remove residual confounding as much as possible, we combined weighting at the design stage with regression adjustment on the same confounders (as listed in online supplemental figure S2 and table S1, appendix 1) at the analysis stage when estimating treatment effects.<sup>20</sup> A robust sandwich-type estimator was used to calculate SEs.

We performed sensitivity analyses to assess the robust-ness of the overall HR associated with invasive proce-dures: initially by using ATT weights truncated at the 5th ş and 95th percentiles, then by using time strata defined by every day, an invasive procedure or death occurred.

copyright, All tests were two sided, and a p value<0.05 was considered statistically significant. The analysis used the SAS Enterprise Guide V.7.15 (SAS Institute Inc., Carv, NC, including for uses related USA) provided by the SNDS infrastructure.

#### Patient and public involvement

None.

#### RESULTS

The final analysis included 107 014 first stays of patients aged 80 years or older who were admitted to an ICU for medical reasons at 822 hospitals, mostly publicly funded (65%), in France between 2013 and 2018. Among those patients, 51 680 (48%) received invasive ventilation or vasopressors, and 55 334 (52%) received neither of the two. A flowchart of patients and stays in the study is shown in figure 1.

Ξ The demographic characteristics and the outcomes since ICU admission are shown in table 1. The mean age was 84.6 years. More than half (52%) were male in the ≥ invasive group, and 52% were female in the conservative group. Overall, 89% were admitted from home, with most of them having a stop at the emergency department ĝ (59%). Patients in the invasive group had a significantly higher severity of illness at admission as reflected by a higher SAPS II but fewer general coexisting conditions as reflected by a lower Charlson comorbidity index. Over the years, the flow of patients was increasingly directed towards the invasive group. Among 51 680 (48%) patients technolog in the invasive group, 70% were dead at 1 year, while among 55 334 (52%) patients in the conservative group, 41% were dead at 1 year ( $\chi^2$  test, p<0.001).

Outcomes of patients in the invasive group since ICU admission are detailed in table 2. Among 38 427 patients who underwent vasopressors, 72% were dead at 1 year. Among 40 495 patients who received invasive ventilation, 72% were dead at 1 year. Patients who received a first invasive procedure were likely to receive the other one in 53% of cases, and 1 year mortality was then 77%, whereas it was 60% and 63%, respectively, for vasopressors only or ventilation only. Among 8761 patients who underwent RRT (regardless of the group), 74% were dead at 1 year. The

đ

ē

and

data



Figure 1 Flowchart of patients and stays in the study. DRG errors correspond to stays that could not be assigned to a DRG, mainly due to coding inconsistencies or inaccuracies in the classification of hospital stays, such as misclassification of diagnoses, procedures or administrative coding discrepancies. DRG, diagnosis-related group; ICU, intensive care unit.

median number of days in the ICU was 4 (IOR 2-8). The median number of days in the hospital was 8 (IQR 2-16). The median duration of ventilation was 3 days (IOR 2–7). There were 2582 patients who underwent prone positioning. In their case, the median number of sessions was 2 (IQR 1-3) per patient. The median duration of vasopressor support was 2 days (IOR 1-4). The time of the initial invasive procedure was the day of ICU admission for 79% of patients in the invasive group and the following day for an additional 9% (online supplemental figure S1, appendix 1). More than half of the patients in the invasive group had both procedures, generally on the same day (86%). If vasopressors predated ventilation (6%) or ventilation predated vasopressors (9%), the median interval of initiation was 1 day (IQR 1-3). 24% of deaths in the invasive group occurred on the day of the initiation of any procedure, and 7% the following day.

After the calculation of the time-stratified PS, the balance obtained on ATT weighted samples was good, with absolute standardised differences less than 0.1 (online supplemental figure S2, appendix 1). The test of Schoenfeld residuals for the PHs assumption was significant, as the HR was decreasing over time (online supplemental figure S4, appendix 1). Kaplan–Meier survival curves obtained before and after the time-stratified ATT weighting are presented in figure 2. ATT weighting

induced a decrease in 1-year survival rate in the conservative group from 59% to 43% (95% CI 0.421 to 0.441) versus 27% in the invasive group (95% CI 0.268 to 0.276, remained unchanged after ATT weighting, as expected). The mortality in the invasive group remained significantly higher after time-dependent IPTW (HR 1.64; 95% CI 1.60 to 1.69; p<0.001). Life expectancy limited to 1 year was 117.5 days in the invasive group versus 185.2 days in the conservative group, resulting in a significant loss of 67.7 days (RMST, 95% CI 65.7 to 69.8).

In the sensitivity analysis, neither the use of ATT weights truncated at the 5th and 95th percentiles nor the use of a different time-stratification pattern changed substantially the HR associated with invasive procedures. Finally, the combination of weighting and further adjustment on baseline covariates (year, age, sex, coexisting conditions, admission source, severity and academic status) produced a similar HR (HR 1.67; 95% CI 1.63 to 1.73; p<0.001) (online supplemental appendix 1).

### DISCUSSION

Several studies support conservative management over invasive approaches,<sup>18 21 22</sup> and there is concern that invasive procedures may worsen the prognosis of older ICU patients.<sup>23 24</sup> Our large nationwide study was designed

Protected by copyright, including for uses related to text and

All Patients (n=107014)	Invasive group (n=51 680)	Conservative group (n=55 334)	P value
100	48	52	
84.6±3.6	84.3±3.4	84.9±3.7	<0.001
53 457 (50)	26 785 (52)	26 672 (48)	< 0.001
			<0.001
17 138 (16)	7756 (15)	9382 (17)	
17 484 (16)	8013 (16)	9471 (17)	
18 286 (17)	8612 (17)	9674 (18)	
18 312 (17)	9143 (18)	9169 (17)	
18 284 (17)	9236 (18)	9048 (16)	
17 510 (16)	8920 (17)	8590 (16)	
			< 0.001
31 703 (30)	15 079 (29)	16 624 (30)	
63 032 (59)	30 446 (59)	32 586 (59)	
12 279 (11)	6155 (12)	6124 (11)	
			<0.001
17 411 (16)	5226 (10)	12 185 (22)	
28 394 (27)	15 024 (29)	13 370 (24)	
61 209 (57)	31 430 (61)	29 779 (54)	
78 973 (74)	41 717 (81)	37 256 (67)	< 0.001
61 089 (57)	33 089 (64)	28 000 (51)	<0.001
			< 0.001
39 659 (37)	18 384 (36)	21 275 (39)	
31 807 (30)	14 046 (27)	17 761 (32)	
28 344 (27)	12 937 (25)	15 407 (28)	
12 062 (11)	6305 (12)	5757 (10)	
10 651 (10)	4996 (10)	5655 (10)	
3622 (3)	1936 (4)	1686 (3)	
16 191 (15)	7723 (15)	8468 (15)	
19 162 (18)	9083 (18)	10 079 (18)	
			< 0.001
2 (1–4)	2 (1–4)	2 (1–4)	
23 972 (22%)	12 698 (25%)	11 274 (20%)	
20 753 (19)	9884 (19)	10 869 (20)	<0.001
45 (34–63)	59 (45–76)	37 (30–46)	<0.001
			<0.001
40 189 (38)	20 773 (40)	19 416 (35)	
29 926 (28)	13 682 (27)	16 244 (29)	
36 899 (35)	17 225 (33)	19 674 (36)	
			<0.001
58 955 (55)	36 019 (70)	22 936 (41)	
32 160 (30)	26 152 (51)	6008 (11)	
37 354 (35)	28 438 (55)	8916 (16)	
			<0.001
4 (2–8)	5 (2–11)	3 (1–6)	
	All Patients (n=107014)   100   84.6±3.6   53 457 (50)   17 138 (16)   17 138 (16)   17 484 (16)   18 286 (17)   18 286 (17)   18 284 (17)   18 284 (17)   17 510 (16)   20   31 703 (30)   63 032 (59)   12 279 (11)   28 394 (27)   61 209 (57)   78 973 (74)   61 089 (57)   31 807 (30)   28 344 (27)   12 062 (11)   10 651 (10)   3622 (3)   16 191 (15)   19 162 (18)   20 753 (19)   45 (34–63)   20 753 (19)   45 (34–63)   20 753 (19)   45 (34–63)   20 753 (19)   45 (34–63)   20 753 (19)   45 (34–63)   21 60 (30)   36 899 (35)   36 895 (55)   32 160 (30)   37 354 (35)	All Patients (n=107014)   Invasive group (n=51 680)     100   48     84.6±3.6   84.3±3.4     53 457 (50)   26 785 (52)     17   138 (16)   7756 (15)     17 484 (16)   8013 (16)     18 286 (17)   8612 (17)     18 312 (17)   9143 (18)     18 286 (17)   826 (18)     17 510 (16)   8920 (17)     17 510 (16)   8920 (17)     17 133 (30)   15 079 (29)     63 032 (59)   30 446 (59)     12 279 (11)   6155 (12)     17 411 (16)   5226 (10)     28 394 (27)   15 024 (29)     61 209 (57)   31 430 (61)     78 973 (74)   41 717 (81)     61 089 (57)   30 3089 (64)     18 07 (30)   14 046 (27)     28 344 (27)   12 937 (25)     12 062 (11)   6305 (12)     10 651 (10)   4996 (10)     3622 (3)   1936 (4)     11 6191 (15)   7723 (15)     19 162 (18)   9083 (18)     20 773 (40)   24 (	All Patients (n=107 014)   Invasive group (n=55 334)   Conservative group (n=55 334)     100   48   52     84.6±3.6   84.3±3.4   84.9±3.7     53 457 (50)   26 785 (52)   26 672 (48)     17   138 (16)   7756 (15)   9382 (17)     17 484 (16)   8013 (16)   9471 (17)     18 286 (17)   8612 (17)   9674 (18)     18 312 (17)   9143 (18)   9169 (17)     18 284 (17)   9236 (18)   9048 (16)     17 510 (16)   8920 (17)   8590 (16)

BMJ Open: first published as 10.1136/bmjopen-2024-089835 on 22 May 2025. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

Continued

#### Table 1 Continued

	All Patients (n=107014)	Invasive group (n=51 680)	Conservative group (n=55 334)	P value
In hospital	8 (2–16)	7 (1–18)	8 (3–14)	
ICU readmission within the year-no (%)				<0.001
In patients from enrolment	23 846 (22)	6894 (13)	16 952 (31)	
In ICU survivors	23 846 (32)	6894 (27)	16 952 (34)	
Hospital discharge for survivors-no (%)				<0.001
Home	35 312 (51)	9016 (39)	26 296 (57)	
Other skilled facility	34 348 (49)	14 226 (61)	20 122 (43)	

P values correspond to statistical tests assessing whether there is a significant difference between the two groups. Variation in comorbidity burden and underlying physiological robustness may have influenced the decision to initiate invasive care, contributing to baseline differences between aroups.

\*Plus-minus values are means ±SD. Percentages may not sum to 100 because of rounding.

+Crude unweighted outcomes since ICU admission, without regards fto the time-to-event analysis.

CCI, Charlson comorbidity index; ICU, intensive care unit; SAPS II, simplified acute physiology score II.

to describe the association between invasive care and mortality in real-world clinical practice. Our findings suggest that invasive procedures are a negative determinant, but as an observational study, it cannot be concluded as evidence of harm or non-inferiority between the two groups.

However, the high mortality rate in the invasive group is per se our main finding. With a 1-year survival rate of 27%, it seems reasonable that a large portion of elderly patients may not be best served by invasive care. This calls into question the upward trend of time-limited trials that could lead to ethical misunderstanding, especially as the survival curves separated early on with a rapid decrease in the invasive group. The high proportion of early deaths in the invasive group most likely reflects the natural progression of an irreversible disease rather than complications from the procedure. This interpretation is supported by the strong culture of safety and patient-family engagement in ICU care, which prioritises harm prevention and appropriate treatment escalation.<sup>25</sup>

The need for invasive care is not merely a treatment choice but also a marker of increased severity. Thus, the

Protected by copyright, includi poor prognosis associated with invasive care is expected and reflects underlying disease severity rather than the d direct impact of invasiveness itself. However, if invasiveness reflects increased severity, then a strict dichotomy gebetween invasive and non-invasive approaches may seem overly simplistic, given that the relationship between the degree of invasiveness and prognosis is likely more gradual. This is supported by the sigmoidal relationship between SAPS II and mortality,<sup>26</sup> resembling a doseresponse effect. Nevertheless, we deliberately adopted this classification to avoid borderline situations and to ar describe the two extremes of the therapeutic spectrum in intensive care.

Admittedly, the non-invasive group likely comprises two distinct populations: patients who are not severe enough to require invasive intervention and those who are too critically ill to benefit from it. However, when considered ⊳ as a whole, the non-invasive group remains fundamentally distinct from the invasive cohort, where a paradigm shift in care is always required. The two populations we studied differ not in the degree of care received but in the nature of care itself. This distinction is crucial, as similar technologies

Table 2   Outcomes in the invasive group (n=51 680)*									
		Mortality—no (%)			Median length of stay- days (IQR)				
	No (%)	ICU	Hospital	1 year	ICU	Hospital			
All vasopressors (± ventilations)	38 427 (74)	20 606 (54)	22 281 (58)	27 694 (72)	5 (2–12)	8 (3–18)			
All ventilations (± vasopressors)	40 495 (78)	22 632 (56)	24 217 (60)	29 331 (72)	5 (2–12)	7 (1–18)			
Vasopressors only	11 185 (22)	3520 (32)	4221 (38)	6688 (60)	5 (2–8)	9 (2–17)			
Ventilations only	13 253 (26)	5546 (42)	6157 (47)	8325 (63)	4 (2–9)	9 (3–18)			
Vasopressors and ventilations	27 242 (53)	17 086 (63)	18 060 (66)	21 006 (77)	6 (2–14)	7 (2–16)			

This table reports the subsets of patients according to the invasive procedures exposure.

\*Crude incidence and unweighted outcomes since ICU admission, without regards to the time-to-event analysis. Percentages may not sum to 100 because of rounding.

ICU, intensive care unit.

ē

ated to

data min

, and



**Figure 2** Probability of survival from ICU admission to 1 year, according to conservative or invasive approach, before and after time-dependent PS weighting (ATT). Kaplan–Meier method adapted to time-dependent covariate (with 95% Cl). Dashed lines represent the time-dependent Kaplan–Meier plot of the probability of survival from ICU admission to 1 year among the original unweighted population. Solid lines represent the time-dependent Kaplan–Meier plot of the probability of the probability of the probability of survival on IPTW-ATT weighted sample using weights trimmed at the 1st and 99th percentile. Invasive curve remained unchanged after weighting, as expected. HR denotes the HR obtained from the ATT99 weighted Cox model and diff-RMST the difference in (1 year) RMST (days). ATT, average treatment effect in the treated; ICU, intensive care unit; IPTW, inverse probability of treatment weighting; PS, propensity score; RMST, restricted mean survival time.

the decision between invasive and non-invasive management is never incidental<sup>27</sup>; it is always an active choice that carries significant implications for the patient, their family and the medical team. For this reason, we did not include different modalities of oxygenation, such as highflow nasal insufflation or NIV, in our analysis.

Furthermore, we aimed for the invasive group to reflect the maximal therapeutic investment—at least at the moment of procedure initiation. In this regard, NIV is a treatment that has been shown to improve survival and, as such, is not purely a palliative intervention. However, its role in alleviating respiratory discomfort is increasingly well documented. NIV has been found to be more effective than oxygen in reducing dyspnoea and decreasing the need for morphine in palliative care patients.<sup>28</sup> This modality is used both to enhance comfort at the end of life<sup>29</sup> and for patients who have declined tracheal intubation.<sup>30</sup> More broadly, it is now integrated into an approach that seeks to improve palliative care in the ICU.<sup>31</sup>

Finally, this distinction between invasive and noninvasive care also implies the notion of immediacy, which is why we excluded chronic conditions requiring invasive procedures. Both NIV and RRT are commonly used in chronic settings—NIV for chronic respiratory failure (eg, amyotrophic lateral sclerosis) and RRT for end-stage renal disease. The coding system does not allow for mining differentiation between acute and chronic indications. Including these cases would have introduced additional confounding factors, whereas our focus was on invasive procedures initiated for acute conditions. Nevertheless, our findings suggest that renal support worsens prognosis regardless of the treatment group, as among the 8761 patients who underwent RRT, 74% died within 1 year.

The strength of this study is the size of the cohort with few missing data and the national-level database needed to overcome sampling biases<sup>32</sup> that often limit epidemiological studies of the critically ill elderly. With 107014 patients under observation, we had the statistical power to robustly assess this issue in the target population of medical ICU patients adjusted for known prognostic factors specified a priori. The comprehensive multicentre design enhances the generalisability of our findings, particularly important given that older patients are frequently excluded from clinical trials<sup>33</sup> but are commonly treated in the ICU. Our study further provides valuable information on the epidemiology of circulatory and respiratory failures in older patients.

The main limitation of our study is the risk of confounding inherent to any observational study, which the PS cannot entirely eliminate. As a summary of measured covariates, the PS cannot account for unmeasured confounding.<sup>34</sup> In contrast to randomised controlled trials, where randomisation is expected to balance both measured and unmeasured covariates across treatment arms, observational studies remain subject to residual confounding.<sup>35</sup> Nonetheless, best practices for the use of PS methods with survival or time-to-event<sup>36</sup> outcomes using IPTW can help mitigate the effects of confounding in observational studies.<sup>37 38</sup>

Residual confounding may result from the lack of detailed clinical or contextual data involved in the decision to initiate an invasive procedure. These parameters not only influence the decision itself but also impact patient outcomes. The initiation of vasopressor therapy relies on critical information, such as arterial pressure, heart rate and urinary output, while the decision to proceed with invasive mechanical ventilation depends on the patient's level of consciousness, signs of respiratory failure and oxygen saturation. Comparing patients without this information is challenging. Nevertheless, although our methods do not directly incorporate these physiological parameters individually, they each contribute to the SAPS II score, which serves as the primary severity adjustment factor in our PS model. Notably, the density plots indicate that the SAPS II distribution is not only the strongest determinant of risk in our model but also closely aligned between invasive and conservative groups after weighting (online supplemental figure S3). In addition, the reason for admission integrates some clinical data.

We acknowledge that clinical parameters influencing invasive procedures are strong predictors of mortality, regardless of the level of invasiveness. Moreover, the need for invasive care serves as a marker of disease severity rather than a direct determinant of prognosis. In our study, the two populations inherently differ in acute severity, which is a key driver of treatment decisions. However, our aim was not to assess the appropriateness of invasive procedures but rather to describe patient outcomes based on treatment intensity, once a treatment pathway has been adopted in real-world practice.

The predominant contribution of SAPS II to our PS substantially mitigates the risk of confounding, although it cannot be broken down into its circulatory and ventilatory components, which would have allowed for a more refined adjustment. Nevertheless, SAPS II integrates various parameters that are associated with both prognosis and the decision to initiate an invasive procedure. This duality reflects the inherent overlap between prognosis and therapeutic decision-making in intensive care, where addressing clinical imbalance is expected to neutralise risk.

For instance, in haemodynamics, the 65 mm Hg mean arterial pressure threshold was originally established based on the retrospective cohort studies<sup>39 40</sup> that demonstrated a strong association between time spent below this threshold and mortality in patients with septic shock. However, vasopressors have since been shown to exert pleiotropic effects,<sup>41</sup> making their overall impact more difficult to predict, or even potentially leading to increased mortality in older patients.  $^{42}$ 

Thus, the traditional perspective in which invasive procedures were assumed to have an inherently positive—or at worst, neutral—impact by counteracting the excess risk associated with a high severity score has evolved. It is now recognised that their effect is far less predictable and, particularly in older patients, unlikely to be neutral.<sup>43</sup>

Our aim was to describe the trajectories of two distinct **T**CU populations rather than to compare treatment efficacy. Thanks to the inclusion of all treated patients nationwide over a 6-year period, any biases in our data are more likely to reflect the overall clinical practice rather than individual decisions regarding the appropriateness of invasive or conservative treatment. This is arguably the main advantage of real-world evidence over randomised trials in informing public health decision-making.<sup>44</sup>

Other limitations of our study include potential biases due to coding errors. Moreover, our study did not include the functional status nor the quality of life among survivors, which are more important than survival for many older persons.<sup>45–47</sup> The study also lacks consideration for pre-existing frailty, despite its recognised importance as a determinant of mortality.<sup>48–50</sup> However, while elderly patients with a higher functional baseline are more likely to survive, their chances of returning to their prior level are reduced compared with those with a lower functional baseline.<sup>51 52</sup> In addition, whoever with a good functional status is resuscitated until it becomes poor is doomed to die with a poor functional status.

The absence of consideration for triage process, treatment appropriateness or therapeutic limitations may introduce selection bias but reflects the real-world shared decision-making process among physicians, patients and families. Current studies suggest that the risk of overutilisation of invasive procedures outweighs the risk of underutilisation.<sup>22 24 53-55</sup>

The Principles of Biomedical Ethics by Beauchamp and Childress, developed in 1979, outlines the four principles of medical care: autonomy, non-maleficence, beneficence and justice. Individuals have a significant preference for non-maleficence over the other principles, but it does not appear to be directly used in the decision-making process.<sup>56</sup> Advance care planning is essential to support clinicians in targeting appropriate invasive, rehabilitative or palliative strategies, which are not exclusive. As stated in a recent review: all critically ill patients, by definition, have serious illness and, thus, have palliative care needs.<sup>57</sup> The retrospective meaning of 'end-of-life care' seems problematic unless considering the oldest patients are living the last part of their lives. Oldest patients, similar to paediatric patients, have distinct healthcare trajectories and goals supported by physiological evidence for geriatric specificities.

To clarify, our study does not suggest that elderly patients should be denied ICU admission. On the contrary, it highlights the potential benefits of an intensive integrative approach in the ICU rather than a purely technical approach that may only prolong the dying process.<sup>58</sup> The conservative group exhibits a low mortality rate, including patients who were refused invasive treatments due to futility, and it is unlikely to be further reduced with a more invasive approach. Similarly, the high mortality rate observed in the invasive group is unlikely to be exacerbated by a less aggressive strategy.

Our findings have strong ethical implications. Despite being highly selected for favourable outcomes in realworld practice, patients who received invasive procedures had a low survival rate. The incentive care policy for a standard of care regardless of age is questionable in the light of medical appropriateness<sup>22</sup> <sup>24</sup> 53-55 and patients' wishes.<sup>24–26</sup> While age should not be the sole criterion for ICU triage, the combination of age and the need for an invasive procedure must be considered attentively when deciding on treatment options. Growing evidence suggests a gap between patient preferences and the actual care provided<sup>59</sup> and that focusing resources on patient preferences is possible.<sup>60</sup> Age remains a potent trigger for clinicians to ensure that patients and families are well informed about the benefits, risks and harms associated with invasive care.<sup>61</sup>

### **CONCLUSIONS**

In conclusion, in our nationwide study, an invasive approach was associated with a lower 1-year survival rate among elderly patients who were admitted to the ICU for medical reasons compared with a conservative approach. Early discussion, including the requirement for an invasive procedure, may reduce the incidence of avoidable aggressive end-of-life care and improve goal-concordant care achievement.

#### X Matthieu de Stampa @matthieudestampa

**Contributors** This analysis is an investigator-initiated study led by CL, he supervised the analyses, drafted the manuscript and is the guarantor. All coauthors contributed to the study design and made substantial contribution. AG and CL conceptualised the study and prepared the original study protocol, which was subsequently reviewed by MdS and PA. CL, AG and PA developed the statistical methods. CL and PA had full access to the data and take responsibility for the integrity of the data and accuracy of the analysis. All authors contributed to data interpretation, critically revised the drafted manuscript and approved the final submitted version. The guarantor accepts full responsibility for the conduct of the study, had access to the data and controlled the decision to publish. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

**Funding** This study was supported by Assistance Publique–Hôpitaux de Paris through an agreement between the Caisse Nationale d'Assurance Maladie and HAD-APHP (signed on 19 October 2020) for the OCTO-Reverse project (962976). The funding sources had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; or decision to submit the manuscript for publication.

#### Competing interests None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

#### Patient consent for publication Not applicable.

Ethics approval The study was submitted to and approved by the independent national data protection authority (CNIL Registration: 920181). All data were

deidentified for research purposes, and French law waives the need for informed consent. An independent institutional review board approved the study protocol (IRB Registration: #00011928).

Provenance and peer review Not commissioned; externally peer reviewed.

**Data availability statement** Data may be obtained from a third party and are not publicly available. The data used in this study are derived from the French National Health Data System, which is managed by the French National Health Insurance Fund. Access to these data is subject to regulatory approval and can be requested through the official data access platform under authorisation number TPS 962976. Further details on data access procedures can be obtained by contacting snds. cnam@assurance-maladie.fr.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

#### **ORCID** iDs

Clement Leclaire http://orcid.org/0000-0001-9162-2574 Matthieu de Stampa http://orcid.org/0000-0001-7238-5913 Philippe Aegerter http://orcid.org/0000-0002-9156-5028

### REFERENCES

- Vallet H, Schwarz GL, Flaatten H, et al. Mortality of older patients admitted to an ICU: a systematic review. Crit Care Med 2021;49:324–34.
- 2 Baldwin MR. Measuring and predicting long-term outcomes in older survivors of critical illness. *Minerva Anestesiol* 2015;81:650–61.
- 3 Boumendil A, Latouche A, Guidet B, *et al.* On the benefit of intensive care for very old patients. *Arch Intern Med* 2011;171:1116–7.
- 4 Biddison LD, Berkowitz KA, Courtney B, et al. Ethical considerations: care of the critically ill and injured during pandemics and disasters: CHEST consensus statement. Chest 2014;146:e145S–55S.
- 5 Soliman IW, Cremer OL, de Lange DW, et al. The ability of intensive care unit physicians to estimate long-term prognosis in survivors of critical illness. J Crit Care 2018;43:148–55.
- 6 Vink EE, Azoulay E, Caplan A, et al. Time-limited trial of intensive care treatment: an overview of current literature. *Intensive Care Med* 2018;44:1369–77.
- 7 Guidet B, Vallet H, Boddaert J, et al. Caring for the critically ill patients over 80: a narrative review. Ann Intensive Care 2018;8:114.
- 8 Ferrante LE, Pisani MA, Murphy TE, *et al.* Functional trajectories among older persons before and after critical illness. *JAMA Intern Med* 2015;175:523–9.
- 9 Flaatten H, de Lange DW, Artigas A, *et al.* The status of intensive care medicine research and a future agenda for very old patients in the ICU. *Intensive Care Med* 2017;43:1319–28.
- 10 Seethala RR, Blackney K, Hou P, et al. The association of age with short-term and long-term mortality in adults admitted to the intensive care unit. J Intensive Care Med 2017;32:554–8.
- 11 Nathanson BH, Higgins TL, Brennan MJ, et al. Do elderly patients fare well in the ICU? Chest 2011;139:825–31.
- 12 Wunsch H, Guerra C, Barnato AE, et al. Three-year outcomes for Medicare beneficiaries who survive intensive care. JAMA 2010;303:849–56.
- 13 Jubran A, Grant BJB, Duffner LA, et al. Long-term outcome after prolonged mechanical ventilation. A long-term acute-care hospital study. Am J Respir Crit Care Med 2019;199:1508–16.
- 14 Biston P, Aldecoa C, Devriendt J, *et al.* Outcome of elderly patients with circulatory failure. *Intensive Care Med* 2014;40:50–6.
- 15 Fassier T, Duclos A, Abbas-Chorfa F, *et al.* Elderly patients hospitalized in the ICU in France: a population-based study using

## **Open access**

secondary data from the national hospital discharge database. *J Eval Clin Pract* 2016;22:378–86.

- 16 Atramont A, Lindecker-Cournil V, Rudant J, et al. Association of age with short-term and long-term mortality among patients discharged from intensive care units in France. JAMA Netw Open 2019;2:e193215.
- 17 Laporte L, Hermetet C, Jouan Y, et al. Ten-year trends in intensive care admissions for respiratory infections in the elderly. Ann Intensive Care 2018;8:84.
- 18 Gaudry S, Hajage D, Schortgen F, et al. Initiation strategies for renal-replacement therapy in the intensive care unit. N Engl J Med 2016;375:122–33.
- 19 Hernán MA, Brumback BA, Robins JM. Estimating the causal effect of zidovudine on CD4 count with a marginal structural model for repeated measures. *Stat Med* 2002;21:1689–709.
- 20 Austin PC, Thomas N, Rubin DB. Covariate-adjusted survival analyses in propensity-score matched samples: Imputing potential time-to-event outcomes. *Stat Methods Med Res* 2020;29:728–51.
- 21 Auriemma CL, Van den Berghe G, Halpern SD. Less is more in critical care is supported by evidence-based medicine. *Intensive Care Med* 2019;45:1806–9.
- 22 Chang DW, Shapiro MF. Association between intensive care unit utilization during hospitalization and costs, use of invasive procedures, and mortality. *JAMA Intern Med* 2016;176:1492–9.
- 23 Guidet B, Leblanc G, Simon T, et al. Effect of systematic intensive care unit triage on long-term mortality among critically III elderly patients in France: a randomized clinical trial. JAMA 2017;318:1450–9.
- 24 Sjoding MW, Prescott HC, Wunsch H, *et al.* Hospitals with the highest intensive care utilization provide lower quality pneumonia care to the elderly. *Crit Care Med* 2015;43:1178–86.
- 25 Thornton KC, Schwarz JJ, Gross AK, *et al.* Preventing harm in the ICU-building a culture of safety and engaging patients and families. *Crit Care Med* 2017;45:1531–7.
- 26 Aegerter P, Boumendil A, Retbi A, et al. SAPS II revisited. Intensive Care Med 2005;31:416–23.
- 27 Burns KEA, Cook DJ, Xu K, *et al*. Differences in directives to limit treatment and discontinue mechanical ventilation between elderly and very elderly patients: a substudy of a multinational observational study. *Intensive Care Med* 2023;49:1181–90.
- 28 Nava S, Ferrer M, Esquinas A, et al. Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. *Lancet Oncol* 2013;14:219–27.
- 29 Azoulay E, Kouatchet A, Jaber S, et al. Non-invasive ventilation for end-of-life oncology patients. Lancet Oncol 2013;14:e200–1.
- 30 Azoulay E, Kouatchet A, Jaber S, et al. Noninvasive mechanical ventilation in patients having declined tracheal intubation. Intensive Care Med 2013;39:292–301.
- 31 Puntillo K, Nelson JE, Weissman D, et al. Palliative care in the ICU: relief of pain, dyspnea, and thirst--a report from the IPAL-ICU Advisory Board. Intensive Care Med 2014;40:235–48.
- 32 Hua M, Gershengorn HB, Wunsch H. Assessing delivery of mechanical ventilation: risks and benefits of large databases. *Intensive Care Med* 2020;46:2297–300.
- 33 Ivie RMJ, Vail EA, Wunsch H, et al. Patient eligibility for randomized controlled trials in critical care medicine: an international two-center observational study. *Crit Care Med* 2017;45:216:216–24:.
- 34 Yang JY, Webster-Clark M, Lund JL, et al. Propensity score methods to control for confounding in observational cohort studies: a statistical primer and application to endoscopy research. *Gastrointest Endosc* 2019;90:360–9.
- 35 Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med* 2009;28:3083–107.
- 36 Austin PC. The use of propensity score methods with survival or time-to-event outcomes: reporting measures of effect similar to those used in randomized experiments. *Stat Med* 2014;33:1242–58.
- 37 Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res* 2011;46:399–424.
- 38 Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using

the propensity score to estimate causal treatment effects in observational studies. *Stat Med* 2015;34:3661–79.

- 39 Dünser MW, Takala J, Ulmer H, et al. Arterial blood pressure during early sepsis and outcome. *Intensive Care Med* 2009;35:1225–33.
- 40 Maheshwari K, Nathanson BH, Munson SH, et al. The relationship between ICU hypotension and in-hospital mortality and morbidity in septic patients. Intensive Care Med 2018;44:857–67.
- 41 Andreis DT, Singer M. Catecholamines for inflammatory shock: a Jekyll-and-Hyde conundrum. *Intensive Care Med* 2016;42:1387–97.
- 42 Futier E, Lefrant J-Y, Guinot P-G, et al. Effect of individualized vs standard blood pressure management strategies on postoperative organ dysfunction among high-risk patients undergoing major surgery: a randomized clinical trial. JAMA 2017;318:1346–57.
- 43 Lamontagne F, Richards-Belle A, Thomas K, et al. Effect of reduced exposure to vasopressors on 90-day mortality in older critically III patients with vasodilatory hypotension: a randomized clinical trial. JAMA 2020;323:938–49.
- 44 Sheldrick RC. Randomized trials vs real-world evidence: how can both inform decision-making? *JAMA* 2023;329:1352–3.
- 45 Philippart F, Vesin A, Bruel Č, et al. The ETHICA study (part I): elderly's thoughts about intensive care unit admission for lifesustaining treatments. *Intensive Care Med* 2013;39:1565–73.
- 46 Behforouz HL, Drain PK, Rhatigan JJ. Rethinking the social history. *Engl J Med* 2014;371:1277–9.
- 47 Le Guen J, Boumendil A, Guidet B, *et al*. Are elderly patients' opinions sought before admission to an intensive care unit? Results of the ICE-CUB study. *Age Ageing* 2016;45:303–9.
- 48 Flaatten H, De Lange DW, Morandi A, et al. The impact of frailty on ICU and 30-day mortality and the level of care in very elderly patients (≥ 80 years). Intensive Care Med 2017;43:1820–8.
- 49 Guidet B, de Lange DW, Boumendil A, et al. The contribution of frailty, cognition, activity of daily life and comorbidities on outcome in acutely admitted patients over 80 years in European ICUs: the VIP2 study. Intensive Care Med 2020;46:57–69.
- 50 Muscedere J, Waters B, Varambally A, *et al*. The impact of frailty on intensive care unit outcomes: a systematic review and meta-analysis. *Intensive Care Med* 2017;43:1105–22.
- 51 Heyland DK, Garland A, Bagshaw SM, et al. Recovery after critical illness in patients aged 80 years or older: a multi-center prospective observational cohort study. *Intensive Care Med* 2015;41:1911–20.
- 52 Griffiths J, Hatch RA, Bishop J, et al. An exploration of social and economic outcome and associated health-related quality of life after critical illness in general intensive care unit survivors: a 12-month follow-up study. *Crit Care* 2013;17:R100.
- 53 Teno JM, Gozalo P, Khandelwal N, et al. Association of increasing use of mechanical ventilation among nursing home residents with advanced dementia and intensive care unit beds. JAMA Intern Med 2016;176:1809–16.
- 54 Sullivan DR, Kim H, Gozalo PL, *et al*. Trends in noninvasive and invasive mechanical ventilation among medicare beneficiaries at the end of life. *JAMA Intern Med* 2021;181:93–102.
- 55 Guidet B, Flaatten H, Boumendil A, *et al.* Withholding or withdrawing of life-sustaining therapy in older adults (≥80 years) admitted to the intensive care unit. *Intensive Care Med* 2018;44:1027–38.
- 56 Page K. The four principles: can they be measured and do they predict ethical decision making? *BMC Med Ethics* 2012;13:10.
- 57 Aslakson RA, Cox CE, Baggs JG, et al. Palliative and end-of-life care: prioritizing compassion within the ICU and beyond. Crit Care Med 2021;49:1626–37.
- 58 Cox CE, Curtis JR. Using technology to create a more humanistic approach to integrating palliative care into the intensive care unit. *Am J Respir Crit Care Med* 2016;193:242–50.
- 59 Heyland DK, Dodek P, Mehta S, et al. Admission of the very elderly to the intensive care unit: family members' perspectives on clinical decision-making from a multicenter cohort study. *Palliat Med* 2015;29:324–35.
- 60 Deniau N, Shojaei T, Georges A, *et al.* Home emergency response team for the seriously ill palliative care patient: feasibility and effectiveness. *BMJ Support Palliat Care* 2024;14:187–90.
- 61 Leblanc G, Boumendil A, Guidet B. Ten things to know about critically ill elderly patients. *Intensive Care Med* 2017;43:217–9.