A three-step support strategy for relatives of patients dying in the intensive care unit: a cluster randomised trial

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Summary

Background In relatives of patients dying in intensive care units (ICUs), inadequate team support can increase the prevalence of prolonged grief and other psychological harm. We aimed to evaluate whether a proactive communication and support intervention would improve relatives' outcomes.

Methods We undertook a prospective, multicentre, cluster randomised controlled trial in 34 ICUs in France, to compare standard care with a physician-driven, nurse-aided, three-step support strategy for families throughout the dying process, following a decision to withdraw or withhold life support. Inclusion criteria were relatives of patients older than 18 years with an ICU length of stay 2 days or longer. Participating ICUs were randomly assigned (1:1 ratio) into an intervention cluster and a control cluster. The randomisation scheme was generated centrally by a statistician not otherwise involved in the study, using permutation blocks of non-released size. In the intervention group, three meetings were held with relatives: a family conference to prepare the relatives for the imminent death, an ICU-room visit to provide active support, and a meeting after the patient's death to offer condolences and closure. ICUs randomly assigned to the control group applied their best standard of care in terms of support and communication with relatives of dying patients. The primary endpoint was the proportion of relatives with prolonged grief (measured with PG-13, score ≥30) 6 months after the death. Analysis was by intention to treat, with the bereaved relatives as the unit of observation. The study is registered with ClinicalTrials.gov, NCT02955992.

Findings Between Feb 23, 2017, and Oct 8, 2019, we enrolled 484 relatives of ICU patients to the intervention group and 391 to the control group. 379 (78%) relatives in the intervention group and 309 (79%) in the control group completed the 6-month interview to measure the primary endpoint. The intervention significantly reduced the number of relatives with prolonged grief symptoms (66 [21%] *vs* 57 [15%]; p=0·035) and the median PG-13 score was significantly lower in the intervention group than in the control group (19 [IQR 14–26] *vs* 21 [15–29], mean difference 2·5, 95% CI 1·04–3·95).

Interpretation Among relatives of patients dying in the ICU, a physician-driven, nurse-aided, three-step support strategy significantly reduced prolonged grief symptoms.

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Introduction

Many families who have a loved one admitted to the intensive care unit (ICU) subsequently experience post-ICU syndrome characterised by symptoms of anxiety, depression, and post-traumatic stress disorder (PTSD).[1–3] Sadly, up to 25% of these relatives lose their loved one in the ICU, placing them at high risk of also developing prolonged grief[4] characterised by persistence of intense grief that is distressing and disabling. Prolonged grief, as well as PTSD, not only significantly affect general health, mental health, and quality of life but are also associated with increased consumption of health-care resources.

Many studies have shown that communication with ICU clinicians is one of the most highly valued aspects of care[5,6] and has a major effect on relatives' experience throughout the patient's stay, including during the end of life (EOL), as well as after the patient's death. Communication difficulties with ICU clinicians at the EOL are well documented.[7] Missed opportunities are common: the family's emotions are not always addressed, non-abandonment not consistently affirmed (providing continuity and facilitating closure), and palliative care not always discussed.[8] Unsatisfactory communication with inadequate quality of information, empathy, support, and attention to the words used and non-verbal cues is associated with an increased risk of post-ICU burden.[9] Communication could be one of the most important aspects of EOL care that needs improvement in ICUs. Guidelines have been developed[10] and randomised controlled trials done with the primary goal of reducing post-ICU burden in relatives of patients at

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Research in context

Evidence before this study

We searched PubMed from Jan 1, 2000, to Jan 1, 2017, using the terms "end-of-life ICU", "family communication ICU", "palliative care ICU", "dying and death ICU", and "bereavement ICU". Studies were included if they evaluated communication and support strategies to improve family experience during and after the patient's stay in the intensive care unit (ICU).

In the months that follow the patient's death in the ICU, bereaved family members are at high risk of presenting symptoms that negatively affect their mental health, such as anxiety, depression, post-traumatic stress disorder (PTSD) symptoms, and complicated grief. Quality of communication is a central component of families' experience, and bereaved relatives reporting poor communication are at increased risk of developing complicated grief and PTSD-related symptoms. Research also highlights the importance of non-verbal communication: relatives who experienced the physician's attitude as non-comforting are at higher risk of developing post-ICU burden. However, only very few randomised controlled trials have tested interventions to improve communication and family experience. In one, providing relatives of patients who are dying in the ICU with end-of-life family conferences that include longer meetings and more time for family members to talk, as well as a bereavement leaflet, was significantly associated with decreased symptoms of anxiety, depression, and PTSD. In another, the intervention of communication facilitators was associated with decreased family depressive symptoms at 6 months, but with no significant difference in symptoms of anxiety or PTSD. In a third, family informational and emotional support meetings led by palliative care clinicians (from outside the ICU) did not improve the family experience.

Added value of this study

This randomised controlled trial provided family members with a direct ICU physician-driven intervention throughout the dying and death period, the most crucial time for family members, targeting three critical moments of the dying process on the basis of evidence provided by previous research. The nurse was actively involved at all three steps. Prolonged grief that includes difficulty accepting the loss, intense yearning, bitterness, emotional numbness, inability to trust others, and the feeling of being trapped in grief has been used for the first time as the primary outcome, and shows to be responsive to change of communication and support practices. Last, this is one of the largest randomised controlled trials on the subject (875 bereaved relatives) with a high response rate during telephone follow-up calls.

Implications of all the available evidence

The findings from our randomised controlled trial show that, compared with standard care, a proactive intervention including a three-step, physician-driven, nurse-aided strategy of support to relatives of patients dying in the ICU significantly decreases the prevalence of prolonged grief 6 months after the patients' death, as well as prevalence of PTSD-related symptoms and symptoms of anxiety. Our study shows that support provided by the same professionals who are in charge of daily patient care is effective and that training in communication, including non-verbal cues and means of expressing empathy, can be effective. The intervention is simple to replicate, adaptable to every country and language, and low cost. Our trial supports the feasibility of training bedside ICU physicians and nurses to deliver the three steps of the strategy as a routine practice, thereby protecting many bereaved relatives from prolonged grief and other components of post-ICU syndrome.

high risk of dying. Proactive interventions such as an EOL family conference coupled with a bereavement leaflet[11] or nurse-led interventions to facilitate communication between the ICU team and the relatives[12,13] have established that behavioural interventions are feasible and can improve relatives' outcomes. Despite these efforts, however, further improvement is urgently needed.

We developed a proactive intervention involving repeated meetings with relatives of patients dying after a decision to withdraw or withhold life-sustaining therapies. We hypothesised that, compared with standard care, the developed proactive intervention based on research into communication and support would decrease the post-ICU burden and, more specifically, the presence of prolonged grief disorder 6 months after the death.

Methods

Study design and participants

The COSMIC-EOL cluster randomised trial compared standard EOL care with a proactive intervention including a three-step, physician-driven, nurse-aided support strategy for relatives of patients with treatment withholding or withdrawal decisions. The protocol and statistical analysis plan have been published.[14]

Full details of the trial centres are in the appendix p 2. 36 French ICUs were invited to participate and all accepted. For each patient who had a treatment withdrawal or withholding decision, the relative who was the most involved with the ICU team was enrolled. Inclusion criteria were relatives of patients older than 18 years, with an ICU length of stay 2 days or longer, and who provided informed consent. We excluded relatives who did not speak enough French for a telephone interview, who did not provide informed consent, or whose loved one was an organ donor because these relatives receive specific support from trained coordination teams.

The study was registered on ClinicalTrial.gov on Nov 4, 2016, and the first relative was enrolled on Feb 23, 2017. A central institutional review board approved

the study (March 27, 2016). We obtained written informed consent from all enrolled relatives before study inclusion. This study was entirely conducted before the COVID-19 pandemic and was thus unaffected by restricted family visitation policies.

Randomisation and masking

The participating ICUs were randomly assigned into an intervention cluster and a control cluster. A randomisation scheme in a 1:1 ratio was generated centrally by a statistician not otherwise involved in the study, using permutation blocks of non-released size. Randomisation was stratified on the recruitment period (three consecutive recruitment periods) and on whether the centre had previously participated in a study from our research group. No centre was masked to cluster assignment.

Intervention and control

The intervention involved three meetings of the physician and nurse in charge of the patient with the relative, with the goal of allowing the relative to express emotions, ask questions, check understanding of the medical information, and be assured that care to the patient would continue until the death. Attentive listening, sensitivity to non-verbal communication, and empathy were the mainstays of these meetings that necessitate awareness and training (appendix p 3). The first meeting was the EOL conference during which the relatives were told about the appropriateness of treatment withholding or withdrawal, encouraged to express their emotions, invited to provide care to the patient, asked whether they wanted to be present at the time of death and whether they had specific requests about spiritual support, and encouraged to say goodbye to their loved one. Then, during the dying process, the physician and nurse in charge of the patient entered the patient's room separately at least once to show non-abandonment, to check on the relatives, and to discuss, as appropriate, the family's spiritual beliefs, the principles of palliative care, the expected time of death, any symptoms that might occur during dying (such as gasping), how the relatives felt, and the need for the relatives to also take care of themselves. Finally, after the patient's death the physician and nurse met the relatives in a dedicated room to express their condolences, elicit and answer questions about the patient's ICU stay and death, provide an opportunity for relatives to express their feelings, acknowledge emotions, indicate the team's availability for a subsequent visit, and invite relatives to seek medical help should they experience difficulties with the grieving process. These meetings could take place within the hours following the patient's death or when the relatives returned to the hospital the next day for administrative formalities. If the relatives were unavailable for such a meeting, the physician was asked to call the relative for a phone meeting during which they were asked to address the same issues. In such an intervention, based on communication and interaction, some items were not always possible to complete depending on each specific situation.

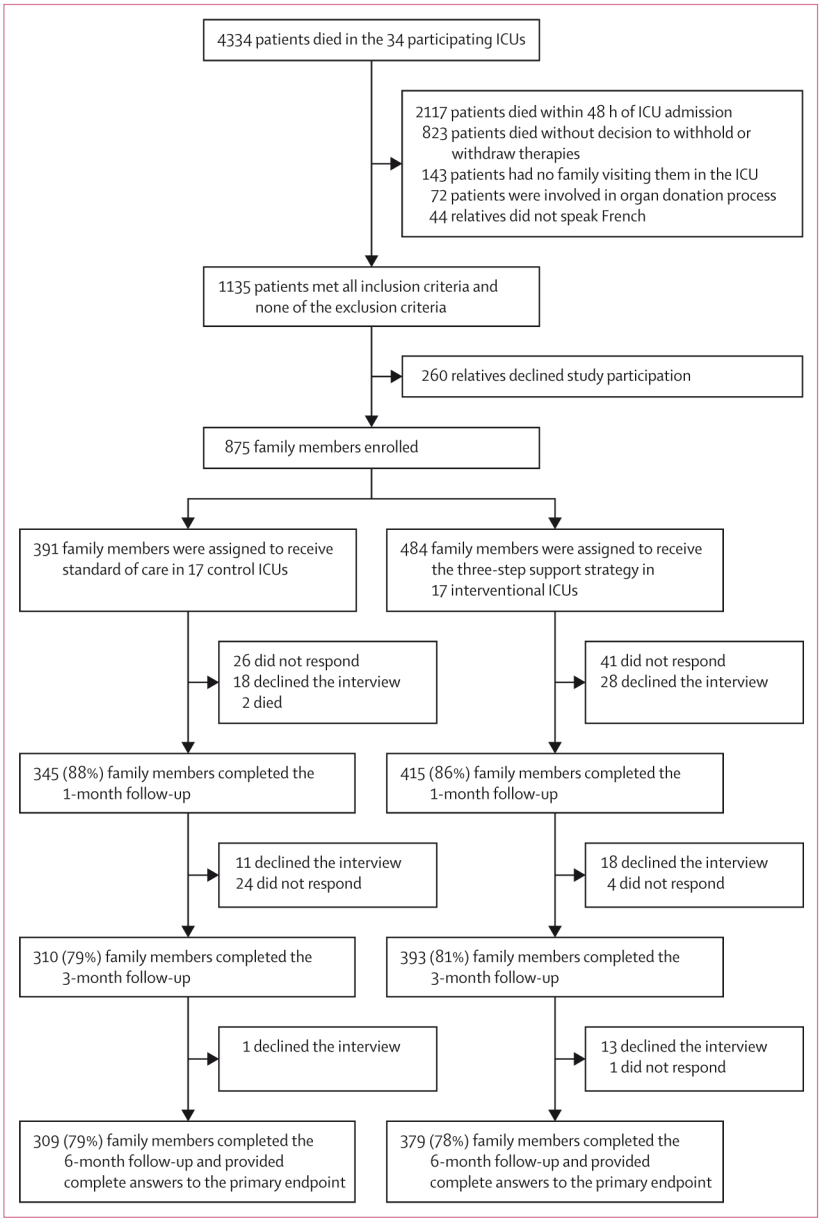

Figure 1: **Patient flow diagram**
ICU=intensive care unit.

In ICUs randomly assigned to the intervention, before the study, the clinicians attended interactive educational meetings led by the lead investigator (NK-B) and focused on EOL communication. All members of the team were required to participate in training sessions. The three-step communication strategy was presented using a video, which was followed by a discussion. A pamphlet summarising the key points of verbal and non-verbal

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	Control group (17 centres, n=391)	Intervention group (17 centres, n=484)
Patients' characteristics		
Gender		
Male	255 (65%)	336 (69%)
Female	136 (35%)	148 (31%)
Age (years)	70·98 (61·76–78·15)	69·7 (61·07–76·7)
Length of ICU stay (days)	7 (3–16)	8 (4–17)
Patient type		
Medical	315 (81%)	405 (84%)
Elective surgery	18 (5%)	16 (3%)
Emergent surgery	58 (15%)	63 (13%)
Impaired performance status*	157 (40%)	190 (39%)
Cancer or haematological malignancy	133 (34%)	170 (35%)
Psychiatric illness	21 (5%)	13 (3%)
Dementia	8 (2%)	10 (2%)
End-of-life characteristics		
Decision to		
Withhold treatment	95 (24%)	81 (17%)
Withdraw treatment	296 (76%)	403 (83%)
Patient sedated at time of death	332 (85%)	380 (79%)
Family present at patient's death	215 (58%)	299 (69%)
Intervention of a chaplain	35 (9%)	120 (25%)
End-of-life family conference	262 (67%)	452 (93%)†
Physician entered the patient's room during the end of life	260 (66%)	448 (93%)‡
Nurse entered the patient's room during the end of life	288 (74%)	446 (92%)‡
Physician and nurse met the relative after the patient's death	114 (29%)	410 (85%)§

(Table 1 continues in next column)

(Continued from previous column)

	Control group (17 centres, n=391)	Intervention group (17 centres, n=484)
Relatives' characteristics		
n	352	433
Gender		
Female	233 (66%)	301 (70%)
Male	119 (34%)	132 (30%)
Age (years)	55·5 (46·25–65)	53 (44–63)
Relationship with the patient		
Spouse or partner	129 (37%)	157 (36%)
Parent	11 (3%)	12 (3%)
Child	149 (42%)	197 (45%)
Sibling	39 (11%)	37 (9%)
Other	24 (7%)	30 (7%)
Educational attainment		
None or <high school	139 (39%)	145 (33%)
High school graduation	73 (21%)	90 (21%)
Bachelor's degree or over	140 (40%)	198 (46%)
Professional activity		
Primary sector (agricultural and allied sector services)	5 (1%)	6 (1%)
Secondary sector (manufacturing sector)	18 (5%)	23 (5%)
Tertiary sector (service sector)	194 (55%)	236 (55%)
Retired	101 (29%)	114 (26%)
Not professionally active	34 (10%)	54 (12%)
Family rating of social support (0=very poor to 7=very strong)	6 (5–7)	6 (5–7)

ICU=intensive care unit. *Previous health status (Knaus): severe activity limitation due to chronic illness plus bedridden patient. †Part of intervention, step 1. ‡Part of intervention, step 2. §Part of intervention, step 3.

Table 1: **Characteristics of the relatives, patients, and end of life measured during the study period**

communication and giving a link to the video was handed out. A local investigator was designated by each team to provide motivation and assistance in implementing the strategy. Clinicians who were unable to participate in training sessions were asked to watch the video and discuss the intervention with the local investigator. A 1-month implementation phase then occurred to allow for clinicians to practise and get familiar with the three-step strategy and for the discussion of any difficulties with the lead investigator (NK-B).

ICUs randomly assigned to the control group applied their best standard of care in terms of support and communication with relatives of dying patients. EOL family conferences that showed benefits in a previous trial of our group[11] are most often part of the standard of care. Nonetheless the first step of our intervention required that clinicians go further by developing active listening and non-verbal communication, as well as systematically discussing issues that are only sometimes broached in standard of care. Furthermore, in standard practice, nurses are not systematically involved in EOL conferences and chaplains are rarely called upon. The two other components of the intervention are not routinely implemented in ICUs. The EOL care received by the relatives of each patient who died during the study period was recorded to determine whether any components of the intervention were used.

Endpoints

The primary endpoint was the proportion of relatives with prolonged grief (score on the prolonged grief-13 questionnaire [PG-13][15] ≥30) 6 months after the death. The secondary endpoints were the relatives' experience, quality of death and dying, and satisfaction with EOL communication evaluated after 1 month; symptoms of anxiety and depression after 1, 3, and 6 months; and PTSD symptoms after 3 and 6 months.

Data collection

Standardised forms were completed after each of the three meetings to collect data describing the meeting (appendix p 6).

In both groups relatives who agreed to participate were contacted by telephone 1, 3, and 6 months after the patient's death. All telephone interviews were done by trained psychologists from our research group who were masked to group assignment.

The PG-13 was administered during the 6-month telephone interview. Scores of 30 or more indicate prolonged grief disorder.

The CAESAR scale[16] was used to assess the relatives' experience. Scores of 59 or less indicate a difficult experience, 60–68 range a fair experience, and 69 or higher a good experience. The quality of death and dying-1 (QODD-1) scale was also administered at 1 month.[17] The hospital anxiety and depression scale was administered at all three timepoints: subscores greater than 7 were taken to indicate symptoms of anxiety or depression, as relevant. Symptoms of PTSD were evaluated using the impact of event scale–revised (IES-R) at 3 and 6 months,[18] with scores of 12–32 taken to indicate a moderate risk and scores of 33 or more a high risk of PTSD. To assess satisfaction with communication with the ICU physician and nurse, the rapport subscale of the medical interview satisfaction scale (MISS-21) was completed 1 month after the death.[19]

Other exploratory tools were also used, including a questionnaire for the relatives describing lifestyle disruptions (at 6 months); a strategy checklist for the intervention centres to assess adherence to the intervention; and, in each centre, a questionnaire describing the ICU characteristics.

Statistical analysis

Summary statistics (median with IQR, or percentages) are reported unless otherwise specified. We hypothesised that the proactive intervention including a three-step, physician-driven, nurse-aided support strategy would, 6 months after the patient's death, decrease the proportion of relatives with prolonged grief symptoms from 50% to 35% on the basis of a previous study that measured prolonged grief in relatives experiencing EOL care as optimal as compared with overall relatives.[16] With the type I error set at 0·05, 454 relatives (227 in each group) were needed to obtain power of 90% to detect such a decrease. Moreover, between-cluster variation was accounted for, using an inflation factor or design effect of $1+\rho n1$, where n=25 is the expected average cluster size and $\rho=0\cdot023$ is the intracluster correlation coefficient, assuming clusters of similar size. The resulting sample size was 704. To further allow for a 25% attrition rate at 6 months,[2,4,11] we planned to enrol 874 relatives (437 in each group).

An intention-to-treat analysis was done, with the bereaved relatives as the unit of observation rather than the cluster, since the intervention occurred at the individual level. Point estimates of effect size, measured on mean differences with 95% CIs were reported for the primary and secondary outcomes. The primary and secondary outcomes were compared across randomised groups, taking into account the correlation induced by the study design through the use of generalised linear mixed-effects models. The intracluster correlation coefficient for the primary outcome provided an indication of the extent of clustering. Proportions of individual answers to the Likert scale of the main outcome in each randomised group were represented.

Post-hoc analyses were done to look at the relationships between receiving these components and the main outcome, using a quasi-Poisson regression model.

The scores were analysed on the basis of original data and, when available, according to established cutoffs. All tests were two-sided, with significance defined as a p value less than 0·05.

The study is registered with ClinicalTrials.gov, NCT02955992.

	Implementation	Both physician and nurse	Either physician or nurse
Step 1: Preparation for death (physician and nurse together)			
Prepare the relative for the patient's imminent death	100%	32%	68%
Give opportunities for relative to ask questions	100%	41%	59%
Give opportunities for relative to express feelings and emotions	83%	44%	56%
Encourage relative to talk to the patient and say goodbye	86%	38%	62%
Discuss being present at time of death	97%	43%	57%
Discuss possible involvement in the patient's physical care	65%	40%	60%
Discuss spiritual beliefs and needs	85%	34%	66%
Step 2: During the dying process and death, in the patient's room (physician and nurse separately)			
Meet relative's emotional needs	85% P, 84% N	..	..
Active listening	97% P, 99% N	..	..
Offer material support (eg, chair, glass of water)	86% P, 96% N	..	..
Discuss spiritual practices	66% P, 64% N	..	..
Discuss relative's implication in patient support and tenets of palliative care	63% P, 62% N	..	..
Clarify and answer any questions	95% P, 92% N	..	..
Highlight the relative's commitment	79% P, 76% N	..	..
Step 3: After the patient's death (physician and nurse together)			
Express condolences	87%	39%	61%
Encourage questions about the patient's ICU stay and death and address doubts	89%	38%	62%
For administrative procedures, guide relatives towards specific professionals	98%	43%	57%
Offer a visit with the ICU team later on	86%	33%	67%
Show empathy and give the relative opportunities to express feelings	92%	59%	41%

ICU=intensive care unit. P=physician. N=nurse.

Table 2: **Implementation of the intervention**

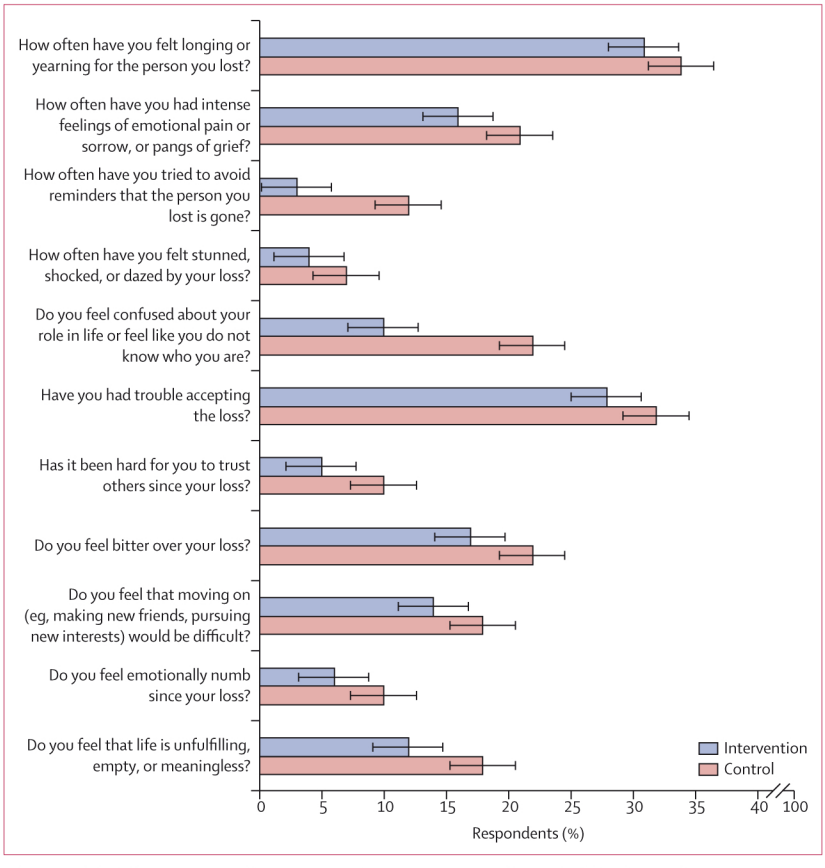

Figure 2: **High-risk responses to the PG-13 questions to measure prolonged grief at 6 months**
The proportion of respondents who answered positively to each of the PG-13 questions is depicted in each randomised group. As required by the PG-13 instructions, for an answer to be positive, the respondent must experience questions 1 and 2 at least daily, and for questions 4–12 at least once a day or quite a bit.

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or decision to submit the manuscript.

Results
Between Feb 23, 2017, and Oct 8, 2019, 4334 consecutive patients died in the 34 participating ICUs (two ICUs subsequently declined participation, 17 ICUs were randomly assigned to the intervention group and 17 to the control group). The study eligibility criteria were met by 1135 patients and relatives, and 875 relatives were included in the trial (391 in control ICUs and 484 in intervention ICUs). 6-month follow-up interviews (ending in April, 2020) were completed by 688 (79%) relatives (figure 1). There were no significant differences in patients' and relatives' characteristics between those who completed follow-up and those who were lost to follow-up (appendix p 14). Appendix p 16 describes the ICU characteristics and table 1 the main characteristics of the patients and study relatives as well as EOL, as measured during the study.

All three steps of the intervention were implemented for most relatives (90%) in intervention centres (table 2 and appendix p 17). Table 1 also shows EOL differences between the two clusters. The intervention was effectively applied for 448 (93%) relatives in step 1, 446 (92%) in step 2, and 410 (85%) in step 3.

The median PG-13 score at 6 months (primary outcome) was significantly lower in the intervention group than the control group (19 [IQR 14–26] *vs* 21 [15–29], mean difference 2·5, 95% CI 1·04–3·95), which also had fewer relatives with scores of 30 and higher (57 [15%] *vs* 66 [21%]; p=0·035) (figure 2).

Post-hoc analysis showed that the PG-13 score was likely to be increased in female versus male relatives (appendix p 18). It decreased with patient age, and also when the relative was not the patient's partner, and when the relative did not feel isolated (appendix p 18).

Among secondary outcomes, most variables studied were significantly better in the intervention than in the control group (table 3). Although HADS depression subscores were signifcantly lower in the intervention group at 3 and 6 months, the proportion of relatives with scores greater than 7 did not differ significantly at any timepoint. At 1 month, the relatives' experience, quality of death and dying as assessed by the relatives, and relatives' satisfaction were all significantly better in the intervention group than the control group, as were the IES-R scores and proportion of relatives whose scores indicated a high risk of PTSD at 3 and 6 months (table 3).

Other secondary outcomes are presented in the appendix p 19.

Discussion
In this multicentre, cluster-randomised trial, we found that, compared with standard care, a proactive intervention including a three-step physician-driven, nurse-aided strategy of support to relatives of patients dying in the ICU (after a decision to withhold or withdraw life support) significantly decreased the prevalence of prolonged grief 6 months after the patients' death, as well as prevalence of PTSD-related symptoms and symptoms of anxiety.

Our innovative proactive intervention targeted three critical moments of the dying process on the basis of evidence provided by previous research.[4,11–13,16] First, the relatives were prepared during an EOL conference, a tool that has shown effectiveness in decreasing symptoms of PTSD, anxiety, and depression in relatives.[11] Second, the physician and nurse were present in the patient's room with the relatives at some point of the dying process, to create opportunities for detecting and addressing unmet needs.[20] This step might be seen as intrusive, as relatives' may want to preserve their privacy, but could occur at the optimal time to provide explanations and reassurance[6] and to encourage families to express their feelings and ask questions.[21] Third, after the death, many relatives still have questions about the illness and death, which, if unanswered, could hinder the grieving process. Furthermore, closure with the team who cared for the patient eases the grieving process.[22]

Our study shows that support provided by the professionals in charge of daily patient care is effective, in keeping with earlier work.[12,13] Support from other clinicians, without the involvement of ICU staff, has led to conflicting results.[23] Non-verbal communication and empathetic support were central components of all three steps and are known to markedly affect patient and family outcomes.[24,25] The intensivists and nurses in the intervention ICUs received training and brief practice in communication, including non-verbal cues and means of expressing empathy, which seems to have been effective. The intervention is simple to replicate and its cost is reasonable (essentially clinicians' time investment). Our trial supports the feasibility of training ICU physicians and nurses to deliver the three steps of the strategy as a routine practice, thereby protecting many bereaved relatives from prolonged grief and other components of post-ICU syndrome.

Previously reported risk factors for prolonged grief are traumatic circumstances of the death, insufficient preparation of the relatives, and conflicts with staff.[26] In the ICU, unsatisfactory communication with the physician, an inability to say goodbye to the patient, and presence at the death without adequate support were also associated with prolonged grief.[4] Our intervention was based on this research. By guiding the relatives through the dying process, it significantly decreased the occurrence of prolonged grief, as well as other adverse outcomes in the relatives. Grief is an emotion shaped by our age, personality, and coping strategies, but it is also a social experience influenced by interactions with others before and after the death. Our study shows that better interactions with others around the patient's death improved outcomes in the relatives.

The SUPPORT investigators initiated interventional research for patient-centred and relative-centred care in the ICU.[27] They maintained that any intervention aimed at improving relatives' experience in the ICU must be subjected to a formal evaluation. Some studies that sought to decrease the frequency of post-ICU syndrome in relatives proved to have the opposite effect.[23,28,29] For instance, in a randomised controlled trial involving more than 200 bereaved relatives, a condolence letter sent by the ICU team increased the risk of developing PTSD-related symptoms, as well as symptoms of anxiety and depression, 3 and 6 months after the death.[29]

Our trial has several limitations. First our study took place in France where ICU practices and admission policies may differ from those in other cultural settings. However, our intervention was rooted in the international literature and should therefore be relevant to other countries. Additionally, 34 centres participated, enrolling a large number of relatives, thereby enhancing the general applicability of our findings. Second, studies have shown that some individuals are unable to improve their communication skills.[30] However, our intervention

	Control group	Intervention group	Effect size (95% CI)*	p value†
Primary endpoint: PG-13 score at 6 months				
Number of respondents	307	379	..	..
PG–13 score ≥30	66 (21%)	57 (15%)	Δ=–6·5 (–0·12 to –0·6); OR=0·6 (0·4 to 1·0)	0·03
PG–13 score‡				
Median (IQR)	21 (15–29)	19 (14–26)	..	..
Mean (SD)	23·4 (10·5)	20·9 (8·4)	Δ=–2·5 (–4·0 to –1·0)	0·003
Secondary endpoints at 1 month				
Number of respondents	352	433	..	..
CAESAR score ≤59 (difficult EOL experience)	77 (22%)	58 (13%)	Δ=–8·5 (–12·9 to –3·1); OR=0·5 (0·4 to 0·8)	0·002
QODD-1				
Median (IQR)§	8 (7–9)	9 (7–10)	..	..
Mean (SD)	7·8 (1·9)	8·5 (1·9)	Δ=+0·4 (0·1 to 0·7)	0·02
HADS¶ total score				
Median (IQR)	14 (9–21)	14 (8–20)	..	..
Mean (SD)	15·2 (8·7)	13·8 (7·9)	Δ=–1·4 (–2·7 to –0·1)	0·036
Anxiety subscale				
Median (IQR)	8 (4–11)	7 (4–10)	..	..
Mean (SD)	7·8 (4·6)	7·1 (4·3)	Δ=–0·7 (–1·5 to 0·0)	0·063
Presence of symptoms of anxiety (subscore >7)	190 (54%)	194 (45%)	Δ=–9·2 (–16·2 to –2·1); OR=0·7 (0·5 to 0·9)	0·01
Depression subscale				
Median (IQR)	6 (3–11)	6 (2–10)	..	..
Mean (SD)	7·3 (5·2)	6·6 (5·0)	Δ=–0·7 (–1·5 to 0·1)	0·095
Presence of symptoms of depression (subscore >7)	148 (42%)	173 (40%)	Δ=–2·1 (–9·0 to 4·8); OR=0·9 (0·7 to 1·2)	0·56
MISS–21 scale				
Median (IQR)‖	6 (5–7)	6 (6–7)	..	..
Mean (SD)	5·8 (1·2)	6·1 (1·1)	Δ=0·3 (0·02 to 0·5)	0·04
Secondary endpoints at 3 months				
Number of respondents	310	393	..	..
HADS¶ total score				
Median (IQR)	13 (8–19)	11 (7–17)	..	..
Mean (SD)	13·7 (8·0)	12·1 (7·3)	Δ=–1·6 (–2·8 to –0·4)	0·009
Anxiety subscale				
Median (IQR)	7 (4–11)	7 (4–9)	..	..
Mean (SD)	7·6 (4·3)	6·9 (3·9)	Δ=–0·7 (–1·4 to 0·0)	0·051
Presence of symptoms of anxiety (subscore >7)	149 (48%)	166 (42%)	Δ=–5·9 (–13·2 to 1·6); OR=0·8 (0·5 to 1·1)	0·18
Depression subscale				
Median (IQR)	5 (2–9)	4 (1–8)	..	..
Mean (SD)	6·1 (4·5)	5·2 (4·8)	Δ=–0·9 (–1·6 to –0·2)	0·016
Presence of symptoms of depression (subscore >7)	109 (35%)	113 (29%)	Δ=–6·5 (–13·3 to 0·6); OR=0·7 (0·5 to 1·0)	0·07
Impact of event scale–revised**				
Median (IQR)	20 (10–31)	15 (7–24)	..	..
Mean (SD)	22·0 (15·6)	17·1 (12·4)	Δ=–4·9 (–7·5 to –2·3)	<0·0001
Presence of PTSD–related symptoms (score ≥33)	68 (22%)	47 (12%)	Δ=–10·0 (–15·6 to –4·3); OR=0·4 (0·2 to 0·8)	0·005

(Table 3 continues on next page)

	Control group	Intervention group	Effect size (95% CI)*	p value†
(Continued from previous page)				
Secondary endpoints at 6 months				
Number of respondents	309	379	..	..
HADS score				
Median (IQR)	11 (7–17)	9 (4–15)	..	..
Mean (SD)	12·2 (7·8)	10·2 (7·0)	Δ=–2·0 (–3·3 to –0·7)	0·003
Anxiety subscale				
Median (IQR)	7 (4–10)	6 (3–9)	..	..
Mean (SD)	7·2 (4·2)	6·0 (4·2)	Δ=–1·2 (–1·9 to –0·5)	0·002
Presence of symptoms of anxiety (subscore >7)	140 (45%)	121 (32%)	Δ=–13·3 (–20·7 to –6·1); OR=0·6 (0·4 to 0·8)	0·002
Depression subscale				
Median (IQR)	4 (1–8)	3 (1–7)	..	..
Mean (SD)	5·0 (4·7)	4·1 (4·0)	Δ=–0·9 (–1·6 to –0·2)	0·02
Presence of symptoms of depression (subscore >7)	82 (27%)	74 (20%)	Δ=–7·0 (–13·4 to –0·7); OR=0·7 (0·5 to 0·9)	0·037
Impact of event scale–revised**				
Median (IQR)	13 (5–25)	10 (4–20)	..	..
Mean (SD)	17·5 (15·6)	13·6 (12·4)	Δ=–3·9 (–6·6 to –1·2)	0·013
Presence of PTSD–related symptoms	51 (17%)	32 (8%)	Δ=–8·1 (–13·1 to –3·0); OR=0·5 (0·2 to 0·9)	0·014

EOL=end of life. *Effect size was measured on mean difference (Δ) across groups, as well as odds ratio (OR) for binary outcomes. †p values were computed from generalised linear mixed-effects models that handled correlation induced by the cluster randomised design. ‡Prolonged grief-13 (PG-13) score; the possible range is 11–55 and a score ≥30 indicates prolonged grief disorder. §Quality of death and dying (QODD) questionnaire; the possible range is 0–10 with higher scores indicating better quality. ¶Hospital anxiety and depression scale (HADS); the total score can range from 0 to 42, with higher scores indicating more distress; the anxiety and depression subscales each can range from 0 to 21 with scores >7 indicating a high risk of developing anxiety or depression. ||21-item medical interview satisfaction scale (MISS), with four subscales (distress relief, communication comfort, rapport, and compliance intent); mean item score ranges from 1 to 7 with higher scores indicating higher satisfaction. **The total score can range from 0 to 88, scores in the 12–32 range indicate a moderate risk and scores ≥33 a high risk of developing post-traumatic stress syndrome.

Table 3: **Primary and secondary endpoints**

is simple and can probably be learned by most people. EOL family conferences, which in 2007 were shown to decrease symptoms of PTSD in relatives,[11] were applied in 67% of cases in the control group of this study, showing that ICU teams adapt their communication practices on the basis of scientific research. Third, the PG-13, used to measure our primary outcome, has not been used before in an interventional trial in the ICU, thus raising the question of the interpretation of the clinical value of the results. There is no established minimal clinically important difference for the PG-13 tool, and little is known about the working mechanisms of grief interventions. Anxiety, depression, and PTSD are more often chosen as important ICU outcomes. However, a previous study by our group showed a very high risk of developing complicated or prolonged grief after the death of a loved one in the ICU.[4] Fourth, only 79% of families provided information at 6 months, so we could not exclude attrition bias given the low effect size; nevertheless, no main differences in terms of patients and relatives were observed according to such a loss to follow-up. Fifth, given that this was a cluster randomised study, we cannot exclude some confounding due to differences in practice at the participating sites; unfortunately, these were not measured before the study onset, limiting the possibility of further adjustment on potential differences. Moreover, we undertook post-hoc analyses of the PG-13 score at 6 months (primary outcome) to ensure that our findings were not only due to unobserved differences across centres. Sixth, relatives were eligible for the trial only after a decision to withhold or withdraw treatment had been taken for their loved one—ie, only when the physicians were confident that the patient would die, which often occurs late in the ICU stay. Our intervention did not involve earlier opportunities for improving support to relatives. Clearly, the attentive, verbal and non-verbal, empathetic communication style used in our intervention could be extended to the entire ICU stay. Seventh, the trial included only French-speaking relatives to ensure quality follow-up; adapted communication strategies remain important for culturally and linguistically diverse populations. Last, even if the study thoroughly guided EOL care practices in the intervention group, clinicians provided the best standard of care in the control group. However, this pragmatic trial intended to improve EOL practices that are already rooted in reality.

In conclusion, a three-step, physician-driven, nurse-aided support strategy decreased the prevalence of prolonged grief disorder among bereaved relatives. PTSD-related symptoms, as well as symptoms of anxiety, were less common in the intervention group than in the control group. The communication style used in the intervention deserves to be used widely in ICUs.

Contributors

NK-B, EA, FP, and VS wrote the study protocol. SC designed the study, and planned and did the statistical analysis. All coauthors approved the study protocol and those in the interventional centres organised the training sessions. NK-B wrote the first draft of the report with input from EA, SC, and FP. SV, SJ, LK, OG, MM, AM, LP, LA, AD, DS, EL, FE, EH, SM, JA, CB, P-YD, AL, OL, AR, DR, NT, BP-J, MF, MR, J-PR, KA, BC, DG-T, J-LD, P-EB, RC, and AC provided substantial contribution to the acquisition of data. AC and SV accessed and verified the data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Declaration of interests

EA reports receiving fees for lectures from Gilead, Pfizer, Baxter, and Alexion. His research group has been supported by Ablynx, Fisher & Payckle, Jazz Pharma, and MSD, outside the submitted work. AC reports receiving fees for lectures from Bard, outside the submitted work. AD reports grants, personal fees, and non-financial support from

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Data sharing

The protocol, statistical analysis plan, definition of outcomes, description of training materials, regulatory documents, and other relevant trial materials are available online. According to the sponsor rules, the Assistance Publique–Hôpitaux de Paris is the owner of the data and no use or transmission to a third party can be made without its prior agreement. The trial steering committee will facilitate the use of the trial data and approval will not be unreasonably withheld. Deidentified participant data will be made available to bona fide researchers registered with an appropriate institution within 3 months of publication. However, the steering committee will need to be satisfied that any proposed publication is of high quality, honours the commitments made to the trial participants in the consent documentation and ethics approvals, and is compliant with relevant legal and regulatory requirements (eg, relating to data protection and privacy). The steering committee will have the right to review and comment on any draft manuscripts before publication.

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