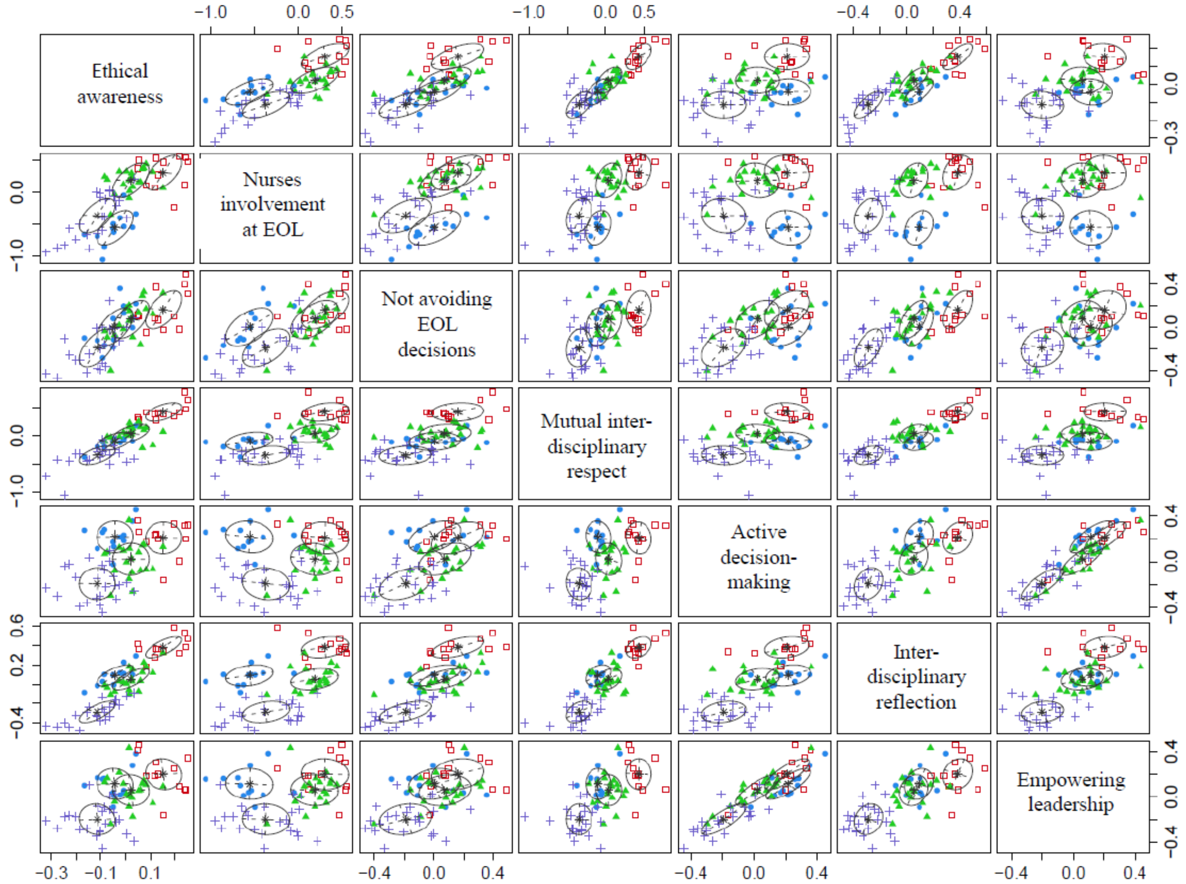
ESM 2. Web appendix 2.

1) Identification of ethical climates : cluster analysis

To identify possible types of ethical climates within all participating ICUs, we explored dimension reduction by means of cluster analysis using the identified 7 factors described in the article by Van den Bulcke et al [1], namely, ethical awareness, active involvement of nurses in end-of-life decisions, culture of not avoiding end-of-life decisions, culture of mutual inter-disciplinary respect, active decision-making by physicians, practice and culture of open inter-disciplinary reflection, and self-reflective and empowering leadership. Each ICU comprises several clinicians, each with their own perception of the ethical climate. The average score across health care providers for each factor in a given ICU was calculated and used as input for the cluster analysis at ICU level. ICUs were subsequently clustered into ethical climates using the partitioning around medoids (PAM) algorithm, which essentially seeks to minimize the similarity of ICUs within each cluster and maximize the dissimilarity of ICUs between clusters.

Similarly as for factor analysis, a conceptual meaning, using Delphi method, was assigned to each cluster. For this purpose, high and low factor scores were identified for each factor and ICU within a cluster. Using this visualization of low and high factor scores, as shown in figure 1, it was clear that there were 2 clusters where either all factors scored “high” (red squares) or “bad” (blue +). The two remaining clusters showed more average scores, however, a difference in decision-making and involvement of nurses in EOL care was observed. ICUs in cluster 3 (blue dots) did not involve nurses in EOL care, while there seemed to be excellent decision-making by physicians. In contrast, cluster 2 (green triangles) showed a better involvement of nurses in EOL care, while a decision-making by physicians was perceived as average. As a result, we named cluster 1, good climate; cluster 2, average climate with involvement of nurses at EOL (average$^{(+)}$); cluster 3, average climate without involvement of nurses at EOL (average$^{(-)}$) and cluster 4, poor climate. In eTable 1 underneath, the results on each single item of the EDMCQ are given.

Figure 1.



eTable 1.

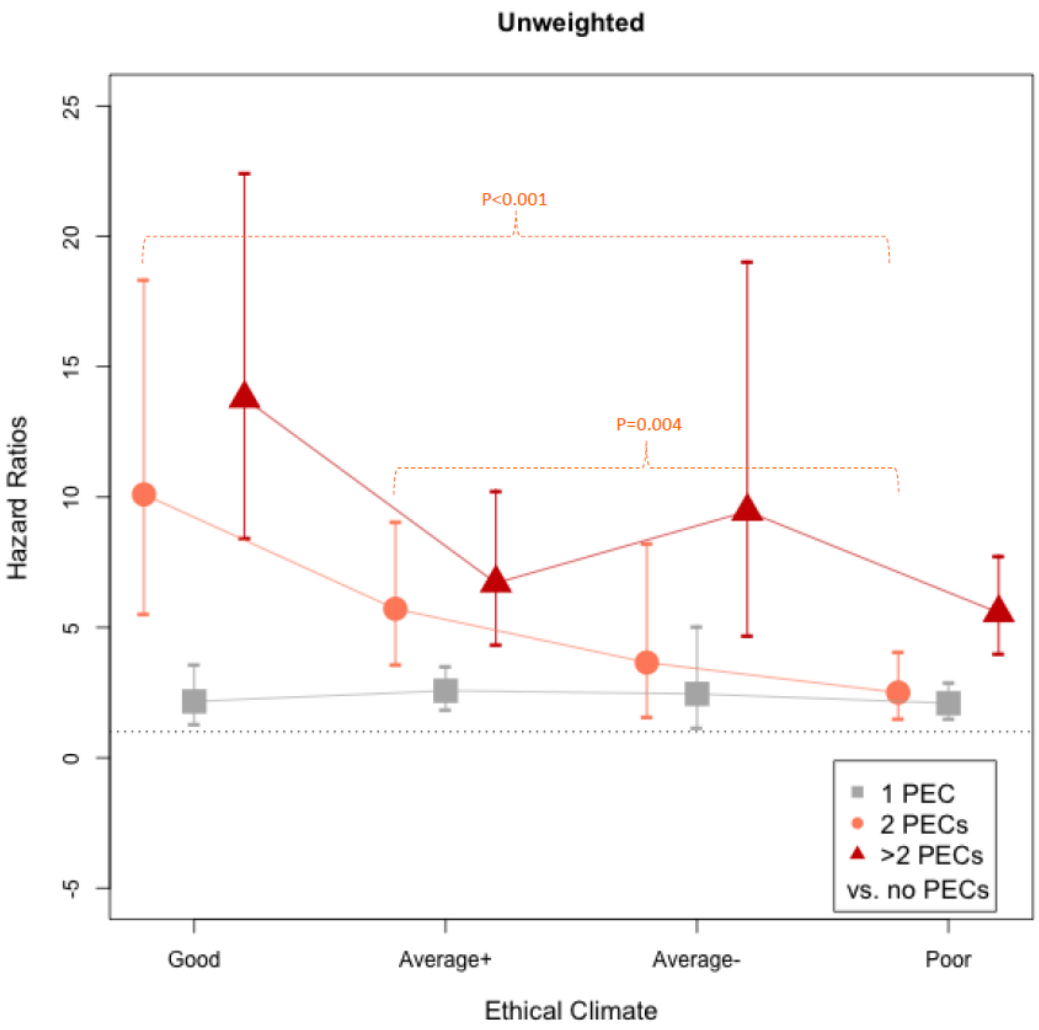
	Ethical climate					
	Overall	**Good**	**Average(+)**	**Average (-)**	**Poor**	**P-value (chi-square)**
Number of clinicians	**n=2992**	**n=535**	**n=1235**	**n=302**	**n=902**	
Culture of not avoiding EOL decisions (agree)						
Patients with little chance of recovery are **not** frequently admitted	30%	37%	36%	31%	18%	<0,001
Patients with little chance of recovery **don't** frequently occupy an ICU bed	45%	48%	66 %	49%	31%	<0,001
EOL decisions are **not** frequently postponed	52%	57%	60%	57%	44%	<0,001
Death is **not** perceived as a treatment failure	81%	86%	88%	82%	67%	<0,001
Active involvement of nurses in EOL care and DM (agree)						
Nurses are involved in EOL DM	55%	68%	70%	15%	40%	<0,001
Nurses are present during EOL family meetings	73%	88%	93%	17%	55%	<0,001
Nurses and physicians collaborate well with one another during EOL care	77%	89%	90%	60%	60%	<0,001
Culture of mutual respect within the interdisciplinary team (agree)						
I am always regarded by everyone as a fully-fledged team member	73%	89%	77%	64%	60%	<0,001
Team members from another discipline respect my work	74%	89%	80%	72%	57%	<0,001
I have confidence in the professional competence of my team members	85%	95%	88%	80%	75%	<0,001
Active decision making by senior physicians (often-always)						
Physicians in charge make accurate and timely decisions	68%	84%	71%	83%	50%	<0,001
Physicians in charge take full charge when emergencies arise	84%	95%	84%	94%	76%	<0,001
Physicians in charge are **not** hesitant about taking initiative in the group	66%	80%	64%	79%	56%	<0,001
Physicians in charge are well aware of their role model function	42%	48%	39%	64%	36%	<0,001
Practice and culture of ethical awareness (agree)						
My colleagues understand my thoughts/feelings about difficult end-of-life decisions.	90%	92%	93%	83%	88%	<0,001
Different opinions and values concerning end-of-life are tolerated.	87%	94%	90%	75%	81%	<0,001
We talk about moral problems	81%	89%	84%	80%	73%	<0,001
There is a structured, formal debriefing after difficult patient care situation	49%	58%	47%	61%	42%	<0,001
Self-reflective and empowering leadership by physicians (often-always)						
Physicians in charge help team members settle their differences	25%	29%	22%	36%	22%	<0,001
Physicians in charge trust the team members to exercise good judgment	70%	82%	76%	68%	54%	<0,001
Physicians in charge permit the team members to use their own judgment in solving problems	51%	67%	53%	55%	36%	<0,001
Physicians in charge encourage initiative in the team members	50%	62%	52%	59%	36%	<0,001
Physicians in charge treat all team members as their equals	49%	72%	50%	57%	33%	<0,001
Physicians in charge are well aware of their own emotions and attitudes	42%	48%	39%	64%	36%	<0,001
Physicians in charge dare to show their vulnerability	14%	16%	12%	19%	12%	<0,001
Practice and culture of open interdisciplinary reflection (agree)						
There are regular opportunities for open informal dialogue between healthcare providers	58%	80%	56%	75%	42%	<0,001
There is regular structured and formal dialogue between the various disciplines within the team to discuss patient care	47%	68%	44%	58%	34%	<0,001
We regularly reflect on the quality of care provided from the various points of view of the staff	59%	82%	62%	68%	36%	<0,001
The teams are well coordinated/managed	73%	89%	77%	64%	60%	<0,001
There is an open and constructive culture in the department such that criticism can be easily expressed	47%	68%	44%	58%	34%	<0,001
Discussions about patients lead to greater understanding and agreements	58%	82%	62%	68%	36%	<0,001
The culture in my ICU makes it easy to learn from the errors of others	57%	79%	55%	67%	43%	<0,001

2) Differences across ethical climates

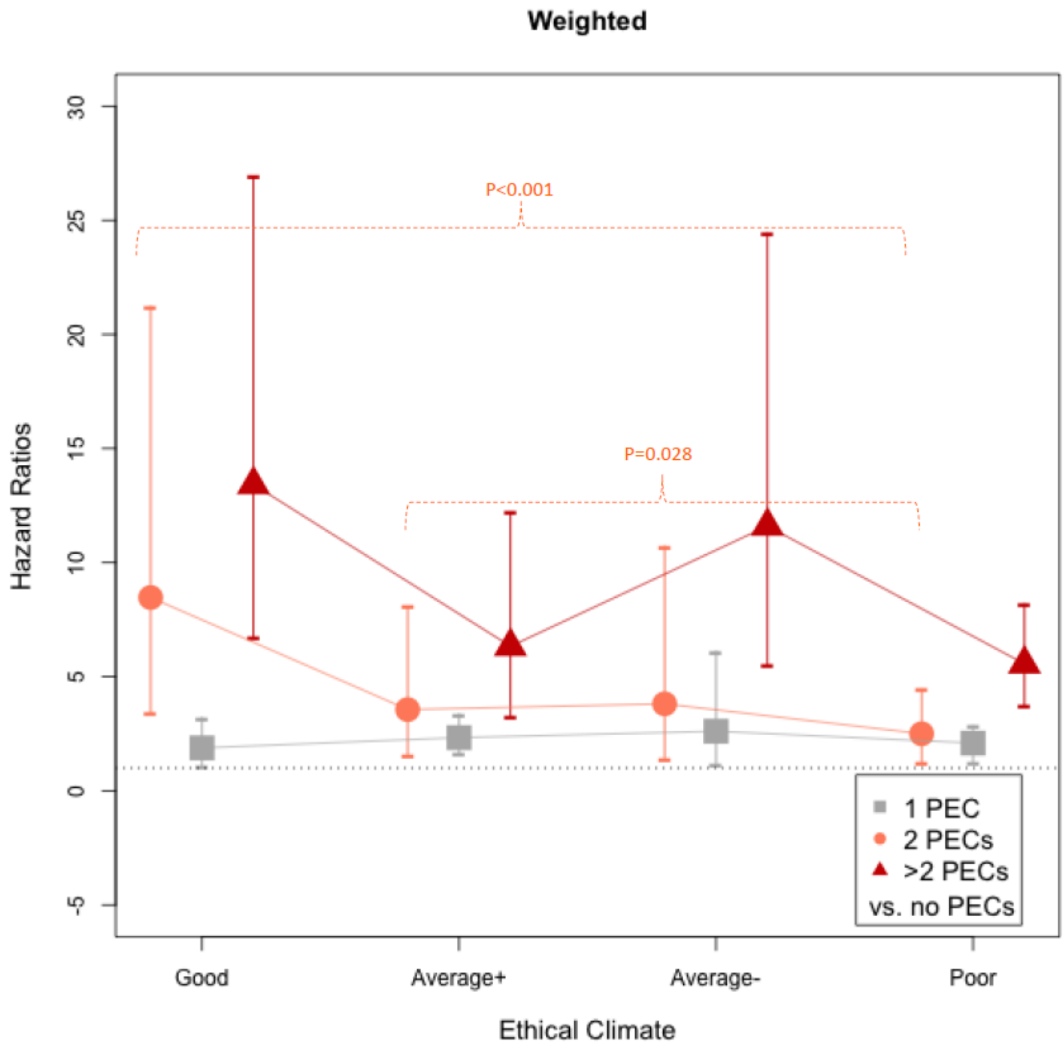
a. Differences in risk of attaining the combined endpoint between patients with PEC by one, two or more than two different clinicians.

We used time-dependent Cox-regression analysis to compare the prognostic value of PEC by one, two or more than two different clinicians with regard to the combined endpoint (death, not home or a utility < 0.5 at one year) across the four ethical climates obtained via cluster analysis. In line with previous studies, we found that PEC by a clinician alone was only moderately informative about the combined endpoint.

We also found that the hazard ratio (HR) of concordant PECs by two different clinicians in the good climate was statistically significantly superior to the poor climate and also in the average$^{(+)}$ versus the poor climate. The average$^{(-)}$ and poor climates required a PEC of at least a third clinician to achieve HRs higher than 5.



This observation was similar after weighting (see next chapter for explanation of used methodology for weighing) for the case-mix, hospital and country characteristics.



Weighted
Hazard Ratios
30
25
20
15
10
5
0
-5
P<0.001
P=0.028
1 PEC
2 PECs
>2 PECs
vs. no PECs
Good
Average+
Average-
Poor
Ethical Climate

b. eTable 2. Differences in country, hospital, ICU and clinicians characteristics

Eighty-six ICUs and 2992 clinicians participated, respectively. This data was used to build the propensity scores (see pg 9).

		Ethical climate			
	Good	Average(+)	Average(-)	Poor	P-value
Number of ICUs	n=12	n=20	n=12	n=24	
Country characteristics					
Number of ICU beds / 100.000 inhabitants[a]	11.6 (10.2-16.9)	6.7 (6.6-15.9)	11.6 (6.0-11.6)	13.2 (6.4-15.9)	0.434
Percentage of population over 65 year[a]	18.0 (17.8-20.0)	18.0 (18.0-18.0)	17.0 (17.0-20.0)	18.0 (18.0-19.0)	0.691
Geographical region					< 0.001
Northern Europe	3 (25.0%)	6 (30.0%)	0 (0.0%)	0 (0.0%)	
Western Europe / USA	7 (58.3%)	11 (55.0%)	0 (0.0%)	10 (41.7%)	
Central Europe	2 (16.7%)	2 (10.0%)	7 (58.3%)	8 (33.3%)	
Southern Europe	0 (0.0%)	1 (5.0%)	5 (41.7%)	6 (25.0%)	
Hospital characteristics					
Hospital type					0.840
University	6 (50.0%)	9 (45.0%)	6 (50.0%)	16 (66.7%)	
University affiliated	2 (16.7%)	4 (20.0%)	2 (16.7%)	2 (8.3%)	
Public	3 (25.0%)	6 (30.0%)	4 (33.3%)	6 (25.0%)	
Private	1 (8.3%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	
Total beds in hospital					0.500
< 250	1 (8.3%)	1 (5.0%)	0 (0.0%)	2 (8.3%)	
250-499	3 (25.0%)	7 (35.0%)	3 (25.0%)	5 (20.8%)	
500-749	6 (50.0%)	3 (15.0%)	3 (25.0%)	5 (20.8%)	
> 750	2 (16.7%)	9 (45.0%)	6 (50.0%)	12 (50.0%)	
ICU characteristics					
Number of beds per ICU	10.0 (8.0-12.3)	10.5 (8.0-16.0)	9.0 (7.5-12.0)	11.0 (8.0-24.3)	0.660
Patient to nurse ratio	2.0 (1.5-3.0)	1.5 (1.2-2.0)	1.9 (1.4-2.1)	2.0 (2.0-2.6)	0.047
Patient to doctor ratio[b]	4.8 (3.1-5.8)	5.1 (2.8-7.5)	3.0 (2.0-4.5)	4.5 (2.9-6.8)	0.613
Clinician characteristics	n=535	n=1253	n=302	n=902	
Age	40.0 (32.0-49.0)	39.0 (31.0-50.0)	36.0 (30.0-42.0)	36.0 (29.0-45.0)	<0.001
Gender (male)	156 (29.2%)	318 (25.4%)	80 (26.5%)	304 (33.7%)	<0.001
Role					<0.001
Nurse	423 (79.1%)	998 (79.6%)	205 (67.9%)	649 (72.0%)	
Doctor[b]	112 (20.9%)	255 (20.4%)	97 (32.1%)	253 (28.0%)	
Years of experience in the ICU	8.0 (3.0-16.0)	8.0 (3.0-18.0)	8.0 (4.0-15.0)	8.0 (3.0-17.0)	0.797

Results are expressed as number (%) and median (25^{th}-75^{th} percentiles).[a]Rhodes A et al[20]. [b]of which respectively 73, 150, 60 and 126 were senior doctors (including ICU heads).

c. eTable 3 : Differences in patients' characteristics

During the study period 1824 patients were admitted for more than monitoring only. The data of these patients was used to build the propensity scores (see pg 9)

		Ethical climate			
	Good	Average(+)	Average(-)	Poor	P-value
Number of patients	n=327	n=733	n=127	n=637	
Characteristics on admission					
Age	64.0 (51.0-74.0)	65.0 (52.0-74.0)	66.0 (48.0-77.0)	64.0 (51.0-75.0)	0.861
Gender (male)	186 (56.9%)	433 (59.1%)	71 (55.9%)	382 (60.0%)	0.725
ECOG performance status					<0·001
Grade 0 (full functional)	102 (31.2%)	252 (34.4%)	43 (33.9%)	240 (37.7%)	
Grade 1 (symptomatic)	94 (28.7%)	159 (21.7%)	29 (22.8%)	160 (25.1%)	
Grade 2 (functional but not able to work)	61 (18.7%)	106 (14.5%)	20 (15.7%)	82 (12.9%)	
Grade 3 (limited functionality)	49 (15.0%)	94 (12.8%)	26 (20.5%)	68 (10.7%)	
Grade 4 (bedridden)	8 (2.4%)	40 (5.5%)	6 (4.7%)	35 (5.5%)	
Unknown	13 (4.0%)	82 (11.2%)	3 (2.4%)	52 (8.2%)	
Nursing home resident	24 (7.3%)	27 (3.7%)	2 (1.6%)	31 (4.9%)	0.021
Moderate to severe comorbidities					
Number					0.001
0	153 (46.8%)	390 (53.2%)	51 (40.2%)	273 (42.9%)	
1	129 (39.4%)	275 (37.5%)	53 (41.7%)	281 (44.1%)	
≥ 2	45 (13.8%)	68 (9.3%)	23 (18.1%)	83 (13.0%)	
Type (in decreasing frequency)					
Solid tumor	48 (14.7%)	129 (17.6%)	23 (18.1%)	139 (21.8%)	0.042
Heart failure (NYHA III or IV)	38 (11.6%)	62 (8.5%)	30 (23.6%)	98 (15.4%)	<0.001
COPD (Gold III or IV or equivalent)[a]	43 (13.1%)	89 (12.1%)	19 (15.0%)	66 (10.4%)	0.376
Neurological (excluding dementia)	15 (4.6%)	42 (5.7%)	10 (7.9%)	49 (7.7%)	0.203
Hematological malignancy	37 (11.3%)	29 (4.0%)	7 (5.5%)	30 (4.7%)	<0.001
Liver cirrhosis (Child Pugh B or C)	13 (4.0%)	31 (4.2%)	5 (3.9%)	39 (6.1%)	0.304
Chronic renal failure requiring dialysis	13 (4.0%)	26 (3.5%)	4 (3.1%)	17 (2.7%)	0.702
Dementia (moderate or severe)[b]	12 (3.7%)	12 (1.6%)	5 (3.9%)	21 (3.3%)	0.120
AIDS	8 (2.4%)	1 (0.1%)	0 (0.0%)	5 (0.8%)	0.001
Abuse					
Alcohol[c]	36 (11·0%)	85 (11·6%)	8 (6·3%)	64 (10·0%)	0·319
Active smoking	67 (20·5%)	114 (15·6%)	32 (25·2%)	115 (18·1%)	0·032
Main admission reason(s)					
Respiratory failure	76 (23.2%)	190 (25.9%)	34 (26.8%)	137 (21.5%)	0.231
Sepsis / severe sepsis / septic shock	75 (22.9%)	126 (17.2%)	28 (22.0%)	131 (20.6%)	0.121
Heart failure / cardiogenic shock	37 (11.3%)	136 (18.6%)	28 (22.0%)	113 (17.7%)	0.011
Neurologic pathology / Stroke / ICB	26 (8.0%)	95 (13.0%)	12 (9.4%)	70 (11.0%)	0.102
Gastro-intestinal pathology / liver failure	33 (10.1%)	77 (10.5%)	7 (5.5%)	65 (10.2%)	0.378

Metabolic / renal	34 (10.4%)	68 (9.3%)	12 (9.4%)	49 (7.7%)	0.529
Polytrauma	18 (5.5%)	45 (6.1%)	13 (10.2%)	35 (5.5%)	0.220
Neurotrauma	5 (1.5%)	30 (4.1%)	7 (5.5%)	26 (4.1%)	0.111
Surgery 48 hrs prior to admission					<0·001
No surgery	264 (80.7%)	514 (70.1%)	83 (65.4%)	339 (53.2%)	
Scheduled surgery	25 (7.6%)	57 (7.8%)	24 (18.9%)	128 (20.1%)	
Unscheduled surgery	38 (11.6%)	162 (22.1%)	20 (15.7%)	170 (26.7%)	
Do-not-resuscitate order before admission					<0.001
Full code	301 (92.0%)	657 (89.6%)	90 (70.9%)	554 (87.0%)	
No CPR	16 (4.9%)	22 (3.0%)	0 (0.0%)	25 (3.9%)	
Withholding of therapy	8 (2.4%)	27 (3.7%)	3 (2.4%)	9 (1.4%)	
Unknown	2 (0.6%)	27 (3.7%)	34 (26.8%)	49 (7.7%)	
Severity of illness < 24 hrs after admission					
Invasive mechanical ventilation	111 (33.9%)	317 (43.2%)	102 (80.2%)	373 (58.6%)	<0.001
Vasopressor need	95 (29.1%)	240 (32.7%)	59 (46.5%)	262 (41.1%)	<0.001
Dialysis	14 (4.3%)	21 (2.9%)	6 (4.7%)	21 (3.3%)	0.550
Written withholding / withdrawing order < 24 h	14 (4.3%)	43 (5.9%)	4 (3.1%)	14 (2.2%)	0.008
Characteristics during ICU stay	n=285	n=673	n=124	n=589	
Invasive mechanical ventilation	126 (44.2%)	362 (53.8%)	105 (84.7%)	395 (67.1%)	<0.001
Duration of invasive ventilation (days)	2.5 (1 – 8)	2 (1 – 6)	4 (1 - 11)	2 (1 - 7)	<0.001
Vasopressor need	105 (36.8%)	304 (45.2%)	76 (61.3%)	317 (53.8%)	<0.001
Duration of vasopressors (days)	2 (1 - 4)	1.5 (1 - 3)	4 (1 – 6.25)	2 (1 - 4)	<0.001
Dialysis	29 (10.2%)	47 (7.0%)	19 (15.3%)	49 (8.3%)	0.016
Duration of dialysis (days)	2 (2 - 4)	3 (2 - 7)	3 (2 - 11)	4 (2 – 8)	0.445

Results are expressed as number (%) and median (25th-75th percentiles). ECOG : Eastern Collaborative Oncology group. NYHA : New York Heart Association. COPD : Chronic Obstructive Pulmonary Diseases. AIDS : Acute Immune Deficiency Syndrome. ICB : Intra-Cranial Bleeding. CPR : Cardio-Pulmonary Resuscitation.

[a]Similar stage according to other definitions in absence of pulmonary function test or chronic oxygen therapy.

[b]Global Deterioration Scale 6 (largely unaware of recent experiences and events in their lives. require assistance with basic ADL's. behavioral and psychological symptoms of dementia are common) or 7 (verbal abilities will be lost over the course of this stage, incontinent, needs assistance with feeding, lose ability to walk).

[c]More than 4 drinks a day for male, more than 3 drinks a day for female

3) Extended methodology

Competing risk analysis

The analysis of time until concordant PECs and from concordant PECs until written treatment-limitation decision (TLD) is affected by the problem of competing risks. In particular, ICU discharge or death prevents observation of the time to TLD or to concordant PEC (or made these times ill defined). In view of this, we present cumulative incidence curves obtained from a competing risk analysis. The cumulative incidence of TLD, for instance, merely expresses the percentage of patients being assigned TLD by a given day. We deliberately chose not to present Kaplan-Meier curves, as these would treat death as a censoring event, and would thereby implicitly assume that the risk of being assigned TLD stays the same for patients who died as for those who stay.

To adjust for case-mix, hospital and country characteristics, we made use of inverse probability weighting. In particular, we first built a multinomial logistic regression model for the probability for a given patient to be treated in a given ethical climate, in function of patient characteristics; see further detail below. On the basis of this model, we calculated for each patient the probability to belong to the ethical climate where he/she is actually treated. The reciprocal of that probability was then used as a weight. Next, to construct the cumulative incidence curve for TLD adjusted for differential case-mix between climates, we calculated the sum of those weights for the patients being assigned TLD by a given day and divided this by the sum of the weights of all patients with concordant PEC in a given ethical climate. As such, the cumulative incidence expresses the weighted percentage of patients being assigned TLD by a given day. A similar reasoning was used to calculate the cumulative incidence of attaining concordant PEC.

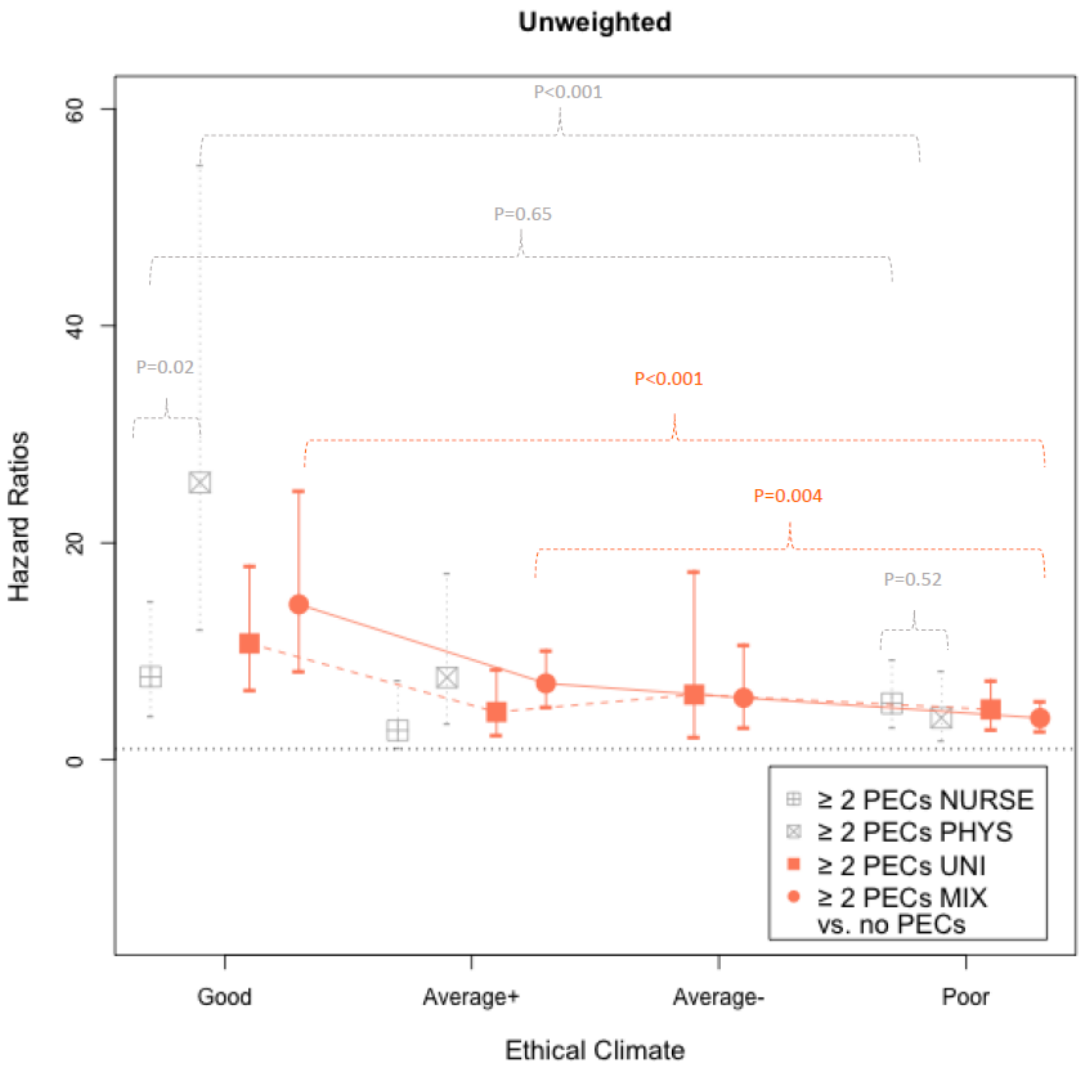
Weighting with propensity scores

The considered weighting strategy to adjust for case mix is well known from the literature on propensity scores. We used unstabilised weights based on propensity scores (1/PS), defined as the estimated conditional probability that a patient would have been assigned to his/her specific ethical climate given one's patient characteristics. We truncated high weights at the 90% percentile. We built a multinomial model to obtain the propensity scores, which we fitted on a subset of 1824 observations, of which 327 in the good climate; 733 in the average$^{(+)}$ climate; 127 in the average$^{(-)}$ climate; 637 in the poor climate. As in Spreeuwenberg et al.[1], we only included (baseline) variables related to the outcome (PEC) in order to avoid imprecision and large finite-sample bias. Thus, variables significantly related to the ethical climate, but not to PEC were not added to the propensity score model. To identify which variables need to be included in the PS model, we conducted several logistic regression analyses with outcome perception of excessive care (PEC) and each time another potential covariate, again working at a 10%-significance level. Because we also planned to use the PS in future analyses (on intent to jobleave, moral distress…) all factors from the CRF (thus more elaborated than the variables shown in eTable 1 and 2) were verified.

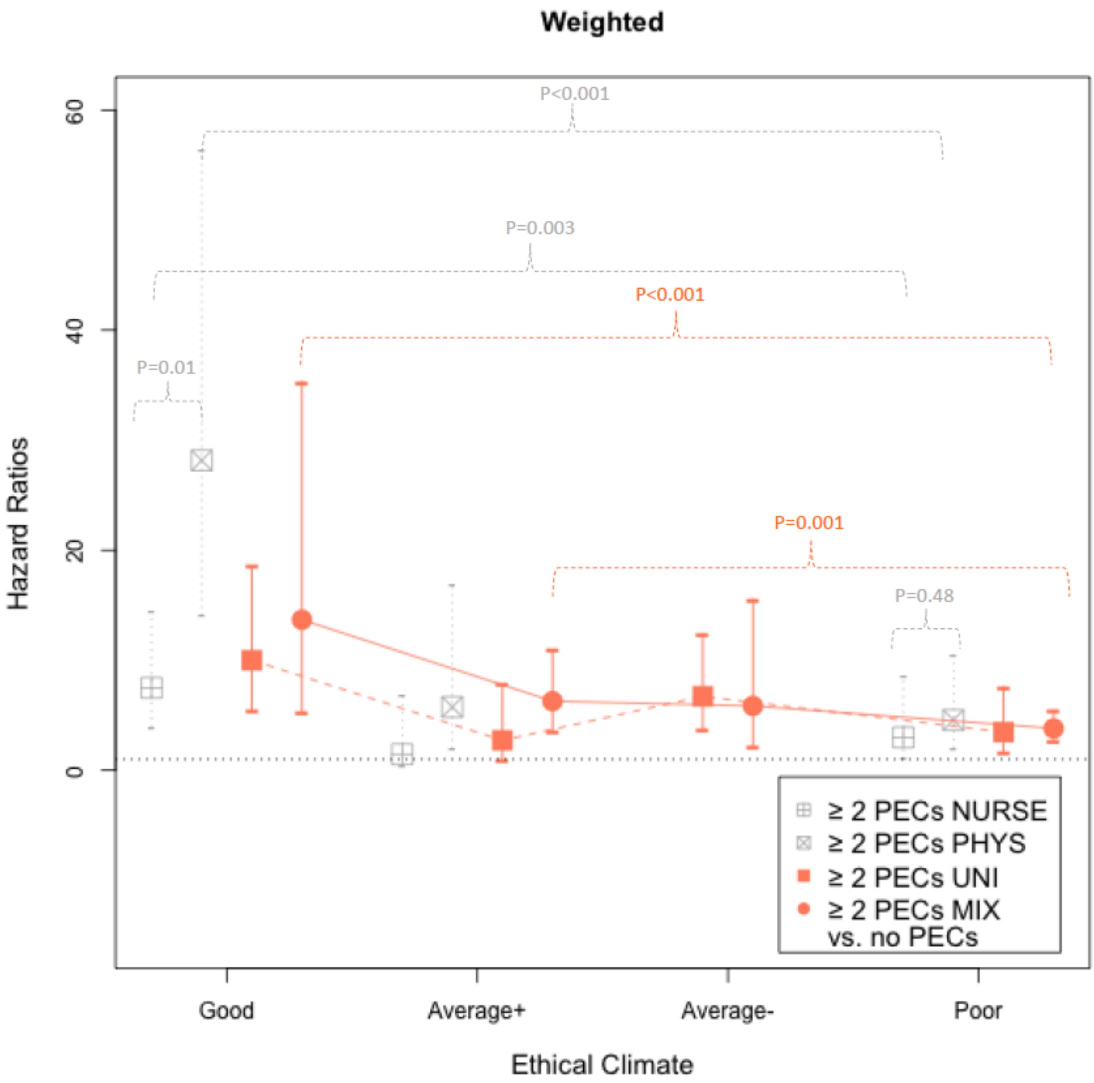
At the country level we included the percentage of the population > 65 years, the bigmac index (http://bigmacindex.org) and the net average salary per month for a nurse. At the hospital level, the type of hospital and the number of total beds. At the ICU level the average 24 hrs patient-to-nurse, patient-to-junior physician and patient-to-senior physician ratio. Since we needed propensity scores per patient, we did not include clinicians' characteristics in the PS model. The following baseline patient characteristics were included: the age of the patient, the functional status 2 weeks before ICU-admission (ECOG score), moderate to severe comorbidities (heart failure, dementia, solid tumor, AIDS, chronic renal failure), reasons for admission (multiple trauma, neurologic, respiratory failure, metabolic), FiO2 in case of mechanical ventilation and whether the patient is an active smoker, a nursing home resident or underwent surgery within 48 hours prior to admission. Vasopressor use and dose, and dialysis at admission were highly correlated with the FiO2 in mechanically ventilated patients and were therefore not included in the model.

4) Differences in time until death in patients with concordant PECs in different decision-making scenarios.

We again used time-dependent Cox-regression analysis to compare the risk until death in patients with concordant PECs by clinicians with different decision-making power (doctor-doctor, doctor-nurse, nurse-nurse). From good to poor climate, 8 (22.2%), 7 (14%), 1 (4.7%) and 9 (18%) patients were identified by two or more doctors, 11 (30.5%), 17 (47.2%), 35 (70.0%), 17 (80.9%), and 50 (67.5%) by at least one nurse and one doctor, and 11 (30.5%), 8 (16%), 3 (14.2%) and 15 (20.5%) by two or more nurses, respectively. The HR of the combination of at least one doctor and one nurse ("mix") was statically significantly higher in the good and average(+) climates compared to the poor. The HR of two or more doctors was also statistically significantly higher in the good compared to the poor climate (P<0.001). The risk of death in the good climate was higher in patients with PECs by two or more doctors than in those with PECs by two or more nurses (P=0.02), with the risk of death in patients with PECs by at least one nurse and one doctor ("mix") being intermediate. There was no evidence of such a difference in risk of death in the poor climate (P=0.52).



After weighing for the case-mix, country and ICU characteristics, the HR of the combination of at least one doctor and one nurse ("mix") remained statistically significantly higher in the good and average(+) climates compared to the poor (P<0.001). The HR of two or more doctors remained also statistically significantly higher in the good compared to the poor climate (P<0.001). This was now also the case for the combination of two or more nurses (not shown on the figure, P=0.003). The risk of death in the good climate remained higher in patients with PECs by two or more doctors than in those with PECs by two or more nurses (P=0.01), with the risk of death in patients with PECs by at least one nurse and one doctor ("mix") being intermediate. There was no evidence of such a difference in risk of death in the poor climate (P=0.48).



5) Analysis of selection bias

We found evidence for a difference in ICU mortality rates and in length of stay across climates in patients admitted during the study period for monitoring only (Table 2. underneath). However, pairwise comparison shows that only the ICU mortality and length of stay of the average$^{(-)}$ climate differs from the other climates. All other pairwise comparisons were not significant. Therefore we can conclude that the attending physicians in good, average$^{(+)}$ and poor climates included patients in a similar way and that our main results for comparison between these climates were not biased by different selection.

Table 2: Comparison of ICU mortality and length of stay between ethical climates

	Ethical climate				
	Good	**Average +**	**Average -**	**Poor**	**p-value**
ICU mortality	**n=178**	**n=415**	**n=82**	**n=541**	
	7.9%	8.0%	22.0%	8.7%	0.001*
Median length of stay in days (IQR)	**n=176**	**n=414**	**n=82**	**n=536**	
	1.2 (0.8-3.1)	1.2 (0.8-3.1)	3.1 (1.5-11.2)	1.6 (0.9-1.6)	< 0.0001

*Pearson Chi-Square, ** Non-parametric test comparing medians

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References of the Webappendix

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2. Spreeuwenberg MD, Bartak A, Croon MA, Hagenaars JA, Busschbach JJ, Andrea H, Twisk J, Stijnen T. The Multiple Propensity Score as Control for Bias in the Comparison of More Than Two Treatment Arms: An Introduction From a Case Study in Mental Health. Medical Care 2010; 166-74.