Outcomes of critically ill patients with and without concordant perceptions of excessive care: A comparison between more religious and less religious ICUs

Short title: Religion, excessive care, and patient outcomes

Lucas Dierickx[1], Hanne Irene Jensen[2,3,4], Hans-Henrik Bülow[5], Stijn Vansteelandt[6], Rosanna Vaschetto[7], Gábor Élő[8], Ruth Piers[9], Dominique D. Benoit[10]

Affiliations:

[1]Department of Marketing, Innovation and Organisation, Ghent University, Tweekerkenstraat 2, 9000 Ghent, Belgium.

[2]Departments of Anaesthesiology and Intensive Care, Vejle Hospital, University Hospital of Southern Denmark, Beriderbakken 4, 7100 Vejle, Denmark

[3]Department of Anaesthesiology and Intensive Care, Kolding Hospital, University Hospital of Southern Denmark, Sygehusvej 24, 6000 Kolding, Denmark

[4]Institute of Regional Health Research, University of Southern Denmark, J.B. Winsløwsvej 19, 5000 Odense, Denmark

[5]Department of Anaesthesiology and Intensive Care, University Hospital Holbaek, Holbaek, Denmark

[6]Department of Applied Mathematics, Computer Science and Statistics, Ghent University, Krijgslaan 281-S9, 9000 Ghent, Belgium.

[7]University of Eastern Piedmont, Via Solaroli 17, 28100 Novara, Italy

[8]Semmelweis University, Üllői út 26, 1085 Budapest, Hungary

[9]Department of Geriatrics, Ghent University Hospital and Ghent University, Corneel Heymanslaan 10, 9000 Ghent, Belgium

[10]Department of Intensive Care Medicine, Ghent University Hospital and Ghent University, Corneel Heymanslaan 10, 9000 Ghent, Belgium

Correspondence address:

Lucas Dierickx, Department of Marketing, Innovation, and Organisation, Ghent University, 9000 Ghent, Belgium

Lucas.Dierickx@UGent.be

Title: Outcomes of critically ill patients with and without concordant perceptions of excessive care: A comparison between more religious and less religious ICUs

Keywords
ICU, Treatment-limitation decisions, perceived excessive care, patient outcomes

Summary

Background
Intensive care unit (ICU) clinicians are frequently confronted with ethical dilemmas surrounding end-of-life decisions. There is little knowledge on the relation between religiosity of clinicians and perceptions of excessive care in real-life patient situations.

Research Question
Are there differences between more religious and less religious ICUs with regard to perceptions of excessive care, treatment-limitation decisions and patient outcomes?

Study Design and Methods
We utilized a multicenter, prospective cohort design. 56 ICUs in 12 European countries and the United States were classified as more religious or less religious based on the median degree of religious beliefs of their clinicians. We compared the cumulative incidence of concordant perceptions of excessive care by two or more clinicians, treatment-limitation decisions during ICU stay and mortality within one year between patients in more religious and less religious ICUs. To adjust for differences in patient, hospital, ICU or country characteristics, inverse probability weighting based on propensity scores was utilized.

Results
Out of 56 ICUs, 15 were categorized as more religious and 41 as less religious. In these ICUs, 1,641 patients were admitted for more than monitoring during the study period, 437 (26.6%) in more religious ICUs and 1,204 (73.4%) in less religious ICUs. After inverse probability weighting to adjust for confounding, we found no evidence for a difference in receiving concordant perceptions of excessive care (8.2% vs 10.7%, HR: 1.41, 95% CI: [0.86, 2.32], p = 0.18), risk of death (92.2% vs 86.9%, p = 0.20) or written treatment-limitation decisions (36.2%

vs 25.8%, $p = 0.37$) between patients in more religious and less religious ICUs. In the absence of concordant perceptions of excessive care, no differences were found with regard to the risk of death (37.6% vs 40.7%, $p = 0.14$) or written treatment-limitation decisions (5.2% vs 7.3%, HR: 1.55, 95% CI: [0.83, 2.89], $p = 0.17$).

Interpretation

We found no evidence that more religious ICUs have different views on what constitutes excessive care in comparison to less religious ICUs. We found also no difference in treatment limitation decisions and 1-year outcomes in patients with and without perceptions in excessive care, suggesting a professional attitude of ICU clinicians towards patients, irrespective of their religiosity.

Title: Outcomes of critically ill patients with and without concordant perceptions of excessive care: A comparison between more religious and less religious ICUs

In intensive care units (ICUs), clinicians are frequently tasked with ethical dilemmas in which decisions have to be made often in the absence of certainty surrounding the outcome of these decisions. It is essential to ensure that care provided to these patients is proportionate, with the goal of reducing morbidity, and ideally at the same time minimizing as much as possible the physical and mental burden of patients and their relatives, and maximizing the quality of life after ICU stay[1,2]. To achieve these goals, it is crucial that patients and their relatives are well-informed about the potential risks of life-prolonging treatments, which should also be in accordance with their personal wishes and values[3]. Coping with uncertainty in these circumstances may be influenced by personal, team and cultural factors[4], which can ultimately lead to disproportionate levels of care (excessive care or insufficient care). For instance, clinicians might experience the burden of choosing between two mutually exclusive actions (e.g., writing an order to withdraw treatment or not) and inadvertently prolonging the suffering of patients and their families[5]. Such outcomes can result in the healthcare provider wondering if they have truly made the 'right' decision, leading to moral distress and in turn resulting in burnout, depression or a decision to resign from their job[6]. In this study, we consider the role of religion with regard to disproportionate care and excessive care in particular, since the perception of excessive care is much more prevalent than "not enough" care[3,6,7].

Previous studies have investigated religion with regard to end-of-life decisions at the level of patients/ relatives and physicians. For instance, Van Ness et al.[8] note that older patients who reported growing closer to their religion are more likely to accept the outcomes and possible risks of life-sustaining treatment. A study by Bülow et al.[9] concludes that religious relatives of patients may prefer more treatment and be more in favour of life-prolonging measures

compared to relatives that are only affiliated with a religion. With regard to clinicians, the findings of Vincent[10] suggest that religious clinicians are less likely to withdraw treatment compared to their less religious counterparts. However, this study was conducted only through questionnaires and therefore considered only hypothetical situations. Sprung et al.[11] reported on specific religions where 'end-of-life decisions varied greatly depending on the clinician's religious affiliation'. For instance, the active shortening of the dying process was only reported among Catholic and Protestant clinicians or those with no religious affiliation. Withholding of treatment occurred more often than withdrawal of treatment among Jewish, Greek Orthodox and Muslim clinicians.

The research question here builds upon two sub-studies that are part of the multicentre DISPROPRICUS study conducted in 2014-2015[3,12]. Both of these studies investigated differences in the time of receiving concordant perceptions of excessive care (when at least two clinicians report that a patient is receiving excessive care), time until written treatment-limitation decisions during ICU stay and time until patient death one year after ICU admission. These differences were assessed across different ethical climates and patient characteristics such as age and cancer diagnosis. In the same fashion, the objectives of this study are split into three parts: are there differences between patients admitted to more religious and less religious ICUs with regard to 1) time until concordant perceptions of excessive care, 2) time until written treatment-limitation decisions and 3) time until reaching the combined endpoint (death, poor quality of life or not living at home)?

Materials and methods

Study design and data collection

This study utilizes data collected in the context of the multicentre DISPROPICUS study conducted in 2014 – 2015. The data in question contain information on 68 adult ICUs and their patients and clinicians in 12 European countries and the United States[3]. The detailed protocol

and study design can be found in previous publications[3,13]. Over a 28-day study period, clinicians were asked to provide daily perceptions of disproportionate care (either "excessive care" or "not enough care") in patients for whom they were directly in charge. Most importantly, information on the time of admission and time until concordant perceptions of excessive care and until written treatment-limitation decisions was collected. Other patient characteristics such as age, gender and the presence of several comorbidities were also collected for patients admitted for reasons other than monitoring only. Exactly one year after the ICU stay of these patients, data were once again collected concerning the quality of life of each of the patients. Patients who had died, were not living at home or had a poor quality of life one year after the ICU stay were considered to have reached the combined endpoint. Health-related quality of life was defined using the EuroQoL-5D questionnaire[14]. The acquired measures are then converted into a utility index, where a utility index score of lower than 0.5 indicates a compromised or poor quality of life.

Moreover, we collected data on demographical factors such as age, gender, years of experience and the role (e.g., junior or senior) of ICU health care providers. Healthcare providers were also asked about their perception regarding each of the 7 factors of the ethical decision-making climate (EDM-C) through self-assessment with the Ethical Decision-Making Climate Questionnaire (EDM-CQ)[13].

Religion among healthcare providers was assessed in two separate items. Firstly, respondents were asked which religion they felt most connected to (the options being Roman Catholic, Protestant, Greek-Orthodox, Muslim, Jewish, Buddhist, Non-Religious, Other or the option 'I do not wish to answer'). Healthcare providers that provided any response other than 'Non-Religious' were asked about the importance of religion in their daily lives. This was assessed with a 4-point Likert scale ranging from 1 (not important) to 4 (very important). Healthcare

159 providers answering ‘Non-Religious’ on the first question automatically received a score of 1
160 on this item.
161 The importance of religion scores of clinicians was aggregated into a median score per ICU.
162 The median was chosen to make the division between more religious and less religious ICUs
163 for two reasons. First of all, we can make a clear distinction between units where there is no
164 importance of religion among the majority of team members and units where there is at least
165 some importance of religion among the majority of its members. Second, upon using the
166 median, we observed remaining variability within country in the sense that some countries have
167 both more religious and less religious ICUs according to this distinction. Variability within
168 countries is desired in this case to distinguish the effects of country and culture with those of
169 religion. The full division with regard to country can be found in Figure 1. ICUs with a median
170 importance of religion score of 2 or higher were judged to be more religious ICUs (e.g., ICUs
171 in which there is some importance of religion among the majority of its team members) and
172 ICUs with a median importance of religion score of 1 were considered as less religious ICUs
173 (in which there is very little to no importance of religion among the majority of its team
174 members).
175

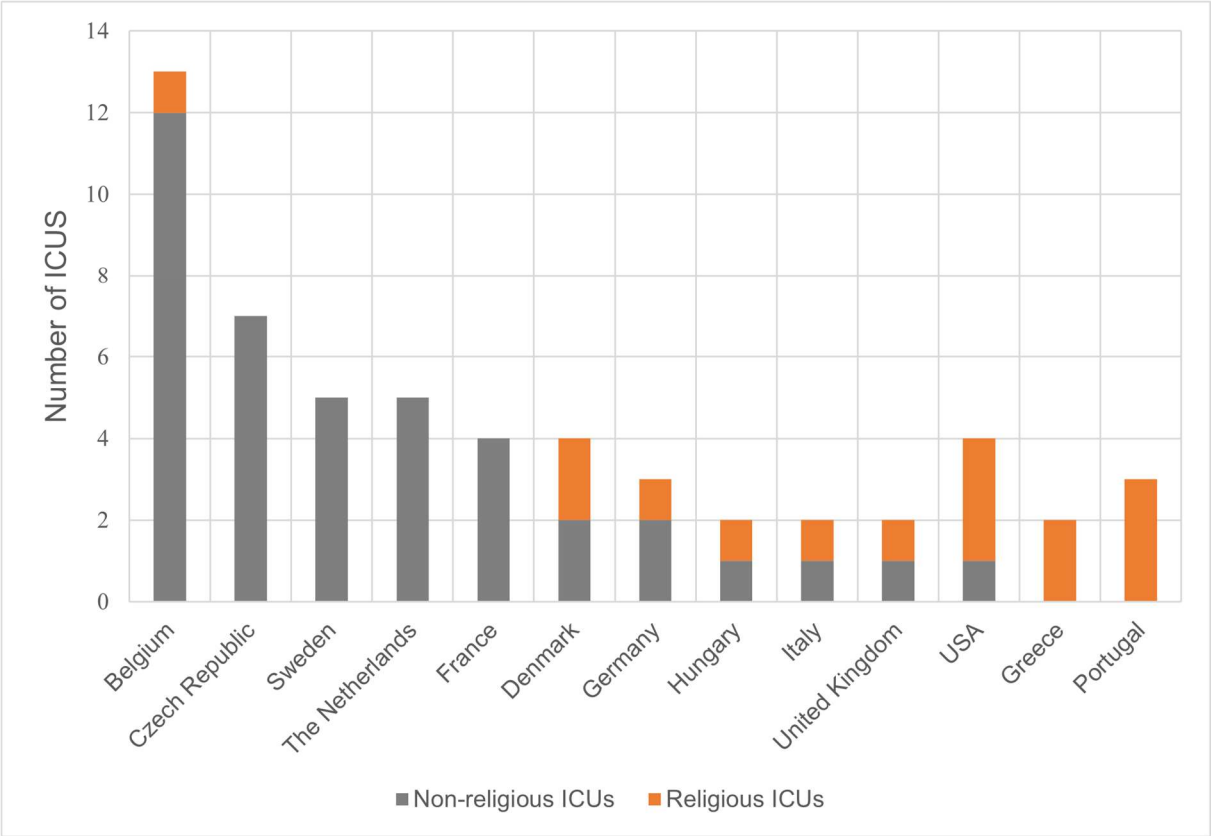


Figure 1. Number of less religious and more religious ICUs in each of the 13 countries, sorted by number of less religious ICUs.

Using the results of the EDM-C questionnaire, four different mutually exclusive ethical climates were identified in the DISPROPRICUS study through the usage of an exploratory and confirmatory factor analysis: good, average with (+) and without (-) involvement of nurses at end-of-life, and poor. ICUs with an average (-) climate were omitted from the analysis to avoid potential selection bias, as it was determined that the clinicians in charge in this climate included patients in a dissimilar manner compared to the other three climates. Specifically, these patients had a significantly higher mortality and median length of stay compared to patients in other climates and are thus not comparable with patients in the other climates[3]. Therefore, the final data are based on 56 ICUs. The study was approved by the ethics committees of all participating centres and the Danish National Health Authority. Informed consent was required in all countries to collect the one-year outcomes.

Data analysis

Outcomes between patients in more religious and less religious ICUs were assessed for patients with and without concordant perceptions of excessive care. Differences in country, hospital, ICU and patient characteristics were assessed using chi-squared tests for categorical outcomes and Mann-Whitney U tests for continuous outcomes. Results are expressed as number and percentage or median and 25-75th percentiles. Cause-specific hazard ratios acquired via Cox regression (accounting for competing risks by ICU discharge) were used to compare time from admission until concordant perceptions of excessive care and time from concordant perceptions of excessive care to written treatment-limitation decisions and reaching the combined endpoint. The cause-specific hazard of an event "expresses the instantaneous risk of that event at a given time for patients who are still alive in the ICU at that time and have not previously experienced that event[3]". Robust standard errors were used to account for clustering within ICUs. For patients with concordant perceptions of excessive care, this methodology was used to compare time from concordant perceptions of excessive care to written treatment-limitation decisions and reaching the combined endpoint. To learn about the time from admission to written treatment-limitation decisions and reaching the combined endpoint in the absence of concordant perceptions of excessive care, we additionally analysed this time for all patients, thereby censoring patients at the time of receiving concordant perceptions of excessive care. Here, we censor patients at the time of receiving concordant perceptions of excessive care (instead of restricting the analysis to the subgroup of patients without concordant perceptions of excessive care) to prevent selection bias due to overadjustment for future perceptions of excessive care status. Inverse probability weighting based on propensity scores was used to adjust for potential systematic differences in ICU ethical decision-making climate, patient, hospital and country characteristics. These propensity scores are calculated as the probability of belonging to a more religious or less religious ICU given a set of patient, ICU, hospital and country characteristics

and are obtained from building a multinomial logistic regression model. The included patient characteristics were age, admission reason, comorbidities, alcohol problems, patient competence, surgery before admission, cancer status and Eastern Cooperative Oncology Group (ECOG) performance status. Number of ICU and hospital beds, patient-nurse ratio and patient-junior physician ratio were included as hospital characteristics. ICU ethical decision-making climate and geographical region were included as additional variables. For a more detailed methodology in obtaining the weights, see Supplementary material 1. Concordant perceptions of excessive care, treatment-limitation decisions and reaching the combined endpoint are expressed as proportions and cause-specific hazard ratios with 95% confidence intervals. Patients in more religious ICUs were used as the reference value in all analyses. Two-sided *p* values were considered significant at the 0.05 level. We used R version 4.2.2 to analyse the data. To adjust for systematic differences in patient characteristics, the weighted analyses are considered as our primary results. Unweighted analyses are also provided in Supplementary material 2.

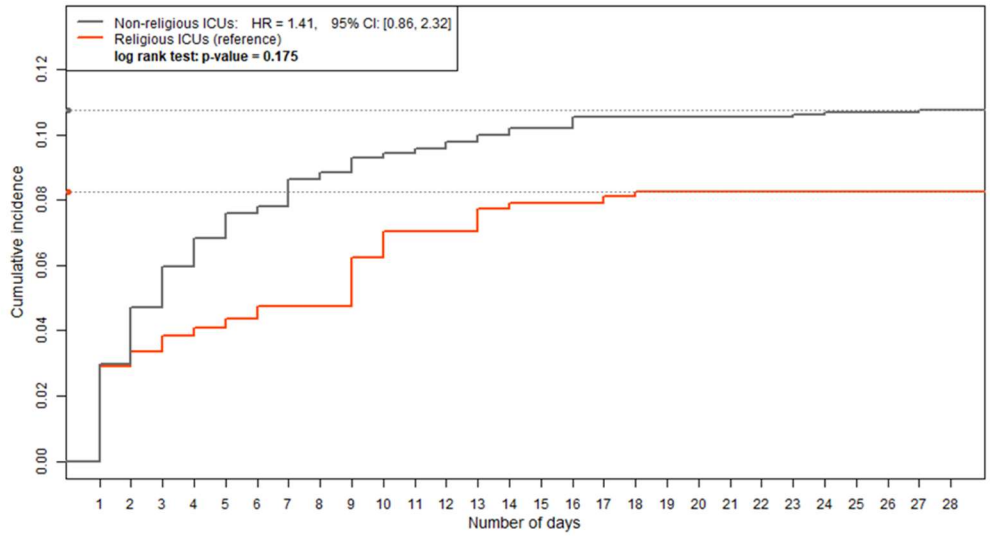
Results

Out of the 56 ICUs included in this study, 15 were categorized as more religious and 41 as less religious. In the 56 ICUs, 1,641 patients were admitted for more than monitoring during the study period, 437 (26.6%) in the more religious ICUs and 1,204 (73.4%) in the less religious ICUs. In less religious ICUs, 129 (10.7%) patients were perceived as receiving excessive care by two or more clinicians. In comparison, perceptions of excessive care were given by two or more clinicians in 31 patients in more religious ICUs (7.1%). Differences in country, hospital, ICU and patient characteristics are reported in Table 1.

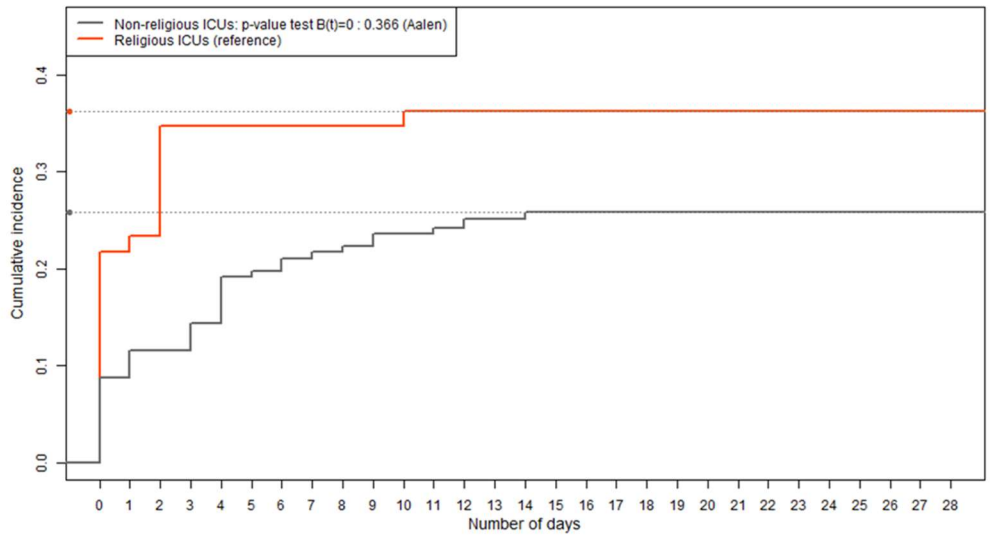
[Insert Table 1 here]

Statistical evidence was found for the unweighted analysis with regard to differences in cumulative incidence of concordant perceptions of excessive care between patients in more religious and less religious ICUs (7.1% vs 10.7%, HR: 1.56, 95% CI: [1.05, 2.30], $p = 0.03$), however, no such evidence was found in the weighted analysis (8.2% vs 10.7%, HR: 1.41, 95% CI: [0.86, 2.32], $p = 0.18$). In patients with concordant perceptions of excessive care, we found no evidence for a difference between patients in more religious and less religious ICUs with regard to time between concordant perceptions of excessive care and written treatment-limitation decisions (36.2% vs 25.8%, $p = 0.37$). Similarly, we found no differences with regard to time between admission and written treatment-limitation decisions in the absence of concordant perceptions of excessive care, using the weighted analysis (5.2% vs 7.3%, HR: 1.55, 95% CI: [0.83, 2.89], $p = 0.17$). Lastly, we found no evidence for a difference in the risk of reaching the combined endpoint between patients in more religious and less religious ICUs for patients with concordant perceptions of excessive care (92.2% vs 86.9%, $p = 0.20$) and without concordant perceptions of excessive care (37.6% vs 40.7%, $p = 0.14$). Each of the weighted analyses and the corresponding cumulative incidence curves can be found in Figure 2 for patients with concordant perceptions of excessive care, and Figure 3 for patients in the absence of concordant perceptions of excessive care.

a


Non-religious ICUs: HR = 1.41, 95% CI: [0.86, 2.32]
Religious ICUs (reference)
log rank test: p-value = 0.175
Cumulative incidence
0.00 0.02 0.04 0.06 0.08 0.10 0.12
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Number of days

b


Non-religious ICUs: p-value test B(t)=0 : 0.366 (Aalen)
Religious ICUs (reference)
Cumulative incidence
0.0 0.1 0.2 0.3 0.4
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Number of days

c

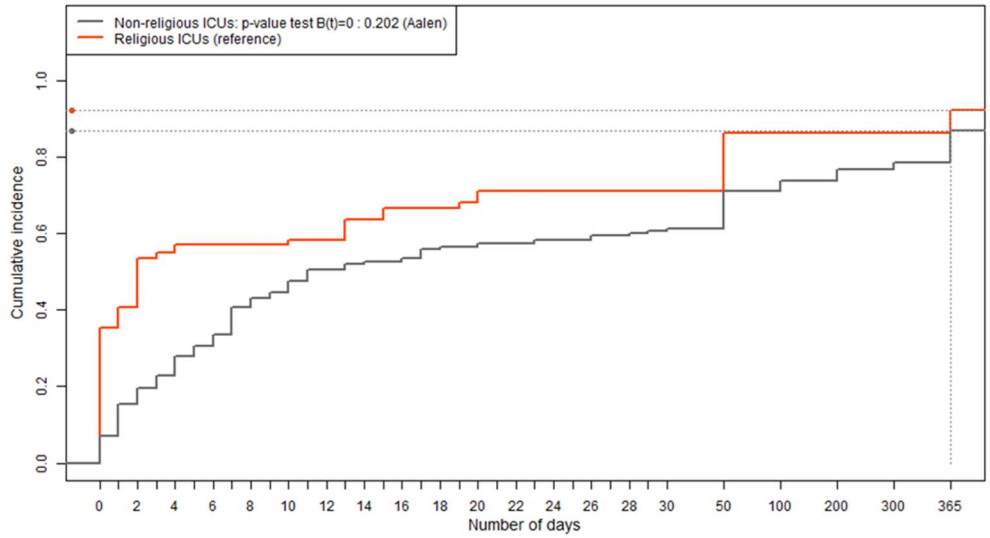

Non-religious ICUs: p-value test B(t)=0 : 0.202 (Aalen)
Religious ICUs (reference)
Cumulative incidence
0.0 0.2 0.4 0.6 0.8 1.0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 50 100 200 300 365
Number of days

Figure 2. a. Time from admission until at least two perceptions of excessive care during ICU stay (weighted) b. Time from at least two perceptions of excessive care until written treatment-limitation decision (weighted) c. Time from at least two perceptions of excessive care until reaching the combined endpoint (weighted).

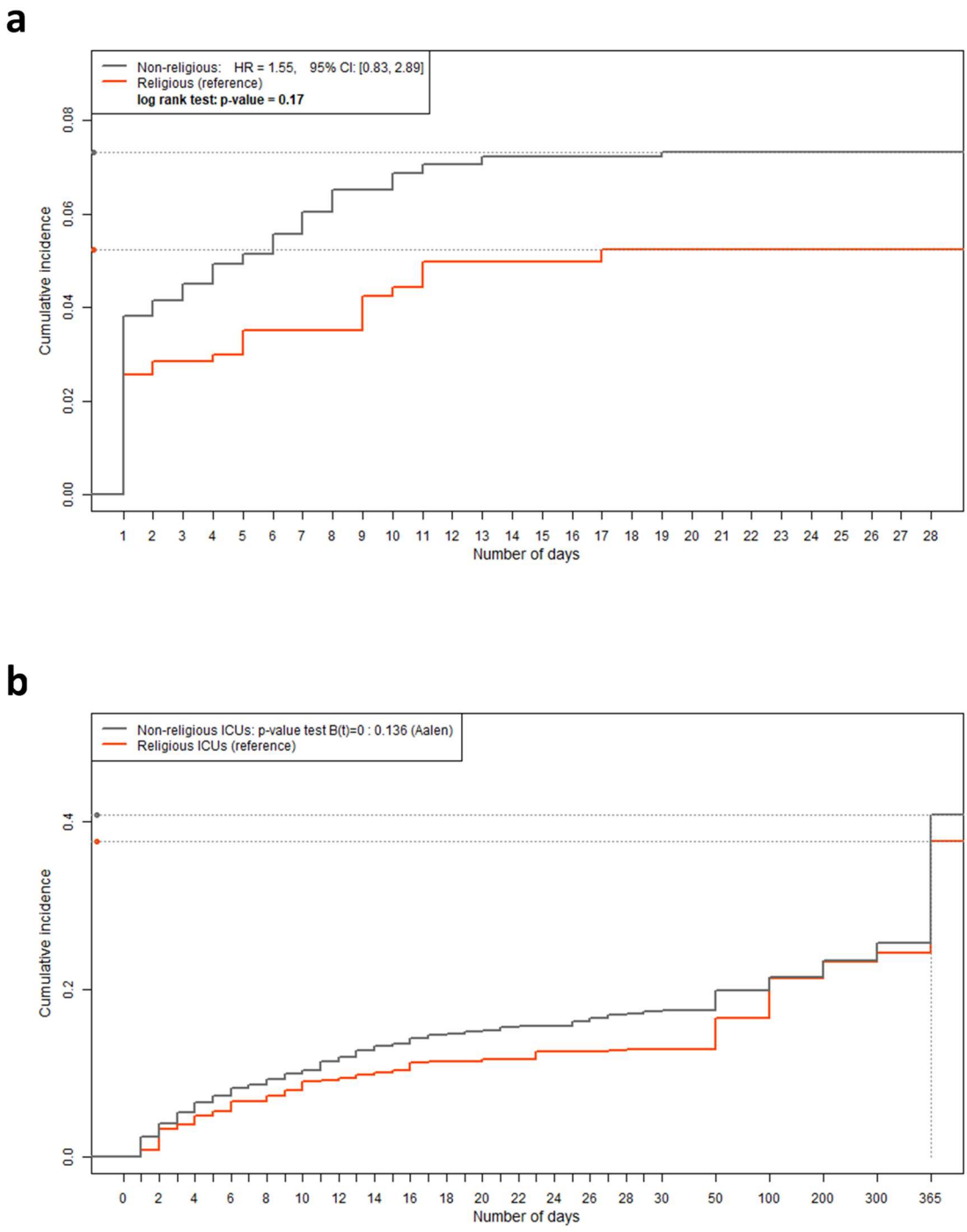


Figure 3. a. Time from admission until written treatment-limitation decision in the absence of concordant perceptions of excessive care (weighted) b. Time from admission until reaching the combined endpoint in the absence of concordant perceptions of excessive care (weighted).

Discussion

The aim of this study was to investigate the association of religious beliefs and perceptions of excessive care, end-of-life decision making and patient outcomes within an ICU setting. After adjusting for patient, hospital and country characteristics, we found no significant difference in patients perceived as receiving excessive care by two or more clinicians. Also, we found no evidence to suggest that more treatment-limitation decisions were made by clinicians in less religious ICUs compared to clinicians in more religious ICUs. Third, patients in more religious ICUs were not more at risk of dying, nor of having a poor quality of life or not residing at home one year after ICU admission compared to patients in less religious ICUs. While more patients are perceived as receiving excessive care in less religious ICUs according to the results of the unweighted analysis, there is thus no evidence to suggest that this is translated to more treatment-limitation decisions or lower patient mortality compared to patients in more religious ICUs.

Altogether, we found no evidence that more religious ICUs have differing views with regard to what constitutes excessive care in comparison to less religious ICUs. However, as said previously, it is possible that clinicians perceiving disproportionate care (including excessive care) may experience acute moral distress resulting in overt conflicts, burnout, depression, substance abuse or a decision to leave jobs[6,15]. What is not known is whether more religious clinicians experience possible moral distress in different ways compared to less religious clinicians. We also found no differences with regard to written treatment-limitation decisions between patients in more religious and less religious ICUs. This is in contrast to previous studies

293 that found differences in end-of-life decision making between religious and non-religious
294 clinicians. A Swiss mortality follow-back study notes that religious physicians (not exclusively
295 ICU physicians) are less likely to make treatment-limitation decisions compared to non-
296 religious physicians, and more inclined to make decisions resulting in the hastening of death[16].
297 A Turkish survey among more than 600 physicians showed that atheists compared to religious
298 physicians were significantly more in favour of do-not-resuscitate orders on patients' request[17].
299 Finally a postal survey among 2923 UK medical practitioners showed independently of
300 specialty, that non-religious physicians were more likely than others to report having taken
301 decisions they expected or partly intended to end life, and to have discussed these decisions
302 with patients judged to have the capacity to participate in discussion[18], while religious
303 physicians express more support for life preservation and are more opposed to euthanasia
304 compared to non-religious physicians[9,19]. However, the results from the current study support
305 the notion of Bopp et al. that evidence for an association between religious beliefs and
306 treatment-limitation decisions is rather weak at the international level[16]. Our study found no
307 differences between religious and less religious ICUs with regard to patient outcomes in the
308 form of patient mortality, patients not living at home or having a poor quality of life one year
309 after the initial ICU stay. It must be noted though, that this study is looking at religion as an
310 overarching principle that apparently has no influence on decisions, but if you dig deeper and
311 look at differences between the individual religions, then marked differences are found in
312 literature[11]. For instance, the aforementioned study of Sprung et al. reports differences in the
313 frequency of withholding and withdrawing treatment between different religions[11]. Another
314 study by Romain and Sprung[20] found that religion was associated with the decision to discuss
315 treatment-limitation decisions with the patient's family, with Protestant clinicians being more
316 likely to discuss these decisions than some other religions. Other studies remark that some
317 religions have differing views on euthanasia, do-not-resuscitate orders, organ donation and

318 what constitutes disproportionate treatment[21,22]. This study thus highlights that further research
319 on religion in an ICU and end-of-life decision-making context should be concerned with
320 different religions and their differing values on the end of life.
321 The strength of this study is its multicentre, international and prospective on-site design of
322 actual bedside practice involving the ICU stay for over 1500 patients. Usually, studies of this
323 kind are surveys, questionnaires or retrospective studies with high risk of bias. Additionally, it
324 can be very difficult to decipher whether decisions are based on religion or culture[11], but in 7
325 of the 13 countries in this study we were able to include both more religious and less religious
326 ICUs, leading to results where the impact of culture probably is minimized.
327
328 This study also has limitations. First, the participating ICUs were not selected at random. This
329 may have affected the external validity of our results[3]. Second, inclusion of patients was left at
330 the discretion of the attending doctors. However, we tried to reduce the risk of selection bias
331 across ICUs by excluding ICUs from average (-) ethical decision-making climates, as it was
332 determined that the clinicians in charge in this climate included patients in a dissimilar manner
333 compared to the other three climates[3]. Third, we used time until death and written treatment-
334 limitation decisions as surrogate markers of withholding or withdrawal of ICU treatment. We
335 did not measure actual withholding or withdrawal of these treatments[3]. Fourth, data from
336 patients admitted before the study period and patients who remained in the ICU for longer than
337 the study period were excluded from the analysis. Therefore, it is possible that the incidence of
338 patients with concordant perceptions of excessive care is underestimated[3]. Fifth, the distinction
339 between more religious and less religious ICUs was made on the basis of individual religious
340 beliefs and then aggregated on the team level. In a good ethical decision-making climate, end-
341 of-life decisions are made e.g., through interdisciplinary collaboration and communication
342 between team members in the ICU and the involvement of nurses in end-of-life decision-

making. Hence, we made the distinction between more religious and less religious ICUs to better reflect the way in which end-of-life decisions are made within an ICU setting. While instruments exist that measure spirituality and religion within clinical settings and among nurses, no such instruments exist which measure religion within a team[23]. Sixth, no distinction was made between different religious affiliations. Further research on disproportionate care, treatment-limitation decisions and patient outcomes should therefore also incorporate views from different religions. Seventh, it is difficult to completely distinguish the effects of religion from the effects of cultural aspects. Although some adjustment was made through the application of inverse probability weighting, it may have been insufficient as a result of residual confounding.

Conclusion

We found no evidence for a difference between patients in more religious and less religious ICUs with regard to being perceived as receiving excessive care. Among patients with and without concordant perceptions of excessive care, no differences were found with regard to treatment-limitation decisions and patient outcomes. Possible explanations for these results may be the professionalism and engagement of ICU clinicians towards patients and their families, independent of religious views.

Abbreviations ECOG performance status: Eastern Cooperative Oncology Group performance status; EDM-C: Ethical Decision-Making Climate; EDM-CQ: Ethical Decision-Making Climate Questionnaire; HR: Hazard ratios; ICU: Intensive Care Unit; 95% CI: 95% Confidence intervals

Supplementary information

Supplementary material 1. Detailed methodology

Supplementary material 2. a. Time from ICU admission until at least two perceptions of excessive care during ICU stay (unweighted). b. Time from ICU admission until combined endpoint (unweighted). c. Time from ICU admission until treatment-limitation decision during ICU stay (unweighted). d Time from ICU admission until treatment-limitation decision during ICU stay in the absence of concordant perceptions of excessive care (unweighted). e Time from ICU admission until combined endpoint in the absence of concordant perceptions of excessive care (unweighted). Combined endpoint: death, poor quality of life or not being at home.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committees of all participating centres and the Danish National Health Authority. All clinical participants received written and oral information about the study. Participation was voluntary, and the local investigators did not have access to the responses. Filling in the questionnaire was considered consent to participate. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

The study was supported by the European Society of Intensive Care medicine/European Critical care research network clinical research, a Fonds voor Wetenschappelijk Onderzoek senior clinical investigators grant (1800513N) and by Fund Marie-Thérèse De Lava, King Baudouin Foundation, Belgium.

Acknowledgements

The authors thank all participating nurses and physicians.

Likewise we would like to thank the national coordinators (please see affiliations below). Johan Malmgren, Victoria Metaxa, Anna K. Reyners, Katerina Rusinova, Danny Talmor, Anne-Pascale Meert, Laura Cancelliere, Laszlo Zubek, Paulo Mai, Andrej Michalsen.

and participating centers and local investigators:

Participating centers and local investigators: Belgium: University Hospital,Vrije Universiteit Brussel, Brussels (Herbert Spapen, Marie-Claire Van Malderen, Godelieve Opdenacker), Leuven University Hospital, Leuven (Geert Meyfroidt, Dieter Mesotten, Joost Wauters, Marie Van Laer and Alexander Wilmer, Joost Wauters, Helga Ceunen), ZNA Stuivenberg, Antwerpen (Inneke E De Laet, Anita Jans), Ghent University Hospital, Gent (Dominique Benoit, Sandra Oeyen, Ingrid Herck, Stephanie Bracke, Charlotte Clauwaert), Institut Jules Bordet, Bruxelles (Meert Anne-Pascale, Leclercq Nathalie), CHU-Brugmann, Bruxelles (Devriendt Jacques), CHU Saint Pierre, Bruxelles (Dechamps Philippe), Czech Republic: Liberec District Hospital, Liberec (Ivana Zykova), Masaryk University, Brno and University Hospital, Brno (Jan Malaska), Third Faculty of Medicine, Charles University, Prague (Matous Schmidt), Hospital and Polyclinic Havirov, Havirov (Igor Satinsky), Institute for Experimental and Clinical Medicine, Prague (Eva Kieslichova), 3rd Medical Department, First Faculty of Medicine, Charles University in Prague and General University Hospital,

Prague (Jarmila Krizova), Karlovy Vary District Hospital, Karlovy Vary (Robert Janda), Pardubice District Hospital, Pardubice (Magdalena Fortova, Jiri Matyas), First Faculty of Medicine, Charles University and General University Hospital, Prague (Katerina Rusinova, Ondrej Kopecky), Denmark: Herning Hospital, Herning (Christian Alves Køhler Pedersen), Kolding Hospital, Kolding (Stine Hebsgaard), Vejle Hospital, Vejle (Rikke Frank Aagaard Johnsen), Holbæk Hospital, Holbæk (Tina Charlotte Bitsch Hansen), France: Saint-Etienne University Hospital and Jacques Lisfranc Medical School, Saint-Etienne (Michael Darmon), Saint-Louis University Hospital, APHP, Université Paris-7, Paris (Danielle Reuter, Elie Azoulay), Institut Paoli Calmette, Marseilles (Djamel Mokart), Montfermeil Hospital, Montfermeil (François Vincent), Germany: University Hospital Jena, Jena (Christiane S. Hartog), Viersen General Hospital, Viersen (Peter Gretenkort), Tettnang Hospital, Tettnang (Andrej Michalsen), Greece: Agia Olga Hospital, Athens (Aikaterini Kounougeri), Evangelismos Hospital, Athens (Serafim Nanas), Agios Pavlos Hospital, Thessaloniki (Despina Papachristou), AHEPA University Hospital, Thessaloniki, (Ioanna Soultati), G.Gennimatas Hospital, Thessaloniki (Dimitrios Lathyris), Hippokratio General Hospital, Thessaloniki (Marili Pasakiotou), Papageorgiou General Hospital, Thessaloniki (Marina Oikonomou), Hungary: Semmelweis University Budapest, Budapest (Gábor Élő, Orsolya Szűcs), Kaposi Mór Teaching Hospital, Kaposvár University, Kaposvár (János Fogas), St. Stephen and St. Leslie Metropolitan Hospital, Budapest (Ilona Bobek), Italy: Azienda Ospedaliero Universitaria, “Maggiore della Carità”, Novara, and Department of Translational Medicine, Università del Piemonte Orientale, Novara (Francesco Della Corte, Carlo Olivieri, Rosanna Vaschetto, Laura Cancelliere), Ospedale Civile San Salvatore, and Department of Life, Health and Environmental Sciences (MeSVA), University of L’Aquila and Department of Emergency, San Salvatore Hospital, L’Aquila (Franco Marinangeli, Tullio Pozone, Alessandra Ciccozzi), The Netherlands: Canisius Wilhelmina Ziekenhuis, Nijmegen (A.

Schouten, Monique Bruns), Medical Center Leeuwarden, Leeuwarden (Rik T. Gerritsen, Matty Koopmans), Erasmus University Hospital of Rotterdam (Erwin Kompanje, Ditty van Duijn), University of Groningen and University Medical Center Groningen, Groningen (Jan G. Zijlstra, Anne KL Reyners), Wilhelmina Ziekenhuis Assen, Assen (Johan G. Lutisan), Portugal: Hospital S.António, Porto (Raquel Monte, José António Pinho, Pedro Pimenta), CHVNG, Vila Nova de Gaia (Paula Fernandes, Ana Isabel Paixão), Instituto Português de Oncologia, Porto (Filomena Faria), Sweden: Sahlgrenska University Hospital, Gothenburg (Johan A. Malmgren), Sahlgrenska University Hospital/Östra, Gothenburg (Bertil Andersson), Skåne University Hospital, Malmö (Eva Åkerman), Karolinska University Hospital, Karolinska (Andreas Hvarfner), The Hospital of Norrköping, Norrköping (Robert Svensson), United Kingdom: King's College Hospital, London (Victoria Metaxa), USA: Beth Israel Deaconess Medical Center and Harvard Medical School, Boston MA (Daniel Talmor, Ariel Mueller, Valerie Banner-Goodspeed), Henry Mayo Newhall Memorial Hospital, Valencia, CA (Dee Rickett), Mayo Clinic, Rochester, MN (Michael E. Wilson, Richard Hinds).

References

1. Aslakson RA, Curtis JR, Nelson JE. The changing role of palliative care in the ICU. Crit Care Med. 2014 Nov;42(11):2418. https://doi.org/10.1097/ccm.0000000000000573
2. Smith AK, White DB, Arnold RM. Uncertainty: the other side of prognosis. N Engl J Med. 2013 Jun 6;368(26):2448. https://doi.org/10.1056/nejmp1303295
3. Benoit DD, Jensen HI, Malmgren J, Metaxa V, Reyners AK, Darmon M, et al. Outcome in patients perceived as receiving excessive care across different ethical climates: a prospective study in 68 intensive care units in Europe and the USA. Intensive care medicine. 2018 Jul;44(7):1039-49. https://doi.org/10.1007/s00134-018-5231-8

4. Oerlemans AJ, van Sluisveld N, van Leeuwen ES, Wollersheim H, Dekkers WJ, Zegers M. Ethical problems in intensive care unit admission and discharge decisions: a qualitative study among physicians and nurses in the Netherlands. BMC Med Ethics. 2015 Dec;16(1):1-0. https://doi.org/10.1186/s12910-015-0001-4
5. Oberle K, Hughes D. Doctors' and nurses' perceptions of ethical problems in end-of-life decisions. J Adv Nurs. 2001 Mar 16;33(6):707-15. https://doi.org/10.1046/j.1365-2648.2001.01710.x
6. Piers RD, Azoulay E, Ricou B, Ganz FD, Max A, Michalsen A, et al. Inappropriate care in European ICUs: confronting views from nurses and junior and senior physicians. Chest. 2014 Aug 1;146(2):267-75. https://doi.org/10.1378/chest.14-0256
7. Piers RD, Azoulay E, Ricou B, Ganz FD, Decruyenaere J, Max A, Michalsen A, et al. Perceptions of appropriateness of care among European and Israeli intensive care unit nurses and physicians. Jama. 2011 Dec 28;306(24):2694-703. https://doi.org/10.1001/jama.2011.1888
8. Van Ness PH, Towle VR, O'Leary JR, Fried TR. Religion, risk, and medical decision making at the end of life. J Aging Health. 2008 Aug;20(5):545-59. https://doi.org/10.1177/0898264308317538
9. Bülow HH, Sprung CL, Baras M, Carmel S, Svantesson M, Benbenishty J, et al. Are religion and religiosity important to end-of-life decisions and patient autonomy in the ICU? The Ethicatt study. Intensive Care Med. 2012 Jul;38(7):1126-33. https://doi.org/10.1007/s00134-012-2554-8
10. Vincent JL. Forgoing life support in western European intensive care units: the results of an ethical questionnaire. Crit Care Med. 1999 Aug 1;27(8):1626-33. https://doi.org/10.1097/00003246-199908000-00042

11. Sprung CL, Maia P, Bulow HH, Ricou B, Armaganidis A, Baras M, et al. The importance of religious affiliation and culture on end-of-life decisions in European intensive care units. Intensive Care Med. 2007 Oct;33(10):1732-9. https://doi.org/10.1007/s00134-007-0693-0
12. Benoit DD, van der Zee EN, Darmon M, Reyners AK, Metaxa V, Mokart D, et al. Outcomes of ICU patients with and without perceptions of excessive care: a comparison between cancer and non-cancer patients. Ann Intensive Care. 2021 Dec;11(1):1-1. https://doi.org/10.1186/s13613-021-00895-5
13. Van den Bulcke B, Piers R, Jensen HI, Malmgren J, Metaxa V, Reyners AK, et al. Ethical decision-making climate in the ICU: theoretical framework and validation of a self-assessment tool. BMJ Qual Saf. 2018;27(10):781–9. https://doi.org/10.1136/bmjqs-2017-007390
14. Rabin R, Charro FD. EQ-SD: a measure of health status from the EuroQol Group. Ann Med. 2001 Jan 1;33(5):337-43. https://doi.org/10.3109/07853890109002087
15. Druwé P, Monsieurs KG, Gagg J, Nakahara S, Cocchi MN, Élő G, et al. Impact of perceived inappropiate cardiopulmonary resuscitation on emergency clinicians' intention to leave the job: Results from a cross-sectional survey in 288 centres across 24 countries. Resuscitation. 2021 Jan 1;158:41-8. https://doi.org/10.1016/j.resuscitation.2020.10.043
16. Bopp M, Penders YW, Hurst SA, Bosshard G, Puhan MA, Swiss End-of-Life Decisions Study Group. Physician-related determinants of medical end-of-life decisions–a mortality follow-back study in Switzerland. PLoS one. 2018 Sep 20;13(9):e0203960. https://doi.org/10.1371/journal.pone.0203960
17. Baykara N, Utku T, Alparslan V, Arslantaş MK, Ersoy N. Factors affecting the attitudes and opinions of ICU physicians regarding end-of-life decisions for their patients and

themselves: A survey study from Turkey. PloS One. 2020 May 20;15(5):e0232743. https://doi.org/10.1371/journal.pone.0232743

18. Seale C. The role of doctors' religious faith and ethnicity in taking ethically controversial decisions during end-of-life care. J Med Ethics. 2010 Nov 1;36(11):677-82. https://doi.org/10.1136/jme.2010.036194

19. Fischer S, Bosshard G, Faisst K, Tschopp A, Fischer J, Bär W, et al. Swiss doctors' attitudes towards end-of-life decisions and their determinants: a comparison of three language regions. Swiss Med Wkly. 2006;136(23-24):370-6. https://doi.org/10.4414/smw.2006.11260

20. Romain M, Sprung CL. End-of-life practices in the intensive care unit: the importance of geography, religion, religious affiliation, and culture. Rambam Maimonides Med J. 2014 Jan;5(1). https://doi.org/10.5041/rmmj.10137

21. Steinberg SM. Cultural and religious aspects of palliative care. Int J Crit Illn Inj Sci. 2011 Jul;1(2):154. https://doi.org/10.4103/2229-5151.84804

22. Bülow HH, Sprung CL, Reinhart K, Prayag S, Du B, Armaganidis A, et al. The world's major religions' points of view on end-of-life decisions in the intensive care unit. Intensive Care Med. 2008 Mar;34(3):423-30. https://doi.org/10.1007/s00134-007-0973-8

23. Austin P, Macdonald J, MacLeod R. Measuring spirituality and religiosity in clinical settings: A scoping review of available instruments. Religions. 2018 Mar 4;9(3):70. https://doi.org/10.3390/rel9030070

542

543

544

545 **Table 1:** to be inserted on page 10

546

547 Table 1. Country, hospital, ICU and patient characteristics across subgroups

	Less religious ICUs (n = 1204)	More religious ICUs (n = 437)	p-value
Country characteristics			
Number of ICU beds/100.000 inhabitants	11.6 (6.4-15.9)	15.9 (6.7-20.0)	<0.001
Geographical region			<0.001
Central Europe	169 (14.0)	33 (7.6)	
Northern Europe	204 (16.9)	87 (19.9)	
Southern Europe	49 (4.1)	88 (20.1)	
Western Europe/USA	782 (65.0)	229 (52.4)	
Hospital characteristics			
Total beds in hospital			<0.001
<250	20 (1.6)	102 (23.3)	
250-499	248 (20.6)	114 (26.1)	
500-749	312 (25.9)	109 (24.9)	
>750	624 (51.8)	112 (25.6)	
ICU characteristics			
Ethical climate			<0.001
Good	311 (25.8)	10 (2.3)	
Average +	428 (35.5)	269 (61.6)	
Poor	465 (38.6)	158 (36.2)	
Number of beds per ICU	14.0 (9.0-40.0)	13.0 (10.0-18.0)	0.051
Patient to nurse ratio	2.0 (1.2-3.0)	2.0 (1.5-2.5)	<0.001
Patient to junior physician ratio	5.0 (3.0-6.0)	4.0 (2.0-4.0)	<0.001
Patient to senior physician ratio	7.0 (5.0-8.0)	6.0 (5.0-7.7)	<0.001
Patient characteristics			
Age	65 (53.0-74.0)	63 (48.0-75.0)	0.41
Gender (female)	495 (41.1)	176 (40.3)	0.80
ECOG performance status			<0.001
Grade 0 (full functional)	395 (32.8)	178 (40.7)	
Grade 1 (symptomatic)	328 (27.2)	76 (17.4)	
Grade 2 (functional, not able to work)	188 (15.6)	52 (11.9)	
Grade 3 (limited functionality)	159 (13.2)	45 (10.3)	
Grade 4 (bedridden)	68 (5.6)	14 (3.2)	
Unknown	66 (5.5)	72 (16.5)	
Nursing home resident	55 (4.6)	23 (5.3)	0.65
Number of comorbidities			0.03
0	556 (46.2)	243 (53.5)	

1	510 (42.3)	156 (35.7)	
≥ 2	138 (11.5)	47 (10.8)	
Type of comorbidities			
Solid tumour	230 (19.1)	74 (16.9)	0.35
Heart failure (NYHA III or IV)	154 (12.8)	38 (8.7)	0.03
COPD (Gold III or IV or equivalent)	133 (11)	57 (13)	0.30
Neurological (excluding dementia)	71 (5.9)	32 (7.3)	0.35
Haematological malignancy	74 (6.1)	18 (4.1)	0.15
Liver cirrhosis (Child-Pugh B or C)	68 (5.6)	14 (3.2)	0.06
Chronic renal failure requiring dialysis	44 (3.7)	10 (2.3)	0.22
Dementia (moderate or severe)	23 (1.9)	16 (3.7)	0.06
AIDS	11 (0.9)	3 (0.7)	1
Substance abuse			
Alcohol	124 (10.3)	57 (13)	0.14
Active smoking	200 (16.6)	90 (20.6)	0.07
Main admission reason			
Respiratory failure	286 (23.8)	104 (23.8)	1
Sepsis/severe sepsis/septic shock	237 (19.7)	86 (19.7)	1
Heart failure/cardiogenic shock	204 (16.9)	75 (17.2)	0.98
Neurological pathology/stroke/ICB	129 (10.7)	53 (12.1)	0.47
Gastro-intestinal pathology/liver failure	116 (9.6)	53 (12.1)	0.17
Metabolic/renal	103 (8.6)	41 (9.4)	0.67
Multiple trauma	63 (5.2)	33 (7.6)	0.10
Head trauma	28 (2.3)	30 (6.9)	<0.001
Surgery 48 hrs. prior to admission	420 (34.9)	140 (32.0)	0.31
Surgery category			0.02
No surgery	774 (64.3)	296 (67.7)	
Scheduled surgery	169 (14.0)	38 (8.7)	
Unscheduled surgery	261 (21.7)	103 (23.6)	
Do-not-resuscitate order before admission			<0.001
Full code	1103 (91.6)	360 (82.4)	
No CPR	49 (4.1)	12 (2.7)	
Withholding of therapy	32 (2.7)	10 (2.3)	
Unknown	20 (1.7)	55 (12.6)	
Severity of illness < 24 hrs. after admission			
Invasive mechanical ventilation	582 (48.3)	202 (46.2)	0.48
Vasopressor need	467 (38.8)	116 (26.5)	<0.001
Dialysis	48 (4.0)	7 (1.6)	0.03
Withholding/withdrawing order	57 (4.7)	10 (2.3)	0.04

548 A p-value of <0.05 was considered statistically significant. Results expressed as number (%) and median
549 (interquartile range).

550

Supplementary material 1.

Application of inverse probability score weighting

In this study, inverse probability score weighting based on propensity scores was used to adjust for potential confounders. The process to acquire the weights was as follows:

1. Building a logistic regression model to acquire the variables related to the outcome variable 'Combined endpoint'.
2. Building a logistic regression model with variables from previous model to acquire the variables also related with admission to a more religious or less religious ICU.
3. Estimating the propensity scores based on fitted values.
4. Calculating the weights.

In the first step, a multinomial logistic regression model is used to find variables that are related to reaching the combined endpoint. If the patient had died, was not at home or had a poor quality of life, the patient was considered to have reached the combined endpoint. If the patient was still alive, living at home and with a good quality of life, the combined endpoint was not reached. For 339 out of a total of 1641 patients, the status of combined endpoint after one year was unknown. These patients were therefore omitted from the model. Variables related to the combined endpoint were obtained by using a forward, backward and both-way stepwise logistic regression with the significance level set to 0.10. Patient, ICU, hospital and country characteristics were considered as possible predictors for the combined endpoint. Five variables representing the five dimensions of the EuroQoL-5D questionnaire contained multiple missing values and were therefore not included in the model building process. Each of the three stepwise models returned the same results, and a total of 16 variables were retained and carried over to the next step of the process. The full overview of this model including coefficient estimates, standard errors and p-values can be found in Table 1.

576 Table 1. Overview of variables related with the combined endpoint including coefficient estimates, standard errors
577 and p-values.

Patient characteristics			
Variable	Log odds ratio	SE	p-value
ECOG			9.65E-13
Fully functional	1.58	0.69	
Functional, not able to work	-1.31	0.36	
Limited functionality	-0.40	0.37	
Symptomatic	-0.91	0.36	
Unknown	0.72	1.34	
Patient competency			1.45E-09
Not competent	0.20	0.32	
Competent	-0.71	0.32	
Surgery category			1.09E-05
Scheduled surgery	-0.78	0.21	
Unscheduled surgery	-0.63	0.17	
Cancer status			0.026
No cancer	-0.84	0.33	
Not active	-0.59	0.34	
Neurological pathology	0.85	0.25	0.0004
Head trauma	1.32	0.42	0.0009
Amount of comorbidities	0.40	0.12	0.001
Age (>= 75 or < 75)	0.36	0.15	0.02
DNR before admission			0.007
Don't know	0.12	0.41	
No CPR	1.17	0.55	
Withholding	1.45	0.64	
Alcohol abuse	0.54	0.23	0.02
Liver cirrhosis	-0.77	0.35	0.03
Gastro-intestinal pathology	0.43	0.25	0.09
ICU characteristics			
Total beds in hospital			0.0009
250-500	0.21	0.38	
500-750	0.18	0.39	
>750	-0.52	0.37	
Patient-nurse ratio	0.20	0.09	0.02
Patient-junior physician ratio	0.08	0.03	0.02
Total beds ICU	-0.02	0.006	0.0001

578

In the second step, a multinomial logistic regression model was again built using the 16 variables of the previous model to find those variables that were related to both the combined endpoint and the patient being in admission in either a more religious or less religious ICU. The 16 variables related to the combined endpoint mentioned in Table 1 and their two-way interactions were considered in building this new model. Again, a both-ways stepwise multinomial logistic regression model was built, this time with the significance level set to 0.05. The significance level was changed in comparison with the previous model in order to prevent overfitting. This resulted in a model containing 8 variables and two-way interactions. As ethical-decision making climate and geographical region were previously found to be important with regard to treatment-limitation decisions[1,2], these variables as well as patient gender were included in the final model to calculate the propensity scores. The weight for a patient in a more religious ICU is then the inverse of the propensity score[3] and thus the inverse of the probability that a patient is admitted in a more religious ICU, which is defined as:

$$w_i = \frac{1}{P(More\ religious\ ICU \mid x_i)}$$

While the weight for a patient in a less religious ICU is defined as:

$$w_j = \frac{1}{P(Less\ religious\ ICU \mid x_j)} - \frac{1}{1 - P(More\ religious\ ICU \mid x_j)}$$

In the calculation of these weights, some outlying weights were detected. In the case of extremely high weights this can lead to estimates with high variance[4]. We applied weight trimming by replacing weights with a value larger than the 99th percentile with the value of this threshold as a way to deal with the issue of these extremely high weights[4]. An overview of the

603 included variables and their interactions, coefficient estimates, standard errors and p-values can
604 be found in Table 2.
605

606 Table 2. Overview of variables related with the combined endpoint and admission in a more religious or less
607 religious ICU, including coefficient estimates, standard errors and p-values.

Main effects			
Patient characteristics			
Variable	Log odds ratio	SE	p-value
DNR before admission			3.61E-08
Withholding	-0.09	0.87	
No CPR	-0.80	0.90	
Unknown	-1.58	1.20	
ECOG			0.004
Full functional	1.21	0.44	
Functional, not able to work	0.77	0.47	
Limited functionality	0.52	0.48	
Symptomatic	0.52	0.46	
Unknown	1.35	0.58	
Head trauma	1.36	0.50	0.005
Gastro-intestinal pathology	0.64	0.27	0.017
Hospital/ICU characteristics			
Total beds in hospital			2.44E-15
250-500	-3.11	0.58	
500-750	-2.90	0.61	
>750	-5.56	0.76	
Total beds in ICU	0.46	0.06	0.002
Patient to junior physician ratio	2.00	0.20	1.76E-12
Patient to nurse ratio	1.08	0.41	< 2.2E-16
Manually added variables			
Geographical region			< 2.2E-16
Northern Europe	1.93	0.53	
Southern Europe	5.06	0.69	
Western Europe/USA	1.27	0.50	
Overall climate patient			< 2.2E-16
Good	-8.15	0.85	
Poor	-5.46	0.72	
Interaction effects			
DNR before admission x total beds in ICU			0.002
No CPR x total beds in ICU	0.04	0.06	
Withholding x total beds in ICU	0.22	0.06	
Unknown x total beds in ICU	0.25	0.08	
Patient to nurse ratio x total beds in ICU	0.17	0.02	1.17E-13
Total beds in ICU x patient competence			0.02
Total beds in ICU x not competent	0.01	0.02	
Total beds in ICU x competent	0.03	0.02	
Total beds in ICU x junior physician ratio	-0.25	0.02	< 2.2E-16

608

Abbreviations ECOG performance status: Eastern Cooperative Oncology Group performance status; ICU: Intensive Care Unit; DNR before admission: Do-not-resuscitate order before admission; CPR: Cardiopulmonary resuscitation

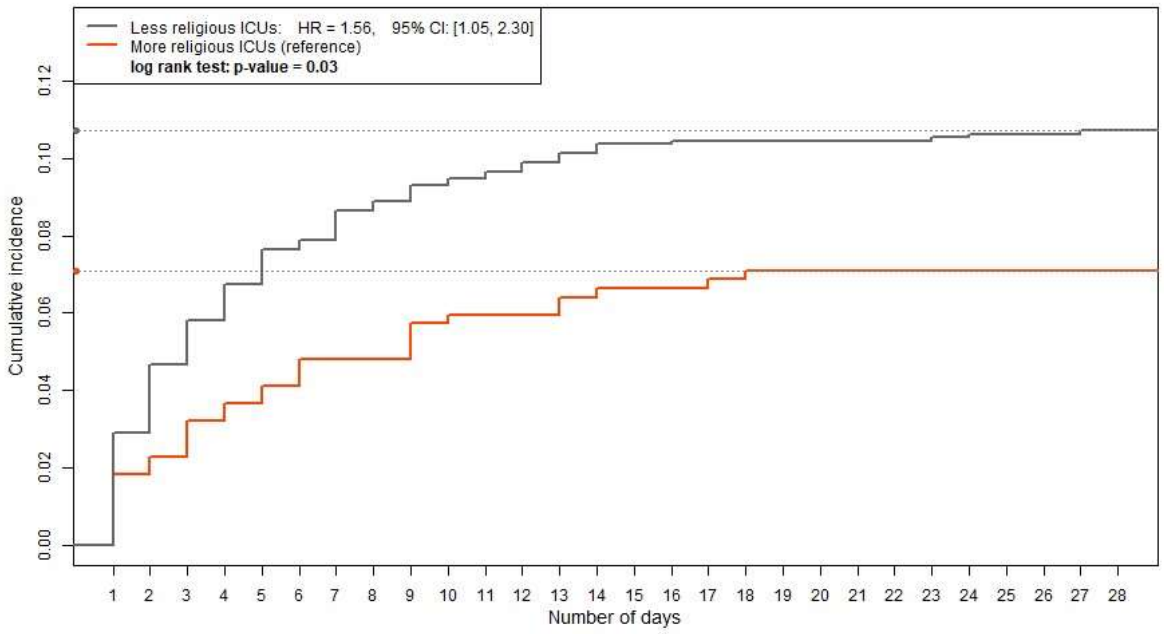
References

1. Benoit DD, Jensen HI, Malmgren J, Metaxa V, Reyners AK, Darmon M, et al. Outcome in patients perceived as receiving excessive care across different ethical climates: a prospective study in 68 intensive care units in Europe and the USA. Intensive care medicine. 2018 Jul;44(7):1039-49. https://doi.org/10.1007/s00134-018-5231-8
2. Benoit DD, van der Zee EN, Darmon M, Reyners AK, Metaxa V, Mokart D, et al. Outcomes of ICU patients with and without perceptions of excessive care: a comparison between cancer and non-cancer patients. Ann Intensive Care. 2021 Dec;11(1):1-1. https://doi.org/10.1186/s13613-021-00895-5
3. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika. 1983 Apr 1;70(1):41-55. https://doi.org/10.1093/biomet/70.1.41
4. Lee BK, Lessler J, Stuart EA. Weight trimming and propensity score weighting. PloS One. 2011 Mar 31;6(3):e18174. https://doi.org/10.1371/journal.pone.0018174

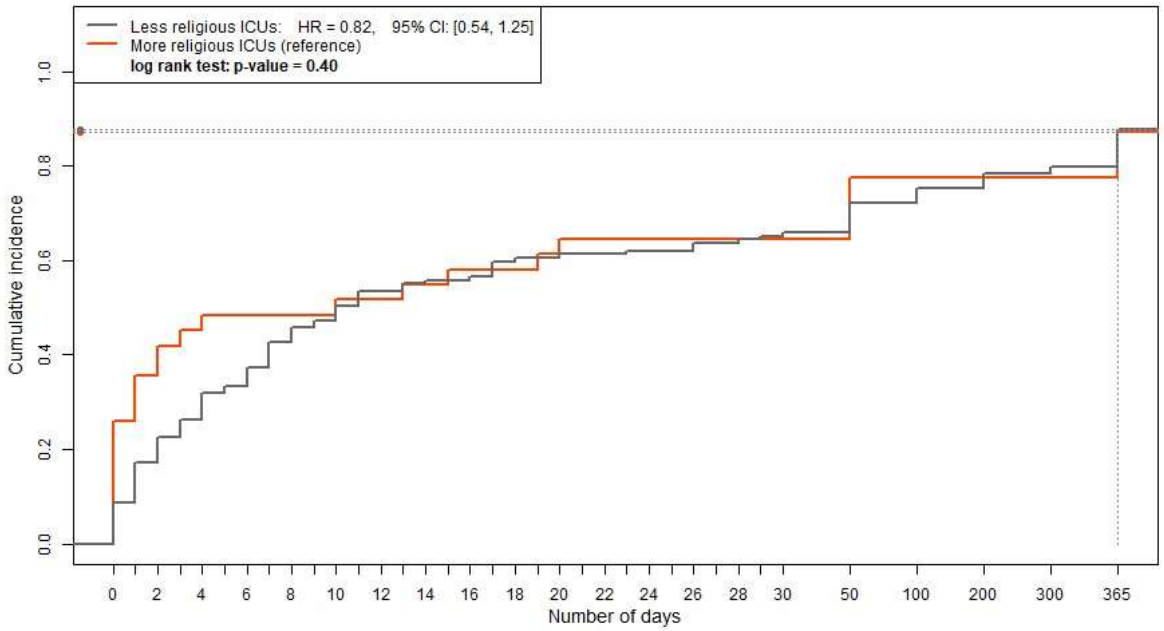
Supplementary material 2.

a Time from ICU admission until at least two perceptions of excessive care during ICU stay (unweighted). **b** Time from ICU admission until combined endpoint (unweighted). **c** Time from ICU admission until treatment-limitation decision during ICU stay (unweighted). **d** Time from ICU admission until treatment-limitation decision during ICU stay in the absence of concordant perceptions of excessive care (unweighted). **e** Time from ICU admission until combined endpoint in the absence of concordant PECs (unweighted). *Combined endpoint:* death, poor quality of life or not being at home.

a



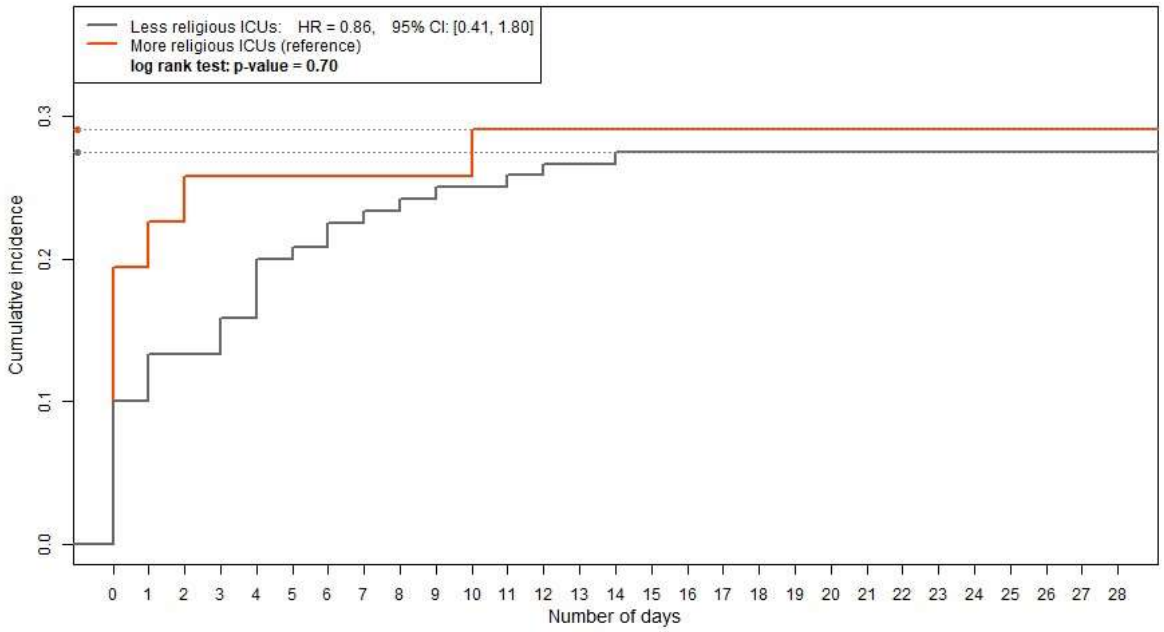
b



667

668

669 **c**



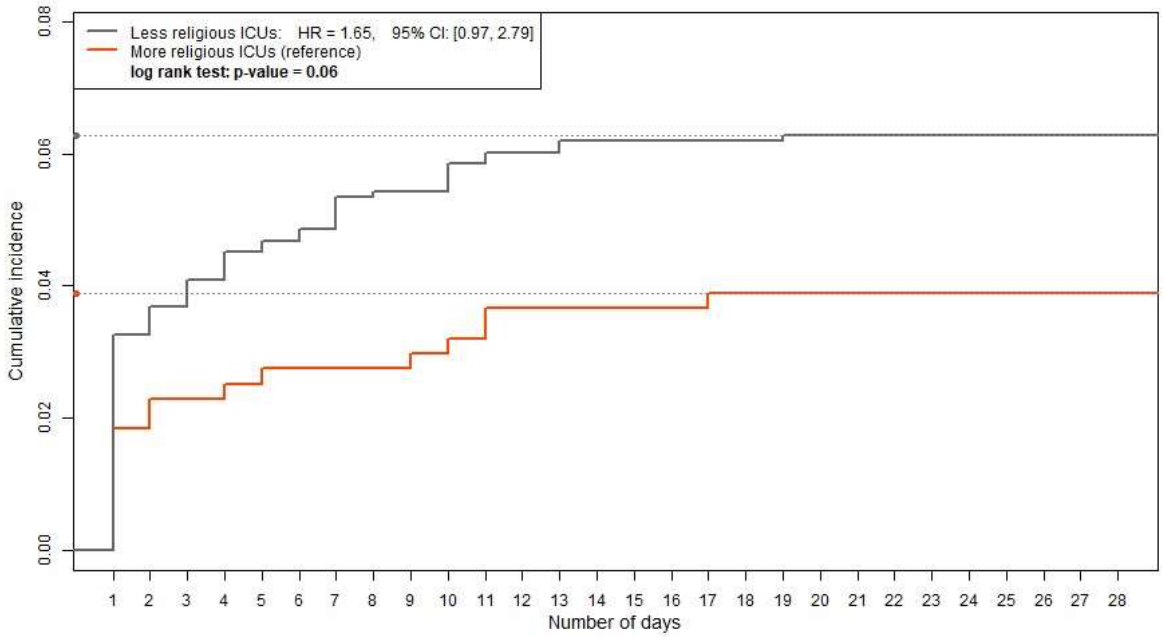
670

671

672

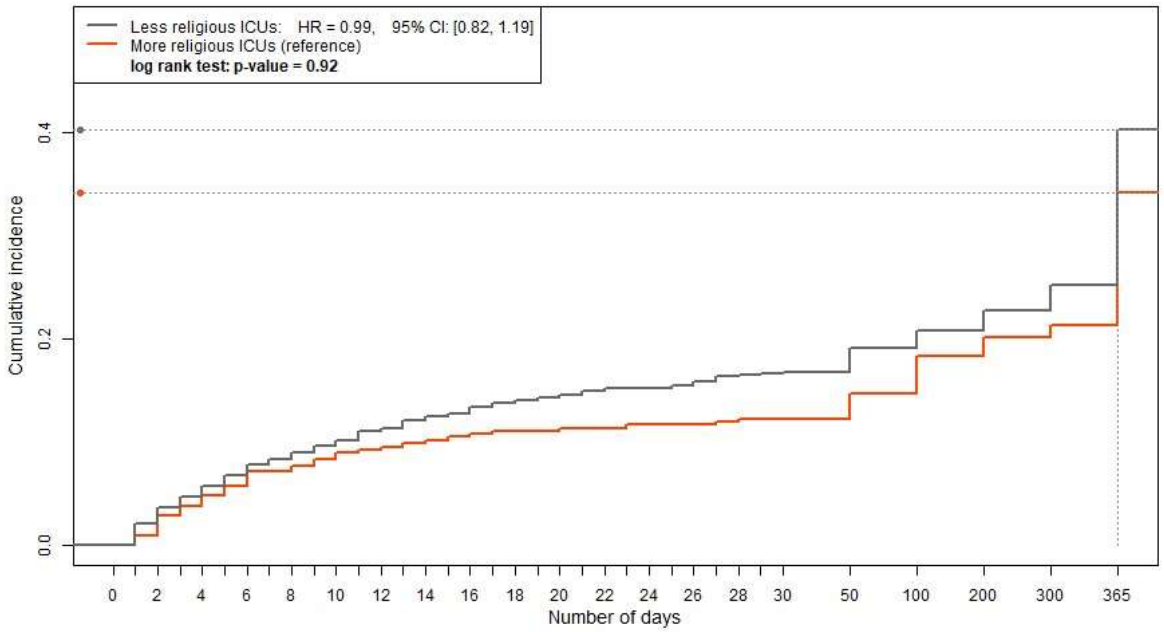
673

674 **d**



675

676 **e**



677

678

679

680